ELECTROGENETICS

Electrogenetics is the basis for designing compounds that can interrupt and offset the energy flow in cancer cells and produce their selective destruction.

Electrogenetics describes the energy requirements, energy exchanges, and electrical communications, which allow gene reactions to occur in the living state.

We will shortly describe the major intracellular and extra-cellular polymers of the tissue oscillation amplifier circuit and identify the key bio-polymers. This will include the major: inductance, capacitance, dielectric transmitter, electric ground and also the resonant frequencies.

Notes toward a Corollary Genetic Code 5/2001

There is a traditional **DNA based genetic code.** Nevertheless, I have found **the dynamic corollaries of the genetic code**. This **second code governs energy exchange** and is the electronic receiver and transmitter of DNA. When it gets out of alignment, it can no longer exchange energy and we die. **Dead things have only the first code; live things have both codes.**

When seeds get wet and warm they induce the onset of the second code. The first code stores traits (protein synthesis). The second code expresses or suppresses traits (protein synthesis). The second code is a musical program of repeated phrases which re-phrases combinations throughout life. It requires alignment of the nucleosomes for transmission. These are specially coiled chromatin. They form a series inductance electronic device and send 50 millivolt signals to the catalytic centers of certain enzymes at ultra-low resonant frequencies. They depend on nucleosome inductance and alignment for charge efflux. Nucleosome alignment becomes critical and is detuned by competing paramagnetic centers at higher frequencies. Our compounds re-introduce the signal devices to mimic the stage in the electronic musical phrase.

When someone says there's a change in the DNA, please be aware that the context implies a change in the genomic sequence. This is always toxic. Much of conventional chemotherapy attempts to alter and break DNA. The things that do are mutagenic and not therapeutic. We do not do that. We do something different. By re-connecting the DNA electronically and thermodynamically, we tune the channel and are greeted by pulses of a musical nature! Transferring the charge in and out of DNA with the palladium lipoic complex changes the DNA charge and the charge on the cell membranes. This happens already in a normal cell in the same specific range. Induction of this normalization charge in tumors provides a novel therapeutic concept.

Garnett Mckeen Laboratory, 2001

Transcription & the Polymer Beat

In terms of major reactions in biochemistry, there are few things as important as **transcription**. Here **the encoded message of the DNA is copied into the RNA messenger form**, which shall later go out into the cytoplasmic world and try to make a life manufacturing proteins. But first the **DNA must be transcribed**.

The helix is sliced open to expose the two delicate single strands and the incision is extended. A team of enzymes is enlisted in the operation: topoisomerases, gyrases, helicases, and polymerases. Looped segments of RNA are brought in and stuck onto the DNA strands, and then connected before being disgorged. And if we can see through biological time we will realize that the old RNA world has found a connection to the future evolving world of DNA. This new state, the DNA and RNA have become closely locked in reciprocal reactions somewhat analogous to a hard drive (DNA), and the activated RAM (RNA) in a computer. Most important is the dynamic interplay between these two realms. As long as these two realms can closely interact the code will go through.

It is this delicate interaction which we must study - after all, this is a **hybrid state**. It is a crucial transient state in which the old and new come together and then separate. And **this coming together of looped RNA and single strand DNA is quintessentially dependent on matched physical configuration and matched frequency of oscillation.**

It is to this oscillation that we should pay attention. This oscillation is the dance of the old with the new in a polymer beat. And the conditions of this molecular dance are very strict so that if there are interferences with the harmonic frequency, the dance will fail, normal transcription will fail, and we must return to the pre-DNA world and its wild single cell behavior.

<u>DNA Reductase: A Synthetic Enzyme with Opportunistic</u> <u>Clinical Activity Against Radiation Sickness</u>

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DNA reductase, a stable synthetic enzyme, gives protection against radiation illness. During oral administration of this material in the emergency treatment of certain brain tumors, it was found that patients receiving concurrent radiation did not develop the usual signs of radiation toxicity such as nausea, exhaustion, disorientation, and depression. This compound is a liquid crystal polymer composed of palladium and lipoic acid. It has been reported to show DNA electronic reducing activity by cyclic voltammetry (1). A charge transfer from membrane phospholipid to DNA is the presumptive mechanism whereby certain tumors, protozoa, and veasts, are inhibited by this complex. The sub cellular site of destruction has been shown to be the membrane (2). The functional catalytic group incriminated by ESR spectroscopy is sequestered peroxide within the polymer, which unlike solvated peroxide, does not form super oxide. We believe this sequestered peroxide is the charge carrier site. This charge carrier is able to discharge into tumor membranes during cellular migration of the complex. The electronic reduction denatures the polar disulfide groups binding peptides together and compromises the integrity of the membrane. Fluorescent probes delineate the increase in cell voltage, and the membrane rupture. This is seen in the facultative protozoan Tetrahymena. While Tetrahymena tolerates DNA reductase under aerobic conditions, it suffers membrane rupture in a similar challenge under anaerobic conditions. Another illustration of this principle occurs when sea urchins are exposed to DNA reductase. Only those cells in the anaerobic archenteron are destroyed. This produces sea urchins without a gastro-intestinal system. In normal cells, the absence of side effects is attributed to the process by which reducing equivalents are rapidly engaged in electron transfer sequences which terminate in oxygen. This textbook metabolic differential protects the host organism and its energy competent cells from electrocution. This is the proposed explanation as to why formal studies in mice and twenty documented human cases testify to the safety of synthetic DNA reductase. It was during the emergency clinical use of orally administered DNA reductase that we learned of its protection against the side effects of radiation. There was both prevention and relief from radiation sickness occurring in patients receiving radiation therapy. Subsequent questioning in more radiated patients indicated this protection was reproducible. We believe the mechanism of the radiation protection by DNA reductase will be found in studies of the vector addition radiative and non-radiative charge transfer at the level of its liquid crystal structure. While radiation protection was not the original therapeutic design for DNA reductase, it appears that quantitative animal and human studies in this are warranted. Critical assays of the dose relationships can develop this material for applications in radiation risk environments in civilian utilities, and military sites. Such studies can lead to commercial development and an advance in public safety procedures.

References: 1. Garnett, M., U.S. Patent no. 5,463,093, Oct. 31, 1995. 2. Garnett, M., J. Inorg. Biochem. 59: nos. 2&3, C48, p.231, Elsevier, 1995.

X-RADIATION ALTERATION OF DNA REDUCTASE IN VITRO

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Introduction - Palladium DNA Reductase (PDR) is a formulation of palladium lipoic acid liquid crystal polymer under active clinical investigation as an oral chemotherapeutic. Opportunistic interference with radiation sickness by this material has been reported (1). I now report an attempt at observing the interaction of the liquid crystal form of PDR with X-radiation.

Results - These changes are the result of the absorption of X-ray energy. The relative importance of this process needs to be evaluated by animal studies. The data sought is how much radiation, and what kinds of radiation, can a standard dose of PDR mitigate to improve survival and protect tissues from degeneration. A variety of radiation challenges will have to be considered in designing these experiments.

Reference

1. Garnett, M., Remo, J.L., <u>DNA Reductase: A Synthetic Enzyme with Opportunistic Clinical Activity Against Radiation</u> Sickness, Int'l Symp. On Applications in Chemical and Biological Defense, Orlando, May 2001, p.41.

The Science

Introduction

The Inductive Phase State of Gene Polymer Pulsation, Compensates for the Absence of Time, Energy and Distance Parameters of the Genetic Code

The modern genetic code is a gene base sequence theory whose regulatory influence is implied from the feedback experiments of bacterial genetics and modern mammalian genetics. **Nevertheless, this intellectual framework failed to disclose the mechanics of differentiation intrinsic to understanding cell development, aging, and cancer. The weakness lies in the absence of dynamical parameters.**

Since 1987 a few investigators have sought and observed other explanations at the DNA level. These reports describe energy storage and retrieval in the unstacked gene base sequences, and DNA oscillations. From measurements with Raman spectroscopy (Volkov & Kosevich), and from theoretical calculations (Bistolfi, also Prohofsky et al., also Chou et al.) an electron dynamic second DNA code emerges. I have reported that measurements with impedance spectroscopy and frequency domain analysis, confirm the oscillatory data. This concept allows the synthesis of drugs designed to act on the exchange of energy at the DNA level. The drugs act as electro-chemical reagents, demonstrating the catalytic addition of electrons to DNA. In so doing it becomes clear that a variety of protozoa and tumor cell lines suffer membrane disruption from the 250 millivolt inward current. In other parallel research, since 1983, workers at Columbia and Caltech have made abundant reports showing stacked sequences of gene bases are able to transfer photo-activated electrons within DNA in the long axis. This is a strong argument for gene to gene signaling or energy transfer when the weak current is amplified in vivo by the oscillating ion fluxes. It becomes necessary to integrate all these reactions into equivalent electronic circuitry as a cell function. To this end the impedance plots were examined from the conventions of electro-chemistry. Since DNA manifests three arcs in the upper right guadrant of the Nyquist plot, it is therefore a variable capacitor at negative voltages. At positive voltages, when exposed to a corrosion driven cation pump, DNA and RNA manifest pseudo-inductance. It is this pulsed inductive magnetic component which is capable of long range penetration of the heterogeneous biological state, and which carries cell to cell integrative biopotential feedback. Fatty acid and phospholipid electron donors are capacitative. Synthetic chemotherapy agents which transfer current to DNA and RNA share with the gene polymers a common ultra-low frequency---demonstrating resonance. These data support

models for a cellular circuit directly analogous to oscillator or tank circuits. These oscillator or pulsed circuits use a frequency at .285 Hertz -- about 17 beats/minute. It is this frequency which is believed to be responsible for the apoptosis effects of DNA reductase.

High flux oscillating electron flow produces clonal selection allowing survival of only the competent electron transfer cell systems, and therefore presents a dynamical model for the design of anti-cancer drugs.

Two catalytic chemotherapeutic agents have been synthesized: **the liquid crystal polymer of palladium and lipoic acid** acts as a **DNA reductase** and its new derivative which acts as a DNA gyrase. These have different anti-tumor spectra and receptor mechanisms. **The DNA gyrase produces dense heterochromatin which is traditionally a gene suppressive action**. We are studying the electrodynamics of DNA gyrase.

In summary, genetic control extends from cell to cell by long range pulsed magnetic induction according to the Faraday-Maxwell-Heaviside law:

curl B = 4 pi C

translated conceptually as:

the net circulating magnetic field around a wire or a long molecule carrying a current is equal to 4 pi times the current density.

In utilizing this electrodynamic model we are switching from traditional coulombic electrostatics to Faraday-Maxwell inductance. This may take on an intellectual adjustment period.

Abstract: The Biological Internet

Biological Polymers & Tissue Synchronization: what are the structures that could produce the inductance between cells?

The cancer cell functions and moves as a single and separate cell and the normal controlling signals are not present. For the normal multicellular state to exist there must be rapid communication between cells. These signals must cross distances considered long range for chemical reactions and for electrostatic charge transfer in biomatter. These signals must cross where there are no neurologic connections and no neural synapses. I have proposed that pulsed magnetic inductance easily penetrates bio-matter over distance. But what are the structures that could produce the inductance between cells? I here recount some of this information, now in press.

----Merrill Garnett, May 28, 2001

Two natural biological polymers, **DNA and prothrombin**, form extensive reversible (liquid crystal) **dendritic networks** as a function of charge and/or field, when they are associated with the intercellular matrix polymer **hyaluronic acid**. When these first two polymers are associated with hyaluronic acid they each form cables microscopically resembling the parallel twin wire transmission cables used in electronics. Such transmission cables are efficient for **signal transfer** at defined electronic impedance, voltage, and frequency. I have reported that these paired polymers **produce an inductance field** when they are exposed to a pulsed **cation current**. This is in keeping with the **Faraday Maxwell law of induction** as in wires, coils, and transformers. **A model for cell DNA-to-cell DNA inductive signaling** is suggested by the intermediate role of prothrombin-hyaluronic acid acting with the coil-to-coil field geometry of an electric transformer. The vascular flow of prothrombin then forms a kind of common **biological internet** for cells to log onto. Hence **tissue synchronization**.

Increased Pseudo-inductance in Paired Mixtures of Biopolymers is a Model for Twin Mutual Induction in RNA & DNA

While not common, inductance in liquids (pseudo-inductance = corrosion production of a magnetic field) has been studied (1, 2) in molten salts. Impedance plots of pseudo-inductive material yield a clockwise circular loop extending from the electrolyte arc in the complex plane. The lower part of this loop represents phase reversal and the current lag typical of inductance (Figs. 1a, 1b). Current lags voltage.

We observe rudimentary pseudo-inductance in **calf liver RNA**, **calf thymus DNA** (Sigma), and **hyaluronic acid** (Hyal Corp.). Such small inductance loops (**Figs. 2a, 2b, 2c**) are variable, abortive, tend to scatter-plot, and are difficult to reproduce. All responses are measured in purged, aqueous 0.1 M Na acetate at pH 5.2 at a DC current of 0.5 V., using an Hg working electrode---**this is the ion pump of the reaction (Hg +1)** ---and an Ecochemie electro-analytic system at room temperature.

Subsequent measurements indicate addition of hyaluronic acid to either DNA or RNA regularly produces large continuous pseudo-inductance responses (**Figs. 1a, 1b**). These spectra initially suggest additive effects. However the new smoothness and reproducibility raise a question. **Are there electronic interactions between those weakly inductive linear polymers expressing clear voltammetric signals, which intermingle in bio-systems? Are we wired?**

Subsequent experiments using gamma globulin as a control at a variety of DC voltages show this **globulin alone produces a poorly developed capacitance plot (Fig. 3a)**. Globulin and hyaluronic acid combined produce a well developed capacitance plot; the loop is reliably interrupted at the critical point before phase reversal and is not additive (**Fig. 3b**). Plots were linear at 0.16 V. **It appears that such mixtures of hyaluronic acid with another bi-polymer are electronically interactive.** This suggests that twin wire-like impedance in liquids occurs, analogous to twin solid wire cables with flux coupling and mutual reactance (**3**). Such a process would enable long range energy transfer in liquids **and signals between cells in the living state.**

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