Thales' Legacy

by

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A book in three parts on the role of water in life



The Living Pixel:

or how the demon made water come alive

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Acknowledgements

Begun in 2000, these books were originally conceived as a single work, but as it grew, it became clear that, because of the breadth of the subject covered, subdivision was needed. In fact, the three parts and their several appendices are still evolving, which means that they will continue to need correction into the future.

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1. Two Views

Each year the divide separating the physical and the biological sciences grows wider. At first we may not find this so Everyone knows that specialization has splintered science into a wide surprising, since differences are expected. variety of distinct fields of study. We know that each field has its own narrow journals, where results obtained using specialised techniques are reported in a language scarcely understood by outsiders. But we would agree, this is an expected, if unfortunate, development that evolved in a natural way over the last century in the wake of the explosive And although this development may be obvious to readers with a scientific increase in scientific knowledge. background, I feel that the majority of non-technically trained readers may not be aware of how extensive the fracturing of science has become. For instance, everyone is familiar with the meaning of the term "genetics" and has a sense of what this branch of science investigates, yet only those people with a grounding in modern biochemistry know that, in addition to our natural interest in human heredity, there are the studies of population genetics, animal genetics, plant genetics, cellular genetics, viral genetics, molecular genetics, as well as the more recent fields of tissue compatibility, cloning and stem cell research. There are even separate organizations for each genetic disease which hold regular conferences attended by specialists in that particular medical condition.

However, it is a different type of division which is to be described in the following chapters -a more fundamental, philosophic division of principle. The technical advances of the closing decades of the twentieth century brought not only the unavoidable diversity of fields, but at the same time brought an unprecedented, ever accelerating expansion in the life sciences. As a result, society is beginning to be affected in a new way by the fruits of science. Accompanying the technical wonders are new unforeseen moral and ethical problems. One need only imagine the emotional debate that will erupt in many quarters of society, when a healthy human cell is created wholly from the chemicals available on Although these technical advances rest squarely on modern methods born of the physical the laboratory shelf. sciences, especially electronics (broadly viewed), the conceptual advances do not. Many readers may be surprised to learn that the leaps in our understanding of biological phenomena have been achieved without reference to the concepts of the physical sciences. In addition, these advances are so rapid at the present time, that biological results taught as fact today must be corrected or even overturned for tomorrow's classes. In the absence of any time for reflection on the part of the researchers at the forefront of recent discoveries, this proliferating body of knowledge has become disconnected from the traditional body of physicochemical knowledge and now exists as if floating above it. To clarify this claim, I recall for readers those physical concepts like time, mass, gravity, velocity, atom, magnet, temperature, force and so on, which we consider to be the very foundations of our scientific understanding of the world. Yet the breathtaking succession of advances that cram the time line from the discovery of DNA to animal cloning, has proceeded over the period of just a few decades without reference to those concepts - the very concepts regarded as basic by us all.

The dichotomy between the physical and life sciences can be understood in broad terms as a difference between a reductionist and holistic approach to nature. According to the physical sciences, natural phenomena can be understood by analysing them in terms of simpler objects existing on a lower hierarchical level of scale. In the reverse direction, higher complex phenomena can be built logically upon the simpler. Adherents of this approach would say that we do not discover the secrets of nature by searching upwards towards the whole, but by analysing downwards to the parts. By extending this philosophy, they come to the conclusion that it is even not necessary to show how life is based on the well known laws of physics, since this is anyway clearly true in principle. They argue that we should not expect to dig deep and rely on those "basic" concepts like time, mass and so on, in explaining life, because biology is not a fundamental science. By way of example, readers can find the reductionist attitude forcefully expressed in Gell-Mann's book "The Quark and the Jaguar", and many others (1).

The basic laws tell scientists about the fundamental particles that everything in the universe is made of. Almost all of us will have heard of some of the more familiar titles such as the law of gravity, the laws of motion and the law of Also included among these laws are the laws of statistical thermodynamics that govern conservation of energy. complex systems composed of a large number of particles, which are the systems thought to include living things – in other words, life can be reduced to statistical thermodynamics. Although it now sounds as if we have suddenly entered a difficult technical area, the basic concept of this field of physics is easy to grasp for any reader, technically trained or All that is needed is enough familiarity with statistics to understand the notion of an average. The laws in not. question tell us that, in a large population, we do not need to study the behaviour of each and every individual, we need to study the average behaviour only. But what are complex systems, and why is information about their average so useful to understanding them? In a gas, a system studied in the physical sciences, the individuals are gas molecules – in air for example, they are the molecules of oxygen and nitrogen. On the other hand, in the living cell, the system studied by biologists, the individuals are protein molecules. By analogy, in a football crowd the individuals are human beings, and here the law of averages works too. It says, that if we want to know the overall feeling of the crowd, then we seek the average spectator. However since there is such a vast range in human behaviour, there is no point seeking

a real average spectator – there is little chance of finding such a person. To find the average, information on all possible types is fed into an exhaustive calculation. The average spectator is a computation. From our first hand experience of sporting crowds, it is common knowledge that some spectators are jumping about excitedly while others remain seated in rapt attention (or boredom). It is of no use waiting for all the spectators to be doing the same thing, because this will never happen. Their behaviour is statistical. Consequently, the chance of all 50 000 people showing average behaviour at the same time is so minute that the probability that it will happen is zero. Like the spectators who are constantly on the move pushing others out of the way in order to get further in front or behind, gas molecules are known to speed about in space in all directions. They are also incessantly pushing their neighbours by colliding with them in the frenzy of their blind chaotic activity. On the other hand, protein molecules in a living cell are trapped within a watery environment and remain in place at the same location. These individuals are constricted within the medium that surrounds them, and so like the excited spectators who jump up and down in their seats, they exert their energy through agitated repetitive movements executed on the spot. In technical language the two types of movements are called translations (energy that is expressed by travelling movement from place to place) and vibrations (energy that is expressed by repeated activity in the same place), but the thermodynamicists tell us that the energies of both types of motion are spread out in a statistical way. Individuals, even if they are identical, exert themselves to different degrees. Put more pictorially, the individuals of each population are all not behaving with the same enthusiasm, neither in the gas, nor the cell, nor the football crowd.

For more than 100 years it has been known that reactions between molecules happen according to this law of averages. Even when very complicated processes are involved, the overall end result can be predicted when we have enough information to calculate the average energies. For example, when we strike a wooden match and let it burn a little, many complicated chemical reactions take place, involving the exotic substances phosphorus and sulfur from the ignition of the match head, as well as the more ordinary carbon in the wood. We do not know, nor need to know, every possible reaction that takes place, because we know the sequence of steps that the average molecules of these chemicals follow through to their final states, where all of the starting material ends up as a statistical mixture of hot gases rising upwards from the tip of the flame. (These gases are called oxides because when substances burn they react with the oxygen in the air to form chemicals known collectively as oxides. One gas with which we are all familiar, carbon dioxide from the carbon in the wood, is in fact the major constituent of this final mixture).

From the point of view of these principles, the chemical reactions that take place within the living cell are in essence no different from a burning match. In the cell, sugars are "burnt" in a cool, watery environment by metabolic processes rather than in a hot flame, to produce carbon dioxide – we eat starch and breathe out carbon dioxide. Sugars are closely related to wood, as both are formed from the sap of plants. Like all the chemicals of life, sometimes called "organic chemicals", sugars contain carbon and react with the oxygen of the air to form carbon dioxide. Thus the chemistry of life must be fundamentally the same as the chemistry of non-living matter. Indeed, when the great German chemist, Wohler, found the organic compound, urea, to be a major constituent in urine in 1828, he established clearly for the first time that the end products of our cellular processes are simple chemicals which can be prepared synthetically in the laboratory test tube. So it appears that this milestone in the history of science supports the reductionist picture in which the molecules in our metabolic reactions, as in the burning match, follow a multitude of different pathways, some fast and violent others slow and weak, to arrive randomly at their final states. And as complicated as this may sound, chemists nevertheless know how to calculate what the average molecules would be doing throughout all stages of these biological reactions. Put succinctly, the environment of the living cell does not justify any holistic claim that biological reactions do not follow the reductionist principles of statistical thermodynamics, because the law of averages holds true there too.

However, biologists do not see the objects of their world in this way at all. They see structure and function, not statistics and averages. When the orb spider pounces on her prey, a sequence of movements is set in train, which is a marvel to watch no matter how familiar this sight may be. In perfect co-ordination, her four hind legs gather the strong sticky thread from the silk organ and bring it forward to wrap around her prey which she simultaneously slowly rotates with her front legs. She manipulates the thread at such a speed that the movement of the hind legs becomes invisible to the eye, and even though all eight legs are involved, she remains attached to her web. In fact, neither the hazards of her sticky surroundings nor the force of gravity perturb the frenzied activity of this skilful hunter, and within seconds, the hapless fly has become a neatly wrapped shiny silver ball.

This ordinary biological scene is one that displays the precision of an expert, and as every expert sportsman knows, perfect co-ordination is the secret of success. Clearly then, such activity cannot be the result of statistical internal events, because allowing a random move at any stage means introducing a fatal error. With a single unsynchronised movement, the sequence would falter and the deadly silk thread would entrap her own legs. Average movements have no part to play in this world. Indeed, everywhere we look we see co-ordination in living things, which we take for granted, believing it to be obviously required for their purposeful function. But is this conclusion valid, or is it, as the reductionists would say, only a false impression hastily arrived at in awe of life's apparently perfect design?

Let's look a little deeper into the spider's structure. For synchronised movement of her numerous legs, the leg muscles must contract and relax in a regulated sequence. So the nerves which stimulate the muscles, must also fire in a regulated sequence to switch the contractions on and off with high precision. Then in turn, so must the brain cells fire in strict co-ordination, since the nerve cells are under their control. But now, at the start of the line of cell-to-cell command, we are confronted by the question, how do the brain cells fire? In answer, cell biologists tell us that the electrical impulse delivered by a brain cell is caused by activity within the cell, in which its proteins collectively function also according to a strict sequence. Or put in the opposite perspective, if these proteins did not work in concert, there would be no regular impulses passed between cells, and further down the line no successful catch. So in this picture of nature structure did not disappear, even though we zoomed in by a factor of about one million down through the hierarchical levels from spider to protein molecule. And although we reached the level of the cell's proteins, we came to entities which behave in the opposite way to the statistical proteins of the reductionist picture.

The biologist's standpoint is a holistic one. The lower parts work together to ensure the larger entity functions as an integrated whole. They co-operate as though under the influence of the whole. From the physicist's standpoint in contrast, the function of the larger can be reduced to the statistical behaviour of the elementary particles which make up everything in the universe. By juxtaposing these counterclaims in this way we have discovered that the two views do not connect. By proceeding in the bottom-up direction from the elementary atoms on the one hand, and descending in the top-down direction from the organism on the other, we did not arrive on common ground. However we naturally expect, or at least we hope, that both approaches would dovetail together at the intermediate hierarchical level, the mesoscopic level between the macro and micro worlds, populated by those objects which possess the sparks of life. And since proteins occupy the lowest rung on the downward ladder from living organisms, and also the highest rung on the upward ladder from fundamental particles, we would further wish to conclude that proteins are precisely those objects. But instead of a merging landscape, we find the canyon illustrated in Figure 1.1, where proteins stand at the edge on either side of a chasm – the ever widening gap referred to at the beginning of this story. To construct a living cell out of its constituent particles, we would expect to proceed logically step by step from atoms upwards, but like Coronado's men forced to realise that their progress was blocked when they stood awe-struck on the southern edge of the Grand Canyon, we also face an impasse. However ours is an intellectual chasm, within whose reaches lurk the forces that give rise to living matter.

Protein was not present on the early Earth where, astronomers tell us, conditions were extremely harsh. Protein is a delicate substance. Perhaps this may seem strange at first, as most readers think of protein in its dietary sense and associate it with a boiled egg or barbecued steak, which could hardly be described as delicate. But in these examples the protein is dead. As an egg cooks, the clear watery gel is transformed by heat into a solid white mass, which would never become a chicken. So although all the atoms of the original gel are still inside the egg, they are no longer in the living state. Where does living quality come from? What is the difference between the hard, tough state of the dead and the soft, fragile state of the living?

Organic chemicals are more complicated than the simple chemicals of the early Earth, whose atmosphere was made up of chemicals composed of single atoms or small groups of atoms bound together as simple molecules. For those who remember their high school chemistry, names such as hydrogen, nitrogen and methane spring to mind as examples of the simple gases which probably made up the early atmosphere, judging from those of our sister planets. Certainly water, whose technical name is hydrogen oxide and whose familiar formula H2O tells us it is made up of just three atoms (two hydrogen plus one oxygen), was abundant, as was probably carbon dioxide, whose formula CO2 indicates its molecule also contains three atoms (one carbon plus two oxygen). Water and carbon dioxide belong to the class of chemicals called the oxides, which we have already met and will meet again in discussing the origin of life at the end of the story. The atoms of these small molecules are locked together by a few strong bonds ensuring a lasting power of billions of years. In contrast however, each protein molecule consists of thousands of atoms held together by weak bonds forming a much larger structure – a protein molecule is an intricate three-dimensional network. It is the way this large number of bonds holds the precise structure in its overall shape that makes it fragile. Notice we meet here the two concepts "precise" and "fragile", as opposed to "average" and "strong", to describe the world of biology. So how did proteins arise?



1.1 The Chasm between the Sciences We begin with a pictorial representation of the chasm which has opened up in our study of nature over the last 50 years. A "Grand Canyon" splits the large-scale map showing an overview of the hierarchy of our scientific understanding into two landscapes. The physical sciences are on the southern and biological sciences are on the northern side of the deep divide. In the reductionist landscape of the physical sciences, a road of deterministic logic leads from the most fundamental particles of all, the quarks, through atoms and molecules to complicated chemicals like amino acids and proteins. Actually, according to this view, the proteins which stand on each side of the canyon are one and the same, and therefore, the road leads straight on from proteins, following its logical direction to living organisms and even minds, without any gaps. Proteins are simply chemicals found midway along the upward road.

However according to the holistic view, there is a difference between the two types of proteins – the northern proteins work, the southern ones do not. In the eyes of biologists, proteins are functioning entities, which work in harmony with the higher activity of the organisms of which they are part. Therefore, there is a top-down non-deterministic logic as well as the bottom-up logic guiding the road through the northern landscape. The story in this book is about bridging the canyon, or in particular, about the problem of what is the difference between living and dead protein. Is there some natural ingredient lurking here at this level of matter but as yet not visible on the map, that can be added to the physical protein and bring it to life?

The scenario generally accepted by scientists from all fields is that the first protein (or DNA or RNA) molecule formed by accident in the rich chemical soup of the primordial sea. Since it was a statistical process, a vast number of protein molecules would have originated in this way, but just one is supposed to have been endowed with that extraordinary power which is the hallmark of life – the ability to copy itself, that is, to replicate. With the appearance of this molecule, life was born. But how did thousands of atoms link together in the correct three-dimensional arrangement needed to give this finished product the amazing, and until then unprecedented, power of self-reproduction? After all, the simple molecules of the stable gases do not react to form new and bigger molecules as a result of being mixed together, as judged from the atmospheres of our sister planets which have not changed over billions of years. High temperatures like those in the flame of a burning match are needed to cause the early gases to react, and this requirement suggests conditions of fiery volcanoes and violent electrical storms. For this reason, many scientists believe that the answer lies in the results obtained in 1953 by Miller and Urey (2).

In this famous experiment, a mixture of the simple gases was subjected to boiling temperatures and electric discharges for several days. Such conditions were chosen because they are thought to represent those on the early Earth, where collisions with asteroids and comets caused constant volcanic eruptions and violent storms. When Miller analysed the resulting chemical mixture, he found a multitude of new molecules had been produced, which were up to about five times larger than the starting molecules, that is, they were composed of 10 to 20 atoms. Most importantly, he detected in his rich soup chemicals called amino acids. Likewise, on the early Earth the primordial seas became enriched with a huge variety of new substances produced by violent high-energy collisions forcing the smaller molecules to bind together. Later, as conditions cooled, these forceful collisions weakened and eventually this type of chemical reaction ceased. The only reactions that could proceed under the new milder conditions were those that can take place in the watery environment of the oceans. It was in this second more peaceful phase of the planet's early life that the amino acids linked together forming long chains, or proteins. Thus in this three-stage scenario, the earliest atmosphere contained the small everlasting molecules, which during the fiery era were fused together in twos and threes to form the intermediate molecules (amino acids), which in the following era were in turn strung together to form the long chain molecules (proteins) – or as we might say more pictorially, sand became bricks and bricks became houses. It can be claimed therefore, that experiments have definitely established that a protein molecule can be produced by purely statistical processes under just those conditions that prevailed on early Earth. This chemical product is the protein that stands on the southern side of the canyon in Figure 1.1 - the "reductionist" protein of physics and chemistry. But did this entity have the uniquely specialised ability to reproduce itself? Indeed, could it do anything at all?

This first biological molecule has captured the imagination of scientists for decades. Once formed, it was able to direct other amino acids remaining unreacted in the soup to link together in its own image. But how could a chance arrangement of atoms have such seemingly magical powers? Much of the discussion has centred on the high improbability that it arose in this accidental way and on proposing strategies to obviate this problem. For example, the pre-eminent scientists Hoyle (3) and Crick (4) both agree that life could not have originated on Earth by chance and propose some other location in the universe where conditions were favourable. The basic form of life then arrived here later, already in working order. Of the thousands of different types of amino acids that could have been present in the rich soup at the end of the fiery high-energy era, nature used only 20 to create proteins. A typical protein in a living cell is a chain about 200 amino acids long, from which we can quickly calculate the number of distinctly different protein molecules that can possibly be made from these 20 types - and it turns out that this number is larger than 10 multiplied by itself 200 times. From the mass of one of these protein molecules, we can then easily calculate the total mass of all these possible proteins -a calculation which gives a number which is vastly in excess of the total amount of matter in the visible universe! Or looked at in reverse: there is not enough matter in the entire universe, let alone on planet Earth, to produce the required number of proteins to check for one with a special quality. From this straightforward argument we can safely conclude, that the probability that a replicating protein molecule appeared in the primordial soup by chance, is zero.

Nevertheless, proponents of the reductionist view claim further that the statistical beginnings are in line with Darwin's Theory of Evolution. We are all familiar with the Darwinian ethos of "the survival of the fittest", which seems so convincingly to explain why some species went on to evolve into higher life forms, while others died out. According to the theory, the environment plays the positive role of the selector, which screens changes occurring in organisms caused by the lottery of random mutations and chooses those organisms with improved fitness for survival. The force of this argument is so strong that almost all biologists with whom I have spoken believe it, and my wider impression is that the majority of people educated in the sciences believe it also.

So with the statistical scenario standing squarely on Darwinian theory, it now appears that all is solved. Just as with the animals which evolved later on, so too with the molecules before even the first living cell had appeared. In the era of the fiery beginnings chemicals were randomly synthesised. Those which were most suited to produce proteins under the conditions of the next era proved the most successful. Likewise, those proteins which could promote reactions

producing copies of themselves during the next era proved again to be the most successful, and so on. And so the same process of natural selection by the environment operated continuously from the beginning. There is no gap in this picture, since present life forms can be traced in a direct lineage of statistical events to the original simple chemicals of the fiery era. For instance, de Duve, the eminent biochemist who popularised this view, believes that selection overrides the chance factor inherent in random events to the extent that he can claim, "my model is emphatically and unambiguously deterministic" (5).

There is however a fallacy in this argument. Random changes do not improve fitness - they destroy it. This criticism is not new, it has been levelled at Darwinian theory many times. It comes, broadly speaking, from those workers influenced by an interdisciplinary approach who see evolution in terms of the processing of order and information. Those of us who have tried their hand at writing a computer program know well the consequences of even just a single comma inadvertently out of place – the program crashes. Hence, people with experience in this technology find it inconceivable that random changes could retain the quality of copied information, not to mention actually improve it! Of course it cannot be denied that our lives are full of accidents, some of which have happy outcomes. For the lucky few, chance even brings good fortune. But this does not convince us to rely on accidents to improve the quality of our lives or the size of our bank balance. Furthermore, on closer inspection such lucky events do not really turn out to be positive purely by chance. They have their unexpected happy outcomes because they fit perfectly into the existing scheme of our needs and desires. They are like the seed that falls on fertile soil rather than on rocky ground. This is certainly a lucky accident from the point of view of that seed, because the seed itself is already replete with sophisticated information on how to relate to this environment, allowing it to germinate and flourish. It is ready to go somewhere. But needs, desires and expectations are not part of the Darwinian mechanistic picture - in fact they are not allowed. Gould puts this point forcefully when he explains how evolving organisms are not going anywhere (6). Genetic mutations are considered to be isolated statistical events, independent of expectations and information, and unrelated to wishes and dreams. It is selection alone that makes them positive or not.

Many authors have analysed in detail the factors that must be considered in calculating the probability that living molecules appeared spontaneously on Earth. I do not intend to review those spectacular numbers here, rather I wish to extend that analysis and emphasize additional serious consequences which flow from the statistical viewpoint. A good place to start the discussion on the odds against the chance appearance of life on Earth is Fred Hoyle's colourful snapshot of a whirlwind sweeping through a junkyard and creating a fully functional jumbo jet (3). Although it is a very illustrative image, it is really only the beginning of the problem. A jumbo jet cannot function in isolation. It needs fuel, runways, maintenance staff, pilots, navigators, passengers and so on. It is intimately connected with certain sections of society and weakly connected with the whole of society. Likewise the functioning protein. It must find itself in a suitable environment containing the correct chemicals, in the right proportions, at the right temperature, and so on, and all these conditions at the appropriate moment when it is ready to react and begin its replication. In other words, the spontaneous genesis of a protein molecule in the primordial seas could not have started life because to function, it would have additionally needed its environmental supplies and infrastructure. Thus we see that the first living molecules could not have arisen in isolation – they were created by the planet acting as a whole. Like a jet plane, they were created by their society. Consequently, in addition to the statistical factors involved in the spontaneous generation of amino acids and the proteins made from them, we must include the likelihood that the first protein found itself in a world made just for it. Clearly these additional requirements vastly increase the already overwhelming odds against the possibility that life arose randomly from the bottom up.

The problem can be ignored while one faithfully believes that, however remote, however minuscule the chance might be, it is still possible to have a random event which improves the survival rate of a developing entity, be it molecule, bacterium, whole organism, or computer program. In his modern popularisation of the theory, the outspoken champion of Darwinian evolution, Dawkins explains how there must have been even many more mutations during life's long history than previously thought, whose visible signs have disappeared (7). In fact, he uses a computer program to show that the smaller the changes produced by accidental mutations, the more efficient selection must be. However, to claim that a study of random numbers generated by a computer program establishes how evolution occurred is to confuse the simulation of something with the thing itself. A simple illustration of this mistake is when we succumb to powerful impressions like those produced in the cinema, and believe for example, that the movie "Gone with the Wind" is an episode from the American Civil War. But historical events on the one hand, and patches of color projected onto a screen on the other, belong to different realms of reality. A simulation is an artificial representation produced by human agency after the fact, and therefore the cinematic images have no causal connection to the events themselves. Likewise, Dawkins' evolution is a result of his mental activity and comes into existence through running his computer program – a predetermined process which is not in any way related to the supposedly unpredictable changes in direction.

Taken at face value, Dawkins' computations support the reductionist view, that complex life forms are the result of a closely packed sequence of lucky accidents that continued to occur over eons of time. At this point, the inquiring mind is surely tempted to conclude that, even if the chance of the appearance of the first molecule were itself not zero, then the chance of living matter reaching the complex forms it displays in our era certainly must be. In this extended reductionist scenario, the appearance of the first protein is but a minor miracle – the real miracle of life has now been elevated to a higher order. It is that each of the multitude of miracles occurred under the correct circumstances at the correct moment in the time line of the evolutionary sequence – the miracle of the miracles.

Why do so many scientists align themselves with this absurdly unrealistic account of events? They do not conduct themselves according to such impractical principles in their private lives, and certainly never do in their professions. "Leave it up to chance" is not a rule you will find in a handbook of laboratory techniques. In planning experiments, scientists take great care to arrange conditions in a way that they think will maximise the chance of success. And when experiments fail, as they invariably do on the first attempt, scientists assiduously re-examine the conditions with the express purpose of intervening to improve that chance. Indeed, this attitude towards the investigation of natural phenomena is demanded by the guardians of the profession. When Maddox, the editor of the pre-eminent journal. Nature, publicly denigrated the work from Benveniste's laboratory, he claimed he had to do so in order to uphold strict Benveniste does not realise "indifference to an ubiquitous source of error should lead to the scientific standards. uncritical acceptance of data which appear to be more consistent among themselves than the simple arithmetic of sampling error would allow" he wrote (8). This wordy sentence means that, had Benveniste analysed his results correctly, he would have seen that they belong to the realm of chance. Maddox even engaged the services of a professional magician to check whether the experiment from Benveniste's laboratory was not a clever fraud! We will return to this unhappy incident later in Chapter 3, when we come to deal with the actual subject matter of this group's innovative research.

We are all familiar with the movie version of evolution, revealed to us as we watch a television naturalist explain the ever increasing complexity of the animals from trilobite to primate in a 20 minute show. However, we too often forget that today's common knowledge is little more than understanding through familiarity – indeed, judging from the controversial history of biology, an understanding of evolution did not come easily at all. The idea that the history of the animals is one full of ever changing scenes, was not obvious in the 19th century. At the time of Lamarck, Wallace and Darwin, the motion picture was not even an imaginary concept, so little wonder that the species were thought of as static, and even unrelated. The trouble is that, in the 20 minute film show, biological history is speeded up about one trillion times, so what people of Darwin's day saw in the natural world around them was a still shot – in fact it was the last frame of the movie. And in a still shot, there is no movement.

On our time scale, evolution is the extremely slow transformation of matter, primarily water and carbon dioxide, into structures of ever increasing complexity. This transformation is so slow that we cannot see it. It had to be deduced. Biologists think of it in materialistic terms of the improvement of organisms from bacterium to human, whereas computational scientists see it more in terms of the enrichment of information from simple algorithm to complex program. But it is of no consequence whether one thinks in materialistic terms on the one hand, or in digital terms on the other – the question is the same: how did a chaotic mixture devoid of information become organised?

In their private and professional lives, scientists, like all of us, behave according to their value judgements. They want action to be effective, so they ask: is this good for that? Similarly, in evolution it is value or quality which improves, not objects like DNA or protein. We should look for the evolution of things-for-other-things, not things-in-themselves. This means that we have to be able to recognise and measure function as well as objects. This is not always easy to do and science has until recently mainly been occupied with the discovery of objects. Indeed, the pursuit of the fundamental particles remains one of the principle activities, some would even say the highest goal, of modern physicists. However, those on the northern side of the canyon, the biologists, have become experts in studying function, almost to the exclusion of objects, and this new direction has proven to be most fruitful. Biochemical research papers often open by introducing the reader to the agent of interest (an enzyme, a hormone, a drug, etc) by describing what it does rather than what it is. It is common for papers to be titled "The effect of agent X on", then in the report of the study, information intrinsic to this agent as an object, like its chemical formula, is not even mentioned. The agent-in-itself is not at issue. In the biological sciences, it is a tacit assumption that life is at bottom concerned with function, not matter. Put another way, the northern and southern landscapes of Figure 1.1 represent different categories of being. Descending from the top down by running evolutionary time backwards, we arrive at the protein molecule which is an entirely different entity to the protein standing opposite on the lower edge. The upper protein is an active agent, the lower is a chain of atoms. The upper protein is alive, the lower one is dead.

The concept of life as function puts the problem of evolution in a new perspective. We all have a clear notion of when things function better, because the ability to make value judgements, especially about actions, is innately human. We know when a function improves, because of the purpose it serves in a bigger picture. We descend from animals who honed their skills of hunting to survive. Our ancestors were always on the lookout for better methods. We may examine a function as though it stands alone, just as the biochemist studies the function of his agent X, but when we do we are aware that this approach is a simplification. Functions do not stand alone, because by the logic of their existence they belong within a bigger scheme. If a function stood alone, it would be just the means to an isolated end. But in real life, the ends of means are simply the means to new ends, which in turn are the means to even more ends further along the sequence of our daily activities. For example, the function of driving a car is to take me to work, of working is to earn money, of having money is to spend it, of spending is to etc, etc. Life runs on these interrelated activities. It is a network of interconnected functions.

Nevertheless, even though biologists see life in these terms of function, they do not extend this frame of thought to include evolution. For those readers not educated in the sciences, this may seem surprising in view of the way in which their professional approach so thoroughly embraces the interconnectedness of things. But a powerful reason underpins The concept of function implies purpose, and with purpose come reasons, design, mind and even this stance. consciousness. In the frame of mind of the 19th century, the century of Wallace and Darwin, these attributes meant one thing, vitalism, and one of the triumphs of Darwinism was the overthrow of vitalism. The claim rang out that there is no divine hand which directs the world of living things – blind natural selection does that. Analyzing living phenomena in terms of means to ends is not valid, because it puts effect before cause, whereas according to reductodeterministic principles, cause precedes effect and the parts determine the whole. Natural selection is the economic rationalism of the biological world, where advances are attributed to the fitness of individuals to survive the marketplace and social benefits may follow on as a consequence, (or may not). So even though biologists do analyze their observations and interpret their experiments in terms of function, they reject applying this standard to the fundamentals of life itself. Their professional lives are conducted in the social world north of the canyon, but their philosophical souls lie over on the southern side. In the strong words of the pre-eminent biologist, Monod, "chance alone is the source of every innovation, of all creation in the biosphere" (9).

I feel that many readers, especially those not educated in the sciences, may find the fact that a trained scientist can hold such conflicting attitudes quite bewildering – even self-contradictory. We may perhaps understand, how those people trained in the physical sciences view the southern side of the canyon with the eyes of deductive practitioners and therefore see the genesis of the first protein as a once-only chance event. Then as time flowed over to the opposite side, they could find it quite logical that natural selection continued to operate and guide the subsequent random modifications of this molecule to finally produce a brain. But as we also saw, belief in such a series of accidents is not in accord with their practice of the scientific method. Rather, it is an act of faith. On the other hand, the everyday experiences of those other practitioners, the biologists, tell them that all the molecules of life fit together functionally as a society. Yet they reject this philosophical notion in their attempts to understand life's origin for fear of being branded "vitalists". So in the final analysis, they too turn to accidents and miracles.

The belief that life arose by accident represents a breakdown in the epistemology of science. In their striving to understand nature, scientists look for interrelationships, for cause and effect, and now following the explosion in biology, for purpose and design. Against this background, the proposal that the main event in the history of our planet was a lucky strike does not constitute an advance in understanding - on the contrary, it shows up failure. In making this proposal, theory is thrown away and the problem removed beyond the realm of science. You cannot do experiments on accidents. In fact, the proposal means that the physical and biological worlds are unconnected, and even that there is no causal thread running through later stages of evolution because mutations are not dependent on prior changes. Darwinists simply proclaim: we exist because we survived. There is then nothing to explain about evolution in their view, since what is meant by this claim is that there is no underlying mechanism for development the mechanism is superficial and obvious. Change happens. An analogy of this type of tautology is when we say that we see things because they are there, in front of our eyes, whereas in reality we see things as a result of powerful information processing by the visual cortex. And similarly, I suggest that evolutionary change also results from information processing by feedback systems operating at deep levels in the biosphere. Surely it is in the nature of scientific inquiry to posit and identify causal interrelationships, and for this reason many readers interested in the history and philosophy of science may well find the denial of a causal mechanism by most of the scientific community quite incredible, and so feel compelled to ask: is the fear of vitalism really worth such a high price?

So we have unearthed a puzzling inconsistency here: biologists do not seem to fear any vitalistic force at all – on the contrary, in their work they actively seek it out. They want to discover what the machinery of living matter can do. They search for that natural power which they know can organise material and direct energy. And learning from their results, I do not conclude that organisms are endowed with magic spirits, yet I certainly do think that they are driven by a hidden energy. So am I a vitalist? Physicists believe that bodies are driven by the force of gravity to fall to the ground – but does this make gravity a vitalistic force? Chemists believe that the match burns because of the drive of reactions to release energy – but does this make chemical energy a vitalist force? And so by extension, is the proposal of a still higher-level energy, which can organize matter, "pseudo science" (as one journal called my work)?

The idea that there are natural forces which can gather energy and manipulate information, may seem like calling up magic spirits to the classically trained scientific mind, but, as Darwin pointed out, the concept of the gravitational field pulling bodies to the ground is pretty weird too. Through education we have become accustomed to the scientific explanation of gravity and so are desensitized to any suspicion of vitalism we could otherwise hold for this strange force. Likewise, we accept without question the laws we use to construct our tools and machines, regarding them as familiar scientific and engineering principles upon which our modern technology is founded. We consider them to be natural and comprehensible – our machines are not magic devices. Nature's biological machines are also built on natural principles, even though their operation may appear in our mechanical eyes to be driven by vitalistic forces. In the chapters that follow, our goal is to discover those principles – but first we must find the machines.

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2. Natural or Man-made

Seventy years ago, the small opus entitled "What is life?" by the great quantum scientist, Schroedinger, first appeared (1). The small size of this book bore no relation to the influence it was to have, for it went on to stimulate discussion among scientists and non-scientists alike, which has persisted to the present day. In it, Schroedinger confronts the chasm between biology and physics head on. The reader is presented with the thought-provoking proposition that the enigma of life can be viewed in terms of two parallel principles: order-from-order and order-from-disorder. Although one of the founders of quantum theory himself, Schroedinger was a reductionist as far as the physical explanation of life is concerned. He felt that the order-from-disorder principle had already been identified and solved by statistical thermodynamics, which was at its zenith at the time of his writing. Thus, as we discussed in Chapter 1, he saw the chemical reactions of the cell, its metabolism, as the average of a mixture of an enormous variety of reactions occurring concurrently at any particular moment.

On the other hand, the creation and maintenance of inheritable information in organisms convinced him, that order can originate from order through natural processes according to some additional physical laws, which were yet to be discovered. He speculated that living systems must somehow feed off information found in the environment, much like we take in food to supply us with energy. As many readers will remember, he introduced the controversial concept of "negentropy" as the basis of this new theory. Living systems, he taught, feed off negentropy, that is to say, order, which is available in their environment, allowing them to process information. Thus life is also an expression of order-from-order.

In the irony of history, it was this order-from-order principle which was first solved – and quite quickly too. Within a decade of the publication of "What is life?", the moment of DNA arrived. In 1953, the mystery of the inheritable information and its mechanism of transmission from parent to offspring was laid bare by Watson and Crick (2). On the other hand, the further discoveries in the life sciences which were to be made in the following decades, showed it to be the order-from-disorder principle which remained unsolved. As we saw, the spectacular successes in recent research reveal that biological reactions are not statistical at bottom, but show order right down at the molecular level inhabited by proteins – a revelation which was unthinkable in Schroedinger's day. To the reductionist mind of his time, the reactions that underpin life are statistical and thus the activity we call "living" is an average activity. The spider's skill might be taken as an outward sign of masterfully designed machinery, but to the reductionist this would be a mistaken conclusion. The visible signs of skill are appearances only – the trillions of molecules which constitute the organism do not behave according to any plan. Co-ordinated though it may seem, life runs without being directed by a program from above.

In contrast, it is all too clear that our man-made machines are designed and built for our purposes. They are built by us for us, and we could hardly be human without this reflective interconnection we have with them. Even though they belong to our world, it is these inventions of ours which provide the clue to how nature also solves the problem of producing special and directed, as opposed to average and accidental, action. Because they touch all aspects of out lives, we have a very broad idea of a machine. We can speak of a "sowing machine" or a "military machine", but in all cases we have in mind what each machine is supposed to do. On the other hand, scientists use the term more narrowly to mean something clear and definite. They have in mind a device rather like what is called an "engine" in the English language -a device which takes in energy from a fuel source and outputs work by achieving a prescribed effect. Likewise, scientists use the term "work" also in a specially defined way, which we can paraphrase as "energy-for-us" or "useful energy". Thus we see that a machine is an energy converter, taking natural energy from the environment and changing it into a form to suit our needs.

Before the industrial revolution, machines were operated using animal power – slaves lifted stones, oxen pulled carts. Following the advent of the steam engine, it became obvious that fuel could replace animal power as the source of energy. Then scientists gradually came to understand that fuel is indeed always needed whenever we want a source of power – there is no such happy scenario where we get "work-for-free". This realization took the form of the First Law of Thermodynamics, which can be succinctly put in the few words: energy can be neither created nor destroyed. Today, two centuries after the industrial revolution, every educated member of society has become acutely aware of this law, as the realization that we cannot simply create energy on demand looms large before us.

A very basic machine would carry out the conversion in a single step, written $E1 \rightarrow E2$, an equation which reads: "energy input equals work output", or, "natural energy in equals useful energy out". Real machines are of course more complicated. For example, the pistons of the car motor are moving parts designed to catch the energy from the explosions of burning petrol inside its cylinders. But even these movements are of no real worth to us – they have to be transferred to axles, wheels and so on, to become energy-for-us. Muscles are also composed of components which move in conjunction to produce the outward movement of the body on the large scale. However, the First Law applies equally to both – and in fact, their fuels are very similar. The organic chemicals, petroleum and sugar, are closely related, being both carbon-based compounds which burn to produce carbon dioxide when they release their stored energy. They are high-energy materials originating in the leaves of plants, which both the man-made and natural machines use as their fuel to produce movement.

Let's look a little closer at the heart of each machine where the energy derived from burning the fuel is released. In the 6-cylinder motor of our design illustrated in Figure 2.1, fuel enters each cylinder where it burns explosively producing high pressure and is then expelled from the cylinders and collected to exit in the form of the exhaust gas. Engineers would say that this is controlled burning – and so it is on our scale. But when we zoom in down to the molecular level, each molecule of petrol undergoes violent collisions, being smashed and broken apart until all its atoms of carbon are converted to separate molecules of carbon dioxide. Viewed on our level it is controlled – the piston is pushed down just at the right moment. But on the molecular level it is statistical – just as in the flame of the burning match.

However, it is precisely down to this level we must go for the biological machine. In this case, each "cylinder" is a protein molecule called an "enzyme". In this motor the fuel is burnt differently – one molecule at a time. Here, timing and sequence are of the essence. Rather than a certain amount of bulk sugar being fed into each cylinder as the fuel and then burnt up explosively, a single molecule of sugar is delivered to the first protein molecule for its first chemical reaction, and then passed to each of the others along the line until all of the 6 carbon atoms in one molecule of sugar are converted to 6 end product molecules of carbon dioxide.

The sugar molecule is consumed in a step-by-step fashion, which we could with some imagination liken to an apple being consumed in 6 bites. It is not a series of violent collisions as in the cylinder of the car motor, because the precision of the sequence of steps must be maintained. As far as we know, there is also no high pressure produced to push pistons – on the contrary, the scene of this action is soft, cool and watery. Because each of the enzyme "cylinders" has its own place in the sequence according to the reaction step it must carry out, it differs chemically and structurally from its neighbours. Following the analogy, a particular enzyme can recognize how many bites of the apple have already been taken, then it accepts and bites only those apples at the correct stage of consumption specified for it alone. Put another way, each enzyme carries out a single chemical reaction, the biological function belonging to it alone, not the vast and varied number of chemical reactions that occur in the car motor. Thus enzymes are probably nature's smallest machines – "nanomachines" in the true sense of this term. It is therefore also probable that enzymes can perform energy conversions in a single step, represented as E1 \rightarrow E2 above, that is to say, they are a form of the most basic machine possible.

Car manufacturers may claim that their motors operate at the high level of say, 30% efficiency. This means that, of the energy released by burning fuel, 30% is used to move the vehicle at a reasonable speed and 70% is wasted. What about nature's machines, the enzymes? We do not know the answer to this important question, because we do not know how protein molecules capture the energy from their bite of the fuel apple. We can feel sure that it is higher than our man-made versions, but nevertheless they cannot operate at 100% efficiency. We know the truth of this assertion from the famous Second Law of Thermodynamics, which states that, in the real world, there is always wastage. So, although the First Law was correct, it did not tell the whole story – in fact, in a way it concealed the nasty truth, which runs $E1 \rightarrow E2 + E3$. This new version of the equation reads: "energy input equals real work output plus wasted energy". We now see that, because of this law, there will always be some energy lost in operating machines, both natural and man-made, and therefore "real work output" will always be less than the "work output" predicted above by the First Law alone, where all the fuel was converted into energy-for-us.

I would not be surprised if many readers, whether technically trained or not, would wonder what is so important about this conclusion, since common sense and everyday experience tell us that there is always unavoidable waste in any operation, no matter how well planned or executed. Yet, as trivial as it may seem to many, I have nevertheless concluded from my reading of science, that this law has occupied the attention of scientific thinkers more than any other, including the laws of gravity and relativity. Indeed, many famous scientists have said that it occupies first place among the laws – a conclusion arrived at in awe of the dramatic consequences it predicts, as we shall now see.



<u>2.1 Two Motors</u> Two versions of motors, man-made and natural, which burn similar chemicals, petroleum and sugar, as their fuel.

Upper panel: The row of 6 cylinders is a schematic representation of a car motor. The pistons are pushed downwards by the force of high pressure inside the cylinders when the fuel suddenly ignites and burns explosively. This is illustrated by the pressure arrows in cylinder numbers 2, 4 and 6, which alternate their action with cylinders 1, 3 and 5, as the cam shaft along the bottom rotates. However this type of reciprocating action is not essential for our story. The important feature of the design is that each cylinder receives the same quantity of fuel, exerts the same force, and produces the same quantity of exhaust. Fuel is fed into each group of three cylinders simultaneously through the fuel line from the left of the diagram, and the hot exhaust gases, mainly carbon dioxide, are expelled simultaneously to the right.

Lower panel: For this illustration we have zoomed in by a factor of about one billion times (from a meter to a nanometer) to the level of the molecular machine of biology. Instead of 6 identical cylinders, we have 6 distinct jack-in-the-box enzymes which burn their fuel in a sequence of steps as it is passed along the row. The fuel, single molecules of glucose represented by the apples, is consumed in 6 different precise chemical steps until it is all converted into the waste products, carbon dioxide and water, as in the car motor. The 6 squares are in keeping with the pictorial jack-in-the-box image of enzymes. They are drawn in order to aid the eye to define a region of space, they do not represent the sides of real boxes. The curved lines inside each box are schematic representations of the protein chains which are the real material of enzymes. Where they make side-to-side contact, a positive glue factor is in force between them. Likewise the apple at a certain stage of consumption has a strong positive glue factor with the enzyme which is designed to take This step then alters the chemistry of the local fuel-enzyme contact region so that the the next bite. attraction between them is switched off. The fuel apple has now a different shape and size, and is attracted instead to the next enzyme in the line. This generalized picture of enzyme function highlights an essential design implicit in biological machinery. Indeed, the fact that the picture is greatly oversimplified suggests that the degree of design surpasses even that of our man-made inventions.

Because the laws of thermodynamics form the backdrop to the story of this book, we will digress here a little to remind ourselves of this famous prediction announcing the inevitability of waste. The German scientist, Clausius, sowed the seeds of dire consequences when he coined the word "entropy" in his enunciation of the Second Law (whence Schroedinger's "negentropy" mentioned above). Clausius realized that some of the energy extracted from the fuel had to be returned to the environment, and that this must tell us something about how and why natural changes occur. In 1865, at the height of the industrialisation of Europe, he published one of the most important papers in the history of science. In it he gave the mathematical proof of energy loss, which immediately took on the mantle of a basic scientific concept rather than remaining just the broad notion of "wastage". The publication ended with the overarching sentence "…the entropy of the universe tends to a maximum", which describes what happens every time energy is used anywhere in the universe. It tells us that we, indeed the universe, will eventually run out of high grade energy, that is, fuel sources to use, because of the inevitable dissipation of wasted heat into the environment. This dramatic scenario is often described as "the heat death of the universe". In more modern parlance, we might say that our energy supplies are unsustainable in the ultimate sense.

A decade or so after this doomsday prediction, the great Austrian scientist, Boltzmann, whom we will meet again as the story unfolds, began a journey which, he hoped, would end with a theory of evolution of the physical world in terms of entropy, in the same way as his hero, Darwin, had explained the evolution of the biological world in terms of natural selection. He conceived of entropy as a process of the on-going randomization of matter, and his famous equation linking entropy to randomization is carved on his tombstone as a mark of honour to this great intellectual achievement. His insight revealed that the fuel of Clausius' machine is not the bottom line, since it is not just heat energy, but everything, including matter, which is getting irrevocably downgraded and lost. Structures are becoming featureless. Order becomes chaos. The universe is running down, energetically and materially.

Although generally accepted by the scientific community today, Boltzmann's giant step caused many ripples among physicists and philosophers, then and now. Many great minds, including those of Planck and Einstein, became preoccupied by the apparently unassailable power of its awful, some even say depressing, consequences. Readers can find the topic extensively discussed in Prigogine and Stenger's book "Order out of Chaos" (3). However, we do not need to belong to the stratum of geniuses to notice that the world views of Darwin and Boltzmann must meet in head-on collision, for they point in opposite directions. Darwin's theory, so admired by Boltzmann, speaks of ever-increasing order and complexity, while Boltzmann's entropy has us descending in some future time to a homogeneous mix resembling a frozen version of the primordial soup. And so the two most important theories we have to explain the relentless march of time cannot be reconciled – an unsatisfactory situation which has troubled thinkers since Boltzmann's day. Physicists, in the main, tend to Boltzmann's interpretation of time as the gradual levelling out of all things as the universe approaches its final, cold, featureless end. Many have therefore proposed that life must have its own special principle, which applies in addition to the Second Law in special corners of the universe such as planet Earth, to explain life's undeniable success story.

However, when we bring nature's machines into the picture, the forecast is not so gloomy. Clausius' downgraded energy refers to wasted heat, but such high-grade energy is not always wasted, and especially so when it passes through a machine. To be sure, some is unavoidably downgraded, however the point of operating a machine is to take energy from the fuel source and to upgrade as much of it as possible. So we cannot say that, overall, energy is always downgraded, until we take into consideration the degree of upgrade produced by the machine at the same time. This means that a lot of misunderstanding has arisen among scientists and non-scientists alike, because thermodynamicists do not calculate the upgrade – they simple ignore it. And so the Second Law owes its doomsday scenario to the wide-spread, but mistaken, belief that only downgrading occurs.

This topic will be discussed in more detail in Chapter 2, "Mechanism or No Mechanism", of the sequel, TPM. But for the moment, I am aware that many readers may have already found the above discussion excessively technical and may well wonder why there is so much discussion about such seemingly simple issues as efficiency and wastage. Some may even think that I am deliberately making a straight forward question abstruse. So for those who are unaware of the historical circumstances, let us summarise the developments without attention to the technicalities. Clausius originally said that with every change some energy gets wasted. Then Boltzmann later widened the scope to include matter as well as energy, claiming that with every change the order of things in the universe decreases. We can sense the deep-seated force of the spell cast by the Second Law over scientific thought in the words of the eminent British cosmologist, Eddington, who warned, "… if your theory is found to be against the Second Law of Thermodynamics I can give you no hope, there is nothing for it but to collapse in deepest humiliation" (4). And from my experience, I am sure that Eddington's opinion remains the consensus view among leading physicists still today.

Notwithstanding the dire predictions of the thermodynamicists, the story that unfolds in this book is about the upgrading that natural changes bring. But if downgraded implies wasted energy, what does upgraded mean? One analogy with an immediately familiar ring to all of us, is the value of money and its many forms. When we change a handful of heavy coins into one note, money is upgraded. And then changing many tiresome notes into, let's say, a diamond, is a further upgrade of even greater value – not monetary value, grade value. We recognize that the many small sheets of printed paper on the one hand, and the diamond on the other, are of vastly different qualities, yet we accept them as equivalent in monetary value. Likewise, upgraded energy produced by a machine does not show any resemblance to heat. For example, the transfer of a jumbo jet from one airport to another is not heat, even though heat was the direct physical cause of this event. A less familiar but more spectacular example is the transformation of sunlight into sugar by the solar powered enzymes at work in the leaves of plants. The story that unfolds in this book traces the development of machines of this latter type, rather than the avgas guzzling type of our human invention. In choosing this direction, we are following the strong hunch, that living processes are about the upgrading of energy into energy-for-us.

The analogy of the 6-enzyme biological machine with the 6-cylinder motor illustrated in Figure 2.1 emphasizes how the 6 elements need to act in co-ordination for the machines to function. In the motor, this requirement is met by the rigid axle or cam connecting the pistons together, thus ensuring that their movements are synchronised. But in the cell there are no steel rods – indeed, we saw that living protein has the consistency of raw egg-white – so what holds the biological machine together, and what ensures that its moving parts remain co-ordinated?

In an important step towards answering this question, biochemists now know that protein molecules which belong together, stay together. Proteins are designed to possess this ability through the sequence of their amino acids. Biochemists find the color coding of amino acids to be a useful intellectual tool in teaching and research, so we will also adopt this simple mode of visualisation here and avoid technicalities. Let's imagine the 20 different types of amino acids used by nature to produce protein molecules to be beads of 20 different colors. Let's further imagine that whitish pale coloured beads are like glue and tend to stick together, while, say blue and green beads prefer contact with water rather than with one another or with other beads. We could readily extend this picture to a rich variety of interplay between beads, but for the development of our story we need to concentrate on these two basic varieties only – those with a positive and those with a negative "glue factor".

Now let us further imagine, that a string of around 200 beads is coiled neatly back and forth into a compact shape in the same way that a string of pearls would be folded to fit snugly into its box. Each stretch is say 10 to 20 beads long before it loops around in a U-turn and stretches back in the opposite direction. The whole chain makes say 10 or more back and forth stretches in all in this folded-up conformation. In examining this three-dimensional compact form biochemists have discovered something both wonderful and amazing, and that is, that although chains of different proteins have different lengths and different sequences, they nevertheless fold in such a way that the same colors are hidden inside while other colors show up on the outside. There are even other trends observable, such as the same colors tend to be found at the ends of the stretches where the chains loop around and turn back inwards. Research into protein structure has thus revealed an enticing harmony of colors, which emerges from the way the chain twists and turns into its three-dimensional shape. So now, if we imagine the string packed tightly into an invisible box, the box would have differently colored surfaces. White and blue would be especially prominent, because a white surface indicates a negative glue factor, so that this side of the box would avoid other boxes, preferring instead to remain in contact with the surrounding water.

Now we can see how the parts of the biological machine get assembled. They are not 6 identical cylinders as in the motor, but 6 distinctly different chain molecules, each folded into its own compact shape, like 6 jack-in-the-boxes linked together in an assembly line. Each is a different enzyme, so each has its correct position in the row. When biochemists use chemical tricks to separate them from one another in a solution, they will come back together in the correct order when returned to their natural environment. This precision is possible because the surfaces with positive glue factors are not really identical, for example not all plain white, but display a variegated pattern of pale colors. Such a pattern matches only one other, which is displayed on the surface of its contact partner, ensuring that the correct partners dock together in the correct relative orientation. In other words, a color code emerges as protein chains fold into their compact forms, which directs the way in which they associate together. This beautiful biochemical concept helps us explain how the cell constructs its complex internal machinery.

It would appear that we have homed in and identified the basic question lying at the bottom of the layers of biological order – the folding of protein chains. Since the findings of the groups of Kendrew and Perutz in the 1950s (5), biochemists have known that identical chains, that is chains of the same length and sequence, all fold up the same way. This means that in a solution of say, pure haemoglobin, each one of the trillions upon trillions of haemoglobin molecules have the same size, three-dimensional form and shape, or in the pictorial analogy used here, all light up with the same spatial color pattern. At first this conclusion was held in disbelief by many people and simply dismissed by physical scientists, since it runs counter to the predictions of statistical thermodynamics. As we saw in the preceding chapter, basic tenets of physics and chemistry dictate that the behaviour of a vast number of molecules, even if identical, must be random - one can speak of averages but not of uniformity. We were earlier reminded that it is inconceivable that the 50 000 spectators at the football match would behave identically, and since we are describing molecules here, we are dealing with a population of quadrillions, not thousands. Biochemists have, however, made the problem even more intriguing, because they know how to unfold the chains and produce exactly that statistical population predicted by physics, where the chains are thrashing about chaotically in their watery world like frenzied sea snakes. And further, provided the measures taken to effect the unfolding were not too harsh, the researchers can then just as easily reverse this process and return the chains to their original natural state of precise uniformity. If on the other hand, the measures were too harsh, then the natural protein cannot be recovered. The reason why the opaque white of the hard-boiled egg will never become a chicken, is because the uniform chains of the clear living gel have all been unfolded by the heat of the cooking and mangled together into a gigantic knot, which, like a multitude of tangled fishing lines, can never be undone.

It is then an established experimental fact, that a vast number of identical chains thrashing about energetically in water in random kicking-and-screaming motion, can all be induced to calm their motion and fold up spontaneously into the same compact conformation by placing them under conditions resembling their natural environment. Now if one begins to contemplate the probability involved in this display of unison, one is immediately confronted by another of those bigger-than-anything-in-the-universe numbers, which constantly arose in the previous chapter when we discussed the spontaneous appearance of the first protein chain. To put this new situation in plain language: the genesis of the first living protein molecule by statistical means required two impossible developments – firstly, the step by step synthesis of a chain of amino acids in the correct sequence, and secondly, once formed, the correct folding pattern of this lucky chain.

In 1999, the multinational computing company, IBM, announced the Blue Gene Project. With the use of massively parallel technology, a futuristic concept to most of us, the project team aims to solve the mystery of protein folding, which they themselves call "a grand challenge problem". From my correspondence with them (or lack of it on their part), I conclude that they view the problem as a computational, rather than a conceptual challenge. In the tradition of statistical thermodynamics, they believe that the correct twist and turn we would make as we step from bead to bead along the chain, can be found by the throw of the dice repeated a sufficient number of times, no matter how vast this number may be. The approach is reductionist theory put into practice. Prior to the development of the technological power of supercomputing, such calculations were unthinkable, and reductionist scientists tacitly claimed that, in principle, life is statistical at bottom. However, the Blue Gene Project promises to demonstrate how the unthinkable is now possible, using a new generation of the same technology that turned chess grand masters into an extinct species. But from the holistic standpoint the project is doomed by its own internal logic, since the stated aim is to find an average – but whatever it may be, a living protein is certainly no average.

The perfect unison in the ballet of protein folding was revealed through biochemical experimentation – no one expected it and no one predicted it. Over the decades of the twentieth century, biochemists learnt how to extract proteins out of the complex mixture that comprises any tissue sample, be it rat liver or spinach leaves, then to home in on one particular protein and isolate it in the pure state. However, the biological engines of the cell's metabolism are not composed of collections of the same protein, because, as we see in Figure 2.1, each has a different job to do in the overall function. In the man-made motor, the cylinders are identical, since each has to catch the optimum average energy from the trillions of burning fuel molecules trapped inside. In the natural machine, each jack-in-the-box enzyme is different, since each has to extract the energy from a single fuel molecule at a different stage of its combustion as it is passed along the metabolic assembly line. By the end of last century, biochemists had learnt how to reconstitute many of these machines, that is to say, to reconstruct them artificially in the test tube, by mixing together the separate proteins in the The chains will then assemble themselves in the right way by utilising the subtle threerequired proportions. dimensional information contained in their glue factors. In many cases this structural information is today very detailed, in fact, in many enzyme complexes biochemists know the spatial positions of all the thousands of atoms relative to one another in the overall assembly. At this stage, I know many readers are thinking that, armed with so much information, biochemists surely understand how enzymes work. But the answer to this is negative, and to illustrate how fascinating, bewildering, intriguing and just how downright frustrating this problem is, we will take a look at the spectacular modus operandi of one of the most scrutinized machines of all, DNA polymerase.

No doubt the most popularly known success story of modern biology is the discovery of DNA. Everyone has heard how this information molecule is different in each living individual. Our genes impart to each one of us our own identity. In every one of the billions of cells of each person, the same DNA is neatly packaged inside, twisted into the familiar double-helix conformation which has become the logo of so many scientific (and not so scientific) TV shows. And we all know too, how its discovery made the names of Watson and Crick inseparable on the roll of fame. However according to Brenda Maddox (6), credit for the achievement of this milestone in human endeavour must also go to the relatively unknown Rosalyn Franklin. During the natural course of events cells must divide from time to time, and each time division occurs the DNA of the dividing cell is carefully unpacked, untwisted, copied precisely, then refolded and repacked into the two new cells, of which each now has its own copy – an identical copy of the original DNA present when each of us was just a single cell at the moment of conception. So it is DNA that is the replicating molecule, and for this reason many biologists propose that it is a DNA, not a protein molecule, which stands on the northern edge of the canyon in Figure 1.1.

But there are problems here. Like protein, DNA is a high level, sophisticated molecule which could not have arisen spontaneously in the primordial sea. Secondly, as far as I know, DNA does not function like a machine and so cannot reproduce itself. Although DNA is the most studied molecule in the history of biological science, there is not a skerrick of evidence of self-replication to date. In all organisms, copies are made by a copy machine, called DNA polymerase, which is a highly organised assembly of jack-in-the-box protein molecules. To help us look more closely at this biological machinery, we'll use another analogy from our human world, just as we have already compared biological machines with car motors. So the problem now is to paint a picture of nature's copy machine in action from the zoom-out perspective of our world.

Compared to proteins, DNA is a very much longer chain. Whereas the linked amino acid beads in a protein string are numbered in the few hundreds, the DNA double-helix is millions of beads long. In this case, the beads are not amino acids, but like amino acids they are molecules of intermediate size chemically related to sugar. In fact, they are close relatives of glucose, the sugar represented by the apple in the diagram of the metabolic machine. We will meet sugar again in later chapters, as it reveals its multifaceted role in living systems. There are however only four of these sugar-related molecules (some readers may recognize the initials A, T, C, G of their technical names), so in this way DNA is much simpler than proteins. Because this DNA analogy is a string of only 4 instead of 20 differently colored beads, it does not have the variety of sequences exhibited in proteins chains – or put another way, although much longer it is not nearly as colorful.

The length of human DNA is about one billion beads, so one might well expect that there must be quite some frenzied activity in a cell's copying rooms when it divides. However this activity is nothing exceptional, because biochemistry has taught us that the replication of DNA is just another enzyme reaction like the burning of the sugar molecule in the biological motor. On the other hand, it has become something certainly quite special to us in social terms, since every educated person is today aware that, by some seemingly magical means, the microscopic amount of DNA in a single cell, taken from say the root of one hair fiber, can be amplified, identified and even presented in courts of law as belonging unambiguously to one particular individual.

In 1983, the biochemist Mullis devised that ingenious Nobel Prize-winning experimental recipe, which is routinely used to achieve this amplification (7). Among the ingredients for his chemical reaction is the DNA to be copied, of which only one molecule will do – a quantity of material that is difficult for any scientist to believe could ever be effective in producing an observable outcome in a test tube. The other crucial ingredient is the copy machine under discussion, DNA polymerase, and within a few hours, the laboratory technician can harvest from the test tube a million faithful copies of the original single stretch of nano-information. Today, the polymerase chain reaction – we will call it "PCR" for short as biochemists do – is routinely carried out in thousands of laboratories by students of biochemistry. So on the one hand, this PCR is a student exercise, while on the other, it is so scientifically fundamental that understanding how it works would throw light on the mysteries of living matter that lurk in the intellectual chasm where our story began. When we return to it in the last chapter, it is hoped we will have laid foundations to help build the bridge that must eventually stretch across that chasm.

Returning to the zoom-out perspective, we will now see how difficult this feat of replication would be in the world of our devices. To set the stage, let us pay a visit to that medieval monastery, famous for the monks who still thread their prayer beads meticulously according to traditional methods. They perform their craft so skilfully, that the prayer beads produced today are exact replicas of the originals first produced many centuries ago. It is the job of the most diligent monk to thread the new string of beads, by following faithfully the sequence of colors set down by their age-old tradition, as illustrated in Figure 2.2. He is supplied with four huge piles of the differently colored beads, which are constantly replenished by other committed monks. These beads are each one centimeter long and so a chain of one billion beads is about 10 000 kilometers long. The old string to be copied is fed into his cell by his neighbor, whose job it is to unwind and separate the twisted strands - strings of prayer beads are stored away in pairs coiled around one another in perfect double-helices – and straighten them out. As our deft monk passes this old string through his fingers, he checks the color of each bead in turn, and threads a bead of the corresponding color onto the new string. With each new addition, he gently entwines the old and new strings together, so that they form the strands of a new double-helix. This double-helix – one strand old plus one strand new – is passed on to his other neighbor, whose job it is to pile it neatly into compact segments for further packaging. He thus carries out a billion cyclic movements with never a missed bead, never a mismatched color, never a wrong turn, never a step backwards, never a knot - in a word, faultlessly. Of course, every reader will agree that such a feat is humanly impossible, yet in the dividing cell, the process is successfully completed within a few minutes.

Biochemists know that the heart of DNA polymerase, the machine's center where the crucial steps of reading and copying proceed, is an enzyme complex of three or four jack-in-the-box components. The size of this copying device is so small that it spans a distance along the double-helix of just one to two turns, that is, a length of about 15 beads measured along one string. Unlike our deft monk though, it possesses no mind, no nerves, no muscles, no eyes, no arms, ..., and additionally is composed of similar material to the DNA beads themselves.

From the reductionist point of view, our analogy of this enzyme's operation to human activity is very misleading. It could even be claimed that I am manipulating readers, since it is self-evident that no chemical reaction needs arms, legs and muscles. Reactions proceed because of jostling movements and random collisions between molecules supplied by the chaotic energy of the watery environment. Therefore, however unlikely it may seem, the PCR, like any other reaction, is the result of statistical events. But as we have learnt earlier in this chapter, biological reactions are carried out by machines, the jack-in-the-box enzymes, and in this case the reductionist claims cannot be applied – car motors do not function chaotically. And just like our machines, enzymes also carry through their operations rhythmically, over and over again. So as with other machines whose make-up and function we do understand, it is legitimate to ask what is its fuel, and further, how does it use this energy? There are no blurred edges here providing openings for alternative statistical interpretations – this time the picture is clear-cut. The PCR is a display of nature producing and propagating order in its environment through proscribed events taking place down at the molecular level.

There are other intriguing questions too. Motors are made of steel, which is material of an entirely different quality to petrol and exhaust gas, and so it is understandable how they can recycle millions of times without being themselves consumed by the fires of internal combustion. But protein is the same material as sugar, so why is it not consumed with the fuel as the PCR machine cycles billions of times? And further, without muscles how does it thread the DNA beads together and how does it move the strings along, one bead at a time? Forceful actions must be exerted to effect these steps, and because these mechanical actions are not random, but show defined direction, it is now legitimate to ask also, how are these forces co-ordinated?

Biochemists cannot answer these questions. They can tell us that when the right ingredients are in the test tube, then the reaction goes. It is for physics to enlighten us about the forces. Nevertheless, from their detailed knowledge of its structure and using the size scale of a DNA bead one centimeter long, biochemists can tell us that the heart of DNA polymerase would be about the size of a human hand – not a hand and an arm and a body and a brain – just a hand, as illustrated in Figure 2.3. But now there seems to be something very wrong indeed. Can a mechanical entity which is so small in comparison to the size of its workload, possess a sufficient number of moving parts and control centers needed to generate and direct the forces exerted in its operation? Or posed more directly: where is the rest of this amazing machine?



2.2 The Human Copy Machine Acting with the precision and regularity of a mechanical device, the skilful monk threads a new string of beads by copying the sequence of beads on the old string which is fed into his cell from his neighbor on the right. He is supplied with sufficient quantities of the 4 differently colored beads called A, T, C and G by biochemists from the initials of their chemical names. At the same time, he carefully twists the strings around one another, creating the familiar double-stranded DNA helix which he passes through to his other neighbor. On the size scale of 1 cm to one bead, the string located in each and every human cell, the human genome, would measure about 10 000 km long.



2.3 The Size of Nature's Copy Machine Biochemists know the real sizes of the beads and the enzyme which carries out the following sequence of steps essential for the PCR: reading the next bead on the old string, choosing the corresponding new bead and threading it onto the growing string. These two beads momentarily at the center of the action are shown as square rather than round shapes. Using the scale of 1 cm to one bead, then the enzyme is roughly the size of a hand loosely clasping one full turn of the double-helix, whereby it is also known, that we can imagine these steps occurring in the vicinity of the thumb and forefinger. Additional steps which must be involved include: twisting the strings precisely to make a double-stranded helix, rotating the whole double-helix a distance of exactly one bead so that the next bead of the old string moves into the thumb region while simultaneously displacing it so that it emerges stepwise from the bottom of the hand. We will return to this illustration in Figure 13.2 at the end of the story. In the meantime, the challenge facing us in the intervening chapters is to present ideas that are coherent enough to help explain how dead molecules successfully carry out this living act.

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3. The Living and the Dead

Cells are not all the same – they are differentiated to do different jobs. In the spider, brain cells send electric signals down nerve wires, whereas muscle cells must contract. But whatever may be their particular role, they are energy converters, causing motion, electricity or making wood out of sunlight. From the zoom-in perspective, each cell can be viewed as a giant factory, full to its walls and ceiling with densely packed machines working together to achieve this designated end.

Let's get an idea of its make-up. Each machine in turn is a jack-in-the-box worker who repeats the same single job over and over, relying on material passed to him by his neighbors, and then passing on his finished products to another neighbor. For example, bacteria are small cells – smaller than most human cells – but contain roughly the same proportions – about 75 % water, 20 % protein and 5 % other chemical ingredients. In a bacterium weighing one billionth of a gram, the 20 % protein translates into about one hundred million jack-in-the-box machines or enzymes.

Enzymes are not distributed at random throughout the cell, but as we saw are stacked together with their correct neighbors. They are thus grouped into enzyme complexes, or supermachines, containing those enzymes which are involved in the same cellular work or metabolic processes. The six boxes shown in Figure 2.1 are a schematic illustration of such a metabolic complex, which is responsible for oxidizing glucose. There are hundreds of thousands of the same supermachine in a single cell, because there are millions of glucose molecules to be consumed to satisfy the cell's constant energy demands. This means that there are millions of copies of the same jack-in-the-box protein chain present at any particular moment.

So we have a picture of the cell as a huge factory of millions of tireless workers each performing a single repetitive task. The workers are assembled together in groups within which they work in synchronization to carry out a predetermined function. In some cases this function is chemical, such as burning sugar, while others are physical like causing the movement that makes muscles contract. Each jack-in-the-box worker knows how to pack in with his neighbors in the correct way. Some of his surfaces make contact with those of his neighbors, which have the mutually positive glue factor, while surfaces with negative glue factors point outwards making contact with the surrounding water. The assembled groups, the supermachines, are themselves also arranged in order so that those with related functions can make contact and pass on their produce, the metabolite molecules, to one another. Somehow the cell operates as a co-ordinated whole.

Between the stacks of jack-in-the-box supermachines, a network of corridors reticulates throughout the internal space of the cell. Traffic along these passageways is always heavy. The raw materials, fuel for the machines and their produce are transported through doors, which in turn are opened and closed by other jack-in-the-box workers acting as ushers. At the ends of the corridors there are more controlled one-way gates through the cell membrane, connecting the inner workings of the busy factory to the outside world. These membrane proteins are so selective about the traffic molecules they allow to pass, that they appear to have truly police powers. In effect however, just as the workers inside, they recognize and operate their gate for molecules of one type only. Each enzyme has its own individual job distinct from that of others, be it chemical, electrical, mechanical or policing traffic with the outside world.

In their language, the Japanese have the useful little expression "like air", used commonly to describe those things in our lives which we take for granted. Like air, such things may be essential, but we don't even notice their existence. In the world of the cell, this expression could be replaced with the expression "like water". For although it occupies three quarters of the space, giving support to the intrinsic construction we have likened to a huge factory, it plays no role in the study of biochemistry. When enzymes, like the PCR machine, are studied, biochemists isolate them from the cell, transfer them to a test tube and examine them as if they exist and function alone in empty space – just as we imagine the monk carries out his appointed task alone in an empty room. Water is like air, and air is like emptiness.

Even the water filling the busy corridors is forgotten. When cell biologists speak of the traffic of metabolites along the thoroughfares of the cell, they have in mind the process of diffusion. They imagine that free molecules pass through the space of the cell by jostling chaotically back-and-forth along the corridors, colliding with one another until they find their destination by chance. Familiar territory? Yes, we are back in the statistical world of physics. Physicists tell us that the water does indeed have a role – that of supplying the energy for the chaotic collisions without which there would be no random motion and therefore no traffic of essential items along the corridors. In technical language, the water is a bath of heat energy driving the diffusion necessary for the cell's transport operations. Thus water has a background role – it can always be relied upon as the basic source of movement, but, because it is always present as the medium filling the environment just as air is for us, it can be taken for granted.

And so, according to the present stage of our knowledge, the two major components of the cell display opposite behavior. Each enzyme has its prescribed task, which it carries out faultlessly, while inert water molecules kick and jostle about aimlessly with the result that everything remains in chaotic motion. The cell is thus divided into two populations – the living and the dead. As an analogy, let us take an aerial view of a busy city. We see cars and buses travelling one behind the other, always following their prescribed routes at the planned speed, stopping at regular intervals to allow others to cross in front of them in an orderly way and to interchange their passengers. Then there are the smaller individual pedestrians crowding the footpath as they move about randomly in all directions at different speeds. Some of these individuals suddenly speed up running erratically across streets, others stop motionless for unpredictable periods of time, still others turn suddenly to retrace their steps. Like the spectators at the football match, there is no overall pattern to their zombie-like behavior.

Ideas of water as inert chaotic matter that fills spaces did not always hold sway. In physics, ideas of water possessing ordered activity of its own go back 100 years, I believe, to Roentgen, the discoverer of X-rays. He thought that water molecules would cluster together to make structures. But in a general sense, it goes back much, much further than this. Archeological evidence indicates that the ancient Egyptians used the power locked in liquid water to quarry the monolithic stones used in the construction of their giant monuments, including the pyramids (1). In order to free blocks of stone from the bedrock of their quarries, dried wooden wedges were fitted tightly into grooves chiselled out along the rock face. Soaking the wedges with water in the cool of the night caused them to swell and crack the rock along the grooves. They had discovered a powerful energy source which they had learnt to put to their own use. We might imagine that some inquisitive ancestors of these early civil engineers had observed how the growing roots of plants readily invade a natural rock face and with time expand to force cracks to open and then boulders to loosen. Subsequently, over the next few generations, such knowledge could have been refined by the early masons, so that the method of production of building materials improved from the simple harvesting of naturally formed boulders to the quarrying of designed blocks. The intellectual step needed for the development of this technology was the realization that the agent causing the enormous sideways pressure exerted by growing roots was the water they imbibed. In other words, the power to be caught and put to work resided within the water itself.

The strong affinity between wood and water has long been recognized by biologists. We cannot imagine plants without water. Age-old experience reminds us that the dawn of civilization is associated with the practical knowledge that we must supply water to crops. This common liquid is taken in through the roots and travels up the plant to make the leaves, flowers and precious grains. Through the edified eyes of a botanist, a tree is seen as a column of wood holding up a column of water within. So perhaps it is no surprise that wood will absorb water. But it is a surprise that it does so, even when we try to stop it! There is a strong force hidden inside, and as the ancient engineers found, this force is strong enough to break bricks and crack rock.

Other creative players on the ancient stage, the potters, also knew of a secret shared, this time, between earth and water. To mould the desired shape, skilled potters kneaded their lumps of clay by repetitive pressing and pushing motions in the same direction while adding a palmful of water with each cyclic action. This water is not squeezed out of the wet clay by the pressure of the potters' thrusts – on the contrary, it is continually absorbed. It can be dried out in the kiln, but it cannot be pressed out. Before firing, the clay form is heavy with water in the potters' hands, but after the intense heat has done its work, the form becomes light and strong. In fact, since the earliest times, craftsmen have known that the kneading of clay is crucial in producing the finest pot. What is the process by which water enters the wet form, and what sort of material is it that the skilful potter creates when the expelled water leaves behind a clear light porcelain?

Wet clay is not like a mixture of finely ground stones in water. Clay is really crystalline, but because they are microscopically thin, we cannot see these crystals with the unaided eye. In the finest clays, the crystals are just one molecule thick! On the other hand, because they are so wide and long, they can be stacked on top of one another like a pack of cards. So rather than shattering into a jumbled pile of nanofragments, as their frailness would suggest must happen, the stacking gives them collective strength. Kneading wet clay is like shuffling slippery cards into a neat deck. The result is a layered array of the thinnest of crystals, whereby the more regular the array, the finer the pot.

When clay returns to our story in later chapters, it will be with the roles reversed – rather than the potter giving form to clay, it will be clay giving form to life. For the moment, we need to know only that clay is composed of silicon dioxide – the sister molecule of carbon dioxide (silicon and carbon belong to the same chemical family). Quartz is the purest form of silicon dioxide and this fact makes it easy to see how silicon dioxide can be crystalline, since quartz crystals are known to all of us as a common show feature in every jeweler's window. However, such crystals are bulky as is evident from their three-dimensional solid form, and they certainly do not absorb water. Being finely ground quartz, sand is also a form of silicon dioxide, but even the finest sand does not absorb water. The key that clay holds is in the molecular form of its crystals – they are sheets, not blocks – and the secret that it shares with water is that water can partake in the three-dimensional structure by forming sheets also.

Thin flat layers of liquid invade the stack and take up position between the crystals. This is an active process – the result of a working partnership. Water molecules do not diffuse inwards like passive zombies wandering aimlessly in crowded streets, but flow inwards creating a new solid material by acting like thin films of glue between the wafers of mineral shown in Figure 3.1. Since earliest times, potters have been amazed by the drawing power of clay which is always active in drying out the palms of their hands, even though they add ample water while shaping their material. As more and more water is absorbed into the multiple stack of alternating layers, the water layers grow thicker than the crystal layers and so the proportion of water becomes greater than that of the original clay mineral. Yet even with this constitution, it is still not a fluid runny mixture resembling a slurry of fine sand – it is on the contrary, a heavy solid material which is hard to work. And just as the living cell, this material can be more than 75 % water.

Looking from a different perspective, the importance of swelling phenomena is also well illustrated by their undesirable effects. In more mundane situations of ordinary life, we have all experienced how wood swells in wet weather and how houses built on clay crack in wet-dry weather cycles. To the construction engineer, soil heave is a nuisance – not an interesting physical phenomenon. And why are such problems so hard to deal with? After all, the ways in which past societies solved the problems of water supply are admired as great achievements, even wonders. We look in awe at the irrigation systems of ancient civilizations, which stand as testament to how early people clearly recognized the need to control water flow. The ingenuity of the Babylonians in raising water to construct their hanging gardens fascinates us all. But in these cases it is human power that supplies the drive and effort, with water playing a passive role. Our machines direct the precious liquid to do our will. But with swelling phenomena the relationship is turned on its head. Water and its partners – wood and clay – are the active agents. Human ingenuity imposed from outside is not required to drive these phenomena – they arise spontaneously from within and impose their unwanted effects on us.

The basic unit of water, the H2O molecule, possesses no special powers of its own. Indeed, as we have seen, in modern physics its movements are believed to be entirely at the mercy of its environment. It is battered in all directions at random as the result of collisions with its equally aimless neighbors. We will see later why the cluster idea suggested by Roentgen is so seminal, but at this introductory stage we will first examine the meanings we attach to our concept of a "group". As a starting point, let us return to the football match. Each and every football fan understands the difference between twelve men and a team. To humans this knowledge seems to be instinctive, and in any case, certainly does not require a scientific education. Although members of the teams enter the arena in loose file one by one, they take up predetermined positions on the field before the game starts. It is unacceptable for players to perform independently as they wish, because then chaos would reign. From team activity we expect an outcome of a higher hierarchical order than that from a collection of individual sportsmen. In fact, most spectators arrive with the outcome already clear in their imaginations and they come to see their home team achieve just that – they do not come to be disappointed by an aimless melee of undisciplined individuals.

Let us develop this picture further – we have already used the energy analogy to describe the enthusiasm of agitated spectators. We saw them then as individuals displaying each their translational or vibrational energy – we remember these technical terms for jumping from place to place, or for jumping up and down on the spot. However, the crowd can also display highly organized group behavior, as in the phenomenon of the Mexican wave. This spectacular social behavior usually takes hold when the crowd as a whole feels a sense of elation (or frustration). Instead of waving frantically in an indiscriminate fashion and shouting abroad strongly held private opinions, each spectator waits for those neighbors on one side, either the right or left, to stand and wave, and then in turn stands and waves in a controlled way. The more regular the seating arrangement and the more precise the timing of the signal from neighbor to neighbor, then the more perfect the wave and the more satisfying to the crowd is their communal effort. As a result of a certain degree of selflessness, they are able to produce an effect on the large scale which is simultaneously visible to all. So just as a team is more than twelve men, the Mexican wave is more than the combined enthusiasm of the crowd.



3.1 Ancient Water Power The ability of water to cause wood and clay to swell has been known since ancient times, yet it remains a mystery to us still today. To illustrate the phenomenon, we have zoomed in by a factor of about one billion down to a small cross section of the stack of parallel sheets (cross-hatched layers) composed of cellulose fibers or clay minerals. The liquid water molecules (circles with two short arms) enter the stack between these sheets making a multilayered sandwich of alternating liquid films and solid wafers. As more and more flow inwards (thin arrows) they push the stack apart against the force of high pressure being applied from outside upon the whole structure (thick arrows). This flow presents us with the following puzzle: since there is no pressure acting sideways to push the water inwards, why is it not squeezed out? It seems indeed that the water is being actively drawn inwards by invisible forces which we do not understand.

At this point I know that readers will immediately want to ask: can water molecules also behave in this collective way? My answer to this question is: yes, this is precisely what Roentgen had in mind – group behavior. All molecules, whatever their type, have their own shape, or anatomy, and as it happens, the anatomy of the water molecule bears some resemblance to that of the human. It has a large round body (the oxygen atom) fitted with two short arms (the two hydrogen atoms). The arms of one molecule tend to link up with the body of its neighbors – indeed scientists know how strong this force of attraction is. In the first half of last century, scientists in general believed that water molecules group together, and that such clusters spread out and grow as long as there are free arms poking out from the edge of the cluster ready to make contact with and incorporate more molecules. Those readers curious about this tendency of the molecules to aggregate can get an early preview of the process by checking the illustration in Figure 8.3.

Notwithstanding that we are still at the beginning of the story, some relevant facts are already known to us. For instance, it is actually common experience that water behaves like a weak glue indicating that its molecules bond together. We all know how sticky wet clothes are compared to dry, how water spreads through paper and soaks into fibrous material, and how drops remain hanging when we try to flick them away. Pond skaters skip about on the top of the pool without sinking and fallen leaves float because of surface tension. We can even see the tension on the top of the water with our own eyes when we look carefully at the edge of a floating leaf. The surface is stretched into a curve as if there is a thin invisible film of some fine elastic material covering the bulk of the liquid below. So 50 years ago, it did not seem unnatural at all to suggest that the molecules constituting liquid water could join together and exert their influence by pulling on one another. At that time, they were not seen as zombies in aimless chaotic motion – they could behave like the orderly traffic, knowing in which direction to go and which way to turn by following the rules that apply to them collectively.

Scientific research that supported the ideas of ordered structure in water, reached its zenith in the 1960s in the depths of provincial Russia (then the Soviet Union). From the laboratory of an unknown scientist came the news that he had succeeded in making fully structured water, later to become known as "polywater". Prepared by condensing steam in thin tubes of the purest glass, quartz capillaries, polywater was heavier and thicker than normal water. The simplest explanation of its properties was that all its molecules were linked together from one side of the tube to the other -adistance spanning tens of thousands of molecules. When news of the Soviet discovery reached the West, it set off a shock wave that was to resound throughout the scientific establishment for a decade. The Soviets had been the first in space – were they now to claim the discovery of the century? Polywater had the potential to change our basic ideas about physics, chemistry and biology. In response to the threat of the Soviets being once more in the lead, huge resources, both public and private, were directed towards research into polywater in the UK and US. But polywater also had its opponents – established scientists openly hostile to both the concept and the amount of money spent on it. The controversy quickly spread from the field of water research to the general scientific community and finally to the popular press, where sensational reporting on claims and counterclaims became commonplace. The level of emotion reached at the height of the debate, around 1970, can still be felt radiating from the sizzling quotes found in Frank's coverage of the episode in his book "Polywater" (2). One reads for example, "Russian's sample contained sweat" or "polywater is polycrap" and the prominent US thermodynamicist, Hildebrand, proclaiming in a furious article debunking polywater printed in the foremost scientific journal, Science, "... I choke at the explanation that glass can catalyze water".

But the quartz capillary was indeed doing something – something so simple that the polywater proponents did not at first suspect it. The pure quartz was dissolving in the water being condensed in such a narrow curved space, and since quartz contains silicon which is denser than water, the solution that formed in the capillaries was thicker and heavier than pure water. Careful analysis of polywater in more and more Western laboratories confirmed that it was simply a solution of silicon dioxide, and when the announcement finally came from the Soviet scientists in 1973 admitting the mistake, those who had been opposed to it came in for the kill.

But it was overkill. Almost overnight, the idea that molecules could link together to build ordered groups became heresy. When scientists threw out polywater, they threw out structure – and with it the possibility that structure facilitated the dissolution of the capillary walls. Water was now completely statistical, and therefore thoroughly featureless. One well respected researcher who had worked closely on polywater, later wrote how the physics of water reveals "the dense molecular disorder which is now the generally accepted major structural characteristic of the liquid state" (3). After the demise of polywater, scientists, especially those who had worked on the topic, began to fear the stigma attached to it. As Franks admits, even 10 years after the fiasco, "we automatically dissociate ourselves from anything that might bear a resemblance to polywater".

And then, a further 10 years later on, the spectre of structured water arose once more – this time in a French laboratory! Benveniste and his group obtained results, from biological rather than physical experiments, showing how water could remember the nature of surfaces with which it made contact, even after these surfaces were no longer present. Armed with this retained information, liquid water can then act upon other surfaces and cause reactions which would normally need the physical presence of the first surface. Put in human terms: water could remember where it had been. As we already learnt in Chapter 1, the results and conclusions of Benveniste's group collided head-on with those of the establishment. In 1988, the journal Nature, regarded by many of the scientific community as the foremost among journals, published their work along with the disclaimer by the editor, Maddox, that the results could not be believed, even though he printed them! As a consequence of the controversy that ensued, Benveniste and his co-workers became ostracized by the scientific community and their laboratory closed down. For those readers interested in more background to this sad episode, I recommend Schiff's account in his book "The Memory of Water" (4). For the present, we need only be aware that mainstream science, now more steadfastly than ever, embraced the view that water is a featureless medium. For instance, the journal Nature, even 16 years later, referred to Benveniste's work as "pseudo science" and "fringe science" (5).

At the outset of this story, we saw how the last two decades of the twentieth century witnessed breathtaking advances in biology. One often hears it quoted that progress over this short period surpasses that of all previous advances taken together – we need look no further than the spectacular results of modern medicine. But this scientific activity belongs exclusively to the landscape well north of the canyon. Unprecedented though it was and continues to be, this research takes living protein, DNA and even the cell for granted. Indeed, over the same period of time, the chasm grew wider as the controversies surrounding ordered water further marginalized ideas of structure. Like air for us, water fills the background space in cells but is not involved in that crucial activity which transforms dead molecules into living ones. But as we will see, the chasm cannot be bridged without the help of nascent structures in water, which have a foot in each landscape. So before the goal of building a bridge can be achieved, we will need to overturn the established view that the liquor of life belongs to the zombie world of dead matter.

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4. The Puzzle of Osmosis

In the first three chapters, the main characters of the story, protein and water, were introduced. We heard how, in the eyes of mainstream science, they are not viewed as playing equal roles in the "living" of living matter. Whereas life sprang forth with the appearance of protein, the ever-present water remained and remains in the background playing the role of a lifeless fluid medium. But in the version of the story told in the following chapters, protein and water are equal partners, and indeed one of the duo, water, must come to the foreground as it was obviously the original player from the historical perspective. The stage is now set for action, and as water predated protein, it is fitting that we start with a scene in which the liquid reveals a glimpse of its inner vital force.

The phenomenon of osmosis is familiar to everyone: the frankfurter sausage swelling in a pot of water, wooden doors jamming in wet weather, the roots of invading grass cracking the bricks of the garden path. When asked what one understands by "osmosis", the layman would probably describe it as an absorbing or swelling effect. This meaning is reflected in the way we use it in general vocabulary – for example, we might say, that children pick up behavior patterns in the playground by osmosis from their peers, or perhaps, that an immigrant newcomer learns the culture of his new country by osmosis. We use it to describe an imbibing process when someone is surrounded by novel or impressive influences. Thus readers will have no difficulty in grasping the simple osmotic experiment illustrated in Figure 4.1, which shows the cross-section of an inverted glass funnel containing a sugar solution, made by stirring a little sugar in water, placed in contact with pure water. This is the same apparatus as was used by the father of research into osmosis in the latter half of the 19th century, the German botanist, Pfeffer. This very basic experimental set-up is used still today in thousands of biology laboratories around the world, because it demonstrates the osmotic phenomenon in such a facile way. The sugar solution is kept separate from the water below by the membrane stretched over the funnel, which allows water, but not sugar, to pass up and down through its pores between the two compartments. Water, known technically as the solvent, flows into the funnel raising the level of the surface of the solution up the funnel tube above the level of the water outside such that, in the language of engineers, the solution inside is now under a hydrostatic head of pressure given by the height, h. Because of this raised level, the pressure in the solution inside is greater than that outside and, pushing downwards, it acts against the tendency of more water flowing upwards through the membrane pores. When the pressure is great enough to stop this upward flow, scientists say that equilibrium has been reached. The extra pressure in the sugar solution which established and maintains this equilibrium is called the osmotic pressure. But what most readers will not be aware of is that, like a levitating Houdini, this behavior defies the laws of physics.

Shocked readers will no doubt demand an immediate explanation of this outrageous claim. So let us digress a little from the watery solutions and recall a couple of these laws. Firstly, the law of gravity: everyone knows that levitation is a conjurer's trick. Things, or bodies (also called mass, matter, material or substance by scientists) cannot rise up spontaneously. According to long known scientific principles, energy must be spent to lift a body against its own weight. Yet in Pfeffer's experiment, water rises spontaneously like the conjurer lifting himself by his bootstraps. To explain this levitation, most physicists favor the theory that water molecules are propelled up into the sugar solution, because those below the membrane have more energy than those in the sugar solution above. This explanation has an analogy in the way in which the sun dries up a pool of water. The sun's rays warm up water molecules on the surface of the pool giving them enough heat energy to propel them up into the air above. In that case, the sun is the source of energy which can indeed lift up mass. But in osmosis there is no sun – in fact experimenters take great care to keep all parts of their apparatus at the same uniform temperature, and hence it cannot be claimed that one portion of water is warmer than another. So even though it is true that the warm water molecules in the air are now moving faster than those still in the cool water below, there are no warmer molecules in osmosis.

But let's pause for a moment: surely it is those molecules above the membrane which are propelled faster, because it is after all they which are exerting the greater pressure. For this reason, many other physicists believe that it is the molecules in the solution above the membrane which have the greater energy. In the final contribution to a discussion on osmosis published in the pre-eminent scientific journal Science in 1976, the thermodynamicist Andrews writes, "...if the pressure is allowed to increase in the solution, solvent molecules are pushed into the membrane with extra force" (1). With this simple picture, Andrews, whose views we will examine again in the sequel TPM, was interpreting in a more straightforward way the explanation originally proposed by the famous thermodynamicist, Scatchard, who put it in these vaguer terms, "...the excess pressure is exerted to increase the tendency of each solvent molecule to diffuse" (2).

But this explanation only deepens the mystery. At this stage, it is difficult to get a clear picture of which molecules have the greater energy, those above or those below the membrane. If, as Scatchard and Andrews say, the molecules above are moving faster and harder than those below, how can molecules move upwards against their extra force? It now appears that the molecules moving upward through the pores of the membrane can somehow avoid confronting the more energized molecules pushing downwards against them from the solution above.

To see this contradiction in better light, let us turn the experiment on its side shown in Figure 4.2A. This eliminates the factor of gravity and focuses purely on the horizontal movement of the water. In this set-up, the water now flows sideways to enter the sugar solution, pushing a small fraction of the solution up the funnel tube again raising the pressure in this solution. So here once more, the water passing through the membrane appears by some means to be propelled by a smaller force against a bigger force. However, a basic law of physics says that a mass moves in the direction of the bigger force and thus the sideways flow breaks another law. This time it breaks Newton's Second Law of Motion.

Some readers may object, quite rightly, that I have not eliminated gravity entirely, because just as in the original apparatus, it is the rise in the level of the solution that produces the osmotic pressure. So in the technical eyes of engineers, it still appears that osmotic pressure is in reality a hydrostatic pressure. But we can prevent the level from rising by closing off the funnel tube as illustrated in Figure 4.2B. Now, no water can flow into the sugar solution, because the solution already fills the funnel, leaving no free space for more solvent. Yet the pressure within the funnel still increases and stops, just as before, when the osmotic pressure is reached! This interesting observation tells us that osmotic pressure is caused, not by a flow of solvent, but by a flow of energy. We are forced to this conclusion because, even though extra water cannot enter the solution, energy must come from somewhere to explain the pressure increase behind the membrane in Figure 4.2B. We will return many times to this intriguing phenomenon.

Although we have eliminated the role of gravity in the pressure build-up, this has not removed the serious difficulties encountered with still other physical laws. For example, the behavior of osmotic systems contravenes one of the most rigorous requirements of thermodynamics. As we saw in Chapter 2, thermodynamicists believe that nothing in the physical or biological world escapes the dictates of the First and Second Laws of Thermodynamics. At an early stage of their studies, students of the subject learn that these two laws can be combined into a single law, which defines a special thermodynamic quantity called the "Free Energy". The Free Energy is a truly powerful tool to the scientist, because knowledge of how it changes allows the prediction of whether any process can happen spontaneously or not – and only when the Free Energy of a system decreases, can the system change spontaneously. Thus this quantity tells us whether a change can occur in a natural way by itself, and for this reason, is often referred to as a thermodynamic potential. For many readers, this line of argument may at first sound a little too difficult to follow, but it can be put in simpler terms: when an event happens naturally, it loses some of its drive, that is, its potential, which caused it to happen in the first place. However thermodynamics also dictates that the Free Energy of a solution – any solution – increases as its pressure increases, and therefore the spontaneous build-up of osmotic pressure breaks this thermodynamic law.

One does not need sophisticated technical knowledge to grasp the essence of this argument. Nontechnical readers can understand its meaning by referring back to the situation in Figure 4.1, where the solution lifted itself against the force of gravity. In the normal world, bodies do not lift up spontaneously – we need machines to lift a load of bricks, and as we learnt in Chapter 2 we need fuel to do that. In lifting loads, the work we do gives them energy or potential. Inanimate loads cannot gain this potential by themselves. In Figure 4.2 however, the pressure increases whether it is physically possible for the solution to rise up the tube (tap open), or not (tap closed), so even when the solution is not lifted, it still gains potential in a natural spontaneous way. This counterintuitive behavior can be likened to a spring becoming squeezed automatically, even though there is no external agent compressing it. It is acting alone, giving us the sense that the spring has the power to concentrate energy within itself. Later we will see how this spontaneous energy build-up played a role in the origin of life. Watch this space!



4.1 Measuring Osmosis The early apparatus for measuring osmosis consisted of a membrane made from animal gut stretched across the wide opening of the bulb of a pouring funnel. The bulb of the funnel holding the solution, say sugar in water, was inverted into a vessel containing pure water. The two remained separate because the sugar does not pass down through the pores of the membrane which is permeable to water only. Today's laboratory osmometer is essentially the same as this simple classic device. As osmosis proceeds, the level of the solution rises up the funnel's run-out tube connected to the narrow opening to a height which causes enough back pressure in the sugar solution inside the funnel to stop any further upward flow of water. When this additional pressure, the osmotic pressure, is reached, scientists say that the system is now at osmotic equilibrium.

On the right is a schematic view of this set-up, in which the membrane is represented by the dashed line to illustrate a barrier with pores through which water passes back and forth. The pressure build-up inside the bulb is illustrated by the slight stretching of the membrane. Since the membrane plays the role of one of the central characters in the story, we will meet this representation again in later diagrams.



4.2 What Causes Osmotic Pressure? In this experimental set-up, the bulb of the funnel is turned on its side, so that water must now flow through the membrane pores horizontally to the right to enter the sugar solution. There is also the additional fitting of a tap connecting the bulb to the run-out tube.

A) The tap is open and the level of the solution rises up to the same height as in the previous diagram where the water flowed vertically upward into the funnel. Here again the membrane is shown stretched outward a little to illustrate the higher pressure in the solution.

B) The tap is closed, however the pressure inside the funnel still rises until the osmotic pressure is reached. Since no additional water can enter the solution in this case, we are faced with the intriguing question: what causes this pressure build-up?

The law of gravity, Newton's laws of motion, the thermodynamic law of Free Energy – serious questions now confront us. Are these breaches real, or are they only apparent? Many readers will be puzzled by this melee of contradictory ideas, especially in view of the conflicts with physical laws which we have been educated to accept without question. You get the feeling that physicists today know more about black holes and the big bang than they do about a glass of salty water. And indeed this feeling is strengthened, when we extend the survey of popular theories of osmosis more widely to cover fields ranging from physics through chemistry to physiology. This book is not the place to examine these various theories, although many readers would be surprised at the variety of contradictory notions which have been used as the basis for the more popular explanations of how osmosis works - so just for a taste: (i) that the extra pressure in the solution is caused by the sugar molecules alone as if they were gas molecules moving in empty space. This was the original explanation and was put forward by van't Hoff in 1886, who discovered that the osmotic pressure behaves mathematically as though it is a gas pressure; (ii) that the lower concentration of solvent molecules in the solution causes the solvent to diffuse into the solution against pressure. This explanation has won a higher rate of acceptance among physical scientists than van't Hoff's and is called the "molecular theory of osmosis"; (iii) that solvent flows into the pores in the membrane because the pressure therein is lowest and then emerges suddenly without opposition into the solution where the pressure is highest; (iv) that solvent is sucked into the solution; (v) that the sugar molecules act as trapdoors at the pore openings on the solution side of the membrane resulting in a ratchet one-way flow of solvent molecules through the pores against pressure. All of these theories involve complicated mathematical treatment and, because they make no reference to one another, reading more than one of them at a time leaves the inquiring mind in a state of dizzy confusion.

Many scientists were unhappy with this unsatisfactory situation – after all, we do not have several theories of why bodies fall to the ground or why a burning match releases heat - we have only one. So in 1978, some prominent scientists who worked on the fundamentals of osmosis during last century, contributed to the "Forum on Osmosis" published by the American Journal of Physiology (3). The discussion was opened by the botanist, Hammel, with his unorthodox proposal that osmosis is caused by stronger tension in solutions compared to pure solvents, or put plainly, by water molecules pulling on one another with more force when the sugar molecules are added to them. This proposal was not only unorthodox, but extremely unpopular – one might even say, heretical. It was dismissed by all the other contributors. The discussion included a short article by Hilderbrand, the eminent thermodynamicist whom we have already quoted in the previous chapter attacking polywater, ridiculing Hammel's proposal. Despite the antagonism, it was Hammel with his simple idea who was able to resolve the apparent conflict between osmotic phenomena and Newton's Law. This follows because, given that there is a higher tension in the water of the solution than in pure water, then water will be pulled into that solution by the stronger tensile force now acting in that direction. In Figure 4.1 for example, it means that water will be pulled upwards by the stronger tension in the solution above. In other words, the water moves in the direction of the bigger force, as is required by Newton's Second Law of Motion. Yet despite this illuminating idea, the moderator of the Forum, editor Yates, showed partiality with Hammel's antagonists by invoking Einstein's name in summing up the discussion in favor of the popular view. Even a non-scientific reader gets the message that the use of the name of this great physicist in association with the opposition sealed the fate of Hammel's tension proposal. Hammel wanted to clarify the mechanical problem posed by osmosis, but his approach met intense confrontation from the thermodynamicists, who were unaware that it was Hammel's simple proposal alone, which had the possibility of removing the contradiction with Newton's Law.

Hammel knew that there is tension in water. He had experimental evidence of it – an overwhelming amount of evidence. In collaboration with Scholander, their research group had extensively studied the state of water in plants over decades and established that sap rises up even the tallest trees under tension. In other words, sap is pulled upwards like a long taut rope by some osmotic mechanism operating in the leaves high above. Today, botanists around the world know that one does not need tall trees to see this phenomenon. So widely spread is it in plants that every blade of grass holds water under tension, and as we shall see in later chapters, so indeed does every living cell.

One of my treasured possessions is a letter I received from Professor Hammel shortly before he retired. In it he describes feelings of despondency and loneliness which he experienced at the end of his career. Rather than recognition and acclaim for original research and fruitful collaboration over his working years, he was faced with rejection and even ridicule. He was a victim of the mass hysteria that prevailed among physical scientists over the perceived threat of innate forces of order in liquid water. We have already heard of the global ramifications following the collapse of polywater a few years prior to the Forum on Osmosis. Here once again we hear the words of Franks (4) "...any researcher still courageous enough to invoke the existence of modified water must be prepared to face a good deal of ridicule. The funding agencies too do not look kindly on any proposal that smacks of polywater....We automatically dissociate ourselves from anything that might bear a resemblance to polywater".

My own experience teaches that little has changed over the intervening decades. Reputable scientific journals have often told me that tension does not exist, and even that the rise of sap is "imaginary". A catalogue of antagonistic editorial reactions, some quite colorful, is included in TPM Chapter 5, "The Establishment". It is surprising that such strong disbelief is so widespread, in view of the fact that the phenomenon has been measured by physicists, chemists and biologists in a variety of experimental setups. The engineer, Hayward, whose name is synonymous with the measurement of tension in liquids, concedes that results from biological groups like Hammel's helped to convince him that plants do indeed hold their sap under tension. In an inspiring article entitled "Negative pressure in liquids. Can it be harnessed by man?" (5), he presents the notion that, since nature manages water under tension so effectively and on such a grand scale, we should be able to also, at least in some small measure. Readers may also be interested in the sociological aspect of his article, in that he makes a plea for a dedicated research effort into developing cheap agricultural equipment based on water tension, which would be of benefit in third world countries.

The puzzle of osmosis sets the stage for the unfolding of a much bigger story. Solving this problem will lead us into seemingly unrelated fields of study ranging from engine mechanics to the chemistry of life. Acting like a seed that becomes a spreading tree, solving the puzzle will grow branches outwards to many sciences – branches long enough and strong enough to overarch the chasm between physics and biology depicted at the outset of this story.

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5. The Machine

In 1824, the young French engineer, Sadi Carnot, published his small book entitled "Reflexions sur la puissance motrice du feu" (On the motive power of heat). This seminal work gave birth to thermodynamics, a study which was to have ramifications not only for its own narrow arcane field of science, but also for general scientific and social thought that arose and flourished during the era of the industrial revolution. We already have a feeling for the authoritative influence that thermodynamics holds over the other sciences from the discussion in Chapter 2. Carnot's machine illuminated what will always be a basic scientific issue – the nature of energy. In a word, it explains the circumstances which allow natural energy (fuel) to be converted into work (energy-for-us). Although not appreciated at the time, this intellectual step led to some of the most abstract thought, associated especially with the names of Mayer, Joule, Kelvin, Clausius, Maxwell and Boltzmann, in the history of science. This may sound rather daunting to the non-technical reader, but his machine is simple in essence, and can be understood in terms of familiar concepts like heat, work and cycle, plus the perhaps more technical concepts of pressure and temperature.

Carnot was interested in the steam engine, and so his machine is depicted as a piston moving in a cylinder in diagram Figure 5.1. Hot, pressurised steam pushes on the piston from inside and the machine expands from A to B in what engineers call the power stroke. At B, the steam starts to cool down and condense into water, and as a result, the pressure inside the cylinder drops to C. So during the return stroke, C to D, the force now being exerted on the piston from outside is much smaller. This means that heat, a natural form of energy, can be converted into work, a useful form of energy, because we can connect the piston to a motor device and use the strong delivery of the power stroke as the heartbeat of an engine. We must however, give back some work by pushing the piston during the return stroke to complete the cycle, but this amount is much smaller, and therefore we gain work overall (or as one might phrase it more dramatically: "and therefore the industrial age was made possible").

Carnot's insight revealed that the machine can contain any gas – it need not be steam. He was able to show that during the high pressure power stroke, the machine must operate at high temperature, and conversely, during the return stroke at low pressure, it must operate at low temperature. Then followed his conclusion: the bigger the temperature difference between steps AB and CD, the more work can be gained from the same fuel source. It was this realization that was to prove so illuminating for later scientists, helping them eventually to unravel the intricate mesh of mathematical relations which embodies the field of thermodynamics. In fact, we can trace a direct line of thought from Carnot's simple idea to the final overarching concept of the heat death of the universe, which we touched on a little earlier in Chapter 2.

Carnot's machine is an idealization. In the real world we cannot simply set up our high and low temperatures as we wish. We have to achieve the high temperature by providing an energy source, say by burning oil, and we have little control over the low temperature where the unused energy is given back. For instance, we cannot run a motor with the return stroke at a colder temperature than that of the environment, although this may be very desirable. Take the common example of a car motor – it is always very hot when it is running and the exhaust is always much hotter than the surrounding air into which it is expelled. This is a clear case of wasted heat. The Carnot cycle is a conceptual tool rather than a description of a real motor. We are able to use it as a basic principle to demonstrate whether we can gain work by operating machines in systems where there is a natural energy source available. It instructs us on how to transform energy from one type into another – from natural energy into energy-for-us.

However, the energy source is not always heat delivered at high temperature. We have become so accustomed to burning fossil fuels that, in this age, we expect to be constantly supplied with high temperature as an essential social service. Our machines run on high temperature – the energy source of the industrial age. But living systems do not, and hopefully one day soon ours also will not. The plankton of arctic waters for example, have little choice but to operate their machines near zero degrees, so clearly heat is not their energy source. In fact they use sunlight, which is energy of a different quality from heat. Osmotic energy is another type of energy which differs from heat. As we saw, solutions can develop high pressures without the need to be heated up by an outside fuel source. To see how an osmotic machine could work, we will incorporate the essence of Pfeffer's osmometer into Carnot's machine and rerun its cycle to establish how this new energy source could be used.


5.1 Carnot's Cycle This cycle is the basis, one might even say, the inner essence, of the vast majority of man-made machines called engines. The machines of Carnot's time were driven by steam, but as he showed, any hot gas will do, for example, the hot gases produced by the burning fuel in the internal combustion engine illustrated in Figure 2.1. At the start, A, hot pressurized steam is directed into the cylinder and pushes the piston delivering the power stroke, A to B (large thick arrows). At the end of this expansion the steam inside the cylinder cools down and consequently there is a big pressure drop in the step B to C. Now the steam is no longer pressurized, so the force on the piston during the return stroke, C to D, is much smaller (small thick arrows). During the power stroke the machine can do work for us, say by turning a set of levers as illustrated here, but during the return stroke the levers must work on the piston to push it back to its starting position. But since the force A to B is much bigger than C to D, the levers have gained energy. Or in the technical language of thermodynamics, the cycle converts thermal into mechanical energy, that is, heat is converted into work.

Let us imagine that biologists have discovered a primitive marine animal whose behavior prompted them to call it a "piston fish". This tiny organism contains a salty solution (as do all real cells) surrounded by a semipermeable membrane (as are all real cells), and is fitted with a tiny piston shaft which it uses to exert push and pull forces on its environment. Like the swelling sausage, it develops an internal pressure when surrounded by water - its osmotic pressure - which is higher than the pressure in its watery environment, in the same way that the pressure in the solution above the membrane is higher than in the water below in Figure 4.1. It uses this extra pressure to push out its piston from A to B as shown in the diagram of Figure 5.2. Our piston fish is performing work during its power stroke AB. Next it is surrounded by salty, rather than pure, water which has the same salt concentration as its internal medium. Now there is no difference between inside and outside, so the internal pressure drops back to the normal surrounding pressure of one atmosphere at C. The piston fish has now no inner force so the piston shaft can easily be pushed back to D, corresponding to its original position at A. During this return stroke CD, a much smaller amount of work is exerted by the environment on the piston fish, because the step CD is down near the zero pressure line shown in the This illustrates that our imaginary mechanical organism effected forceful action on its diagram. environment, but it cycled back to the starting position unchanged. It is the Carnot machine of the biological world of cool waters, as opposed to the power houses of our industrial world of hot gases.

Following one turn around the osmotic cycle helps pose the problem of the energy source in a clear, understandable way. Here we have no fuel burning at high temperature to cause the high pressure which powers the expansion step AB. So where does the energy come from and when does it enter the machine? After all, the water molecules entering the swelling piston fish from outside come from the normal low pressure of one atmosphere, so how do they supply the molecules inside with the energy to produce the high pressure needed to do the work? And can we even be sure that it is they, which really do supply this extra energy? This is the puzzle of osmosis now seen in a brighter practical light.

In the case of Carnot's original machine the answer is easy. One of the triumphs of 19th century science was the development of a thorough explanation of the behaviour of gases in what is called "The Kinetic Theory of Gases". In this theory, a gas possesses more energy at a high temperature because its molecules are moving at higher speeds – the agitated spectators who are constantly on the move. Hotter molecules speed through space faster, colliding with one another and the inside face of the piston with greater force. At the lower temperature during the return stroke their movement becomes sluggish, they collide against the piston with weaker force and so this stroke is performed with much less effort compared with the force of the power stroke. This simple explanation of hot gases at high temperature in terms of higher speeds and more forceful collisions is today universally accepted as the correct molecular interpretation of events during the work cycle – or put in simpler terms, why the outward force is strong and the backward force is weak. The Kinetic Theory has given us a clear picture of what the molecules are doing when heat enters and is converted into mechanical work in Carnot's machine.

So can the osmotic machine, which operates by absorbing and releasing water, be redesigned to use a gas instead of a liquid as the medium inside the cylinder? This would offer the possibility of throwing light on the problem of the energy source, since gas machines are so well understood in terms of the Kinetic Theory. And indeed, this can easily be done. Figure 5.3 shows the workings of the tiny creature known to biologists as the "piston fly" – a close evolutionary relative of the piston fish. This delicate insect possesses a vapor sack, fitted with a piston shaft, in which the pressure responds in harmony with the humidity in the surrounding air. The piston fly is so fragile, that it ventures out from its hiding place at the water's edge only when the air is dead calm. Hovering above the surface of the water, it absorbs the humidity, which is greatest above clean fresh water, and builds up high pressure in its vapor sack. Just as with the piston fish, it expands while in this pressurized state, doing work on its surroundings during its power stroke AB. It then flies to the region where the water is salty and the humidity lower. Hovering over the calm surface, the piston shaft is pushed back during the return stroke CD, and because the humidity is lower here, less work is exerted on the insect's body machinery than was done by it during the power stroke.



5.2 The Piston Fish - or - The Osmotic Machine The cycle of the piston fish operates in the same way as Carnot's steam engine. When the piston fish is surrounded by fresh water, it becomes pressurized inside because its body is a specialized osmotic bladder containing a solution of salty water. It starts to swell and expands from A to B. Because there is higher pressure inside pushing on its piston than outside, it uses this expansion as a power stroke. But when it is surrounded by water which is just as salty as inside its specialized bladder, the pressure inside drops to normal (one atmosphere), and its piston can be easily pushed back to its starting position without using up much energy. So the step C to D is used as the return stroke. Therefore this machine operates just as Carnot's heat machine, except that the high pressure power stroke is not driven by high temperature. In this cycle it is cool osmotic energy that is converted into work.



5.3 The Piston Fly - or - Steam Engine with a Difference To become pressurized, the piston fly hovers above the fresh water reservoir where the humidity is high (shown by the dots). It expands its specialized vapor chamber from A to B, while taking in water vapor under these high pressure conditions, and as before, this step is the power stroke because the piston pushes on its environment. Over the surface of salty water however, the humidity is always lower, so the return stroke, C to D, is performed in this environment to ensure that less work is done pushing the piston back than the piston delivered during the power stroke. By cycling in this manner between high and low humidities, the piston fly is operating in the same way as other gas engines. This is what the editors meant by the retort "the engine is driven by the expansion of the high pressure gas. This is elementary and well known". But now the question: where does the energy come from? Technically rigorous cycles for the piston fish and piston fly are given in Appendix 1, "Work Cycles and Boltzmann's Constant".

Although the work cycle of the piston fish was derived in analogy to Carnot's cycle, we need not qualify the cycle of our imaginary piston fly with the label "analogy", since, just as Carnot's machine, it is also a steam engine – a steam engine with a difference. Here the "steam" is of course cool water vapor at very low pressure – the "steam" that is reported by the weather man when forecasting tomorrow's humidity. Yet it can still do work, just as hot steam does.

Since our imaginary creatures use the same fuel source, the fresh water reservoir, they will deliver the Their cycles, compared in technical detail in Appendix 1, reveal two same amount of work. interesting results. The first has to do with Boltzmann's Constant. Boltzmann, whom we recall from Chapter 2 and will meet again many times in the chapters to come, linked entropy and disorder in the universe via a proportional measure known today as Boltzmann's Constant. This physical quantity tells us how much spring there is in molecules. If we imagine all the molecules that make up matter to be tiny springs, then Boltzmann's Constant tells us that they all have the same strength. Comparison of the work output of the two machines shows that Boltzmann's Constant is lower in the salty water compared to the pure water. This means that pure water has more spring than salty, and consequently energy would naturally flow from the pure to the salty if they were in contact. This explains why our imaginary creatures, the piston fish and piston fly, both first become charged from the fresh water reservoir, then perform work, and finally return the remaining unused energy to the salty reservoir. Carnot's machine (Figure 5.1) takes energy from the hot boiler and returns it to the cool atmosphere, whereas our creatures take energy from the strong springs of pure water and return it to the weak springs of salty water.

The second result follows as a consequence of the drop in Boltzmann's Constant, since it means that one and the same solution can have different spring strengths. This ability is illustrated by the intriguing phenomenon where the pressure of the solution trapped in the container with the tap closed in Figure 4.2B increased, even though water could not enter it. On making contact with their stronger neighbors through the membrane, the weak springs of the solution inside increased their energy and so pushed up the pressure on their side of the membrane. This picture of different springs will prove very fruitful when we come to discuss structure in liquid water in following chapters.

However, physical journals are not at all impressed by the working of our piston creatures. "Like the jackhammers that break up the pavement on our streets, the engine is driven by the expansion of the high pressure gas. This is elementary and well known", thundered the Journal of Chemical Physics in their criticism of the mechanism of the piston fly. But in their haste to dismiss it, the editors neglected to consider the osmotic energy source causing the high pressure, and hence their rejection was based on the absurd notion, that a jackhammer and a growing root use the same mechanism to crack the pavement. An air compressor is powered by an electric motor, whereas the wooden wedges of the Egyptians were powered by natural forces between water molecules – forces that remain unidentified to this day. Let us be clear: the Egyptians employed a method based on a technology which predated the wheel, let alone the jackhammer! Happily, not all editors have responded with the same antagonism towards publicizing this interesting unsolved problem, and I can report that the machine eventually appeared in the biological journal, Progress in Molecular and Subcellular Biology in 1991 (1). The attitude of the scientific establishment to the osmotic machine and to the challenging puzzles it reveals is covered in Chapter 5, "The Establishment", of the sequel the sequel, TPM.

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6. The Impossible

The story does not suddenly end here in a kneejerk reaction to the rebuff from the organs of conventional wisdom. Indeed the refusal of mainstream science to acknowledge that there may be a problem with our understanding of osmosis, sets the scene for us to dig even deeper.

Let's return for a moment to our piston fish and follow the work cycles of those who live in river estuaries. In this environment, they experience the fresh-salt-fresh daily changes in their external water reservoirs brought about by the tidal flows in and out of the river mouth. Sea water is an important osmotic agent for real organisms, not just our imaginary ones, and in view of this it is an interesting fact that it develops an osmotic pressure of a staggering 24 atmospheres! This means that, if the sugar solution in Pfeffer's apparatus (Figure 4.1) were replaced with sea water, the level would rise up the tube to a height of 240 meters. To get an idea of the forces involved under these conditions, this is the pressure that your ears would feel if you could dive (and survive) to a depth of 240 meters. This fact itself raises fascinating questions on how real estuarine organisms deal with such seemingly deadly physical stresses. It also offers us the opportunity to exploit a clean energy source by tapping into the natural water cycle at this point where the renewed fresh water mixes into the sea – its final salty sink.

The energy conversion effected by our imaginary piston fish has recently been turned into practical reality by projects underway at present in Europe. A prototype power plant built by the Norwegian energy agency, Statkraft, is already operational to study engineering involved in construction of osmotic clean energy technology. In The Netherlands, projects Redstack and Realpower aim to extract energy from the forces unleashed at the mouth of the Rhine river, where the waters of the river mix into the North Sea, using a technology based on salt gradients.

As the tide goes out, the piston fish develops its normal high osmotic pressure internally, because it is surrounded by fresh river water. In this energised state, it can deliver the power stroke AB in Figure 6.1, just as in Figure 5.2. As the tide comes in, it becomes surrounded by higher and higher concentrations of salty water, reaching say, 5 times more than its own internal salt concentration. This has the opposite effect on the osmotic pressure, which now drops below zero to negative pressures. This means that the solution inside it goes under tension, and therefore begins to pull, rather than push, on the piston. So we find ourselves now in a situation where the operation of the osmotic machine exhibits the very phenomenon described by botanists like Hammel and his coworkers in their observations on the movement of sap. Here the water molecules inside our imaginary creature, like those inside real plants, have locked arms in such a way, that the links between them make an unbroken connection stretching from wall to wall and pull on the piston.

Readers with an engineering bent will immediately notice that in this new situation the return stroke CD makes a positive contribution to the work done, because the piston fish is actively contracting. In other words, the piston is now moving backwards under its own power and therefore does not have to be forced back. This means in turn, that the piston shaft is pulling on the environment. This is not the case in Figure 5.2, where there was still pressure inside. In that case, the piston had to be pushed back so that during the return stroke some of the work was returned to our imaginary fish. As we recall from Chapter 2, "Natural or Man-made", the Laws of Thermodynamics stipulate that we cannot get more work from a machine than the amount of energy drawn from the fuel source – in fact we must always get less. During the return stroke the machine always takes back some of the energy which it used in performing the power stroke. Yet in this new situation, the piston fish acts as the driver during both the expansion and the contraction. Steps AB and CD are both power strokes, in defiance of the Second Law of Thermodynamics.



6.1 The Piston Fish Delivers the Unbelievable When the piston fish is surrounded by fresh river water, it draws in water and expands performing its power stroke, A to B, as we saw before in Figure 5.2. However, this time it experiences a bigger change in its surrounding conditions because during the step B to C, the incoming sea water raises the salt level outside to more than 5 times the level inside its osmotic bladder. Now water is drawn out, so the piston fish contracts during the return stroke C to D. In this cycle, our piston fish performs more work than is allowed by the Second Law of Thermodynamics, since its piston is actively pushing during the power stroke, A to B, and is actively pulling during the return stroke, C to D.

thick arrows = pressure thin arrows = tension



6.2 The Impossible Equilibrium To help throw light on the opposite natures of pressure and tension, we can draw analogies with springs. In this illustration, we have zoomed in down to the size of a membrane pore separating two solutions whose mechanical states are indicated by two springs:

A) the springs are undisturbed at rest, indicating that neither the solution on the left nor that on the right is pushing or pulling on the other,

B) both springs are squeezed, indicating that both solutions are under pressure,

C) both springs are extended, indicating that both solutions are under tension,

D) here the springs indicate that the solution on the left is under pressure while that on the right is under tension.

The solutions in A), B) and C) are at equilibrium because the opposing forces are balanced, so in these cases the solutions remain static and there is no flow through the pore. But in D), equilibrium is impossible because the spring on the left is pushing and that on the right is pulling. According to Newton's Second Law of Motion which we have already met playing its decisive role in Chapter 4, the water located at the point of contact of these solutions must move through the pore to the right. However in biology this type of equilibrium is common.

thick arrows = pressure thin arrows = tension We can examine this puzzling result in a more concrete way by following the mechanical forces acting on the membrane walls surrounding the osmotic bladder of our fanciful organism. It is here in the membrane where the molecules of water belonging to the internal and external solutions make contact. Here, flowing in and out, they establish the osmotic equilibrium – just as happens in the pores of the membrane in Pfeffer's simple apparatus. What happens in this region when, on the incoming tide, the salt concentration outside becomes greater than inside during the step BC? How does an equilibrium of forces arise at the point of contact where molecules on one side of the junction are pulling and those on the other side are pushing? Such a situation runs counter to our intuition, because, as illustrated in Figure 6.2, it is impossible for solid bodies to exist in this state. Our concept of equilibrium means that opposing forces are balanced, and so now it appears that liquids have presented us with not just a puzzle, but with a clear-cut self-contradiction.

One simple and direct response is disbelief – it does not happen! Of course tension can happen when one artificially produces it in the laboratory, but it is argued, it does not happen spontaneously. When I have asked scientists directly about the contradiction shown by osmotic forces I am mostly ignored, or, less often, the question is avoided by generalizations such as: "…the clearest explanation for osmotic pressure is as Gibbs explained, the chemical potential of the solvent in the two compartments must be equal"….see Chapter 5 of TPM. Overarching thermodynamic explanations like these are so powerful in the minds of scientists, especially those working in the life sciences, because they give the general impression that all is understood even though there is no reference to the problem at hand. It is surprising how widespread is this attitude of denying the problems posed by tension, in view of the fact that the examination of living cells in high salt media like sea water is an oft used technique to study the shrinkage of real cells, not just our fanciful piston fish!

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7. The Demon

In 1871, at the height of an intellectual joust between two giants of nineteenth century science, Maxwell and Boltzmann, Maxwell introduced his infamous "demon" to the world. The action of this mischievous spirit, if he existed, would lead to a breakdown of the Second Law of Thermodynamics, and so it is no surprise that he has attracted the attention of a long list of notable physicists and philosophers for more than a century, including names such as Kelvin, Planck and Einstein, around the turn of the 20th century (1). These early concerns about the demon, even if he should be only imaginary, found expression in a long and intense debate over the meaning of the Second Law, which was to rage for decades. The later developments were thoroughly reviewed by Brillouin, himself an expert on the subject, in the pages of his book "Science and Information Theory" (2). Brillouin tells us how the demon was eventually exorcised by Szilard and Garbor in the 1930s and 40s, both famous names in physics, who proved theoretically that the demon would need information to be able to operate. Their arguments were based on Jacobson's imaginary situation, in which the demon sets up a pressure difference in a body of gas occupying a double-compartment container by operating a trapdoor between the two compartments illustrated in Figure 7.1. Brillouin then quotes Gabor's famous conclusion: "we cannot get anything for nothing, not even an observation". Garbor's argument showed that the demon could produce a pressure difference, but that to do so he must receive information about what the molecules are doing - or put another way: to produce order you need information. However, gathering and using information without effort contravenes the Second Law, because natural occurrences must all follow the one-way street of time's arrow. We recall from Chapter 2 that the inexorable increase in entropy points the arrow in the direction of universal degradation as information is continually lost and order slides into chaos. And therefore according to the Second Law, Maxwell's demon is an impossibility.

How remote and arcane these circular deliberations sound when one comes back down to earth and considers osmosis – the spontaneous generation of pressure differences! Here we are faced with the problem of explaining how the demon's actions do in fact lead to a pressure difference, not how his actions are pure fantasy. Our aim is not to discuss whether or not the demon is conceivable on scientific grounds – we have to accept his actions as common occurrences. In plain language, this means we have to tackle the blunt question: how does the demon raise water from the lower to the upper compartment in Pfeffer's apparatus in Figure 4.1 -or in other words, lift a weight against gravity? In the previous chapters we found that the water must be pulled up, and in order for the demon to be able to do this, he must have support on the top side of the membrane. The forces involved in his operation can be analysed in terms of actions and reactions, in the same way that engineers analyse mechanical problems. In Figure 7.2A, we see the actions he exerts in pulling up the pail of water and pressing on the membrane surface for support, while in Figure 7.2B, we have the opposing reactions of the rope and the membrane floor exerted on the demon in response to his actions.

Non-technical readers may perhaps be a little bewildered, or even bemused, by the idea of the floor pushing on the demon's feet, but this is a reactive force, not the type of action we usually understand as force. As Newton taught, reactive forces are always present – and indeed are necessary for motion. He explained how the horse pulls the cart by using the reactive force of the ground pushing on the horse's hooves. And we ourselves could not walk without the help of the floor pushing on our shoes. In any case, we see in the next diagram how the demon can use his body as a lever and with the help of support from the floor can lift the weight of water. The heavier the weight, the more tension he creates in the rope, and the bigger will be the reactive force of the floor on his feet to balance that load. In other words, the greater the tension, the greater the pressure.



7.1 The Demon's Unnatural Act A) The scene is set in this zoom-in view of a pore in a membrane separating two compartments containing gas under the same conditions. According to the Kinetic Theory of Gases, the gas molecules are speeding through space chaotically moving back-and-forth between the compartments, as illustrated by the arrows pointing randomly in all directions.

B) The demon enters the scene. He interferes with the natural course of events by operating the microscopic door at the pore opening to let through those molecules of his own choosing. For example, he lets through only those molecules which would hit this spot from the right.

C) Because of the demon's selective actions, there are now fewer arrows in the right compartment but more in the left. The Kinetic Theory tells us that there is now a higher pressure on the left than the right. According to the Szilard-Gabor interpretation of the Second law of Thermodynamics, this situation cannot arise naturally. This intriguing question of the connection between spontaneous changes and information is a major theme of the sequel, "The Pixel Machine".



<u>7.2 The Demon's Actions and Reactions</u> This illustration analyses the forces exerted by and on the demon as he pulls up the pail of water through a hole in the membrane.

A) His arms cause tension in the rope as he pulls upwards, while his feet push on the membrane floor to carry the weight of his body plus the load of the pail.

B) The load reacts by pulling downwards on the rope, while the floor pushes upwards against his feet in a reaction that keeps the floor in place by preventing it from being pushed downwards by his weight.

thick arrows = pressure thin arrows = tension



7.3 The Demon Defies Gravity The support offered by the reaction of the membrane floor enables the demon to lift the load, just as the floor we stand on helps us lift our own weight when we raise ourselves up on our toes. If he must pull harder, then the floor also increases its reaction in response as shown by the pressure arrows. These arrows correspond to the force of the ground pushing on the horse's hooves in Newton's explanation of how the horse pulls the cart.

thick arrows = pressure thin arrows = tension Diagrams 7.2 and 7.3 may seem like an unduly detailed and overly academic account of an ordinary event depicting how any human lifts a load with a rope. However, the analysis is needed to show the interconnection between pressure and tension, because we will soon find that the interplay of these two forces is a crucial clue to solving our puzzle. The task is now to apply them to the fundamental reality we face: that there is really only water at the pore openings connecting the upper and lower solutions in Pfeffer's apparatus. To play the role of the demon, water molecules in the region of the openings must lock together in such a way, that they all pull on one another and on those within the pore through to those in the compartment below. Such co-operative groupings of molecules are none other than the clusters we met in Chapter 3, "The Living and the Dead". The force inside a cluster is tensile, or inward-pulling. If the clusters above the membrane can exert greater tension than those below, then water will be pulled up through the pores into the solution above. As more and more water is pulled into the top compartment, the pressure rises due to the weight of water and this increase supports the superior pulling strength inside the clusters there. The greater the tension, the greater the pressure. However, continued increase eventually becomes counterproductive and as the clusters begin to push against one another with greater force, water will be pushed back downwards. Osmotic equilibrium is set up when the pressure exerted by clusters on one another balances the tension pulling within each one.

So here we have at last pieced together the explanatory model based on clusters. But of course clusters imply structure and as reported in Chapter 3, scientific evidence for clusters was discarded following the demise of polywater. As a consequence, the idea of liquid molecules building structures became anathema, especially in the case of water. Even the thousand year old human experiences of water uptake by wood and clay were ignored, although they clearly pointed to a powerful pull exerted from inside these materials. As the story advances to the study of living systems, we will be confronted by even more fundamental questions that thermodynamics cannot answer.

In the opening chapters, I have already introduced some of the more spectacular examples, like the PCR reaction, which remain unexplained, even uninvestigated, by the physical sciences. And we are still at an early stage with the intriguing problems presented by the demon yet to solve before we meet the PCR again. So we will forge ahead with the structuralist approach on the promise that it will deliver a measure of understanding which the statistical approach has not. Following this path we will hopefully discover how clusters transform themselves into the demons, who turn the chaos of molecules in motion into an underlying vital force for order.

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8. The Pressure Pixel

With a new concept come many new questions. If there are clusters in liquids, one naturally wants next to know: how many and how big? Do they populate a liquid uniformly throughout the medium, or are they, like the demon, located in special places only, such as the openings to membrane pores?

In the simple diagram of Figure 8.1, we see the everyday picture of water filling the lower portion of a drinking glass. Air fills the top half of the glass, which we can clearly distinguish because the water interferes with the transmission of light through it in a different way to air. Many readers will recall from their high school science days, properties of light such as reflection and refraction, which cause these optical effects. But if our human eyes could detect pressure (and temperature) only, then we would not see the water as distinct from the air. The contents of the glass would appear uniform, without a division between the upper and lower portions.

The way in which a gas like air exerts pressure is described in complete detail by the Kinetic Theory of Gases. We called upon this theory in Chapter 5, "The Machine", to tell us how pressure is generated. We found that pressure is the result of individual molecules of air colliding chaotically with the walls and with one another as they speed through the space in the upper portion. Although this ceaseless activity is totally random, their vast number produces an evened-out collision force which is the same everywhere – the pressure. So pressure is a measure of the average behavior of this enormous crowd. But if we zoom in, we will eventually come to a region of space so small that, instead of an even pressure, we would feel individual molecular impacts battering us about in every direction. Then proceeding still further down to a region smaller than the volume occupied by one molecule, we would feel no pressure and no impacts, because we would now find ourselves in the empty space between the molecules. We would have zoomed into a volume smaller than the pressure pixel.

I have borrowed the term "pixel" from the information sciences, for it describes very aptly the concept of the indivisible basic bit. For example, as you zoom in on a visual image, you eventually come to the dots composing the picture. This is so for an image printed on a page, projected on your monitor screen or the retina of your eye. Further magnification destroys resolution – single dots have no meaning. A quantum or a binary bit is an analogous concept, as is a gas molecule – the entity we are concerned with here. But a liquid molecule is not. When liquid molecules join together and pull on one another, they are no longer individual basic units. They are physically linked, or bonded, together forming a cluster. In a liquid, the cluster becomes the basic entity.

The Kinetic Theory of Gases tells us the size of the pressure pixel. At normal pressure and temperature at sea level – the environment of the biosphere – it is a volume of about 40 cubic nanometers. In the air, this volume contains just a single molecule, and in water, just a single cluster. In an idealised picture, the volume of the beaker can be divided up into a grid of equally sized pixels. In the upper portion they are almost empty, because the molecules in air are widely separated from one another, but in the lower portion each pixel is totally filled with water, because the molecules in liquids are in contact with one another leaving no empty spaces. Thus in the lower portion, each pressure pixel corresponds to the space occupied by a cube of water containing about 1400 molecules.

The Kinetic Theory is such an all-embracing theory, that it is able to explain the macroscopic properties of a gas, its pressure, temperature, energy, entropy and so on, in terms of the motion of its molecules. When a gas is compressed into a smaller volume, the pressure increases as the volume available to each molecule decreases. This result is as we would expect intuitively from the meaning of "pressurized", that is, the more closely the colliding particles are squeezed together, the more strength is needed to contain them. This is just the everyday experience we have when using a bicycle pump. So at higher pressure, the grid size would need to be finer in order to represent smaller pressure pixels, or in the case of liquids, smaller clusters. For instance, in the schematic representation of osmotic equilibrium in Figure 8.2, the pure solvent is at lower pressure and has larger clusters than the solution, which has developed the extra, that is the higher, osmotic pressure.



8.1 The Pressure Pixel This diagram shows four views of a glass of water. On the left is the normal depiction of water in the bottom half and air in the top. The glass is covered with a lid to prevent the water from drying out due to evaporation. We know that liquid water is a continuous medium, but that the air in the upper half is almost empty space, being occupied by separate molecules of gases (oxygen and nitrogen). Or seen is another way, the molecules of water are everywhere in contact, while the molecules of air are separated from one another by a distance of roughly 10 to 20 times their own sizes. Thus in the second glass, the air is depicted as a grid of nanosized volumes with air molecules occupying just one unit each. So here, the volume of air has been subdivided into a grid of tiny pixels of pressure.

However if our eyes could detect pressure only, then we would see the third glass with no difference between the upper and lower halves, since the air and water are both exerting the same pressure (atmospheric pressure). Because the contents can now be represented as being uniform throughout, so too can its microstructure as in the fourth glass – the grid of pixels. In the water, each pixel contains a cluster of about 1400 water molecules, and is in direct contact with the molecules in its neighboring pixels. In the upper half, each pixel contains a single gas molecule, while in the lower half, each pixel contains a single cluster.



8.2 Clusters in Osmosis This diagram zooms in on a section of the membrane in Pfeffer's osmometer in Figure 4.1. Water moves through the holes, or pores, in the membrane, M, separating the sugar solution above from the pure water below. The grid of pixels shows that the clusters are smaller above the membrane than below, because it follows from the pixel concept, that when the pressure on a gas or liquid increases, the grid becomes finer as the pixels get smaller.

The claim that opens this chapter, "a new concept", is, as it stands, not true. In discussing historical points of interest in Chapter 3, "The Living and the Dead", we learnt that the notion of liquid molecules associating together goes back more than a century to Roentgen. As a student, I was lectured on the topic of water structure in the 1960s, when it was generally accepted as a major factor underlying the behavior of liquids. It became a heretical idea only after 1973 following the dramatic final rejection of polywater by the scientific establishment. Since then, liquids, and in particular water, have remained structureless to science. I have spoken with scientists on occasions since 1973, who I know had earlier proposed ideas of molecular clusters, but who now lack any memory of having worked in the field!

One of the most influential ideas from those earlier times was the "flickering cluster" concept of Frank and Wen which appeared in 1957 (1). Although I have reproduced it in several papers, I include it here again in Figure 8.3, since I found it, and still find it, a profound inspiration. Its ingenuity lies not only in its depiction of a cluster, but also in its suggestion of oscillating motion. Like the spectators at the football match, molecules possess their own energy, and so they are constantly jostling each other. Therefore, a cluster of molecules cannot be truly represented as a fixed or static structure, like a microscopic crystal of ice embedded within the liquid, but as a fluctuating assembly – with some imagination you might almost say, a living assembly. Frank and Wen saw a cluster as an active entity with a certain lifetime. As water molecules link together to form these entities, they co-operate, or pass on information about their movement and orientation. It is this transmitted information that underlies the rhythmic build-up and break-down of clusters. Such studies support the picture of cluster formation as an ordering process displaying regularity of motion. To highlight this dynamic behavior I superimposed the symmetrical wave over the flickering cluster. The new representation suggests in a natural way, that clusters travel through the liquid medium rather than "flicker on and off" appearing and disappearing unpredictably at random. These simple notions became the foundation of the wavecluster model, which depicts ordering in liquids as a travelling co-operative phenomenon occurring as naturally as the Mexican wave.



The Flickering Cluster 8.3 This diagram after Frank and Wen depicts their concept of a cluster composed of 16 water molecules. Although drawn here in isolation, we must imagine them embedded in an endless sea populated with the same molecules. Using the same imagery already introduced in Figure 3.1, each circle and its two short arms represents one molecule consisting of an oxygen atom joined to two hydrogen atoms according to the familiar chemical formula, H2O, whereby a dot in the circle indicates an arm pointing out of the page. Because of electrical forces, the arms tend to point towards neighboring circles which has the effect of aligning the molecules. However, we do not need such detailed technical knowledge to appreciate the essence of this creative idea. On the left and the right, the molecules are seen grouped in an orderly way in an arrangement of 4 hexagons, while in the middle they are shown as a random jumble. If we interpret the arrangement on the left as having a general orientation, say facing left, then, as a result of the constant jostling and tumbling of the molecules, we see the structure first destroyed, as it switches through the disordered state, and then rebuilt with the opposite orientation facing right. Put another way: we have a mirror reflection between the left and right structures. The wave superimposed on these three states of the cluster helps to illustrate its oscillating motion, and suggests in a natural way a sustained co-operative motion like a Mexican wave, involving not just these 16, but extended to all the molecules in the entire population.

Reference

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9. Cluster as Wave

The bonds between molecules make a temporary network throughout the liquid, linking molecule to molecule to molecule. It is via these bonds that tension is exerted through the space of the medium. But tension cannot be exerted beyond a break in this bonded network - instead pressure is exerted there, because contact is made by collisions at a break. Within clusters there is tension, but between clusters there is pressure. Or put another way: molecules exert tension on one another, clusters exert pressure on one another. Molecules located on the outside edge of a bonded network form new links with their neighbors and pull them into the cluster. During this activity, the new members are forced to orientate themselves and each must take up a position that fits the overall pattern. This build-up of structure is co-operative, that is it helps itself, so that the edge of the cluster travels through the medium like the front of a wave. Likewise, the break-down process. Molecules which have sufficient energy for independent agitation, can break free of the local network, destabilising it, helping further breakdown. These principles of growth and decay operate simultaneously in such a way that the cluster travels as a wave through the liquid medium. It is important to see that it is the cluster, not the molecules, which moves forward in this case - the molecules remain in their locality and carry out their movements on the spot, so to speak. Or put another way - the molecules are behaving just as our spectators did at the beginning of the story when they participated in the Mexican wave.

As most readers will not be familiar with the physics of wave motion, I think it would be appropriate to digress a little for the purpose of illustrating how versatile this type of motion is in general. An endless variety of shapes, sizes and movement can be generated from superimposing simple waves onto one another. In Figure 9.1A, an asymmetrically shaped, long, narrow wave moves across or down the page, like an ocean wave approaching the beach. Waves readily add on top of one another when their motion occurs simultaneously in the same location. If several of these long waves are superimposed in this way, we can create geometric shapes moving about the page. Of particular interest is the pattern which results from superimposing sets of waves travelling back and forth and up and down the page. Then we have a regular pattern of equally sized squares which are not moving at all, called "stationary waves". Movement has not stopped however. They have their own mode of internal movement arising from the ceaseless molecular movement underlying all these examples. This type of stationary wave motion is often seen on the surface of swimming pools when the water is being disturbed by active children jumping about. Between the playful children, patches of the surface can be seen where the water is bobbing up and down in the form of waves, yet these waves are not moving in any direction. In our case, we have a grid of square waves, which are themselves no longer moving, although their internal motion has not stopped. The squares depict a regular array of alternating "on and off" flickering, strongly reminiscent of the flickering clusters of Frank and Wen's model of water structure illustrated in the previous chapter.

Another versatile characteristic of waves is their ability to undergo harmonic transitions. A well known phenomenon in music is the halving or doubling of the wavelength of a vibration as the pitch of a note jumps up or down an octave. Another is how a vibrating string can stimulate a second one to resonate in harmony, as long as the second string is tuned to the first. And so, the harmonies of music imply that cluster size is flexible. In the simplest case, two small neighboring clusters each with the basic size of the pressure pixel, can fuse to give a single cluster of double that size. Furthermore, if enough of these fusion steps happen in succession, they could produce a cluster so large that it becomes even macroscopic in proportion. In this way, harmonic transitions can change a large region of water initially under pressure, to one under tension over its whole length. These harmonics can also change cluster shape, depending on the directions that the fusion steps take relative to one another. Cluster growth does not have to be symmetrical and equal in all directions. This is because wave motion and its transitions are guided by surfaces which are already present in the medium. For example, water is usually in contact with the air making a flat air-water surface. This physically precise boundary has a strong orientational influence on water molecules, inducing the formation of a large flat cluster in the form of a thin sheet of water, which is microscopically thin but macroscopically wide and long. The phenomenon of surface tension is a consequence of this layer extending itself laterally across the surface of liquids in all directions. It has the form of a delicate film stretched over the surface like an imaginary taut drumskin made of water. So now we have found the invisible film that supports the pond skaters mentioned in Chapter 3 – it is a wafer-thin water cluster.

In addition to flat surfaces, any interface, any solute or indeed any material other than water will influence cluster size and shape. The presence of other molecules in general interferes with the orientation and motion of the water molecules, and this in turn causes the structure wave to change its regular rhythm. We can readily imagine how breaks in the regularity of the seating arrangement would disrupt the perfect form of the Mexican wave – for example, people in seats which are out of line, too wide, pointing backwards and so on, could not synchronize their movements with those of the crowd, and so their actions would disturb the smooth transfer of information. It is how the structure wave responds to local restrictions affecting its speed, direction and form, that determines cluster size and shape. Of special interest, is the effect of small solute molecules which are about the same size as the water molecules themselves. What happens to the interactions within a uniform population, when a foreigner is introduced into their midst? We are now turning attention to those ordinary salt and sugar solutions, which lie at the heart of the puzzle of osmosis – the place where this story began to unfold.

By interfering with the uniform water-to-water linkages, those foreign molecules obstruct the cooperative influence that molecules have on one another. This disruption prevents the influence extending as far as it normally would, shortening the distance between successive waves as if compressing them together. Thus clusters are smaller in the sugar solution than in pure water. Thinking of this process in the opposite way we can say, that only in the bulk of the pure medium away from disturbing influences like boundaries and inserted foreign bodies, can the wavelength grow to its maximum size. In other words, it is only in that environment where there are no localised irregularities, that the mutual influences of the liquid molecules on one another will be most farreaching.

In this wave-cluster model, the structure wave carries the clusters as it travels through the liquid. The propagation of the wave means that clusters are colliding with the surfaces, walls and membranes at the boundaries of the container, just as ocean waves crash against the breakwater. In gases, individual molecules speed about at random in empty space, whereas in liquids, the waves are all connected together as one entity filling all the space occupied by the medium. Yet both forms of movement produce the same pressure as indicated in Figure 9.2. At higher pressure, the increase in the number of collisions means more molecules in the space occupied by the gas, or more wave crests in the volume occupied by the liquid. In other words, at higher pressure the pixel grid is finer. The picture evoked by the analogy in Figure 6.2, which uses a metal spring to illustrate water being compressed or stretched, can be extended here a little further. As shown in that diagram, the spring is continuous through the space between its ends, and when pressure is applied to it, the spring is squeezed and the distance between the turns becomes smaller. Here again we see how shortening the wavelength as the turns get closer together corresponds to increasing the pressure.

The conclusions reached by following these rather pictorial lines of argument, are in agreement with the general way in which physicists view gases. The Kinetic Theory of Gases which we have already called upon, is itself founded on just these concepts. Readers who are past students of the sciences, will almost certainly remember the famous "Boyle's Law". It is from this seed that The Kinetic Theory of Gases grew, eventually achieving such fineness of detail that we know the length of each turn of the spring and thus the size of the pressure pixel. Indeed, Boyle's original work was entitled "On the Sprynge of the Aire"! When a solution is made by adding a little sugar to water, the system is thrown out of its "normal" state of high spring strength, since now the pixels have diminished in size without increasing the pressure. It is as if the material of the spring has been degraded by addition of the foreign matter, because the wave has been squeezed without it being forced to do so by extra compression imposed from outside. In technical terms, this new state is a consequence of the fall in Boltzmann's Constant as we saw in Chapter 5, "The Machine", for which the explanation in terms of wave velocity and momentum will be presented at a later stage in Chapters 8, "Hard and Soft Clusters", and 9, "Uncoupling M and v", of the sequel TPM. But if this system is put in contact with pure water, so that its shortened wave joins with the longer to form a continuous structure through the membrane pores, then these connected waves can carry energy and information to-and-fro between the two liquid It is this transfer of information between the long waves in the pure water and the short media. weakened waves in the sugar solution, which causes the pressure build-up in osmotic phenomena.



<u>9.1 Wave Patterns</u> The panels show progressively more complex patterns resulting from superposition of simple waves.

A) A wave with a long front moves across the page from left to right like an ocean wave approaching the shore.

B) A similar wave now moving down the page is added. Where they meet, they produce a localised wave peak of double the height which moves diagonally from top-left towards bottom-right.

C) Several waves follow one another in succession across and down the page. Their superposition produces a regular pattern of square shapes moving in the diagonal direction.

D) When two more sets of waves moving from right to left and up the page are added, the pattern of squares becomes stationary. Motion has not ceased however. The surface of each square is bobbing up and down in the opposite direction to its 4 neighbors, so that the entire surface is divided up into a grid of alternately vibrating squares which we could call "wave pixels".



Particle Pressure or Wave Pressure ? <u>9.2</u> Let us imagine there is a thin weak film (FF) stretching down the middle of a chamber separating a gas on the left from a liquid on the right. Because the film is not bulging in either direction, the pressures on both sides are equal, or in the language of physics, the energy densities in both media are equal. From the Kinetic Theory of Gases we know that there are gas molecules speeding through space in all directions causing the pressure by colliding with the film from the left. On the right however, there is no empty space in which molecules can speed about at random, because the liquid molecules are in contact with one another filling the whole space. Here it is the motion of the structure wave that causes the pressure, by colliding with the film and reflecting off it back into the medium. For the pressures to be equal, the size of the grid showing the pressure pixels must be the same on both sides. As depicted earlier in the glass of water illustration in Figure 8.1, each pixel on the left contains just one gas molecule, and on the right just one cluster, or in more technical language of physics, the energy densities in both media are equal, because each unit or quantum of energy occupies the same volume of space in the liquid as in the gas.

As we go in the reverse direction towards lower pressure, we reach zero pressure and then pass to negative pressure. Now we find ourselves under those circumstances where liquids show a versatility not possessed by gases. With decreasing pressure there are fewer and fewer molecules in a gas, until only a single molecule remains in the container – in other words, the pressure pixel grows in size until it equals the volume of the container. In a perfect or total vacuum, there are no gas molecules, and the pressure pixel has become larger than the container itself. In a liquid on the other hand, the container is filled with a single cluster, so the bonded network now stretches unbroken from boundary to boundary. In this state, the molecules pull on one another and on the walls through a continuous linkage reaching right across the medium. The liquid becomes a gel.

As with osmosis, the phenomenon of gelation is familiar to everyone. Children wait eagerly for their favorite sweet to gel in the refrigerator, and each one knows that a premature disturbance by impatient fingers will only ruin the beautiful smooth form of their shocking-green delight. The word of interest to us here is, of course, "form". Even when cut through by the spoon, the watery contents of the bowl remain standing alone as a rigid form without the aid of the container as illustrated in Figure 9.3. But how can water stand up? And again, as with osmosis, we are confronted by the apparition of levitating water. So once again we ask, is it a conjurer's trick or is it just an unexplained curiosity ignored by basic science?

If it is merely an illusion, then a gel is really a solid in disguise. But ice is the solid form of water, and every child knows that their favorite sweet is not a block of ice. On the other hand, if it's not a trick but a natural state of water, then we will need the demon again to help explain its existence. Physical measurements which detect the movements of single independent molecules, show that they are jostling and spinning about just as in the familiar fluid state of water. The message from these results is that, at the deep down molecular level, a gel is still liquid. The molecules are not held in a static location by the strong forces between molecules as in a true solid like the block of ice. In a solid, permanent pulling forces operate throughout its form extending from boundary to boundary overpowering individual movement. A brick cannot change its shape because its molecules are not free to move about as jostling molecules do. In a gel likewise, there must be tensile forces pervading the whole body making sure it keeps its shape – but here, the linkages locking molecule to molecule and maintaining this tension must be fleeting only.

So liquids inhabit a double world. On one side, there are the "gas" liquids we are familiar with. They live under pressure and are fluid. In the obverse world are the "solid" liquids – the gels of biology. Energy tends to flow outwards from the world of the "gas" liquids. These liquids constantly strike at their boundaries trying to escape. The "solid" liquids inhabit the world of tension where energy flows inwards. But scientists do not consider these two worlds on an equal footing. Because we live in the expanding world of pressure – the world of the industrial revolution and its enormous scientific legacy – we are familiar with the world of the "gas" liquids, regarding them as the normal, natural state of liquids. On the other hand, the world of the "solid" liquids remains unexplored, because the gel state is considered a curious anomaly and is thus relegated to the periphery of science. Yet it is not uncommon. It pervades every niche of the biosphere. It is only hard to see.



9.3 Solid Liquids What is the secret behind the formation of the children's dessert familiarly called "jelly" or sometimes "jello" by English-speaking kids? A gel behaves like solid water. It can defy gravity because the water does not flow. It is held in place by tension stretching right through its form from one side to the other and from top to bottom. There is no pressure inside a gel. The wobbly shape on the plate is a single, enormous, macroscopic cluster.

10. Pixel and Antipixel

For water to enter the mirror world inhabited by gels, it has to go under tension. In the laboratory, scientists have used clever tricks to design apparatuses that pull on liquids held inside them. Hayward, whom we have already met in Chapter 4, gives a readable description of the difficulties that must be overcome in creating and measuring tension. He also points out that natural systems, especially in the plant kingdom, seem on the contrary, to be able to develop tension with relative ease – and a major theme of this book is that osmotic systems develop tension spontaneously. This applies not just to plants, but to every living cell, since they all contain water as a gel. Pollack's recent books provide the interested reader with a comprehensive and colorful account of the state of water in cells (1).

We have also seen how such osmotic systems present us with that "impossible" situation, where water on one side of the membrane is under pressure while in equilibrium with water on the other side under tension. Now we have arrived at a stage in the story where we can launch an attack on this problem. Actually, the problem was always present. For instance, already in Pfeffer's common osmotic set-up the problem was lurking in disguise. In terms of mechanics, we had there two bodies, in that case two liquid media, pressing on one another with unequal forces, and since this is clearly not an equilibrium – at least to an engineer – some additional hidden force must have been present to explain this imbalance.

The cluster provided that extra force. Clusters build and maintain themselves by internal tension – not just with the help of, but because of, internal tension. This force also explained the movement of water through the membrane in the wrong direction, apparently contradicting physical laws and common sense. In Figure 10.1 we see this tension in the solution pulling away from the membrane in the opposite direction to the pressure. This third force can balance out the unequal pressures acting on both sides. In fact there are of course four forces: the two unequal pressures which exist in our macro world and two unequal tensions which exist in the micro world below the pressure pixel in the hierarchy of sizes. The higher tension is exerted in clusters exerting the higher pressure – in this case in the solution – since, as the demon demonstrated, the clusters on that side are stronger and pull solvent into themselves from the weaker clusters on the pure water side.

If we invert this constellation of forces, we obtain instead the situation shown in Figure 10.2 where tensions now pervade the macro world of the "solid" liquids. In this experimental set-up, both the pure water and the solution have to be held in closed containers to prevent contact with the air, which would immediately introduce a pressure of one atmosphere into the system. When osmotic equilibrium is now established, we have two liquid bodies pulling on one another through the membrane. But as with the pressures, the tensions are unequal and must be balanced. This time, the balancing force is a pressure acting at the micro level below the size of the inverted pressure pixel. In volumes smaller than this size, pressure replaces tension as the operative force in the medium – the pixel has become the antipixel.

What is the nature of the cluster that occupies this inverted pixel? How are we to picture the molecules in this new entity which was previously held together as a single structural unit? Since pressure is exerted internally, individual molecules are pushing and colliding with one another. The new clusters have no internal structure. They are islands of internal chaotic movement in an overall order that fills the background.

This random motion down at the molecular level explains how osmotic tension develops. Just as with osmotic pressure, tension develops in solutions by movement of solvent in the direction defying our common sense and apparently contradicting Newton's Second Law of Motion. If we reverse the roles of pure solvent and solution illustrated in Figure 4.2, so that now it is the pure water which is constrained by the closed volume inside the funnel, then a small amount will flow out into the solution seen in Figure 10.3. But the flow immediately stops, because the tension suddenly rises becoming strong enough to hold it back and halt it. So now the old question poses itself again here, only in a new guise: how is there flow at all, if the molecules are in a medium where they are being pulled back? And again, the answer is the same as the old answer: individual molecules feel the force operating at the microscopic level below the pixel size. In the solution this force is tension while in the pure water it is pressure, and therefore molecules naturally exit the pure water side, because in the contact region both these forces drive in this same direction. Now we can understand how all three types of equilibrium are set up and maintained. The solutions in contact may be under unequal pressures, unequal tensions, or one under pressure and the other under tension. But each of these circumstances is mechanically stable because of the balance between four forces – two acting on the macroscopic and two on the microscopic hierarchical level.



10.1 Clusters Pulling from Within A) A zoom-in view of forces acting at the membrane in Pfeffer's osmometer of Figure 4.1. There is more pressure pushing on the water in the membrane pores from above than pushing up from below. How does this unbalanced situation remain stable?

B) The full thick arrows show the pressure in the solution caused by clusters. They are macroscopic forces, that is, they exist in our world and so are measured by our instruments. But in the microscopic world inside clusters, the water molecules feel tension, which is invisible to our instruments. The dashed thin arrows show the tension within the stronger clusters in the sugar solution pulling water upwards through the pores from the weaker cluster in the pure water below. The direction of this flow tends to correct the imbalance between the pressures.

C) In the complete picture, we must have all four forces, two measurable macroscopic pressures and two invisible microscopic tensions, which cancel each other at equilibrium.

full thick arrows = macroscopic pressure dashed thin arrows = microscopic tension



10.2 Anticlusters Pushing from Within A) In the mirror world of gels the solutions are solid, but down at the micro level the individual water molecules possess the same energy and freedom of movement as in the fluids. So this time, our macroscopic instruments measure tension, while the pressure in volumes smaller than pixel size remains invisible. The solid thin arrows show that the measured tension pulling downwards on water in the membrane pores is stronger than pulling upwards from above. So again we have an imbalance of macroscopic forces at equilibrium.

B) The pressures exerted on individual molecules down at their level are shown by the empty thick arrows. In this case, all four forces include the two measurable macroscopic tensions balanced by the two invisible microscopic pressures.

C) A third arrangement of the forces analyses the most intriguing situation of all – the sugar solution under pressure in equilibrium with pure water under tension. The full thick arrows above show water being pushed, and the full thin arrows below show water being pulled, through the membrane. This mechanical impossibility, which we recall was experienced by our imaginary piston fish in Figure 6.1, is explained by the invisible balancing forces exerted in the micro worlds smaller than the pressure pixel.

full thick arrows = macroscopic pressure empty thick arrows = microscopic pressure full thin arrows = macroscopic tension dashed thin arrows = microscopic tension



10.3 The Puzzle of Osmosis Returns In the previous two diagrams we saw how the undetectable forces acting on individual molecules balance the unequal forces measured in osmosis. Now we see that they also explain how the "impossible" situation of Chapter 6 arises.

A) The intriguing question of what causes the pressure increase illustrated in Figure 4.2B, can be made even more baffling by switching the places of the pure water to inside and the sugar solution to outside the funnel. In this arrangement, tension, not pressure, develops in the funnel, even though the water in the funnel was originally at the same outside atmospheric pressure as the sugar solution when it was immersed into the solution. This pressure, which is normal for our environment, is indicated by the full thick arrows, and the tension inside by the full thin arrow. The development of tension can be seen by the stretching of the membrane inwards as the water tends to flow outwards. Outwards? – against these forces which must move matter inwards according to Newton's Laws of Motion?

B) The zoom-in view of the membrane pore shows the forces exerted at the molecular level. The tension in clusters on the left (dashed thin arrows), and pressure in those on the right (empty thick arrows) are stronger than the large scale macroscopic forces, even though they are active only in the microscopic world below pixel size. It is these forces which move the water molecules. But because the tap is closed, the water inside cannot continue to exit, and this causes the tension inside to build up rapidly, halting flow to the left and producing the balance of the four forces illustrated above in Figure 10.2C.

full thick arrows = macroscopic pressure empty thick arrows = microscopic pressure full thin arrows = macroscopic tension dashed thin arrows = microscopic tension Let us consider what happens when a liquid is put under a pulling force in an apparatus like Hayward's which is designed to measure tension. In the wave-cluster model, the pixel size in a solution increases as the pressure decreases until, at zero pressure, there is just one large single cluster occupying the container. The network of bonds now stretches throughout the whole volume of the container making an unbroken connection to all its boundaries. Then as we proceed further, tension starts to develop. The network strengthens as a reaction to this new force of extension. But more stretching causes breaks to appear as some of the links between molecules spring open. This action stimulates neighboring bonds to open also, such that single molecules break free and together they form islands of jostling unconnected molecules. This co-operativity means that the reaction causing bonds to open is constantly propagating through the medium, in the same way that bonded clusters form and propagate in liquids under pressure. It is the same process, whether bonds are making under pressure or breaking under tension. Under the usual conditions of pressure, cluster size is set by the pressure pixel, but now under tension, the size of the unbonded regions is set by the antipixel.

Normally liquids are under pressure, which means, like gases they have a tendency to expand, or as one of the fathers of liquid physics, Lewis, put it: a tendency to escape (2). They are the "gas" liquids. It is our everyday experience that a liquid dries up if it is not kept in an airtight container. In fact we live in a world of pressure. The Earth's atmosphere is always tending to expand, but fortunately, the Earth's gravity is strong enough to prevent it from escaping into outer space. Even so, the lighter gases have been lost long ago from our planet's atmosphere. This natural drive to disperse can be represented by "lines of force" directed outwards, hitting the boundary walls of the container holding the liquid as depicted in Figure 10.4. These lines illustrate that the space occupied by a "gas" liquid possesses a directional quality in addition to the immediate quality of volume, which we automatically attribute to space. For us, volume is a positive space – something that can be used up or taken away, as in the case when a body occupies a certain amount of space. We know for instance, that putting too much furniture in a room uses up its space. And even on a human level, each of us feels our own personal space as projecting outwards around our body, because we sense it is diminished when it becomes intruded upon by somebody else.

Conversely, the "solid" liquids are held together and so the "lines of force" point inwards from the boundaries. Volumes measured in this space are taken as negative, because they occupy negative space, and therefore anticlusters have negative size. The mathematical reasoning behind this convention is found in Appendix 2. I realize that here again, it sounds as though we have entered a difficult area, but in fact we do not need the equations in the appendix to grasp the concept. An easy analogy to help the non-technical reader understand these extra qualities possessed by space is the way we see money in terms of credit and debit – debit is negative credit. In fact we have already used the expression "negative pressure" for "tension". These two basic forces which are the central characters of this story are simply two forms of the same energy. The forms differ by acting in opposite directions in three-dimensional space – one outwards and the other inwards. Pressure particles occupy positive space, tension particles occupy negative space.

Another intriguing consequence of the pixel-antipixel symmetry is revealed when we examine the effect of foreign molecules on cluster size. We have already seen how dissolving sugar or salt in water produces more, but smaller, clusters. The size of clusters decreases because introduction of the foreign molecules disrupts their formation. However these disruptive influences increase the size of anticlusters. When pure water is under tension, the network of interconnecting linkages stretches from boundary to boundary without a break, reaching right through the medium. There are islands of broken structure – the anticlusters – but as depicted in Figure 10.5, these are isolated. Because the foreign solute molecules encourage breakdown of structure, the links maintaining tension begin to disappear as more solute is added, and consequently the isolated islands grow bigger. To help illuminate this process, we refer again to our simple money analogy and liken two solutions, one under pressure and the other under tension, to two bank accounts – the pressure account contains pixels and so is in credit, while the tension account contains antipixels and is in debit. A deposit of money into each account will increase the credit but decrease the debit. In a similar way, an increase in the number of positive pixels increases the pressure in the solution under pressure but decreases the tension in the one under tension.

Such circumstances sound very pertinent for our piston fish, who must live in environments alternating between pressure and tension. But real cells are far more instructive than any imaginary organism we might devise. Internally they experience both forces being exerted simultaneously in a dynamic yet controlled way. One region of the cellular medium, the cytoplasm, can be extending under pressure, while another is contracting under tension. The capacity they show for flexibility of movement driven by the twin actions, extension and contraction, implies that adjacent cytoplasmic regions can be each under mutually opposite forces. Cells are living demonstrations that the two physical states of water – the "gas" liquid and the "solid" liquid – can co-exist, and further, that the basic units of energy – pixel and antipixel – are interchangeable.



10.4 The Two Types of Liquid Space Physicists frequently use "lines of force" as an illustrative tool to convey the concept of direction where there is a natural flow of energy through space. For example, the Earth's gravitational pull is often shown as lines through space pointing inwards towards the Earth's center. Here this tool is used to illustrate the directional quality of pressure and tension. The diagram shows a box, which we imagine is located inside some uniform material. In the panel on the left, the lines of force point towards the sides of the box from within, illustrating an "outward-directed" or "positive" space. Matter in this type of space tends to repel and escape. In the panel on the right, the lines of force point from the sides of the box towards its center, illustrating an "inward-directed" or "negative" space. Matter in this type of space tends to attract and fuse together. We will see these opposing forces in action later on in Chapter 3, "Four Machines" of the following book, TPM.



10.5 Opposite Changes in Clusters and Anticlusters In this diagram the areas of crosshatching indicate regions in the water medium where the molecules form an interlinked cluster because they are momentarily bonded together. The open areas are regions lacking this structure with the dots representing separate unconnected molecules involved in collisions as opposed to linkages. The wave is included here to show the correspondence of this type of illustration with the flickering cluster of Figure 8.3, where the molecules were shown in more detail as circles with two arms. The introduction of foreign molecules into the medium causes the cluster pattern to change from A to B, as a result of disruption to the network stemming from interference with the water molecule-tomolecule bonds. This disruption to structure explains how the size of the clusters becomes smaller.

When the medium is under tension however, the network stretches throughout its space, so that the regions of nonbonded molecules are isolated, forming the anticlusters. In this case, the disruptive effect of foreign molecules breaks down the network even more, reducing the number of molecules involved in the connected structure and setting them free as separate dots. This causes the pattern to change from C to D, resulting in an increase, rather then a decrease, in the size of the anticlusters (for technical detail see Appendix 2).

References

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11. Cluster as Demon

The previous chapter in our story opened doors onto a new world inhabited by liquids – the taut world of gels. The unusual nature of this inward environment offers us the opportunity to attack the puzzle of osmosis from a fresh perspective because new forces, once hidden from view, have been revealed to us. To guide us through this unfamiliar new dimension, we need to call upon the help of Maxwell's demon once again. We now know that the state of equilibrium is a balance between four forces, two pressures and two tensions. The actions of the demon helped to explain how water molecules flow in the wrong direction in the traditional osmotic system involving the "gas" liquids – he pulled them through the membrane against pressure. Here, in the mirror world of the "solid" liquids, we have individual molecules being pushed out of their medium even though this medium is pulling them back.

In Figure 11.1, we see the demon performing the inverse of his earlier trick. This time, up-side-down, he pushes the pail of water up through the membrane pore. Like a gymnast somersaulting on training rings, his weight is supported by ropes hanging from the ceiling. To lift the additional weight of the pail with his feet, he pulls even harder on the rings and hence the supporting tension in the ropes increases. In other words, the greater the pushing force he must exert to lift the water, the stronger he must pull on his surroundings to support his efforts. So while the roles played out by the forces have been reversed compared to those depicted in Chapter 7, Newton's action and reaction law still strictly applies, -- the greater the pressure, the greater the tension. The problem is not yet solved however, because we cannot accept this pictorial representation as a scientific explanation – in fact it immediately leads us to the obvious question: do clusters act in the same way as the demon? Certainly his actions depicted in Chapter 7 were illuminating, but can liquids go through spatial motions like those of the demon?

The answer is of course: no, they cannot. Clusters cannot act like the demon, who has arms and legs which move unhindered in empty space. The demon is depicted with a human anatomy and, like the gymnast, he is really a set of freely moving levers, carefully arranged so that he can raise loads by pulling and pushing actions which are not obstructed by direct contact with the surrounding medium. But in water, clusters and the surrounding medium are as one. The form and body of the clusters fill the space. There is no empty room to accommodate swinging arms and legs. In the real world, the demon is made of water, and water is everywhere.

We recall how easy it seems for the demon to lift the pail of water in Figure 7.3 using the levers of his body like the moving parts of a machine, mechanical or human. Clearly, his actions would be prevented if he had no room for these manoeuvres. Being an integral part of the liquid medium, his new form must fill the space as a block like that depicted in Figure 11.2. He is now a single large cluster, pulling all his body parts inwards but being pressed upon by the surrounding clusters at his edges. Once a single continuous cluster is formed connecting the compartments on both sides of the membrane, the water medium on one side exerts a pull on that in the other, because, like the demon's rope, the tension extends from one solution through the pore into the other. The clusters made of stronger bonds win this tug-of-war, and water will be pulled into that solution. The same interplay of forces underlies the mechanism for the rise of sap up tall trees discovered by the botanists - a scenario which reminds us what elongated proportions and what enormous dimensions clusters can adopt as a result of their wave harmonics. Returning to Pfeffer's osmometer in Figure 4.1, this means that water flows from the pure solvent side below into the sugar solution above. We have at last arrived at the explanation of how clusters move water against pressure in a way that seemingly contradicted physical laws. These tug-of-war forces operate on the micro level and so are invisible to our instruments.

To complete the puzzle however, we must still explain how this movement causes the pressure to build up. In Figure 11.3, water is pulled up through the membrane pores into the flat cluster layered over the membrane, swelling this layer outwards across the surface. This action increases the pressure in the upper chamber, because its expansion is eventually transmitted in all directions, even though in this diagram it is initially exerted parallel to the surface only. The water at the ends of the layer is pushed outwards and upwards as the flow of water into this upper solution increases. From the zoom-out perspective, the sideways pressure caused by the swelling layer becomes randomised, that is, it pushes in all directions throughout the solution.



11.1 The Demon Inverts his Act The demon defies the forces once more, but this time he raises the load against gravity by a pushing action. In Figure 7.3, reproduced here on the left, he acted in the sugar solution above the membrane in Pfeffer's apparatus to move water upwards against the measured pressure operating inside the funnel. In the pictorial language of the illustration, he used the pressure of the membrane floor on his feet to generate tension in the rope. However now, as shown on the right, he acts below the membrane to move water upwards against the measured tension operating in the water reservoir below. To push the load, he needs the support of the membrane pulling him upwards preventing his fall. By hanging on rings below the membrane, the demon positions his body in such a way that this tension supports the upward thrust of his feet. We saw him acting again in this way under different circumstances in Figure 10.3B, indicated by the small empty arrows representing the pressure inside anticlusters pushing water molecules through the pores to the left. In that case, water tends to exit the funnel in its horizontal position, even though there is measurable tension behind and pressure in front both opposing this molecular movement.

full thick arrows = macroscopic pressure full thin arrows = macroscopic tension empty thick arrows = microscopic pressure dashed thin arrows = microscopic tension



11.2 The Battle of the Clusters For the demon's actions illustrated in the previous diagram to become a liquid mechanism, the demon, his ropes and the pail of water must all be made of water. Following harmonic fusion of clusters located in the sugar solution above the membrane, with those in the pore and those in the water below, they would together become a single cluster. In fact, the upper and lower surfaces of the membrane itself stimulate the formation of such clusters with extended branched shapes, because water has a positive glue factor with the material of porous membranes and so naturally spreads across and attaches to these surfaces as it wets them. In this idealized representation, clusters appear as rectangles and combinations of rectangles as depicted earlier in Figure 8.2.

A) In Pfeffer's experiment shown in Figure 4.1, the clusters in the solution above the membrane have a higher tension within them than those below, so when the extended cluster forms, water will be pulled upwards. Just as the demon pulls up the pail in the previous illustration, the supporting pressure in the surroundings (full thick arrows) aids the cluster within the pore to generate an upward tension (dashed thin arrows).

B) The physical restrictions of Pfeffer's experiment can be altered slightly, so that the pure water in the reservoir below is totally enclosed in a container and no longer in contact with the atmosphere. Then measurable tension will immediately develop as soon as any water flows upwards into the sugar solution exerting a pull backwards preventing further flow. To exit the enclosed container, water must be pushed up, as the demon does in the previous diagram, by using this tension (full thin arrows) to help him generate pressure. Here, pressure within the extended anticluster (empty thick arrows) lifts water molecules into the solution above, until the developing tension in the pure water below becomes strong enough to halt this upward flow and we have equilibrium again.

full thick arrows = macroscopic pressure full thin arrows = macroscopic tension empty thick arrows = microscopic pressure dashed thin arrows = microscopic tension



11.3 The Pixel Turns Tension into Pressure

A) An elongated cluster on top of the membrane in Pfeffer's apparatus actively pulls up water into itself through the pore (dashed thin arrows). At its ends it exerts pressure on its neighbors in the regions labelled X and Y (full thick arrows). Layered on top are clusters which belong to the normal grid of pressure pixels, exerting the experimental pressure measured in the sugar solution as illustrated by the grid of smaller squares in Figure 8.2. To make room for the extra water molecules drawn up into it, the long cluster reverts to a layer of normal sizes, and in so doing, pushes sideways into the neighboring regions. As a result, a single cluster has been pumped up through the pore against pressure.

B) In the switch from tension to pressure, water that was compressed into the space of 6 cluster sizes has expanded to 7 clusters, and consequently pushed the water of the regions X and Y further apart. In this way, the switch spreads pressure up and out into the bulk of the solution, until the pressure becomes high enough to prevent this expansion step and consequently halt the upward tensile flow.

The waves on the right illustrate the operation of the pressure-tension switch resulting from the harmonic transition in the structure wave, in which the long wave reverts to several short ones. Through the suggestion of a spring at work, this type of representation helps to explain how energy accumulates in the solution as its pressure builds up.

full thick arrows = macroscopic pressure dashed thin arrows = microscopic tension

To follow the action more closely, let us return to the large cluster pulling water upwards in the previous diagram. As it is shown there, it cannot expand, because, by the nature of its intrinsic action, it is under tension. It could contract in this state, but not expand. The additional water drawn up from below is now compressed, since the cluster did not grow in size. However expansion could subsequently take place if a harmonic step reverts it to a multiple of smaller clusters, because a population of clusters exerts pressure. With each cycle of fusion and splitting of the wave additional new clusters appear, born out of the additional water drawn up into the large cluster. They push laterally after the transition to smaller clusters and, as a result, there is movement of water as layers of clusters slide over one another. Thus if we again zoom out and view the scene from a macro perspective, we would see a general streaming of water into the upper sugar solution. But this flow is caused by a pump-like action on the micro level which we cannot see.

We can now construct a more detailed picture of the region where the demon is active. Large clusters appear and disappear as a result of the harmonics of fusion and splitting, and accompanying these structural fluctuations the water medium experiences to-and-fro switching between tension and pressure. As explained in Chapter 9, it is the labile nature of wave motion that underlies the flexibility of the pressure pixel and thus cluster size. We see now that the wave-cluster model of the osmotic mechanism predicts the operation of a pressure-tension switch, which is innate to the liquid medium.

In Figure 11.3, the switch to pressure causes clusters to push laterally, producing local relative movement of one layer of water over another. If this form of motion could be controlled, then we would have the means of sliding clusters along in line by repeatedly flicking the switch on and off. The clusters would appear to march forward in register, slotting into position with each step, because the step size is determined by the wavelength. In the words of physics, the movement is proceeding in quantized steps.

More complicated patterns of apparently ordered movement can be produced by aligning the clusters in simple geometric arrangements. For example, the four clusters in Figure 11.4 are under the influence of two sets of parallel layers, horizontal and vertical. In the horizontal layers, the relative movement tends to displace the top clusters to the right and the bottom to the left, while in the vertical layers, the left tends to move up and the right tends to move down. The group of four would tend to rotate as one cluster, as long as each corner experienced the correct sequence of alternating forces at the same time. Thus, when the wave transitions lead to such an arrangement of pressure and tension, rotation of the group would ensue, like an island of ordered water spinning in a wider environment of disorganized clusters.

In this chapter, we have extended the activities of the demon to include dynamic effects in addition to his original narrow role of causing the build-up of osmotic pressure. In fact, the movements in layers and circles do not involve build-up of pressure at all. And there are neither membranes, funnels nor even two solutions. The movements described occur in the pure liquid in the bulk of the medium. The scene has moved beyond that set up by the simple props needed for Pfeffer's experiment in Figure 4.1 – the sugar, the membrane and the funnel-shaped container – so that we see osmosis from a new and wider perspective. Until now, it has been viewed as a special phenomenon requiring its own special explanation, and this approach has been responsible for it having been sidelined into a scientific cul-de-sac, where it represents a curiosity displayed by particular biological solutions. It is customarily understood that physicists have relegated the study of solutions to the field of chemistry, while chemists have in turn relegated natural solutions to the field of biology. So as we saw in Chapter 4, in the end, osmosis became automatically accepted as a peculiarity encountered in the study of complex systems, certainly not in basic physics. But we have reached a point where we now see that osmosis is only the tip of the iceberg, so to speak. It is a sign of much more happening at a lower level. The clusters are ubiquitous and constantly active, whether membrane pores are present in their midst or not. Only when the stage is set with the correct props (membranes, containers, taps), do their dynamics lead to the special case of the paradoxical build-up of pressure and the puzzle of osmosis.


11.4 The Spinning Cluster Let us consider the movement of the 4 clusters seen here in cross-section. They are located in the bulk of liquid water away from any external influence such as a boundary, membrane or foreign molecule. Let us further speculate that the spontaneous flickering of the form of the structure wave has led to the spatial arrangement of forces as indicated. With tension in front (thin arrows) and pressure behind (thick arrows) we have: clusters 1 and 2 tend to move right, clusters 2 and 3 tend to move down, clusters 3 and 4 tend to move left, clusters 4 and 1 tend to move up. Under this constellation of influences, the group would move as a unit and rotate clockwise as shown on the right. Thus, even though this arrangement has occurred by chance, the type of motion it produces appears to be a coherent effort by the thousands of water molecules in this unified spinning cluster. The curved arrow shows the direction of the circular motion of the four clusters fused into one, it is not a tension arrow.

12. The Protein Pixel

The story of the pixel seems to have taken us far from the goal of understanding life's vital force. At the outset, it was promised that searching down to the level of water molecules would produce new concepts of matter - concepts that would bridge the gap between the macro and micro levels and so reveal the existence of objects which inhabit this crucial intermediate world. The point of departure was a thorough examination of the osmotic mechanism beginning with blunt but clearly posed statements of how osmotic phenomena appear to contravene well established physical laws. We then learnt that, more than 100 years ago, Maxwell had already proposed his infamous demon to illustrate how a being of just this mesoscopic size, small enough to see individual molecules but yet large enough to have power over them, could defy physical laws. This imaginary being had the ability to split systems of an even, uniform composition into two uneven halves with different pressures - in other words, to reverse the direction of the natural course of spontaneous events. With the words of Gabor still in our ears, we recall further, how this action implied he was also a source of information on the movement of molecules. In the ensuing chapters, the help of this cunning imp was enlisted to develop the wave-cluster model of liquids, which proposed that clusters built of linked water molecules are responsible for the puzzling behavior of osmotic systems. It is clusters which are the inhabitants of the intermediate world in the chasm between the sciences. Like the demon, they are large enough to have control over the way individual molecules move.

It also became clear that clusters are not just simple structural objects with the right size, but, like the demon, they are dynamic entities. They exert forces, both pressure and tension. This ability clearly means that they are agents which manipulate energy. Another dynamic characteristic is that they show both versatility and lability in their sizes and shapes. And as the diagrams of the previous chapter illustrate, it is these characteristics which give clusters the power to determine what force is acting and what movement ensues at any given time and place.

The flexible behavior – sometimes pressure, sometimes tension – is achieved through the to-and-fro interchange between different forms of the structure wave – sometimes short, sometimes long – that is to say, through the operation of the pressure-tension switch. This switch was seen as necessary to explain osmotic processes, because they require the exertion of both forces at the same location and on the same body of liquid medium. In such basic situations as a pure liquid or a solution like sugar in water, the switch operates back-and-forth at random. For the osmotic mechanism we did not need to control the switch, since wave harmonics occur spontaneously in any case. But now we proceed on to imagine what consequences would arise if the switch could be controlled, for then we could have directed movement of matter under our command.

Enter the protein molecule. From Chapter 2, we recall that enzymes are the protein nanomachines which perform the chemical reactions of life. Every cell is neatly packed with enzymes. These large molecules have a common physical characteristic – they are all roughly the same size. At first sight, they do not appear to be the same to the biochemist, because they vary in length, that is, some enzymes are longer chains than others. However, when they are folded into their correct natural shape to play their jack-in-the-box role as they do in the cell, they occupy the same volume. This volume is equivalent to about 1400 water molecules – the size of a single cluster.

What determined this uniformity? After all, the biological functions of enzymes are many and varied. For example, comparing the function of carrying oxygen in the blood, with digesting food in the gut, with causing electrical impulses in the brain, with acting as an antibody fighting infection, does not suggest commonality, or even similarity. So these protein molecules perform tasks which are entirely different from one another, yet they are all made of the same stuff and there is a high degree of resemblance in the way they are folded up to fill their unit of space. They are the smallest components of the cell to perform biological work but like other machines, enzymes need fuel to function. Each is a quantised structural element carrying its unit of energy. In the wave-cluster model, that unit of energy defines the pressure pixel. It is this pixel of space that determines the size of a water cluster and a protein molecule.

What is the difference between a water cluster and a protein molecule? A cluster is composed of hundreds or thousands of small water molecules temporarily linked together – and this fleeting existence means they are fragile. In a cluster of 1400 molecules, there are 1400 atoms of oxygen and 2800 atoms of hydrogen, according to the familiar chemical formula, H2O. Protein molecules, on the other hand, are permanent, because the amino acids comprising them are chemically bonded together in a long chain. The amino acids contain atoms of carbon and nitrogen as well as oxygen and hydrogen.

But carbon and nitrogen atoms are the same size as the oxygen atoms, and in a chain of 200 amino acids (the average length), there are together about 1400 of these three types of atoms, and additionally, the number of hydrogen atoms is again about two to one, as in water. So from the point of view of numbers and sizes of atoms, clusters and proteins are remarkably similar.

However, the composure of proteins is not affected to any large degree by the random jostling motion in the surroundings. Firstly, in the natural state inside the cell, there is no disruption to structures since, unlike normal water in the drinking glass, the medium is in the gel state. Secondly, when proteins are extracted out of the cell and isolated out of that protective environment, they still tend to calm the chaos in their watery neighborhood. We remember from Chapter 2 that, provided conditions of their isolation are not too harsh, the chains all fold into the same compact shape. Then, adopting the role of permanent clusters, they extend a wide-ranging stabilising influence over their erratically flickering neighbors. Protein molecules and water clusters exercise mutual interactions, which are transmitted throughout the medium – the permanent proteins aligning the labile clusters. The diagram in Figure 12.1 shows that, even when protein molecules are distant from one another in a solution, they are able to judge their mutual positions and orientations (1). Clearly then, proteins transmit information through the water medium, from which we may conclude that they are in tune with the structure wave. Or expressed more pictorially we might say, the flickering of the structure wave is in synch with the rhythmic dance of the jack-in-the-box proteins.

When protein molecules are close enough to be almost touching, they orientate themselves to form the most highly ordered gel we know – the protein crystal. Although called a crystal, this material is not what readers would usually associate with a crystal, as it is soft and delicate, being half protein and half water. The name "crystal" is in recognition of the fact that the large protein molecules in this fragile environment are just as ordered in their spatial arrangement as are the small molecules in hard, shiny minerals we know as gem stones. In fact they are so ordered, that the positions of individual atoms, the carbon, nitrogen, oxygen and hydrogen atoms we spoke of above, can be mapped using the technique known as X-ray crystallography. When the group of Kendrew published the first such map in 1958 (2), they showed that the protein molecule, myoglobin, is folded into a form which is just the same size as the pressure pixel.

The tendency for perfect crystalline alignment of protein molecules is used by the cell. It provides us with the answer to the puzzle of the biological motor illustrated in Figure 2.1 where our story began. As in the 6-cylinder motor, the enzyme units must be interconnected in a stable sequence, since each first accepts fuel from the preceding and then donates new fuel to the next. But in detail, their functions are different. We recall that with each step the fuel molecules are altered, and so the job of each enzyme is to extract energy from a slightly different supply. Hence, this assembly does not show the ultraperfect order of the protein crystal where all the protein molecules are identical. However, each enzyme unit fits like a building block into the overall assembly. Each is a distinct piece of a jig-saw puzzle and when they all slot together the working supermachine emerges. This assembly therefore shows an order of a different type – an order of higher quality than in the flawless gem stone. The physical alignment of these motor parts directed by their glue factors must have the correct sequence, so that the chemical steps involved in metabolizing the fuel are carried out in the right order – otherwise the motor cannot function. Biochemists have learnt how to extract supermachines intact and in working order from living cells, showing that they do exist as large integrated entities which can retain their interconnected form and function even in isolation.

But of course, there are no pistons, valves and pipes. The fuel must be delivered molecule by molecule from enzyme to enzyme. To avoid clogging of the system, each fuel molecule, or metabolite as we now call them, must pass to each enzyme in turn at the right moment, just as piston and valve movements in the car motor are synchronised. To achieve this smooth running, metabolite molecules must travel through the surrounding water in a co-ordinated way, meaning that adjacent water layers act in co-operation with the enzyme assembly. It is clear that this high degree of organisation is needed to prevent malfunction and ensure that each fuel molecule which enters the supermachine passes through to the end with certainty.





12.1 Proteins and Clusters Slot Together Proteins which have a negative glue factor for one another dissolve well in water. They prefer to be dispersed from one another so that they are surrounded by water, rather than to stick together in aggregates. When a solution is left undisturbed, the separate protein molecules will slowly distribute themselves uniformly throughout the volume of the solution and align themselves in an orderly way, even though they are distant from one another. The transfer of information needed for this mutual orientation passes through the intervening water medium on the structure wave, shown schematically by the waves connecting the boxes together.

When the concentration of protein is about 50 %, so that the amounts of protein and water are about equal, then that most ordered of gels – the protein crystal – can form. The separate protein molecules are only minimally in contact along their edges, being still surrounded by water on all sides. But now the number of protein molecules equals the number of water clusters, so that the oscillations of the structure wave fit the dimensions of this geometrically perfect assembly (vertical wave). In this construction the wave is so regular that it can trigger a harmonic jump to a long wave stretching right through the crystal and hold it together under tension (horizontal wave).

In this diagram, the regular spacing suggests a strong parallel with the schematic representation of layers of swelling clay illustrated in Figure 3.1 before the introduction of the structure wave concept. Inside each shaded box is an identical string of amino acids folded up in the same way, while the alternating spaces are filled with water. We can now build further on this representation by extending it to a picture of the internal architecture of the cell.



^{12.2} The Cell's Six-cylinder Engine We can now look in more detail at the enzyme motor introduced at the beginning of the story in Figure 2.1. In contrast to the cylinders of a car motor, the biological machine consumes the fuel in a orderly sequence, in which each step is carried out by its own enzyme designed to effect the chemical reaction corresponding to that step. Schematically, the initial metabolite fuel molecule A is converted stepwise into the final waste molecule G, for example, we can imagine a sugar molecule, A, in various stages of its decomposition to waste carbon dioxide, G.

1) The six different jack-in-the-box enzymes are in their correct positions in line, and each has its corresponding metabolite (A,B,C,D,E,F) attached ready to react. The folded protein chains inside the boxes are not shown here for clarity. The metabolite molecules act as positive glue factors linking the proteins together forming a long wave, and so tension is exerted right along the line. However, the upper surfaces of the proteins have a negative glue factor, and so are in tight contact with the water layer stretching along the top of the line. Thus this diagram actually shows the cross-section of two layers or extended clusters, water above and protein below, both under lateral tension (thin arrows).

2) The long wave in the protein layer stimulates the chemical reactions to occur so that each metabolite is changed into its corresponding product. These new molecules bind in a different way to the protein surfaces, and the glue factors between the proteins become negative, that is, repulsive. The protein layer is now a line of smaller clusters exerting pressure between themselves, as shown schematically by the short waves. These chemical reactions thus trigger the pressure-tension switches.

3) The pressures generated (thick arrows) now expel the product molecules into the water layer above, where they are held in place by its lateral tension. They do not diffuse away as assumed in accepted theories of enzyme action, because this layer is a gel.

4) A new fuel molecule A, binds to the initiating enzyme at the start of the line because it has a stronger positive glue factor to the surface of this protein than to the surrounding water. This step reverses the attraction between the protein and water at the start of the line, switching the force in the water layer to pressure at this location (thick arrow). With tension still in front and pressure now behind, the layer moves one cluster unit to the right, transporting the dissolved products like a conveyor belt to their next positions in the metabolic pathway.

5) The products are now positioned close to the locations where the next chemical change in their metabolism takes place. Once rebound to their new reaction sites, the pressure (short waves) reverts back to tension (long wave in step 1), because they are so compatible within this protein environment that they switch the glue factor from repulsive to attractive. On reverting back to step 1, the assembly is now ready as a whole to restart the cycle. Although several models of synchronized function are imaginable, only the highly oversimplified version illustrated in Figure 12.2 is discussed now. As little is yet known about the behavior of whole enzyme complexes, the picture we can draw today is necessarily speculative. Nevertheless, I feel it worthwhile to propose a model in order to highlight the remarkably coherent design features exhibited by living systems. In taking this step, we are returning to the contentious territory of a fundamental issue of the chasm, since physics does not allow co-ordinated enzyme action.

In this model, the metabolites, A, B, C, ... attach to their enzymes simultaneously, chemically react there simultaneously, are released as products into the water layer simultaneously, are transported along one cluster spacing simultaneously and are finally rebound to the next enzyme along the line simultaneously. The triplet of steps, binding-reaction-release, between a metabolite and its enzyme partner are today thoroughly understood, having been the core study of biochemistry since its beginnings over a century ago. For example, let us imagine that the biochemist has in his test tube a solution of the purified jack-in-the-box enzyme called Jack, which has been isolated out of the cell away from all the other proteins. To this solution he adds metabolite, A, which is the molecule that Jack acts on. He then studies the steps

 $Jack + A \rightarrow JackA \rightarrow JackB \rightarrow Jack + B$

in which the enzyme captures molecule A, converts it into B and releases it back into the surrounding water. Since such reactions proceed in a purified solution lacking the other parts of the supermachine, they do not help throw light on the question of co-ordination. On the contrary, they lead biochemists to believe that the steps occur by accident, or in the technical language of thermodynamics, the steps are controlled by random diffusion. As will be discussed in more detail in Chapter 15, "The Supermachine", of TPM, under such conditions there is no certainty that a metabolite, once released after a reaction step, would find its next enzyme partner. But the unavoidable consequence of this picture is that the action-packed world inside the cell would soon become crowded with all types of metabolic debris and cease to function. The real picture of living cytoplasm is just the opposite – metabolism proceeds with both efficiency and reliability. There are no out-of-synch enzymes and no free-floating metabolic fragments obstructing the smooth operation of the busy factory.

If we are to depict the assembly acting as a coherent whole, we cannot escape introducing directed movement, and therefore controlled mechanical forces. At a very minimum, the triplet must be extended to the four-step sequence: binding-reaction-release-transfer. A simple solution to this problem is provided by the relative movement of the water and protein layers. In Figure 11.3, we saw how the operation of the pressure-tension switch could produce this type of motion in layer-shaped clusters. The two dynamic features of the wave-cluster model, switches and harmonics, are again the key players in producing the sequence of events depicted in the present diagram, Figure 12.2. By operating in the correct sequence, they control the metabolic pathways of the cell, ensuring that metabolites reach their end state without relying on chance.

The displacement of cellular material, whether water or protein, evidently implies some type of circular movement. The space of the cell interior is full – there is no free space or empty room to accommodate the shifting medium. For instance, the water at the leading end of the sliding layer must displace more water as it advances into its new location. But this displacement means in turn, that even more water further on must also be moved, and so on in a chain of relocations down the line. We can now easily see how a cyclic arrangement would solve this problem, since there is free room made available at the trailing end of the sliding layers. This would allow local clusters to move around in a circle, obviating the need for distant clusters to be displaced further away along the layer.

The four spinning clusters of Figure 11.4 provide a basis upon which models of cyclic movement can be built. We need to find appropriate switching mechanisms, by which the rotation of the group can be controlled. A possible solution to this problem is already known to biochemists, since one of the most significant achievements of their field is the discovery that the binding of metabolites to enzymes acts to a large measure just like a switch. Older biochemists will remember the discussion which took place during the 1960s and 70s surrounding the "lock-and-key" versus the "induced fit" mechanisms. These mechanical models refer to the structural changes which ensue when the small metabolite molecules attach to their large protein partners. Speaking figuratively, something happens to Jack when A binds to it as set out in the first step of the equation shown above

$Jack + A \rightarrow JackA \rightarrow$

To illustrate a small change in the structure of the enzyme this step might be modified to read something like

$$Jack + A \rightarrow JockA \rightarrow$$

Today everyone agrees that changes do occur, in fact some are so large that they can be seen in powerful microscopes. We can now apply this concept to a simplified model of a spinning group and suggest how protein movement might be controlled. The four clusters of Figure 12.3 are initially immobile because they are embedded in two horizontal layers similar to those in Figure 11.4, which are under tension from both sides. They also feel pressure from above and below, exerted by the surrounding medium. Clusters 1 and 3 are similar or identical enzymes which bind the metabolite T (an example of T is triphosphate), which in turn causes the glue factor of their contact surfaces with their neighbors to interchange. In other words, the binding of T operates a pressure-tension switch. We now have the correct constellation of forces acting on the group to produce the rotational movement, which occurred in Figure 11.4 by chance. After one quarter of a rotation, the enzymes are in a new environment and there are new influences on T, preparing it for the chemical reaction which modifies it slightly to the molecule D (diphosphate). This chemical change occurs in the next step of the Because it is smaller, this new truncated form of the metabolite, D, does not have the powerful rotation. influence on the contact surfaces as had T, and they revert to their initial states. However, the group of four enzyme units has rotated through half a complete cycle.

Readers unfamiliar with enzyme mechanisms may find this type of proposal quite fanciful. In disbelief they may even react with the pertinent question: do biological molecules really perform such acts which appear to rely on so much design? However, there need be no doubts. The cyclic activities of enzyme complexes many times larger and far more intricate than four clusters are well established experimentally. Furthermore, proposals of sophisticated models of protein machinery involving reciprocating actions paralleling those of car motors are commonplace in biochemical research publications. Such models are widely accepted by the biological world and are to be found in the most prestigious journals, even though their strictly ordered mode of sequential operation contravenes thermodynamic principles.

On the other hand, readers familiar with biochemistry will have no qualms with the role of the triphosphate, ATP, depicted here. ATP is the wonder metabolite. It is known to bind to over 100 different enzymes and to be involved in a myriad of cellular activities ranging from changing the shape of amoeba to causing electrical impulses in the brain. It has been given the title of the energy molecule of the cell, because it was recognized at an early stage to be involved in reactions causing movement. It fuels the cell's motors. Indeed, the work of Lipmann's group in the 1940s on phosphate metabolism led to the concept of the "high energy phosphate bond", which has remained biochemical dogma to this day. This concept refers to a chemical bond in ATP which is split by enzymes when ATP is broken down to ADP, releasing large amounts of energy which the enzyme can then use to do the physical tasks of the cell.

However, careful measurements have shown that the energy in ATP is not large at all - in fact it turns out to be rather small (3). For example, it is smaller than the carbon bonds in sugar (which the cell uses as its primary source), and is much smaller than the carbon bonds in fat (the cell's back-up fuel reserves). Nevertheless, the term "high energy phosphate bond" is still used, and taught, perhaps because it seems reasonable to assume that nature would maintain a supply of high energy to fuel its more difficult mechanical jobs. But the puzzle remains: ATP is not a source of high energy.

In the rotation mechanism illustrated in Figure 12.3, ATP plays the role of a trigger. When it binds, the machine is switched on, then when it changes to ADP, the machine is switched off. It does not supply the energy for the movement – the energy was already there. It was always there, because it is in water. The energy delivered by ATP changes the chemistry of the contact region – the glue-factor – so that clusters will fuse together or split apart as they perform their harmonic dance. This switching step would be similar whatever may be the mechanical task to be carried out, since all the machines of the cell – bicycles or locomotives – are composed of clusters in contact. Only a similar small amount of energy is needed to operate switches, even when they control machines performing work loads with widely different energy demands. In this picture, ATP is the universal switch molecule, rather than the universal energy molecule. It is not the supplier, it is the controller.



12.3 The Spinning Protein The four central water clusters of Figure 11.4 are replaced by protein clusters seen again schematically in cross-section. The folded chains inside each box are again not shown for clarity.

A) They are held stationary in position by the actions of equal forces, two opposing pressures from above and below (say), and two opposing tensions from left and right.

B) The units 1 and 3 possess surfaces which bind strongly a molecule of the metabolite T (for example, the energy molecule of the cell, ATP). This event reverses the nature of their surfaces in contact with the surrounding water, that is, the binding of T operates a glue factor switch.

C) As a result of the switch, the forces now acting on the group have the correct arrangement to cause a clockwise rotation, which in turn chemically modifies T to a slightly altered form, t.

D) A further step in the rotation completes the chemical reaction changing t into D (ADP) which is a smaller molecule than T. As a consequence, D does not have as big an influence on the surface structure of the protein as did T, and the forces revert to their initial arrangement. Also, because they are now only weakly bound to the protein, the two D molecules detach easily, leaving the group of four as they began without their metabolites, but now displaced through half of a clockwise rotation.

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13. Dead or Alive

An old rule of thumb in the study of cell biology runs: if you can see Brownian motion in your cell then your cell is dead. For us, this specialist knowledge translates to: the contents of a living cell are not in random motion. There is a lot of movement inside a cell of course, but it is not the type of chaotic motion observed with the new invention, the microscope, by the English botanist, Brown, two centuries ago. Using that instrument today, biologists are able to recognize living from dead movement. However, as we have seen, physicists' models of biological machines rely on Brown's random motion. So on the one hand, we have the practitioners dismissing chaotic life, while on the other, we have the theoreticians still today requiring the aimless activity of the zombie molecules. These opposing outlooks bring us back once again to the basic problem laid out in the introductory chapters. This time however, we look back with a fresh perspective from a holistic standpoint, which has been clearly developed step by step throughout the foregoing chapters.

Let us recall in a few sentences the two views of Chapter 1. The cell biologist views his field in the topdown direction. Through the microscope he sees first the intact cell, then deeper down he finds the ordered structure of its internal medium, the cytoplasm. All functions as if by design. The physicist, on the other hand, views biology in the bottom-up direction. The higher levels are explained, even determined, by the lower. Biology is based on biochemistry, biochemistry is based on chemistry and chemistry is based on physics. Thus all can be reduced to randomness, and therefore the order displayed by biological systems is apparent only. Biological order does not really exist.

From this bottom-up perspective, there is no break in the road – the world is statistical all the way up. One can read this reductionist philosophy in the writings of many modern physicists. Some quantum physicists do raise the theoretical problem of downward causation in the tradition of Bohr (1), but such arcane deliberations are not related to the holistic perspective of the biosphere discussed in this book. From the biologists' top-down point of view, the question becomes: how far down do we go before we meet the random world of physics and chemistry? In general, biologists do not concern themselves with this problem and assume only that structure persists down far enough to permit the coherent activity of their proteins. They know that the cell's jack-in-the-boxes work in masterful co-operation. To clarify this point, let's consider the example of the working model of the enzyme that makes ATP in the cell's energy factories, which took Nobel honours in the year 2000 (2). Biologists believe that this large complex protein supermachine is driven by osmotic forces which cause it to rotate in precise steps in one direction like a spinning top under the control of a ratchet mechanism. The proposal of this built-in oneway mechanism is essential in order to prevent the disorderly steps which would cause it to run backwards with equal likelihood as forwards, and so consume the ATP it makes! An example like this highlights the problem well, for it contains no mention of how this ratchet works, or in other words, how the protein successfully avoids those disorderly steps required by physics. And so just as physicists proclaim that biology can be reduced to chaos, biologists build their three-dimensional models of how living machines work without incorporating physical principles. We have arrived again at the chasm of Chapter 1 – in a state of mutual denial, each discipline ignores the other.

So how do enzymes work? The argument developed in this book is that the orderliness of their stepwise dance is real, because it is based on natural principles. The argument is not that it is only apparent, because the creation of order is forbidden by basic principles – as the classical physicist would say – nor is the argument that it is a useful concept even though mistaken at bottom – as the classical biologist would say. No, the argument found herein is that biological order is real, being the expected outcome of an early stage in evolution involving already existing physical entities – a prebiotic stage. There were no lucky strikes – natural evolutionary advances bridged the gap between the worlds on the upward road. The core theme developed in the preceding chapters is that the intriguing osmotic phenomena reveal themselves to us just there, where the worlds meet. And further, because these phenomena cannot be explained by the behavior of molecules inhabiting the chaotic world below, they must rely on the existence of new physical entities – the pixels – which belong to this intermediate mesoscopic level, where they lay the foundation of the structured world above.

But we cannot call osmotic phenomena "alive". The fleeting pixels of energy in liquids are physical rather than biological objects, on the other hand though, the clusters which occupy their space do show some of the basic characteristics of life. With their demon-like ability to concentrate energy and thwart the destructive effects of random collisions, clusters are the precursors of their more talented offspring, the proteins. Clusters therefore predate proteins, suggesting that it is liquid water itself which harbors the life force. This idea in turn suggests the unfolding of a historical scenario, in which a prebiotic form of life thrived during the evolutionary stage preceding carbon-based organic life. So just as clusters inhabit the middle level in the hierarchy from physics to biology, they also inhabit a middle slot in the temporal progression from dead to alive.

With our understanding of osmosis, we are now able to speculate on the connection between mechanical forces and early prebiotic chemistry. During that era, the chemistry of the surface of our planet underwent a wide-ranging and thorough irreversible change: the carbon of the oceans and atmosphere became locked up in organic material where it has remained to this day. Except for the buried deposits like limestone and fossil fuels, which themselves were also once living, all the carbon on our planet cycles and recycles through the biosphere. To understand this development, let's imagine that the Earth's early atmosphere was what the chemists call "oxidized". Under such conditions, the carbon was distributed freely and uniformly through the oceans and atmosphere as carbon dioxide – the same chemical substance that figured so prominently in the early stages of this story. Recalling the discussion in Chapter 2, carbon dioxide is the low-energy end product of our energy-hungry human activities. It is the dead state of carbon – the state that we know prevails on our sister planets, Venus and Mars.

To become energized, that is to take a step towards becoming alive, a molecule of carbon dioxide must undergo a chemical reaction stripping it of its oxygen and adding instead a molecule of water to its carbon. The oxygen is then set free as a gas into the atmosphere. When the oxygen is replaced by water we get carbohydrate (literally carbon-water), in a process we can represent by the simple chemical equation

carbon dioxide + water \rightarrow carbohydrates + oxygen (released into the air)

From our everyday knowledge of diet, carbohydrates are readily recognized as a high-energy food source by both the technical and non-technical readers alike. Comprising as they do sugars, starches, saps, the gooey insides of plants and animals, the wood of trees and the gossamer thin threads of gel strewn throughout the oceans, carbohydrates no doubt account for most of the carbon locked up in the entire biosphere. Indeed cellulose, the chemical name for wood, makes up the major fraction of organic matter on Earth today. And since "higher" animal life remains dependent on "lower" plant life in the food chain, it is likely that cellulose-like material was always the basic form of energized carbon since that time when life began.

We recall from Chapter 1, that in popular theories of the origin of life, a high-level complicated molecule – a protein or DNA molecule – appeared miraculously in the primordial sea as a finished product. At that moment life sprang into action. The emphasis is on molecules, the sticks-and-stones, or in more modern terminology, the hardware of life. Naturally then, there is usually an attempt to explain how replicating molecules arose, since, if life is seen as material at bottom, then its most important attribute would be the ability to make hard copies of itself in order to ensure survival. Hence we find an emphasis on the original gene, that is, the original replicating hard object.

In contrast, the formation of early clays did not happen with the odds of a once-only cosmic event. Such mineral deposits are vast and continuous throughout geological time. Nor was their association with water a freak accident never to be repeated. In fact, the reaction of older volcanic rock with water is a requirement for their formation. Indeed this process is an older version of the chemical equation we have already used to describe prebiotic carbon chemistry. It describes how water energizes the mineral, quartz:

silicon dioxide + water \rightarrow silicates (layers of clay crystals)

Silicon dioxide (the scientific name for quartz, silica and sand) is, chemically speaking, the sister molecule of carbon dioxide. Furthermore, it is the major component of many volcanic rocks, especially the granites. Geologists call the physical breakdown and chemical transformation of rocks "weathering". It is a long slow process, but it doubtless began as soon as there was liquid water available on Earth to rain down and wash over the rocks formed from volcanic lava flows of the fiery era. When the dissolved silicon dioxide crystallizes under cool conditions in intimate contact with water, as opposed to the furnace-like conditions of volcanoes, it forms delicate microscopically thin sheets. Singly, each is a fragile wafer, but stacked together they make the robust, active material we met in Chapter 3 - the material of the potter's craft. They are the offspring of the marriage of solid rock and liquid water, the endless supply of which gradually laid down the vast geological beds of clay minerals found today on every continent in the world.

In his stimulating book "Seven Clues to the Origin of Life", Cairns-Smith presents a convincing case for the role of clays as the primitive genes in the prebiotic era before the appearance of complicated, high-level organic molecules like DNA (3). In this model of replication, the molecular patterns present in the topmost sheet could be copied into the new sheet as it crystallises on top of the stack. But the crystal sheets are separated by a layer of water, in much the same way that a layer of glass separates the copy from the copied in a familiar Xerox machine. So the question that now confronts us is: how can faithful copies be produced without there being direct contact between the surfaces of the old crystal and the new emerging one?

A fruitful approach is offered by Good in a seminal article on clay-water interactions, in which he describes how synthesis of organic precursors of proteins and DNA, those molecules of intermediate size, was able to proceed successfully (4). He gives special informational properties to the water between the sheets. This sandwiched "hydrogel", as he calls it – the layer labeled "liquid" back in Figure 3.1 – takes on a structure under the influence of the adjacent clay surfaces, which can fit, or not fit, other surfaces presented to it. The hydrogel is, in effect, a memory of the intimate clay-water contact, and can "read" or "scan" new molecules to check whether they are faithful copies of the original clay surface. In this way, "life" chemistry was able to take off in the water, while the mineral crystals sank into the background as the original "genes".

I feel that most readers, whether they are familiar with the technical terms used here or not, sense that this line of thought has the potential to be far more productive in explaining life's origin than that proposing a series of lucky strikes. To clarify this claim, let's pause a moment to reflect on some points of difference. Firstly, the well known strong affinity between clay and water was discovered long ago quite independently of the field of biological evolution. Secondly, clay crystals have a natural ability to copy themselves. Such duplication is a primitive type of reproduction, and since it is a natural mineral process, it is not an event occurring against galactic odds. Thirdly, since this crystallization occurs in water, the atomic arrangements in the new crystal are being copied from the old at a distance across the water layer. This knowledge led Good to develop a model where water is the medium which actively transferred, not obstructed, the patterns presented on the crystal surfaces. In other words, his model implies flickering water structure as a hidden but crucial factor in the origin of life. In this picture the transmission of information is made a foundation stone of evolution. The contrast with the popular lifeby-roulette theories could hardly be greater. Good's model illustrates for us in a concrete way, what was argued in an abstract way at the outset of our story, namely, that random collisions and information are mutually exclusive. As we can see in Figure 13.1, if the water layers were composed of a structureless medium, then they could not carry information from the surface of one clay crystal across to the next.

In general, scientists do not associate clay and wood together. One belongs to the field of mineral chemistry and the other to biological chemistry. As these fields of study are widely separated, a common approach would need a high degree of interdisciplinary exchange not achieved to date. However, as the wooden wedges of the Egyptians demonstrated, there is a remarkable similarity between these materials in their interaction with water. Both are able to concentrate osmotic energy so effectively that they can generate powerful forces. This ability is a result of the similar molecular patterns on the surfaces of clay and wood, which closely mimic the patterns in ordered water. So when contact with water is made, both materials are able to marshal osmotic energy through their influence on its structure. In other words, the patterns on the fixed surfaces of silicate and carbohydrate crystals exert a similar ordering effect on the flexible arrangement of their neighboring water molecules, and in so doing, force a primitive level of organization on the clusters. With this in mind, it seems reasonable to ask whether clay minerals played a central role in incorporating carbon from the dead atmosphere into prebiotic life by directing the synthesis of carbohydrates. Did the ordered water layer in contact with the clay surface operate as a machine converting the physical energy of osmosis into the chemical energy of organic molecules?

In Figure 13.1, these ideas are translated into a simple scheme. If water layers rich in carbon dioxide became squeezed between sheets of clay particles, the high pressures could have been relieved by a chemical reaction producing simple carbohydrates, because the resulting molecules occupy less room than the original carbon dioxide and water. Oxygen is also produced, but unlike carbon dioxide, this gas is not very soluble and so could not have remained in the watery environment. From its point of production inside the clay stack it would be expelled into the surrounding bulk water, and from there into the atmosphere. Indeed, a fundamental feature of this early process was the ability of the silicate beds to move layers of water through them, because it enabled the two new energized chemical players on the scene to be separated into different compartments of the Earth's surface – one, carbohydrate, remained in its watery environment while the other, gaseous oxygen, accumulated in the atmosphere. We can speculate that, because this dynamic feature proved to be so effective, it was carried through to later stages. When plants eventually took their place in evolutionary history and superseded the beds of clay, they continued to use osmotic flow between the cellulose sheets of their woody tissue to transport their nutrients and deliver oxygen upwards into the air. So if silicate crystals are the precursors of wood, we may now ask, is clay swelling the early version of the rise of sap?

Oxygen levels in the atmosphere gradually built up as more and more carbohydrate was synthesized, and more and more oxygen expelled. The overall effect of this early prebiotic stage of evolution was the replacement of carbon dioxide in the atmosphere by oxygen. In this picture, the osmotic energy stored in pressure was converted into the chemical energy we know as high-energy carbohydrates. Thus, in the search for life's beginnings, the emphasis is now removed from the material sticks-and-stones basis of life and placed instead on the process that might have led to directing the way energy became organised – or again in modern terminology, shifted from the hardware of living matter to the software of energy manipulation.

Readers will notice the strong resemblance between Figure 13.1 and Figure 12.2. But we also notice a difference – there are no enzymes in the present diagram, because there were no proteins in the prebiotic era. At that time, the reactions synthesizing energy-rich molecules were carried out by water clusters under the direction of minerals, and the required energy was delivered in pixel units to the locations of the chemical events. As pixels and anti-pixels appeared and disappeared throughout the length and breadth of the water layer, the mechanical energy residing in high pressure was pumped into more complicated chemicals, and the new organic molecules were born. This picture of evolving life forms in terms of evolving energy forms will be expanded in Chapter 5, "The Matrix", of the third book, TLM.

The traditionally accepted signs of life such as growth and reproduction, deal with carbon-based matter and so the origins of life are traced back to the first appearance of that type of material. It might seem therefore to be a natural conclusion that life must have originated by chance with the spontaneous synthesis of proteins (or DNA or RNA). For this reason, scientists do not search for the first signs of energy concentration – energy was always abundantly present in the form of random collisions pervading the watery environment, produced by the aimless activity of the zombies. Energy is like air and so does not need to be accounted for. In any case, it was never considered to be part of the problem, because the dictates of thermodynamics on the ability of energy to become spontaneously organized are blunt: it cannot, and it did not. As we recall from chapter 2, the power of this dogma has discouraged discussion on the possibility that it can happen, because non-physicists feel intimidated when entering the realm traditionally regarded as belonging exclusively to the scientific priesthood. Many readers who are not familiar with the social stratification of the scientific fraternity may be surprised to learn of such a nonegalitarian attitude towards basic questions. In her engaging book, Wertheim examines how a quasireligious order grew from its historical roots to establish itself among physical scientists, and explains how physicists naturally adopted the exalted role of the guardians of science's innermost secrets (5).



13.1 Early Machines of Life Although the six cylinder engine of Figure 12.2 is a much oversimplified schematic model of a real cellular supermachine, it nevertheless represents a highly evolved system full of regularity and control. On the other hand machines of the prebiotic era were composed of the materials available at the time – water and minerals. They functioned without controls since the pressure-tension switches operated without regularity. In this diagram, we will build up a speculative model of the earliest engine that harnessed the available environmental energy to take the first steps in the development of carbon chemistry, later to become the chemistry of life.

A) Water molecules (circles with two short arms) are shown sandwiched between two clay crystal sheets (horizontal hatched areas). We have zoomed in by a factor of more than a million for this diagram, in which the sheets shown in cross-section are just a few atoms across. The + signs indicate locations on the top side of the crystals, which attract carbon dioxide molecules. This ability of clays to absorb chemical substances is well known and is used in many industrial processes. The water molecules are depicted in a regular array as if this layer is also crystalline, although they are constantly moving and not frozen in any arrangement. The array is a schematic representation of a cluster which stretches the distance of millions of water molecules in the four horizontal directions, left and right as well as in and out of the page, even though it is only a few molecules thick (as depicted here by four rows). The arrangement is constantly changing to other similar patterns as described in the oscillations of the flickering cluster in Figure 8.3. This flat cluster of gelled water is under tension in the extended directions (thin arrows), but under pressure in the vertical direction through the layered stack (thick arrows), as we originally saw in Figure 3.1. The extended tense state is represented by the long structure wave shown on the right.

B) In the following panels most of the water molecules have been omitted for clarity. Carbon dioxide molecules (three circles joined in a line) dissolved in the water layer attach onto the attraction sites. Because of the positive glue factor between these molecules and the clay surface, some of them remain locked in position for a time. The presence of the stationary carbon dioxide molecules modifies the ordering in the water layer splitting it into two sublayers, the lower one containing both types of molecules and the upper one containing pure water still in the same state as in the original single layer in A). The split layer is shown in the wave representation on the right.

C) Held in position, the carbon dioxide molecules experience strong mechanical forces exerted in definite directions because of the geometry of the environment, tension laterally and pressure vertically. These energetic influences stimulate a chemical reaction to occur converting a carbon dioxide plus a water molecule into a carbohydrate (two circles with two short arms) and an oxygen molecule (two circles). These foreign molecules interfere with the structure in the water layers stimulating transitions back-and-forth between long and short waves. The short waves which appear in the lower layer represent small clusters which now exert lateral pressure, and the carbohydrate molecules produced by the chemical step are pushed into the upper layer. The oxygen molecules remain bound to the attraction sites at the location of their parent carbon dioxide.

D) The switch to pressure in the lower layer means that it is now mechanically labile and could be removed. For instance, when tension is also exerted somewhere along its length, then it could be transported and even removed from the clay stack relieving the high pressure imposed from outside. In this illustration it would flow to the right pulled by tension in front and pushed by pressure behind. The separation of the products, carbohydrate and oxygen, from one another is an important step, because it removes the chemically reactive oxygen from the site of reaction, allowing it to escape out of the clay material into the atmosphere where it accumulates as a free gas in the state we know today. Its physical removal from the watery clay environment ensures that the synthesis of carbohydrate continues by preventing the reaction from reversing and recreating the original carbon dioxide. That their separation can be maintained is made possible by the chemical facts that carbohydrates are quite soluble in water whereas oxygen is not. In this case, the pressure-tension switches are not under the control of special proteins as in Figure 12.2, but occur spontaneously. However the relative movement of the layers introduces the possibility of a one-way step into the overall process, which was later refined in biological systems. The importance of irreversibility in machine action is discussed more deeply in Chapter 3, "Four Machines", of the second book, TPM. In the embryonic process illustrated here, mechanical energy in the environment drives the chemical reactions and transports the oxygen away from the location.

This diagram does not claim to be a description of how life originated, but is a speculative model suggesting how energized carbon chemicals could have been synthesized in the watery environment of the primitive Earth prior to the emergence of the biosphere.

Because the main player in the picture is water, its organization is hard to see, and therefore also hard to believe. About 50 years ago, when powerful microscopes began to peer into living cells, they found a transparent empty cytoplasm. At the time, the pre-eminent cell biologist, Frey-Wyssling, concerned by these negative results, warned against the generally accepted interpretation depicting the cell's interior as a featureless medium. He held that the aim of microscopy is to explain "the double nature of the cytoplasm", for it is "solid and liquid at the same time" (6) – in other words, he hoped to see living matter in action. Since then, the more powerful electron microscopes have revealed the cell's inner world down to the level of its protein machinery, but to see these co-ordinated components in action we must zoom in and magnify them more than a million times. We achieved this in a fanciful way earlier in Chapter 2 with the pictorial analogy of our deft monk, who could thread and wind his precisely coiled 10 000 kilometer-long string of prayer beads without making a mistake. In close-up perspective we see how his task would be made all the more difficult than earlier imagined, since we now know he cannot move unhindered in free space. Additionally, his movements must be executed in a closely packed world, because he is forced to share his overcrowded workroom with other monks, all just as busy as he is. Yet the cell unwinds and rewinds its meter-long DNA chains with never a hitch.

We have returned to the wonders of the polymerase chain reaction, or PCR for short, which figured so spectacularly at the outset. This reaction is performed by that remarkable machine, DNA-polymerase illustrated here anew in Figure 13.2, which can copy a string of DNA beads faultlessly thousands of times alone in a test tube. With each new bead it adds onto the end of the growing string, it performs its dance steps in the correct sequence over and over until the string is complete. All this machine needs is an original string to copy and a plentiful supply of beads. I share the feelings of awe with those readers who find such apparently purposeful behavior of dead molecules hard to believe, yet the truly astonishing fact is that this machine runs without energy input -a high precision motor that runs without fuel! So what drives this spontaneous creation of free order?

To remind us of its breathtaking performance, in this updated version of the original Figure 2.3 we see again two strings emerging from the machine – an existing string synthesized earlier which acts as the template, and the new growing string whose sequence of beads is being copied from that template. As the machine steps along the template one bead at a time, it pauses to recognise the next bead and then adds a corresponding bead onto the growing string. The two strings exit from the bottom of the machine twisted around one another in the form of the universally recognized double-helix. Since the distance between successive beads in the double-helix is just the width of one water molecule, the enzyme marches forward with steps of this size. Knowing these dimensions, we can build a picture of the DNA double-helix surrounded by a gel of structured water composed of layers of water one molecule thick. These layers are stacked on top of one another like thin flat donut rings with the double-helix acting as an axle running through their centers. The internal strength of this solid gel keeps the enzyme from slipping up and down the axle – chaotic behavior is prevented.

Encased in this highly ordered environment, the enzyme responds to the forces exerted by the thin flat clusters. During the pauses in its marching progression, its front and back ends experience the same force being exerted upon them, so that it is held in place by equal influences, for example, two pressures. Then, as the next bead is locked into place, the force in front switches to tension and the enzyme moves forward a distance of one bead along the DNA chain. To see it in action, we can imagine a rotating mechanism similar to that depicted in Figure 12.4. One of the four beads, A, is in fact ATP which we have already empowered with the role of a switch controlling cyclic steps. In the present case of the PCR, there are ten steps in one complete turn, because there are just ten beads stretched along the chain in one turn of the DNA helix. Each time the next bead (A,T,C or G) enters the enzyme to be threaded onto the growing chain, it triggers a rotation of one tenth of a turn (36 degrees), so that the DNA axle appears to move through the machine like a screw as more and more beads are added. With each stepwise turn of the screw, a layer of water is displaced from immediately in front of the enzyme by an outward-pushing force, and another is replaced behind it by an inward-pulling force.





Mechanical Action in the PCR 13.2 The diagram on the left is a schematic representation of the essential elements of the protein machine that copies a new strand of DNA from an old one to form the familiar double helix. The old string of beads, or template, is seen at the top of the diagram and runs down into the center where it becomes entwined into the double-helix motif with the new string. The central rectangular section represents the It is composed of 3 or 4 protein clusters forming a shape which is often protein machine. described by biochemists as being like the palm of a hand loosely clasping the double string of beads. They know it as the Klenow fragment after Klenow, who discovered that this is the smallest portion of the larger DNA polymerase which can produce double-stranded DNA. lt spans one whole turn of the double string stretching a distance of ten beads on each string. The top section of the enzyme identifies the next bead on the old string as it enters the palm area, and then chooses the corresponding bead to add onto the new string (square beads). As we recall from Figure 2.3, this thumb-forefinger area is the location of these chemical steps at the growing end of the new string. The enzyme then moves forward (upward in this diagram) in a stepwise manner to begin the next identification. Because the double-helix has the cylindrical shape of a screw, this physical step must involve a rotation of the enzyme hand through an angle of 36 degrees relative to the DNA running through it.

The active complex, protein plus DNA, is surrounded by water (circles with two short arms), which also contains a small amount of some salts and a supply of the beads A, T, C and G as single molecules dissolved in this water (not shown). The region in contact with the back end where the double-helix exits from the enzyme as a finished product, has a highly ordered structure of the type found in swelling clay and wood, and therefore exists in the state of a solid gel. Each time the enzyme moves a step forward (upward), a new layer of water is pulled inwards behind it (small curved arrows) as a result of the strong lateral tension exerted through these layers of gelled water. Even when isolated by itself from the enzyme, the double-helix is known to have this powerful influence on water structure. This influence and the negative glue factor between water and the end surface of the enzyme generate the arrangement of forces seen at the bottom of the diagram on the right, lateral tension (thin arrows) and forward pressure (thick arrows).

When the arrangement of forces at the front end where the template strand enters the enzyme is identical to that at the back end, there would be no movement of the enzyme relative to the DNA. During these pauses, the precise chemical reactions can proceed. When the new bead has been added onto the growing string however (small square in the diagram on the right), its fixation into this reactive position in the complex causes a pressure-tension switch at the protein-water contact surface at the front disrupting the ordered water layers. As illustrated in Figure 12.3, the switch reverses the arrangement of forces there, resulting in lateral pressure and forward tension. The new direction of the pressure helps to remove water from in front by pushing a layer sideways. We now have the required physical circumstances, tension in front and pressure behind, for an overall concerted action that effects a forward step of the enzyme along the DNA template strand.

With this picture we can finally compare the two views of how living machines operate at the molecular level. The orderly workings of the large construction made of water, protein and DNA depicted here stands in stark contrast to the accepted picture in which the sequence of steps is said to proceed in a chaotic fashion. Furthermore, the biologists continue to present us with new, larger and even more complex protein supermachines of whose existence they are certain. An example here is the ratchet machine we met above that puts osmotic energy into ATP. These developments will eventually turn the spotlight onto the contradiction underlying the traditional approach, since they announce loudly that the cell contains components of highly complex design, yet all operating against unimaginable odds by accident. And since, in the final analysis, natural events are certain, reactions like the PCR must be viewed as unnatural in the extreme, and their occurrence be seen as another example of Hoyle's whirlwind spinning its magic – this time not in the primordial soup creating life, but in every living cell constantly maintaining life!

That same spotlight will thus reveal how the dogma of structureless water will have to be taken to extraordinary lengths in order for the traditional view to remain a convincing alternative. This trend can already be seen in the final sentence of a review on the physics of the effects of DNA on water, which concludes: ".... the nature of the interaction is generally non-specific and with no special effect on the water dynamics or structure" (7). In this interpretation, the fact that 1% DNA renders 99% water immobile as a gel, is not considered to be a physical observation relevant to water dynamics or structure. This quote is an example of how researchers can be selective in regard to the scientific importance, or otherwise, they place on their observations – we learnt already early in the story, how swelling and gelling have been ignored by serious science. The prevailing philosophy of rejecting structured water in biological systems is another illustration of the power of thermodynamics in the minds of scientists to explain these phenomena, however contrived the explanation may seem. Nevertheless, I feel sure that, in the end, structure at biology's deepest level will be needed to replace Hoyle's whirlwind at the bottom of life's processes, and make the unnatural natural.

But returning to the PCR itself, we find the bigger question still looms: where does the energy to run this amazing machine come from? Where can it come from, but from underlying organized forces at work in the surroundings which have so far remained invisible to researchers? The organic matter – the enzyme and the DNA beads – can be seen with today's experimental techniques, but the process cannot. On this point it is instructive to remember that, before the discovery of DNA-polymerase and the invention of the electron microscope about 50 years ago, the enzyme itself was also invisible. With this in mind, the proposal of the deeper and more fragile pixel machine is not at all a fanciful speculation. And we must not think that the PCR is a special case – it is really the theme of DNA that makes this chosen example dramatic, not the PCR itself. In fact, each and every enzyme must perform its dance routine without fault, so in this light the example of copying DNA is no special case after all. In calling upon our hardworking monk in Chapter 2 we could have chosen any biological machine to set the scene for our story, since all tasks must be done with equal diligence. All enzymes are sign posts pointing in the direction of the living pixels below – it is just that Mullis's sign reading "polymerase chain reaction", because of DNA itself, is lit up in universally recognised neon letters we cannot ignore.

In the natural state, living matter is a compact array of delicate machinery. Viewing this dense organization from the zoom-out perspective, the cell is a highly energized, tiny droplet of water. This droplet is not surrounded by a concrete wall, nor do steel cables fortify its soft internal medium, yet it actively absorbs, converts, concentrates, stores and releases energy. Such a scenario sounds like a recipe for disaster, but rather than self-destruct, the cell goes on to multiply as it gathers even more energy from its surroundings. And all the while cells remain perfectly stable! Even during heightened activity, the urgent call on its reserves does not cause its internal machinery to run amok, releasing uncontrollable forces of disintegration – there is no explosion inside this cylinder. Chaotic events have no place in the world of the cell. The smooth manipulation of energy is not just a sign of, but surely the essence of life, contrasting so strongly as it does with the powder-keg technology of our man-made machinery.

The organic carbon-based chemistry of the biological world, is layered on top of a more primitive mineral-based chemistry. During that prebiotic era, pixels took their first steps to becoming organized and gave birth to elementary systems of energy management. These early structures slowly incorporated carbon into their chemistry through synthesis of molecules, perhaps carbohydrates, which were able to act as energy stores. This transition lifted nature's ability to concentrate energy to a new level, because these high-energy products turned out to be more versatile chemical agents than their mineral forebears, and eventually took control over their creators. Yet even after the organic molecules had become the rulers of their new realm, the biosphere, their chemistry still involved minerals for a long time, reminding us that from the distant past the watery medium has remained the chronological continuum. The striated rock beds that bear stromatolite fossils are testimony to that early period when mineral and carbon chemistry were still intertwined. That time saw the dawn of biological evolution, which emerged out of simpler mechanical processes located in regions where earth and water were in osmotic contact. And so now in the present era, as then, organic matter owes its living quality to the pixels - those tiny, flickering energy quanta on the lowest level of all, which through their physical expression as water clusters became the sparks of life. This version of the story of early evolution tells us that the vital force of life is hidden in water.

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Appendix 1

Work Cycles and Boltzmann's Constant

The work cycle of the vapor pressure machine was published in Progress in Molecular and Subcellular Biology 12: 113-134 (1991), where details may be found. In summary, the cycle ABCD of Figure 1 represents the operation of a piston in a cylinder of which the walls contain an opening to permit the entry and exit of gas molecules. During the power stroke AB, the machine is in contact with the vapor above the first liquid reservoir, say, the pure solvent. During the step B to C, the piston does not move while the machine is equilibrated sequentially with the vapors above solutions of increasing concentrations of a non-volatile solute in the solvent, so that there is an incremental fall in the pressure inside the machine with each equilibration. During the return stroke CD, the machine is in contact with the vapor of the last of the series of solutions, let us say the second reservoir, of the lowest vapor pressure, and the piston is pushed back to its original position. The step D to A reverses the series of equilibrations, so that gas molecules enter the machine at constant volume increasing the pressure inside to the original value P_0 .

The work is delivered by the gas which is evaporated from the pure solvent reservoir at P_0 and returned to the solutions at lower vapor pressures. From Figure 1

$$W = (P_0 - P_1)(V_2 - V_1)$$
$$= (P_0 - P_1) c \Delta V kT / P_0$$

where P_1 is the vapor pressure of the second reservoir, c the concentration of molecules per unit volume in the pure solvent, ΔV the volume of liquid solvent that evaporates, k is Boltzmann's Constant and T temperature.

It is an experimental fact, described by Raoult's Law, that the fractional drop in pressure is given by the mole fraction of the solute in a solution and therefore

$$W = zkT \Delta V$$

where z is the concentration of solute molecules per unit volume in the second reservoir.

The cycle can also be performed by transferring the volume ΔV directly in liquid form from the first to the second reservoir using the osmotic machine. In this case, the walls of the cylinder transmit solvent but not solute while executing the cycle EFGH in Figure 2, that is, the walls function as semipermeable membranes. During the successive equilibration steps F to G, the pressure inside the machine falls continually because the pure solvent remains inside while placed in contact with the series of solutions which are at their respective lower pressures on the outside. Finally, after the pressure inside has fallen to P₂, the volume ΔV is returned to the second reservoir, giving the work done

$$\mathbf{W} = (\mathbf{P}_0 - \mathbf{P}_2) \Delta \mathbf{V}$$

Comparison with the work done by the vapor pressure machine gives

$$P_0 - P_2 = zkT$$

This well known result is van't Hoff's equation for a solution at pressure P_0 in equilibrium with a pure solvent reservoir at the lower pressure P_2 . It is sometimes quoted by thermodynamicists as showing the equivalence between the phenomena of vapor pressure reduction, as studied by Raoult, and osmotic pressure, as studied by van't Hoff.

During the return stroke of the osmotic machine GH however, the solvent inside is in equilibrium with the solution reservoir of solute concentration z at pressure P_1 outside. Using an equation analogous in form to van't Hoff's we write for this reversed osmotic situation

$$\mathbf{P}_1 - \mathbf{P}_2 = \mathbf{z}\mathbf{k}^{\prime}\mathbf{T}$$

Then because $P_1 < P_0$, k' < k.

Interested readers can check forward to Chapters 8 and 9 of TPM for an interpretation of the fall in the value of k from a structural perspective..



Figure 1. The Vapor Pressure Machine During the step AB the machine is open to the vapor of the pure solvent reservoir at its vapor pressure, P_0 , and expands its volume from V_1 to V_2 . From B to C, the machine is placed in contact with the vapor above a large number of solutions of increasing solute concentrations in succession and the cylinder is opened each time to allow a small amount of vapor to exit and the pressure to drop incrementally. During the step CD the machine is open to the vapor of the second reservoir which is the last solution of the series and therefore has the lowest vapor pressure, P_1 . From D to A, the large number of equilibration steps from B to C are reversed.



Figure 2. The Osmotic Machine During the step EF the machine is immersed in the pure solvent reservoir and expands its volume by the amount $\Box V$ at pressure P₀. From F to G, the machine is immersed in the series of solutions in succession and allowed to adjust to osmotic equilibrium each time. During the step GH the machine is immersed in the second reservoir at P₁, while executing the return stroke at the pressure P₂. From H to E, the sequence of equilibration steps F to G is reversed.

Appendix 2

Pressure and Tension Pixels

According to the arguments developed in Chapter 10, the equilibrium between two solutions in contact is a balance of four forces: -- two macroscopic forces operating in volumes greater than the pressure pixel, and two microscopic forces operating within clusters. Or simply

$$P_1 + Q_1 = P_2 + Q_2$$

where P_1 and P_2 are the macroscopic forces (with units of energy density) in solutions 1 and 2, and Q_1 and Q_2 are the microscopic forces. The macro- and micro-forces are opposite in sign, so under normal conditions P_1 and P_2 are pressures while Q_1 and Q_2 are tensions. The osmotic pressure is then given by

$$\mathbf{P}_1 - \mathbf{P}_2 = -(\mathbf{Q}_1 - \mathbf{Q}_2)$$

The volume of a cluster, u, is given by the Gas Law

$$P u = kT$$

so that at normal temperature and pressure u is about 40 cubic nm. In a pure solvent we can write $P_0 = ykT$, where y is the number of clusters per unit volume (cluster density), such that $y = 1/u_0$. In Chapter 10 we learnt that the presence of solute molecules increases the cluster concentration, because these molecules shorten the wavelength of the structure wave, so that for a solution of solute concentration, z, we can write

$$P = (z + y) kT$$

Although this expression refers to a single solution, it can be used to link any number of solutions as long as they possess the same energy per cluster, kT, for example rearrangement gives

$$P - P_0 = z kT$$

which is van't Hoff's equation describing the relationship between the pressure of a solution of solute concentration, z, in equilibrium with its solvent at pressure P_0 . In fact, the equation describes a P,V isotherm (Fig 1) analogous to that for gases used by Carnot to analyse a general heat machine, and is the basis of the osmotic machine introduced in Chapter 5.

As explained in Appendix 1, in contrast to gases solutions can have lowered values of k. In these cases the isotherm is displaced downwards, just as the P,V curve for a gas is displaced to lower values of P when the temperature is decreased.

A further contrast with gases is that liquids can go under tension and then the variables P, u and y take negative values (Fig 2). This mathematical consequence is the rationale for calling the unit of space defined by the volume, u, the "antipixel", and because its corresponding variable, Q, now takes positive values, the particle occupying it is internally under pressure.



Figure 1. Family of Equilibrium Curves The osmotic machine contains Z molecules of solute which cannot exit the machine, so the solute concentration of the solution inside is z = Z/V, when the machine has expanded to volume V. Curve A shows the pressure inside when the machine is immersed in the pure solvent reservoir at pressure P_1 (or in any solution reservoir provided that this reservoir is at the equilibrium pressure on the curve corresponding to its solute concentration). Curve B shows the pressure inside when the machine is immersed in the pure solvent under tension at the negative pressure P_2 (or in any solution at its corresponding equilibrium pressure also on curve B). P_1 and P_2 are the asymptotes to curves A and B as they approach large values of V.



Figure 2. Gas Law Relationship between Pressure and Pixel Size The solid portion of the Pu = kT hyperbola covering the range of pressures greater than P_1 corresponds to curves A and B of Figure 1. The dashed curve covering pressures from P_1 down to P_2 corresponds to curve B. It shows how the pixel size becomes negative for solutions under tension.