

Anti-Radical Activity of Low Frequency and Low Amplitude PEMF

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ABSTRACT

Many hypotheses have been done to understand how Pulsed Electromagnetic Fields (PEMF) at low frequency (LF) and low intensities/amplitude (LA) impact on biological tissues. One of the responses it is aimed to investigate is the LF LA PEMF capability of promoting an oxidative stress modulation and anti-radical activity. Nonlinear models and, upon all, Schrödinger equations explains what could be the energy activation which drives these changes: the soliton wave. This solution finds its biophysical and biological demonstration in oxidative stress changes, disease or sport related. *In vitro* test was performed to demonstrate this model. Fibroblast and endothelial cells were exposed to PEMF LFLA 0-300Hz, 100uT emitted from a solenoid for 30 minutes for 21 Days. The assay kit revealed a progressive reduction of oxidative stress after the 8th day, in both cultures. This test was followed by an explorative clinical test report involving n.5 professional running athletes who were exposed for 21 days, once a day, to PEMF LFLA (variable frequencies 0-300Hz and 100uT mean peak) through a multi-solenoid mattress. The photometric analysis done every week (0, 7th, 14th, 21st day) showed a mean reduction of oxidative stress before and after each treatment, and in the overall treatment. The theoretical and experimental evidence described in this report illustrate the working principle of PEMF LF LA inducing responses in oxidative stress levels of biological tissues, both *in vitro* and *in vivo*. Further studies in wider population need to be done in order to confirm these assumptions.

Introduction

If we expose biological tissue to Pulsed Electromagnetic Fields (PEMF) we can induce a measurable biological response and modulate inflammatory processes, promote bone repair, repair of skin wounds, even chronic ones, improve metabolic processes. Electromagnetic fields can interact with biological tissue inducing responses depending on their frequency and intensity. In the therapeutic field, the most promising results are obtained with the use of low intensity and very low frequency pulsed electromagnetic fields, or Extremely Low Frequency, indicated by the acronym PEMF LFLA. In fact, exposing cultures of fibroblasts and endothelial cells to PEMF LFLA, which vary during the stimulation process, we can quantitatively measure a reduction in the free radicals produced.

Recent evidence has demonstrated that LPEMFs can prevent inflammation and oxidative stress as a non-invasive therapeutic method for various diseases. As an example, in 2019 a study [1] presented how, in an *in vivo* test, PEMF LFLA promote functional recovery following spinal cord injury, potentially by modulating inflammation, oxidative stress and HSP70. Furthermore, studies confirmed that PEMF LFLA can reduce ROS levels and enhance antioxidative stress responses in osteoblasts [2]. A polish clinical research [3] in 2018, attested that variable low frequency PEMF therapy meaningfully improved the overall condition of 57 patients through a decrease of oxidative stress markers while significantly affected positively their psychophysical abilities after stroke. In the

present study it is presented a biophysical hypothesis of interaction between PEMF and biological working principle regarding the oxidative stress modulation PEMF derived, particularly in sport activities. Finally, we evidenced some results *in vitro* in fibroblast and endothelial cells and *in vivo*, in a case report on professional running athletes.

Biophysical Hypotheses Of Interaction between PEMF and Biological Tissues

There are several hypotheses of interaction between electromagnetic fields and cellular structures. Among the various hypotheses proposed in the scientific literature, the use of non-linear physical descriptive models, seem to be the best tools for describing the induced biological phenomena. In particular, the use of solutions of Schrödinger equation, relating to waves with constant amplitude, called "solitons", which will be better described below, allows to explain, as a theoretical model, the effects of PEMFs on the modulation of oxidative stress. The magnetic field can, in fact, induce variations in electrical charges through the insulating effect of the plasma membrane, acting on electrons, ions, radicals, molecules and macromolecules.

The hypothesis of interaction of PEMF LFLA with cellular structures includes (1):

1. Action on RNA polymerase and stimulation of cell replication
2. Action on the synthesis and hydrolysis of ATP
3. Effectiveness of oxidation-reduction reactions

Electro-magnetic fields can influence biological redox processes. The electron transport chain, involved in the synthesis of ATP and in respiration, is a process of oxygen reduction (by NADH and FADH₂) through electron transfer in the mitochondria (it is the initial part of oxidative phosphorylation). The relatively small mass molecules involved in the chain, such as cytochrome-c, can move quite "easily" out of the mitochondrial membrane, carrying electrons from donor to acceptor [4]. This electron transport can be described using very complex physical theoretical modelling. Trying to simplify, the various models consider electron donor molecules loosely bound to "bridging" molecules, in turn loosely bound to acceptor molecules. But if we consider high molecular weight molecules such as the NADH-ubiquinone oxidoreductase proteins and cytochrome c-oxidase, which are also involved in the electron transport chain, these result to be practically fixed in the inner mitochondrial membrane. Most of these proteins have an alpha-helix conformation. When the electrons are released from the donor molecule, they are transferred into the protein and accompanied by a deformation of the endoplasmic reticulum which forms a potential barrier that attracts the electron itself. A relationship between protein conformation and formation of the electron-lattice deformation bond is hypothesized.

The charges then propagate, accompanied by a deformation of the lattice. Mathematically, through the solutions of non-linear equations, it is possible to describe this propagation which assumes a waveform with particular characteristics, such as the amplitude that remains constant. We will see that this wave has been called "soliton". To demonstrate this result, the ion-resonance frequency relationship can be inserted into the solution of the non-linear Schrödinger equation, defined in quantum mechanics [5]. If we consider the presence of potential $U(x,t)$ the formula of the equation can be written as follows:

$$\text{Eq.1} \quad i\hbar \frac{\partial \psi(x,t)}{\partial t} = -\frac{\hbar^2}{2m} \frac{\partial^2 \psi(x,t)}{\partial^2} + U(x,t)\psi(x,t)$$

Cyclotron ion resonance is a phenomenon related to moving ions immersed in a magnetic field and is based on the Lorentz force. The magnetic field acts on electronically charged elements such as ions (eg Na⁺, K⁺, Ca⁺⁺) and electrons, certainly available in biological systems. The magnetic field can act on the movement of these electric charges through a force called Lorentz and defined by

$$\text{Eq.2} \quad F = qE + qvB$$

where the contribution of the electric field E which acts on the charge q , and the contribution of the magnetic field of intensity B , which acts on the same charge as a function of its speed v , determines the intensity of the force F . Thanks to the Lorentz force, a free ion immersed in a magnetic field of intensity B , moves on a circular trajectory with an angular velocity ω , dependent not only on the intensity of the magnetic field but also on its own charge and mass. Using the information of the Lorentz force and the circular trajectory, the following formula can be obtained:

$$\text{Eq.3} \quad f = \frac{q}{2\pi m} B$$

If we insert this frequency value into Schrödinger's equation and solve it, the solution obtained is the wave function of the electron $\psi(x,t)$.

More correctly, its square provides information on the probability of finding the electron when trying to measure its position. Applied to the electron transport chain, the wave function provides information on the position of the particle along the protein lattice. Considering an alpha polypeptide chain, the solution of this equation is a particular wave, which indefinitely maintains its amplitude. In the literature this wave has been described through the shape of a "soliton".

$$\text{Eq.5} \quad \psi(x,t) = f(x-vt)$$

The soliton is a solitary wave that keeps its amplitude constant and represents the "module" for transporting energy and information at the cellular level. With the same solution we can calculate the deformation of the lattice (chain) in the "soliton"

state, which is proportional to the probability of the presence of the electron (x). From the mathematical demonstration we obtain that the electron and the deformation of the lattice together, propagate along the polypeptide chain, with constant speed, from a donor molecule to an acceptor molecule, as a localized wave. This wave is exceptionally stable, able to propagate along macroscopic distances, thanks to the combination of low energy dispersion and non-linear phenomena (non-linear nature of its formation). The oscillatory character of soliton propagation with frequency given by Equation 1 is accompanied by the propagation of the local deformation of the polypeptide chain.

At a “macroscopic” level, solitons are well known and used in some fields of application. For example, in optical fibre transport networks, the non-monochromatic light, due to the Kerr effect, can propagate without changing over time. Tsunamis are common in seismology, generated by submarine earthquakes, capable of spreading for kilometres without dispersing energy, before impacting the coasts, with all their destructive force. They are therefore waves that do not lose their energy and their intrinsic characteristics by propagating and this is due to the combination of dispersion and non-linear effects, which interact by cancelling each other. The name “soliton” is due to their characteristic of remaining unchanged in the event of reciprocal interaction: two soliton waves that collide do not add up their effects. The hypothesis that some biological phenomena are based on the presence of solitons is due to Alexander Davydov who in 1979 and then in 1985 hypothesized their existence in alpha polypeptide chains [4]. Davidov demonstrated, mathematically, that the energy from ATP hydrolysis could be stored as a vibration of the amide group of the alpha helix protein, through a non-linear interaction that traps, the energy into a soliton [6,7]. The energy comes from the hydrolysis of ATP, as widely known in biology, but this is stored in the form of mechanical vibration of the amide, with constant amplitude. The subsequent propagation of this energy can explain the muscle contraction [8] (Figure 1). Over the years, scientific literature has shown, mathematically, how the solitons mechanism was a good solution to explain biological phenomena. It therefore becomes clear how PEMF LFLA can interact with these mechanisms, promoting biological phenomena.

Biological Working Principle of ROS Regulation with PEMF Exposure

Both in the therapeutic and sports fields, an important effect of PEMF LFLA is the reduction or, more correctly, the regulation of oxidative stress. This plays an important role in numerous pathological conditions on an inflammatory basis, involving the cardiovascular, neurological, metabolic and respiratory compartments. In the respiratory tree, free radicals cause epithelial and vascular necrosis, connective tissue degradation and activation

of pro-inflammatory factors [9]. Sports-related oxidative stress slows post-workout recovery, increases fatigue and the risk of myocyte injury. ROS free radicals are produced during physiological chemical reactions that use oxygen. These molecules are particularly reactive and unstable due to at least one unpaired electron in their outer orbital. To reach an electromagnetic equilibrium state, they try to “recover” that electron binding other atoms and leading to new and further unstable molecules. Modulated PEMF LF LA can reduce the average “duration” of the oxidative free radical, limiting its damage action, in particular during inflammatory processes, both acute and chronic, which limit the physiological healing processes or sports recovery. The “spin chemistry”, through the “radical pair mechanism”, can describe the mode of action of the low intensity magnetic field with chemical reactions [10].

During an oxidative reaction, radical pairs are formed, therefore, as known, with “unpaired” electrons. These electrons can be “parallel” or “antiparallel”. In the first case the radical couple will be in the electronic “triplet” state, while in the second case the couple will be in the “singlet” state [11]. During the chemical reaction, with the formation of the radical pair, there is an interconversion between singlet and triplet states. This reaction influences the speed and the course of the chemical process and can be influenced by applied magnetic fields, in particular if they have low energy and variable frequency. The PEMF LFLA fields therefore promote the transition to a more stable state, that is the “triplet” state, reducing the “average life”, that is the duration, of the free radical [12].

***In vitro* tests**

In order to demonstrate the ROS-reducing action, PEMF LF LA was applied to *in vitro* cultures of fibroblasts and endothelial cells [5]. By means of a solenoid with 54 coils and a generator of sinusoidal electrical signals that allowed the combination through DDS of several sinusoids at different frequencies and above all, to make the frequencies vary during the treatment, impulsive e.m. fields have been generated. at frequencies that can be varied in the range 0-300Hz and with average intensities of 100 μ T. In conditions of oxidative stress, free radicals accumulate, but by exposing cell cultures to modulated pulsed electromagnetic fields, it is possible to limit their production, or, more correctly, reduce the duration of activity of ROS by reducing their quantity overall. The following figure (Figure 2) shows the comparison of the quantities of ROS, measured by the Oxiselect kit in cultures of fibroblasts and endothelial cells [5], exposed to the described LF LAPEMF 20 minutes/day for 21 days [13]. The curves show the progressive variations of ROS species on a daily basis: in fibroblasts a reduction is observed, compared to the control, starting from the 8th day, while in endothelial cells the reduction of ROS is evident from the first exposure to PEMF LFLA 0-300Hz, 100 μ T.



Figure 1: Alexander Davydov was the first to hypothesize the action of solitons in biological systems.

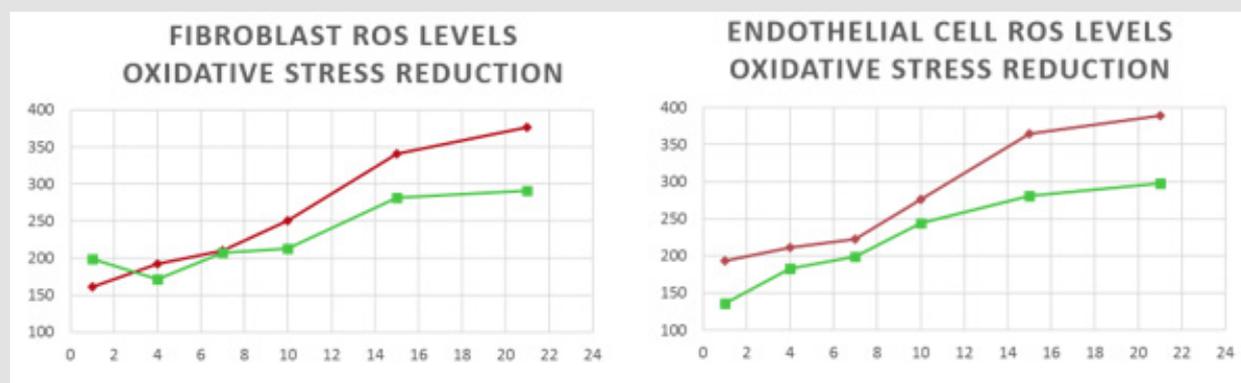


Figure 2: Quantity of ROS species in fibroblast (left) and endothelial (right) cells vs treatment days (20min / d): green line with squares represents the treated cells, while the red line with rhombuses the control cultures.

Clinical Test Report on Athletes

An explorative clinical test report was performed in order to evaluate the ROS influence as a systemic effect after low intensity and low frequency PEMF exposure. The PEMF emitting systems was composed by a mattress with three pairs of solenoids at increasing numbers of coils (18, 36, 50). The coils are connected to a generator which supplies the therapy as per *in vitro* tests (variable frequencies 0-300 Hz and variable intensity 100 μ T mean). We measured systemic ROS levels of n.5 professional athletes with the use of a portable system (FRAS 5, H&D S.r.l. – Italy) before and after exposure with PEMF at different timepoints during their training session. A small amount of capillary blood was taken from the

fingertip and analysed through photometer which determines the blood concentration of ROM (Reactive Oxygen Metabolites = Free radicals) in U CARR (10). Patients undergo a 30-minute PEMF exposure lying on the mattress with solenoids once a day. At time 0, 7, 14 and end time (21 days) the analysis of the values of free radicals (d-ROMs) were carried out, before and after a treatment session with PEMF, and then athletes continued the treatment at home. The points in the above figure (Figure 3) showed a decrease of the measurement of systemic ROS after 30 minutes of exposure with PEMF in every session resulting in an overall decrease at the end of the study. This is confirmed by the mean between the measurement before and after PEMF treatment throughout the study in five professional running athletes (Figure 4).

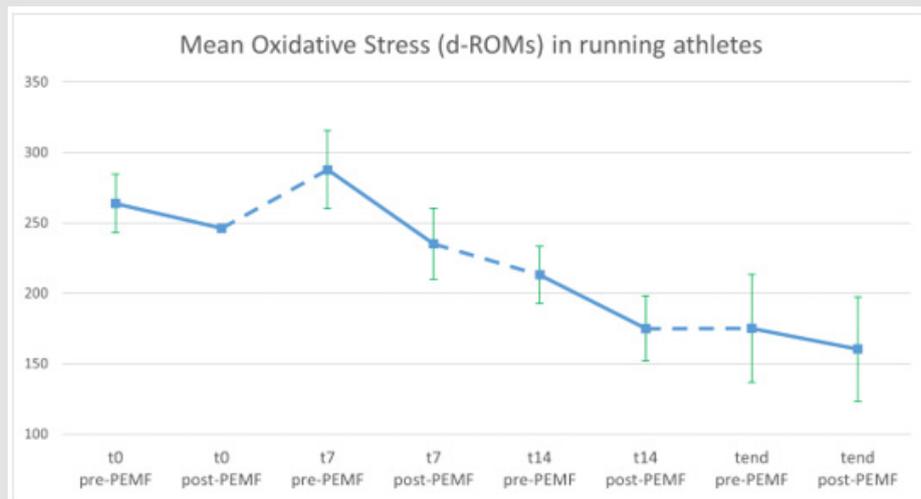


Figure 3: Mean of d-ROMs in U CARR in capillary blood of 5 athletes before (pre-PEMF) and after (post-PEMF) exposure with PEMF treatment at start of treatment (t0) and after 7, 14 and 21 days (tend). In green the standard deviation.

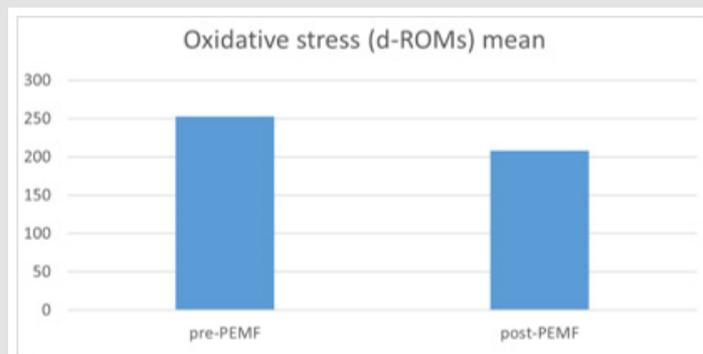


Figure 4: Overall Mean of d-ROMs in U CARR in 5 athletes before (pre-PEMF) and after (post-PEMF) exposure with PEMF treatment of the 4 sessions.

Discussion

LFLA PEMFs are able to interact with biological tissue and modify its responses, for example by reducing free radicals and consequently their action in inflammatory processes. The theoretical hypothesis is based on the modulation of soliton waves capable of acting on cellular elements with an electric charge, in the processes of cellular respiration, realizing the transport of electrons, and promoting the formation of stable states and reducing the duration of action of the free radical. Initial evidence has been found *in vitro* in fibroblast and endothelial cells, where the exposure to PEMF resulted in a decrease of ROS levels. Clinical exploratory test report on professional athletes showed a decrease of systemic ROS levels after PEMF exposure. LFLA PEMF showed capability to reduce ROS level *in vitro* and *in vivo*, but further studies need to be implemented in a wide population in order to confirm this first experimental results.

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