Power, Sex, Suicide

Mitochondria and the Meaning of Life

Part 2. The Vital Force: Proton Power and the Origin of Life

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About

Dr Nick Lane is a British biochemist and writer. He was awarded the first Provost's Venture Research Prize in the Department of Genetics, Evolution and Environment at **University College London**, where he is now a Reader in Evolutionary Biochemistry. Dr Lane's research deals with evolutionary biochemistry and bioenergetics, focusing on the origin of life and the evolution of complex cells. Dr Lane was a founding member of the UCL Consortium for Mitochondrial Research, and is leading the UCL Research Frontiers Origins of Life programme. He was awarded the 2011 BMC Research Award for Genetics, Genomics, Bioinformatics and Evolution, and the 2015 Biochemical Society Award for his sustained and diverse contribution to the molecular life sciences and the public understanding of science.

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Energy and life go hand in hand. If you stop breathing, you will not be able to generate the energy you need for staying alive and you'll be dead in a few minutes. Keep breathing. Now the oxygen in your breath is being transported to virtually every one of the 15 trillion cells in your body, where it is used to burn glucose in cellular respiration. You are a fantastically energetic machine. Gram per gram, even when sitting comfortably, you are converting 10,000 times more energy than the sun every second.

This sounds improbable, to put it mildly, so let's consider the numbers. The sun's luminosity is about 4 x 1026 watts and its total mass is 2 x 1030 kg. Over its projected lifetime, about 10 billion years, each gram of solar material will produce about 60 million kilojoules of energy. The generation of this energy is not explosive, however, but slow and steady, providing a uniform and long-lived rate of energy production. At any one moment, only a small proportion of the sun's vast mass is involved in nuclear fusions, and these reactions take place only in the dense core. This is why the sun can burn for so long. If you divide the luminosity of the sun by its mass, each gram of solar mass yields about 0.0002 milliwatts of energy, which is 0.0000002 joules of energy per gram per second (0.2 mJ/g/sec). Now let's assume that you weigh 70 kg, and if you are anything like me you will eat about 12,600 kilojoules (about 3,000 Calories) per day. Assuming barely 30% efficiency, converting this amount of energy (into heat or work or fat deposits) averages 2 millijoules per gram per second (2 mJ/g/sec) or about 2 milliwatts per gram – a factor of 10,000 greater than the sun. Some energetic bacteria, such as Azotobacter, generate as much as 10 joules per gram per second, out-performing the sun by a factor of 50 million.

At the microscopic level of cells, all life is animated, even the apparently sessile plants, fungi and bacteria. Cells whirr along, machine-like in the way that they channel energy into particular tasks, whether these are locomotion, replication, constructing cellular materials, or pumping molecules in and out of the cell. Like machines, cells are full of moving parts, and to move they need energy. Any form of life that can't generate its own energy is hard to distinguish from inanimate matter, at least in philosophical terms. Viruses only 'look' alive because they are organized in a way that suggests the hand of a designer, but they occupy a shadowy landscape between the living and the nonliving. They have all the information they need to replicate themselves, but must remain inert until they infect a cell, as they can only replicate themselves using the energy and cellular machinery of the infected cell. This means that viruses could not have been the first living things on Earth, nor could they have delivered life from outer space to our planet: they depend utterly on other living organisms and cannot exist without them. Their simplicity is not primitive, but a refined, pared-down complexity.

Despite its obvious importance to life, biological energy receives far less attention than it deserves. According to molecular biologists, life is all about information. Information is encoded in the genes, which spell out the instructions for building proteins, cells and bodies. The double helix of DNA, the stuff of genes, is an icon of our information age, and the discoverers of its structure, Watson and Crick, are household names. The reasons for this status are a mixture of the personal, the practical and the symbolic. Crick and Watson were brilliant and flamboyant, and unveiled the structure of DNA with the aplomb of conjurors. Watson's famous book narrating the discovery, The Double Helix, defined a generation and changed the way that science is perceived by the general public; and he has been an outspoken and passionate advocate of genetic research ever since. In practical terms, sequencing the codes of genes enables us to compare ourselves with other organisms and to peer into our own past, as well as the story of life. The human genome project is set to reveal untold secrets of the human condition, and gene therapy holds a candle of hope for people with crippling genetic diseases. But most of all, the gene is a potent symbol. We may argue over nature versus nurture, and rebel against the power of the genes; we may worry about genetically modified crops and the evils of cloning or designer babies; but whatever the rights and wrongs, we worry because we know deep down, viscerally, that genes are important.

Perhaps because molecular biology is so central to modern biology we pay lip service to the energy of life in the same way that we acknowledge the industrial revolution as a necessary precursor of the modern information age. Electrical power is so obviously essential for a computer to function that the point is almost too banal to be worth making. Computers are important because of their data-processing capacity, not because they are electronic. We may only appreciate the importance of a power supply when the batteries run out, and there's no plug to be seen. In the same way, energy is important to supply the needs of cells, but is plainly secondary to the information systems that control it and draw on it. Life without energy is dead, but energy without information to control it might seem as destructive as a volcano, an earthquake or an explosion. Or is it? The flood of life-giving rays from the sun suggests an uncontrolled flow of energy is not inevitably destructive.

In contrast to our worries over genetics, I wonder how many people exercise themselves over the sinister implications of bioenergetics. Its terminology is what the Soviets used to call obscurantist, as full of mysterious symbols as a wizard's robes. Even willing students of biochemistry are wary of terms like 'chemiosmotics' and 'proton-motive force'. Although the implications of these ideas may turn out to be as important as those of genetics, they are little known. The hero of bioenergetics, Peter Mitchell, who won the Nobel Prize for chemistry in 1978, is hardly a household name, even though he ought to be as well known as Watson and Crick. Unlike Watson and Crick, Mitchell was an eccentric and reclusive genius, who set up his own laboratory in an old country house in Cornwall, which he had renovated himself, following his own designs. At one time, his research was funded in part by the proceeds from a herd of dairy cows, and he even won a prize for the quality of his cream. His writings did not compete with Watson's Double Helix – besides the usual run of dry academic papers (even more obscure than usual in Mitchell's own case), he expounded his theories in two 'little grey books', published privately and circulated among a few interested professionals. His ideas can't be encapsulated in a visually arresting emblem like the double helix, redolent of the standing of science in society. Yet Mitchell was largely responsible for articulating and proving one of the very greatest insights in biology, a genuine and bizarre revolution that overturned long-cherished ideas. As the eminent molecular biologist Leslie Orgel put it "Not since Darwin has biology come up with an idea as counterintuitive as those of, say, Einstein, Heisenberg or Schrödinger… his contemporaries might well have asked 'Are you serious, Dr Mitchell?' "

Part 2 of this book is broadly about Mitchell's discovery of the way that life generates its energy, and the implications of his ideas for the origin of life. In later chapters, these ideas will enable us to see what the mitochondria did for us: why they are essential for the evolution of all higher forms of life. We'll see that the precise mechanism of energy generation is vital: it constrains the opportunities open to life, and it does so very differently in bacteria and eukaryotic cells. We'll see that the precise mechanism of energy generation precluded bacteria from ever evolving beyond bacteria – from ever becoming complex multicellular organisms – while at the same time it gave the eukaryotes unlimited possibilities to grow in size and sophistication, propelling them up a ramp of ascending complexity to the marvels that we see all around us. But this same mechanism of energy generation constrained the eukaryotes, too, albeit in utterly different ways. We'll see that sex, and even the origin of two sexes, is explained by the constraints of this same form of energy generation. And beyond that we'll see that our terminal decline into old age and death also stems from the small print of the contract that we signed with our mitochondria two billion years ago.

To understand all this, we first need to grasp the importance of Mitchell's insights into the energy of life. His ideas are simple enough in outline, but to feel their full force we'll need to look a little deeper into their details. To do this, we'll take a historical perspective, and as we go along we can savour the dilemmas, and the great minds that wrestled with them in the golden age of biochemistry, littered with Nobel Prizes. We'll follow the shining path of discovery, which showed how cells generate so much energy that they put the sun in the shade.

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