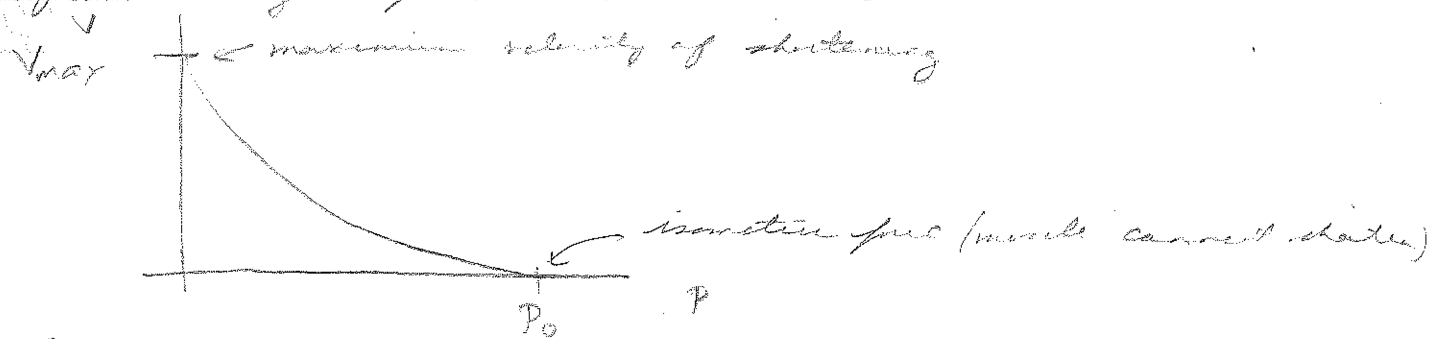
Muscle Mechanics

The goal of this chapter is to understand how the microscopic behavior of muscle dictates its macroscopic behavior

<u>the force-velocity curve</u> * (against which it works)

Property of muscle force P that it generates vs. velocity V of shortening. Experimental observation:



Experimental measurement closely matches equation of the form

$$V = b\left(\frac{P_0 - P}{P + a}\right)$$

where P_0 = isometric force, a and b are constants that can be determined from experiment.

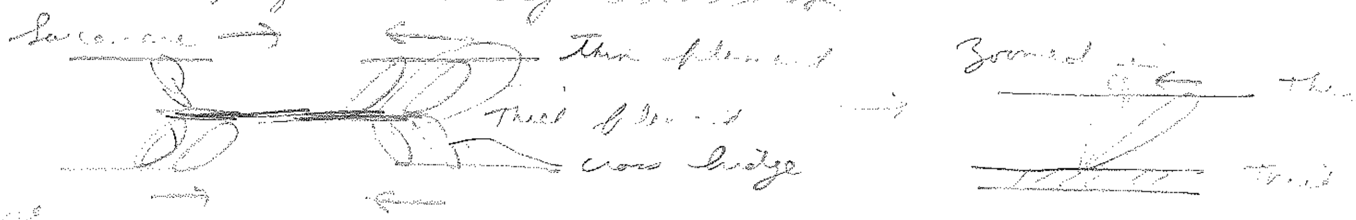
We will now try to derive this equation from microscopic muscle mechanics

<u>Microscopic view of muscle</u>

Basic unit of muscle function is the sarcomere.

Contains thick filaments (myosin) and thin filaments (actin)

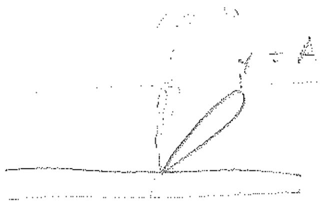
Motion brought about by cross bridge.



Emph: When CB slides, the force on the thin filament [illegible] this happens faster at higher velocities, which qualitatively explains the force-velocity curve

A quantitative explanation is as follows.

ATTACH + DETACH



Let x = displacement from eq. configuration

$p(x)$ = force on thin filament when displacement = x

Linear spring $p(x) = kx$

$p(0) = 0$, $p(x)$ is increasing function of x

n_0 = # of CBs in half sarcomere, connected in parallel (forces add). Half sarcomeres in series (lengths add)

Force on all muscle if all CBs had displacement $x = n_0 p(x)$

But in general CBs have different values of x. Describe the statistical distribution in terms of a population density function

$$\int_{x_1}^{x_2} u(x)\,dx = \text{fraction of CBs with } x_1 < x < x_2$$

discrete $\sum u_i$ ... the $\sum x = U_i$ = density ... $\int x \to 0$

x only defined for attached CBs

$$U = \int_{-\infty}^{\infty} u(x)\,dx < 1 = \text{total fraction attached}$$

$$P = n_0 \int_{-\infty}^{\infty} p(x)\,u(x)\,dx$$

Motivate these definitions ~~through~~ discrete case.

4 people weigh 120, 5 160, 1 300. Average wt?

$$\underbrace{\frac{4}{10}\cdot 120 + \frac{5}{10}\cdot 160 + \frac{1}{10}\cdot 300}_{\text{average wt. Like integrating}}$$ total wt = 10 × avg wt.

Crossbridge cycle assume all attachments form at $x = A > 0$.

Rate of attachment proportional to # available for attachment $= n_0(1-U)$. (at A)

Rate of formation: $\alpha n_0(1-U)$. (#/time)

Motion: $\frac{dx}{dt} = -v$ where v = velocity of shortening/sliding

$v = V/2N$, where N = # of sarcomeres,

V = total macroscopic velocity

v = half sarcomere.

Rate of breaking = β(# of attached bridges)

$$= \beta n_0 \int_{x_1}^{x_2} u(x)\,dx$$

Steady state equation for CB population density $u(x)$.
Consider population $u(x)$ in $x_0 < x < A$.
New CBs attach at A.
Detach [illegible] and get [illegible]

$$\frac{du}{dt} = 0 = (\text{Amt entering}) - (\text{Amt leaving}).$$

sliding out

$$= \underbrace{r_0\alpha(1-U)}_{\text{form}} - \Big(\underbrace{\beta n_0 \int_{x_0}^{A} u(x)\,dx}_{\text{detach}} + \underbrace{v n_0 u(x_0)}_{\text{slide}}\Big)$$

$n_0 u(x_0) = \#$ density at x_0.
$v n_0 u(x_0) = \#/\text{time}$ leaving the boundary
[Think this way: in 1 second, you can "see" bridges which are $v \cdot 1$ away. So if $u(x_0)$ were constant, would see $v \cdot u(x_0) n_0$ bridges in that time].
Steady state assumption

$$\alpha(1-U) = \beta \int_{x_0}^{A} u(x)\,dx + v u(x_0).$$

Differentiate wrt x_0 and use FTC

$$0 = -\beta u(x_0) + v\, u'(x_0).$$

$$\boxed{v \frac{du}{dx} = \beta u.}$$

Exercise: solve this ODE assuming $u(A) = u(A)$ given.
Solution: $u(x) = c e^{\beta x/v}$

$$u(A) = c e^{\beta A/v} \rightarrow c = u(A) e^{-\beta A/v}$$

$$\rightarrow \boxed{u(x) = u(A)\exp(\beta(x-A)/v)}$$

Determine the constant via integral eqn.
at $x = A$:

$$\alpha(1-U) = v u(A) \rightarrow u(A) = \frac{\alpha}{v}(1-U).$$

But exercise

$$U = \int_{-\infty}^{A} u(x)\,dx = \frac{v u(A)}{\beta} \exp\left(\cancel{\frac{\beta(A-A)}{v}}\right).$$

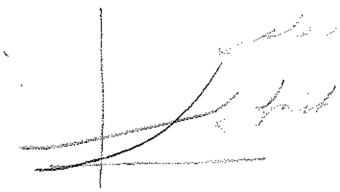
So

$$u(A) = \frac{\alpha}{v}\left(1 - \frac{v}{\beta} u(A)\right) \rightarrow u(A)\underbrace{\left[1 + \frac{\alpha}{\beta}\right]}_{\frac{\alpha+\beta}{\beta}} = \frac{\alpha}{v}.$$

$$\rightarrow \boxed{u(A) = \frac{\alpha\beta}{v(\alpha+\beta)}} \rightarrow \boxed{U = \frac{\alpha}{\alpha+\beta}}$$

Substituting, we get

$$\boxed{n(x) = \frac{\alpha\beta\exp(\beta(x-A)/v)}{v(\alpha+\beta)}} \quad \text{for } x < A.$$



as the density of attached bridges.

Zero v – CBs are clustered near $x = A$.

Force velocity curve.

$$P = n_0\int n(x)\,p(x)\,dx$$

$$= \frac{n_0\alpha\beta}{v(\alpha+\beta)}\int \exp(\beta(x-A)/v)\,p(x)\,dx.$$

Possibilities for $p(x)$ – linear spring shown to reproduce data (HW).

$$p(x) = p_1(e^{\gamma x} - 1)$$

Gives the force velocity curve observed experimentally

$$P = \frac{\alpha n_0 p_1}{\alpha+\beta}\,\frac{(e^{\gamma A} - 1) - (\gamma v/\beta)}{1 + (\gamma v/\beta)} \qquad (*)$$

Empirical curve:

$$V = \frac{b(P_0 - P)}{P + a}$$

Can put $(*)$ in this form by solving for $\gamma v/\beta$ and recalling $V = 2Nv$.

$$P_0 = \text{force when } v = 0$$

$$= \frac{\alpha n_0 p_1}{\alpha+\beta}(\exp(\gamma A) - 1) \qquad \left[\text{all CBs at } A,\; n = \frac{\alpha}{\alpha+\beta} \Rightarrow n = \frac{n_0\alpha}{\alpha+\beta},\; p = p_1 e^{\gamma A}\right]$$

$$V_{max} = V(P=0) = \frac{bP_0}{a} = \frac{2N\beta A}{\gamma A}[\exp(\gamma A) - 1]$$

Negative forces by CBs balance positive ones.