Docosahexaenoic Acid and Cerebral Evolution: Past Present and Future.

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The introduction to evolution as dictated by the conditions of existence:

600 million years ago, the evolution of the brain and nervous system originated in the marine environment in a rich supply of docosahexaenoic acid (DHA). This essential fatty acid has been conserved since then for the structure and function of neurological and visual membranes. It is the major ω3 component of the inner cell membrane lipids of the brain[1] and constitutes some 50% or more of the fatty acid component of the photoreceptor membranes where rhodopsin sits with vitamin A as the photon sensitive system[2]. The origins of both vitamin A and DHA have their parenting in the photosynthesis of plants. For the first 3.0 - 2.5 billion years or more since life evolved, algal photosynthetic life dominated the proto oceans of the planet. They converted sunlight into carbohydrates, proteins, lipids and more. Some 600 million years ago, the oxygen tension had risen above the Pasteur point and air breathing systems became thermodynamically possible. An explosion of evolution took place and within a short period of geological time, all 32 phyla known today had appeared on the planet. The trick used by the first primitive air breathing systems was to convert sunlight not into carbohydrate and proteins but into electricity. This was achieved by the combination of rhodopsin, vitamin A and DHA.

The conservation of brain chemistry but not size.

The brain and indeed the photo receptor, is a fat rich organ in which 60% of its structural material is lipid. DHA is selectively taken up by the brain[3] and concentrated in synapses and photoreceptors. Andrew Sinclair and I found that in all 42 mammalian species studied, DHA was the major component of the fatty acids in neural cell membranes (Figure 1) and photoreceptors despite wide variations in diet and liver lipid stores (figure 2)[3]. This high degree of conservation implies DHA has a 600 million year track record in neural and visual function. Interestingly, the difference between species is not the chemistry but the extent to which the brain is developed[4,5]. This difference, combined with the animal experiments showing deficiency of brain DHA[6] induced cognitive[7] and visual loss[8], led to the idea that a rich source of DHA would have provided a selective advantage for cerebral expansion. The conservation of DHA is all the more remarkable because its immediate precursor would, by force of the metabolic synthetic sequence, have been more abundant[9]. It has the same 22 carbon chain length but one less double bond (C22:5ω3)(see Figure 3). Yet despite it being easier to synthesise and less susceptible to peroxidation, the C22:5ω3 has not been found to replace DHA in the photoreceptor or synapses of the fish, amphibia, reptiles or mammals so far studied.

Odd things about the savannah hypothesis for the origin of H. sapiens.

Originating from Raymond Dart early last century and adhered to this day, the conventional view was that humans evolved on the hot, dry savannahs of Africa where competition with the top carnivores furnished the selective pressure to evolve a large brain. Upright stance evolved out of the need to stand up right to throw spears at animals. The success in killing large animals was a prerequisite for the selection pressure necessary for cerebral expansion. Having lived and worked in East Africa for several

years and experiencing its contrasting peoples, wild life and geography, this again was a curiosity to me. Hunting big game in Africa, whether with rifle or camera, required that you crawled on the ground to get as close as you could. Darwin comments on Aboriginal hunting prowess in his "Voyage Around the World" that "crawling after wild animals, they could conceal themselves on almost bare ground". It is difficult to conceive how anyone who has worked in Africa could draw the conclusion that standing up to chase wild animals was a good idea!

Hairlessness is another feature which we share with the marine mammals in contrast to the dry savannah species. Richard Dawkins on a BBC programme, claimed hairlessness evolved because males preferred copulating with the less hairy females. Using the Dawkins idea of logic, I would guess that the sight of the men all copulating only with the naked female would have elicited some kind of a response. As the hairy women would have undoubtedly been the stronger, I would not fancy her chances in the Dawkins sexist world of evolution. Indeed, the macho concept of humans killing and copulating their way to cerebral expansion has a remarkable Lamarkian feel. There is little if any science base to these notions.

Physiological inconsistencies

Sir Alistair Hardy had a different view[10] . Hardy suggested that the line which came down to humans, may have had an aquatic phase with wading and swimming accounting for up right stance and hairlessness from the familiarity with the aquatic habitat. Again , based on the similarity to the marine mammals, he argued that we share a layer of subcutaneous fat and moreover human babies are born with fat sufficient for buoyancy, consistent with their ability to swim after birth. Whilst being born knowing how to swim, they have to learn to walk some several years later. Interestingly, Dolphins have up right stance. They can and do walk on water on their tails. This physiological contrast with the land based animals was followed up by Elaine Morgan who has commented extensively in her books on the naivety of the savannah hypothesis and its inconsistency with human physiology[11],[12]. Yet undaunted, the paleonanthropologist response was to simply ignore both Hardy and Morgan. Elaine herself felt that their deliberate silence was explained by their lack of a logical response[13].

Personal demonstration of the inconsistency

I came to question the savannah view when working in East Africa in the 1960s and 70s. My first concern with the Savannah hypothesis came on my first foot safari when my companion Neil Casperd and I, became severely dehydrated. To make matters worse, at the end of the day, we had to climb a 2,000 foot escarpment to return to our base. Never did water taste so good. Suffering with serious nausea, we lay down and drank straight from the Jerry cans. We returned the following week with physiologists and found we were loosing water at the rate of 1.5 litres per hour on the savannah. That suggested to me the savannah might be an inhospitable habitat for a primate with a high requirement for water to keep cool. Dick Taylor and others at that time were demonstrating that the physiology of savannah species was devoted to extreme water conservation[14]. They allowed their body temperatures to rise in the day and fall at night rather than waste precious water in evaporation to keep cool. They also had lung and intestinal adaptations to avoid water loss. Humans are inconsistent as they loose water by the litre on the savannahs!

Food selection has also been addressed by several authors[15],[16],[17] with many authors emphasising meat eating. However, a most serious criticism against the savannah hypothesis arose from our discovery that the savannah food chain and its meat in particular, is a very poor source of DHA. The large mammals

accumulated the plant essential fatty acids but their chain elongation and desaturation proves seemed to come to stop at docosapentaenoic acid (ω3). In their muscle and liver stores there was relatively little DHA[18]. The richest source of DHA is the marine food chain[19]. It was during this time, that I and my colleagues found the biochemistry questioned the savannah hypothesis. Some years later, Stephen Cunnane drew my attention to the writings of Hardy and Morgan. The physiology and the biochemistry dovetailed scientifically.

Iodine adds further support for a coastal origin

Another nutrient which is richest in sea foods and disadvantaged inland is iodine. According to WHO, 1.6 billion people are at risk to iodine deficiency disease today. These are all inland and flood plain people. In Indonesia, where I wrote a report for Indonesian Government and WHO in 1992, there were 60% of the school children with palpable goitre. There were 1.5 million, severely mentally retarded children and 800,000 cretins. This problem was all inland. There was no goitre, cretinism or mental retardation that I observed, in the fishing villages. A similar situation was described in India at a subsequent conference on Nutrition and the Brain in New Dehli organised by Gopalan.

In classical Darwinian terms the evolutionary advantage of the chemistry of the marine food chain would have been enormous and not just confined to DHA. Indeed, Thompson has analysed data which suggests that Neanderthals may have suffered from iodine deficiency. Many of the facial and skeletal structures are similar to that seen in cretinism. He moreover suggests that iodine deficiency would have restricted human evolution on inland regions.[20]

The universal degenerative evolution of the brain in land based mammals.

Another piece of evidence which convinced me of the fallacy of the savannah hypothesis was that the brain/body weight ratio of all land species diminishes logarithmically as they increased body size. The rhinoceros reaches a one ton of body weight by four years of age. The animal obtains all the protein, calories and minerals it needs to support this prodigious rate of body growth from the simplest food resource, namely grass. It has only a tiny brain – less than 0.05% of its body weight. Small mammals such as the squirrel or capuchin monkey have 2.1-2.3% of their body as brain. The chimpanzee has about 0.45%. The gorilla, with a larger body size has actually less brain and a smaller proportion of only 0.25%. All the marine mammals are far in advance of the land mammals. In a 70 Kg human with 1,3 Kg brain, the proportion is 1.8% and the only species which comes close to that is the dolphin at 1.1%.[4]. The dolphin has a quite different brain design to humans but none the less, there is no large land mammal which comes remotely close to it.

Arachidonic acid is also required:

The problem with the marine food chain is that it is dominated by ω3 fatty acids[21]. Both arachidonic (C20:4ω6) and docosahexaenoc (C22:6ω3) acids are used exclusively in the brain in roughly similar proportions[22]. So whilst land mammals have a problem accessing DHA, the marine mammals have a problem with AA. However, this simplistic rule breaks down in the tropics where the marine and indeed fresh water products contain substantial amounts of arachidonic acid. This distinction applies to the East Coast of Africa and the Rift Valley lakes, which we have studied[23],[24].

Absence of fossil evidence of living beside water is contrary to a coastal/lacustrine habitat.

One of the few criticisms the paleoanthropolgists voiced about the coastal origin of H. sapiens was that there was no fossil evidence. That seemed to be the end of the story. The fact that coastlines, lakes and rivers have been changing with time and that the Olduvai gorge was a river bed, did not seem to count. As it happens the large majority of the fossils discovered were in the Rift Valley or Chad where at the time they were living, they were beside inland seas, lakes or rivers. According to the geophysicist Leigh Broadhurst, the Gulf of Aden and Red Sea was in the process of creating an ocean down the African valleys when tectonic plate movements isolated the Rift Valley. None the less, the Rift Valley is still dotted with very large lakes. Studies on Rift Valley fishing communities by Claudio Galli and ourselves, testify to the arachidonic and docosahexaenoic acid value of the lake fish as well as he superior cardio-vascular risk factors of these lake fishing peoples. In addition, their status for plasma fatty acids with regard to both AA and DHA was substantially greater than that of their inland cousins with little access to fish, and greater than the Europeans living in East Africa at the time[21,22]. Indeed, the blood cholesterol levels of the El Molo children and also the blood pressures, which Claudio and we separately studied, remained steady as they grew up. The blood cholesterols of European children living in East Africa, although the same at in their first year of age, rose with age and the separation reached a statistically significant level above the El Molo children in the 6-8 year age group[25]. The El Molo and European children were born the same but their dietary practices differentiated their cardiovascular risk factors in childhood.

Consequently, we developed the hypothesis that the cerebral expansion which led to the evolution of H. sapiens occurred in association with the use of sea and lacustrine foods. The paleonthropologists would not consider this evidence until the Dual Congress in South Africa in 1998 where Professor Tobias, a world leader in paleoanthropology invited presentations on the topic. In December 1998, Professor Tobias wrote "Where ever humans were evolving they had to have water to drink" and of the savannah hypothesis he said 'We were all profoundly and unutterably wrong!'[26,27] He concedes that the paleontological evidence fits far better with an evolutionary history at the water's edge. Apart from explaining cerebral expansion, it is consistent with the water crossings as early as 800,000 years ago and Chris Stringer's view of way the planet was populated around coast-lines[28]. They were certainly not eating Cape buffalo as they made this journey. Of course, the conventional paleoanthropologists may eventually find this type of evidence convincing. As so often happens in a paradigm change, they will claim it as their own idea. The signs of this happening appeared in the New Scientists report on the discovery of a 7 million year old skull in the deserts of Chad. Today, the Djurab desert is little more than sand as far as the eye can see. However, 6-7 million years ago it was forested with abundant game and "fish were plentiful" in the nearby lakes. "Some experts have already questioned the conventional wisdom that hominin evolution was somehow triggered by the appearance of savannah grasslands …. "The new finds confirm that this scenario must be thrown out".[29]

Recent fossil discoveries provide incontrovertible evidence of intense exploitation of the marine food chain dating to 120,000 - 80,000 years ago, which fits with the period of the recent cerebral expansion and the appearance of humans[30,31]. Discoveries in the coral reefs at the Red Sea coastline of Eritrea similarly provide evidence of early human locations at the coast, again coincident with evidence of habitation by early humans[32]. Moreover, the origins of civilisations were geographically located beside water. Indeed, the first written languages, which heralded the beginnings of civilisations, were beside water. Some have said this juxtaposition was for trade. But before trade could begin, people were fishing and utilising the best resources of both land and water. They built boats as we have seen as early as 800,000 years ago[33]. All of that, including the brain, had to come first. Even recent history from the Egyptians, Minoans, Greeks, Romans, 1492 and dare one say it, Rule Britannia, were deeply embedded in origins that started with harvesting the products of the lakes, rivers and seas. The Museum of London

contains exhibits of amphora, which the Romans used to import fish oils from Spain. At the turn of last century, the bars in the East end of London served oysters free with the beer as they were so plentiful along the Thames shore line. The productivity of the marine and fresh water systems was so rich and the oceans so vast, that they were taken for granted. Whilst humans developed land based agriculture 10,000 years ago we are still hunting and gathering the sea foods with the same primitive philosophy that dates back to unrecorded history. The continuation of this naïve policy has been to our cost in the death by pollution of the rivers and estuaries and the decimation of marine resources.

DHA could be obtained from buffalo brains

There is a further and interesting comment on the macho view of human evolution – what Robert Ardrey called "The Killer Ape"[34]. In support of the savannah hypothesis, Loren Cordain maintains that DHA could have been provided on the savannahs from the brains of the animals they killed[13]. Bear in mind the very small size of the brains of the savannah species and one wonders if this was enough? Moreover, it is a formidable task to cut through a rhinoceros's or buffalo's skull to get at the brain and then the balance between meat and brain would be about 1,000 to 1. So there would not be much there. Bear in mind that the journey back to camp where the women and children were would at the high temperatures of the savannahs, have resulted in considerable deterioration with precious little to share around the community.

My argument is not that people did not eat meat but that a coastal/estuarine habitat would have provided a massive competitive advantage in the provision of DHA and trace elements. By contrast with the savannah, the coast lines would have been extremely rich and particularly so in food rich in DHA. Land mammals migrated from land to the oceans over a 60 million year period. This migration came to an end about 10-5 million years ago by which time, these originally land based species had become fully aquatic. The end of the migration left the coastal and estuarine resources empty. Now Nature exploited all possible extremes in search of food – the desert rat, polar bear, snow leopard, the tree eating giraffe to name but a few extreme examples. It is unthinkable that the vacated coastal resources would have been left vacant. It may be a coincidence but it is noteworthy that the vacation of the coastal resources occurred at the time the geneticists tell us the line that came to us humans separated from the great apes. Bearing in mind that we separated. That means we were in a geographically different location so we did not continue to interbreed. The coastlines would have provided for that requirement.

Forget about the macho men it is the women and children who are important.

This brings us to another key point. It is not the macho men that matter. It is the women, the embryo, fetus and new born child that need the proper nourishment. Seventy percent of the brain cells in the human divide before birth and the remainder are largely in place by 2 years of age. The post-natal period would have been encouraged in that latter phase by the mother's milk which itself would have been rich in DHA.

The women would be all important biologically to secure the increasing supply of neural nutrients so that brain size evolved in harmony with body size. A coastal or best an estuarine habitat would enable even heavily pregnant women to wander around the coast and gather as much food as she needed. Indeed, the children would have done the same and enjoyed the fun as they do today, of searching rocky pools for crabs and fish as the tide receded. . If the men brought back some meat that would be well and good. But it would not matter one little bit if their macho efforts went unrewarded. A coastal habitat would not have furnished the challenge of a struggle for survival. It would have furnished the rich environment that would have stimulated the evolution and growth of the brain. This idea is not a concept

based on the need to evolve a large brain because of some challenge. It is an evidence based account that the brain requires specific constituents for growth and function. Depletion leads to the degenerative evolution as seen in the large land mammals. Provision, allows body size and brain size to expand in harmony. Indeed, there is now evidence that DHA is not only a ligand for the retinoid X receptor, an obligatory step in communicating to the genome[35], but it also stimulates neural gene expression in a manner consistent with neural growth and development[36].

DHA driven brain evolution supported by molecular biology and evidence on gene expression.

The importance of the relationship between DHA and gene expression and its 600 million year conservation, is that it explains a puzzle, which only really can now be understood with the solution of the human genome. With only 35,000 genes discovered instead of an expected 150,000 Craig Ventor, head of the USA genome project declared that we can forget about genetic determinism: there are not enough genes to explain human behaviour. It is the way the genome is influenced and its expression controlled that matters. Like DHA, many of our genes have been conserved over great periods of geological time. The Puffer Fish genome has recently been published[37]. Professor Ted Tuddenham of Imperial College described in a recent lecture to the McCarrison Society how its blood clotting factors are the same as in humans and share much the same coding which stretches from 50-80% identity. In other words the essence of our coagulation factors was in place 450 million years ago. He said that the explanation for the epidemic of thrombosis which began last century, cannot be explained by a change in genes. It is a change in diet operating on ancient genes that has done the trick. Our genome is only about 1.5% different from the chimpanzee. It is quite plausible that again the change in diet was a key to the ultimate change from a chimpanzee to a human. In view of the experimental and gene expression evidence, nothing more complex is needed.

The evidence for the requirement of the brain for DHA is now robust and confirmed in two, joint International Expert Consultations by FAO and WHO on "The Role of Dietary Fats and Oils in Human Nutrition" (1978, 1994). Animal experiments have shown that deficiency of essential fatty acids during early development resulted in reduced cognitive and visual function, which was later irreversible[38]. DHA is the major ω3 fatty acids in neural and other cell membranes (see figure 2). Deficiency of ω3 fatty acids during brain development has been found to result in primate behavioural abnormality[39], loss of cognitive function in rodents[40] and primates[41] and in the extreme case, in brain hemorrhage and death in chickens[42]. Feeding infants on formula without DHA result in a loss of DHA from the infant's circulating triglycerides, plasma and red cell phosphoglycerides and even infant brain phosphoglycerrdes[43]. Maternal milk replacement formulae with and without AA and DHA have provided further evidence of the requirement for developing cognitive and visual function in the human infant[44],[45],[46] Human studies in peroxisomal disease indicate the adverse effects of deficiency on very early neural development. During treatment with DHA, Manuela Martinez witnessed MRI evidence of myelination in response to DHA supplementation[47].

In the contemporary health scene, there is now evidence of a sharp, recent rise in mental ill health, which is following from country to country the previous rise in death from coronary heart disease. Dr. Joe Hibbeln of the National Institutes of Health in the USA points to the correlations for the increase in mental ill health and depression inversely with fish intakes[48],[49],[50]. The rise in mental ill health he also says is amongst young people born after 1950. It is predicted to be in the top three burdens of ill health by the year 2020 (www.globalburdenhealth.org).

Conclusion and implications

The implications of this new paradigm of human evolution are wide reaching. If food was only gathered because of its protein and calorific value, the past and future food policies would only be concerned with procurement of such foods. However, if as we suggested, lipids were determinants of brain evolution and function then it is a very different story, which will requite substantial adjustments in education, food policy and academic pursuits[51].

Last century, protein and body growth dominated nutrition thinking. However, this new body of evidence on lipid and neural requirement says that marine and lacustrine foods from the beginning of time played a critical role in the supply of brain and vascular specific nutrients. For 99.8% of our time we were eating wild foods largely exploiting the extremely rich lacustrine and coastal resources and making use of the best of both worlds of surf and turf. This means that sea and lake foods are not important for protein. Their importance lies in the DHA and trace elements.

During the last century there has been a nutrition driven rise in average height of 0.4 inches per decade. This has been associated with cardio-vascular disease rising from a rarity to be no 1 killer. It is noteworthy that a major cause of the rise in blood lipids, atherosclerosis and cardio-vascular disease, was the rise and excessive use of land animal fats this century. Marine fats have been found to be protective. WHO now considers diabetes and heart disease will become the major cause of death in developing countries in the next decade. Heart disease is already the no 1 cause of mortality in Manila. The rise in obesity is spreading from North to South. That is we were changed in shape, size and disease pattern in one century. If nutrition can underpin such a rapid change in such a short time, think what it could do over evolutionary times scales.

The case now to be addressed is the health and abilities of children to be born in this new century. A new approach to nutrition education in primary, secondary and medical schools is urgently needed to empower children and indeed adults to make informed decisions about their nourishment and health. A new and urgent approach is required to arrest the continued pollution of the lakes, river, estuaries and coastlines. The productivity of the oceans, rivers and lakes needs to be restored. The size of budgets devoted to space exploration need to be invested in the estuaries, oceans and fresh water systems. Mars will not feed us in the foreseeable future.

In particular the pivotal importance of the mother and her young needs proper recognition. What is at stake is the health and abilities of the children yet to be born. Without action, the mistakes in food policy of last century which are now so visible, will continue to exert their multi-generational affect to the detriment of health, intelligence and the social cohesion of human society.

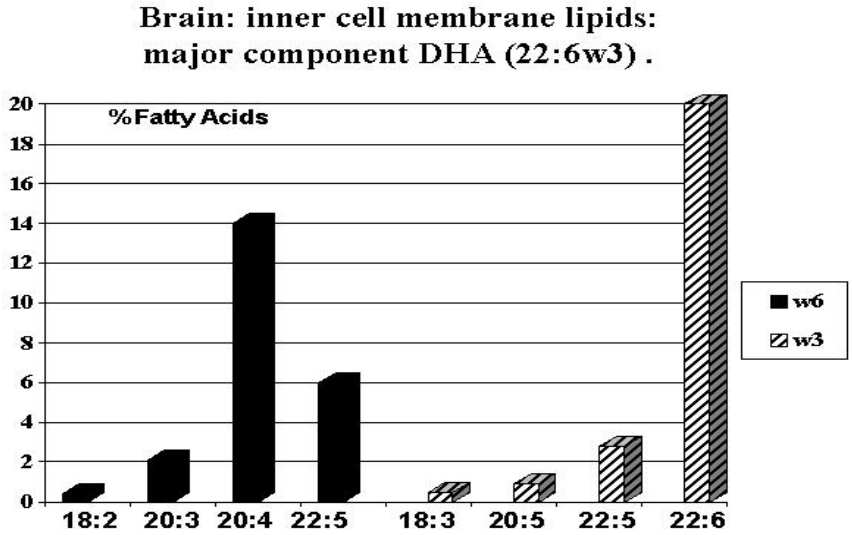


Figure 1

Fig 2: 42 species: inner membrane lipid varies widely in the liver but not the brain.

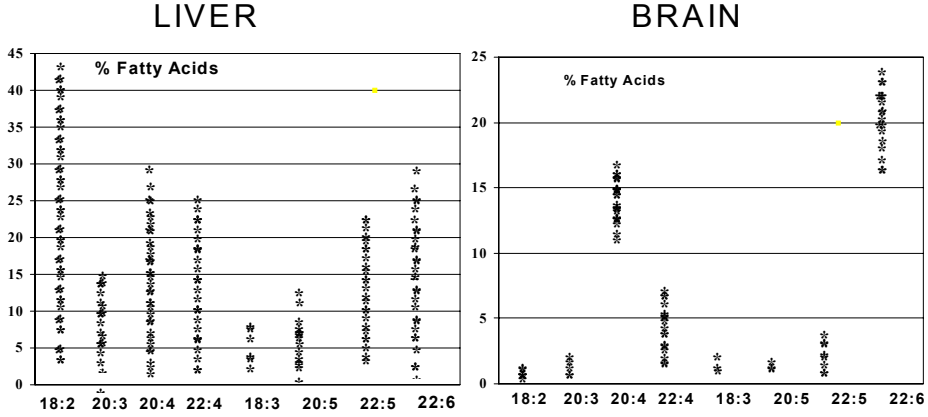
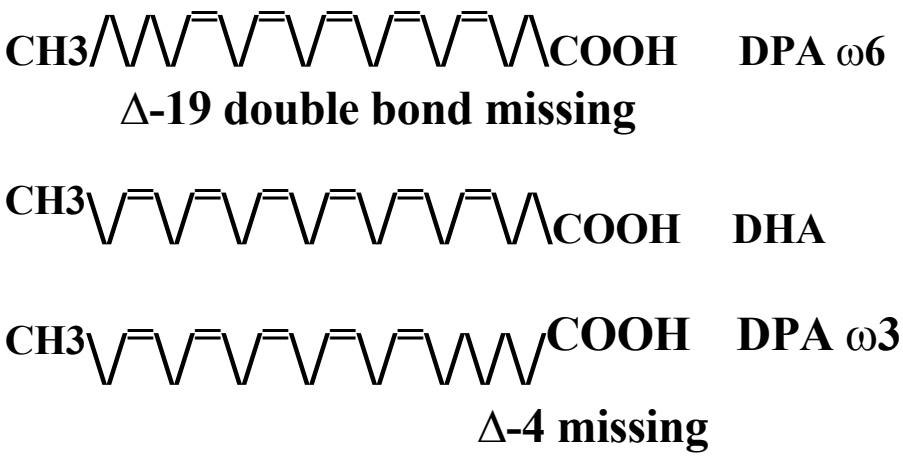


Figure 3. THE OPTIMUM PHYSICAL HYPOTHESIS (OPH)[52]
DHA - A 600 million year track record?



Neither the ω3 or ω6 were used in the synapse or photoreceptor.

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