

# Pulsed electromagnetic field therapy history, state of the art and future

Marko S. Markov

© Springer Science+Business Media, LLC 2007

**Abstract** Magnetic and electromagnetic fields are now recognized by the 21st century medicine as real physical entities that promise the healing of various health problems, even when conventional medicine has failed. Today magnetotherapy provides a non-invasive, safe, and easy method to directly treat the site of injury, the source of pain and inflammation, and other types of diseases and pathologies. Millions of people worldwide have received help in treatment of musculoskeletal system, as well as pain relief. Pulsed electromagnetic fields are one important modality in magnetotherapy and recent technological innovations, such as Curatron pulsed electromagnetic field devices, offer excellent, state of the art computer controlled therapy system. In this article the development, state of the art and future of pulsed electromagnetic field therapy are discussed.

## 1 Introduction

This article was triggered by information found on Internet that a new, computerized system for pulsed electromagnetic field (PEMF) therapy has been introduced on the market. It appears that the Curatron system marks a new era in the biomagnetic technology: use of computer during the planning and executing of the therapy (<http://www.curatron.com>).

It is recognized that the use of magnetic fields for therapy has a long history. Physicians from ancient Greece, China, Japan, and Europe successfully applied natural

magnetic materials in their daily practice. The contemporary magnetotherapy has begun immediately after the World War II by introducing both magnetic and electromagnetic fields, generated by various waveshapes of the supplying currents. Starting in Japan, this modality quickly moved to Europe, first in Romania and the former Soviet Union. During the period 1960–1985 nearly all European countries designed and manufactured own magnetotherapeutic systems. Indeed, the first book on magnetotherapy, written by N. Todorov, was published in Bulgaria in 1982 and summarizes the experience of utilizing magnetic fields for treatment of 2700 patients, having 33 different pathologies.

During the 1970s, the team of Andrew Bassett introduced a new approach for treatment of delayed fractures, that employed a very specific biphasic low frequency signal (Bassett et al. 1974, 1977). This signal was allowed by FDA for application in the USA only for non-union/delayed fractures. A decade later, FDA allowed the use of pulsed radiofrequency electromagnetic field (PRF) for treatment of pain and edema in superficial soft tissues.

It is now commonly accepted that weak electromagnetic fields (EMF) are capable of initiating various healing processes including delayed fractures, pain relief, multiple sclerosis, and Parkinson's disease. (Rosch and Markov 2004). This proven benefit could be obtained by using both static and time-varying magnetic fields.

This article discusses only the modalities that utilize time varying low frequency EMF, known as PEMFs. Therefore, a large body of research, including many clinical studies that report the successful application of static magnetic fields and high frequency EMF as well as electroporation and electrical stimulation will remain outside this article. Several excellent reviews concerning these stimulation modalities (Gardner et al. 1999; Rushton 2002;

---

M. S. Markov (✉)  
Research International, Williamsville, NY 14221, USA  
e-mail: msmarkov@aol.com

Sluka and Walsh 2003; Ojingwa and Isseroff 2003; Rosch and Markov 2004).

It should be noted, that, thus far, the medical community approach to magnetotherapy is as to an adjuvant therapy, especially for treatment of a variety of musculoskeletal injuries. There is a large body of basic science and clinical evidence that time-varying magnetic fields can modulate molecular, cellular, and tissue function in a physiologically and clinically significant manner. (Markov 2002; Rosch and Markov 2004).

The fundamental questions related to the biophysical conditions under which EMF signals could be recognized by cells in order to modulate cell and tissue functioning remains to be elucidated. The scientific and medical communities still lack the understanding that different magnetic fields applied to different tissues could cause different effects.

The medical part of the equation should identify the exact target and the “dose” of EMF that the target needs to receive. Then, physicists and engineers should design the exposure system in such a way that the target tissue receives the required magnetic flux density. One should not expect, for example, that the magnetic field which is beneficial for superficial wounds, might be as good for fracture healing. Particular attention must be paid to the biophysical dosimetry, which should predict which EMF signals could be bioeffective and monitor this efficiency. This raises the question of using theoretical models and biophysical dosimetry in selection of the appropriate signals and in engineering and clinical application of new PEMF therapeutic devices.

## 2 Some examples for target populations

The largest populations of patients that have received, or could benefit from magnetic field therapy are victims of musculoskeletal disorders, wounds and pain. Following is a summary of information for the number of people in the USA who need help in above-mentioned areas.

Five million bone fractures occur annually in the United States alone. About 5% of these became delayed or non-union fractures (Ryaby 1998). According to National Osteoporosis Foundation about 10 million Americans have osteoporosis and 34 millions of US citizens have low bone density, which put them at risk for further musculoskeletal disorders.

Chronic wounds and their treatment are an enormous burden on the healthcare system, both in terms of their cost (\$5 billion to \$9 billion annually) and the intensity of care required. There is even more cost to society from human suffering and reduced productivity. More than 2 million people suffer from pressure ulcers and as many as

600,000–2.5 million more have chronic leg and foot wounds (Wysocki 1996).

Diabetic foot ulcers are probably the most common chronic wounds in western industrialized countries. Of the millions who have diabetes mellitus, 15% will suffer foot ulceration which often leads to amputation (100,000 per annum in the US alone) (Pilla 2006).

The National Institutes of Health estimate that more than 48 million Americans suffer chronic pain that results in a 65 billion loss of productivity and over \$100 billion spent on pain care (Markov 2004c). Better part of this money is spent for pain-relief medications.

Recent advances in magnetotherapy suggest that carefully selected magnetic fields might be helpful in treatment of diseases as Parkinson’s, Alzheimer, as well as Reflex Sympathetic Disorders which have relatively small number of potential users.

## 3 Cost and benefit of EMF therapy

Improvement in only a small percentage of above-mentioned cases would be of great benefit: less suffering, reduced expenses, and decreased duration of treatment should be considered in parallel with individual and social welfare. Thus, the clinical effects of PEMF on musculoskeletal system repair are physiologically significant and often constitute the method of choice when the conventional standard of care has failed to produce adequate clinical results.

PEMF modalities are usually applied directly on the targeted area of the body. Compared to regular pharmaceuticals, PEMF offers an alternative with fewer, if any, side effects. This is a tremendous advantage versus pharmaceutical treatment at which the administered medication spreads over the entire body, thereby causing adverse effects in different organs, which sometimes might be significant. One should not forget that in order to deliver the medication dose needed to treat the target tissue/organ, patients routinely receive medication dose hundreds of times larger than the dose needed by the target.

However, regulatory and reimbursement issues have prevented more widespread use of PEMF modalities, especially in the USA. The FDA policy toward magnetotherapy is unnecessarily restrictive. In concert with this policy, the Center for Medicare Services (CMS) for a period of time refused to allow reimbursement even for modalities cleared by FDA. It took several years of court fighting until CMS reversed its position. This was a result of the pressure from general public and physical therapy communities. In fact, the CMS has been now recognized that PEMF is a plausible therapeutic modality which produces sufficient clinical outcome to permit, and reimburse

for, use in the off-label application of healing chronic wounds, such as pressure sores, diabetic leg, and foot ulcers (Pilla 2006).

### 3.1 PEMF signals

Today, magnetic-field-dependent modalities could be categorized in six groups, but this article is discussing only the PEMF signals (for details see Markov 2004c). An excellent review of the physics and engineering of low frequency signals was published by Liboff (2004).

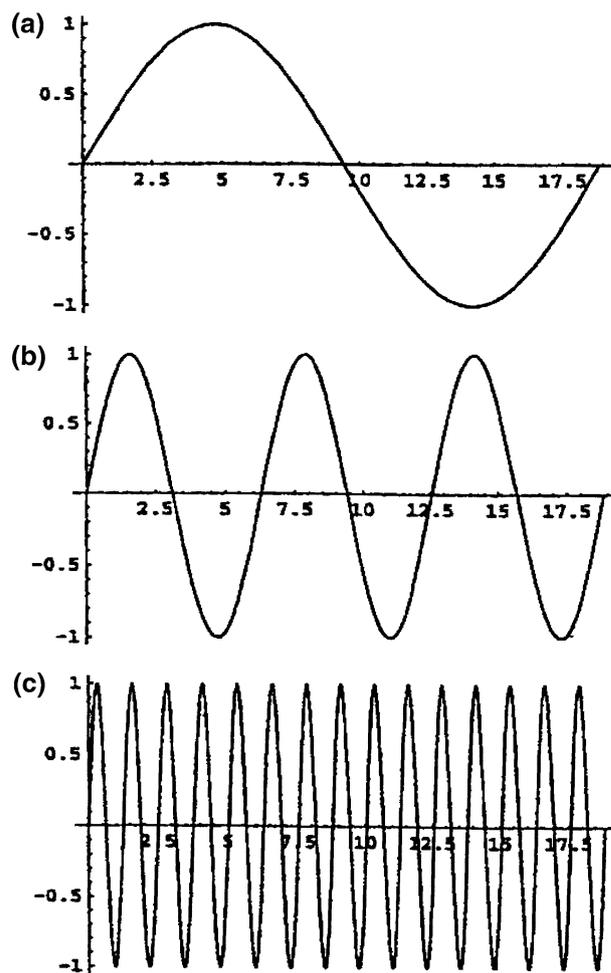
The PEMF signals in clinical use have variety of designs, which in most cases are selected without any motivation for the choice of the particular waveform, field amplitude or other physical parameters.

### 3.2 Sinewave type signals

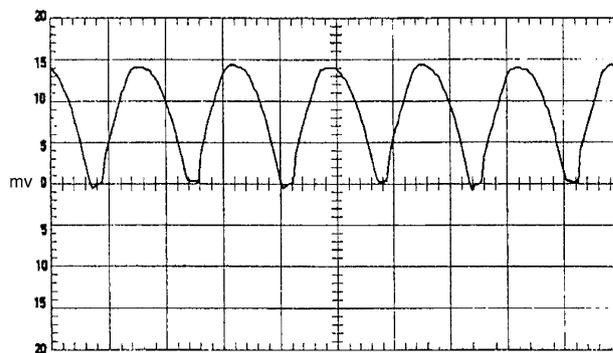
It seems reasonable that the first and widely used wave-shape is the sine wave with frequency of 60 Hz in North America and 50 Hz in the rest of the world (Fig. 1). Though not a subject of this article, it should be noted that the 27.12 MHz continuous sinewave have been used for deep tissue heating in fighting various form of cancer.

From the symmetrical sinewaves engineers moved to an asymmetrical waveform by means of rectification. These types of signals basically flip–flop the negative part of the sinewave into positive, thereby creating a pulsating sine-wave. The textbooks usually show the rectified signal as a set of ideal semi-sinewaves. However, due to the impedance of the particular design such ideal waveshape is impossible to be achieved. As a result, the ideal form is distorted and in many cases a short DC-type component appears between two consecutive semi sinewaves (Fig. 2). This form of the signals has been tested for treatment of low back pain and Reflex sympathetic disorder (Ericsson et al. 2004). However, the most successful implementation of this signal is shown in animal experiments as causing anti-angiogenic effects (Williams et al. 2001; Markov et al. 2004d). Investigating a range of amplitudes for 120 pulses per second signal, the authors demonstrated that the 15 mT prevents formation of the blood vessels in growing tumors, thereby depriving the tumor from expanding the blood vessel network and causing tumor starvation and death.

In the middle of 1980s the Ion Cyclotron Theory was proposed by Liboff (1985), Liboff et al. (1987) and shortly after that a clinical device was created based on the ICR model (Orthologics, Temple, AZ). This device is in current use for recalcitrant bone fractures. The alternating 40  $\mu$ T sinusoidal magnetic field is at 76.6 Hz (a combination of



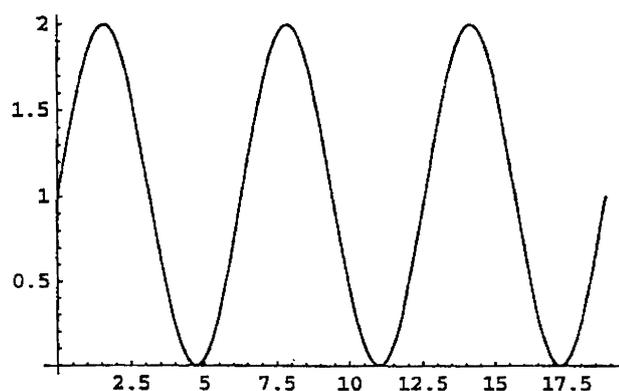
**Fig. 1** Three types of sinewave signals with the same amplitude, but different frequencies



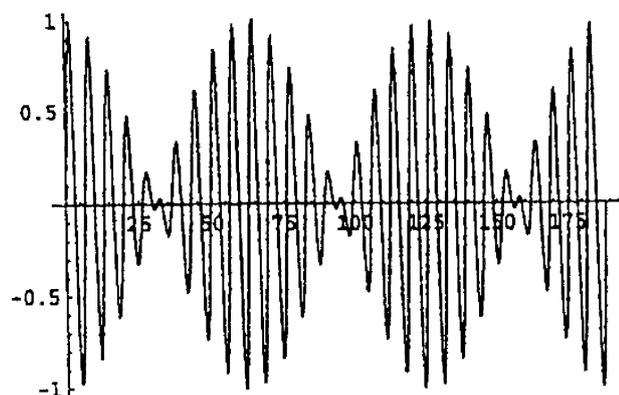
**Fig. 2** Example of real bridge rectified signal: a small DC component occurs between two semi sine waves and a slight distortion of the front part of semi sine wave might be observed

$\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  resonance frequencies). This signal, shown in Fig. 3 has oscillating character, but due to the DC magnetic field it oscillates only as a positive signal.

The other type of sinewave-like signals might be seen when a sinewave signal is modulated by another signal.



**Fig. 3** Adding a DC signal to sinusoidal signal might cause the positive only signal to originate

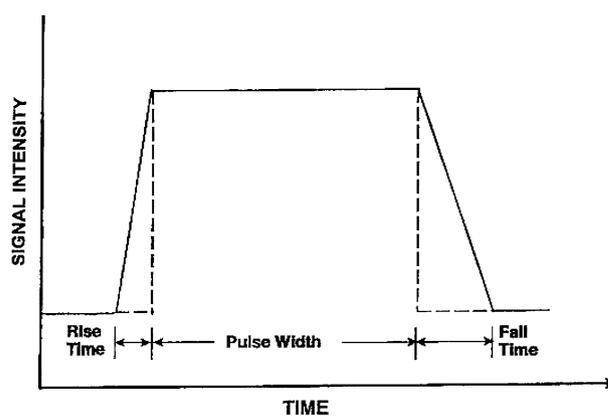


**Fig. 4** Example of amplitude modulation of a high frequency sinusoidal signal

This exploits the principle of amplitude modulation, used in radio-broadcasting (Fig. 4). Usually, the sinewave signal is at high frequency (in kHz and MHz range), while the modulating signal is a low frequency signal. There are also devices that apply two high frequency signals and the interference of both signals results in an interference magnetic field (Todorov 1982).

### 3.3 Rectangular type of signals

In addition to sinewave type signals, a set of devices which utilize unipolar or bipolar rectangular signals is available at the market. Probably for those signals the most important is to know that due to the electrical characteristics (mostly the impedance) of the unit, these signals could never be rectangular. It should be a short delay both in raising the signal up and in its decay to zero. The rise-time of such signal could be of extreme importance because the large value of dB/dt could induce significant electric current into the target tissue. Some authors consider that neither frequency, nor the amplitude are so important for the biological



**Fig. 5** Trapezoid signal minimizes the problems with the rising time in case of rectangular signals

response, but the raising time dB/dt rate is the factor responsible for observed beneficial effects. There are recent suggestions that the rectangular signals should be replaced by more realistic trapezoid signals (Kotnik and Miklavcic 2006) (Fig. 5).

### 3.4 Pulsed signals

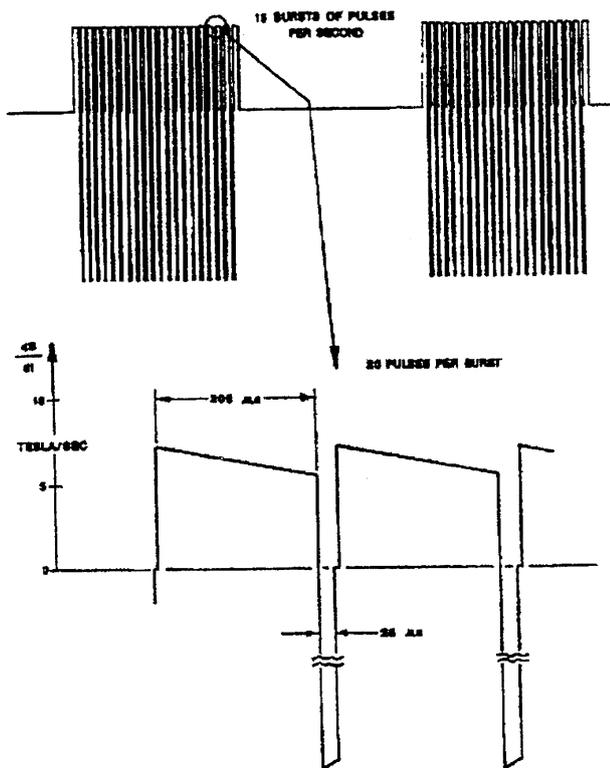
The first clinical signal approved by FDA for treatment of nonunion or delayed fractures (Bassett et al. 1974, 1977) exploited the pulse burst approach. Having repetition rate of 15 burst per second, this asymmetrical signal (with a long positive and very short negative component) has more than 30 years of very successful clinical use for healing nonunion bones (Fig. 6) It was assumed that the cell would ignore the short opposite polarity pulse and respond only to the envelope of the burst which had a duration of 5 ms, enough to induce sufficient amplitude in the kHz frequency range.

A series of modalities utilizes signals that consist of single narrow pulses separated by a long “signal-off” intervals. This approach allows modification not only of the amplitude of the signal, but also of duty cycle (time on/ time off) as well.

The pulsed radiofrequency signal, originally proposed by Ginsburg in 1934 and later allowed by FDA for treatment of pain and edema in superficial soft tissues (Diapulse) utilizes the 27.12 MHz in pulsed mode. Thus, having short 65  $\mu$ s burst and 1,600  $\mu$ s pause between pulse bursts, the signal does not generate heat during 30 min use.

## 4 Clinical benefit

A large number of scientific and clinical studies have been reporting that PEMF help in bone unification; reduce pain,



**Fig. 6** The original signal for treatment of non-union fractures proposed by Bassett et al

edema and inflammation; increase blood circulation; stimulate immune, and endocrine systems. Most wounds studies involve arterial or venous skin ulcers, diabetic ulcers, pressure ulcers as well as surgical and burn wounds. Since cells involved in wound repair are electrically charged, some endogenous EMF signals may facilitate cellular migration to the wound area (Lee et al. 1993), thereby restoring normal electrostatic and metabolic conditions. An important concept was proposed, that at any injury site of the musculoskeletal system an injury current occur (Canaday and Lee 1991). Since the main goal of any therapy is to restore normal function to the organism, electric, magnetic or electromagnetic modalities appear suitable to compensate the injury currents. Of course, the optimal parameters to achieve this goal would depend on the type and extent of the injury that cause the specific injury current to originate.

PEMF have also been beneficial in treatment of chronic pain associated with connective tissue (cartilage, tendon, ligaments and bone) injury and joint-associated soft tissue injury (Rosch and Markov 2004; Hazlewood and Markov 2006).

Numerous cellular studies have addressed the effects of EMF on signal transduction pathways. It is now well accepted that the cellular membrane is a primary target for

magnetic field action. (Adey 2004) Evidence is collected that selected magnetic fields are capable of affecting the signal transduction pathways via alteration of ion binding and transport. The calcium ion is recognized as a key player in such alterations. In a series of studies of calcium-calmodulin dependent myosin phosphorylation my group demonstrated that specific static magnetic fields, PEMF and 27.12 MHz PRF could modulate  $Ca^{2+}$  binding to CaM to a twofold enhancement in  $Ca^{2+}$  binding kinetics in a cell-free enzyme preparation. (Markov et al. 1992, 1993, 1994; Markov and Pilla 1993, 1994a,b; Markov 2004a,b) The ion binding target pathway has been confirmed in other studies using static magnetic fields (Engstrom et al. 2002; Liboff et al. 2003).

A meta-analysis performed on randomized clinical trials using PEMF on soft tissues and joints showed that both PEMF and PRF were effective in accelerating healing of skin wounds (Ieran et al. 1990; Itoh et al. 1991; Stiller et al. 1992; Comorosan et al. 1993; Seaborne et al. 1996; Canedo-Dorantes et al. 2002), soft tissue injury (Bental 1986; Foley-Nolan et al. 1990; Vodovnik and Karba 1992; Pennington et al. 1993; Pilla et al. 1996), as well as providing symptomatic relief in patients with osteoarthritis and other joint conditions (Fitzsimmons et al. 1994; Zizic et al. 1995; Ryaby 1998).

We, as scientists, are guilty of making statements like this: "Today there is abundance of in vitro and in vivo data obtained in the laboratory research as well as clinical evidence that time-varying magnetic fields of various configurations can generate beneficial effects for various conditions, such as chronic and acute pain, chronic wounds and recalcitrant bone fractures. This has been achieved with low intensity, non-thermal, non-invasive time-varying EMF, having various configurations within a broad frequency range." (Pilla 2006). What is wrong with this statement? One only word is missing "some". By not saying that some or selected PEMF could initiate plausible therapeutic effects, we simply say that *all* magnetic fields could achieve the goals.

Which signals and at which conditions could be effective? Are any signal parameters better than others? It should be pointed out that many EMF signals used in research and as therapeutic modalities have been chosen in some arbitrary manner. Few studies assessed the biological and clinical effectiveness of different signals by comparing the physical/biophysical dosimetry and biological/clinical outcomes. With the exponential development of Internet it is easy to find tens, if not hundreds of devices, which promise to cure each and any medical problem. A careful look at these sites would show that no engineering, biophysical and clinical evidence is given to substantiate the claims.

It has been three decades since the concept of “biological windows” was introduced. In fact, three groups, unknown to one another, published, almost simultaneously that during evolution Mother Nature created preferable levels of recognition of the signals from exogenous magnetic fields. The “biological windows” could be identified by amplitude, frequency and their combinations. The research in this direction requires assessment of the response in a range of amplitudes and frequencies. It has been shown that at least three amplitude windows exist: at 50–100  $\mu\text{T}$  (5–10 Gauss), 15–20 mT (150–200 Gauss) and 45–50 mT (450–500 Gauss) (Markov 2005). Using cell-free myosin phosphorylation to study a variety of signals, my group has shown that the biological response depends strongly on the parameters of applied signal, confirming the validity of the last two “windows” (Markov 2004a,b). Interestingly, a new PEMF system, developed by Curatron Ltd. generates electromagnetic signals within the range of these amplitude windows and exploit amplitude signals already proven to be biologically and clinically effective (<http://www.curatron.com/>).

## 5 Mechanisms of action

The biophysical mechanism(s) of interaction of weak electric and magnetic fields with biological systems, as well as the biological transductive mechanism(s), have been vigorously studied by the bioelectromagnetics community. Both experimental and theoretical data have been collected worldwide in search of potential mechanisms of interactions. As of today, a number of mechanisms have been proposed, such as ion cyclotron resonance (ICR), ion parametric resonance (IPR), free radical concept, heat shock proteins, etc. One of the first proposed models uses a linear physicochemical approach (Pilla 1972, 1974), in which an electrochemical model of the cell membrane was employed in order to assess the EMF parameters for which bioeffects might be expected. It was assumed that non-thermal EMF may directly affect ion binding and/or transport and possibly alter the cascade of biological processes related to tissue growth and repair.

This electrochemical information transfer hypothesis postulated that one plausible way for interactions between the cell membrane and the EMF could modulate the rate of ion binding to receptor sites. Several distinct types of electrochemical interactions can occur at cell surfaces, but two deserve special attention: non-specific electrostatic interactions involving water dipoles and hydrated (or partially hydrated) ions at the lipid bilayer/aqueous interface of a cell membrane as well as voltage dependent ion/ligand binding (Pilla et al. 1997).

It should be noted the significant contribution of late Ross Adey in studying biophysical mechanisms of interactions of EMF with biological membranes which has both fundamental and clinical importance (Adey 1986, 2004).

ICR proposed during the mid-1980’s by Liboff (1985, 1987), described specific combinations of DC and AC magnetic fields which can increase the mobility of specific ions near receptor sites and/or through ion channels.

Any discussion of the possibility for EMF to cause biological/clinical effects must involve a discussion of the problem of thermal noise (“kT”). Physicists and physical chemists, for example, have rejected the possibility that static and low frequency magnetic fields may cause biological effects because of the “thermal noise.” Indeed, thermal noise has been cited as the main objection to the ICR model (Muesham and Pilla 1996; Pilla et al. 1999; Zhadin 1998). Bianco and Chiabrera (1992) have provided an elegant explanation of the inclusion of thermal noise in the Lorentz-Langevin model which clearly shows the force applied by a magnetic field on a charge moving outside the binding site is negligible compared to background Brownian motion and, therefore, has no significant effect on binding or transport at a cell membrane.

In order to resolve the thermal noise problems in the ICR model, Lednev (1991) formulated an IPR model which was further developed during the 1990’s (Blanchard and Blackman 1994; Blackman and Blanchard 1995; Engstrom 1996). In this quantum approach, an ion in the binding site of a macromolecule is considered to be a charged harmonic oscillator. It was proposed that the presence of a static magnetic field could split the energy level of the bound ion into two sublevels with amplitudes corresponding to electromagnetic frequencies in the infrared band. The difference between these two energy levels is the Larmor frequency.

For me, the most important contribution of Lednev is the experiment he designed to estimate the validity of his ICR model: myosin phosphorylation in a cell-free mode (Shouvalova et al. 1991). The calmodulin molecule provides ideal model for investigating ion binding without and with the presence of exogenous magnetic field. This molecule has 4 molecular clefts ready to bind Calcium ion. Moreover, calmodulin undergoes conformational changes at each filling of the binding sites. The experiment proposed by Lednev, and further elaborated by my group (Markov 2004a,b), allows the Pilla’s group to propose a model that overcomes the problem of thermal noise. In addition, evidence showing both low frequency sinusoidal magnetic fields, which induce electric fields well below the thermal noise threshold, and weak static magnetic fields, for which there is no induced electric field, can have biologically and clinically significant effects (Shouvalova et al. 1991; Markov et al. 1992, 1993, 1994; Markov and

Pilla 1993, 1994a,b; Liburdy and Yost 1993; Engstrom et al. 2002; Liboff et al. 2003) have been collected.

Larmor precession, which describes the effects of exogenous magnetic fields on the dynamics of ion binding, when the ion is already bound, has been suggested, as a possible mechanism for observed bioeffects due to weak static and alternating magnetic field exposures (Zhadin and Fesenko 1990; Edmonds 1993; Muehsam and Pilla 1994a,b, 1996; Pilla et al. 1997a,b).

A bound ionic oscillator in a static magnetic field will precess at the Larmor frequency in the plane perpendicular to the applied field. This motion will persist in superposition with thermal forces, until thermal forces eventually eject the oscillator from a binding site. The threshold for Larmor precession model is determined only by the bound lifetime of the charged oscillator, allowing extremely weak magnetic fields to affect its dynamics. It should be taken into account, that when an ion is approaching the binding site, the molecular cleft is already occupied with water molecules. Therefore, the ion must compete with the water molecules. The geometry of the binding site can create a locally hydrophobic region, from which water molecules could be repelled. Weak static magnetic fields have been reported to accelerate Ca/CaM dependent myosin light chain kinase (MLCK) and protein kinase C (PKC) dependent processes up to twofold (Markov and Pilla 1994a).

The further development of this approach leads to the dynamical systems model which assumes the ion binding as a dynamical process wherein the particle has two energetically stable points separated by a few kT (double potential well), either bound in the molecular cleft, or unbound in the plane of closest approach to the hydrated surface (Helmholtz plane) at the electrified interface between the molecular cleft and its aqueous environment. Ion binding/dissociation is treated as the process of hopping between these two states driven by thermal noise and EMF effects are measured by modulation of the ratio of time bound (in the molecular cleft) to time unbound (in the Helmholtz plane) (Pilla et al. 1997).

This dynamical system uses the thermal noise as the driving force for ion binding and dissociation. The external force could modulate the relative depth of the wells thereby affecting the ratio of time bound to time unbound and thus the kinetics of the binding process. A weak magnetic field can indirectly affect the double well, which, in turn, modulates the ratio of time bound to time unbound and therefore reaction rate (Pilla et al. 1997).

The biophysical dogma prevailing until the late 1980s and lingering to this day is that, unless the amplitude and frequencies of an applied electric field were sufficient to trigger membrane alterations, to produce tissue heating or to move an ion along a field gradient, there could be no effect. This was a serious obstacle in the search for

biological mechanisms and therapeutic applications of weak EMF signals.

The underlying problem for any model of biophysical mechanism of weak EMF bioeffects relates to the signal detection at the molecular/cellular/tissue target in the presence of thermal noise, i.e., signal to thermal noise ratio (SNR).

Clinical experience, as well as numerous animal and in vitro studies, suggest the initial conditions of the EMF-sensitive target pathway determine whether a physiologically meaningful bioeffect could be achieved. For example, when broken bone received treatment with PEMF, the surrounding soft tissues receive the same dose as the fracture site, but physiologically important response occurs only in the injured bone tissue, while changes in the soft tissue have not been observed.

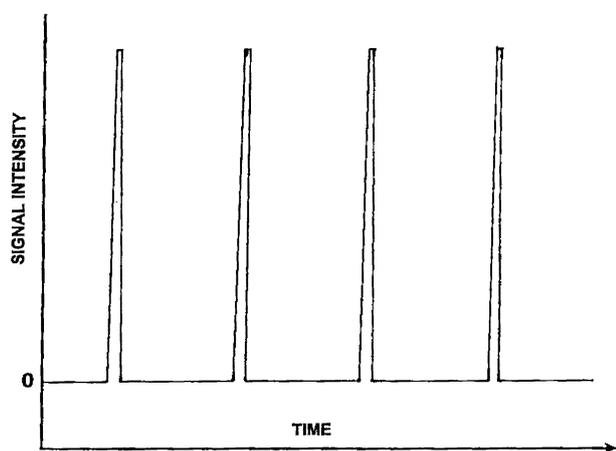
This is crucially important behavior, indicating that magnetic fields are more effective when the tissue is out of equilibrium. Therefore, the experiments with healthy volunteers are not always indicative for the potential response of patients who are victims of injury or disease. The healthy organism has much larger compensational ability than the diseased organism, which in turn would reduce the manifestation of the response.

Support for that notion comes from a study of Jurkat cells in which the state of the cell was found to be important in regard to the response of tissues to magnetic fields: normal T-lymphocytes neglect the applied PEMF, while being stimulated by other factors. Furthermore, the response of lymphocytes to magnetic fields clearly shows a dependence on the stimulation with other factors. In other words, it might be approximated with pendulum effect—the larger is the deviation from equilibrium, the stronger is the response (Nindl et al. 2002; Markov et al. 2006). For example, Nindl has demonstrated, in an in vitro study, that the initial conditions of lymphocytes are important in terms of the biological effects of those cells to magnetic fields.

## 6 The future

Even with the large variety of devices and signals in use for PEMF therapy, some general categories have been identified as more promising for the future development of the magnetic field therapy. It appears that semi sinewaves are more effective compared to continuous sine waves.

This approach is based on rectification of the continuous sinusoidal signal, described earlier. It is too preliminary to generalize, but the future research should clarify the importance of the short DC component between the consecutive semi sinewaves (Fig. 2). In an unpublished study, we have found that the duration of this DC component is



**Fig. 7** Some therapeutic modalities use monophasic pulsed (both with low and high frequency components) with different duty cycles

associated with different biological response in several outcomes Fig. 7, 8.

There are at least two different approaches for utilization of these signals. One relies on constructing an elliptical or spherical coil which could be moved around the patient body (Williams et al. 2001) and the other, applies the magnetic field on the upper or lower limbs, assuming that the results appear following systemic effects when the benefit is obtained at site distant from the site of application (Erickson et al. 2004).

Living in the era of computers, we should expect that the advantages of powerful computer technologies should be implemented in designing new magnetotherapeutical devices. At first, it should be the computerized control of the signal and maintenance of the parameters of the signal during the whole treatment session. Next, inclusion of user-friendly software packages with prerecorded programs, as well as with the ability to modify programs depending the patient needs. With appropriate sensors, the feedback information could be recorded and used during the course of therapy. Last, but not least, is the possibility to store the data for the treatment of individuals in a large database and further analyze the cohort of data for particular study or disease.

One of the most promising PEMF units available now worldwide is the Curatron system, designed and distributed by Curatronic Ltd. (Israel). The Curatron system generates a sinusoidal dual rectified waveform, subjected to Fast Fourier Transformation. This way the signal contains at a given time only one frequency component, resulting in a single peak at the frequency of the wave. Gating of the above waveform with a precise time window creates the pulsing frequency. The process of creating the pulse waveform, pulsing frequency, zero crossing, timing and impulse intensity is completely software controlled by the built-in computer (<http://www.curatron.com>).

By utilizing the precise computer-controlled timing for gating of the time window, responsible for the actual pulse frequency, the maximum utilization of the energy contents of the modulated sinusoidal signal is obtained. Very fast pulse rise time guarantees maximum electromagnetic energy transfer deep inside the tissue and cells, explaining the high efficacy for the Curatron. The strength of the PEMF generated by the coil applicators is monitored and controlled by a laser-calibrated Hall-effect sensor.

By connecting the unit to a standard Personal Computer (PC) a large database with readily pre-programmed therapy, protocols becomes available. Thus, the specially designed software package takes full control of the Curatron unit and all therapy parameters are under direct command and control of the PC program.

Therapy setting can be selected from a database, which contains an extensive list of preprogrammed treatment protocols, applicable for various diseases. Besides the pre-programmed protocols the therapist can easily compile his own therapy protocols and save it in the database for future use. The complete program runs fully automatic in sequence, according to the corresponding frequencies and intensities for each stage, during the total treatment time of each session. The inventors of Curatron assume that the automatic parameters change is important to avoid adaptation of the body to repeated stimulus. As an example, the therapy program developed for osteoporosis monitors the bone density and the bone densitometry values and scores are used for calculating automatically the optimal therapy parameters for each individual patient.

**Fig. 8** Curatron therapeutic system



## 7 Conclusions

The author strongly believes that a lot of work remains to be done in designing both technology and methodology of application of magnetotherapeutic devices. One of the very important issues that engineers and biophysicists neglect, is the frequency spectrum of the signal. At any PEMF, a large spectrum of harmonics, up to 3 kHz exists with the first harmonic usually having the amplitude close to 20% of the amplitude of basic signal. In that aspect, the computerized system, offered and already in use, by Curatron is of great importance. The computer technology allows a collection of feedback information, analysis and monitoring of the signal during the entire treatment session and opportunities for Fourier analysis of the signal during the use. Shortly, computer link to PEMF is the future of the therapy with PEMF.

**Acknowledgment** The author express his deep gratitude to Dr. A.R. Liboff for his kind permission to use figures from his excellent article published in “Bioelectromagnetic Medicine”

## References

- Adey, W. R. (1986). The sequence and energetics of cell membrane transducing coupling to intracellular enzyme systems. *Bioelectrochem Bioenergetics*, *15*, 447–456.
- Adey, W. R. (2004). Potential therapeutic application of nonthermal electromagnetic fields: Ensemble organization of cells in tissue as a factor in biological tissue sensing. In P. J. Rosch, & M. S. Markov (Eds.), *Bioelectromagnetic medicine* (pp. 1–15). New York: Marcel Dekker.
- Bassett, C. A. L., Pawluk, R. J., & Pilla, A. A. (1974). Acceleration of fracture repair by electromagnetic fields. *Annals of the New York Academy of Sciences*, *238*, 242–262.
- Bassett, C. A. L., Pilla, A. A., & Pawluk, R. (1977). A non-surgical salvage of surgically-resistant pseudoarthroses and non-unions by pulsing electromagnetic fields. *Clinical Orthopaedics*, *124*, 117–131.
- Bental, R. H. C. (1986). Low-level pulsed radiofrequency fields and the treatment of soft-tissue injuries. *Bioelectrochem Bioenergetics*, *16*, 531–548.
- Blackman, C. F., Blanchard, J. P., Benane, S. G., & House, D. E. (1995). The ion parametric resonance model predicts magnetic field parameters that affect nerve cells. *Federation of American Societies for Experimental Biology Journal*, *9*, 547–551.
- Blanchard, J. P., & Blackman, C. F. (1994). Clarification and application of an ion parametric resonance model for magnetic field interactions with biological systems. *Bioelectromagnetics*, *15*, 217–238.
- Bianco, B., & Chiabrera, A. (1992). From the Langevin-Lorentz to the Zeeman model of electromagnetic effects on ligand-receptor binding. *Bioelectrochem Bioenergetics*, *28*, 355–365.
- Canaday, D. J., & Lee, R. C. (1991). Scientific basis for clinical applications of electric fields in soft-tissue repair. In C. T. Brighton, & S.R. Pollack (Eds.), *Electromagnetics in Biology and Medicine* (pp. 275–291). San Francisco Press Inc.
- Canedo-Dorantes, L., Garcia-Cantu, R., Barrera, R., Mendez-Ramirez, I., Navarro, V. H., & Serrano, G. (2002). Healing of chronic arterial and venous leg ulcers with systemic electromagnetic fields. *Archives of Medical Research*, *33*, 281–289.
- Comorosan, S., Vasilco, R., Arghiropol, M., Paslaru, L., Jianu, V., & Stelea, S. (1993). The effect of Diapulse therapy on the healing of decubitus ulcer. *Romanian Journal of Physiology*, *30*, 41–45.
- Edmonds, D. T. (1993). Larmor precession as a mechanism for the detection of static and alternating magnetic fields. *Bioelectrochemistry and Bioenergetics*, *30*, 3–12.
- Engstrom, S. (1996). Dynamic properties of Lednev’s parametric resonance mechanism. *Bioelectromagnetics*, *17*, 58–70.
- Engstrom, S., Markov, M. S., McLean, M. J., Holcomb, R. R., & Markov, J. M. (2002). Effects of non-uniform static magnetic fields on the rate of myosin phosphorylation. *Bioelectromagnetics*, *23*, 475–479.
- Ericsson, A. D., Hazlewood, C. F., Markov, M. S., & Crawford, F. (2004). Specific Biochemical changes in circulating lymphocytes following acute ablation of symptoms in Reflex Sympathetic Dystrophy (RSD): A pilot study. In P. Kostarakis (Ed.), *Proceedings of 3rd international workshop on biological effects of EMF* (pp. 683–688). Kos, Greece, October 4–8, 2004, ISBN 960-233-151-8.
- Fitzsimmons, R. J., Ryaby, J. T., Magee, F. P., & Baylink, D. J. (1994). Combined magnetic fields increase net calcium flux in bone cells. *Calcified Tissue International*, *55*, 376–380.
- Foley-Nolan, D., Barry, C., Coughlan, R. J., O’Connor, P., Roden, D. (1990) Pulsed high frequency (27 MHz) Electromagnetic therapy for persistent neck pain: a double blind placebo-controlled study of 20 patients. *Orthopedics*, *13*, 445–451.
- Gardner, S. E., Frantz, R. A., & Schmidt, F. L. (1999). Effect of electrical stimulation on chronic wound healing: A meta-analysis. *Wound Repair and Regeneration*, *7*, 495–503.
- Ginsburg, A. J. (1934). Ultrashort radio waves as a therapeutic agent. *Medical Record*, *19*, 1–8.
- Hazlewood, C. F., & Markov, M. S. (2006). Magnetic fields for relief of myofascial and/or low back pain through trigger points. In P. Kostarakis (Ed.), *Proceedings of Forth International Workshop Biological effects of electromagnetic fields* (pp. 475–483). Crete 16–20 October 2006, ISBN# 960-233-172-0.
- Ieran, M., Zaffuto, S., Bagnacani, M., Annovi, M., Moratti, A., & Cadossi, R. (1990). Effect of low frequency electromagnetic fields on skin ulcers of venous origin in humans: a double blind study. *Journal of Orthopaedic Research*, *8*, 276–282.
- Itoh, M., Montemayor, J. S., Jr., Matsumoto, E., Eason, A., Lee, M. H., & Folk, F. S. (1991). Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). *Decubitus*, *4*, 24–25, 29–34.
- Kotnik, T., & Miklavcic, D. (2006). Theoretical analysis of voltage inducement on organic molecules. In P. Kostarakis (Ed.), *Proceedings of forth international workshop biological effects of electromagnetic fields* (pp. 217–226). Crete 16–20 October 2006, ISBN# 960-233-172-0.
- Lee, R. C., Canaday, D. J., & Doong, H. (1993). A review of the biophysical basis for the clinical application of electric fields in soft-tissue repair. *The Journal of Burn Care and Rehabilitation*, *14*, 319–335.
- Lednev, V. V. (1991). Possible mechanism for the influence of weak magnetic fields on biological systems. *Bioelectromagnetics*, *12*, 71–75.
- Liboff, A. R. (1985). Cyclotron resonance in membrane transport. In A. Chiabrera, C. Nicolini, & H. P. Schwan (Eds.), *Interactions between in interactions between electromagnetic fields and cells* (pp. 281–396). New York: Plenum Press.
- Liboff, A. F., Fozek, R. J., Sherman, M. L., McLeod B. R., & Smith, S. D. (1987). Ca<sup>2+</sup>-45 cyclotron resonance in human lymphocytes. *Journal of Bioelectricity*, *6*, 13–22.

- Liboff, A. R., Cherng, S., Jenrow, K. A., & Bull, A. (2003). Calmodulin-dependent cyclic nucleotide phosphodiesterase activity is altered by 20 mT magnetostatic fields. *Bioelectromagnetics*, *24*, 32–38.
- Liboff, A. R. (2004). Signal shapes in electromagnetic therapies: A primer. In P. J. Rosch & M. S. Markov (Eds.), *Bioelectromagnetic medicine* (pp. 17–37). NY: Marcel Dekker.
- Liburdy, R. P., & Yost, M. G. (1993). Time-varying and static magnetic fields act in combination to alter calcium signal transduction in the lymphocyte. In M. Blank (Ed.), *Electricity and magnetism in biology and medicine* (pp. 331–334). San Francisco Press.
- Markov, M. S., & Pilla, A. A. (1993). Ambient range sinusoidal and DC magnetic fields affect myosin phosphorylation in a cell-free preparation. In M. Blank (Ed.), *Electricity and magnetism in biology and medicine* (pp. 323–327). San Francisco Press.
- Markov, M. S., Ryaby, J. T., Kaufman, J. J., & Pilla, A. A. (1992). Extremely weak AC and DC magnetic field significantly affect myosin phosphorylation. In M. J. Allen, S. F. Cleary, A. E. Sowers, & D. D. Shillady (Eds.), *Charge and field effects in biosystems-3* (pp. 225–230). Boston: Birkhauser.
- Markov, M. S., Wang, S., & Pilla, A. A. (1993). Effects of weak low frequency sinusoidal and DC magnetic fields on myosin phosphorylation in a cell-free preparation. *Bioelectrochem Bioenergetics*, *30*, 119–125.
- Markov, M. S., Muehsam, D. J., & Pilla, A. A. (1994). Modulation of cell-free myosin phosphorylation with pulsed radio frequency electromagnetic fields. In M. J. Allen, S. F. Cleary, & A. E. Sowers (Eds.), *Charge and field effects in biosystems 4* (pp. 274–288). New Jersey: World Scientific.
- Markov, M. S., & Pilla, A. A. (1994a). Static magnetic field modulation of myosin phosphorylation: Calcium dependence in two enzyme preparations. *Bioelectrochem Bioenergetics*, *35*, 57–61.
- Markov, M. S., & Pilla, A. A. (1994b). Modulation of cell-free myosin light chain phosphorylation with weak low frequency and static magnetic fields. In A. Frey (Ed.), *On the nature of electromagnetic field interactions with biological systems* (pp. 127–141). R.G. Landes Co., Austin.
- Markov, M. S. (2002) How to go to magnetic field therapy? In P. Kostarakis (Ed.), *Proceedings of second international workshop of biological effects of electromagnetic fields* (pp. 7–11). Rhodes, Greece, October 2002, ISBN #960-86733-3-X. 5–15.
- Markov, M. S. (2004). Magnetic and electromagnetic field therapy: Basic principles of application for pain relief. In Rosch, P. J., & Markov, M. S. (Eds.), *Bioelectromagnetic medicine* (pp. 251–264). NY: Marcel Dekker.
- Markov, M. S. (2004a) Myosin light chain phosphorylation modification depending on magnetic fields I. *Theoretical Electromagnetic Biology and Medicine*, *23*, 55–74.
- Markov, M. S. (2004b). Myosin phosphorylation – a plausible tool for studying biological windows. Ross Adey Memorial Lecture. In P. Kostarakis (Ed.), *Proceedings of third international workshop on biological effects of EMF* (pp. 1–9). Kos, Greece, October 4–8, ISBN 960-233-151-8.
- Markov, M. S., Hazlewood, C. F., & Ericsson, A. D. (2004c). Systemic effect – a plausible explanation of the benefit of magnetic field therapy: A hypothesis. In P. Kostarakis (Ed.), *Proceedings of 3rd international workshop on biological effects of EMF* (pp. 673–682). Kos, Greece, October 4–8, 2004, ISBN 960-233-151-8.
- Markov M. S., Williams C. D., Cameron I. L., Hardman W. E., & Salvatore J. R. (2004d). Can magnetic field inhibit angiogenesis and tumor growth. In Rosch P. J., & Markov M. S. (Eds.), *Bioelectromagnetic medicine* (pp. 625–636). NY: Marcel Dekker.
- Markov, M. (2005). Biological windows: A tribute to Ross Adey. *The Environmentalist*, *25* (pp. 67–74).
- Mir, L. M. (2001). Therapeutic perspectives of in vivo cell electroporomeabilization. *Bioelectrochemistry*, *53*, 1–10.
- Muehsam, D. J., & Pilla, A. A. (1994). Weak magnetic field modulation of ion dynamics in a potential well: Mechanistic and thermal noise considerations. *Bioelectrochem Bioenergetics*, *35*, 71–79.
- Muehsam, D. J., & Pilla, A. A. (1994). Weak magnetic field modulation of ion dynamics in a potential well: Mechanistic and thermal noise considerations. *Bioelectrochem Bioenergetics*, *35*, 71–79.
- Muehsam, D. S., & Pilla, A. A. (1996). Lorentz approach to static magnetic field effects on bound ion dynamics and binding kinetics: Thermal noise considerations. *Bioelectromagnetics*, *17*, 89–99.
- Nindl, G., Johnson, M. T., Hughes, E. F., & Markov, M. S. (2002). Therapeutic electromagnetic field effects on normal and activated Jurkat cells-International Workshop of Biological effects of Electromagnetic fields. Rhodes, Greece, 7–11 October 2002, (pp. 167–173). ISBN #960-86733-3-X.
- Ojingwa, J. C., & Isseroff, R. R. (2003). Electrical stimulation of wound healing. *The Journal of Investigative Dermatology*, *121*, 1–12.
- Pennington, G. M., Danley, D. L., Sumko, M. H., et al. (1993). Pulsed, non-thermal, high frequency electromagnetic energy (Diapulse) in the treatment of grade I and grade II ankle sprains. *Military Medicine*, *158*, 101–104.
- Pilla, A. A. (1972). Electrochemical information and energy transfer in vivo. In *Proc. 7th IECEC* (pp. 761–764). Washington, D.C.: American Chemical Society.
- Pilla, A. A. (1974). Electrochemical information transfer at living cell membranes. *Annals of the New York Academy of Sciences*, *238*, 149–170.
- Pilla, A. A., Martin, D. E., Schuett, A. M., et al. (1996). Effect of pulsed radiofrequency therapy on edema from grades I and II ankle sprains: A placebo controlled, randomized, multi-site, double-blind clinical study. *Journal of Athletic Training*, *S31*, 53.
- Pilla, A. A., Muehsam, D. J., & Markov, M. S. (1997). A dynamical systems/Larmor precession model for weak magnetic field bioeffects: Ion-binding and orientation of bound water molecules. *Bioelectrochem Bioenergetics*, *43*, 239–249.
- Pilla, A. A. (2006). Mechanisms and therapeutic applications of time-varying and static magnetic fields. In F. Barnes & B. Greenebaum (Eds.), *Handbook of biological effects of electromagnetic fields* (3rd ed.). Boca Raton, FL: CRC Press.
- Rosch, P. J., & Markov, M. S. (2004). *Bioelectromagnetic Medicine*. NY: Marcel Dekker.
- Rushton, D. N. (2002). Electrical stimulation in the treatment of pain. *Disability and Rehabilitation*, *24*, 407–415.
- Ryaby, J. T. (1998). Clinical effects of electromagnetic and electric fields on fracture healing. *Clin Orthopaedics*, *355*(suppl), 205–215.
- Seaborne, D., Quirion-DeGirardi, C., & Rousseau, M. (1996). The treatment of pressure sores using pulsed electromagnetic energy (PEME). *Physiotherapy Canada*, *48*, 131–137.
- Shuvalova, L. A., Ostrovskaia, M. V., Sosunov, E. A., & Lednev, V. V. (1991). Weak magnetic field influence of the speed of calmodulin dependent phosphorylation of myosin in solution. *Dokladi Akademii Nauk USSR*, *217*, 227.
- Sluka, K. A., & Walsh, D. (2003). Transcutaneous electrical nerve stimulation: Basic science mechanisms and clinical effectiveness. *J Pain*, *4*, 109–121.
- Stiller, M. J., Pak, G. H., Pack, J. L., Thaler, S., Kenny, C., & Jondreau, L. (1992). A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers:

- A double-blind, placebo- controlled clinical trial. *The British Journal of Dermatology*, 127, 147–154.
- Todorov, N. (1982). *Magnetotherapy* (106 p). Sofia: Meditzina i Physcultura Publishing House.
- Vodovnik, L., & Karba, R. (1992). Treatment of chronic wounds by means of electric and electromagnetic fields. *Medical & Biological Engineering & Computing*, 30, 257–266.
- Williams, C. D., Markov, M. S., Hardman, W. E., & Cameron, I. L. (2001). Therapeutic electromagnetic field effects on angiogenesis and tumor growth. *Anticancer Research*, 21, (pp. 3887–3892).
- Wysocki, A. B. (1996). Wound fluids and the pathogenesis of chronic wounds. *J Wound Ostomy Care Nursing*, 23, 283–290.
- Zhadin, M. N. (1998). Combined action of static and alternating magnetic fields on ion motion in a macromolecule: Theoretical aspects. *Bioelectromagnetics*, 19, 279–292.
- Zhadin, M. N., & Fesenko, E. E. (1990). Ionic cyclotron resonance in biomolecules. *Biomed Sci*, 1, 245–250.
- Zizic, T., Hoffman, P., Holt, D., Hungerford, J., O'Dell, J., Jacobs, M, et al., (1995). The treatment of osteoarthritis of the knee with pulsed electrical stimulation. *The Journal of Rheumatology*, 22, 1757–1761.