

## Adenosine Triphosphate, An introduction, A First and Second Year Blog

(for the week commencing the 26<sup>th</sup> of January 2020)

As scientists we rely very heavily on the peer-reviewed work done by other scientists, who in turn relied on the work done by their predecessors ..... and so on. (Please see my Blog "*Participants in the development of Molecular Biology, UK 1920-1970*" where I emphasise that we all stand on the shoulders of our predecessors.) As a child I had a very devout religious upbringing (and in fact entered the priesthood when I was 18 years of age) and, until many years later, it never occurred to me to even *try to understand* nor question what my religion taught me to believe.

As I read (present tense) material on Biology, *I get the same feeling about Biology*. There is an element of unchallenging acceptance about it. Textbooks seem to take for granted that we actually know what "life" is and how it arose. The fact however is that we appear to know neither 'fact'. Solar systems obey all the conditions required of a "living" entity, and indeed James Lovelock's "Gaia" hypothesis is now accepted by nearly all scientists. However, what is equally accepted by nearly all scientists is that there **is** a difference between plants, animals, fish, insects, etc on the one hand and let's say stones and Water on the other hand. For a novice Biologist such as myself therefore, I am very happy to make a distinction between a stone and a bird or a bee even though I cannot encapsulate that difference in a definition. The problem then becomes more complicated when we try to work out how life on Earth began. As a child I just accepted (because that is what I was taught) that "God" had created life on Earth, and then as an adult and as a scientist I just accepted that life had somehow *evolved* on Earth. However, I have recently been reading Michael Marshall's <http://www.bbc.com/earth/story/20161026-the-secret-of-how-life-on-earth-began> , and now I am not at all certain about how life on Earth 'evolved'. My acceptance of the thesis that a flash of lightning had somehow converted a soup of early chemicals into a life-form is now clearly just too naïve, because if that were so then scientists today would be able to create life forms from just Carbon, Oxygen, Hydrogen and Water – but it would appear that scientists have not been able to do that. However, that does not perturb me. I am very happy to accept that in time my colleagues in the world of science will soon (or will eventually) be able to do so.

In the olden days, Education in Europe and in the Middle East was heavily controlled by the Judaeo-Christian-Islamic culture<sup>1</sup>, and we European scientists used to define "life" in a way that made it clear that we had a pre-conception of what we wanted to include and what we wanted to exclude from the definition. This pre-conception derived from the old religious descriptions of "life" in the Bible, and this pre-conception was, of course, not shared by scientists in the Far East who knew nothing whatsoever about the Bible (any more than we in the West had any idea about what was contained in the Upanishads in India, or whatever was contained in the sacred books of the Burmese/Chinese/Laotian/Cambodian/Vietnamese/Korean/and other Far Eastern peoples). In modern times, we have rightly gradually moved away from religiously influenced pre-conceptions and beliefs, and moved more to things that can be *proved (or disproved) by scientific methodology*.

Even today, scientists are heavily influenced in their thought processes about "life", by the life forms that exist on Earth. However, there is no necessity *whatsoever* for life in other parts of the Universe to be Carbon, Oxygen and Water based. **There could easily be life forms that have evolved in a manner that is so 'alien' to our own life that we have no idea of what to look for to recognise other forms of "life"**<sup>2</sup>. **If as scientists we cannot explain 85% of the matter (the so-called 'dark matter') in the Universe, then we may have almost no chance (as yet) of understanding what 'life' actually is.**

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<sup>1</sup> From about 800-1200 AD, the Muslims were the main repository of virtually all European scientific knowledge. While we were dressing up in suits of armour and killing each other, they placed a huge value on *knowledge*, and people who could translate Greek and Latin and Hindi texts into Arabic were paid the equivalent of what Beckham and Ronaldo are paid today – and held in the same awe as footballers are today! The Roman Catholic Church controlled all education at that time, and when our biggest monasteries contained a few hundred books at most, the great library in Cordoba (the centre of European Islamic culture at the time) apparently contained some **400,000 books**. The Muslims made us look like ignorant little peasants (which at the time we were)!

<sup>2</sup> If you can get hold of a copy of Sir Fred Hoyle's "The Black Cloud", then I would strongly urge you to read it. Hoyle (a Fellow of St John's, Cambridge) was one the greatest Astronomers that this country has ever produced (he was the man who invented the phrase "Big Bang"), and in his book he puts forward a description of life that is as startling as it is revolutionary.

The things that we on Earth call “living things” may or may not have a non-material dimension to them and there is no scientific way of clarifying the issue – but it certainly **looks as though** plants/animals/ insects/etc are in *some* way different from pieces of rock/the oceans/water/fire/etc. It is possible to (and we do) divide things on our planet into two groups: living things and non-living things. One definition of a living thing is covered by the mnemonic “MRS GREN” where the capitals stand for

- **M**ovement - all living things move, even plants
- **R**espiration - getting energy from food
- **S**ensitivity - detecting changes in the surroundings
- **G**rowth - all living things grow
- **R**eproduction - making more living things of the same type
- **E**xcretion - getting rid of waste, and
- **N**utrition - taking in and using food

and another definition says that

“All groups of living organisms share several key characteristics or functions (viz.) order, sensitivity or response to stimuli, reproduction, adaptation, growth and development, regulation, homeostasis, and energy processing. When viewed together, these characteristics serve to define life.” (Source: <https://courses.lumenlearning.com/wm-biology2/chapter/properties-of-life/>)

but it is possible to argue that the Earth/the solar systems (and even the Universe itself) do all these things. However, if everything is considered to be “alive” then the distinction that we make about rocks versus animals would cease to have any meaning – and [the discussion about Biology therefore has to start with the assumption that there really is a difference between what are called living things and non-living things, or that for the purposes of the science of Biology that there is such a difference.](#)

What is incontrovertible is that living things have evolved over time. The evidence for this is in the “fossil record”. When a living thing dies, if it is an aquatic creature then its body falls to the bottom of the river/lake/sea/ocean where it lived and becomes covered by growing layers of mud/silt and becomes a “fossil”; and, if it had been a land-creature, then its body would have fallen to the earth and become covered in leaves/dust/mud/etc and would also have become “fossilised” (*and Susannah Maidment of the Natural History Museum in South Kensington believes that we have a fossil record of only a very few percent of all the species that have **actually** lived on the Earth.*) From radio-active dating we can date the different layers of rock in the Earth’s surface with considerable accuracy, and we can therefore use fossils to see how life forms have evolved through time. Sadly Professor Aubrey Manning (UCL and Merton, Oxford) who was a Zoologist and Professor of Natural History at Edinburgh University for a quarter of a century died last year (2018). He was a pioneering evolutionary geneticist, and if you can get hold of a copy of his dvd “Earth Story” then you could not get a better introduction to Biology (and Geology) than that seminal work<sup>3</sup>.

What troubles me more is that whilst I am very happy to accept that I evolved by accident from some sort of primordial soup, and that Darwin’s and Alfred Russell Wallace’s magnificent insight into the workings of natural selection account for the evolution of Man from an Ape some 200,000 years ago, nevertheless (rather like Sheldon in the “Big Bang Theory”) I am still not entirely clear as to what it is that distinguishes me from a computer. There are scientists who believe that “life” is merely the appearance that enormously sophisticated **material entities manifest**, and that there is no non-material element to such entities (and this lies behind the ‘Deus ex Machina’ mechanical contraptions built in some German towns in the 17<sup>th</sup> and 18<sup>th</sup> centuries). There is a similar debate as to whether or not there is such a thing as a non-corporeal “mind”, or whether entities such as consciousness/emotions/etc are merely the manifestation of the enormously complicated/sophisticated computer that we call the “brain”. (Margaret Boden has written an extremely interesting two volume essay called “Mind as Machine” on this subject – and the first volume *alone* runs to 700 pages!)

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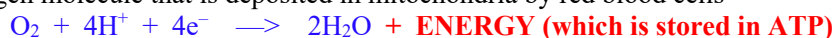
<sup>3</sup> Aubrey Manning did his Doctoral work under the renowned Nobel Laureate Niko Tinbergen who also supervised Richard Dawkins (the author of “The Selfish Gene”).

One of the greatest Astronomers that this country has ever produced was the late great Sir Fred Hoyle (Bingley Grammar School, Emmanuel Cambridge, and Plumian Professor of Astronomy at Cambridge). It was Hoyle who coined the term ‘Big Bang’, and conceived the idea of nuclear synthesis in 1946<sup>4</sup>, and with Fowler and the two Burbidges demonstrated that it needed the extreme temperatures and pressures generated by a Supernova<sup>5</sup> to create elements above Iron in the Periodic Table. He was cruelly robbed of his Nobel Prize (which was instead awarded to Fowler and Chandrasekar) because Hoyle had a habit of being blunt to the point of rudeness and, if I remember rightly, he was one of the few male scientists who stood up and pointed out that Hewish and Ryle should **not** have been awarded the Nobel Prize for the discovery of pulsars because it was the immeasurably modest Jocelyn Bell (now Dame Professor Jocelyn Bell Burnell) who had actually discovered pulsars – and indeed, Hewish had actually tried to **discourage** Bell from working on pulsars when Bell was his Doctoral student. How more unjust can you get! We men (even today) are such ignoble petty creatures when it comes to our female colleagues. Hoyle’s blunt Yorkshire outspoken-ness did not go down well with ‘the Establishment’, and Hoyle never received the recognition that he rightly deserved, and if I remember rightly, even Fowler admitted that everyone at Caltech had to be pushed into pursuing Hoyle’s ideas on nuclear synthesis.

Now, I do not even reach ankle high when I stand next to men like Fred Hoyle or women like Jocelyn Bell, and if you read (past tense) my recent Blogs on Mitosis and Meiosis, you will know that I know nothing whatsoever about Biology, but that I have started to study the subject in earnest in order to help my grandchildren with their GCSEs. I have as yet not formed any attachment to Physical Biology (and at the age of 80 I have almost no interest in birds and bees and bodies heaving rhythmically up and down) – **but I am becoming deeply interested in Genetic Biology.**

I do not as yet understand what exactly defines a ‘living entity’ nor why living things feel the necessity to promulgate/to ‘procreate’, but clearly they *do* feel this need<sup>6</sup>. After a few short weeks of studying Biology, I am only in the foothills of trying to understand the subject – but, rightly or wrongly, I have already formed one very strong conviction viz. from the way that I see things as a Chemist, everything in Genetic Biology depends on the chemical molecule Adenosine TriPhosphate (ATP) because every cell on Earth needs **ENERGY** to stay alive for even a very few moments (and well before a cell can divide and multiply and any gene can replicate, the cell **must** have energy), and apparently it is ATP that provides that energy. It seems to me therefore (*that in my current state of unenlightened ignorance*) it is not DNA that is the essence of life – **but that it is ATP that is the very essence of life!** DNA is merely about reproduction (the need for which I am still unclear).

In Marshall’s essay (quoted earlier), he describes the contributory work of many scientists including that of the late and not very well known 1978 Nobel Laureate in Chemistry Peter Mitchell<sup>7</sup> (1920-1992, Queen’s, Taunton / Jesus, Cambridge / and Edinburgh University) who was awarded his Nobel Prize for the discovery of the chemi-osmotic mechanism of ATP synthesis. Apparently, in order to *literally* turn the molecular ‘wheels’ that convert ADP into ATP, every mitochondrion needs a proton gradient between the fluid in the Intermembrane Space and the Inner Matrix of a cell, and the ultimate recipient in the electron ‘pass-the-parcel’ chain is an Oxygen molecule that is deposited in mitochondria by red blood cells



and it is this process that provides the energy required by cells<sup>8</sup>.

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<sup>4</sup> The Hoyle/Fowler 1960 paper “Nucleosynthesis in Massive Stars and Supernovae” has stood unread on a bookshelf in my Study for more than half a century because I just do not understand enough of the Mathematics therein.

<sup>5</sup> “Supernova” is the singular form of the noun, and “Supernovae” is the plural form.

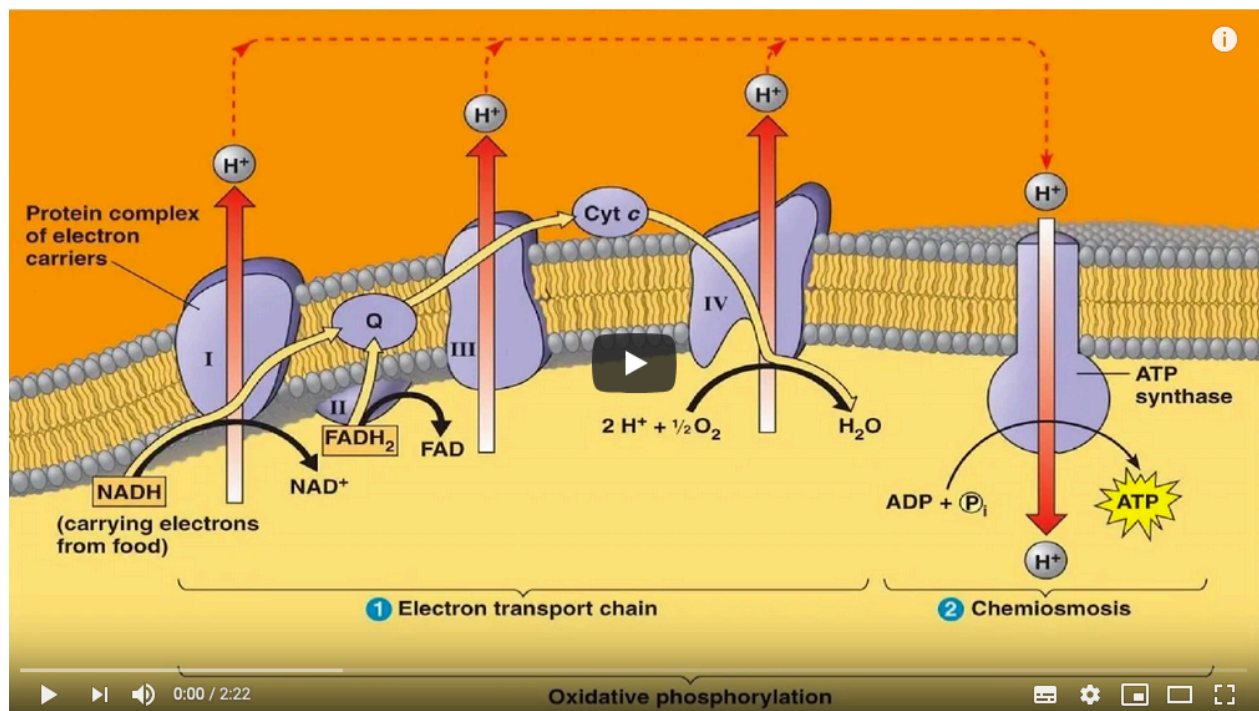
<sup>6</sup> Perhaps I should go back and re-read Dawkins’ “The Selfish Gene”. In the late 1970s I sat next to him in a plane coming back from California where one of the West Coast Universities had just awarded him a prize, and when I got back to England I bought his book and read it – but that was *half a century ago* and I have forgotten the details of his thesis. When I have learnt a bit more about Biology I will re-read the book (perhaps in my 2021 Summer hols).

<sup>7</sup> Whose famous uncle, Sir Godfrey Mitchell, was the man who created the UK Construction company “Wimpey”.

<sup>8</sup> “The electron transport chain (ETC) is a process in which the NADH and FADH<sub>2</sub> produced during glycolysis, β-oxidation, and other catabolic processes are oxidised thus releasing energy in the form of ATP. The mechanism by which ATP is formed in the ETC is called chemiosmotic phosphorylation” (Source: [Chemistry Libre Texts](#)) – and that is where Peter Mitchell comes in.

However, despite Mitchell's enormous contribution (and his Nobel Prize), one should not ignore the work of Otto Meyerhof and his colleagues Lipmann/Ochoa/Kalckar/and Belitzer in this field. There are many videos on [Oxidative Phosphorylation](#) and the [Electron Transport Chain](#) and Chemiosmosis on *youtube*, and I attach hereto a slide by "EDGE" – but there are much longer and more informative explanations on *youtube* (e.g. those by the exceedingly good [Khan Academy](#), and a short video with *excellent* graphics by [North Dakota State University](#) on the proton gradient, and one by [Harvard Biovision](#) on the F<sub>0</sub>-F<sub>1</sub> complex).

If you want to become a Doctor/Dentist/or anything in Medicine, then you **must** know the workings of the Electron Transport Chain and the F<sub>0</sub>-F<sub>1</sub> complex intimately. **The provision of energy to a cell is (in my opinion) absolutely fundamental to all life forms as we on Earth know them.**



Source: <https://www.youtube.com/watch?v=8XISfi7OpzY>

As yet I understand hardly anything about the details of these topics, but it looks as though the smattering of Chemistry that I possess will help me to understand the mechanisms involved. However, at this stage I would caution you not to overemphasise the importance of DNA (which rightly receives almost universal adulation), but instead I would urge you to pay slightly more attention to the humble Cinderella chemical molecule **ATP**, which ought to be allowed to don its glass slippers and attend the ball. The Nobel Committee has made some notable errors in the past (but luckily not many), and similarly *it would be unfair to ATP if scientists were to accord it less credit than it is rightly due*. (I rather feel as though an outsider should don gladiatorial armour and go forth and do battle for the honour of poor little neglected ATP, and that is what I am now doing.)

I am beginning to quite like Biology – but then how can you not like any of man's intellectual pursuits. Man is not even a speck of dust in the immensity of the Universe, and yet with our puny miniscule brains we are desperate to try to understand the workings of everything. **Goodness me, what a noble endeavour!**