The previous sections have described what is meant by fields, and how exposure to fields is measured in actual and laboratory settings. The understanding of what the effects of this exposure may be comes from three kinds of studies.

- 1. Laboratory experiments using animal or human tissues or cell cultures exposed to fields. These experiments are termed 'in vitro" (in glass) experiments.
- 2. Laboratory and field experiments using live animals and people exposed to fields. These experiments are termed "in vivo" (in a live state) experiments.
- **3.** Epidemological studies involving human populations exposed to fields at work (occupational studies) or at home (residential studies).

The following sections describe these in order.

## **3. Cellular Level Experiments**

Until the mid-1970's few conjectured that there could be any effect on a biological system from electric or magnetic fields of the strengths usually present in the environment. This was in part due to the fact that these fields can transfer only minute amounts of energy to the cell, and hence can not disrupt chemical bonds in the cell **as** ionizing radiation can. There is not even enough energy in 60 Hz fields to heat the cell to any significant extent as microwave or radiofrequency radiation does.

A considerable body of evidence has emerged that points to the cell membrane (the membrane enveloping the cell) as the primary site of interaction between ELF fields and the cell [Adey 86]. In addition to sewing as the boundary and maintaining the structural integrity of the cell, the cell membrane is responsible for some of the critical functions of the cell such as controlling the flows of material and energy signals into the cell and transmitting information arriving at its surface to the interior of the cell so that appropriate life processes can take **place.** It is a highly selective filter that maintains an unequal concentration of ions (charged atoms) on either side and allows nutrients to enter and waste products to leave the cell. This is made possible by very specialized components of the cell membrane.

Unequal concentrations of ions are used by the cell for transmitting external signals to the interior; and for allowing or preventing the entry of selected molecules and ions into the cell. The most important ions are potassium (K+), sodium(Na<sup>+</sup>), chlorine (Cl-), hydrogen (H+), and calcium(Ca<sup>+2</sup>). The actual entry of many molecules and ions occur through channels in the cell called '\*ion channels". These close or open in response to the ion concentrations and thus regulate the flows. There are also some enzymes that are attached to the membrane. These "membrane-bound" enzymes take part in the synthesis of molecules as well as in controlling initial actions of external molecules such as drugs.

ELF field experiments on the cellular level have concentrated on examining how some of the specific processes governed by the membrane change as a result of exposure to the ELF fields. When reading the results, it is important to understand that even when an effect is observed at the cellular level, it is still hard to extrapolate what, if anything, that effect implies for the organism as a whole.

In this section, experimental results on effects of ELF field exposure on cell cultures are discussed under six classes:

- 1. modulation of ion flows [Bawin 76, Bawin 75, Blackman 82, Blackman 85a];
- **2.** interference with DNA synthesis and RNA transcription [Liboff 84, Goodman 86, Goodman 87]

- interaction with the cell response to different hormones and enzymes including those that are involved in cell growth processes and stress responses [Luben 82, Lymangrover 83, Lymangrover 87];
- 4. interaction with the cell response to chemical neurotransmitters [Vasquez 86];
- 5. interaction with the immune response of cells [Lyle 83]; and
- 6. interaction with cancerous cells [Cain 86, Winters 86]

The observed effects have certain peculiarities. Some effects described below occur at some frequency and intensity values but not at others. Some effects depend upon the duration of the exposure. Some effects persist only for a brief period of time after the exposure is discontinued. These peculiarities make it difficult to extrapolate experience from the more familiar chemical and ionizing radiation toxicology to the realm of ELF exposure and effects.

Many of the studies described below have been carried out in single laboratories and, with a few exceptions, have not been replicated in other laboratories. Although a number of high quality experiments have been performed in the last decade, we still do not have enough robust, replicated results to build a coherent scientific or phenomenological picture of the spectrum of effects and we are far from having a good theoretical model. Generally, when the background science is clear and developed, experimental research on a new phenomenon proceeds by a series of steps usually referred to as "the scientific method". The first step in this method is to make a hypothesis (educated prediction) of the expected result. Experiments are then designed and conducted to "test the hypothesis\*". In the field of biological effects of ELF fields, there are not yet theories to make firm hypotheses and test them. Therefore, some of the experiments described in this paper are attempts to see if there are any effects at all. Other experiments examine if there are simple hypothetical connections between experimental observations and possible health effects. We are not at the stage where experiments can be designed to test hypotheses based on a coherent framework.

The most concerted of the studies on cellular level have been conducted by an interdisciplinary group of biologists, biochemists, physicians, physicists and psychologists at the Jerry L. Pettis Memorial Hospital at Loma Linda. This group has examined the various aspects of the interaction of ELF fields with the cell, paying particular attention to understanding the role of the cell membrane in the interaction.

Because of the rapidly evolving nature of this subject, **a** few of the results we discuss have been reported only in professional meetings and have not yet appeared in refereed journals. These distinctions are made clear in the references.

### 3.1. Modulation of Ion and Protein Flow across the Cell membrane

The phenomenon most studied at the cellular level is the nonlinear pattern of calcium ion efflux from cells which results after exposure to 60 Hz fields. Before discussing these experiments it is useful to briefly review the role of calcium in the regulation of cellular processes.

The flow of calcium ions (Ca<sup>+2</sup>) across the cell membrane in response to extracellular signals is an important means of transmitting signals from the outside to the interior of the cell. Calcium flow governs physiological processes such as muscle contraction, egg fertilization, and cell division. Most of the intracellular calcium (Ca present in the cell) is normally bound to molecules in the cell. Calcium is also

present in the structure of the membrane itself, to be released in the event of an appropriate triggering signal.

When information in the form of electrical or chemical impulses arrives at the cell membrane, the membrane binding as well as permeability to calcium is altered and the subsequent transport of calcium across the membrane transfers the information signal to the interior of the cell. Because of this function, calcium is said to be a "second messenger".

Calcium acts in a multitude of **ways** in its capacity as a second messenger. For example, among the proteins on the surface of nerve cells are certain enzymes called calcium-dependent protein kinases which, when activated by the calcium changes, cause actions on other cell surface proteins that are important in cell adhesion during development and growth. Calcium signals also regulate processes such as muscle contractions including heartbeats, developmental processes such as egg maturation and ovulation and several others. The quantity as well as the rate of calcium ion transport are important in this regulation.

Unusual behavior of calcium efflux (or, outward flow) from cell membranes in brain tissue in vitro was the first clear, reproducible effect of ELF fields observed in biological tissue. Bawin and coworkers took the two halves of the brain of freshly killed chicks maintained in solutions to continue the natural cellular processes ("tissue preparation of chick cerebral hemisphere"). They exposed one half to an ELF field, keeping the other half unexposed to field. They then compared the calcium efflux from the two halves and found that the efflux was decreased in the exposed, compared to the unexposed half. This effect of decreased calcium efflux was noted to have frequency and amplitude "windows" around 6 and 16 Hz and at 10V/m. That is, the effect occurred when the field value was 10V/m and the frequency 6 Hz or 16 Hz. [Bawin 76].

In an independent set of experiments, Blackman and coworkers also observed a change in calcium efflux, although it was an increase rather than decrease, with a complex pattern of several "windows". The frequency ranges they examined were 1-30 Hz and 45-105 Hz, and the intensity range, 1 to 70 V/m. [Blackman 82, Blackman 85a, Blackman 85b]

Figure 3-1 summarizes the ELF frequency and intensity combinations found to cause changes in calcium-ion efflux from chick brain tissue in vitro. [Blackman 85a] For example, the figure shows that in this experiment, at 60 Hz, six field intensity values were examined : 25, 30, 35, 40, 42.5 and 45 V/m . These voltage values to the peak-to-peak voltage (abbreviated as  $V_{PP}$ ) of the field applied during the experiments. In all other experiments the field intensity is expressed in terms of root-mean-square (rms) voltage, as defined in Section 2.2.2. Figure 3-1 also shows the equivalent rms values. The effect appeared only at three of these values, 35, 40 and 42.5 V/m. The lower values of 25 and 30 V/m as well as the higher value of 45 V/m showed no significant difference between the efflux from the exposed and the unexposed halves of the brain. That is, for the frequency of 60 Hz, there is an intensity window between about 35 V/m and 43V/m. There is no effect observed immediately above or below this range of values. Similarly, if the intensity is kept at 42.5 V/m and the effect explored at various frequencies, the effect is seen at several values (15, 45, 60, 75, 90 and 105 V/m) but not at values in between.

Further experiments by Blackman et al., showed that the position of frequency and amplitude windows was influenced by the strength and relative orientation of any static magnetic field superimposed on the AC field [Blackman 85 b]. That is, the position of the windows depended on constant or static (not

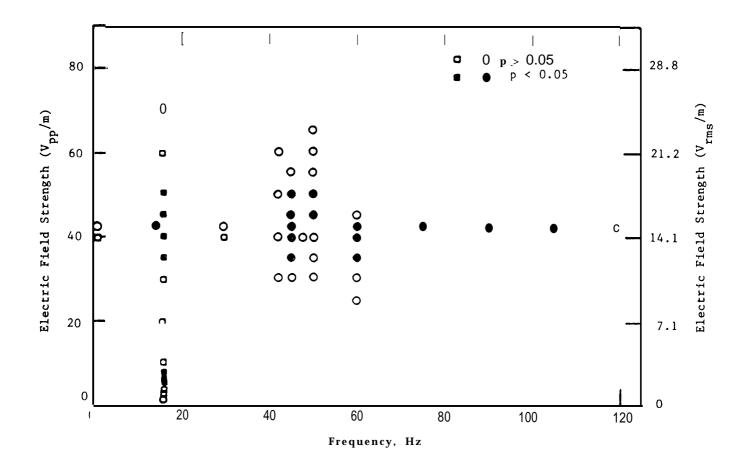


Figure 3-1: Frequency and intensity windows in the efflux of calcium from chick brain tissue : This figure shows the results of Blackman's experiments on calcium efflux in chick brain exposed to ELF electric fields.' The horizontal axis shows the frequency of the sinusoidal ELF exposure. The left hand vertical axis shows the peak-to peak electric field strength. The right hand vertical axis denotes the root-mean-square field strength (See section 2.2.1 for an explanation). The efflux of calcium from one half of the brain exposed in vitro to ELF electric fields was found to be significantly higher than from the other half which was not exposed. The graph shows the values of frequency and field intensities for which there was an effect. Dark circles show the presence of an effect and the open circles show values which were examined, but no effect was found. Instead of showing an effect that increased or decreased with increasing or decreasing frequency or intensity, the effect appeared at certain values of frequency and intensity but not at others. For example, note that when the frequency of the applied field is 60 Hz, an effect is seen at 3 values of field, at 35, 40 and 42.5 Vpp/m. When the field is **above** or below this range, such as at 45 V/m or at 30 Vpp/m, there is no effect. So when the "applied frequency is 60 Hz, there is an 'intensity window" between about 35 and 42.5Vpp/m at which there is an effect. Along similar lines, it can be seen that there are "frequency windows" at 15, 45, 60, 75, 90 and 105 Hz when the applied field value is kept at 42.5Vpp/m. Similar observations can be made about other values of frequency and field. [Blackman 85a]

AC) magnetic fields present in the labortory setup. In a recent experiment, Bellossi has found that a replication of the efflux experiment with only <u>static</u> (frequency = O Hz) magnetic fields produces no effect.. [Bellossi 86].

Blackman has recently found that 16Hz, 40V/m fields affect the efflux from brain tissue not only of calcium ions which are charged but also of the neutral sugar molecules, mannitol and sucrose. Further experiments are being carried out to see if the window pattern seen for calcium ions persists for these neutral molecules [Blackman 87].

Gundersen et al. [Gundersen 86] studied the effects of electric and magnetic fields on calcium efflux from cells of chick spinal cord. For exposure to 60 Hz fields of 1 G, 30 kV/m for varying periods of upto 72 hours, no change was found between sham and experimental cases. [Gundersen 86] Because of the use of different cells - spinal cord rather than brain- and of a single pair of field values, these results should be viewed as a separate observation rather than an attempt to replicate the Bawin and Blackman work.

The calcium efflux experiments described above point up several peculiarities of the ELF-tissue interaction at least in this one effect:

. A. Frequency and Intensity Windows: For a particular value of frequency, some field intensities produce the effect but others do not. Conversely, if an effect is observed at a particular value of field, it might be "tuned out" by changing the frequency of the field. The "windowed'\* nature of these effects imply that when one looks at experimental results, one must bear in mind that even when there is no effect at some field values there may be effects at other, lower or higher values.

- . B. Background static field conditions may matter: The effect may be influenced by how the field is applied relative to earth's natural static magnetic field.
- . C. "More is worse" paradigm does not hold: For this cellular level phenomenon at **least**, it is not true that a larger value of the field shows a larger, or even any effect, compared to a smaller value of field.

The features described above have been observed in the cell in vitro. Blackwell and Reed of the National Radiological Protection Board in the United Kingdom attempted to see if the calcium efflux effect seen in vitro in the chick brain, could be detected through an effect in an intact animal [Blackwell 85]. They looked for signs of change in exploratory activity and of barbiturate-induced sleeping time in male mice exposed to 50 to 400V/m at 15, 30, and 50 Hz, Both of these parameters are sensitive to changes in the central nervous system (CNS) associated with calcium changes. Their experiments failed to show any effect. The authors suggest that the results indicate that the fields used may not be of the right magnitude, or that the calcium efflux change that may have been induced in the brain by the fields were not large enough to produce changes in the CNS function. Blackwell [Blackwell 86] has also studied the activity of spontaneously firing neurons in anesthetized rat exposed to 100 V/m field at 15 and 30 Hz, both of which were resonant frequencies for the chick brain and for 50 Hz which is the frequency for power transmission in the United Kingdom. He found no change at 50 Hz. However, the time, but not the rate, of firing was changed for 15 and 30 Hz signals. It is not clear what if any implication this has for the functioning of the animal.

Other than the work described above, no work has been done to see if similar effects exist in whole

organisms and if they do, whether these too show windows in the effects. However, if biological effects of ELF fields on whole organisms show similar dependencies, then setting exposure standards would be a problem, because the "more is worse" maxim which applies for most agents such as environmental chemicals may not hold true in the case of ELF field exposure.

# 3.2. Chromosomal Damage and Interference with DNA Synthesis and RNA Transcription

DNA and RNA are the primary biomolecules in the cell. Nuclear DNA which is the primary constituent of the chromosomes carries the genetic code while the extranuclear RNA transcribe the DNA command codes into proteins for the physiological functioning of the cell. Well-studied cancer- initiating agents such as ionizing radiation and chemicals cause direct damage to DNA by mutations. As mentioned earlier, ELF fields do not have enough energy to break bonds or otherwise disrupt the structure of DNA.

Chromosomes from blood samples of mice chronically exposed to 60 Hz fields of 50 kV/m, 10 G, and from human lymphocytes and Chinese Hamster Ovary (CHO) cells exposed in vitro were examined for sister chromatid exchange (SCE)<sup>3</sup> and other forms of chromosomal damage [Benz 87, Cohen 86, Livingston 86]. These experiments were all negative and the extensive nature of these studies leads to the conclusion that it is quite unlikely that ELF fields induce SCE's or other standard chromosomal aberrations.

However, changes in DNA synthesis rates and alterations in the transcription patterns of RNA, with the resultant production of structurally changed proteins have been observed in cells exposed to low intensity ELF fields. LibOff [Liboff 84] showed that the rate of DNA synthesis in human fibroblasts<sup>4</sup> is increased on exposure to ELF magnetic fields with intensities comparable to the earth's magnetic field. Goodman and coworkers [Goodman 86] showed that 60 Hz fields both qualitatively and quantitatively change the pattern of translation (or, perhaps transcription) in cells from the salivary gland of a particular insect<sup>5</sup>. The rate of production of the normal proteins made by the cell is increased. In addition, the field causes new proteins to be made. Protein synthesis is a very complicated process and the experiments yield no simple interpretation about the mechanisms or about potential effects on the organism.

### 3.3. Interaction with Response to Hormones and Effects on Endocrine Tissue

Only a few experiments have studied the effects of ELF fields on endocrine parameters. These involve responses of various tissues to the corresponding hormones in the presence of an ELF fields. Some interesting effects have been found. But, it is impossible at this point to draw any inference about the effects of fields on the endocrine system in a human or animal, other than to say that fields do exert an action on endocrine tissue and endocrine processes in vitro and these effects too show windows.

Luben et al. [Luben 82] reported a reduction in the cell response to parathyroid hormone (PTH) in

<sup>&</sup>lt;sup>3</sup>SCE's are a well-characterized chromosomal defect known to result from agents such as ionizing radiation

<sup>&</sup>lt;sup>4</sup>Fibroblasts are cells in the "extracellular matrix" or the network of molecules connecting the space outside the cells. Fibroblasts are responsible for producing material such as fibrin and other collagens, which form a large fraction of the matrix.

<sup>&</sup>lt;sup>5</sup>Protein synthesis is a complex process that begins in the cell nucleus. The first step is transcription, the Process <sup>by</sup> which 'he information in the DNA in the genes is used to form the molecule **mRNA** (messenger RNA). After some modifications, this **mRNA** is translated into a sequence of **aminoacids** which rearrange to form proteins.

mouse cranial bone cells, exposed to 72 Hz and 15 Hz pulsed magnetic fields. This response was measured as reflected in the cyclic AMP (cAMP) accumulation and collagen synthesis which normally result from administration of PTH<sup>6</sup>. Although not a 60 Hz field experiment, this study is significant in that it demonstrated rather clearly that, for this action at least, the membrane is the site of action.

The only studies on endocrine tissue in vitro have been done by Lymangrover and coworkers who investigated the effects of 60 Hz electric fields on the adrenal tissue<sup>7</sup> (Lymangrover83, 87). They found that a 60-Hz electric field caused an increase in the production of corticosterone in response to the hormone ACTH (adrenocorticotropical hormone). Corticosterone is a hormone of the steroid family involved in stress response and in anti-inflammatory reactions of the body. ACTH is a hormone one of whose functions is to stimulate the production of corticosterone by the adrenal tissue. In the present context, the production of corticosterone in response to ACTH is used **as a** biological process to examine a possible effect of electric field exposure on a specific tissue function. The tissue level effect noted below cannot be simply interpreted in terms of consequences in the whole animal.

The field did not produce any change in the amount of hormones produced by the tissue alone (basal activity of the tissue). But when the tissue was activated with ACTH, and the resulting production of corticosterone was measured, there was an increase in corticosterone production for certain values of the field, for certain durations of exposure. That is, the effect showed intensity windows combined with an exposure time dependence. Specifically, a 10 kV/m field intensity produced a fourfold increase in corticosterone production on 5.5 to **7** hours exposure and a 1,000 kV/m intensity produced a twofold increase during 2 hours of exposure. Fields of 5 and 100 kV/m produced no effect for any of these durations. The complex intensity and time dependence are the most notable features of these experiments. Although corticosterone level increase in response to ACTH is a stress response, tissue level experiments do not necessarily act as indicators of response in situ [AxeIrod 84].

#### 3.4. Interaction with the Cell Response to Neurotransmitters

As much of the activity in the brain takes place through electrical signals, it is reasonable to examine whether some of the chemical production in the brain are affected by exposure to electric fields. Rates of neurotransmitter secretion especially of norepinephrine and dopamine by the hypothalamic section of the brain in chicks and rats were found to change upon exposure to electric fields [Vasquez 86]. This effect is detailed in the subsection 4.2 on experiments in the whole animal.

#### 3.5. Interaction with Immune Response of Cells

The immune response of the cells, that is the ability of the cells to act against foreign agents such as viruses and toxic chemicals, is important in combating infection and maintaining a healthy function. The several types of blood cells responsible for immune response have been examined in electric fields to see if any change in their function can be observed. Decreased immune response could lead to decreased resistance to disease or other harmful agents and is also suspected of accelerating the growth of some cancers.

<sup>&</sup>lt;sup>6</sup>Cyclic AMP or cyclic Adenosine Monophosphate, is an intracellular signaling molecule, or, "second messenger" like calcium. PTH is a hormone that activates bone absorption of calcium using cAMP as the second messenger.

<sup>7</sup>Tissue from adrenal glands, situated over the kidney

Winters examined human and canine leukocytes<sup>®</sup> under different combinations of ELF electric and magnetic field exposure to see if immune response is modified by field exposure. [Winters 86]. Leukocytes taken from these dogs and people were examined under two conditions. First, immune properties of normal, unstimulated white blood cells (that is, healthy white blood cells that was not exposed to any known challenge to the immune system) were measured during exposure to fields. Second, the dogs and human volunteers were injected with antigens<sup>®</sup> and the white blood cells thus stimulated to an immune response. The cells were then exposed to combinations of electric and magnetic fields. The exposed cells were examined for immune responses . Tests showed no significant effects of ELF field exposure on immunologic functions of normal or specifically immunized cells.

It is worth noting in this context that some authors have found responses when the cell was first stimulated by antigens and then exposed to fields, and when the cells were subjected to <u>pulsed</u> fields<sup>10</sup> Most of the results discussed in this paper are for fields which are not pulsed [Chiabrera 84, Hellman 85]. These observations point to two possibilities: that field effects on immune system response are complicated ; and that there is a marked difference between cell behavior in sinusoidal regularly alternating) and pulsed fields.

Lyle (1986) reported an alteration in the cytotoxicity (that is, the ability to kill cells) of T-lymphocytes of the type CTLL-1 which are purified mouse lymphocytes that specifically attack cancer cells. The cells were exposed to 60 Hz electric fields for 48 hours and their cytotoxicity measured. In general, the fields inhibited the ability of these cells to kill cancer cells. A 0.10 mV/cm field inhibited the ability by 7%, a field of 1 mV/cm by 18% and a field of 10 mV/cm by 30%. In this experiment, therefore, one sees a "dose-response" type of relationship between the effect the magnitude of the effect and the intensity value of the applied field. That is, in this range, the effect (inhibition of cytotoxicity) increases in proportion to the intensity of the applied field. If the reduced immune capacity exhibited in this experiment by one particular type of lymphocytes when exposed to low intensity electric fields, against a particular type of cancer cell) turns out to be present also when the cell is in the whole organism, it may be one mechanism by which the field inhibits the body's resistance to cancer or cancer growth.

#### 3.6. Interaction with Cells Relevant to Cancer

One hypothesis for potential carcinogenesis by ELF fields is that the fields promote cancer formation or cancer growth rather than initiating cancer. This is discussed in the Endnote 2 on cancer. The fact that ELF fields have not been known to cause alterations in DNA structure (see Section 3.2), is consistent with the observation that ELF fields do not initiate cancer.

Several authors have looked for a response of leukemia cells to ELF field exposure [Liboff 84, Winters 86, Cain 86]. LibOff and Kaplow found that mouse leukemia cells exhibited increased DNA synthesis [Liboff 84]. Winters and Phillips found increased DNA synthesis in human colon cancer cells after 24 hours of exposure to 60Hz magnetic field. Field-exposed cancer cells also showed an increased

<sup>&</sup>lt;sup>8</sup>Leukocytes is the general term for white blood cells, types of which destroy invading bacteria, modulate allergic reactions, evoke several immune responses and kill some infected and tumor cells.

<sup>&</sup>lt;sup>9</sup>Antigens ar substances that elicit an immune response from the body. Examples are infection-causing ViruSes, pollen, etc.

<sup>&</sup>lt;sup>10</sup>Pulsed fields are fields which are turned on quickly for only a brief period. Most of the results discussed in this paper are 'or fields which ar not oulsed.

capacity to proliferate compared to unexposed cancer cells. At the request of the New York State Power Lines Study Project, which sponsored the Winters study, Cohen attempted to replicate the Winters results. [Cohen 871. He found no significant effects of the fields to affect the proliferative ability of the same two lines of cells. For this and other reasons, the validity of the Winters results has been questioned.

The group at the J.B. Pettis Veterans Hospital at Loma Linda have examined the tumor promotion hypothesis by looking at effects of ELF fields on specific biochemical processes in the cell rather than by looking at the cell growth itself. Their results are described below. They have so far examined :

- 1. Decreased immune response depicted by the CTLL-1 experiment described in the previous section [Lyle 86],
- 2. Accelerated growth potential as measured by the increased activity of ornithine decarboxylase (ODC), described below [Cain 86, Byus 86],
- 3. Loss of the ability of cells to communicate because of the loss of gap junctions, described below [Fletcher 87].

Ornithine decarboxylase (ODC) is present in all cells and is an essential enzyme for cell growth because it helps synthesize biochemical that are necessary for DNA and protein syntheses. Any agents promoting cell growth also increase ODC activity. Examples of biochemical that cause increased ODC activity when administered to cells are : hormones and growth factors in the **case** of normal cells, and tumor promoters such as phorbol esters that promote uncontrolled growth of tumor cells. Hence factors that increase ODC activity can, but do not necessarily, lead to tumors. Highly increased ODC activity has been used as an indicator of malignancy.

Cain's experiments used normal fibroblasts which are a classical system for tumor promotion. There was a two-fold increase in ODC activity in cultured fibroblast cells exposed to 60 Hz electric fields at 10 mV/cm.

Fletcher's experiments are based on the observation that gap junctions which help cells communicate with each other lose their function in many tumor models in which there is evidence for promotion. An example is the skin tumor in mice, a classical model of tumor promotion. He also notes that tumor promoters have no effect on cells that do not express gap junctions. Fletcher reported that while the field by itself has no effect on gap junctions in fibroblast cell lines, the field enhances the effect of the tumor promoter chemical TPA<sup>11</sup>. This experiment **was**, however, with modulated microwaves rather than with 60 Hz fields.

Byus exposed human lymphoma cells to 60 Hz fields and reported both intensity and time windows for increase in ODC activity. The same value of increase **was** noted for 10mV/cm and 0.1 mV/cm field intensities, with no effect by field values in between. On continuous exposure to field, the effect was maximum at 1 hour of exposure time, and fell to control values at 2 hours of exposure. Beyond two hours exposure, ODC activity continued to decrease, so that the phenomenon changed from one of enhancement to one of inhibition of ODC activity after two hours. The activity went back to normal values when the field was removed [Byus 86].

<sup>&</sup>lt;sup>11</sup>TPA, or .1,2-o-tetradecanoyl phorbol-13-acetate, is a potent promoter of cancer often used as an experiment standard in cancer promotion experiments

All the observations above, except the last, are consistent with a hypothesis that fields can promote tumors but again carry with them the warning that any potential relationship between the field intensity and the degree of promotion and may be highly complex. The last experiment shows that continuing to remain in the field once an organism has entered it may be less perturbing than a pattern that involves frequent periods of exposure and non-exposure.

### 3.7. General Observations on Cell Level Experiments

Despite many negative results, a significant number of cell level experiments have shown positive effects from exposure to ELF fields. These are summarized in Table 3-1. These results do not yet indicate any clear adverse impacts at the level of the whole animal. They do clearly demonstrate that:

- . the cell membrane is one site of action of the field; and, therefore, processes governed by the cell membrane may be candidates for disruption by field exposure, the immune response and cell-cell communication being two such processes;
- . the fields do not appear to act directly on the DNA structure; but may alter cellular processes by interfering with the transcription by RNA, a process in the chain of command from DNA to protein production;
- . the effects may show a complex dependence on the intensity and frequency of the field and the time pattern of exposure to the field; further, the effects of fields may depend on the direction of the applied field in relation to the earth's magneitc field or, upon whether the field is a simple alternating field or a pulsed field. (i.e., a field turned on rapidly for brief periods)

Table 3-1: Cellular Lev	el Experiments: Effects	and possible significance
A Summary of results described in this section		

Experiment	Effects Noted	Possible Significance
Calcium efflux from cell membrane (6 experiments)	Efflux is dramatically changed. The change occurs only at some frequency and intensity values, but not at others.	Significance not clear But points up the possibility that effects of fields may not be such that "higher field intensity is worse than lower".
Chromosomal Damage (3 experiments)	No chromosomal damage detectable.	Does not cause the damage that usually initiates cancer.
DNA Synthesis Rate (1 experiment)	Rate change at low magnetic field.	Extremely low AC magnetic fields as small as the earth's natural DC field may affect cell process rates.
RNA Translation (1 experiment)	New proteins made by the cell. Rate of trans- cription altered.	Fields may alter rates of primary cell processes.
Cell Response Modifi- cations: Response to: A. hormones (1 experiment)	Modifications in adrenal and bone tissue and connective cell response. to hormones	Significance not clear. Adrenal response shows intensity windows. Bone tissue experiment points to membrane as site of action.
<ul><li>B. Neurotransmitters</li><li>(1 experiment)</li></ul>	Phase shifts in the periodicity of secretion rhythms	If true in humans, might have implications for psychological disorders, such as chronic depression.
C. immune system (5 experiments)	Not clear that there are significant effects except in special cases.	Implications not clear.