## **Powerfrequency EMFs and Health Risks**

This article is separated into 12 sections, each of which can be individually downloaded. It is a 'work in progress' incorporating new information whenever time permits.

# Section 4

## Cellular changes and potential mechanisms

- 1. Introduction; electricity consumption; measuring meaningful exposure; static electric field from high voltage direct current transmission; precautionary recommendations; EMFs interacting with the environment or other substances; geomagnetic field (GMF) changes; a French study in 2009; residential exposure; mitigating biological effects; campaigning organisations
- 2. Occupational exposure; occupational research
- Cancer; leukaemia; Sources of magnetic field exposure and cancer risk; brain 3. cancer; breast cancer; neuroblastoma; other cancer; immune system effects; tamoxifen, doxorubicin and other drug effects; similarities to other chemical effects
- 4. Cellular changes and potential mechanisms; DNA breaks and changes; EEG changes; other cellular changes; potential mechanisms for interaction between exogenous EMFs and biological processes; free radical effects; effects on other cellular processes; airborne pollutant effects; other potential synergistic effects
- 5. MRI; contrast enhancement; individual experiences of reactions; MRI vs CT; cardiac scan; the European Physical Agents Directive; research
- 6. Electronic surveillance systems in shops, airports, libraries, etc.
- 7. Light at Night and Melatonin; circadian rhythm disruption; clock genes; plant, animal and insect effects
- 8. General reproductive effects; miscarriage and other effects of female exposure; powerfrequency exposure and male sperm; protective treatments
- 9. Other effects; ageing; amyotrophic lateral sclerosis (ALS); animal effects; anxiety; asthma; autism; bacteria; behaviour changes; birth defects; effects on blood; bone changes; brain damage; cardiovascular effects; dementia; developmental effects; depression and suicide; EEG changes; energy metabolism; eye effects; gastric effects; genetic defects; hearing effects; heart; insulin and electric fields; interference problems; kidney effects; learning and memory effects; lung, spleen and liver; medical implants; mental health problems; nervous system; neurobehavioural effects; neurodegenerative effects
- 10. Other effects; obesity; olfactory effects; other neurological and psychological effects; pain perception; Parkinson's disease; protective effects of EMFs; skin;

sleep; synergistic effects; teeth; thyroid; weight change; some experimental problems; government advisory bodies

- 11. Positive health effects; apoptosis; cancer treatment; cell survival and differentiation; wound healing
- 12. References 937 references

#### Cellular changes and potential mechanisms

In this section we look at EMFs and the changes that they have been found to make in DNA in cells, or in other cellular processes. We then look at some of the theories that have been proposed for the interaction between biological processes and external sources of EMFs.

The results of a study by Kesari (2016) indicated that the threshold for biological effects of ELF MFs is 10  $\mu$ T or less. Many papers frequently quoted use exposures very much higher than 10  $\mu$ T. Because of the variability of findings from the different studies it may be that the expected dose-response relationship is not a valid one, and there may be windows of effects. Bae (2013, Koziorowska 2018) concluded that the observed differences in the study on cancer cell proliferation, which showed both showed positive and negative differences, may partially explain the poor reproducibility and controversial results of many experimental and epidemiological studies. Farina's study (2010) indicated that cell response, including oxidative stress, after acute exposure to ELF EMFs strictly depended on the cell model rather than on the applied magnetic field strength or duration of exposure. Ayşe (2010) found that a single exposure to an ELF EMF resulted in a decrease in cell differentiation, while ELF EMF applied every day for 1 h caused an increase. These findings imply that the amount of exposure time is important in determining the physiological response of cells to ELF EMFs.

A problem that was pointed out by Mild (2009) that could be occurring to confuse research findings is that ELF electromagnetic fields caused by electronic equipment such as laboratory incubators is largely unrecorded and uncontrolled. These can generate significant amounts of EMFs, up to tens of microtesla. Portelli (2013) found that the background magnetic field in biological incubators can vary by orders of magnitude within and between incubators. Exposure to such altered magnetic field environments has been experimentally shown to be sufficient to cause numerous effects in cell cultures. Examples of the effects reported vary from differential generation of free radicals and heat shock proteins to differences in cellular proliferation, differentiation, and death. Electric fields have also been shown to accelerate cell differentiation at the expense of cell proliferation (Collard 2011, 2013). The inhomogeneity of the background magnetic field in incubators is a potential confounding source of the variability and reproducibility for studies performed on cell cultures.

The experimental data in the paper by Belyaev & Alipov (2001) support the idea that both harmonics and subharmonics of several biologically important ions are involved in frequency-dependent ELF effects in cells of different types.

Hasanzadeh (2014) found that the expression of 189 proteins in in a neuroblastoma cell line exposed to magnetic fields changed.

### **DNA Breaks and Changes**

For some time, DNA breaks were thought to be caused only by ionising radiation (like an X-ray or a nuclear bomb) acting directly on exposed cells. However, Professor Lai and others have consistently found single and double DNA strand breaks as a result of powerfrequency magnetic

fields (Lai <u>1998</u>, <u>2004</u>, Markkanen <u>2008</u>, Chen <u>2008</u>, Kim <u>2012</u>, Nakayama <u>2016</u>) and a review by Phillips (<u>2009</u>), concluded that such breaks may have consequences for carcinogenesis and neurodegenerative diseases. The fields they exposed rat cells to were higher than are likely to be found in the normal residential environment, but were lower than the level at which DNA breaks would have been expected. Ivancsits and colleagues also found that intermittent EMF exposure led to a significant increase in single and double-strand breaks in DNA (<u>2002</u>, <u>2003</u>), as did Nikolova (<u>2005</u>). This effect seemed stronger in women than in men (Ahuja <u>1999</u>). Focke (<u>2010</u>) and Kim (<u>2010</u>) confirmed these findings, suggesting that the effects could be explained by disturbances in S-phase processes and triggering of apoptosis rather than the generation of DNA damage. Ivancsits (<u>2003</u>) also suggested that there was an age-related slowdown of DNA repair efficiency.

A meta-analysis of 87 ELF-MF studies carried out between 1990 and 2007 found that ELF-MF exposure carried a significant risk of causing genetic damage (Vijayalaxmi & Prihoda 2009). Rageh (2012) concluded that there was an association between DNA damage and ELF-MF exposure in newborn rats.

Sarimov (2011) found that chromatin conformation (the combination of DNA and proteins that make up the contents of the nucleus of a cell) was affected by magnetic field exposure at high levels, but the effect differed between individuals, over time and altered according to the temperature at the time of exposure. Despite these variations, though, the authors concluded that the cells were changed by magnetic fields.

This concept that only ionising radiation could cause DNA breaks was challenged by Professor Eric Wright (2004) of Dundee University, who found effects of ionizing radiation in cells that had received no direct radiation exposure, what has become known as the bystander effect. Professor Denis Henshaw in a private communication (December 2008) said "the word 'breakage' is a misnomer because it is not usually the site where the DNA was "hit" or "attacked" (by chemicals, radiation or whatever), rather the so-called breaks represent points of failure of the DNA replication template. The best examples here are genomic instability and the bystander effect, both nothing to do with direct 'hits' on the (parent) cell DNA". The bystander effect is where cells that have never been hit by ionising radiation, but were in the vicinity of those that were, or even were cultured in a culture medium which had previously had cells in them that were irradiated, had DNA strand breaks induced in them. This occurs by a signalling effect from hit cells. Rossi (2011) found that cell proliferation rate and morphology of cells in one petri dish was affected by cells in a neighbouring one with no apparent chemical communication. A filter was used to screen EMFs and the changes didn't happen, leading the authors to conclude that it was intercellular electromagnetic communication, an example of the bystander effect. However Professor Henshaw continues "Chromosomal aberrations reflecting DNA strand breaks represent replication failures in the DNA template. Such failures are associated with coding information and not necessarily quantum energy at the level associated with ionising radiation. The myriad of responses involving genetic damage seen following exposures to magnetic fields are consistent with such loss of coding information."

In a review of 29 studies (genotoxic and epigenetic) about DNA strand breaks and magnetic fields (MFs) by Ruiz-Gómez & Martínez-Morillo (2009), the authors concluded that the differences in conclusions could be explained if "*MF could act as a co-inductor of DNA damage rather than as a genotoxic agent per se.*" Okudan (2010) found no genotoxic changes in mice as a result of magnetic field exposures between 1 and 5 microtesla, although they did find higher micronucleus numbers, especially among males, at some frequencies. Luukkonen (2014) found persistently elevated levels of micronuclei in the progeny of cells exposed to 50 Hz magnetic fields, indicating an induction of genomic instability.

DNA damage was found in all cerebral areas of mice exposed to low frequency magnetic fields (Mariucci <u>2010</u>). The damage seemed to be repairable after a 7-day exposure.

Blank & Goodman (2009, 2011) reviewed reports of increased stress protein levels and DNA strand breaks due to EMF interactions, both of which are indicative of DNA damage. They suggested that the range of interaction with EMF is a characteristic of a fractal antenna, and DNA possesses 2 characteristics of a fractal antenna, electronic conduction and self symmetry. They concluded that these properties contribute to greater reactivity of DNA with EMF in the environment, and the DNA damage could account for increases in cancer epidemiology.

Parham (2016) in a review of ELF EMF papers on links to disease reported that ELF EMF datasets were sporadically linked to human diseases, but no clear pattern emerged. Individual datasets showed some linkage to cancer, chemical dependency, metabolic disorders, and neurological disorders.

Winker (2005) found that intermittent low-frequency EMFs led to considerable chromosomal damage in dividing cells.

Miyakoshi (2000) found that exposure to high density ELF-MF at more than 50 mT may potentiate X-ray-induced DNA strand breaks.

Findings by Y Liu (2016) demonstrate that miR-26b-5p could serve as a potential biomarker following 50 Hz ELF-EMF exposure, and miR-26b-5p-CCND2-mediated cell cycle regulation might play a pivotal role in the biological effects of ELF-EMFs.

## **EEG changes**

In a study by Marino (2004), each subject exhibited statistically significant changes in the EEG during presentation of the low-strength, low-frequency magnetic field. The 100% response rate suggests that the ability to detect such magnetic fields is a common property of the human nervous system. Carrubba (2009) also found changes in the EEG triggered by an external electric field. Joe Kirschvink from the California Institute of technology has been working for many years to find out about the magnetic sense detection ability in humans.

He found that when a magnetic field was rotated counterclockwise – the equivalent of the person taking part in the experiment looking to the right – there was sharp drop in alpha waves. The suppression of alpha waves, in the EEG world, is associated with brain processing: A set of neurons were firing in response to the magnetic field, the only changing variable. The neural response was delayed by a few hundred milliseconds, and Kirschvink says the lag suggests an active brain response. A magnetic field can induce electric currents in the brain that could mimic an EEG signal – but they would show up immediately.

Demir (2014) found that MF exposure has a negative effect on brain waves, and this effect becomes more evident with prolonged exposure.

Shafiei (2014) observed that significant changes in different EEG bands were caused by locally exposing different points of the brain to ELF-MF.

Magnetic fields increased the uptake of glucose into the brain, depending on the direction of the field, affecting EEG (Frilot 2nd 2011).

## Other cellular changes

Santini (2009) concluded in a review of papers looking at ELF cellular effects "the majority of the in vitro experimental results indicate that ELF fields induce numerous types of changes in cells. Whether or not the perturbations observed at the cellular level can be directly extrapolated to negative effects in

humans is still unknown. However, the myriad of effects that ELF fields have on biological systems should not be ignored when evaluating risk to humans from these fields and, consequently, in passing appropriate legislation to safeguard both the general public and professionally-exposed workers". The results of a study by Ke (2008) suggested that membrane receptors could be one of the most important targets where extremely low frequency (ELF) MF interacts with cells, and Ras may participate in the signal transduction process of 50 Hz MF. A 'noise' MF could inhibit these effects caused by ELF-MF.

Adherens (AJ) and tight junctions (TJ), as integrated parts of the junctional complex, are specialized regions of the cell membrane in epithelial cells. They are responsible for cell-to-cell interactions and also have great importance in cellular signalling. Somosy (2004) demonstrated that magnetic fields are able to modify the distribution of TJ and AJ structural proteins.

Lahijani (2009) also found a variety of cellular changes which resulted in deformities when chicks were exposed to EMFs before hatching.

Kaune (2002) found that the membranes of living cells may be affected by power frequency electric and/or magnetic fields at levels below those set by thermal noise limits. Cellini (2008) found changes in cell division in E. Coli exposed to EMFs. Sert (2011) found intracellular Ca(2+) accumulation in cardiac ventricles increased in rats exposed to ELF magnetic field. No effect of ELF-EMFs was found in the proteins of the autonomic nervous system (Benfants 2008).

Blank (2005) suggested that transient charges in the particular enzymes could provide a trigger for the sequence of conformation changes that are part of the ion transport mechanism. If the distributions of transient electrons and protons in the membrane are affected by their concentration and the membrane potential, as expected from electric double layer theory, this can account for the different effects of low frequency electric and magnetic fields, as well as for the observation that membrane hyperpolarization reverses the ATPase reaction to generate ATP.

In 2004 Blank & Goodman suggested that EMFs could stimulate transcription by interacting with electrons in DNA to destabilize the H-bonds holding the two DNA strands together. Such a mechanism is consistent with the low electron affinity of the bases in previously identified electromagnetic response elements (EMREs) needed for EM field interaction with DNA. It is also in line with both endogenous and in vitro stimulation of biosynthesis by electric fields. The frequency response of several EM sensitive biological systems suggests that EM fields require repetition and are most effective at frequencies that coincide with natural rhythms of the processes affected.

Bone marrow cells were affected by ELF-MF (Erdal 2007), without any chemicals or differentiation factors (Cho H 2012).

In 2006, Blackman reviewed work on EMF exposure, asking whether it could cause alterations in the physiology of developing organisms. He particularly mentions reports that indicate that exposure of chicken eggs to electric fields of 10 volts per metre could cause the brain tissue of the hatched chickens to respond differently in a particular test, and subsequently that chemical sensitivity could develop in individuals with a history of power-line exposure. He wondered whether the ambient electromagnetic environment can leave an imprint on developing organisms and if such imprint changes have the potential for health consequences.

Gok (2016) felt that prenatal and/or postnatal exposure of rats to a 50 Hz electric field might influence evoked potentials. Lipid peroxidation in the brain and retina might be associated with this effect.

Fifty Hz electric field may decrease plasma total cholesterol and triglyceride levels in rodents significantly, especially with long-term exposure (Coskun & Comlekci 2010). Coskun (2009) also found that intermittent and continuous magnetic field exposures affect various tissues in a distinct manner because of having different tissue antioxidant status and responses. Torres-Duran (2007) found that single exposures to ELF-EMF increased the serum values of high density lipoproteins (HDL-C), the liver content of lipoperoxides and decreased total cholesterol of the liver. The mechanisms for the effects of ELF-EMF on lipid metabolism are not well understand yet, but could be associated to the nitric oxide synthase EMF-stimulation.

Gerardi (2008) found "evidence that long term exposure to electromagnetic fields with a well defined frequency may have relevant effects on parameters such as body weight, blood glucose and fatty acid metabolism." Touitou (2012) reported that long-term exposure to 50 Hz magnetic in healthy men could induce some biological modifications of certain blood parameters (sodium, chloride, phosphorus, glucose). Giorgi (2011) found that ELF magnetic field exposure affected cell transposition activity, and the effects critically depend on the wave shape of the field, but not on the frequency and the exposure time, at least in the range observed in that particular study. ELF-Lin (2016) found that EMF and RF-EMF exposure can upregulate the expression of genes involved in glucose transportation. Energy metabolism is closely related with the cell response to environmental stress including EMF exposure.

Bonhomme-Faivre (<u>1998</u>a) measured changes in hematological, biochemical and cortisol parameters in 6-week-old Swiss mice continuously exposed to ELF generated by a transformer station. Changes were observed over time, including both decreases and increases in numbers. Individual differences in sensitivity were observed, as some mice showed a significant decrease in the leukocyte, neutrophil and other counts, whilst in others there was a significant increase (de Kleijn <u>2016</u>).

Power frequency magnetic fields can be one of the factors involved in the aetiology of semicircular lipoatrophy (SL), an idiopathic condition characterized by atrophy of subcutaneous fatty tissue (Martínez <u>2015</u>).

Makarov & Khmelinskii (2014) found that a combination of environmental three-dimensional oscillating low-frequency electric and magnetic fields increased or decreased the lifespan of drosophila melanogaster. They hypothesised that they slowed down or accelerated metabolic processes by inducing vibrational motions at a sub-cellular or larger scale.

Exposure to 50 Hz EMFs increased the frequency of micronucleated polychromatic erythrocyte in mouse bone marrow, expressing a genotoxic capacity (Alcaraz <u>2014</u>).

Repeated exposure to extremely low frequency magnetic fields (ELF-MF) increases locomotor activity (Shin 2011).

# Potential mechanisms for interaction between exogenous EMFs and biological processes

Magnetic material is present in a wide range of grain sizes in parts of the brain (Schultheiss-Grassi <u>1999</u>). This is likely to be involved in the interaction with external magnetic fields. It has been suggested that there may be a relationship between excess iron accumulation in the brain and neurological and neurolegenerative diseases. Brem (<u>2006</u>) found that brain tumour tissue contained an elevated amount of iron oxide.

Though experiments may be contradictory or inconclusive, nevertheless, it is suggested that EMFs could act by:

- Directly increasing the level of harmful free radicals within the body
- Affecting other cellular processes, including tumour promotion, some of which may not even have been investigated as yet, including quantum-like processing of mental information in the brain (Khrennikov 2011)
- Decreasing the level of the protective hormone melatonin
- Affecting exposure to airborne pollutants, making them more harmful
- Other synergistic effects

#### Free radical effects

In body tissue free radicals are dangerous high-energy particles that damage cells and can both cause and accelerate the progression of cancer. Timmel & Henbest (2004) were among the first to show that exposure to EMFs can increase the yield of free radicals by more than 60%. The theory was reviewed by Simkó & Mattsson (2004), who concluded that EMFs cause a general increase in the levels of free radicals, including field polarisation differences (Mannerling 2010), which could explain the diverse and often inconsistent nature of observed effects of EMFs, free radicals being intermediaries in many natural processes. Martínez-Sámano (2010) found that 2 hours of 60 Hz EMF exposure might immediately alter the metabolism of free radicals decreasing antioxidant activity in the heart and the kidneys, and systems controlling the brain oxidative balance (Martínez-Sámano 2012), including reducing melatonin levels (Tiwari 2013). Ciejka (2011) showed that ELF-MF applied for 30 min/day for 10 days could affect free radical generation in the brain. Prolongation of the exposure to ELF-MF (60/min/day) caused adaptation to this field. The effect of ELF-MF irradiation on oxidative stress parameters depends on the time of animal exposure to magnetic fields. ELF-EMFs were found to interfere with chemical reactions involving free radical production (Patruno 2015).

Experiments on mice (Rollwitz 2004, Crumpton 2005, Frahm 2006) found that magnetic fields (or electric fields Guler 2008) stimulated the formation of free radicals and also macrophage activity. Some applications of EMFs were found to increase free radicals, whilst others did not (Güler 2007). Exposure to some, but not all, frequencies changes the cell cycle of human fibroblasts (connective tissue involved in wound healing), which may be an effect of free radical concentration (Cridland 1999).

Wolf (2005) found a dose-dependent increase in DNA damage after exposure to EMFs. Antioxidant administration reduced the damage, suggesting that redox reactions were involved. DNA damage could arise as a result of persistently elevated free radical concentrations (Lupke 2004), caused by long-term EMF exposure, or via the radical pair mechanism (Montoya 2017), by which magnetic fields increase the lifetime of free radicals, allowing more DNA damage to occur (Rollwitz 2004, Henshaw 2008, Eleuteri 2009, Buchachenko 2016). Yokus found in his studies (2005, 2008) that magnetic field exposure prolonged the life of free radicals detectable up to 100 days after exposure. There seemed to be a window effect and the higher levels of exposure did not have the same effect as lower ones.

Yoshikawa (2000) found that low frequency EMFs enhanced the level of nitric oxide that had been experimentally induced, thus increasing oxidative stress. Nitric oxide has been associated with obsessive compulsive disorder-like behaviour (Salunke 2014). Falone (2007) and Di Loreto (2009) found that 50 Hz EMFs reduced cell tolerance to oxidative attacks and Emre (2011) suggested a link between magnetic field exposure, oxidative stress, and induced cell death. Tayefi (2010) found that prenatal exposure to EMF causes oxidative stress, apoptosis and morphological pathology in myocardium of rat pups. Türközer (2008) and Akdag (2010) found no change in cell death, but increased oxidative stress, and diminished antioxidant defence system. Selaković (2013) found the amount of oxidative stress was higher in middle-aged animals. Regoli (2005), Chu (2011, 2012), Akpinar (2012), Seifirad (2014), Manikonda (2014) and Gok (2014) also found an

increase in oxidative stress after ELF exposure. Some of these results were at exposure levels which would be rarely encountered even in occupational circumstances, so the relevance may not be clear. The ELF electric fields used in a study by Harakawa (2005) decreased the lipid peroxide level in an oxidatively stressed rat.

Polanaik (2010) suggested that vitamin E supplementation might decrease susceptibility to liquid peroxidation in tumour cells and that EMFs would reduce its effectiveness.

A review of the epidemiologic and experimental research on the potential carcinogenic effects of extremely low frequency electromagnetic fields (ELF EMF) by Simkó (2007) led her to conclude that "modulations on the oxidant and antioxidant level through ELF-EMF exposure can play a causal role in cancer development".

The increase of free radicals generation was observed after 30 and 90 min exposure of platelets to magnetic fields found in cars (Buczyński 2005).

#### Effects on other cellular processes

Binhi (2008) suggested that magnetic nanoparticles in the human body may be one of the avenues by which EMFs may be implicated in the development of childhood leukaemia. Changes in levels of cellular proteins or ions can affect cell function (such as removing unnecessary or damaged cells) and cause cancer cells to develop. Some experiments have shown that EMFs affect these functions (Sulpizio 2011), though they have been difficult to reproduce and therefore remain controversial.

Delle Monache (2008) found low frequency fields affected angiogenesis (the growth of new blood vessels, which can change tumours from a dormant state to a malignant one). Calcium ions play a critical role in determining the rate of cell division, and the overall evidence is that magnetic fields induce changes in apoptosis (cell death), according to a review & paper by Santini (2005b, 2005), and a study by McCreary (2006).

Luo (2014) found that ELF-EMF exposure specifically influences some intracellular calcium dynamics. Changes in B lymphocytes can also change cellular division rates. Y Li & Héroux (2014) found that biological effects of MFs are connected to an alteration in the structure of water which they felt may be environmentally important, in view of the central roles played in human physiology by ATPS and AMPK, particularly in their links to diabetes, cancer and longevity. A series of studies (Dibirdik 1998, Kristupaitis 1998) demonstrated EMF effects that made cells more likely to become cancerous. Basile (2011) found that the expression of the anti-apoptotic protein BAG3 was changed as a result of ELF exposure. The authors suggested that this may contribute to melanoma cell survival and/or resistance to cancer therapy. Boscolo (2001) demonstrated a reduction of blood NK lymphocytes and of the production of interferon in workers exposed to low frequency EMFs in a museum. However, the original results have not yet been replicated, perhaps pointing to the need to tighten experimental protocols. D'Angelo (2015) found that the expression of chemokine MCP-1 which regulates the migration and infiltration of memory T cells, natural killer (NK), monocytes and epithelial cells, and which has been demonstrated to be induced and involved in various diseases, was modified by EMF exposure in different cell types. It might affect the metabolism and functions related to neurodegenerative processes.

Wahab (2007) proposed that DNA crosslinking at the replication fork is a model which could explain the mechanistic link between ELF EMF exposure and increased sister chromatid exchange (SCE) frequency.

Electromagnetic fields were found to regulate the orientation of epithelial cell (epithelial cells include secretion, selective absorption, protection, transcellular transport and detection of

sensation) division and cause their directional movement (Zheleznov 2009). Applied electric fields of physiological strength were shown to produce significant mechanical torques at the cellular level (Hart 2010).

ELF-EMF exposure was found to exert significant effects on synaptic activity, dependent on the structure and neuronal network of the affected region (Varro 2009, Azanza 2013, Komaki 2014). EMFs were found to have different neuronal effects depending on the neuron spiking pattern. The authors (Yi 2014) concluded "Compared with tonic spiking, bursting dynamics are less sensitive to the perturbations of ELF MF exposure. Further, ELF MF exposure is more prone to perturb neuronal spike times relative to spiking frequency. Our finding suggests that the resonance may be one of the neural mechanisms underlying the modulatory effects of the low-intensity ELF MFs on neuronal activities."

ELF EMFs induced molecular changes during the differentiation of embryonic neural stem cells (Ma 2014). Yan (2010) found that exposure to extremely low frequency magnetic fields could influence the growth (decreased cell number under exposure) and metabolism (increased osmolality and increased extracellular sodium and potassium concentrations) of human mesenchymal stem cells, but had no significant effect on cell differentiation.

Cells are not autonomous units responding to damage as independent entities. Recently, there have been many reports of effects arising in non-irradiated cells as a consequence of inter-cellular communication. These non-targeted effects have been demonstrated in the descendants of irradiated cells (radiation-induced genomic instability) and in cells that have received signals produced by neighbouring irradiated cells (radiation-induced by stander effects) but the expression of such effects is significantly influenced by genetic factors (Wright 2008).

Evidence for indirect effects as a result of the 'bystander effect' has been shown by Wright and Mair (2008). Mair suggested that "EMF carcinogenesis involves the transport by macrophages of toxins (possibly including free radicals) to sites of infection or tumour localisation. This could increase mutation rates at these sites, perhaps promoting malignancy by introducing mutations, or by increasing the DNA instability of small early tumours, thereby engendering a more aggressive phenotype." Mair also suggested that EMFs could be mutagenic on their own, or could potentiate ionizing radiation mutations. Pokorný (2009) also suggested that "Local invasion, detachment, and metastasis of cancer cells are subsequent events of disturbed electromagnetic interactions."

Repacholi & Greenebaum (<u>1999</u>) suggested that induced currents circulate mostly in the extracellular medium, and may be responsible for alterations in ion transport across membranes, voltage sensitive or other channels, membrane protein function, or binding of hormones or mitogens at the cell surface (Calabrò <u>2013</u>). To have a meaningful biological effect, signals from external fields must be either greater than the endogenous levels, or discernible in a different manner. This study was reported by McNamee (<u>2009</u>) who commented that EMFs may act on a molecular, cellular or organ level.

Sun (2010) concluded that 50-Hz magnetic field (MF) exposure for 72 hours could inhibit the hormone secretion of trophoblasts, and an incoherent MF of equal intensity could completely eliminate the effects induced by the 50-Hz MF.

Atasaoy (2009) suggested that electromagnetic fields could affect the functional capacity of the peripheral blood mononuclear cells by changing their adhesion ability. They wondered if these alterations were the signs of immune system changes. Selmaoui (2011) showed that 50-Hz magnetic field exposure significantly increased IL-6, a protein that is part of the human immune response. Qiu (2010) indicated that protein kinase C signalling was involved in electromagnetic pulse-induced blood brain barrier permeability change. The magnetic field levels were at the top of ICNIRP-allowed occupational levels, but these effects should be looked at again. A study by Di Giampaolo (2006) found that high magnetic field levels in a museum workplace affected the

immune systems of those working there; the women more than the men. Johansson (2009) reviewed papers on the effects of EMFs on the immune system and concludes that "EMFs disturb immune function through stimulation of various allergic and inflammatory responses, as well as effects on tissue repair processes. Such disturbances increase the risks for various diseases, including cancer."

Fonken (2012) found that light at night affected immune parameters in diurnal rodents. She also found (2013) that chronic exposure to even very low levels of light pollution may alter inflammatory responses, including a greater reduction in locomotor activity, increased anorectic behaviour and increased weight loss. She suggested that light at night disrupted core circadian clock mechanisms.

Ravera (2011) reported that only membrane-anchored enzymes decreased their activity as a result of exposure to specific levels of EMFs, and that this change was reversible.

John Howard, at a conference in November 2008, introduced a paper describing how he had used fluorescent stains to show that exposure to chemicals (to which the cells were sensitised) and electromagnetic radiation caused almost identical rapid influxes of calcium into living cells. He suggested that Multiple Chemical Sensitivity (MCS) and Electrical Hypersensitivity (EHS) may be very similar and centred on changes in membrane permeability.

Zhang (2010) found that 50 Hz 0.8µT magnetic field can induce the uptake of intracellular calcium in osteoblasts. Morabito (2010a, 2010b) found that acute exposure decreased calcium activity and increased reactive oxygen species (ROS) levels (Rosenspire 2000, Jeong 2017), and nitric oxide levels (Pall 2013). Chronic exposure resulted in levels returning to non-exposure levels. Cui (2014) concluded that 50Hz ELF-EMF inhibits T-type calcium channels through AA/LTE4 signaling pathway. Another pathway was identified by C Huang (2014), where the authors showed that ELF-EMFs activated the ATM-Chk2-p21 pathway in HaCaT cells, inhibiting cell proliferation. An (2015) found that 50Hz PF-EMF exposure could affect cell proliferation and cell cycle by down-regulation the expression of PCNA and CyclinD1 protein.

Results of a study by Wei (2015) indicated that ELF-EMF could regulate calcium-associated activities in heart muscles.

Chiu & Stuchly (2005), using two modelling techniques, found that imperceptible contact currents could potentially induce biologically significant changes in transmembrane potential across cellular gap junctions from "several to over 200 microV". It has been suggested by others (Peck & Kavet 2005) that contact currents (such as may be found on domestic water pipes) may be one of the causative mechanisms for leukaemia.

Studies with electric and magnetic fields in the extremely low-frequency range have shown that weak fields can cause charge movement (Albanese 2009). Redistribution of charges in large molecules can trigger conformational changes that play a key role in membrane transport proteins, including ion channels, and probably account for DNA stimulation to initiate protein synthesis (Blank 2008, Ye & Curcuru 2016). He concluded that weak EMFs can control and amplify biological processes.

Liboff (2009) found that changes in human body bioimpedance are significantly altered during exposure to ion cyclotron resonance (ICR) magnetic field combinations. Some of the effects were only found at ultra-low AC magnetic intensities. These findings reinforce the idea that "physical factors acting to influence the electric polarization in living organisms play a key role in biology."

Dendrites in the brain have been reported to be electrically excitable, requiring less stimulation than is normally required for biological changes (Sastre & Kavet 2002). Changes in dendrites in the medial entorhinal cortex (a part of neural network that is closely related to learning and

memory), were identified by Xiong (2013), who felt that these findings may help explain the ELF magnetic field exposure-induced impairment in cognitive functions.

Davanipour & Sobel (2009) reviewed the research into EMF and the risks of Alzheimer's disease and breast cancer. They concluded that long-term significant occupational exposure increased the risk of both and suggested two biological processes that may be responsible; increased production of amyloid beta and decreased production of melatonin, as did Noonan (2002). Del Giudice (2007) found a significant increase of amyloid-beta peptide secretion following overnight exposure to low frequency EMFs.

Contalbrigo (2009) said that exposure to different electromagnetic fields is responsible for the variations of some haematochemical parameters in rats, which could explain some of the variability in experimental findings (Cakir 2009). Magnetoreception may be more common than has been allowed for which could explain some of the variability, too, as in the preceding experiment. Robertson (2010) found changes in brain activity from pulsed EMFs, using functional brain imaging to observe them, and explained them in terms of brain changes involved in the processing of acute thermal pain.

Simkó (2004), in an overview of cellular studies, presents a model describing potential mechanisms for EMF exposure causing cell changes, which could lead to carcinogenesis. Pokorný (2008) suggested that the interaction forces between cancer cells may be smaller than the interaction between healthy cells and cancer cells, and that the "mechanism of malignity, i.e. local invasion, detachment of cancer cells, and metastasis, is assumed to depend on the electromagnetic field" which presumably is open to disruption.

In a study by Zhang (2013), low frequency EMFs significantly enhanced the proliferation of human epidermal stem cells (hESC) in a frequency-dependent manner, with the highest cell proliferation rate at 50 Hz. Razavi (2014) found enhanced proliferation of hADSCs at 50 Hz. Exposure to a low frequency EMF significantly increased the percentage of cells at the S phase of the cell cycle, coupled with a decrease in the percentage of cells in the G1 phase, but the effect was not frequency dependent.

Park (2013) found that neural differentiation of human bone marrow stem cells were induced by EMF through mild generation of ROS.

The effect of EMF exposure on gene induction has been investigated using heat shock proteins, which play a role in cellular signal transduction pathways and are involved in essential cellular functions such as cell proliferation, differentiation and the initiation of apoptosis (Morano & Thiele 1999). Other methods have also demonstrated the potential mechanism by which MF influence cell growth and differentiation (RY Wu 2000). Lin (2001) found that responses to magnetic fields were dependent on particular gene sequences, or cell status (Garip & Akan 2010) and changed when these mutated, and Tokalov & Gutzeit (2004) found that responsiveness was dependent on field strength, with 'windows' of maximum response, or which cells were targeted (Ivancsits 2005). ELF magnetic fields stimulated cell growth under specific conditions of exposure (Belyaev 2011), whilst other studies (Lee 2015) showed decreased cell growth. Lin (1998a, 1998b) suggested that the heat shock factor was activated in exposed cells, and also that there was a increase in c-myc transcripts. Lin said "Because magnetic fields penetrate the cell, they could well react with conducting electrons present in the stacked bases of the DNA," though the response did seem to depend on the presence of elevated protein levels. Strasák (2009) found protein (c-Jun) changes in the brains of mice exposed to magnetic fields. Both protein carbonyl and malondialdehyde levels in rat brains were altered by long-term exposure to either 100 or 500 µT ELF-MF (Akdag 2013). These are very high levels of exposure, and would not be found in places of normal human exposure. Balassa (2013) found changes in synaptic efficacy in the brains of rats exposed to ELF-MFs during pregnancy, or postnatally.

Yang (2008) found genetic markers that showed those carrying this gene variant were four times more likely to develop childhood leukaemia if they also live within 100 metres of powerlines or transformers, compared to those with a fully functioning version of the gene. This groundbreaking piece of research indicates a potential for identifying individual susceptibility.

Cells which clump together take up less oxygen and also raise the risk of thrombosis.

Liboff (2014) offers an explanation for the effect of weak magnetic fields with biological systems. He says "the biological basis is likely to be found in the weak (-50 nT) daily swing in the geomagnetic field that results from the solar tidal force on free electrons in the upper atmosphere, a remarkably constant effect exactly in phase with the solar diurnal change. Because this magnetic change is locked into the solar-derived everyday diurnal response in living things, one can argue that it acts as a surrogate for the solar variation, and therefore plays a role in chronobiological processes. This implies that weak magnetic field interactions may have a chronodisruptive basis, homologous to the more familiar effects on the biological clock arising from sleep deprivation, phase-shift employment and light at night. It is conceivable that the widespread sensitivity of biological systems to weak ELF magnetic fields is vestigially derived from this diurnal geomagnetic effect."

Liboff (2016) also hypothesises "Many reports over the last few decades have provided evidence that living tissue is robustly sensitive to ultrasmall (1–100 nT) ELF magnetic fields overlapping the  $\gamma$ -frequency range often associated with awareness. An example taken from animal behaviour (coherent bird flocking) lends support to the possibility of a disembodied electromagnetic consciousness."

#### Airborne pollutant effects

Airborne pollutant particles are known to have a significant effect on health. The strong electric fields associated with high voltage power lines may affect the charge on the chemicals found in traffic pollution, making them more likely to be absorbed by the body. This effect can be observed up to 7 kilometres downwind of a high voltage powerline (Fews <u>1999a</u>). The older the cable and the wetter the weather the more charged ions are emitted (Fews <u>1999b</u>). These small particles are in the size range where electrical charging can significantly increase lung deposition on inhalation.

#### Other potential synergistic effects

Soffritti (2016) studied groups of male and female Sprague-Dawley rats exposed from prenatal life until natural death to 20 or 1000  $\mu$ T sinusoidal 50Hz magnetic fields and also to 0.1 Gy gamma radiation delivered as a single acute exposure at 6 weeks of age. The results of the study showed significant carcinogenic effects for the mammary gland in males and females and a significant increased incidence of malignant schwannomas of the heart as well as increased incidence of lymphomas/leukaemias in males. The authors felt that the results called for a re-evaluation of the safety of non-ionizing radiation.

Yoon (2014) found that magnetic field exposure and gamma radiation could act synergistically to damage DNA in human lung fibroblasts and human lung epithelial cells.

Lead contamination in the presence of an EMF exacerbates the oxidative damage to plasma proteins which could be a health problem for workers in industrial fields, battery manufacturing companies, and power plants (Ansarihadipour & Bayatiani <u>2016</u>). Hassan & Abdelkawi (<u>2014</u>) suggested that the combination of cadmium and magnetic field exposure could increase the risk of plasma damage in rats via oxidative stress.

Low magnetic fields could enhance the process of mutation in human lymphocytes caused by benzo(a)pyrene rather than initiating mutations itself (YH Cho & HW Chung <u>2003</u>).

Soffritti (2016b) also concluded that there might be a synergy between life-span exposure of rats to a 50 hz magnetic field and formaldehyde in terms of carcinogenicity.

ZY Zhang (2016) investigated the effect of ELF-EMFs on flies which were also exposed to stressinducing temperatures of 25°C and 35°C and found that dual exposure accelerated the death rates of CS and w1118 flies, shortened their lifespan, and influenced their locomotion rhythm and activity.

Belova & Acosta-Avalos (2015) reviewed animal magnetoreception and the effects of alternating magnetic fields in living beings. It is suggested how alternating magnetic fields can interfere in the magnetic alignment of animals and a general conclusion is obtained: alternating magnetic field pollution can affect the magnetic sensibility of animals.

The results of a study By Osipova (2016) showed that geomagnetic field and its variations should be taken into account when interpreting the zebrafish's directional preferences and locomotor activity in mazes and other experimental devices.

A study by Vanderstraeten & Gillis (2010) found that magnetic fields over 0.5 microtesla combined with the geomagnetic field to exceed the threshold of magnetoreception in migrating animals. As humans also have magnetite in their cells, this may explain one of the more subtle cellular processes (Kirschvink 2001). It has also been found that the human flavoprotein crytochrome, CRY2, has the molecular capability to function as a light-sensitive magnetosensor (Foley 2011).

Hajnorouzi (2011) found that an appropriate combination of a geomagnetic field and an alternative magnetic field resulted in the promotion of maize seedling growth by an alleviation of an excess production of reactive oxygen species.

Wu & Dickman (2012) spotted a group of 53 cells in pigeons' brains that respond to the direction and strength of the Earth's magnetic field. Each cell also showed a sensitivity to field strength, with the maximum sensitivity corresponding to the strength of the Earth's natural field. Where these cells are is a bit of a mystery. Ideas have included:- in their noses or beaks, in an inner ear organ, or even the compass cells in pigeon beaks are a type of white blood cell. As with most life processes, the answer may be complex, and more than one mechanism may be at work in bird navigation.

Pica (2006) found that changes in viruses exposed to EMFs occurred only when they were stimulated with TPA.

Although individual chemicals are typically present at low concentrations, they can interact with each other resulting in additive or potentially synergistic mixture effects, such as benzpyrene (. Radiation actions such as electromagnetic fields can change the effects of chemicals, such as pesticides, and metal trace elements on health (Ledoigt <u>2015</u>).