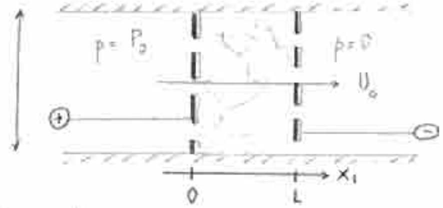
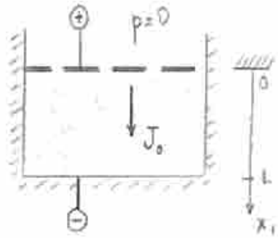
Problem 1





a) 1D equations of motion

(i) conservation of momentum (neglecting inertia) $\dfrac{\partial \sigma_{11}}{\partial x_1} = 0$ (1)

(ii) conservation of mass – from the class notes, with U_1 being the relative fluid velocity with respect to the solid network and averaged by the "total area $\pi \frac{D^2}{4}$", and with v_s and v_f being the local solid & fluid velocities, respectively.

$\nabla \cdot \bar{U}_1 = -\nabla \cdot \bar{v}_s$ and $U_1 = \phi\,(v_f - v_s)$, hence $U_1 = -\dfrac{\partial u_1}{\partial t} + U_0$ (2)

ϕ ↳ porosity

(iii) stress - strain constitutive law

$$\sigma_{11} = H\,\varepsilon_{11} - p$$
$$\varepsilon_{11} = \frac{\partial u_1}{\partial x_1} \qquad (3)$$

(iv) constitutive laws for U_1 and J_1.

$$U_1 = -k_{11}\frac{\partial p}{\partial x_1} + k_{12}\frac{\partial V}{\partial x_1} \qquad (4)$$
$$J_1 = k_{21}\frac{\partial p}{\partial x_1} - k_{22}\frac{\partial V}{\partial x_1} \qquad (5)$$

(v) conservation of charge (charge relaxation in $\tau \sim ns$) $\dfrac{\partial J_1}{\partial x_1} = 0$ (6)

b) Steady state velocity U_0 caused by a steady state pressure drop across the tissue

(i) Electrodes shorted together $V = 0$

here $\dfrac{\partial V}{\partial x_1} = 0$ and (4) becomes $U_1 = -k_{11}\dfrac{\partial p}{\partial x_1}$. The hydraulic permeability of the tissue is $\boxed{k_{11}}$

(ii) Electrodes left open-circuited $J = 0$

(5) becomes $k_{12}\dfrac{\partial p}{\partial x_1} = k_{22}\dfrac{\partial V}{\partial x_1}$; injecting into (4) we get $U_1 = -k_{11}\dfrac{\partial p}{\partial x_1} + k_{12}\left(\dfrac{k_{21}}{k_{22}}\cdot\dfrac{\partial p}{\partial x_1}\right)$

The hydraulic permeability of the tissue is $\boxed{k_{11} - \dfrac{k_{12}\,k_{21}}{k_{22}}}$

c) Differential equation for $u_1(x_1, t)$

$$\frac{\partial \sigma_{11}}{\partial x_1} \underset{(1)}{=} 0 \underset{(3)}{=} H\frac{\partial \varepsilon_{11}}{\partial x_1} - \frac{\partial p}{\partial x_1} \underset{(3)}{=} H\frac{\partial^2 u_1}{\partial x_1^2} - \frac{\partial p}{\partial x_1} \qquad (7)$$

$k_{22} \times (4)$: $\quad k_{22}\,U_1 = -k_{22}\,k_{11}\dfrac{\partial p}{\partial x_1} + k_{22}\,k_{12}\dfrac{\partial V}{\partial x_1}$

$k_{12} \times (5)$: $\quad k_{12}\,J_1 = k_{12}\,k_{21}\dfrac{\partial p}{\partial x_1} - k_{12}\,k_{22}\dfrac{\partial V}{\partial x_1}$

adding these two equations yields

$$\frac{\partial p}{\partial x_1} = \frac{k_{22}\,U_1 + k_{12}\,J_1}{k_{12}\,k_{21} - k_{11}\,k_{22}}$$

and injecting into (7):

$$0 = H\frac{\partial^2 u_1}{\partial x_1^2} - \frac{k_{22}}{A}U_1 - \frac{k_{12}}{A}J_1, \quad \text{where } A = k_{12}\,k_{21} - k_{11}\,k_{22}$$

$$\underset{(2),(6)}{=} H\frac{\partial^2 u_1}{\partial x_1^2} + \frac{k_{22}}{A}\frac{\partial u_1}{\partial t} - \frac{k_{22}}{A}U_0 - \frac{k_{12}}{A}J_0$$

, which can be written

$$\boxed{\frac{\partial u_1}{\partial t} = H\left(k_{11} - \frac{k_{12}\,k_{21}}{k_{22}}\right)\frac{\partial^2 u_1}{\partial x_1^2} + U_0 + \frac{k_{12}}{k_{22}}J_0} \qquad (8)$$

hydraulic permeability $k' = k_{11} - \dfrac{k_{12}\,k_{21}}{k_{22}} > 0$

Problem 1 (cont'd)

d) Steady state solution for constant and steady applied current J_0 . $\frac{\partial}{\partial t} = 0$

Boundary conditions $u_1(x_1 = 0) = u_1(x_1 = L) = 0$

(8) becomes $U_0 + \frac{k_{12}}{k_{22}} J_0 = -Hk' \frac{\partial^2 u_1}{\partial x_1^2}$ or $\frac{d^2 u_1}{dx_1^2} = -\frac{k_{22} U_0 + k_{12} J_0}{k_{22} H k'} = B$ constant

solving with BCs above yields, with $\underline{U_0 = 0}$ in this confined configuration, $u_1(x_1) = \frac{B}{2}(x_1^2 - L x_1)$

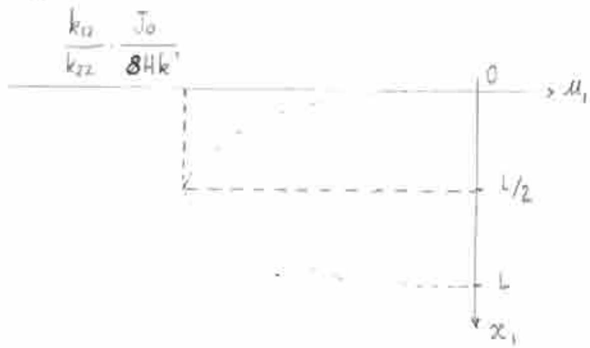
$$\boxed{u_1(x_1) = \frac{k_{12} J_0}{2H(k_{12}k_{21} - k_{11}k_{22})}(x_1^2 - L x_1) = \frac{k_{12}}{k_{22}} J_0 \frac{L x_1 - x_1^2}{2Hk'}} \quad (9)$$

• Current-generated stress $\sigma_{11} = H \frac{\partial u_1}{\partial x_1} - p$ from (3).

(9) gives $\frac{\partial u_1}{\partial x_1} = B\left(x_1 - \frac{L}{2}\right)$ and at $x_1 = 0$ we have $p = 0$,

$$\boxed{\sigma_{11}(x_1 = 0) = -\frac{k_{12} J_0 L}{2(k_{12}k_{21} - k_{11}k_{22})} = \frac{k_{12}}{k_{22}} J_0 \frac{L}{2k'}}$$

Because $k' > 0$, $k_{22} > 0$, $L > 0$ and $J_0 > 0$, the sign of $\sigma_{11}(x_1 = 0)$ is the same as the sign of k_{12}. The latter takes on the effect of the net charge of the fixed network.

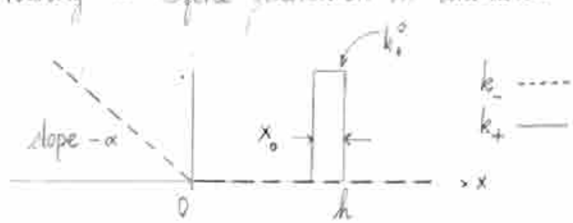


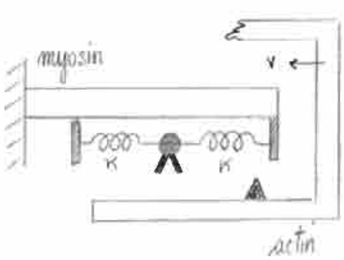
This plot corresponds to the $\underline{\text{case } k_{12} < 0}$, for a negatively charged network: the applied current J_0 is equivalent to imposing a ⊕ electrode on top of the tissue, and a ⊖ electrode below it. Therefore, the ⊖ solid phase will tend to move towards the top; conversely, the ⊕ charged fluid will move downwards (and $u_1(x_1) < 0$ when $k_{12} < 0$)

Problem 2

a) Cross-bridge model

. assumptions: only the case of constant (time-invariant) sliding velocity & force generation is considered
the muscle is maximally activated throughout
attachment & detachment obey the kinetics.
effects of other elastic components in muscle are ignored





myosin head

actin binding site

$n(x,t) = n(x)$ probability of binding at steady state

$$\frac{dn}{dt} = \frac{\partial n}{\partial t} - v\frac{\partial n}{\partial x} = -v\frac{\partial n}{\partial x} = [1 - n(x)]\,k_+(x) - n(x)\,k_-(x) \quad (1)$$

↳ attachment rate ↳ detachment rate

$\boxed{\text{Problem 2 (cont'd)}}$

- Expression for the binding probability $n(x)$

  - $x > h$: $k_+(x>h) = k_-(x>h) = 0$, hence from (1), $\boxed{n(x>h) = n(h) = 0}$
  - $h - x_0 < x < h$: $k_+ = k_+^0$ and $k_- = 0$

    (1) becomes $-v \dfrac{dn}{dx} = (1-n)\,k_+^0$

    $\dfrac{dn}{n-1} = \dfrac{k_+^0}{v}\,dx$, integrating $\displaystyle\int_{h-x_0}^{h} \frac{dn}{n-1} = \frac{k_+^0}{v}\int_{h-x_0}^{h} dx$ or $\ln \dfrac{n(h)-1}{n(h-x_0)-1} = \dfrac{k_+^0 x_0}{v}$

    and with $n(h) - 1 = 0 - 1 = -1$, we get

    $$\boxed{\begin{aligned} n(x = h - x_0) &= 1 - \exp\left(-\frac{k_+^0 x_0}{v}\right) \\ n(x = h - x_1) &= 1 - \exp\left(-\frac{k_+^0 x_1}{v}\right) \end{aligned}}$$

    and for $x_1 < x_0$

  - $0 < x < h - x_0$ $k_+ = k_- = 0$ $\boxed{n(0 < x < h - x_0) = n(x = h - x_0)}$
  - $x < 0$ $k_+ = 0$ $k_-(x<0) = -\alpha x$

    (1) becomes $-v\dfrac{dn}{dx} = \alpha n x$ or $\dfrac{dn}{n} = -\dfrac{\alpha}{v}\,x\,dx$

    integrating $\displaystyle\int_x^0 \frac{dn}{n} = -\frac{\alpha}{v}\int_x^0 x\,dx$, $\ln \dfrac{n(x=0)}{n(x)} = -\dfrac{\alpha}{v}\left(-\dfrac{x^2}{2}\right)$

    $$\boxed{n(x<0) = n(x=0)\exp\left(-\frac{\alpha}{2v}x^2\right)}$$

- Work done in contraction by a cross-bridge

attachment at $x = a$
detachment at $x = -b$ $\Big\}$ $W = \displaystyle\int_{-b}^{a} \kappa\, x\, dx = \frac{\kappa}{2}\left(a^2 - b^2\right)$

Now consider muscle of length l, cross-sectional area A, taking into account the probability distribution that a bond exists:

$$FAl = \int_{-\infty}^{+\infty}\left(n(x)\,\rho_s\, A\, \frac{s}{2}\right)\kappa\, x\, dx \quad , \text{ where } \begin{cases} \rho_s & \text{density of sarcomeres} \\ s & \text{total sarcomere length} \end{cases}$$

The force per unit area is:

$$F = \frac{\rho_s\, s\, A\kappa}{2Al}\int_{-\infty}^{+\infty} n(x)\,x\,dx = \frac{\rho_s\, s\,\kappa}{2l}\left[\int_{-\infty}^{0} n(x<0)\,x\,dx + \int_0^{h-x_0} n(0<x<h-x_0)\,x\,dx + \int_{h-x_0}^{h} n(h-x_0<x<h)\,x\,dx\right]$$

$$= \frac{\rho_s\, s\,\kappa}{2l}\left[\int_{-\infty}^{0}\left(1-\exp\left(\frac{-k_+^0 x_0}{v}\right)\right)\exp\left(\frac{-\alpha}{2v}x^2\right)x\,dx + \int_0^{h-x_0}\left\{1-\exp\left(-\frac{k_+^0 x_0}{v}\right)\right\}x\,dx + \int_{h-x_0}^{h}\left(1-\exp\left(-\frac{k_+^0(h-x)}{v}\right)\right)x\,dx\right]$$

$$= \frac{\rho_s\, s\,\kappa}{2l}\left[1-\exp\left(\frac{-k_+^0 x_0}{v}\right)\right]\left\{\left[-\frac{v}{\alpha}\exp\left(\frac{-\alpha}{2v}x^2\right)\right]_{-\infty}^{0} + \left[\frac{x^2}{2}\right]_0^{h-x_0}\right\} + \frac{\rho_s\, s\,\kappa}{2l}\left\{\left[\frac{x^2}{2}\right]_{h-x_0}^{h} - \exp\left(-\frac{k_+^0 h}{v}\right)\int_{h-x_0}^{h}\exp\left(\frac{k_+^0 x}{v}\right)x\,dx\right\}$$

$$= \frac{\rho_s\, s\,\kappa}{2l}\left[1-\exp\left(\frac{-k_+^0 x_0}{v}\right)\right]\left(\frac{(h-x_0)^2}{2} - \frac{v}{\alpha}\right) + \frac{\rho_s\, s\,\kappa}{2l}\left\{\frac{x_0}{2}(x_0 - h) - \exp\left(\frac{-k_+^0 h}{v}\right)\left(\left[\frac{vx}{k_+^0}\exp\left(\frac{k_+^0 x}{v}\right)\right]_{h-x_0}^{h} - \frac{v}{k_+^0}\int_{h-x_0}^{h}\exp\frac{k_+^0 x}{v}\,dx\right)\right\}$$

$$= \frac{\rho_s\, s\,\kappa}{2l}\left\{\left[1-\exp\left(\frac{-k_+^0 x_0}{v}\right)\right]\left[\frac{(h-x_0)^2}{2} - \frac{v}{\alpha}\right] + \frac{x_0}{2}(x_0 - h) - \exp\left(\frac{-k_+^0 h}{v}\right)\left[\frac{vh}{k_+^0}\exp\left(\frac{k_+^0 h}{v}\right)\left(1-\exp\left(\frac{-k_+^0 x_0}{v}\right) - \frac{k_+^0 h}{v}\right) + \frac{v}{k_+^0}\left(x_0 + \frac{v}{k_+^0}\right)\exp\left(\frac{k_+^0(h-x_0)}{v}\right)\right]\right\}$$

note : if we consider $\boxed{x_0 \ll h}$

and $\displaystyle\int_0^{h-x_0} n(x)\,x\,dx + \int_{h-x_0}^{h} n(x)\,x\,dx \simeq \int_0^{h} n(h-x_0)\,x\,dx = \left(1-\exp\left(\frac{-k_+^0 x_0}{v}\right)\right)\frac{h^2}{2}$

then $F = \dfrac{\rho_s\, s\,\kappa\, h^2}{4l}\left[1 - \dfrac{2v}{\alpha h^2}\right]\left[1-\exp\left(\dfrac{-k_+^0 x_0}{v}\right)\right]$ and maximum force generated for $v = 0$

$$\boxed{F_{max} = \frac{\rho_s\, s\,\kappa\, h^2}{4l}}$$

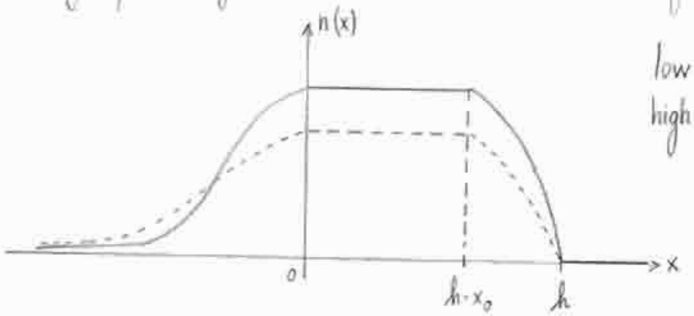
$$\boxed{\frac{F}{F_{max}} = \left(1 - \frac{2v}{\alpha h^2}\right)\left[1-\exp\left(\frac{-k_+^0 x_0}{v}\right)\right]}$$

Problem 2 (cont'd)

- Maximum shortening velocity v_{max} for $F = 0$ $\Rightarrow$ $\boxed{v_{max} = \frac{\alpha h^2}{2}}$
- Normalized power

$$\boxed{\frac{Fv}{F_{max}\, v_{max}} = \frac{2v}{\alpha h^2}\left(1 - \frac{2v}{\alpha h^2}\right)\left[1 - \exp\left(\frac{-k_+^o x_o}{v}\right)\right] = \frac{v}{v_{max}}\left(1 - \frac{v}{v_{max}}\right)\left[1 - \exp\left(\frac{-2k_+^o x_o}{\alpha h^2} \cdot \frac{v_{max}}{v}\right)\right]} \quad (2)$$

b) Binding probability distribution for different sliding velocities v



The slower the sliding velocity v, the more numerous the bonds formed (the myosin & actin binding sites are in proximity for a longer time), but the more quickly they disappear (short tail for $x < 0$).

c) Hill's equation : We want equate (2) with $\frac{v}{v_{max}} = \frac{1 - F/F_{max}}{1 + C\frac{F}{F_{max}}}$ and $C = 5$ (3)

- From (3) $1 - \frac{F}{F_{max}} = \frac{v}{v_{max}} + C\frac{v}{v_{max}} \cdot \frac{F}{F_{max}}$

$$\frac{F}{F_{max}} = \left(1 - \frac{v}{v_{max}}\right) \cdot \frac{1}{1 + C\frac{v}{v_{max}}} \quad (4)$$

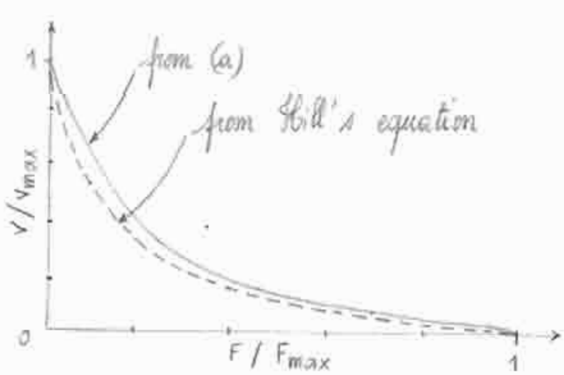
- From (2) $\frac{F}{F_{max}} = \left(1 - \frac{v}{v_{max}}\right)\left[1 - \exp\left(-A\frac{v_{max}}{v}\right)\right]$ where $A = \frac{2k_+^o x_o}{\alpha h^2} = \frac{k_+^o x_o}{v_{max}}$ (5)

Equating (4) & (5) yields

$$\left(1 + C\frac{v}{v_{max}}\right)\left[1 - \exp\left(-A\frac{v_{max}}{v}\right)\right] = 1 \quad \text{or} \quad \exp\left(-A\frac{v_{max}}{v}\right) = \frac{C\frac{v}{v_{max}}}{1 + C\frac{v}{v_{max}}} = \frac{1}{1 + \frac{v_{max}}{vC}}$$

- To agree with Hill's equation, we need our parameter A:

$$\boxed{A = \frac{k_+^o x_o}{v_{max}} = \frac{v}{v_{max}} \ln\left(\frac{1}{C} \cdot \frac{v_{max}}{v} + 1\right)}$$



d) Comparison of the case derived in class, $k_-(x<0) = k_-^o$, with the situation in which $k_-(x<0)$ is very large as soon as $x < 0$:
In the latter case, all the cross-bridges release immediately. Since allowing binding to persist as $x < 0$ extracts energy from the system (work done in stretching the spring for $x < 0$, which is lost when the bond breaks), the extent to which the bond persists reduces the efficiency of the cross-bridge.