

# Power, Sex, Suicide

Mitochondria and the Meaning of Life

Part 3. Insider Deal: The Foundations of  
Complexity

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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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### Part 3. Insider Deal: The Foundations of Complexity

Here is a list of words to make an evolutionary biologist spill their beer: purpose, teleology, ramp of ascending complexity, non-Darwinian. All these terms are associated with a religious view of evolution – the sense that life was ‘programmed’ to evolve, to become more complex, to give rise to humanity on a smooth curve from the lowest animals to the angels, each approaching closer to God – the great ‘chain of being’. Such a view is popular not just with religious theorists, but nowadays with astrobiologists too. The idea that the laws of physics virtually summon life forth in the universe that we see around us is a comforting one, and evokes the idea that even human sentience may be an inevitable outcome of the workings of physics. I disagreed in Part 1, and we will consider the theme further in this Part by looking at the origin of biological complexity.

In Part 1, we observed that all complex multicellular organisms on earth are composed of eukaryotic cells; in contrast, bacteria have remained resolutely bacterial for the best part of four billion years. There is a chasm between bacterial and eukaryotic cells, and life elsewhere in the universe might well get stuck in the bacterial rut. We have seen that the eukaryotic cell was first formed in an unusual union between a bacterium and an archaeon. The question we’ll look into now is the ‘seeding’ of complexity in eukaryotes: what exactly is it about the eukaryotic cell that seems to encourage the evolution of complexity? However misleading the impression may be, surveying the grand canvas of evolution after the appearance of the eukaryotic cell does engender a sense of purpose. The idea of a great chain of being, striving to approach closer to God, is not accidental, even if it is wrong. In this Part, we’ll see that the seeds of complexity were sown by mitochondria, for once mitochondria existed, life was almost bound to become more complex. The drive towards greater complexity came from within, not from on high.

In his celebrated book *Chance and Necessity*, the committed atheist and Nobel Prize-winning molecular biologist Jacques Monod tackled the theme of purpose. Plainly, he said, it is pointless to discuss the heart without mentioning that it is a pump, whose function is to pump blood around the body. But that is to ascribe purpose. Worse, if we were to say that the heart evolved to pump blood, we would be committing the ultimate sin of teleology – the assignment of a forward-looking purpose, a predetermined endpoint to an evolutionary trajectory. But the heart could hardly have evolved ‘for’ anything else; if it didn’t evolve to pump blood, then it is truly a miracle that it happened to become so fine a pump. Monod’s point was that biology is full of purpose and apparent trajectories, and it is perverse to pretend they don’t exist; rather, we must explain them. The question we must answer is this: how does the operation of blind chance, a random mechanism without foresight, bring about the exquisitely refined and purposeful biological machines that we see all around us?

Darwin’s answer, of course, was natural selection. Blind chance serves only to generate random variation within a population. Selection is not blind, or at least not random: it selects for the overall fitness of an organism in its particular environment – the survival of the fittest. The survivors pass on their successful genetic constitution to their offspring. Thus any changes that improve the function of the heart at pumping blood will be passed on, while any that undermine it will be eliminated by selection. In each generation (in the wild) only a few per cent might survive to reproduce, and they will tend to be the luckiest or best adapted. Over many generations luck no doubt balances out, so natural selection tends to select the best adapted of the best adapted, inevitably refining function until other selective pressures balance out the tendency to change. Natural selection therefore works as a ratchet, which turns the operation of random variation into a trajectory. In retrospect this may well look like a ramp of ascending complexity.

Ultimately, biological fitness is written in the sequence of the genes, for they alone are passed on to the next generation (well, almost alone: mitochondria are, too). Over evolutionary time, alterations in the genetic sequence, subjected to round after round of natural selection, build tiny refinement upon tiny refinement, until finally erecting the

dizzying cathedral of biological complexity. Although Darwin knew nothing of genes, the genetic code at once suggests a mechanism for producing random variation in a population: mutations in the sequence of 'letters' in DNA can change the sequence of amino acids in proteins, which might have a positive, or a negative, or a neutral, effect on their function. Copying errors alone generate such variation. Each generation produces perhaps several hundred small changes in the DNA sequence (out of several billion letters), which may or may not affect fitness. Such small changes undoubtedly occur, and generate some of the raw material for the slow evolutionary change anticipated by Darwin. The gradual divergence in the sequence of genes of different species, over hundreds of millions of years, shows this process in action.

But small mutations are not the only way to bring about change in the genome (the complete library of genes in one organism), and the more we learn about genomics (the study of genomes), the less important small mutations seem to be. At the least, greater complexity demands more genes – the small bacterial genome could hardly code for a whole human being, still less the myriad genetic differences between individuals. Surveying species, there is a general correlation between the degree of complexity and the number of genes, if not the total DNA content. So where do all these extra genes come from? The answer is duplications of existing genes, or whole genomes, or from the union of two or more different genomes, or from the spread of repetitive DNA sequences – apparently 'selfish' replicators, which copy themselves throughout the genome, but may later be co-opted to serve some useful function (useful, that is, to the organism as a whole).

None of these processes is strictly Darwinian, in the sense of gradual, small refinements to an existing genome. Rather, they are large-scale, dramatic changes in the total DNA content – giant leaps across genetic space, transforming existing gene sequences at a single stroke – even if they generate the raw material for new genes, rather than the new genes themselves. Excepting these leaps across genetic space, the process is otherwise Darwinian. Changes to the genome are brought about in an essentially random manner, and then subjected to rounds of natural selection. Small changes hone

the sequence of new genes to new tasks. So long as the big jumps in DNA content do not generate an unworkable monster, they can be tolerated. If there is no benefit in having twice as much DNA, then we can be sure that natural selection will jettison it again – but if complex organisms need a lot of genes, then the elimination of superfluous DNA surely puts a ceiling on the maximum possible complexity, for it eliminates the raw material needed to form new genes.

This brings us back to the ramp of complexity. We have seen that there is a big discontinuity between bacteria and eukaryotes. It is remarkable that bacteria are still bacteria: while enormously varied and sophisticated in biochemical terms, they have resolutely failed to generate real morphological complexity in 4 billion years of evolution. In their size, shape and appearance, they can hardly be said to have evolved in any direction at all. In contrast, in half the time open to bacteria, the eukaryotes unquestionably ascended a ramp of complexity – they developed elaborate internal membrane systems, specialised organelles, complex cell cycles (rather than simple cell division), sex, huge genomes, phagocytosis, predatory behaviour, multicellularity, differentiation, large size, and finally spectacular feats of mechanical engineering: flight, sight, hearing, echolocation, brains, sentience. Insofar as this progression happened over time, it can reasonably be plotted out as a ramp of ascending complexity. So we are faced with bacteria, which have nearly unlimited biochemical diversity but no drive towards complexity, and eukaryotes, which have little biochemical diversity, but a marvellous flowering in the realm of bodily design.

When confronted with the divide between bacteria and eukaryotes, the Darwinian might reply “Ah, but the bacteria did generate complexity – they gave rise to the more complex eukaryotes, which in turn gave rise to many organisms of inordinately greater complexity.” This is true, but only in a sense, and here is the rub. The mitochondria, I shall argue, could only be derived by endosymbiosis – a union of two genomes in the same cell, or a giant leap across genetic space – and without mitochondria, the complex eukaryotic cell simply could not evolve. This viewpoint stems from the idea that the eukaryotic cell itself was forged in the merger that gave rise to mitochondria, and that

the possession of mitochondria is, or was in the past, a sine qua non of the eukaryotic condition. This picture differs from the mainstream view of the eukaryotic cell, so let's remind ourselves quickly why it matters.

In Part 1, we examined the origin of the eukaryotic cell, as surmised by Tom Cavalier-Smith, which best represents the mainstream view. To recapitulate, a prokaryotic cell (without a nucleus) lost its cell wall, perhaps through the action of an antibiotic produced by other bacteria, but survived the loss, as it already had an internal protein skeleton (cytoskeleton). The loss of the cell wall had profound consequences for the cell in terms of its lifestyle and manner of reproduction. It developed a nucleus and a complicated life cycle. Using its cytoskeleton to move around and change shape like an amoeba, it developed a new, predatory lifestyle, engulfing large particles of food such as whole bacteria by phagocytosis. In short, the first eukaryotic cell evolved its nucleus and its eukaryotic lifestyle by standard Darwinian evolution. At a relatively late stage, one such eukaryotic cell happened to engulf a purple bacterium, perhaps a parasite like Rickettsia. The internalised bacteria survived and eventually transmuted, by standard Darwinian evolution, into mitochondria.

Notice two things about this line of reasoning: first, it exhibits what we might call a Darwinian bias, in that it limits the importance attributed to the union of two dissimilar genomes, a basically non-Darwinian mode of evolution; and second, it limits the importance of mitochondria in this process. Mitochondria are incorporated into a fully functional eukaryotic cell, and are readily lost again in many primitive lines such as Giardia. Mitochondria, in this view, are an efficient means of generating energy, but no more nor less than that. The new cell simply had a Porsche engine fitted, in place of its old-fashioned milk-cart motor. I think this view gives little real insight into why all complex cells possess mitochondria, or conversely, why mitochondria are needed for the evolution of complexity.

Now consider the hydrogen hypothesis of Bill Martin and Miklos Müller, which we also discussed in Part 1. According to this radical hypothesis, a mutual chemical dependency

between two very different prokaryotic cells led to a close relationship between the two. Eventually one cell physically engulfed the other, combining two genomes within a single cell: a giant leap across genetic space to create a 'hopeful monster'. This genetic leap, in turn, set up a series of Darwinian selection pressures on the new entity, leading to a transfer of genes from the guest to the host. The critical point of the hydrogen hypothesis is that there never was a primitive eukaryote, one that supposedly possessed a nucleus and had a predatory lifestyle, but did not have any mitochondria. Rather, the first eukaryote was born of the union between two prokaryotes, a fundamentally non-Darwinian process – there was no halfway house.

Just look at Figure 5, a tree of life drawn in 1905 by the Russian biologist Konstantine Merezhkovskii, to see what an uncomfortable reversal of the standard branching tree of life this creates. There has been plenty of controversy over trees of life in the past, notably from Steven Jay Gould, who claimed that the Cambrian explosion inverted the usual tree. The Cambrian explosion refers to the great, and geologically sudden, proliferation of life around 560 million years ago. Later on, most of the major branches were ruthlessly pollarded, as whole phyla fell extinct. Daniel Dennett, in *Darwin's Dangerous Idea*, lambasts Gould's apparently radical evolutionary trees for being the same as any other evolutionary tree, except with distorted axes – a low-lying scrub bush, throwing up a few scraggly shoots, rather than a lofty tree of life. But there is no danger of this in Merezhkovskii's case. His evolutionary tree is a genuinely upside down. Here, the branches fuse, rather than bifurcate, to generate a new domain of life.

I'm not trying to cry revolution. There is nothing exceptional about these arguments, and symbiosis is part of the standard evolutionary canon, even if it is played down as a mechanism of generating novelty. For example, the late, great John Maynard Smith and Eörs Szathmáry, in their stimulating book *The Origins of Life*, argue that biological symbiosis is analogous to a motorbike, which is a symbiosis between a bicycle and the internal combustion engine. Even if we view this symbiosis as an advance, they say, with rather crusty humour, someone still had to invent the bicycle and the internal combustion engine first. Likewise in life, natural selection must invent the parts first, and symbiosis

just makes creative use of the available parts. Thus symbiosis is best explained in Darwinian terms.

All this is true, but it obscures the fact that some of the most profound evolutionary novelties are made possible only by symbiosis. Presumably, if we follow Maynard Smith and Szathmáry, if a bicycle and an internal combustion engine can evolve independently by natural selection, then so too, in principle, could the motorcycle. No doubt it's faster to evolve a motorcycle by shuffling existing components, but there is no fundamental reason why it should not have evolved anyway, given enough time, in the absence of symbiosis. In the case of the eukaryotic cell, I disagree. Left to themselves, I will argue, bacteria could not evolve into eukaryotes by natural selection alone: symbiosis was needed to bridge the gulf between bacteria and eukaryotes, and in particular a mitochondrial merger was necessary to sow the seeds of complexity. Without mitochondria, complex life is simply not possible, and without symbiosis, mitochondria are not possible – without the mitochondrial merger we would be left with bacteria and nothing but. Regardless of whether we consider symbiosis Darwinian or not, an understanding of why symbiotic mitochondria are necessary is paramount to an understanding of our own past, and our place in the universe.

In this Part, we will see why there is such a yawning chasm between the prokaryotes and the eukaryotes, and why this deep divide can only be bridged by symbiosis – it is next to impossible, given the mechanism of chemiosmotic energy production (discussed in Part 2) for eukaryotes to evolve by natural selection from prokaryotes. This is why bacteria are still bacteria, and why it is unlikely that life as we know it, based on cells, carbon chemistry and chemiosmosis, will progress beyond the bacterial level of complexity anywhere else in the universe. In Part 3, we'll see why mitochondria seeded complexity in the eukaryotes, placing them at the beginning of the ramp of ascending complexity; and in Part 4, we'll see why mitochondria impelled the eukaryotes onwards up the ramp.

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