Influence of Dynamical Load on Mechanical Features of Bone

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10. Kubátův podologický den

Outline

1. Motivation
   - The problem that we studied and previous work
2. Our Contribution
   - Analysis of the model
   - Modification of the model
   - Analysis of the modificated model
   - Results from the modificated model

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Dynamics is crucial for bone formation

Example

If neonate does not move around enough in uterus in prenatal age, his bones are much less evolved (high ratio of cartilage) and often deformation of joints can be seen.

Schematic description of bone remodeling

$$D_1 + D_2 \overset{k_1}{\rightleftarrows} D_3 + D_4 \tag{1.1}$$

$$D_3 + D_5 \overset{k_2}{\rightleftarrows} D_6 \tag{1.2}$$

$$D_2 + D_5 \overset{k_3}{\rightleftarrows} D_7 + D_8 \tag{1.3}$$

$$D_9 + D_7 \overset{k_4}{\rightleftarrows} D_{10} + D_{11} \tag{1.4}$$

$$D_{12} + D_{10} \overset{k_5}{\rightleftarrows} D_{13} + D_{14} \tag{1.5}$$

Reactions proceed in both ways, but $\rightarrow$ are much more probable.

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Outline

Transfering to mathematical description I

- change of concetration of chemical subst. in time:

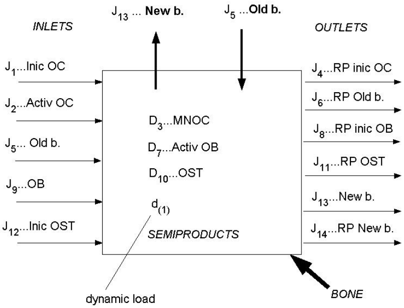
$$\dot{n}_j = \sum_{\rho=1}^{5} (\nu`_{\rho j} - \nu_{\rho j}) \cdot \omega_\rho \tag{2.1}$$

where $j = 1, 2, \ldots, 14$ and refers to chemical substance $D_1, D_2, \ldots, D_{14}$;
ω_ρ is rate of $(1.\rho)$ reaction which depends on dynamical load;

- affinity

$$\omega_\rho = k_\rho \mathcal{A}_\rho + l_{\rho v} d_{(1)}$$

Transfering to mathematical description II



Mathematical description of bone remodeling

$$
\begin{aligned}
\dot{N}_2 &= -\delta_1(\beta_1 + N_2 + N_7 + N_{10} + N_{13})N_2 - \\
&\quad -\delta_3 N_2 N_5 + \mathcal{J}_3 + \mathcal{J}_5 + \mathcal{D}_1 + \mathcal{D}_3 \\
\dot{N}_5 &= -(\alpha + N_5)N_5 - (\delta_3 - 1)N_2 N_5 + \mathcal{J}_5 + \mathcal{D}_3 + \mathcal{D}_2 \\
\dot{N}_7 &= \delta_3 N_2 N_5 - \delta_4 N_7(\beta_9 - N_{10} - N_{13}) - \mathcal{D}_3 + \mathcal{D}_4 \\
\dot{N}_{10} &= \delta_4 N_7(\beta_9 - N_{10} - N_{13}) - \delta_5 N_{10}(\beta_8 - N_{13}) - \mathcal{D}_4 + \mathcal{D}_5 \\
\dot{N}_{13} &= \delta_5 N_{10}(\beta_8 - N_{13}) - \mathcal{J}_{13} - \mathcal{D}_5
\end{aligned}
$$

Stationary solution='state of stabilization'

$$\overline{N}_5 = \frac{-\alpha + \sqrt{\alpha^2 - 4(\mathcal{J}_{13} - \mathcal{J}_5 - B - \mathcal{D}_2)}}{2}$$

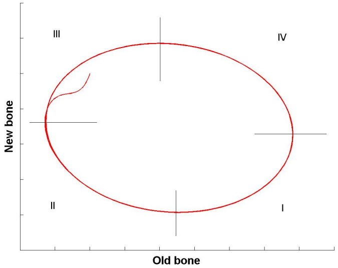
$$\overline{N}_2 = \frac{B}{\overline{N}_5}$$

$$\overline{N}_7 = \frac{-(\beta_9 + \beta_1 + \overline{N}_2 - \frac{-\mathcal{J}_{13}+\mathcal{D}_1+\mathcal{J}_3+\mathcal{J}_5}{\delta_1 \overline{N}_2)}}{2} + \\ + \frac{\sqrt{(\beta_9 + \beta_1 + \overline{N}_2 - \frac{-\mathcal{J}_{13}+\mathcal{D}_1+\mathcal{J}_3+\mathcal{J}_5}{\delta_1 \overline{N}_2)})^2 + 4\frac{\mathcal{D}_4+\mathcal{J}_{13}}{\delta_4}}}{2}$$

$$\overline{N}_{10} = \frac{-\beta_8 + \beta_9 - \frac{\mathcal{J}_{13}+\mathcal{D}_4}{\delta_4 \overline{N}_7} + \sqrt{(\beta_8 - \beta_9 + \frac{\mathcal{J}_{13}+\mathcal{D}_4}{\delta_4 \overline{N}_7})^2 + 4\frac{\mathcal{D}_5+\mathcal{J}_{13}}{\delta_5}}}{2}$$

$$\overline{N}_{13} = \frac{\beta_8 + \beta_9 - \frac{1}{\delta_4 \overline{N}_7} - \sqrt{(\beta_8 - \beta_9 + \frac{\mathcal{J}_{13}+\mathcal{D}_4}{\delta_4 \overline{N}_7})^2 + 4\frac{\mathcal{D}_5+\mathcal{J}_{13}}{\delta_5}}}{2}$$

Our visualization



Why?

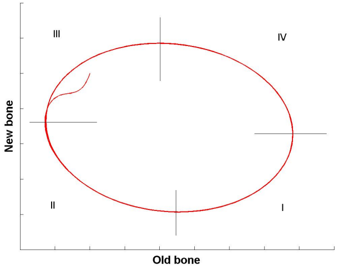
I resorbtion

II resorbtion and formation(calcification)

III formation(calcification) and changeover from New b. to Old b.

IV changeover from New b. to Old b.

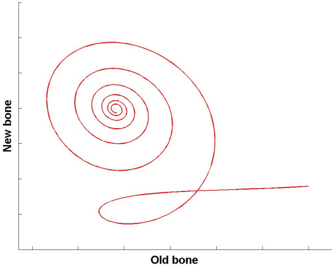
Our visualization



Why?

- I resorbtion
- II resorbtion and formation(calcification)
- III formation(calcification) and changeover from New b. to Old b.
- IV changeover from New b. to Old b.

Change in our visualization



Why?

- still describes reality
- can lead to suppression of osteoporosis

Demandingness

very complicated (much more, than finding periodical solution)

Real dynamical load

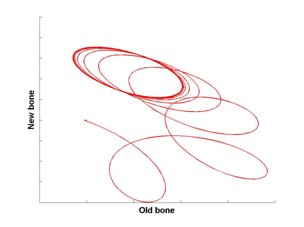
Idea

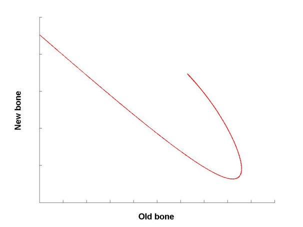
$$\mathcal{D}_i = A\sin(2\pi freq \cdot \tau)$$

Problem: determination of frequency

Solutions

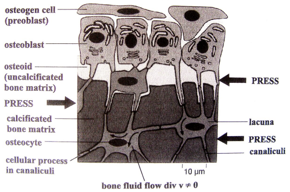
Two results





Time step transformation

Mechanical stimuli transfer



- microlevel $\sim 4.2 \cdot 10^{-7}$ sec.

$$\frac{2\pi}{\triangle\ t} 10^{-5} = 1.5 \cdot 10^{3}$$

$$\Downarrow$$

$$\triangle\ t = 4.2 \cdot 10^{-7}$$

-determined by corticalis bone structure

- macrolevel $\sim$ 25 days

$$\frac{\triangle\ n_5}{n_{50}} = -k_{+2} n_3 \triangle t$$

-determined by model

Simplification: constant density of osteoid, old and new bone

$$
\begin{aligned}
\dot{N}_2 &= -\delta_1(\beta_1 + N_2 + N_7 + N_{10} + N_{13})N_2 - \\
&\quad -\delta_3 N_2 N_5 + \mathcal{J}_3 + \mathcal{J}_5 + \mathcal{D}_1 + \mathcal{D}_3 \\
\dot{N}_5 &= 0 \\
\dot{N}_7 &= \delta_3 N_2 N_5 - \delta_4 N_7(\beta_9 - N_{10} - N_{13}) - \mathcal{D}_3 + \mathcal{D}_4 \\
\dot{N}_{10} &= 0 \\
\dot{N}_{13} &= 0
\end{aligned}
$$

Outline

Modification of model-Model II

$$D_1 + D_2 \overset{k_1}{\rightleftarrows} D_3 + D_4 \tag{1.1}$$

$$D_3 + D_5 \overset{k_2}{\rightleftarrows} D_6 + D_7 \tag{1.2}$$

$$D_7 + D_5 \overset{k_3}{\rightleftarrows} D_8 + D_9 \tag{1.3}$$

$$D_{10} + D_8 \overset{k_4}{\rightleftarrows} D_{11} + D_{12} \tag{1.4}$$

$$D_{13} + D_{11} \overset{k_5}{\rightleftarrows} D_{14} + D_{15} \tag{1.5}$$

Reason: in nature is everything well utilized (little of waste)

Outline

Mathematical description of Model II

$$
\begin{aligned}
\dot{N}_2 &= -\delta_1(\beta_1 + N_2)N_2 + \mathcal{J}_3 + \mathcal{J}_{14} - \mathcal{D}_1 \\
\dot{N}_5 &= -(\beta_3 - N_2 + N_5 + N_8 + N_{11} + N_{14})N_5 - \\
&\quad -\delta_3(\beta_7 - N_5 - 2(N_8 + N_{11} + N_{14}))N_5 + 2\mathcal{J}_{14} - \mathcal{D}_2 - \mathcal{D}_3 \\
\dot{N}_8 &= \delta_3(\beta_7 - N_5 - 2(N_8 + N_{11} + N_{14}))N_5 - \\
&\quad -\delta_4(\beta_{10} - N_{11} - N_{14})N_8 + \mathcal{D}_3 - \mathcal{D}_4 \\
\dot{N}_{11} &= \delta_4(\beta_{10} - N_{11} - N_{14})N_8 - \delta_5(\beta_{13} - N_{14})N_{11} + \mathcal{D}_4 - \mathcal{D}_5 \\
\dot{N}_{14} &= \delta_5(\beta_{13} - N_{14})N_{11} - \mathcal{J}_{13} + \mathcal{D}_5
\end{aligned}
$$

Stationary solution of Model II

$$\overline{N}_2 = \frac{-\beta_1 + \sqrt{\beta_1^2 + 4\frac{-\mathcal{D}_1+\mathcal{J}_3+\mathcal{J}_{14}}{\delta_1}}}{2}$$

$$\overline{N}_5 = \frac{-(\beta_7 + 2\beta_3 - 2\overline{N}_2) + \sqrt{(\beta_7 + 2\beta_3 - 2\overline{N}_2)^2 + 4(\frac{\mathcal{J}_{14}-\mathcal{D}_3}{\delta_3} + 2(\mathcal{J}_{14} - \mathcal{D}_2))}}{2}$$

$$\overline{N}_8 = \frac{-(\beta_{10} + \frac{1}{2}(\overline{N}_5 - \beta_7 + \frac{\mathcal{J}_{14}-\mathcal{D}_3}{\delta_3\overline{N}_5}))}{2} + \\ + \frac{\sqrt{(\beta_{10} + \frac{1}{2}(\overline{N}_5 - \beta_7 + \frac{\mathcal{J}_{14}-\mathcal{D}_3}{\delta_3\overline{N}_5}))^2 + 4\frac{\mathcal{J}_{14}-\mathcal{D}_4}{\delta_4}}}{2}$$

$$\overline{N}_{11} = \frac{-(\beta_{13} - \beta_{10} + \frac{\mathcal{J}_{14}-\mathcal{D}_4}{\delta_4\overline{N}_8}) + \sqrt{(\beta_{13} - \beta_{10} + \frac{\mathcal{J}_{14}-\mathcal{D}_4}{\delta_4\overline{N}_8})^2 + 4\frac{\mathcal{J}_{14}-\mathcal{D}_5}{\delta_5}}}{2}$$

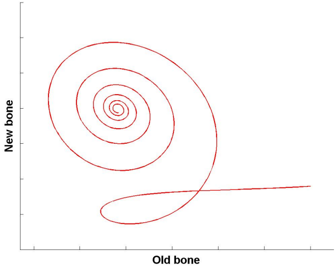
$$\overline{N}_{14} = -\overline{N}_{11} + \beta_{10} - \frac{\mathcal{J}_{14} - \mathcal{D}_4}{\delta_4\overline{N}_8}$$

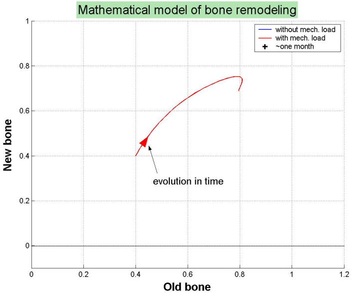
Finding periodical solution of Model II

Theorem

There is no positive periodical solution of Model II with any set of parameters.

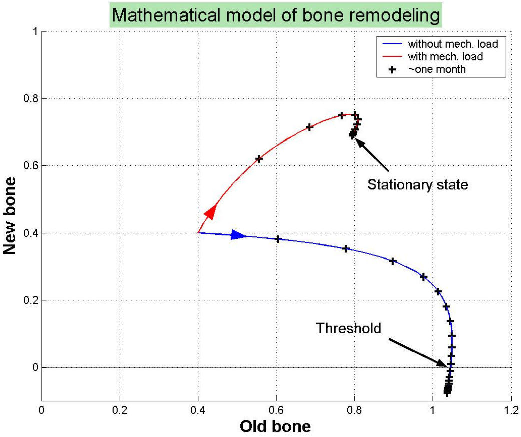
Our visualization with Model II



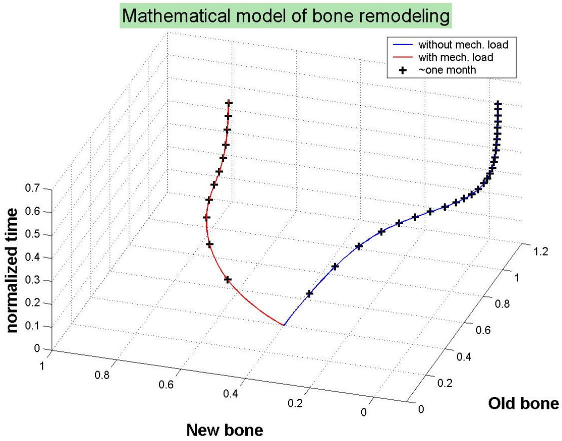


Outline

Influence of mechanical loading on bone remodeling I.
D(1)=2.44, D(2)=1.26, D(3)=5.85, D(4)=1.30, D(5)=5.68

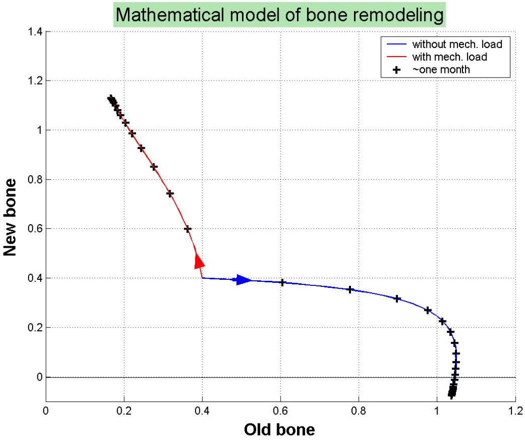


Influence of mechanical loading on bone remodeling I.
Time evolution



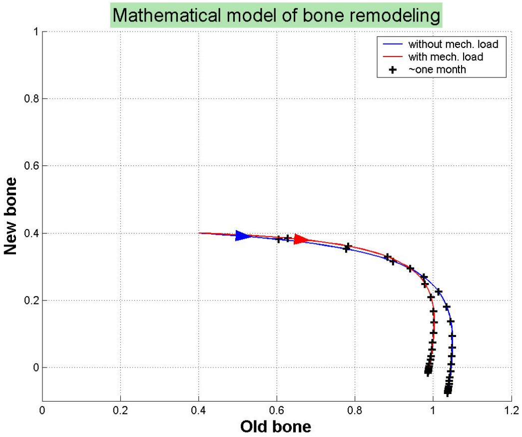
Influence of mechanical loading on bone remodeling II

D(1)=5, D(2)=5, D(3)=5, D(4)=5, D(5)=5



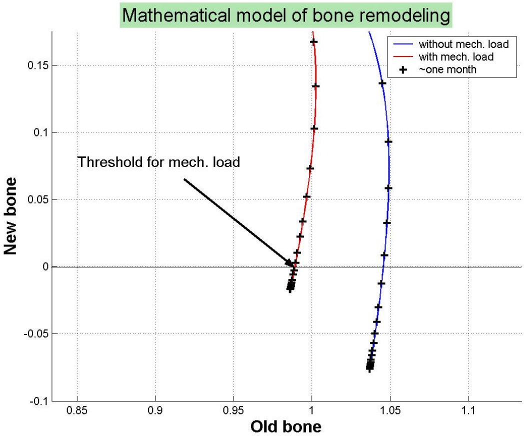
Limits of mechanical loading - lower limit

D(1)=0.3, D(2)=0.3, D(3)=0.3, D(4)=0.3, D(5)=0.3



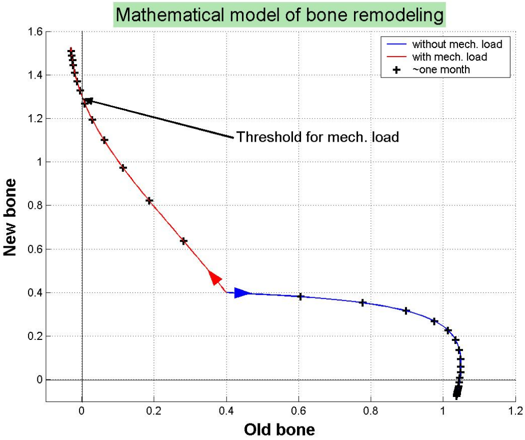
Limits of mechanical loading - lower limit

Zoomed critical area

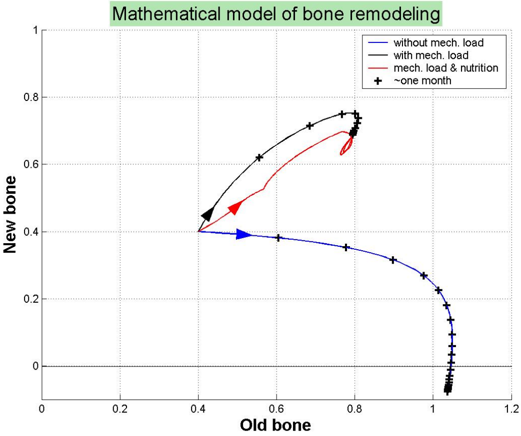


Limits of mechanical loading - upper limit

D(1)=6, D(2)=6, D(3)=6, D(4)=6, D(5)=6

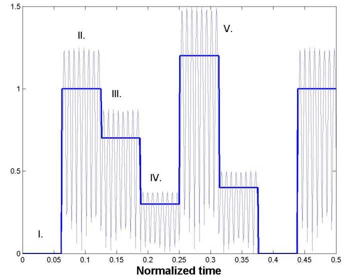


Influence of nutrition - changes during year

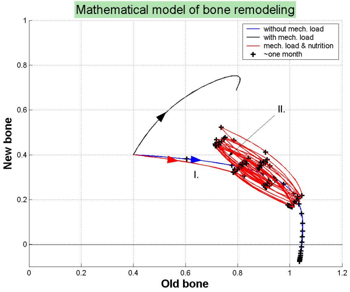


Approximation of reality of bone remodeling

Approximation of walking (generalization of dyn. load)



Approximation of reality of bone remodeling



Interpretation of previous pictures

Deliberation

- Still the same excercise and nutrition $\Rightarrow$ stationary state = equilibrium of bone resorbtion and formation
- 'Nutrition' may be influenced by chemical processes $\Rightarrow$ reality is much more complicated

Summary

- This model has many features that well corresponds to reality, but it is needed to examine this model in more detailed way
- Even here can be seen the importance of mechanical loading

- Outlook
  - Adjust parameters so that they corespond to real patients
  - Create another models with new ideas - still trying to find the limit cycle

Acknowledgement

Support

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