Mitochondria that ignite life: Science and imagination

Introduction

Imagination is perhaps the most powerful tool we have to create the future and to construct the history of the past, especially to explore the origins of life. About three or four years ago, I read an article in douban Internet popular science works: the 20th century's most great biology "Counter-intuitive" : chemical infiltration "[i], this paper construct, fascinating, including the principles which are very imaginative and want to be counter-intuitive and counter common sense. The proton pump in cell biology at the university are something boring as hell and now it be that colourful, just like opening a new door to me. "This article is by no means altogether original," writes Mance Reid, "there is a mass of data, theories and historical evidence derived from the books Oxygen and Mitochondria, by The British biochemist and popular science author Nick Lane." I couldn't help saying, Oh, Nick Lane is amazing.[ii]

The greatest biological discovery of the twentieth century (even to the extent of "scientific discovery") is credited to Watson and Crick's determination that biological genetic material is DNA and the biochemical mechanism by which DNA is passed on. This is a standard intuitive finding. "I think I've discovered the secret of life," Watson told Crick, less than two weeks after he had figured out the double helix structure of DNA. This breakthrough leap from structure to function came from Watson's intuition as a chemist and his genius imagination: molecular structure proclaimed molecular function. The double helix means each other's templates and infinite expansion. Pairwise pairing of four bases means accurate, lossless information replication. The simple syntax for translating from bases to amino acids implies a limited, succinct set of basic instructions.

The stability and precision of biological inheritance are fully explained in the structure of DNA, and from a biochemist's point of view, the jump is simple and clear enough to make anyone but Watson and Crick blow their brains out. The theory caught fire, washing out the brains of all researchers overnight and changing the landscape of biology.

For me, as a computer science student, the wonderful implications of this beautiful bold hypothesis are novel and rare. In my field of study, things are often simple and straightforward: we have a need, and we implement it. We are like a bunch of engineers in the skin of scientists, but in the real world of science, this kind of beautiful imagination and hypothesis is often crucial.

As an evolutionary biochemist at University College London, Nick Lane ponders big questions about life: How did it begin? And how does it survive? Why do we age and die? Why do we have sex? Regardless of the habits of our time, Lane examines these issues from an evolutionary genetics perspective.

He believes that our underlying biochemical mechanisms, particularly the energy production of living cells, may be the key to determining this question.

Lane has been trying to construct a new evolutionary theory that is complementary to the one that currently holds that genes compete for reproduction and survival. Energy limits, he argues, need to be taken into account to fully understand important changes in evolutionary history, such as the emergence of eukaryotes and multicellular organisms.

Life Ascending: The Ten Great Inventions of Evolution, by Lane, is a 2010 Royal Society

Science Book award winner. His 2015 book The Vital Question: Why Is Life The Way It Is has also been described as a "game-changing piece", "full of bold, critical ideas", etc. It provides a new, detailed model of the origin of life, explaining how life evolved from the chemical energy of deep-sea hydrothermal vents. According to Gates, The Vital Question is a "wonderful inquiry into The origin of life."

In "Power, Sex and Suicide", Mr Lane sums up a number of ideas about mitochondria and the meaning of life. The relationship between neutrality, energy constraints and mitochondria can turn our imaginations upside down.

Intuition and counterintuition

Intuitive and counterintuitive are common dichotomies in scientific discussions when describing a scientific theory or discovery. The term itself is not so scientific or rigorous, but its implications are profound.

Since it is not rigorous, I will not define it, just look at the example:

The simplest and most straightforward theory of intuition, there are many examples in ancient Greek science. For example, "The amount of water an object displaces is equal to its volume." Such as the postulates and simple theorems in Euclidean plane geometry. "Every right Angle is equal", "the straight line between two points is the shortest", the beginner of geometry, will think this is not nonsense. It is only when this nonsense is used as a weapon, gradually disintegrated, and other hideously complex theories proved, that we know what nonsense is good for. This is the most primitive characteristic of intuitive theory: it speaks for itself. Even in this budding wisdom, however, the seeds of counterintuitive theories were sown, such as Roche's geometry, which had broken new ground by merely "tampering" with a Euclidean postulate.

Background

The study of molecular biology has three macroscopic aspects: matter, information and energy. Matter is the common foundation, while information and energy are two different research directions. The brilliant achievement of DNA inheritance theory has completely focused the public's vision on the direction of information, and even the academic world itself has produced a deviation in understanding. In many people's minds, molecular biology is information biology.

The genome of an organism is a library of code. Life activity is the aggregation of these information interactions. The other big picture, cellular energetics (or energy biology), is very unfamiliar to the public. In fact, the understanding and discovery in this field in the 20th century is as subtle, profound and exciting as the information. The ups and downs, however, are very different from the boom-time scenes of information biology.

The central question of energy biology in the twentieth century is the chemical nature of cellular energy metabolism. Or the chemical nature and details of aerobic respiration. An intuitive sense of direction leads biologists to approach the subject from two directions in an attempt to complete the puzzle. It's like building a bridge from both ends. By the 1950s, the bridge seemed close to the solitaire point. The following results have been achieved:

* The nature of aerobic respiration is not different from that of aerobic combustion; both are oxidation-reduction reactions. The oxidant is oxygen, and the reducing agent can be simplified as

glucose.

* Unlike normal combustion, which is out of control naturally, aerobic breathing is controlled step by step in the cells. And it involves a complex set of biocatalysts.

* The site of aerobic respiration is the mitochondria in the cell. The mitochondrial inner membrane is embedded with a series of miniature catalytic factories: cytochrome enzyme protein complex. In these different catalytic plants, one electron is removed from the sugar, the intermediate molecules are gradually transferred, releasing chemical potential energy, and the oxygen takes these electrons and combines them with the hydrogen atoms in the sugar, gradually forming water.

* The common currency of energy in all living cells is adenosine triphosphate (ATP). It's a high-energy form of a molecule. The corresponding low energy form is ADP.

* All energy-consuming life activities consume ATP, convert it into ADP (and lose a phosphate group: P), and use the energy released by the conversion. The role of aerobic respiration, therefore, is the reverse of these activities: the production of energy that can be used to convert low-energy ADPs into high-energy ATPs.

* ATPase, another protein complex embedded in the inner membrane of mitochondria, is where ATP is produced. These micro-catalytic plants consume ADP and release ATP. And, in some cases, these plants also work in reverse, consuming ATP to make ADP.

Please note that I have divided the above results into two groups with blank lines. Lacking a step in between, cytochrome enzyme and ATPase are different protein complexes, which are physically isolated from each other in the mitochondrial inner membrane. Chemical reactions, on the molecular level, are 100% physical. So how does energy travel from cytochrome enzyme to ATPase? This is called a solitaire point.

The first group is molecular biochemistry, the second group is molecular biochemistry, and there is no chain in the middle. What's your intuition? Molecular biochemistry, of course. We need to find a vector molecule that is produced in the REDOX reaction at the cytochrome enzyme plant, consumed at the ATPase plant, that carries a high energy state of the chemical bond. Let's just call this vector X.

The energy biology of the '40s and' 50s was filled with optimism that the building was only a step away, and that scientists and research groups were in a race to find molecules of X. However, after 20 years of searching, more than a dozen candidate molecules have been proposed, and all of them have been rejected by research and experiments. In the process of searching, as the details of the whole process become more and more in-depth, a series of seemingly trivial, but inexplicable and disturbing questions emerge:

* We already know that ATP and ADP are both positive and negative forms of the universal currency of energy. In chemistry, a self-evident intuitive understanding is that high energy states are unstable, low energy states are stable, the so-called "water flows downwards." If pure ATP is placed in a solution outside the body of a living organism, it will naturally convert rapidly into ADP and release heat energy. However, in biological cells, the proportion of ATP and ADP is usually very high, with ATP accounting for more than 90%. This global high energy state requires

a continuous supply of energy to maintain. The intensity of aerobic respiration in cells, as measured by the rate of sugar and oxygen consumption, varies widely and can be quite debilitating. However, regardless of the intensity of aerobic respiration, the ATP ratio remains at a stable high level. It's like a huge rock hanging from a wall. It won't fall off whether you use it or not. It was an incomprehensible scene in the chemical world, but there was nothing to support it.

* The production of ATP and the consumption of glucose, this reaction equation, actually does not match in the actual measurement. Anyone who's taken high school chemistry should know what a balanced equation is. Molecules of A and molecules of B react to form molecules of C. Once balanced, the ratio is fixed. This is "mathematics," the fundamental truth of all science. However, measurements show that a molecule of glucose is completely oxidized to produce between 28 and 38 ATPs, any number is possible, but most of the time is near the lower limit. In the chemical reaction equation, what is 28 minus 38? You need integers for balance! This is another crazy anti-chemical scene. The measurement experiment is done over and over again, and the result is always the same.

* The energy and matter of a chemical reaction are conserved, that is, after the chain of reactions is established, the previous reaction takes place, and the subsequent reaction should be driven to take place simultaneously. Oxidation consumes glucose first, and then it drives it to produce ATP. This is called coupling, or coupling, in chemical terminology. The process of consuming glucose is coupled to the process of producing ATP (ignoring the mismatch problem mentioned earlier). Specific chemicals, however, can disrupt the stability of the coupling, which is called "uncoupling". The decoupling of aerobic respiration is universal, and the glucose oxidation process is completely normal and ATP production is completely halted when some substances are involved. It's like the pulley system breaks the belt, the front wheels are idling, the back wheels are ignored. Chemically, this is acceptable. Because decoupled substances always have a chemical property that can disrupt a link in the continuous chain of reactions (for example, if you have an X-medium molecule, some decoupled substance tends to bind to the X-medium to make it lose concentration and disrupt energy transfer, of course you can decouple.) But the problem now is that substances that have been experimentally shown to decoule aerobic respiration, such as salicylic acid (aspirin), diphtherithromycin and ecstasy, are so diverse in their chemical composition and properties that they have little in common. In their failure to find molecules of X, biologists had high hopes for decoupling, because once they discovered the common chemistry of the decoupled substances, they could probably deduce what the molecule of X was -- because that was the only unknown part of the bridge. The reality, however, is that the more decoupled substances are found, the less chemistry there is.

The genius American physicist and science expert Feynman once had a hilarious description of some of the difficulties in physics: "If you haven't been completely confused, you just don't understand the field." In the late fifties, the study of aerobic respiration and the mystery of the identity of the X molecule was exactly this scenario. The more thoroughly studied, the more contradictory and unreasonable the theory and reality become. Each hypothesis has untreatable painful feet, and no leading researcher knows exactly what went wrong. Optimism has given way to chaos.

Discoverer of chemical osmosis: Peter. Mitchell, from the inside out, reeks of eccentric genius. When Mitchell dropped his bombshell in 1961, he really had no basis for experimentation, which is the main reason why most academics instinctively did not accept him. However, this hypothesis, which pioneered a new system of its own, was based on Mitchell's in-depth analysis of known scientific facts and experimental results. Through his strange vision and misty language, more and more people realized that Mitchell's chemosmosis hypothesis was an odd-looking, but well-placed Mosaic that explained many of the mysteries of the study of aerobic respiration.

Sex is closely related to death

By death, I mean "programmed cell death".[iii] The process is genetically controlled, energy-consuming and entirely intentional. The damaged cells actively kill themselves, remove themselves from their place, and are replaced by new cells created by stem cells. Sexual intercourse performs the same task at the level of the individual organism. From the point of view of natural selection, the purpose of sexual intercourse is to promote natural selection by increasing differences between individuals and diversity within the population. From the point of view of natural selection, the differences between people go back to sexual intercourse. How many offspring will you leave? In humans, the problem is mostly male. Natural selection favors fewer men, but more sons and daughters. From a natural selection point of view, the goal of sex is to leave as many copies as possible of the best genes. This can increase the diversity within the population. There will be some very "effective" men in the population, and some "ineffective" men, and the "effective" men will get more opportunities. From a human point of view, this may not be nice. But that's what evolution is all about.

Mitochondria are closely related to aging

The mitochondria are actually bacteria that get mixed up in another cell. Exactly what the cell looks like and what it is is a matter of great debate, but it is almost certainly a very simple cell. Ultimately, the mitochondria become the energy factories of the cell. All the energy we need to survive comes from our mitochondria.[iv]

Survival comes at a price. Whatever you do, you must pay the price. To some extent, this price depends on the speed of our lives. If we have a fast pace of life, our physical strength will soon be exhausted. There is a strong correlation between metabolic rate (the rate at which we consume oxygen and digest food) and longevity. When conditions are good, we allocate more resources to sexual maturation and reproduction. But when conditions are not good, such as during a famine, we shift the focus from sexual intercourse, protein synthesis and weight gain to survival, putting reproduction on hold until the hard times are over. This switch has been the focus of aging research over the past decade. It's not just about metabolic rate, it's also about the way we prioritize our resources. Resources are allocated to either mating or survival. For simple organisms, genetic variation can increase their lifespan by two or three times. But it's much more difficult for complex creatures like us.

But we still have a strong desire to live longer. So what's the best strategy for prolonging life? Some studies have shown that calorie restriction seems to significantly extend the lifespan of mammals. Decades of studies have been conducted on rhesus monkeys, but the results have always been contradictory. Some studies have shown that this approach works well, extending lifespan by 30-40%. But some studies have shown that letting control rhesus monkeys eat as much as they like can actually harm their health or cause them to live longer than normal. So there's a lot of uncertainty in the design of these experiments. And most people don't want to cut calories by 40 percent. Of course, there are some people who would like to do this, but it's not clear that it would actually add years to life. I've heard of people who have osteoporosis from dieting and are more likely to break bones when they fall. So there are side effects.

Think of reptiles, turtles, etc., and they all live incredibly long lives. The reason is that their metabolic rate is extremely low. These animals live very long because they rarely move and their cells are rarely stressed. Birds are at the other extreme. They have a much higher metabolic rate than humans, have a higher body temperature and use more oxygen, but they live much longer than mammals of the same size and at the same metabolic rate. This seems to be because they have more and better quality mitochondria, which improve overall system function. The ratio of longevity to metabolic rate forms a U-shaped curve. This is very sobering.

Conclusion

This article is about the biology, genetic evolution, the imagination of mitochondria, science and some gossip and wander, think of where writes, are introduced from the double helix structure, tells the story of biological energy research background: a big difficulty and its story full of imagination of genius solver, then this paper expounds the main point of the "Power, Sex and Suicide". We saw many concepts, some of which may be common sense now, but at the time were contrary to the prevailing way of thinking, and some of which are still contrary to our common sense. We've seen how some of the wildest imaginings might work in science, but they might not be accepted at first. Here I do not want to make too many comments on imagination and scientific research, I just want to use the way of topic setting to arouse readers' thinking.

Reference

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ii Nick Lane. Power, Sex and Suicide

[iii] https://zhuanlan.zhihu.com/p/57197823

[iv] http://tech.hexun.com/2014-08-01/167166449.html