Effects of electric and magnetic loadings on bone surface remodeling: a model modification and simulation

Anahita Fathi Kazerooni1,2, Mohsen Rabbani3,4,*, Mohammadreza Yazdchi5, Saeid Kasiri6 and Hamidreza Saligheh Rad1,2

1 Department of Biomedical Systems and Biophysics, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2 Research Center for Science and Technology in Medicine (RCSTIM), Emam Hospital, Tehran, Iran
3 Faculty of Biomedical Engineering, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran
4 Nanomedicine and Tissue Engineering Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5 Department of Biomedical Engineering, Faculty of Engineering, University of Isfahan, Isfahan, Iran
6 Trinity Center for Bioengineering, University of Dublin, College Green, Dublin 2, Ireland

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Introduction

Living bone senses the mechanical loads applied upon it, occurring, for example during walking and running and adapts its structure to the applied loadings to preserve its functionality. Bone adaption to the external forces is achieved by transducing the applied forces into bioelectrical or biochemical signals through a mechanism called ‘‘mechanotransduction’’, which induces cellular responses [17, 23]. In fact, bone is a porous fluid-filled solid. In response to mechanical strain, the pores of bone release their fluid content. When the strain is released, the pores can resorb the fluid. This way, the mechanical loading can be detected by bone cells [4].

The flowing fluid is electrically charged. On the compression side under applied strain, negative electric charges are induced, which initiate bone formation. On the other hand, when bone is under tension and positive charges are generated that cause bone absorption. The induced potentials are known as ‘‘strain generated potentials’’ [2, 14, 31]. Bone formation and absorption ultimately result in bone remodeling [5].

In addition through extensive researches, it has been shown that bone shows piezoelectric effects under applied mechanical loadings, due to its asymmetric structure [11, 18, 20]. It has also been indicated that bone generates electric currents and potentials when it fractures [9, 22]. Therefore, it was suggested that applied electric signals can stimulate bone growth [11].

Based on these findings, electric and electromagnetic bone growth stimulators were developed as rehabilitative tools for bone repair. In the experiments performed on the effectiveness of bone healing stimulators, different electric and magnetic fields with various amplitudes and waveforms have been employed including direct current (DC) as well as sinusoidal and pulsed fields. The two latter categories have been applied in wide ranges of frequencies and duty cycles [3, 13]. Experiments concerning the application of electric and electromagnetic bone healing devices have been reviewed by Pickering and Scammell [24]. Although vast trials have been performed, there is no standard protocol for bone treatment using these stimulators yet and this is an issue which has to be handled in bone healing devices.

A convenient way to resolve this problem is to use an appropriate bone model to approximate its responses to electrical and magnetic fields with various characteristics, such as waveforms, frequencies and pulse duty cycles. This paper...
intends to obtain the solution to the aforementioned problem using modeling approach.

Several mechanical models have been suggested for modeling the adaptive behavior of bone under applied strain [6, 12, 21]. One of the important models among the others is the theory of adaptive elasticity of bone internal remodeling proposed by Cowin and Hegedus in 1976 [6, 7, 16]. In this theory, bone is assumed to be a porous elastic solid, in which the porosity is modified through adaptation to mechanical strains. Then in 1979, Cowin and Van Buskirk proposed the model of bone surface remodeling [8]. In this model, bone matrix is assumed as a regular elastic solid on the interior and adaptive elastic solid on the surface. Through adaptation process, the mass is deposited or resorbed on the surface resulting in surface growth or absorption [8]. Qin et al. in 2005 [27] extended this model to include piezo-electro-magneto effect. They also suggested solutions for thermo-electro-magneto-elastic equations [27]. They presented these solutions for internal and surface remodeling of bone under various loadings [25]. In addition, they simulated the effects of static electric and magnetic loadings on bone internal and surface remodeling [25–27].

Although taking into account electric and magnetic terms in the equations of adaptive elasticity of bone remodeling has been a significant progress, this model is still not capable to completely describe the physiological behavior of living bone in response to long-term continuous loadings. It has been indicated that in response to long-term loading, bone cells reduce the effect of the stimulus in order to counterbalance the environmental forces, i.e., they become “desensitized” to further loadings. In other words, bone cells adapt themselves with the applied loadings through “desensitization” [29, 30, 33]. Therefore, it is essential to insert rest or recovery periods to allow desensitized bone cells to become sensitive again, or “resensitized”. Previous models have not taken this phenomenon into account.

This problem is properly addressed in this paper by modifying the theory of adaptive elasticity extended by Qin et al. for bone surface remodeling [25, 27], referred to as “thermo-piezoelectro-magneto-elastic model”. The modification of the bone model is accomplished by inserting recovery periods to meet the demand of cells to resensitize. Therefore, the model becomes compatible with this physiological phenomenon. Furthermore, instead of investigating the effects of static electric and magnetic loadings on bone model, as in previous modeling simulations [25], the response of the modified model to various frequencies is studied. Moreover, the modified model is explored to obtain the optimal frequency at which the bone remodeling approaches its maximum value. This issue has not been considered in previous studies.

In this paper, bone desensitization is inserted in the original model, as will be discussed in Materials and methods. In Results section, several electric and magnetic fields which have been utilized in bone healing stimulators including static, sinusoidal and pulsed waveforms are applied to the modified model, and the behavior of the model under different frequencies and pulse duty cycles will be investigated. Then, these results will be compared to the results obtained by the original model. Furthermore, based on the modified model, sub-optimal frequency and pulse duty cycles to induce highest osteogenic response are explored. Finally, comparisons will be presented in the Discussion.

Materials and methods

Electromagnetic equations for bone surface remodeling

Based on thermo-piezoelectro-magneto-elastic model of bone surface remodeling presented by Qin et al. [25, 27], and by assuming small strain, the speed of surface undergoing remodeling is linearly proportional to strain tensors, electric and magnetic fields as expressed in the following equation:

\[ U(n,\mathcal{Q}) = C_{ij}(n,\mathcal{Q})\varepsilon_{ij}(Q) + C_{ii}(n,\mathcal{Q}) + G_{ii}(H_i(Q)) \]

in which, \( U \) denotes speed of the surface undergoing remodeling normal to the surface at point \( Q \) on the surface. \( n \) is normal to the surface at point \( Q \). \( \varepsilon_{ij} \), \( E_i \), and \( H_i \) indicate the reference values of strain, electric and magnetic fields, respectively, where no remodeling occurs and \( C_{ij}, C_{ii}, G_i \) represent surface remodeling rate coefficients [25, 27].

Bone surface consists of two layers, endosteal and periossteal layers on the inner and outer sides of bone, respectively, where both undergo surface remodeling. The surface remodeling rate is characterized by the equations given below [27]:

\[ U_i = \frac{\partial a}{\partial t}, \quad U_p = \frac{\partial b}{\partial t} \]

in which \( U_i \) and \( U_p \) are the velocities normal to the inner and outer surfaces of the cylinder, respectively, in which “a” indicates inner radius (the side facing the endosteal) and “b” the outer radius (the side facing the periosteal envelope).

The thermo-electro-magneto-elastic equations for surface remodeling proposed by Qin et al. [27], and expressed in Eqs. (1) and (2), are employed as the bone model in this study. Analytical solution proposed in the same paper is used for solving the equations of the model. Also, the boundary conditions and numerical examples used by Qin et al. [27] are applied for simulating the model. Accordingly, bone is considered as a hollow circular cylinder subjected to several loadings, i.e., external temperature changes, semi-static axial load, external pressure, electric potential and magnetic field. In response to these loadings, bone undergoes remodeling process [25, 27].

For simplicity, here we assume that the applied electric and magnetic fields have no propagation in other tissues around the bone, such as muscle, fat and blood.

Model modification

Continuous application of electric or magnetic fields for stimulation of bone means that bone undergoes remodeling
every second of the simulation duration, but this is not the case in reality. It is shown that 8 h of recovery is necessary to restore mechano-sensitivity of adapted bone cells [29, 30]. The model presented in the previous section does not consider bone recovery (desensitization phenomenon).

Governing equation for recovery as fully explained by Robling et al. [30] is as follows:

\[
\text{Recovery}(\%) = 100(1-e^{-t/\tau})
\]

in which \(t\) is time between bouts (rest periods) and \(\tau\) is a time constant approximately equal to 6 h. Based on Eq. (3), 98% of bone mechano-sensitivity returns after 24 h of rest [29, 30]. Therefore, inserting rest times between electric and/or magnetic loadings is essential for bone to recover.

In order to modify the model, we considered a rest period of 12 h between loadings. By inserting this value in Eq. (3) and considering \(\tau\) equal to 6 h, 86% of the sensitivity returns, after the rest period is passed. In other words, bone cells become resensitized to further loadings by 86%. Therefore, by considering the ability of bone cells to remember the previous loadings, for the days after the first day, a coefficient value equal to 0.86 is multiplied by the results of Eq. (3).

Accordingly, each day, 86% of the bone cells are activated and potentiated to perform the remodeling with respect to the previous day, i.e., the bone remodeling is performed by a fraction of the previous day remodeling capability.

**Simulation**

To exclude the effects of changes of temperature and semi-static axial loads and the external pressure, these values are set to their threshold values, adopted from analytical data calculated by Qin et al. [27] as 30°C, 1500 N and 1 MPa, respectively. Accordingly, the initial values of the inner and outer radii of human bone (\(a_0, b_0\)) are assumed to be 25 mm and 35 mm, respectively. The values of coefficients as well as the amplitudes of electric and magnetic fields are adopted from the numerical examples used by Qin et al. [25, 27]. Because of unknown interaction between electric and magnetic fields during the surface remodeling, these effects are evaluated separately. Therefore, the value of the magnetic field is assumed to be zero when the electric field changes. While the magnetic field changes, the electric field value is set to zero. Therefore, the effects of superimposition are excluded.

In response to the strain, bone would enlarge its cross sectional area to counterbalance the applied strain [27]. The changes of cross sectional area due to different types of loadings are obtained to evaluate electric and magnetic loading effects on bone remodeling.

Here the effects of various electric and magnetic loadings on bone surface remodeling are investigated in three stages:

First, the static electric and magnetic fields with specific amplitudes, 30 Volts (V)/m and 0.1 Amperes (A)/m, for electric and magnetic fields, respectively, in the case of recovery consideration are compared with the case of no recovery.

Second, the effects of various frequencies of sinusoidal electric and magnetic fields on surface remodeling with and without recovery are investigated. Again the amplitudes are selected to be 30 V/m with 30 V/m bias and 0.1 A/m with 0.1 A/m bias for electric and magnetic loadings, respectively. In the experiments, it has been shown that electromagnetic devices are mostly used in the frequency range of 6–12 Hertz (Hz); however, 16 Hz is an optimal frequency for ion transport [32]. Based on this observation, we performed the simulation of sinusoidal fields in frequencies: 0, 0.5, 1, 5, 10 and 15 Hz. This type of loading is searched for the optimal phase delay and the resulting phase delay was obtained as 150°. This is done by testing the model with sinusoidal inputs with a specific amplitude and frequency but in various phase delays as in the function that follows:

\[
\text{Input} = \text{Amplitude}*\sin(\text{Freq}*t+\text{phase}) + \text{bias}
\]

Finally, the effects of pulsed fields are studied. By observing the response of the proposed model to the frequencies of previous simulation, we selected the optimal frequency to be 1 Hz for the pulses. Pulsed fields with various duty cycles as 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100% are selected to study the behavior of bone surface remodeling. Figure 1 illustrates an example of a pulse with 20% duty cycle. The amplitudes are chosen as 30 V/m for electric loading and 0.1 A/m for magnetic loading.

The commercial software, Simulink [Mathworks version 7.8 (2009a)] was used for simulations. The simulation time for all the loadings is 1000 days (≈2.8 years).

**Results**

The results of both electric and magnetic loadings are summarized in the following subsections. The following figures indicate that surface remodeling exhibits similar trends under both electric and magnetic loadings, so the results are restated in the same subsections. However, the effects of magnetic fields are drastically higher than those of electric fields.

**Static electric and magnet loadings**

Figure 2 shows the effects of static electric/magnetic loadings with and without recovery. It can be observed that in the case of recovery, the increase in the cross sectional area is lower than in the case of no recovery by approximately 21% for both electric and magnetic loadings. In fact, surface remodeling increases more smoothly by considering recovery period. In addition, the static loading with no recovery reaches steady state around 800th day. In contrast, the static loading with recovery reaches its steady state after 2000 days.

**Sinusoidal electric and magnetic loadings**

In Figure 3, the results of sinusoidal fields on bone surface remodeling in the model without recovery (square dots) are compared with the model with recovery consideration (diamond dots). Sinusoidal fields are applied in different frequencies, i.e., 0, 0.5, 1, 5, 10 and 15 Hz. In order to reduce data, given a specific frequency for each of the loading cases,
Figure 1  An example of pulsed signal with 20% duty cycle. The frequency of the pulse is 1 Hz. The pulse period and the concept of pulse duty cycle are shown in the Figure with double arrows. As it can be observed, the pulse duty cycle is the ON time of a pulse in its period.

Figure 2  The effects of (A) static electric loadings (30 V/m) and (B) static magnetic loadings (0.1 A/m) on the increase of bone cross sectional area during simulation time (1000 days) with considering two situations of recovery and no recovery. The final values reached in the models with and without recovery for electric loading are 1 and 1.27, and for magnetic loading in the models with and without recovery are 4.45 and 5.57, respectively.

Figure 3  The effects of (A) sinusoidal electric loadings (30 V/m and offset = 30 V/m) and (B) sinusoidal magnetic loadings (amplitude = 0.1 A/m and offset = 0.1 A/m) with various frequencies (0, 0.5, 1, 5, 10, 15 Hz) on the increase of bone cross sectional area with considering models with and without recovery.

the final value that surface remodeling reaches over the simulation duration is shown in the figure. It can be observed from the figure that in contrast to the modified model, the original model is not able to show the effects of electric and magnetic frequency variation. Moreover, the model with recovery has significant progress over the model without recovery in 1 Hz, in contrast to other frequencies. Therefore, the optimal frequency of the modified model is around 1 Hz.
Pulsed electric and magnetic loadings

In the previous work published by some of the authors of this paper [10], the effects of pulsed electric fields on cross sectional area were investigated. The results showed that by increasing the pulse width of the signal, the inner and outer diameters of bone increase, which also raises the rate of increase in cross sectional area.

From the outcomes obtained in the previous subsection, the optimal frequency of 1 Hz was chosen as the frequency of pulses and the impact of variation in pulse duty cycles on surface remodeling were examined. The results in recovery and no recovery situations are illustrated in Figure 4A and B. It can be inferred from the figure that in the absence of recovery, the rate of increase in cross sectional area increases linearly with the increasing duty cycles. By considering recovery in the model, the changes are higher than those of the model without recovery, up to 50% duty cycle. The rate of increase in cross sectional area in the model with recovery remains steady and saturates in response to duty cycles larger than 50%.

Discussion

In this paper, the thermo-electro-magneto-elastic model of bone surface remodeling was modified in order to include bone recovery which is a physiological phenomenon. The effects of various loadings on the surface remodeling were studied with and without recovery. It was indicated that the model with recovery in contrast to the model without recovery is capable of detecting variations of frequencies and adapting itself appropriately with the applied loadings. In addition, it can respond to various loading waveforms. The results of static and sinusoidal fields, as summarized below, are consistent with the results obtained by previous experimental trials. However, there has been no specific studies on comparing the effects of changing pulse durations in electric and magnetic fields. Therefore, the results of pulsed fields could not have been compared to experimental data.

Static electric and magnetic fields

It was shown that static electric/magnetic fields affect the model with recovery consideration in the same trend as the model without recovery, but the values are lower. In fact, surface remodeling reaches a steady state in the model with recovery in a longer duration than the model without recovery. This means that the responses in the model with recovery are slower than the model without recovery and further loading to a specific time point, i.e., approximately 2000th day causes the remodeling to improve. This is in agreement with the hypothesis stated by Spencer and Genever [31], which yields that bone cells can remember earlier periods of loading. Thus, responses produced by further loadings and those generated by the previous loadings are accumulated; therefore, the whole response is strengthened [31].

Sinusoidal electric and magnetic fields

It was demonstrated that surface remodeling under sinusoidal loading in the model with recovery demonstrates obvious progress over the model without recovery, since the model without recovery is not sensitive to the changes in frequency of loading. In experiments performed before, it has been shown that dynamic strains rather than static strains increase bone formation. Also, it has been confirmed that loading frequency and strain rate are important in determining the bone adaptation [19]. Therefore, results of the modified model are consistent with the experimental observations.

As it can be seen from Figure 3A and B, bone cross sectional area in frequencies lower than 0.5 Hz is slightly less than its value around frequencies higher than 0.5 Hz. In addition, in frequencies more than 2 Hz, more bone cross sectional area is induced in comparison with what is achieved in frequencies <1 Hz.

In the trials performed on the effects of various biomechanical loadings, it has been shown that these loadings have no effects on bone formation, unless it is applied at frequencies larger than 0.5 Hz [30]. Moreover, recent experiments have shown that when loading frequency surpasses 10 Hz, variation of the sensitivity of bone is small [30]. The results obtained in this paper are similar to these findings; however, in the modified model used here after 10 Hz, the value of bone cross sectional area slightly increases.

In addition to biomechanical data, experimental observations on the effects of Pulsed ElectroMagnetic Field (PEMF) stimulators demonstrate that chondrocyte in bone, responds to low frequencies of <15 Hz [32]. Stimulation of chondro-
genesis is one of the ways in which PEMF affects the early stages of bone repair. Therefore, PEMF technique can be used for treating osteoarthritis [1, 32]. As mentioned in Materials and methods, most of the PEMF devices are used in frequency range of 6–12 Hz for inducing osteogenic response, however, 16 Hz is an optimal frequency for ion transport [32]. The results of this study show that the modified model is sensitive to frequency of loading in the range of 0.5–15 Hz. However, this model has not been studied for the effects of electric and magnetic fields simultaneously, as in electromagnetic fields. Also, the original model and the recovery periods inserted in this work have been adopted from mechanical studies. Therefore, the results show more agreement with mechanical experiments.

As it was mentioned in the previous section, the simulated results of this paper demonstrate the maximum osteogenic response at 1 Hz. Levy (1974) indicated that a peak osteogenic response occurs at an electrical firing rate of 0.7 Hz [15]. To test this hypothesis, several implantable oscillators were used. Richez et al. observed that a firing rate of 0.5 Hz was more efficient than 0.1 Hz [28]. Thus, the outcome of the modified model (with recovery) demonstrated in Figure 3A and B is in agreement with experimental data.

Pulsed electric and magnetic fields

In both cases of electric and magnetic fields, it was shown that as the pulse width increases, the surface remodeling is enhanced. The saturation of pulsed fields after 50% of duty cycle demonstrates that there is no need to increase duty cycle to enhance bone formation, because the modified model cannot distinguish between duty cycles larger than 50%. This is related to the necessary time for resensitization. In other words, this modified model as well as its desensitization to the long-term loadings, shows sensitivity to shorter time durations and reaches a saturation model after 50% duty cycle.

In conclusion, the modified model for bone recovery is compatible with the experimental data regarding the sensitivity of model to the frequency variations. The original model did not indicate the importance of rest times required for bone resensitization which is crucial in healing procedure of bone fractures. In contrast, the modified model predicts the behavior of bone in response to various waveforms with various characteristics. The results are valuable to be employed in electromagnetic therapy of bone fractures.

However, the modified model needs to be verified based on real clinical data. Moreover, parameters of the model can be carefully optimized employing the same data. In addition, simulation of the model by considering electric and magnetic fields simultaneously as in electromagnetic field healing stimulators is proposed for future works.

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References


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