Modelling the Temporal Dynamics of Cortical Bone Adaptation to Mechanical Loading

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Summary

This study proposes a temporal model to predict bone formation rate (BFR) from cellular biomarkers, focusing on COL1A1 gene expression under mechanical loading. A novel model identifies key parameters influencing BFR, and a new approach is introduced to estimate instantaneous BFR from experimental data of COL1A1 gene expression and average BFR. The model bridges cellular mechanotransduction and bone adaptation, offering insights for exercise planning, sports medicine, and skeletal treatments.

Introduction

Bone adapts dynamically to mechanical stimuli through mechanotransduction, where osteocytes convert mechanical signals into biochemical responses [1]. While spatial models for bone formation exist, temporal predictions from cellular biomarkers are limited. This study develops a mathematical model using COL1A1 gene expression to predict instantaneous bone formation rate (BFR) over time, offering insights for optimizing skeletal health strategies [2].

Methods

Previous research has demonstrated that bone formation rate is directly proportional to the square root of dissipation energy density ($\sqrt{\phi_0}$) per loading cycle above a specific threshold and the square root of the number of cycles [1]. Additionally, studies indicate a delay (τ) of approximately 96 hours between mechanical loading and the initiation of new bone formation [3]. Based on these findings, we modelled the instantaneous BFR in the time domain as follows:

$$f(t) = \begin{cases} k\sqrt{\phi_0}(t-\tau)^n e^{-a(t-\tau)} & t \geq \tau \\ 0 & t < \tau \end{cases} \quad (1)$$

If the fluorochrome labels are administered at time t_1 and t_2, then the average BFR is given by:

$$g(t) = \frac{\int_{t_1}^{t_2} f(t)\,dt}{t_2 - t_1} \quad t_1 \leq t \leq t_2 \quad (2)$$

Roosa et al. [2] performed a time-sequenced loading experiment, applying daily axial mechanical loading to the ulnae of Lewis rats using an oscillating Haversine waveform (360 cycles at 2 Hz frequency with a peak load of 13 N) to assess the relative gene expression of COL1A1. Based on this, we hypothesise that the instantaneous bone formation rate (BFR) induced by external loading is directly proportional to the relative expression of COL1A1 but delayed by a dead time. The COL1A1 expression is thus given by:

$$h(t) = \begin{cases} k_1\sqrt{\phi_0}(t-\tau_1)^n e^{-a(t-\tau_1)} & t \geq \tau_1 \\ 0 & t < \tau_1 \end{cases} \quad (3)$$

Results and Discussion

The nonlinear curve fitting of the function h(t) in equation (3) to the experimental values in [2] obtained the following optimal parameters: $\tau_1 = 0$ days; $a = 0.3083$ per day; $n = 3.6712$; $k_1 = 2.12 \times 10^{-2}/\sqrt{\phi_0}$. The model COL1A1 expression has been compared to the experimental values, in Figure 1.

With τ (= 96 hours) and a known, the value of k can be found out from equation (2) by fitting it to the average BFR results given in [4], where t_1 and t_2 are respectively 5 days (120 hours) and 12 days (288 hours). The value of k was found to be $8.5013 \times 10^{-3}/\sqrt{\phi_0}$. The instantons BFR can now be predicted using equation (1), which has also been plotted in Figure 1.

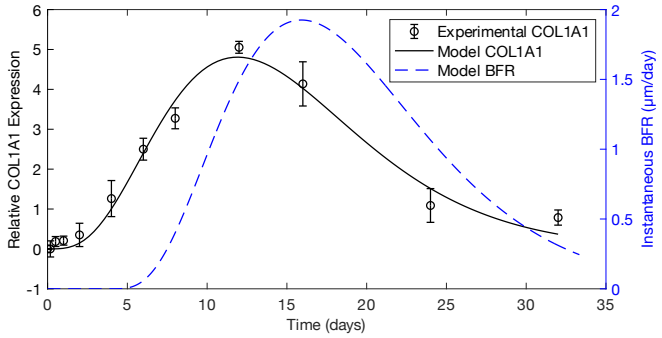

Figure 1: The relative expression of COL1A1 fitted by the model and compared with the experimental values. The predicted instantaneous BFR is also plotted.

Conclusions

The proposed model effectively predicts temporal bone formation rate from COL1A1 gene expression, offering insights into mechanotransduction and skeletal adaptation under mechanical loading.

References

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