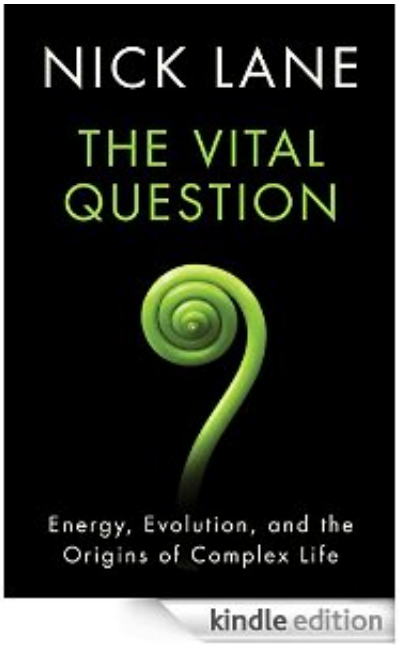
The vital question: Why is life the way it is?

April 1 2015, by John Hewitt



The Vital Question. Credit: Nick Lane

The Vital Question: Why is life the way it is? is a new book by Nick Lane that is due out on April 23rd. His question is not one for a static answer but rather one for a series of ever sharper explanations—explanations that apply at different resolutions to specific increments in the continuous chain of life, to the whole, and to generalizations of the process to other instances. For example, we might now boldly assert that an explanation for whether life evolved, or could have evolved, in the same way more than once on our own planet might also describe the same for any other planet. In reading Nick's staggeringly broad and

indelible new synthesis, we reach the conclusion that in it's most rough top-level form this explanation must be that any sufficiently advanced chemiosmotic geochemistry is indistinguishable from life.

Chemiosmosis refers to the movement of ions down an electrochemical gradient and across a selectively permeable membrane. This process was there at the begining in what is now widely held to be life's most diffuse state, the alkaline hydrothermal vent. The incidentals of a chemiosmotic lifestyle have continued to exert their influence at every major subsequent induction of new form since, each time further encapsulating both the primal elements of, and various substitutions in the original geochemistry. The explanation for why all life conserves energy in the form of proton gradients across membranes contains within itself the reason why one bacterium was ultimately able to get comfortable living inside another.

As Nick details, the constraints imposed on the evolution of life by chemiosmotic coupling ultimately dictate what he calls the greatest paradox in biology: that all life on earth is divided into prokaryotes, which lack morphological complexity, and eukaryotes, which share a massive number of perplexing traits never found in bacteria or archaea, including genome-wide sex, two sexes, and ageing. The gulf between the two families, and also among individual prokaryotic domains accordingly had less to do with adaptations for unique or extreme environments and more to do with the divergence of a group whose 'membranes were obliged to remain leaky for bioenergetic reasons.'

The main idea here is that without leaky membranes, the accumulation of protons inside a cell (or on the relavent side of a vent system operating at a specific pH) would quickly lead to a buildup of positive charge that opposes the influx of more H+. In this seemingly trivial description at least, activity across primitive membranes would

eventually grind to a halt. In recent times Lane and his group have taken to the computer to provide insight into some of these effects, running all kinds of simulations to vet their hypotheses. We might mention here that these same simplistic intuitions apply to ATP accumulation in mitochondria. If ATP is generated at a higher rate than it is used, respiration grinds to a halt through the action of various inhibitory feedbacks. Low ATP consumption drives higher membrane potentials to higher levels making it even harder to pump protons. The respiratory complexes therefore gradually back up with excess electrons and leak away free radicals.

Any planet with rock, water, and CO_2 has a more-or-less completed shopping list for life. Between 25 and 125°C biomass formation from H_2 and CO_2 is actually exergonic, ie. it should spontaneously be generated according to chemistry and geology provided two important kinetic barriers can be overcome. The trick for life is to clear the first barrier to get to formaldehyde or methanol without running the reaction straight through all the way to methane. If the latter happens, you miss the sweet spot where you score on life's shuffleboard, and all your efforts are dispersed away as methane gas.

Lane prefers to think of CO_2 as a lego brick that can be plucked from the air carbon-by-carbon to build up strongly bonded molecules (at least stronger than silicon). Oxygen, by the same token, is an ideal photosynthetic waste product since it can simply diffuse away as a gas. Anoxygenic photosynthesis, on the other hand, may use 'easier' electron donors than water, however, it begets cells that ultimately get encased in their own waste.

A key insight into chemiosmotic coupling of proton pumping to ATP generation is that, as Nick observes, it transcends chemistry. Other than the occasional fermentation, it's really the only game in town. For a cell, simple biochemical accounting tells us that from any single reaction 1

whole ATP must be spent to generate fewer than 2 whole ATPs for growth based on H2 and CO2. If it takes an ATP to make an ATP, normal chemistry gets you nowhere. The beauty of chemiosompsitc coupling is that it allows the cell to save up the fractional ATPs, the loose change, and put it all to good use.

It may not be surprising that bacteria typically respire on average about three times faster (per gram) than single-celled eukaryotes. What might be more surprising is that according to Lane's calculations, the average eukaryote has over 1200 times more energy available to it per gene than does the average prokaryote, and in some cases as much as 200,000 times as much. We might think of an organsim's characteristic 'Lane number"—its energy per gene—to be a kind of scale-free descriptor of its general behavior, perhaps in the way engineers use the so-called 'Reynold's number' to describe abstracted aerodynamic flow conditions.

When you take a look at the largest bacteria, you find that rather than evolving themselves a gigantic nuclear genome what they usually do is simply hoard thousands of copies of their standard-issue tiny bacterial genome. This situation is much different than for eukarytotes which instead use a larger nuclear genome while retaining the services of thousands of copies of minimal respiratory genomes stashed in their mitochondria. One major side effect in the transition to eukaryotes that is important for understanding differences in genome organization was their acquisition of tens of thousands introns. Just to note, by comparison, a typical circular bacterial genome may have just 30 mobile introns spread across some 4000 genes.

We have taken stock of some of the recent research on the origins the eukaryotic cell in a previous two part post. Namely, part I dealing specifically with endosymbionts and part II dealing with membranes and nuclear structure. Lane's grand synthesis of the issue, which is detailed throughout the second part of his book, is simply stunning in its reach.

It begins with the realization that the only practical way to explain the chimeric mix of bacterial- and archeael- derived structural proteins that now create the modern nucleus (the nuclear pores, lamins, and nucleolus) is to assume that the nucleus evolved after the acquisition of mitochondrial precursors and their subsequent bombardment of the host with new DNA. The nuclear pore complexes appear to have created the double nuclear membrane by flattening and riveting together the internalized lipid bags that would have spontaneously precipitated out of the cytoplasm after excess bacterial-style lipids were synthesized by the still unregulated genes that were transferred along from the newly endocytosed endosymbionts.

These new genes would have been made available for integrating into the host (presumably of archeal origin) along with rogue introns similarly transferred when the endosymbionts expired. In order to splice out these aquired introns (which eventually proved to be a feature rather than a bug) the relatively slow-operating spliceosomal machinery that had evolved from earlier bacterial precursor versions needed to buy some time to work. This was achieved by fencing out the ribosomes that were standing by ready to grab onto any newly transcribed RNA. This fence, conveniently, was the nuclear membrane.

While that description is obviously condensed and storified, the truth can not now be so far off. Many of the larger implications for organisms with mitochondrial symbionts were explored years ago by Lane in his book 'Power, Sex, Suicide, Mitochondria and the Meaning of Life." New insights gained since that time have profound implications for new technologies currently being bandied-about, like for example, mitochondrial transfer in the creation of three-parent embryos. In particular, this work highlights a central challenge in all higher endosymbiotic life: the need to get the right match between the nuclear and mitochondrial encoded protein subunits that make up the respiratory chain.

As mosaics built from two genomes, any changes to protein sequences that increase the distance through which electrons must travel to get to the next membrane reaction center in the respiratory chain will have predictable negative effects on fitness, or even fertilization outcome. Lane notes that beyond separations of about 14 angstroms, quantum tunneling of electrons gets becomes unlikely. For each angstrom increase between redox centers the speed of electron transfer will fall approximately 10-fold.

One of the more intriguing connections made in the book is when Lane revisits the older ideas on sex and gender originally laid out in the work of Ursula Mittwoch in light of what is now known about mitochondria. Whereas we usually imagine the Y chromosome as the main determinant of our gender, the Y might be better described as a transitory reservoir of genetic keys. In other words, a controller of an even more fundamental trigger of gender, namely, temperature and/or energy. Mittwoch describes gender determination across different species where it is independent of chromosomes and relies instead on direct thermal effects, or specific molecules and other environmental cues. In this view, mitochondria function in gender specification becomes more important, and reports of the imminent demise of the 'Y' may might not give us too much pause for concern.

Mittwoch also convincingly portrays several less commonly observed phenomena regarding lateralized growth retardation (or acceleration) during early development according to gender and successfully predicts the related effects seen in hermaphroditism. Today we regularly hear incredible stories that defy traditional understanding of gender genetics. One recent example was a woman walking around with 95% of her cells in possession of an XY male karyotype. With the aid of specific drugs to fast-track the maturation of her proto-uterus into a functional organ she was able to bear healthy child.

Birds have figured into the mitochondria picture in many unique ways by virtue of their genetic arrangement of having homozygous males and heterozygous females. The vibrancy of their colored plumage, among other things, can in some sense be viewed as a direct map of their mitochondrial function, particularly with regard to the pigments that are synthesized within them. Birds also are a prime species to look at the above mentioned problem of mitonuclear coadaptation. In specific instances there are other names applied here, names like mitonuclear mismatch, mitonuclear breakdown, or even hybrid breakdown. The latter, a subject to which we will hopefully return to say more about later, generates specific mitochondrial ills in the first generation which can be predictably cured in the second by backcrossing with an appropriately matched mitochondrial mate.

The influence of mitochondria on nearly every imaginable function, and dysfunction, of the cell now permeates new research. The primary determinants in many metabolic diseases, cancers, aging, and death are increasingly described in terms of specific energetic and respiratory behaviors of the cell. Nick leaves us with a simpler answer to the riddle of life, a quote from biophysicist Albert Szent-Györgyi "Life is nothing but an electron looking for a place to rest."

More information: The Vital Question: Energy, Evolution, and the Origins of Complex Life: www.amazon.com/The-Vital-Quest … -ebook/dp/B00OD8Z4JW