Research Article

Open Access
CrossMark

Evaluation of the effects of using low-frequency stimulation (ELF) in the biophysical and immune context

Abstract

Electronic bioregulation techniques are mainly of German origin. The fields of biophysics are increasingly advanced in studies of low-frequency electrostimulation in the spectrum of non-ionizing radiation, which is represented by frequencies lower than 3 × 10^15 Hz. The work carried out with cells uses the spectrum between 3 Hz and 10^3 kHz, that is, extremely low frequencies. However, when evaluating the devices sold, each company adopts a range of electromagnetic spectrum, according to its studies and objectives, and what they have in common would be biological work with very low non-ionizing radiation. Most devices have the function of tissue regeneration and neuromodulation with fixed frequencies. The objective of the manuscript to evaluate the effects of the use of Low-Frequency Electro Stimulation (ELF) in the physical and biophysical context in the areas of application of its application and the context of the immune response. Systematized bibliographic study, of the descriptive and exploratory type, on ELF. The bibliographic search included the LILACS databases (Latin American and Caribbean Literature in Health Sciences) at the address: http://www.bireme.br/, electronic journals available in the SciELO database, and dissertations and theses available in the Library of the University of São Paulo at the address: http://www.usp.br/.

Keywords: biophysics, interleukins, b lymphocytes, t lymphocytes, nk cells

Volume 10 Issue 3 - 2025

Klebert de Paula Malheiros,[1,2] Fernanda de Oliveira Feitosa de Castro,[1] Valéria Bernadete Leite Quixabeira,[1] Hermínio Maurício da Rocha Sobrinho,[1] Irmtraut Araci Hoffmann Pfrimer,[1] Carlos Henrique Marchiori[2]

[1]Pontifícia Universidade Católica de Goiás, Brazil
[2]Teachers and Researchers of the Institute Marco Santana, Brazil

Correspondence: Carlos Henrique Marchiori, Instituto Marcos Santana, Goiânia, Goias, Brazil, Tel +55 62 99105-9988

Received: August 13, 2025 | **Published:** September 02, 2025

Introduction

Low-frequency electro stimulation (ELF) concept

Low-Frequency Electrical Stimulation (LFS) is unique to living organisms and has specific wavelengths. Therefore, an ionized or electrical signal is much more than just a new type of tool. On the contrary, it may represent an entirely new way of clinical management, both for diagnosis and treatment. LFS has broad and indisputable effects on cellular characteristics, causing changes in membrane permeability, cell proliferation, membrane chromatin conformation, and compaction, and raising the hypothesis that endogenous microtubular signals function as a resonance modulator to maintain cellular osmotic balance (Figure 1)[1-3]

Figure 1 Functional low-frequency electrical stimulation (ELF).

This led to the development of a new concept called "bionomics," also known as cellular sound, where an excess or deficiency of a single biological cation can selectively increase the frequencies of cyclic resonant fields and trigger cellular changes. ELF techniques use low frequencies at points of lower electrical resistance in the human body, specifically at acupoints. These were studied by German biophysics professor Fritz-Albert Popp. He was the first to show that the low-frequency electromagnetic vibrations emitted by the human body could be explained by the biophoton theory. In explaining biophotons, he stated that living beings emit electrical vibrations at very low frequencies and that these vibrations photons act as high-level control mechanisms for living beings. This method of therapy was called bioresonance.[2-5]

In 1980, the Graduate School of Biological Sciences and the School of Medicine at Mount Sinai University in the United States made references to these biophotons. According to Oster and Jaffe (1980), audible low-frequency vibrations are produced by human skeletal muscles undergoing sustained contraction. The effect is easily demonstrable with an electronic stethoscope that amplifies the sound below 50 Hz. Autocorrelation analysis of the signal shows that it is periodic with a frequency of 25 to ± 2.5 Hz.[1,3,4]

Due to the advancement of the field, the main event on bio electromagnetism was created in the international context with a series of conferences, the International Conference on Biomagnetism (BIOMAG), which began in 1976 in the city of Cambridge, Massachusetts, in the United States of America. In this first edition, the number of participants was 23 individuals. Currently, BIOMAG is a series of biannual conferences that have been held in several countries, including the United States, Japan, Germany, Austria, Finland, and Canada, among others. Contrary to the small number of participants in the first event, BIOMAG 2004 (Boston, USA) had the participation of more than 600 representatives from more than 15 countries, and more recently, the 17th edition held in 2010 in the city of Dubrovnik, Croatia, had the contribution of 416 authors from 22 countries (Figure 2).[3,4,6]

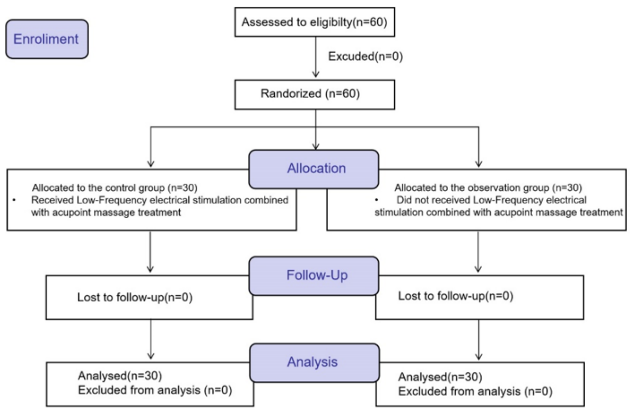

Figure 2 Patient flow diagram.

ELF is based on the concept of non-ionizing radiation. The action of the non-ionizing radiation spectrum can be subdivided into three broad categories: Optical, radiofrequency, and electrical. optical is the energy associated with light, infrared, and ultraviolet. Radiofrequency is radio waves, which range from 10KHz to 300GHz and electrical is that in which energy is usually transmitted by wires or cables with a frequency of 50 to 60Hz with an upper limit of 20KHz. The action of the low-frequency electric field is a spectrum of radiation that is incapable of producing ionization, that is, it does not have enough energy to remove electrons from atoms. When talking about biological stimuli for cellular balance, the use of extremely low non-ionizing frequencies is observed, starting with 3 Hz until the lower limit in kHz.[7-9]

EMFs are widespread in the environment, especially at extremely low frequencies ELF 30 to 300Hz, where they are emitted by electrical appliances and overhead power lines. The effects of EMF exposure on humans are considerable, as there is potential for negative health effects from high levels of exposure. For this reason, the European Union suggests an occupational exposure level of 1mT (Directive 2013/35/EU) to reduce the potential for harm. Insects, birds, butterflies, ants, flies, bees, and cockroaches have been shown to have a "magnetic" sense and are able to detect very low levels of static magnetic fields and use them to drive oriented movements.

There is also evidence of different mechanisms of magnetoreception by organisms that respond to these low-level static magnetic fields in the environment, including direct detection through deposits of ferromagnetic crystals, or through cryptochrome molecules.[7-9]

Certain electromagnetic frequencies must be used with caution and can interact with molecules present in living organisms, through a phenomenon called resonance. The oscillation of the electromagnetic wave and its effect depend on its intensity, and can result in burns, modification of the molecular structure or simply heating. It is also observed that low-frequency magnetic fields induce circulating currents within the human body, and the intensity of these induced currents depends on the intensity of the external magnetic fields and the path through which the current flows, as well as the exposure time.[7-9]

ELF fields pass through the body, while high-frequency fields are partially absorbed and penetrate the body. Medicine has been using high-frequency fields in a controlled and targeted manner for diagnostic testing and treatments. The effects of electrical stimulation on cell alignment and migration have as underlying mechanisms the action of voltage-dependent ion channels of G-protein coupling receptors, integrins, cell polarization, and endogenous electric fields. The physical method has attracted much attention since it can activate specific signaling pathways in cells near the cathode or anode and induce cell migration and alignment.[7]

Low- and high-frequency electric fields can act to activate multiple cellular signaling pathways, such as PI3K/PTEN, the KCNJ15/Kir4.2 membrane channel, and intracellular polyamines. These pathways are involved in the detection of physiological electric fields, directional cell migration (galvanotaxis, also known as electrotaxis), and possibly other cellular responses. Asymmetric ionic fluxes of mobile charged ions generate the endogenous electric potential. Na+, Cl−, K+, and Ca 2+ are the main components of endogenous electric currents.[10,11]

Biomagnetism and the measurement of magnetic signals are associated with a specific physiological activity that is usually linked to an accompanying electric field in a specific tissue or organ. Biomagnetism has played an increasingly important role in medicine since 1936, when Linus Pauling and Charles Coyer published two studies related to the effect of magnetism on hemoglobin and its derivatives. The magnetic properties of biological substances have been increasingly investigated. For example, the magnetic susceptibilities of cellular contents are represented by water, lipids, and proteins. Tao et al.[11] examined the susceptibility in human nasopharyngeal carcinoma CNE-2Z cells. Another study demonstrated paramagnetic increases at low temperatures, indicating the presence of paramagnetic components in CNE-2Z cells.[11,12]

Ultra-low magnetic fields of 50µT to strong artificial magnetic fields (>1T) can affect biochemical reactions by influencing the spin of particles. This can affect biological metabolism, including diffusion processes, chemical reactions, and complex interactions between the electronic and nuclear spins of reagents. Furthermore, audible sound waves through the property of bioresonance can produce sound waves between 46 and 3333.33Hz. These sound vibrations can be modulated or not with ON-OFF cycles. The emitter 19 of the equipment requires gel as a coupling substance. The sound wave is captured by amino acids and proteins and causes these elements to oscillate, mobilizing them from the interstitial medium to the lymphatic, facilitating their absorption. Following these principles, the molecules formed by amino acids and proteins in the lymph move through harmonics generated by the acoustic wave system, which begin to oscillate until they disintegrate, leaving the extracellular space and migrating through lymphatic pathways to the kidney. This entire process was demonstrated by lymphoscintigraphy (Figure 3).[12-14]

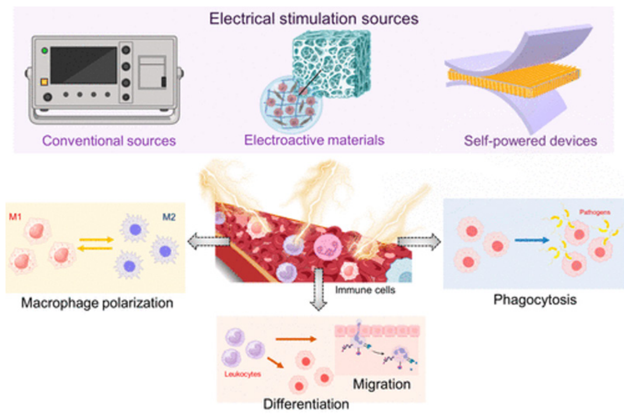

Figure 3 Schematic representation of different electrical stimulation strategies employed for immunomodulation and how they might affect the processes of immune cells.

Citation: Malheiros KP, Castro FOF, Quixabeira VBL, et al. Evaluation of the effects of using low-frequency stimulation (ELF) in the biophysical and immune context. *MOJ Biol Med.* 2025;10(3):126‒133. DOI: 10.15406/mojbm.2025.10.00253

Extremely Low-Frequency Electromagnetic Field (ELF-EMF) stimulation readily interacts with the Central Nervous System (CNS). Although high-frequency EMFs found in industries may expose workers to increased risk, they can also induce amyotrophic lateral sclerosis and multiple sclerosis. Increased intracellular Ca2+ is one of the immediate effects of ELF on cellular response. Calcium ions are important cellular mediators that play a role in many important life activities such as proliferation, differentiation, and apoptosis.[13,15,16]

At the cellular level, when external electric fields are applied, increases in the circulation and migration of epithelial cells, neutrophils, macrophages, and various growth factors have been found, as well as an increase in the production of fibroblasts, collagenase levels, and a reduction in edema, inhibiting the emergence of mast cells and bacteria. However, within the *in vitro* and *in vivo* experimental studies related to stimulation by electric fields, the literature continues to report more and more applications in different diseases.[13,15,16]

It has been hypothesized that the increased production of free radicals caused by EMFs may be associated with Fenton reactions. This phenomenon was discovered by Henry John Horstman Fenton in 1894 and is directly related to unbound iron within cells. According to classical theory, iron ions can catalyze the decomposition of hydrogen peroxide with the generation of hydroxyl radicals. It has been identified that EMF 60 Hz affects the expression of human transferrin receptors, which play a crucial role in iron homeostasis in the body. In addition to transferrin, other metal proteins (cytochromes) and metal enzymes (catalases) may be a subject of interest for future electromagnetic applications.[16,17]

Objective

The objective of the manuscript to evaluate the effects of the use of low-frequency stimulation (ELF) in the physical and biophysical context in the areas of application of its application and the context of the immune response.

Methods

Systematized bibliographic study, of the descriptive and exploratory type, on Low-Frequency Electro Stimulation (ELF). The bibliographic search included the LILACS databases (Latin American and Caribbean Literature in Health Sciences) at the address: http://www.bireme.br/, electronic journals available in the SciELO database, and dissertations and theses available in the Library of the University of São Paulo at the address: http://www.usp.br/

Selected studies

ELF application areas

In a review study, a total of 48 studies were evaluated, using different Magnetic Fields (ELF) modalities, including direct current, alternating current, low-intensity direct current, and electrical stimulation by electro biofeedback. All electrical stimulation modalities demonstrated positive effects on the healing of skin wounds due to different causes.[18]

Regarding pain, studies have shown that transcutaneous electrical nerve stimulation is a non-invasive therapeutic resource, based on the delivery of low-frequency electrical current over the skin through surface electrodes. Its effect is due to the stimulation of sensory nerve fibers, which modulate the process of neuro-conduction of pain and the increase in the release of endogenous opioids at the medullary and pituitary levels. The use of ELF in 935 patients with arthrosis, polymyalgia rheumatica, and postoperative neuralgia who presented with gait dysfunctions. The researchers demonstrated that there was an improvement in the gait alteration index (GDI) of 72.4% in the ELF group.[3,18]

The Bio-Electro-Magnetic-Energy Regulation (BEMER) is a device that uses a low-frequency pulsed magnetic field of 35ÿT with a series of sinusoidal intensity variations in the form of a half-wave. This BEMER system has been shown to address imbalances related to the circulatory system, such as vasomotion and microcirculation, to improve blood flow to organs and facilitate the supply of nutrients and removal of metabolites. Cystinosis is an autosomal recessive hereditary disease that causes dysfunction in multiple organs. The application of the low-frequency modulation device bio-resonance-bicom for treating childhood nephropathic cystinosis, administered weekly over four years, stopped the formation of kidney stones and allowed the left kidney, which had largely lost its filtering ability, to recover its functions. In allergy treatment, the scanning frequencies, certified by the European Community, range from 1Hz to 800kHz. Modified (inverted) electromagnetic vibrations of the allergens are transmitted to the body, which is placed in a container connected to the device (Figure 4).[18-20]

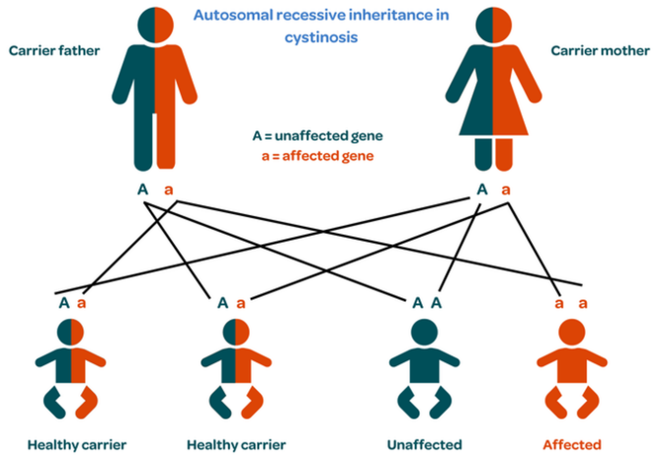

Figure 4 Autosomal recessive inheritance in cystinosis.

It has been found that ELF induces the attraction of cancer cells due to electrolyte imbalance. Thus, in a study, it was observed that through a low-frequency electric field, it is possible to distinguish the surface charge of cancer cells that are more negative compared to normal cells. In a retrospective study, from 2017 to 2018, using bioresonance, in selected patients at the Psychiatric Clinic of the Mureÿ County Clinical Hospital in Târgu Mureÿ, they were subjected to frequencies from 0.1Hz to 480,000Hz, and a frequency filter from 1Hz to 500,000Hz. After the application of low frequency, there was a significant reduction in depression levels according to the HAM-D 17 scale, Hamilton Depression Rating Scale, between the first evaluation and after the fifth bioresonance therapy session.[20-22]

Patients suffering from illnesses across the internal-orthopedic-neurological spectrum, as well as particularly in the areas of allergies, pain, and infections, can also benefit from ELF. ELF therapy showed high practical-therapeutic efficacy. The exact mode of biophysical and physiological functioning has not yet been physiologically well clarified.[23]

A randomized, blinded, crossover study with two treatment phases separated by a one-month washout period compared the efficacy of low-frequency, low-intensity electrotherapy and manual lymphatic drainage in the treatment of chronic lymphedema related to upper limb breast cancer. Treatment was performed using a carrier frequency wave ranging from 0.31 to 6.16 Hz and a modulation between 400 and 120 Hz; the low displacement voltage is always between +12 and 12 V. Although the benefits of low-frequency, low-intensity electrotherapy on most symptoms and health-related quality of life were statistically significant, they were not significantly different from those of manual lymphatic drainage. Thirty patients completed treatment. However, low-intensity ELF did not reduce lymphedema volume (mean change = 19.77 mL, p=0.36). However, significant reductions in pain and weight were observed, and a trend toward improved health-related quality of life is notable with low-frequency, low-intensity electrotherapy.[20,21,24]

In Turkey, 44% of adults are smokers, which can result in lung cancer, chronic bronchitis, and emphysema, which is the most common cause of death in adults over 35 years of age. Therefore, a study was developed at the Istanbul Medical School together with the Institute of Biophysics in Germany, a study using ELF for drug addicts. The frequencies with the success rate of electro versus conventional treatments were then applied. In the 1st week (success rate 77.2% vs. 54.8%), 2nd week (62.4% vs. 34.4%), 1 month (51.1% vs. 28.6%), and 1 year (28.6% vs. 16.1%) after treatments. A study carried out on an individual with a corneal ulcer, until previously considered untreatable, was treated with a low-frequency electromagnetic field for 1 year.[23-25]

The patient was regularly using sodium chloride and tetracycline eye drops, and the wound was burned five times with laser surgery due to a lack of healing. After a year of electrotherapy, the ophthalmologist's final report stated that the lens dressing was removed, and the ulcer was stable without any fluid. After treatment, the patient no longer wore contact lenses and did not experience severe pain or sensitivity to light. However, although promising, the success of a single case report is limited, and it is essential to confirm this with further research.[24,26]

Sixteen human cell lines, 17 dipteran eggs and 18 planarians were exposed to field conditions at ELF levels below 0.1 mT, which led to increased levels of HSP70 during a single exposure, while in chicken embryos repeated exposure led to a reduction in HSP70, which is the expression of the stress-related chaperone protein. Cryoprotection had an elevating effect on the expression of HSP70 levels. Above 1 mT the effects were limited for in vitro cellular systems, but in some experiments, they were effective, with an increase in HSP70 transcription leading to protection from chronic hypoxia and expression of Ca2+ channels in neuronal synapses, improving neuronal activity.[7,24,26]

Cardiac stem cells expanded *ex vivo* are susceptible to exposure to 7-Hz sonic stimulators and likely express a modulation of myogenic versus angiogenic differentiation. This may provide fertile ground for further investigations into tissue engineering and cell therapies in the future. Cytosolic calcium (nuclear calcium) has long been understood as an influencer in the regulation of cellular and molecular interactions and has been identified in this process. Molecular factors related to Ca2+ oscillations provide molecular signals that influence cellular behavior, including differentiation and proliferation (Figure 5).[2,7,26,27]

ELF may enhance axon regeneration after peripheral nerve injury in animal models and humans. One-hour, 20-Hz stimulation has been applied to injury sites in humans and rats (following chronic axotomy and/or chronic denervation). Indeed, ELF was found to be very effective in promoting the growth of motor and sensory neuron axons. The efficacy of a 1-hour, 20-Hz electrical stimulation regimen has also been demonstrated in patients undergoing carpal tunnel release surgery to promote regeneration of injured median nerves that were severed by ligament constriction at the wrist. The most important point of this study is that there was a similar rate of axon regeneration in both humans and animals.[2,26,28]

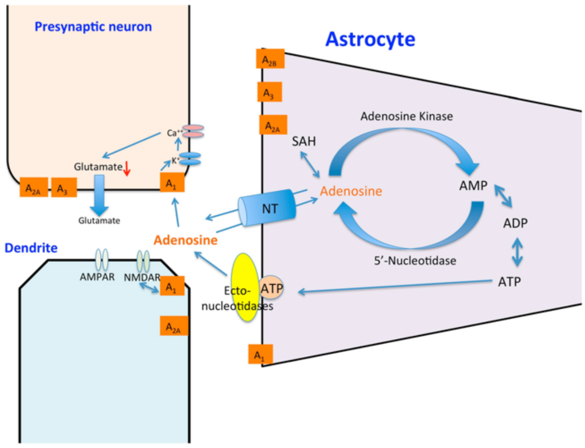

Figure 5 The effects of hypoxia on adenosine release in the Central Nervous System (CNS). Hypoxia causes a breakdown of extracellular ATP and AMP along with activation of membrane-bound transporters such as ectonucleotidases, leading to a build-up of extracellular adenosine. Adenosine binds presynaptically to A_1Rs, attenuating Voltage-Dependent Calcium Channel (VDCC) function and thus neurotransmitter release, and also binds postsynaptically to A_1Rs receptors, Inactivating Glutamatergic (NMDARs). Adenosine is released from astrocytes in response to chronic hypoxia.

Human chromatin can change with ELF exposure *in vivo*, and it has been shown that exposure of human cells to ELFs has pronounced effects on chromatin conformation. Lymphocytes were exposed to ELF at predefined amplitudes of 50 Hz with peaks in the range of 5 to 2 mT for 15 to 180 min. The exposure system consisted of two pairs of Helmholtz coils, one horizontal and one vertical, which produced relatively homogeneous magnetic fields. It was shown that chromatin conformation depends on the concentration of Na+, Cu2+, Ca2+, Mg2+, and Zn2+ ions. Na+ ions resulted in chromatin relaxation, and Mg2+ ions resulted in chromatin condensation in V-79 cells. Almost all proteins involved in various enzymatic reactions at the DNA level, such as replication, recombination, transcription, and repair, contain divalent ions in their active site.[26,28,29]

Acute exposure of Human Adipose Tissue-Derived Stem Cells (hASCs) to low-frequency 1Hz sinusoidal Alternating Current (AC) electric fields induced an increase in cytoplasmic calcium in response to the magnitude of the electric field, as observed by fluorescence microscopy. Based on observations that electrocorticography synchronization closely follows the level of brain excitability, the effects of low-frequency 1Hz intracranial brain stimulation on cortical phase synchronization levels before, during, and after 1Hz electrical stimulation were evaluated in twelve patients. This effect persisted for at least 30 minutes after stimulation. Overall, these findings demonstrate that ELF reduces phase synchronization and thus cortical excitability in the human brain. ELF could therefore contribute to the prevention of impending epileptic seizures.[28-30]

Biomagnetic fluid is an electrically conductive magnetic fluid with the capacity for magnetization. Blood is a biomagnetic fluid that exhibits such properties. Voltages and currents generated by conductive fluids in the presence of a magnetic field can result in reduced flow rates. Changes in the electrical conductivity of blood due to blood flow have been examined in several studies. And that iron oxide in the form of hemoglobin in the blood reacts with magnetic fields.[12,31]

Other studies suggest that electrical stimulation increases cell proliferation, production of extracellular matrix, secretion of various cytokines, tissue regeneration in multiple tissues, and may also increase the proliferation of immune cells and vascular development. Several types of cells align perpendicularly and parallel to the direction of the electric field vector. The current causes a flood of ions through ion channels and transporters (Na +, Cl -, K+ +, Ca 2+). In response to the electrical stimulus, intracellular molecular polarization and polarization of the transport channel occur, then the flow of ions and changes in the cytoskeleton cause persistent cell migration to the cathode.[30-32]

Many cell types can respond to electrical stimuli with cellular actions such as proliferation, morphological changes, and growth factor release. Specifically, neuronal growth increases and Schwann cells, the glia of the peripheral nervous system, increase nerve growth factor over 3 days in response to a single electrical stimulus of 50 mV/mm DC. Electrical stimuli have been used successfully in human nerve crush injuries and with some limited success in rat models. The application of electrical stimuli *in vivo* impacts not only the glia and neurons but also the site of injury, impacting all resident cells, including immune cells. Macrophages are rapidly recruited after injury and assume much of the responsibility for inflammation at the wound site (Figure 6).[29-34]

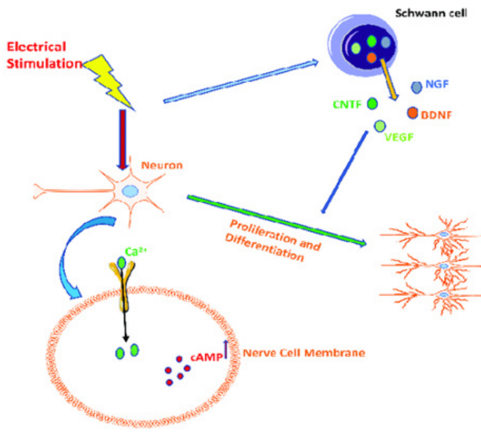

Figure 6 The effect of electrical stimulation on neurons. Electrical stimulation increased the secretion levels of Nerve Growth Factor (NGF), Brain-Derived Neurotrophic Factor (BDNF), Ciliary Neurotrophic Factor (CNTF), and Vascular Endothelial Growth Factor (VEGF) in Schwann cells, enhancing the activity of Ca 2+ channels in nerve cell membranes, which in turn activated related effector proteins and increased cAMP levels, ultimately promoting neuronal proliferation and differentiation.

AC electric fields with capacitive characteristics were used to modulate macrophage phenotypes in a self-designed system. Cells grown in Petri dishes were placed between two parallel electrodes connected to the oscilloscope power supply to generate homogeneous electric fields between the electrodes. The frequency of the electric field was adjusted employing a DC direct current module using batteries; and AC alternating current – transmission lines (AC/DC). Interestingly, it was observed that the frequencies of the applied electric fields significantly influenced the polarization of macrophages from M1 to M2, with 10 and 60Hz increasing the expression of CD206 markers that validated the polarization.[30,32,33,35]

According to Zhong et al.[33] there is evidence indicating that electrical or electromagnetic stimuli increase the proportion of cells in specific phases of the proliferative cycle. Thus, it was reported that a 50Hz and 0.5mT field induces proliferation in human Bone Marrow-Derived Stem Cells (BMSC) from mice, increasing the proportion of cells that enter the S and G2 phases of the cycle. In recent years, Extremely Low Frequency Electromagnetic Fields (EMF-ELF) therapy has gained significant interest due to its potential protective impact on cardiovascular functions. A controlled pilot trial in healthy adults showed that a 50Hz magnetic field had therapeutic effects in stimulating parasympathetic activity, resulting in increased vasodilation and blood flow through a nitric oxide-dependent mechanism.[33,35,36]

Oxidative stress can be modulated by ELF-EMF, which significantly improved the functional and mental state of patients with a 7mT field at 40Hz. In a follow-up study in post-stroke patients, they found that exposure to ELF-EMF led to a significant elevation in the levels of growth factors and cytokines associated with neuroplasticity and facilitated a remarkable improvement in functional recovery. However, the wide range of possibilities in terms of frequencies, magnitudes, stimulation times, population differences, among others, continues to make it difficult to create standards that differentiate their application in pathological processes.[35]

ELF versus immune response

The immune system is made up of an intricate network of organs, cells, and molecules, and its purpose is to maintain the body's homeostasis. Innate immunity works in conjunction with adaptive immunity and is characterized by a rapid response to aggression, regardless of prior stimulus, and is the body's first line of defense. Pluripotent stem cells in the bone marrow give rise to myeloid and lymphoid progenitor cells. Lymphoid progenitors, in turn, give rise to T lymphocytes, B lymphocytes, and NK cells. Monocytes are a subtype of leukocytes that can differentiate into macrophages and dendritic cells. Their population is heterogeneous and the subpopulations of these cells are divided according to the expression profile of membrane receptors. There is great interest in science today in studying the reactions of the immune system to the action of low-frequency electromagnetic fields (Figure 7).[1,37-39]

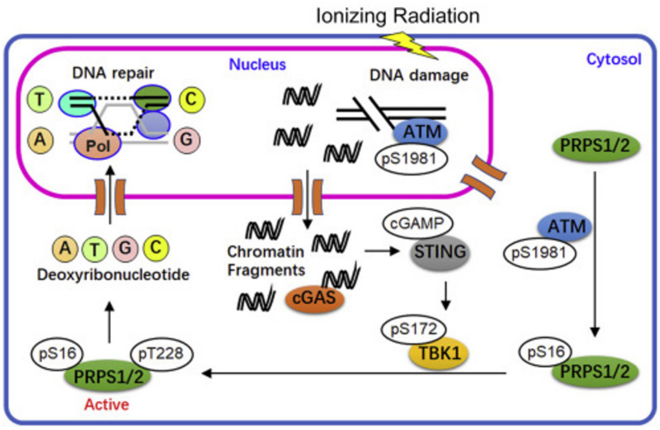

Figure 7 Model of innate immune machinery-mediated PRPS1/2 activation and deoxyribonucleotide synthesis in response to ionizing radiation. Ionizing radiation-induced DNA fragments activate the GAS/STING/TBK1 axis, leading to phosphorylation of PRPS1/2 T228, which is dependent on ATM-mediated PRPS1. /2 S16 phosphorylation. T228-phosphorylated PRPS1/2 enhances deoxyribonucleotide synthesis, which facilitates DNA repair.

The ELF stimuli were observed in this study by using membrane markers, where cells can detect what is happening around them and can respond in real-time to signals sent from their neighbors and the external environment. This type of signaling is especially important in the immune system, where immune cells use cell surface markers

Citation: Malheiros KP, Castro FOF, Quixabeira VBL, et al. Evaluation of the effects of using low-frequency stimulation (ELF) in the biophysical and immune context. *MOJ Biol Med.* 2025;10(3):126–133. DOI: 10.15406/mojbm.2025.10.00253

to recognize "self" cells (the body's cells) and cells infected by pathogens.[1,37,38]

However, other avenues of studies regarding the action of ELF concerning the immune system have been developed, among them, a study is reported in which a single uninterrupted 24-hour exposure to 50Hz, 7mT of ELF-EMF in human cells, resulted in notable elevations in the plasma levels of the agents mediating the immune responses of interleukins IL-1β, IL-6 and IL-2, as well as an increase in blood parameters, such as white blood cells, lymphocytes, hemoglobin and hematocrit levels.[37,38]

Macrophages can also be polarized to the M2 phenotype when subjected to an electric field of 12.7–30.5 V/s from a conventional DC source for 2 h with glass microelectrodes. A gradual increase in intracellular Ca 2+ was observed after 2 min of low-intensity electrical stimulation, promoting repetitive Ca2+ -dependent spikes that were related to M2 polarization.[40]

Human T cells can also migrate toward the cathode under directional electric fields. The applied electric field increased T cell migration by 3-fold at 50 mV/mm, which further increased to 6-fold at 150 mV/mm. These findings suggest that the electric field may help position T cells at wound sites where the epithelium is damaged in order to aid in the healing process. Furthermore, macrophage viability decreased with increasing frequency, with the highest viability at 10 Hz, while macrophage viability decreased at 110 Hz, indicating that the electric field frequency is an important parameter governing immune cell differentiation. Studies have further demonstrated that immune cells, including macrophages, T cells, and B cells, are electrically excitable due to the presence of specific ion channels that tune their membrane potentials in the presence of endogenous and exogenous electric fields.[38,40]

Studies were also conducted with BALB/c mice bearing MC-4L2 tumors that were exposed to a 100mT 10Hz ELF-EMF for 2 hours daily for 28 days. The research revealed a significant increase in pro-inflammatory reactions together with inhibition of tumor growth and also verified through in vitro experiments that the phenomenon was partially caused by the accumulation of oxidative stress and necroptosis induced by Ca2+ overload.[41]

Another study reported that exposure of mouse macrophages to 1.0 mT EMF showed a significant increase in the extracellular release of IL-1beta, which increased continuously after 12 to 24 hours of exposure. These data suggest that EMF stimulation is capable of increasing cytokines in macrophages and beyond these results. It is important to reiterate the importance of the fact that the cellular effects of ELF-EMFs depend largely on their intensity and time of exposure, as well as on the cellular phenotype and interactions with intracellular structures.[15,41]

Human monocyte-derived macrophages and neutrophils were isolated from the blood of healthy adult donors. Using live-cell video microscopy, it was shown that macrophage migration is driven anodically by low electric fields of 5 mV/mm and depends on the electric field strength, with peak effects at 300 mV/mm. Monocytes, as precursors of macrophages, migrate in the opposite, cathodic direction. Surprisingly, for the first time, it was reported that electric fields significantly enhance the phagocytic uptake of macrophages, including carboxylate spheres, apoptotic neutrophils, and the opportunistic pathogen *Candida albicans*, involving different classes of surface receptors.[15,41]

A study also using electrotherapy with 0.6 and 1.0 mA in immunocompetent mice produced a significant delay in tumor growth compared to immunodeficient mice, demonstrating that the immune system is an important component that aids in the effectiveness of electrotherapy. Results showed that the number of T lymphocytes measured in the spleen increased. CD3 + CD4 + T cells and CD3 + CD8 T cells demonstrated an increase, while regulatory T cells (which regulate and suppress other cells of the immune system) decreased. In addition, the levels of cytokines TNF-α and IL-2 increased, and the level of IL-10 decreased. Using a device called NPS (30kV/cm, 100Hz, 200p) in a mouse model of malignant melanoma.[15,41,42]

Most cancer patients have an immune system that is unable to recognize and target cancer cells. Immunotherapy is becoming a very common treatment for cancer, using approaches such as checkpoint inhibition, T-cell transfer therapy, monoclonal antibodies, and cancer vaccination. A promising approach to reduce the dose of immunotherapeutic agents administered to cancer patients and simultaneously with ELF, can act by modulating the immune system. Nanopulsed electrical stimulations are used to activate the immune system and direct it against tumor cells and these approaches have been used for different types of cancer, such as fibrosarcoma, hepatocellular carcinoma, human papillomavirus, etc. Another common approach is to combine electrochemotherapy with immune modulation, either by inducing immunogenic cell death or by injecting immunostimulants that increase the efficacy of treatments (Figure 8).[15,41-44]

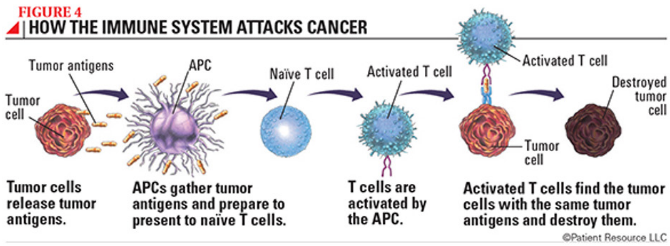

Figure 8 The DNA changes that cause the cancer may be different enough to stimulate an immune response similar to the response described for invading virus cells. If the immune system detects the cancer, the APCs must share the information with the T cells, which are the primary players in the fight against cancer.

ELF has demonstrated anti-inflammatory properties through its *in vivo* application, which by stimulating the vagus nerve, promotes a modulation in the immune system and may thus delay tumorigenesis, suggesting that it could potentially contribute to cancer treatments in the future. Electrical stimulation of the vagus nerve can trigger the production and activation of anti-tumor immune cells and immunological responses. Vagus nerve stimulation is successful in studies performed in cardiac tissue, the circulatory system, the nervous system, and the digestive system. The vagus nerve detects peripheral inflammation and generates action potentials through vagal efferents, resulting in an inhibition of increasing levels of pro-inflammatory cytokines (Figure 9).[41-44]

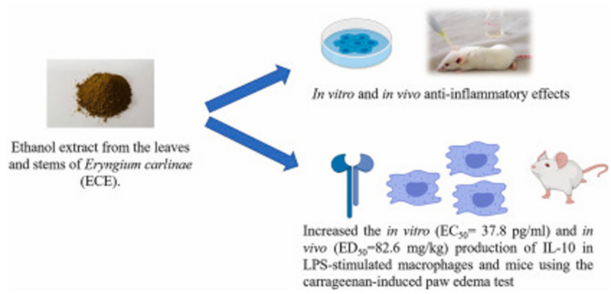

Figure 9 ECE exerts *in vitro* and *in vivo* anti-inflammatory effects by increasing the release of IL-10.

Exposure of human peripheral blood mononuclear cells to extremely low-frequency Pulsed Electromagnetic Fields (PEMFs) increased both spontaneous and induced production of interleukin-1 (IL-1) and IL-6. Our results suggest that monocytic cells, which are good producers of both IL-1 and IL-6, could be important cellular targets for PEMFs. Given that these cytokines are among the most pleiotropic, these data may help to understand the previously reported effects of PEMFs on human lymphocyte proliferation and the effects of such fields on cartilage and bone cells, whose physiological activities are highly dependent on IL-1 and IL-6. This indicates robust mitogenic responses in human lymphocytes to low-frequency electromagnetic fields. The effects of low-frequency magnetic fields on both B and T lymphocytes are noteworthy. In some cases, with remarkably weak magnetism and field intensities, this alone provides sufficient reason to believe that there may be an electromagnetic component to the immune response.[41,44,45]

Conclusion

Electrical states in the brain can be altered by light and electromagnetic fields EMFs with frequencies in the range of 1–20 Hz. The absorption of electromagnetic waves by the human body varies according to tissue characteristics, exposure time, field strength, and tissue composition. The organism's sensitivity to external low-frequency oscillations is associated with specific evolutionary detection mechanisms developed to derive valuable biological information from the Earth's normal magnetic field or to compensate for the effects of geological and meteorological EMFs. These EMFs are subject to some amplification in the organism and have been shown to affect different physiological systems.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Mesquita Júnior D, Silva WN, Moraes-Fontes MF, et al. Immune system - part II: fundamentals of the immune response mediated by T and B lymphocytes. *Braz J Rheumatol*. 2010;50(5):552–580.
2. Venter RL. Environmental energy for cellular growth and repair, especially by bio-resonance focused ultrasound: a literature review. *Indo Am J Pharm Sci*. 2021;8(4):59–64.
3. Teker A, Işik ES. Rezonans therapy bioresonance. *Anatol Med J*. 2022;1(2):1–12.
4. Oster G, Jaffe JS. Low-frequency sounds from sustained contraction of human skeletal muscle. *Biophys J*. 1980;30(1):119–127.
5. Zou X, Cai M. Effect of low-frequency electrical stimulation combined with abdominal acupoint massage on postoperative gastrointestinal function recovery after cesarean section: a prospective randomized study. *Clin Exp Obstet Gynecol*. 2024;51(7):164.
6. Silva SL, Silva LB. *Non-ionizing Radiation and Workplace Environments*. João Pessoa: Editora UFPB; 2020.
7. Wyszkowska J, Shepherd S, Sharkh S, et al. Exposure to extremely low-frequency electromagnetic fields alters the behavior, physiology, and stress protein levels of desert locusts. *Sci Rep.* 2016;6:e36413.
8. Silva C, Ribeiro S, Gonçalves D, et al. Electrical stimulation as a novel tool for regulating cell behavior in tissue engineering. *Biomater Res*. 2019;23(25):1–12.
9. Andrade LP, Marinho R, Souza AP, et al. Brazilian state-of-the-art on the effects of non-ionizing radiation on human health. *Braz J Dev*. 2021;7(8):80876–80893.
10. Guangping T, Michael T, Min Z. Electrically stimulated cell migration and its contribution to wound healing. *Burns Trauma.* 2018;6(20):1–7.
11. Tao Q, Zhang Y, Liu Y, et al. Magnetic susceptibility difference-induced nucleus positioning in a gradient ultrahigh magnetic field. *Biophys J.* 2020;118(3):578–585.
12. Zhang B, Zhang M, Chen Z, et al. Biophysical mechanisms underlying the effects of static magnetic fields on biological systems. *Prog Biophys Mol Biol.* 2023;177:14–23.
13. Meyer PF, Gomes MC, Pereira JA, et al. Effects of low-frequency sonic waves on geloid fibroedema: case study. *Braz J Ther Health*. 2011;1(2):31–36.
14. Snigdha RB, Jhunjhunwala S. Electrical stimulation for immunomodulation. *ACS Omega.* 2024;1:52–66.
15. Guerriero F, Ricevuti G. Extremely low-frequency electromagnetic field stimulation modulates autoimmunity and immune responses: a possible immuno-modulatory therapeutic effect in neurodegenerative diseases. *Neural Regen Res.* 2016;11(12):1888–1895.
16. Leppik L, Oliveira KMC, Bhavsar MB, et al. Electrical stimulation in bone tissue engineering treatments. *Eur J Trauma Emerg Surg.* 2020;46(2):231–244.
17. Saliev T, Begimbetova D, Masoud AR, et al. Bio-effects of non-ionizing electromagnetic fields in the context of cancer therapy. *Front Biosci (Landmark Ed).* 2014;6(1):175–184.
18. Ud S, Bayat A. Electrical stimulation and cutaneous wound healing: a review of clinical evidence. *Healthcare (Basel).* 2014;2(4):445–467.
19. Storch K, Dickreuter E, Artati A, et al. BEMER electromagnetic field therapy reduces cancer cell radioresistance by enhanced ROS formation and induced DNA damage. *PLoS One.* 2016;11(12):e0167931.
20. Saglam H. Response of cystinosis to frequency therapy (bioresonance treatment): a case report. *J US-China Med Sci.* 2017;14:90–97.
21. Jahangiri M, Mohammadi M, Saberi H, et al. Low-frequency stimulation induces polarization-based capturing between normal, cancerous, and white blood cells; a new separation method for circulating tumor cells enrichment or phenotypic cell sorting. *Analyst.* 2020;145(23):7636–7645.
22. Muresan D, Vlad A, Bogdan I, et al. Evaluation of an alternative depression therapy using bioresonance. *J Interdiscip Med*. 2021;6(2):82–86.
23. Galle HPE. The autobiographical writings of Josef Mengele. *Adv Stud.* 2011;25(71):269–286.
24. Belmonte R, Cuesta-Vargas AI, Arroyo-Morales M, et al. Efficacy of low-frequency low-intensity electrotherapy in the treatment of breast cancer-related lymphoedema: a cross-over randomized trial. *Clin Rehabil.* 2012;26(7):607–618.
25. Pihtili A, Koyuncu T, Akyüz M, et al. Evidence for the efficacy of a bioresonance method in smoking cessation: a pilot study. *Forsch Komplementmed.* 2024;21(4):239–245.
26. Imanzade M, Farajzadegan Z, Rajabi A, et al. Bioresonance treatment of intractable corneal ulcer. *Ann Mil Health Sci Res*. 2021;19(3):e117099.
27. Mukandala G, Tynan R, Lanigan S, O'Connor JJ. The effects of hypoxia and inflammation on synaptic signaling in the CNS. *Brain Sci.* 2016;6(1):6.
28. Rottmann S, Jung K, Ellrich J. Electrical low-frequency stimulation induces long-term depression of sensory and affective components of pain in healthy men. *Eur J Pain.* 2010;14(4):359–365.
29. McCullen SD, Zhu Y, Bernacki SH, et al. Application of low-frequency alternating current electric fields via interdigitated electrodes: effects on

cellular viability, cytoplasmic calcium, and osteogenic differentiation of human adipose-derived stem cells. *Tissue Eng Part A.* 2010;16(6):1377–1386.

30. Manzouri F, Zoghi M, Rogasch NC, et al. Low-frequency electrical stimulation reduces cortical excitability in the human brain. *NeuroImage Clin.* 2021;31:e102778.

31. Shen H, Sun J, Wu X, et al. Effects of the arterial radius and the center-line velocity on the conductivity and electrical impedance of pulsatile flow in the human common carotid artery. *Med Biol Eng Comput.* 2019;57(2):441–451.

32. Ferrigno B, Stigliano C, Puca A, et al. Bioactive polymeric materials and electrical stimulation strategies for musculoskeletal tissue repair and regeneration. *Bioact Mater.* 2020;5(3):468–485.

33. Kearns KR, Thompson DM. Macrophage response to electrical stimulation. In: 41st Annual Northeast Biomedical Engineering Conference (NEBEC). IEEE; 2024.

34. Zeng Z, Yang Y, Deng J, et al. Physical stimulation combined with biomaterials promotes peripheral nerve injury repair. *Bioengineering (Basel).* 2022;9:292.

35. Jia Y, Li J, Sun H, et al. Study on the effects of alternating capacitive electric fields with different frequencies on promoting wound healing. *Med Nov Technol Devices.* 2022;16:e100142.

36. Okano H, Taki M, Nakagawa M, et al. A 50 Hz magnetic field affects hemodynamics, ECG, and vascular endothelial function in healthy adults: a pilot randomized controlled trial. *PLoS One.* 2021;16(8):e0255242.

37. Reece JB, Taylor M, Simon EJ, et al. *Cell communication*. 2025.

38. Raven PH. *Cell communication*. In: Raven PH, ed. *Biology*. New York: McGraw-Hill. 2014:168–185.

39. Rui L, Zhang Y, Huang H, et al. Innate immune response orchestrates phosphoribosyl pyrophosphate synthetases to support DNA repair. *Cell Metab.* 2021;33(10):2076-2089.e9.

40. Barman SR, Jhunjhunwala S. Electrical stimulation for immunomodulation. *ACS Omega.* 2023;9(1):52–66.

41. Tian H, Wang L, Liu Q, et al. System-level biological effects of extremely low-frequency electromagnetic fields: an in vivo experimental review. *Front Neurosci.* 2023;17:e1247021.

42. Zhong Z, Wen Y, Zhu M, et al. Chondrolectin mediates growth cone interactions of motor axons with an intermediate target. *J Neurosci.* 2012;32(13):4426–4439.

43. Payne SC, Furness JB, Stebbing MJ. Bioelectric neuromodulation for gastrointestinal disorders: effectiveness and mechanisms. *Nat Rev Gastroenterol Hepatol.* 2019;16(2):89–105.

44. Das R, Zarei M, Ghatak S, et al. Electrical stimulation for immune modulation in cancer treatments. *Front Bioeng Biotechnol.* 2022;9:e795300.

45. Liboff AR. Electromagnetic vaccination. *Med Hypotheses.* 2022;79(3):331–333.

Citation: Malheiros KP, Castro FOF, Quixabeira VBL, et al. Evaluation of the effects of using low-frequency stimulation (ELF) in the biophysical and immune context. *MOJ Biol Med.* 2025;10(3):126–133. DOI: 10.15406/mojbm.2025.10.00253