KEY TO UNDERSTANDING THE EMF ISSUE: PIECING TOGETHER THE EMF PUZZLE TO VIEW THE TOTAL PICTURE

- How low-level EMFs affect cell function
- Why, how and when low-level EMFs are adverse
- How adverse effects of low-level EMFs may be avoided

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INTRODUCTION

The purpose of this paper is to piece together a large number of reported specific scientific findings on the various biological effects of low-level electromagnetic fields (EMF) into a coherent picture that provides an understanding of how EMF affect cell function and under what circumstances these effects are adverse to cells. Furthermore, it is presented how a solution to the EMF problem can be derived from this understanding.

In this presentation, low-level EMF means extremely low frequency (ELF) EMF (frequencies below 3000 Hz) and radio frequency (RF) EMF at levels below current safety standards and guidelines. No distinction will be made between effects induced by ELF and RF fields, as the effects have been shown in numerous studies to be identical.

Despite hundreds of reports on effects induced by low-level EMF in cells, whole animals end even humans, it is still a subject of substantial controversy and skepticism. The biggest problem in accepting all these findings is that our current level of knowledge does not offer a proper explanation for the observed effects, which seem to occur virtually without the involvement of energy, making it almost impossible to establish relevant safety standards and guidelines.

It is a very important part of the puzzle that the same scientific and regulatory communities (including the FDA), who are skeptical even towards the concept of low-level EMF being able to produce **any effect at all** in biological systems, have already approved devices that use the very same type of low-level pulsed EMF therapeutically in hospitals. This is based on hundreds of clinical, double-blinded and peer-reviewed studies showing a statistically significant effect of EMF on the growth of cells in human tissue – in live human beings.

Since 1979, FDA has approved pulsed EMF generators for three different established medical uses. The pulsed EMF generating devices are used frequently to treat bone fractures that have stopped healing. EMF treatment is also increasingly being applied to fuse spinal vertebrae in people with intractable back pain. Several US-based medical firms – e.g., EBI Medical, Inc. and Orthofix – generate annual revenues in the order of hundreds of million dollars on MD prescription based sales of pulsed EMF emitting bone growth stimulators. EBI alone has published several hundred double-blinded and peer-reviewed clinical studies confirming the effectiveness of pulsed electromagnetic fields in promoting bone cell growth.

The U.S. FDA has also approved – after extensive clinical trials that were highly successful – a device that emits ELF-modulated microwaves in treatment of psycho physiological insomnia. The device emits microwaves at a maximum power output of 0.1 watt – more than an order of magnitude lower than current guidelines for cell phone radiation [1]. In reference [45] a large number of scientific publications describing successful human clinical trials and uses of pulsed EMF are reviewed.

Whereas low-level EMF has been clinically proven in humans to stimulate cell growth, it is beyond discussion that the biological mechanisms of low-level EMF are not related to any form of direct damage to the structures and substances of a biological cell. For example, EMF that is unable to heat tissue by as much as a millionth of a degree has been reported to increase DNA strand breaks and chromosomal damage in cells, and even so in human beings. Swedish researchers have found chromosomal aberrations in lymphocytes of engine drivers exposed to ELF fields in their occupation.

The only possible explanation to the mechanism, and broadly available research strongly support this, is that low-level EMF presents itself to the cell as a **signal**, triggering a response – a cascade of signaling substances changing gene expression, enzyme activities and cell metabolism. This triggering results in cell stress, a well-defined biological reaction, known to be caused by damaging agents such as X-rays, UV, toxic chemicals and overheating. The stress response involves the expression of specific genes – stress genes – that control production of protecting stress proteins, a vital part of the cell's defense system.

It is well known from biology that some level of stress may constitute a beneficial stimulation to a cell, but chronic, repetitive stress cause a down-regulation in the stress response, which will relatively quickly weaken the cell. Research referred to in this presentation show that just 30 minutes of daily exposure to EMF – ELF or RF – for three consecutive days in a row will cause down-regulation and thereby a weakening of heart cells in live chicken embryos.

That this actually takes place in humans is supported by a study on electric utility workers, showing that the more years they have been exposed to EMF in their occupation, the higher their likelihood of dying from a heart attack.

Recent research from Hong Kong University of Science and Technology suggest that stress proteins are a necessary factor in efficient repair of DNA damaged by free radicals – which are always present in our body – and that EMF exposure indirectly induces DNA degradation by down-regulating stress proteins.

In effect, it emerges from the scientific findings that low-level EMF – despite the fact that it has no ability to cause direct damage to a cell – **triggers a response as if it was a direct threat to the cell**. In a way, EMF triggers a "false alarm", and it is this triggering that eventually results in various damages to the cell, by down-regulating the cell's defense system against real threats such as free radicals, which are always present in the interior environment of our body.

RESEARCH UPON WHICH THIS PRESENTATION IS BASED

This presentation is based upon studies and clinical trials generally available in peer-reviewed scientific journals, combined with a compilation of experience obtained through an extensive 15 year research effort conducted at the Catholic University of America (CUA) in Washington DC, initiated by the US Army Medical Command and sponsored by:

1) The United States Department of the Army, Walter Reed Institute of Research;
2) The United States National Institute of Environmental Health Sciences (NIEHS), a sub-division of the National Institute of Health (NIH);
3) The United States Department of Energy (DOE);
4) Maryland State Department of Natural Resources;
5) EMX Corporation.

The main findings obtained through the research project have been peer-reviewed and published in leading journals, and confirmed by studies at four other universities, three of which have published their confirmation in peer-reviewed journals, the fourth university has not yet submitted final papers for publication.

In overview, this research project has provided important insights as to the conditions under which biological effects are induced by low-level electromagnetic fields, under what circumstances the biological effects may be beneficial – low-level EMF has been used for medical therapy in hospitals for decades – and under what circumstances and how the biological effects may be adverse to the cell and thereby increase the risk of disease: It is a question of structure and dose of the EMF.

The research revealed that the effects induced by radio frequency (RF) fields (microwave) and extremely low frequency (ELF) fields (largely below 1000 hertz) are identical, and therefore research results from ELF can be used to interpret and predict effects of RF, and vice versa.

The research also revealed that it is the **temporal information** of the EMF that is sending a "signal" to the cell – the temporal characteristics of the EMF (periodic constancy) determine if the biological cell will respond or not. This is described in-depth for cellular phone radiation induced biological effects in [2].

The research further showed that the biological impact of the EMF might result in physiological stress, which may be adverse if the exposure is repetitive or chronic. These findings are consistent with experience from hospital magneto therapy, where they expose patients to low-level EMF with certain pulse characteristics (temporal properties) – if the field is applied too frequently, the effect turns from beneficial to adverse.

Finally, the research has revealed that superimposing a "noise field" – an EMF with random temporal characteristics – on the biologically active EMF can eliminate induced biological effects and potentially adverse physiological stress. The studies showed that an ELF "noise field" may be used to block the biological effect of an RF (microwave) field, showing the way to mitigating effects of radiation in practice from devices such as cell phones without interfering with the operation of the devices. The Catholic University of America has patented this technique, and the main sponsors, the U.S. Government and EMX Corporation, have reserved rights to practical applications of this technology.

EMF-induced biological effects and the ability of the "noise" technology to mitigate such effects have been shown, replicated and confirmed by the following universities:

Catholic University of America, Washington DC: EMF enhanced activity of growth enzyme ODC (used as diagnostic marker for cancer, related to DNA synthesis) [3; 4; 13; 14; 48]; EMF-induced chicken embryo abnormalities [4], EMF-induced stress-related responses in chick embryos [6; 7; 49; 50; 51].

University of Western Ontario, **Canada**: EMF induced changes in nucleotidase levels [8].

Columbia University, New York: EMF enhanced gene expression (oncogenes, stress genes, household genes), EMF-induced stress response, EMF-induced suppression of neurotransmitter dopamine [9-11].

Aarhus University, Denmark: EMF induced acceleration of cell proliferation rates of human amniotic cells [12].

University of Washington, Seattle: EMF induced memory loss in rats [46] and DNA strand breaks in rat brain cells [47].

Zheijiang University School of Medicine, Hangzhou, China: EMF induced changes in cell membrane cytokine factor receptors [52] and stress-activated protein kinase (SAPK) phosphorylation [53].

In addition, researchers from **Colorado State University** [15] have investigated in humans the effect of EMF reducing levels of hormone melatonin. They found that in electric utility workers the melatonin reducing effect was dependent on the **temporal stability** of the EMF – the more constant the EMF properties, the larger the induced reduction in melatonin levels.

All of this research strongly suggests that the biological cell reacts to EMF as a **signal**; the EMF triggers a chain of events in the cell, unrelated to direct effects such as heating.

OVERVIEW OF SCIENTIFIC FINDINGS REPORTED IN THE LITERATURE

There is ample evidence that low-level EMF of both ELF-type and microwaves affect cell physiology and under controlled exposure conditions may have a marked clinical effect in humans, such as the enhancement of growth in bone tissue cells [45]. This form of therapy was approved by the FDA in 1979, and millions of patients have been treated in hospitals and doctors' clinics for the past almost four decades. Manufacturing and distributing medical devices emitting therapeutically active low-level EMF is a multimillion dollar industry.

Since it is well-established from traditional western medicine that agents affecting cell physiology – i.e., drugs – are beneficial in the right doses, but harmful in over-dose conditions, it should be obvious that this is the case with low-level EMF as well, as this has been scientifically and clinically shown and federally approved to be a highly active "medicine" for cells, animals and humans. However, for some reason there is still considerable controversy over the issue of EMF and health effects, and even the issue of low-level EMF and biological effects is still not widely accepted despite overwhelming scientific evidence.

Human exposure to physiologically active emissions of low-level EMF from mobile devices and other equipment is largely unregulated, and existing regulations are based on irrelevant, heat absorption based standards even though it can be clearly demonstrated that heat is not the cause of low-level EMF health effects, whether therapeutically beneficial or adverse depending on dose – i.e., exposure conditions. The effects are occurring at levels orders of magnitude below levels where any heating can be detected. They have been shown to be associated with signaling mechanisms inside and between the cells – membrane receptors, kinase enzymes, gene transcription and gap junctions – causing the EMF to act in effect as a "stressor" and a growth factor, much like a hormone [6-14; 46-53].

Results of epidemiological studies regarding the association between EMF exposure and disease through the past more than 20 years have been contentious, although several countries now are beginning to adopt the assumption that the risk is real, especially for children. Numerous epidemiological studies, at least 50 on ELF exposures, and 5 on microwave exposures, do suggest that EMF is associated with an increased risk of disease. Most studies are focusing on cancer, but there are studies available suggesting an association of EMF and Alzheimer's disease. Even research funded by the CTIA (Cellular Telephone Industry Association) in USA found an association between cellular phone radiation and cancer [16]. Epidemiology alone is not going to resolve the EMF health issue for a long time, therefore laboratory experiments are necessary to evaluate the risk.

Several in vivo studies have demonstrated that EMF may induce cancer in animals. The most prominent example of this is the Royal Adelaide Hospital study [17], showing that two times half an hour per day of mobile phone signals increased the number of tumors in exposed mice by more than a factor of two compared to unexposed mice. This study was also funded y the cellular phone industry (Telstra).

Some studies have found evidence of chromosomal damage in human cells and even in humans after exposure to EMF. Maes et al. [18] found chromosomal aberrations in human lymphocytes after exposure to microwaves, and Nordenson et al. [19] found chromosomal aberrations inhuman amniotic cells after exposure to 50 Hz ELF fields. Nordenson et al. [20] as well found chromosomal aberrations in lymphocytes of Swedish engine drivers exposed to ELF fields. In 1966, Dr. G. Jacobson of George Washington University examined 34 selected employees from the US embassy in Moscow, which had by then been subject to three years of microwave exposure by the Russians. Of the 34 employees examined, more than half were recommended not to reproduce over a six months period following the examination, due to chromosomal damage [21].

Several studies have found evidence of the special form of EMF induced chromosomal damage, **micronuclei**. Micronuclei are used as a clinical marker for increased cancer risk in nuclear exposure victims. It was used as such after the Chernobyl accident in the former Soviet Union. At least four studies,

including studies done as part of the $27 million research effort on behalf of the U.S. CTIA, Cellular Telephone Industry Association [16; 18; 22].

At least four studies have reported increased DNA strand breaks in whole animals and human cells as a consequence of low-level EMF exposure (ELF and microwave) [23-27].

At least 12 studies have replicated EMF induced increases in the activity of the important DNA-related enzyme ornithine decarboxylase (ODC), for an overview see [2]. ODC has been used as a diagnostic marker for cancer. Other enzymes reported to be influenced by EMF are for example nucleotidase [8], Na/K-ATPase, tyrosine kinases and other protein kinases.

At least four universities have reported EMF induced changes in gene expressions [9; 10; 28-31]. Genes activated by EMF include stress response genes, proto-oncogenes (known to be involved in carcinogenesis), household-genes, apoptosis-related (cell death) genes, etc. In [31], Dr. James Trosko et al. from Michigan State University in October 2000 reported that EMF blocks **cell differentiation** in human blood cells. This is exactly the characteristics of a tumor promoter.

There are numerous reports (at least 50) showing that EMF induce changes at the cell membrane level, for a review, see [32]. There are also reports providing evidence for the triggering of inward signaling enzymes in cells by EMF [30; 33; 34; 52; 53]. In 1999, a cooperative research effort between four laboratories – University of Minnesota, Minneapolis, University of California, Riverside, Wayne Hughes Institute, Roseville, Minnesota, and Kansai Medical University, Japan – found that low-level EMF stimulate tyrosine kinases, known to be involved in the activation of oncogenes. Tyrosine kinases are also known to be stimulated by ionizing radiation and believed to be responsible for the final damage that ionizing radiation induces, according to Dr. Uckun, one of the researchers involved in the study.

Studies at the Zheijiang University School of Medicine demonstrated that a group of cell membrane receptors (cytokine factor) associated with cellular signaling was affected by magnetic fields [52]. The researchers also demonstrated that the very important signaling enzyme stress-activated protein kinase (SAPK) is enhanced by low-level EMF [53]. They concluded that signal transduction pathways are the mediators of EMF for the induction of biological effects.

The individual findings of biological effects and potential health effects of EMF revealed in the studies are very disturbing from a public health perspective. But what makes the findings very much more disturbing is the fact that they all fit like pieces of a puzzle into an overall picture, which makes sense from a conventional scientific perspective: One biological effect reported is known to lead to the other.

It is known in biology that triggering of membrane signaling enzymes like tyrosine kinases and protein kinases is involved with changes in the expression of genes, especially genes known to be involved in carcinogenesis. Gene expression changes are known to be involved in changes of the activity of important enzymes, some of which involved in cellular repair function such as DNA repair. It makes sense that changed efficiency of repair enzymes may lead to accumulation of unrepaired biomolecules such as DNA, which are constantly being damaged by free radical activity. Accumulation of damaged DNA may of course lead to chromosomal damage. Chromosomal damage is known to increase the risk of cell death or cell transformation, which is directly related to diseases such as Alzheimer's and cancer.

This presentation will focus on DNA breaks and chromosomal damage and show how available scientific evidence already provide a plausible explanation for how such dramatic effects can occur.

LOW-LEVEL EMF IS A SIGNAL TO THE CELL – NOT A DIRECT THREAT IN ITSELF

It is an odd thought that subtle energies as low-level EMF should be a threat to the cell, causing such dramatic effects as DNA breaks, chromosomal damage and increased risk of serious diseases.

The only possible answer – and numerous available reports support this – is that the effect is not related directly to energy or heating, but to EMF as a signal, triggering a cascade of events, which are identical to the way the cell would respond to a **real** threat such as ionizing radiation, toxic chemicals or heat shock.

In fact, EMF is able to induce the exact same response as a heat shock – a dramatic rise in temperature – without any rise in temperature at all. It is known that a temperature rise of 5.5˚C (10˚F) is a threshold for the induction of heat shock proteins in a cell. The energy density required for such an effect to occur by direct heating is approximately 23,000,000 J/m^3. An ELF field of barely 8 mG is the threshold of an ELF electromagnetic field inducing the same heat shock response. The energy involved with such a field is approximately 0.00000026 J/m^3, a factor of almost 10^{14} lower than the threshold for heat shock by direct heating [10].

It is well known from physics that an EMF has two properties: Energy and information (structure). This is the reason for EMF to be used in communication, which is transportation of information.

In a microwave oven, the intensity of the microwave is very high, that is why it can be used for cooking food. In a cellular telephone, the energy density is too low to cause any significant heating. However, the cellular telephone emits microwave in a certain structure: Packages (bursts) of radiation at a very specific, constant frequency, amplitude and waveform.

Research at the Catholic University of America in Washington, DC has established that a field only affects cells when it has these constancy characteristics. This finding has been confirmed by research at five other universities [2-15; 46-54].

According to available research, the EMF – supposing it has the right constancy characteristics – triggers membrane receptors [32; 52], which release inward signaling enzymes such as tyrosine kinases [30; 33; 34; 53]. The tyrosine kinases activate specific genes in the cell nucleus, which then change expression [9; 10; 28-31]. Also intercellular signaling – gap junctions – have been shown to be affected by EMF [54].

This changed gene expression have a series of consequences. Some of the genes expressed are oncogenes, which control the activity of important enzymes such as ODC (ornithine decarboxylase) that is involved in DNA synthesis [2].

Other genes expressed are stress genes, causing a stress response in the form of stress proteins, which are only present in the cell when exposed to a threat.

Researchers at the Catholic University of America have determined the temporal characteristics of this triggering mechanism [2]. The targets of the EMF – the membrane receptors – take a few milliseconds to sense and activate inward signaling enzymes. The signal transduction process, which is the time it takes for the chromosomes to determine the constancy of the EMF, happens in a matter of approximately one second. The biochemical response – the biological effect – starts to build after approximately one second, reaching its maximum in 10-20 minutes. The temporal response characteristic of a constant ELF field is identical to the characteristics of a microwave field, thus confirming what many studies have reported, that the bioeffects induced by ELF fields are identical to the bioeffects induced by microwave fields.

THE EFFECT OF EMF ON CELLULAR REPAIR FUNCTION: THE ROLE OF STRESS

In order to stay healthy, a cell has to maintain efficient repair of biomolecules such as DNA, which are constantly bombarded by reactive oxygen species – free radicals – that are breaking chemical bonds. Free radicals are formed continuously in our cells as a result of respiration and metabolism. Antioxidants such as melatonin scavenges most of the free radicals, but still a large number remains and cause damage to biomolecular structures such as DNA strands. The reason why the cell survives is because efficient repair enzymes repair the broken biomolecules.

Accumulation of damage to cell structures, which may lead to cell death or transformation, can be the result of either increased direct damage or insufficient repair.

Ionizing radiation cause increased direct damage, as it increases levels of free radicals in the cell cytoplasm.

Low-level EMF is unable to do so, but there is ample evidence that low-level EMF affect cellular repair mechanisms, which is responsible for the build-up of damage such as DNA strand breaks that may result in chromosomal damage.

Efficient repair mechanisms depend on functional repair enzymes, which catalyze the formation of chemical bonds. If repair enzymes become dysfunctional, cellular repair will become reduced.

Just like the DNA-molecules they repair, repair enzymes are themselves macromolecules bombarded by free radicals causing damage by breaking chemical bonds. When the repair enzyme becomes permanently damaged, it is repaired by – **stress proteins**.

Stress proteins are the cell's universal response to stressors that cause damage to proteins such as repair enzymes. Functional enzymes need to be folded in a certain way, stressors such as X-rays, UV, toxic chemicals, heat shock, lack of oxygen, etc., cause enzyme molecules to unfold. Stress proteins function by refolding enzymes into their proper shape, so they become functional again.

Stress proteins are only produced when needed, i.e., when the level of damage demands it. Stress protein production is induced through expression of stress genes. Stressors such as X-rays, UV, toxins or heat shock trigger stress gene expression. In these cases, the stress proteins are really needed, as the stressors are able to directly damage biomolecules such as repair enzymes.

All of this is well known from traditional cellular biochemistry.

The big surprise is, however, that low-level EMF – ELF fields or microwave – is able to induce the exact same stress response, even though there is no way such agents can cause any direct harm. In a way, the triggering of the stress response to low-level EMF is a "false alarm". At least 10 different universities have found that EMF – ELF fields or microwave – trigger the stress response [6; 7; 10; 28; 29; 35-44].

The reason why this "false alarm" becomes a problem is the well-established biological phenomenon of **down-regulation** of the stress reaction as a function of repetitive or chronic stresses. This will suppress the production of stress proteins, and when they are really needed to repair the damage caused by free radicals or heat shock, they are not available and the cell will weaken because of insufficient repair.

Down-regulation of the stress response as a consequence of repeated EMF-exposures has been demonstrated in particular by the research team at the Catholic University of America on chicken embryo hearts [6; 7]. When chicken embryos were exposed to EMF for a single period of 30 minutes, their hearts were protected against subsequent stressors such as hypoxia (simulated heart attack). However, when the EMF-exposure was repeated for four consecutive days, the result was the opposite: The chicken embryo heart cells became weakened and fewer cells survived a subsequent stress (hypoxia).

This seems to be the case as well for humans exposed to EMF in their occupation. In a study published 1999 by Savitz (American Journal of Epidemiology, 1999) on electric utility workers it was demonstrated that the more years of exposure, the higher the risk of acute myocardial infarction.

On this background the following EMF-induced chain of events leading to a build-up of DNA damage, as observed by researchers, seems plausible:

Constantly pulsing EMF presents itself as a signal to the cell and triggers the cellular stress response, both on the genetic level as a stimulation of stress genes, and as a production of stress proteins, even though the EMF is in effect not a "real" stressor like ionizing radiation, toxic chemicals, etc. Repetitive EMF-induced stress leads to down-regulation of the stress response and a suppression of stress protein production. This leads to inefficient maintenance by the stress proteins of DNA repair enzymes, and subsequently there will be a build-up of DNA damage caused by free radicals, which are always present in the cells.

That DNA repair is influenced by EMF, and that indeed stress proteins are the determining factor, was described in three recent papers from University of Hong Kong, Department of Biochemistry. When the levels of stress proteins were increased by EMF-exposure (as in one-time exposures), the DNA repair was enhanced. When levels of stress proteins were reduced by EMF (as in repetitive exposures), DNA repair was suppressed and DNA degraded. This finding is supported by reports of chromosomal damage such as micronuclei in human blood cells, which has been established in research funded by the U.S. Cellular Telephone Industry Association and other research studies.

Exposure to EMF from devices such as cell phones tends to be repetitive. It should therefore be expected that cellular phone radiation induce cell stress, reduced DNA repair and chromosomal damage, which increase the risk of diseases such as cancer and Alzheimer's. In a brain, cancer may be the result of genetic damage if the troubled cells are able to multiply such as glial cells. If the troubled cells are neurons, which cannot multiply, the result of genetic damage is likely to be Alzheimer's. There are indeed health data available, which support this hypothesis.

THE SOLUTION TO THE PROBLEM

As shown by the researchers at the Catholic University of America, and confirmed by their colleagues at six other universities [2-15; 46-53], it is a requirement for the EMF to have an effect on cells that it is constant for at least one second. If this is not the case, the EMF is no longer a **signal** to the cell, and no triggering results. Litovitz and Penafiel [2] have determined that cellular phones, even with DTX and power regulation, still have such constant properties that it triggers a response.

Litovitz and Penafiel have suggested [13; 14] that superimposing a random ELF field on a bioeffecting microwave field such as cell phone radiation will mitigate induced bioeffects. The same principle may of course be used to mitigate effects of constant ELF fields.

The experiment of mitigating effects of a constant field – ELF or microwave – by superimposing a random ELF field is the most replicated experiment in bioelectromagnetism. Six universities have participated in this research, which has been performed on a large number of biological markers [2-15; 46-54], every time with the same results: All bioeffects measured were eliminated.

EMF-induced biological effects shown in scientific studies to be eliminated by the noise-field technology:

- Increased ODC activity (marker for cancer);
- Chicken embryo abnormalities;
- Oncogene activation (human cells);
- Stress gene activation (human cells);
- Stress protein production (human cells);

- Neurotransmitter dopamine;
- Cell proliferation acceleration (human cells);
- Rat memory;
- DNA breaks in rat brains;
- Membrane growth factor and cytokine membrane receptor changes;
- Signaling stress enzyme (SAPK) enhancement;
- Intercellular communication pathway (gap junction) suppression.

Furthermore, Colorado State University have tested and confirmed the hypothesis in humans (melatonin in electric utility workers) [15].

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