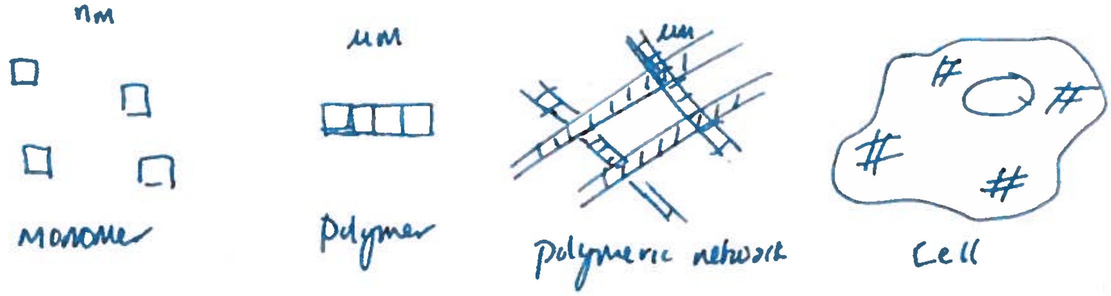
Lecture #5 Notes: Adhesion, Migration, and Contraction

Let's review what we have learned so far!



$\psi = W - TS$

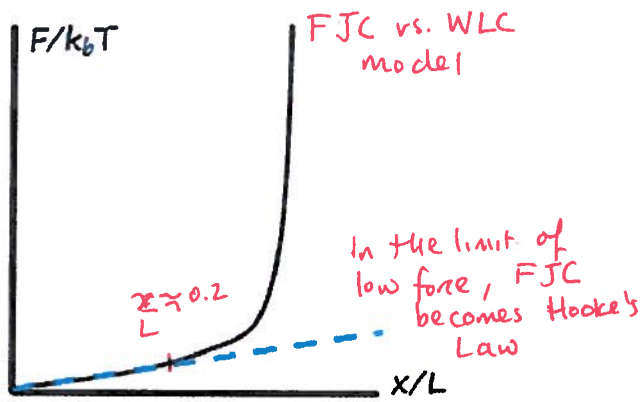
Energy vs. Entropy

Axial Tension vs. Bending for CSK proteins → stiffer in tension but flexible in bending.

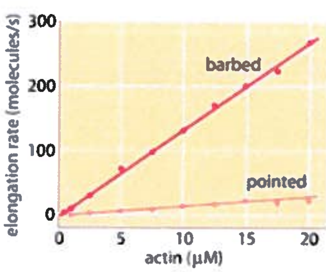
↳ Persistence Length

$$L_p = \frac{EI}{k_B T} = \frac{\text{energetic}}{\text{entropic}}$$

"characteristic length"



Polymerization Kinetics



$$\frac{dn}{dt} = k_{on}C - k_{off} \rightarrow \frac{dn}{dt} = 0, \quad C_{crit} = \frac{k_{off}}{k_{on}}$$

For actin polymerization ⇒ Steady state

$$\frac{dn^+}{dt} + \frac{dn^-}{dt} = 0. \qquad C^+_{crit} \leq C_{SS} \leq C^-_{crit}$$

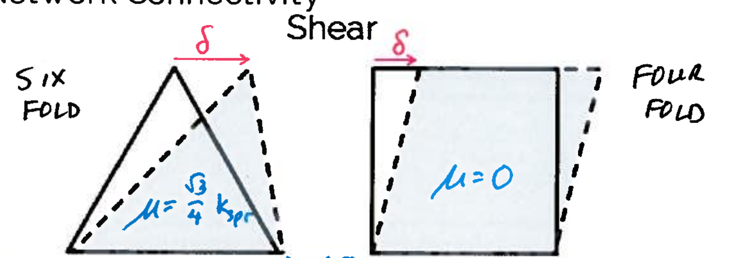
Fiber Bundle Model (Filopodia)

→ tightly crosslinked actin bundles probe the membrane with critical force defined by buckling.

$$F_{Buckle} = \frac{\pi^2 EI}{4L^2} \rightarrow L = \sqrt{\frac{\pi E_{actin} \pi (\sqrt{n} R_{act})^2}{4 F_{mem}}}$$

$$F_{mem} = 2\pi R N \approx 50\,pN$$

Network Connectivity



Hill: $W^{macro} = W^{micro}$

$$W^{macro} = \tfrac{1}{2} K [\varepsilon_{xx} + \varepsilon_{yy}]^2 + \tfrac{1}{2}\mu[\varepsilon_{xx} - \varepsilon_{yy}]^2 + 2\mu\varepsilon_{xy}^2$$

$$W^{micro} = \frac{\sum_1 W_{sp,i}}{\sum A_{i\,spr}}$$

Membrane Mechanics (Soap Bubble)

$$n[\nabla^2 w] - K_B[\nabla^4 w] + p_z = 0$$

surface tension

$$\frac{K_B}{n\lambda^2} = \begin{cases} \ll 1 & \text{tension} \\ \gg 1 & \text{bending} \end{cases} \text{ dominates.}$$

characteristic length

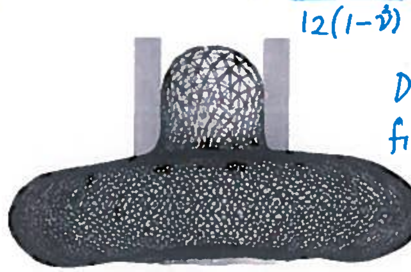
Equibiaxial tension; for equal radii $p_z = \frac{2n}{r}$

Expansional modulus $K_A = \frac{Eh}{2(1-\nu^2)}$ → Huge

Membrane shear stiffness $K_S = \frac{Eh}{1+\nu}$

Bending stiffness $K_B = \frac{Eh^3}{12(1-\nu^2)}$

→ Very Small



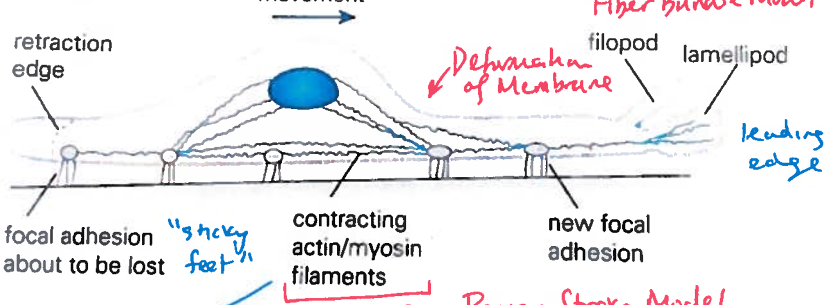
Discher's finite element model of a RBC in micropipette aspirations.

He modeled the network as 6 fold.

Experimentally, you get macro via MPA

Migration (Speed, Persistence, and Traction Forces)

Release	Translocation	Attachment	Protrusion
actin filament contraction and focal adhesion sacrifice	actin/myosin contraction	focal adhesion formation	actin polymerization (Kinetics)



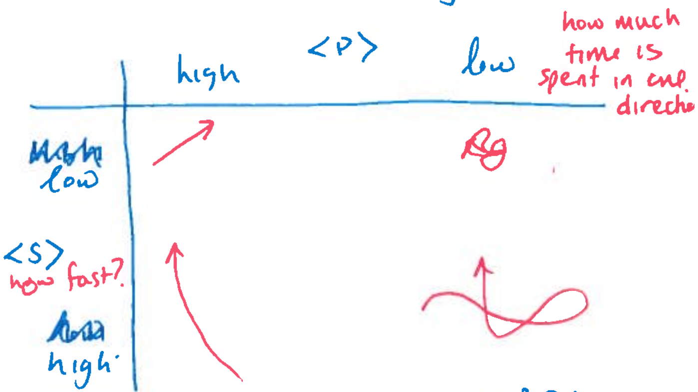
HW 3 : Power Stroke Model

Traction forces

→ as cells crawl, they exert force to their surface

Typically characterization

1. Speed [$\mu m/min$]
2. Persistence time [min]
3. Traction [nN]

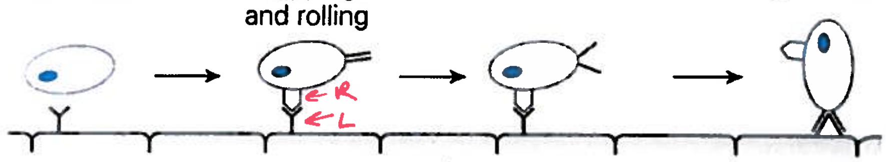


mean square distance $\langle d^2 \rangle = \underbrace{2S^2P}_{D}t$ D diffusion constant

Adhesion (The Bell Model)

Classic Example: White Blood Cells and Endothelial Layer one of the fastest

$$\underset{\text{ligand}}{L} + \underset{\text{receptor}}{R} \underset{k_-}{\overset{k_+}{\rightleftharpoons}} \underset{\text{bound}}{B}$$



Y selectin ‖ unactivated integrin

U selectin ligand \/ activated integrin

Λ intercellular adhesion molecule (ICAM)

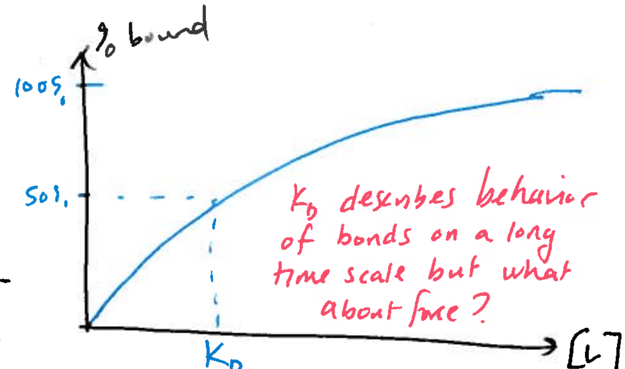
Use Law of Mass Action for Kinetics

$$\boxed{k_+[L][R] = k_-[B]}$$

$$\boxed{K_d = \frac{k_+}{k_-} = \frac{[L][R]}{[B]}}$$

equilibrium or dissociation constant.

$$\%\text{ bound} = \frac{[B]}{[B]+[R]} = \frac{[B]\frac{[L]}{[B]}}{[B]\frac{[L]}{[B]} + [R]\frac{[L]}{[B]}} = \frac{[L]}{[L]+K_d}$$



K_D describes behavior of bonds on a long time scale but what about force?

<u>In 1978</u>: George Bell article in <u>Science</u>

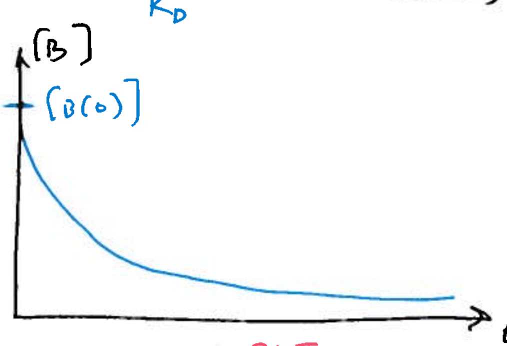
Consider the kinetics of force induced bond rupture between a single R-L pair

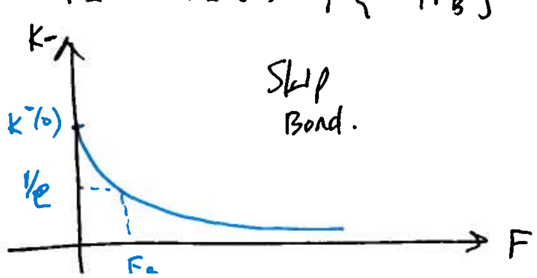
$$k_- = k_-(0)\exp\left\{\frac{\sigma F}{k_B T}\right\}$$

$[\sigma F] = $ energy

$$k_- = k_-(0)\exp\{F/F_B\}$$

$F_B = \frac{k_B T}{\sigma}$ characteristic measure of bond strength



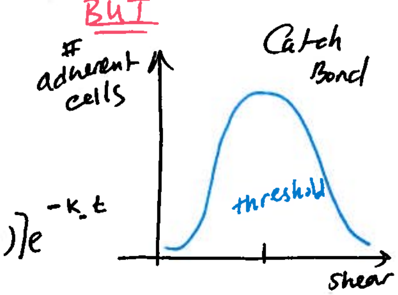


<u>In simple model</u>

Only bond rupture and no rebinding

$$\frac{d[B]}{dt} = -k_-[B] \rightarrow [B(t)] = [B(0)]e^{-k_- t}$$

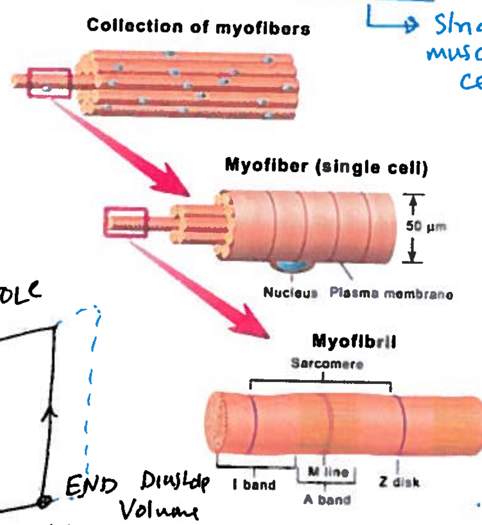
<u>BUT</u>

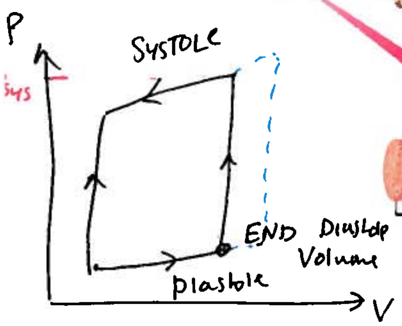


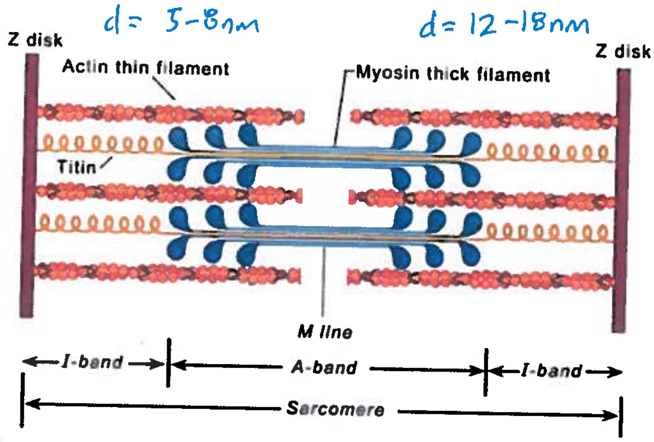
Contraction (Intracellular Contractile Forces)

Muscle Cells: Smooth, ***Skeletal & Cardiac***

→ Striated muscle cells



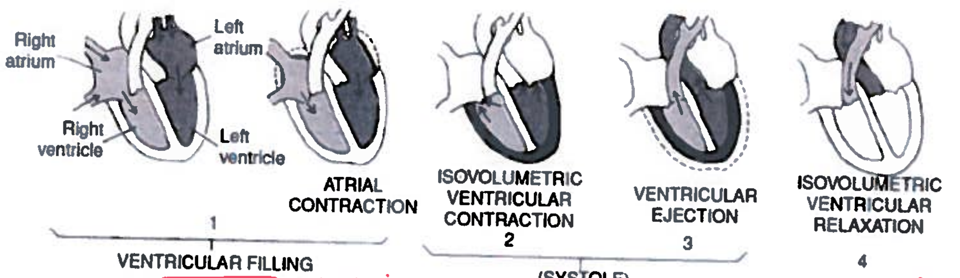




Actin: semiflexible polymer

Myosin: molecular motor

Titin: resting elasticity



Our understanding of muscle force generation comes from understanding the pumping action of the heart. Frank Starling Law states that as the heart stroke volume increases, owing to more diastolic filling, the muscle contracts with more force, leading to higher systolic pressure.

→ stretching ⇒ ↑ stretch, ↑ contraction force

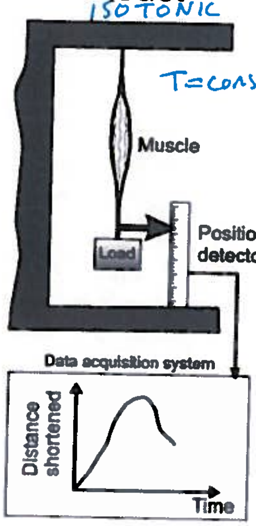
higher EDV → more stretching of muscle fibers and more forceful ejection

→ the tension a sarcomere is able to generate must increase with its initial stretch of length

Hill's Model [Frog muscle]

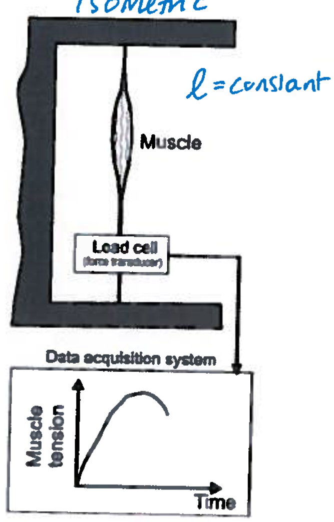
ISOTONIC

$T = \text{constant}$

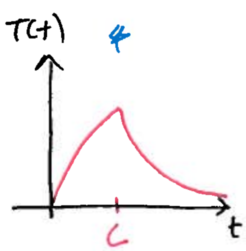


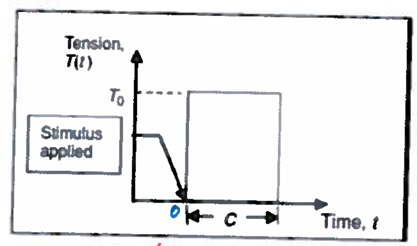
Isometric

$\ell = \text{constant}$

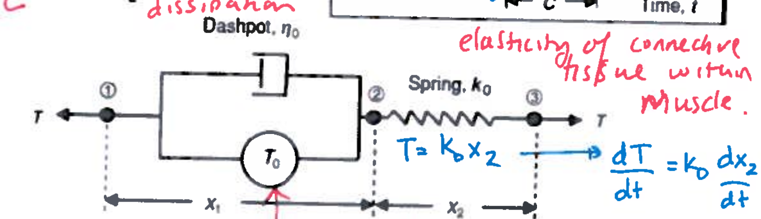


Spring-Mass-Damper Model





frictional dissipation



elasticity of connective tissue within muscle.

$T = k_0 x_2 \rightarrow \frac{dT}{dt} = k_0 \frac{dx_2}{dt}$

active element w/ actin-myosin complex

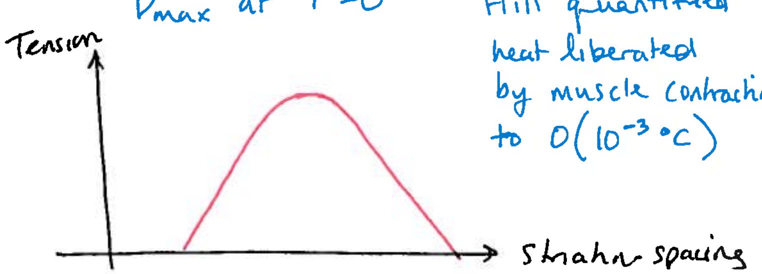
Hill's equation $(F + a)(b + v) = b(F_0 + a)$

F_{max} at $v = 0$

V_{max} at $F = 0$

Fun fact

Hill quantified heat liberated by muscle contraction to $O(10^{-3}\,°C)$



Isometric $x_1 + x_2 = \text{constant}$

$\frac{dx_1}{dt} + \frac{dx_2}{dt} = 0.$

For $0 \le t \le c$ $\quad T = T_0 + \eta_0 \frac{dx_1}{dt}$

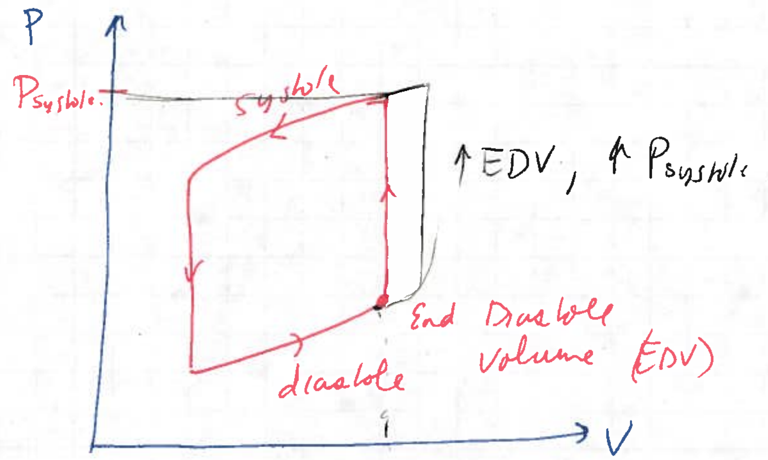
$t > c$ $\quad T = \eta_0 \frac{dx_1}{dt}$

$\frac{T - T_0}{\eta_0} + \frac{1}{k_0}\frac{dT}{dt} = 0 \qquad 0 \le t \le c$

$\frac{T}{\eta_0} + \frac{1}{k_0}\frac{dT}{dt} = 0 \qquad t > c$

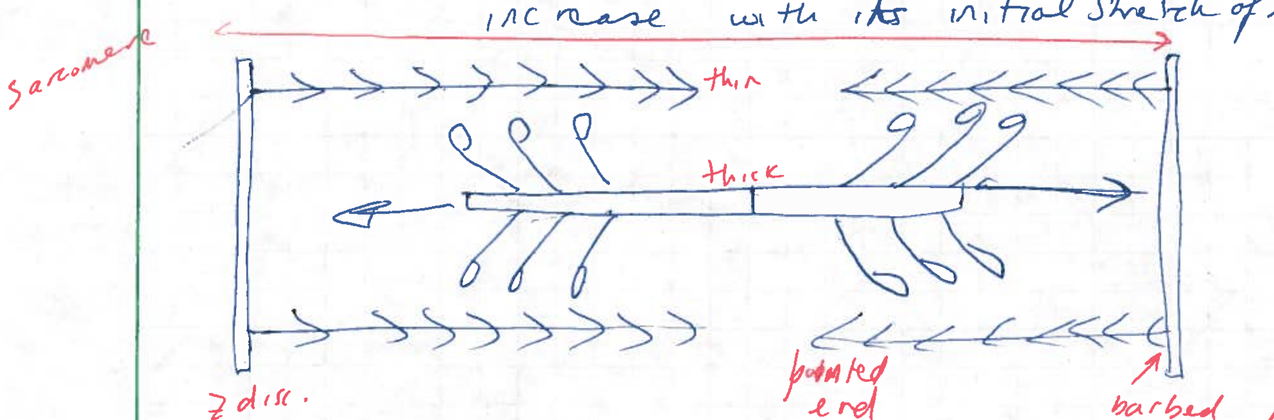
Contraction

Frank Starling law states that as heart stroke volume increases owing to more diastolic filling, the muscle contracts with more force, leading to higher systolic pressure.



higher EDV → more stretching of heart muscle fibers and more forceful ejection.

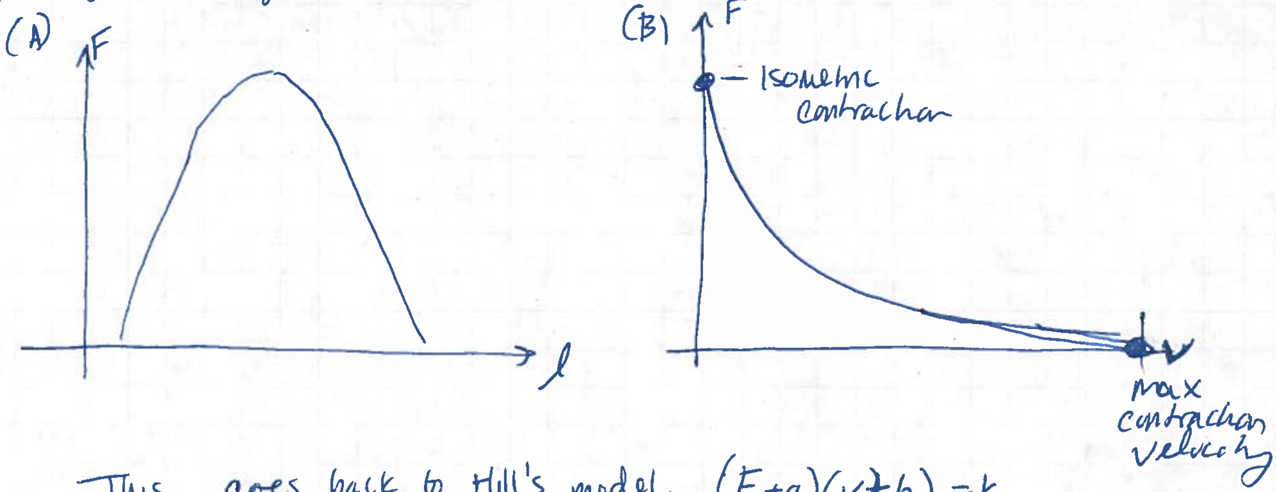
→ the tension a sarcomere is able to generate must increase with its initial stretch of length.



- Skeletal muscle is very organized tissue — composed of muscle fibers = smaller units called myofibril and along the length you find repeated units of sarcomeres as illustrated above.

- the two most important parameters affecting muscle force generation are length & velocity.
  - → isotonic: muscle tension held constant and length changed
  - → isometric: muscle length held constant.

Typically, you get two different plots as a result.



This goes back to Hill's model, $(F+a)(v+b) = k$.

F_{max} at $v=0$.

V_{max} at $F=0$

In Hill's original experiment, he quantified heat liberated by muscle contraction to $O(10^{-3}\,°C)$.

He observed heat released $\propto$ shortening distace x_{sh}.

total energy liberate: $E_1 = \underbrace{F x_{sh}}_{\text{mechanical work done}} + \underbrace{a x_{sh}}_{\text{heat released}}$.

Experimentally, he found

$$(F+a)\frac{dx_{sh}}{dt} = (F+a)v = -bF + c$$

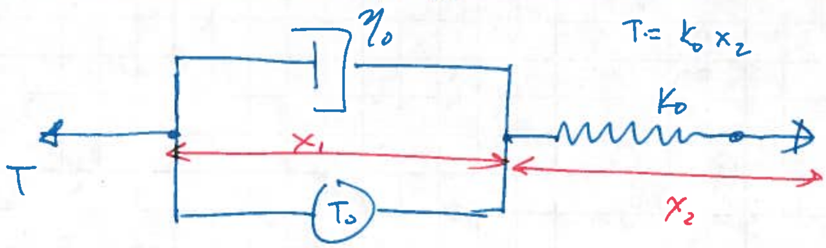
$$(F+a)(v+b) = c + ab = k.$$

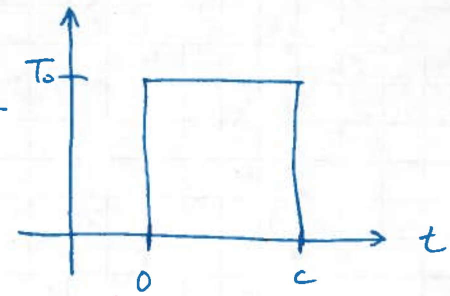
I have also seen it written in this manner

$$(a+F)(b+V) = b(F_0 + a)$$

You will learn more about this later on with tissue/musculoskeletal.

$$T = \eta_0 \frac{dx_1}{dt}$$





$$x_1 + x_2 = \text{constant.}$$

<u>Isometric</u>

$$\frac{dx_1}{dt} + \frac{dx_2}{dt} = 0$$

$$x_2 = \frac{T}{k_0} \rightarrow \frac{dx_2}{dt} = \frac{1}{k_0}\frac{dT}{dt}$$

$$T = T_0 + \eta_0 \frac{dx_1}{dt} \qquad \text{or} \qquad T = \eta_0 \frac{dx_1}{dt}$$

$$0 \le t \le c \qquad\qquad t > c$$

$$\frac{T - T_0}{\eta_0} + \frac{1}{k_0}\frac{dT}{dt} = 0 \qquad\qquad \frac{T}{\eta_0} + \frac{1}{k_0}\frac{dT}{dt} = 0$$

$$T(t) = T_0\left[1 - \exp\left\{-\frac{k_0}{\eta_0} t\right\}\right] \qquad T(t) = T_0\left[1 - \exp\left\{-\frac{k_0}{\eta_0} c\right\}\right] e^{-\frac{k_0(t-c)}{\eta_0}}$$

for $0 \le t \le c$ for $t \ge c$