Ray Peat's Newsletter

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Bioelectric Fields, Regeneration, and the Lactic Acid Myth

Exercise physiologists, knowing that lactic acid is produced during intense exercise, and cancer biologists (especially since Warburg's work showing that all cancers have a respiratory defect) who know that cancer tends to produce lactic acid, almost always talk about the "acidity" of the fatigued muscle or of the cancer cell.

While it is true that the entry of lactic acid into the blood tends to produce metabolic acidosis, the cell which is producing the lactic acid is actually more alkaline than normal cells. The simplest way to think of it is that "acid leaving the muscle makes it less acidic." But still, even though the chemical formula for producing lactic acid directly shows the consumption of acidity, and direct measurements confirm that the cells become more alkaline when they produce lactate, the average biochemist or physiologist is likely to think the opposite.

> ***What we call inflammation offers a good conceptual link between the studies on excitotoxicity or cellular stress, and the newer approaches to the treatment of aging and degenerative diseases, based on ideas of regeneration and development. Controlling inflammation becomes part of promoting regeneration. Injury potential and inflammation are closely related; for example, I found that sunburned skin, or skin irritated by the application of a prostaglandin, had a negative polarity relative to normal adjacent skin.***

Lactic acid (or its ion, lactate) is involved in stress, aging, edema, inflammation, rheumatic diseases, bioelectricity, nerve-muscle interactions, cancer, and the antiinflammatory actions of the thyroid hormone, among other things, so a fundamental confusion about what it does to cells means that much of biological and medical opinion has been unfounded. When I discussed the cellular alkalinizing effect of lactic acid formation in my dissertation in 1972, it wasn't a matter of scientific dispute, and since then, the newer techniques of measurement have made the situation even clearer. But, even today, almost always when conclusions are drawn about muscle fatigue, cancer, radiation damage, etc., they are based to a large extent on the false assumption about lactic acid and cellular pH. A specialist too often builds on the generalizations that are propagated by textbooks and other mass media.

When the pH of a cell or tissue changes, its electrical properties change.

In the normal body, repair is going on constantly, and generally the new substance conforms to the existing pattern. The systems of signals that govern these patterns are called "developmental fields," and during the last 80 years, evidence has accumulated showing that electrical fields participate in these processes of organization. (Child, 1921; McCaig, 1996.)

There is an electrical field around organisms and, internally, electrical fields contribute to the development and maintenance of anatomical structure. Sharks are able to find small fish buried under sand by detecting their electrical fields; they will dig for electrical devices that have similar fields. Large electrical fields have been demonstrated extending away from the surface of skin, and since these fields have some of the properties of a "static electrical field," many people have assumed that the charge was just something that passively accumulated by friction.

Le champ est aligne les molecule de la substance et ca comme une charge polarize

But an experimenter demonstrated the presence of an electrical field extending outward from the external surface of pieces of skin grown in a culture dish. When cyanide was added to the medium, blocking respiration, the field collapsed, and when the cyanide was washed out of the skin, allowing respiration to continue, the field reappeared. The intensity of respiration clearly governs the intensity of the field. The researcher suggested that the field had the characteristics of an "electret" field. An electret is a charge polarization that results when the molecules of a substance (wax or ceramic) are aligned by an external field while at a relatively high temperature, and then cooled.

He implied that the energy of respiration was causing an alignment of molecules, resulting in the polarization of charges. Any field of this sort will influence other charged particles, and so it is obvious that it will participate in the arrangement and organization of particles. The existence of such fields probably influences the alignments of particles within cells, and of cells within organs. There is a tremendous difference in the strength of the field produced by different individuals, but the pattern is always essentially the same, except when it is distorted by pathological conditions; tumors, for example, distort the field.

L'énergie de la respiration cause un alignement des molécules ce qui résulte
en polarization des charges

In general, cell excitation or stimulation increases the intensity of cellular respiration, but when oxygen isn't available, the stressed or dying cell may become hyperactive. Epileptic seizures, for example, can be produced by hypoxia or hypoglycemia, as well as by other stimuli such as imbalances of salts and water.

Textbooks often represent cellular electricity with a diagram showing the outside of a cell as "positive" relative to the "negative" inside of the cell. And researchers who have read those textbooks uncritically sometimes speak of the "positive" charge or field outside a cell. I'm sure they won't feel humiliated if I point out that the whole thing is an artifact of their experimental setup. Isolated cells in a liquid will move toward the positive pole in an electrical field, showing that the cell outwardly has a negative charge. This is called the sigma potential, or surface potential. And if the cell is pulverized, again, nearly all of its large molecular componenents and organelles will move toward the positive pole.

When an electrode is poked into a cell, it registers a negative polarity relative to the neutral outside. On a larger scale, if you put one electrode on moist skin, and put another electrode on a cut, the cut skin will be negative relative to the intact skin. This is called an "injury potential." But the intact skin is itself negatively charged, in the same way that any whole cell is negatively charged.

It has been suggested that sharks are attracted to wounded animals by the electrical field caused by the injury, rather than by the odor of the blood, since they can detect the injured animal from distances far beyond the spread of chemical substances from the blood. The animal's "injury potential" is apparently just an intensification of the animal's normal electrical field. (Although much of the research on electrical sensing has been done on fish, I suspect that land animals sometimes use electrical sensing. For example, dogs can sense an impending epileptic seizure of their owner; the electrical fields created--by the brain or the skin--during an extreme metabolic disturbance might be larger than those of a small fish buried under sand. People are able to detect the flow of a weak current in a buried wire, as discussed by Barnothy and Barnothy in *Biomagnetics.)*

I have seen articles in major science journals that draw important conclusions from the nonexistent positive charge supposed to be on the outside of cells, and those things have got past the editors and referees because those ideas are so current in our scientific culture. Less blatant, but equally false, ideas are even more prevalent. The use of various microelectrode techniques has produced an abundance of information on cellular electrical responses, but with the exception of the work of Gilbert Ling and a few others, the meaning of the data is obscured by a huge culture of phantasy theories.

With this sort of fundamental confusion about bioelectricity, it isn't surprising that there is so little interest in the morphogenetic influences of

excitation ou stimulation ↑ l'inten de la respi, mais si l'O2 n'est pas disponible les cellule mourante ou stressé peuvent devenir hyperactive electrical fields. The textbook images of "membrane potential" give the impression either that relevant fields don't exist, or that they are the opposite of those observed experimentally, and those mistaken textbook images overwhelmingly dominate the scientific-political-economic scene.

The overall charge on proteins and other macrolecules is, in general, a matter of the pH of their environment. Usually, cellular proteins have a negative charge above a pH of 5. The ionization of chemical groups such as hydroxyl, amino, and sulfhydryl are responsible for the overall charge. The degree of oxidation or reduction affects the number of sulfhydryl groups, and the structural state of the protein also influences the charge. At high pH the charge is high, and the number and arrangement of sulfhydryl groups can affect the charge. The presence of small ions, carbon dioxide, and oxygen also influence the charge of proteins. When the whole living system is involved, bioelectricity interacts with other electron-related phenomena, including oxidation-reduction, pH, donor-acceptor and free radical reactions.

When the pH of blood is high, the cells of blood vessels are excited into contraction. When the pH of the blood is low, nerve activity can be dulled to the point of coma, as in diabetic acidosis. I think these effects of pH, and the simpler effects of pH on protein charge, are closely related to each other, and to the phenomenon of the injury potential.

Since proteins are generally negatively charged, and tend to move toward the positive pole when they are in an electrical field, a membrane made up of proteins (sheets or layers of cells, for example) will move in the same direction relative to the water that permeates it, meaning that the water will move in the opposite direction, i.e., toward the negative pole. This is called electroosmosis. Since the electrical charge on proteins becomes more strongly negative when the pH is high, and less strongly negative when the pH is low, water will tend to move across membranes from acidic regions into alkaline regions.

The contracting muscle tends to take up water, and forcing it to take up water increases its tendency to contract.

Oxygen, producing carbon dioxide, acidifies the cell, and carbon dioxide influences the cell's handling of water. Carbonic anhydrase inhibitors are commonly used to regulate conditions involving edema, including adaptation to high altitudes.

During intense contraction, especially when oxygen and carbon dioxide are limited, muscles produce lactic acid, and **the specific reaction in which lactic acid is formed causes protons to be consumed, that is, it raises the pH.**

Increased pH, decreased osmolarity, and the associated movements of ions increase the cell's excitability.

Because of the long history of thinking of muscle fatigue and hypoxia in terms of lactic acid production, and the mistaken idea that intracellular pH is more acidic in proportion to the production of lactic acid, the confusion of biolectrical ideas has been compounded by the confusion about pH.

Cellular excitation, exhaustion, and injury will affect the cell's electrical fields in different ways depending on the availability of oxygen, glucose, salts, etc., but **in each of those states, there is increased entry of calcium into the cytoplasm.**

Calcium's entry into cells in itself can lead to increased excitation (muscle contraction, cramps, and seizures, for example), to cell death, or to increased proliferation. (It has also been thought that sodium and water can stimulated proliferation. For example, Berman, et al., 1995.)

Something as simple as reducing the pH can prevent apoptotic ("organized" or "programmed") cell death. (K.P. Hanson and V. E. Komar, *Molecular Mechanisms of the Radiation Death of Cells*, Energoatomizdat, Moscow, 1985).

Carbon dioxide, produced by respiration, and ATP hydrolysis, are two powerful acidifiers of the cell; with sufficient stimulation both can probably act simultaneously, and in this situation the pH decrease will tend to oppose the exciting stimulus. Without sufficient oxygen to make CO2, a given stimulus might cause greater excitation and probability of death. The insufficiency of oxygen also leads to a relatively reduced state of the cytoplasmic proteins, increasing their electrical charge at a given pH. **CO2 has many other effects that act in the same protective direction, such as calcium removal, iron binding, and water binding,** and these other effects are at least as important as the pH effect. (Badylak and Babbs, 1986 showed that the combination of a calcium blocker and an iron chelator with carbon dioxide tripled the survival after 7 minutes of cardiac arrest.) Adequate CO2 is intimately involved in the disposition of calcium, and calcium's regulatory significance is universally recognized.

K. P. Buteiko believed that increased carbon dioxide in the body fluids sometimes caused cancers to disappear. In many studies over the last 40 years (and the trend can also be seen in insurance statistics published in 1912), it is clear that cancer mortality is much lower at high altitude. Under all conditions studied, the characteristic lactic acid metabolism of stress and cancer is suppressed at high altitude, as respiration is made more efficient. The Haldane effect shows that carbon dioxide retention is increased at high altitude.

Studying athletes at sea level and at high altitude, it was seen that less lactic acid is produced by maximal exercise at high altitude than at sea level. Since oxygen deficiency in itself tends to cause the formation of lactic acid, this has been called the "lactate paradox"; the expectation was that more lactic acid would be formed, yet less was produced. Something was turning off the production of lactic acid. Normally, it is oxidative respiration that turns off glycolysis and lactic acid production, so that in exercise beyond the ability of the body to deliver oxygen, and in cancer with its respiratory defect, glycolysis produces lactic acid. So, something is happening at high altitude which turns off glycolysis.

The Haldane effect is a term for the fact that hemoglobin gives up oxygen in the presence of carbon dioxide, and **releases carbon dioxide in the presence of oxygen.** It is the increased retention of carbon dioxide that accounts for the "lactate paradox." Carbon dioxide activates the Krebs cycle, but it also combines with ammonium, and in doing so, deactivates glycolysis because ammonium activates a regulatory enzyme. At high elevation, carbon dioxide is retained, and lactic acid formation is suppressed. (This is called the Pasteur effect, but altitude physiologists haven't begun thinking in these directions.) Comparing very low altitude (Jordan valley, over 1000 feet below sea level) with moderate altitude (620 meters above sea level), ACTH was increased in runners after a race only at the low altitude, **indicating that the stress reaction was prevented by a moderate increase of altitude.** (el-Migdadi, et al., 1996.)

The perspective we get on cancer, from the high altitude studies, allows us to go beyond the specific issue of cancer, to the more general issue of stress and regeneration. In outline, stress alters the physical nature of the cellular substance in a way that activates the cell, in which case it will either die from exhaustion, or grow into new cells. The replacement of injured cells means that mutations need not accumulate, and this renewal with elimination of mutant cells has been observed in sun-damaged skin. Among the many layers of form-generating and form-sustaining systems, the balance of electrical fields has a basic place.

Several investigators have demonstrated that internal cancers altered the external electrical polarity of the animal, increasing the negative polarity in a region near the tumor. In the late 1960s, I suspected that irritation or inflammation created an injury potential, similar to the "demarcation potential" of a cut nerve or muscle. I covered one arm so that a small spot would sunburn without exposing the surrounding skin, and in other spots I applied small amounts of prostaglandins, the "hormones" derived from unsaturated fatty acids. The sunburned area was distinctly negative relative to adjacent areas, and some of the prostaglandins (PGF, for example) produced a slight increase of negative charge. I think these changes reflect both intensified metabolism and increased pH caused by interfering with efficient cell metabolism. Lactic acid production raises the pH, and high pH increases the ionization of most proteins.

The localized distortion of the electrical fields will participate in adjustments that should tend to restore the normal fields, with different processes occurring depending on how long the distortion continues. Ordinarily, the fields change in concerted ways during the rhythmic events of eating, excreting, breathing, and sleeping.

When a state of excitement persists long enough for the cell to produce an excess of lactic acid, causing it to become more strongly charged electrically, nearby blood vessels and nerves will tend to grow into the area, restoring normal energy supply and integrated functioning. (Lactic acid can be demonstrated to stimulate vascular growth by putting it near the eye's cornea, causing blood vessels to invade previously clear areas. In cell culture, McCaig demonstrated that nerve cells grow toward the negative electrode.)

When a cell has been damaged (as by radiation or toxins), its inefficiency creates a small *localized distortion* in the fields, which will stimulate processes of repair or removal and replacement, as far as the organism's resources allow. When a stress is great enough that the *entire organism* is exposed to lactic acid, the organism's adaptive resources are being challenged, and potentially harmful responses are evoked. For example, a sluggish liver can allow the blood lactate concentration to rise during stress, and this can lead to secretion of endorphins GH and pituitary hormones (Elias, et al., 1997). The endorphins can increase histamine release, and growth hormone increases free fatty acids; increased permeability of blood vessels can allow ? proteins and fats to leave the blood stream with cumulatively harmful effects.

In general, the factors that protect against harmful local activation of cells are also protective against maladaptive general responses.

The doctrines that explain aging, cancer, and other diseases in terms of the "wearing out of cells" have been based on the denial of the role of organismic patterns and fields in the regulation of events on the cellular and molecular levels. Those theories or doctrines have been popular because they fit the "reductionist" idea of science, which tries to explain the organism as a whole in terms of its smallest parts. The investigation of regeneration, which requires thinking in terms of patterns and fields, has been retarded by that essentially antibiological culture of reductionism.

Sodium and carbon dioxide are essential for maintaining the normal fields, and these substances interact in ways that cause both of them to be lost during stress. In hypothyroidism, sodium is persistently lost, as carbon dioxide is chronically replaced by lactic acid.

Both sodium (Veech, et al.; Garrahan and Glynn) and carbon dioxide--by stimulating the Krebs cycle, and keeping the respiratory enzymes active--help to maintain the normal level of ATP, protecting against stress and shock.

The interlocking fundamental features of cell excitation/relaxation, electrical potential, lactic acid/carbon dioxide, water retention/water loss, salt regulation, pH and energy level, allow us to visualize in a coherent way the biological meaning of stress and adaptation. Interacting with those physical-chemical events, there are many layers of biochemical and physiological processes that reinforce or modify them, including regulatory systems such as hormones and other biological signaling substances, nutritional adequacy, and the type of fuel used. The safest and most effective interventions will be those which support our basic organizational fields (sodium, carbon dioxide, balanced proteins, fruits, thyroid, pregnenolone, for example), and don't introduce distortions, as some drugs, foods, hormones, and supplements do.

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compared with liver the Na+ content was 2-fold higher, K+ was 20% lower, total Ca2+ was 8-fold higher (7.4 mumol/g wet wt) and total Pi 2-fold higher (8.5 mumol/g wet wt), suggesting the presence of insoluble calcium phosphate, **HCO3- was lower, total Mg2+ was similar in both tissues, but free [Mg2+] (calculated by two different methods) was approximately 5-fold lower in the hepatoma, as was [ATP]/[ADP][P(i)]. Because of an inadequate blood supply, tumors are often hypoxic with impaired Krebs cycle activity, low [ATP]/[ADP][P(i)] and rely mainly on glycolysis for energy. The rapid production and subsequent export of anionic lactate-from the tumor cell would be accompanied by H+.** This would account for reversal of the proton gradient and activation of the Na+/H+ exchange. The elevated [Na+]i would decrease the Na+/Ca2+ exchange, which would in turn tend to cause the accumulation of Ca2+ (and P(i)). Such calcification is a very common feature of tumor pathology. The data indicate the change in gradient of one ion (H+) involves alterations in the linked equilibria of many ions and also of energy metabolites and offers new insights into properties of tumors important both diagnostically and therapeutically.

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Notes:

[The living cell is different from most other electrically polarized materials in being able to adjust its charge, its affinity for small molecules and ions, and its shape. During stimulation (and contraction of a muscle), the phase potential may momentarily disappear as proteins' affinity for potassium, sodium, and calcium change, but the sigma potential doesn't, and may even increase slightly. The nature of the excited state is different in different environments, for example, at high altitude or in the presence of increased carbon dioxide, muscles don't contract as fully, and don't produce as much lactic acid during their maximal activity, as they do under conditions of high oxygen and low carbon dioxide pressure.]

[Increased carbon dioxide lowers the so-called membrane potential (Ling and Gerard, 1949), which I interpret as being almost equivalent to a lowering of the "injury potential." There are several more direct indications that carbon dioxide protects against destructive excitation. Muscle contraction is limited by increased carbon dioxide, and at high altitude, maximum exertion is limited, very probably because of the Haldane effect, in which carbon dioxide is retained in proportion to the oxygen deficit.

Carbon dioxide increases the association of water with proteins, a process analogous to lowering the temperature; both cold and high CO2 concentrations have a similar effect on muscle relaxation after contraction. (Howell, 1920)

A deficiency of carbon dioxide (as in hyperventilation) tends to cause epileptic seizures and muscle cramps, and is a factor in asthma and several other diseases (Buteiko) which seem to involve excessive cellular excitation. I think it acts by way of reducing the overall electrical charge of proteins, probably acting as a "cardinal adsorbant," in Gilbert Ling's sense--a molecule which, when bound to a protein, changes the protein's affinity for other molecules.]

[When a needle is poked into a cell, it obviously injures the cell, but the doctrine of the "plasma membrane" leads people to deny that what they are measuring is a type of "injury potential." They want to say that they are measuring a disequilibrium between the inside of the cell and the outside. (A disequilibrium has to be maintained by some charging mechanism such as a "pump.") They talk about the significance of the "membrane potential" as if the presence of the electrode hardly had an effect on the cell. And the surface (or sigma) potential always seems to be forgotten by these people, who think of the outside of the cell as "positive."]