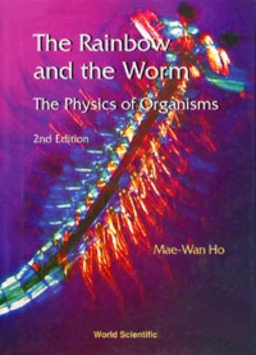


The Rainbow and the Worm

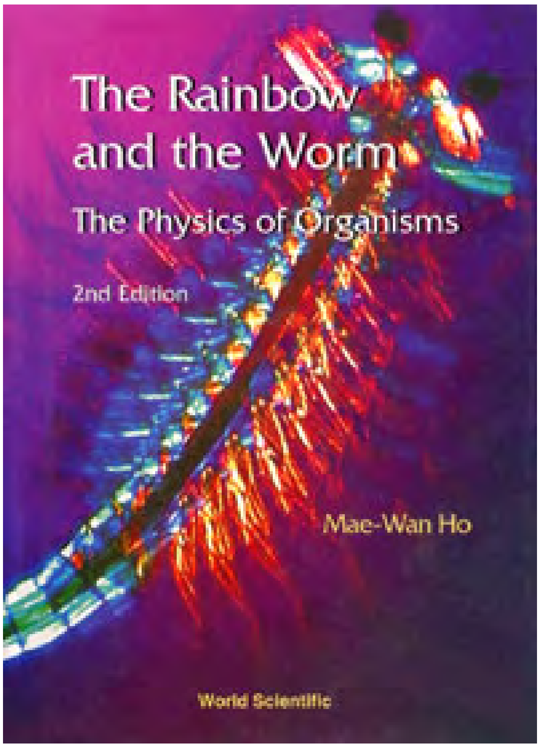
The Physics of Organisms

2nd Edition

Mae-Wan Ho

World Scientific

Cover



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Preface to Second Edition

Why produce a new Edition of this book?

First, it is still the only book of its kind. Second, it has made me many friends since it appeared in print in 1993, some of whom became my collaborators in research. Third, all the friends I have made taught me a great deal more about the subject, thus revealing the shortcomings of my book. Fourth, while the book has lost little of its original appeal, there has been significant progress in the subject matter, both in the general scientific literature, and in research done by myself and my collaborators since the book was published. For all those reasons, I believe a new Edition is necessary to do justice to the book and its subject matter. Indeed, the progress made since 1993 warrants at least 3 new Chapters: 6, 11 and 12. Chapter 6 presents a “thermodynamics of organized complexity” especially applicable to living systems, and contains work that I have done since 1993, which, in many ways, extends and completes the thermodynamic enquiry into the living system presented in the early Chapters. Chapters 11 and 12 deal with the idea that organisms are liquid crystalline, again, extending work which began in 1993, to which my coworkers and collaborators have contributed an enormous amount. The liquid crystalline nature of organisms, may, to a large extent, account for their most paradoxical properties, including pattern formation and the faculties of consciousness.

The additional Chapters have been intercalated into the previous Edition, which has been preserved in its form and substance, with extensive up-dating throughout. I have been able to simplify and clarify the narrative with the benefit of hindsight, at the same time fleshing out the original account with fresh evidence. All the Chapters are inevitably longer, but that is more than justified by the wealth of additional material which is beginning to give clear definition to a theory of the organism. Let me list some of the highlights.

Chapter 3 contains new evidence for resonant energy transfer in living systems. Chapter 4 contains new information on the Bénard cells from Koschmeider's book on the subject published in 1993. Chapter 7 includes extra material on the structure of water. Chapter 8 includes a description of Donald Ingber's model of the cell as a tensgrity system. Chapter 9 has been sustantially edited, with more evidence on the biological effects of electromagnetic fields. Chapter 10 contains a substantial update on research into biophotons and their relationship to energy mobilization. Chapters 13-15 connect entropy generation with quantum decoherence and refer to recent experimental work demonstrating quantum superposition on the mesoscopic scale. There is a new Section on the fractal structure of organic space-time. There are, of course, numerous extra references.

I hope the reader will find much to think about and will continue to point out to me the shortcomings of this volume.

It remains for me to thank the many friends who have helped shape this Edition. David Knight introduced me to much of the literature on liquid crystals, collaborated with us in the experimental work, offering expert advice and brilliant ideas at all times. Eric Schneider told me about Koshmeider's work and a wealth of other literature on the thermodynamics of living systems, including his own excellent work on ecosystems. I benefited enormously by having been guest of him and his wife Carol in their beautiful home in Montana, where I learned a lot, not only about thermodynamics, but also ecology and energy metabolism of organisms. Philip Herbomel brought zebrafish to our laboratory and spent a week with us, studying its development. He acquainted me with many exciting developments in France, including Nottale's work on fractal space-time. Clive Kilmister suggested to me the interesting analogy between noninvasive and adiabatic measurements. Ervin Laszlo inspired me with his book, The Interconnected Universe, to the possibility that the liquid cyrstalline continuum of the body may be a quantum holographic medium. He has also kindly arranged for my book to be translated into German, which is another reason for this new Edition.

Douglas Kell and Rickey Welch connected me to the whole radical world of biothermokinetics, which shows that there is life after the chemiosmotic theory. Franklin Harold wrote to tell me he swallowed neither worm nor rainbow whole, and challenged me to think more deeply on bioenergetics. James Clegg initiated me into the mysteries of Artemia, the brine shrimp whose portrait graces the front cover of this book. Rufus Lumry taught me everything I have always wanted to know about the bioenergetics of enzyme action and the importance of water and hydrogen bonds.

Walter Freeman introduced me to his fascinating work on the collective, possibly nonlocal synchronization of brain waves. Alex Andrews spurred me on to write a paper on the subject. Peter Marcer drew my attention to quantum holography, quantum computing and his fascinating model of quantum perception. Michael Conforti brought me into the world of Jungian archetypes and the collective unconscious.

I would like mention all my old friends who continue to share my enthusiasm for the physics of organisms, especially the following with whom I have discussed many ideas during their formative phases: Kenneth Denbigh whose work was the major inspiration for the thermodynamics of organized complexity, Lynn Trainor on liquid crystals and the morphogenetic field, Franco Musumeci and Fritz Popp on the coherence of biophotons, Charles Jencks whose book, the Jumping Universe, inspired me to think about achitecture and space-time, and hence, the architecture of space-time; Nick Furbank on determinism and freewell; and Geoffrey Sewell, as always, who answers any random question on physics that presents itself during our happy lunch hours at the Spaniard.

I am grateful to all who have supported and sustained us in our experimental research efforts: Steve Swithenby for his abiding interest and support, as well as his expert advice on electromagnetism; Lyndon Davies who coordinated the only major grant I have recieved in support of research into the physics of organisms; Gordon Evans, Alex Todd and Derek Welsh of Prior Scientific, Mark Willamson, Mark Norris and Ian Young of Data Cell, Lynn Yeates, Derek Batchelor, Barry Hollis, Alan Bassindale, Jim Iley and Mike Mortimer of the Open University, all of whom took some of the ideas expressed in this book seriously; and Ron Hussey, Martin Bellis, Fraser Robertson and others, of the Open University Workshops, who skilfully constructed crucial pieces of laboratory equipment. I am also deeply appreciative of Franco Musumeci's efforts to keep us involved in biophotons research in sunny Catania.

Finally, I would like to thank my coworkers during the past 5 years, without whom this Edition would not have been possible. Julian Haffegee, Zhou Yu-Ming, Stephen Ross, John Bolton and Richard Newton, who have done much of the work described in Chapters 10, 11 and 12.

Milton Keynes
July, 1997

Preface to First Edition

This book began 30 years ago when as a young undergraduate, I came across Szent Györgyi's idea that life is interposed between two energy levels of the electron. I was so smitten with the poetry in that idea that I spent the next 30 years searching for it. Naturally, I went at once into biochemistry. But I arrived too late. For the heady days of unity in diversity, the wine-and-roses days of discoveries in the universal energy transformation processes in living organisms had long been eclipsed by the new excitement over the molecular basis of heredity: the structure of the DNA double-helix and the cracking of the genetic code whereby the linear structure of DNA specifies the linear structure of proteins. So I became a geneticist; but found to my dismay that no one cared about unity anymore. Instead, almost everyone was obssessed with diversity and specificity: each biological function has a specific protein encoded by a gene ‘selected by hundreds of millions of years of evolutionary history’ to do the job.

After some years getting acquainted with a group of enzymes involved in a number of hereditary neurological disorders, I became an evolutionist. Together with Peter Saunders, we set out to try to understand the relevance of thermodynamics to evolution, and other ‘big’ questions such as how life began. Sidney Fox's work on thermal proteins was the antithesis to the then dominant ‘frozen accident’ theory of prebiotic evolution, and impressed on me the nonrandomness, or I should say, non-arbitrary nature of life's physicochemical beginnings. I spent the next years working towards an alternative research programme to the neo-Darwinian theory of evolution by the natural selection of random mutations. This involved investigations on the relationship between development and evolution, the physicochemical and mathematical bases of biological form and organization, on ‘rational taxonomy’—the classification of biological forms based on the developmental process generating the forms, as well as the wider social implications of evolutionary theory; all in the inspiring company of Peter Saunders, and later, also Brian Goodwin.

Yet something was still missing. I still did not understand how catching the electron between the excited and the ground state could make life go round. A chance meeting with Fritz Popp in 1985 changed all that. Although I understood then almost not a word of his lecture, I was convinced what he said was very significant: that coherence held the key to living organization. And so I plunged into quantum physics, with the help and encouragement of Fritz, who also invited me to work on light emission from living organisms in his laboratory. With immense patience and panache, he taught me quantum physics, taking me straight into the exotic world of quantum optics. Having got in at the deep end, I could do little else but swim to shore! Suddenly, everything begins to make sense.

When Brian Goodwin said to me: ‘‘Why don't you write a book on what is life?” I thought, why not? A month later, I put pen to paper, and the first draft was complete by the time another month had elapsed.

This book is patterned — roughly — after Schrödinger's What is life? (Cambridge University Press, 1944), and addresses the same question: Can living processes be explained in terms of physics and chemistry? His preliminary answer, in the 1940s, is that the inability of the physics and chemistry of his day to account for living processes is no reason for doubting that living processes could be so explained. For, on the one hand, there has not been an adequate experimental investigation of living processes, and on the other, physics and chemistry are both evolving disciplines, and some day, they may just succeed in accounting for life.

Indeed, physics and chemistry have developed a great deal since Schrödinger's time. Whole new disciplines became established: synergetics, nonequilibrium thermodynamics, quantum electrodynamics and quantum optics, to name but a few. There have already been several suggestions that the new physics and chemistry may be particularly relevant for our understanding of biological phenomena. I, for one, believe it is time to examine Schrödinger's question again, which provides a ready structure for this book.

I shall be ranging widely over the different physical disciplines already mentioned, starting from first principles; as well as the relevant physiology, biochemistry and molecular biology of cells and organisms. Those who expect details of molecular genetics and gene control mechanisms, however, will be disappointed. They should consult instead the numerous volumes of excellent texts that already exist. In this book, it is the bare-bones sketch that I shall be concerned with — the fundamental physical and chemical principles which are relevant for life.

At the risk of giving the story away, I shall say a few words on what this book is about. The first chapter outlines the properties of organisms that constitute ‘being alive’, and hence that which is in need of explanation. Chapters 2 to 5 show how a living system differs from a conventional thermodynamic machine. The organism's highly differentiated space-time structure is irreconcilable with the statistical nature of the laws of thermodynamics. And hence, the laws of thermodynamics cannot be applied to the living system without some kind of reformulation. The space-time structure of living organisms arises as the consequence of energy flow, and is strongly reminiscent of the non-equilibrium phase transitions that can take place in physicochemical systems far from thermodynamic equilibrium. Energy flow organizes and structures the system in such a way as to reinforce the energy flow. This organized space-time structure suggests that both quasi-equilibrium and non-equilibrium descriptions are applicable to living systems, depending on the characteristic times and volumes of the processes involved. Hence, an appropriate thermodynamics of the living system may be a thermodynamics of organized complexity involving, among other things, replacing the concept of free energy with that of stored energy.

Thermodynamics has its origin in describing the transformation of heat energy into mechanical work. As shown in Chapters 6, 7, 8 and 9, the predominant energy transductions in the living system are instead, electronic, electric and electromagnetic, as consistent with the primary energy source on which life depends as well as the electromagnetic nature of all molecular and intermolecular forces. Furthermore, given the organized, condensed state of the living system, it is predicted that the most general conditions of energy pumping would result in a phase transition to a dynamically coherent regime where the whole spectrum of molecular energies can be mobilized for structuring the system, and for all the vital processes which make the system alive. Chapters 8 and 9 summarize experimental evidence for coherence in living organisms, some of the findings pushing at the frontiers of quantum optics and quantum electrodynamics. The relevance of quantum theory to coherence in living systems is treated in more detail in Chapter 10.

The summary of the enquiry suggests that organisms are coherent space-time structures maintained macroscopically far from thermodynamic equilibrium by energy flow. This has profound implications on the nature of knowledge and knowledge acquisition, as well as on the nature of time as it relates to issues of determinism and freewill, which are dealt with in Chapters 11 and 12. There, I try to show how, by following to logical conclusions the development of western scientific ideas since the beginning of the present century, we come full circle to validating the participatory framework that is universal to all traditional indigenous knowledge systems the world over. This enables us to go some way towards restoring ourselves to an authentic reality of nonlinear, multidimensional space-time as experienced by the truly participatory consciousness, who is also the repository of free will and coherent action.

I have been asked whether it is necessary to do the science before getting to the point, which is the validation of participatory knowledge. Why not just develop the ‘rhetoric’? That would have defeated one of the main purposes of this work, which is to show how science can reveal in a precise way the deeper wonders and mysteries of nature which are currently in danger of being totally obscured by the kind of superficial woolly misrepresentation that many people, especially the young, mistake to be ‘new age philosophy’. Another motivation for writing this book is to show that science, when properly perceived, is far from being alienating and dehumanizing. Instead, it is consonant with our most intimate experience of nature. To me, science is surely not about laying down eternal ‘laws of nature’ to dictate what we can or cannot think. It is to initiate us fully into the poetry that is the soul of nature, the poetry that is ultimately always beyond what theories or words can say.

This book is the most exciting thing I have ever written. I would like to dedicate it to everyone young or youthful who has ever looked upon the living process in wonderment. I cannot express my gratitude enough to all those already mentioned, who have both inspired and encouraged me in realizing this work. Peter Saunders, as always, gives up much of his time to help me with the mathematics and the physics. Very special thanks are due to my former colleagues, Oliver Penrose (Professor of Applied Mathematics and Theoretical Physics at the Open University, now at Herriot-Watt University, Edinburgh) and Kenneth Denbigh (Prof. of Physical Chemistry and Principal at Queen Elizabeth College, London) for reading an earlier version of the entire manuscript, commenting in substantial detail, correcting errors in my presentation, and stimulating me to new levels of understanding. To my present colleague, Nick Furbank (Professor of English at the Open University), I owe the title of this book and much more: he read and gave me helpful suggestions on the penultimate draft, and restored my faith that the book will reach a wider readership, including those without any scientific training who nevertheless love the subject as much as I do. Comments, suggestions and corrections are also gratefully acknowledged from Ronald Pethig, R.J.P. Williams, Clive Kilmister, Geoffrey Sewell, Wolfram Schommers, Francisco Musomeci, T. M. Wu, K.H. Li, R. Neurohr, Konrad Kortmulder, Lev Beloussov, Hansotto Reiber, Charles Jencks, Willis Harman, Lynn Trainor, Guiseppe Sermonti, Sheila Higham, Viven Thomas, and Katy Bentall. Last, but by no means the least, I would like to thank my brother, Li Poon and my son Adrian Ho for giving me their support as well as valuable comments and suggestions. The shortcomings which remain are all my own.

Milton Keynes,
July, 1993

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CHAPTER 1

What is it to be Alive?

The 'Big' Questions in Science

There are 'big' questions and 'small' questions in science. Most scientists in their work-a-day life confine themselves to asking small questions such as: Which gene is involved in a given hereditary defect? How will a certain organism react to such and such a stimulus? What are the characteristics of this or that compound? What is the effect of A on B? How will a given system behave under different perturbations? Yet, it is not a desire to solve particular puzzles that motivates the scientist, but rather the belief that in solving those little puzzles, a contribution will be made to larger questions on the nature of metabolic or physiological regulation, the generic properties of nonlinear dynamical systems, and so on. It is ultimately the big questions that arouse our passion — both as scientists and as ordinary human beings. They can inspire some of us as the most beautiful works of art that nature has created, whose meaning is to be sought as assiduously as one might the meaning of life itself.

For me, the big motivating question is Erwin Schrödinger's 'What is life?'1 That it is also a question on the meaning of life is evident to Schrödinger, who closes his book with a Chapter on philosophical implications for determinism and freewill. This is as it should be. I do not agree with those scientists for whom scientific knowledge has no meaning for life, and must be kept separate from real life in any event; perhaps an attitude symptomatic of the alienation that pervades our fragmented, industrial society. I will not dwell on that here, as it is not the main thesis of my book. Instead, I want to concentrate, for now, on Schrödinger's original question:

‘‘How can the events in space and time which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?”2

The same question has been posed in one form or another since the beginning of modern science. Is living matter basically the same as non-living only more complicated, or is it something more? In other words, are the laws of physics and chemistry necessary and sufficient to account for life, or are additional laws outside physics and chemistry required? Descartes is famous not only for separating mind from matter; he also placed living matter, alongside with non-living matter, firmly within the ken of the laws of physics; more specifically, of mechanical physics. Since then, generations of vitalists, including the embryologist Hans Driesch and the philosopher Henri Bergson, have found it necessary to react against the mechanical conception of life by positing with living organisms an additional entelechy, or elan vital, which is not within the laws of physics and chemistry.3

The vitalists were right not to lose sight of the fundamental phenomenon of life that the mechanists were unable to acknowledge or to explain. But we no longer live in the age of mechanical determinism. Contemporary physics grew out of the breakdown of Newtonian mechanics at the beginning of the present century, both at the submolecular quantum domain and in the universe at large. We have as yet to work out the full implications of all this for biology. Some major thinkers early in the present century, such as the philosopher-mathematician, Alfred North Whitehead, already saw the need to explain physics in terms of a general theory of the organism,4 thus turning the usually accepted hierarchy of reductionistic explanation in science on its head. Whitehead's view is not accepted by everyone, but at least, it indicates that the traditional boundaries between the scientific disciplines can no longer be upheld, if one is to really understand nature. Today, physics has made further in-roads into the ‘organic’ domain, in its emphasis on nonlinear phenomena far from equilibrium, on coherence and cooperativity which are some of the hallmarks of living systems. The vitalist/mechanist opposition is of mere historical interest, for it is the very boundary between living and non-living that is the object of our enquiry, and so we can have no preconceived notion as to where it ought to be placed.

Similarly, to those of us who do not see our quest for knowledge as distinct from the rest of our life, there can be no permanent boundary between science and other ways of knowing. Knowledge is all of a piece. In particular, it is all of a piece with the knowing consciousness, so there can be no a priori dualism between consciousness and science. Far from implying that consciousness must be ‘reduced’ to physics and chemistry, I see physics and chemistry evolving more and more under the guidance of an active consciousness that participates in knowing.5 Some of these issues will be dealt with in the last two Chapters.

The Physicochemical Underpinnings of Life

Schrödinger's preliminary answer to the question of what is life is as follows:

“The obvious inability of present-day [1940s] physics and chemistry to account for such events [as take place within living organisms] is no reason at all for doubting that they can be accounted for by those sciences.”6

He is saying that we simply do not know if events within living organisms could be accounted for by physics and chemistry because we have nothing like living systems that we could set up or test in the laboratory. There is a serious point here that impinges on the methods and technologies we use in science. Until quite recently, the typical way to study living organisms is to kill and fix them, or smash them up into pieces until nothing is left of the organization that we are supposed to be studying. This has merely reinforced the Newtonian mechanical view of organisms that has proved thoroughly inadequate to account for life. The situation is changing now with great advances in the development of non-invasive technologies within the past twenty years. We can ‘listen in’ to nature without violating her. I shall have more to say on that in later Chapters.

Another reason for not doubting that physics and chemistry can one day account for living systems is surely that they are both evolving disciplines. Who knows what the subjects will look like in twenty years’ time? Already, physics and chemistry today look quite different from the subjects half a century ago. The transistor radio, the computer and lasers have been invented since Schrödinger wrote his book. One major current obsession is with nano-technologies, or technologies which are precise to the molecular level because they make use of actual molecules. Whole new disciplines have been created: synergetics — the study of cooperative phenomena, nonequilibrium thermodynamics, quantum electrodynamics and quantum optics, to name but a few. In mathematics, non-linear dynamics and chaos theory took off in a big way during the 1960s and 70s. Perhaps partly on account of that, many nonlinear optical phenomena associated with quantum cavity electrodynamics and coherent light scattering in solid state systems are being actively investigated only within the past 15 years. Meanwhile the race is on for the ultimate in high temperature superconducting material.

There have been several suggestions that these recent developments in physics and chemistry are particularly relevant for our understanding of biological phenomena. But there has not been a serious attempt to re-examine the issue in the way that Schrödinger has done in his time. I believe we have made substantial progress since, and it is the purpose of this book to substantiate that claim. By way of exploration, I shall range widely over equilibrium and nonequilibrium thermodynamics, aspects of quantum theory, solid state physics, physics of liquid crystals as well as the relevant physiology, developmental biology, biochemistry and molecular biology of cells and organisms. I shall not be referring much to the details of molecular genetics and gene control mechanisms which already fill volumes of excellent texts, and which I simply take for granted. They are all part of the rich tapestry of life that will find their rightful place when our life-picture has been sufficiently roughed out. It is indeed the bare-bones sketch that I shall be concerned with here — the fundamental physical and chemical principles which make life possible.

I promise neither easy nor definitive answers. Our education already suffers from a surfeit of facile, simplistic answers which serve to explain away the phenomena, and hence to deaden the imagination and dull the intellect. An example is the claim that the natural selection of random mutations is necessary and sufficient to account for the evolution of life. As a result, whole generations of evolutionary biologists are lulled into thinking that any and every characteristic of organisms is to be 'explained' solely in terms, of the 'selective advantage' it confers on the organism. There is no need to consider physiology or development, nor indeed the organism itself; much less the physical and chemical basis of living organization.7

To me, science is a quest for the most intimate understanding of nature. It is not an industry set up for the purpose of validating existing theories and indoctrinating students in the correct ideologies. It is an adventure of the free, enquiring spirit which thrives not so much on answers as unanswered questions. It is the enigmas, the mysteries and paradoxes that take hold of the imagination, leading it on the most exquisite dance. I should be more than satisfied, if, at the end of this book, I have done no more than keep the big question alive.

What is life? Can life be defined? Each attempt at definition is bound to melt away, like the beautiful snowflake one tries to look at close-up. Indeed, there have been many attempts to define life, in order that the living may be neatly separated from the nonliving. But none has succeeded in capturing its essential nature. Out of the sheer necessity to communicate with my readers, I shall offer my own tentative definition for now, which to me, at least, seems closer to the mark: life is a process of being an organizing whole. In the course of this book, you will come across other more precise or more encompassing definitions. It is important to emphasize that life is a process and not a thing, nor a property of a material thing or structure. As is well known, the material constituents of our body are continually being broken down and resynthesized at different rates, yet the whole remains recognizably the same individual being throughout. Life must therefore reside in the patterns of dynamic flows of matter and energy that somehow makes the organisms alive, enabling them to grow, develop and evolve. From this, one can see that the 'whole' does not refer to an isolated, monadic entity. On the contrary, it refers to a system open to the environment, that enstructures or organizes itself (and its environment) by simultaneously 'enfolding' the external environment and spontaneously 'unfolding' its potential into highly reproducible or dynamically stable forms.8 To be alive and whole is a very special being. Let us dwell on that for a while.

On Being Alive

Biology textbooks often state that the most important characteristic of organisms is the ability to reproduce, and then proceed to give an account of DNA replication and protein synthesis as though that were the solution to the fundamental problem of life. The ability to reproduce is only one of the properties of living organisms, and it could be argued, not even the most distinguishing one. For there are a number of other characteristics, scientifically speaking, which leave us in no doubt that they are alive: their extreme sensitivity to specific cues from the environment, their extraordinary efficiency and rapidity of energy transduction, their dynamic long range order and coordination, and ultimately, their wholeness and individuality.9

For example, the eye is an exquisitely sensitive organ, which in some species, can detect a single quantum of light, or photon, falling on the retina. The photon is absorbed by a molecule of rhodopsin, the visual pigment situated in special membrane stacks in the outer segment of a rod-cell (Fig. 1.1). This results eventually in a nervous impulse coming out at the opposite end of the cell, the energy of which is at least a million times that contained in the original photon. The amplification of the incoming signal is in part well understood as a typical 'molecular cascade' of reactions: the specific receptor protein, rhodopsin, on absorbing a photon, activates many molecules of a second protein, transducin, each of which then activates a molecule of the enzyme phosphodiesterase to split many molecules of cyclic guanosine monophosphate or cGMP. The cGMP normally keeps

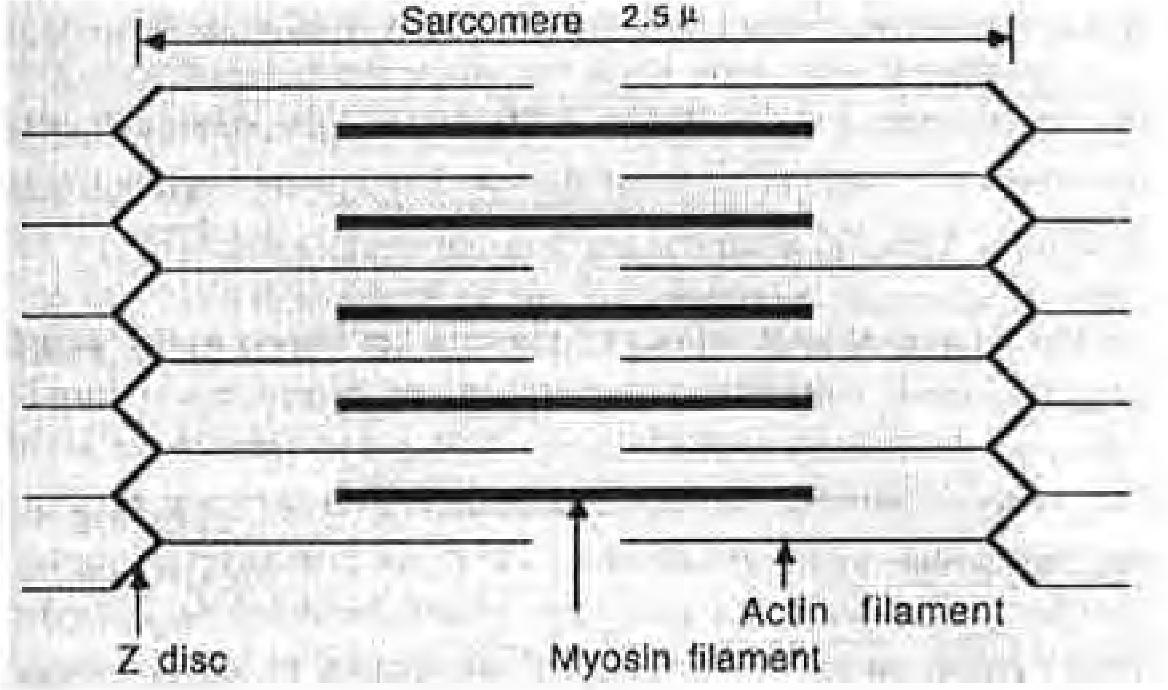
Figure 1.1 Diagram of a light sensitive rod cell. The top part (to the left) is the 'rod' containing membrane stacks in which the light sensitive pigments are situated. The resultant nervous impulse goes out at the bottom.

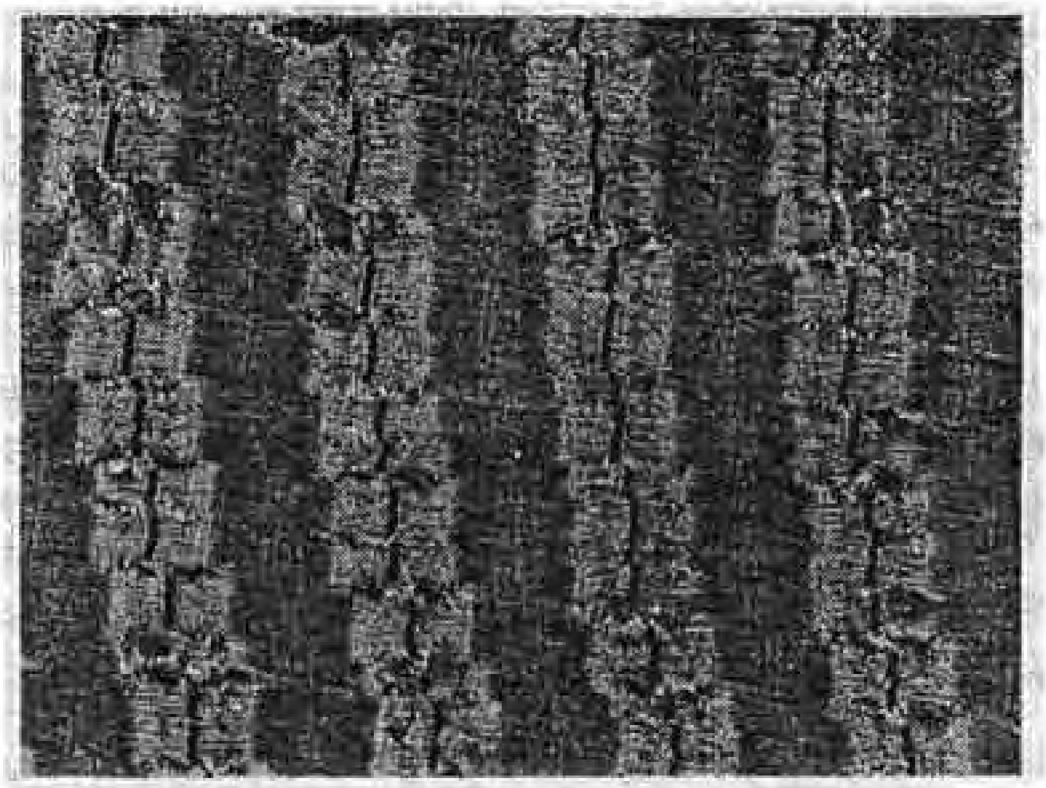
sodium ion channels open in the otherwise impermeable cell membrane, whereas the split non-cyclic GMP cannot do so. The result is that the sodium channels close up, keeping sodium ions out of the cell and giving rise to an increased electrical polarization of the cell membrane — from about -40mV to -70mV, which is sufficient to initiate the nerve impulse.10

Molecular cascades are common to all processes involved in signal transduction, and it is generally thought that one of their main functions is to amplify the signal. Let us examine the visual cascade reactions more closely. There are notable caveats in the account given in the last paragraph. For one thing, the component steps have time constants that are too large to account for the rapidity of visual perception in the central nervous system, which is of the order of 10-2s. Thus, it takes 10-2s just to activate one molecule of phosphodiesterase after photon absorption. Furthermore, much of the amplification is actually in the initial step, where the single photon-excited rhodopsin passes on the excitation to at least 500 molecules of transducin within one millisecond. How that is achieved is still a mystery, except that as rhodopsin and transducin molecules are bound to a common membrane, the membrane must play a crucial role in both the amplification and the long range transfer of excitation.

Another instructive example is muscle contraction.11 About 40% of our body is made of skeletal muscle, i.e., muscle attached to bones, like those in our arms and legs and trunk. Another 5 to 10% is smooth muscle such as those in the gut and body wall, and cardiac muscle which is in the heart. Skeletal muscle consists of bundles of long, thin muscle fibres, which may be discerned under a magnifying glass. These fibres are several centimeters in length, each of which is actually a giant cell formed by the fusion of many separate cells. A single muscle fibre, magnified a hundred times or more under the light microscope, can be seen to be made up of a bundle of 20 to 50 much smaller fibres, or myofibrils, each 1 to 2µ in diameter. A myofibril has regular, 2.5µ repeating units, called sarcomeres, along its length. Adjacent myofibrils are aligned so that their sarcomeres are in register. Under the much higher magnifications available from the electronmicroscope — thousands to tens of thousand times — one will see extremely regular arrays of the periodic structures (Fig. 1.2). One will also see that each sarcomere consists of alternating thin and thick filaments, made up respectively of the two main muscle proteins, actin and myosin. In three dimensions, there are actually six thin actin filaments surrounding each thick myosin filament, and the six actin filaments are attached to an end-plate, the Z-disc. Contraction occurs as the actin filaments surrounding the myosin filaments slide past each other by cyclical molecular treadmilling between myosin 'head' groups and serial binding sites on the actin filament, forming and breaking cross-bridges between the filaments, in all three dimensions in the entire array.

The actin and myosin molecules are packed and arranged very precisely, approaching the regularity of crystals, and the study of the detailed structure of resting as well as contracting muscle is done by means of X-ray crystallography. There are 624 myosin head groups on each myosin filament, and when the muscle contracts,


Sarcomere 2.5 μ
Actin filament
Z disc
Myosin filament



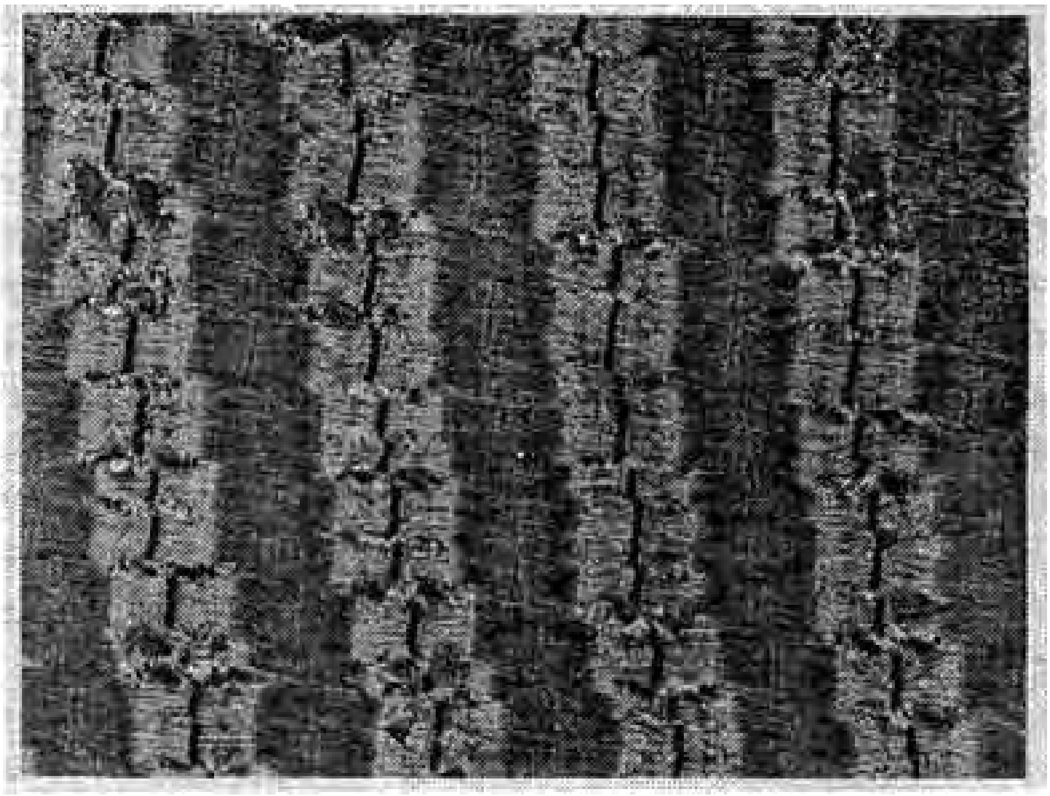


Figure 1.2 Ultrastructure of rabbit muscle. Top, diagram of a sarcomere; bottom, electronmicrograph.

each sarcomere shortens proportionately. Thus, when a myofibril containing a chain of 20,000 sarcomeres contracts from 5 to 4 cm, the length of each sarcomere decreases correspondingly from 2.5 to 2µ. The energy for contraction comes from the hydrolysis of a special molecule that acts as the universal energy transacting intermediate in the body. In its “charged up” form, it is ATP, or adenosine triphosphate — with three phosphate groups joined one to another and to the chemical group adenosine. ATP ‘‘discharges” its energy by splitting off a phosphate group at the end, to give the “discharged” form, ADP or adenosine diphosphate.

Muscle contraction is triggered by an action potential at the site where a nerve impinges on the muscle-cell membrane. An action potential is a quick electrical discharge followed by recovery of the pre-existing baseline electrical potential. This releases calcium ions, Ca2+, from intracellular calcium ion stores to initiate contraction simultaneously in the entire cell within a millisecond.12 Contraction involves numerous autonomously occurring cycles of attachment and detachment of all the individual myosin heads to and from the binding sites on the actin filaments at the rate of 50 cycles or more per second13 — each of which molecular event requiring the transfer of energy contained in one molecule of ATP — precisely coordinated over the whole cell.

In a typical muscle contraction, all the cells in the muscle — billions of them at the very least — are executing the same molecular treadmilling in concert. Simply waving our arms about is a veritable feat requiring a series of actions coordinated instantaneously over a scale of distances spanning nine orders of magnitude from 10-9 metre (one billionth part of a metre) for intermolecular spacing between the actin and myosin heads, to about one metre for the length of our arm; each action, furthermore, involving the coordinated splitting of 1019 individual molecules of ATP. Now, then, imagine what has to happen when a top athlete runs a mile in under four minutes! The same instantaneous coordination over macroscopic distances involving astronomical numbers of molecules, only more so, and sustained for a long period without break.14

It is truly remarkable how our energy should be available to us at will, whenever and wherever we want it, in the amount we need. Moreover, the energy is supplied at close to 100% efficiency. This is true for muscle contraction, in which the chemical energy stored in ATP is converted into mechanical energy,15 as well as for all the major energy transduction processes, as for example, in the synthesis of ATP itself in the mitochrondria16 where carbon compounds are oxidized into carbon dioxide and water in the process of respiration. If that were not so, and energy transduction can only occur at the efficiency of a typical chemical reaction outside living organisms, which is 10 to 30% efficient at best, then we would literally burn out with all the heat generated.

To summarize, then: being alive is to be extremely sensitive to specific cues in the environment, to transduce and amplify minute signals into definite actions. Being alive is to achieve the long range coordination of astronomical numbers of submicroscopic, molecular reactions over macroscopic distances; it is to be able to summon energy at will and to engage in extremely rapid and efficient energy transduction.

So, how is this sensitive, vibrant whole that is the organism put together? An organism that, furthermore, develops from a relatively featureless fertilized egg or seed to a complicated shapely creature that is nonetheless the same essential whole?

We have certainly not exhausted the wonders of being alive, and shall continue our investigations from the standpoint of thermodynamics in the next five Chapters.

Notes

1. Schrödinger, (1944).
2. Schrödinger (1944). p. 3.
3. Needham (1935).
4. Whitehead, (1925).
5. I have written several papers recently on the need to recover a way of knowing in science that involves the complete participation of the knowing being: intellect and feeling, mind and body, spirit and intuition. Authentic science and art are both creative activities arising out of this total engagement of nature and reality. See Ho, (1989a; 1990a; 1993).
6. Schrödinger (1944), p. 4.
7. For alternative approaches to neo-Darwinism in the study of evolution, please see Ho and Saunders (1984); Pollard (1984); Ho and Fox (1988); Kauffman (1993); Goodwin (1994); Cohen and Stewart (1994); Saunders (1998).
8. See Ho (1988a).
9. See Ho (1989b).
10. See Stryer (1987).
11. See Alberts et al. (1983).
12. Rios and Pizarro (1991).

13. See Pollard (1987).
14. A detailed account of muscle contraction may be found in Ho, (1995a).
15. Hibbard et al. (1985).
16. Slater (1977).

CHAPTER 2

Do Organisms Contravene the Second Law?

Life and the Second Law

Many scientists have remarked that whereas the physical world runs down according to the second law of thermodynamics such that useful energy continually degrades into heat, or random molecular motion (expressed in the technical term, entropy), the biological world seems capable of doing just the opposite in increasing organization by a flow of energy and matter. Physicists and chemists have long felt that as all biological processes require either chemical energy or light energy and involve real chemical reactions, the second law, as much as the first law of thermodynamics (the conservation of energy) ought to apply to living systems. So, what is the secret of life? One explanation offered by Schrödinger1 is that because living systems are open to the environment, they can create a local decrease in entropy at the expense of the surroundings, so that the entropy of living systems plus the surroundings always increases in all real processes, and there is no violation of the second law. But there are more fundamental problems, which Schrödinger was also aware of, as were the founding fathers of thermodynamics (see Chapters 5 and 14). We cannot appreciate those problems before we know what the laws of thermodynamics are, and to which systems they are supposed to apply.

What are the Laws of Thermodynamics?

Classical thermodynamics deals with the laws governing the conversion of heat into work or other forms of energy. It arose as a science giving an exact description of macroscopic systems of gases expanding against an external constraint such as a piston driving a steam engine, for example, for which the important parameters are pressure, volume and temperature. Its major foundations were laid long before detailed atomic theories became available. The possibility that the thermodynamic behaviour of matter could be derived from the mechanical properties (such as mass and velocity) of its constituent molecules forms the basis of statistical mechanics, which is supposed to give a rigorous deductive framework for thermodynamics.[2]

There are two main laws of thermodynamics. The first is usually written as the equation,

$$\Delta U = Q + W, \qquad (2.1)$$

which says that the change in the total internal energy of a system, ΔU, is equal to the heat absorbed by the system from its surroundings, Q, plus the work done on the system by the surroundings, W. (The sign Δ — Greek letter delta — is shorthand for 'change in'.) It is based on the law of the conservation of energy, which states that energy is neither created nor destroyed in processes, but flows from one system to another, or is converted from one form to another, the amount of energy 'in the universe' remaining constant. The total internal energy, U, is a function of the particular state of the system, defined by temperature and pressure, and does not depend on how that state is arrived at. The heat absorbed, Q, and the work, W, are by contrast, not state functions and their magnitudes depend on the path taken. The first law tells us that energy is conserved but it does not tell us which processes can occur in reality. This is done by the second law.

The second law of thermodynamics tells us why processes in nature always go in one direction. Thus, heat flows from warm to cold bodies until the two are at the same temperature, but nobody has ever observed heat flowing spontaneously from cold to warm bodies. A drop of ink placed into a jar of water soon diffuses to fill the whole jar. And we would be surprised indeed, if, some time later, the original ink drop were to reconstitute itself. In the same way, machines run down unless constantly supplied with energy. Nobody has ever succeeded in building a perpetual motion machine which turns heat into mechanical work, then turns mechanical work back to its original equivalent in heat and so on again and again — which does not contradict the first law of thermodynamics.

Thus, spontaneous processes in nature appear to define a time's arrow: they go in one direction only, never in reverse. Physical systems evolve from order to homogeneous disorder, eventually running down until no more useful work can be extracted from them. To explain these phenomena, the second law defines a quantity, entropy, which increases in real processes and never decreases. Thus, at the end of a process, the change in entropy is always positive, or in the limiting case of a process which is reversible, the change in entropy is zero. This is expressed in the equation,

$$\Delta S_{sys} + \Delta S_{surr} \geq 0 \, , \qquad (2.2)$$

which says that sum of the changes in entropy in the system, ΔSsys, and its surroundings, ΔSsurr, is greater than or equal to zero in all real processes. The change in entropy in each case is equal to the heat absorbed in a reversible process divided by the temperature at which the process occurs in degrees Kelvin, or K (which starts at -273.15°C, so that for example, 25°C would be 298.15K). For simplicity, we consider an isothermal process, i.e., one occurring in a system at constant temperature T,

$$\Delta S = Q_{rev}/T \, . \qquad (2.3)$$

A reversible process, in thermodynamic terms, is one that occurs very, very slowly, so that it is at equilibrium the whole way through. This means that the heat energy absorbed at every stage has time enough to spread or equilibrate throughout the system. In a reaction occurring reversibly, the net change of entropy in the system is exactly compensated by the change in entropy of the surrounding in the opposite direction, so that the net change in entropy is zero:

$$\begin{aligned}\Delta S_{sys} &= -\Delta S_{surr}\\ \Delta S_{sys} + \Delta S_{surr} &= 0\end{aligned} \tag{2.4}$$

Another point about entropy is that it is a state function (like internal energy U above), and is therefore independent of the path taken to arrive at the particular state. If the process occurs irreversibly, the heat, Q, absorbed is less than that in the reversible process, but the entropy production does not change, so,

$$Q_{irrev}/T < \Delta S_{sys} \tag{2.5}$$

On account of the reduction in the amount of heat lost by the environment to the system, the required compensatory change in entropy in the environment cannot take place in accordance with Equation 4. That means the increase in entropy in the system is not compensated by an equal decrease in entropy in the environment, so

$$\begin{aligned}\Delta S_{SYS} &> -\Delta S_{surr}\\ \Delta S_{SYS} + \Delta S_{surr} &> 0\end{aligned} \tag{2.6}$$

An example of an irreversible process is the expansion of a perfect gas against a vacuum. Here, no heat is absorbed from the surroundings and no work is done. The change in entropy of the system is the same as if the process occurred reversibly, but the change in entropy of the surroundings is zero, and so a net increase in entropy (so to speak, ‘of the universe’) results.

We can see that in the case of living systems, a decrease in entropy can indeed be achieved at the expense of a compensating increase in entropy in its surroundings, and there is no need to contravene the second law in that respect.

Another way to state the second law is that all isolated systems (those which exchange neither energy nor matter with their surroundings) run down so that useful energy is degraded into entropy. The point at which all useful energy is degraded into entropy is the state of thermodynamic equilibrium. Thermodynamic equilibrium is thus an end-state characterized by a maximum in entropy, when no useful energy is left. Entropy is thus made up of a kind of incoherent energy that is no longer available for work. (Entropy is, however, technically not the same as energy, as it has different dimensions, Joules per deg. K compared with Joules.) We can then define a number of functions for the free energy, or energy which is extractable for work: the Helmholtz free energy, A, for systems at constant volume, and the Gibbs free energy, G, for other systems.

$$A = U - TS \tag{2.7}$$

$$G = U + PV - TS \tag{2.8}$$

(Note that for simplicity, we have dropped the subscript "sys", for all the symbols referring to the system.) For isothermal processes at constant temperature T, the changes in free energies are,

$$\Delta A = \Delta U - T\Delta S \tag{2.9}$$

and

$$\Delta G = \Delta H - T\Delta S \tag{2.10}$$

ΔH is the change in a quantity called enthalpy, or heat content, which is defined as

$$H = U + PV \tag{2.11}$$

$$\Delta H = \Delta U + \Delta(PV) = \Delta U + P\Delta V + V\Delta P + \Delta P\Delta V , \tag{2.12}$$

where U, P and V are the internal energy, pressure and volume of the system. At constant pressure, the last two terms disappear, and

$$\Delta H = \Delta U + P\Delta V \tag{2.13}$$

At constant volume, the last three terms of Eq. 2.12 disappear; we get

$$\Delta H = \Delta U \qquad (2.14)$$

and the free energy change of the system is ΔA, as given in Eq. 2.9.

In both expressions for free energy — Eqs. 2.7 and 2.8 — it can be seen that free energy is just that part of the internal energy or enthalpy that can be extracted for work. The part that is unavailable for work is entropy. So, as entropy increases in a system, free energy decreases, until, at thermodynamic equilibrium, entropy reaches a maximum and there is no free energy left. The concept of thermodynamic equilibrium is central to the second law. It is a state of maximum entropy towards which all isolated systems evolve. A system at equilibrium is one in which no more changes can occur unless it is removed from isolation and placed in contact with another system.

The laws of classical thermodynamics describe how one equilibrium replaces another. They say very little about the changes that happen in between when systems are not in equilibrium. In that respect alone, classical thermodynamics is quite inadequate to deal with living systems where things are happening all the time (In Chapter 4, we shall see how thermodynamicists try to overcome that limitation with some success). A more serious problem is that the laws of thermodynamics, as usually formulated, apply to homogeneous, or 'bulk phase' systems consisting of a large number of identical components.3

Thus, entropy can be given an exact formulation in statistical mechanics by considering a large ensemble of identical systems at a given internal energy, volume and composition (a 'microcanonical ensemble' in the language of statistical mechanics), each of which can exist in a vast number of different microstates or more precisely, 'quantum states' (to be described in detail in Chapter 14). The entropy of the system is given as

$$S = k\,\ln W\,, \qquad (2.15)$$

where the Boltzmann's constant, k = 1.3805x10-23J K-1, is a measure of the thermal energy in Joules associated with each molecule per degree K. W is the number of possible microstates that the system can exist in, and ln is the natural logarithm. (It should be apparent to you by now that physicists may use the same symbols for different entities: I have used W for work above for the first law of thermodynamics, whereas here it stands for microstates.) It can readily be appreciated that the greater the number of possible microstates, the greater the entropy, hence, of ‘randomness’, or ‘disorder’. The system consisting of the ink drop in a jar of water, for example, starts from a state of low entropy because the molecules are confined to a small region in the glass. Entropy increases as the molecules diffuse, so that finally, at equilibrium, a given molecule has the probability of being found in a small volume located anywhere in the glass. The equilibrium state is thus the one in which the entropy function given in Eq. (2.15) is a maximum. Another way to say the same thing is that the equilibrium state is the most probable state.

Similarly, the total energy of a system corresponds to the sum of all the molecular energies of translation, rotation, vibration, plus electronic energy and nuclear energy (see Chapter 5); whereas temperature is proportional to the sum of the kinetic energies of all the molecules and, for a monatomic system, is defined by the formula:

$$nkT = \sum_{i=1}^{n} m_i C_i^2 \qquad (2.16)$$

where n is the number of molecules, mi is the mass of the ith molecule and Ci its velocity. The term kT is often referred to as the thermal energy of a molecule at temperature T.

The translation of macroscopic parameters into microscopic properties of molecules is by no means straightforward. For example, the statistical entropy function, elegant though it is, cannot easily be used for systems involving chemical reactions, which include all living systems as well as all chemical systems.

It is only an analogue of the macroscopic entropy. As physical chemist, Kenneth Denbigh4 reminds us, there is no necessary connection between entropy and either 'orderliness' or 'organization'. Along with concepts like energy, work, heat and temperature, entropy does not bear up to rigorous analysis.5 We shall leave these difficulties aside for the moment (to be dealt with in Chapter 5), and concentrate on the limitations of the second law of thermodynamics which arise on account of its statistical foundations.

Is Maxwell's Demon in the Living System?

In his physical chemistry textbook, Glasstone6 expresses a very commonly held view, that the second law of thermodynamics is a statistical law which can only be applied to a system consisting of a large number of particles, and that, ''If it were possible to work with systems of single, or a few, molecules, the law might well fail."

A major difficulty, already pointed out by Schrödinger, is that single molecules, or very few of them, are the active agents in living systems. Thus, each cell contains only one or two molecules of each sequence of DNA in the nucleus. Each bacterium of E. coli contains several molecules of the protein that enables it to respond to the presence of lactose in its environment, resulting in the induced synthesis of several enzymes involved in metabolizing the sugar, enabling the bacterium to grow and to multiply. This is typical of whole classes of metabolic regulators. Similarly, it takes no more than several molecules of a given hormone to bind to specific receptors in the cell membrane in order to initiate a cascade of biochemical reactions that alter the characteristics of the whole cell. Does this mean the second law cannot be applied to living systems?

Actually, this difficulty is not restricted to biology, but occurs in physical systems as well. The most colourful statement of the problem is in the form of Maxwell's demon7 — an hypothetical intelligent being who can operate a microscopic trapdoor between two compartments of a container of gas at equilibrium so as to let fast molecules through in one direction, and the slow ones in the other. Soon, a temperature difference would be created by the accumulation of fast, energetic molecules on one side and slow ones on the other, and work can then be extracted from the system. Maxwell invented this demon in 1867 to illustrate his belief that the second law is statistical, and had no intention of questioning the second law itself. The trapdoors, after all, would also be subject to the same statistical fluctuations as the molecules, and would open and close indiscriminately so that the separation of fast from slow molecules could never be achieved, unless we had the magical demon — small and clever enough to observe the fluctuations.

Thirty-eight years later, however, Einstein showed that the fluctuations can be observed, and in fact, were first observed in 1827 by Robert Brown — as Brownian motion. This is the random movements of microscopic particles (observable under the microscope) as they are jostled about by the fluctuations of the water molecules. It also became evident in the 1950s that something like a Maxwell's demon could be achieved with little more than a trapdoor that opens in one direction only and requires a threshold amount of energy (activation energy) to open it. This is realizable in solid-state devices such as diodes and transistors that act as rectifiers.[7] Rectifiers let current pass in one direction only but not in reverse, thereby converting alternating currents to direct currents. That means they can convert randomly fluctuating currents, in principle, into an electrical potential difference between the two sides from which work can then be extracted.

Similar situations are commonly found in biological membranes which have electrical potential gradients of some 107 V/m across them and have bound enzymes involved in the vectorial transport of ions and metabolites from one side to the other, as for example, the transport of Na+ out of, and K+ into the cell by the enzyme

Na+/K+ ATPase. It has been demonstrated that weak alternating electric fields can drive unidirectional active transport by this enzyme without ATP being broken down. In other words, the energy from the electric field is directly transduced into transport work by means of the membrane-bound enzyme. Moreover, randomly fluctuating electric fields are also effective, precisely as if Maxwell's demon were involved in making good use of the fluctuations!8 Actually, there is no violation of the second law here simply because cells and organisms are not at thermodynamic equilibrium.

The problem of Maxwell's demon is generally considered as having been ‘solved’ by Szilard, and later, Brillouin, who showed that the demon would require information about the molecules, in which case, the energy involved in obtaining information would be greater than that gained and so the second law remains inviolate (see Chapter 14). What they have failed to take account of is that the so-called information is already supplied by the special structure or organization of the system (see Chapter 11). In the next chapter, I will concentrate on how the problem of Maxwell's demon might be solved.

Notes

1. Schrödinger (1944).
2. See Penrose (1970).
3. Statistical mechanics can be formulated to deal with a mixture of chemical species, and to a limited extent, with space-time structure, but not yet of the kind that exists in living systems. I thank Geoffrey Sewell for pointing this out to me.
4. See Denbigh (1989), pp. 323–32.
5. See Bridgman, (1941). Geoffrey Sewell disagrees with my statement, pointing out that a lot of effort has since been devoted to translating/relating macroscopic entropy to degree of molecular disorder either in a system (von Neumann entropy) or in a process (Kolmogorov entropy). However, I believe it is still true to say that the relationship between the macroscopic and microscopic entities remain conjectural. There is no necessary logical connection between the two (see Chapter 5).
6. Glasstone (1955).
7. Ehrenberg (1967).

8. See Astumian et al. (1989). The authors are at pains to point out that noise internal to the system, however, cannot be used in the same way to generate work, because electrical correlations would be induced to oppose it, and hence the second law is by no means violated. A more detailed model of how “non-equilibrium fluctuations” can bias the Brownian motion of a particle in anisotropic medium without thermal gradients is presented by Astumian (1997). See also Tsong and Gross (1994) for an electroconformation model of membrane-bound enzymes that can efficiently carry out vectorial transport with random electrical energy.

CHAPTER 3

Can the Second Law Cope with Organized Complexity?

The Space-time Structure of Living Processes

One cannot fully appreciate the problem of Maxwell's demon in the context of living organisms without taking full account of the complexity of the organism's space-time structure, which demonstrates clearly the limitations of thermodynamics applied to living systems.

To begin, we can take it as obvious and given that the organism is an open system, which moreover, qualifies as a dissipative structure1 in the sense that its organization is maintained in some kind of ‘steady state’ by a flow of energy and chemicals. (We shall say more about energy flow in the next Chapter.) As soon as that flow is interrupted, disintegration sets in and death begins. That steady state, however, is not a static bulk phase in a rigid container such as the physical chemists’ continuously stirred tank reactor (CSTR) or, as microbiologists prefer to call it, the chemostat. The CSTR has long served as the model for the steady state, and a lot of useful analyses have been achieved. But as far as a representation of living organization is concerned, it introduces some quite misleading features. Indeed, in typical models of dissipative structures such as the Bénard-Rayleigh cells (see next Chapter) which develop in a shallow pan of water heated from below, or the famous Beloussov-Zhabotinsky oxidation-reduction reaction, which gives oscillating, concentric red and blue rings and various spiralling patterns in a petri dish (see Fig. 3.1), the dynamical structures — the objects of interest — are obtained precisely because the system is not stirred. Stirring would obliterate those structures and featureless homogeneity would result.2

What do we find in the organism? Organized heterogeneities, or dynamic structures on all scales. There is no homogeneity, no static phase held at any level. Even a single cell has its characteristic shape and anatomy, all parts of which are in constant motion; its electrical potentials and mechanical properties similarly, are subject to cyclic and non-cyclic changes as it responds to and counteracts environmental fluctuations.

Spatially, the cell is partitioned into numerous compartments by cellular membrane stacks and organelles, each with its own 'steady states' of processes that can respond directly to external stimuli and relay signals to other compartments of the cell. Within each,

Figure 3.1 The Beloussov-Zhabotinsky reaction.3

compartment, microdomains4 can be separately energized to give local circuits, and complexes of two or more molecules can function as ‘molecular energy machines’ which can cycle autonomously without immediate reference to its surroundings. In other words, the steady ‘state’ is not a state at all but a conglomerate of processes which are spatiotemporally organized, i.e., it has a deep space-time structure, and cannot be represented as an instantaneous state or even a configuration of states.5 Characteristic times of processes range from < 10-14 s for resonant energy transfer between molecules to 107 s for circannual rhythms. The spatial extent of processes, similarly, spans at least ten orders of magnitude from 10-10 m for intramolecular interactions to metres for nerve conduction and the general coordination of movements in larger animals.

The processes are catenated in both time and space: the extremely rapid transient flows (very short-lived pulses of chemicals or of energy) which take place on receiving specific signals, are propagated to longer and longer time domains of minutes, hours, days, and so on via interlocking processes which ultimately straddle generations. These processes include the by now familiar enzyme activation cascades (see Chapter 1) which occur in response to specific stimuli, and often end in the expression of different genes and in morphological differentiation.

For example, repeated stimulation of the same muscles encourages the growth of those muscles and make them function more efficiently, as body builders are well aware! The intermediate events include changes in innervation, and the expression of genes which code for different sets of muscle proteins.6 The graph in Fig. 3.2 depicts the catenated sequence of events and their approximate timescales.

A transient pulse of a chemical signal, acetylcholine, sent out by the nerve cell at its junction with the muscle, opens the sodium ion channels in the membrane of the muscle cell and depolarizes the cell membrane within 10-3 s (peak 1), triggering an influx of Ca2+ from the sarcoplasmic reticulum which lasts for 10-2 s (peak 2). This in turn sets off the reactions between actin and myosin in a contraction, which involves many cycles of molecular tread-milling

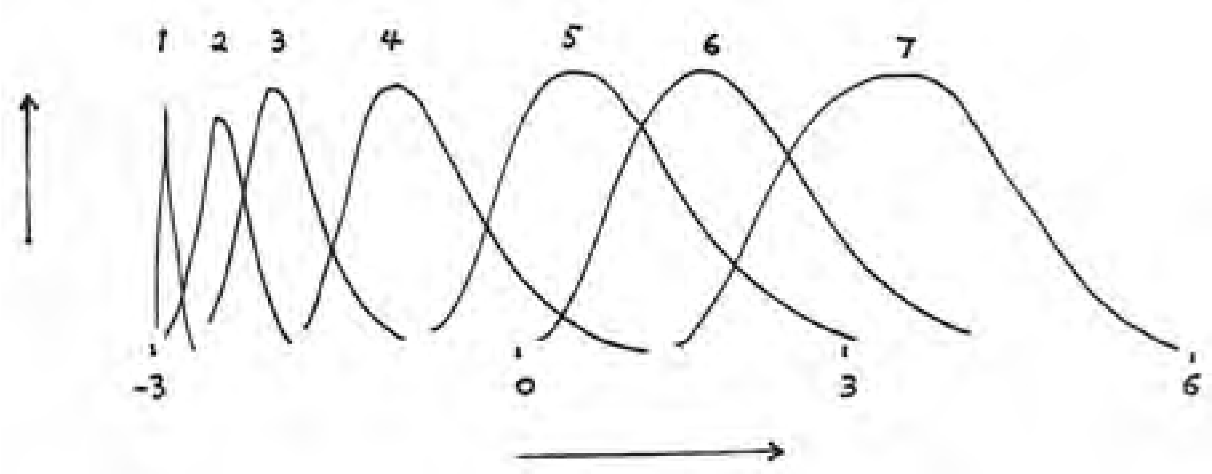


Figure 3.2 The catenation of living processes in time. The vertical axis represents the magnitude, or amplitude, of change; the horizontal axis is time in seconds in logarithm to the base ten. The amplitudes are represented as equal for all the processes, but in reality, they may be progressively amplified or diminished at longer and longer time scales see text.

where ATP is split into ADP and Pi. Each individual cycle is some 10-2 to 10-1 s long (peak 3), whereas a contraction may last 1 to 10 s (peak 4). Sustained muscular activities, consisting of numerous cycles of contraction and relaxation of entire muscles, go on typically for 102 – 103 s (peak 5). This stimulates the transcription of specific genes to increase the synthesis of special muscle proteins in 103 s or longer (peak 6). Over a period of days, weeks and months, repetition of the same sequence of activities in regular exercises gives rise to the desired changes to the muscles involved (peak 7): enhancement in anatomy and improvement in performance.

These catenated processes are responsible for the phenomenon of ‘memory’ so characteristic of living systems. In reality, the processes are projections or propagations into the future at every stage. They set up influences to determine how the system develops and responds in times to come. Typically, multiple series of activities emanate from the focus of excitation. The mere anticipation of muscular activity is accompanied by the secretion of adrenaline, which in turn causes the blood vessels to dilate, increasing the heart rate, and thus enhancing the aeration of muscles and the synthesis of more ATP to supply the sustained activity of the muscle. While the array of changes in the positive direction is propagating, a series of negative feedback processes is also spreading, which has the effect of dampening the change. It is necessary to think of all these processes propagating and catenating in parallel in many dimensions of space and time (see Fig. 3.3). In case of disturbances which have no special significance for the body, homeostasis is restored sooner or later as the disturbance passes. On the other hand, if the disturbance or signal is significant enough, a series of irreversible events brings the organism to a new ‘steady state’ by developing or differentiating new tissues. The organism may even act to alter its environment appropriately.

The living system is so thoroughly dynamic that each single cell in the body is simultaneously criss-crossed by many circuits of flow, each circuit with its own time domain and direction, specified by

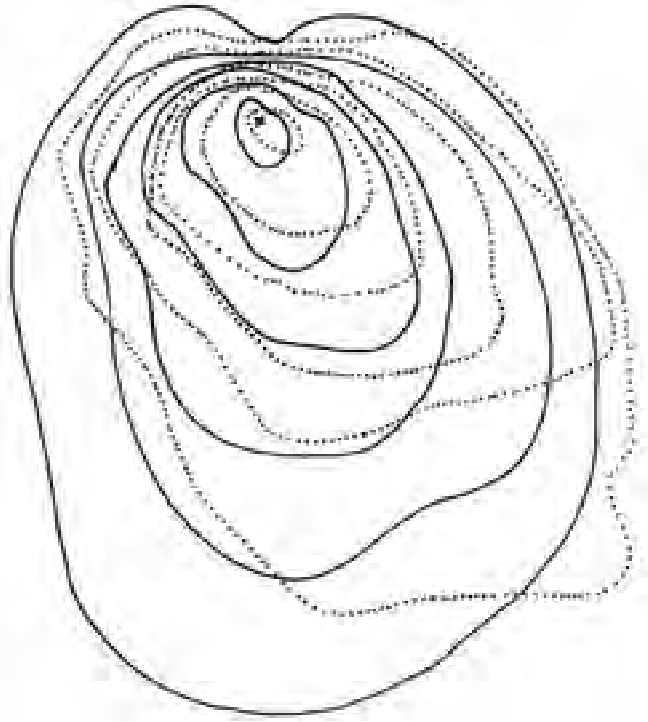


Figure 3.3 The propagating of processes in many dimensions of space and time. The spot marked x is the initial signalling process. The dotted lines and solid lines represent two series of catenated processes spreading out from the initial event.

local pumping, gating and chemical transformation. Thus, classical equilibrium constants are quite irrelevant for each ‘constant’ is in reality a continuous function of variables including the flow rates, the electrical and mechanical field intensities and so on. Furthermore, as the reaction products change the chemical potentials of all the components by altering the variables, the equilibrium ‘constants’ will also be functions of time. How can we describe such a space-time structure? The inorganic chemist, R.J.P. Williams,4 who has considered this problem with the refreshing eye of ‘first looking into nature's chemistry’, advocates a shift from a conventional thermodynamic approach to a dynamic approach, which would involve a description of the living system in terms of forces and flows rather than a succession of equilibrium states. This has already begun, to some extent, with non-equilibrium thermodynamics (see the next Chapter). But the fundamental difficulty of the statistical nature of a thermodynamic description remains practically untouched. There is as yet no science of organized heterogeneity or complexity such as would apply to living systems.

As is clear from the description above, living systems consist of nested compartments and microcompartments down to single macromolecules which can cycle autonomously as efficient molecular energy machines. At the very least, this implies that if thermodynamics were to apply to living systems, it must apply to individual molecules. Such is the physiologist Colin McClare's5 contention.

The Second Law Restated

In order to formulate the second law of thermodynamics so that it applies to single molecules, McClare introduces the important notion of a characteristic time interval, τ within which a system reaches equilibrium at temperature θ. The energies contained in the sytem is then partitioned into stored energies versus thermal energies. Thermal energies are those that exchange with each other and reach equilibrium in a time less than τ (so technically they give the so-called Boltzmann distribution characterized by the temperature θ). Stored energies are those that remain in a non-equilibrium distribution for a time greater than τ, either as characterized by a higher temperature, or such that states of higher energy are more populated than states of lower energy. So, stored energy is any form which does not thermalize, or degrade into heat in the interval τ.

McClare goes on to restate the second law as follows: useful work is only done by a molecular system when one form of stored energy is converted into another. In other words, thermalized energy is unavailable for work and it is impossible to convert thermalized energy into stored energy.

McClare is right in identifying the problem of Maxwell's demon in relation to the living system, and in stressing that useful work can be done by a molecular system via a direct transfer of stored energy without thermalization. The significance of this alone requires much more thought. Photosynthesis, on which practically all life on earth depends, involves the direct, nonthermal absorption of the energy of photons, and non-thermal energy transfer may indeed play a much larger role in living processes than hitherto recognized. However, his restatement of the second law is unnecessarily restrictive, and possibly untrue, for thermal energy can be directed or channelled to do useful work in a cooperative system, as in the case of enzymes embedded in a membrane described at the end of the previous chapter. Furthermore, thermalized energy from burning coal or petrol is routinely used to run machines such as generators and motor cars (which is why they are so inefficient and polluting). In the case of the motor car, the hot gases expand against a constraint,6 the piston, which, in taking up the thermalized energy, is in a position to do work against the system external to the combustion chamber. This suggests ‘the system’ must be more explicitly defined in relationship to the extent of equilibration, which naturally brings into the second law considerations of space as well as time. A more adequate restatement of the second law, is as follows: Useful work can be done by molecules by a direct transfer of stored energy, and thermalized energy cannot be converted into stored energy within the same system, the system being the extent over which thermal and other rapidly exchanging energies equilibrate.7

The first half of the formulation, much as McClare has proposed, is new and significant for biology, as well for the non-equilibrium phase transitions associated with laser action, for example (see Chapter 8). The second half of the statement, which I have modified, introduces the concept of a ‘system’, defined as the spatial extent to which thermalized and other rapidly exchanging energies equilibrate. It allows for the possibility that thermalized energies from one (sub)system can do work in a larger encompassing system for which the thermalized and other energies are in a nonequilibrium distribution. This is highly relevant for the nested dynamic organization of the living system. What I am proposing is that the living system is effectively partitioned into a dynamic hierarchy of subsystems defined by the spatiotemporal extent to which rapidly exchanging energies equilibrate (see below).

The major consequence of McClare's ideas arises from the explicit introduction of time, and hence time-structure. For there are now two quite distinct ways of doing useful work, not only slowly according to conventional thermodynamic theory, but also quickly — both of which are reversible and at maximum efficiency as no entropy is generated. This is implicit in the classical formulation, $dS \geq 0$, for which the limiting case is $dS = 0$, as explained in the previous chapter. But the attention to time-structure makes much more precise what the limiting conditions are.

Let us take the slow process first. A slow process is one that occurs at or near equilibrium. According to classical thermodynamics, a process occurring at or near equilibrium is reversible, and is the most efficient in terms of generating the maximum amount of work and the least amount of entropy (see p. 15). By taking explicit account of characteristic time, a reversible thermodynamic process merely needs to be slow enough for all exchanging energies to equilibrate, i.e., slower than τ, which can in reality be a very short period of time, for processes that have a short time constant. Thus, for a process that takes place in 10-12 s, a millisecond (10-3 s) is an eternity. Yet for the cell in which it occurs, it is about the ‘normal’ timescale, and for us, a millisecond is an order of magnitude below the level of our time awareness. So high efficiencies of energy conversion can still be attained in thermodynamic processes which occur quite rapidly, provided that equilibration is fast enough. Seen in this light, the nested dynamic compartmentation of the living system is thermodynamically (as well as kinetically) extremely important. It effectively restricts the spatial extent within which equilibration occurs, thus reducing the equilibration time.8 This means that local equilibrium may be achieved for many biochemical reactions in the living system. We begin to see that thermodynamic equilibrium itself is a subtle concept, depending on the level of resolution of time and space. I shall have more to say on that in a later Chapter.

At the other extreme, there can also be a process occurring so quickly that it, too, is reversible. In other words, provided the exchanging energies are not thermal energies in the first place, but remain stored, then the process is limited only by the speed of light. Resonant energy transfer between molecules is an example of a fast process. As is well known, chemical bonds when excited, will vibrate at characteristic frequencies, and any two or more bonds which have the same intrinsic frequency of vibration will resonate with one another. (This happens also in macroscopic systems, as when a tuning fork is struck near a piano, the appropriate string will begin to vibrate when it is in tune.) More importantly, the energy of vibration can be transferred through large distances, theoretically infinite, if the energy is radiated, as electromagnetic radiations travel through space at the speed of light, though in practice, it may be limited by nonspecific absorption in the intervening medium. Resonant energy transfer occurs typically in 10-14 s, whereas the vibrations themselves die down, or thermalize, in 10-9 s to 101 s. (On our characteristic time-scale — roughly 10-2 s — the vibrations would persist for as long as one year to one thousand years!) It is 100% efficient and highly specific, being determined by the frequency of the vibration itself; and resonating molecules (like people) can attract one another. By contrast, conventional chemical reactions depend on energy transfer that occurs only at collision, it is inefficient because a lot of the energy is dissipated as heat, and specificity is low, for non-reactive species could collide with each other as often as reactive species.

Does resonant energy transfer occur in the living system? McClare9 is the first to suggest it occurs in muscle contraction. Subsquently, it has been found that the energy released in the hydrolysis of ATP is almost completely converted into mechanical energy (see previous Section) Recent experiments with isolated muscle proteins show that the energy of one ATP molecule may be effectively shared over 4 cycles of cross-bridge formation between actin and myosin. That would indeed involve a form of resonant energy transfer.10 Ultrafast, resonant energy transfer processes have been well-recognized in photosynthesis.11 Chlorophyll molecules in the light harvesting 'antenna complex' transfer the energy of the photons absorbed to the 'reaction centre' by a form of resonant energy transfer known as exciton migration. In the reaction centre, the separation of positive and negative charges in the 'special pair' of chlorophyll molecules has also been identified to be a readily reversible reaction that takes place in less than 10-13 s. This is possibly the fastest chemical reaction on earth, as well as being 100% efficient.

Finally, within the past ten years, molecular and electronic engineer Irena Cosic,12 has put forward the radical idea that protein-protein, as well as protein-DNA interactions are not due to complementary shapes — the mechanical 'lock and key' model — as they are supposed to be by the vast majority of molecular biologists in the mainstream, but due to electromagnetic resonance recognition. In other words, the molecules attract each other by vibrating at the same frequencies. We shall look at this idea in more detail in a later Chapter.

Thus, the living system may use both means of efficient energy transfer: slow and quick reactions, always with respect to the relaxation time, which is itself a variable according to the processes and the spatial extents involved. In other words, it satisfies both quasi- equilibrium and far from equilibrium conditions where entropy production is minimum.13 This insight is offered by taking into account the space-time structure of living systems explicitly. We shall have the occasion to return again and again to entropy production and space-time structure in the living system in later Chapters.

McClare's ideas have been taken up and developed by Blumenfeld,14 and more recently, Welch and Kell, among others.15 particularly in the concept of nonequilibrium, ‘quantum molecular energy machines’, which is now increasingly accepted among protein biochemists and biophysicists. I suspect, however, that most molecular energy machines may be functioning in the quasi-equilibrium mode.16

I have effectively generalized McClare's notion of ‘characteristic time’ of energy storage to ‘characteristic space-time’ which captures the space-time differentiation of living processes more precisely. 17 Stored energy, being capable of doing work, is also mobilizable energy or coherent energy. (Coherent energy comes and goes together so it can do work, as opposed to incoherent energy which goes in all directions and cancel itself out.) As the energy is stored over all space-times, so it is mobilizable all over the system. Stored energy is really a more precise formulation of the usual ‘‘free energy” you have come across in the previous Chapter, which has no space-time characterization. This generalization turns out to be crucial for our understanding of the living system, as you shall see later on.

Quantum Molecular Machines in Living Systems

Another important insight is the fundamental quantum nature of biological processes. McClare18 defines a molecular energy machine as one in which the energy stored in single molecules is released in a specific molecular form and then converted into another specific form so quickly that it never has time to become heat. It is also a quantum machine because the macroscopic action is produced by the sum of all the individual molecules involved. Muscle contraction is the most obvious example, as described in Chapter 1.19

Even in conventional enzyme kinetics, more and more quantum mechanical effects are recognized. Electron tunnelling (going ‘under’ an energy barrier by virtue of an overlap of the quantum mechanical wave functions of the electron in different neighbouring states) is already well known to be involved in the separation of charges and electron transport across the biological membranes of the chloroplasts of green plants20 as well as across electron transport proteins such as cytochrome c.21 Hydrogen transfer reactions may also involve tunnelling across energy barriers via an overlap of quantum mechanical wave functions between enzyme complexes of substrates and products.22 It may be that very few reactions occurring in organisms involve thermalization of stored molecular energy.23 This does not preclude thermal excitation where the activation energy barrier is sufficiently low, as for example, in making and breaking the hydrogen bonds involved in maintaining the three-dimensional shapes or conformations of protein molecules (see Chapter 7). Indeed, such fluctuational changes in conformation occur within nanoseconds (10-9 s), and they have been observed in a large number of proteins. But, in order to do useful work, the fluctuations have to be coordinated. Otherwise there will be equal probability for the reaction to go forwards as backwards and cancel out — precisely as predicted in statistical mechanics.

There seems to be no escape from the fundamental problem of biological organization: how can individual quantum molecular machines function in collective modes extending over macroscopic distances? Just as bulk phase thermodynamics is inapplicable to the living system, so perforce, some new principle is required for the coordination of quantum molecular machines. This principle is coherence, perhaps even quantum coherence; but we shall leave that for later. In the next Chapter, we consider the consequences of energy flow in biology in greater detail.

Notes

1. This term has been invented by Nobel laureate physical chemist Ilya Prigogine in order to capture what he believes to be the essential nature of the living system that is shared with certain non-equilibrium physical and chemical systems. See Prigogine (1967).

2. Physical chemist, Michael Menzinger and his co-workers, have shown that even stirred reactors can maintain a variety of dynamic oscillatory structures. It seems clear that coupling between flow and chemical reaction plays a crucial role in generating structural complexities. See Menzinger and Dutt (1990).
3. From Winfree and Strogatz (1983) p. 37.
4. See Williams (1980).
5. McClare (1971).
6. McClare had difficulty envisaging obvious constraints against which thermalized energy could be converted into work in the living system. See McClare (1971), Lomo et al. (1974); Laing and Lamb (1985).
7. This formulation has evolved through a number of versions. See Ho (1994a, 1995a, 1995b and 1997a).
8. See Ho (1995a) Chapter 5 for detailed arguments on why the nested compartmental organization of living system optimizes energy transfer both thermodynamically, in terms of efficiency, and kinetically, in terms of reaction rates.
9. McClare (1972).
10. See Douglas (1995) reporting on the work of Japanese muscle protein biophysicist, Toshio Yanagida; also Yanagida et al. (1985).
11. Fleming et al. (1988); Fleming and van Grondell (1994).
12. See Cosic (1994).
13. Denbigh, K. (personal communication) comments as follows: "… the applicability, or the non-applicability of McClare's theory can best be grasped by using $S = k \ln W$. In any proposed application, one asks: will the number of quantum states, W, increase or not? If the answer appears to be no, then reversibility can be assumed, and entropy remains constant. Otherwise, entropy increases."
14. Blumenfeld (1983).
15. Welch and Kell (1985); see also Chapters in Welch (1986).
16. See Ho (1995a).
17. See Ho (1994a, 1995a, 1995b).
18. McClare (1971).
19. See Ho and Harris (1995).
20. Tien (1989).
21. Bechtold et al. (1986).
22. Klinman (1989).
23. See Ho and Popp (1993) for a review of nonthermal energy transfer processes in living systems.

CHAPTER 4

Energy Flow and Living Cycles

The Probability of Life

The chemical constituents of a typical living cell, say, an E. coli bacterium, are known in considerable detail. The major elements are carbon, hydrogen, nitrogen, oxygen, phosphorous and sulphur, in that order, or CHNOPS for short, making a sound like a cow munching on fresh, green grass. These go to make up the organic polymers such as proteins, nucleic acids, membrane lipids, carbohydrates, and small molecular weight cofactors and intermediates of metabolism. A question of great interest to scientists is: how probable is life in its simplest form of the cell? The problem can be considered as follows. Suppose one were to mix together the chemical elements in their appropriate amounts and proportions in each of an infinite array of sealed containers kept indefinitely in a very big water bath (or reservoir) at 300°C, say, what fraction of them would eventually develop into living cells? The answer is 10-10 11 — an infinitesimally small number, so small that there has not been time, nor matter enough in the whole of the universe for it to happen even once. How is such a number arrived at? Is there any basis to this kind of estimate?

The (hypothetically) infinite array of systems with the same chemical composition, volume and temperature, is a ‘canonical ensemble’, in the language of statistical mechanics, which is allowed to go to equilibrium. The theory is that eventually, every possible configuration of the atoms or microstates, i, with corresponding energy level, ei, will be explored, some of which would correspond to those in the living system. But because the energy level of the living state is so much higher than the average in the equilibrium ensemble, the probability of those states occurring is vanishingly small.

The living cell has a very large amount of energy stored in covalent bonds as electronic bond energies — considerably more than the thermal energies which exist in the equilibrium state. So large, in fact, that the probability of getting there by chance fluctuation around the equilibrium state is essentially nil. So how come there are living organisms at all? The immediate answer is energy flow. Energy flow greatly increases the probability for life, and is absolutely essential for its maintenance and organization. These are some of the insights offered by physical chemist, Harold Morowitz, in his wonderful book, Energy Flow in Biology.1 We shall explore some of his ideas in the pages following.

Energy Flow and Material Cycles

The concept of energy flow in biology is familiar to every biochemist and ecologist. It is the energy from sunlight, trapped by green plants, which flows through the whole biosphere, beginning with herbivores and insects which feed directly on green plants, through to other ‘trophic layers’ of animals that in turn feed upon them. At every stage, the energy is further transformed, rearranged and degraded, and a fraction lost as heat. Accompanying the energy flow is a cycling of materials through the biosphere: carbon dioxide, water, nitrogen, sulphates and phosphates are ‘fixed’ by green plants and bacteria into high electronic energy compounds which cycle through the bodies of animals in the biosphere before they are broken down and returned to the soil and the atmosphere for general recycling. (Cycling and re-cycling are indeed nature's way.) The relationship between energy flow and the cycling of the elements in the biosphere is represented very schematically in Fig. 4.1. The ‘cycle’ is actually a lot more complicated. It is a composite of many parallel cycles and epicycles variously connected, and branching at different points.

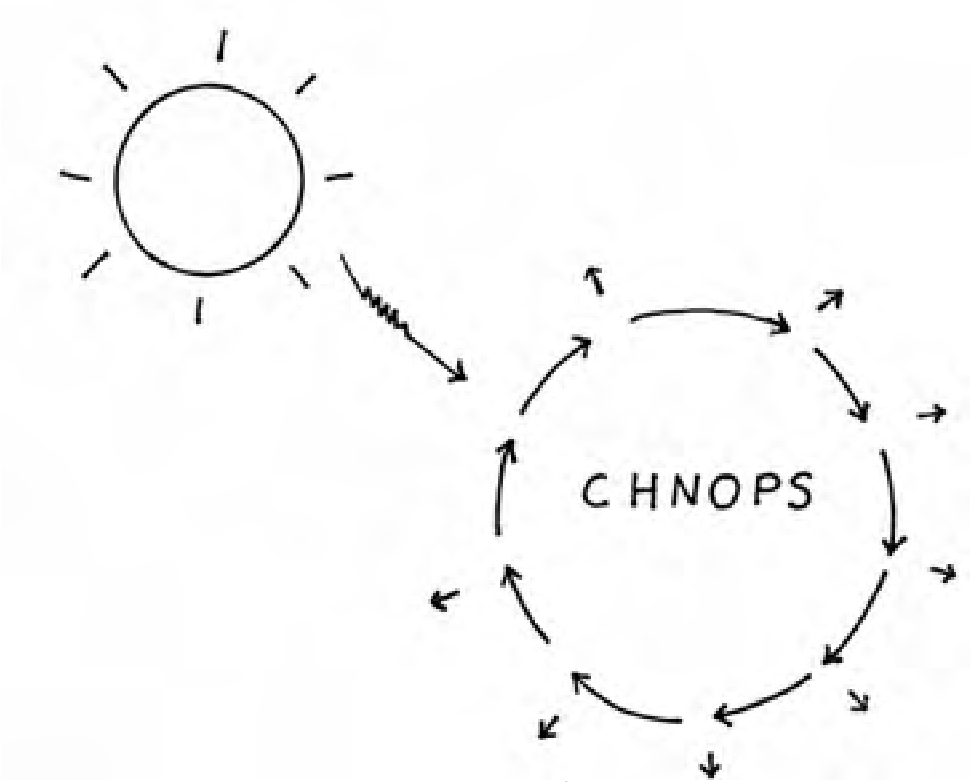


Figure 4.1 The CHNOPS cycle and energy flow.

This intimate relationship between energy flow and the cycling of the elements turns out not to be at all fortuitous. For it is the energy flow which organizes the material system, taking it far away from thermodynamic equilibrium by raising its energy level, producing gradients, and cyclic flow patterns of materials (and energy), in short, generating a hierarchy of space-time structures which in turn organizes the energy flow. The key to life is in this mutuality of spontaneous relationship between the system and the environment, each in turn the organizer and the organized (Fig. 4.2).

The same space-time catenation of processes occurs on the ecological level as in individual organisms, involving larger dimensions and longer durations, of course. Ecological processes are continuous with,

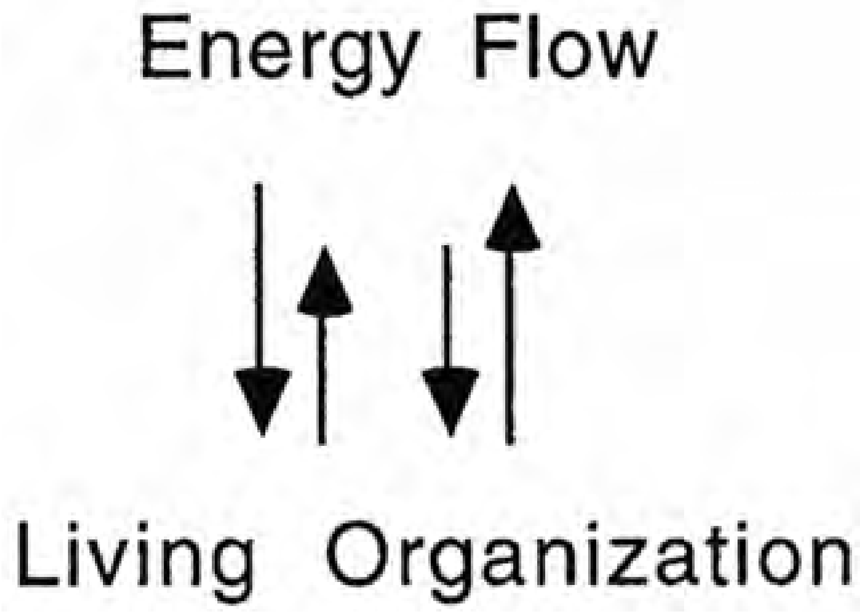


Figure 4.2 Energy flow and living organization.

and impinge upon individual organismic processes, and are subject to similar cybernetic principles of regulation; so much so that James Lovelock, who calls himself a “geophysiologist”, has proposed that the earth is like a superorganism.2 And hence, a lot could be learned by concentrating on the global homeostatic, feedback mechanisms that account for the stability of the earth's ecological system as a whole. Many other scientists, including Sidney Fox3 who works on the origin of life, also believe that biological evolution is continuous with the evolution of the solar system and chemical evolution, and is by no means the result of a series of lucky ‘frozen accidents’.

These fascinating aspects are beyond the scope of the present book, but they do emphasize the continuity between the living and non-living, which is my thesis. Without further ado, let us go on to consider Morowitz's idea that energy flow leads to space-time structures, in particular, to cycles.

Dynamic Molecular Order from Energy Flow

Some simple examples will illustrate how molecular order can arise from energy flow. Figure 4.3 is a model system consisting of a chamber containing an ideal gas (i.e., at low enough concentrations such that the volume of individual molecules do not matter, and the individual molecules do not interfere much with one another). The left side is kept indefinitely at temperature T1 by contact with a large reservoir at the same temperature, and the right side kept by contact with an equally large reservoir, at temperature T2; with T1 > T2. A steady flow of heat is therefore maintained across the chamber from left to right, or from ‘source’ to ‘sink’.

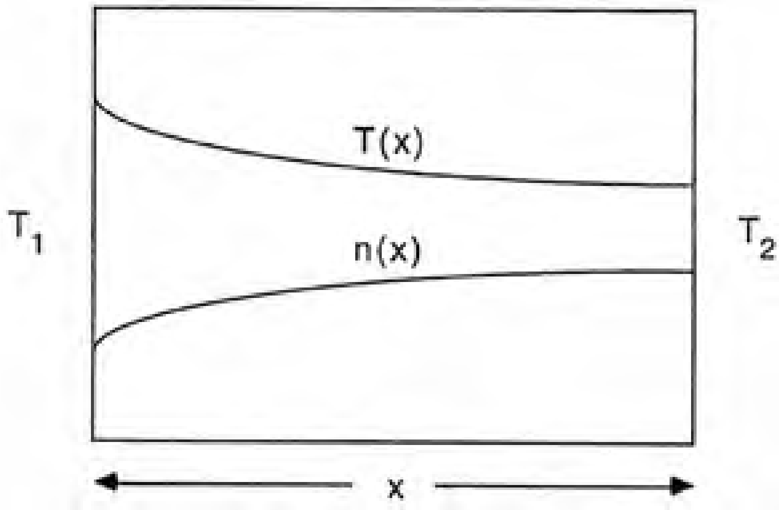


Figure 4.3 Heat flow and the formation of a concentration gradient in a volume of ideal gas.

The result is a temperature gradient from left to right, and at the same time, a concentration gradient of the molecules increasing from the ‘hot’ end to the ‘cold’ end. This has been theoretically predicted and experimentally observed. The calculations are quite complicated, but it is intuitively easy to see how the concentration gradient arises. The hotter molecules at the left have more kinetic energy (which is proportional to kT, see p. 19); therefore, they tend to have higher velocities than those on the right, and there is a net (convectional) movement of molecules towards the right where they cool down and lose kinetic energy. At steady state, this is balanced by diffusional movement from the right back to the left.4 This would go on indefinitely as long as the temperature difference is maintained. If now the chamber is ‘adiabatically’ isolated from the reservoirs, i.e., isolated so that there is no heat exchange with the reservoirs, it would soon decay back to uniform equilibrium in which the temperature and concentration everywhere will be the same. This is the simplest version of a ‘dissipative structure’5 which must be maintained by a continuous flow and dissipation, of energy. The next example involves the formation of more complicated structures.

A shallow pan of water is heated uniformly from below (Fig. 4.4). For a small temperature difference, the situation is similar to the previous example, a temperature gradient is maintained across the depth of the water from the bottom to the top, and a density gradient in the opposite direction. The one difference here is that the heat transfer will occur by conduction rather than convection, for the water molecules themselves do not alter their mean position in the process.

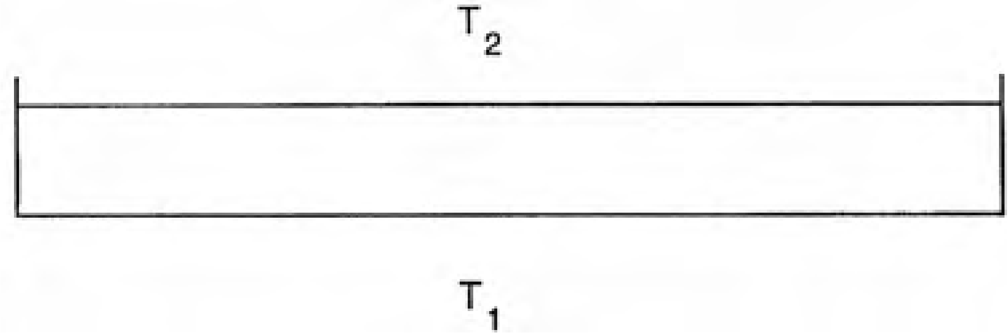


Figure 4.4 Heat flow in a shallow pan of water.

If we increase the temperature difference, a critical value will be reached at which bulk movements will occur in the liquid. A series of regular, convection cells are formed, giving a honeycomb appearance when viewed from above (Fig. 4.5). These so-called Bénard convection cells (or more accurately, Bénard-Rayleigh cells6) arise as the low density, lighter water at the bottom of the pan repeatedly rises to the top while the denser water at the top sinks to the bottom, and so on in a cyclic manner. As convectional movements begin in different parts of the pan and increase in magnitude, the system would eventually end up in a situation where all the convection cells are of the same size and are cycling together, as that is the most stable dynamical state.

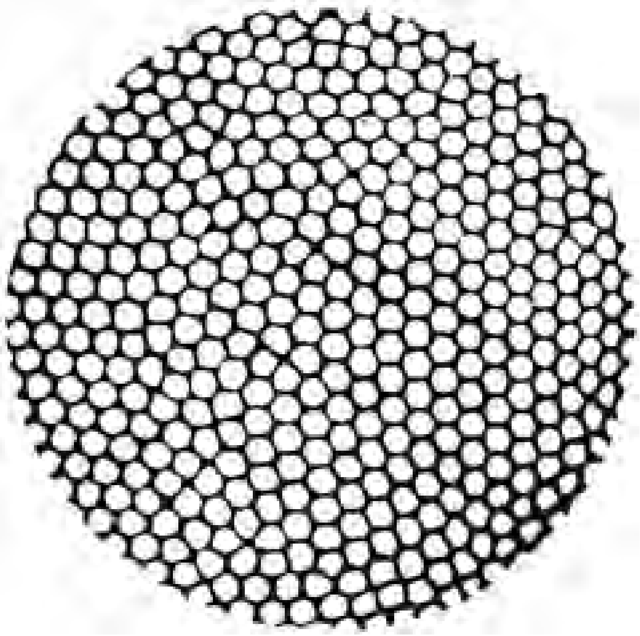


Figure 4.5 The Bénard-Rayleigh convection cells.7

Let us dwell on this remarkable state in terms of what is happening at the molecular level. Each cell involves the concerted cyclical movement of some 1023 individual water molecules (as schematically represented in Fig. 4.6). Furthermore, all the cells in the pan are synchronized with respect to one another. In technical language, a non-equilibrium phase transition to macroscopic order has taken place. Before phase transition, the individual water molecules move around randomly and aimlessly without any order or pattern. At phase transition, however, they begin to move collectively until all the molecules are dancing together in cellular formations as though choreographed to do so. Like the previous example, the convection cells are dissipative structures dependent on the flow of energy for their continued existence. It is appropriate also to refer to them as ‘coherent structures’ which are dynamically maintained. Do keep in mind this wonderfully evocative picture of global order constituted of microscopically coherent motions when we try to imagine what happens in a living system later on.

In both examples of non-equilibrium structures just described, there is a net cycling of molecules around the system, from the

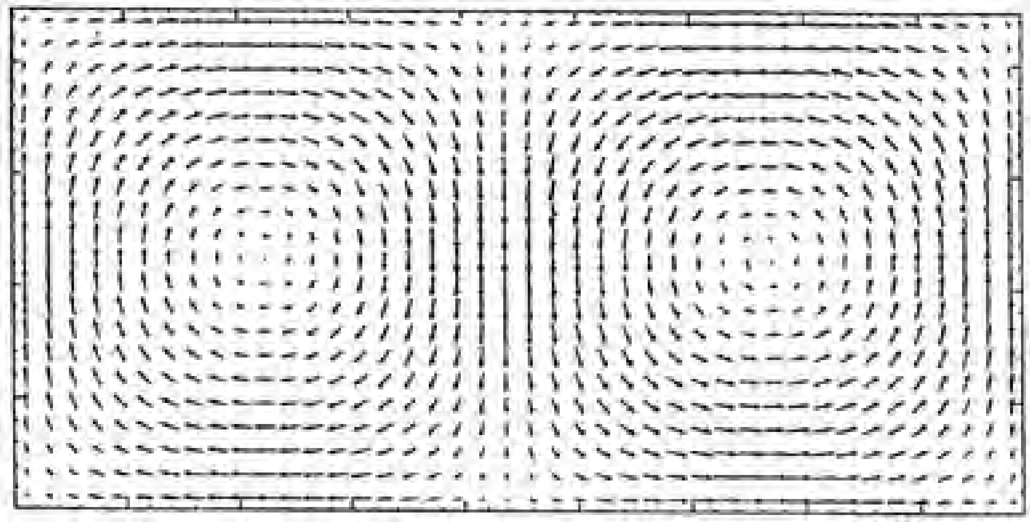
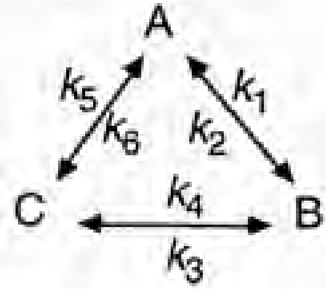


Figure 4.6 Coherent molecular motions in the convection cells.8

hot end to the cold end and back again, the situation being more visually dramatic in the second case. What happens when chemical reactions are involved? Does chemical cycling also take place as the result of energy flow?

A Theorem of Chemical Cycles

Consider a reactor maintained by contact with a large reservoir at temperature T, in which are three chemical species, A, B, and C, reacting according to the following scheme:9



where the k's are the rate constants: the odd numbered ones refer to rates in the forward direction — A to B to C, and the even numbered ones in the reverse direction. At equilibrium, i.e., without energy flow, forward and backward reactions are equal. This is the principle of microscopic reversibility or detailed balance, which is of great importance in chemistry. Hence,

$$\begin{aligned} k_1[\mathrm{A}] &= k_2[\mathrm{B}] \\ k_3[\mathrm{B}] &= k_4[\mathrm{C}] \;, \\ k_5[\mathrm{C}] &= k_6[\mathrm{A}] \end{aligned} \tag{4.1}$$

where the bracketed letters represent concentrations of the respective chemical species. Thus, at equilibrium, there is no net flow around the system, as the forward and backward reactions are occurring at the same rate and are therefore in detailed balance at every step. Under the additional constraint that the total amount of material in the reactor is constant, i.e.,

$$[\mathrm{A}]+[\mathrm{B}]+[\mathrm{C}]=\mathrm{M} \tag{4.2}$$

we can solve for the equilibrium concentrations of each species. These are,

$$\begin{aligned} [\mathrm{A}]_{eq} &= k_2 k_4 \mathrm{M}/k' \\ [\mathrm{B}]_{eq} &= k_1 k_4 \mathrm{M}/k' \;, \\ [\mathrm{C}]_{eq} &= k_1 k_3 \mathrm{M}/k' \end{aligned} \tag{4.3}$$

where k’ = k2k4 + k1k4 + k1k3.

If energy now flows into the system so that a steady state is maintained with a net flow of material around the system from A to B to C, the principle of microscopic reversibility will no longer hold: there will not be a detailed balance in every step. In the three species system,

$$\begin{aligned} k_1[\mathrm{A}] &> k_2[\mathrm{B}] \\ k_3[\mathrm{B}] &> k_4[\mathrm{C}] \\ k_5[\mathrm{C}] &> k_6[\mathrm{A}] \end{aligned} \tag{4.4}$$

In other words, the material must cycle around the system. The flow, or rate at which the material is cycling around the system is given by,

$$\mathcal{J} = k_1[A] - k_2[B] = k_3[B] - k_4[C] = k_5[C] - k_6[A]. \qquad (4.5)$$

This result can be restated in a formal, general way. A canonical ensemble of systems is at equilibrium with i possible states, where fi is the fraction of systems in state i (also referred to as occupation numbers of the state i), and tij is the transition probability that a system in state i will change to state j in unit time. The principle of microscopic reversibility requires that every forward transition is balanced in detail by its reverse transition, i.e.,

$$f_i t_{ij} = f_j t_{ji}. \qquad (4.6)$$

If the equilibrium system is now irradiated by a constant flux of electromagnetic radiation such that there is net absorption of photons by the system, a steady state will be reached at which there is a flow of heat out into the reservoir (sink) equal to the flux of electromagnetic energy into the system. At this point, there will be a different set of occupation numbers and transition probabilities, f•i and t•ij; for there are now both radiation induced transitions as well as the random thermally induced transitions characteristic of the previous equilibrium state. This means that for some pairs of states i and j,

$$f_i^{\prime} t_{ij}^{\prime} \neq f_j^{\prime} t_{ji}^{\prime}. \qquad (4.7)$$

For, if the equality holds in all pairs of states, it must imply that for every transition involving the absorption of photons, a reverse transition will take place involving the radiation of the photon such that there is no net absorption of electromagnetic radiation by the system. This contradicts our original assumption that there is absorption of radiant energy (see previous paragraph), so we must conclude that the equality of forward and reverse transitions does not hold for some pairs of states. However, at steady state, the occupation numbers (or the concentrations of chemical species) are time independent (i.e., they remain constant), which means that the sum of all forward transitions equals to the sum of all backward transitions, i.e.,

$$df_i^s/dt = 0 = \Sigma(f_j^s t_{ji}^s - f_i^s t_{ij}^s)\,. \qquad (4.8)$$

But it has already been established that some f•it•ij - f•it•ij are non-zero. That means other pairs must also be non-zero to compensate. In other words, members of the ensemble must leave some states by one path and return by other paths, which constitutes a cycle.

The above line of reasoning led Morowitz to an important theorem: In steady state systems, the flow of energy through the system from a source to a sink will lead to at least one cycle in the system.

The formation of steady state cycles has the important thermodynamic consequence that, despite large fluxes of materials and chemical transformations in the system, the net change in entropy of the system is zero, because entropy is a state function (as mentioned in Chapter 2), a return to the same state will always entail no net entropy change. Of course, the compensatory change in entropy of the surroundings could be greater than zero, but entropy does not accumulate in the system, provided that the cycles are perfect in the sense that exactly the same state is reproduced, which is definitely not the case in real life (see Chapter 11). But the steady state approximation leads to some quite remarkable consequences, as I shall describe in a later Chapter.

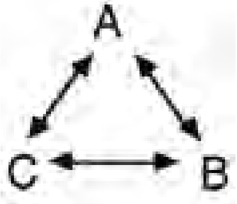
More mathematical treatments of the consequences of energy flow may be found in the writings of Ilya Prigogine and his colleagues in the Brussels School,10 who show how 'dissipative structures' can arise in systems far from thermodynamic equilibrium based on the analysis of entropy production. Theoretical physicist Hermann Haken,11 taking a different approach, identifies 'order parameters' as macroscopic descriptors of cooperative phenomena in systems far from equilibrium, which include the Bénard-Rayleigh convection cells we have just seen, as well as lasers

(Chapter 8). In such instances, random energy fed into the system will nevertheless lead to macroscopic organization as the system passes from the thermodynamic regime of random microscopic motion of many degrees of freedom to a dynamic regime which has only one or a few degrees of freedom. This is also the characteristic to be expected of a system in which all the processes are linked, or coupled together in a symmetrical way.12 Let us explore further what that means.

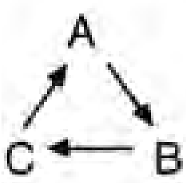
Coupled Cycles and the Steady State

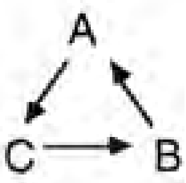
Physical chemist, Lars Onsager, used the same principle of microscopic reversibility (p. 45) to derive another significant result in non-equilibrium thermodynamics — the Onsager reciprocity relation — which shows how symmetrical coupling of processes can arise naturally in a system under energy flow.13

The principle of microscopic reversibility can be expressed as follows: under equilibrium conditions, any molecular process and its reverse will be taking place on the average at the same rate. As we have seen in the previous Section, that implies equilibrium is never maintained by a cyclic process at the molecular level. To return to the three species system (p. 38), the principle of microscopic reversibility, as conventionally interpreted by chemists, requires that the balance be maintained at every step:



However, the interconversions could be legitimately considered as occurring in a forward sequence, A → B → C → A, linked or coupled to a backward sequence, C → B → A → C, so that they balance each other on the whole, i.e.,





It turns out that the rate equations (which are like those on p. 45, and I shall not write down again here) have the same form, whether one assumes detailed balance at every step or merely overall balance. In other words, detailed molecular balance at every step is not required for thermodynamic equilibrium. (This is what I had in mind when I drew your attention to the subtlety of the concept of thermodynamic equilibrium in the previous Chapter.) So a system in equilibrium may nevertheless have within it balanced flows of energy and material, as long as the flows are linearly proportional to the forces. This is not surprising in retrospect, as the laws of thermodynamics were themselves a generalization of macroscopic phenomena, and do not depend on the knowledge of what is happening in detail at the molecular level.

What this means is that many locally non-equilibrium situations involving cyclic flow processes can be described as near approximations to the equilibrium situation, more specifically, as fluctuations occurring within a larger, encompassing equilibrium system, so long as the flows and forces which tend to restore the equilibrium are linearly proportional to one another.

We have come across such situations already. In the example on heat flow in a volume of an ideal gas (p. 41), a steady state is arrived at in which the convectional flow of hot molecules to the right is balanced by the diffusional movement of cooler molecules back to the left. So the transport of energy from left to right is linked or coupled to the diffusion of molecules from right to left (to maintain a concentration gradient). In the case of heat flow in a pan of water (p. 42), we have two different ‘steady states’ depending on the temperature difference, only the first of which — at small temperature differences — can be regarded as an approximation to equilibrium: the flow of heat by conduction from the bottom to the top is coupled to the maintenance of a density gradient in the reverse direction. Many other non-equilibrium processes may be approximated in this way. The flow of electrons across a biological membrane, for example, can couple linearly to the diffusion of inorganic ions.

Onsager set out to describe by means of general ‘thermodynamic equations of motion’, the rates of processes such as energy flow and diffusion, which are assumed to be linearly proportional to the ‘thermodynamic forces’ generating them. These forces are just the gradients of temperature, or of chemical/electrical potentials, which may be seen to be the causes of the flows. If we let J1 and J2 represent two coupled flow processes, and X1, X2, the corresponding forces, then,

$$\begin{aligned} J_1 &= L_{11}X_1 + L_{12}X_2 \\ J_2 &= L_{21}X_1 + L_{22}X_2 \end{aligned} \qquad (4.9)$$

The coefficients L11 and L22 are proportionality constants relating the flows each to their respective force. L12 and L21 are the cross coefficients representing the extent to which coupling occurs: in other words, how the force of one process influences the flow of the other process. For example, the two flows could be electricity and inorganic ions, due respectively to an electric potential gradient and an ionic concentration gradient. The cross coefficients tell us the extent to which the electric potential gradient influences the diffusion of ions, and conversely, how the ionic concentration gradient affects the flow of electricity.

Onsager then shows that if the principle of microscopic reversibility is true for a system in equilibrium and near equilibrium, it implies that,

$$L_{12} = L_{21}\,. \qquad (4.10)$$

This means that the coupling of the two processes becomes completely symmetric, even in states of non-equilibrium at the molecular level. In other words, the force of each process has the same reciprocal effect on the other process. This result can be generalized to a system of many coupled processes described by a set of linear equations of the same form as Eq. (9),

$$J_i = \Sigma_k L_{ik} X_k \, . \qquad (4.11)$$

where Ji is the flow of the ith process (i = 1, 2, 3,…n), Xk is the kth thermodynamic force (k = 1, 2, 3,…n), and Lik are the proportionality coefficients (where i = k) and coupling coefficients (where i ≠ k). It may happen that some of the coupling coefficients are zero (in cases where the processes do not interact at all). Some may be positive while others are negative. Still, for such a multicomponent system, certain of the couplings will be symmetrical; in other words, for some i and k, (i ≠ k),

$$L_{ik} = L_{ki} \, . \qquad (4.12)$$

The mathematical entities of the Onsager's thermodynamic equations of motion (Eq. 11) can all be experimentally measured and verified, although it has not yet been systematically applied to the living system.14 Nevertheless, as we shall see, it captures a characteristic property of living systems: the reciprocal coupling of many energetically efficient processes. This raises once again the interesting question as to whether most of the processes in the living system may be operating near to local equilibrium.

As we have seen in the previous Chapter, the intricate space- time differentiation of the organism specifically allows for the establishment of a hierarchy of local near-equilibrium regimes, even though the organism as a whole is a system far from equilibrium. Perhaps one of the raisons d'etre of development is to set up the nested hierarchies of space-time domains where local equilibrium can be maintained in a macroscopically non-equilibrium system. Thus, paying attention to space-time structure leads us to a much more subtle view of both equilibrium and non-equilibrium. A system in equilibrium can have local non-equilibrium regimes; conversely, a system in non-equilibrium can also possess domains in local equilibrium.

Another intriguing question is, what sort of couplings of processes can arise far from thermodynamic equilibrium? In the system of Bénard-Rayleigh convection cells, for example, the flow of heat is obviously coupled to the convectional movement of molecules, although the flows and forces are not linearly related in such systems far from equilibrium, which include the Beloussov- Zhabotinsky reaction (Chapter 3). Nevertheless, these ‘dissipative structures’ arise in such a regular, predictable way that one cannot help wondering whether a general, or ‘canonical’ mathematical relationship concerning the coupling of processes far from equilibrium is hovering in the wings, awaiting discovery by some mathematically able physical chemists.15 There is, indeed, already a balance theorem due to Chandresekhar,16 which states that instability of the linear steady state of the Bénard-Rayleigh problem (where the flow of heat by conduction exactly counteracts the density gradient) occurs at the minimum (critical) temperature gradient at which a balance can be steadily maintained between the kinetic energy dissipated by viscosity and the internal energy released by the buoyancy force. Similarly, Glansdorff and Prigogine17 state that the Bénard-Rayleigh instability occurs at the minimum temperature gradient at which a balance can be steadily maintained between the entropy generated through heat conduction by the temperature fluctuations and the corresponding entropy flow ‘‘carried away” by the velocity fluctuations. These are deep problems to which we shall return in Chapter 6.

The Manyfold Coupled Cycles of Life

Based on the above insights, we can begin to understand two main aspects of the living system: the ubiquitous cycling as the means for structuring at every level of living organization, and the coupling of all the cyclic processes. This is so from the ecological cycle of the biosphere to the biochemical metabolic cycles in organisms down to the whirring of molecular machines, all meticulously choreographed, like the molecules in the Bénard-Rayleigh convection cells, to spin and turn at different rates, each in step with the whole.

The biochemical outline of the ecological cycle is very simple. The photons absorbed by green plants split water molecules and reduce carbon dioxide, resulting in the formation of carbohydrates and oxygen. In respiration, the converse takes place: carbohydrates are oxidized to restore carbon dioxide and water:

$$H_2O + CO_2 \overset{h\nu}{\rightleftharpoons} \text{carbohydrates} + O_2$$

(The letters hv represent a photon, or more accurately the energy of a photon; h, Planck's constant, equal to 6.6256 x 10-34 J s, is the smallest quantum of action and has the unit of energy in Joules multiplied by time in seconds; v is the frequency of vibrations per second associated with the photon.)

Many secondary and tertiary cycles and epicycles feed off, or are coupled to the primary cycle above, constituting metabolism in living systems. Metabolism refers to the totality of chemical reactions which make and break molecules, whereby the manifold energy transformations of living systems are accomplished. The secret of living metabolism — which has as yet no equal in the best physicochemical systems that scientists can now design — is that the energy yielding reactions are always coupled to energy requiring reactions. The coupling can be so perfect that the efficiency of energy transfer is close to 100%. Central to the coupling of energy yielding and energy requiring processes is the cyclic interconversion of adenosine triphosphate (ATP) and adenosine diphosphate (ADP). The terminal phosphate of ATP is added on to ADP by energy yielding processes such as photosynthesis and respiration. In photosynthesis, the energy of sunlight goes to excite electrons. As the electrons flow ‘downhill’ via a chain of electron transport proteins back to the ground state, the energy is tapped at several places along the way to make ATP from ADP. In respiration, similar processes of oxidative phosphorylation of ADP to ATP take place by using energy from the oxidation of complex foodstuffs. ATP is in turn converted into ADP in the biosynthesis of all the constituents of organisms and in all the energy transducing processes that enable them to grow and develop, to sense, to feel, to move, to think, to

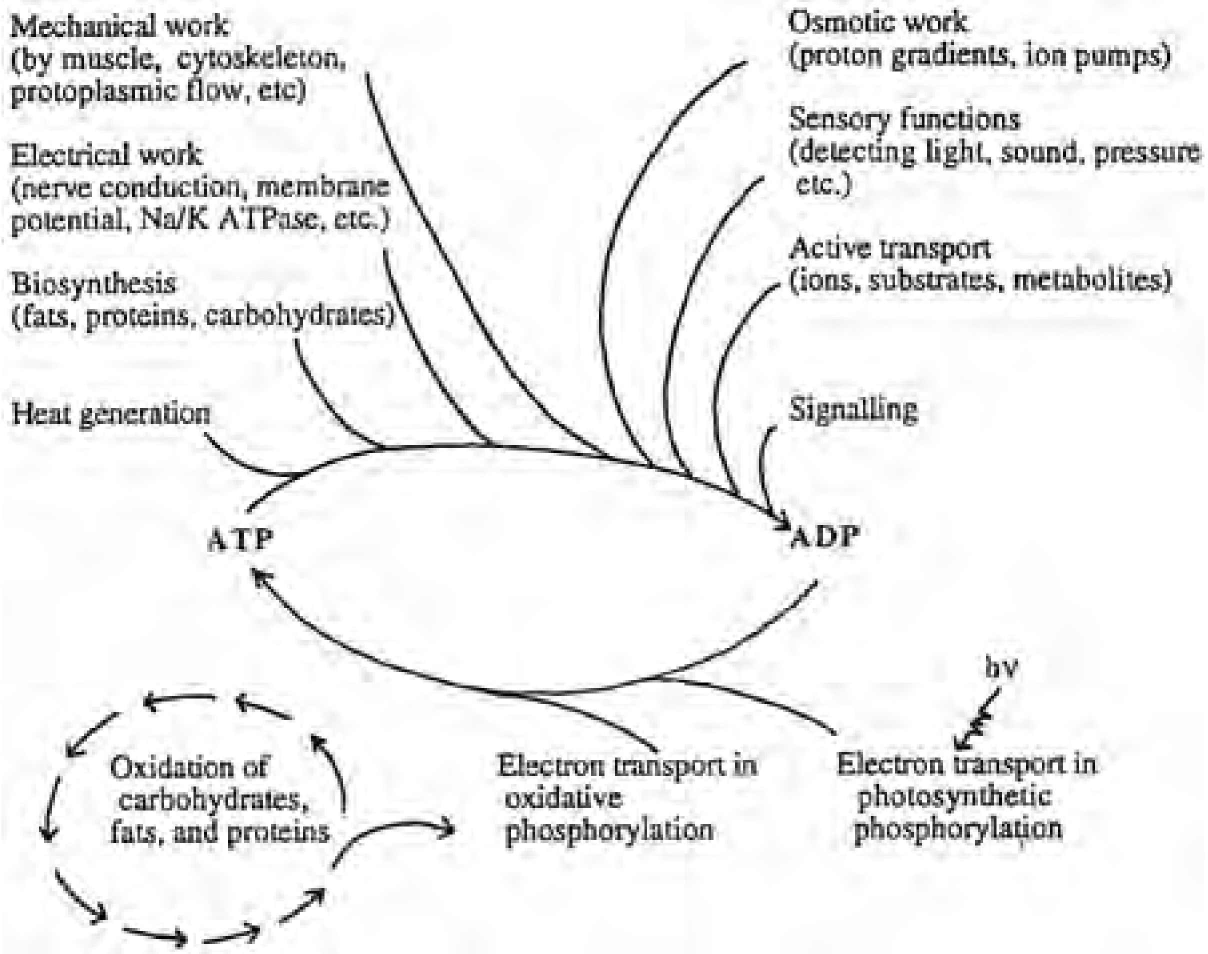


Figure 4.7 The coupled cycles of life: energy flow in living systems. The photon energy absorbed by green plants and cycles of oxidation of foodstuffs provide mobile electrons (and protons) to make ATP. The cycles of energy charging and discharging between ATP and ADP run all the rest of the other vital activites.

love, … in short, to live (see Fig. 4.7). I leave it as an exercise for readers, if they so wish, to trace out the many metabolic cycles by a careful scrutiny of a metabolic chart of ‘biochemical pathways’ (an assigment normally set for intransigent students).

Coupled cycles are the ultimate wisdom of nature. They go on at all levels, from the ecological to the molecular through a wide range of characteristic timescales from millennia to split seconds. Thus, the transformation of light energy into chemical energy by green plants yields food for other organisms whose growth and subsequent decay provide nutrients in the soil on which green plants depend. The energy in foodstuffs is transformed into the mechanical, osmotic, electrical and biosynthetic work both within the plants themselves and in other organisms in all the trophic levels dependent on green plants. Each kind of energy transduction in individual organisms is carried out by its own particular troupe of busy cyclic molecular machines. And upon all of these turn the innumerable life cycles of multitudinous species that make up the geological cycles of the earth.

One is reminded here of the Earth Spirit's speech in the opening scene of Goethe's Faust,

In the torrents of life,
in action's storm
I weave and wave
in endless motion
cradle and grave
a timeless ocean
ceaselessly weaving
the tissue of living
constantly changing
blending, arranging
the humming loom of Time I ply
and weave the web of Divinity.18

Energy Storage in the Biosphere

The cycling of material and energy within the biosphere automatically involves the storage, not only of material in the biosphere as biomass, but also of energy. At the beginning of this Chapter, I have alluded to the large amount of energy stored in living systems, but exactly how much energy is stored? In particular, if the living system is far away from thermodynamic equilibrium, it must be free energy which is stored, for free energy disappears at equilibrium.

There have been several attempts to estimate the relative free energy content of the biosphere. One method is to compare the energy level associated with the known molecular contents of a cell with that of the appropriate mixture of small molecular weight precursors by looking up standard tables of bond enthalpies and free energies of formation which have been published for many compounds.19 For example, Morowitz's calculations led to an estimate that the free energy level of biomass is 5.23 kcal/gm higher than the starting materials. This is approximately the energetic content of one gram of carbohydrates. A slice of bread, for example, will have about 10 to 15 times this amount of energy. The calorie is a unit of heat energy and is equivalent to 4.184 Joules. The same kind of estimates gives values of entropy content in biomass as 0.421 cal/ gm lower than the starting materials, so one could say that biomass has a ‘negative entropy’ of 0.421 cal/gm. We shall examine negative entropy in greater detail in the next chapter.

There have also been direct measurements carried out in a ‘constant volume adiabatic bomb calorimeter’. This device enables us to measure the heat of combustion of substances. It consists of a tightly sealed, heavy-walled stainless steel container, thermally isolated from its surroundings. The ‘biomass’, usually in a dehydrated form, is placed inside the container, which is filled with O_2 at a pressure of 30 atmospheres. The combustion is started with an electrical spark through a pair of wires in contact with the biomass. The heat released is then measured by a thermometer. From the first law of thermodynamics, the change in internal energy is equal to the heat change plus the work done:

$$\Delta U = Q + W \qquad (4.13)$$

However, as the volume is constant, the work done is zero, and the decrease of internal energy is just equal to the heat released:

$$\Delta U = Q \qquad (4.14)$$

These measurements give values not too dissimilar to those obtained by calculation, and represent an energy enrichment on average of

0.07 eV/atom. (The electron volt, eV, is a unit of electric energy, especially useful in characterizing electronic energy levels of atoms and molecules, it is 1.602 x 10-19 J, a very minute amount of energy.)

A lot is missing from these estimates of free energy and negative entropy content. They do not take into account the space-time organization of the molecules into tissues, cells and organelles. This organization corresponds in some respect, to what Morowitz20 has referred to as the ‘configurational improbability’ of the living state, in addition to its ‘energetic improbability’. But far more significantly, a lot of energy is actually stored in the organization of the living system. For instance, gradients and potentials involving chemical species, ions and especially protons — can readily be converted into work as fluxes and flows across membrane-bound compartments to drive the transport of metabolites or movements of cilia and flagella. Nevertheless, let us take the estimate as a reasonable figure for the moment, and see what it tells us about energy flow on earth.

If we designate the average energy enrichment of biomass as ε, and the average residence time of the energy in the system as t, then the necessary flow rate per atom is,

$$J = \varepsilon / t \,, \qquad (4.15)$$

This has the same form as the chemical equation for the flow of species of atoms and molecules through a system,

$$\text{Flow of species} = \frac{\text{Total amount of the species in the system}}{\text{mean residence time}} \,. \qquad (4.16)$$

Unlike chemical species, however, energy cannot be ‘tagged’, for example, with a radioactive label, and its fate followed through the system; so the residence time for energy cannot be measured directly. However, as the flow of energy into the biosphere is always accompanied by the flow of materials — especially CO2 — into the system, the mean residence time for energy can be taken as the mean residence time for carbon in the system. The size of the various carbon pools on the surface of the earth has been estimated, giving the total biomass (both living and dead) on land and in the sea as 2.9 X 1018 gm and 10.03 x 1018 gm respectively. The values for carbon flow, i.e., the total fixed by photosynthesis per year, on land and in the ocean, are respectively, 0.073 ± 0.018 X 1018 gm and 0.43 ± 0.3 x 1018 gm. Putting these values into Eq. (14) above gives residence times of 40 years and 21.8 years. In terms of energy, an average flow of 0.003 eV per atom of biomass per year suffices to maintain the level of the biomass. This flow corresponds to a total annual flow of energy of 4.8 x 1017 kcal, a value in good agreement with the estimated yearly fixation of energy by photosynthesis, which is 13.6 ± 8.1 X 1017 kcal.21

An interesting question arises here: what is the significance of the long residence time of the energy that comes to the biosphere in photons from the sun? The energy of the photon meanders through innumerable cycles and epicycles of metabolism such that it is released and stored in small packets (in the ATP molecules, for example) ready for immediate utilization or in medium term depots such as gradients and fields to longer term deposits in the form of glycogen and fat, and even longer term deposits in the form of fossil fuels. The efficiency (and perhaps stability) of metabolism is associated with this drawn-out web of coupled energy transfer, storage and utilization within the highly differentiated space-time structure of the organism and ecological communities of organisms. Metabolic and structural complexity prolongs the energy residence or storage time, perhaps by an equal occupation of all storage times (or all storage space-times), affording the organism an efficient and stable living. I have suggested that the equal population of energy in all space-time modes is the thermodynamic extremum (i.e., end state towards which systems evolve) for open systems under energy flow, analogous to the maximum entropy state of thermodynamic equilibrium for isolated systems.22 However, the maximum entropy state of the open system is also a minimum entropy state, as all the space-time modes are effectively coupled together. And, in contradistinction to the maximum entropy state of isolated systems where no energy is stored, the open system has a maximum of stored energy. As long as the energy remains stored, it can be utilized for work (see Chapter 3). We shall have the occasion to return yet again to the importance of energy storage for vital functions in later Chapters.

A similar significance may well attach to the ecological cycles where the stability of the planetary system is concerned. There has been a great deal written on ecological sustainability, as well as the need to preserve genetic diversity within the past several years. Diversity may be much more important for the homeostasis — and hence sustainability — of planet earth than is generally recognized. The residence time of the energy within the biosphere is directly related to the energy stored, and hence, to species diversity or equivalently, the size of the trophic web (see Eq. 4.16), which, on the planetary level, is the space-time organization of the global ecological community. Could it be that in the 'geophysiology' of planet earth there is the same wisdom of the body that is in metabolism? The relationship between complexity of ecological communities and stability has already captured the attention of some ecologists,23 and fascinating investigations into the space-time "architecture" of ecosystems have also begun.24

In the next Chapter, we shall examine more closely the molecular basis of energy and entropy, where it will become clear that the quantity of energy in biomass as such cannot be the whole story to the success of living organisms. It is the quality of the energy, the structure of the living system and the way energy is stored and mobilized in coupled flows and fluxes that are most crucial for life.

Notes

1. See Morowitz (1968).
2. Lovelock (1979).
3. Fox (1986).
4. The account given is a simplified version of that given in Morowitz (1968) pp. 23–25.
5. See Prigogine (1962).

6. Koschmeider (1993) distinguishes between two kinds of convection cells, Bénard cells — driven by surface tension gradient — and Rayleigh-Bénard cells — driven by density gradient. The original Bénard cells, which appear as photographs or diagrams in most subsequent literature, have been mistakenly interpreted as Rayleigh-Bénard cells. I thank Eric Schneider for drawing my attention to this error.
7. See Nicolis and Prigogine (1989) p. 12.
8. Nicolis and Prigogine (1989) p. 12.
9. The following account is based on that given in Morowitz (1968) pp. 29–33.
10. See Prigogine (1962, 1967); Glansdorff and Prigogine (1967); Nicolis and Prigogine (1989).
11. Haken (1977).
12. I am indebted to Kenneth Denbigh for suggesting that coherence in the living system may have something to do with the coupling of processes. This encouraged me to study Onsager's reciprocity relation more carefully and started me thinking about the consequences of coupling in equilibrium and non-equilibrium systems.
13. Onsager (1945). See Denbigh (1951) for a very clear and accessible account on which the following description is based.
14. See Westerhof and van Dam (1987), however, for a non-equilibrium thermodynamics treatment intended for living systems.
15. Geoffrey Sewell has recently obtained a nonlinear generalization of the Onsager reciprocity relations for a class of irreversible processes in continuum mechanics. See Sewell (1991).
16. Chandresekhar (1961), cited in Koschmeider (1993).
17. Glansdorff and Prigogine (1967) p. 159.
18. MacDonald (1989).
19. See Ho (1995a).
20. See Morowitz (1978) pp. 252–3.
21. See Morowitz (1968) pp. 68–70.
22. See Ho (1994, 1995b).
23. See May (1973); DeAngelis (1992); Pimm (1996); Moffat (1996).
24. See Holling (1992) and references therein.

CHAPTER 5

How to Catch a Falling Electron

Life and Negative Entropy

In the last Chapter we saw how energy flow leads to material cycling and energy storage in living systems. But in what forms is the energy stored, and how is energy storage related to living organization?

Here is Schrödinger's famous statement about life: “It is by avoiding the rapid decay into the inert state of ‘equilibrium’ that an organism appears so enigmatic… What an organism feeds upon is negative entropy. Or, to put it less paradoxically, the essential thing in metabolism is that the organism succeeds in freeing itself from all the entropy it cannot help producing while alive.”1

In a footnote Schrödinger explains that by ‘negative entropy’, he perhaps should have said free energy. “But,” he continues, “this highly technical term seemed linguistically too near to energy for making the average reader alive to the contrast between the two things. He is likely to take free as more or less an epitheton ornans without much relevance, while actually the concept is a rather intricate one, whose relation to Boltzmann's order-disorder principle is less easy to trace than for entropy and ‘entropy taken with a negative sign’…’’2

Despite Schrödinger's apology for the term ‘negative entropy’, it continues to be used, and by the most authoritative among scientists: “It is common knowledge that the ultimate source of all our energy and negative entropy is the radiation of the sun. When a photon interacts with a material particle on our globe it lifts one electron from an electron pair to a higher level. This excited state as a rule has but a short lifetime and the electron drops back within 10-7 to 10-8 seconds to the ground state giving off its excess energy in one way or another. Life has learned to catch the electron in the excited state, uncouple it from its partner and let it drop back to the ground state through its biological machinery utilizing its excess energy for life processes.”[3] So writes Nobel laureate biochemist Albert Szent-Györgi, who has inspired more serious students in biochemistry than any other single person.

What exactly is this negative entropy, and how is it related to free energy and the manner in which the living system avoids the decay to equilibrium? Schrödinger uses the term ‘negative entropy’ in order to describe a somewhat fuzzy mental picture of the living system, which not only seems to avoid the effects of entropy production — as dictated by the second law — but to do just the opposite, to increase organization, which intuitively, seems like the converse of entropy. Szent-Györgi, on the other hand, has conveniently included the notions both of free energy and of organization in his use of the term. I think that both scientists have the right intuition — energy and organization are inextricably bound up with each other. Hence energy is not something associated merely with molecules. In order to appreciate that, we need to follow through the argument of those who have attempted to translate thermodynamic concepts, such as energy and entropy, into molecular motions and configurations.

Many thermodynamicists have already cautioned us (see Chapter 2) that the thermodynamic entropy, $\Delta S = Q_{rev}/T$, for example, has no direct connection with the statistical mechanics term by the same name, $S = k \ln W$[4], nor with notions of ‘order’ and ‘disorder’, and even less with ‘organization’.

Actually, even the relationships among all the thermodynamic entities: entropy, free energy, total energy, heat and temperature, are by no means straightforward. The physicist-philosopher, P.W. Bridgman, has often been criticized for pushing the ‘operationalist’ positivist approach in science, which says that science ought only to be about entities that one can measure or define by means of an operation. However, Bridgman's primary motivation was to expose the shaky foundations of fuzzy concepts to which scientists attribute an undeserved and misplaced concreteness, extrapolating the concepts indiscriminately to situations where they may no longer apply. Scientists, he says, should always keep before themselves the ‘man-made’ nature of their science (instead of treating it as though God-given). He has presented a thorough and rigorous critique of the thermodynamic concepts in his book, The Nature of Thermodynamics,5 and as far as I am aware, no one has successfully replied to his criticisms.6 Let us take a closer look at the thermodynamic concepts and their statistical mechanical interpretations.

Free Energy and Entropy

In Chapter 2, I have written down some equations for the change in free energy which are most relevant for biological systems: the Helmholtz free energy for processes occurring at constant temperature and volume,

$$\Delta A = \Delta U - T\Delta S \qquad (5.1)$$

and the Gibbs free energy for processes at constant temperature and pressure,

$$\Delta G = \Delta H - T\Delta S \qquad (5.2)$$

The criterion for all spontaneous processes is that free energy always decreases, i.e.,

$$\Delta A < 0 \qquad (5.3)$$

and,

$$\Delta G < 0 . \qquad (5.4)$$

Or, in the limiting case that the process occurs at equilibrium, the free energy change is zero. Processes which involve a negative free energy change (loss of free energy to the surroundings) are said to be exergonic — and are thermodynamically ‘downhill’ or spontaneous; those which involve a positive free energy change, or gain in free energy, are endergonic, and are thermodynamically ‘uphill’ and non-spontaneous.

As the free energy term is a difference between two other terms: total energy or enthalpy, and entropy, we have to see how the two change in a reaction. For example, if ΔH is negative and TΔS positive, they reinforce each other and ΔG will also be negative (i.e., free energy is lost to the system), so the reaction would proceed spontaneously. In other situations, ΔH and TΔS may work against each other, then ΔG would depend on the relative magnitudes of the two terms. If |ΔH| >> |TΔS|, then the reaction is said to be enthalpy driven because the sign of ΔG is predominantly determined by ΔH. Conversely, if |TΔS| > |ΔH|, then the reaction is entropy driven. In case of an adiabatic process occurring reversibly, which involves no heat exchange with its surroundings, Q = 0, hence ΔS = 0, and the change in free energy is simply equal to the change in internal energy or enthalpy, i.e.,

$$\Delta A = \Delta U \qquad (5.5)$$

$$\Delta G = \Delta H . \qquad (5.6)$$

We have already mentioned such reactions in the living system towards the end of Chapter 3. There can also be cases where the enthalpy and entropy changes have the same sign, so that they compensate or balance each other, leading to a reduction in free energy change. When the compensation is exact, the free energy change becomes zero, i.e.,

$$\Delta G = \Delta H - T\Delta S = 0$$
$$(\Delta H = T\Delta S) \qquad (5.7)$$

There are, in fact, no absolute measures for the quantities such as U, H, and G which enter into the equations of thermodynamics. Only the changes can be calculated and a zero point for the quantity is arbitrarily fixed at standard conditions of 298.15 K and one atmosphere. The one exception may be entropy.

According to Boltzmann's equation given in Chapter 2,

$$S = k \ln W , \qquad (5.8)$$

where entropy is proportional to the logarithm of the number of microstates, W, in the macroscopic system. In a perfect crystal, there can be only one arrangement of the atoms and so there must only be one single microstate at absolute zero, i.e.,

$$S = k \, ln 1 = 0 , \qquad (5.9)$$

This gives rise to the so-called third law of thermodynamics, which states that:

Every substance has a finite positive entropy, but at the absolute zero of temperature, the entropy may become zero, and does so become in the case of a perfect crystalline substance.7

Not all substances have only one microstate at absolute zero. Nevertheless, one can appreciate that the entropy of a substance is related to the random thermal motion of the molecules — a thermal energy that is somehow not available for work, and tends to disappear at absolute zero temperature. This is in opposition to the free energy, which is somehow available for work. But as pointed out above, there need be no entropy generated in an adiabatic process. From that we suspect that the division into available and nonavailable energy cannot be absolute: the energy associated with a molecule simply cannot be partitioned into the two categories.

The second law identifies the direction of processes which can occur spontaneously. However, it says nothing about the rate of the processes. Many thermodynamically favourable, or downhill processes do not actually proceed appreciably by themselves. The reason is that every substance sits inside its own individual energy well, separated from others by a hump which is the energy barrier (see Fig. 5.1). In order for a reaction to take place, an amount of energy, known as the activation energy, must first be supplied to overcome this barrier.

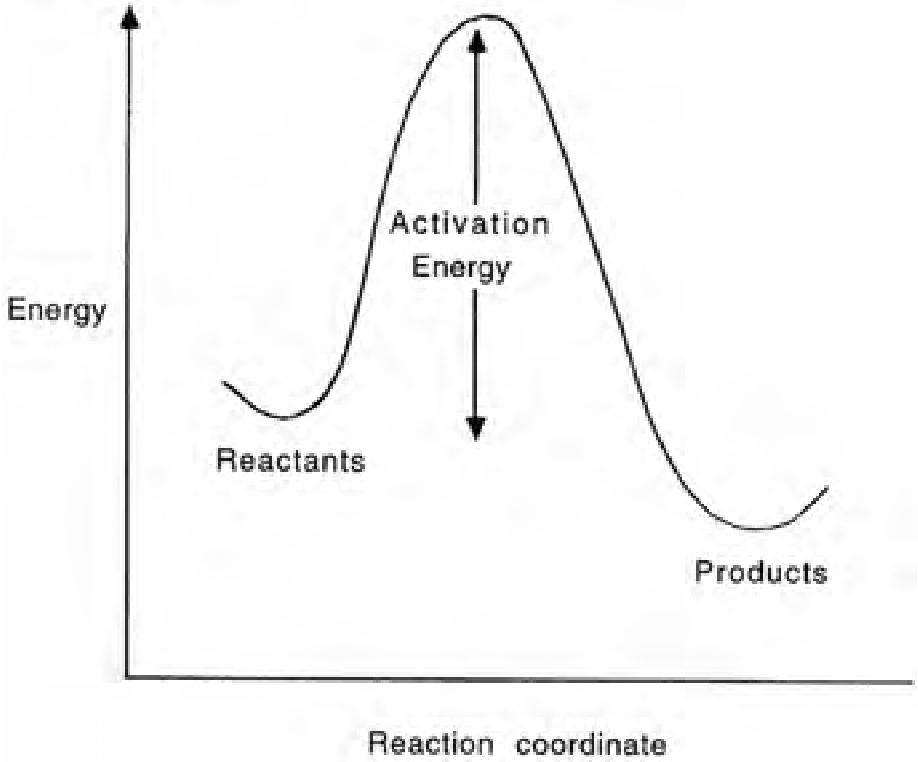


Figure 5.1 Activation energy for chemical reactions.

That is why the rate of almost all reactions goes up with temperature. With increase in temperature, the random motion of the molecules becomes exaggerated, increasing the likelihood of collisions on which reaction depends. This is the basis of Arrhenius' law of the dependence of reaction rates on temperature. But if increasing the temperature increases reaction rates, then not all random thermal motion can be regarded as entropy, some of that must actually contribute to the free energy of activation, and indeed, such a term has been invented for chemical kinetics. So again, this warns us that useful energy and the random kinetic energy that goes to make up entropy cannot be so neatly distinguished.

Why Don't Organisms Live by Eating Diamonds?

This question was raised by F. Simon, who pointed out to Schrödinger that his simple thermodynamical considerations cannot account for our having to feed on matter in the extremely well-ordered state of more or less complicated organic compounds rather than on charcoal or diamond pulp, which are crystalline substances with regular molecular order, and consequently, have little or no entropy.8

After all, according to thermodynamic principles, organisms could make their living by eating carbon or diamond pulp (for negative entropy), and absorbing energy as heat directly from its surroundings, say, by taking up residence inside a volcano. But they do not. So there may be something special about the precise form, or quality, of energy that is taken up, or how that energy is taken up by living systems that perhaps enables them to build organization, which is not the same as crystalline order. For one thing, the former is dynamic through and through, whereas the latter is static.

To explore further the interrelationships among the concepts of heat, energy, entropy, negentropy and organization, we need to know something of the description as to how energy is distributed at the molecular level.

According to the principle of equipartition of energy, which is based on classical (as opposed to quantum) theory, the energy of a molecule is equally divided among all types of motions or degrees of freedom. For mon-atomic gases, each atom has three translational degrees of freedom. For molecules containing more than one atom, there will be other motions, notably, rotation (moment) about the centre of mass on the interatomic bonds and vibration (stretching and compressing) along the bonds. For a molecule containing N atoms, we need 3N coordinates to describe all its complete motion. Of these, three are for translational motion, three angles are needed to define the orientation of the molecule about the three mutually perpendicular axes through the centre of mass, and that leaves 3N — 6 degrees of freedom for vibrations. If the molecule is linear, only two angles are needed to specify rotation, leaving 3N — 5 degrees of freedom for vibrations. For one single molecule, each translational and rotational degree of freedom possesses energy ½kT, whereas each vibrational degree of freedom possesses energy kT. This is so because the vibrational energy contains two terms, one kinetic and one potential, each of which is ½kT. For one mole of a gas (the molecular weight in grams), there are N0 molecules, where N0 is Avogadro's number and is equal to 6.02217 x 1023; and the corresponding energies for each degree of translation and rotation is ½N0kT, or ½RT, and for vibration, RT, where R = N0k is the gas constant and is equal to 8.314 JK-1 mol-1.

We can now calculate the total internal energy U for any system of gases. For a diatomic gas such as O2, for example,

$$U = \underset{\text{(translation)}}{\tfrac{3}{2}RT} + \underset{\text{(rotation)}}{RT} + \underset{\text{(vibration)}}{RT} = \tfrac{7}{2}RT \, . \qquad (5.10)$$

How can we test whether the derivation of U based on the kinetic theory of gases corresponds to the same entity in thermodynamics? This can be done by heat capacity measurements. The specific heat of a substance is the energy required to raise the temperature of 1 g of the substance by 1 degree. For the chemist, the mole is a more convenient unit of mass, and the corresponding specific heat is the molar heat capacity, C, the energy required to raise 1 mole of the substance by 1 degree. The heat capacity at constant volume is defined by the equation,

$$C_v = (\partial U/\partial T)_v \, , \qquad (5.11)$$

where ∂U/∂T represents the partial derivative of internal energy with respect to temperature. According to the derivation above, for a diatomic gas,

$$C_v = (\partial U/\partial T)_v = \tfrac{7}{2}R = 29.10\,\mathrm{JK^{-1}\,mol^{-1}} \, . \qquad (5.12)$$

It turns out that the predicted values agree with experimental measurements for monatomic gases, but show considerable discrepancies for molecules containing two or more atoms (see Table 5.1).

9

Gas	Cv(JK-1 mol-1)Calculated	Cv(JK-1 mol-1)Measured
He	12.47	12.47
Ne	12.47	12.47
Ar	12.47	12.47
H2	29.10	20.50
N2	29.10	20.50
O2	29.10	21.05
CO2	54.06	28.82
H2O	49.87	25.23
SO2	49.87	31.51

The discrepancies can be explained on the basis of quantum theory, which we shall deal with in more detail in a later Chapter. For the moment, it is sufficient to recognize that according to quantum theory, the electronic, vibrational and rotational energies of a molecule are ‘quantized’, which means that they do not exist in a continuum, but only at discrete levels (see Fig. 5.2). Thus, the spacing between successive electronic levels is much larger than that between vibrational energy levels; which is in turn larger than that between rotational energy levels. The spacing between successive translational energy levels is so small that the levels practically merge into, a continuum. In that respect, translational energy is classical rather than quantum mechanical.

When a system absorbs heat from its surroundings, the energy is used to promote various kinds of molecular motion. The heat capacity is hence an energy capacity, or the system's capacity to store energy.

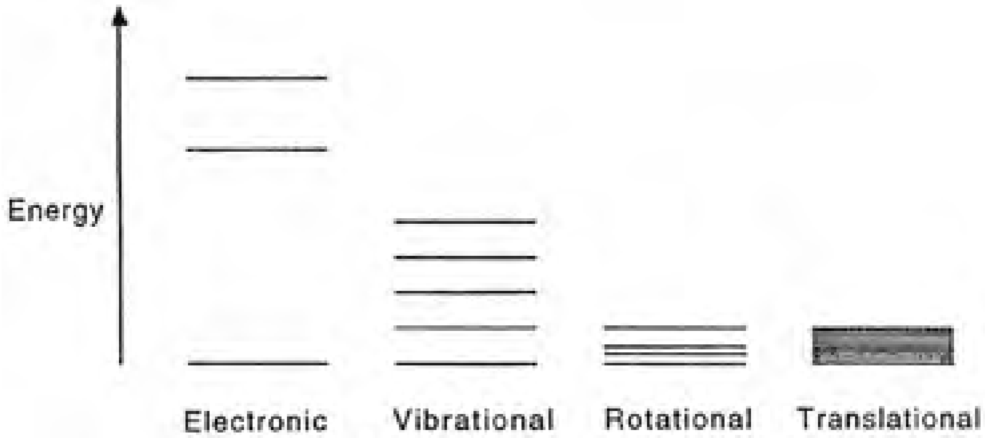


Figure 5.2 The quantized energy levels for the different forms of molecular motion.10 The lowest energy levels, associated with translational motion, are so close together that they form a continuum. Translational energies are hence, classical.

Theoretically, energy may be stored in any mode. But it is much easier to excite a molecule to a higher rotational energy level than to a higher vibrational or electronic energy level. Hence, molecular energies can at least be quite unambiguously classified in terms of the levels of excitation and storage.

Quantitatively, the ratio of the occupation numbers (i.e. the number of molecules in each energy level), N2/N1, in any two energy levels, E2 and E1 is given by Boltzmann's distribution law, which applies to thermodynamic equilibrium:

$$N_2/N_1 = e^{-\Delta E/kT} \tag{5.13}$$

where ΔE = E2 - E1, k is Boltzmann's constant and T the absolute temperature. For translational motion, ΔE is about 10-37 J, so ΔE/kT at 298 K is,

$$\frac{10^{-37}\,\mathrm{J}}{(1.38\times 10^{-23}\,\mathrm{JK^{-1}})(298\,\mathrm{K})} = 2.4\times 10^{-17}$$

The resulting figure is so close to zero that the value for the ratio, N2/N1, is very nearly unity. In other words, the successive levels of translational energy are about equally populated at room temperatures. On the other hand, for vibrational energy, where ΔE is about 10-20J, repeating the calculation done above gives ΔE/kT = 2.431, so N2/N1, is much smaller than unity in this case. That means only a very few molecules will be in the higher energy levels at 298K. For electronic energies, the population of higher energy levels is even much less likely, and at 298 K, almost all of the molecules will be in the lowest energy levels.

From these considerations, one would expect that at room temperatures, we can neglect both vibrational and electronic energies, so the energy of the diatomic system becomes,

$$U = \underset{\text{(translation)}}{\tfrac{3}{2}RT} + \underset{\text{(rotation)}}{RT} = \tfrac{5}{2}RT, \qquad (5.14)$$

This give Cv = 5/2 RT = 20.79 JK-1 mol-1, which is quite close to the measured value (see Table 5.1). When the temperature increases, however, the vibrational levels will be expected to make a substantial contribution to the heat capacity. And this is indeed the case. At 1500 K, the heat capacity of O2 closely approaches the theoretical value of 29.10 JK-1 mol-1. At 2000 K, the measured value of 29.47 JK-1 mol-1 actually exceeds the theoretical value, suggesting that electronic motion is beginning to make a contribution to heat capacity (see Table 5.2).

The alert reader will have already noticed by now that the above account describes quite adequately what happens when energy is supplied as heat to a system of unorganized molecules, which is what physics and chemistry usually deal with. The heat absorbed saturates all the lower energy levels before the upper levels become populated, and a large spectrum exists ranging from the translational energies at the low end to the electronic energies at the high end. The higher the level at which energy is stored, the less the increase in temperature per unit of energy stored, i.e., the greater the heat capacity. Much of the energy stored in living system is in the high vibrational and electronic levels. In particular, macromolecules such as proteins and nucleic acids have

2 at different temperatures12 T(K) Cv(JK-1 mol-1298 21.05600 23.78800 25.431000 25.561500 28.252000 29.47

many, many more vibrational motions for storing energy than small molecules. And heat capacity measurements typically show exponential increases with increase in temperature.11 In the language of quantum theory, the living system has achieved a ‘population inversion’ deviating from the equilibrium prediction of Boltzmann's law, i.e., the upper energy levels are much more populated than they should be for the temperature of the system, which is typically about 300 K.

It has been said that our bodies have a high ‘electronic’ temperature and that if we were equilibrium thermodynamic systems, we would have a temperature of up to 3000 K. But that too, is misleading. For at those temperatures, the high molecular weight constituents could no longer exist; they would be subject to denaturation and dissociation long before those temperatures are attained. And perforce neither cells nor tissues could exist. Temperature is not an apt description for living systems, as we shall see later, they do not work by heat transfer.

With regard to the wide spectrum of energies associated with the molecules, one finds that a priori, they cannot be clearly apportioned into free energies, or entropy, or heat; much less can we say which parts correspond to work. These can only be apportioned a posteriori — after the reactions have taken place, and furthermore, depending on how the reactions have taken place. That may seem contrary to the textbook assertion that unlike work or heat, entropy is a state function; which means that it is a property of the state as much as its temperature, volume and pressure, and does not depend on how that state is arrived at. However, there are no operational measures of absolute entropy content, except by spectroscopic methods at absolute zero. And only changes in entropy are defined in terms of a reversible process. Yet, there are many natural irreversible processes in which the change in entropy simply cannot be defined (see Chapter 13). So, the change in entropy is just due to the energy which has gone missing, or has somehow become dissipated. To work out how much has gone where is rather like an accountant balancing the books at the end of the year! And just as it is misleading to base next year's budget on this year's accounts, one cannot hope to explain how the organism works by laws governing steam engines, or an unorganized collection of molecules. Let us try to be more precise about this.

What Kind of ‘Engine’ is the Organism?

In discussing the limitations of the second law of thermodynamics as usually formulated, Morowitz lists 4 types of engines (see Fig. 5.3). The first three, the Carnot engine, the industrial engine and the fuel cell, are all equilibrium devices. As the first two engines operate by converting chemical energy into heat which is then converted into work, they are both subject to Carnot's efficiency theorem, which places an upperbound to the efficiency — when operated reversibly — as (1 - Tsink/Tsourse). In other words, efficiency is determined by the temperature difference between source and sink, or the boiler and the exhaust in the heat engine.

The fuel cell, however, operates isothermally, converting chemical energy directly into electricity, and so its efficiency is no longer limited by the temperature difference between source and sink. Instead, the maximum efficiency is given by $(1 - T\Delta S/\Delta U)$, where ΔS and ΔU are the changes in internal entropy and energy of the fuel cell and T is the temperature of the surroundings. If entropy change is zero, as would be the case if the energy is transferred at equilibrium, the efficiency becomes one.

The fourth type is the far-from-equilibrium machine that can in principle operate at very high efficiencies without any heat loss. Living systems, Morowitz suggests, could be isothermal

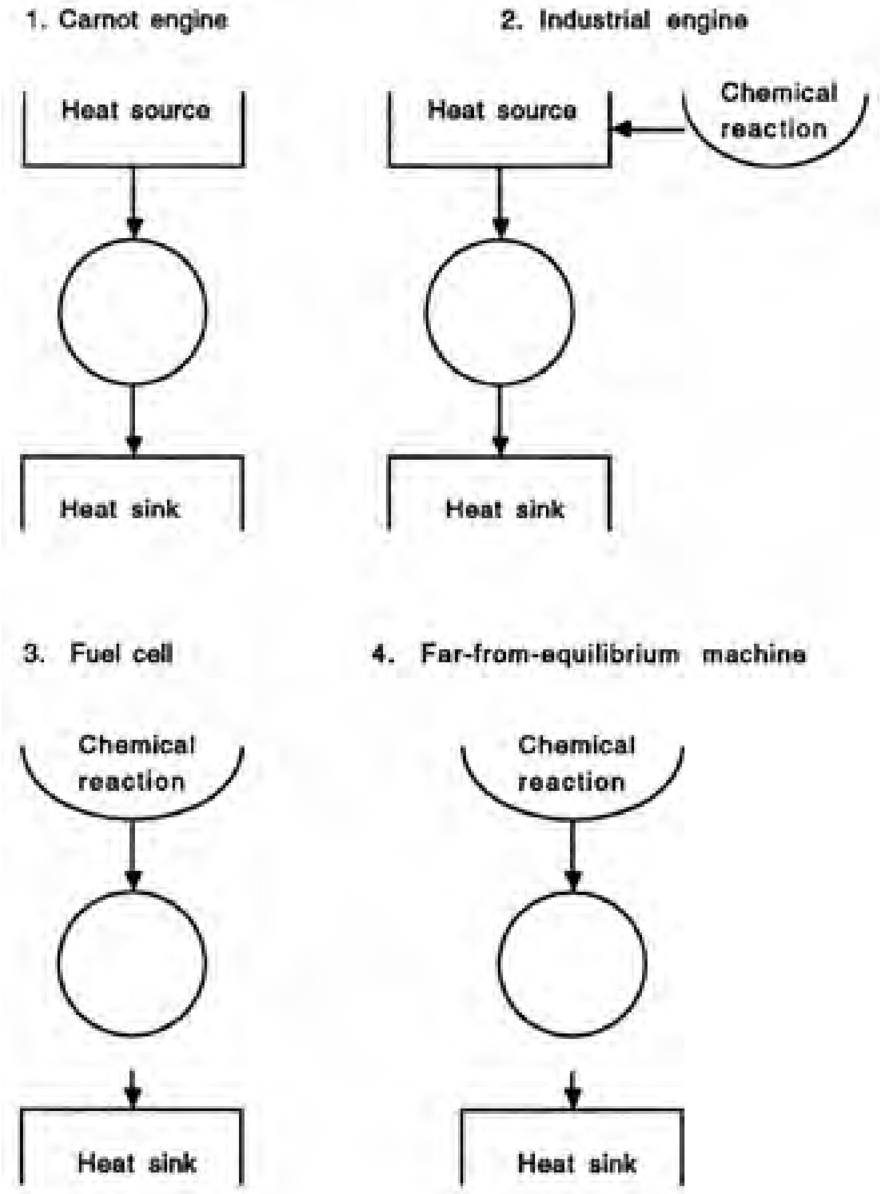


Figure 5.3 Four types of engines. Carnot and industrial engines are subject to Carnot's efficiency theorem as they depend on heat exchange. The fuel cell and far from equilibrium machines do not depend on the conversion of energy into heat, and hence are not subject to the same constraints (see text). The incomplete arrows leading from the fuel cell and far-from-equilibrium engines to the heat sink indicate that the heat loss is not a necessary part of the working cycle.14

equilibrium machines, like the fuel cell; or it could be a non-equilibrium, type 4 machine. ‘‘It is also possible,” he continues, “that they operate on a molecular quantum mechanical domain that is not describable by any of the macroscopic engines…”13

Energy transfer via heat, on which the science of thermodynamics is based, is by far the least efficient and nonspecific form of transfer. The biosphere, as we have seen, does not make its living by absorbing heat from the environment. No organism can live like a heat engine, nor can it obtain its energy or negative entropy by feeding on carbon or diamond pulp and burning it with oxygen. Instead, life depends on catching an excited electron quite precisely — by means of specific light absorbing pigments — and then tapping off its energy as it falls back towards the ground state. Life uses the highest grade of energy, the packet or quantum size of which is sufficient to cause specific motion of electrons in the outer orbitals of molecules. It is on account of this that living systems can populate their high energy levels without heating up the body excessively, and hence contribute to what Schrödinger intuitively identifies as ‘negative entropy’. But what enables living systems to do so? It is none other than their meticulous space-time organization in which energy is stored in a range of time scales and spatial extents. This is what I meant at the beginning of the previous Chapter (p. 40) when I say that energy flow organizes the system which in turn organizes the energy flow. Stored energy is in the organization, which is what enables the living system to work so efficiently on a range of timescales.

It is of interest to compare the thermodynamic concept of ‘free energy’ with the concept of ‘stored energy’. The former cannot be defined a priori, much less can be it be assigned to single molecules, as even changes in free energy cannot be defined unless we know how far the reaction is from equilibrium. ‘Stored energy’, originally defined by McClare with respect to a characteristic time interval (see Chapter 3), is readily be extended, in addition, to a characteristic spatial domain. As such, stored energy is explicitly dependent on the space-time structure of the system, hence it is a precise concept which can be defined on the space and time domain of the processes involved. Indeed, stored energy has meaning with respect to single molecules in processes involving quantum molecular machines as much as it has with respect to the whole organism. For example, energy storage as bond vibrations or as strain energy in protein molecules occurs within a spatial extent of 10-9 to 10-9m and a characteristic timescale of 10-9 to 10-8s. Whereas in terms of a whole organism such as a human being, the overall energy storage domain is in metre-decades.

Stored energy, as you will recall from Chapter 4, is coherent energy capable of doing work. And that may be the clue to understanding the thermodynamics of living systems. In the previous Chapter, we also discovered how the living system, though macroscopically far from thermodynamic equilibrium, may yet harbour a hierarchy of local domains of equilibrium defined by the space-time magnitude of the processes involved. Thus, equilibrium and non-equilibrium may be less important a distinction between living and non-living systems, than space-time structure, or organization. What we really need, in order to understand the living system, is a thermodynamics of organized complexity which describes processes in terms of stored energy instead of free energy. (Alternatively, we can define the hierarchy of local equilibria in terms of the energy storage domains.) Thus, the living system could contain isothermal equilibrium machines, non-equilibrium machines, as well as quantum molecular machines. We shall explore these ideas further in the next Chapter.

The crucial difference between living and non-living systems lies in how energies are stored, channeled and directed in a coherent way. It is of interest to note that Lord Kelvin, one of the inventors of the second law, has stated it as follows: “It is impossible by means of an inanimate material agency to derive mechanical effect from any portion of matter by cooling it below the temperature of the coldest of the surrounding objects.” Lest there should be any ambiguity as to what is intended by the reference to ‘inanimate material agency’, he adds, “The animal body does not act as a thermodynamic engine… whatever the nature of these means [whereby mechanical effects are produced in living organisms], consciousness teaches every individual that they are, to some extent, subject to the direction of his will. It appears therefore that animated creatures have the power of immediately applying to certain moving particles of matter within their bodies, forces by which the motions of these particles are directed to produce derived mechanical effects.”15 The secret of the organism is that it can mobilize the whole spectrum of energies for work, from the translational to the electronic, making scant distinction between ‘bound’ and ‘free’ energy, between that which is ‘unavailable’ and otherwise.

To both summarize and anticipate the story thus far: ‘negative entropy’ in the sense of organization, or simply ‘entropy with the sign reversed’ has not so much to do with free energy (as Schrödinger also indicates), but with the way energy is trapped, stored and mobilized in the living system. Energy is trapped directly at the electronic level. It is stored not only as vibrational and electronic bond energies, but also in the structure of the system: in gradients, fields and flow patterns, compartments, organelles, cells and tissues. All this in turn enables organisms to mobilize their energies coherently and hence make available the entire spectrum of stored energies for work, whenever and wherever energy is called for.

Notes

1. Schrödinger (1944) pp. 70–71. See Gnaiger (1994).
2. Schrödinger (1944) p. 74.
3. Szent-Györgi (1961).
4. K. Denbigh is of this opinion, although Oliver Penrose (personal communication) disagrees! Both scientists are authorities in the field of thermodynamics and statistical mechanics. This illustrates precisely the complexity of the issues involved.
5. Bridgman (1961).
6. Oliver Penrose disagrees with this statement (personal communication). In his book, Foundations of Statistical Mechanics, he has shown that a non-decreasing function corresponding to entropy can be derived from a Gibbs ensemble by the mathematical technique of ‘coarse-graining’. See also Penrose (1981).
7. This statement is due to Chang (1990) p. 140.

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8. See Schrödinger (1944) p. 74.
9. From Chang (1990) p. 43.
10. Modified from Chang (1990) p. 44.
11. See Ho (1995a) Chapter 2.
12. From Chang (1990) p. 45.
13. See Morowitz (1978) pp. 74–6.
14. Modified from Morowitz (1978) p. 75.
15. Cited in Ehrenberg (1967) p. 104.

CHAPTER 6

Towards a Thermodynamics of Organized Complexity

The Continuing Enigma of Organisms

We will take for granted, by now, the idea that organisms are open systems dependent on energy flow. Energy flows in together with materials, and waste products are exported, along with the spent energy that goes to make up entropy. And that is how living systems can, in principle, escape from the second law of thermodynamics. The second law, as you will recall, encapsulates the monotonous, unexceptional experience of everyday life: that all physical systems run down, ultimately decaying to homogeneous disorganization when all useful energy is finally exhausted, being converted into entropy. So organisms are anti-entropic as long as they are alive. Not only do they keep their organization intact, but also manage to have lots of energy for their activities. But how do they really manage their anti-entropic existence? What would a thermodynamic description of organisms be like?

The project is to come up with something like “a thermodynamics of organized complexity” left hanging in the air at the end of the previous Chapter.

The Organism as an Energy Storage Domain

Many physicists and chemists have stressed the importance of energy flow and dissipation to living organization. But, in order to benefit from energy flow, the system must have some means of capturing and storing the energy, to lift it up from thermodynamic equilibrium. Solar energy flows through Mars and Venus just as it flows through Earth, yet only Earth can capture the energy by means of the chlorophyll of green plants. In common with all other organisms, green plants have an impressive metabolic network of biochemical reactions “down-stream’’ of the energy capture, which stores the energy, not just for the plants, but also to pass along to the other organisms in the food web. The entire ecosystem on earth is one big energy store maintained far away from thermodynamic equilibrium, and at the end of Chapter 4, an estimate of the energy residence time was made.

The key to understanding the thermodynamics of organisms is, therefore, neither energy flow nor energy dissipation, but energy storage under energy flow (see Fig. 6.1).

Energy flow is of no consequence unless the energy is trapped within the system where it circulates, to build up structures for storing the energy, and to do work before it is dissipated. An organism arises when the loop of circulating energy somehow closes on itself to give a regenerating, reproducing life-cycle within which energy is mobilized, remaining stored as it is mobilized. The energy goes into complex cascades of coupled cyclic processes within the system before it is allowed to dissipate to the outside. These cascades of cycles span the entire gamut of space-times from slow to fast, from local to global, that all together, make up the life-cycle.

Each cycle is simply a domain of coherent energy storage. As you will recall, coherent energy is energy that can do work because it is all coming and going together. The cycles within the life-cycle are all interlinked in a very special way, in order to feed off the one-way energy flow. Picture them as a complicated system of eddies forming in a pool off the main river stream. The more eddies or

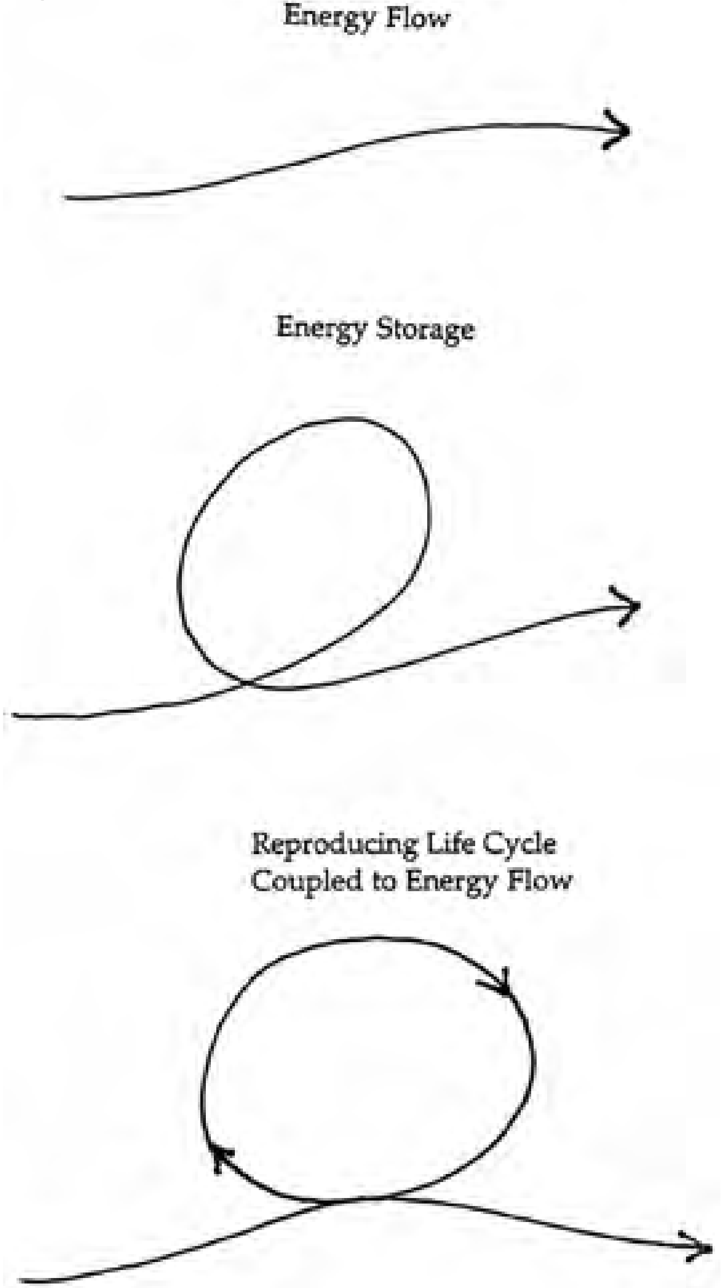

Figure 6.1 Energy flow, energy storage and the reproducing life-cycle.

cycles there are, the more energy is stored, and the longer it takes for the energy to dissipate. The average residence time of energy (see Chapter 4)2 is therefore a measure of the organized complexity of the system. An intuitive representation is given in Fig. 6.2.

Coupled processes are familiar in biochemistry: practically all thermodynamically uphill reactions, i.e., those requiring energy

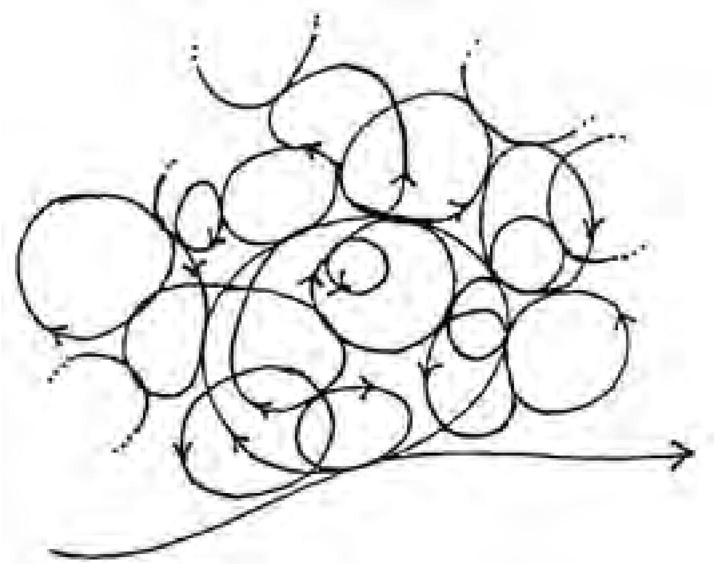

Figure 6.2 The many-fold cycles of life coupled to energy flow.

(ΔG positive), are coupled to the thermodynamically downhill ones, i.e., those yielding energy (ΔG negative). The ATP/ADP couple, ubiquitous is to the living system, effectively turns all biosynthetic and other energy requiring uphill-reactions downhill.3 Life is literally downhill, or, on a more optimistic and cheery note, effortless and spontaneous, all the way.4

That living processes are organized in cycles is also intuitively obvious by a casual examination of the metabolic chart. Apart from the prominent cycles such as the tricarboxylic acid cycle and the cyclic interconversion of ATP/ADP, NADH/NAD and other redox (reduction-oxidation) intermediates, many more cycles and epicycles are entangled in the metabolic network (see Chapter 4).5

Another prominent way in which cycles appear in living systems is in the familiar form of the wide spectrum of biological rhythms — with periods ranging from milliseconds for electrical discharges of single cells to circadian and circa-annual cycles in whole organisms and populations of organisms.6 These cycles also interlock to give the organism a complex, multidimensional, entangled space-time, very far removed from the simple, linear Newtonian space and time of mechanical physics. There are some very suggestive observations that all these rhythms are indeed entangled, or coupled together. Geneticists have discovered that mutations in two genes of Drosophila, period and timeless, which speed up, slow down or abolish circadian rhythm, also cause corresponding changes in the millisecond wing beat cycle of the male fly's love song.7 This correlation spans seven orders of magnitude of characteristic timescales, reflecting the full extent of coupled energy storage and mobilization in the living system. We shall come back to organic space-time in later Chapters.

Energy Storage and Mobilization is Symmetrical

Energy is stored and mobilized over all space-times according to the relaxation times and volumes of the processes involved. The result, as stated in Chapter 3, is that organisms can take advantage of two different ways to mobilize energy with maximum efficiency — non-equilibrium transfer in which stored energy is transferred before it is thermalized, and quasi-equilibrium transfer, which is slow enough to allow all thermalized, and other exchanging energies to equilibrate, for which the free energy change approaches zero, in accordance with conventional thermodynamic considerations. Because all the modes of activity are coupled together, energy input into any mode can be readily shared, or delocalized over all modes, and conversely, energy from all modes can become concentrated into any mode. Another way to express the same thing is that energy from any point can spread throughout the system, or become concentrated to any point from all over the system. In technical terms, energy coupling in the living system is symmetrical, as I have begun to argue in Chapter 4.8

I also showed that symmetrical energy coupling and cyclical flows are both predicted from the thermodynamics of the steady state, in the form, respectively, of Onsager's reciprocity relationship and of Morowitz' theorem. Let me briefly recapitulate before presenting the full argument here.

Onsager's reciprocity relationship states that for a system of many coupled linear flows under conjugate forces,

$$J_i = \Sigma_k L_{ik} X_k \quad (6.1)$$

where Ji is the flow of the ith process (i = 1, 2, 3…n), Xk is the kth thermodynamic force (k = 1, 2, 3,…n), and Lik are the proportionality coefficients (where i = k) and coupling coefficients (where i ≠ k), the couplings for which the Xks are invariant with time reversal (i.e., velocity reversal) will be symmetrical; in other words,

$$L_{ik} = L_{ki} \quad (6.2)$$

so long as the Js and the Xs satisfy Tθ = ΣJiXi where T is temperature in deg. K, and θ is the rate of entropy increase per unit volume.9

Morowitz' theorem states that the flow of energy through the system from a source to a sink will lead to at least one cycle in the system at steady state, provided that the energy is trapped and stored within the system (italics mine). This important theorem is, as far as I know, the only attempt to account for cycles in the living system, it implies that the steady state — at which global balance is maintained — must harbour nonlinear processes. It also implies that the steady state necessarily violates the principle of microscopic reversibility, which, as Onsager originally argued, is a principle extraneous even to thermodynamic equilibrium.10

Onsager's reciprocity relationship has been extended to the far from equilibrium regime for systems containing many enzymes working together11 and more recently, for “infinite” (or sufficiently large) quantum systems.12 However, the validity and the theoretical basis for extending Onsager's reciprocity relationship to biological systems are still under debate within the community of biochemists.13

I believe some form of Onsager's reciprocity relationship does hold in living systems if only to account for the ready mobilization of energy on the one hand — why we can have energy at will — and on the other hand, for the linear relationships between steady-state flows and thermodynamic forces outside the range of equilibrium,14 which is actually observed in many biological systems.

According to biochemist, Rothschild and his coworkers15 linearity in biological processes can arise in enzymes operating near a "multidimensional inflection point" (i.e., a local minimum or maximum) far away from thermodynamic equilibrium, if some of the rate constants of different reactions are linked. That is realistic for living systems which are now known to have highly organized flows in the cytoplasmic matrix due to dynamic compartmentation and microcompartmentation (as you will see in greater detail in Chapter 8). Theoretical physicist Geoffrey Sewell,16 on the other hand, shows how Onsager's reciprocity relationship applies to locally linearized combinations of forces and flows, which nonetheless behave globally in nonlinear fashion. Again, that is relevant for the living system, where nested compartments and microcompartments ensure that many processes can operate locally at thermodynamic equilibrium even though the system or subsystem as a whole is far away from equilibrium (Chapter 3).17

Furthermore, as each process is ultimately connected to every other in the metabolic net through catenations of space and time, even if truly symmetrical couplings are localized to a limited number of metabolic/energy transducing junctions, the effects will be shared, or delocalized throughout the system, so that symmetry will apply to appropriate combinations of forces and flows over a sufficiently macroscopic space-time scale. That is perhaps the most important consideration. As real processes take time to occur, Onsager's reciprocity relationship (or any other physical relationship) cannot be true for an arbitrarily short instant, but must apply at a sufficiently macroscopic time interval when overall balance holds. The same argument applies to the spatial extent of the processes involved.

By now, you will have realized that a constant theme running throughout this book is the space-time differentiation of real processes, and the consequent need to distinguish between microscopic and macroscopic descriptions.

Thermodynamics of the Steady State vs Thermodynamics of Organized Complexity

Denbigh18 defines the steady state as one in which "the macroscopic parameters, such as temperature, pressure and composition, have time independent values at every point of the system, despite the occurrence of a dissipative process.” That is too restrictive to apply to the living system, which, as mentioned earlier, has coupled processes spanning the whole gamut of relaxation times and volumes.

A less restrictive formulation — one consistent with a “thermodynamics of organized complexity’’ — might be to define the living system, to first approximation, as a dynamic equilibrium in which the macroscopic parameters, such as temperature, pressure and composition have time-independent values despite the occurrence of dissipative processes.[19] My formulation significantly omits the phrase, “at every point of the system” on grounds that microscopic homogeneity is not crucial for the formulation of any thermodynamic state, as the thermodynamic parameters are macroscopic entities quite independent of the microscopic interpretation. Like the principle of microscopic reversibility, it is extraneous to the phenomenological laws of thermodynamics as Denbigh himself has convincingly argued.

In order to fully appreciate the above formulation, it is necessary to go into the history of the thermodynamics of the steady state. It began with W. Thomson's (Lord Kelvin) treatment of the thermoelectric effect.[20] This arises in an electrical circuit in which heat is absorbed and rejected at two junctions (the Peltier heat), and in addition, heat is absorbed and given off due to current flows between two parts of the same metal at different temperatures (the Thomson heat). Both of these heat effects are reversible, in that they change sign but remain the same in magnitude when the direction of the current is reversed. On the other hand, there are two other effects which are not reversible: heat conduction along the wires and dissipation due to the resistance. It is thus impossible to devise a reversible thermoelectric circuit even in principle. Nevertheless, Thomson took the step of assuming that, at steady state, those heat effects that are reversible, i.e., the Peltier heat and Thomson heat balance each other so that no net entropy is generated,

$$\Delta S_p + \Delta S_T = 0 \qquad (6.3)$$

On that basis, he derived the well-known relations between the Peltier and Thomson heats and the temperature coefficient of the electromotive force. It was a bold new departure in the application of the second law, but one which was subsequently justified by experimental evidence.

Very similar methods were used later by Helmholtz in his treatment of the electromotive force and transport in the concentration cell, where he states clearly that the two irreversible process in the cell, heating and diffusion, are to be disregarded and the second law to be applied to those parts of the total process which are reversible. Most modern accounts of this system follow the same procedure. A virtual flow of current is supposed to take place across the liquid junction, resulting in a displacement of the ions. The process is taken to be reversible and to generate no net entropy. The justification,21 is that the two processes, diffusion and flow of current across the junction, “take place at rates which vary according to different laws” when the composition gradient across the boundary is altered, and so it seems reasonable to suppose that the two processes are merely superposed, and that the one may be ignored when considering the other. Thus, the steady state is treated as if there were no dissipative processes, and it is this assumption which is later validated by Onsager's reciprocity relationship.

Superposition of Cyclic Non-dissipative Processes Coupled to Dissipative Processes

In the same spirit, I propose to treat the living system as a superposition of non-dissipative cyclic processes and dissipative irreversible processes, so that Onsager's reciprocity relationship applies only to the former. In other words, it applies to coupled processes for which the net entropy production is balanced out to zero,

$$\Sigma_k \Delta S_k = 0 \qquad (6.4)$$

This will include most living processes on account of the ubiquity of coupled cycles, for which the net entropy production may indeed balance out to zero. Cycles are states of perpetual return, so entropy does not accumulate, and also, no net entropy need to be generated.

The principle of net entropy balance applies, in fact, to the smallest unit cycle in the living system — enzyme catalysis — on which all energy transduction in the living system is absolutely dependent. Over the past 30 years, enzyme chemist, Rufus Lumry and his coworkers22 have shown convincingly how the flexible enzyme molecule balances out entropy with enthalpy to conserve free energy (i.e., stored or coherent energy in the present context) during catalysis, in accordance with the relationship for isothermal processes,

$$\Delta G = \Delta H - T\Delta S = 0 \qquad (6.5)$$

It is also possible to balance out positive entropy with negative entropy directly (see later).

The organism can be regarded, in effect, as a closed, self-sufficient energetic domain of cyclic non-dissipative processes coupled to irreversible dissipative processes. In the formalism of conventional thermodynamics, the life cycle, or more precisely, the living system in dynamic equilibrium, consists of all cyclic processes for which the net entropy change is zero, coupled to dissipative processes necessary to keep it going, for which the net entropy change is greater than zero (Fig. 6.3).

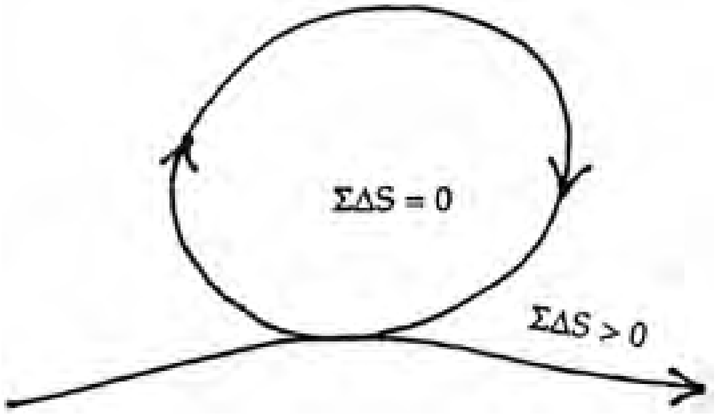

Figure 6.3 The organism frees itself from the immediate constraints of thermodynamics.

In other words, there is an internal entropy compensation as well as coherent energy conservation due to the predominance of coupled cyclic processes and the nested space-time organization of the processes. That means the system maintains its organization (or negative-entropy state) while it is metabolizing and transforming energy.

This formulation of the living system is in accord with our common intuition of an organism. Each of us, for example, is recognizably the same person, with well-defined boundaries from moment to moment, even as we are constantly breathing in oxygen and exporting carbon dioxide and entropy, dying little deaths and undergoing little rebirths as we metabolize. We are, to all intent and purposes, closed systems full of stored energy, fed by an open circuit, an exotic golden flower powered by the green fuse of life.

The Principle of Internal Entropy Compensation

Let us see how this formulation matches up with previous ideas on the thermodynamics of the steady state. There is a well-known theorem of minimum entropy production derived by Prigogine,23 which states that entropy exported from a system reaches a minimum, or becomes zero, at thermodynamic equilibrium and at steady states close to thermodynamic equilibrium. Prigogine's theorem is a direct consequence of Onsager's reciprocity relationship which holds at steady states close to thermodynamic equilibrium (see Chapter 4). The principle of internal entropy compensation which I am proposing here, is in addition to, and implies the principle of minimum entropy production, and may even be valid in regimes far from thermodynamic equlibrium.

As pointed out in Chapter 4, there is already a balance theorem due to Chandresekhar,24 which states that instability of the Bénard-Rayleigh cells occurs at the minimum (critical) temperature gradient at which a balance can be steadily maintained between the kinetic energy dissipated by viscosity and the internal energy released by the buoyancy force. Glansdorff and Prigogine,25 for their part, state that the Bénard-Rayleigh instability occurs at the minimum temperature gradient at which a balance can be steadily maintained between the entropy generated through heat conduction by the temperature fluctuations and the corresponding entropy flow “carried away” by the velocity fluctuations.

Prigogine's theorem of minimum entropy production was derived for homogeneous systems where all volume elements are uniform and locally at equilibrium. On the contrary, internal entropy compensation applies to systems with organized heterogeneity — such as organisms — so that positive entropy production in some space-time elements may be compensated by negative entropy production in other elements. Alternatively, positive entropy flows in some directions may be compensated by negative entropy flows in other directions. Another possibility is some form of enthalpy-entropy compensation, as mentioned above in connection with enzyme catalysis, so that coherent energy is conserved, with no entropy generated. The system could be arbitrarily far away from equilibrium, so long as, at some sufficiently macroscopic space-time of interest, overall balance is attained, and the net entropy production of the system either vanishes or reaches a minimum. The internal balance of entropy production means that the system maintains its organized heterogeneity or dynamic order. It is in turn dependent on energy flow being symmetrically coupled, and cyclically closed over the system as a whole. In other words, it depends on the validity of Onsager's reciprocity relationship in systems far from thermodynamic equilibrium, as argued above.

While most current thermodynamical analyses ignore space-time structure, the “thermodynamics of organized complexity” applying to living systems depends on space-time heterogeneity, which allows ‘free’ variation of microscopic states within macroscopic constraints. Thus, stability criteria which apply to the system as a whole need not be satisfied in individual space-time elements. Each element may be defined by the extent of equilibration according to the characteristic timescale of its constituent process(s), and so the local equilibrium assumption can still be satisfied. But each space-time element need not be in equilibrium with other elements.

Dynamic Closure and the Autonomy of Organisms

My formulation of the organism in terms of dynamic closure converges formally with several other representation of living organization: theoretical biologists Maturana and Varela's concept of life as autopoesis26 — a unitary, self-producing entity; theoretical chemists Eigen and Schuster's hypercycle27 of RNA-directed protein synthesis, in turn directing RNA polymerization; and theoretical biologist Kauffman's catalytic closure of polypeptide formation in the origin of life.28 However, none of the previous representations is based explicitly on physical, thermodynamic principles. The present formulation offers new and important physical insights into living systems relevant, not only to organisms, but also to ecosystems29 and sustainable economic systems,30 both of which are beyond the scope of this book. So, let us concentrate on organisms here.

The dynamic, energetic closure of the living system proposed here gives rise to a number of important consequences. First and foremost, it frees the organism from the immediate constraints of energy conservation — the first law — as well as the second law of thermodynamics, thus offering a solution to the enigma of the organism posed by Lord Kelvin and Schrödinger (see Chapter 5). There is always energy available within the system, for it is stored coherently, and ready for use, over all space-time domains. That is the basis of the autonomy of organisms. Organisms are never simply at the mercy of their environments on account of the coherent energy stored. More to the point, we don't have to eat constantly, leaving plenty of time for other useful, pleasurable activities.

The other consequences are that, the organism is exquisitely sensitive and free from mechanical constraints; and satisfies, at least, some of the basic conditions for quantum coherence.

Exquisite Sensitivity and Freedom

One of the hallmarks of the living system is that it is exquisitely sensitivity to specific, weak signals. As pointed out in Chapter 1, the eye can detect single photons falling on the retina, where the light sensitive cell sends out an action potential that represents a million-fold amplification of the energy in the photon. Similarly, a few molecules of pheromones in the air is sufficient to attract male insects to their mates. This sensitivity is characteristic of all parts of the system and is a consequence of the energy stored. No part of the system has to be pushed or pulled into action, nor be subjected to mechanical regulation and control. Instead, coordinated action of all the parts depends on rapid intercommunication throughout the system. The organism is a system of “excitable media”,31 — excitable cells and tissues poised to respond specifically and disproportionately to weak signals, because the large amount of energy stored everywhere automatically amplifies weak signals, often into macroscopic actions.

Do take note of the radically anti-mechanistic nature of organisms. Mechanical systems work by a hierarchy of controllers and the controlled that returns the systems to set points. One can recognize such mechanistic systems in the predominant institutions of our society. They are undemocratic and non-participatory. Bosses make decisions and workers work, and in between the top and the bottom are “line-managers’’ relaying the unidirectional “chain of command”. Organic systems, by contrast, are truly democratic, they work by intercommunication and total participation. Everyone works and pays attention to everyone else. Everyone is simultaneously boss and worker, choreography and dancer. Each is ultimately in control to the extent that she is sensitive and responsive. There are no predetermined set points to which the systems have to return.32 Instead, organisms live and develop from moment to moment, freely and spontaneously. All that is a consequence of the energy stored, aided and abetted by the special physicochemical properties of living matter, which will be dealt with in Chapters 11 and 12.

Remember that stored energy is coherent energy. The organism is, therefore, a highly coherent domain possessing a full range of coherence times and coherence volumes of energy storage. In the deal, it can be regarded as a quantum superposition of coherent space-time activities, each itself coherent, and coupled to the rest. We shall deal with the remarkable state of quantum coherence in Chapter 13.

Notes

1. See Ho (1996a, 1996b; 1997a).
2. See Morowitz (1968), also Chapter 5.
3. c.f. Harold (1986).
4. Ho (1995a).
5. Ho (1995a).
6. Breithaupt (1989); Ho (1993).
7. Zenk et al., 1996.
8. The arguments presented below have been developed in the course of several papers: Ho (1994; 1995b, 1996b, 1997a).
9. I thank Denbigh (personal communication) for this formulation.
10. See Denbigh (1951).
11. Rothschild et al. (1980).
12. Sewell (1991).
13. Westerhof and van Dam (1987).
14. See Berry et al. (1987) and references therein.
15. Rothschild et al. (1980).
16. Sewell (1991).
17. Ho (1995a).
18. Denbigh (1951) p. 3.
19. See Ho (1996b, 1997a).
20. See Denbigh (1951).
21. According to Guggenheim, cited in Denbigh (1951).
22. See Lumry (1991).
23. See Glansdorff and Prigogine (1967).
24. Chandresekhar (1961), cited in Koschmeider (1993).
25. Glansdorff and Prigogine (1967) p.159.
26. Maturana and Varela (1987).
27. Eigen and Schuster (1977).
28. Kauffmann (1993).
29. See Schneider and Kay (1994) for an important thermodynamic approach to ecosystems deriving from Eugene and Howard Odum, which has substantial connections with the perspective in this book.

30. See Ho (1997c) for a model of sustainable economic systems.

31. See Goodwin, (1994, 1995).

32. Saunders et al. (1997) have presented a mathematical model of homeostasis which maintains accurate concentrations of glucose in the blood, without setting fixed points. It accounts for the nonlinear responses of different kinds of diabetic patients to treatment.

CHAPTER 7

The Seventy-Three Octaves of Nature's Music

Reductionism Versus Integration

Western science is dominated by an analytical tradition that progressively separates and fragments that which for many of us, appears to be the seamless perfection that once was reality.1 Yet beneath this reductionistic tendency runs a strong countercurrent towards unity and integration, particularly within the past hundred or so years. I am motivated to write this book partly by a confluence of ideas which is drawing together the hitherto divergent streams of physics, chemistry and biology. I have a strong feeling that this is how we can begin to understand the organism, and in so doing, restore to some extent the sense of unity that once gave meaning to life.

The two great unifying concepts in physics and chemistry that are most relevant for understanding the organism are the laws of thermodynamics and the electromagnetic theory of light and matter. We have dealt with thermodynamics at some length in the preceding chapters, showing, among other things, how the organism differs from a thermodynamic engine and from a collection of unorganized molecules, and how a thermodynamics of organized complexity may be formulated which takes full account of the space-time differentiation of living system. In this and the Chapters following, we shall concentrate on the electromagnetic theory of light and matter, to show how electromagnetic energy animates and coordinates the living system. Electromagnetic theory also places both light and matter within the central conundrum of the wave particle duality of physical reality. This has far reaching implications on the nature of biological processes, indeed, of consciousness and free will. Before we launch into examining the relevance of electromagnetic energy for living systems and the deep philosophical issues raised by the quantum theory of reality, let us review classical electromagnetic theory as put forward by James Clerk Maxwell.

Electricity and Magnetism

The fundamental relationship between electricity and magnetism was discovered in the last century from observations on electromagnetic induction. Charges moving in a wire induce a magnetic field around the wire. Conversely, moving a conducting wire through a magnetic field induces a current to flow in the wire. These phenomena are brought together first by Michael Faraday, and then formalized in Maxwell's electromagnetic theory. Maxwell reasons that moving charges in the wire give rise to an electric field surrounding the wire, which induces a magnetic field. The magnetic field in turn, induces another electric field which induces a further magnetic field, and so on. Actually, the continuous mutual induction only occurs in an oscillating electrical circuit, or from a pair of oscillating charges. This is because, just as the charges have to be moving in order to induce a magnetic field, the magnetic field has to be changing to induce an electric field. Figure 7.1 gives the electric field lines in the neighbourhood of a pair of oscillating electrical charges. The spreading electric field lines are accompanied by magnetic field lines which are at right angles to them (not shown in the diagram). This gives rise to electromagnetic waves that propagate away from the oscillating charges.

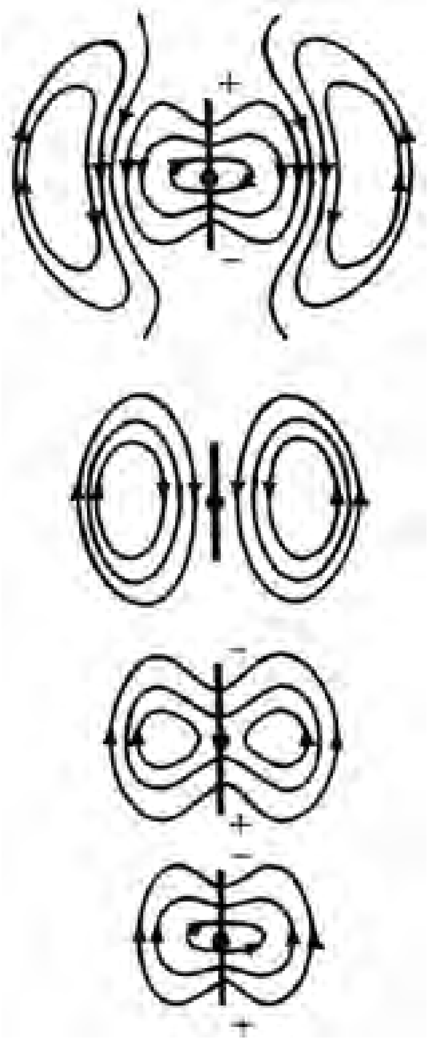

Figure 7.1 Electric field lines near a pair of oscillating charges. The lines have the same appearance in any plane containing the charges. The lines of the magnetic field induced are perpendicular to those of the electric field. The electric and magnetic fields propagate together as waves through space. The sequence is read from bottom to top.

In the course of this work, Maxwell made a second sensational discovery concerning light. The phenomenon of light has been studied from the time of the Greeks, and after many experiments, two competing theories were advanced. One maintains that light consists of tiny, invisible particles that move along rays, like a continuous series of minute shots fired from a gun. The other theory claims that light is a motion of waves propagating from a source. Both theories explain reflection, as from a mirror, and refraction, the change in the direction of light rays when passing from one medium to another, say from air to water. However, the diffraction of light — light bending around an obstacle — is more reasonably explained by a wave theory. But if it were a wave, there must be a medium through which it propagates through space. This medium was given the name of ether. From astronomical studies, the velocity of light had been determined in 1676 by the Danish astronomer Roemer to be about 186,000 miles per second. Maxwell found that the velocity of electromagnetic waves is also 186,000 miles per second. The identity of these figures, and the fact that both electromagnetic radiation and light were known to be wave motions immediately suggested to Maxwell that light must consist in the transverse undulations of the same medium (ether), which is the cause of electric and magnetic phenomena. In other words, light consists of a succession of electric and magnetic fields. With one stroke of genius, Maxwell had connected phenomena as widely disparate as cosmic radiation, sunlight, the microwave oven, radio and television broadcast, and all the uses of electricity. The electromagnetic spectrum starts from wavelengths of 10-14 m at one extreme to 108 m at the other, spanning a range of 1022. In terms of doublings, 1022 ≈ 273, or 73 octaves. This is the range of nature's music, of which we ourselves are part, and which we can tune into in its entirety, for better or for worse. The organism's own music — of a somewhat more restricted but still enormous range between 10-7 m and 108 and beyond — is both exquisite and subtle. With the present level of ‘man-made’ electromagnetic pollution of the environment, one might very well ask whether the organism's melody is in grave danger of being drowned out altogether.

The Electromagnetic Theory of Light and Matter

The 50 years straddling the end of the last century and the beginning of the present century must have been a heady era for western science. It began with Maxwell's theory that light is a form of electromagnetic radiation, essentially the same as that emitted by an oscillating electric circuit, only at much higher frequencies. This wave theory of light was soon thrown into doubt, however, by its failure to account for a number of observations, among which, is the so-called blackbody radiation emitted by all bodies at temperatures above absolute zero, and the photoelectric effect, the ejection of electrons from a metal surface when light of a definite threshold frequency is shone upon it. (Albert Einstein was awarded the Nobel prize for a theory of the photoelectric effect.) Both phenomena require the explanation offered by Max Planck: that the energy in electromagnetic radiation comes only in packets, or quanta, the size of which depends on the frequency, i.e.,

$$E = h\nu , \qquad (7.1)$$

where E is energy, h is Planck's constant, and v, the frequency. These quanta are absorbed, one by one, as though they were particles, resulting in the ejection of an equal number of electrons in the photoelectric effect:

$$h\nu = W + \tfrac{1}{2} m\upsilon^2 , \qquad (7.2)$$

where W represents the energy that the photon must possess in order to remove an electron from the metal and ½mv2 is the kinetic energy of the ejected electron, m being its mass, and v its velocity. W is a measure of how strongly the electrons are held in the metal. Thus, one must regard light not only as waves, but also as particles under some circumstances.

This dual character — the wave particle duality of light — was soon extended to matter. Particles of matter, under certain circumstances, will also exhibit wave properties. De Broglie proposed in 1924 the following relations:

$$\lambda = h/m\upsilon = h/p . \qquad (7.3)$$

where p is the momentum, mass x velocity, λ is the wave length, and v the frequency. This was experimentally confirmed several years later when diffraction patterns of electron waves by aluminium powder were obtained. The electron microscope, now routinely used in biology, is based on just this wave-like behaviour of accelerated electrons.

In parallel with these developments, the structure of the atom was also being defined. It was known in the 1930s that atoms consist of a nucleus containing positively charged particles, called protons, and neutral particles, called neutrons. As atoms are electrically neutral, there must be an equal number of negatively charged particles, or electrons present. These are found outside the nucleus. In order to account for the emission spectra of excited atoms, which were known since the 19th Century, and for the stability of atoms, Niels Bohr incorporated Planck's hypothesis to develop his theory of the atom. Our present picture is a later refinement of the Bohr atom, described in 1913.

Essentially, Bohr supposed that electrons are not found just anywhere outside the nucleus, but are confined to ‘shells’ for which the angular momentum is given by,

$$p = mvr = nh/2\pi \,, \tag{7.4}$$

where m and v are the mass and velocity of the electron, r is the radius of the shell, n is an integer, 1,2,3… Within these shells, the electrical attraction between the electron and the nucleus just balances the outward acceleration due to the circular motion of the electron, i.e.,

$$Ze^2/r^2 = mv^2/r \tag{7.5}$$

where Z is the atomic number (the number of protons in the nucleus), e is the electronic charge. Combining Eqs. (7.4) and (7.5) gives the permitted radii of successive shells, ie.,

$$r_n = \frac{n^2h^2}{4p^2me^2Z} \tag{7.6}$$

Thus, the radii of stable shells are proportional to n2, i.e., 12, 22, 32,… or 1, 4, 9… whereas the angular momentum, p, goes up in proportion as n, i.e., 1, 2, 3… (see Eq. (7.4)). The ground state is n = 1. It is closest to the nucleus and corresponds to a radius of r = 0.529 Å, which is called Bohr's radius. Successively higher energy levels are represented by n = 2, 3, 4,… and so on. The total energy of the electron at each level is the sum of the kinetic and potential energies, i.e.,

$$E = \tfrac{1}{2}mv^2 - Ze^2/r \qquad (7.7)$$

The negative sign associated with the potential energy (the second term on the right of the above equation) indicates an attractive interaction between the electron and the nucleus. From Eq. (7.5), we have,

$$mv^2 = Ze^2/r \qquad (7.8)$$

Substituting into Eq. (7.7) gives,

$$E = -Ze^2/2r = -\tfrac{1}{2}mv^2 \qquad (7.9)$$

Combining Eqs. (7.6) and (7.9) gives,

$$En = \frac{-2mp^2Z^2e^4}{n^2h^2} \qquad (7.10)$$

Thus, the energy levels go up in proportion as $-1, -\tfrac{1}{4}, -\tfrac{1}{9}$ and so on. At sufficiently large distances away, the energy is almost zero, and that is where the electron, being no longer attracted to the nucleus, becomes mobile. In other words, it becomes a little electric current until it drops into a vacant electron shell of another atom. Usually, only electrons in the outermost shell can be excited into mobility. The difference between the energy level at infinity and the outermost populated electron shell defines the ionizing potential of the atom (see Fig. 7.2).

The shells are successively filled with electrons as we proceed along the periodic table of the elements in accordance with four quantum numbers: n, l, ml and ms. The value of n gives the total energy of the electron; l, its angular momentum, ml determines the angle between the angular momentum of the electron and an

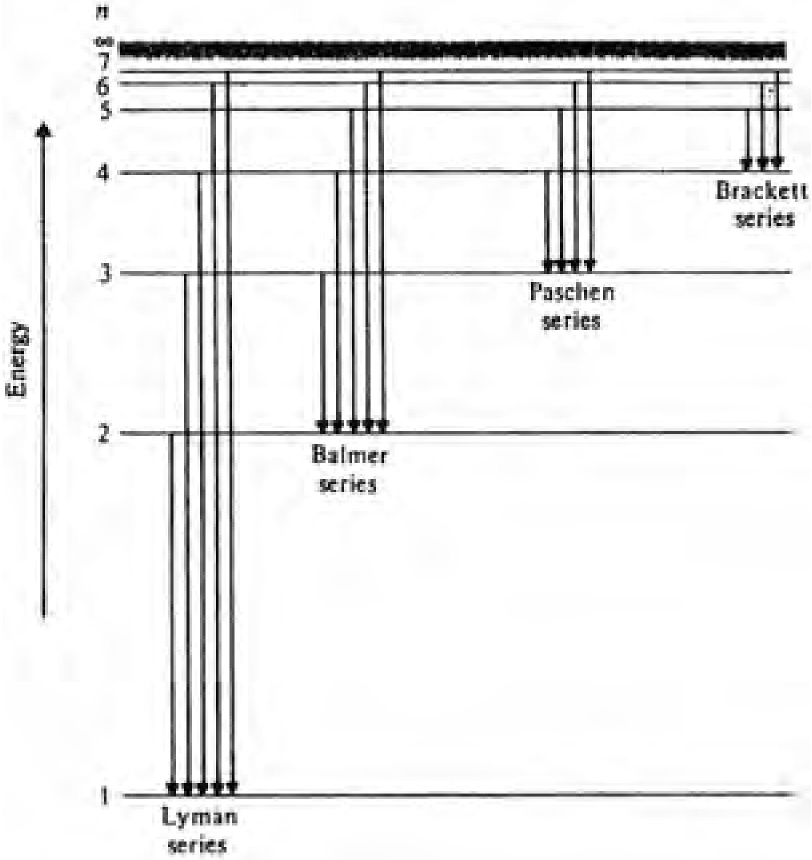

Figure 7.2 Energy levels of the electron shells in a hydrogen atom, and the different emission spectra obtained when excited electrons move from a higher to a lower energy shell.

external magnetic field, and hence the extent of the magnetic contribution to the total energy of the atom. All three numbers are quantized. Thus, n can take any integer from 1 to n, l can take any integer from 0 to n - 1, and ml can take any integer from - 1 through 0 to +1. In addition, each electron carries a spin, described by the fourth quantum number, ms, which can take values of +1/2 or -1/2, according to the two opposite directions of spin. The other major principle determining the distribution of electrons around an atom is Pauli's exclusion principle: no two electrons in an atom can exist in the same quantum state. That means each electron in a complex atom must have a different set of the four quantum numbers. The quantum number n defines the energy level of a shell, within which different subshells are specified by the quantum number l, and within each subshell, ml defines pairs of states, of opposite spins, or ms ± ½. In this way, the atomic structure of all the elements in the periodic table can be specified. The first shell (n = 1) has only one subshell containing the single electron of hydrogen. Adding another electron of opposite spin gives helium, which completes the first shell. The next element, lithium, has three electrons, so the additional one has to go to the l = 0 subshell of the n = 2 shell, which has two subshells, the other being l = 1, and so on.

A final word of caution about the picture of the atom presented above: it would be wrong to think of the electron as a minute charged particle orbiting the nucleus, possessing definite position and momentum. Quantum theory tells us, instead, it is more like a complex probability cloud distributed over the whole of the three-dimensional orbital, as consistent with the wave-particle duality of all matter (as well as light). We shall deal with the wave particle duality in more detail in Chapter 13.

Molecular and Intermolecular Forces

Atoms are most stable when their electron shells are closed or fully filled, and tend to gain or lose electrons in order to secure closed shells by joining with other atoms. That is the basis of chemical reactivity. Two principal binding mechanisms are known, ionic and covalent. In ionic bonds, electrons are effectively transferred from one atom to another, e.g.,

Na + Cl = Na+ + Cl-

The resulting positive and negative ions attract each other with an electrostatic force given by Coulomb's law:

$$F = Q_1 Q_2 / \epsilon r^2 , \qquad (7.11)$$

where F is the force; Q1, Q2 are the electric charges of the ions; r is the distance between them and e is the dielectric constant (or, to physicists, the permittivity) of the medium. The dielectric constant measures how effectively the medium shields the negative and positive charges from one another and hence reduces the force between them. Water, a major constituent of living systems, is an excellent dielectric because of its large effective dipole moment (see below). Water molecules can surround the ions in solution and effectively neutralize their charges.

In a covalent bond, which is the majority of chemical bonds in biological molecules, two atoms share one or more pairs of electrons in order to provide each with a closed outer electron shell. Molecules formed by covalent bonds, in which the centres of the positive and negative charges are separated, or do not exactly coincide, are said to be dipolar, and possess a dipole moment:

$$m = Qr\,, \qquad (7.12)$$

where Q is the charge separated and r the distance between them. Dipolar molecules interact electrostatically with one another, the magnitude of the force being proportional to 1/d4, where d is the distance separating the two molecules. The magnitude of the dipole moment in each case depends on the difference in electronegativity between the atoms involved in bonding. The order of electronegativity is, for example,

H < C < N < O

Water has a dipole moment of 1.85 debye (where 1 debye = 3.38 × 10-30 Coulomb meter). Polypeptide chains in the α-helical configuration have enormous dipole moments upwards of 500 debye, as the individual moments of the peptide bonds are all aligned. In the double helical DNA, on the other hand, the antiparallel arrangement of the two strands means that there is no net dipole moment, even though the single strands have their dipole moments due to the sugar-phosphate bonds in the backbone all aligned in the same direction 2 (see Fig. 7.3).

A third bonding mechanism is the hydrogen bond, which arises from dipole interactions in molecules where hydrogen is bonded to an electronegative atom such as oxygen, or nitrogen. This results

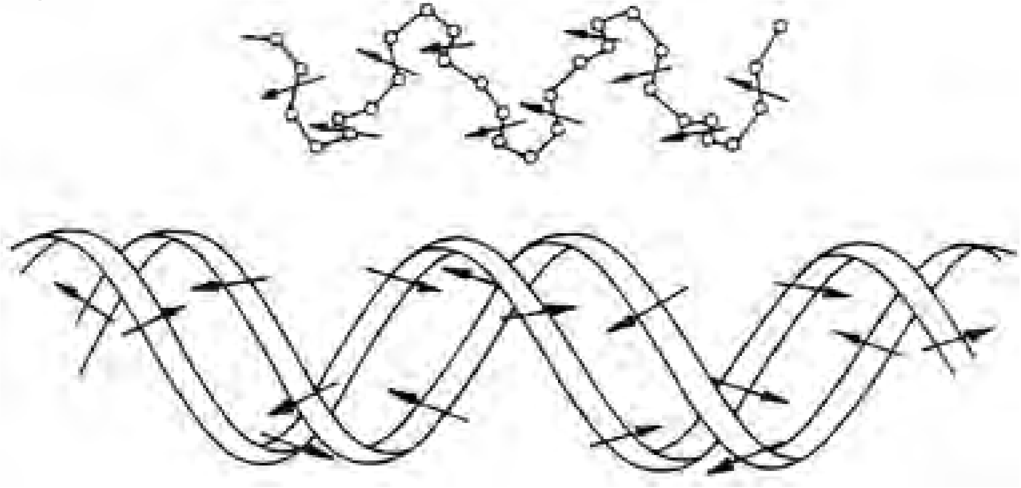

Figure 7.3 The dipole moments of the α-helix in a polypeptide (above) and a double helix of the DNA (below).3

in the bonding electrons being closer to the other atom than to the hydrogen, leaving a net positive charge on the non-bonded side of the hydrogen atom. The latter can thus be involved in bonding with other electronegative atoms, constituting the hydrogen bond.

Hydrogen bonds are responsible for stabilizing the α-helical secondary structure of the polypeptide chain, as well as the β-pleated sheet structures between polypeptide chains. They also stabilize various ‘conformations’ or folded tertiary and quarternary structures of polypeptides and proteins. The hydrogen bonds between base-pairs in the DNA double helix are responsible for the templating mechanism which ensures the faithful reproduction of the base sequence of the DNA molecule during replication.

Hydrogen bonds form between water molecules, giving rise to supramolecular aggregates or clusters. The clustering of water is a cooperative phenomenon, which means that forming one hydrogen immediately favours the formation of several other hydrogen bonds, and vice versa, breaking one bond leads to breaking up a whole cluster. Thus clusters are dynamic flickering networks with lifetimes of 10-11 to 10-10 s (see Fig. 7.4). This structure of water accounts for many of its unusual properties that are essential for supporting life. Treatises have been written on the structure of

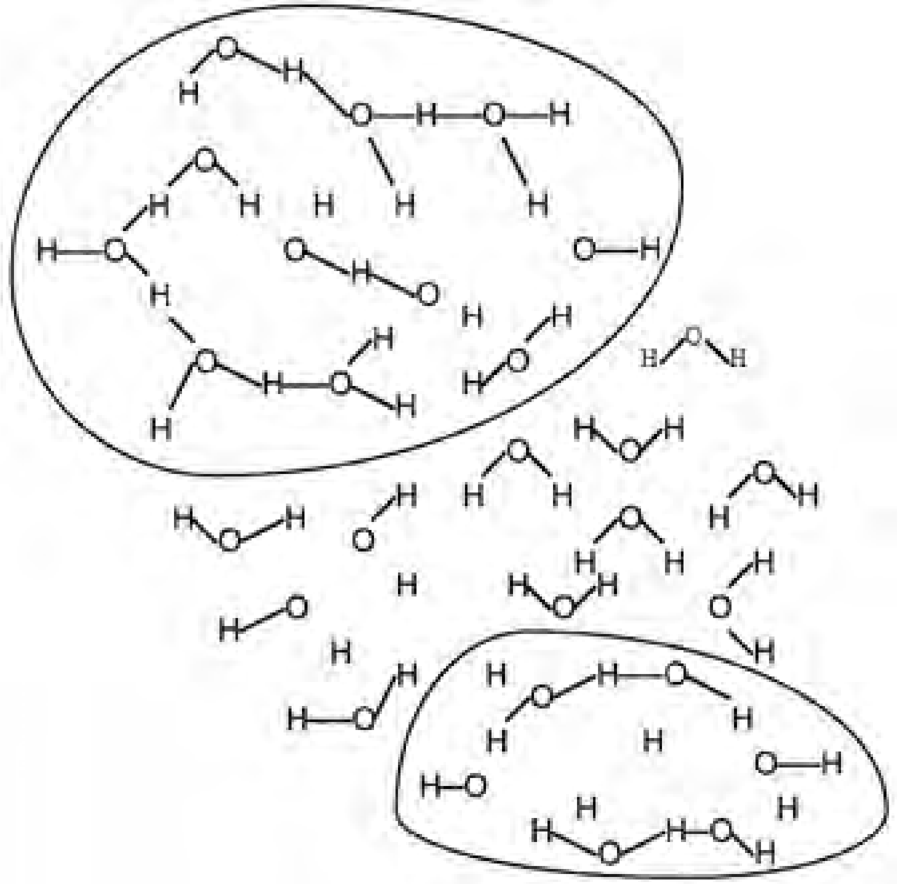

Figure 7.4 Supramolecular aggregates of water molecules formed by hydrogen bonding.4

water, and it is a much researched area in contemporary physical chemistry.5 Water makes up 70–80% of all organisms and active live is impossible without it, yet practically no mention of water is made in most biochemical textbooks. Enzyme chemists and cell biologists have recently come to recognize the importance of water for living organization and function.6 For example, no enzymes can work unless they are ‘‘plasticized” by water. The interaction between water bound to the macromolecule and free water are key determinants of enzyme catalysis, and of the self-assembly of cytoskeleton and cellular organelles and the extracellular matrices. You will see in Chapters 11 and 12 how water may play a major role in intercommunication within the organism.

Finally, nonpolar molecules, or molecules which are electrically neutral, are nonetheless subject to short range attraction by so-called dispersion or London forces. It turns out that these forces can be explained in terms of the instantaneous configuration of the field around the atom, creating temporary dipoles. One especially important form of bonding due to London forces in the living system is the hydrophobic (literally, water fearing) interaction, which accounts for why oil and water do not mix. Hydrophobic interaction is responsible for structuring lipid molecules into biological membranes, and for the folding of polypeptide chains into specific shapes or conformations so suited to their functioning.

Thus, electric and electromagnetic forces underlie all molecular and intermolecular interactions. The situation is best summarized in 1966 by the chemist, Peter J.W. Debye, after whom the unit of dipole moment is named:7

“Forty years ago discussions started about the interpretation of van der Waals' universal molecular attraction as a result of the Coulombic interactions of the electrical components of the molecule. The average electrical field around a molecule was analyzed, which led to its characterization by dipole-, quadrupole- and higher moments. The mutual orientation effect of such molecules was recognized as a reason for attraction. However, the higher the temperature, the smaller the effect of such an orientation has to become. So the conclusion to be drawn was that at high enough temperatures molecular attraction should vanish. This obviously was in contradiction to the experimental facts, and so the picture of molecules as rigid electrical structures was abandoned. Instead, their structure was recognized as deformable under the influence of an electric field: polarizability was introduced. The result was that, under the combined influence of the electrical field carried by one molecule and the polarization induced by it in its partner an additional potential energy emerges which is proportional to the square of the field and drives the molecules to each other. This still was not enough, since it made the mutual attraction of single atoms like neon or argon, around which the average field is zero, not understandable. The last difficulty was overcome by London when he recognized that the field important for the interaction should be taken as the instantaneous field. This introduced, unavoidably, quantum theory as a new and essential background …

“It was at this juncture that colloid chemistry entered into the field with the recognition that the attraction between colloid particles was the result of essentially the same molecular forces as those which determine, for instance, the heat of vaporization of a liquid. Calculations appeared concerning the van der Waals attraction between spheres and plates, giving rise to a series of brilliant experiments, which directly measured van der Waals' forces between plates at distances of the order of the wavelength of visible light, and which also demonstrated that indeed van der Waals' attraction is a result of the electromagnetic interaction of the molecular stray fields.

“However, the theory of molecular interaction had first to be refined. The molecular field introduced by London was an electrostatic field. Casimir recognized that its finite velocity of propagation had to be taken account of. One of the most characteristic results of this refinement is the calculation of van der Waals' attraction between two perfect mirrors. This attraction depends solely on two fundamental constants, Planck's quantum of action h and the light velocity c, and illustrates emphatically how intimate the relation is between van der Waals' universal attraction and the quantum fluctuations of the electromagnetic field.

“In recent times observations on the critical opalescence have also entered the field as appropriate for the measurement of molecular forces. In the vicinity of the critical point [for phase transitions, interactions are observed which are apparently of long-range character extending over distances of the order of the wavelength of visible light. …this can be understood as a result of long-range correlation, based on short-range interactions…”

The last paragraph in Debye's summary makes it clear that the same electromagnetic attractive forces are responsible for long range order during equilibrium phase transitions. We shall continue our exploration of how these same intermolecular forces may be involved in the organization of the living system in the next Chapter.

Notes

1. I have written on this myself, see Ho (1991, 1993, 1994a, 1994c).
2. see Pethig (1979).
3. From Pethig (1979) p. 50.
4. Modified from Chang (1990) p. 500.
5. See Franks (1985–90); Luzar and Chandler (1996). See Coats (1996) on the work of the remarkable Austrian scientist, Viktor Schauberger on the relationship between water and energy; also Endler and Schulte (1994) on water structure and homeopathy.
6. See Ho (1995a), Chapters 3 and 5.
7. Debye's Foreword to Chu (1967).

CHAPTER 8

Coherent Excitations of the Body Electric

Collective Versus Statistical Behaviour

The living system is a bewildering mass of organized heterogeneity. Its molecular diversity alone would defy description in terms of any statistical mechanisms involving large numbers of identical species. Within the confines of a volume less than 1 μm3 bound by a cell wall of woven complex proteins and carbohydrate fibres, each E. Coli bacterium has a single copy of a gigantic DNA molecule con-sisting of 106 non-periodic base-pairs (monomeric units) coding for the 103 different cellular proteins, the majority of which exists in no more than 100 copies, and a minority considerably less. Within the same volume, there are 103 species of RNAs, mostly represented by a few copies; and in addition, there are diverse membrane lipids, carbohydrates, fats and other metabolites, small molecular weight cofactors, and inorganic ions, all together in a minute, highly indented and wormholed droplet of water (precious water!). And yet, this vastly complicated mixture of molecules, within a volume smaller than a pin-head, behaves with such order and regularity that Schrödinger concludes it must be “guided by a ‘mechanism’ entirely different from the ‘probability mechanism’ of physics.”1 What is the mechanism that Schrödinger has in mind? It is none other than the collective behaviour of physical systems at low temperatures when molecular disorder — entropy — disappears and the systems no longer behave statistically but in accordance with dynamical laws. These collective behaviours are the subject matter of solid state physics, or condensed matter physics, as it is called nowadays.

Thus, the molecules in most physical matter have a high degree of uncoordinated, or random thermal motion; but when the temperature is lowered to beyond a critical level, all the molecules may condense into a collective state, and exhibit the unusual properties of superfluidity, when all the molecules of the system move as one, and superconductivity, in which electricity is conducted with zero resistance (see Fig. 8.1) by a perfectly coordinated arrangement of conducting electrons. Liquid helium, at temperatures close to absolute zero, is the first and only superfluid substance known thus far; and various pure metals and alloys are superconducting at liquid helium temperatures. Today, technology has progressed, at least, to superconducting materials which can work at 125 K.2

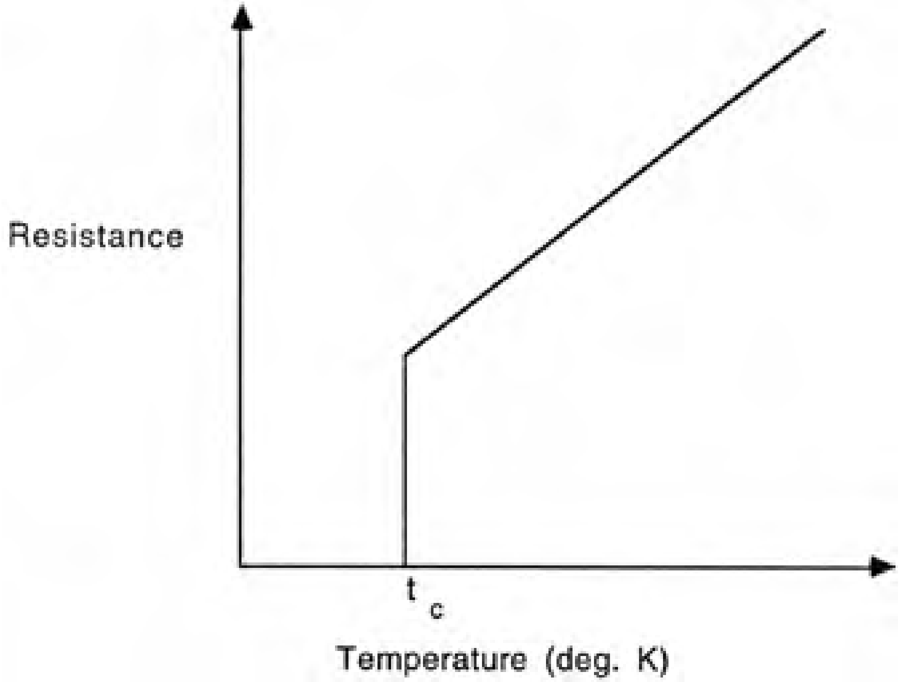

Figure 8.1 Graph of electrical resistance versus temperature in a superconductor.

Since Schrödinger's time, a number of people have suggested that collective modes of activity may arise in living systems which are analogous to those occurring at low temperatures in physical systems. But how can that take place, given that living systems typically work at around 300 K? A clue is supplied by the observation that non-equilibrium systems subject to energy flow can also undergo transitions to coherent, macroscopic activity, as we have seen in the Bénard-Rayleigh convection cells in Chapter 4.

Non-Equilibrium Transitions to Dynamic Order

The similarity between equilibrium and non-equilibrium phase transitions has been noticed by Hermann Haken.3 Both involve an abrupt change from a state of molecular chaos to one with macroscopic order — as though the different subsystems are cooperating with one another. Equilibrium phase transitions include the familiar solid-liquid, liquid-solid changes of states all pure substances as well as mixtures of substances undergo at characteristic temperatures; other less familiar examples are transitions to ferromagnetism, superfluidity and superconductivity at low enough temperatures. All of these involve a reduction in the number of possible microstates in the system ultimately to a single one. The type of order achieved is essentially static — being that of a perfect crystal. In the non-equilibrium system, however, the transition is always to a regime of dynamic order where the whole system is in coherent motion. Let us consider laser action, which is representative of non-equilibrium phase transitions.

In a solid state laser, specific atoms are embedded in a block of solid-state material (Fig. 8.2), at the ends of which are reflecting mirrors. Energy can be supplied in the form of light, electric current, or even heat, in order to excite the atoms. The atoms re-emit light tracks and those running in the axial direction will be reflected back and forth several times before going out. At low levels of energy pumping, the laser operates as an ordinary lamp, and the atoms emit randomly. As the pumping power is increased, a level is reached,

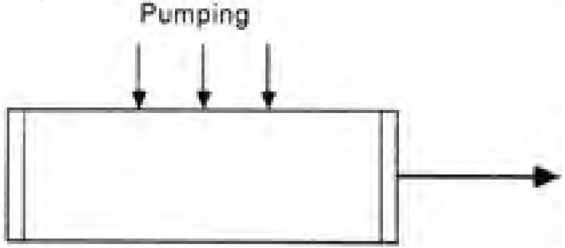

Figure 8.2 A solid state laser.

called the laser threshold, when all the atoms will oscillate in phase and emit together, sending out a giant wave train that is 106 times as long as that emitted by individual atoms.

In this example, as in the Bénard-Rayleigh convection cells (Chapter 4), we can clearly see the transition from a regime where individual molecular motions are random with respect to one another, and hence no macroscopic or long range order is present, to a regime where all the molecules are moving coherently, with the concomitant dramatic appearance of long range macroscopic order. In both systems, random energy is channeled into coherent modes of activity at phase transition. This is a characteristic feature of non-equilibrium phase transitions as it makes them stable to thermal noise or other perturbations, thus distinguishing them from equilibrium phase transitions such as superconductivity and ferromagnetism which are destroyed by thermal energies. The two non-equilibrium systems, however, differ in an important respect. The Bénard-Rayleigh convection cells result from a classical phase transition, which typically occurs over a long timescale. The solid state laser, by contrast, results from a quantum phase transition which takes place very rapidly. This difference in timescale, in my opinion, tips the balance in favour of biological organization being essentially a quantum rather than a classical phenomenon (see later).

Coherent Excitations of the Body Electric

Can it be that similar non-equilibrium phase transitions to macro-scopic dynamic order occur in living systems? And if so, what may be the sort of energy involved? Solid-state physicist Herbert Fröhlich4 points out that, as living organisms are made up predominantly of dielectric, or dipolar molecules packed rather densely together, they may indeed represent special solid state systems where electric and viscoelastic forces constantly interact. Under those conditions, metabolic pumping may result in a build-up to collective modes of vibration, rather like the laser action just described.

Specifically, thermal energies arising from metabolism can be retained in the system by the excitation of giant dipolar molecules such as proteins, nucleic acids and cellular membranes, which typically have an enormous electrical field of some 107 V/m across them. The excited molecules vibrate at various characteristic frequencies involving the coupling of electrical displacements and mechanical deformations. This eventually builds up into collective modes of both electromechanical oscillations (phonons, or sound waves) and electromagnetic radiations (photons) that extend over macroscopic distances within the organism and perhaps also outside the organism. Recently, the emission of electromagnetic radiation from coherent lattice vibrations in a solid-state semi-conductor has been experimentally demonstrated.5 The radiated mode arises also because oscillating charges always emit electromagnetic waves (see previous Chapter). Fröhlich refers to these collective modes of vibrations as ‘coherent excitations'. There are three kinds of coherent excitations. The first is a stable or metastable highly polarized state where the separation between positive and negative charges are maximum; this results from mode softening of interacting frequencies towards a collective frequency of 0. The second is a limit cycle oscillation, a limit cycle being a cycle which has a stable orbit that neither gets smaller nor bigger. The third mode arises when the energy supply exceeds a certain threshold, and oscillations of much higher frequencies occur. Each collective ‘mode’ can be a band of frequencies, with varying spatial extents, as consistent with the spatiotemporal structure of the living system. Nevertheless, the frequencies are coupled together so that random energy fed into any specific frequency can be communicated to other frequencies. This is reminiscent of non-equilibrium phase transitions in which random energy becomes channeled into macroscopic order as in the Bénard-Rayleigh convection cells and the solid state laser.

To what extent is Fröhlich's hypothesis tenable for living systems? In his model, energy is exchanged via a ‘heat-bath', which constitutes a quasi-equilibrium approximation. Does the living system with its highly differentiated space-time structure constitute a heat-bath for energy exchange. I have already argued in earlier Chapters that it does. The nested compartmental structure of the living system is both thermodynamically and kinetically optimized. Energy ‘‘thermalized” from one compartment is still retained within a larger encompassing compartment in which the energy is in a non-equilibrium distribution. The energy can effectively remain stored within the larger encompassing compartment. The “heat-bath” is no ordinary heat-bath working by incoherent jostling of energy quanta, but a highly efficient medium for energy conservation and mobilization, on account of its liquid crystalline structure (see Chapter 12).

What one must imagine is an incredible hive of activity at every level of magnification in the organism — of music being made using more than two-third of the 73 octaves of the electromagnetic spectrum — locally appearing as though completely chaotic, and yet perfectly coordinated as a whole. This exquisite music is played in endless variations subject to our changes of mood and physiology, each organism and species with its own repertoire. It would be wonderful if we could tune in and discover how some of us are made of Schubert, and others of Beethoven, or Bach…

Coherent excitations can account for many of the most characteristic properties of living organisms that I have drawn your attention to at the beginning of this book: long range order and coordination; rapid and efficient energy transfer, as well as extreme sensitivity to specific signals. An intuitive way to appreciate how coherence affects the rapidity and efficiency of energy transfer is to think of a boat race, where it is paramount for the oarsmen and oarswomen to row in phase; and similarly, in a line of construction workers moving a load, as the one passes the load, the next has to be in readiness to receive it, and so a certain phase relationship in their side-to-side movement has to be maintained. If the rhythm (phase relationship) is broken in either case, much of the energy would be lost and the work would be slower and less efficient. Songs and dances may have their origin primarily in the pleasurable sensations arising from the entrainment of one's own internal rhythms to those of the collective, they also serve to mobilize the energies of the collective in an efficient and coherent way.

How would coherent excitations make the system sensitive to specific, weak signals? Such a weak signal will be received by the system only when the system is ‘in tune’ — rather like a very sensitive radio receiver, which can resonate to the signal. Furthermore, a small signal will be greatly amplified for it will not only affect one molecule, but because many other molecules are in the same state of readiness, they too, will be affected in the same way, and the signal is correspondingly multiplied as many times as there are molecules responding to it. A situation where this is most dramatically illustrated is the crystallization of a solid from a supersaturated or supercooled solution: a tiny speck of dust would nucleate the process all at once in the entire volume of fluid. Something analogous may be involved in the functioning of living systems, except that there would be much more specificity. Whole populations of cells may be poised in critical states so that a small, specific signal would set off a train of macroscopic, coherent reactions.

The idea of coherence is so foreign to most western-trained scientists that there has been a lot of resistance to it from the mainstream. It is easy to blame this just on the reductionistic tendencies of western science for which cooperativity and coherence are anathemas. There is a more immediate aspect that comes from the practice and methodology of biological sciences itself, which is all of a piece with the conceptual framework.

‘The Cataclysmic Violence of Homogenization’

As biochemists brought up in the early 1960s, we were schooled to the idea that the cell is, to all intents and purposes, a bag of concentrated solution of enzymes and metabolites mixed up at random, save for a few organelles and intracellular membranes. Enzymes enable reactants to overcome often very large activation energy barriers so that the reaction can take place at physiological temperatures. In other words, enzymes are the reason why organisms can work isothermally, at physiological temperatures (and pressures), and they and other proteins are reponsible for all the energy transformation that take place in living organisms. On account of their important role in metabolism, much of biochemistry is given over to the study of the mechanism of enzyme action in vitro, (that is, isolated and outside of the cell), although how they actually work in vivo, within the cell, is still a mystery. As good biochemists then, we found this ‘mixed-upness’ — which we supposed to exist inside the cell — an irritating obstacle to analysis and something one has to overcome. The standard procedure is to grind up the organisms or cells to a pulp, or ‘homogenate’ — in which everything is well and truly mixed up, and then proceed to separate out the different ‘fractions’ according to size or density, to extract, and to purify until we have stripped off all contaminating ‘impurities’ surrounding the enzyme of interest, to end up triumphantly with a single species ‘purified to homogeneity'. This precious preparation is then dissolved in pure, double- distilled, deionized water to which ultrapure substrates are added, and the long process of ‘characterization’ of enzyme activity begins, based on the notion of random diffusion of enzyme and substrate molecules through the aqueous solution. All this, of course, goes to reinforce the idea we begin with — that the cell is a bag of enzymes and metabolites dissolved in solution.

As electron microscopy and other specific staining techniques became available, it gradually dawned on us that the cell is highly structured. Nowadays, the generally accepted picture of a cell is quite sophisticated. It is bound by the cell membrane — a double layer of lipids with dissolved proteins, which is supported by and attached to the membrane skeleton composed of a basketwork of contractile filamentous proteins lying immediately underneath it. The membrane skeleton, in turn, connects with the three-dimensional network of various fibrous proteins collectively known as the cytoskeleton, which links up the inside of the cell like a system of telegraph wires terminating onto the membrane of the nucleus. In the nucleus, the chromosomes (organized complexes of DNA and proteins) are anchored directly to the inside of the nuclear membrane. The nuclear membrane and the cell membrane are also in communication via concentric stacks of membranous vesicles, the Golgi apparatus — with special secretory functions, and the endoplasmic reticulum — a system of three-dimensional canals and spaces believed to be involved in intracellular transport and occupying a large proportion of the cell volume. A substantial proportion of the intracellular volume is also taken up by organelles (diminutive organs) such as the mitochrondria, where simple carbohydrates are oxidized to CO2 and H2O with the generation of ATP, and ribosomes on which polypeptide chains are synthesized. Finally, what is left over is the cytosol (or 'soluble' cytoplasm).

Despite this much improved picture, most biochemists still believe that organelles are made up of structural proteins which are relatively inert, and that the 'functional' proteins or enzymes are dissolved at random in the cytosol, where the main metabolic theatre of the cell is being played out. There are a few possible exceptions, of course, such as the proteins involved in oxidative and photosynthetic phosphorylation located inside the mitochondria and the chloroplasts respectively, which make ATP for the cell.

However, a number of different lines of investigation began to suggest that perhaps no protein is dispersed at random in solution, but practically all of them are organized in specific complexes with other proteins, and furthermore, a high proportion of the cell water may actually be bound or structured on the enormous amount of surfaces formed by proteins within the cell.6 What would cause proteins and other molecules such as lipids to aggregate into complexes? How could cellular organization ever get started?

Intermolecular complexes giving rise to the submicroscopic cellular organization are usually attributed to steric factors, due to the precise shape specific to the different molecular species involved. And textbooks in biochemistry are filled with beautiful diagrams to illustrate this static, ‘lock and key’ principle of ‘recognition’ between enzymes and their respective subtrates, between signal molecules and their respective receptor proteins, as well as between different species of proteins. Yet, everything in quantum theory tells us that molecules never stand still, and proteins are no exception. Indeed, the most mobile proteins are enzymes which generally have great specificities for their substrates, and the most mobile parts of the antibody molecules are precisely those containing the recognition sites for corresponding antigens.7 These observations are difficult to reconcile with the lock and key model.

What is more likely to be responsible for intermolecular complexes in cellular organization is the universal electromagnetic attractive forces between molecules that we have considered in the last Chapter. This also provides an extremely potent source of specificity and selectivity within the electromagnetic spectrum itself. Even a small fraction of the 73 octaves would far out-perform any specificity in shapes of molecules. It is already well-known that molecules with the same intrinsic frequency of vibration not only resonate over long distances, and hence undergo coherent excitations, but can also attract one another over long distances (see Chapter 3). Furthermore, frequency specificity is generally accurate to within 1%.8 Some biochemists studying enzyme kinetics are coming around to the idea that coherent excitations may have more relevance for enzyme action than the conventional ‘lock and key’ principle. 9 Cosic has provided fascinating evidence for his claim that resonance recognition is general to all protein-protein and protein-nucleic acid interactions (see Chapter 3). He found that groups of proteins with the same function or recognize each other share the same periodicity in electronic potential along the polypeptide chain, which is related to the frequency of electromagnetic radiation they absorb, and by implication, emit, when electrons are conducted along the polypeptide. If he is right, it would change the whole complexion of biomolecular engineering.

The importance of recognition by resonance cannot be over- emphasized. Thermal energies, particularly at equilibrium, possess no information; whereas an excitation of a specific frequency at a temperature where no other excitation of the same energy exists — in a system far from equilibrium — not only has just the requisite information to do the work, but the inherent power to do it as well.10 It provides the motive force of attraction between appropriate reactive species and enables energy exchange to take place. Thus, 'information' is not something separate from energy and organization.

The most general considerations tell us that structuring, or 'self-assembly' is the most probable, one might say, inevitable consequence of the range of intermolecular forces that exists. So part of the 'negentropy' that Schrödinger was searching for is simply located in the chemistry of matter, which physicists have a tendency to forget. For example, bilayer lipid membranes form spontaneously at water/water interfaces to maximize intermolecular hydrophobic and hydrophilic interactions, with the nonpolar side chains of the lipid molecules buried within the membrane, and the polar groups exposed to the water on either side. In dilute solution, these bilayer lipid membranes form vesicles that many chemists have looked upon as the precursors to cells.11 Hydrophobic interactions between lipids and proteins, similarly, account for the localization of many proteins in membranes. Hydrogen bonding is responsible for stabilizing supramolecular aggregates, as we have seen, resulting in complexes in which the dipole moments of individual bonds are either vectorially oriented in the same direction, as in α-helical contractile proteins, or they can form antiparallel complexes in which their dipole moments neutralize each other. Intramolecular and intermolecular hydrogen bonding are also involved in stabilizing protein conformations. Spontaneous self-assembly of supramolecular structures such as microtubules and actin filaments (both important constituents of the cytoskeleton) may involve such oriented dipole interactions and can indeed take place outside the living organism.12 Similarly, the adsorption of water molecules onto the surfaces of membranes and proteins is to be expected on the basis of polar interactions, just as much as water is excluded from the interior of proteins on the basis of hydrophobic interactions between the nonpolar amino acids. The tendency of water to form hydrogen bonded networks is also important in the self-assembly of complex proteins.

For many years now, the physiologist, James Clegg,13 among others, has championed the idea that the cell is meticulously ordered down to the detail of individual protein molecules. It is, in effect, a solid state system.14 Within this system, each protein has its own community of other proteins and small molecular cofactors and metabolites. In other words, an enzyme in isolation — stripped of its rich 'cytosociology'15 —is merely a shadow of its real identity. Its natural highly diverse neighbourhood is the key to its efficient functioning. This is a fascinating microcosm of the same principle of diversity that operates in ecology (see Chapter 4), and perhaps also in societies. (My own experience is that multicultural societies make for a richer social and intellectual life and are more vibrant than closed monolithic communities.)

Clegg summarizes an impression conglomerate of evidence suggesting that even the cytosol is filled with a dense network of actin-like protein strands — the "microtrabecular lattice11 — connecting all cytoplasmic structures and to which practically all of the enzymes and many of the substrates are attached (see Fig. 8.3). The surface area of the microtrabecular lattice is estimated to be about 50 times that of the cell, and its volume about 50% that of the cytosol. Thus, very little of the macromolecular constituents of the cytosol is dissolved in the cell water. On the contrary, up to 60% of the cell water itself might be bound, or structured by the surfaces of the microtrabecular lattice, the intracellular membranes, and the cytoskeleton.

A similarly dense, solid matrix fills the nucleus.16 All the DNA packaging and replication enzymes, transcription factors, growth factors and other proteins regulating gene expression, are bound to an insoluble "nuclear scaffold", which gives a precise spatial organization to the chromosomes, to DNA replication, transcription and RNA processing.

Inspite of, or perhaps because of its highly condensed nature, the whole cell is extremely dynamic, the connections between the

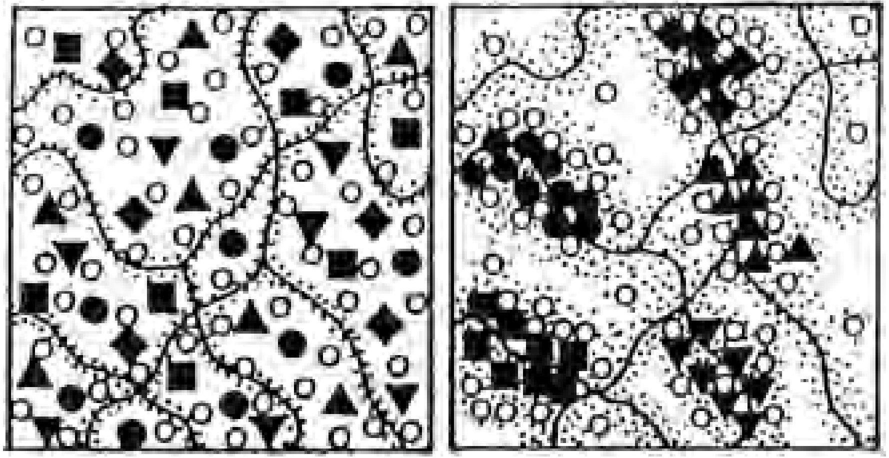

Figure 8.3 Diagrammatic representation of the soluble (left) versus solid state (right) description of the cytosol. Wavy lines are cytoskeletal elements of the microtrabecular lattice (see text), dots are structured water molecules, open circles are metabolites and cofactors, and filled symbols are macromolecules.17

parts as well as the configurations of the cytoskeleton, the membranes and the chromosomes, all, can all be remodelled within minutes subject to appropriate signals from the environment, such as the presence of food and light, hormones, growth factors, mechanical or electrical stimulation. The entire cell acts as a coherent whole, so information or disturbance to one part propagates promptly to all other parts.

Biomechanist and cell biologist, Donald Ingber proposed the idea that the whole cell and its “solid state” of membrane skeleton, cytoskeleton, microtrabecular lattice and nuclear scaffold, form an interconnected “tensegrity” system18 that always deforms or changes as a whole when local stresses and strains are experienced. (The term “tensegrity” originates with architect-polymath Fuller,19 who suggested a method of building from the principle of tensional integrity — ‘‘a structural system based on dynamic interaction of discontinuous compression elements connected by continuous tension cables”.)

Evidence for the detailed organization of the entire cell comes from many sources, including high voltage electronmic roscopy on unfixed cells, measurements of physical parameters of the cell water relative to ‘free’ water outside the cell, and various cytological manipulations to establish the location of cellular enzymes and substrates. I shall describe several kinds of experiments, which seem to me the most decisive.

The first involves centrifuging live cells such as the unicellular alga, Euglena, with a cell wall thick enough to withstand the centrifugal forces. After centrifuging at 100,000 xg (where g is the earth's gravitation force) for 1 h — a standard condition used in the laboratory — the cellular constituents became stratified according to density (see Fig. 8.4), which is as expected. What is unexpected, is that the soluble phase near the top was found to contain no macromolecules at all: sensitive tests for the presence of a long list of enzymes, proteins, and nucleic acids were all negative. This contrasts with results from the routine fractionation of the homogenate — obtained by pulping the cell under generally very disruptive conditions — in which the 100,000 g supernatant or soluble phase contains many proteins, enzymes as well as nucleic acids. Centrifuging other intact, live cells gave essentially identical results: no macromolecules were found in free solution. As remarked by

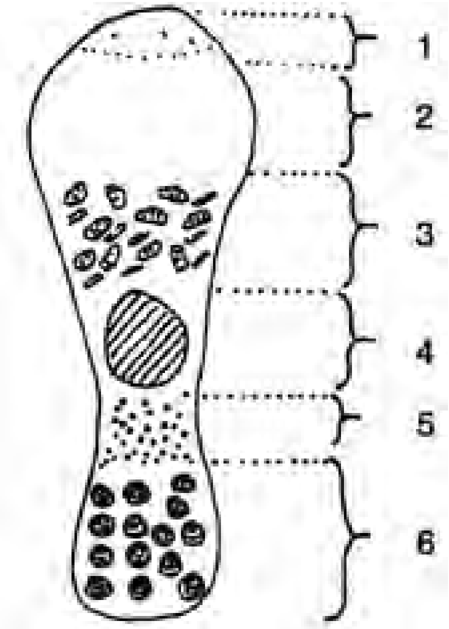

Figure 8.4 Diagram of the layers of cellular structures formed after centrifugation of Euglena. 1. Fat droplets, 2. Soluble supernatant, 3. Mitochondria, Golgi apparatus and endoplasmic reticulum, 4. Nucleus, 5. Ribosomes, 6. Starch grains.20

one advocate of the organized, solid state cell,"…the empirical fact that a given molecule appears primarily in the ‘soluble’ fraction may divert attention from the cataclysmic violence of the most gentle homogenization procedure."21

In another kind of experiment, holes were created in the cell membrane by mild treatments with Dextran sulphate (a complex sulphated carbohydrate) in such a way that the cells remained alive, so that when the Dextran sulphate was removed, the cells recovered and resealed themselves. The holes were big enough to allow subtrates and metabolites to go through. Yet, 60 mins. After treatment, the metabolic rate of the permeabilized cells was only decreased by about 50% compared to untreated controls, suggesting that not only are the macromolecular enzymes bound within the cell, but many of the small molecular weight metabolic intermediates and cofactors may also be bound or compartmentalized so that they cannot diffuse freely away from the cell even when the membrane is full of holes.

Evidence that the entire cell behaves as one tensegrity system is elegantly provided by Donald Ingber and his coworkers, who devised ingenious ways to apply precise, local mechanical forces to the cell membrane.22 For example, when specific receptor-proteins in the membrane, individually tagged with a microscopic ferromagnet, are twisted in a magnetic field, the entire cell stiffens up to resist the twisting. These and other experiments have shown that mechanical signals are involved in regulating many cellular functions.

In the highly structured, interconnected cell, electrial dipole interactions will be just as important as mechanical interactions in determining metabolic function. That is because mechanical deformations automatically generate electrical disturbances, and vice versa. The cell is a electromechanical continuum, as Fröhlich has envisaged. (In fact, the entire organism works in the same way, as you will see in a later Chapter.) Successive enzymes in a metabolic pathway will move in a correlated fashion, as will enzyme and substrate, which account for the characteristically rapid and efficient catalysis in living organisms that has yet to be achieved in the test-tube. Structured water layers on membranes and macromolecular surfaces transmit dipole interactions, and oscillations and proton currents can flow in the layer of water molecules immediately next to membranes and macromolecules. Local proton currents along the membrane are thought to be involved in both oxidative and photosynthetic phosphorylation.23 The flow of protons has been experimentally demonstrated in artificial monolayers of membrane phospholipids,24 as well as along hydrated proteins and nucleic acids.25

All the evidence in support of the organized, interconnected cell comes from investigative methods designed to minimize disruption to endogenous cellular structure, so that the cell can be observed as nearly as possible in its natural functioning state. It is a general approach towards the ideal of 'non-invasiveness', where the cell or organism is allowed to tell its own story, as it were, to inform us of its internal processes as it is living and developing. As techniques become more and more sensitive and precise, we can for the first time, analyse without destroying. The picture we obtain is far from atomistic and reductionist. On the contrary, we begin to appreciate the full extent of the cooperativity and coherence of living processes right down to the scale of individual molecules.

'Life is a Little Electric Current'

So far, we have been concentrating on dynamic electromechanical forces. Should we not also consider other types of forces and flows such as heat conduction and convection, and diffusion of molecules? We have dealt at some length in previous chapters on why heat transfer cannot be the major form of energy transduction in living systems. This does not preclude thermal energies being used for work, as in a coherent system, even thermal energies can be channeled into coherent excitations. Convective effects are unlikely because of the predominant "solid state" nature of the cell. Passive diffusion is simply too slow, particularly as there is very little direct free path for diffusion in the densely packed cell. On the contrary, there is now good evidence that intracellular water channels exist for transport, in much the way that the circulatory system works in the whole organism.26 Heat conduction also cannot play a substantial role, as dielectric activities will quickly come into effect. Besides, living systems are, to all intent and purposes, isothermal (see Chapter 5). Warm-blooded animals, in particular, keep their body temperature constant, and even have special mechanisms to generate heat in order to keep the body above ambient temperatures; heat is not an inevitable byproduct of metabolic reactions.

All the more reason, then, for concentrating on electric and electrodynamical forces. Significantly, even the energy that first enters into the biosphere is electromagnetic radiation. Living systems may indeed be electrodynamical through and through. As Szent-Györgi27 writes,

“…life is driven by nothing else but electrons, by the energy given off by these electrons while cascading down from the high level to which they have been boosted up by photons. An electron going around is a little current. What drives life is thus a little electric current.”

If the organism is like a solid state system, as has been suggested more and more by cell biologists and biochemists, then many of the basic principles of condensed matter physics will have applications in the living system. The important difference we should always bear in mind, is that the living system has a much more complex and dynamic organization that somehow empowers it to metabolize, grow, differentiate and maintain its individuality and vibrant wholeness, something no physical system can yet do. Nevertheless, let us explore what condensed matter physics can tell us about the living system.

I have given reasons why intermolecular dipole attractive forces may be responsible for much of the cellular organization. We also know that mobile charges, carried by both electrons and protons, play a major role in energy transduction and transformation in the living system. Szent-Györgi among others, has noted that the sites of primary energy transduction, the cell membranes, are closely analogous to the pn junction, a semiconductor device which facilitates the separation of positive and negative charges, and is capable of generating an electric current when excited by energy in the form of heat or light.28 It is the basis of the solar cell, which will yet prove to be the cleanest and most efficient source of renewable energy, if that is the lesson we can obviously learn from nature.

In common with these semiconductor devices, various biological membranes and artificially constituted phospholipid membranes also exhibit thermoelectric, photoelectric and piezoelectric effects due respectively to heat, light and mechanical pressure.29 In addition, many semiconductor devices are luminescent, producing light as the result of heating, electrical pumping (the basis of electroluminescent devices which are used in producing laser light) and also stimulation, by light.30 We shall see later that organisms do indeed exhibit luminescence, which can be stimulated in a highly nonlinear way with heat and light. The basis for generating electricity is the electron in the outermost orbital of atoms and molecules — the valency electron — which becomes mobile on absorbing enough energy (corresponding to the ionizing potential). Mobile electrons constitute electric currents, which can flow to the nearest neighbouring molecule, or it can go further afield.

Actually, the electric currents in living organisms flow simultaneously in two opposite directions because there are both positive and negative charges. The molecule from which the electron is lost — the electron donor — acquires a net positive charge, or hole, in the language of solid state physics; while the molecule to which the electron goes — the electron acceptor — acquires a negative charge. Both positive and negative charges can propagate further by moving down an electronic cascade represented schematically in Fig. 8.5.

The molecules, D, A1, A2 and A3 with decreasing electronic energy levels, sit in close juxtaposition in a biological membrane (as is the situation in the electron transport chain involved in photosynthetic and oxidative phosphorylation). The molecule D, on being excited, donates a valency electron from its ground level to the excited level of A1. The hole in D is filled by an electron coming from another molecule on the outside to the left, while the excited electron progresses through the excited levels of the molecules, A2 and then

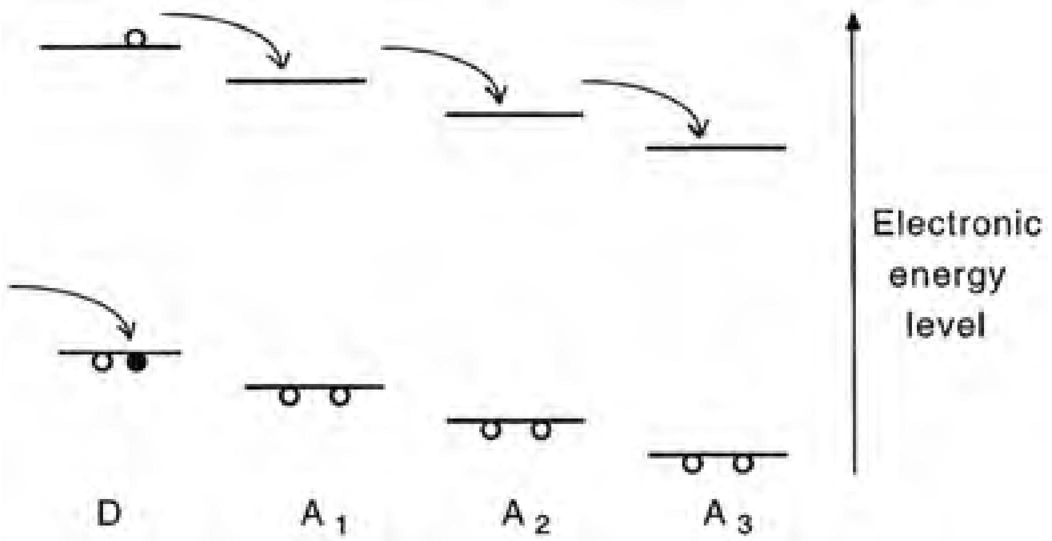

Figure 8.5 The electronic cascade. The molecule D is the electron donor, while A1, A2 and A3 are the electron acceptors.

A3. Positive and negative charges propagate in opposite directions. Electric currents are thus readily generated by such mechanisms of charge separation and transfer which are quite rapid, as they involve no substantial molecular reorganization or chemical change that would otherwise have slowed the process down and caused a lot of unnecessary disturbance.

The first step in photosynthesis is just this kind of charge separation and vectorial transfer: a chlorophyll molecule, on absorbing a photon, donates an electron to an acceptor which flows down the electron transport chain, generating ATP on the way. The ‘hole’ left in the donor chlorophyll is filled by an electron from another donor on the outside, i.e., water. The ‘hole’ in this case becomes a proton, which is also mobile, and it can either accumulate in the bulk phase on one side of the membrane to create a gradient for the transport of metabolites and ions across the membrane, or it can flow in a local circuit along the surface of the membrane. Some people believe that in addition to electricity or the flow of electrons, substantial proticity also flows in the living system in the form of protons.31 Many microorganisms move by means of a single flagellum. That of bacteria such as Salmonella can rotate up to 100 times a second, being driven by a molecular motor attached to its base and embedded in the cell membrane. The motor is entirely powered by the flow of protons (proticity) from one side of the cell membrane to the other. In some marine organisms and organisms living in an alkaline medium, the motor can even be powered by a transmembrane flux of sodium ions.32 Many other ionic currents flow through the cell and out into the extracellular medium.33

What I have given above is an oversimplified description of electron transport. In particular, I have been speaking of the outer electrons (again!) as though they were particles localized to the orbit of one molecule or another, which is far from the case.

This is perhaps the place to make a more general point about the scourge of the language we have to communicate in. If we let this language dominate our thoughts, as some philosophers seem to believe we must, it will surely reduce us all to idiots who take everything literally. Actually, we never take anything just literally, even in ordinary discourse. If we did, we would not only lose all the meaning behind the words, but also the unfathomable magic. It is just the same in science. As in any attempt to understand, we use whatever tools we have at our disposal to help us think, and good scientific theories are just that — a superior kind of tools for thought. They help us clear our minds in order to receive the greater mysteries of nature. It is in this spirit that I am engaging this whole narrative, the purpose of which is to arrive at an intimate understanding of nature beyond theories and beyond words…

To return to quantum theory, it tells us that the wave-function of each electron (a function of its position weighted by complex numbers, or in standard quantum mechanical language, “a complex-valued function of position”) is actually delocalized or spread out over the whole system, so that the electron has a finite probability of being found anywhere within the system. Furthermore, because the molecules are packed so closely together in a solid state system, the energy levels are no longer discrete, as they are subject, not only to attractive forces from the nuclei, but also repulsive forces from other electrons, as well as vibrations in the molecular lattice.

The result is that the outermost electrons are not in discrete energy levels associated with particular atoms or molecules, as they would be in a very dilute ideal gas; but instead, occupy broad bands (of quantum states) delocalized over the lattice, separated in energy by regions where there are no energy levels at all. The lowest energy band involved in bonding — the valency band — is filled with electrons. The next higher band is the conduction band to which electrons can be promoted by absorbing energy. Electrons in this band are the mobile charge carriers. Between the highest valency level and the lowest conduction level lies the band gap, corresponding to the threshold of energy which has to be absorbed to promote a valency electron to a conducting one (see Fig. 8.6).

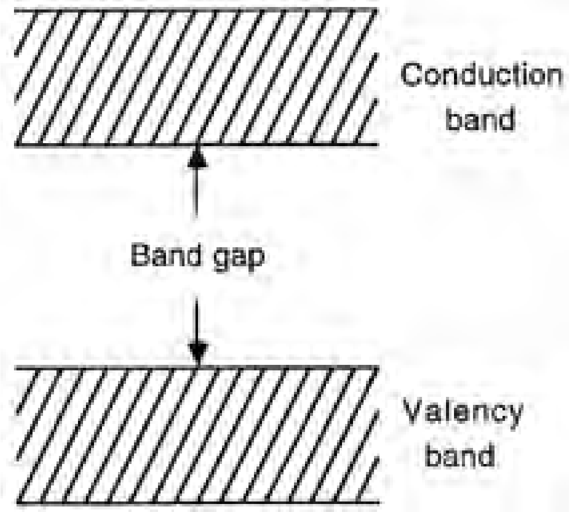

Figure 8.6 The electronic energy bands of the solid state semi-conductor

During conduction in a solid state system, similarly, we should not be thinking of charged particles moving one by one around an obstacle course as in a pin-ball machine. Instead, the wave nature of the electron comes into play, so that the charges seem to move much more readily around obstacles than if they were particles, and all kinds of tunnelling effects can occur (literally going ‘under’ an energy barrier instead of over it), making it necessary to bring in a quantum mechanical description. Readers should bear this in mind whenever and wherever I describe electrons or photons flowing from one place to another. They should automatically add the phrase, ‘quantum mechanically', and imagine all that the phrase entails. We shall venture further into the strange world of quantum theory in Chapters 13 and 15.

The chloroplast and mitochondrial cell membranes are the major sites of charge separation and charge transfer in the living system. There may, however, be other sites associated with macromolecules and macromolecular complexes made up of proteins and nucleic acids. Both theoretical calculations and experimental observations suggest that these too, behave like semiconducting devices when excited by electrical, mechanical or light energy, and can conduct both electricity and proticity.34 Well-documented quantum tunnelling effects have already been mentioned in connection with the electron and proton transfer proteins in Chapter 3. Some scientists have already suggested the possibility that a protoneural network links up the entire cell, which is involved in regulating and coordinating cellular function.35

The Body Electric Flows and Flows

Thus, electrons (and protons) can flow between molecules and along macromolecules. These local flows are organized or coordinated into spatially more and more extended flow patterns, the entire concerted action of which ultimately empowers the organism to be alive. Each flow pattern catenates with larger patterns in space and time, and constitutes part of a macroscopic flow which can often be observed in living systems. Indeed, large electric fields are found in tissues and whole organisms,36 which change with injury and anaesthesia. And all developing and regenerating systems have been found to drive steady currents of the order of 1 to 1000 mA/cm2 through themselves.37

This organized flow of electric currents — meticulously coordinated from the very short range intermolecular charge transfers right up through many intermediate levels of space and time to currents traversing the whole organism — constitutes what I have referred to elsewhere as the coherent electrodynamical field that underlies living organization.38 We shall see how electric currents can flow throughout the body in Chapters 11 and 12.

Let us briefly revisit Fröhlich's idea of coherent excitation in the light of what has been described so far. I have said that coherent excitations can give rise to long range order in the living system, as well as rapid and efficient energy transfer. We can now see in a more concrete way how that may be achieved. Fröhlich39 proposes that biological membranes, by virtue of their dipolar structure and the existence of large transmembrane potentials, are particularly prone to such collective vibrational modes. This could explain how the absorption of a single photon, or the binding of a single chemical ligand by a receptor protein could excite hundreds of membrane bound molecules simultaneously as a first step in the amplification of an external signal arriving on the cell membrane. For all these proteins embedded in the membrane will be vibrating in phase, and hence be in the same state of readiness for receiving the signal. Oscillations in the lipid network could induce simultaneous conformational changes of various proteins anchored in the membrane, and via the interconnected membrane skeleton and cytoskeleton, influence the entire cell.40

Proteins are themselves giant dipoles which can undergo coherent dipole excitations over the entire molecule. And in an array of densely- packed giant dipoles such as muscle and the cytoskeleton, the excitation could be coherent throughout the array, accounting for the kind of long-range coordination of molecular machines that is required in biological functioning. For example, McClare41 suggests that the internal energy of ATP, initially released as a bond-vibration, is resonantly transferred to a pair of oscillators in the actomyosin complex in muscle where the energy is held jointly by the excited pair (excimer) as an ‘exciton'. As the exciton is converted into mechanical work, its energy is conducted along the length of the actin filament to activate another ATP molecule, and so on. In that way, the excitation energy is propagated rapidly along the muscle fibre, giving rise to long range coordination of muscle activity. Since then, theoretical and numerical studies suggest that binding energy from ATP could be resonantly transferred via the hydrogen bond to the peptide bond which in turn interacts with the polypeptide lattice nonlinearly to generate a propagating packet of energy, the 'soliton'.42 Solitons are stable mechanical deformations of the polypeptide chain, in particular, in the α-helical configuration, which can propagate without change in shape or size. Their stability is connected with the competition between two processes: the tendency of the excitation to spread by resonance interaction as against the tendency for the excitation to stay localized due to the mechanical 'softness' or floppiness of the polypeptide chain.41 (See Chapter 3 for evidence suggesting resonant energy transfer in muscle contraction.)

Similarly, RNA and especially DNA are also enormous dielectric molecules that can sustain coherent excited modes which may have important biological functions,44 say, in determining which genes are transcribed or translated. We can begin to see how a coherent electro-dynamical field makes the organism a vibrant, sensitive whole. In the next two Chapters, we shall review some observations and experimental results which lend support to the idea of coherence in living systems, and also present deep challenges to our understanding of the coherent regime in living organisms.

Notes

1. Schrödinger (1944) p. 79.
2. Batlogg (1991).
3. Haken (1977).
4. Fröhlich (1968, 1980). There has been a lot of debate as to whether the 'Fröhlich state' is realizable in practice in living systems. It is thus of great interest that theoretical physicist Duffield (1988) has recently proved that under the most general conditions of energy pumping, the Fröhlich state is globally, asymptotically stable. That means systems will tend to evolve towards that state, and more over, stay in that state and return to it on being perturbed. See also Wu (1994).
5. Dekorsky et al. (1995).

6. See Clegg (1984, 1992) and references therein; also Ingber (1993).
7. See Williams (1980) p. 336-8.
8. McClare (1972) points out that the precision in a chemical system can be greater than 10-2%.
9. See Somogyi et al. (1984);
10. c.f. McClare (1972) p. 571.
11. See Morowitz (1992), for example.
12. See Meggs (1990) and references therein.
13. Clegg (1984, 1992).
14. See Cope (1975) and references therein; also Porter (1984).
15. See Welch and Clegg (1987).
16. See Ingber (1993) and references therein.
17. From Clegg (1984) p. R134.
18. See Ingber (1993).
19. Fuller (1975).
20. Redrawn after Clegg (1984).
21. McConkey (1982).
22. Wang et al. (1993).
23. See Kell et al. (1983); Williams (1980).
24. Sakurai and Kawamura (1987).
25. See Pethig (1979) Chapter 9. Also Pethig (1992); Scott (1984).
26. See Wheatley and Clegg (1991).
27. Szent-Györgi (1960) p. 21–22.
28. Thornton (1967).
29. See Tien, (1989).
30. See Thorton (1967).
31. See Kell et al. (1983); Williams (1980).
32. See Meister et al. (1989).
33. See Nucitelli (1988) and references therein.
34. See Pethig (1979) Chapter 9. Also Pethig (1992, 1994); Scott (1984).
35. Welch and Berry (1985).
36. Becker (1990).
37. See Nucitelli (1988) and references therein.
38. Ho et al. (1992c).
39. Fröhlich, 1980.
40. Welch et al. (1982); see also Ingber, 1993.
41. McClare, 1972.
42. See Scott (1984); and Davydov (1982).
43. See Davydov (1977); also Davydov (1985, 1994). I am grateful to Prof. Davydov for sending me his papers.
44. Li et al. (1983).

CHAPTER 9

How Coherent is the Organism?

How to Detect Coherence

There is as yet no direct evidence that organisms are coherent, although there are clear signs of that from many areas of biological research. Part of the difficulty is that we do not yet know what we should be looking for. In the absence of an appropriate theory, there are no acceptable criteria which would satisfy the skeptic as to whether a given observation constitutes evidence for coherence. Another difficulty is that until quite recently, there have been very few experiments set up to observe the living system, as Schrödinger has already pointed out. Biology has a long tradition of fixing, pinning, clamping, pressing, pulping, homogenizing, extracting and fractionating; all of which gave rise to, and reinforced, a static, atomistic view of the organism. It is no wonder that most biologists still find it difficult to even think of coherence, let alone contemplate how to go about investigating it. And it is with the increasing use of sensitive, relatively non-invasive techniques that we shall begin to recognize the animated, sensitive and coherent whole that is the organism.

There are a number of general observational criteria that a coherent system ought to exhibit. I have mentioned them at the beginning of this book, and have dealt with some of them in the earlier Chapters: long range order, rapidity and efficiency of energy transduction and transfer, extreme sensitivity to external cues, and symmetrical coupling of energy transfer. Another criterion is fluctuationless (noiseless) functioning of entire populations of molecules. The basis for all those criteria are in the physics of quantum coherence, which will be considered in Chapter 13. For now, I shall review relevant observations, starting with those in ‘conventional’ biology and progressing to the more unconventional areas.

Evidence from ‘Conventional’ Biology

One class of evidence for coherence is the existence of biological rhythms as such, together with the observation that these rhythms are frequently coupled to one another.1 For example, respiratory and heart-beat frequencies show harmonic relationships, and sub-harmonic resonance has been observed in metabolic oscillations, where entrainment of the metabolic rhythm is obtained to driving frequencies which are approximately integer (i.e., whole number) multiples of the fundamental frequency.2 As mentioned in Chapter 6, at least two genes in Drosophila reveal coupling relationships over 7 orders of magnitudes of time periods linking the circadian to the wing-beat rhythm of the male fly's love-song.3 These couplings are possible because there is a precise coordination of each mode of activity in the living system.

Insect flight muscle oscillates synchronously with great rapidity, supporting wing beat periods of milliseconds. Many organisms, tissues and cells show spontaneous oscillatory contractile activities that are coherent over large spatial domains with periods ranging from 10-1s to minutes.4 Similarly, spontaneous oscillations in membrane potentials can occur in a variety of ‘non-excitable’ cells as well as in cells traditionally regarded as excitable — the neurons — and these oscillations range in periods from 10-3s to minutes, involving entire cells, tissues or organs (such as the heart, stomach and the intestine). Recent applications of supersensitive SQUID magnetometers to monitor electrical activities of the brain have revealed an astonishing repertoire of rapid coherent changes (in milliseconds) which sweep over large areas of the brain.5 These findings, and the observations on synchronous firing patterns (40 to 60 hz) in widely separated areas of the brain recorded by conventional electroencephlogram (eeg) techniques, are compelling neurobiologists to consider mechanisms which can account for long-range coherence.6 They suggest that the synchronization of the oscillatory response in spatially separate regions may serve as ‘a mechanism for the extraction and representation of global and coherent features of a pattern’, and for ‘establishing cell assemblies that are characterized by the phase and frequency of their coherent oscillations’.

It has recently been proven mathematically that synchronization is the rule in any population of oscillators where each oscillator interacts with every other via the absorption of the energy of oscillation, thus resulting in phase locking (that means they are oscillating together in phase).7 The coupling between oscillators is fully symmetric, i.e., they have completely reciprocal influences on one another, and once they have locked together, they cannot be unlocked. There are many examples of phase-locked synchronously oscillating systems. They include the large populations of fireflies flashing together in perfect time in various parts of Southeast Asia, and crickets chirping in unison. Within the body, the pacemaker cells of the heart, the networks of neurons in the circadian pacemaker of the hippocampus, and the insulin-secreting cells of the pancreas, all show synchronized electrical activities. During an olfactory experience, oscillations in the olfactory bulb in the brain are in phase with the rhythmic movement of the lungs.8 Synchronization is only one among an infinite possibility of coupled phase relationships. In locomotion, for example, the movement of the limbs bear a definite phase relationship to one another, which are simultaneously reflected in the electrical activities of the motor centre in the brain.9 All this suggests that individual rhythms are precisely timed and phase discernment may be extremely accurate.10

This accurate, noiseless functioning applies all the way down to the molecular level. It has been claimed that muscle contraction occurs in definite quantal steps which are synchronous, at least, over entire muscle fibres, and measurements with high speed ultrasensitive instrumentation show that the contraction is essentially fluctuationless (as characteristic of a coherent quantum field (see Chapter 13).11 High speed synchotron X-ray diffraction measurements confirm that crystal-like supramolecular order is maintained in isometrically contracting muscle.12 Similarly, the beating of cilia in mussels and other organisms takes place in synchronized quantal steps with little or no fluctuations.13 These are examples of collective behaviour which are completely anti-statistical.

It appears that physiologists and cell biologists alike have taken these remarkable phenomena for granted. There has been no adequate explanation for the precision of the synchronization which occurs right down to the molecular level, nor for the accuracy of phase coupling relationships.

Sensitivity of Organisms to Weak Electromagnetic Fields

As consistent with the view, developed in the last Chapter, that the flow of electricity at all levels may be responsible for living organization, cells and organisms are extremely sensitive to external electric and magnetic fields. Research on the sensitivity of living organisms to weak electromagnetic fields began in the former Soviet Union early this century, and it is only since the 1970s that similar research has been carried out in the west. Soviet biologist Presman reports many observations suggesting that diverse organisms are sensitive to electromagnetic fields of extremely low intensities — of magnitudes that are similar to those occurring in nature.14 These natural electromagnetic sources, such as the earth's magnetic field, provide information for navigation and growth in a wide variety of organisms; while major biological rhythms are closely attuned to the natural electromagnetic rhythms of the earth, which are in turn tied to periodic variations in solar and lunar activities.

In many cases (described below), the sensitivity of the organisms to electromagnetic fields is such that organisms must be detecting fields below the energy level of thermal noise (~ kT). This points to the existence of amplifying mechanisms in the organisms receiving the information (and acting on it). Specifically, the living system itself must also be organized by intrinsic electrodynamical fields, capable of receiving, amplifying, and possibly transmitting electromagnetic information in a wide range of frequencies — rather like an extraordinarily efficient and sensitive, and extremely broadband radio receiver and transmitter, and much as Fröhlich has suggested (see previous Chapter).

It is known, for example, that nerve cells growing in culture will respond to electric fields as weak as 0.1 V/cm — six orders of magnitude below the potential difference that exists across the cell membrane, which is about 105V/cm. Similarly, skin cells from fish and other animals, and bone cells tend to move towards either the positive or the negative pole in a steady electric field while orienting their long axis at right angles to the field.15 Orientation is accompanied by shape changes which involve the remodelling of the cytoskeleton. Polymerization of cytoskeletal elements possessing dipole moments will proceed much faster in an electric field,16 which in turn suggests that many, if not all, processes involving changes in cell shape and reorganizations of the cytoskeleton may be associated with endogenous electric fields.

Very weak pulsing electromagnetic fields induce transcription of genes in cultured salivary gland cells of the fruitfly after 15 to 45 mins of exposure.17 Both static and oscillating magnetic fields have been found to affect biological functions, including enhanced cell growth in culture by superhigh frequency fields, inhibition of growth of normal and malignant human cells by low frequency fields, the enhancement of collagen and proteoglycan synthesis in cultured chondrogenic cells treated with inflammatory bacterial lipopolysaccharides, as well as the rapid healing of non-united fractures in patients exposed to pulsed electromagnetic fields.18 Combinations of static and extremely low frequency oscillating fields, as well as microwave frequency fields modulated by much lower frequencies, cause changes in Ca^{2+} efflux in cells and tissues, and affect the permeability of artificial membrane lipid vesicles to drugs.19

Despite the wealth of experimental data, perhaps half of the findings are disputed by others. It has become an especially controversial area because of the increasing public concern over the possible harmful effects of all forms of 'man-made' electromagnetic fields20 associated with high tension power lines, power generators, electrical installations, and various radio-frequency communication devices in the environment. They cover a wide range of frequencies and the intensities are at least five orders of magnitude above natural sources. If our bodies are organized by exquisite electronic music, then these artificial electromagnetic fields may well constitute the worst kind of cacophonous interference. A recent report suggests that mice genetically engineered to be prone to cancers of the white blood cells developed more than twice as many cancers when exposed to microwave pulses similar to those experienced by cellphone users.21

One major difficulty in reproducing experimental observations is that the biological effects may depend crucially on the precise physiological state or the developmental stage of the systems concerned. We experimented on populations of synchronously-developing Drosophila embryos whose development can be timed to within a minute. Our results showed that brief exposures of early embryos to weak, static magnetic fields, during the period when cryptic pattern determination processes are taking place, resulted in a high proportion of characteristic body pattern abnormalities in the larvae hatching 24 hours later (see Fig. 9.1). The energies of the magnetic fields causing such abnormalities are several orders of magnitude below the thermal threshold — the energy of individual molecules due to random fluctuations characteristic of the temperature (see Chapter 2, p. 19). That means there can be no significant effect unless there is a high degree of cooperativity or coherence among the movements of the molecules involved in the pattern determination processes reacting to the external fields. This would be like the fluctuationless movements of muscle proteins or the cilia of mussels mentioned earlier. You will see further evidence for the coherence of molecular movements within the living organism later in this Chapter.

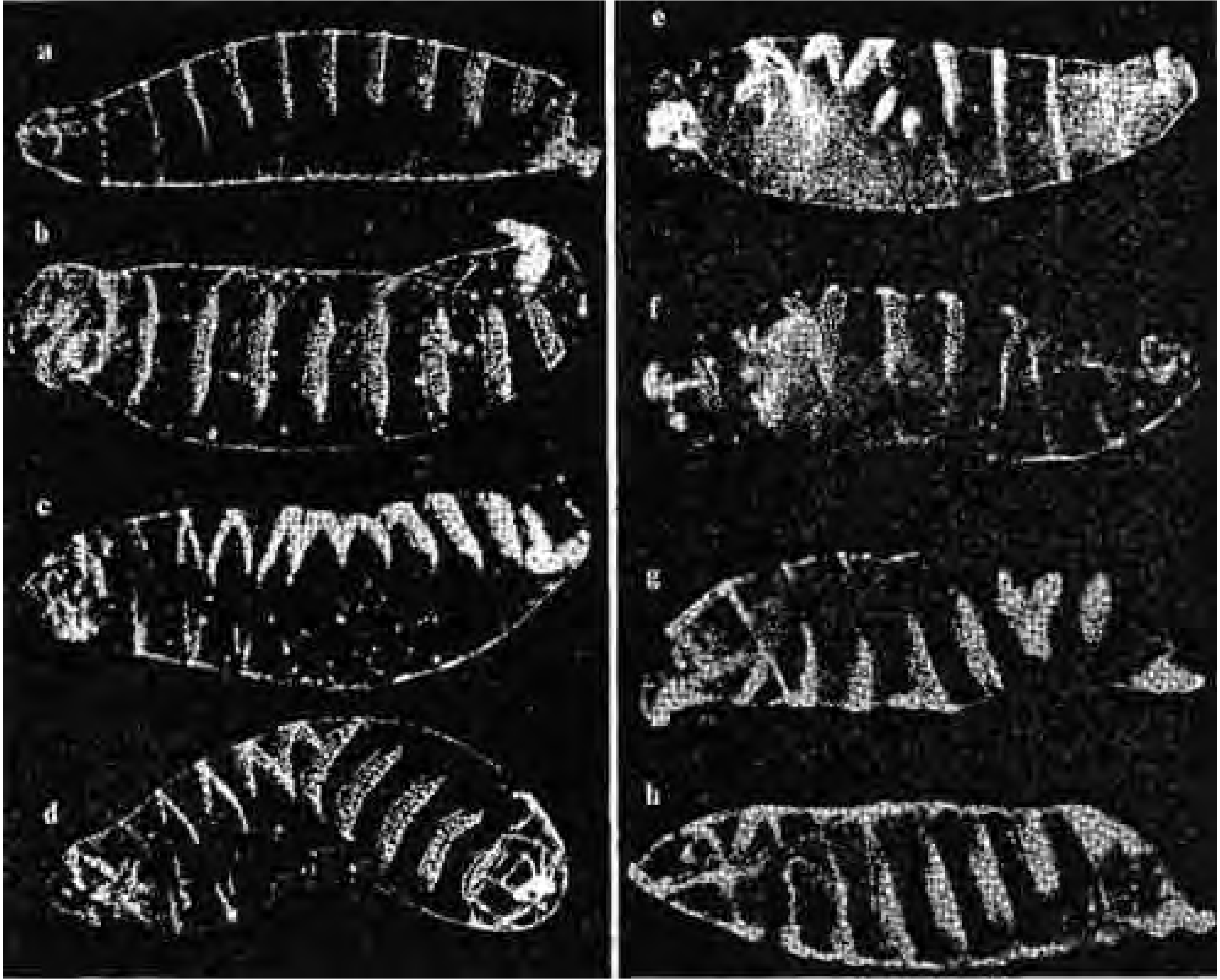

Figure 9.1 Tranformed segmentation patterns in Drosophila larvae hatching from embryos exposed to weak static magnetic fields. The consecutive segmental pattern in the normal (a) is converted to various helical or twisted configurations, (b) to (f).22

The sensitivity of organisms to electromagnetic fields has its basis in the electric and electromagnetic nature of all molecular and intermolecular interactions, and in the ubiquitous charge separation and transfer mechanisms involved in primary energy transductions (see previous Chapter). High sensitivity to electromagnetic fields would be predicted if a ‘‘protoneural network” — a flow of positively charged protons — is involved in regulating and coordinating biological activities, not only at the level of the cell but also at the level of whole organisms (see Chapters 11 and 12). Our body is generally electrically insulated by a covering of skin, but high frequency alternating electromagnetic fields can penetrate owing to the breakdown of successive dielectric shielding layers as frequency increases.23 Furthermore, biological effects can result simply from the build-up of the shielding charges themselves, because that disturbs the electrical balance of the body, which is essentially an electrodynamical continuum (as you will see in Chapters 11 and 12). So it would be a mistake to underestimate the possible effects of electric fields. The body is, however, not at all insulated against magnetic fields. Let us examine the effects of magnetic fields in more detail.

How Magnetic Fields Can Affect Organisms

Organisms are in general much more sensitive to weak magnetic fields than to weak electric fields. What is the basis of the organism's sensitivity to magnetic fields, often with infinitesimal amounts of energy? Time-varying magnetic fields will induce electric currents in the organism (see Chapter 7), which may be quite effective as organisms are transparent to magnetic fields. Static magnetic fields, however, cannot induce currents, so how do they produce biological effects? Static fields affect organisms by their ability to orientate magnetically sensitive molecules and by deflecting endogenous electrical currents.

Some molecules can orientate themselves in a magnetic field. As a consequence of their spin (see Chapter 7), electrons behave as though they are tiny bar magnets each possessing a magnetic moment, called the Bohr magneton, and is of the order of 10-23J/Tesla, where the Tesla is a unit of magnetic flux density. As mentioned in Chapter 7, the electrons in an atom are arranged in shells about a central nucleus. A complete shell always contains pairs of electrons with opposite spins. Hence a complete shell has no net magnetic moment. In elements such as iron, cobalt and nickel, there are unpaired electrons, not only in the outer shell but also in an inner shell. In iron, for instance, five of the six electrons in the $n = 3$, $l = 2$ subshell have parallel spins, so that iron atoms have appreciable magnetic moments and are referred to as ferromagnetic. In an unmagnetised sample, the material is characterized by the presence of domains or groups of atoms with all their magnetic moments aligned, but the alignment of different domains are random with respect to one another. On being magnetized, the domains progressively align themselves until all are oriented in the same direction in parallel with the external field. Beyond a certain temperature, the atomic alignment within the domains disappears, and a ferromagnetic material becomes merely paramagnetic (see below). The temperature at which this happens, the Curie point, is 770°C for iron.

Atoms and molecules with fewer unpaired electrons do not form domains at ordinary temperatures, and are simply paramagnetic or diamagnetic. A paramagnetic atom or molecule has a permanent dipole moment, and therefore tends to align itself in the direction of the applied field. A diamagnetic atom or molecule, on the other hand, has no permanent dipole moment; the applied magnetic field affects the orbital motion of the electron in such a way as to produce a magnetic moment in the opposite direction to the applied magnetic field. Pure samples of membrane lipids are known to align themselves in an external magnetic field. It has been suggested that the effect of static magnetic fields on the permeability of lipid vesicles to drugs is due to the summation of diamagnetic alignments of large molecular aggregates to the external field occurring near membrane phase transition temperatures.24 Proteins are also diamagnetic due to the planar peptide bonds, which, in the α-helix, in particular, are all aligned along the axis, and this will give rise to substantial diamagnetic anisotropy.25 Similar anisotropies exists for other regular arrangements of the peptide bond as well as for nucleic acids. Thus, chloroplasts, the outer segment of the rods in the retina (see Chapter 1), photosynthetic algae and bacteria, the purple membrane of the latter and nucleic acids have all been successfully oriented in moderately strong static magnetic fields of several kilogauss.

Could orientation effects be involved in the changes in segmentation pattern of Drosophila larvae exposed to static magnetic fields? This would not have been due to the simple diamagnetic orientation effects, as the magnetic fields used were far too weak (90 gauss at most). The normal pattern consists of separate consecutive segments, whereas a continuous helical pattern tends to appear in larvae exposed to the magnetic fields (see Fig. 9.1). It must be stressed that this transformed morphology, which I call ‘twisted’, is highly unusual. I have worked with Drosophila for 15 years and never have I, or anybody else come across this kind of body pattern under a variety of pertubations such as heat or cold shocks or exposure to chemicals or solvents.26 Similarly, tens of thousands of genetic mutants of body pattern have been isolated by Drosophila geneticists over the years and until then, not a single one of them has the “twisted’ morphology. This indicates that the static magnetic field exerts its effect in a most specific way, perhaps via orientation of membrane components during a dynamic instability.

Membrane lipids (as well as proteins) belong to a large class of molecules called liquid crystals which can exist in a number of mesophases, i.e., phases that are neither solid nor liquid, but in between (see Chapter 11). These mesophases are characterized by long range order in which all the molecules are arranged in a quasi-crystalline arrays. Liquid crystals are relatively easily aligned with electric and magnetic fields, which is the basis of the liquid crystal display screens that come with watches, calculators, computers and computer games.27 The cell membrane is also known to play a major role in pattern determination.28 One way in which an external static magnetic field can affect body pattern is if a global alignment of membrane components — as a kind of phase transition brought on normally by an endogenous electric field — is involved in pattern determination. In that case, a weak external magnetic field could easily interact with the endogenous electric field to alter the alignment on a global scale. Significantly, alternating magnetic fields invariably fail to produce the ‘twisted’ morphology although other abnormalities are produced in large numbers.29 This is consistent with the hypothesis that static fields act via the alignment of macroscopic arrays of molecules, which alternating fields are unable to achieve. We shall look at pattern determination and liquid crystal alignment in more detail in the next Chapter.

A second orientation effect is Larmor precession30 due to oscillating paramagnetic atoms or ions. When exposed to a magnetic field, the oscillating magnetic atom tries to align itself, and in so doing, precesses like a top around the direction of the magnetic field; the frequency of precession (the Larmor frequency) being proportional to the intensity of the magnetic field. This is an instance where the effect could appear at low field intensities and disappear at high intensities. Thus, the effect of electromagnetic fields on the movement of the paramagnetic ion, Ca^{2+}, across the cell membrane exhibits both frequency and intensity windows.31

Another orientation phenomenon is well documented in chemical reactions.32 This occurs in reactions where a covalent bond is split, resulting in ‘free radicals’ each carrying a single unpaired electron. As the covalent bond was formed originally by two electrons of opposite, or antiparallel, spins, the radicals resulting from the reaction will also have antiparallel spins, and is said to be in the singlet state, as both states have the same energy level,

$R1 - \downarrow\uparrow - R2 - R1\downarrow + R2\uparrow$.

However, it often happens that the separated radicals may have parallel spins (that is, with the arrows in the separated radicals pointing in the same direction), referred to as the triplet state, as they will populate three different energy levels in a magnetic field (see below). This would cause them to drift apart so that one or the other of the radicals can react with another molecule yielding another pair of free radicals also with parallel spins. In order for covalent bonds to form, the spins must be antiparallel, and in the absence of an external magnetic field, all the triplet states have approximately the same energies so the relative spins soon change and bond formation will take place.

In the presence of an external field, however, the spins align themselves so that they are both either in the direction of the field, T_{+1}, or in the opposite direction, T_{-1}, or they can be perpendicular in the field direction, To. These different orientation states no longer have the same energies, and as the magnetic field increases in intensity, they diverge more and more (see Fig. 9.2). The T±1 states become trapped, and can no longer get back to the antiparallel configuration which is necessary to form covalent bonds. Hence the reaction rate in the presence of the magnetic field will be greatly diminished. By contrast, oscillating or alternating magnetic fields will be expected to enhance reactions rates, as they facilitate the changes in relative spins. Here is another instance where static

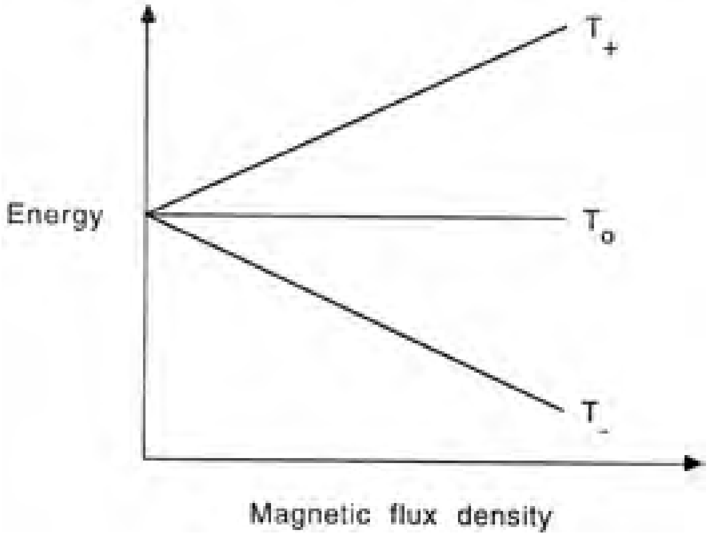

Figure 9.2 The separation of the triplet energy levels due to different alignments of the magnetic free radical pairs as the magnetic flux density increases.

magnetic fields will have very different effects from oscillating magnetic fields.

Finally, static magnetic fields will deflect endogenous electric currents flowing at right angles to the direction of the imposed field. During early embryogenesis in Drosophila, when pattern determination is taking place, considerable electrical activities are also evident (see next Chapter), quite apart from the transembryonic ionic currents which have been found flowing through and around all developing organisms. The ionic currents have a drift velocity far too slow to be appreciably deflected by the external magnetic field.33 Furthermore, it is difficult to see how the deflection of ions in free solution can affect the cell membrane and influence pattern determination. If there is an electric current which is sensitive to the magnetic field in the manner suggested by the specific ‘twisted’ transformations, it would have to flow along the surface of the cell membrane and be coherent throughout the entire surface. There is no evidence for the existence of such a current, although it is possible for electric currents — in the form of electrons or protons — to flow along membranes (see Chapter 8).

We have only scratched the surface of the coherence of living organization. The sensitivity of organisms to weak magnetic fields, strange as it may seem, can in principle, though not in practice, be explained in terms of classical physicochemical phenomena that are relatively well understood.34 In the next Chapter, I shall describe some novel observations in living organisms that have as yet no definite analogy in non-living systems, and have no classical explanations.

Notes

1. Breithaupt (1989).
2. Hess (1979).
3. See Kyriacou (1990); Zeng et al. (1996).
4. See Berridge et al. (1979); Glass and Mackey (1988); Lloyd and Rossi (1992).
5. Ribary et al. (1991); Ioannides (1994).
6. Gray et al. (1989); Freeman (1995); Freeman and Barrie (1994); See also Ho (1997b).
7. See review by Stewart (1991) and references therein. See also Winfree (1980).
8. Freeman and Barrie (1994).
9. Kelso (1991).
10. See Ho (1997b) and references therein.
11. Iwazumi (1979).
12. Bordas et al. (1993).
13. Baba (1979).

14. Presman (1970). The orientation effect of the Earth's magnetic field on a single electron spin associated with a molecule is of the order of 10-8 electron volt, far too weak to be detectable by ordinary mechanisms. Leask (1977) first proposed that detection of magnetic fields in birds is through the eye, in the light sensitive rhodopsin molecules, which, on absorbing photons excites electrons into the triplet state. A population of these excited electrons in the triplet state would be highly sensitive to magnetic field orientation, as explained later in this Chapter. The biological effects of weak electromagnetic fields have been reviewed by Smith (1994).
15. See Ferrier (1986) and references therein.
16. See Meggs (1990) and references therein.
17. Goodman et al. (1983).
18. See Mohamed-Ali et al. (1995) and references therein.
19. See Liburdy and Tenforde (1986); also Adey (1989); Becker (1990); Ho et al. (1994b).
20. See Ho et al. (1994b).
21. Fist (1997).
22. From Ho et al. (1992a).
23. See Pethig (1994).
24. See Liburdy and Tenforde (1986); Liburdy (1994).
25. See Worcester (1978).
26. See Ho et al. (1987) and references therein. Since we published our results, however in Ho et al. (1992a), there has been isolated reports of such mutant phenotypes in Drosophila.
27. See special issue on liquid crystals, Physics Today, May, 1982.
28. See Ho et al. (1987).
29. See Ho et al. (1994a).
30. See Edmonds (1992, 1994).
31. Adey (1989).
32. See McLauchlan (1992)
33. Ho et al. (1992a).
34. We have preliminary evidence, however, that the effect of static magnetic fields on body pattern may be nonclassical. The “twisted” transformations are still produced in the middle of a toroidal coil, in a region where the static magnetic field is essentially zero, but the vector potential which alters the phase of moving charges is non-zero. We suggest that the embryos may be biological detectors of the Aharanov-Bohm effect. See Ho et al. (1994a). Applications for funding for further research were unsuccessful.

CHAPTER 10

Life is All the Colours of the Rainbow in a Worm

Light and Living Matter

Light and matter are intimately linked. The first inkling of that comes from observations showing how, at the quantum level, both light and matter exist as wave and particle. I shall deal with the wave-particle duality of light and matter more substantially in Chapter 13. In this Chapter, I describe some unusual experimental observations suggesting that light and living matter may have such a special relationship that it pushes at the very frontiers of current research in quantum optics and other nonlinear optical phenomena in condensed matter physics.

The Light That Through The Green Fuse

Quantum physicist turned biophysicist, Fritz Popp, and his group in Kaiserslautern, have been investigating light emission from living organisms for nearly 20 years. They find that practically all organisms emit light at a steady rate from a few photons per cell per day to several hundred photons per organism per second.1 The emission of biophotons, as they are called, is somewhat different from well-known cases of bioluminescence in isolated species such as fireflies and luminescent bacteria. Biophoton emission is universal to living organisms, occurring at intensities generally many orders of magnitude below that of bioluminescence, and in contrast to the latter, is not associated with specific organelles. Nevertheless, biophoton emission is strongly correlated with the cell cycle and other functional states of cells and organisms, and responds to many external stimuli or stresses. The response to temperature, for example, is highly nonlinear: a sharp increase in emission rate as temperature rises followed by oscillations before decaying back to a steady level.

Analyses of the emitted light reveal that it typically covers a wide band (wavelengths from about 250 to 900 nm), with an approximately equal distribution of photons throughout the range. That means the energy levels are approximately equally populated, deviating markedly from the Boltzmann distribution characteristic of systems at thermodynamic equilibrium (see Chapter 5 p. 70), giving us yet another indication that the living system is far, far away from thermodynamic equilibrium in its energy profile.

Biophotons can also be studied as stimulated emission after a brief exposure to ordinary white light, or light of different spectral compositions (different combinations of frequencies). It has been found, in all cases without exception, that the stimulated emission decays, not according to an exponential function characteristic of non-coherent light, but rather to a hyperbolic function (see Fig. 10.1) which Popp regards as a sufficient, or diagnostic, condition for a coherent light-field.2 It implies that photons are held in a coherent form in the organism, and when stimulated, are emitted coherently like a very weak, multimode laser. (Such a multimode laser has not yet been made artificially, but it is fully consistent with the theory of coherence in quantum optics as developed by Glauber.3) ‘Biophotons’ include electromagnetic radiation below the visible range, which could extend all the way through microwave and radio frequencies to the extremely low frequency (ELF) end of the spectrum. Organisms may be emitting in the entire electromagnetic range, but sensitive detectors currently exist only for visible photons.

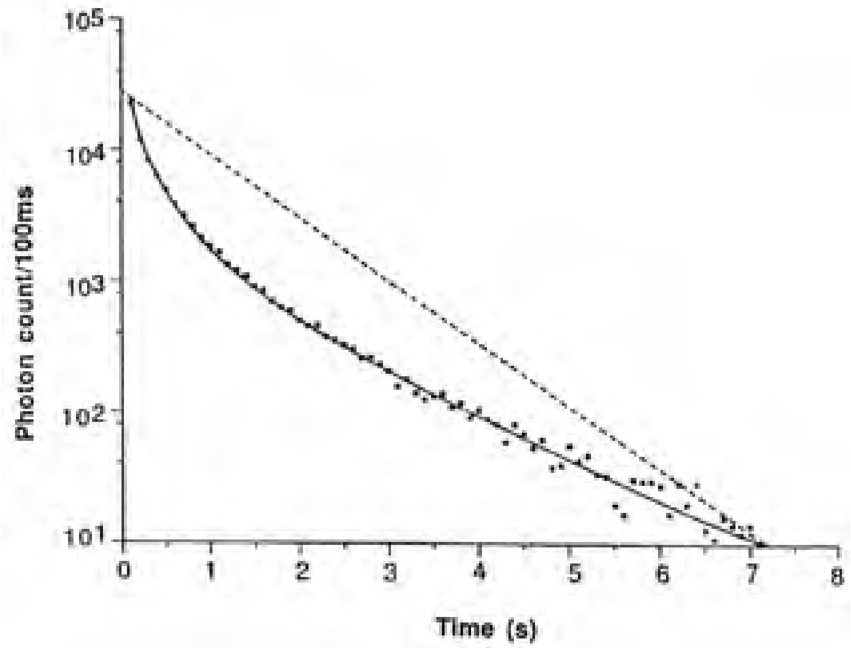

Figure 10.1 Hyperbolic decay kinetics of stimulated light emission from a batch of synchronously developing early Drosophila embryos.4

The hyperbolic function takes the general form,

$$x = A(t + t_0)^{-1/\delta} \tag{10.1}$$

where x is the light intensity, A, t0 and δ are constants, and t is time after light exposure. The equation expresses the characteristic that light intensity falls off as a power of time, pointing to the existence of memory in the system.

The phenomenon of hyperbolic decay can be intuitively understood as follows. In a system consisting of non-interacting molecules emitting at random, the energy of the emitted photons are completely lost to the outside, or converted into heat, which is the ultimate non-coherent energy. If the molecules are emitting coherently, however, the energy of the emitted photons are not completely lost. Instead, part of it is coupled back coherently, or reabsorbed by the system (rather like the interaction between coupled oscillators described in the previous Chapter). The consequence is that the decay is delayed, and follows typically a hyperbolic curve with a long tail. Other nonlinear forms of delayed decay kinetics, such as oscillations, are predicted for a coherent field, and are also often observed.

The hyperbolic, nonlinear decay kinetics is uniform throughout the visible spectrum as shown by analyzing the spectral composition of the emission stimulated by monochromatic light or light of restricted spectral compositions.5 Furthermore, the stimulated emission always covers the same broad spectrum. Regardless of the composition of the light used to induce it, and may retain this spectral distribution even when the system is perturbed to such an extent that the emission intensity changes over several orders of magnitude. These results indicate that energy input into any mode is rapidly delocalized, or shared throughout all the modes, as characteristic of systems mobilizing energy in a fully symmetrical way (see Chapter 4 and 6).

Atomic physicist, Franco Musumeci and his colleagues in Catania, Sicily, have carried out systematic investigations into the nonlinearity of biophotons, with the critical eye of physicists well-attuned to atomistic physical system.6 They found that living systems are unique in their specifc response to light stimulation, which are clearly distinguishable from one another, and from solid state devices. Moreover, the parameters of the decay kinetics are very highly correlated with the physiological state, and cannot be explained in terms of a mere sum of microscopic, independent phenomena.

Instead, those observations are consistent with the idea that the living system is one coherent ‘photon field’ bound to living matter. This photon field is maintained far from thermodynamic equilibrium, and is coherent simultaneously in a whole range of frequencies that are nonetheless coupled together to give, in effect, a single degree of freedom. That means energy input to any frequency will become readily delocalized over all the frequencies, precisely as predicted from the thermodynamic considerations in the first six Chapters of this book.

It must be stressed that the ‘single degree of freedom’ of organisms is a very special one due to quantum coherence which maximizes both local autonomy and global correlation, as you will see in Chapter 13. It does not mean uniformity, or that every part of the organism must be doing the same thing or vibrating with the same frequencies. According to arguments presented in Chapter 6, living systems with internal entropy compensation cannot be uniform. On the contrary, there must be a degree of reciprocal variation of the parts, or space-time differentiation, to achieve an overall balance in entropy production. There can also be domains of local autonomy such as those that we know to exist in the organism. For systems like organisms which have a highly differentiated space-time structure, any measurement of the degree of freedom performed within a finite time interval will deviate from the ideal of one, which is that of a fully coupled system with little or no space-time structure. A real source of variation from the single degree of freedom may arise because some parts of the system are temporarily decoupled from the whole, and the degree of coherence will reflect changes in the functional state of the system. Or else parts of the system may be more permanently decoupled from the whole, as appears to be the case with malignant tumour cells (see later).

Long-Range Communication between Cells and Organisms

In considering the possibility that cells and organisms may communicate at long range by means of electromagnetic signals, Presman7 points to some of the perennial mysteries of the living world: how do a flight of birds, or a shoal of fish, move so effortlessly, spontaneously and freely in unison without following marching orders from a leader? During an emergency, organisms can mobilize prodigious amounts of energy almost instantaneously. The motor nerve to the muscle conducts at 100 times the speed of the vegetative nerves that are responsible for activating processes leading to the enhancement of the contractile activity of the muscles required in a crisis: adrenalin release, dilatation of muscular vessels and increase in the heart rate. Yet, it appears that the muscle actually receives the signals for enhanced coordinated action long before the signals arrive at the organs responsible for the enhancement of muscle activity! This suggests that there is a system of communication that sends emergency messages simultaneously to all organs, including those perhaps not directly connected with the nerve network. The speed with which this system operates seems to rule out all conventional mechanisms. (This is also true for normal visual perception and muscle contraction described in Chapter 1.) Presman proposes that electrodynamical signals are involved, which is consistent with the sensitivity of animals to electromagnetic fields.

Electrodynamical signals of various frequencies have been recorded in the vicinity of isolated organs and cells, as well as close to entire organisms.8 In our laboratory, we have recorded profuse electrical signals from fruitfly embryos (1 hz to 30 hz, 1 hz = 1 cycle per second) during the earliest stages of development when the embryos are not yet cellular.9 Whether these signals are involved in communication is not yet known. (In Chapters 11 and 12, you will see how the connective tissues may support jump conduction of positive electric currents, thus providing intercommunication channels much faster than the fastest nerves.) That electromagnetic signals may be involved in intercommunication is suggested by the photon-emission characteristics of normal and malignant cells.10 While normal cells emit less light with increasing cell density, malignant cells show an exponential increase in light emission with increasing cell density. This shows that long-range interactions between the cells may be responsible for their differing social behaviour: the tendency to disaggregate in the malignant tumour cells, as opposed to attractive long range interactions between normal cells. The difference between cancer cells and normal cells may lie in their capacity for intercommunication, which in turn depends on their degree of coherence. The parameter $1/\delta$ in the hyperbolic decay function (Eq. 10.1) can be taken as a measure of incoherence, as it is directly correlated with the inability of the system to re-absorb emitted energy coherently. This parameter is shown to increase with increasing cell density in the malignant cells, and to decrease with increasing cell density in normal cells. These results are consistent with the suggestion that tumour cells have a diminished capacity for intercommunication.

Similar long range interactions between organisms have been demonstrated in Daphnia where the light emission rate varies periodically with cell number in such a way as to suggest a relationship to the average separation distances between individual organisms which are submultiples of the body size — of about 3 mm (see Fig. 10.2). That indicates individuals in an intercommunicating population tend to adopt optimal separation distances between neighbours, which may explain the formation of swarms, shoals and other collective behaviour in many animal species.

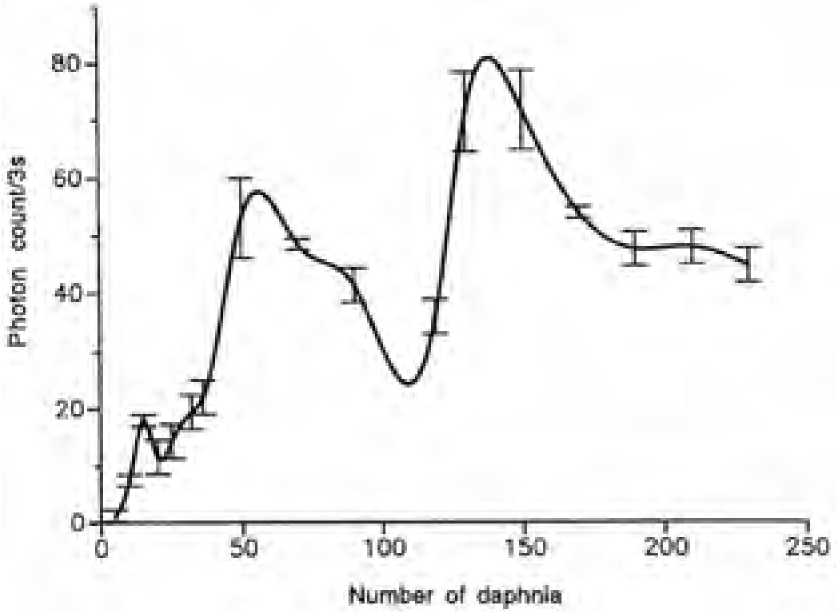

Figure 10.2 Spontaneous light emission in Daphnia as a function density.11

Direct intercommunication between separate populations of the luminescent bacteria, Gonyaulax, have been demonstrated by Popp and his coworkers.12 Two identical quartz cuvettes, filled with the same numbers of bacteria from the same culture, are found to synchronize their light flashing when they are in optical contact, but not when separated by an opaque barrier.

Finally, synchronously developing populations of early Drosophila embryos are found to re-emit intense, often prolonged and multiple flashes of light minutes to hours after a single brief light exposure. We have referred to this phenomenon as ‘‘super-delayed luminescence”. Some examples are presented in Fig. 10.3. The phenomenon depends, among other factors, on the existence of synchrony in the population. Although the timing of light exposure must fall within the first 40 minutes of development in order to obtain superdelayed luminescence, the occurrence of the flashes themselves do not obviously correlate with specific embryonic events. The flashes,

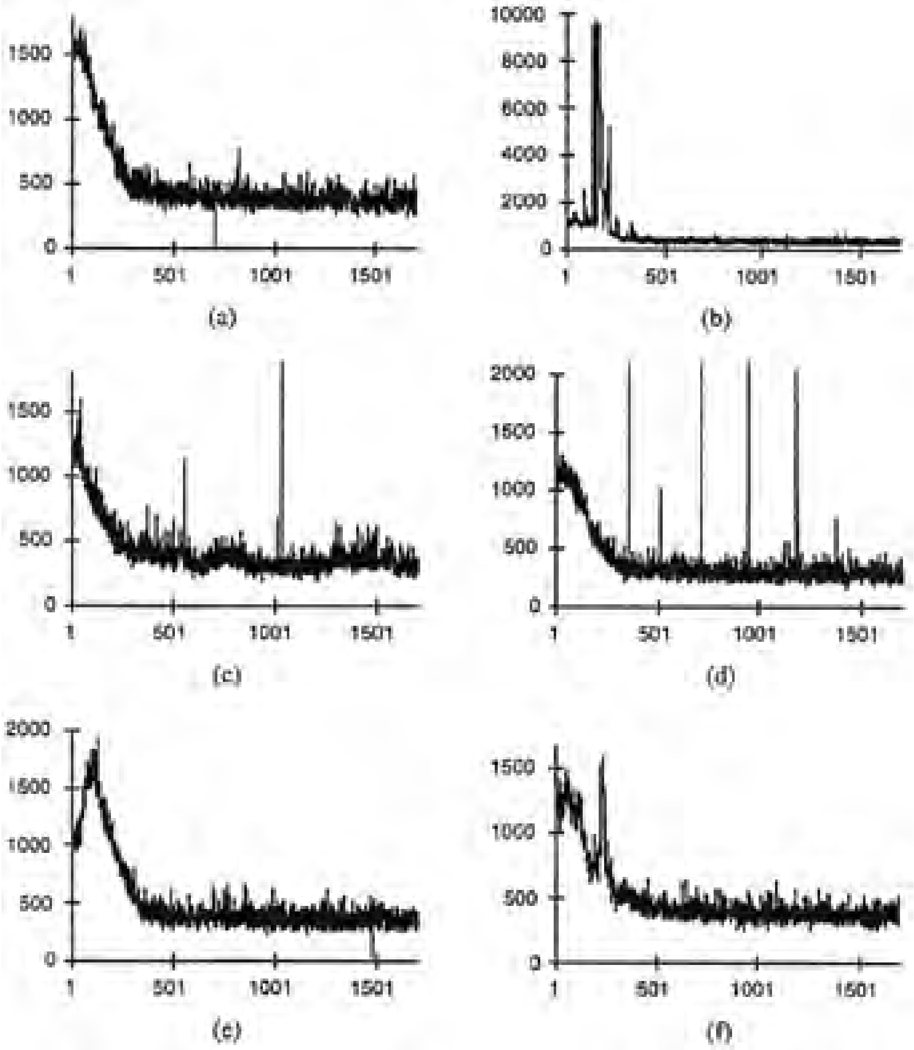

Figure 10.3 Superdelayed luminescence in Drosophila.13 Continuous recordings of aggregated photon count per 20s from synchronously developing embryos. a, control batch without light stimulation, b–f, experimental batches with light stimulation.

therefore, give information concerning the physical state of the embryos at the time of light stimulation — such as the existence of a high degree of coherence — rather than at the time during which the flashes themselves occur.

Superdelayed luminescence takes many forms. It may consist of a single sharp burst of light (< 20 s) or of several sharp bursts separated by long periods of background emission (Fig. 10.3d). It may also come in a single prolonged burst (Fig. 10.3e) or, more dramatically, and most frequently, as a series of prolonged bursts (Fig. 10.3b in particular, but also, Figs. 10.3c, 10.3f). The duration of each prolonged burst varies from 1 to 30 minutes or more. For the multiple prolonged flashes, the total luminescence produced — in excess of the background emission — shows significant first and second order dependence on the number of embryos present. All these observations suggest that superdelayed luminescence results from cooperative interactions among embryos within the entire population, so that most if not all the embryos are emitting light simultaneously. Each embryo has a certain probability to re-emit after light stimulation, so that it can either trigger re-emission in other individuals or alternatively, its re-emission could be suppressed by them. So most or all the individuals in the population may re-emit at the same time giving rise to the high intensity flashes registered by the photoncounting device. Alternatively, re-emission in the entire population could be suppressed, so that in approximately 30% to 40% of the cases, there is no clear indication of superdelayed re-emission even when all the necessary criteria have been satisfied.

The phenomenon resembles various nonlinear quantum electro-dynamic effects (see next Section). It has been qualitatively modelled as a phase-correlated collective emission from an initially uncorrelated population of emitters.14 As yet, we do not know whether any functional significance could be attached to superdelayed luminescence. Drosophila females typically lay eggs just before sunrise, so the external light source could be an initial synchronizing signal or Zeitgeber, which entrains circadian and other biological rhythms. The superdelayed re-emission could be a means of maintaining intercommunication and synchrony among individuals in the population. On the other hand, the flashes may simply be the embryos' way to inform us of their globally coherent state at the time when light stimulation is applied. This enables the embryos to interact nonlinearly to generate light emission that is coherent over the entire population, and orders of magnitude more intense than the spontaneous emission rate.

While the above phenomena cannot be accounted for in terms of classical mechanisms, we do not yet have a satisfactory explanation for any of them. There are, nevertheless, some strong hints as to how they might be understood.

Where Do Biophotons Come From?

Let us consider some possibilities regarding the source of biophotons. I have suggested that single embryos have a probability of re-emission, and indeed, we have succeeded in obtaining an image of single Drosophila embryos built up by integrating the photons from their superdelayed luminescence.15 The results indicate that the light is emitted over the entire embryo, though certain areas may be emitting more strongly than others at different times. The dynamics of emission can be quite complex, as we were able to demonstrate in video recordings of the image in real time, which we subsequently succeeded in obtaining.16 This lack of specific localization of the light emitted is consistent with its broad spectrum, and also with a priori expectations as explained below.

Light is generally emitted from an excited atom or molecule, when an electron in the outermost shell, having been promoted to an excited energy level by, say, a collision with another molecule or absorption of energy by other means, falls back into a lower energy level. Light emission does not always occur, however. The excited electron can often start to move, thus becoming an electric current, or it can be involved in a chemical reaction as explained in the previous chapter. The electron can also relax back to the ground state non-radiatively, that is, instead of emitting photons, it can give off energy as phonons (sound waves), or as heat. In the case of light emission, the energy of the emitted photon will be equal to the difference between the energy levels of the excited and the ground state, which determines the frequency of the photon emitted,

$$E_e = E_1 - E_0 = h\nu \qquad (10.2)$$

where Ee, E1 and E0 are respectively, the energies of the photon emitted, the excited level, and the ground level, h is Planck's constant, and v is the frequency of the emitted photon.

This will prove to be an oversimplified account, as photons are even more intimately involved with matter than the impression I have given so far. In quantum electrodynamics, it is supposed that the orbital electrons and the nucleus are exchanging ‘virtual’ (i.e., not quite real) photons all the time, which is why the electrons can manage to ‘move around in their orbits’ without radiating electromagnetic energy outside.17

In a solid state system, as explained in Chapter 7, outer electrons are neither localized to single atoms or molecules, nor do they have single energy levels. Instead, continuous, delocalized bands of frequencies are separated by band gaps. The low energy valency band, filled with electrons, is separated by a band gap from the conduction band containing mobile electrons to which electrons can be promoted by absorbing energy such as heat or light. If the excited electron is not conducted away, it may relax back to the ground state (to recombine with the positively charged ‘hole’ left behind) by radiating a photon, or non-radiatively as described above. Another source of photons in a solid state system is from ‘excitons’, i.e., an excited electron-hole pair which can propagate over long distances within the system before giving up the energy by emitting a photon.

As we have seen, charge separation underlies the primary bioenergetic transduction processes associated with biological membranes, and the formation of excitons and their propagation is believed to be involved in major energy transductions and in biocommunication (see Chapters 3 and 8). Rattemeyer and Popp18 suggest that the DNA molecule is an excited duplex, or exciplex, in which photons are effectively stored between the two DNA strands, and hence can be a source of emitted biophotons. Exciplex formation in DNA has been shown to predominate even at room temperature.19 So it is not surprising that living systems could emit light from processes taking place all over the cell. And on account of the solid state nature of the cell, one must also suppose that as all the electrons are delocalized, so too, must all the photons in the system be delocalized. Therefore, it is probably misguided and quite fruitless to try to identify from which specific chemical reactions biophotons originate. And this would be consistent with Musumeci's conclusion referred to above.

However, it is one thing to suggest that biophotons come from all over the cell or organism which constitutes a coherent photon field, and quite another to imagine how coherence would manifest itself in light emission. Or, put the other way round, it remains a problem to work out precisely what the characteristics of light emission are telling us about coherence in the living system.

Spontaneous light emission is generally too weak to be analyzed in detail. There is the possibility of observing interference effects directly, which would present a technical challenge necessitating beam splitters and designs for optimizing signal to noise ratios. More immediate opportunity presents itself in the analysis of stimulated light emission. As mentioned earlier, the hyperbolic decay kinetics is considered by Popp as a sufficient condition for a coherent field. This is consistent with the observation that the hyperbolic decay kinetics is uniform over the entire optical spectrum, and that random energy of any frequency fed into the system is rapidly delocalized over all frequencies, implying that all the frequencies are coupled in a single degree of coherence as required for freedom.

In the case of superdelayed luminescence in Drosophila embryos, we have to explain both the extraordinarily long delay in re-emission, and the greatly enhanced re-emission rate. There are two kinds of quantum electrodynamical phenomena in physics which bear certain formal similarities to superdelayed luminescence in our biological system. (The similarity is formal only because the long time constants — tens of minutes and even hours before re-emission — involved in the biological systems have as yet no equal in physical systems.) One of these phenomena, cavity quantum electrodynamics, is the control of spontaneous radiation from excited atoms in resonant cavities;20 the other is the localization of light in semi-conducting material containing dielectric microstructures.21 Both physical phenomena depend on the quantum delocalization of electromagnetic energy and cooperative interaction which is the hallmark of biological organization.

Cavity quantum electrodynamics is associated with experiments demonstrating that spontaneous radiation from excited atoms can be greatly suppressed or enhanced by placing them in a special reflecting cavity which restricts the modes that the atom can radiate into. Strong coupling between the atoms and the radiation field within the cavity can then lead either to a suppression of spontaneous emission of excited atoms or its great enhancement, corresponding to the subradiant and superradiant modes, respectively. The early embryo can be regarded as a cavity resonator in which the spontaneous emission of atoms coherently excited by light exposure has become suppressed for various periods of time before they become re-emitted in a greatly enhanced rate, possibly as the result of some natural change of state as development proceeds subsequent to light stimulation. Or, as mentioned above, the re-emission can be suppressed indefinitely, in the subradiant mode. (The light exposure has no deleterious effects on development, and qualifies as a non-invasive probe.) The situation is further complicated because we are not dealing with one single cavity resonator, but rather with a population of nearly identical resonators which can further interact, within the resonating chamber housing the entire batch of embryos, to emit cooperatively and simultaneously, over the entire population.22

The general formal resemblances between superdelayed luminescence and cavity quantum electrodynamics include the characteristic multiple emission peaks (the most frequently observed emission pattern), the stochastic nature of the delay times, and the size and shape of the peaks. The dramatic multiple peaks occur between half to one-third of the time. The next most frequent forms are single long-lasting intense peaks, and single to multiple sharp bursts of light (each less than 20 s duration). In some cases, no re-emission at all is observed, even though all the controllable parameters such as age and degree of synchrony of the embryos are the same. This is consistent with the observation in cavity quantum electrodynamics that the geometry of the cavity, and the precise distribution of the embryos which are placed in the quartz cuvette by the mother flies themselves, can affect whether superradiance, or its converse, subradiance occurs. When superradiance occurs, the light also tends to be directional, which means that not all of the emissions may be detected by the photomultiplier placed in one definite orientation.

Localization of light is a related quantum electrodynamic effect which occurs as the result of coherent scattering and interference in semi-conducting materials containing dielectric microstructures which are close to the dimensions of the wavelength of light that is being scattered, i.e., $a \sim \lambda/2\pi$. Under those conditions, there are no propagating modes in any direction for a band of frequencies. Any ‘impurity’ atom — i.e., atoms different from the bulk dielectric medium — with a transition frequency in this band gap will not exhibit spontaneous emission of light. Instead, the emitted photon will form a bound state to the atom. In other words, the photon will be trapped indefinitely in the material. When a collection of ‘impurity’ atoms is present in the dielectric, a single excited atom can transfer its bound photon to neighbouring atoms by resonant dipole-dipole interactions. The distance for such photon tunneling is approximately ten times the dimension of the microstructures. Thus, a photon-hopping conduction results, involving a circulation of photons among a collective, which greatly increases the likelihood of coherent stimulated emission or laser action.

The conditions for light localization and subsequent coherent stimulated emission may well be present in the early embryo. There are many candidates for dielectric microstructures of the dimensions of the wavelengths of light, and, on account of the molecular diversity of the biological system, there is no shortage of species acting as so-called ‘impurities’. For example, globular proteins range from 5 to 10 nm; protein complexes and ribosomes, 20 to 30 nm. These can all contribute to the localization of various frequency bands of photons. As the embryo develops, however, conditions favourable for stimulated coherent emission of the trapped photons may become realized. In connection with the trapping or storage of photons, it has been observed that death in organisms invariably begins with a sharp increase in the intensity of light emission (at least 3 orders of magnitude above the self-emission rate) which can persist undiminished for more than 48 hours.23

The phenomena of light emission from living organisms are so unusual that they would certainly be dismissed as curiosities or artifacts were it not for the existence of a general theory of coherence in biological systems within which these phenomena could begin to be understood. There is another reason why new theories in general are important for science: they direct us to new observations which may very well not be made otherwise. This has been my experience in years of scientific research in many areas. All of the most recent discoveries in my laboratory have been inspired by the theory of coherence; in particular, I was very interested in the role played by coherence in body pattern determination,24 which motivated our collaborative work with Frtiz Popp, and more recently with Franco Musumeci's group in Catania.25 The subsequent findings on light emission in Drosophila embryos encouraged me to explore further the optical properties of the developing embryo. This has led to more exciting discoveries, I shall describe one of these.

Life is All the Colours of the Rainbow in a Worm

It had occurred to me quite some time ago that coherence in the organism ought to be reflected in its molecular organization, so one should be able to see evidence for that, say, with the polarizing microscope, which has been routinely used to study rock crystals and various ‘inert’ biological material with regular structures such as fibres, bones, teeth, and more recently, liquid crystals. Polarized light microscopy has also been used to study isolated, contracting muscle fibres before it was supplanted by X-ray diffraction. If organisms are indeed special solid state systems with coherent, quasi-crystalline structure, then there is every reason the polarizing microscope may reveal the regimes of dynamic molecular order in its cells and tissues. As I was most interested in the early stages of pattern determination, I had expected to see some kind of 'prepatterning' in the early embryo which would mirror the body pattern that develops overtly much later on. This idea remained at the back of my mind, but I never seriously pursued it because we did not have a polarizing microscope in the Biology Department, and there were many other things to do besides.

As luck would have it, Michael Lawrence, a colleague who worked as a microscopist and designer in the BBC, came over to visit our laboratory one day in 1992, and told me he was filming crystallization under the polarizing microscope in the Department of Earth Sciences. I persuaded him to look at some Drosophila embryos. He agreed to do so almost immediately. And as a result, we discovered an imaging technique that enables us to see all the colours of the rainbow in a living, crawling, first instar Drosophila larva.

To see it for the first time was a stunning, breathtaking experience, even though I have yet to lose my fascination for it after having seen it many, many times subsequently. The larva, all of one millimeter in length and perfectly formed in every minute detail, comes into focus on the colour-TV monitor as though straight out of a dream. As it crawls along, it weaves is head from side to side flashing jaw muscles in blue and orange stripes on a magenta background. The segmental muscle bands switch from brilliant turquoise to bright vermillion, tracking waves of contraction along its body. The contracting body-wall turns from magenta to purple, through to iridescent shades of green, orange and yellow. The egg yolk, trapped in the ailmentary canal, shimmers a dull chartreuse as it gurgles back and forth in the commotion. A pair of pale orange tracheal tracts run from just behind the head down the sides terminating in yellow spiracles at the posterior extremity. Within the posterior abdomen, fluorescent yellow malpighian tubules come in and out of focus like decorative ostrich feathers. And when highlighted, white nerve fibres can be seen radiating from the ventral nerve cords. Rotating the microscope stage 90° causes nearly all the colours of the worm instantly to take on their complementary hues.26 It is hard to remember that these colours have physical meaning concerning the shape and arrangements of all the molecules making up the different tissues.

It was some time before we realized that we have made a new discovery. The technique depends on using the polarizing microscope unconventionally, so as to optimize the detection of small birefringences or coherently aligned anisotropies in the molecular structures of the tissues. We now have a good idea on how to interpret the colours in terms of molecular structures.27 As with ordinary crystalline and liquid crystalline material, they do tell us about long-range order in arrays of molecules. The full colours only appear under our conditions, and leads us to think we are picking up phase ordering in biological molecules in living organisms that have never been observed before, and cannot be observed under conventional conditions. Furthermore, we have accomplished the first ever, high resolution and high contrast imaging of an entire, living, moving organism. Finally, the very idea of using polarizing light microscopy to look at dynamic order within the organism is also new.

What is so suggestive of dynamic order is that the colours wax and wane at different stages of development. The early stages associated with pattern determination are some of the most colourful ones. We have also been able to discern traces of the prepatterning of the body plan, though not quite in the way expected,28 I am far from disappointed. It confirms my belief that the best experiments always tell one something unexpected, as they are acts of communicating with nature. (More about that in Chapter 14.)

The most dramatic change is in the final stages when the colours intensify in the embryos that have started to move several hours before they are due to hatch.29 It is as though energy, say in the form of an endogenous electric or electrodynamical field, is required to order the molecules, so that even though the structures are formed, the molecules are not yet coherently arranged, and require something like a phase transition to do the job. The closest analogy one could think of is the phase ordering of liquid crystals in electric and magnetic fields, for biological membranes and muscle fibres in particular, have properties not unlike those of liquid crystals (see next Chapter). As consistent with the above interpretation, the colours fade when the organism dies or becomes inactive due to dehydration or to the cold. In the latter cases, the colours return dramatically within 15 minutes when the organism is revived.30

It is also highly significant that in all live organisms examined so far — the Drosophila larva, Daphnia, rotifers, nematodes, larval and adult stages of the brine shrimp, hydra, and embryo and hatchling of the zebra fish and the crested newt — the anterior-posterior body axis invariably corresponds to the major polarizing axis of all the tissues in the entire organism. This is a further indication that some global orienting field is indeed responsible for polarizing liquid crystalline phase alignement, and hence, in determining the major body axis.

The technique works on all live biological tissues. Tissues which have been fixed and stained often fail to show any colours, unless they are very freshly fixed and well preserved. Thus, we seem to have a technique for imaging dynamic order which is correlated with the energetic status of the organism. This could be evidence for the non-equilibrium phase transition to dynamic order that Fröhlich and others have predicted.

All our investigations on the optical properties of living organisms described in this Chapter have been done using relatively non-invasive techniques that enable us to study living organization in the living, organized state. That is, in itself, a major motivation towards the development of non-invasive technologies. Ultimately, they lead to a different attitude, not only to scientific research or knowledge acquisition (see Chapter 14), but to all living beings. For as these technologies reveal the immense subtlety and exquisite sensitivity of biological organization, they engender an increasingly sensitive and humane regard for all nature.

The most remarkable implication of our findings is that organisms are completely liquid crystalline. We shall explore the implications of the liquid crystalline organism in the next two Chapters.

Notes

1. See Popp (1986); Popp and Li (1993); Popp et al. (1981). The first studies on biophoton emission were actually carried out by Soviet scientist, Alexander Gurwitsch and his sister and co-worker, Anna Gurwitsch. The latter has continued the investigations up to the time of her death in 1995. They showed that certain frequencies of uv radiation from dividing cells were ‘mitogenic’ in that the uv light could stimulate otherwise resting cells to divide. This research is currently undergoing a revival in the hands of Russian developmental biologist, Lev Beloussov. See Gurwitsch (1925); also A. Gurwitsch (1992) in Popp et al. (1992). I am very grateful to Lev Beloussov for unpublished information on his efforts to extend Gurwitsch's observations to developing embryos.
2. The proof for hyperbolic decay being a sufficient condition for coherence depends on the ergodic assumption, that time average of the system taken over a long time series equals to the ensemble average taken over many spatial points, see Popp and Li (1993).
3. Glauber (1969).
4. From Ho et al. (1992c).
5. See Musumeci et al. (1992).
6. Musumeci et al. (1997).
7. See Presman (1970).
8. Pohl (1983).
9. See Ho et al. (1992b).
10. Schamhart and van Wijk (1986).
11. Galle et al. (1991).
12. See Popp et al. (1994).
13. From Zhou et al. (1996); See also Ho et al. (1992c).
14. See Zhou et al. (1996).
15. Video sequences shown in public in the 1993 International Science Festival, April 14, Edinburgh.
16. Much thanks to help from Patricia Thomkins and Paul Gibson of Photonics, U.K.
17. See Richard Feynman's book, Q.E.D. The Strange Theory of Light and Matter.
18. Rattemeyer and Popp (1981).
19. Vigny and Duquesne (1976).
20. See Gross and Haroche (1982); Haroche and Kleppner (1989).
21. John (1991).
22. The delayed emission is more like a superfluorescence rather than superradiance because the latter starts from an initially highly correlated state, whereas the former starts from an initially uncorrelated, or weakly correlated state. See Zhou et al. (1996).

23. Neurohr, R. unpublished observation (1989).

24. See Ho et al. (1992b, 1992c).

25. Working with Musumeci's group in Catania, we have since confirmed the existence of superdelayed luminescence in synchronously developing Drosophila embryos, as well as brine shrimp embryos.

26. See Ho and Lawrence (1993a, 1993b). Actually, as with most discoveries, we found that several people had stumbled on the same setting before, but none of them had been looking at living organisms nor did they realize the full potential of the technique for studying liquid crystalline regimes in living organisms. See Newton et al. (1995).

27. Ho and Saunders (1994); Newton et al. (1995); Ho et al. (1996); Zhou et al. (1996b); Ross et al. (1997).

28. Ho et al. (1996).

29. Zhou et al. (1996b).

30. See Ho and Saunders (1994).

CHAPTER 11

The Liquid Crystalline Organism

The Mystery of Artemia — Life Without Energy Flow

The most amazing scientific discoveries are often made away from the headlines. At around the time the media were preoccupied with the possibility that there might have been life on Mars, based on the slimmest evidence, marine biologist James Clegg (whose work was mentioned in Chapter 8) published the results of four years of painstaking research on the brine shrimp, Artemia, that ‘‘challenge [the] meaning of life” itself.1 The brine shrimp is known to all goldfish enthusiasts as fish feed. It is unusual among higher animals in that its eggs can withstand long periods of complete dehydration and lack of oxygen (anoxia), and still retain the ability to develop and hatch when water is added. This dormant state, though unusual among higher organisms, is shared by many simple animals, bacteria and all plants; and is already mysterious enough. What Clegg did was to rehydrate some brine shrimp eggs until they were developing, then sealed them in nitrogen, so they cannot breathe, and left them at room temperatures on the shelf. Four years later, he breaks the seal, and finds that 60% or more of the embryos resume development to hatching. How do the embryos manage to survive under conditions that would have killed most ordinary animals in a few minutes? It appears that they simply stop breathing and metabolizing completely. Using radioactive carbon to label the proteins, Clegg showed that there had been practically no turnover (breakdown and resynthesis) of proteins during the four years. Nor were there any significant changes in the content of a variety of carbohydrates that might have been used to generate metabolic energy. In short, the embryos have remained alive, in a state of truly suspended animation at ordinary temperatures, without energy flow. This contradicts one of the most general axioms of contemporary biology, that energy flow is necessary to maintain the dynamic organization of the living system, and that disintegration and death would result as soon as energy flow is interrupted (see Chapter 4).

Evidently, the cessation of energy flow does not necessarily lead to disintegration and death. The secret lies in the structure of living matter, which, when properly preserved, can retain the memory of life itself, so, like the proverbial sleeping princess, it will resumes active life when conditions are favourable. Clegg attributes this life-preserving quality to an abundant protein found in the embryo, which is similar to the "chaperones" that bind to other proteins. But it is really the structural organization that protein has helped to preserve that holds the key to this remarkable state of suspended animation. The brine shrimp embryo has accomplished something which can only be achieved in other embryos (including those of humans beings) and small organisms that have been rapidly cooled down to liquid nitrogen temperatures, (-70°C) in the now commonplace technique of cryo-presevation. At these low temperatures, random thermal motions are minimized, and metabolism is reduced to very low levels. It is the physicochemical structure of living matter that holds the key to this long-term memory of living organization.

Living Versus Non-Living Matter

Is there something special about the physicochemical properties of living matter that distinguishes it from nonliving matter? This question has been asked since the dawn of biological science in the

West, which goes back at least as far as Aristotle. If one performs chemical analysis on an oyster, say, as is done routinely in food laboratories, one gets a composition of the main ingredients — proteins, carbohydrates and fats — as percentage of the dry weight. And if more details are needed, one can include the minor ingredients — cofactors, vitamins, minerals and so on down to minute amounts of trace elements. You might think all that is missing is the water. But you can add the water back to the ingredients, and no amount of mixing and stirring would bring the organism back to life. We would only end up with a thick (no doubt, delicious) oyster soup.

So, there is something special about living matter in an organism that is alive. The cell has a detailed organization (described in Chapter 8) which once disrupted, is extremely difficult, if not impossible to reconstitute. This detailed organization is more than the precise arrangement of the molecules which have to fit together like a microscopic jigsaw puzzle. The same molecules, from big to small, made up of atoms of different kinds, the electrons around the atoms, all, are transformed by being in an organism that is alive. They are no longer the same electrons, atoms, or molecules.

In the early days of cell biology, biologists examined sea-urchin eggs in an ultra-violet spectrophotometer before and after the eggs were killed by being burst open in distilled water, or crushed, to see how they absorb the uv light. Such physical measurements are routinely used for characterizing molecules in solution, as each species of molecules would have its own signature absorption spectrum — the degree to which light of different wavelengths are absorbed. They found that the spectra for the intact, live eggs differed completely from those of dead mixtures in solution (see Fig. 11.1). Thus, the same molecular species in random solution, are not recognizably the same in a cell that is alive; indicating that living matter is a very special physicochemical state in which characteristics of the isolated, separate molecules are no longer recognizable as such.

This is confirmed by the observation that picric acid, at a concentration high enough to coagulate protein solutions in the test-tube, had no effect at all on the cytoplasm when microinjected into

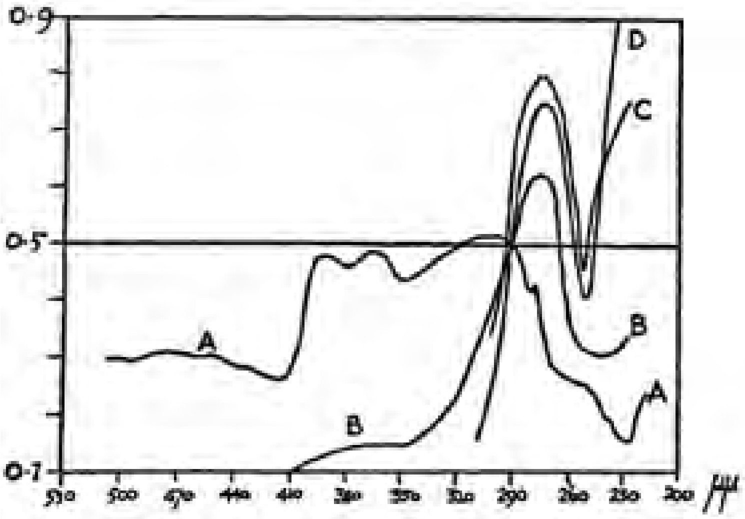

Figure 11.1 Ultra-violet absorption spectra of intact sea-urchin eggs compared with the homogenate.2 A, intact eggs; B, eggs burst open with hypotonic solution; C, eggs crushed open; D, solution of albumin.

an amoeba, a small, single-celled animal.3 The proteins within the live organism have the ability to resist being denatured, but not when they are isolated in solution. These are just two manifestations of the remarkable way in which the living cytoplasm differs from a mere homogeneous mixture of the same constituents in solution.

It is clear that there can be no real understanding of living organization without addressing the physicochemical properties of living matter, which to first approximation are those of liquid crystals.

Liquid Crystals and Organisms

Liquid crystals should be quite familiar to everyone by now, as they are so much part of our daily life, from computer display screens to household detergents. They are special phases of matter which have only been discovered at the end of the nineteenth century. A botanist observed that when the normally solid substance, cholesterol benzoate is heated just above 145°C, it turns into a turbid, viscous liquid before clearing.4 The substance undergoes a phase transition from a solid to a liquid crystalline state before becoming an ordinary liquid. What is the liquid crystalline state?

It is a state or phase of matter in between the solid and the liquid, hence the term, mesophase. Unlike liquids which have little or no molecular order, liquid crystals have an orientational order, in that the molecules are aligned in some common direction(s), rather like a crystal. But unlike solid crystals, liquid crystals are flexible, malleable, and responsive. There are many kinds of liquid crystals, from those which are most like liquids, to ones that most resemble solid crystals. Those that are like liquids can flow in the way water does, and even though all molecules tend to be aligned in one direction, individual molecules can move quite freely and change places with one another while maintaining their common orientation. The ones that resemble solid crystals will have order in all three dimensions, so that the movement of individual molecules will be much more constrained, but they will remain flexible and responsive. Liquid crystals typically undergo rapid changes in orientation or phase transitions when exposed to electric (and magnetic) fields — which is why they are useful as display screens — or to changes in temperature, pressure, pH, hydration, and concentrations of inorganic ions.5 They have even been found to respond to visible light by undergoing structural transformations that make them luminesce, i.e., to re-emit light.6 The chemist, George Gray, who has studied liquid crystals for many years, refers to liquid crystals as “tunable responsive systems”, and as such, are ideal for making organisms.7 It is already recognized that all the major constituents of living organisms may be liquid crystalline — lipids of cellular membranes, DNA in chromosomes, possibly all proteins, especially cytoskeletal proteins, muscle proteins, and proteins in the connective tissues such as collagens and proteoglycans (macromolecules that are part protein and part carbohydrate). These diverse molecular species can adopt a multiplicity of mesophases that may be crucial for biological structure and function at all levels of organization, from processing metabolites in the cell to pattern determination in development, and the coordinated functioning of whole organisms.8 Recent nuclear magnetic resonance (nmr) studies of muscles in living human subjects provided evidence of their “liquid-crystalline-like’’ structure.9

However, very few people have yet come to grips with the idea that organisms may be completely liquid crystalline.

The importance of liquid crystals for living organization was actually recognized some time ago. The biologist, Hardy, began his career in 1890 as a rather conventional comparative morphologist studying small invertebrate animals. Nine years later, he began to write on the special physical properties of protoplasm, recognizing it as a "colloid", which is neither a liquid nor a solid. The protoplasm of the living cell is a continuous medium which is full of strain energy, so much so that protozoa may explode if its surface membrane is cut. By 1927, Hardy already suggested that molecular orientation may be important for living protoplasm. Biochemist, Peters, commenting on Hardy's work two years later, made the explicit link between molecular orientation and liquid crystals.10 But it was Joseph Needham who proposed that all the properties of protoplasm can be accounted for in terms of liquid crystals. "…Liquid crystals, it is to be noted, are not important for biology and embryology because they manifest certain properties which can be regarded as analogous to those which living systems manifest (models), but because living systems actually are liquid crystals…"

Needham, indeed, suggests that living systems actually are liquid crystals, and that many liquid crystalline mesophases may be present in the cell, although no direct evidence exists, until the technique for detecting biological liquid crystals was discovered in our laboratory.

Liquid crystals are typically long molecules. This asymmetry in shape is why they tend to align, with their long axis parallel to one another, giving rise to a property called birefringence, or double refraction of light, that shows up clearly when viewed between two "crossed" polarizers. A polarizer is a sheet of material, like the polaroid dark glasses, that filters out ordinary light, which vibrates in all possible directions, and lets through only those rays vibrating in a single plane. Light filtered in this way is referred to as plane-polarized light. If a second polarizer is placed behind the first so that it only lets in light vibrating in a plane at right angles to the first, then no light will get through at all, and the field will appear completely dark. Birefringent materials, when placed between the two ‘‘crossed” polarizers, will appear characteristically bright in a certain orientation, and the more birefringent the material, the brighter it will be. Cellulose and other synthetic fibres are very birefringent, but most biological liquid crystals are only weakly birefringent and they will not easily be detected. Until, that is, we discovered how a small modification of the optical system makes all the difference in detecting the dynamic, liquid crystalline continuum that makes up the whole organism. I shall describe the technique below, for the benefit of those who would like to take advantage of the hours of pleasure in simply observing small organisms that could easily be found in a pond. Put the organisms in a drop of water under a small cover slip, so as not to squash them. And don't leave the organisms in the full glare of light for long periods, as they may experience different degrees of stress. If you are careful, you can return the organisms to the pond or the aquarium afterwards.

Interference Colours and Liquid Crystals

The colours generated in the organisms are interference colours, which can be produced in birefringent materials viewed in transmitted white light between two crossed polarizers as described above. The easiest way to understand how colours are generated is to follow a ray of plane-polarized light as it emerges from the first polarizer. When it passes through the birefringent material, it is split into two mutually perpendicular vibrating rays that propagate at different velocities. The retardation of the slow ray relative to the fast ray — relative retardation measured in nanometres (nm) — generates a phase difference between the rays as they emerge from the specimen. The slow and fast rays are then recombined into a single ray as they pass through the second polarizer, so they interfere either destructively, if out of phase, or constructively, if in phase. For white light with a full spectrum of wavelengths in the visible range, from 390 nm to 780 nm, the phase difference will vary across the spectrum, so that a precise hue of interference colour will result depending on the relative retardation (of the slow versus the fast ray). Coloured light is simply white light with different components missing.

When the material is not strongly birefringent, i.e., the relative retardation introduced between fast and slow ray is below the wavelength of visible light, no interference colours will be generated unless a mineral crystal plate (compensator plate) causing sufficient relative retardation is added in series with the sample. This brings the net retardation to within the wavelengths of light in the visible range. For weakly birefringent materials with relative retardations less than 50 nm, which is the case for most biological liquid crystals, little or no colour contrast is obtained even with the compensator plate, which is conventionally placed with its vibrational directions at an angle of 45° from the crossed polarizers. Instead, colour and colour contrast are greatly enhanced when that angle is small.11 For best results over the range of weak birefringences frequently found in organisms, the angle is between 4.5° and 7.5°; and the relative retardation of the compensator plate approximately 560 nm, which is the wavelength of green/ yellow light. That particular compensator plate is also known as a full wave-plate, or red tint-plate due to the reddish-violet background produced.

Since our discovery of the technique, we found that several microscopists had found the same setting before us, but none of them had been looking at living organisms nor did they realize the full potential of the technique for studying liquid crystalline regimes in living organisms. Even now, most biologists still regard the idea of the liquid crystalline organism as “mysticism”. But then, very few biologists know physics, and some have never even heard of liquid crystals. Such is the wonder of our over-specialized education system.

The Dynamic Liquid Crystalline Whole

Let us dwell on the significance of the brilliant colours observed in living organisms, some images of which are shown in the figures on the front and back covers of this book. What one sees in each of the image is the whole of the organism at once, from its macroscopic activities and features down to the long-range order of the molecules that make up its tissues. The colour generated and its intensity (the brightness) depend on the structure of the particular molecules (the intrinsic anisotropy of the molecules) and their degree of coherent order. This relationship has been theoretically derived by my colleague, Zhou Yu-Ming, and experimentally verified.12 If there were no molecular order, there would not be any anisotropy in the tissues and no colour would be generated. As pointed out in the previous Chapter, that is what happens when the organism dies, and random thermal motions take over to destroy the coherent molecular orientation. The principle is exactly the same for detecting mineral crystals in geology. But, with the important difference that the living liquid crystals are dynamic through and through, for they depend directly or indirectly, on energy input; and in the case of the muscles, the "molecular machines" of actomyosin are themselves in motion, busily transforming energy (see Chapter 1). So, how can they still appear crystalline?

Because visible light vibrates much faster than the molecules can move, the tissues will appear indistinguishable from static crystals to the light transmitted, so long as the movements of the constituent molecules are sufficiently coherent. Watch any live organism under the microscope, or in a video-recording, and you will see that the most actively moving parts of the organism are always the brightest, implying that their molecules are moving all the more coherently. (This is consistent with measurements on isolated muscle fibres made with other techniques, as described in Chapter 9.) With our optical technique, therefore, one can see that the organism is thick with coherent activities at all levels, which are coordinated in a continuum from the macroscopic to the molecular. The organism really has no preferred levels. That is the essence of the coherent organic whole, where local and global, part and whole are mutually implicated at any time and for all times.

These images draw attention to the wholeness of the organism in another respect. All organisms — from protozoa to vertebrates without exception — are polarized along the anterior-posterior axis, or the oral-adoral axis, such that all the colours in the different tissues of the body are at a maximum when that axis is appropriately aligned in the optical system, and they change in concert as the axis is rotated from that position. The fruitfly larva has neatly demonstrated that for us by curling its body around in a circle (see Figure on the back cover). Thus, the major body axis is also the main axis of molecular orientation for the entire organism. The organism is in effect one uniaxial crystal.

The recognition that organisms are liquid crystalline offers fresh insights into some of the deepest unsolved mysteries of the organism, which we shall now go on to explore.

Liquid Crystals and Pattern Determination

The correspondence between the major body axis and the main axis of molecular orientation for the entire organism is itself significant, and suggests an entirely new perspective to the age-old conundrum of body pattern determination in development. How does the organism decide on its head and tail ends, its back and front, and so on? Development is a fascinating subject which deserves a whole book devoted to it. It is a miracle every time a featureless egg manages to transform into the shapely organism with intricate structures characteristic of the species to which it belongs. This development happens almost as regularly as the sun rises and sets to mark the passing of each day, and yet it has remained as mysterious as if some cosmic censor has decided to draw a thick veil over it for the scientist, right from the beginning.

One of the first generalizations to emerge from developmental biology is that early embryos and isolated parts of early embryos possess a strong tendency to form whole organisms. Thus, if some part is removed from the embryo, the embryo will regenerate the missing part. If the embryo is fragmented into pieces, each piece will develop into an organism, albeit diminished in proportion to the original whole. There appears to be an organizing morphogenetic field directing the embryo to form a whole organism and to regenerate the whole from a part.

At the start of development, the embryo is ‘pleuripotent’ or ‘totipotent’, in other words, all parts of it have the potential to become many structures, or any structure of the adult organism. In the course of early development, however, a hierarchy of determination events occur, so that the different parts of the embryo become more and more restricted in their developmental potential. Little or no sign of the structures yet to be formed some time in the future can be discerned after each of these determinative events. The determined state could only be demonstrated by transplantation and grafting experiments.

A piece removed from an embryo before determination and transplanted to a different location, or grafted to another embryo, will develop in harmony with its surroundings. If the same experiment is carried out after determination, however, the graft will develop into the structure it was determined to be, irrespective of its surroundings. Thus, the graft may develop into a limb on the back of the host, for example. The process of determination was discovered a century ago, but its basis remains largely unknown despite impressive advances in the molecular genetics of morphogenesis in recent years. There are now detailed maps of which genes are expressed where and when for a number of organisms, especially Drosophila.13 Different genes are expressed before, during and after determination, they come and they go. And even though the expression of some genes may coincide with the time of determination, the conundrum remains of what really constitutes the determined state.

The paradoxical nature of the determined state is that the determinative influences not only possess field-like properties, but are also material and transplantable. This has spurred generations of developmental biologists to hunt, in vain, for specific chemical ‘morphogens’. This began with a putative organizing substance that is supposed to exist in the ‘organizer’, a part of the amphibian embryo in gastrulation — the stage at which the main layers of the body begin to be laid down by in-foldings and cellular movements.14 The 'organizer', when transplanted onto the belly of a second embryo, induces the formation of yet another whole embryo, but years of trying to isolate that chemical morphogen proved fruitless.

In the late 1980s, biophysicists, John Totafurno and Lynn Trainor, decided to re-examine the results of classical experiments in which limb-buds (literally precursors of limbs on the body) of the salamander were transplanted upside-down, or left-right interchanged, or variously rotated. When these limb-buds eventually developed, extra limbs were often induced in weird configurations. Totafurno and Trainor successfully interpreted all those results in terms of a nonlinear vector field, i.e., a directed, or oriented field, whose field lines need to reconnect as smoothly as possible after transplantation.15 That offers a vital clue. The vector field is precisely what one would expect for oriented liquid crystals. Could it be that the major polarities and body axes — anterior-posterior and dorsal-ventral — are due to oriented liquid crystals, a correlation that remains in every developed, adult organism we have seen?16 I thought this was a new idea, but it turns out it was at least 50 years old.

Joseph Needham had proposed the same in 1936 — that liquid crystals determine polarities and body axes — and in a more concrete form.17 He drew attention to the similarity between the successive stages of "dimensional rigidity" that liquid crystals go through in transition from the liquid to the relatively solid state, and the successive stages of determination of the limb-buds in amphibian: the anterior-posterior axis is determined before the dorsal-ventral, or the proximal-distal. There is indeed a wide range of liquid crystalline mesophases, from the most liquid — with orientational order in one dimension only and no translational order — to the most solid — with orientation order in three dimensions and also translational order. (Translational order just means the molecules are not free to move or translate from one place to another.) It is conceivable that, in the course of development, the relevant liquid crystalline mesophases undergo transition from the fluid state to metastable patterned regimes, which may then be further stabilized by chemical cross-linking, and even mineralization, as in the formation of bone in vertebrates, or the exoskeleton in insects, crustaceans, and radiolarians. The beautifully intricate and diverse microscopic crystal skeletons of radiolarians are much photographed under the scanning electron microscope, as material chemists are making a range of microcrystalline sculptures using liquid crystals as templates on which minerals are deposited.18

Liquid crystals make up the cell membrane, the membrane cytoskeleton and the cytoplasm of the egg. A special layer of the cytoplasm under the cell membrane — the cortex — has long been implicated as the site of pattern determination.19 A detailed study of the liquid crystalline structure of the cortex at the critical stages of development may reveal the correlations between successive stages of body axes determination and liquid crystalline phase transitions that Joseph Needham has proposed.

The stages at which body pattern is determined in the fruitfly embryo turns out to be quite birefringent (see previous Chapter), and faint, banded patterns can also be seen, which do not correspond to any structural features in the embryo. The early embryo is providing a liquid crystal display of the activities of its own morphogenetic field, rather in the manner that a computer display screen reflects underlying changes in its electric or magnetic field. And that may offer a clue to the concurrent pattern determining processes. We have attempted to map those patterns using a quantitative image analysis package based on our interference colour technique. The patterns show definite periodicities, which evolve in the course of the two hours it takes for the full body pattern to become progressively determined.20 We proposed that electrodynamical activities may be involved in patterning the liquid crystalline domain of the morphogenetic field (which would be consistent with the sensitivity of the patterning to weak static magnetic fields as described by Chapter 9). Electrodynamics of liquid crystals is a well-established and active field of research in physics at least since the 1980s.21 Homogeneous layers of liquid crystals break up into different domains under the influence of applied electric fields, which resemble the Bénard cells and Bénard-Rayleigh cells.

Liquid crystals may thus be involved in registering the longterm memory that enables developing organisms to make specific structures and organs later on in development.22 (As pointed out in Chapter 1, ‘memory’ is always a projection to the future.) Memory is one aspect of conscious experience. We shall see how liquid crystals may be much more concretely involved in consciousness than anyone has suspected.

Notes

1. Clegg (1997); see also Holmes (1997).
2. Vlés and Gex, 1928, cited in Needham, 1936, p. 118.
3. Pollack, 1927, cited in Needham, 1936, p. 119.
4. See Reinitzer (1989). I am also grateful to Alan Mackay for drawing my attention to the history of liquid crystals.
5. See De Gennes (1974); Blinor (1983); Collings (1990).
6. See Danilov (1993).
7. Gray (1993).
8. See Ho et al. (1996).
9. Kreis and Boesch (1994) found evidence of “liquid-crystalline structures of human muscle’’ by in vivo proton magnetic resonance spectroscopy.
10. The fascinating story of the protoplasm is related in detail by Needham, 1936, Chapter III.
11. See Ho and Lawrence (1993); Ho and Saunders (1994); Newton et al. (1995). Polarized light microscopy U.K. patent GB2270774A, US patent, 5559630, developed for quantitative imaging by S.R., J. H., R.N., Y.M.Z. and M.W.H. in collaboration with Prior Scientific and Data Cell under an EPSRC-LINK scheme; the software is an extension of the Media Cybernetics Image Pro image processing program.
12. See Ho and Saunders (1994); Ho et al. (1996); Zhou et al. (1996); Ross et al. (1997).
13. See Bate and Martinez Arias (1993).
14. Reviewed by Needham (1936).
15. Totafurno and Trainor (1987).
16. We first put forward this suggestion in Ho et al. (1996).
17. Needham (1936).
18. These have applications in large-molecule catalysis, formation of semi-conductor nonstructures, biomolecular separations, and development of medical implants. See Yang et al. (1997).

19. See Malacinski (1990).

20. See Ho et al. (1996).

21. See Blinov (1983); Rehberg et al. (1989); Kishore et al. (1993).

22. I have been describing some promising lines of research into the major outstanding problem of morphogenesis. However, almost none of these, nor other promising lines of research described elsewhere in this book, is being pursued, through lack of research funding. Meanwhile, the mainstream in developmental biology, as in all of biological sciences, remains committed to chasing genes.

CHAPTER 12

Crystal Consciousness

The Liquid Crystalline Continuum and Body Consciousness

Determination in morphogenesis involves a cellular memory, rather like the one preserved in suspended animation under cryo-preservation or in the brine shrimp embryo under anoxia. In the determined state, the cells somehow remember which structure they are committed to develop into, even when removed from their original milieu. These structures typically do not become manifest until much later on in development. In a literal sense, the embryo is conscious of its body, and remembers what grows and develops where and when. This memory remains when the organism is fully developed. The salamander is an example of organisms which can regenerate amputated parts of its body even as an adult. Biologist Robert Becker and others before him linked the capacity for regeneration to a direct current (DC) electric field which can be found in all organisms (see Chapter 8).1 When a part of the body is cut or amputated, electrical currents are found to issue from the wound (as though from the ends of live wires in a circuit which have been cut). These currents are crucial for the processes of healing and regeneration. One reason organisms, like human beings, do not normally regenerate amputated parts is because the wound heals over too quickly, so the electrical currents stop flowing before regenerative influences are complete. Successful regeneration was indeed reported for a child's lost finger-tip by keeping the wound open until regeneration was well on its way.

You may think I have been using the word "consciousness" rather loosely in referring to the embryo, which after all, does not have a brain. Whenever people speak of "consciousness", they usually locate it to the brain, where ideas and intentions are supposed to flow, and which, through the nervous system, is supposed to control the entire body. I have always found that odd, for like all Chinese people, I was brought up on the idea that thoughts emanate from the heart. I have come to the conclusion that a more accurate account is that our consciousness is delocalized throughout the liquid crystalline continuum of the body (including the brain), rather than being just localized to our brain, or to our heart. By consciousness, I include, at the minimum, the faculties of sentience (responsivieness), intercommunication, as well as memory.

You have seen how the entire cell is mechanically and electrically interconnected in a ‘‘solid state" or "tensegrity system" (Chapter 8). Actually all the cells in the body are in turn interconnected to one another via the connective tissues, as has been pointed out by biochemist James Oschman nearly 15 years ago.2 The connective tissues include the extracellular matrix surrounding all cells, the skin, bones, cartilage, tendons, filaments, the wall of arteries, veins, alimentary canal, air-passages, and various membranous layers covering the internal organs and tissues. The connective tissues are also liquid crystalline, and fresh-frozen or well-fixed sections of the skin, cartilage and tendons, all exhibit the same brilliant interference colours typical of living organisms. Liquid crystals happen to be ideal for the rapid intercommunication required for the efficient and highly coordinated energy transductions that enable organisms to act as a coherent whole (see Chapters 4, 6 and 10). And the liquid crystals of living organisms are especially good at intercommunicating and responding, as you shall see.

The connective tissues are regarded by most people in purely mechanical terms — their functions are to keep the body in shape, to act as packing between the major organs and tissues, to strengthen the wall of arteries, veins, intestines and air passages, and to provide the rigid elements (bony skeleton) for the attachment of muscles. The proteins of the connective tissues have always been seen as poor cousins to the many “sexy”(!) growth factors, hormones, transmitters, signalling proteins, receptors, regulators and enzyme cascades that currently plague our biochemical and medical texts. We really have not done sufficient justice to the connective tissues. For they may be largely responsible for the rapid intercommunication that enables our body to function as a coherent whole, and are therefore central to our health and well-being.

Oriented Collagens and Intercommunication

The clue to the intercommunication function of connective tissues lies in the properties of collagen, a special protein which makes up 70% or more of all the proteins of the connective tissues. Connective tissues, in turn form the bulk of the body of most multicellular animals. Collagen is therefore the most abundant protein in the animal kingdom.

There are many kinds of collagens, all sharing a general repeating sequence of the tripeptide, (X-Y-glycine) — where X and Y are usually proline or hydroxyproline. They also share a molecular structure in which three polypeptide chains are wound around one another in a triple-helix, with the compact amino acid glycine in the central axis of the helix, while the bulky amino-acids proline and hydroxy-proline are near the surface of the helix.3 The triple-helical molecules aggregate head to tail and side-by side into long fibrils, and bundles of fibrils in turn assemble into thicker fibres, sheets or other more complex three-dimensional liquid crystalline structures. These structures are formed by self-assembly, in the sense that they need no specific ‘instructions’ other than certain conditions of pH, ionic strength, temperature and hydration. The process seems to be predominantly driven by hydrophilic interactions due to hydrogen-bonding between water molecules and charged amino-acid side-chains.4 However, the precise mesophase structures resulting from different conditions of self-assembly show endless variations, as Julian Haffegee has discovered in our laboratory.5 It is clear that the different kinds of collagen assemblies in different connective tissues are well-suited to the mechanical tasks performed by the connective tissue concerned.

Recent studies reveal, however, that collagens are not just mechanical fibres and composites. Instead, they have dielectric and electrical conductive properties that make them very sensitive to mechanical pressures, pH, and ionic composition,6 and to electromagnetic fields. The electrical properties depend, to a large extent, on the bound water molecules in and around the collagen triple-helix. X-ray diffraction studies reveal a cylinder of water surrounding the triple-helix which is hydrogen-bonded to the hydroxyproline side-chains.7 Nuclear magnetic resonance studies (which measures the relaxation times of magnetically sensitive atomic nuclei subjected to magnetic fields) have provided evidence of three populations of water molecules associated with collagen. These are interstitial water, very tightly bound within the triple helix of the collagen molecule, and strongly interacting with the peptide bonds of the polypeptide chains; bound water, corresponding to the more loosely structured water-cylinder on the surface of the triple helix; and free water filling the spaces between the fibrils and between fibres.8 Evidence for bound water in collagen also comes from studies using another popular physical measurement technique, Fourier Transform InfraRed (FTIR) spectroscopy, which measures how the absorption peaks of different chemical groups in the protein are changed by interaction with water.9

All the evidence from physical measurements points to the existence of an ordered network of water molecules, connected by hydrogen bonds, and interspersed within the protein fibrillar matrix. Such a configuration of bound water is expected to support rapid jump conduction of protons — positive electric charges — and this has been confirmed by dielectric measurements.10 In these measurements, the material is subjected to alternating (AC) electric fields of different frequencies to induce separation of charges so that the dielectric and conductive properties of the material can be deduced from the responses. The measured conductivity of collagen increases strongly with the amount of water absorbed (from 0.1 to 0.3 g/g collagen), in accordance with the power-law relation,

$$\sigma(\phi) = X\phi^{Y}, \qquad (12.1)$$

where ø is the water content, and X and Y are constants. The value of Y is found to be 5.1 to 5.4, and is a function of the collagen fibrillar structure. These results suggest that continuous chains of ordered water molecules join neighbouring ion-generating sites enabling proton jumps to occur. (Does the high value of the exponential suggest that up to 5 or 6 neighbours may be involved in the jump conduction?) Based on these findings, it is estimated that conductivity along the collagen fibres is at least one-hundred time that across the fibre.11 The increase in conductivity is most marked around 310 K, which interestingly, is the normal temperature of our body.12 It is to be noted that the triple-helix of collagens in dilute solutions "melt" at 40°C,13 which may enable the collagen fibres to better realign for increasing conductivity. The collagenous liquid crystalline mesophases in the connective tissues, with their associated structured water, therefore, constitutes a semi-conducting, highly responsive network that extends throughout the organism. This network is directly linked to the intracellular matrices of individual cells via proteins that go through the cell membrane. The connective tissues and intracellular matrices, together, form a global tensegrity system,14 as well as an excitable electrical continuum for rapid intercommunication through-out the body.15

A major factor contributing to the efficiency of intercommunication is the oriented nature of collagen liquid crystalline mesophases in all connective tissues. Each connective tissue has its characteristic orientation of fibrous structures which are clearly related to the mechanical stresses and strains to which the tissue is subject. This same orientation is also crucial for intercommunication. Collagen alignment has long been recognized to be important in the structure of bone and cartilage. Less well known are the "Langer lines"16 in the skin, corresponding to predominant orientations of collagen fibres, which are determined, at least in part, by stresses during development and growth.17

It occurred to my colleague David Knight and I that the collagen fibre alignments in connective tissues may also be correlated with the acupuncture system of meridians and points in traditional Chinese medicine, which is also related to the DC body field identified by scientists in the west. The acupuncture system has puzzled generations of western scientists as it does not seem to have any definite anatomical correlates. There is already a suggestion that the acupuncture system is related to the DC electric field.18 Robert Becker has found that 25% of the acupuncture points on the human forearm have specific, reproducible and significant electrical properties in all human subjects tested, and the acupuncture meridians connecting those points have the electrical characteristics of transmission lines while non-meridian skin did not.19 Becker did not locate the DC body field to the connective tissues. Instead, he thought it is associated it with ‘‘perineural” tissues.

As mentioned earlier, collagen fibres are expected to preferentially conduct (positive) electricity along the fibres due to the bound water, which are predominantly oriented along the fibre axis; so these conduction paths may well correspond to acupuncture meridians. By contrast, acupuncture points typically exhibit low electrical resistances compared with the surrounding skin, and may therefore correspond to singularities or gaps between collagen fibres, or, where collagen fibres are oriented at right angles to the dermal layer. Conducting channels may bear a more subtle relationship to the actual orientation of the collagen fibres, as conductivity depends predominantly on the layer(s) of bound water on the surface of the collagen molecules rather than the collagens themselves. So-called free water may also take part in proton conduction as the result of induced polarization, particularly as water molecules naturally form hydrogen-bonded networks (see Chapter 7). This would be consistent with the increase in conductivity of collagen as hydration increases to a level well beyond the bound water fraction, which is probably around 0.15 g/g. (The normal hydration level of tendon is about 65%.) That conductive pathways actually link the entire body is demonstrated by Han Wan and Robert Balaban of the Canadian National Heart, Lung and Blood Institute,20 who are taking advantage of the variation in conductivity of different layers of tissues in the body to develop a new, non-destructive imaging technique to aid clinical diagnosis.

Patterns of collagen fibre alignment are important for biological organization and function. These patterns affect, not only the mechanical properties of the connective tissues, but, through the network of associated structured water, also the electrical conductivity and detailed circuitry for intercommunication, on which the health and well-being of the individual depends.21

I mentioned at the beginning of this Chapter that electrical injury currents flow from skin wounds and sites of amputation, which are involved in healing and regeneration. This is itself evidence that conductive circuits link the entire body, so that cuts result in leakage currents, which are involved in mobilizing cells to migrate to the site of injury in order to initiate the healing and regenerative processes. Electromagnetic stimulation have been used for stimulating regeneration or healing, with conflicting results. Part of the problem is that the strengths of electromagnetic fields used were far stronger than the endogenous fields.22 Another important factor which has received little attention may be the alignement of the applied electromagnetic field with respect to the collagen fibres at the site of injury. If the alignment is inappropriate, then application of an external field will not only be ineffective, but will even delay recovery.23 On that basis of the 100-fold difference in electrical conductivity along the fibre compared to that across the fibre, it would be expected that collagens fibres will align in the direction of the applied electric field. Julian Haffegee in our laboratory has confirmed this, and has achieved the first successful alignment of collagen fibres under self-assembly by weak electromagnetic fields.24 This work has important implications for wound healing and regeneration, as the movement of cells are known to be guided by oriented collagen fibres in the extracellular matrix.

The liquid crystalline continuum of collagen fibres and associated bound water is therefore ideally suited for mediating rapid intercommunication and responsiveness throughout the body. I suggest that it constitutes the body's “consciousness” which, apart from the capacity for intercommunication and responsiveness, also includes the faculty of memory. This exquisitely sensitive body consciousness is the basis of the body's responsiveness to “subtle energy medicines” such as acupuncture (c.f. Oschman).25 Let us examine this hypothesis in more detail.

Oriented Collagens and Body Consciousness

Proteins in liquid crystals have coherent motions, if only because the molecules are aligned, so that not all the degrees of freedom of movement that individual molecules have will be available in the liquid crystal mesophase.26 Protein motions involve vibrational deformations of peptide bonds, which will generate polarization waves along the proteins accompanied by proton conduction in the structured water shell. These coherent vibrations are especially likely as the result of metabolic pumping, much as Fröhlich has suggested (see Chapter 8). Very weak signals of mechanical pressure, heat or electricity, will be readily amplified and propagated by a modulation of the proton currents or coherent polarization waves.27 The hydrogen-bonded water network of the connective tissues extends through ordered water dipoles in the ion-channels of the cell membrane that allow inorganic ions to pass in and out of the cell.28 There is thus a direct electrical link (in addition to the mechanical link described above) between distant signals and the intracellular matrix, leading to physiological changes inside the cells, including nerve cells. This electrical channel of intercommunication is in addition to and coupled with the mechanical tensegrity interactions of the connective tissue and intracellular matrix continuum, because any mechanical deformations of the protein-bound water network will automatically result in electrical disturbances and conversely, electrical disturbances will result in mechanical effects. The new imaging technique that Han and Balaban (see above) are developing depends specifically on detecting ultrasound emissions from mechanoelastic vibrations caused by electrical pulses applied to the tissues. Muscle physiologists have long detected sounds from working muscles, but have treated them as distracting noise when electrical or mechanical signals are being recorded.

Proton jump-conduction belongs to a form of semi-conduction in condensed matter, and is much faster than conduction of electrical signals by the nerves. Thus the ‘ground substance’ of the entire body has a much better intercommunication system than can be provided by the nervous system alone. That is why lower animals which do not have a nervous system are nonetheless sensitive. Watch how a hydra or a sea-anemone contract its entire body when one of its tentacles is touched. At the other end of the evolutionary scale, note the alarming speed with which a hypersentive response occurs in human beings. There is no doubt that a body consciousness exists prior to the ‘brain’ consciousness associated with the nervous system. This body consciousness also has a memory.

Crystal Memory

Many studies on the conformation (three-dimensional shape) of the collagen triple-helix have shown that subtle changes are correlated with specific biological activities.29 Cells are guided in their growth and movement by contact with collagens, and specific sites are recognized by a host of cell membrane proteins. Mutations altering amino-acid sequences give subtle changes in the conformation30 which are associated with hereditary diseases, such as osteogenesis imperfecta, chondrodysplasias and Ehler-Danlos syndrome. Changes in collagen conformation also alters the bound water. Conformations of proteins are by no means static, all proteins undergo a hierarchy of conformational changes on a range of timescales, and collagens will be no exception. The conformations are clustered in groups of nearly identical energy content, with very low energy barriers between individual members of the group, but separated from other groups by higher energy barriers.31 Collective changes (or phase transitions) can readily be triggered, that will in turn alter the liquid crystalline structure and the bound water network, as dielectric studies on chemical liquid crystals have documented.32 As the collagens and bound water form a global network, there will be a certain degree of stability, or resistance to change. Memory may be further stabilized by cross-linking and other chemical modifications of the collagens. The network will retain tissue memory of previous experiences, but it will also have the capacity to register new experiences, as all connective tissues, including bones, are not only constantly intercommunicating and responsive, they also undergo metabolic turnover like the rest of our body. Memory is thus dynamically distributed in the structured network and the associated, self-reinforcing circuits of proton currents, the sum total of which will be expected to make up the DC body field itself.

Coupled Body and Brain Consciousness

Body consciousness possessing all the hallmarks of consciousness — sentience, intercommunication and memory — is distributed throughout the entire body. Brain consciousness associated with the nervous system is embedded in body consciousness and is coupled to it.33 That bound water plays a crucial role in conscious experience is supported by recent evidence that anaesthetics act by replacing and releasing bound water from proteins and membrane interfaces.34 Significantly, Becker found that general anesthesia leads to the complete attenuation of the DC body field.35

Although brain and body consciousness are normally coupled to each other, they may decouple under certain circumstances. Surgicial patients under general anaesthesia have been known to regain (brain) consciousness of pain, but not the ability to move or to express their distress. In contrast, acupuncture has been successfully used to anaesthesize patients who are fully awake. Further evidence that brain and body consciousness are to some extent independent is Becker's observation36 that during a perceptive event, local changes in the

DC field can be measured half a second before sensory signals arrive in the brain, suggesting that the activities in the brain is preconditioned by the local DC field.

It is reasonable to conclude that brain and body consciousness mutually inform and condition each other, and that the unity of our conscious experience depends on the complete coherence of brain and body.

The Unity of Conscious Experience37

From the perspective of the whole organism, one might think that the brain's primary function is the mediation of coherent coupling of all the subsystems of the body, so the more highly differentiated the organism, the bigger the brain required. Substantial parts of the brain are indeed involved in integrating inputs from all over the body, and over long time periods. But not all the ‘‘processing” that goes on in the brain is involved in the coherent co-ordination of parts of the body, for this coordination seems instantaneous by all accounts.

Thus, during an olfactory experience, slow oscillations in the olfactory bulb in the brain are in phase with the movement of the lungs.38 Similarly, the co-ordinated movement of the four limbs in locomotion is accompanied by patterns of activity in the motor centres of the brain which are in phase with those of the limbs.39 That is a remarkable achievement which physiologists and neuroscientists alike have taken too much for granted. The reason macroscopic organs such as the four limbs, the heart and lungs can be co-ordinated is that each is individually a coherent whole, so that a definite phase relationship can be maintained among them (see Chapter 9). The hand-eye coordination required for the accomplished pianist is extremely impressive, but depends on the same inherent coherence of the subsystems which enables instantaneous intercommunication to occur. There simply is not time enough, from one musical phrase to the next, for inputs to be sent to the brain, there to be integrated, and coordinated outputs to be sent back to the hands.40 I suggest that the instantaneous (nonlocal) coordination of body functions is mediated, not by the nervous system, but by the body conscousness inhering in the liquid crystalline continuum of the body. Implicit in this suggestion is the idea that living systems have a special kind of coherence or wholeness, which is characteristic of macroscopic quantum systems. Quantum coherence will be treated in more detail in the next Chapter. For now, let us assume that is the case, and see how the unity of experience, or, the “unity of intentionality”41 can arise.

The unity of experience depends, in the first instance, on the organism's experience of itself as a unity, and not as a collection of disparate parts. It is the “I” that each and everyone of us experience ourselves to be. Not only are we conscious of ourselves as a unity, but we have a total grasp of different parts of our body working together as a coherent whole. We have a self-image of our body, which is located exactly where our body is. So, we can reach out instantly to touch our face or scratch our ear, without missing the target. How do we manage that?

That can be achieved if the memory of our body, inhering in the liquid crystalline continuum, were to exist in a quantum holographic form. An ordinary hologram is an interference pattern produced by two intersecting, coherent beams of light, which is stored in a holographic media, such as a photographic plate or film. (In the case of the body, it would be the liquid crystalline continuum that constitutes the holographic medium). One beam, the reference, reaches the plate directly, while the other is scattered off the object to be recorded. As the interference pattern is spread over the entire plate, all parts of it receive information regarding the object. A quantum hologram involves quantum processes. The interference patterns are due to Schrödinger waves with linear superpositions of complex amplitudes. (see next Chapter), but the principle is the same.42 Consequently, memory is distributed over the entire liquid crystalline medium. And, as each part of the medium receives information from all over the body, the entire body can be reconstructed from a small part, albeit with loss of detail. That may be how development works in principle. The egg, having been part of the whole adult organism, has a memory of the organism which it reconstructs during embryonic development, aided by the genes. Similarly, in the case of consciousness, it means that the whole can be accessed or grasped from any local part. So, regardless of whether we think our conscious awareness is in the brain or in the heart, we may literally have an image of ourselves in both the brain and the heart, or in our ear or our hand. Each part, may literally be a microcosm of the whole.

Computer scientist Peter Marcer has proposed a quantum holographic model of (brain) consciousness in which perception involves converting an interference pattern (between a coherent wave-field generated by the perceiver and the wave-field reflected off the perceived) into an image of the object which is coincident with the object itself.43 This is accomplished by a process known as phase conjugation, whereby the wave reflected from the object is returned (by the perceiver) along its path to form an image where the object is situated. According to psychologist Gibson,44 perception of the environment and proprioception of the self are simultaneously one and the same. Within the perceptive realm of the organism, there will always be an image of the self to which all features in the environment are related. Marcer's quantum holographic model of self-consciousness would therefore involve an image of the self coincident with the perceiving organism, so “self” and ‘‘other” are simultaneously defined. What is the source of the coherent wave-field generated by the perceiver? Could it be the body field itself? Or the body field as modulated by the central nervous system? These are subject for empirical investigations. The body field, as suggested earlier, is probably related to the “coherent excitations” in the liquid crystalline continuum, which are expected to build up from metabolic pumping. These would naturally serve as coherent reference waves in the body. But would they be emitted from the body? Physical theory predicts they would be radiated, and very weak magnetic fields around the body are indeed detected with the highly sensitive SQUID magnetometer (see Chapter 9).

I have argued that quantum coherence is the basis of conscious experience, which involves the possibilities of nonlocal intermunication between distant parts of the brain, the simultaneous recognition of whole and part in our perceptive field, and the distinctive quality of each experienced occasion.45 All that is beyond the scope of the present discussion. I shall mention just one aspect of (brain) memory here.

Many people have already remarked on the holographic nature of brain memory in that it is able to survive large brain lesions. The possibility, from what has been said above, is that memory is not only delocalized over the entire brain, but over the entire liquid crystalline continuum of the body which serves as a holographic medium. Ervin Laszlo,46 philosopher and systems theorist, has recently proposed that much of personal memory may be stored in an ambient, collective quantum holographic memory field delocalized from the individual — in the universal holographic medium of the quantum vacuum — and that memories are accessed by the brain from the ambient field. This is fully consistent with the 'romantic' idea, increasingly validated by the foundations of quantum theory, that all nature is interconnected, and that the separateness and discreteness of things in the common sensible world are illusory.

Notes

1. See Becker (1990).
2. See Oschman (1984, 1993); Pienta and Hoover (1994).
3. See Van der Rest and Garrone (1991) and references therein; also Knight and Feng (1993).
4. Leikin et al. (1995).
5. Haffegee et al. (1997).
6. Leikin et al. (1995).
7. See Bella et al. (1994).
8. See Peto and Gillis (1990).
9. See Renugopalakrishnan et al. (1989).
10. Sasaki (1984).
11. Ron Pethig, personal communication.
12. Jaroszyk and Marzec (1993).
13. Leikin et al. (1995).
14. See Pienta and Hoover (1994).

15. See Oschman (1984, 1993); also Ho (1997b).
16. See Langer (1978). These lines guide surgical incisions, as wounds heal more readily when cuts are made along the lines rather than across the lines.
17. See Reihsner et al. (1995).
18. Ho and Knight (1997).
19. See Becker (1990).
20. See Ehrenstein (1997).
21. David Knight and I and two other colleagues have made repeated attempts, without success, to obtain research support for investigating collagen fibre alignments in connective tissues in health and disease. The quantitative image analysis package we have developed in our laboratory is especially suited for the purpose.
22. See Becker (1990).
23. Watkins et al. (1985).
24. See Haffegee et al. (1997b); Dickinson et al. (1994).
25. Oschman (1993).
26. Searle and Williams (1992).
27. Mikailov and Ertl (1996).
28. Williams (1993); Chiu et al. (1993).
29. Fields (1995).
30. See Bella et al. (1994).
31. See Welch (1985).
32. See Leikin et al. (1993); Wrobel et al. (1988).
33. The following account is abstracted from Ho (1997b), which should be consulted for more details.
34. See Tsukamoto and Ogli (1995) and references therein.
35. Becker (1990).
36. Becker (1990).
37. What follows is taken from Ho (1997b).
38. Freeman and Barrie (1994).
39. Kelso (1991).
40. See Hebb (1958).
41. Freeman (1995).
42. I have drawn inspiration for the idea of the quantum holographic body memory from Laszlo's (1995) suggestion that the zero point field (quantum vacuum) of the universe is just such a quantum holographic medium.
43. Marcer (1992, 1995).
44. Gibson (1966).
45. Ho (1997b).
46. Laszlo (1995).

CHAPTER 13

Quantum Entanglement and Coherence

What is Coherence?

A key notion in the new perspective of living organization developed in the previous Chapters is ‘coherence’. Coherence in ordinary language means correlation, a sticking together, or connectedness; also, a consistency in the system. So we refer to people's speech or thought as coherent, if the parts fit together well, and incoherent if they are uttering meaningless nonsense, or presenting ideas that don't make sense as a whole. Thus, coherence always refers to wholeness. However, in order to appreciate its full meaning, and more importantly, the implications for the living system, it is necessary to make incursions into its quantum physical description, which gives insights that are otherwise not accessible to us.

Before we do that, we must venture more deeply into the mysterious world of quantum physics. We have already been using a good deal of quantum physics in previous Chapters, as when dealing with statistical mechanics, the structure of atoms, the physics of solid states, and so on, which shows how important quantum physics is for understanding contemporary physics and biochemistry. Here we shall delve into the fundamental nature of physical reality revealed to us by quantum theory, and we shall do so with the help of two kinds of observations, which illustrate most clearly how the quantum world is completely at odds with the classical world of Newtonian mechanics.

The first kind of observations demonstrates the wave-particle duality of physical reality, and the second, the phenomena of nonlocality and entanglement. These experiments also impinge upon the central issue of the role of the observer in science. Within the classical framework, the role of the observer is strictly external to the system observed and it is supposed that no influence passes from the one to the other. By contrast, the observer and observed in the quantum world is inextricably entangled. As we shall see, quantum entanglement has a lot to do with quantum coherence.

Wave-Particle Duality

We have seen in Chapter 7 that even within classical physics, light exhibits properties which are consistent with its being composed of waves or of particles. However, in quantum physics, we must think of light as simultaneously wave-like and particle-like. Most quantum physicists have given up trying to say what it really is by calling this property (which belongs to both light and matter), the wave-particle duality. It manifests itself most graphically in one of the earliest quantum-mechanical experiments.

In the simplest version of this experiment, a beam of light is shone through a screen containing a pair of narrow slits onto a photographic plate (see Fig. 13.1).

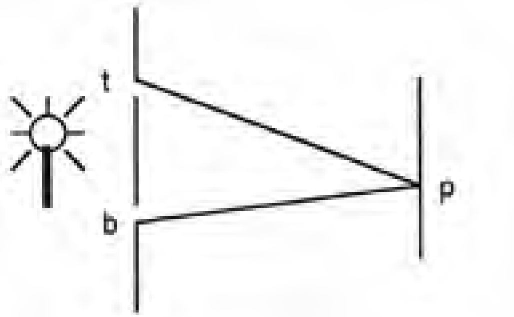

Figure 13.1 The two-slit experiment. (See text)

When only one of the slits is opened, an image of the slit is recorded on the photographic plate, which, when viewed under the microscope, would reveal tiny discrete spots (see Fig. 13.2). And this is consistent with the interpretation that individual particle-like photons, on passing through the slit, have landed on the photographic plate, where each photon causes the deposition of a single silver grain.

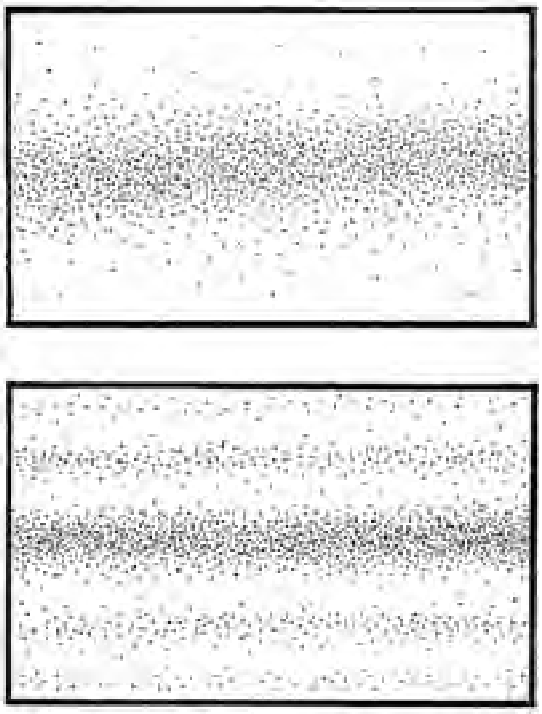

Figure 13.2 The exposure pattern on the photographic plate. Top, with one slit open; bottom, with both slits open.

When both slits are opened, however, an interference pattern arises on the photographic plate, which is consistent with a wave-like behaviour of the light: the two wave trains on passing through the slits, arrive at different parts of the screen either in phase, when they reinforce each other to give a bright zone, or out of phase, so that they cancel out each other to give a dark zone. On examining the photographic plate under the microscope, however, the same graininess appears, as though the light waves become individual particles as soon as they strike the photographic plate (Fig. 13.2).

The result is the same even if the light intensity is reduced to such an extent that only individual photons will pass through the slits and arrive on the screen one at a time. This means that each photon has somehow passed through both slits and interfered with itself, i.e., each particle behaves in a wave-like way entirely on its own in being able to pass through both slits. Yet on encountering the photographic plate, it becomes a particle again! If one tries to be clever and place a photon-detector at one of the slits so that the observer can tell which slit the photon has passed through, then the interference pattern will disappear. In order for interference to take place on the photographic plate, it seems that we must remain 'ignorant' as to which slit the photon has 'actually' passed through. The photons retain both alternatives of going through the top and the bottom slits. Similar experiments have been done with electrons, or recently, with neutrons, which are 1800 times as massive as the electron, and the results tell us the same thing. The neutron can be 'split' into two (by a suitable beam splitter), and on recombining gives an interference pattern exactly as the single photon does. If we were to put detectors in either path, then we would always find the whole neutron in either one or the other, but never in both simultaneously. Numerous other more sophisticated experimental configurations have been devised to investigate this phenomenon, with always the same result.1 Photons 'split' into superposed reflected and transmitted states, or into opposite polarized states are capable of interfering when brought together again.

The way quantum mechanics explains this result is to 'say' mathematically that the photon has a 'probability amplitude' — expressed as a complex number, of passing through the top or the bottom slit. These amplitudes express the quantum mechanical alternatives available to the photon. But they are not probabilities in the classical sense. In order to get the correspondence to classical probabilities (and hence the correct interference pattern), we must square those amplitudes or complex number weightings.2

The fundamental picture of reality in quantum mechanics is that all alternative possiblities open to the system co-exist in a ‘pure state’ rather than a mixture of states until the instant when we observe it. It is important to get this distinction between a ‘pure’ and a ‘mixed’ state. A pure state is indivisible, it is a unity which we can represent as a ‘superposition’ of all the possible alternatives. The mixed state, however, is a mixture where the different states really exist in different proportions. The act of observation seems to put an end to this dream-like pure state into one of the possibilities that previously existed only as a potential. Hence, the observer seems to somehow determine the fate of the particle by ‘collapsing’ all its possibilities into a state of definiteness.

This is often told as the parable of Schrödinger's cat, kept in a box with a radioactive nuclide which might undergo radioactive decay and trigger a mechanism releasing cyanide gas to kill the cat. The quantum state of the cat therefore, is a superposition of being dead and being alive, until the instant when the observer opens the box, when it is either definitely dead, or definitely alive. Apart from being unkind to cats, this parable also suffers from human-observer chauvinism. One might raise the serious objection as to whether the cat, too, has a right to observe. Nevertheless, there is a school of thought which believes that it is the act of observation by the human consciousness which makes definite things happen.

The problem of quantum superposition is real, in the sense that it is not just a philosophical or psychological quirk, and it is not confined to microscopic systems. It has been suggested that quantum superposition depends on the quantum coherence of the superposed states, which disappears when the system decoheres on interacting with the environment.3 (We shall deal with quantum coherence later on.) Experimental support for this idea was provided recently when a group of experimental physicists succeeded in preparing a single atom in a quantum superposition of two spatially separate positions more than 80 nanometers apart, which is large compared with the atomic dimension of 0.1 nm. This was achieved by forming a superposition of two coherent state wave-packets of a single trapped atom using a precise sequence of laser pulses.4

We can generalize this picture to a particle, or a system that can exist in n possible states, then all of those possibilities are given a complex number weighting, the sum of all of which constitutes its quantum state, or wave function, ψ (Greek letter 'psi'). Classically, a particle has a definite position in space, and a definite momentum, which tells one where it is going to go next. Quantum mechanically, however, every single position that the particle might have is available to it, which together make up its wave function. A corresponding wave function can be composed of all the possible momenta it could have. The position and momentum wave functions are connected by a mathematical transformation called the Fourier transform. Position and momentum are related by a deep complementarity: a particle which has a precise position in space is completely indeterminate in its momentum; conversely, one which has a definite momentum will be completely delocalized in space, as can be seen in the Fourier transform diagrams (Fig. 13.3).

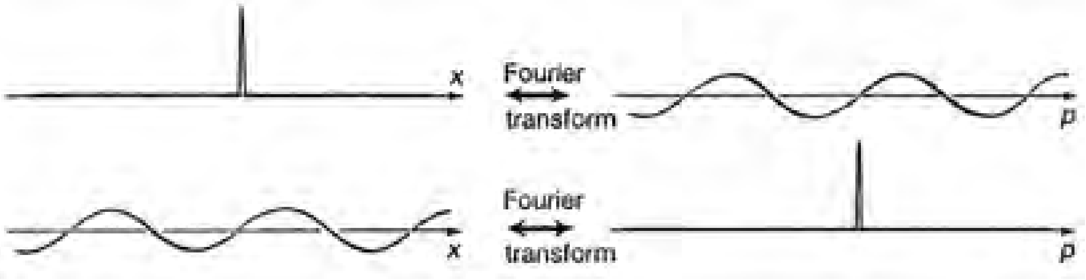

Figure 13.3 Fourier transforms between position (x) and momentum (p) (see text).

A particle with definite position has a position wave function which is very sharply peaked at the value of x in question, all the amplitudes being zero elsewhere. Such a position wave function is a delta function. The momentum wave function corresponding to it is completely spread out in momentum values. Conversely, a particle with a delta function in momentum will be completely delocalized in space.

Another way to express the same thing is in terms of Heisenberg's uncertainty principle, which states that position and momentum of a particle cannot both be known precisely,

$$\Delta x \, \Delta p \geq h/4\pi \tag{13.1}$$

where Δ means 'uncertainty of' x and p are position and momentum respectively, and h is Planck's constant. That means a measurement which gives a precise position value will be completely uncertain with respect to momentum, and vice versa, one giving a precise momentum value will be completely uncertain with respect to position. An analogous relationship for time, t, and energy, E, exists,

$$\Delta E \, \Delta t \geq h/4\pi \tag{13.2}$$

although, as we shall see in Chapter 15, this relationship is really quite different from the position/ momentum uncertainty. The latter refers to the quantities measured at the same instant of time. The energy/ time relationship refers instead to the difference in energy which can be measured to any degree of accuracy at two different instants, and hence, is not the uncertainty in energy at a given instant.

The EPR Paradox and Quantum Entanglement

No description of quantum mechanics at any level is complete without the Einstein, Podolsky and Rosen paradox (the EPR paradox for short). Although Einstein contributed substantially to the development of quantum theory, he could never accept the description of reality in terms of the wave function consisting of a combination of complex amplitudes. This indefiniteness bothered him as something told him that, "God does not play dice!". He assumed there must be a deeper structure beneath quantum mechanics which presents reality without the contradictions inherent in the accepted theory.

Some people have continued in this line of thinking, as for example, David Bohm and Basil Hiley (see Chapter 15).

In order to try to show that a deeper, definite structure of reality exists. Einstein, Podolsky and Rosen proposed a thought experiment, or gedanken experiment (which in the end overcame their objections, especially when the experiment was eventually, actually carried out). The following is a later version due to Bohm.5 Suppose two particles which are prepared in pairs — say an electron and a positron — with complementary properties such as spins up and down, move apart in opposite directions. By the conservation of momentum, the spins must add up to zero, because that is the spin of the initial central particle from which the pair has been generated. This has the implication, according to quantum theory, that if we measure the spin of the electron in whatever direction we choose, the positron must spin in the opposite direction, and vice versa. The two particles could be miles or light-years apart, yet the very choice of measurement on one particle seems instantaneously to fix the axis of spin of the other.

This remarkable result — which has been predicted and subsequently confirmed by experiment — cannot be explained by assuming that there are pre-set probabilities of the electron and positron pair to be in different combinations of spins, or that the two measuring machinery produces ordinary probabilistic responses, the probabilities being determined by the machinery.

One can increase the number of possible alternative settings for different directions of spins in the measurement process, say, in addition to spin ‘up’ or ‘down’, also ‘left’ or right’ and other angles in between, but that does not alter the findings: If the settings on both sides are the same, the results of the two sides always disagree. If the settings are spun at random, completely independently of each other even after the two particles have separated, then the two measurements are as equally likely to agree as to disagree.

This combination of results is incompatible with any local interaction model as the signals cannot propagate faster than light, and there is no set of prepared answers which can produce the quantum mechanical probabilities. The obvious conclusion that has to be drawn is that the effect of measurement (or ‘collapse of the wave function’) of one particle is instantaneously communicated to the other one. It is as though they are still one single coherent system, or in a pure state (see above), much like the single photon that passes through two slits at once, the neutron that interferes with itself, and the atom that is effectively in two places simultaneously. A coherent system has neither space nor time separation, so the ‘collapse’ of one part is ‘instantaneously’ communicated to the other part, regardless of how great a distance exists between the two parts. By extrapolation of the experimental results, it must mean that the two parts could be light years apart, and still the ‘collapse’ of the wave function of one particle instantaneously collapses that of the other as well.

The concept of ‘entanglement’ was introduced by Schrödinger in 1935 to describe this phenomenon as part of his formal discussion of the EPR paper proposing the experiment. The two particles are, as it were, entangled with each other in a pure, coherent state.6 It turns out that the two particles do not even have to be prepared together so that they are originally one system. Experimentally, one can even allow any two particles, neutrons, electrons, or photons, to be produced at distant and unrelated sources. As soon as they have come together and interacted, they become entangled with each other long after they have collided and separated. They have become one7 quantum system. This result is very significant, and I shall come back to it in the final Chapter.

Quantum Coherence

The previous experiments bring out the paradoxical characteristics of the coherent quantum state: quantum superposition, delocalization, inseparability, nonlocal interactions. In order to examine further what quantum coherence entails, let us return to the two-slit experiment as depicted in Fig. 13.1. Recall that when both slits are open, even single photons — generated one at a time at very low light intensities — behave as waves in that they seem to pass through both slits at once, and, falling upon the photographic plate, produces a pattern which indicates that each photon, in effect, interferes with itself. The intensity or brightness of the pattern at each point depends on a ‘probability’ that light falls on to that point.

The ‘probability’ is placed between quotation marks because, as said before, it is not probability in the ordinary sense. One way of representing these special probabilities is as correlation functions consisting of the product of two complex amplitudes. Light arriving at the point p on the photographic plate (Fig. 13.1) has taken different paths, tp and bp. The intensity at p is then given as the sum of four such correlation functions:

$$I = G(t,t) + G(b,b) + G(t,b) + G(b,t)\,, \qquad (13.3)$$

where G(t,t) is the intensity with only the top slit opened, G(b,b) the intensity with only the bottom slit opened, and G(t,b) + G(b,t) = 2G(t,b) is the additional intensity (which take on both positive and negative values) when both slits are opened. At different points on the photographic plate, the intensity is

$$I = G(t,t) + G(b,b) + 2\left|G(t,b)\right|\cos\theta\,, \qquad (13.4)$$

where θ is the angle of the phase difference between the two light waves.

The fringe contrast in the interference pattern depends on the magnitude of G(t,b). If this correlation function vanishes, it means that the light beams coming out of t and b are uncorrelated; and if there is no correlation, we say that the light at t and b are incoherent. On the other hand, increase in coherence results in an increase in fringe contrast, i.e., the brightness of the bands. As cosθ is never greater than one (i.e., when the two beams are perfectly in phase), then the fringe contrast is maximized by making G(t,b) as large as possible and that signifies maximum coherence. But there is an upper bound to how large G(t,b) can be. It is given by the Schwarz inequality:

$$G(t,t)G(b,b) \geq |G(t,b)|^2 . \qquad (13.5)$$

The maximum of G(t,b) is obviously obtained when the two sides are equal:

$$G(t,t)G(b,b) = |G(t,b)|^2 . \qquad (13.6)$$

Now, it is this equation that gives us a description of quantum coherence. A field is coherent at two space-time points, say, t and b, if the above equation is true. Furthermore, we have a coherent field if this equality holds for all space-time points, X1 and X2. This coherence is called first-order coherence because it refers to correlations between two space-time points, and we write it more generally as,

$$G_{(1)}(X_1,X_1)G_{(1)}(X_2,X_2) = |G_{(1)}(X_1,X_2)|^2 . \qquad (13.7)$$

The above equation tells us that the correlation between two space-time points in a coherent field factorizes, or decomposes neatly into the self-correlations at the two points separately, and that this factorizability is a sufficient condition for coherence. It is important to remember that the coherent state is a pure state and not a mixture of states (see previous sections). Factorizability does not mean that it can be factorized into a mixture. But it does lead to something quite unusual. What it means is that any two points in a coherent field will behave statistically independently of each other. If we put two photon detectors in this field, they will register photons independently of each other.

Coherence can be generalized to arbitrarily higher orders, say, to n approaching ∞, in which case, we shall be talking about a fully coherent field. If nth order coherence holds, then all of the correlation functions which represent joint counting rates for m-fold coincidence experiments (where $m < n$) factorize as the product of the self-correlations at the individual space-time points. In other words, if we put n different counters in the field, they will each record photons in a way which is statistically independent of all the others with no special tendency towards coincidences, or correlations. Coherence can therefore exist to different orders or degrees.8

The theory of quantum coherence, as developed by quantum physicist Roy Glauber9 does not require the existence of a single mode, or frequency, of light. There can be many modes, so long as they are coupled. Nor does it require the existence of high intensities of light. The factorizability of coherent states has been experimentally verified, and high degrees of coherence — six or more orders — have also been measured in commercial lasers.

Quantum Coherence and Living Organization

A coherent state thus maximizes both global cohesion and also local freedom. Nature presents us a deep riddle that compels us to accommodate seemingly polar opposites. What she is telling us is that coherence does not mean uniformity: where everybody must be doing the same thing all the time. You can begin to understand it by thinking of an orchestra, or a grand ballet, or better yet a large jazz band, where everyone is doing his or her own thing, as yet keeping perfectly in tune or in step with the whole. But even that is a paltry representation.

‘‘Imagine an immensely huge superorchestra playing with instruments spanning an incredible spectrum of sizes from a piccolo of 10-9 metre up to a bassoon or a bass viol of 1 metre or more, and a musical range of seventy-two octaves. The amazing thing about this superorchestra is that it never ceases to play out our individual songlines, with a certain recurring rhythm and beat, but in endless variations that never repeat exactly. Always, there is something new, something made up as it goes along. It can change key, change tempo, change tune perfectly, as it feels like it, or as the situation demands, spontaneously and without hesitation. Furthermore, each and every player, however small, can enjoy maximum freedom of expression, improvising from moment to moment, while maintaining in step and in tune with the whole.”10

That is precisely the biochemical picture we now have of the living system: compartment, microcompartments and microdomains, right down to molecular machines, all functioning autonomously, doing very different things at different rates, generating flow patterns and cycles of different spatial extensions, yet all coupled together, in step with one another and hence, with the whole organism.

Many of the most paradoxical properties of the living system follow from coherence defined in this more rigorous sense. For example, factorizability optimizes communication by providing an uncorrelated network of space-time points which can be modulated instantaneously by specific signals. Furthermore, it provides the highest possible fringe contrast (or visibility) for pattern recognition, which may account for the great specificities in the response of organisms to diverse stimuli. The factorizability of coherent fields may also underlie the efficiency of bioenergetic processes in two respects. First, it concentrates the highest amount of energy of the field in localized zones by constructive interference, as well as creating effectively field-free zones within the field by destructive interference. Second, since the higher order correlations are the lowest in a completely coherent field, the smallest possible amount of energy is subject to correlated transfer between an arbitrarily large number of space-time points in the field with minimum loss. A coherent field is also fluctuationless or noiseless, the sort that any communications engineer working in radio-frequencies, for example, would say is coherent.11

As mentioned above, coherence does not require the existence of a single frequency; it is only necessary for the different frequencies to be coupled together so as to represent effectively a single degree of freedom. Hence, there can be a broad band of frequencies coupled together or intercommunicating, so that energy fed into any frequency can be propagated to all other frequencies, which is, in fact, what happens in the living system (see Chapters 6 and 10).

I have argued in earlier Chapters that quantum coherence is characteristic of living systems for two reasons. First, as molecular machines are quantum machines, quantum coherence must necessarily be involved in their coordination. Second, the rapidity of long range coordination in the living system is such as to rule out classical coherence due to classical phase transitions as exemplified by the Bénard-Rayleigh convection cells. However, time is a subtle (and difficult) concept, as pointed out in connection with the space-time structure of living organisms.

Consider the consequence of coherence on energy storage in the living system. Coherence is associated with a time and a volume over which phase correlation is maintained. The coherence time for a quantum molecular process is just the characteristic time interval τ over which energy remains stored in McClare's formulation of the second law given in Chapter 3. So, in conformity with the second law of thermodynamics, the longer the coherence time, τ, the more extended is the timescale over which efficient energy transfer processes can take place, provided that the relaxation times are either much less than τ, or, in the quasi-equilibrium approximation, if they take place slowly with respect to τ. In other words, efficient energy transfer processes can in principle occur over a wide range of timescales, depending on the coherence space-time structure of the system.12

The existence of space-time structure in living systems also has its own interesting consequences of which I can only give a hint here. Time structure manifests itself most clearly in the range of biological rhythms that extend over some ten orders of magnitude from the millisecond oscillations of membrane action potentials to 107s for circannual rhythms, which are coherent over varying spatial domains from single cells to entire organs and from whole organisms to populations of organisms (see Chapter 9). A coherent space-time structure theoretically enables ‘instantaneous’ communication to occur over a range of time scales and spatial extents. What this implies in practice is a vast unexplored area, as the notion of nonlinear, structured time this entails is alien to the conventional, western scientific framework that this book is largely based upon. We shall go into the problem of time in more detail in the final Chapter.

I have been presenting heuristic arguments throughout many of the previous Chapters on why the wholeness of organisms has to be understood as quantum coherence. First, there is increasingly compelling evidence that the organisms are organized to approach the 'solid state', (Chapter 8) or, more accurately, the liquid crystalline state, in which much of the water is structured on the large amount of surfaces available in the matrices of cells and the connective tissues (Chapters 10, 11 and 12). That, and the dynamic and energetic closure of the living system (Chapters 4 and 6) provide both the necessary and sufficient conditions for coherent excitations to occur, rather as suggested by Fröhlich (see Chapter 8). The predominant interactions in the liquid crystalline organism, as in any liquid crystalline systems, are electric, electromagnetic and electro-mechanical, and necessarily so, for those are the only ways in which molecules interact and form the various hierarchies of supramolecular assemblies that make up living organisms themselves (Chapter 7). Living organisms depend on quantum reactions, not only in the sense that quantum tunneling is explicitly recognized in electron and proton transfer, but especially in the sense that all energy transductions are carried out by individual enzymes and other molecules acting as "quantum energy machines" in which individual quanta of energy released are directly transferred from the point of release to the point of use (Chapter 3). The coordination of such activities requires nothing short of quantum coherence, especially in view of the rapidity and specificity with which responses or intercommunication can take place in the living system.

By far the most persuasive argument for quantum coherence, to my mind, is the nature of the coordination that is achieved in the organism, where every single part in its magnificently diverse and pluralistic multiplicity, down to an individual quantum molecular energy machine, is able to work autonomously while keeping in step and in tune with the whole. That requires none other than the factorizability of the quantum coherent state, as I have just explained.

We may now offer a tentative answer to at least part of a question which was posed at the beginning of this book: what is it that constitutes a whole or an individual? It is a domain of coherent, autonomous activity. The coherence of organisms entails a quantum superposition of coherent activities over all space-time domains, each correlated with one another and with the whole, and yet independent of the whole. In other words, the quantum coherent state, being factorizable, maximizes both global cohesion and local freedom. It is that which underlies the sensitivity of living systems to weak signals, and their ability to intercommunicate and respond with great rapidity. Within the coherence volumes and coherence times of energy storage, there is no space-like, nor time-like separation, and that is why organic space-time can be nonlocal.

The organism is, in the ideal, a quantum superposition of coherent activities over all space-times, this pure coherent state being an attractor, or end state towards which the system tends to return on being perturbed.13

The fully coherent state (to order m, where m approaches ∞) is an idealization which is almost never realized. That is because the system, despite its dynamic, energetic closure, is constantly interacting with its environment, which would tend to decohere the system, or take it away from the fully factorizable pure state. Nevertheless, it will tend to return to the coherent pure state, which is an attractor. In quantum optics and quantum electrodynamic theory, the coherent state is indeed asymptotically stable.14 Similarly, Duffield15 has provided a proof that the “Fröhlich state” of coherent excitation also exhibits global asymptotic stability. In analogy with the pumped laser, one might even consider the stronger hypothesis that phase correlations between different modes in the living system are actively determined and maintained (c.f. Haken).16

Another useful representation of the organism is in terms of a coherent quantum electrodynamical field of many modes,17 with an uncertainty relationship between energy and phase,18 such that when phase is defined, energy is indeterminate, and vice versa. This captures a phase-amplitude relationship between macroscopic physiological rhythms frequently observed. Accurate phase correlations are usually accompanied by wide variations in amplitudes, whereas rhythms with constant amplitudes are not perfectly periodic, which lead to the idea that healthy rhythms exhibit deterministic chaos.19 In reality, they reflect the constant intercommunication between different biological rhythms that must take place in a healthy organism.20

A group of physicists and cardiologists used a new approach to analyze the heartbeat, based on wavelet and Hilbert transforms, and obtained a remarkable result. The distributions of the variations in the beat-to-beat intervals for all healthy subjects can be described by a single function, while those from unhealthy subjects cannot.21 Although the authors do not say so in their paper, these results suggest that there is a high degree of phase correlations among the different rhythmic frequencies in healthy subjects, as indicative of quantum coherence, which is not the case in cardiac patients.

The individual organism, defined as a domain of coherent activities, opens the way to envisaging individuals which are aggregates of individuals, as, for example, a population or a society engaging in coherent activities.22 As coherence maximizes both local freedom and global cohesion, it defines a relationship between the individual and the collective which has previously been deemed contradictory or impossible. The ‘inevitable’ conflict between the individual and the collective, between private and public interests, has been the starting point for all social as well as biological theories of western society. Coherence tells us it is not so ‘inevitable’ after all. Eminent sociologists have been deploring the lack of progress in sociology, and saying that it is time to frame new questions. Perhaps sociology needs a new set of premisses altogether. In a coherent society, such conflicts do not exist. The problem is how to arrive at such an ideal state of organization that in a real sense, nurtures diversity (and individuality) with universal love.23

Let us recapitulate the main results of the enquiry thus far into Schrödinger's question of ‘what is life?’, or ‘can life be accounted for by physics and chemistry?’. I have shown how the intricate space-time structure of the living system cannot be accommodated within the statistical nature of the laws of thermodynamics, which therefore, cannot be applied to the living system without some kind of reformulation. This reformulation leads to a thermodynamics of organized complexity, in which the living system is understood as a domain of coherent energy storage where coupled cyclic non-dissipative processes constituting the life cycle are superposed on the irreversible dissipative processes.

Organisms are isothermal systems in which the predominant energy transductions are electric, electromagnetic and electro-mechanical, as consistent with the primary energy source on which life depends, as well as the electromagnetic nature of all molecular and intermolecular forces. Furthermore, given the dynamic energetic closure achieved in living systems, and the organized, liquid crystalline state of living matter, the most general conditions of energy pumping from metabolism would result in a phase transition to a coherent regime where the whole spectrum of molecular energies can be mobilized for structuring the system, and for all the vital processes which make the system alive. Consciousness — the faculties of sentience, responsiveness and memory — may all be understood as properties of the liquid crystalline continuum which is the organism. Organisms are quantum superpositions of coherent activities that are actively maintained. This has profound implications on the nature of knowledge and knowledge acquisition, as well as issues of determinism and freewill, which we shall explore in the final Chapters.

I make no claims to having solved the problem of life. I have sketched with a very broad brush where some of the clues may lie, pointing to a number of new and promising areas of investigations on electrodynamics, nonlinear optical properties, the liquid crystalline nature of living organisms and quantum coherence. In the process, I have also raised many more subsidiary questions which I hope will keep the 'big' question alive.

Notes

1. See Laszlo (1995); Penrose, R. (1994) for clear descriptions on later variations of the two-slit experiment.
2. For a readable and authoritative account see Penrose, R. (1989), Chapter 6.
3. See Zurek (1991).
4. Monroe et al. (1996).

5. I thank Oliver Penrose for pointing this out to me.
6. See Li (1992) for a formal argument which throws further light on this idea.
7. See Zajonc (1991).
8. See Glauber (1969).
9. Glauber (1969).
10. From Ho (1997c).
11. See Ho and Popp (1993).
12. Ho (1993, 1995b).
13. See Ho (1997a).
14. Goldin (1982).
15. Duffield (1988).
16. Haken (1977).
17. Ho (1996c).
18. Preparata (1994).
19. See Glass and Mackey (1988); Goldberger (1991); Kelso (1991); Breithaupt (1989); Freeman and Barrie (1994).
20. See Ho (1996a).
21. Ivanov et al. (1996).
22. I have discussed the possibilities for a 'coherent society' in Ho (1996c).
23. See Ho (1992b, 1993, 1996c) for a more detailed discussion on these points.

CHAPTER 14

The Ignorance of the External Observer

The Meaning of Life and All That

Time has come for us to consider some of the implications of all that has been gone before. Any answer, however tentative it may be, to the question of “what is life?” naturally has something to say on the meaning of life, as I intimated right at the beginning. This Chapter continues our enquiry on consciousness begun in Chapters 11 and 12, but concentrates on knowledge itself, on our relationship to the known, which ultimately encompasses all of nature.

Let us begin by looking more closely at the relationships between entropy and the concepts of knowledge, information and order in the context of the living system. These relationships have exercised western scientists and philosophers from the very first, and have remained the subject of lively debate to the present day. I believe that our new understanding of the living system may have something to offer towards resolving some of the central issues.

Is Entropy Subjective?

The concepts of thermodynamics took shape during the industrial revolution when attempts were made to determine how much mechanical work can be made available from steam engines. In the process, it was noticed that not all of the heat energy supplied can be transformed into work — some of it invariably gets lost, or becomes dissipated. This dissipated energy goes to make up entropy. Statistical mechanics interprets entropy in terms of the number of microstates the system can have, but it remains a mere analogue of the thermodynamic entity. Many irreversible processes have a well-defined and measurable macroscopic entropy change, and yet cannot be consistently represented in statistical mechanical terms.

One of these situations, described by Gibbs, concerns the entropy of mixing of perfect gases, and has become known as ‘Gibbs paradox’. The entropy of mixing generated by, say, removing a partition separating the two gases occupying equal volumes on either side of the divide is always the same, and does not depend on how similar or otherwise the gases are. However, if the gases were identical, then the entropy of mixing has to be zero. But what if the two samples of the gas, previously thought to be identical are then found to be different after all? We must now say there is an increase in entropy to their mixing where previously we said it was zero. Maxwell writes,

‘‘It follows from this that the idea of dissipation of energy depends on the extent of our knowledge… Dissipated energy is energy which we cannot lay hold of and direct at pleasure, such as the energy of the confused agitation which we call heat. Now confusion, like the correlative term order, is not a property of things in themselves, but only in relation to the mind which perceives them.”1

Maxwell's idea — that entropy is a subjective concept which measures our ignorance — is all of a piece with the marked tendency among scientists in the 19th Century to regard any manifestation of randomness in natural phenomena as simply due to a lack of sufficient knowledge on our part, rather than as something inherent in nature.2 Although Maxwell emphasized the statistical nature of the second law, he believed it was merely our knowledge of the world that is statistical, and not the world itself. Similarly, Gibbs, commenting on the probabilistic foundations of statistical mechanics, said that probability refers to something which is ‘imperfectly known’. And G.N. Lewis writes in 1930, “The increase in entropy comes when a known distribution goes over into an unknown distribution… Gain in entropy always means loss of information, and nothing more. It is a subjective concept, but we can express it in its least subjective form, as follows. If, on a page, we read the description of a physicochemical system, together with certain data which help to specify the system, the entropy of the system is determined by these specifications. If any of the essential data are erased, the entropy becomes greater; if any essential data are added the entropy becomes less.”3

The same general viewpoint has been adopted by many scientists, the belief that entropy is a measure of the incompleteness of knowledge is one of the foundations of modern information theory, as we shall see. Denbigh and Denbigh comment that although the use of less information than is available in certain aspects of statistical mechanics does result in a greater calculated entropy, more information can also lead to an increase in entropy. For example, information is gained when a spectral line of a substance, previously believed to be a singlet — one corresponding to a single electronic transition — is actually found to be a multiplet corresponding to transitions involving multiple electronic levels. This gain in information, however, will require the revision of the spectroscopic entropy upwards, as it implies the existence of previously undetected microstates accessible to the system.

Furthermore, entropy cannot be entirely subjective because it is an observable quantity, and its value can be determined by the observable data such as energy, volume and composition. And in that sense, entropy is no more subjective than any physical property, such as density, or vapour pressure, which is a function of all variables determining the state of the system.

However, entropy may not be a property of a system as such, for its absolute magnitude cannot be determined directly — even though it is supposed that all substances have zero entropy at absolute zero temperature (see Chapter 5). For one thing, we do not know anything about the entropy within the nucleus of the atom. In practice, we can only measure a change in entropy between two states along a reversible path. Thus, it should be called a dispositional property — one which can be observed only under certain circumstances, or when certain operations are carried out.

My own sympathy lies with the Denbighs especially with regard to entropy being a dispositional property. However, it is a dispositional property, not just of the system, but also of the processes that take place in it. The dispositional nature of entropy can take on a strong form in that it is generated only under certain circumstances or when the system is prepared in certain ways, as opposed to a weaker form where it may be generated under all or most circumstances but only observed in some of them. If my conjecture concerning the thermodynamical description of the living system is right (see Chapter 6), internal entropy compensation can result in little or no net entropy being generated in living processes.

Of course, as active agents who can set up experiments and choose what to measure or observe, we can influence the generation of entropy as well, so one might say that entropy is also a measure of our inability to influence the system. This demonstrates that in a very real sense, we participate in defining a process of measurement in partnership with nature, and out of this act, properties emerge which are neither those of things in themselves nor pure mental constructs, but an inextricable entanglement of both. This is a generalization of the inseparability of observer and observed that is at the heart of quantum measurement. Thus, the subjectivist-objectivist dichotomy is falsely drawn. Subjectivity is an anthropomorphic, anthropocentric concept, and suffers from the same human chauvinism that attributes to the human observer alone the power to make definite things happen in the act of quantum mechanical measurement (see previous Chapter). After all, other natural entities are entitled to their properties and propensities which are not just subject to our arbitrary intellectual whim and dictate. On the contrary, they require our active participation in the process of measurement in order to make manifest those properties which become part of our knowledge,[4] the other part being the theory which relates those properties to one another.[5]

To return to the dispositional nature of entropy, it is now becoming increasingly evident that many of the energy transducing processes in the living system may generate no net entropy at all (see Chapter 6). And, if the living system does represent a coherent regime with, in effect, a single degree of freedom, then its entropy must certainly be close to zero. This has important implications for knowledge and knowledge acquisition. Before we come to that, let us deal more precisely with the measurement of entropy and of information.

Entropy and Information

Entropy, as we have seen, may be defined in terms of the number of possible microstates in a closed system with a given volume, chemical composition and energy:

$$S_{BP} = k \ln W \, , \qquad (14.1)$$

where SBP is Boltzmann-Planck's entropy, as they were the first to use this analogue. The microstates are actually all the quantum states of the macroscopic system defined in terms of the wave functions of the coordinates of the particles in the system.[6] An astronomical number of quantum states are always comprised within a given thermodynamic system: a single gram of hydrogen already contains 1023 molecules. In the Boltzmann-Planck formulation, all the quantum states have the same energy and are by hypothesis, equally probable, i.e.,

$$P_i = 1/W \qquad \Sigma_i P_i = 1 \, , \qquad (14.2)$$

where Pi is the probability of the ith quantum state and all of the Pi sum to 1.

In order to allow for fluctuations in energies, Gibbs put forward an alternative formulation for a system at thermal equilibrium with a large reservoir at a given temperature where there are now quantum states with different quantized energies, e1, e2,… ej. The probability of the jth energy state (or energy eigenstate as it is technically called), is then,

$$p_j = \frac{\exp(-e_j/kT)}{\Sigma_j \exp(-e_j/kT)} \qquad \Sigma_j P_j = 1 , \qquad (14.3)$$

where k is Boltzmann's constant and T the temperature. Entropy now takes the form,

$$S_G = -k\Sigma_j\, p_j \ln p_j , \qquad (14.4)$$

where SG is Gibbs entropy which sums over the j energy states accessible to the system. Equation (14.4) reduces to Eq. (14.1) when all of the pj s are equal to 1/W. Both entropy measures become zero in the pure or coherent state, and take on maximum values at equilibrium, which is the maximally mixed state.

In l949, Claude Shannon put forward an expression for the amount of information which is contained in messages sent along a transmission line. Suppose a message is to be composed of a string of four symbols which can only take one of two alternatives, 0 or 1, e.g., 0101, 0011, 1101, etc., then there are 24 = 16 possible messages. If the zeros and ones are equally probable, then the ‘information’ contained in each message can be defined as being log2 24 = 4 ‘bits’. And the information per symbol is hence one bit. The sequence of 4 symbols actually involves a succession of binary choices. If there are 4 alternative symbols instead of two, then each decision would have involved a choice of one out of 4, and any sequence of four symbols would have the information,

log2 44 = log2 28 = 8 bits

so the information per symbol being now 2 bits. Of course, the number of alternative symbols may vary, and they may not be equally probable. An example is the English alphabet, which has 26 alternative symbols of widely different probabilities of occurrence. In general, a simple logarithmic formula could be written down for the measure of information or ‘uncertainty’ per symbol:

$$H = -\Sigma^n p_i \log_2 p_i \, , \qquad (14.5)$$

where n is the number of alternative symbols and pi is the probability of the ith symbol. Now, the similarity between Eqs. (14.4) and (14.5) is such that it is indeed tempting to equate information with entropy, as Shannon has done.

Right from the beginning however, there were difficulties with both concepts, let alone the legitimacy of equating one with the other. Whose information is it anyway? The transmitter's or the receiver's? And where is the entropy? Is it located in the physical communication system which is after all indifferent to the actual messages sent?7

Information, Entropy, Order and Knowledge

A possibly more rigorous application of the concepts of information and entropy may be in the process of knowledge acquisition. The similarity of the H function and the S function suggests that the entropy is directly proportional to the information we would have if we know which microstate the system is in. Thus, when we say that thermodynamic equilibrium is a state of maximum entropy, we are at the same time asserting that we are maximally ignorant about which microstate it is in — as it has equal probability of being in any one of the astronomical number of them. As Brillouin writes,

“Entropy is usually described as measuring the amount of disorder in a physical system. A more precise statement is that entropy measures lack of information about the actual structure of the system. The lack of information introduces the possibility of a great variety of microscopically distinct structures, which we are, in practice, unable to distinguish one from another.”8

In this passage, Brillouin on the one hand acknowledges and asserts that the system subject to measurement has a structure of its own, and on the other hand, adopts a completely subjectivist view of entropy. So, who has the entropy? The observer or the observed? Morowitz9 offers the following examples to illustrate more concretely the relativity of work and entropy, or rather, their dispositional character according to the information available. It shows that entropy and energy are both dependent on the state of the knower, whether she has knowledge, and more importantly, how she has set up the system.

A single molecule of a perfect gas is in one of two adjacent chambers connected by a valve, and the whole is immersed in a large reservoir at temperature T (see Fig. 14.1). On opening the valve, a change in entropy will occur. We recall that Boltzmann's entropy is, S = k ln W, where W is the number of possible microstates of the system. The change in accessible microstates will be proportional to the change in volume, hence,

$$\begin{aligned}\Delta S &= k \ln V_2/V_1 \\ &= k \ln 2\end{aligned} \tag{14.6}$$

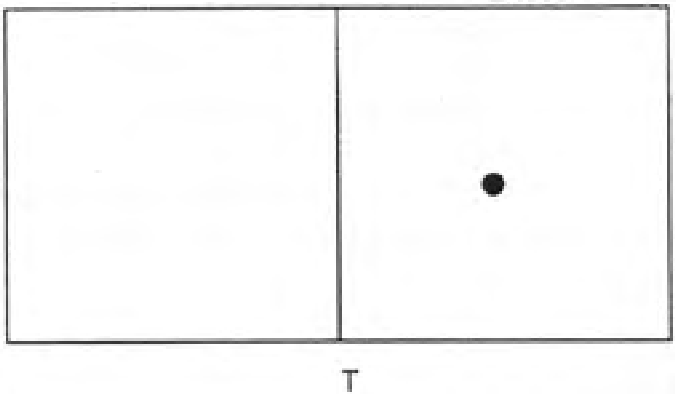

Figure 14.1 A single molecule of a perfect gas in one of two chambers connected by a valve at equilibrium at temperature T.

If an observer knew which chamber contains the molecule, then she would have one bit of information, which is the amount involved in a binary choice. Moreover, this knowledge would enable her to rig up the valve to a piston and get work out of it. As this is an ‘expansion’ occurring isothermally, the total energy — which is a function of temperature only — does not change, i.e.,

$$\begin{aligned} \Delta U &= T\Delta S - \Delta W = 0 \\ \Delta W &= T\Delta S \\ &= kT \ln 2 \end{aligned} \qquad (14.7)$$

If the information, as to which chamber the molecule is in, could be obtained without doing work, we would have a violation of the second law. So one must conclude that in order to obtain one bit of information, one has to do at least Kt ln 2 units of work, or alternatively, cause an increase in k ln 2 units of entropy somewhere in the system. This is Brillouin's general conclusion on the relationships between information, entropy and work.

Consider now the same two adjacent chambers of equal volume immersed in a large reservoir at temperature T, but one of the chambers contains a mole of a perfect gas i.e., N0 molecules, where N0 is Avagadro's number, while the other is empty (see Fig. 14.2, top left diagram).

When the connecting valve is opened between the two chambers, an increase in entropy results:

$$\Delta S = N_0 k \ln(V_2/V_1) = R \ln 2 \qquad (14.8)$$

where R = N0k is the gas constant. As before, the maximum amount of work which can be extracted from the system is,

$$\Delta W = RT \ln 2 \qquad (14.9)$$

This amount of work is the same even if we increase the number of chambers to 4, 8, 16, 32 or more, so long as only half of the chambers are filled with the mole of gas initially. If we carry this argument to molecular dimensions, we will have a distribution of gas hardly different from the completely random distribution that we would have obtained if the gas were originally at thermodynamic equilibrium within the entire volume. But the amount of work obtained in a reversible isothermal expansion is still RT ln 2, just as

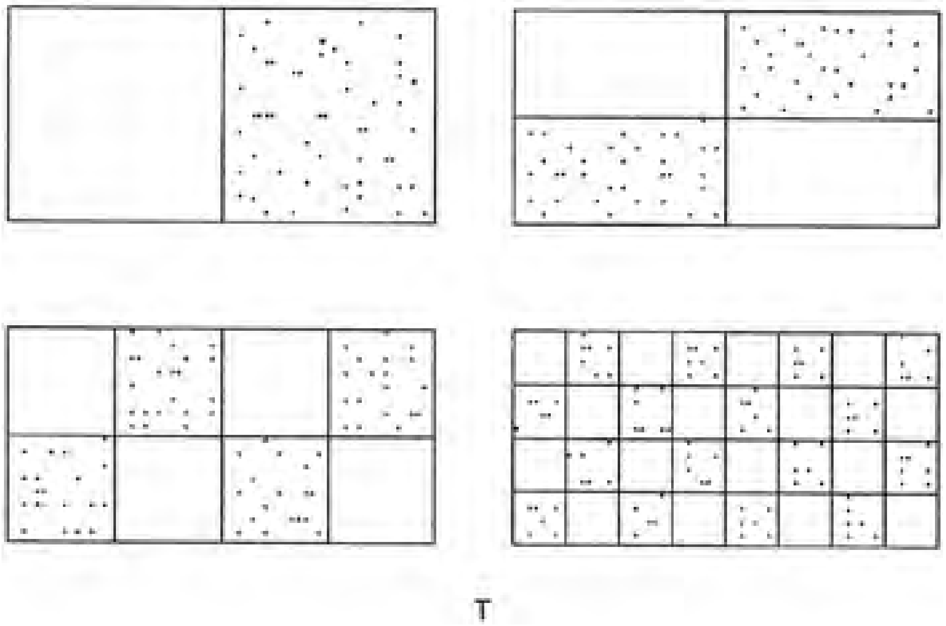

Figure 14.2 One mole of a perfect gas in different number of chambers at equilibrium at temperature T.10 the entropy change is still R ln 2; whereas in an equilibrium system both measures would be zero. This is paradoxical, as entropy is supposed to be a state function. We now have two systems in the same state (at equilibrium) but with different entropy measures depending on how the systems arrived at their final states. The resolution to this paradox is that in the first case, we assumed that the work available is RT ln 2. But in order to get the actual work, we have to know which chamber is filled and which empty. This is a binary decision requiring kT ln 2 work units per molecule, as shown above. For a system with 1 mole or N0 molecules, the work required would be N0KT ln 2 or RT ln 2. Now, an experimenter who has prepared the system, and therefore knows which chambers contain gas and which do not, will be able to get the maximum work of RT ln 2 out of the system. However, for anyone else who has not prepared the system, and has no knowledge of it, at least the same amount of energy would have to be expended in order to get the information, and hence no net work can be obtained from the system.

This appears to be a no-win situation as far as getting knowledge of the system is concerned. The system may have a very well defined coherent structure, which means that its real entropy is very low, as the number of microstates that the system accesses may be close to one. Yet the ignorance of the external observer seems to necessitate an exhaustive series of tests for the occupancy of each and every microstate that the system could exist in. As if that were not bad enough, if we were to actually carry out all those tests, the disturbance to the system would be such that we would no longer have the same system that we started with. Elsasser11 states the problem as follows:

"If we try to predict with precision the future behavior of an organism we must, according to physics, know the initial values of the positions and velocities of its constituent particles with sufficient accuracy… [Otherwise] prediction of the future behavior of the system becomes correspondingly limited. Now, even in a relatively simple organism, a cell say, there are billions of orbital electrons which maintain a most intricate system of chemical bonds. The vital activities of the cell, especially metabolism, consists exactly in the changing of bonds, in the transfer processes which these bonding electrons undergo as time goes on. But quantum mechanics tells us that in order to localize an electron to within a reasonable accuracy… a physical interaction of the electron with the measuring probe (e.g., X-rays) must take place which, in the average, transmits a certain amount of interaction energy to the electron… The energy conferred upon the tissue by virtue of the measurements becomes then so large that vast changes must take place: the system will be radically altered and disrupted and is no longer even approximately equal to the system which was at hand before the measurements were undertaken."

Ignorance of the External Observer

Elsasser's remark encapsulates the dilemma of the external observer who has to determine the structure (microstate) of a living organism without disturbing it out of all recognition.

However, the ignorance of the external observer is really of no consequence to the system itself, which is far from ignorant of its own microstate. The problem of a system knowing its own microstate is vastly different from an external observer knowing its microstate. As Morowitz remarks, ‘‘The system is the microstate and by virtue of being the microstate has a great deal more knowledge of the microstate than is ever possible for an outside observer… This fact is implicitly used in the design of experiments for molecular biology. We do not, as implied by the Bohr-Elsasser argument, set up experiments to measure the position and momentum of all atoms in a living system; we rather use a different strategy of allowing the experimental living system to generate answers to questions that we pose by the experimental set-up…”12

Furthermore, a system such as the organism, which is far from equilibrium, yields a lot more information about its microstates because it possesses macroscopic parameters which can readily be measured. In Chapter 4, we saw how macroscopic organization can spontaneously arise as energy flows through open systems, so much so that they can undergo non-equilibrium phase transitions to macroscopically coherent states characterized by a few macroscopic parameters (see also Chapter 8).

From the previous Chapter, we also know that a coherent system is totally transparent to itself, as all parts of the system are in complete, instantaneous communication. So in a precise sense, it knows itself completely. There is literally a “wisdom of the body” that generations of physiologists have spoken of. The effective degree of freedom of the system is one, and hence the entropy is zero. The entropy here is related to the algorithmic entropy proposed by theoretical physicist Zurek and others.13 A coherent system is one with the highest degree of algorithmic simplicity in that the instructions specifying it is a macroscopic wave function,14 and is hence, much, much shorter than, say, a complete specification of its microstate, volume element by volume element, which would be required if the system were completely random (c.f. Saunders and Ho).15

This suggests that the entropy of the living system can be expressed in terms of its deviation from coherence, i.e., where the degree of freedom becomes greater than one. Such an expression has the advantage that it naturally relates entropy to decoherence or the decay of coherent energy. In practice, in order to measure a system's deviation from coherence, we have to take into account its coherent space-time structure, a quality which cannot be represented by the instantaneous Newtonian time that all western scientific theories are still based upon. l have suggested that time itself (as well as space) is generated by process, specifically by the incoherence of action.16 In that respect, time has the same sense and direction as entropy (see Chapter 15).

There is another important implication as regards knowledge acquisition. The dilemma of the absolutely ignorant external observer betrays the alienation from nature that the traditional scientific framework of the west entails, for western science is premissed on the separation of the observer as disembodied mind from an objective nature observed.17 That is also the origin of the subjective-objective dichotomy, which, when pushed to its logical conclusion, comes up against the seemingly insurmountable difficulty that in order to have sufficient information about the system, one has in effect to destroy it.

But as pointed out above, one can infer a great deal about the microstate of the system by allowing the system to inform. In other words, we must find ways of communicating with the system itself, rather than interrogating it, or worse, testing it to destruction. That is the reason why sensitive, non-invasive techniques of investigation are essential for really getting to know the living system. This is related to the issue of “adiabatic measurement” that allows the detection of quantum superposition in recent experiments (see previous Chapter).

Ideally, we ought to be one with the system so that the observer and observed become mutually transparent or coherent. For in such a pure, coherent state, the entropy is zero; and hence uncertainty and ignorance are both at a minimum. Perhaps such a state of enlightenment is just what Plato refers to as being one with the Divine Mind; or, as the taoists of ancient China would say, being one with the tao, the creative principle that is responsible for all the multiplicity of things.18 It involves a consciousness that is delocalized and entangled with all of nature, when the awareness of self is heightened precisely because self and other are simultaneously accessed. I believe that is the essence of aesthetic or mystical experience.

This manner of knowing — with one's entire being, rather than just the isolated intellect — is foreign to the scientific tradition of the west. But I have just demonstrated that it is the only authentic way of knowing, if we were to follow to logical conclusion the implications of the development of western scientific ideas since the beginning of the present century. We have come full circle to validating the participatory framework that is universal to all traditional indigenous knowledge systems the world over.19 I find this very agreeable and quite exciting.

Notes

1. Cited in Denbigh and Denbigh (1985) p. 3.
2. The description on entropy as a subjective concept is largely based on the excellent summary in Chapter 1 of Denbigh and Denbigh (1985).
3. Cited in Denbigh and Denbigh (1985) p. 4.
4. This issue is discussed at some length in Ho (1993).
5. See Ho (1992b).
6. This account is based on Denbigh (1981).
7. See Denbigh and Denbigh (1985) p. 104.
8. See Brillouin (1962).
9. See Morowitz (1968) pp. 124–8.
10. After Morowitz (1968) p. 127.
11. Elsasser (1966), cited in Morowitz (1968).
12. See Morowitz (1968) pp. 131–2.
13. Zurek (1989).
14. Fröhlich and Hyland (1995).
15. Saunders and Ho (1981).
16. See Ho (1993).
17. See Ho (1990a).
18. See Ho (1992a).
19. See Ho (1993).

CHAPTER 15

Time and Freewill

There is No Glass Bead Game

In this final Chapter, I shall on the one hand, give free rein to my imagination without apology, as I try to convey what the physics of organisms means to me personally, and on the other, demonstrate explicitly that there is no discontinuity between the so-called 'hard' sciences such as physics and chemistry and the 'soft' sciences such as psychology and philosophy. This Chapter is not just the icing on the cake, but stems from a deep conviction that knowledge, especially participatory knowledge, is what we live by, and so, there should also be no discontinuity between knowledge and action. There can be no 'glass bead game' to knowledge,1 especially scientific knowledge, for it matters far too much.

Bergson's 'Pure Duration'

The title of this chapter is taken from the philosopher, Henri Bergson's fascinating book,2 with which I have established a relationship for at least 15 years, before I finally understand the message in the poetry in a way that allows me to write about it.

The second law of thermodynamics defines a time's arrow in evolution3 and in that sense, captures an aspect of experience which we know intuitively to be true. By contrast, the laws of microscopic physics are time reversible: one cannot derive a time's arrow from them, nor are they affected by a reversal of time.4 There is another sense in which time (as well as space) in physical laws does not match up to our experience. Newtonian time, and for that matter, relativistic time and time in quantum theory, are all based on a homogeneous, linear progression — the time dimension is infinitely divisible, so that spatial reality may be chopped up into instantaneous slices of immobility, which are then strung together again with the ‘time line'. Real processes, however, are not experienced as a succession of instantaneous time slices like the successive frames of a moving picture. Nor can reality be consistently represented in this manner.

The mismatch between the quality of authentic experience and the description of reality given in western science has long been the major source of tension between the scientists and the ‘romantics'. But no one has written more vividly on the issue of time than Bergson, with so few who could really understand him. He invites us to step into the rich flowing stream of our consciousness to recover the authentic experience of reality for which we have substituted a flat literal simulacrum given in language, in particular, the language of science.

In the science of psychology, words which express our feelings — love and hate, joy and pain — emptied of their experiential content, are taken for the feelings themselves. They are then defined as individual psychic entities (or psychological states) each uniform for every occasion across all individuals, differing only in magnitude, or intensity. Should we connect our mind to our inner feelings, what we experience is not a quantitative increase in intensity of some psychological state but a succession of qualitative changes which “melt into and permeate one another” with no definite localizations or boundaries, each occupying the whole of our being within this span of feeling which Bergson refers to as ‘pure duration'.

Pure duration is our intuitive experience of inner process, which is also inner time with its dynamic heterogeneous multiplicity of succession without separateness. Each moment is implicated in all other moments (c.f. the organism's space-time structure described in Chapter 3). Thus, Newtonian time, in which separate moments, mutually external to one another, are juxtaposed in linear progression, arises from our attempt to externalize pure duration — an indivisible heterogeneous quality — to an infinitely divisible homogeneous quantity. In effect, we have reduced time to Newtonian space, an equally homogeneous medium in which isolated objects, mutually opaque, confront one another in frozen immobility.

Bergson emphasizes the need for introspection in order to recover the quality of experience. He opposes an inner “succession without mutual externality” to an outer “mutual externality without succession”. He distinguishes two different selves, one the external projection of the other, inner self, into its spatial or social representation. The inner self is reach “by deep introspection, which leads us to grasp our inner states as living things, constantly becoming.’’ “…But the moments at which we thus grasp ourselves are rare, and that is just why we are rarely free. The greater part of the time we live outside ourselves, hardly perceiving anything of ourselves but our own ghost, a colourless shadow which pure duration projects into homogeneous space. Hence our life unfolds in space rather than in time; we live for the external world rather than for ourselves; we speak rather than think; we ‘are acted’ rather than act ourselves…”5

This passage anticipates the sentiment of the existentialist writers such as Camus and Sartre. A similar sentiment pervades T.S. Eliot's poetry. The following lines evoke strong echoes of Bergson's projected being outside ourselves,

We are the hollow men
We are the stuffed men
Leaning together
Headpiece filled with straw. Alas!
Our dried voices, when
We whisper together
Are quiet and meaningless

As wind in dried grass
Or rats’ feet over broken glass
In our dried cellar
Shape without form, shade without colour,
Paralysed force, gesture without motion;

Bergson's protests were directed against one of the most fundamental assumptions underlying modern western science. It claims to express the most concrete, common-sensible aspect of nature: that material objects have simple locations in space and time. Yet space and time are not symmetrical. A material object is supposed to have extension in space in such a way that dividing the space it occupies will divide the material accordingly. On the other hand, if the object lasts within a period of time, then it is assumed to exist equally in any portion of that period. In other words, dividing the time does nothing to the material because it is always assumed to be immobile and inert. Hence the lapse of time is a mere accident, the material being indifferent to it. The world is simply fabricated of a succession of instantaneous immobile configurations of matter (i.e., a succession of equilibria), each instant bearing no inherent reference to any other instant of time. How then, is it possible to link cause and effect? How are we justified to infer from observations, the great ‘laws of nature'? This is essentially the problem of induction raised by Hume.6 The problem is created because we have mistaken the abstraction for reality — a case of the fallacy of misplaced concreteness.

Whitehead's ‘Organism’ and Bohm's ‘Implicate Order'

In order to transcend the philosophical ruin left in the wake of mechanical materialism, Whitehead6 attempts to return to a kind of native realism, not unlike the panpsychism or pananimism that is usually attributed to the so-called primitive mind by western anthropologists. He rejects the existence of inert objects or things with simple location in space and time. As all nature is process, there is only the progressive realization of natural occurrences. For mind, he substitutes a process of ‘prehensive unification’ — a kind of perception that may or may not involve human consciousness. The realization of an occurrence is “a gathering of things into a unity” which defines a here and a now, but the things gathered into a unity always refer to other places and other times. The totality of occurrences thus consists of a pattern of flows and influences now diverging from one locus, now converging towards another in such a way that “each volume of space, or each lapse of time includes in its essence aspects of all volumes of space, or of all lapses of time”.

An organism, according to Whitehead, is “a locus of prehensive unification”. This corresponds to a field of coherent activities which is sensitive to the environment, drawing on its experience of the environment to make itself whole. Whitehead asserts that the fundamental particles of physics such as protons and electrons are organisms, as much as, at the other extreme, entire planets such as the Earth, even entire galaxies. Nevertheless, he does recognize gradations of organisms and hence of consciousness.7 Each organism, in the act of prehensive unification, enfolds the environment consisting of others into a unity residing in a ‘self', while aspects of the self are communicated to others. The realization of ‘self’ and ‘other’ are thus completely intertwined. The individual is a distinctive enfoldment of its environment, so each individual is not only constituted of others in its environment, but also simultaneously delocalized over all individuals. The society is thus a community of individuals mutually delocalized and mutually implicated. Individuality is also relative, for an organism can be part of the life history of some larger, deeper, more complete entity.

An obvious situation where nested individualities occur is in a society or a community of species. Societies evolve slowly, its slowly- changing variables define parameters for the evolution of individuals within it. The picture of nested individuality and constitutive mutuality is also consistent with Lovelock's Gaia hypothesis:8 that the earth is one cybernetic system maintained far from thermodynamic equilibrium in conditions suitable for life by the actions of the ‘organisms’ (both physical and biological) within it. Not only are individuals part of a larger organism, but the substance, the very essence of each individual is constitutive of every other. This is all of a piece with the concepts of nonlocality and quantum entanglement described in Chapter 13, giving further substance to the participatory worldview.

In a very real sense, we participate not only in our knowledge of nature but in creating reality in partnership with all of nature. A truly participatory consciousness would perceive this coherent delocalization of self and other as constitutive of its own being (see also previous Chapter) which not only gives it authentic knowledge, but also empowers it to act appropriately and coherently. The moral feeling arises from this primary perception of the mutual entanglement of self and other, ultimately, of all life.

The mutual enfoldment and unfoldment of the ‘implicate’ and ‘explicate', between organism and environment, is precisely David Bohm's account of the quantum universe.9 In analogy to the hologram, the implicate order of an object is contained in an interference pattern of light distributed throughout space, in which it can be said to be enfolded. By an act of unfoldment, however, the original form of the object could once again be made explicate.

In the latest version of Bohm's theory, the universe is pictured as a continuous field with quantized values for energy, momentum and angular momentum. Such a field will manifest both as particles and as waves emanating and coverging on the regions where particles are detected. This field is organized and maintained by the ‘superquantum potential’ which is a function of the entire universe: ‘‘…What we have here is a kind of universal process of constant creation and annihilation, determined through the superquantum potential so as to give a world of form and structure in which all manifest features are only relatively constant, recurrent and stable aspects of the whole…”10

Whitehead's organicist philosophy is in many ways a logical progression from the demise of mechanical materialism which began towards the end of the previous century. The rise of thermodynamics introduced a new kind of conservation law: that of energy in place of mass. Mass was no longer the pre-eminent permanent quality. Instead, the notion of energy became fundamental, especially after Einstein worked out the famous mass- energy equation, and nuclear fission in the atomic bomb proved him right, with devastating consequences. At the same time, Maxwell's theory of electromagnetism demanded that there should indeed be energy, in the form of electromagnetic fields pervading throughout all space, which is not immediately dependent on matter. Finally, the development of quantum theory reveals that even the atoms of solid matter are thought to be composed of vibrations which can radiate into space. Matter loses solidity more and more under the steady scrutiny of relentless rationality.

Meanwhile, the Newtonian picture of homogeneous absolute time and space gives way to relativity. Each inertial frame of reference (associated with its own observer or prehensive organism) must be considered as having a distinct space-time metric different from those of other inertial frames. (That means it not only has its own clock but also its own map.) The organism has no simple location in space-time. Moreover, an organism can alter its space-time by its own motion or activity. It is possible that some organisms will no longer 'endure' under changes of space-time. Thus, the organism's space-time metric, and perforce, its internal space-time, cannot be regarded as given, but arises out of its own activities. The organization of those activities is also its internal space-time structure, which is not a quantity but a quality, as Bergson's 'pure duration' is a quality of the same cloth.

Space-Time Structure and Quantum Theory

The nature of space and time is fundamental to our theory of reality. The mismatch between the Newtonian universe and our intuitive experience of reality hinges on space and time. In fact, all developments in western science subsequent to Newton may be seen as a struggle to reinstate our intuitive, indigenous notions of space and time, which deep within our soul, we feel to be more consonant with authentic experience. But there has only been limited success so far.

Einstein's theory of special relativity substitutes for absolute space and absolute time a four-dimensional space-time continuum which is different for each observer in its own inertial frame. Space and time have become symmetrical to each other, but they remain definite quantities. In the usual quantum theory, on the other hand, space coordinates lose definiteness in becoming complex statistical quantities (see Chapter 13), but time remains a simple parameter as in classical mechanics.

Another problem with time is that the laws of physics in both classical and quantum mechanics as well as in relativity, are time- symmetric, i.e., they do not distinguish between past and future. Yet real processes have an ‘arrow of time'. So time ought to be related to real processes. If so, it would have the quality that Bergson refers to as pure duration. In other words, it would have a structure. Theoretical physicist, Wolfram Schommers11 has taken up just this problem. Like both Whitehead and Bergson, he argues for the primacy of process, and in an interesting reformulation of quantum theory, shows how time and space are tied to real process.

He begins from a consideration of Mach's principle, according to which, particles do not move relative to space, but to the centre of all the other masses in the universe. In other words, absolute space and time coordinates cannot be determined empirically. Any change in position of masses is not due to the interaction between coordinates and masses, but entirely between the masses. However, neither relativity nor quantum mechanics have incorporated Mach's principle in their formulation.

If one takes account of Mach's principle, space-time must be considered as an auxiliary element for the geometrical description of real processes. In other words, real processes are projected to space-time or ‘(r, t)-space’ from perhaps a more fundamental space — that which represents reality more authentically in terms of the parameters of interactions, i.e., momentum and energy — the ‘(p, E)-space’. The two spaces are equivalent descriptions and are connected by the mathematical device of a Fourier transformation (see Chapter 13). (Intermediate spaces, (r, E) and (p, t), can also be formed which are similarly connected.) The result is that time, as much as space, becomes statistical quantities in (p, E)-space where momentum and energy are parameters and take on definite values. Conversely, momentum and energy are statistical quantities in (r, t)-space where space and time are definite parameters. The wave function for space-time, $\psi(r, t)$ leads to probability distributions for both space and time in (p, E)-space. This means that processes consisting of matter interacting generate space-time structures. In other words, space-time structures are caused by action, and in the limiting case of a stationary (or equilibrium) process and a free particle (one that is not subject to any external influence), no time- and space-structures are defined, i.e., the wave function $\psi(r, t) = 0$.

In Schommer's scheme, energy and time representations are complementary, and for nonstationary processes, an uncertainty relationship exists between them which is of the same form as that between position and momentum in conventional quantum theory. The consequence is that both energy structure and the internal time structure are different for different systems when compared to an external reference time structure such as a clock. For nonstationary processes, there will be probability distributions for all the variables, p, r, E and t, which are internal to the system; whereas for stationary processes, there is no system-specific time definable, and the energy is constant, so only position and momentum take on probability distributions.

Another consequence is that wave and particle are no longer in contradiction. They coexist simultaneously in this representation. For a particle is a point with definite momentum and energy in (p, E)-space, but simultaneously a wave in the (r, t)-space. Conversely, a particle in the (r, t)-space is simultaneously a wave in the (p, E)-space, and so wave and particle co-exist in different spaces independently of the measurement process. This removes the observer paradox, or the ‘collapse of the wave function’ mentioned in Chapter 13. In Schommer's scheme, the wave function never collapses, it only becomes either a particle or wave in one space, and its complement in the other space. This has fundamental implications for the nature of consciousness as we shall see.

By the same token, a free particle cannot be observed in (r, t)-space, for by definition, it does not interact with any other system, i.e., there is no exchange of momentum and energy. An observation implies an interaction process so that the particle is no longer free. That is why knowledge acquisition is always participatory: a partnership between the knower and the known. It is both subjective and objective, as we have already concluded in connection with considerations on entropy and information in the previous Chapter.

Organisms as Coherent Space-time Structures

Schommer's reformulation of quantum theory is especially relevant for understanding the space-time structure of living systems. If organisms are coherent space-time structures, then certain consequences should flow from that. As stated in Chapter 13, an individual is simply a field of coherent activity. Defined in this way, we can readily appreciate the sort of nested individualities that Whitehead speaks of, but with the added insight that individualities are spatially and temporally fluid entities, in accordance to the extent of the coherence established. Thus, in long-range communication between cells and organisms, the entire community may become one when coherence is established and communication occurs without obstruction or delay. Within the coherence time, there is no space separation, i.e., the usual spatial neighbourhood relationship becomes irrelevant. Similarly, within the coherence volume, there is no time separation, hence ‘instantaneous’ communication can occur. (Feelings can indeed spread ‘like wild fire', and people everywhere can get caught up simultaneously in a sudden fervour.)

In the living system, coherence times and coherence volumes are themselves determined by the relaxation times and volumes of the processes involved. We may envisage biological rhythms as manifesting a hierarchy of coherence times that define the time frames of different processes. This fits with Bergson's concept of pure duration, which, in one sense, we may identify as the time taken for the completion of a process. A heartbeat requires a full cycle of contraction and relaxation before we recognize it as such — the duration of a heart-beat is about one second in external reference time. Similarly, neurobiologists have discovered an endogenous 40 hz rhythm that is coherent over the entire brain (see Chapter 9). This may define the duration of primary perception. Within that duration, which we can regard as the coherence time in that level of the nested hierarchy of time structure, processes coherent with it will generate no time at all. The coherence volume, similarly, is the extent of spatial coherence within which there is no time separation.

This representation of individuals as coherent space-time structures implies that space and time, in terms of separation and passage, are both generated, perhaps in proportion to the incoherence of action. I have suggested in Chapter 13 that entropy is generated in decoherence, in proportion to the loss of coherent energy, which has the same direction as the arrow of time. Thus, a coherent sage may well be living in a truly timeless-spaceless state, which is beyond our comprehension. I believe some of us get glimpses of that in a particularly inspired moment, or during an aesthetic or religious experience.

In ordinary perception, on the other hand, the organism interacts with the environment, a decohering perturbation propagates within the organism and is registered or assimilated in its physiology (in other words, enfolded). This results in time generation. The greater the wave function $\psi(r, t)$ changes (see below), or the greater the mismatch between object and subject, the longer the time generated. Conversely, the more match or transparency between object and subject, the less.

From the foregoing discussion, one can see that a coherent society (mentioned in Chapter 13) must obviously be one where social space-time structure matches both natural astronomical space-time as well as individual private space-time. This has considerable relevance for Illich's idea of convivial scales of machinery as well as communities and institutions.12 When the latter become too large, as Illich points out, they have a way of enslaving us instead of serving and supporting us.

Organic Space-Time and Fractal Space-Time13

It is clear that the organism's space time, or organic space-time, has a structure which differs from the linear, infinitely divisible Newtonian space-time that still to a large extent dominate the present scientific worldview. Can anything be said concerning the structure of organic space-time?

There are several lines of recent evidence converging to a new picture of the "texture of reality"14 suggesting that organic space-time does have a structure, and that this structure may be fractal. One of the most exciting discoveries in recent years, which has given rise to the "science of complexity" is that natural processes and natural structures have fractal dimensions. That means they have dimensions in between the one, two or three to which we are accustomed. Fractals capture a new kind of order characterized by self-similarity — the similarity of part to whole over many different scales. Snowflakes, clouds, ferns, coastlines branching patterns of blood vessels, and the "cytoskeleton" inside each cell are all examples of fractal structures. Natural processes, from weather patterns to the healthy heart-beat and electrical activities of the brain, similarly, are thought to exhibit "chaotic dynamics" that when spatialized as a "Poincaré section'', gives rise to "strange attractors" that again have fractal dimensions. If space-time is indeed generated by processes as I have proposed here, then it should also be fractal, or more accurately, multi-fractal, as organic space-time is multi-dimensional (see Chapter 2).

According to theoretical physicist Nottale and others,[15] the whole of present day physics relies on the unjustified assumption of the differentiability of the space-time continuum, which stems from classical Newtonian physics, whereas Feynman and Hibbs[16] have already shown that the typical path of a quantum particle is continuous but nondifferentiable. This is the failure of present-day physical description to capture the organic quantum reality that I have alluded to earlier: the description is still based on a mathematical representation of space-time as continuous and homogeneous, i.e., as infinitely divisible or “differentiable”. It so happens that a structure that satisfies the requirement for continuity and non-differentiability is fractal. Nottale writes,[17]

“Giving up the hypothesis of differentiability has an important physical consequence: one can show that curves, surfaces, volumes and, more generally, spaces of topological dimension DT, which are continuous but non-differentiable, are characterized by a length, an area and, more generally a DT measure which becomes explicitly dependent on the resolution at which they are considered,… and tends to infinity when the resolution interval ϵ tends to zero. In other words, a non-differentiable space-time continuum is necessarily fractal… This result naturally leads to the proposal of a geometric tool adapted to construct a theory based on such premises, namely, fractal space-time.”

The author then proceeds to describe a new approach that generalizes Einstein's principle of relativity to scale transformations. Specifically, the equations of physics are required to keep their form under scale transformation, i.e., to be scale covariant. It allows physicists to recover quantum mechanics as mechanics on a fractal space-time, in which Schrödinger's wave equation is a geodesic equation.

I wonder if that is not the beginning of an approach towards the quantization of space-time which, I believe, is a necessary consequence of the quantization of action that Planck's constant already involves. This quantized space-time is also Bergson's “duration’’, which expresses the indivisible multiplicity of our subjective experience of organic process. It is, perhaps, the experience of processes cascading through the continuous scales of fractal space-times entangled through the coherence of the "ground" or asymptotic state, over which the scale covariance is defined.

Determinism and Freewill

At the end of his book, "What is Life?", Schrödinger has this to say on determinism and freewill,

"… let us see whether we cannot draw the correct, non-contradictory conclusion from the following two premises:

(i) My body functions as a pure mechanism according to the Laws of Nature.

(ii) Yet I know, by incontrovertible direct experience, that I am directing its motions, of which I forsee the effect, that may be fateful and all-important, in which case I feel and take full responsibility for them.

"The only possible inference from these two facts is, I think, that I — I in the widest meaning of the word, that is to say, every conscious mind that has ever said or felt 'I' — am the person, if any, who controls the 'motion of the atoms' according to the Laws of Nature…"

He continues,

"…Consciousness is never experienced in the plural, only in the singular…''18

That is just what the state of coherence entails: a multiciplicity which is singular, the 'self' is a domain of coherence, a pure state which permeates the whole of our consciousness, much as Bergson has described. The positing of 'self' as a domain of coherent space-time structure implies the existence of active agents who are free. Freedom in this context means being true to 'self', in other words, being coherent. A free act is thus a coherent act. Of course not all acts are free, since one is seldom fully coherent. Yet the mere possibility of being unfree affirms the opposite, that freedom is real,

"…we are free when our acts spring from our whole personality, when they express it, when they have that indefinable resemblance to it which one sometimes finds between the artist and his work."19

But as the 'self' is also distributed — being implicated in a community of other entities (see p. 174) — to be true to 'self' does not imply acting against others. On the contrary, sustaining others sustains the self, so being true to others is also being true to self. It is only within a mechanistic Darwinian perspective that freedom becomes perverted into acts against others.20

According to John Stuart Mill,21 to be free, "must mean to be conscious, before I have decided, that I am able to decide either way." So defenders of freewill claim that when we act freely, some other action would have been equally possible. Conversely, proponents of determinism assert that given certain antecedent conditions, only one resultant action was possible.

As Bergson remarks, the problem itself is posed on the mechanistic assumptions of immobility and mutual externality of events. This gives rise to two equally unacceptable alternatives: either that an immobile configuration of antecedents is supposed to 'determine' another immobile configuration of resultants, or that at any frozen instant, to be or not to be are equally likely choices for a consciousness that is external to itself, which immediately leads us back to Cartesian mind-matter dualism that makes us strangers to ourselves. In the reality of process, where the self is ever becoming, it does not pass like an automaton from one frozen instant to the next. Instead, the quality of experiences permeates the whole being in a succession without separateness in ''a self which lives and develops by means of its very hesitations until the free action drops from it like an over-ripe fruit."22

One might represent consciousness as a wave function that evolves, constantly being transformed by experience as well as overt acts. And this would be perfectly in line with the idea that organisms are asymptotically quantum coherent systems. The issue of quantum indeterminism is a very deep one, but the picture of a wave function — a pure state — consisting of a total interfusion of feelings each of which occupying the whole being — is very like what Bergson describes. Such a pure state is an indivisible unity and must be distinguished from a mixture of states (see Chapter 13). Thus, the overt act, or choice, does follow from the antecedent, but it cannot be predicted in advance. One can at best retrace the abstract ‘steps’ and represent the evolution of the consciousness as having followed a ‘trajectory'. In truth, the so-called trajectory has been traced out by one's own actions, both overt and covert up to that point. When one reinstate the full quality of our consciousness, we can see that there can be no identical or repeatable states, which, when presented again at any time, will bring about identical resultant states.23

I suggest that the ‘wave function’ that is consciousness never collapses (c.f. Schommers, p. 24), but is always changing and always unique as it is ‘coloured’ by all the tones of our personality and experience. Each significant experience becomes entangled in our being, constituting a new wave function, in much the same way that particles of independent origins become entangled after they have interacted (see Chapter 13). This would also be in line with Bohm and Hiley's24 ontological interpretation of quantum theory which does not recognize the collapse of the wave function. In their model, the wave function, with quantum potential playing the role of active information to guide the trajectories of particles, simply changes after interaction to become a new one. The possibility remains that there is no resolution of the wave functions of the quantum objects after interacting. So one may remain entangled and indeed, delocalized over past experiences (i.e., in Laszlo's25 ambient quantum holographic field). Some interactions may have timescales that are extremely long, so that the wave function of interacting parties may take a correspondingly long time to become resolved, and large-scale nonlocal connectivity may be maintained.

The reason we experience our macroscopic world so differently from the microscopic world may be tied up with the space-time structure of reality (see above). It could be that, were we the dimensions of elementary particles, we too would experience our world as being inhabited by self-possessed, coherent beings with a free-will, and we would be most surprised to find that human-sized observers are trying to predict which state we are going to ‘collapse’ into next. In the same way, an external observer of galactic dimensions would find our human behaviour completely ‘quantum’ and unpredictable.

Gibson, a chief exponent of a process ontology in perception, has this to say on consciousness,

“The stream of consciousness does not consist of an instantaneous present and a linear past receding into the distance; it is not a ‘travelling razor's edge’ dividing the past from the future. Perhaps the present has a certain duration. If so, it should be possible to find out when perceiving stops and remembering begins. But it has not been possible… A perception in fact, does not have an end. Perceiving goes on.”26

Nature is ever-present to us, as we are to ourselves. This ever-present is structured, as we have seen. Our experience consists of the catenation of events of different durations, which propagates and reverberates in and around our being, constantly being registered and recreated. What constitutes memory of some event is the continuing present for the over-arching process of which the event is part.27

The universe of coherent space-time structures is thus a nested hierarchy of individualities and communities which come into being through acts of prehensive unification. It is a truly participatory, creative universe. Just as the organism is ever-present to itself during its entire life history, and all other individualities are ever-present to it, the universe is ever-present to itself in the universal duration where creation never ceases by the convocation of individual acts, now surfacing from the energy substrate, now condensing to new patterns, now submerging to re-emerge in another guise.

Reality is thus a shimmering presence of infinite planes, a luminous labyrinth of the active now connecting ‘past’ and ‘future’, ‘real’ with ‘ideal', where potential unfolds into actual and actual enfolds to further potential through the free action and intention of the organism. It is a sea awash with significations, dreams and desires. This reality we carry with us, an ever-present straining towards the future. The act is the cause, it is none other than the creation of meaning, the realization of the ideal and the consummation of desire.

Notes

1. See Ho (1993), referring to Hesse (1943, 1970). Hermann Hesse's famous last novel describes the life of Joseph Knecht, Magister Ludi, or the supreme master of the Glass Bead Game. The game is one of pure intellect directed at the synthesis of the spiritual and aesthetic abstractions in diverse disciplines of all ages, and is the prerogative and raison d'etre of an entire spiritual institution, Castalia. Isolated within its enclaves and unsullied by reality, the chosen elite undertook arduous scholastic studies, the sole purpose of which was to create ever more intricate themes and variations of the game. Castalia and the Glass Bead Game developed as antithesis to the philistine, superficial bourgeoise society, intent on its own pursuit of conventional, establishment values. In the end, however, Joseph Knecht turned his back on Castalia, disillusioned with a life consecrated exclusively to the mind, recognizing not only its utter futility, but also its inherent danger and irresponsibility.
2. Bergson (1916).
3. See Saunders and Ho (1976), and references therein.
4. For an excellent accessible survey of time in physics and philosophy, see Flood and Lockwood (1986).
5. Bergson (1916) p. 231.
6. See Whitehead (1925).
7. See Ho (1993).
8. See Lovelock (1979, 1988).
9. See Bohm (1987).
10. Bohm (1987) p. 43.
11. See Schommers (1989).
12. Illich (1973).
13. This Section is taken from Ho (1997d).
14. See Stewart (1989).
15. Nottale (1996).

16. Feynman and Hibbs (1965).
17. Nottale (1996) p. 877.
18. Schrödinger (1944) pp. 86–8.
19. Bergson (1916) p. 172.
20. See Ho (1993).
21. Mill (1878) pp. 580–583, cited in Bergson (1916) p. 174.
22. Bergson (1916) p. 176.
23. I have argued explicitly for a biology of free will based on quantum coherence in Ho (1996a).
24. Bohm and Hiley (1993).
25. Laszlo (1995).
26. Gibson (1966).
27. See Ho (1993).

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