Charge Transfer Medicine

The Underlying Forces

The challenge in research is :

- Finding alternative ways to think about difficult problems.

Why Charge Transfer ?

- The study of the effects of palladium-lipoic acid complexes has grown to add neurology applications to its use in oncology. This is due to the independent research of Frank Antonawich on ischemic stroke. Such broad effects require us to look again at the basic physical chemistry and biochemistry and find a completely new paradigm, presumably interacting the electronics of charge transfer with apoptosis.

I hope to show :

- Charge transfer medicine is a new technology – it is not just a group of drugs.
- Charge transfer unites multi-cellular systems as an integrated organism composed of integrated tissues.
- Charge transfer in the living state uses the **Nano-Vascular** circulation.

Nano-Vascularity – the paramagnetic film of water surrounding proteins, DNA,& RNA.

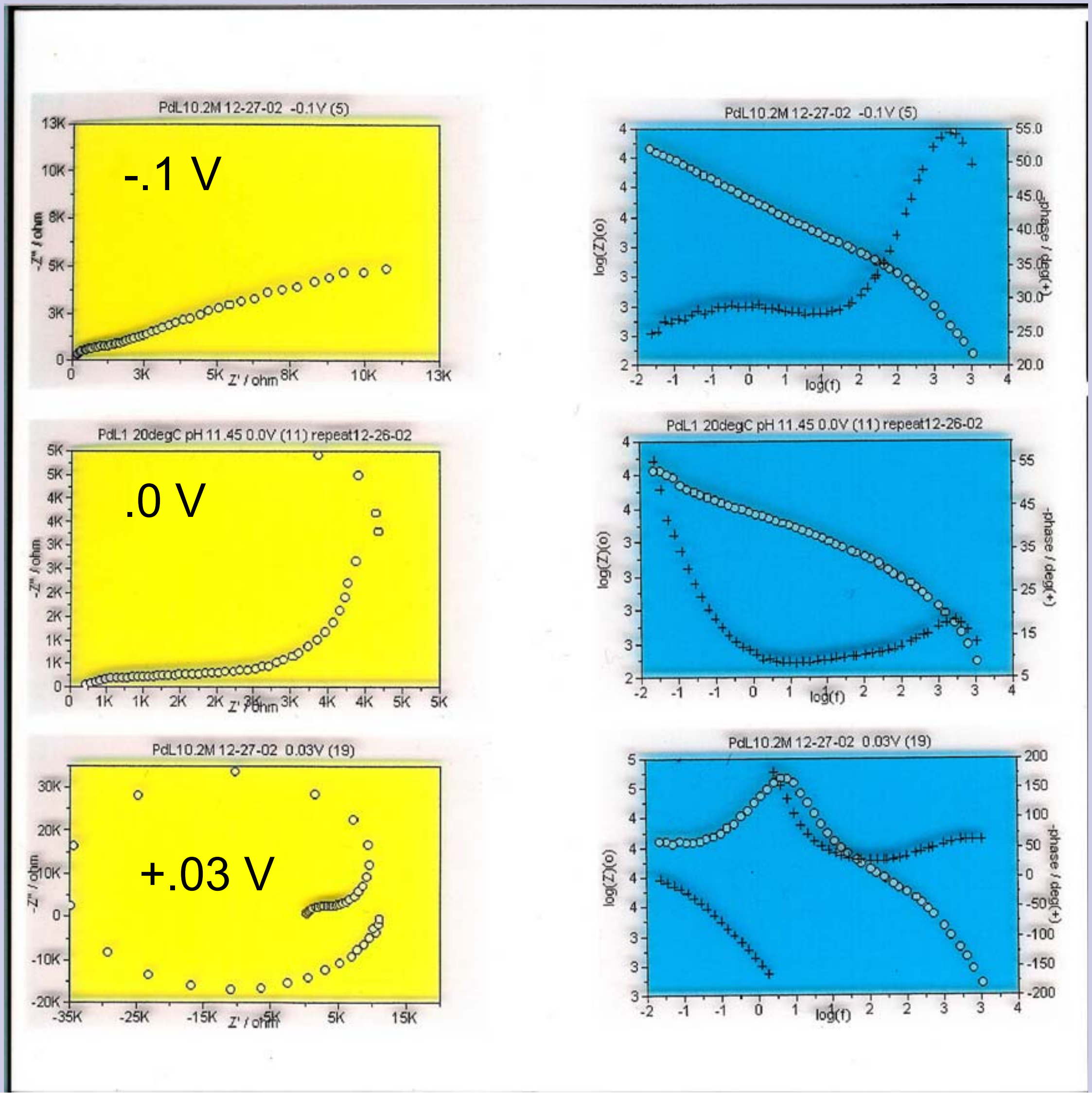
- Mysterious long range signaling has been theorized to be at the heart of genetic control of multi-cellularity.
- We can show that the liquid crystal states of DNA and proteins, in the presence of para-

  magnetic molecular species such as oxyradicals, are **semiconductive. Semiconduction** is the preferred mode for charge transfer and long range signaling.

This phenomenon relies on a second form of water polarization at the surfaces of large molecules :

. **PARALLEL POLARIZATION**

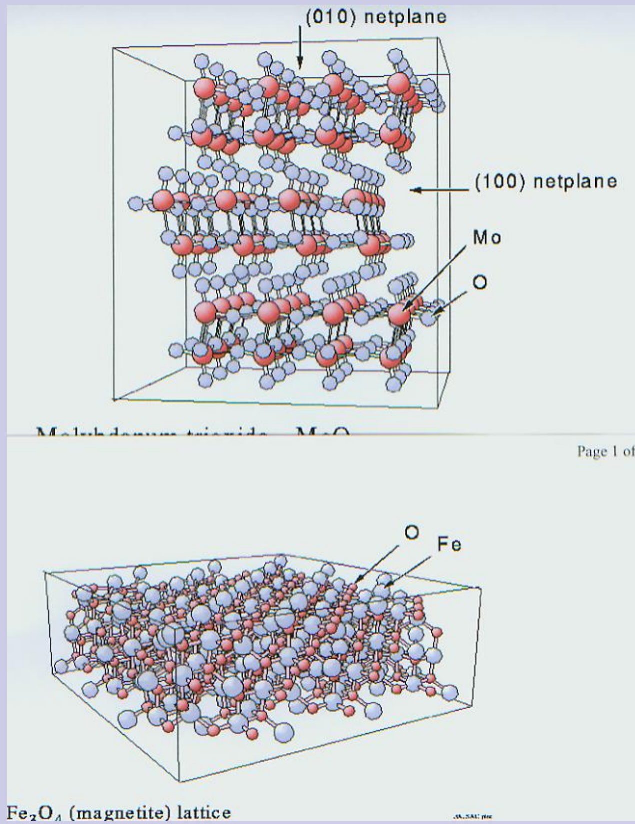
Impedance Bands of Pd-Lipoic Acid by Voltage and Dopant Control



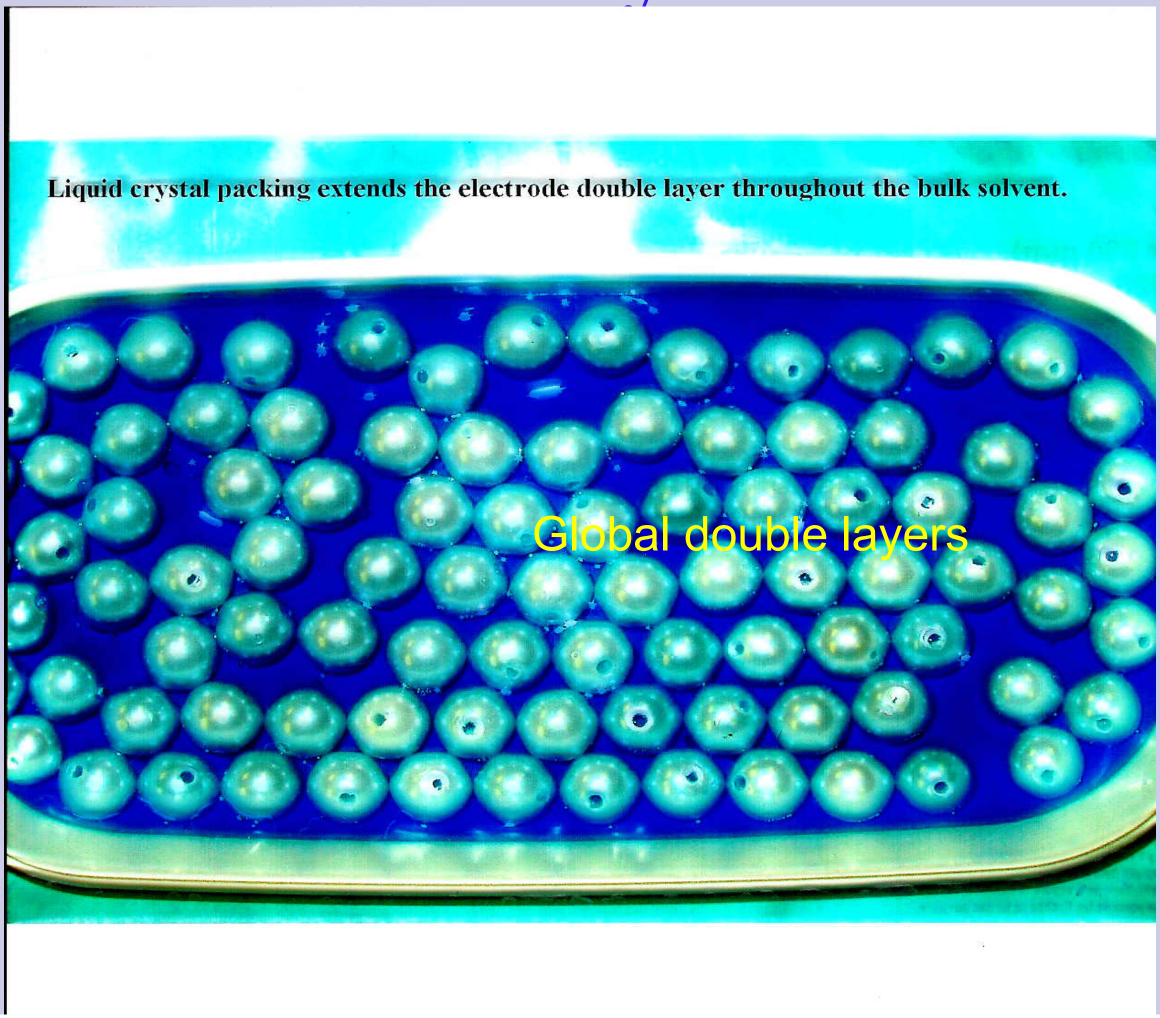
<u>Two Types of H2O Polarization</u>

- <u>PRIMARY</u>: A traditional surface hydration film with both uncharged and **ionic species aligned towards and attracted to the surface** and separated by coulombic repulsion. Capacitance type behavior.
- <u>SECONDARY</u>: An added paramagnetic agent introduces **magnetic H-bond alignment and interaction parallel to the surface,** and semiconduction behavior. This parallel interacting film is the nano-vascular basis of development. **This film acts like a crystal.**
- **CRYSTALs** are the key to computational electronics.
- **Free-radical water films** are the **CRYSTAL** pentiums of the body.

Crystal Lattices Are Always Racked Up And Waiting For The Impact.



Biologic liquid crystal lattices are interlaced with water films, acting as an electric double layer :



Peroxide Structure Can Form Infinite Chains :

The molecule H_2O_2 has a skew, chain structure (Fig. 13-2). There is only a low barrier to internal rotation about the O—O bond. In the liquid state H_2O_2 is even more highly associated via hydrogen bonding than is H_2O.

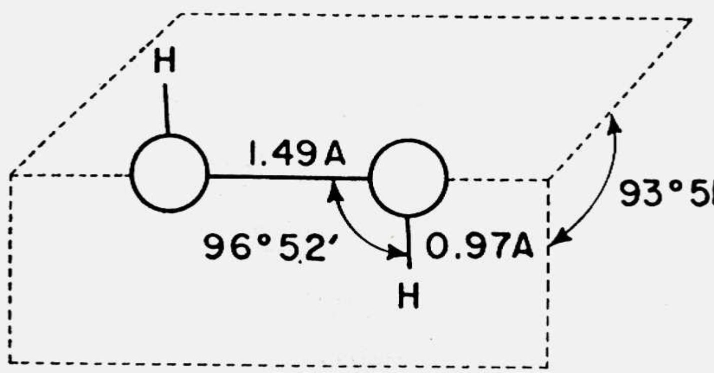


Fig. 13-2. The structure of hydrogen peroxide.

Coil Polymer Simulations

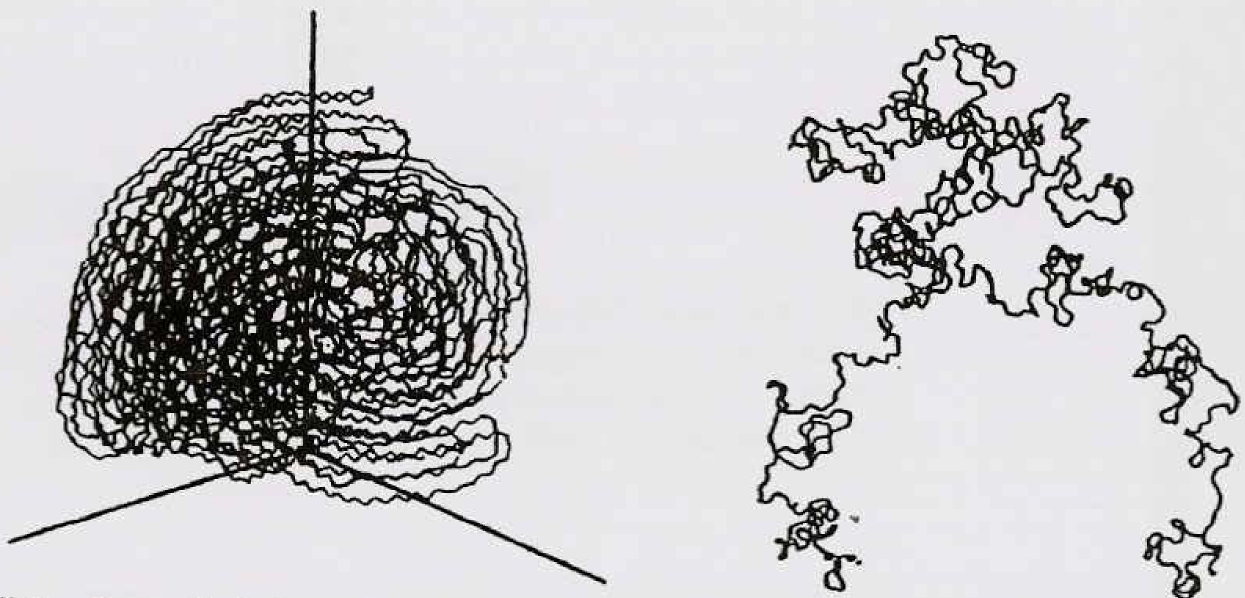


Fig. 5.1. Looped chain and Gauss chain. *Left* — a looped chain of 4000 CH_2 units from molecular dynamics simulation after the collapse of a fully extended chain (from Q. Liao); *right* — a Gauss coil of 1000 CH_2 units from Monte Carlo simulation (from L.R.G. Treloar, *The Physics of Rubber Elasticity*, Clarendon, Oxford, 3rd ed., 1973, Fig. 3.3, reproduced by permission of Oxford University Press).

Allegra’s Model of Polymer Crystal

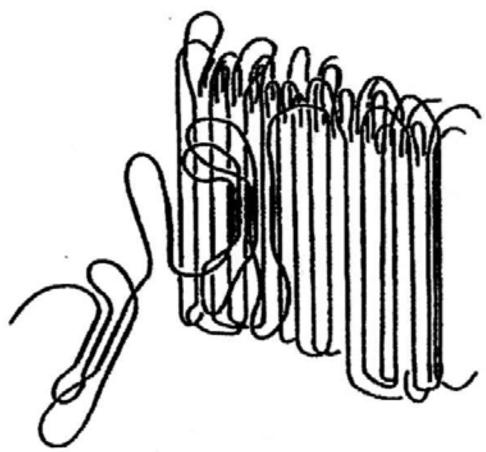
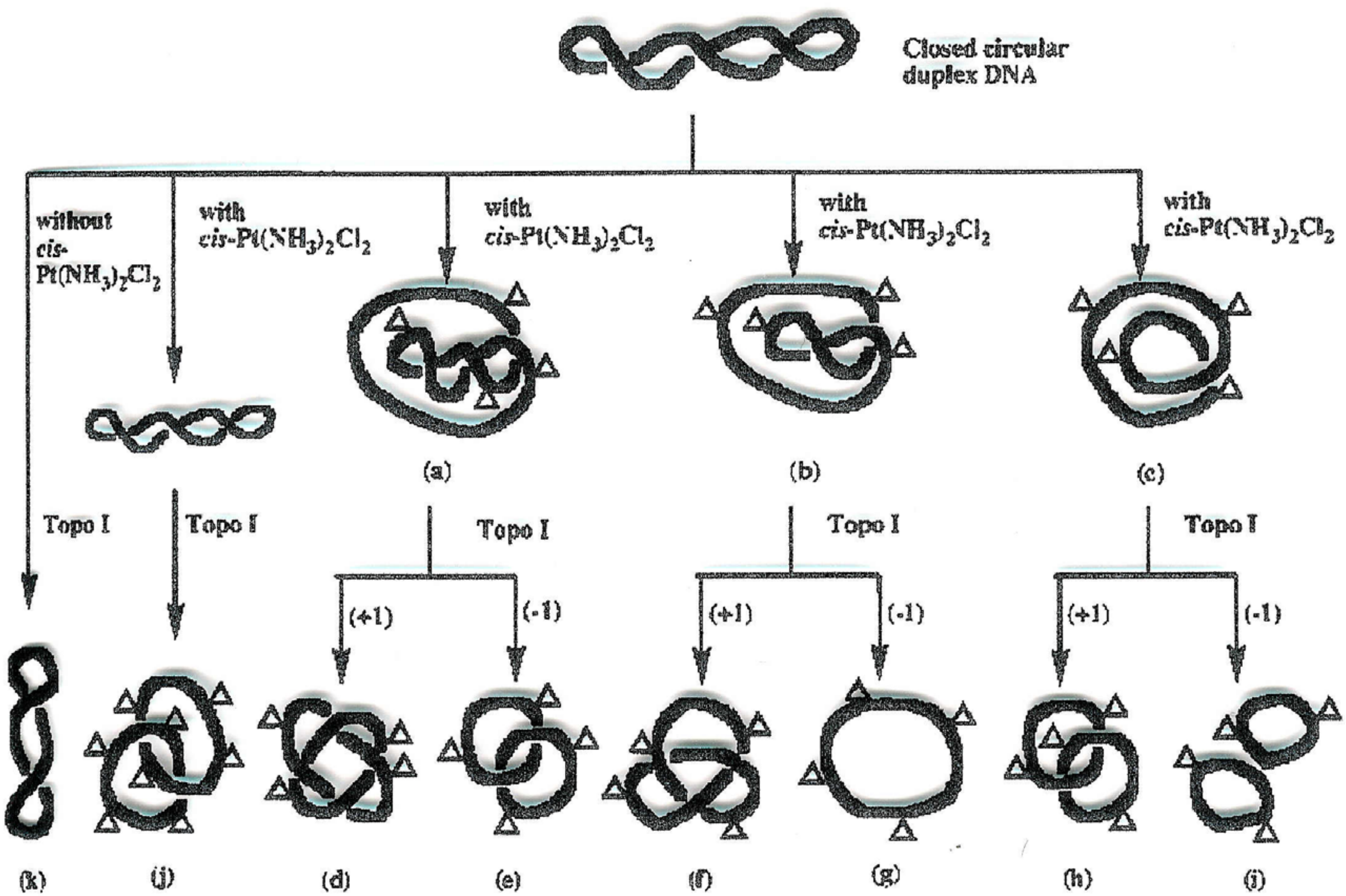


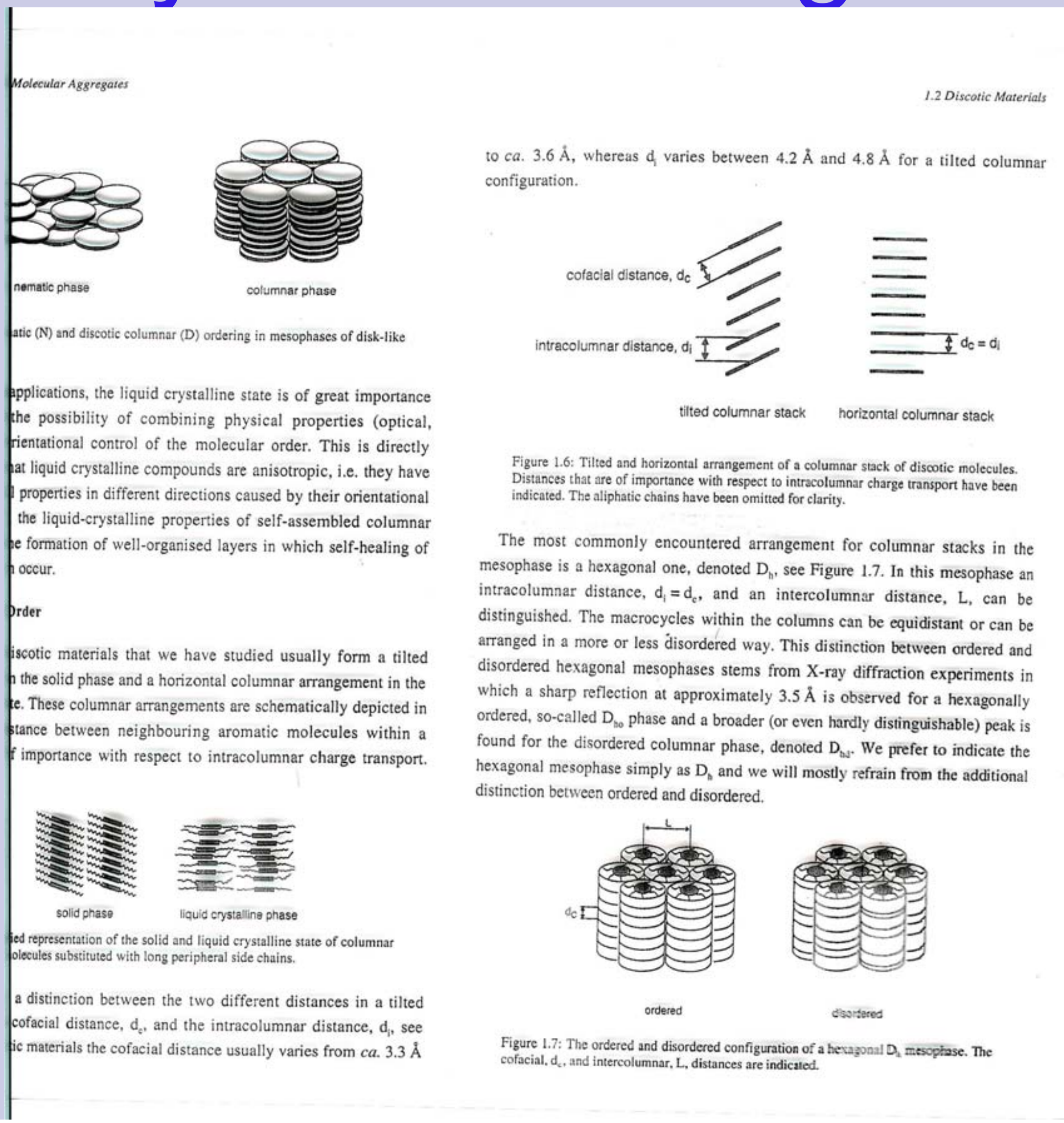
Fig. 4.2. Allegra’s idea of the bundle model of polymer crystallization from a dilute solution, showing a looped coil in solution approaching the crystallization front by diffusion. (From Ref. 14, reproduced by permission of Taylor & Francis, Inc., <http://www.routledge-ny.com>.)



le Topological Mechanisms on Recombination of *cis*-Pt$(NH_3)_2Cl_2$–DNA Adducts by calf Thymus DNA Topoisomerse I

ber ($\langle Wn \rangle$) of intra-twisted loop is 3; (b) $\langle Wn \rangle$ is 2; (c) $\langle Wn \rangle$ is 1; (d) redrawing of catenane in drawing, 4^2_1; (e) singly linked catenane, 2^2_1; (f) trefoil knot, 3_1; (
ingly linked catenane, 2^2_1; (i) trivial knot, 0^2_1; (j) dimetric catenane, 2^2_1, and (k) supercoiled DNA.

Liquid Crystal Stacking



atic (N) and discotic columnar (D) ordering in mesophases of disk-like

applications, the liquid crystalline state is of great importance the possibility of combining physical properties (optical, rientational control of the molecular order. This is directly at liquid crystalline compounds are anisotropic, i.e. they have l properties in different directions caused by their orientational the liquid-crystalline properties of self-assembled columnar e formation of well-organised layers in which self-healing of n occur.

rder

iscotic materials that we have studied usually form a tilted n the solid phase and a horizontal columnar arrangement in the e. These columnar arrangements are schematically depicted in tance between neighbouring aromatic molecules within a f importance with respect to intracolumnar charge transport.

ied representation of the solid and liquid crystalline state of columnar olecules substituted with long peripheral side chains.

a distinction between the two different distances in a tilted cofacial distance, d_c, and the intracolumnar distance, d_i, see ic materials the cofacial distance usually varies from *ca.* 3.3 Å

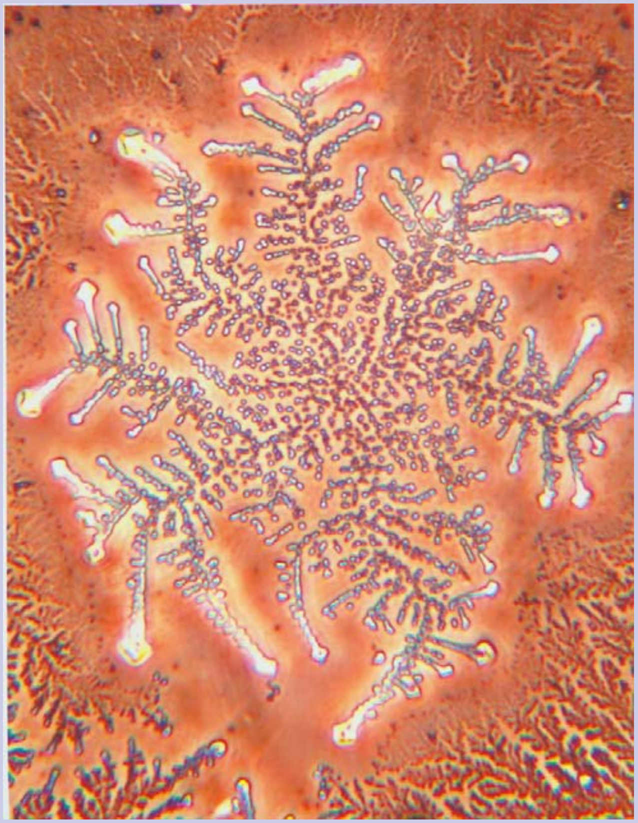
to *ca.* 3.6 Å, whereas d_i varies between 4.2 Å and 4.8 Å for a tilted columnar configuration.

Figure 1.6: Tilted and horizontal arrangement of a columnar stack of discotic molecules. Distances that are of importance with respect to intracolumnar charge transport have been indicated. The aliphatic chains have been omitted for clarity.

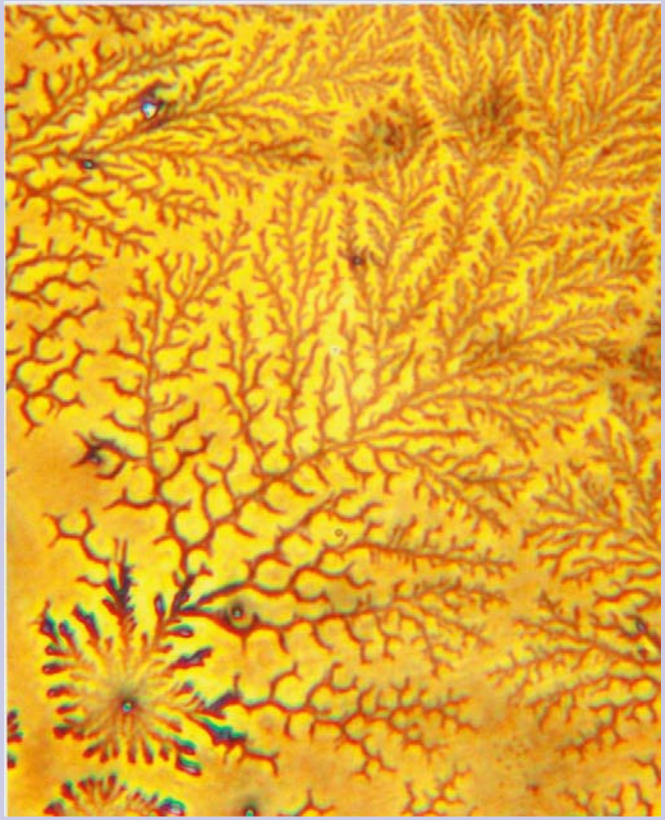
The most commonly encountered arrangement for columnar stacks in the mesophase is a hexagonal one, denoted D_h, see Figure 1.7. In this mesophase an intracolumnar distance, $d_i = d_c$, and an intercolumnar distance, L, can be distinguished. The macrocycles within the columns can be equidistant or can be arranged in a more or less disordered way. This distinction between ordered and disordered hexagonal mesophases stems from X-ray diffraction experiments in which a sharp reflection at approximately 3.5 Å is observed for a hexagonally ordered, so-called D_{ho} phase and a broader (or even hardly distinguishable) peak is found for the disordered columnar phase, denoted D_{hd}. We prefer to indicate the hexagonal mesophase simply as D_h and we will mostly refrain from the additional distinction between ordered and disordered.

Figure 1.7: The ordered and disordered configuration of a hexagonal D_h mesophase. The cofacial, d_c, and intercolumnar, L, distances are indicated.

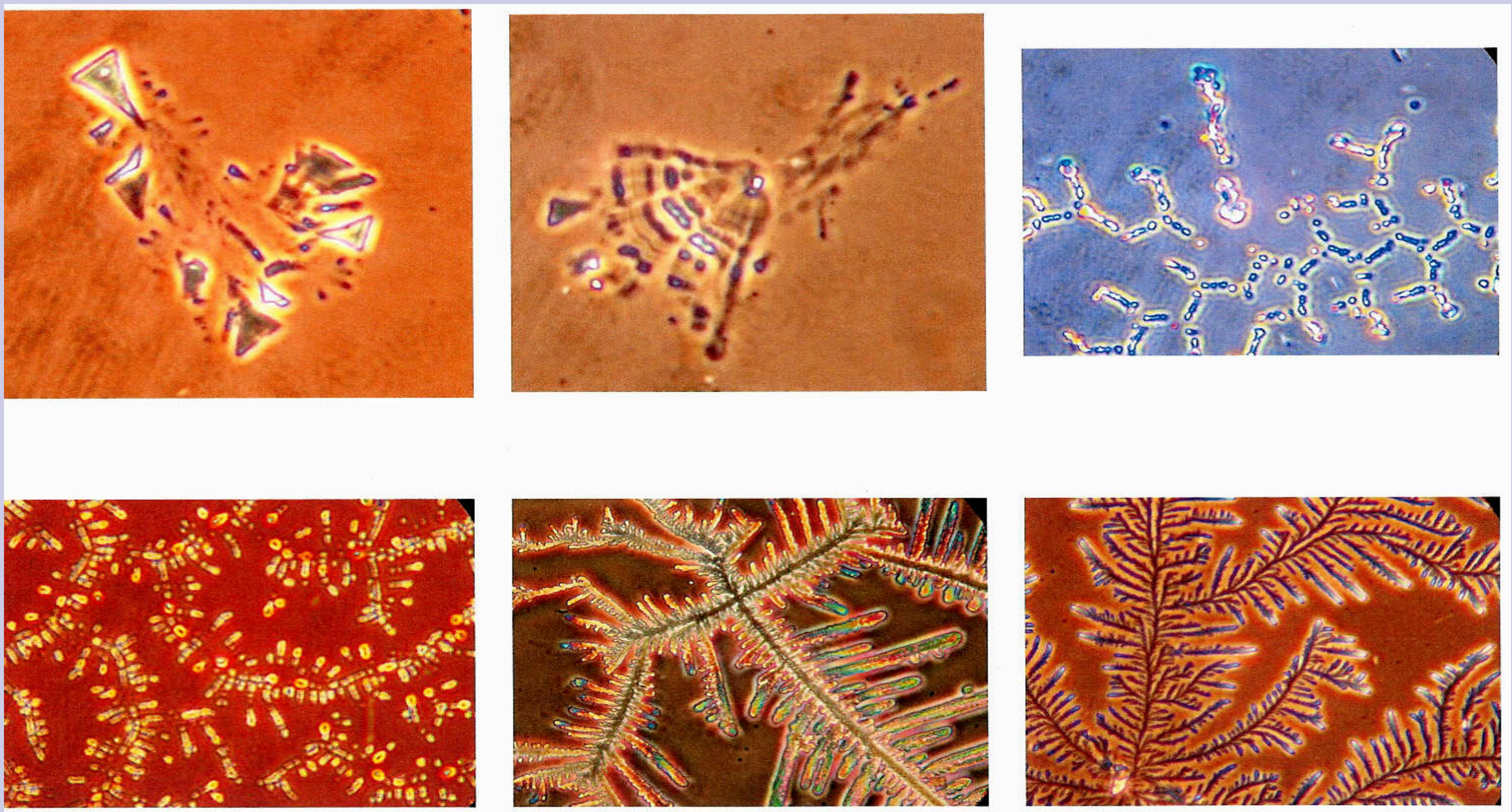
RNA-KCL-H2O2



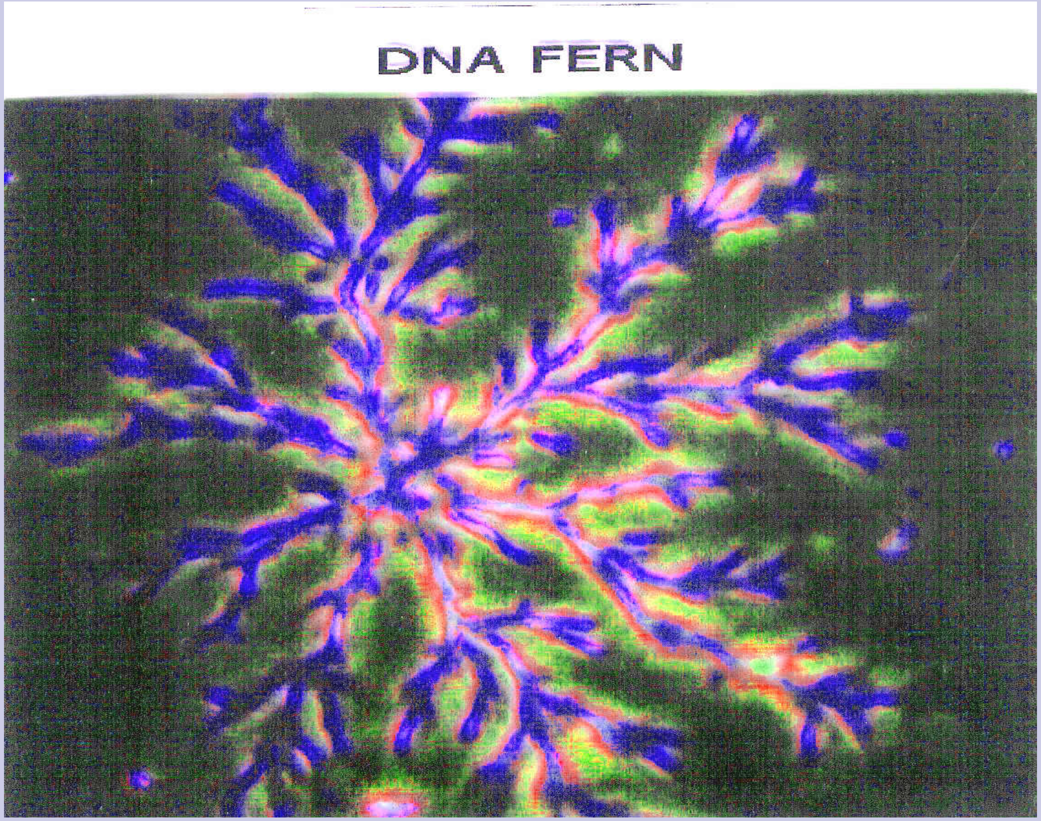
Metallo-Flavin-H2O2



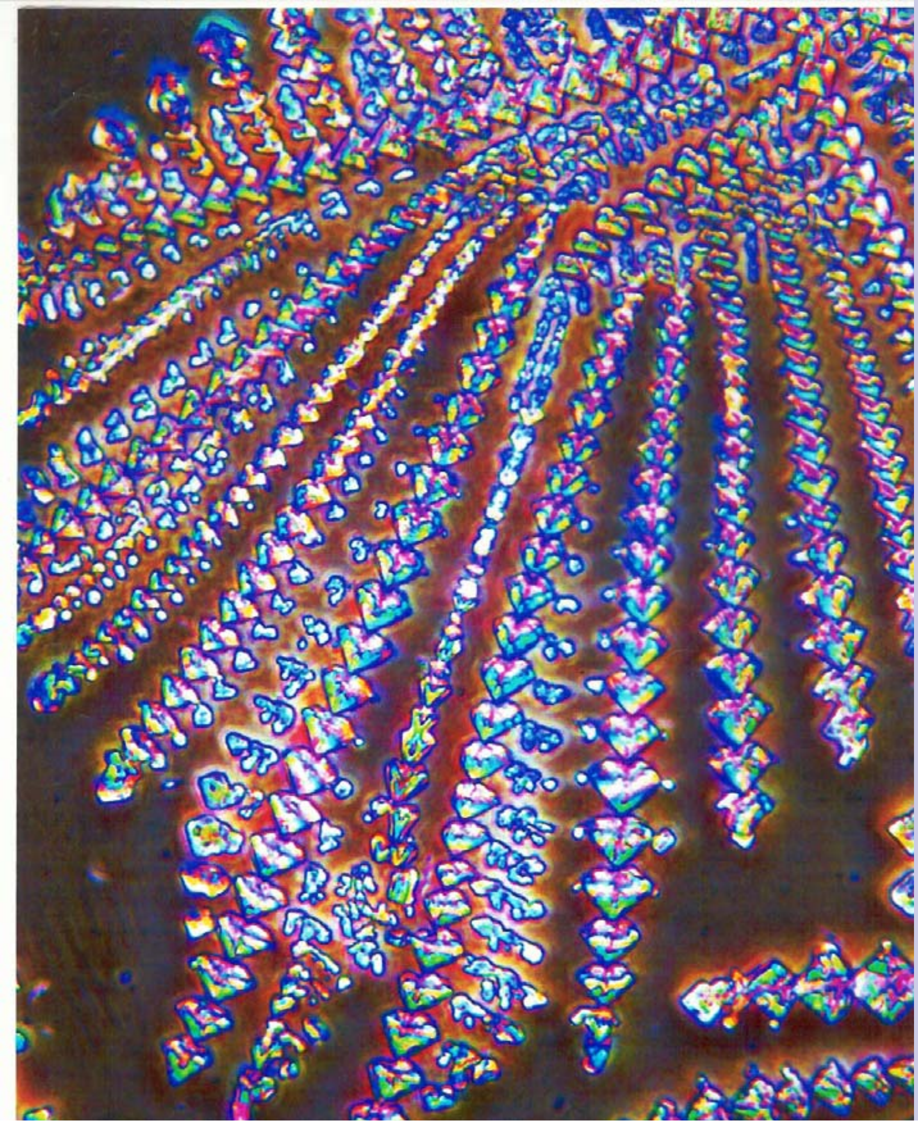
Varied DNA Liquid Crystals



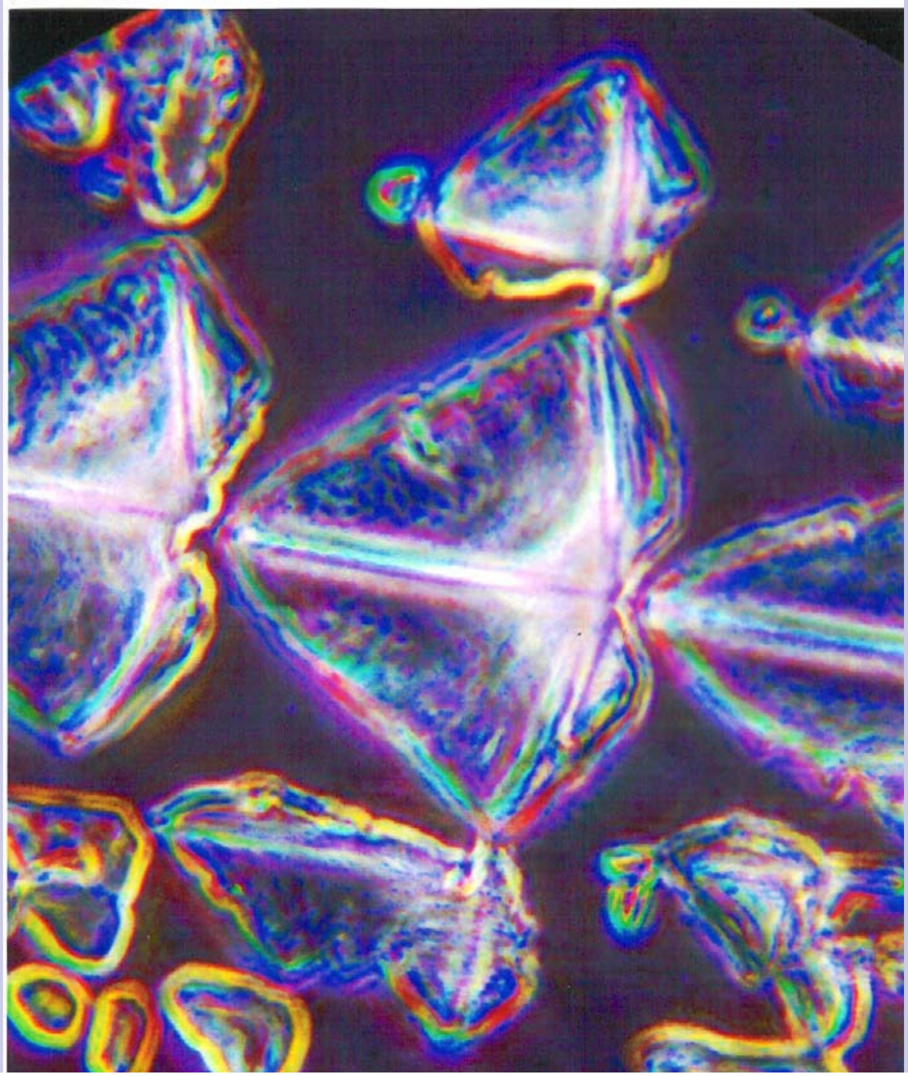
Transient Crystalloid of DNA Doped With H_2O_2



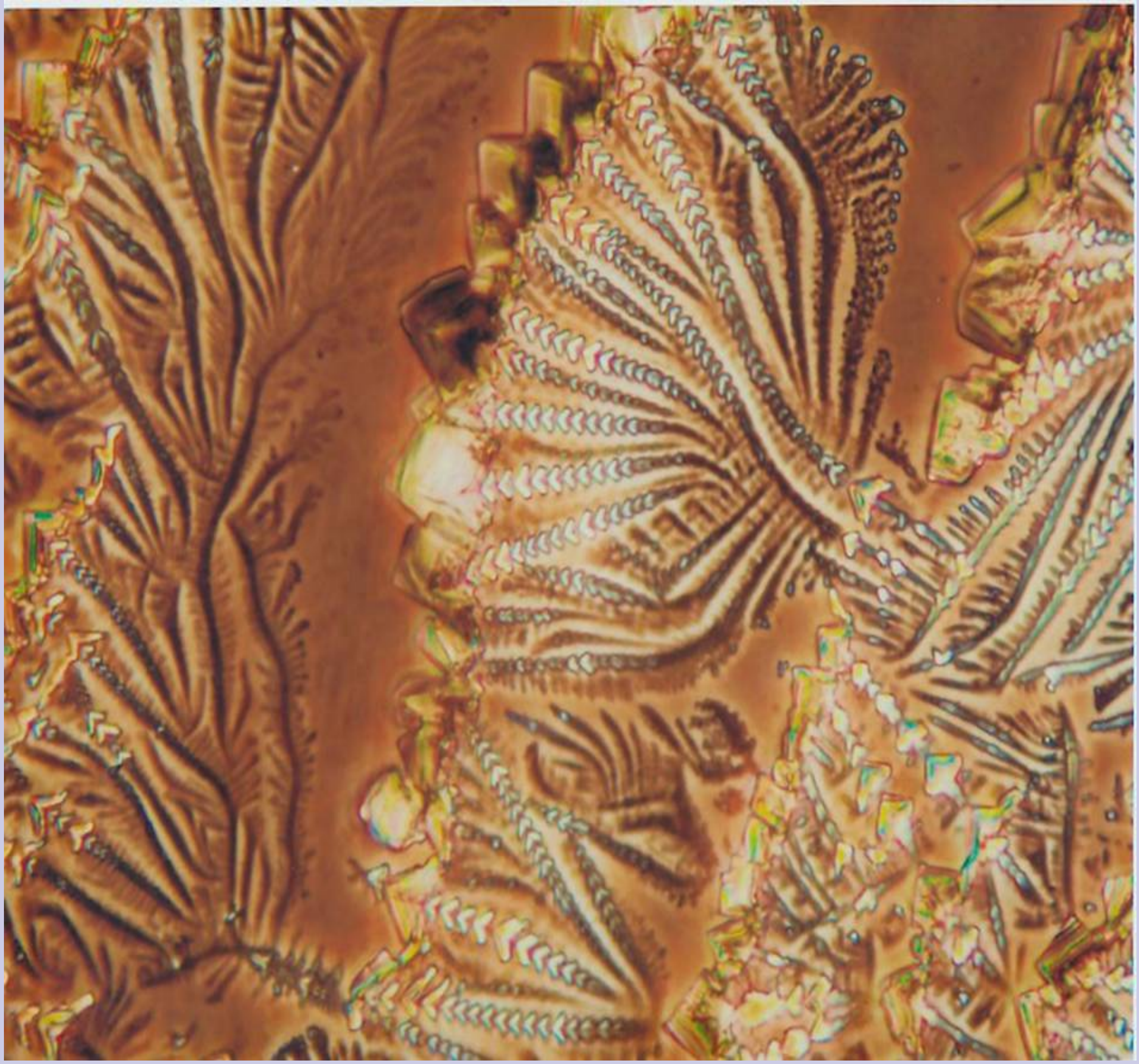
DNA Crystal Array



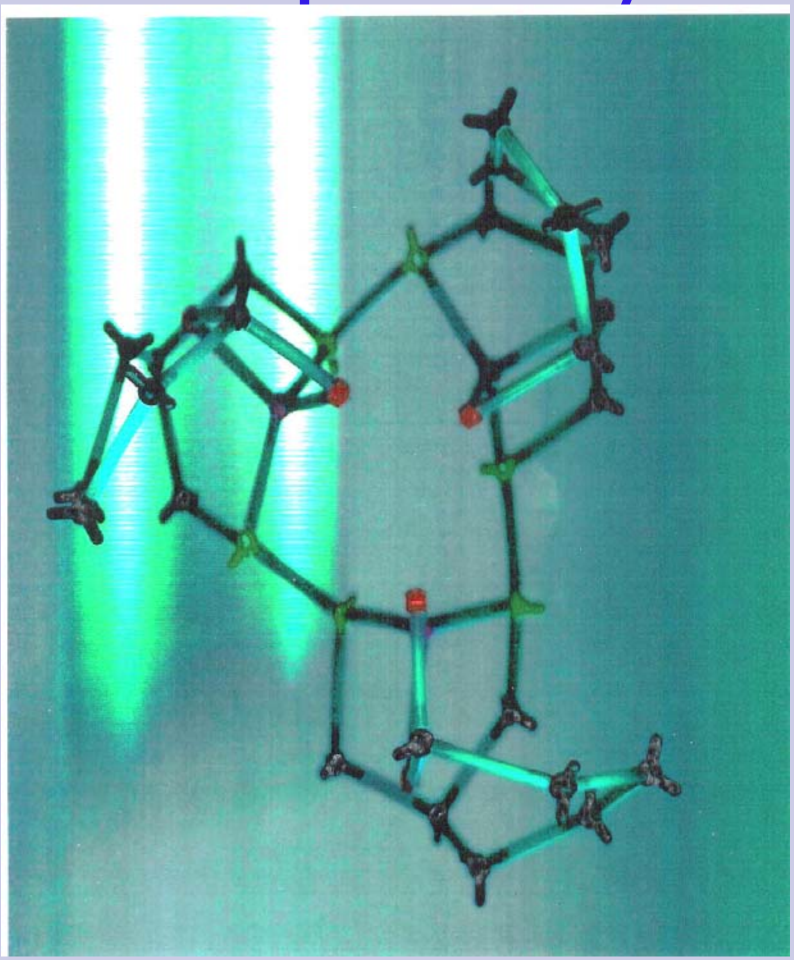
DNA Tetrahedra



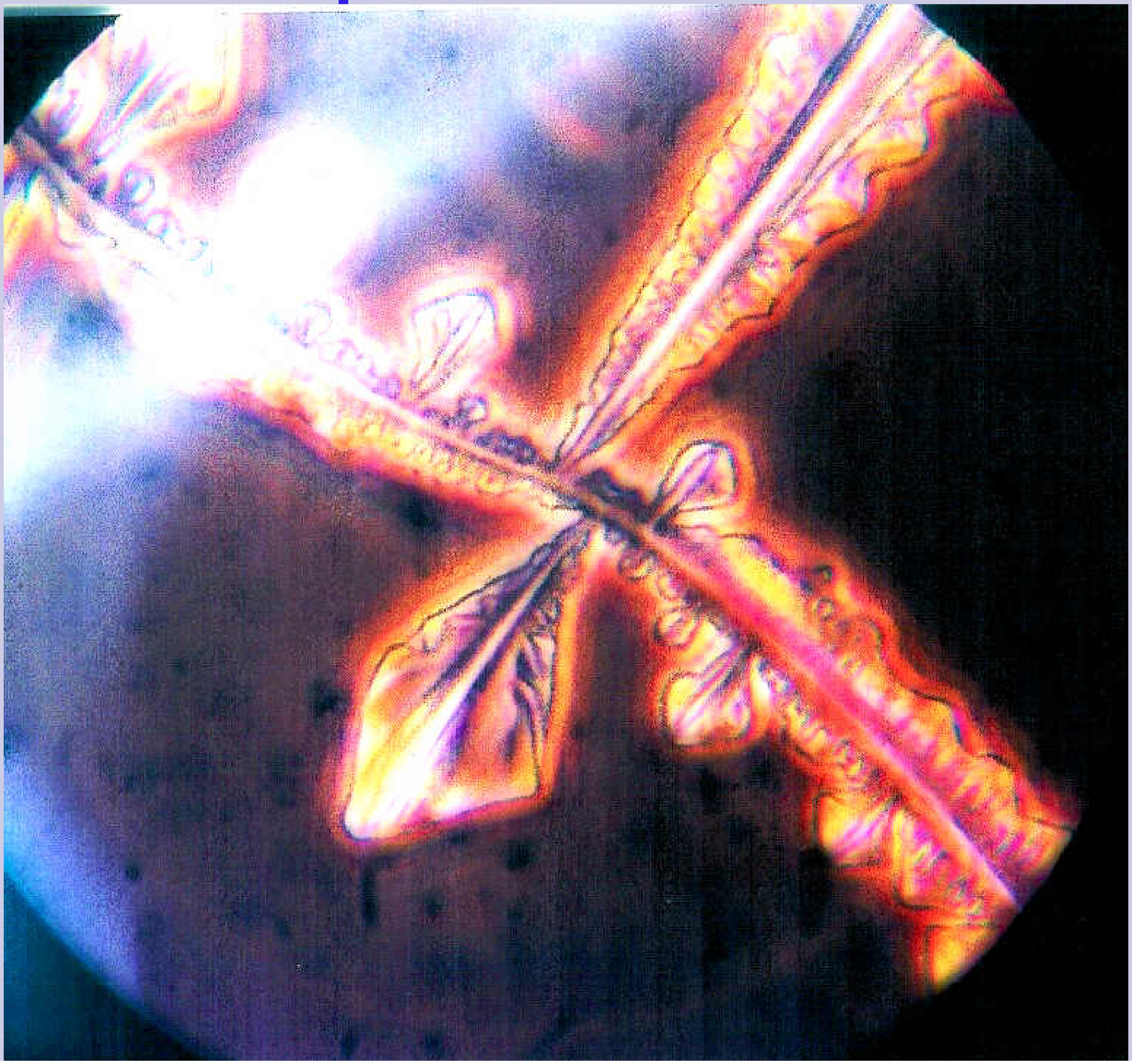
DNA-Prothrombin Array

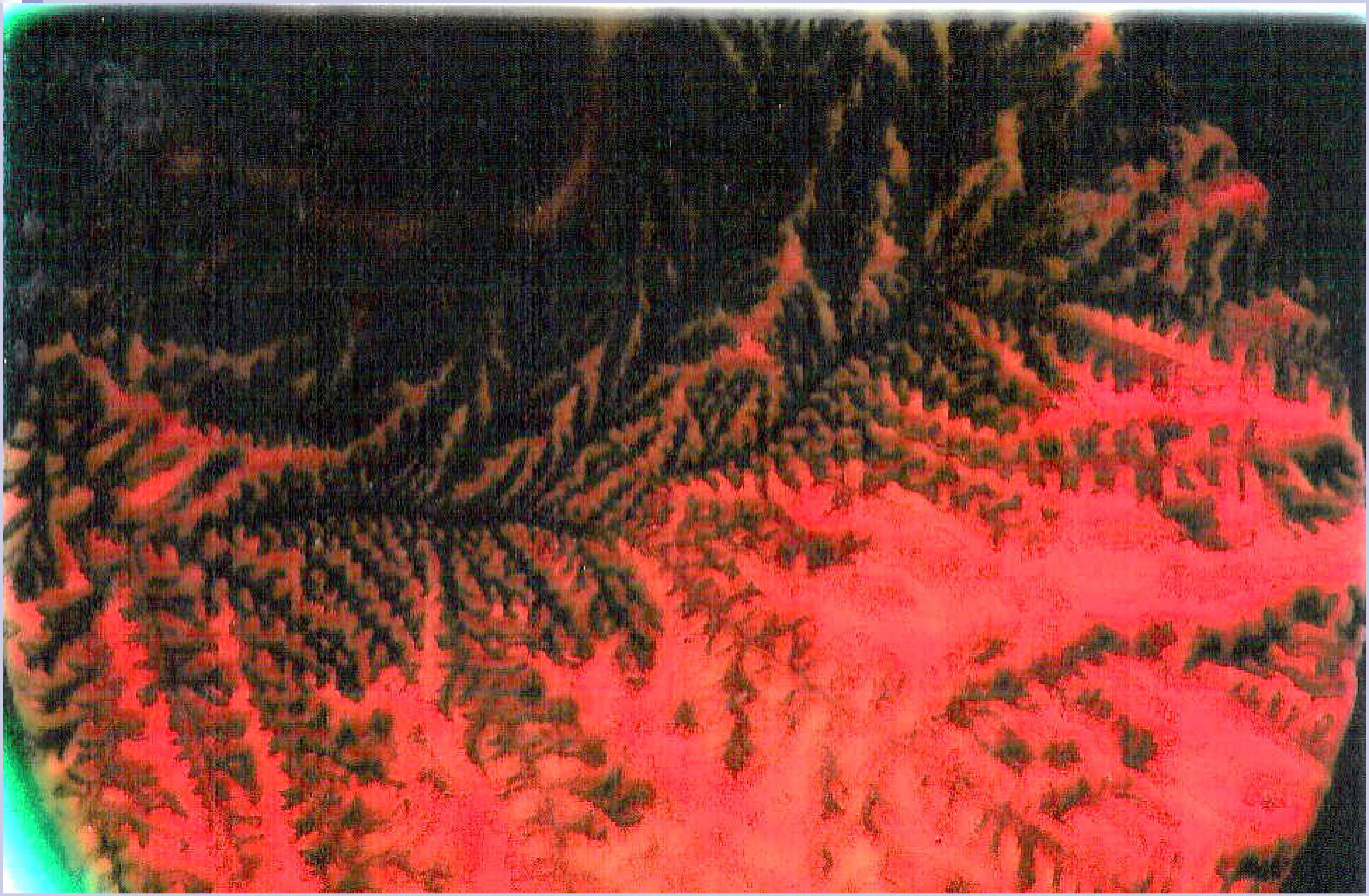


Palladium Lipoic Acid Trimer is an Investigative Chemotherapy Agent which Forms Liquid Crystals

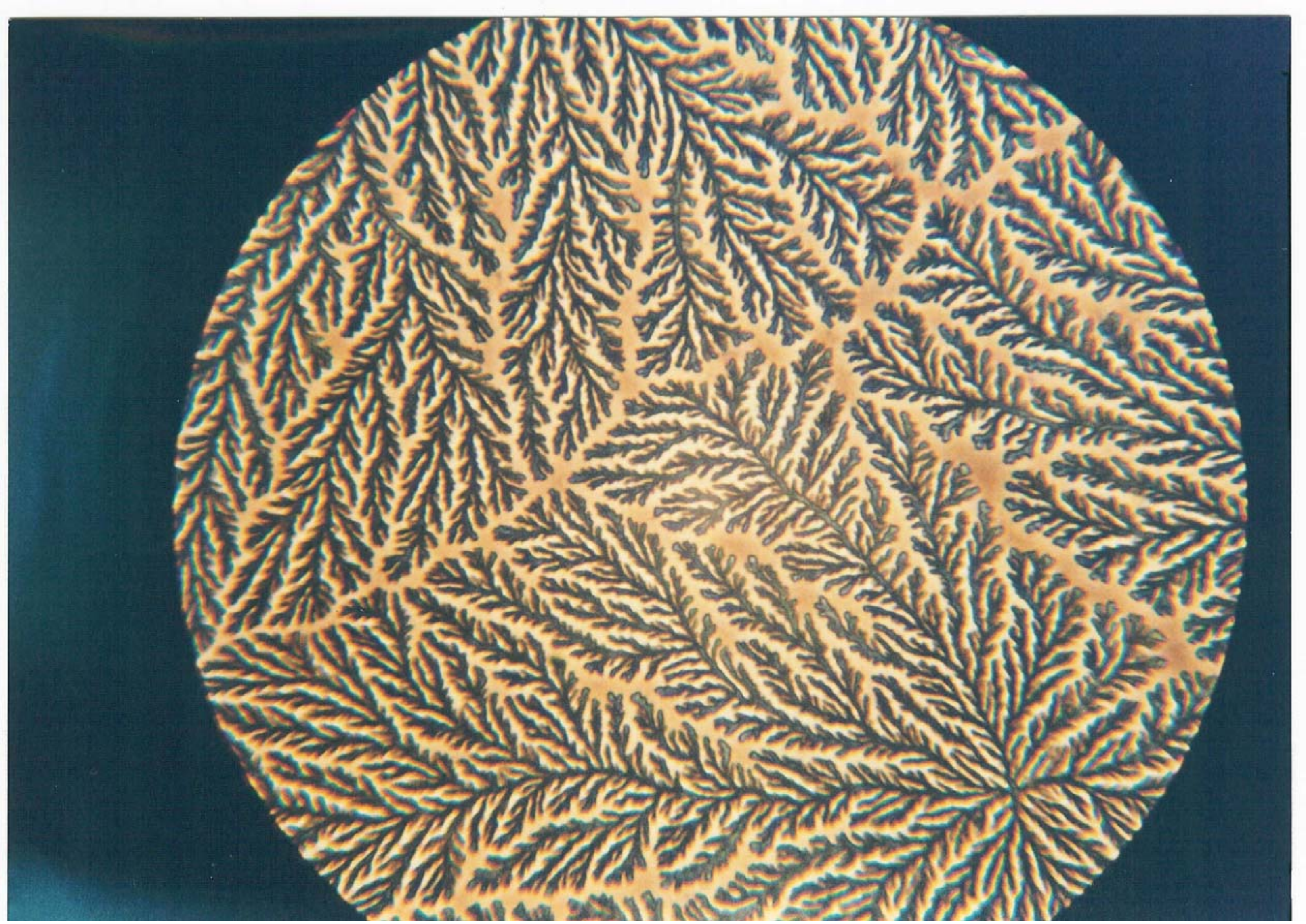


Palladium Lipoic Acid Fern Unit

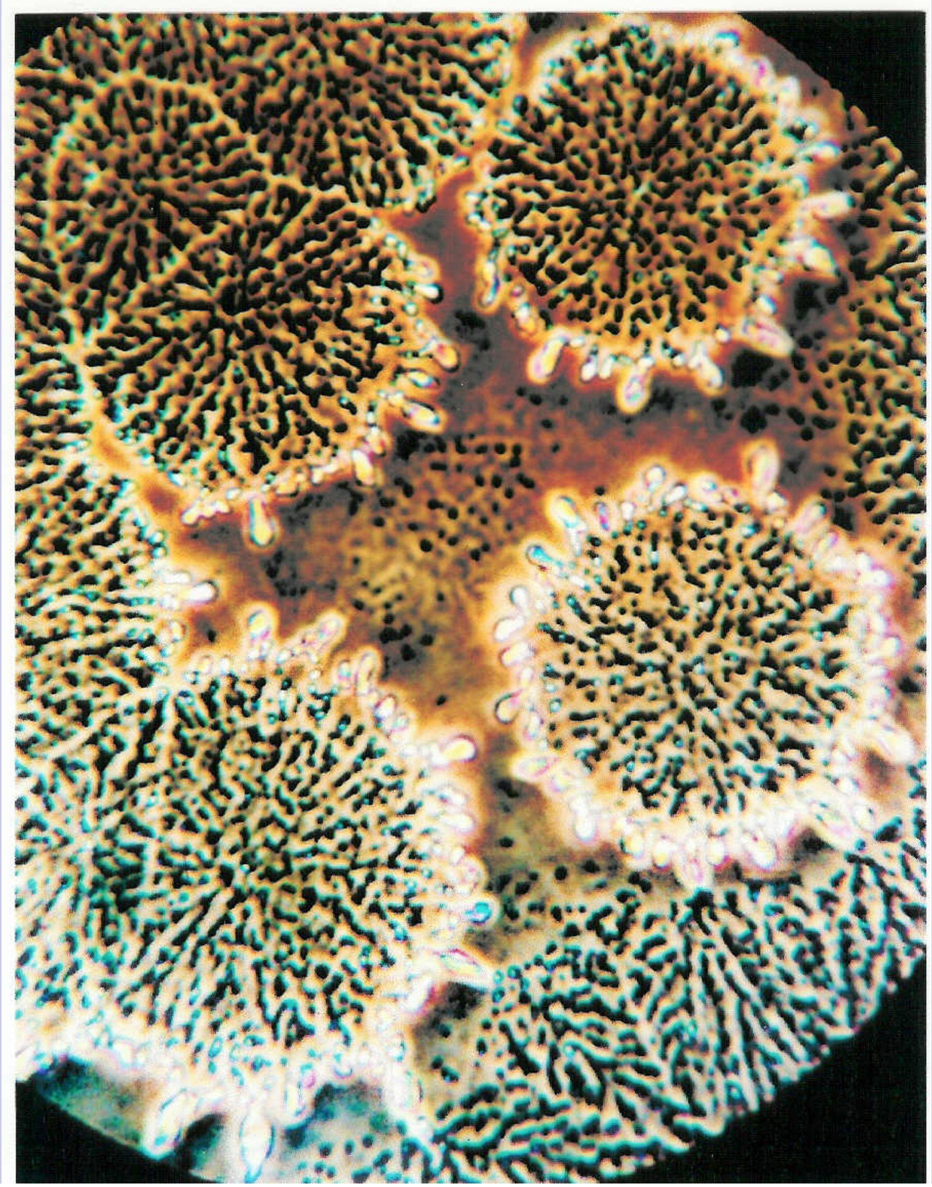




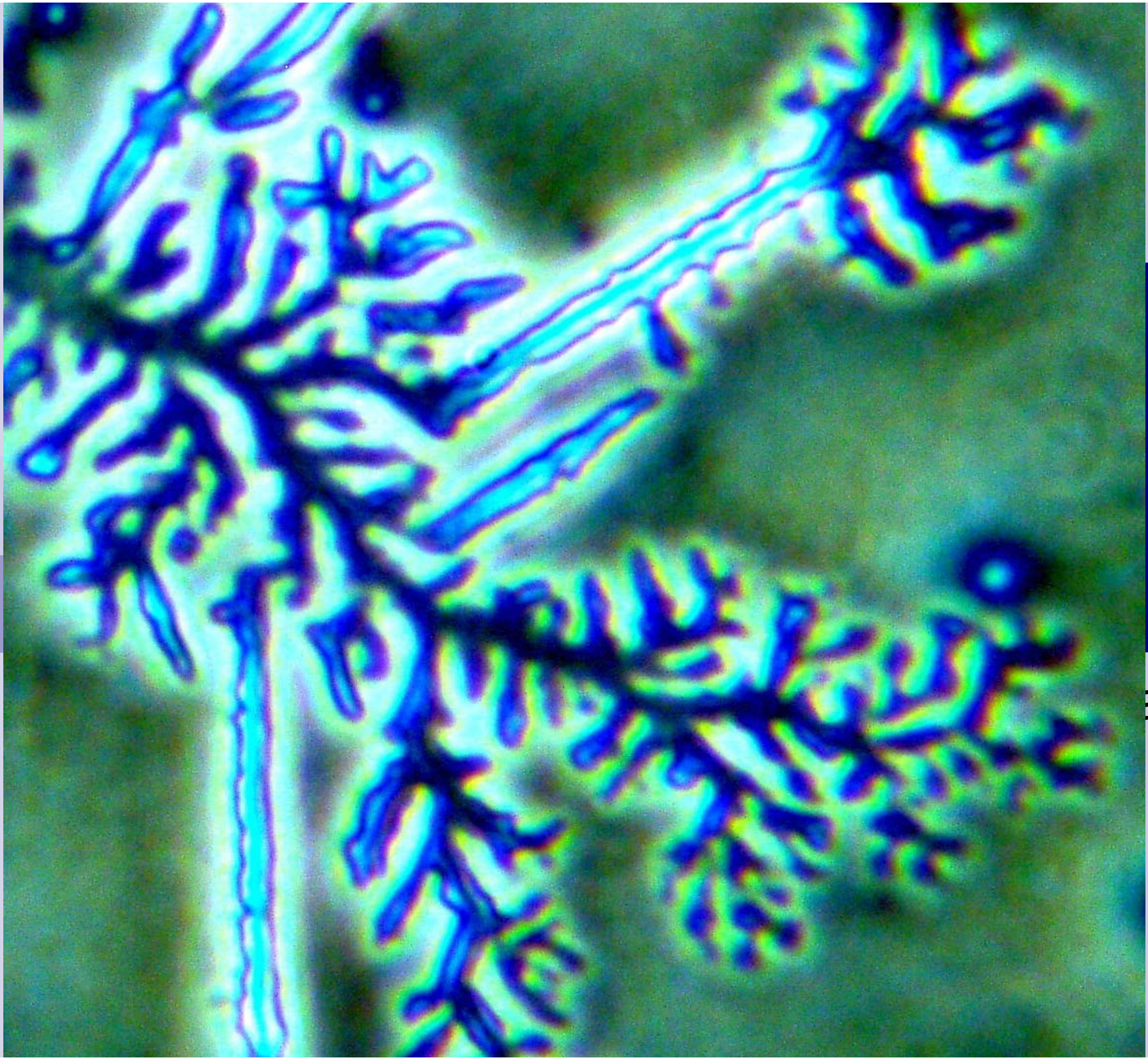
Palladium Lipoic Acid Fern Network



Magnetic Transition of Liquid Crystal Palladium Lipoic Acid

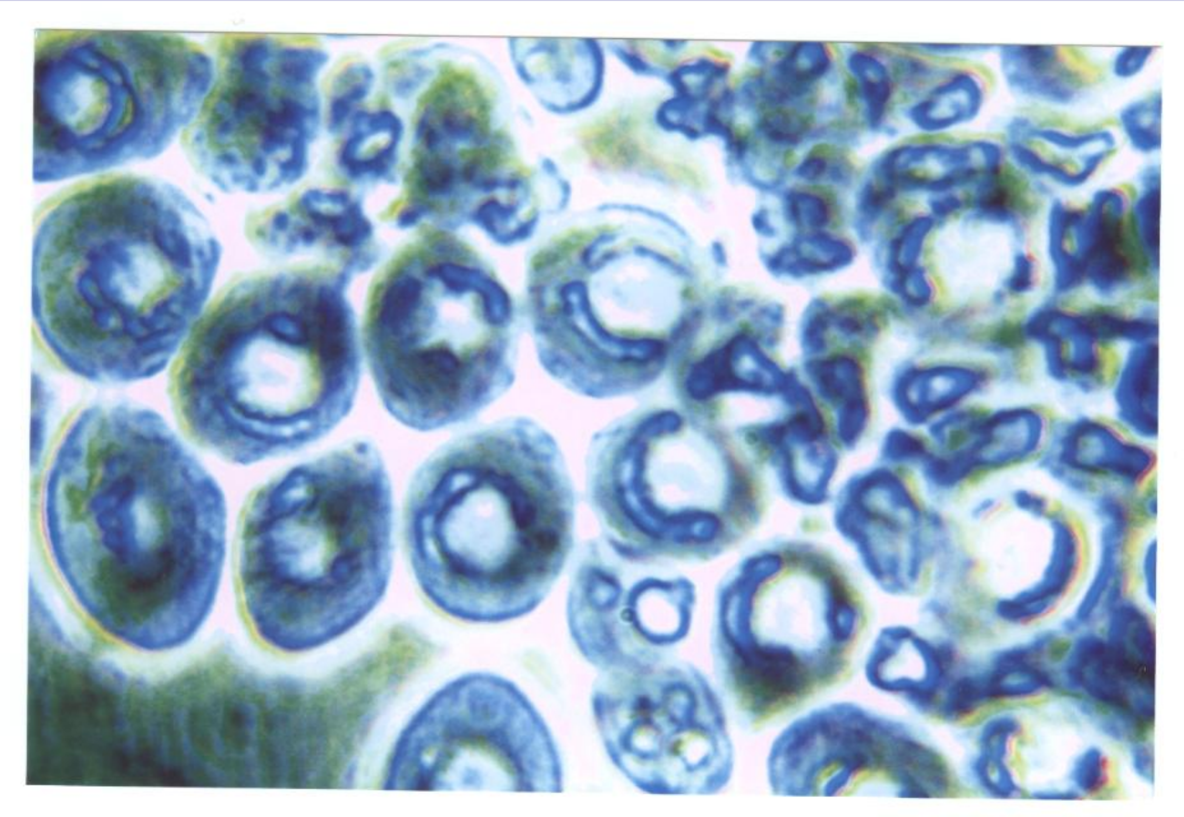


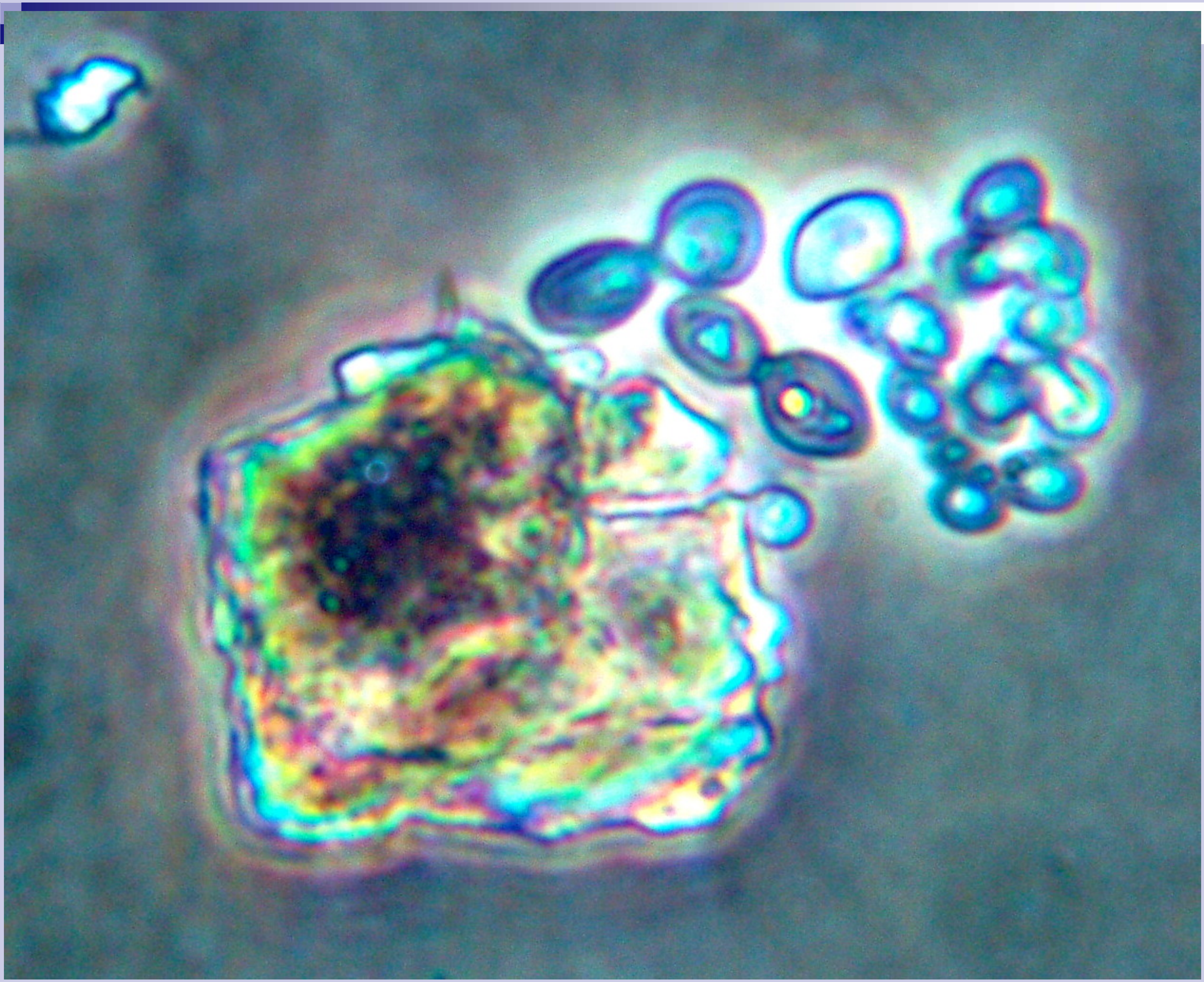
Of



an

Hetrochromatin





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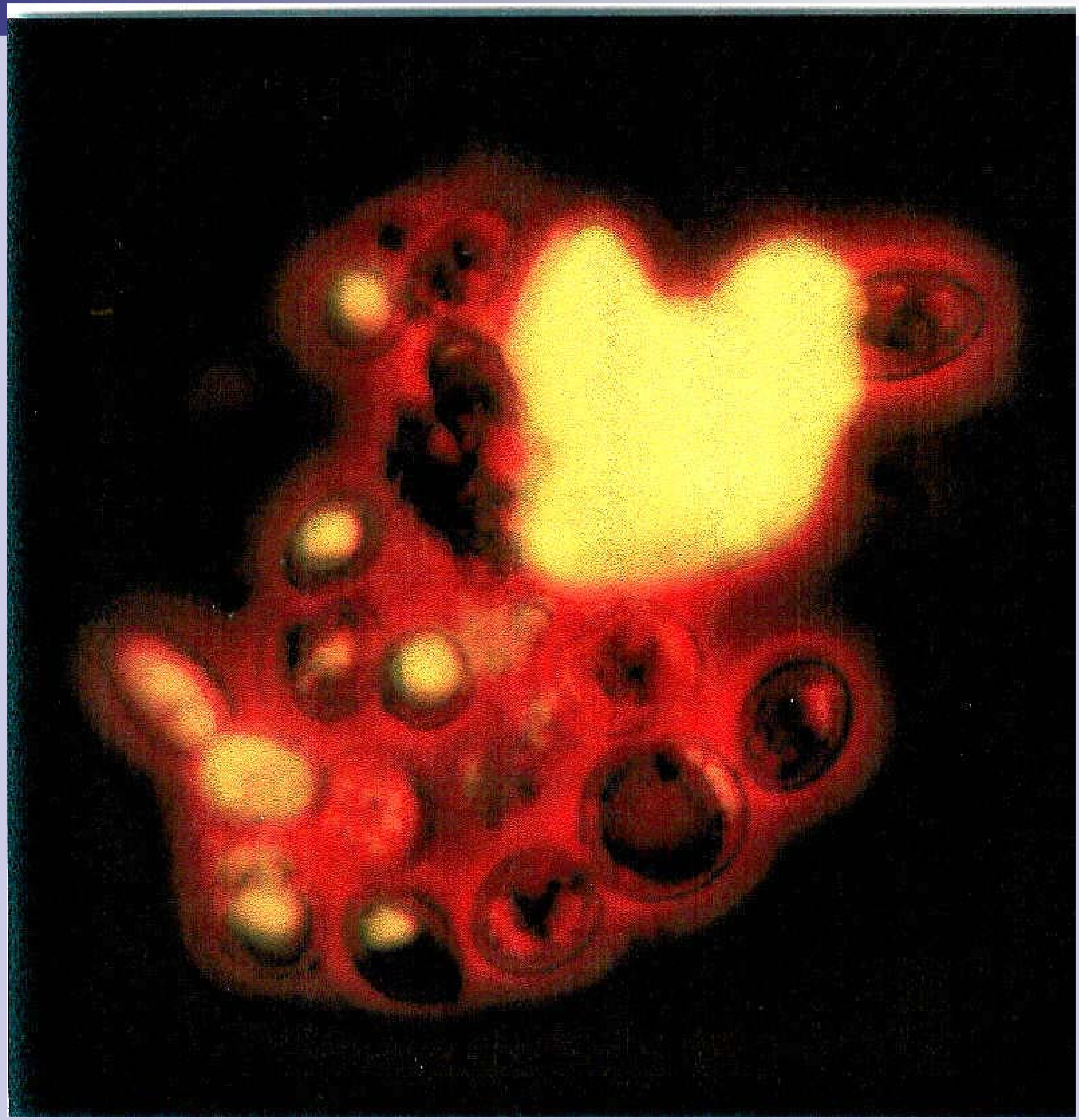


EFFECT OF SYNTHETIC REDUCTASE ON TETRAHYMENA

FIG. Tet 2

MEMBRANE FAILURE AFTER CONCURRENT NITROGEN PURGING

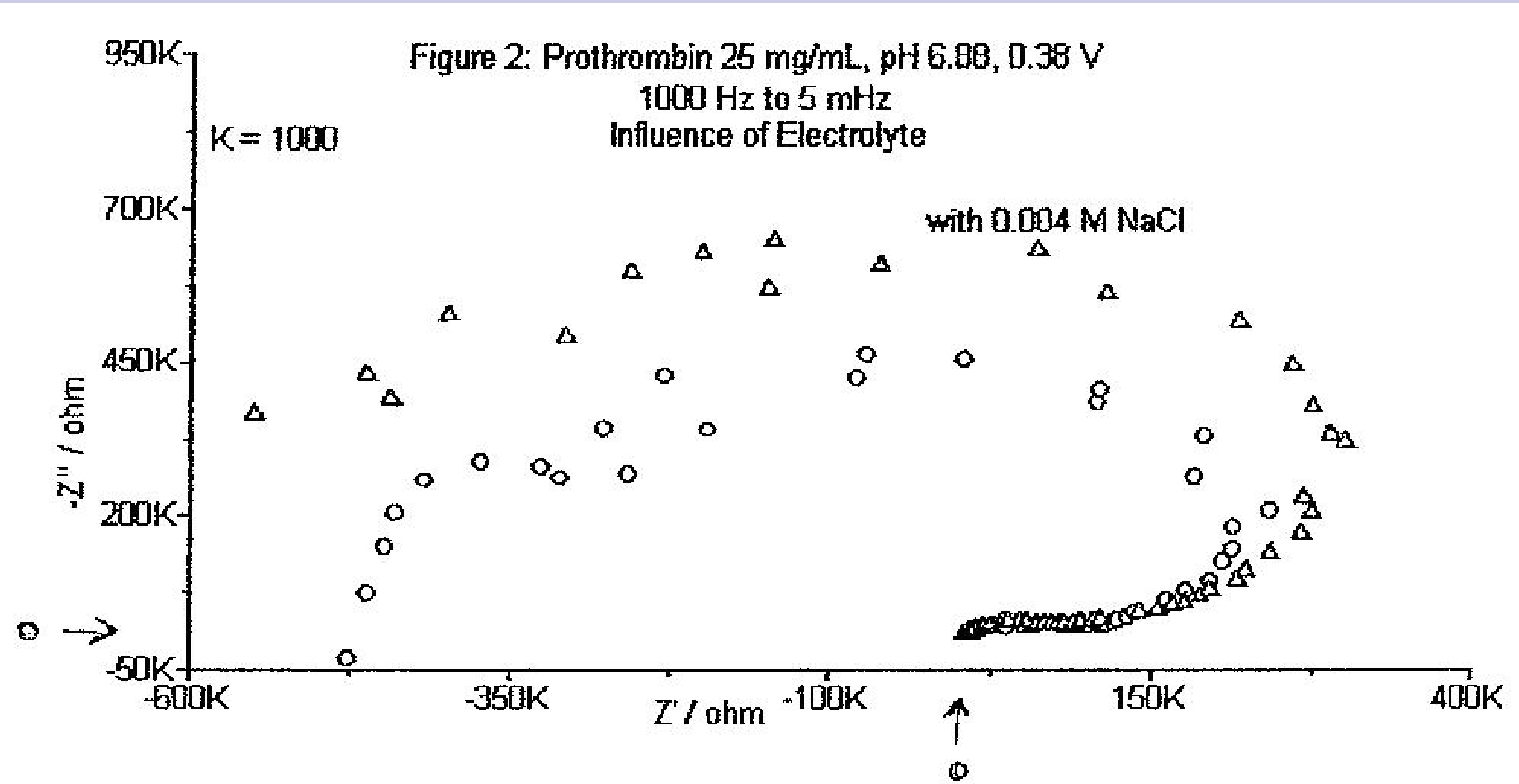
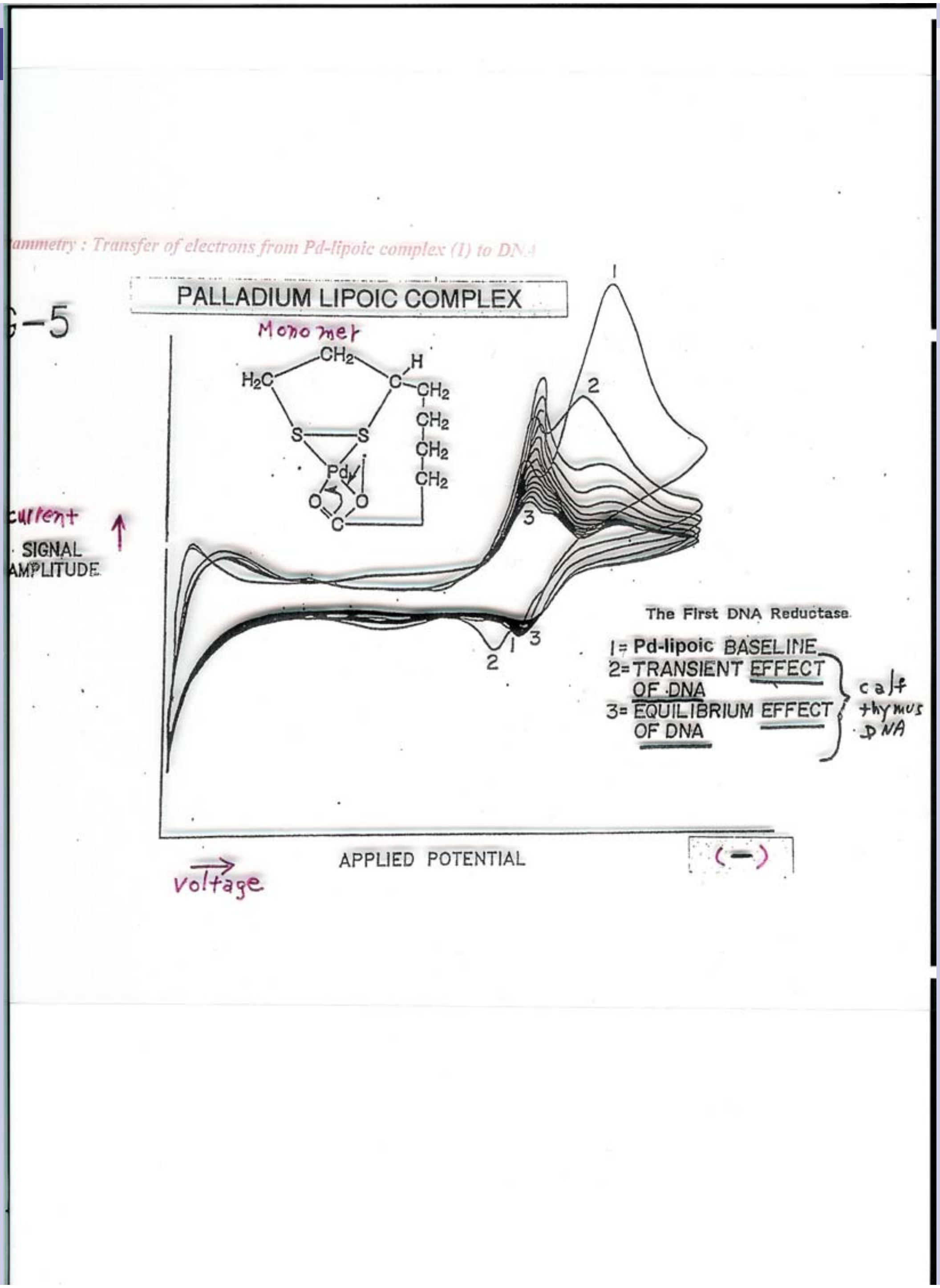
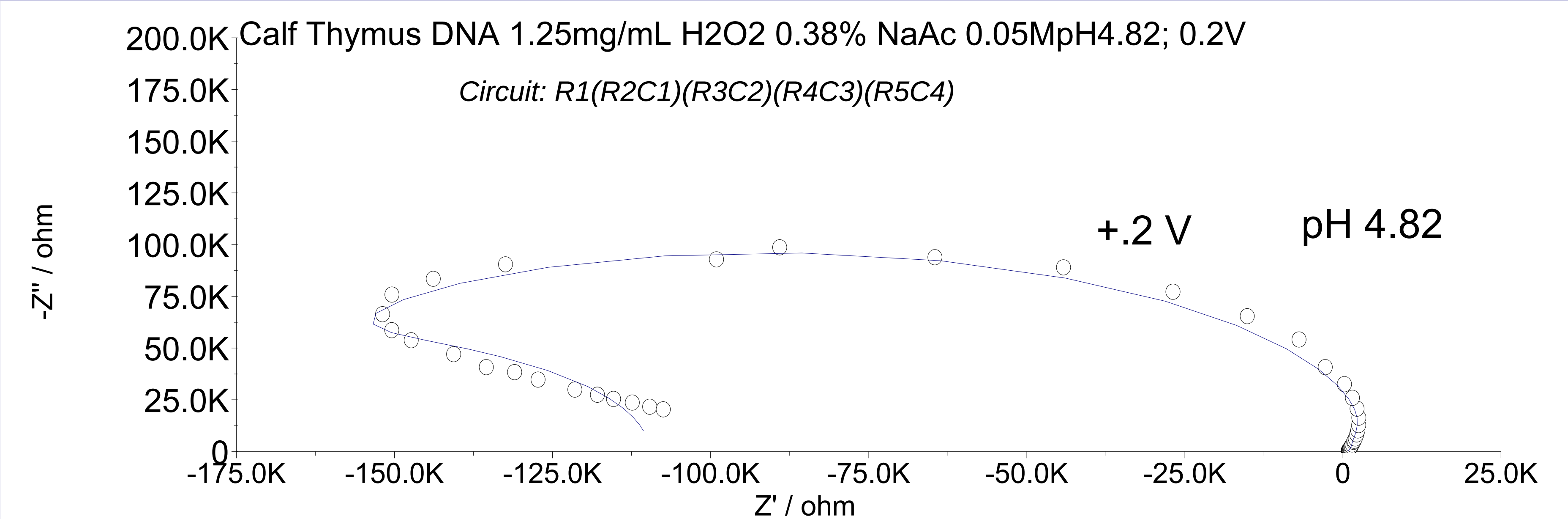


Figure 2: Prothrombin 25 mg/mL, pH 6.88, 0.38 V
1000 Hz to 5 mHz
Influence of Electrolyte
K = 1000
with 0.004 M NaCl
950K
700K
450K
200K
-50K
-Z'' / ohm
-600K
-350K
-100K
150K
400K
Z' / ohm



ammetry : Transfer of electrons from Pd-lipoic complex (1) to DNA
PALLADIUM LIPOIC COMPLEX
-5
Monomer
current
SIGNAL
AMPLITUDE
The First DNA Reductase
1= Pd-lipoic BASELINE
2= TRANSIENT EFFECT OF DNA
3= EQUILIBRIUM EFFECT OF DNA
calf thymus DNA
APPLIED POTENTIAL
voltage
(−)

DNA-NaAc-H_2O_2



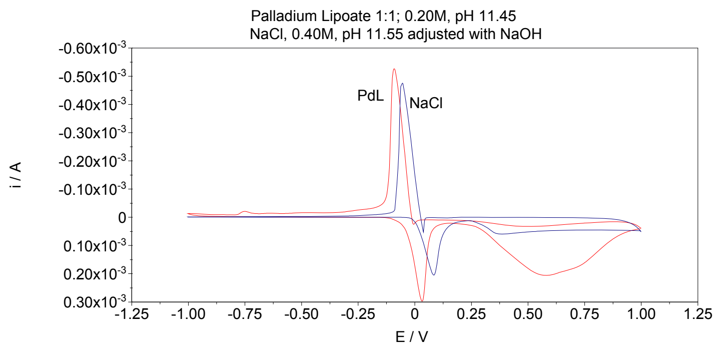
Two Quadrant Impedance
IN DNA Requires Dopant
Peroxide

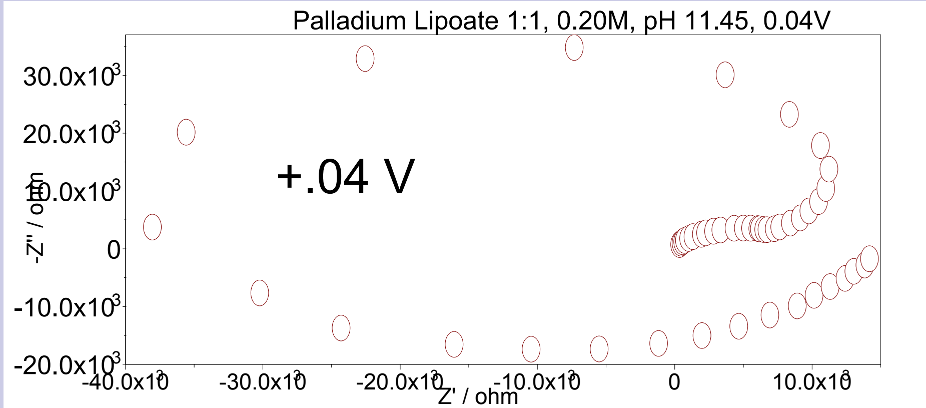
Baseline for Negative Resistance

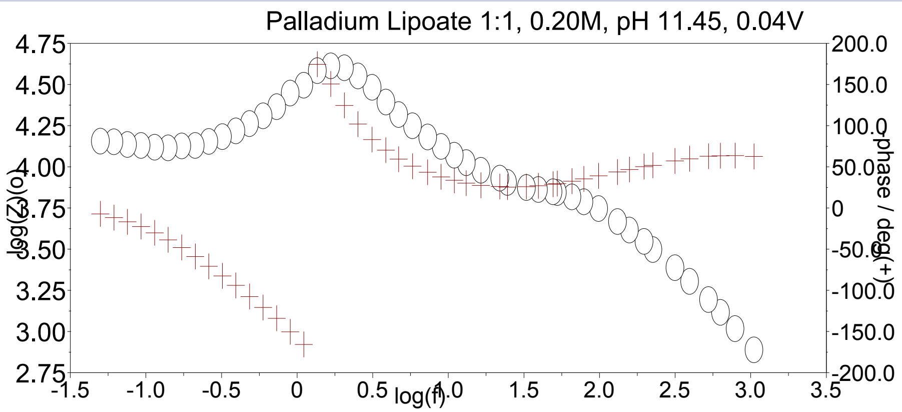
- Notice the reversing impedance curve of a conducting polymer first requires completion of the steady state curve.
- Curvilinear discharge tells us the electrons are in an organized structure.
- This structure is the Secondary (Type 2)

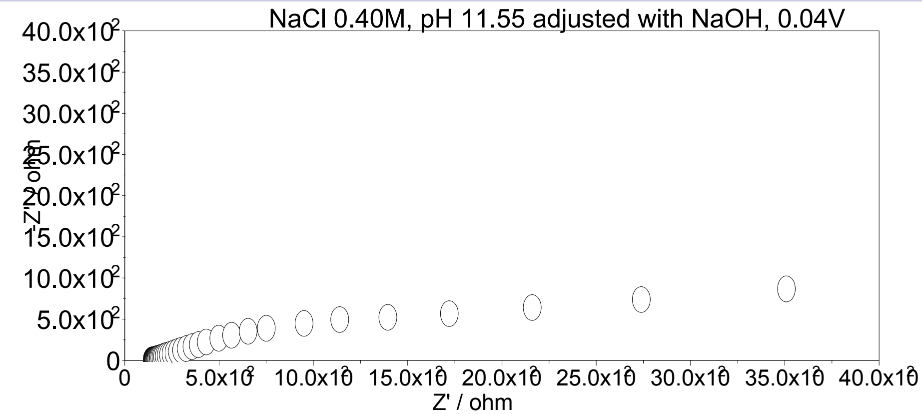
Polarization parallel to the polymer surface.

Unusual Impedance of Pd-Lipoic Acid Liquid Crystal Complex









Semiconduction Requisites :

- 1. polymer-specific counter-ion
- 2. periodic lattice array (liquid crystal)
- 3. paramagnetic surface film (free radical or paramagnetic metal)
- 4. specific ligand redox voltage
- 5. specific low frequency pulse – probably supplied by the EKG

Semiconduction Charge Transfer With Palladium Lipoic Acid :

1. Supplies electro-equivalents for contributions to apoptosis, and to DNA packing.
2. Provides electron energy for oxygen competent ATP synthesis for healing and normal growth.
3. Transfers oxy-radicals from bulk solution to polarized hydration films, then to mitochondria and to DNA.
4. Spin reinforces water structure at H bonds.
5. Clonally selects Type 2 polarized cells by apoptosis.
6. Unites cells as tissues by the nano-vascular route.

This kind of charge transfer affects many biochemical systems :

- 1. mitochondria – apoptosis
- 2. chromatin – packing configuration
- 3. cell size and shape
- 4. regeneration of neuronal filaments
- 5. unified signal transmission and reception throughout the organism

(eg. Prothrombin to DNA)

L = E V B sin Theta
(the Physics model)

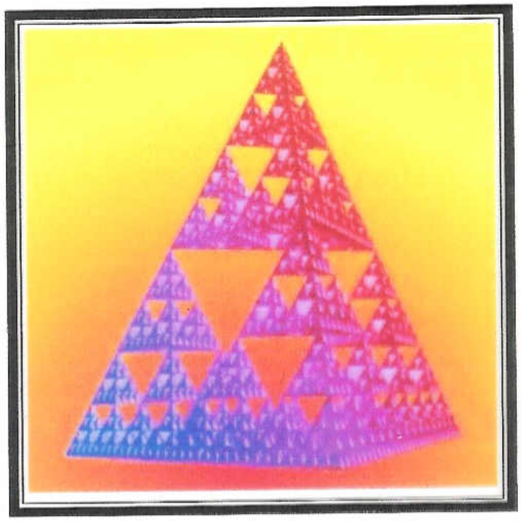
- **Lorentz Force = Electric field x**

Magnetic field x sin Theta.

Where Theta is the angle between the fields.

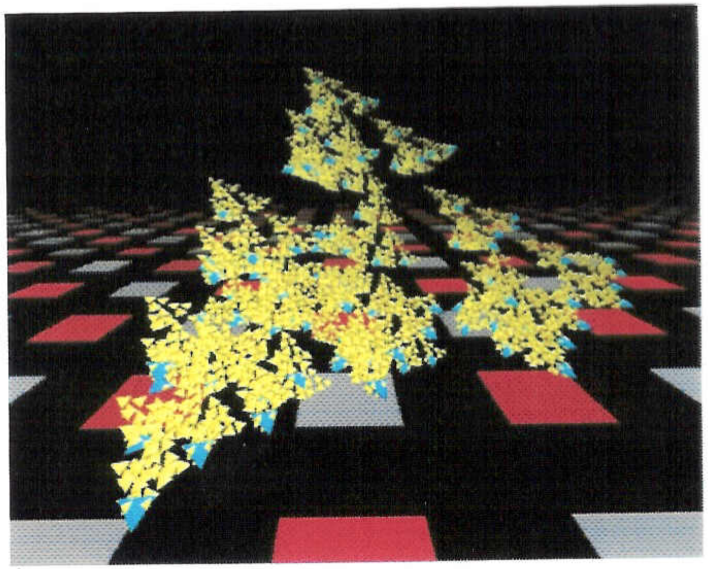
…This is the charge transfer low frequency force and wave process which provides signal and structure unification for the multi-cellular state, and which must be electronically maintained for the health of the organism.

actal Gallery Tour



Sierpinski Tetrahedron

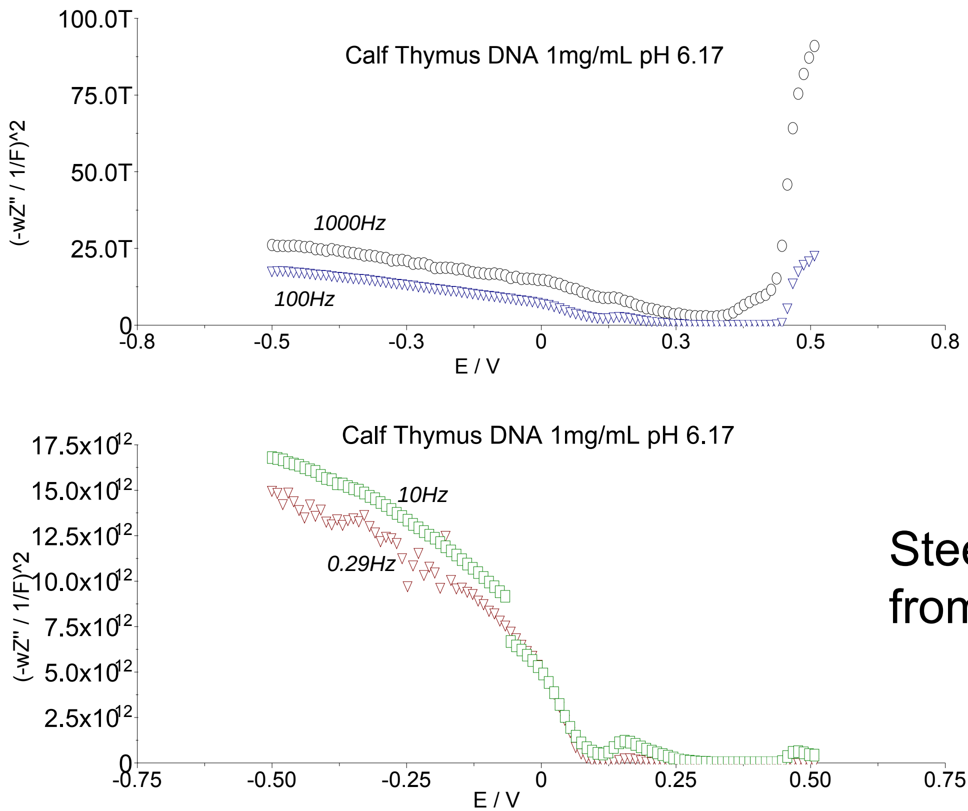
Fractal Application



DNA Frequency Sensitivity

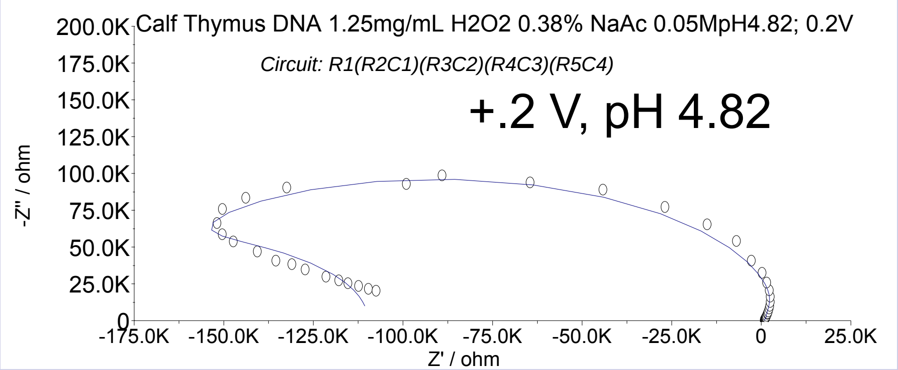
Mott-Schottky Plots for Calf Thymus DNA 1.0mg/ml

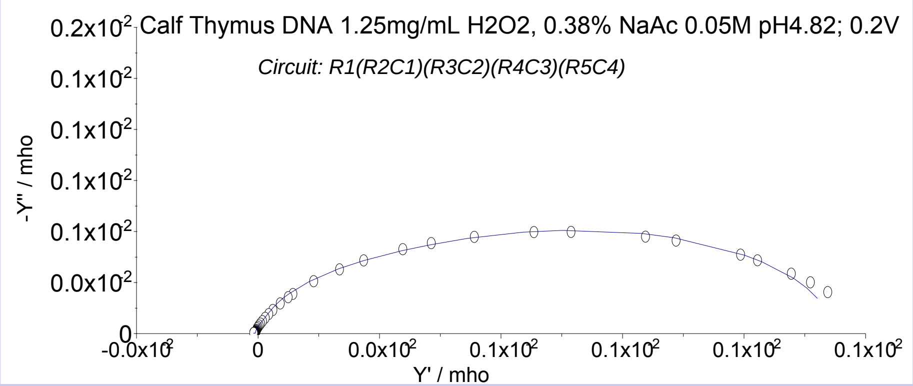
Mott-Schottky Plots for 1mg/mL Calf Thymus DNA



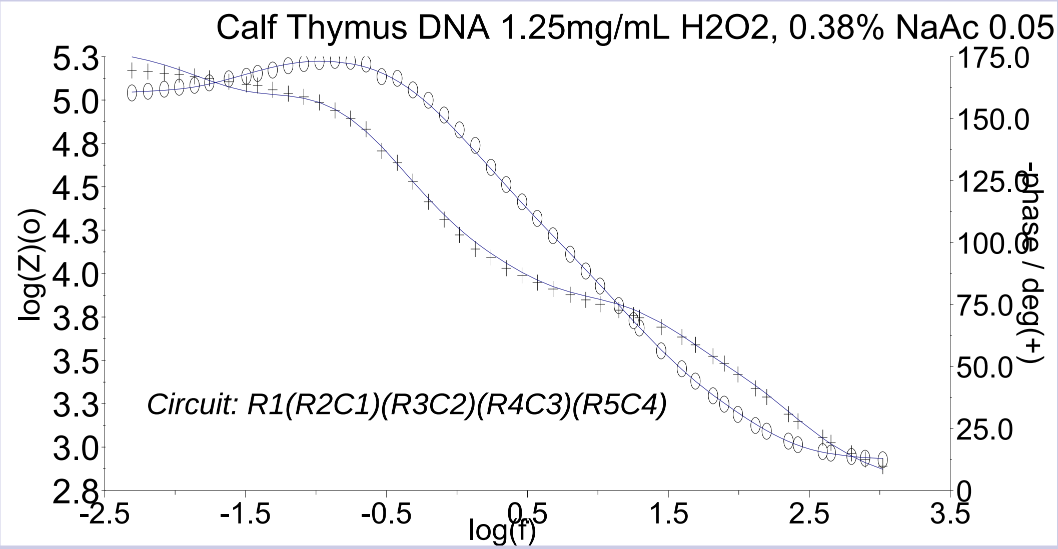
Steep inflection from 10. Hz

Equivalent Circuit DNA-H_2O_2-NaAc





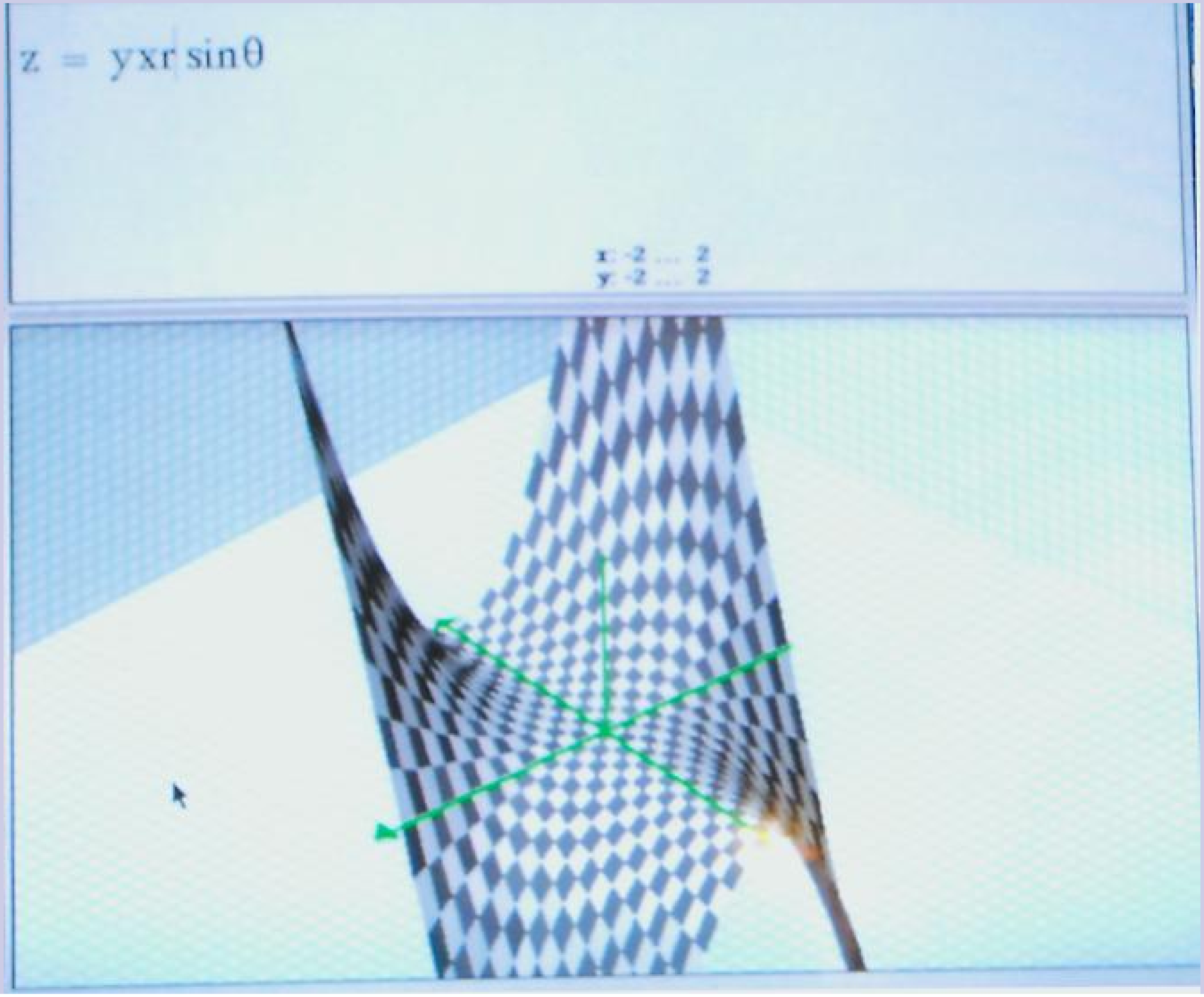
Note the impedance enters the upper left quadrant



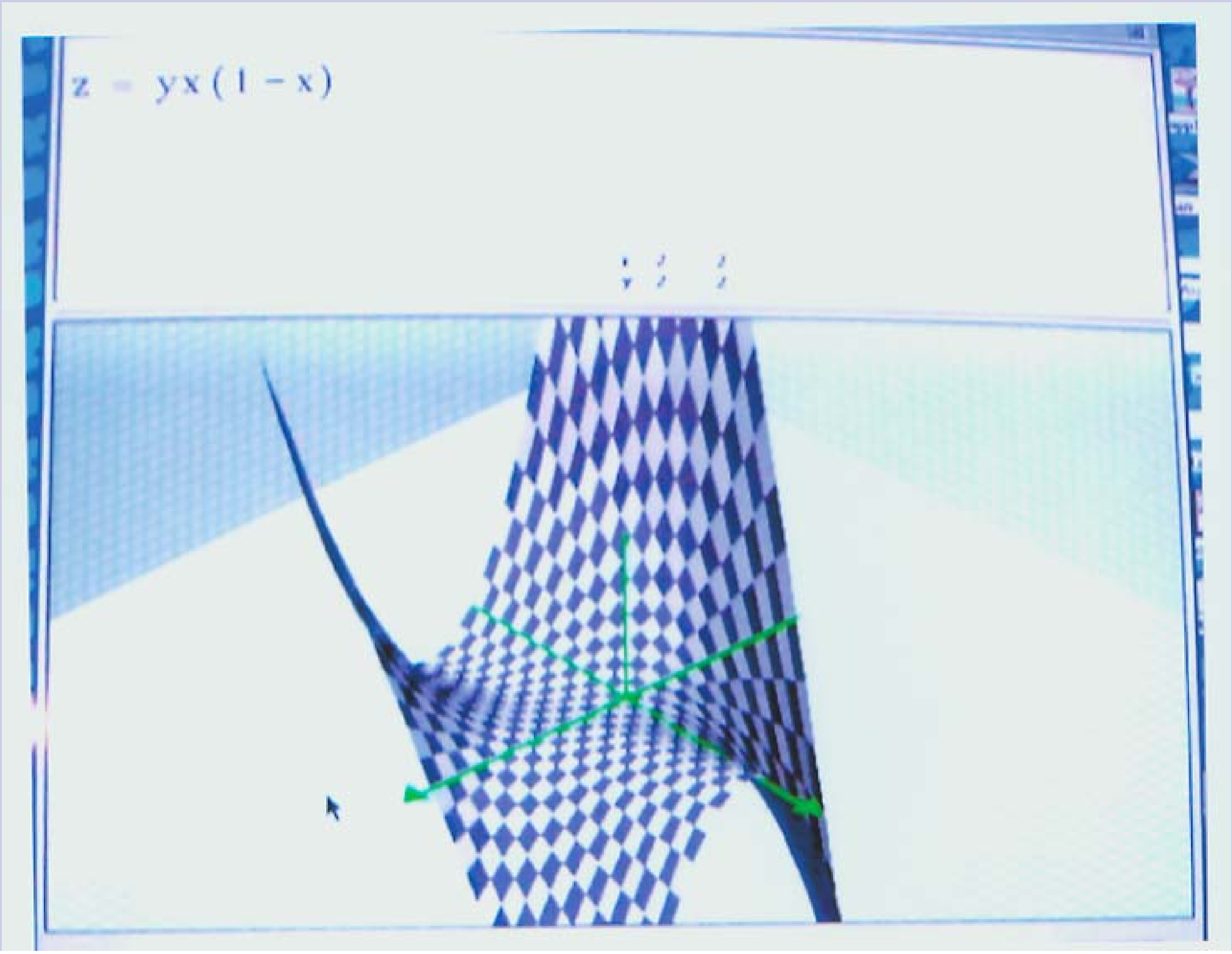
DNA-NaAc-H_2O_2 Circuit Fit : R (RC)(RC)(RC)

R1	.884 kOhm	2.3% error
R2	2.04 kOhm	12.276%
C1	3.89 uF	7.852%
R3	-178.9 kOhm	1.749%
C2	2.274 uF	1.859%
R4	65.6 kOhm	5.71%
C3	54.9 uF	12.144%

Lorenz Equation Surface Plot



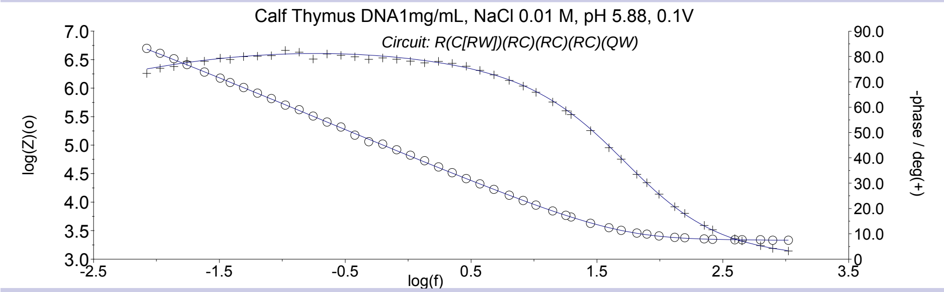
Fractal Equation Surface Plot

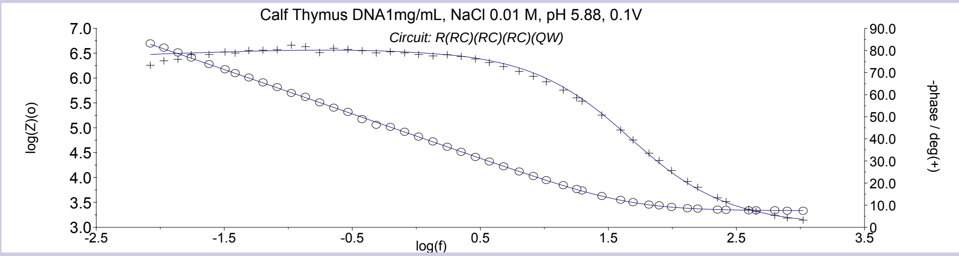


L.C. Multi-Quadrant Impedance

- To analyze liquid crystal multiple double layer systems, we located narrow (5.mv) polarization conduction bands on the Hg electrode: Bands near zero volts provide dopant Hg ion. This is controlled corrosion.
- This reverses impedance curve direction and opens all quadrants of complex plane data as forecast by Cao using 5 parameters.

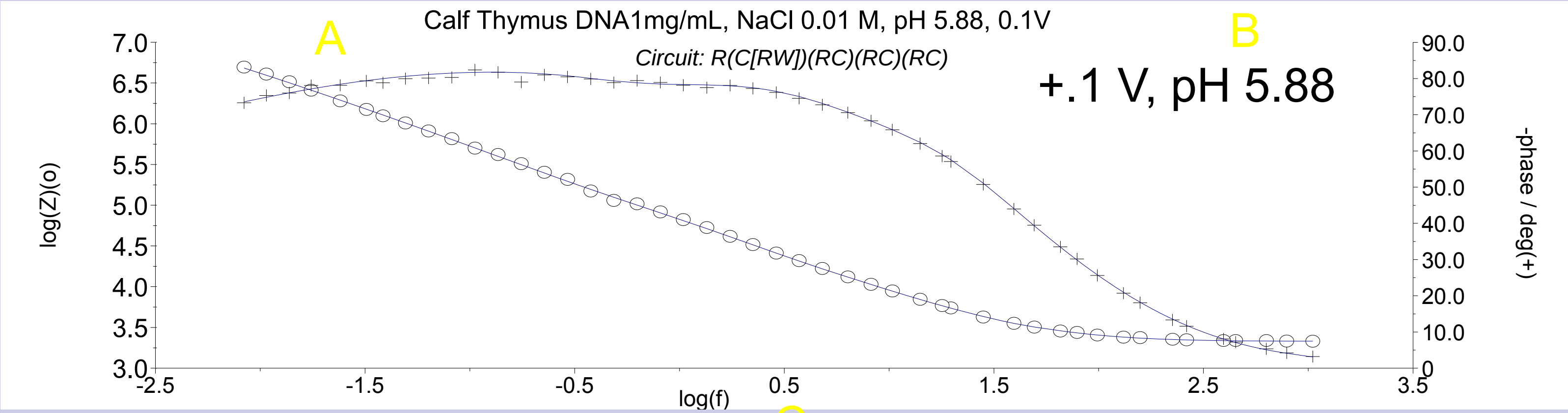
Calf Thymus DNA 1mg/mL, NaCl, 0.01M Equivalent Circuits, Bode





A

B

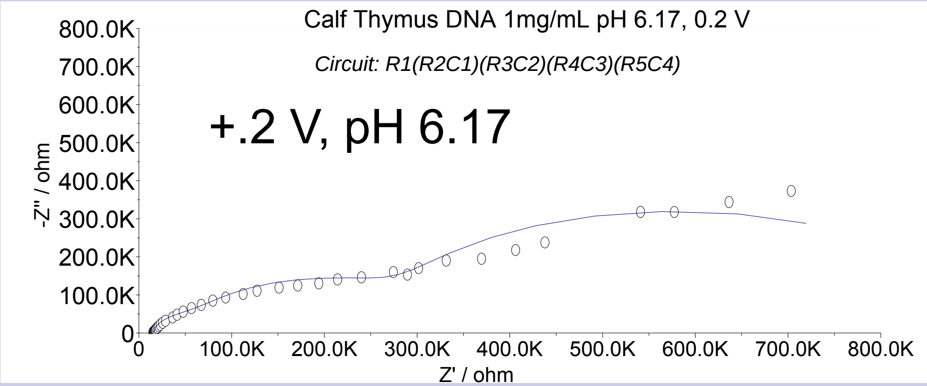


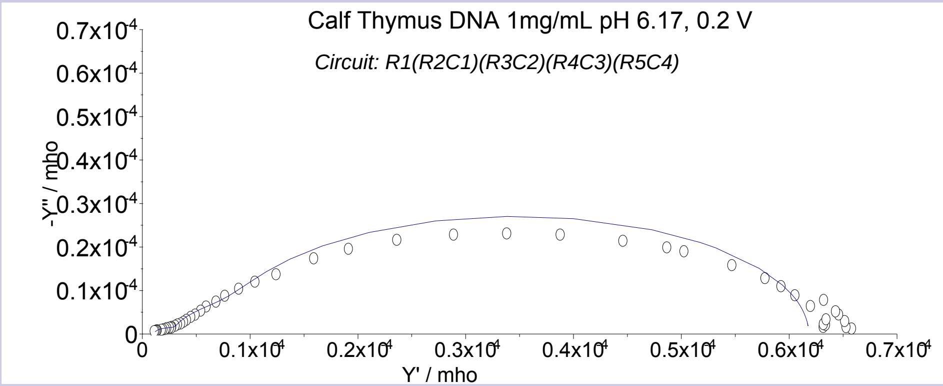
C

Which circuit do you prefer? We prefer C, a Randles circuit with 3 RC units.

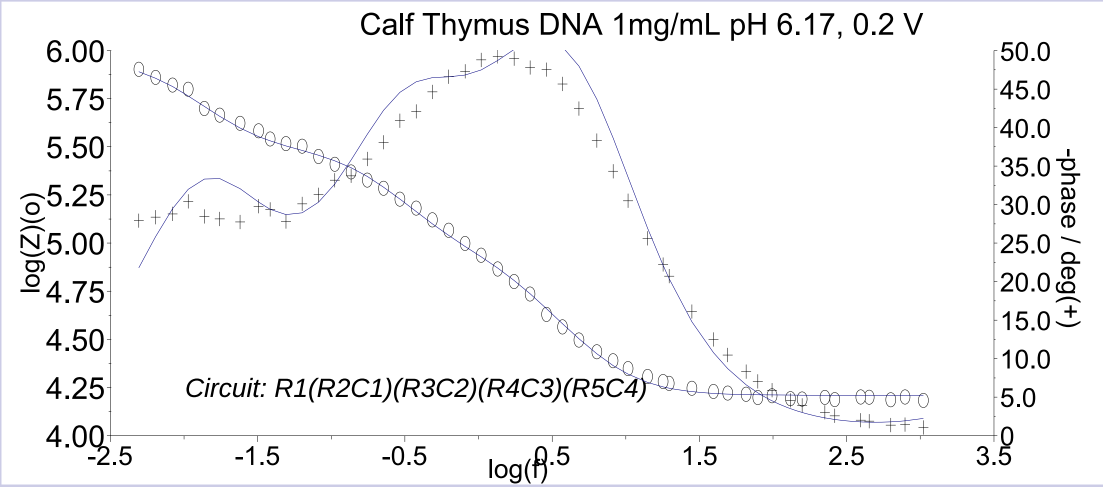
Equivalent Circuit for DNA

Without H_2O_2

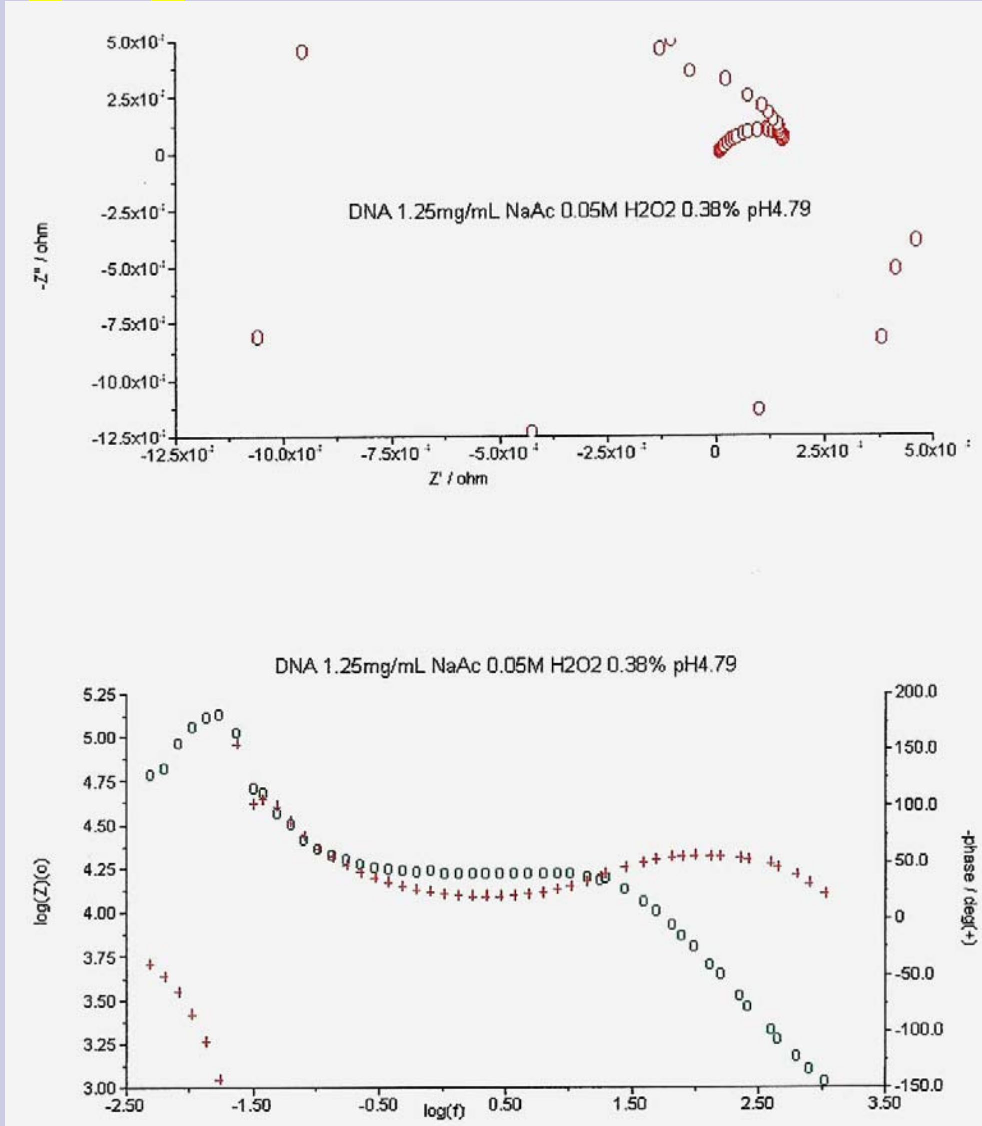




Note the impedance stays in the first quadrant



DNA-H_2O_2, 360 Degree Impedance



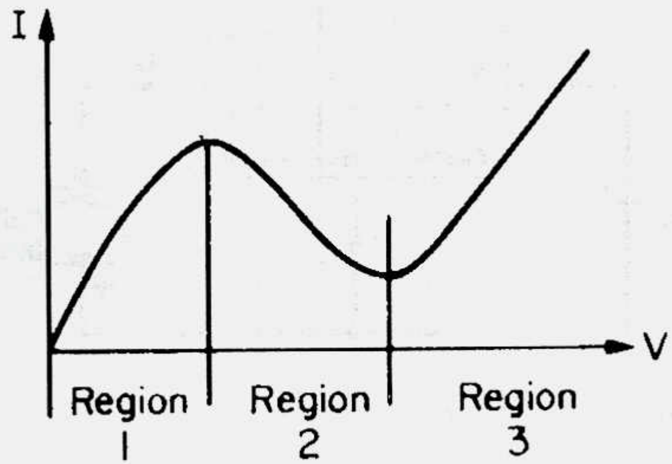
R [RC] [RC] [RC] [RC]

- The 4 RC units have different values. Only the dissipative RC has a negative value for R.
- 3 RC units may represent 3 different double layers . Sometimes a 4th RC fits. One model is :
- 1. electrode-L.C. double layer
- 2. extended L.C. packing layers
- 3. internal polymer surface – eg.
- DNA hydration grooves
- 4. gene base pi-way activation

Tunnel diode

The tunnel diode (sometimes called the Esaki diode, after its inventor) is a p-n junction in which the doping is very heavy. This results in a narrow depletion layer, and breakdown occurs without any external bias at all.

The forward characteristics of the diode are shown below. There are three distinct regions. In region 1, breakdown is occurring and forward current is increasing. In region 2, the device comes out of breakdown and exhibits negative resistance (falling I for increasing V). In region 3, the device is completely out of breakdown and behaves like a normal diode.



Tunnel diode V/I characteristic curve

The useful portion of the characteristic is region 2, the negative resistance making the device useful as an oscillator or storage device.

Transmission Cable=[RC] Sequence

Bisquert

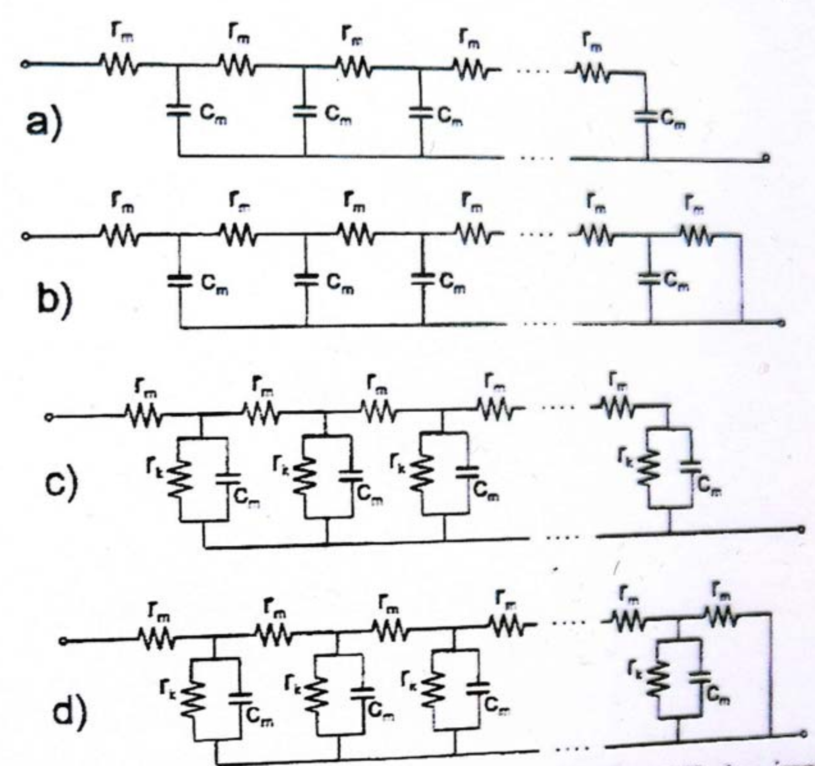


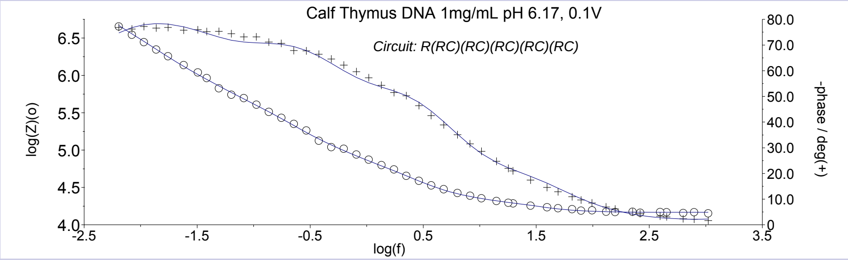
Figure 4. Transmission line representation of the diffusion impedance: (a) simple diffusion with the reflecting boundary condition; (b) simple diffusion with the absorbing boundary condition; (c) diffusion coupled with a homogeneous reaction with the reflecting boundary condition; (d) diffusion coupled with a homogeneous reaction with the

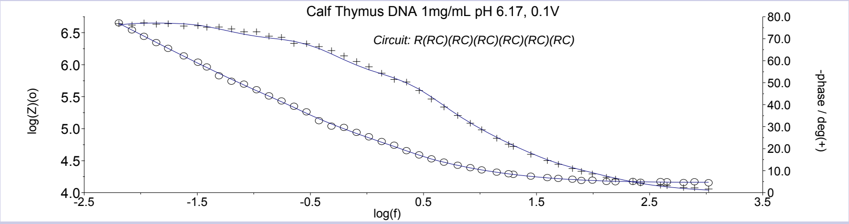
Range of DNA Electronic Identities

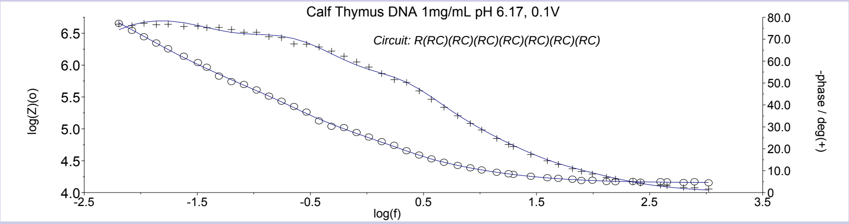
- 1. Tunnel diode (negative resistance RC)
- 2. Transmission Cable (sequential RC units)
- 3. Multi-stranded transmission cable
- with mutual inductance between the pi-ways and the hydration grooves
- 4. Semiconductor = coherent signaling –
- (Mott-Schottky)
- 5. Wire, including twisted pair balanced line

6. Diode-Oscillator circuit

Calf Thymus DNA 1mg/mL Equivalent Circuits

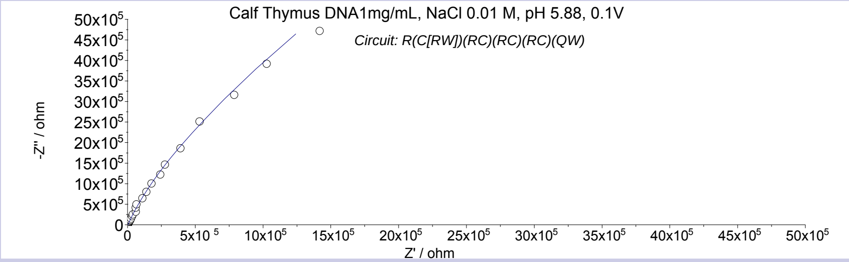




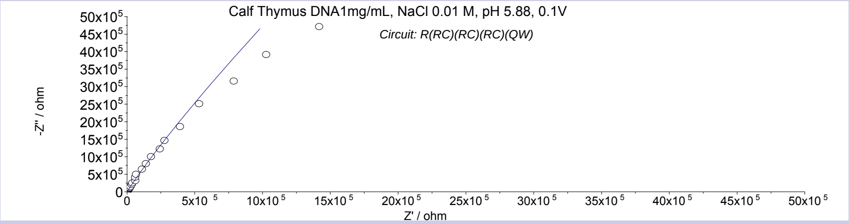


The circuit with 6 or 7 RC units seems better than the one with 5 RC units.

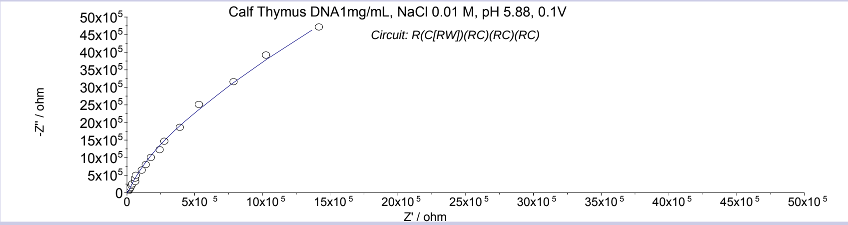
Calf Thymus DNA 1mg/mL, NaCl 0.01M Equivalent Circuits



A



B



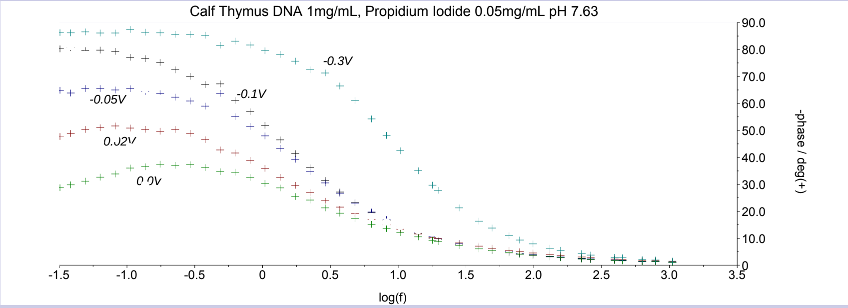
C

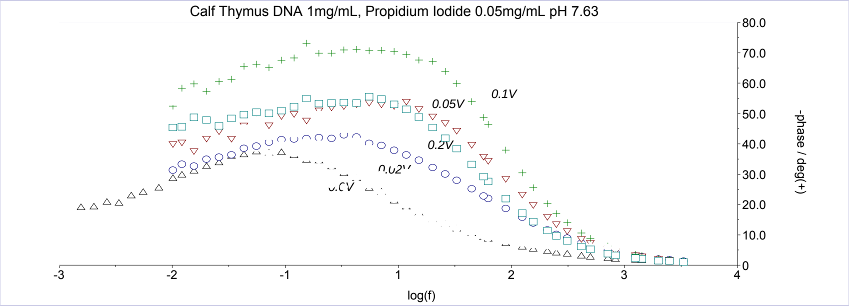
Which circuit do you prefer? We prefer C, a Randles circuit with 3 RC units.

Equivalent Circuit Summary

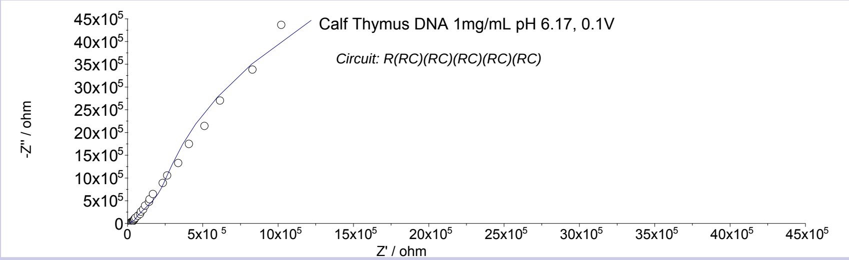
- DNA 1mg/mL, 0.1V : $R_1(R_2C_1)(R_3C_2)(R_4C_3)(R_5C_4)(R_6C_5)(R_7C_6)$
- DNA 1mg/mL, NaCl 0.01M, 0.1V: $R_1(C_1[R_2W_1])(R_3C_2)(R_4C_3)(R_5C_4)$
- DNA 1mg/mL, NaCl 0.01M, CH_3OH 10%(V/V), 0.1V: $R_1(C_1[R_2W_1])(R_3C_2)(R_4C_3)(R_5C_4)(Q_1W_1)$

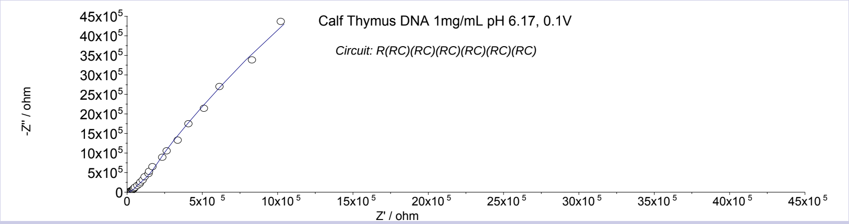
DNA-Propidium Iodide

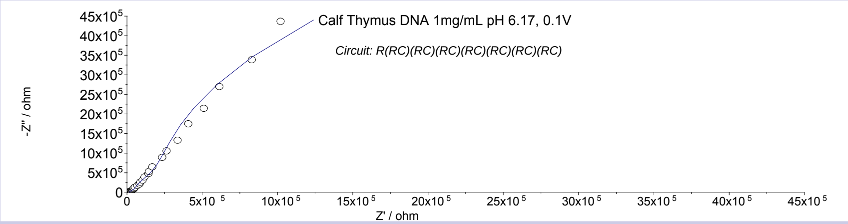




Calf Thymus DNA 1mg/mL Equivalent Circuits

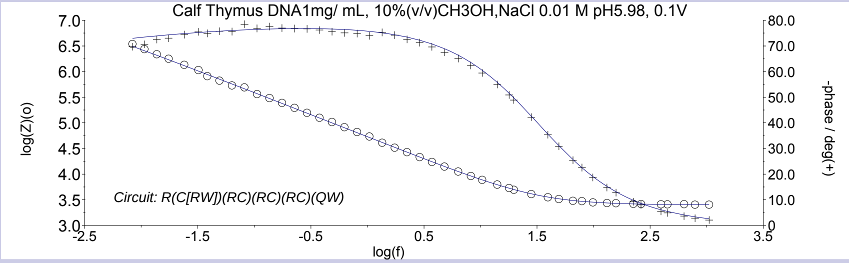


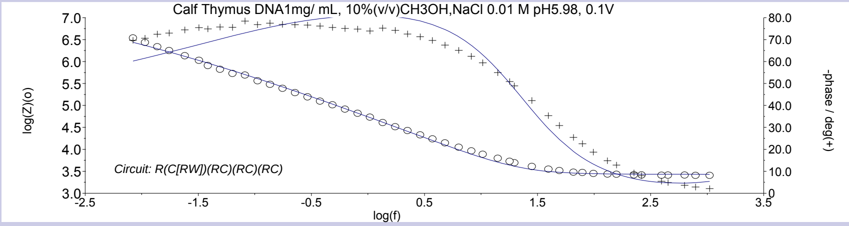


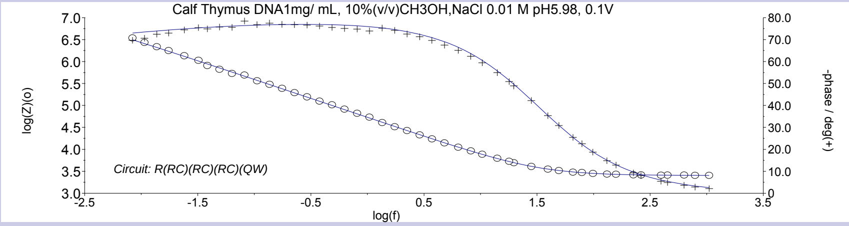


The circuit with 6 RC units seems better than the one with 5 or 7 RC units.

Calf Thymus DNA-NaCl-CH_3OH Equivalent Circuits

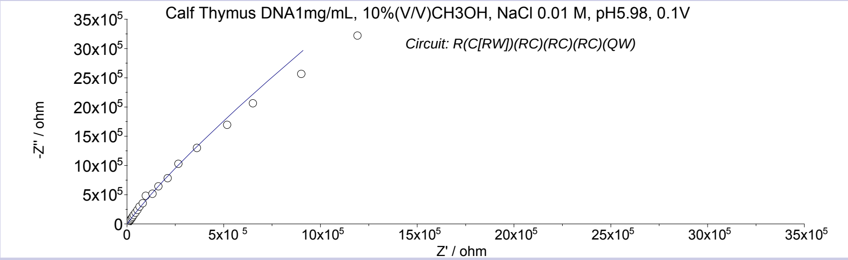


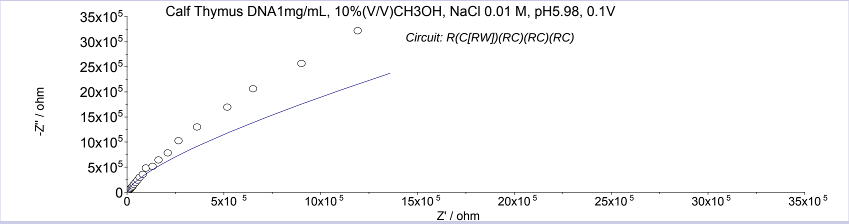


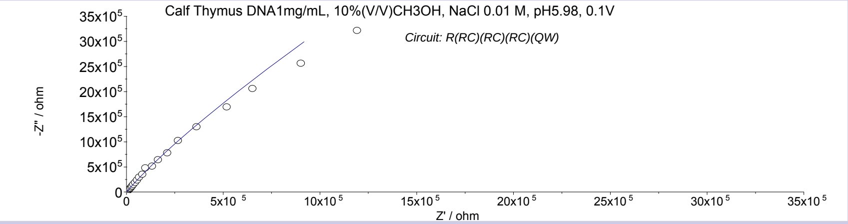


We need the three RC units and QW for the fit. (C[RW]) not critical.

Calf Thymus DNA-NaCl-CH_3OH Equivalent Circuits

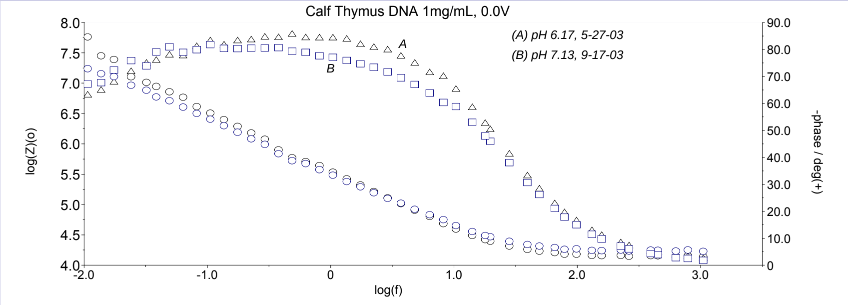


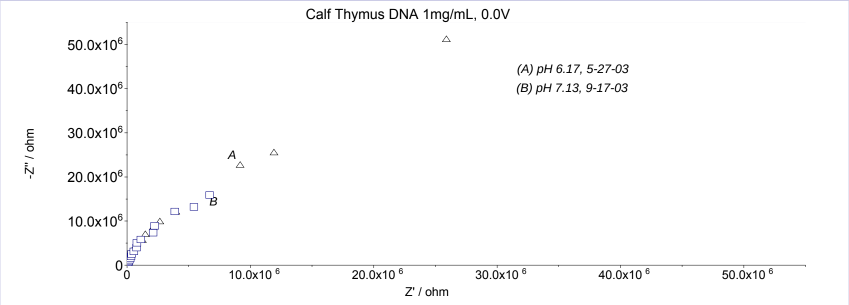




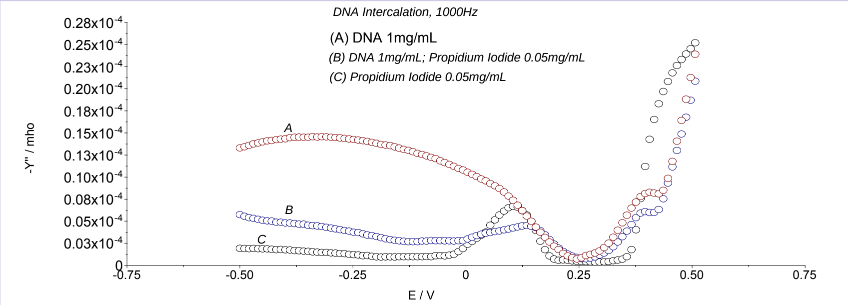
We need the three RC units and QW for the fit. (C[RW]) not critical.

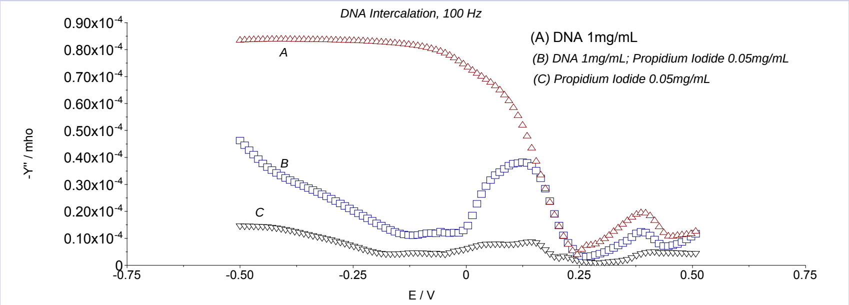
Consistency in DNA samples
Two different samples and dates

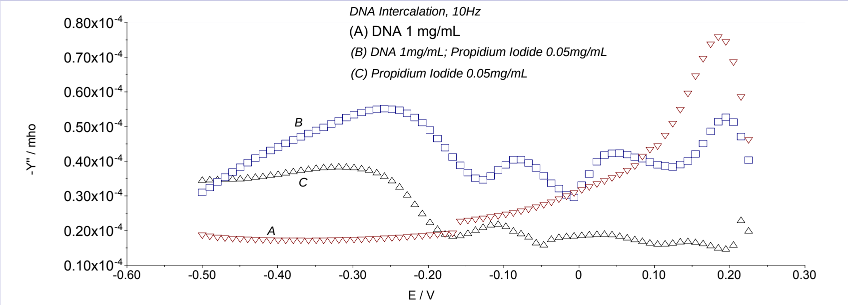


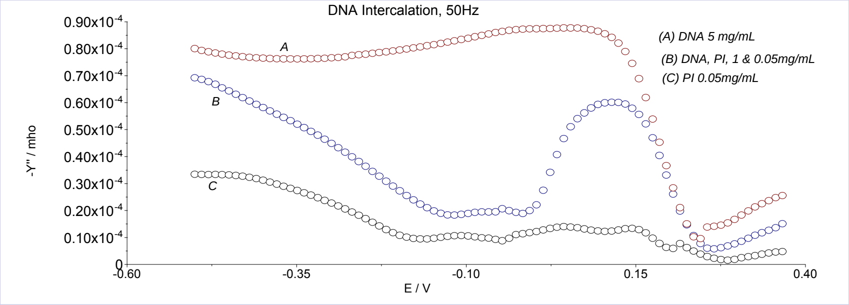


DNA Intercalation with Propidium Iodide

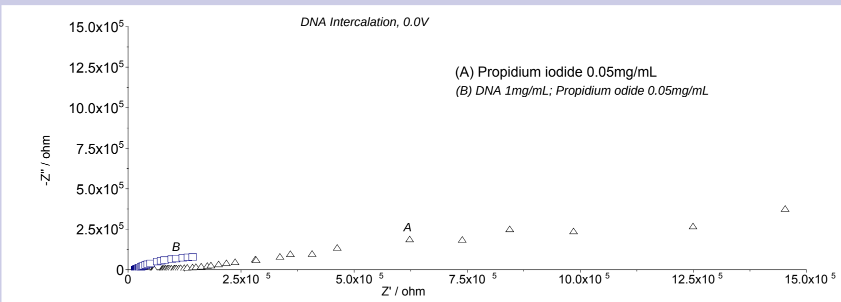


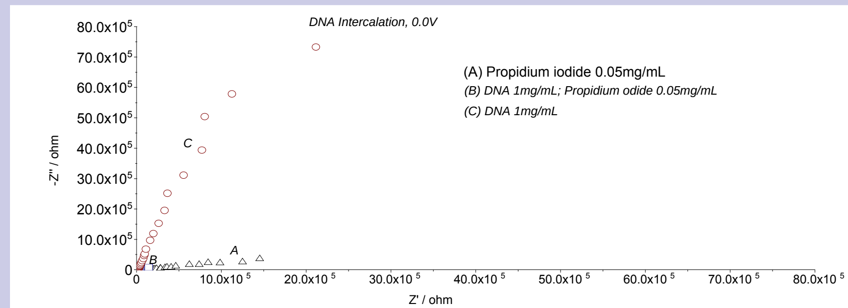




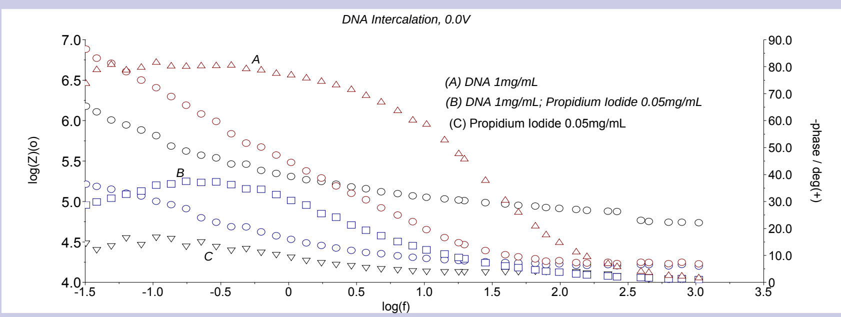


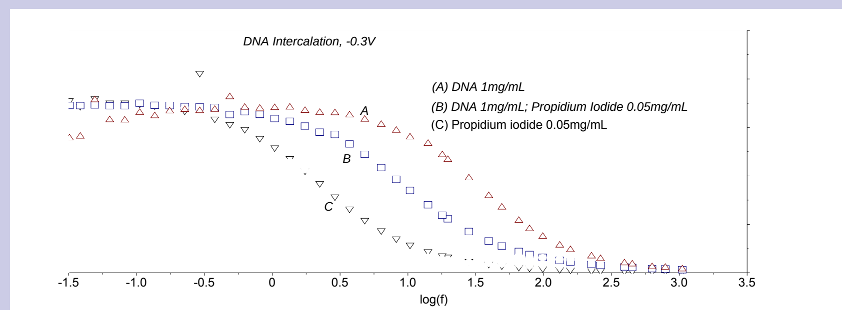
DNA Intercalation with Propidium Iodide





The impedance is much less after intercalation.





Equivalent Circuit Summary

- DNA 1mg/mL, 0.2V : $R_1(R_2C_1)(R_3C_2)(R_4C_3)(R_5C_4)$
- DNA 1mg/mL, NaAc 0.04M, H_2O_2 0.38%(V/V), 0.2V: $R_1(R_2C_1)(R_3C_2)(R_4C_3)(R_5C_4)$
  R_2 is negative because impedance extends into the second quadrant.

Beta Values

- The 1993 data for DNA gave a β value of 0.2 $Å^{-1}$. Since then β values in the range 0.1 to 1.4 have been obtained from various experiments that created the comment, “β was hopping around like a flea on a dog”. The general conclusion is “DNA is by no means a wire, but it still conducts charge better than proteins.”

Why is DNA diode behavior important ?

- Since the discovery of the double helical structure of the B form of DNA, the question arose as to whether DNA's internal tunnel of stacked π orbitals might serve as a molecular wire.
- How and how fast an electrical charge goes through DNA has significant bearings on DNA damage, genetic detection and microelectronics.
- The consequences of long range radical migration through DNA are important with respect to understanding carcinogenesis and mutagenesis.

Retrospect

- One has to carefully look at both the Nyquist and Bode plots before deciding the most probable equivalent circuit.
- The phase angle seems to be a powerful tool to gain fundamental information on solute-solvent interactions at or near the electrical double layer.
- L.C.polyanions such as DNA extend the double layer through the bulk of the solution.
- The equivalent circuit suggest a transmission line model for DNA. However it is more dynamic than that suggested for polymeric semiconductors.

Conclusions

- Intercalation of DNA with propidium iodide suggests a direct evidence for an enhancement of the π way in the conduction properties of DNA.
- Our results suggest DNA can enhance its conduction properties by appropriate association with other molecules and ions and appropriately modify its equivalent circuit.

Conclusions

- DNA transmission line impedance is dependent on extended organized films of water, electrolytes and radicals.
- Water, “the matrix of life”, plays a dominant role in forming equivalent circuits in life processes. Water geometry is dependent on ion streams, radicals, and liquid crystal packing. The liquid crystal state supports signaling processes across the solvent space.
- Dopant peroxide may introduce a paramagnetic thin film influence. This may account for Interaction of the hydration layers and dissipative charge transfer between domains.
- Under controlled conditions, DNA charge transfer resembles that of a diode oscillator.

Conclusions

- An extraordinarily fast, distance independent electron transfer behavior observed in 1993 suggest a wire-like behavior for DNA. This was based on the parameter, β, from the electron transfer theory, that describes the distance dependence of charge transfer rate.
- For proteins, where charge does not travel well, the rate drops off exponentially with distance and β is around 1 $Å^{-1}$. Transfer rates for proteins decrease by a factor of 10 for every 1-5 Å separation between reaction centers.