Bone Remodelling Induced by Dynamical Load - Biochemical Model

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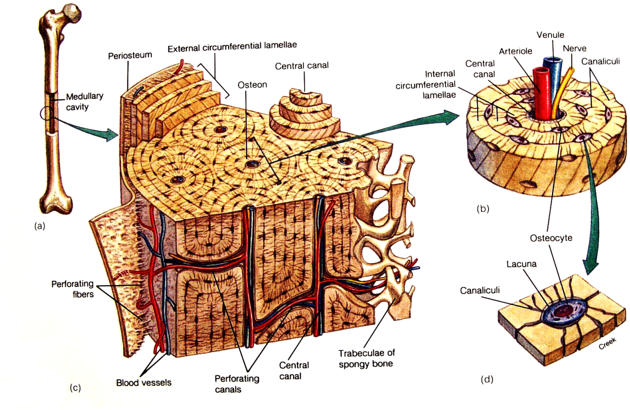
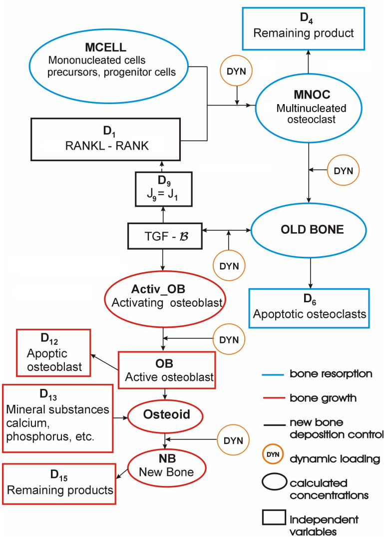
Bone and BR



Functions of BR in bone

- to keep bone alive
- to alter the shape of bone
- repair damages in bone tissue
- part of metabolism

Our model


D4
Remaining product
MCELL
Mononucleated cells
precursors, progenitor cells
DYN
MNOC
Multinucleated
osteoclast
D1
RANKL - RANK
DYN
D9
J9 = J1
TGF - B
OLD BONE
DYN
Activ_OB
Activating osteoblast
D6
Apoptotic osteoclasts
D12
Apoptic
osteoblast
DYN
OB
Active osteoblast
bone resorption
bone growth
D13
Mineral substances
calcium,
phosphorus, etc.
Osteoid
new bone
deposition control
DYN
NB
New Bone
DYN
dynamic loading
D15
Remaining products
calculated
concentrations
independent
variables

Simplified model

$$D_1 + MCELL \overset{k_{\pm 1}}{\rightleftarrows} MNOC + D_4 \quad (1)$$

$$MNOC + Old\_B \overset{k_{\pm 2}}{\rightleftarrows} D_6 + D_7 \quad (2)$$

$$D_7 + Old\_B \overset{k_{\pm 3}}{\rightleftarrows} Activ\_OB + D_9 \quad (3)$$

$$Activ\_OB + OB \overset{k_{\pm 4}}{\rightleftarrows} Osteoid + D_{12} \quad (4)$$

$$D_{13} + Osteoid \overset{k_{\pm 5}}{\rightleftarrows} New\_B + D_{15} \quad (5)$$

Mathematical model & Biochemical condition

$$\dot{\overline{MCELL}} = -\delta_1(\beta_1 + MCELL)MCELL + \mathcal{J}_3 + \mathcal{J}_{14} - \mathcal{D}_1 \tag{6}$$

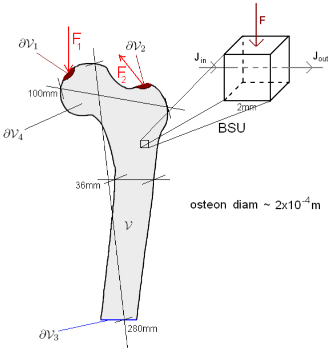
$$\begin{aligned}\dot{\overline{Old\_B}} = &-(\beta_3 - MCELL + Old\_B + Activ\_OB + Osteoid + New\_B)Old\_B - \\ &-\delta_3\left(\beta_7 - Old\_B - 2(Activ\_OB + Osteoid + New\_B)\right)Old\_B + \\ &+ 2\mathcal{J}_{14} - \mathcal{D}_2 - \mathcal{D}_3\end{aligned} \tag{7}$$

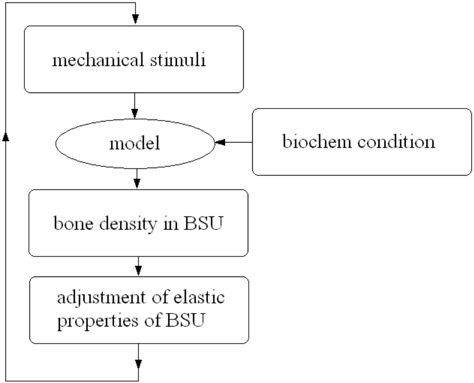
$$\begin{aligned}\dot{\overline{Activ\_OB}} = &\,\delta_3\left(\beta_7 - Old\_B - 2(Activ\_OB + Osteoid + New\_B)\right)Old\_B - \\ &-\delta_4(\beta_{10} - Osteoid - New\_B)Activ\_OB + \mathcal{D}_3 - \mathcal{D}_4\end{aligned} \tag{8}$$

$$\begin{aligned}\dot{\overline{Osteoid}} = &\,\delta_4(\beta_{10} - Osteoid - New\_B)Activ\_OB - \delta_5(\beta_{13} - New\_B)Osteoid + \\ &+ \mathcal{D}_4 - \mathcal{D}_5\end{aligned} \tag{9}$$

$$\dot{\overline{NewB}} = \delta_5(\beta_{13} - New\_B)Osteoid - \mathcal{J}_{14} + \mathcal{D}_5 \tag{10}$$

Algorithm

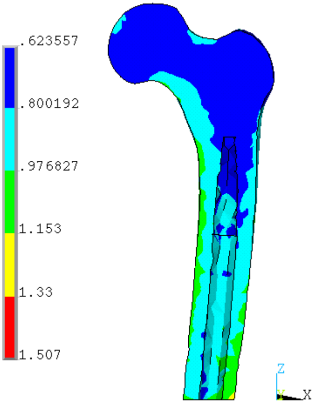

∂V1
F1
∂V2
F2
F
J in
J out
100mm
2mm
BSU
∂V4
36mm
osteon diam ~ 2x10^-4 m
V
∂V3
280mm


mechanical stimuli
model
biochem condition
bone density in BSU
adjustment of elastic properties of BSU

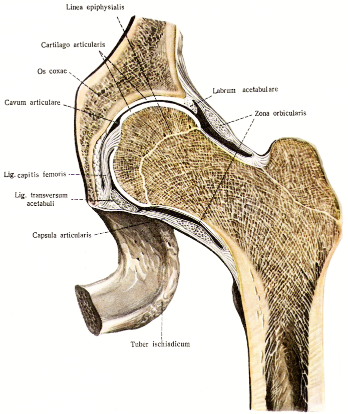
'Healthy person' $\sim$ 10 000 steps a day

Density distribution throughout the bone $E = c \cdot \rho^3$

Model simulation



Cut of femur and hip joint



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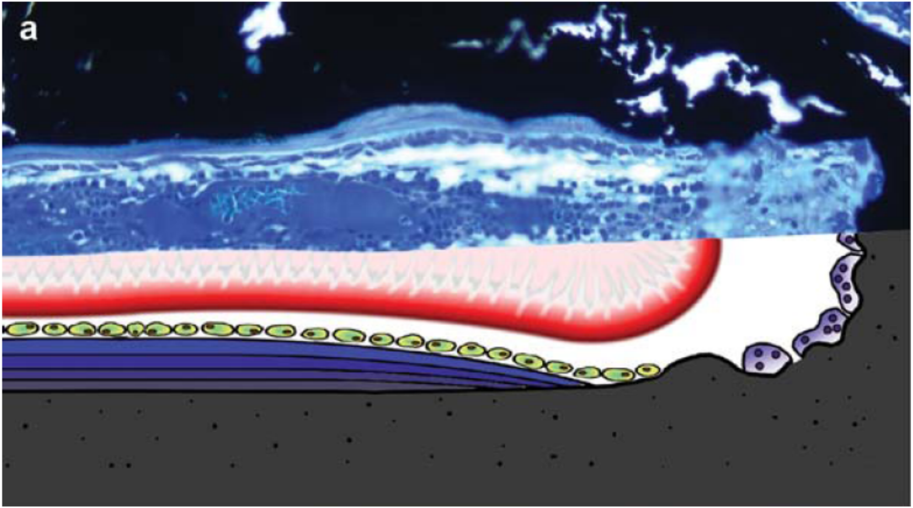
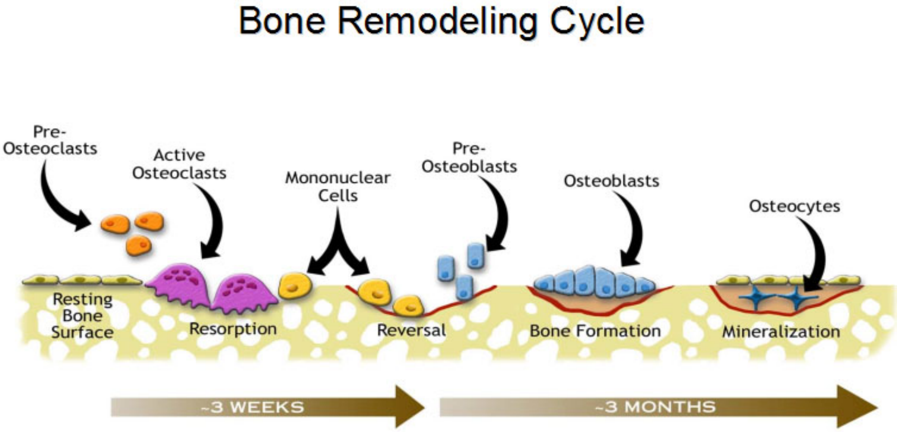
BR process

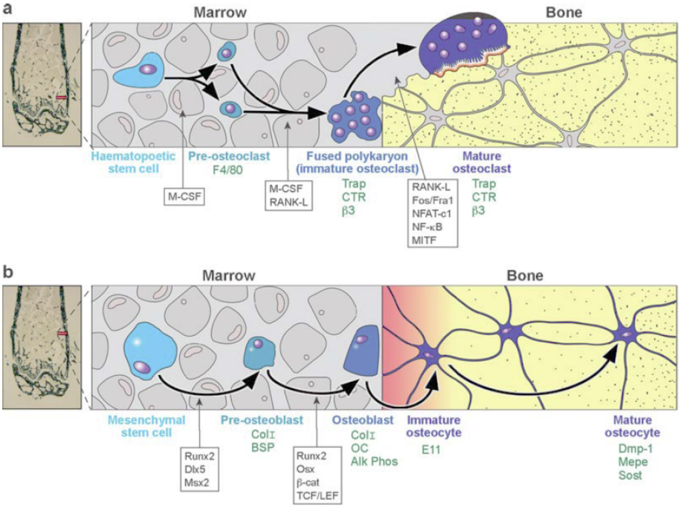


Robling AG et.al. 2006. Biomechanical and Molecular Regulation of Bone Remodeling. *Ann Rev Biomed Eng.* 8:455-498

BR cycle


Bone Remodeling Cycle
Pre-
Osteoclasts
Active
Osteoclasts
Mononuclear
Cells
Pre-
Osteoblasts
Osteoblasts
Osteocytes
Resting
Bone
Surface
Resorption
Reversal
Bone Formation
Mineralization
~3 WEEKS
~3 MONTHS

Control of BR



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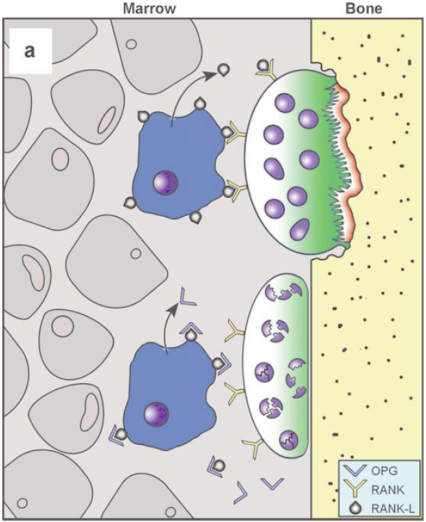
Control of BR



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Mechanical stimuli & elastic properties

Balance of forces

$$\rho \dot{v}_i + \frac{\partial \tau^{ij}}{\partial x_j} = 0$$

Hook's law (bone as an ortothropic material assumed)

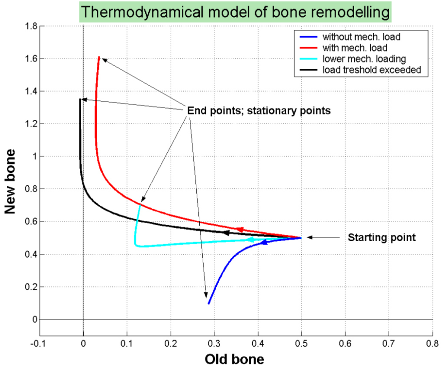
$$\tau^{ij} = C^{ijkl} e_{kl}, e_i j = \frac{1}{2}\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right)$$

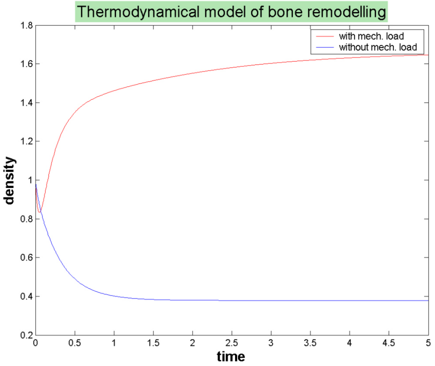
Fundamental idea of our model

$$C^{ijkl} = C^{ijkl}\left(New\_B, Old\_B\right) = C^{ijkl}\left(New\_B(d_{(1)}), Old\_B(d_{(1)})\right),$$

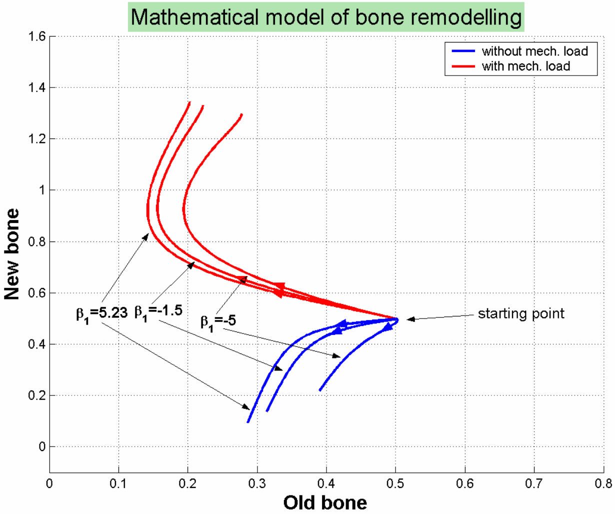
$$d_{(1)} = \frac{\partial \sum_i e_{ii}(I)}{\partial t} \approx \frac{\Delta \sum_i e_{ii}(I)}{\Delta t} = \frac{\Delta \mathcal{V}}{\mathcal{V}_0 \Delta t} = \text{rate of volume change}$$

Phase space diagram - I





Phase space diagram - II



Coupling effect

$$T\sigma(S) = pd_{(1)} + w_\rho \mathcal{A}_\rho \geq 0,$$

p is a mechanical energy concentration, w_ρ and $\mathcal{A}_\rho$ are rate and affinity of $\rho - th$ reaction, respectively.
Following cross-effect is valid:

$$p = l_{vv} d_{(1)} + l_{v\rho} \mathcal{A}_\rho \quad (11)$$

$$w_\rho = l_{\rho v} d_{(1)} + l_{\rho\rho} \mathcal{A}_\rho, \quad (12)$$

By substituting into the second law of thermodynamics it follows:

$$l_{vv} > 0 \quad \wedge \quad l_{\rho\rho} > 0$$

and

$$q \stackrel{def}{=\!=} \frac{l_{v\rho}}{\sqrt{l_{vv} l_{\rho\rho}}} \in (-1, 1).$$

'Healthy person' ∼ 10 000 steps a day

Osteons - isovalues of stresses