Calcium Mineralization in Bone

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Assumptions

- Collagen matrix is produced by cells at constant rate
- Inhibitor is injected through osteoblasts as matrix is produced
- Inhibitor degrades at a constant rate
- Individual crystals can reach a maximum volume
- Growth of crystals is promoted by absence of inhibitor (very steep transition)
- Cells don't stop producing collagen matrix

Mathematical Model

$$\frac{\partial I}{\partial t} + \lambda \frac{\partial I}{\partial x} = -kI, \quad I(0,t) = I_0, \quad I(x,0) = 0$$

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \alpha f(I, I_{\mathrm{TH}})(V_{\max} - V), \quad V(0) = 0 \ \forall x$$

- f is a penalty function which promotes or inhibits crystal growth
- Steep transition from $f = 1$ where there is no inhibitor to $f = 0$ where none of the inhibitor has been degraded
- We consider $\lambda = \lambda^H$ and $V_{\max} = V_{\max}^H$ for healthy individuals

Non-Dimensionalization

$$x = L\hat{x}, \quad t = T\hat{t}, \quad V = V_{\max}^{H}\hat{V}, \quad I = I_0\hat{I}$$

- Take $\lambda^H = \frac{L}{T}$ and $kL/\lambda^H = 1$ to define a collagen osteoid time scale and degradation length scale.
- Define $\mu = \alpha/k$ as a growth to degradation ratio, $\hat{I} = I_{\mathrm{TH}}/I_0$ as a growth activation ratio, $\hat{\lambda} = \lambda/\lambda^H$ as a collagen deposition ratio, and $\beta = V_{\max}/V_{\max}^{H}$ as a crystal volume ratio
- Take as parameter values

$$\lambda^H \approx 10^{-12}\mathrm{m/s}, \quad V_{\max}^{H} \approx 10^{-24}\mathrm{m}^3, \quad k \approx 10^{-6}\mathrm{s}^{-1},$$
$$L \approx 10^{-6}\mathrm{m}, \quad T \approx 10^{6}\mathrm{s}$$

Inhibitor Problem and Penalty Function

- Non-dimensional problem for inhibitor is

$$\frac{\partial I}{\partial t} + \hat{\lambda}\frac{\partial I}{\partial x} = -I$$

- We can solve this by the method of characteristics to get

$$I(x,t) = \exp\left(-\frac{x}{\hat{\lambda}}\right), \quad x < \hat{\lambda}t$$

- We feed this into ODE model for volume
- For the penalty function we take

$$f = \begin{cases} 1 - \hat{I}\left(\frac{I}{\hat{I}}\right)^{\gamma}, & 0 < I < \hat{I} \\ (1-\hat{I})\left(\frac{I-1}{\hat{I}-1}\right)^{\gamma}, & \hat{I} < I < 1 \end{cases}$$

Estimating $\hat{I}$ and μ

- Take as a penalty function, a step-impulse
- Define x^* when $I = \hat{I}$ via $x^* = -\hat{\lambda} \log \hat{I}$
- Measure x^* experimentally, approximate $\hat{I}$
- V has an analytic solution on $0 < x < \hat{\lambda} t$

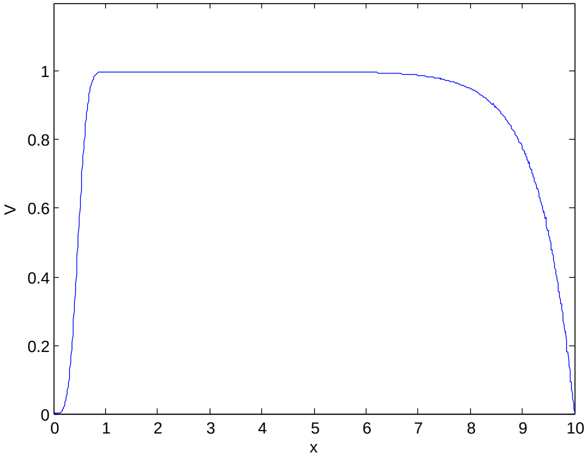
$$V = \begin{cases} 0, & x < x^* \\ 1 - \exp\left(\frac{\mu}{\hat{\lambda}}(x - x^*)\right), & x > x^* \end{cases}$$

- Approximate curve secant slope is 3 ($\mu/\hat{\lambda} \approx 3$)

Front Evolution-Healthy individual

- For a healthy individual take

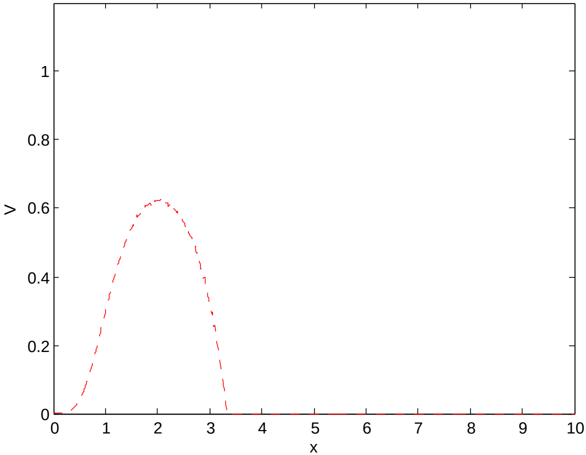
$$\hat{\lambda} = 1, \quad \beta = 1, \quad \hat{I} = 0.37, \quad \mu = 3, \quad t = 10$$



Unhealthy Cells

- For an unhealthy individual take

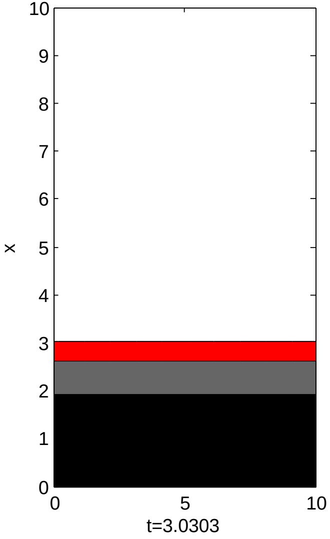
$$\hat{\lambda} = 1/3, \quad \beta = 1, \quad \hat{I} = 0.0015, \quad \mu = 1, \quad t = 10$$



Mineralization Well

(Loading Video...)

Depth Comparison



Future Work

- Investigate hyper-mineralization
- PDE model for volume fraction of mineralized and unmineralized collagen
- Evolution of crystal growth through inter/intra mineralization

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