Presentation for the Steering Committee

at the Public Hearing on the Southeast Metro Transmission Line

PREFILED DIRECT TESTIMONY OF DR. MARTIN BLANK

Q. What is your name and business address?

A. My name is Martin Blank, Ph.D. My business address is Department of Physiology and Cellular Biophysics, College of Physicians and Surgeons, Columbia University, New York, NY 10032.

Q. Where do you work?

A. I am Associate Professor of Physiology and Cellular Biophysics, College of Physicians and Surgeons, Columbia University, New York, NY 10032.

Q. What is your educational background?

A. I have a Ph.D. from Columbia University (1957) in physical chemistry, and a Ph.D. from Cambridge University (1959), England, in colloid science, an interdisciplinary (biology, physics and chemistry) department.

Q. Where have you worked in addition to Columbia University and Cambridge University?

A. My experience includes research, teaching and management of research programs in various academic, industrial and US government settings, including:

- Polymer Department, Weizmann Institute (Israel);
- Bioengineering Department, University of California-Berkeley;
- Pharmacology Department, Hebrew University (Israel);
- Biochemistry Department, Monash University (Australia),
- Frumkin Institute of Electrochemistry (Moscow, USSR),
- Biophysics Department, University of Warsaw (Poland),
- Chemical Physics Department, Tata Institute for Fundamental Research (India),

- Chemistry Department, University of the Negev (Israel) and
- Biology Department, University of Victoria (Canada).

My industrial research experience includes:

- California Research Corporation, Richmond, CA,
- Esso Research and Engineering Corporation, Linden, NJ, and
- Unilever Research Laboratories in Port Sunlight and Welwyn, England and Vlaardingen, the Netherlands.

I have also worked for the US Office of Naval Research (ONR) as a Liaison Scientist in London (UK) and as a Program Officer in Arlington (US), where I developed and managed a research program in biomembrane electrochemistry. I have also consulted for other research agencies, including American Institute of Biological Sciences (AIBS) and Electric Power Research Institute (EPRI), as well as private corporations. This wide range of professional experience has given me a broad perspective on scientific research, and has made me receptive to a variety of approaches in bioelectromagnetic research.

Q. What are your responsibilities at Columbia University?

A. My primary responsibility is to conduct research, which for the last twenty years has focused on electromagnetic (EM) fields and their effects on cell biochemistry and cell membrane function. I have recently specialized in the study of stress proteins and charge transport enzymes (specific biological catalysts). I have also taught Medical Physiology to first year medical, dental and graduate students, including a year as Course Director in charge of 250 students. Throughout my career, I have served as officer of scientific societies, editor of scientific journals, reviewer of scientific papers for publication and proposals for funding, as well as expert advisor, as in the evaluation of the performance of research laboratories for government agencies.

Q. How have your professional experiences contributed to a better understanding of biological effects of EM fields?

A. My experience has impressed upon me the value of interdisciplinary approaches to complex problems. Of particular relevance have been my roles:

- at ONR-London, where I wrote a report on the importance of interdisciplinary research in scientific progress

- as Chairman of the Organic and Biological Division of the Electrochemical Society, President of the Bioelectrochemical Society, and President of the Bioelectromagnetics Society, in which I organized interdisciplinary symposia.

- as organizer of large interdisciplinary meetings, including the 4th International Symposium on Bioelectrochemistry (1976), the first Gordon Research Conference on Bioelectrochemistry (1980), and four interdisciplinary courses at Erice (Italy). The Gordon Conference catalyzed the organization of the First (1992) and Second (1997) World Congresses on *Electricity and Magnetism in Biology and Medicine*, meetings that brought together experts from the different areas needed for understanding all aspects of the EM field problem.

- as editor of the *Journal of the Electrochemical Society* (Divisional Editor for Biology) and *Bioelectrochemistry and Bioenergetics* (North American Editor), where I encouraged contributions using interdisciplinary approaches.

- as author of over 200 papers and reviews, as well as twelve edited books on electrical properties of biological systems. Among these books are the

Proceedings of the First World Congress on "Electricity and Magnetism in Biology and Medicine",

"Biomembrane Electrochemistry", based on the ONR program,

"Nerve-Muscle Function", based on the 4th Erice (Italy) course,

"Electromagnetic Fields: Biological Interactions and Mechanisms" for the authoritative American Chemical Society series, *Advances in Chemistry*. The book focuses on cellular mechanisms in biological interactions of EM fields.

Q. What is your professional assessment regarding the safety of human exposure to low frequency EM fields?

A. Concern about health risks from low frequency EM fields in the environment arose from epidemiological studies linking certain cancers with exposure to power frequency (50-60Hz) EM fields, and the focus has remained on the epidemiology. In 1979, Wertheimer and Leeper showed a doubling in the incidence of leukemia in children associated with EM fields, but epidemiology studies since then have not been conclusive. A consensus appeared to be developing after the NIEHS instituted a comprehensive review of a wide range of evidence that included three symposia of experts, a critical review of the peer-reviewed literature and a detailed written report. The NIEHS-EMF review panel announced in June 1998 that magnetic fields should be considered a **"possible human carcinogen**" based primarily on epidemiological studies, but including some laboratory research as well. Since then two meta analyses (*Greenland et al, Epidem 2000; Ahlbom et al, Brit J Cancer 2000*), of 15 and 9 major studies respectively, have shown a statistically significant doubling of the risk of childhood leukemia when exposures exceed 3-4mG.

Epidemiology can demonstrate association, not causation, but the results of the meta analyses appear convincing. A doubling of risk of leukemia has persisted in many studies near the "significant" level (as in the National Cancer Institute study), and the lack of statistical significance has been due to the low number of cases at high exposure in individual studies. By pooling the cases of many studies in a meta analysis, it has been possible to demonstrate statistical significance.

The epidemiological evidence is strong enough to serve as a basis for practical decisions, but this is only one approach to the problem. Controlled laboratory research is needed to provide a rationale, to make the association plausible, and a detailed mechanism to help develop mitigation strategies. This is the area in which laboratory research in several disciplines has provided important insights that have strengthened the mechanistic basis for the epidemiology conclusions.

Q. Can you explain how your research has contributed to understanding interactions of cells with low frequency EM fields, and how this elucidates the epidemiology results?

A. Let me start by explaining some scientific terms **(in bold).** The **DNA** molecule in a cell nucleus is a long, tightly coiled, double helix. The two strands of the helix are connected by four interacting chemicals called **bases** given the symbols C, G, A, and T. In human DNA there are about 3 billion bases that interact as pairs, C with G and A with T, one base from each strand. The sequence of the bases along the DNA is in a code needed to make the **protein**s essential for life, a code that is being deciphered in the "Human Genome" project. Each protein is encoded in a separate segment called a **gene**, and specific genes are activated by specific chemicals in regions called **promoters**. After activation, proteins are synthesized in two steps, **transcription** (making a copy of the DNA code of the gene in the form of messenger RNA (**mRNA**), and **translation** (using the mRNA to synthesize the protein). The integrity of the DNA is essential for life, since the information for making proteins cannot be changed without damage to the cell. An accumulation of changes **(mutations)** in the DNA is associated with the development of **cancers,** diseases that are believed to arise from a multi-step process: **initiation** (damage to DNA in at least two places)**, promotion** (effect on cellular processes that causes loss of control) and **progression** (tumor growth)**.** EM fields have been mentioned as possible promoters, and Trosko et al. (*Environ Health Perspec*, *2000*) showed that **40mG fields can mimic the effects of chemical promoters**. Cancer mechanisms are not well understood, and different mechanisms may be operating in each specific tissue.

The synthesis of proteins in a cell is regulated by feedback control that supplies particular proteins as needed. When there is a potentially harmful change in a cell's environment (a **stress**), **stress proteins** are synthesized. The **stress response**, first identified in reaction to elevated temperatures, is used by all species in response to harmful environmental stimuli (e.g., low oxygen, toxic metal ions). **My studies with my colleagues concerning changes in both transcription and translation induced by EM fields, have shown that cells react to 60Hz EM fields as a stress and make stress proteins.**

Now in response to the question, **stimulation of the stress response by EM fields:**

- **indicates that cells react to EM fields as a harmful stimulus**
- **shows that EM fields activate DNA and protein synthesis**
- **occurs at field strengths slightly above normal background levels.**

Q. How do the stress proteins activated by EM fields differ from those thermally activated?

A. The stress proteins stimulated by EM fields are identical to those stimulated by an increase in temperature, and both use the same protein synthesis pathway. However, in response to EM fields, cells also use a pathway that requires remarkably low energy input. In Sciara salivary gland cells, the threshold energies of the EM field and thermal stimuli needed to evoke a stress response differ by 14 orders of magnitude, as shown in the Table below.

ENERGY to STIMULATE STRESS RESPONSE

Form of Energy	**Stimulus**	**Energy Density (joules/m^3)**
Magnetic	**0.8μT**	**2.6×10^{-7}**
Thermal	**5.5°C**	**$2.3 \times 10^{+7}$**

Q. Are specific regions of DNA associated with the response to EM fields?

A. Since reviewing EM field stimulation of the stress response (*Goodman and Blank, Cell Stress and Chaperones 1998*), we have identified specific DNA sequences that are EM field-responsive. There are three -CTCT- sequences in the promoter of the major stress protein (hsp70) and eight in the promoter of another EM field-responsive protein. Inactivating these sequences by removal or mutation, eliminates the response to EM fields. Inserting sequences into an artificial construct containing a gene, makes the gene EM field-responsive. Linkage of EM field responses with specific regions of DNA is important for gene therapy, since this provides a non-invasive, precise technique for gene activation. Columbia University has filed a patent application for this process based on our research.

Q. Do the specific DNA sequences suggest how EM fields activate DNA?

A. Stimulation of transcription may occur when magnetic fields accelerate electrons moving within DNA (*Blank and Goodman, Bioelectromagnetics 1997*). Recent studies show that DNA conducts electrons along the bases within the double helix, and we have shown that EM fields accelerate electron transfer reaction rates. The velocity of charge movement calculated from experiments with the enzyme, Na,K-ATPase, 1000 m/s, is similar to ultrafast electron transfer in DNA of 400 m/s. At these velocities, the forces at low field strengths affect enzyme reactions, and so they may be large enough to interact with moving electrons in DNA and generate repulsive forces that cause chain separation. From estimates of the balance of forces (repulsion-attraction) at the DNA bases, sites rich in C and T, as in the identified -CTCT- sequences, appear to be more likely to come apart when repulsive forces are generated by EM fields. **These calculations (*Blank and Goodman, J Cell Biochem, in press*) suggest a plausible mechanism for initiation of transcription by EM fields, and provide a rationale for EM field specific sequences.**

Q. Are there studies showing interaction of EM fields with charge movements in other biological molecules?

A. EM fields accelerate moving charges in any conductor. To determine how EM fields affect charges in biological molecules, we have studied two relatively simple systems, the enzymes Na,K-ATPase and cytochrome oxidase. A summary of changes in their activity in EM fields is given below:

- magnetic fields accelerate both enzyme reactions

- for both enzymes, the acceleration increases with EM field strength.

- the EM field competes with the chemical forces driving the reaction, i.e., when the enzyme rate is very fast, there is no increase due to the field.

- **for both reactions, the threshold EM field is below 5mG.**

- the rate constant for cytochrome oxidase has a broad maximum about 800Hz, and for Na,K-ATPase the frequency maximum is about 60Hz. Both frequencies are close to the optimal enzyme reaction rates and suggest that the EM field coordinates with the enzyme reaction.

- EM fields accelerate electron transfer reactions in the absence of cells, enzymes or membranes. We have studied electron transfer in malonic acid solutions, and found results similar to the two enzyme reactions (including competition between EM field and intrinsic chemical driving forces).

Q. Is there other evidence for interaction of EM fields with DNA?

A. Many studies (laboratories of *Phillips, Woloshack*) have shown that EM fields stimulate transcription (DNA into mRNA). There are also studies that show increases in cell proliferation (an acceleration of cell division) as a result of exposure to EM fields (laboratories of *Kwee, Berg, Parola*). Also, **the many clinical studies showing effects on the rate of healing of bone fractures and soft tissues (pioneering research of *Bassett, Becker*) indicate effects of EM fields on cellular processes at the level of DNA.**

Q. How do the molecular mechanisms stimulated by EM fields relate to cancer mechanisms?

A. As mentioned above, cancer mechanisms are not well understood, but over-expression of stress proteins has been linked to a number of human tumors. The high concentrations of stress genes in a number of human tumors has made them markers for the disease, e.g., hsp90 is a marker for breast cancer. Hsp70 stress proteins are known to interact with proteins, such as c-myc and mutant p53, that cause cellular transformation and are associated with many cancers. The hsp70 promoter is regulated by the tumor suppressor p53, a transcription factor implicated in over 50% of human cancers.

> Another link of EM field exposures to cancer is modification of the tumor suppressing action of melatonin secreted by the pineal gland in the brain. **Studies replicated in four labs show that a low EM field strength of 12mG blocks the growth-inhibiting action of melatonin on human estrogen receptor-positive, breast cancer cells, as well as the near-complete blockage of the anticancer (chemotherapeutic) drug Tamoxifen**. A field strength of 2mG has no effect, indicating that the threshold lies between 2mG and 12mG.

Q. What have we learned from threshold measurements for biological effects of EM fields?

A. Low thresholds have been measured in several independent systems, and the values have been published in peer review journals. The Table below shows that the measured thresholds for changes in enzyme activity and in biosynthesis of stress proteins are within an order of magnitude, and in the range of cut-off thresholds in epidemiological studies. The last entry is for EM field blockage of the inhibition of breast cancer cell growth by melatonin is an upper limit. **All the thresholds are below field strengths measured near transmission lines, so the biological systems would be stimulated.**

Biological EM Field Thresholds

Enzymes:	**Na,K-ATPase**	**2-3mG**
	Cytochrome C Oxidase	**5-6mG**
	Ornithine decarboxylase	**20mG**
DNA:		
	Stress proteins (HL60 Cells)	**8mG**
	Stress proteins (Sciara Cells)	**8mG**
Cells:		
	Block inhibition by melatonin (Breast cancer cells)	**12mG**
	Epidemiology threshold	**3-4mG**

Q. How do you address the criticism that is raised when some biologists cannot repeat published experiments showing positive effects of EM fields on transcription?

A. The biological research has been distorted by the emphasis on cancer research. Instead of studying well defined, reliable biological models, such as E. coli, yeast and drosophila, there has been a focus on transformed cells, such as leukemia cells (e.g., HL60), that have the disadvantage of being highly variable. It is now clear that conflicting results about a central problem in EM field effects, the stimulation of transcription, arose because HL60 cells were used, and the cell populations used in different laboratories have very different properties. HL60 cells from the ATCC (American Tissue Culture Center) grow at half the rate of those supplied by the CUCC (Columbia University Cancer Center), and are also much less reactive to chemical agents and to EM fields. In a recent paper (*Jin et al, 1997*), the conflicting results were shown to depend on the very different growth rates and reactivities of the HL60 cells. **The positive reports that EM fields stimulate transcription were replicated, and the conflicting reports explained.**

Q. The American Physical Society has written a report saying that biological effects at low field levels (below the noise level) are theoretically not possible. How do you reply?

A. It is tempting to simply dismiss the statements of a group whose expertise is so far afield from medical and biological issues, but the issue can be answered with two questions.

Q. Are the physicists aware of research in biology that contradicts their conclusion?

Q. Are the models they use relevant to cellular processes?

The answers to both questions are NO. From my replies to earlier questions it should be clear that many laboratories have shown that weak EM fields can have significant effects on cells (e.g., reaction rates and protein synthesis as in the stress response). The task of the theoretician is to develop realistic models for the observations. The commonly used models for cells, where a membrane is the only cell structure, are unrealistic and not even relevant for stimulation of transcription in the DNA of the cell nucleus. **Calculations based on unrealistic models can only lead to irrelevant conclusions**.

A famous example is Lord Kelvin, the most respected physicist of his time, who used an unrealistic model and came to the wrong conclusion about the age of the earth. Geologists correctly proposed that the earth was billions of years old, but Kelvin calculated that if the earth were that old, heat at the earth's core would have diffused away, and the earth would have cooled into a solid mass. Since the earth had a molten core, the age estimated by geologists was wrong. Kelvin's model did not take into account heating from radioactive decay, a phenomenon that was not discovered until many years later. **Theoreticians must use models that relate to transcription, if they hope to arrive at reasonable conclusions about effects of EM fields on transcription**.

Theoreticians who claim that biological effects of EM fields are impossible at levels weaker than thermal noise (the energy due to random molecular motion) must acknowledge that the extreme sensitivity of sharks to electric fields is well below the thermal noise limit. Sharks have an elaborate inter-connected system of sensors that is able to detect fields as low as nanovolts/cm. Biological systems often have unusual properties (e.g., retinal cells can react to a single quantum of light). Physicists must develop models that are appropriate for the biological measurements they are meant to explain.

Q. How would you summarize the current strength of the evidence on the linkage between EM fields and cancer?

A. As more is learned about EM field interactions with cells, the plausibility of a link between low frequency EM fields and childhood leukemia can be put forward with growing confidence.

- epidemiological results point to a doubling of the risk of childhood leukemia associated with exposure to EM fields in excess of 3-4mG.

- stimulation of the cellular stress response (a cellular protective mechanism) by EM fields indicates that cells react to EM fields as a harmful stimulus

• laboratory studies show that weak EM fields can affect cellular processes, thresholds for cellular effects are in the range of environmental EM fields.

• **a cellular mechanism has been identified**, the cellular stress response, which is an appropriate response to a potentially harmful environmental influence.

• **a molecular mechanism, interaction of EM fields with moving charges, is physically reasonable**, and has been shown to apply in several molecular systems.

• stimulation of protein synthesis by EM fields is probably due to direct interaction with DNA, since a specific DNA sequence has been associated with the response.

• **clinical studies with therapeutic EM devices show accelerated healing, indicating effects on biological growth processes.**

Q. In light of what is known about the epidemiology and the laboratory studies on EM fields, what do you think is a reasonable practical policy to follow?

A. The recommendations of the NIEHS Report to the Congress (May 1999) are the most reasonable ones to follow while we continue to study the problem. Kenneth Olden, the Director of NIEHS, wrote that "...ELF-EMF exposure cannot be recognized at this time as entirely safe... passive regulatory action is warranted such as a continued emphasis on educating both the public and the regulated community [i.e., the power companies] on means aimed at reducing exposures." On page 38 of the Report, the recommendation is more explicit. "The NIEHS suggests that the power industry continue its current practice of siting power lines to reduce exposures and continue to explore ways to reduce the creation of magnetic fields around transmission and distribution lines without creating new hazards."