Membranes, plasma membranes, and surfaces

From the original article in 2009. Author: Ray Peat.

The "essential fatty acids":

Suppress metabolism and promote obesity; are immunosuppressive; cause inflammation and shock; are required for alcoholic liver cirrhosis; sensitize to radiation damage; accelerate formation of aging pigment, cataracts, retinal degeneration; promote free radical damage and excitoxicity; cause cancer and accelerate its growth; are toxic to the heart muscle and promote atherosclerosis; can cause brain edema, diabetes, excessive vascular permeability, precocious puberty, progesterone deficiency....

Twice, editors have printed my articles on unsaturated fats, with adjoining "rebuttals," but I was disappointed that all of my points were ignored, as if you could rebut an argument by just saying that you emphatically disagree with it. I think it is evident that those people don't know what would be involved in refuting an argument. They are annoyed that I have bothered them with some evidence, but not sufficiently annoyed to cause them to try to marshal some evidence against my arguments.

Marketing and medical claims are intertwined with a view of life that permeates our culture. I am aware that my criticism of the doctrine of the essentiality of linoleic acid threatens the large profits of many people, and threatens the prestige of the most popular "theory of cell structure," but I think it is important to point out that nutritional and medical advice depend on the truth of the theory of cell structure and function which supports that advice, and so it is reasonable to see how sound that theory is.

As I understand it, the doctrine of the "essential fatty acids" goes this way:

1. They are essential because they are required for making cell membranes and prostaglandins.

2. Rats deprived of the unsaturated fatty acids develop a skin disease, and "lose water" through the skin.

3. Human skin diseases (etc.) can be cured with polyunsaturated fats.

In fact, rats may get a skin disease when fed a fat-free diet, but the observation that vitamin B6 cures it should have laid to rest the issue of the dietary essentiality of the polyunsaturated oils more than 50 years ago. Scientifically, it did, but forces greater than science have revivified the monster. Experiments that confirm the disproof are done periodically--animals living generation after generation without unsaturated oils in their diet or any evidence of harm, human cells growing in culture-dishes without polyunsaturated fats, for example--without noticeable effect on the doctrine, which is perpetuated in many effective, nonscientific ways--textbooks, advertisements, college courses, for example.

Now, instead of demonstrating harm from a dietary lack of the "essential" fats, the presence of the Mead acid or omega-9 fatty acids is taken as evidence of a deficiency. Our cells (and animal cells) produce these unsaturated fats when their special desaturase enzymes are not suppressed by the presence of exogenous linoleic or linolenic acids. Normally, the inactivation of an enzyme system and the suppression of a natural biological process might be taken as evidence of toxicity of the vegetable oils, but here, the occurrence of the natural process is taken as evidence of a deficiency. To me, this seems very much like the "disease" of having tonsils, an appendix, or a foreskin--if it is there, you have a problem, according to the aggressive surgical mentality. But what is the "problem" in the case of the natural Mead or omega-9 acids? (I think the "problem" is simply that they allow us to live at a higher energy level, with greater resistance to stress, better immunity, and quicker healing.)

There have been arguments based on "membranes" and on prostaglandins. The absence of "good" prostaglandins would seem to be an obvious problem, except that the "good" prostaglandins always turn out to have some seriously bad effects when examined in other contexts. Animals that lack dietary unsaturated fats appear to escape most of the problems that are associated with prostaglandins, and I think this means that many of the toxic effects of the unsaturated vegetable oils result from the quantity and type of "eicosanoid"/lipoxygenase products made from them.

One type of membrane argument had to do with the fragility of red blood cells, reasoning, apparently, that the cells are "held together" by a lipid bilayer membrane. (Just what is the tensile strength of a lipid bilayer? Why do fatty acids or saponins weaken blood cells, instead of reinforcing them? If the "tensile strength" of a lipid layer exists, and is positive rather than negative, it is negligible in relation to the tensile strength of the cytoplasm.) Another type of :"membrane" argument was that the mitochondria are abnormal when animals don't get the essential fatty acids in their diet, because the mitochondria are supposed to be essentially membranous structures containing the essential fatty acids. (Actually, the deficient mitochondria produce more ATP than do mitochondria from animals fed the vegetable oils.) Another argument is that "membrane fluidity" is a good thing, and that unsaturated essential fatty acids make the membranes more fluid and thus better--by analogy with their lower bulk-phase melting temperature. (But the measure of fluidity is a very limited thing on the molecular level, and this fluidity may be associated with decreased cellular function, instead of the postulated increase.)

The most addled sort of argument about "membranes" is that animals on the diet lacking polyunsaturated oils have skin that is unable to retain water because of "defective cell membranes." The skin's actual barrier function is the result of mulptile layers of keratinized ("cornified," horny) cells, which have become specialized by their massive production of the protein keratin--very much as red blood cells become specialized by producing the protein, hemoglobin. Since these cells lose most of their water as they become horny, the issue of whether they still have a "plasma membrane" seems to have little interest to researchers; the same can be said regarding the cells of hair and nails. After the epidermal cells have become keratinized and inert, the sebaceous glands in the skin secrete oils, which are absorbed by the dense, proteinaceous cells, causing increased resistance to water absorption. The ideas of a plasma membrane on the cell, and of the water-barrier function of the skin, are two distinct things, that have been blurred together in a thoughtless way. It has been suggested that vitamin B6 cures the characteristic skin disorder of a vitamin B6 deficiency by altering fat metabolism, but the vitamin is involved in cell division and many other processes that affect the skin.

Given the fact that the "essential" oils aren't essential for the growth of cells, they can't be essential for making plasma membranes (if cells must have plasma membranes), or mitochondrial membranes, or any kind of membrane, but as long as there is the idea that fats mainly have the function of building membranes, someone is going to argue that membranes containing vegetable oils are more fluid, or more youthful, or more sensitive, or better in some way than those containing Mead acids, palmitic acid, oleic acid, stearic acid, etc.

For over a century, people have suggested that cells are enclosed in an oily membrane, because there are higher or lower concentrations of many water-soluble substances inside cells, than in the blood, lymph, and other extracellular fluids, and the idea of a membrane was invoked (W. Pfeffer, 1877; E. Overton, 1895, 1902) to explain how that difference can persist. (By 1904, the idea of a membrane largely made of lecithin was made ludicrous by A. Nathansohn's observation that water-soaked lecithin loses its oily property, and becomes very hydrophilic; the membrane was supposed to exclude water-soluble molecules while admitting oil-soluble molecules.)

Inside the cell membrane, the cell substance was seen as a watery solution. Biochemistry, as a profession, was strongly based on the assumption that, when a tissue is ground up in water, the dilute extract closely reflects the conditions that existed in the living cell. Around 1970, when I tried to talk to biochemists about ways to study the chemistry of cells that would more closely reflected the living state, a typical response was that the idea was ridiculous, because it questioned the existence of biochemistry itself as a meaningful science.. But since then, there has been a progressive recognition that organization is more important in the life of a cell than had been recognized by traditional biochemistry. Still, many biochemists thoughtlessly identify the chemistry of the living cell with their study of the water-soluble enzymes, and relegate the insoluble residue of the cell to "membrane-associated proteins" or, less traditionally, to "structural proteins." It has been several decades since the structural/contractile protein of muscle was found to be an enzyme, an ATPase, but the idea that the cell itself is a sort of watery solution, in which the water-soluble enzymes float, randomly mingling with dissolved salts, sugars, etc., persists, and makes the idea of a semipermeable membrane seem necessary, to separate a "watery internal phase" from the watery external phase. Physical chemists have no trouble with the fact that a moist protein can absorb oil as well as water, and the concept that even water-soluble enzymes have oil-loving interiors is well established. If that physical-chemical information had existed in Overton's time, there would have been no urge to postulate an oily membrane around cells, to allow substances to pass into them, in proportion to their solubility in oil.

Because biochemists like to study their enzymes in watery test-tube solutions, they find it easy to think of the cell-substance as a watery solution. With that belief, it is natural that they prefer to think of the primeval ocean as where life originated. Their definitions of chemical reactions and equilibria in the water-phase (and by extension in cells) ignore the alternative reactions and equilibria that would occur in an environment in which ordinary water was not the dominant medium. By this failure to consider the alternatives, they have created some problems that are hard to explain. For example, the polymerization of amino acids into protein is energetically expensive in water, but it is spontaneous in a relatively dry environment, and this spontaneous reaction creates non-random structures with the capacity for building larger structures, with stainable bilayer "membranes," and with catalytic action. (Sidney Fox, 1965, 1973.) Similarly, the problem of ATP synthesis essentially disappears when it is considered in an environment that controls water. The scientific basis for the origin of life in a "primeval soup" never really existed, and more people are now expressing their scepticism. However, biochemists have their commitments:

"In the course of biological evolution, one of the first developments must have been an oily membrane that enclosed the water-soluble molecules of the primitive cell, segregating them and allowing them to accumulate to relatively high concentrations. The molecules and ions contained within a living organism differ in kind and in concentration from those in the organism's surrounding." (Principles of Biochemistry, supposedly by Lehninger, Nelson, and Cox, though Lehninger is dead and I think his name is attached to it to exploit his fame.# Worth Publishers, 1993.)

Hair is composed of thoroughly dead cells, but if it is washed until it contains no sodium or potassium, and then dipped in serum, or a solution of sodium and potassium, it takes up much more potassium than sodium, in the way a living cell does, concentrating potassium "against the gradient." That is the sort of behavior that led to the postulation of a plasma membrane, to maintain the organization that was created by expending energy. "Membrane pumps" use energy, supposedly, to establish the concentration difference, and the barrier membrane keeps the solutes from diffusing away. The lipid bilayer membrane was an early guess, and the pumps were added later, as needed. Gilbert Ling reviewed the published studies on the various "membrane pumps," and found that the energy needed to operate them was 15 times greater than all the energy the cell could possibly produce.

Water softeners contain an ion-exchange resin, that uses the same principle hair does to concentrate ions, which is simply a selectivity based on the acidity of the resin, and the size of the ion. The resin binds calcium more strongly than it binds sodium, and so the water gives up its calcium in exchange for sodium.* Gilbert Ling devised many experiments that demonstrated the passivity of ion-accumulation by living cells.

Usually, cells are surrounded by and imbedded in materials that they have secreted, and their surfaces are often covered with materials that, while remaining anchored to the cell, have a considerable affinity for water. Physically, many of the molecules attached to cells are "surfactants," making the cell wettable, though it isn't customary to describe them as such. The glycoproteins that give cells their characteristic immunological properties are among these materials. At a certain point, there is a transition between the "outside" of the cell, which is relatively passive and water-friendly, and the cell itself, in which water is subordinated to the special conditions of the cell. (The postulated lipid bilayer membrane, in contrast, has two phase discontinuities, one where it meets the cytoplasm, another where it meets the outside world.) At this phase boundary, between two different substances, it is normal to find an electrical potential difference. When two electrically different substances are in contact, it isn't surprising to find an electrical double-layer at the surface. This is a passive process, which doesn't take any energy to maintain, but it can account for specific arrangements of molecules in the region of the phase boundary, since they are exposed to the electrical force of the electrical double-layer. That is to say that in a completely inert and homogeneous substance, a "surface structure" will be generated, as a result of the electrical difference between that substance and the adjoining substance. (This surface structure, if it is to be described as a membrane, must be called a "wet membrane," while the lipid bilayer would be a "dry membrane," since exclusion of water is its reason for existing.) Too many biologists still talk about "electrogenic membrane pumps," indicating that they haven't assimilated the results of Gilbert Ling's research.

To say it another way, there are several kinds of physical process that will govern the behavior of fats, and fats of different types will interact in different ways with their environments. They interact complexly with their environment, serving in many cases as regulatory signal-substances. To describe their role as "membranes" is worse than useless.

Cells can be treated with solvents to remove practically all fats, yet the cells can still show their characteristic membranes: Plasma membrane, mitochondrial membranes, even the myelin figures. The proteins that remain after the extraction of the fats appear to govern the structure of the cell.

A small drop of water can float for a moment on the surface of water; this is explained in terms of the organization of the water molecules near the surface. No membrane is needed to explain this reluctance to coalesce, even though water has a very high affinity for water.

People believed in the "lipid bilayer membrane" for decades before the electron microscope was able to produce an image that could be said to correspond to that theoretical structure. Osmic acid, which is believed to stain fats, does produce a double layer at the surface of cells. However, the arrangement of fat molecules in the lipid bilayer is such that the fatty tails of the two layers are touching each other, while their acidic heads are pointed away from each other. A lipid bilayer, in other words, contains a single zone of fat, bounded by two layers of acid. The "fat-staining" property of osmic acid, then, argues against the lipid bilayer structure.

Osmic acid is very easily reduced electrically, forming a black product. Proteins with their sulfur molecules in a reduced state, for example, would cause an osmium compound to be deposited, and the appearance of two layers of osmium at the cell's phase boundary would be compatible with the idea of an electrical double-layer, induced in proteins.

Electrically charged proteins, which are able to interact with glutathione to increase or decrease their degree of reduction/electrical charge, distributed throughout the cytoplasm, would explain another feature of osmic acid staining, which is incompatible with the "fat-staining" concept. Asphyxia increases the stainability of cells with osmic acid, and this change seems to represent the availability of electrons, rather than the distribution of fats, since the change can appear within 3 minutes. (C. Peracchia and J. D. Robertson, **"Increase in osmiophilia of axonal membranes of crayfish as a result of electrical stimulation, asphyxia, or treatment with reducing agents,"** J. Cell Biol. 51, 223, 1971; N. N. Bogolepov, Ultrastructure of the Brain in Hypoxia, Mir, Moscow, 1983) The amino groups of proteins might also be stained by osmic acid, though asphyxia would more directly affect the disulfide groups. The increased staining with silver in asphyxia similarly suggests an increase in sulfhydryls.

Freezing cells, and then fracturing them and coating the fragments with metal or carbon is often used to "demonstrate the lipid bilayer," so it is interesting that the **osmium compound that "reveals" the lipid bilayer for the electron microscope destroys the apparent membrane in the freezing technique.** (R. James and D. Branton, "The correlation between the saturation of membrane fatty acids and the presence of membrane fracture faces after osmium fixation," Biochim. Biophys. Acta 233, 504-512, 1971; M. V. Nermut and B. J. Ward, **"Effect of fixatives on fracture plane in red blood cells," J. Microsc. 102, 29-39, 1974.)**

So, when someone says "we need the essential fatty acids to make cell membranes," my response is likely to be "no, we don't, and life probably originated on hot lava and has never needed lipid membranes."

On the third argument, that vegetable oils can be used therapeutically, I am likely to say yes, they do have some drug-like actions, for example, linseed oil has been used as a purgative, but as with any drug you should make sure that the side effects are going to be acceptable to you. Currently, it is popular to recommend polyunsaturated oils to treat eczema and psoriasis. These oils are immunosuppressive, so it is reasonable to think that there might be some pleasant consequences if a certain immunological process is suppressed, but they are also intimately involved with inflammation, sensitivity to ultraviolet light, and many other undesirable things. The traditional use of coal tar and ultraviolet light was helpful in suppressing eczema and psoriasis, but its tendency to cause cancer has led many people to forego its benefits to protect their health.

If you want to use a polyunsaturated oil as a drug, it is worthwhile to remember that the "essential fatty acids" suppress metabolism and promote obesity; are immunosuppressive; cause inflammation and shock; are required for alcoholic liver cirrhosis; sensitize to radiation damage; accelerate formation of aging pigment, cataracts, retinal degeneration; promote free radical damage and excitoxicity; cause cancer and accelerate its growth; are toxic to the heart muscle and promote atherosclerosis; can cause brain edema, diabetes, excessive vascular permeability, precocious puberty, progesterone deficiency, skin wrinkling and other signs of aging.

Whether any of the claimed pharmaceutical uses of the polyunsaturated oils, besides purgation, turn out to be scientifically valid remains to be seen. The theoretical bases often used to back up the claimed benefits are confused or false, or both.

People who are willing to question the validity of an "orthodox method," such as the glass microelectrode, are in a position to make observations that were "forbidden" by the method and its surrounding ideology. (See Davis, et al., 1970.) Their perception is freed in ways that could lead to new understanding and practical solutions to old problems.

But sometimes experiments seem to be designed as advertising, rather than science. Recent studies of the effects of fish oils on night vision or development of the retina, for example, seem to forget that fish oil contains vitamin A, and that vitamin A has the effects that are being ascribed to the unsaturated fatty acids.

With the financial cutbacks in university libraries, there is a risk that the giant seed-oil organizations will succeed in using governmental power to regulate the alternative communication of scientific information, allowing them to control both public and "scientific" opinion more completely than they do now.

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Notes

In their preface, Nelson and Cox say their book has retained "Lehninger's ground-breaking organization, in which a discussion of biomolecules is followed by metabolism and then information pathways," but that at every other level "this second edition is a re-creation, rather than a revision, of the original text. Every chapter has been comprehensively overhauled, not just by adding and deleting information, but by completely reorganizing its presentation and content...." This is reminiscent of the book published under the name of Max Gerson after his death, which inserted essentially fraudulent material to support an approach that is exactly what Gerson strongly advised against.

* This principle might be applicable to the removal of calcium from living cells, with a procedure that wouldn't have the dangers of chelation. Increased consumption of sodium and magnesium should facilitate the removal and excretion of abnormally retained calcium. Sodium has been found to protect tissues against oxidative damage, for example during cancer therapy with cis-platinum.