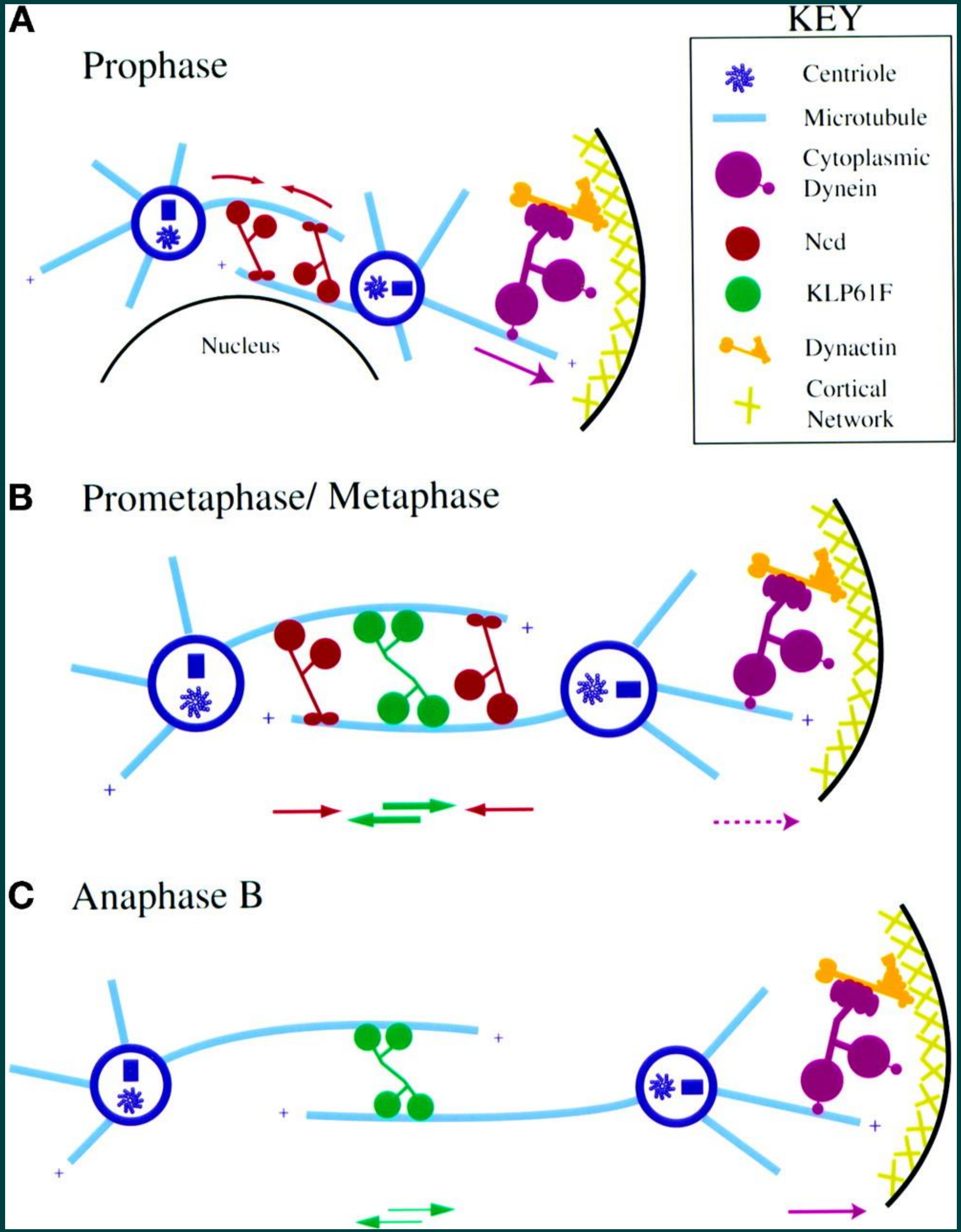
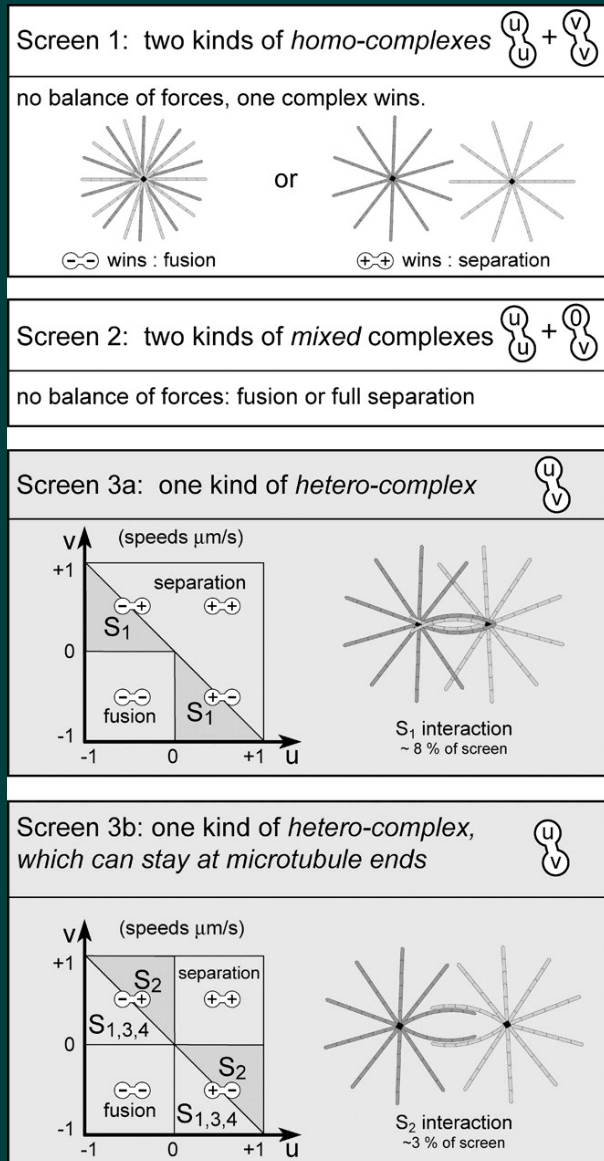
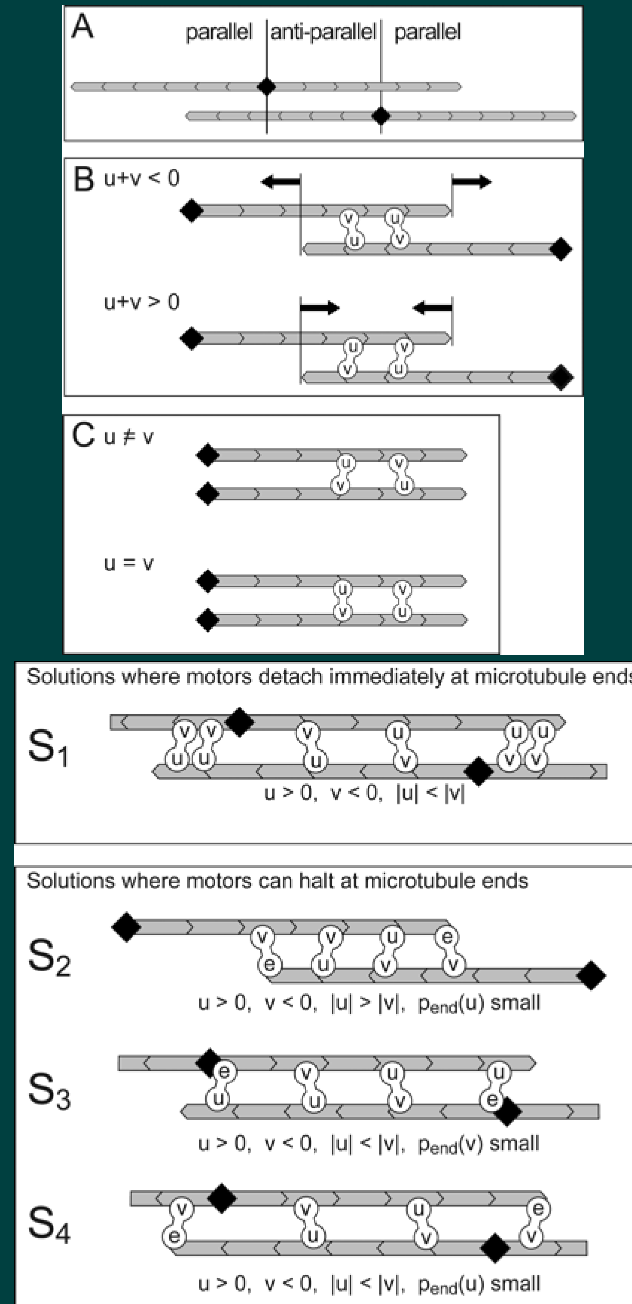
last time: motor proteins in mitosis



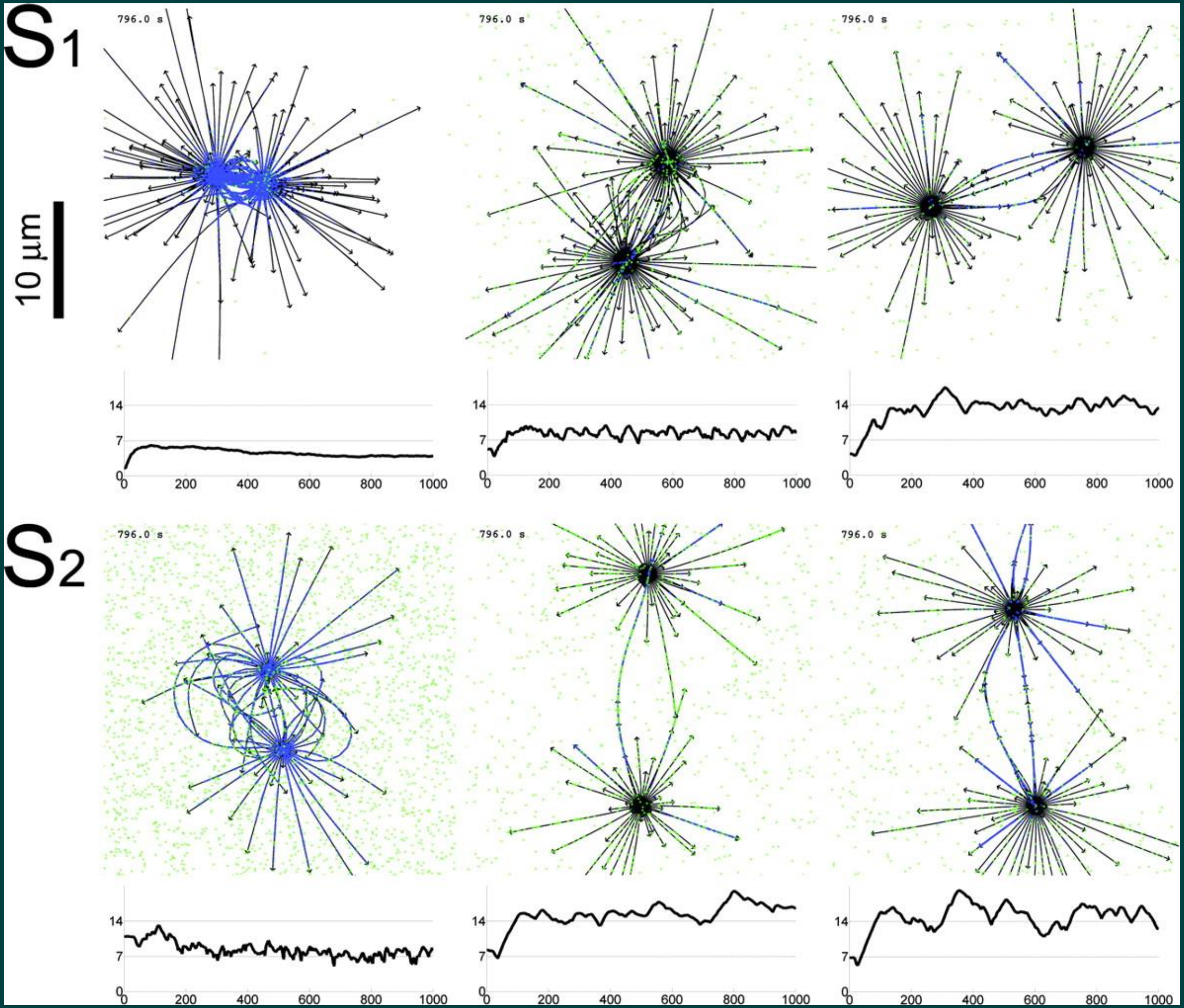
Sharp et al.,
Mol. Biol. Cell, 2000

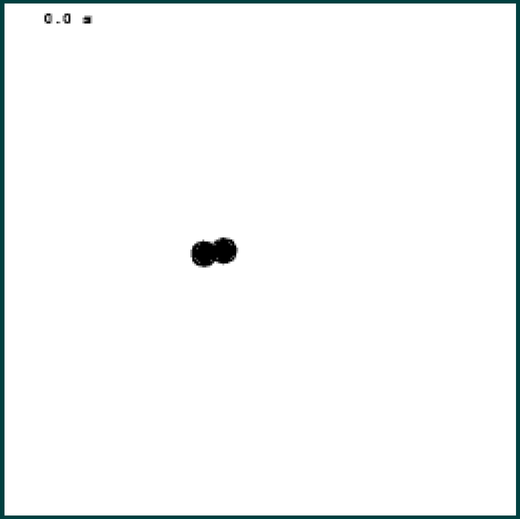
Conditions for steady-state pole separation





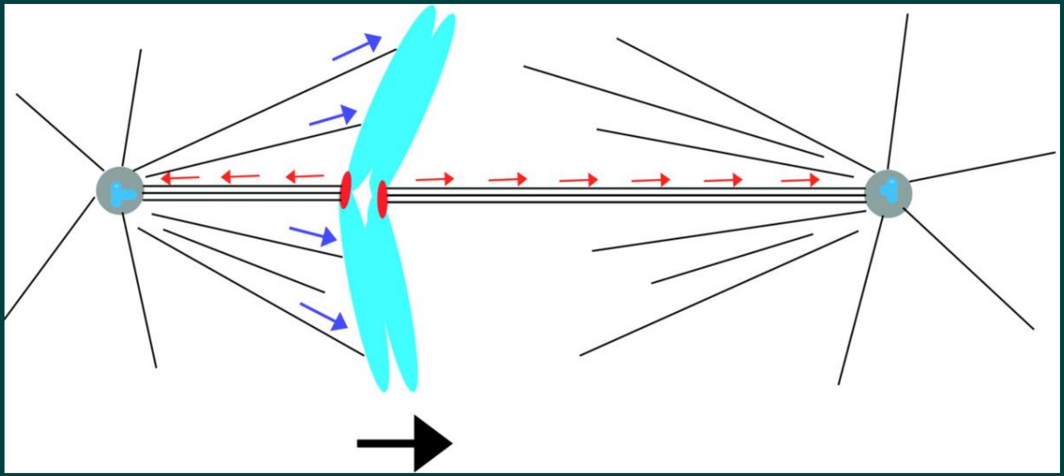
Nedelec, J. Cell Biol., 2002

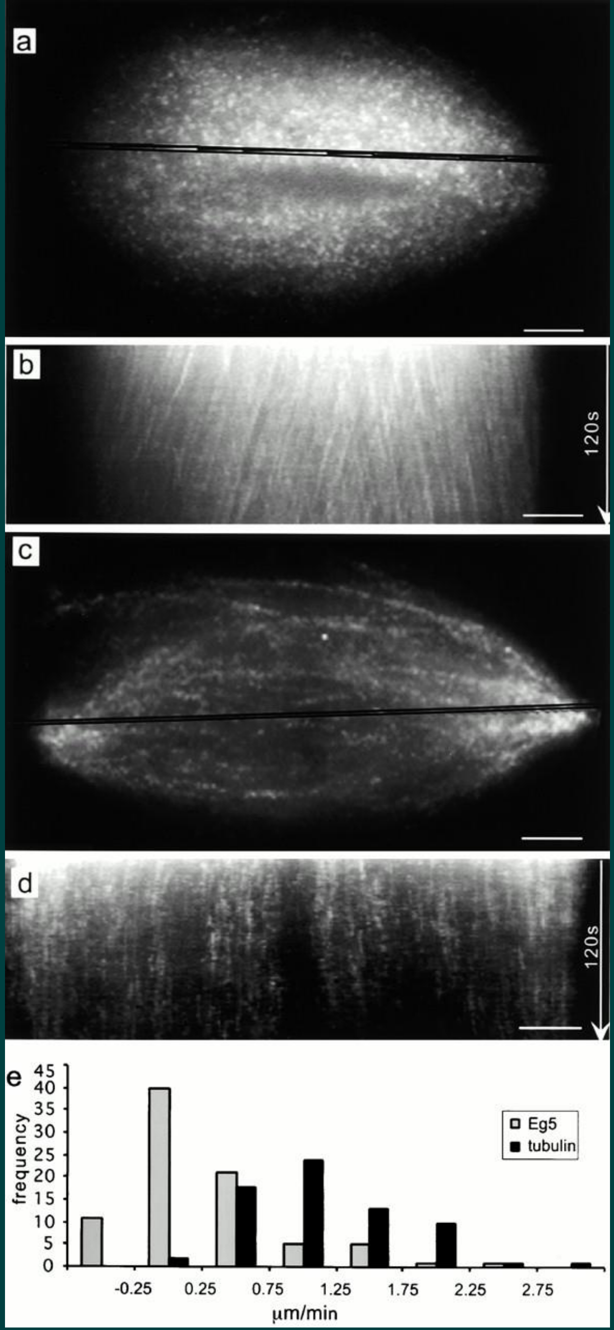




Nedelec, J. Cell Biol., 2002

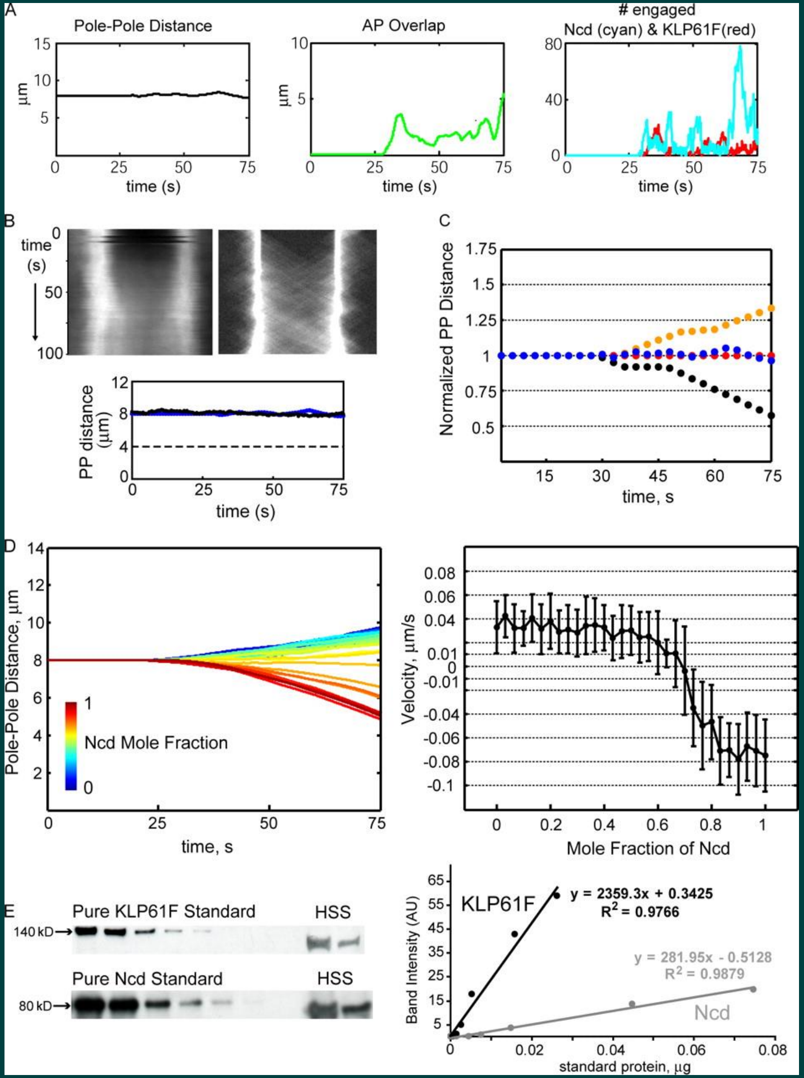
Early ideas about forces in mototic spindle: traction fiber, polar wind and spindle matrix

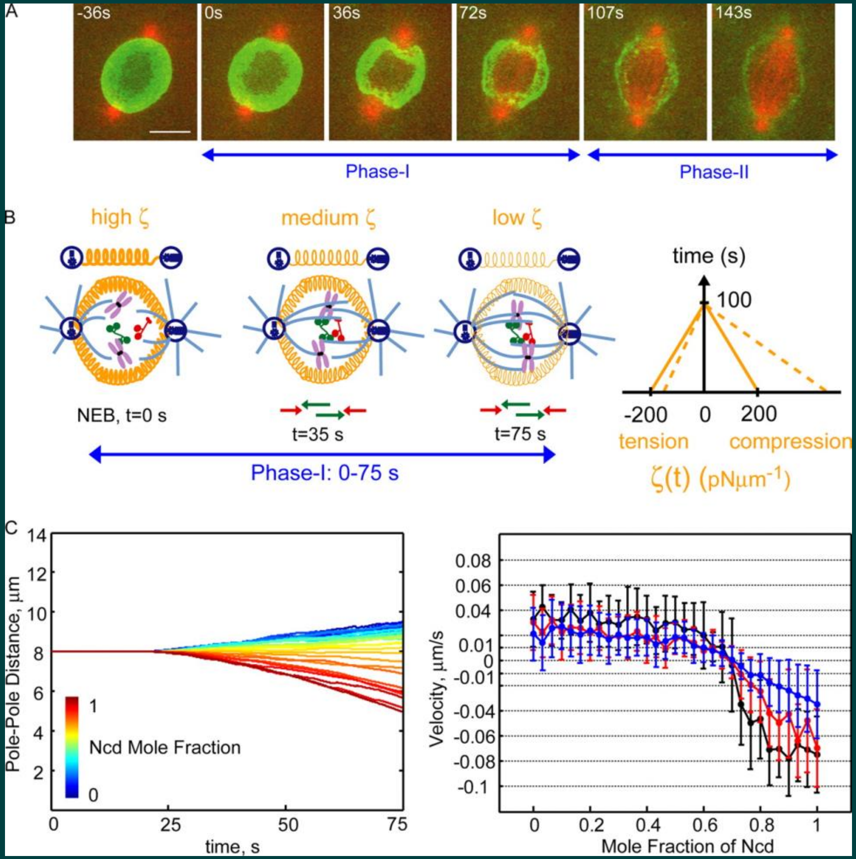




Kapoor and Mitchison, J. Cell Biol., 2001

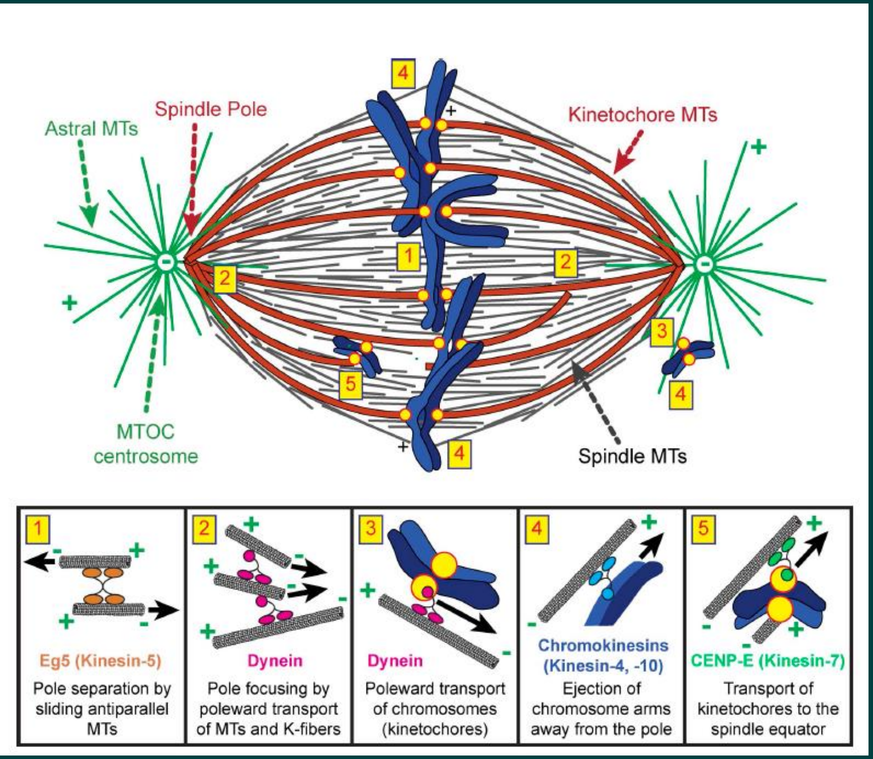
more recent force-balance model: force-dependent detachment of motors
Nuclear lamina can stabilize the separation

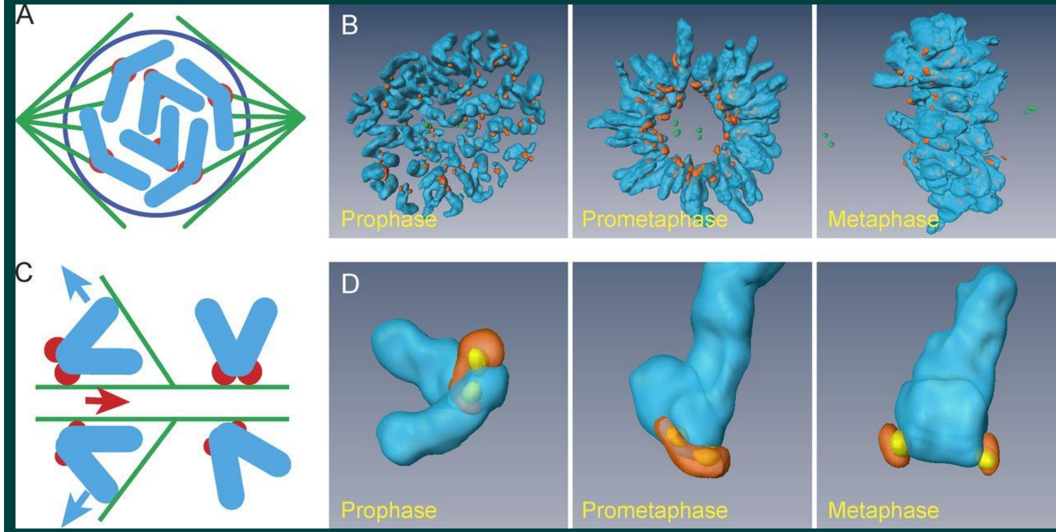




Civelekoglu-Scholey et al., JCB, 2010

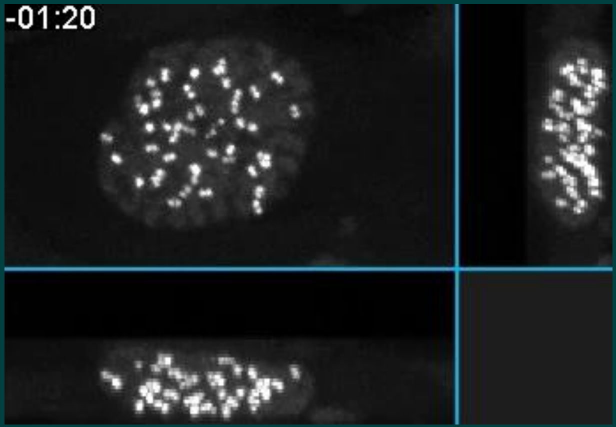
How do microtubules (kinetochore fibers) find chromosomes (kinetochores): search and capture hypothesis and what makes it work

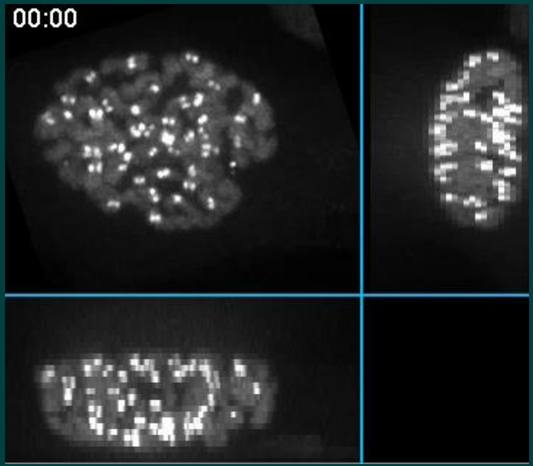


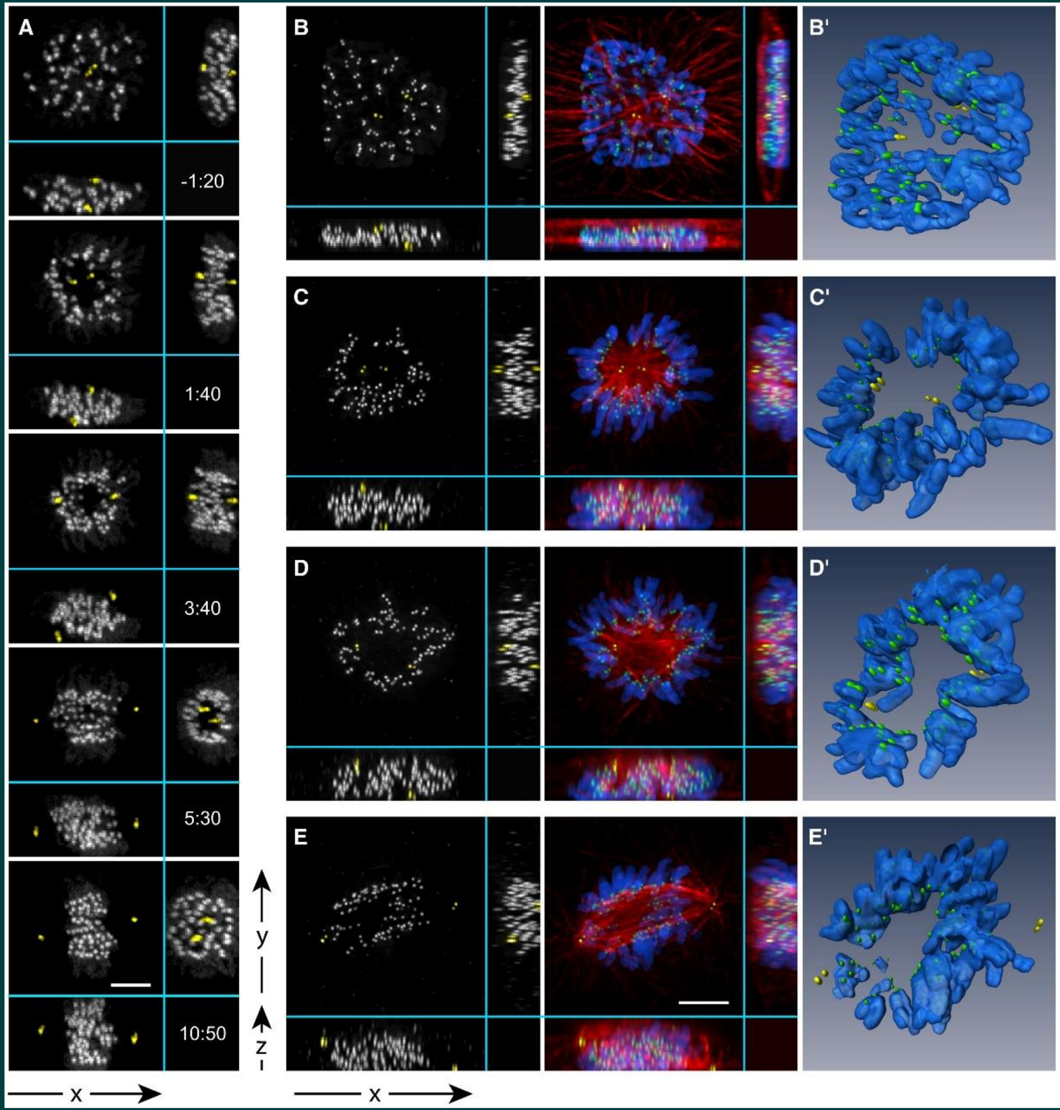


Heald and Khodjakov, 2015

Chromosome ring at the spindle periphery helps search and capture

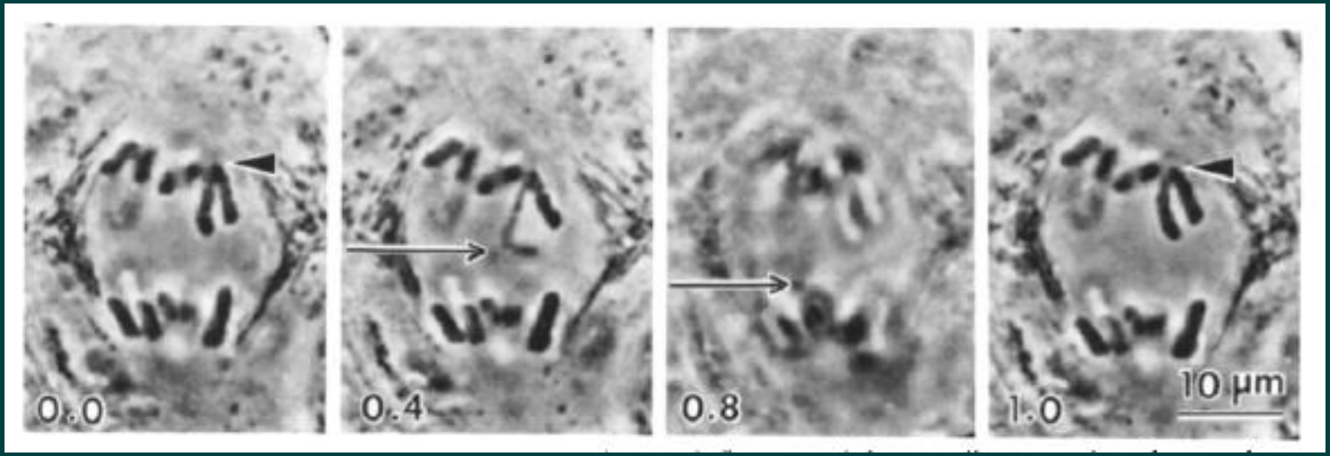






Magidson et al., 2011

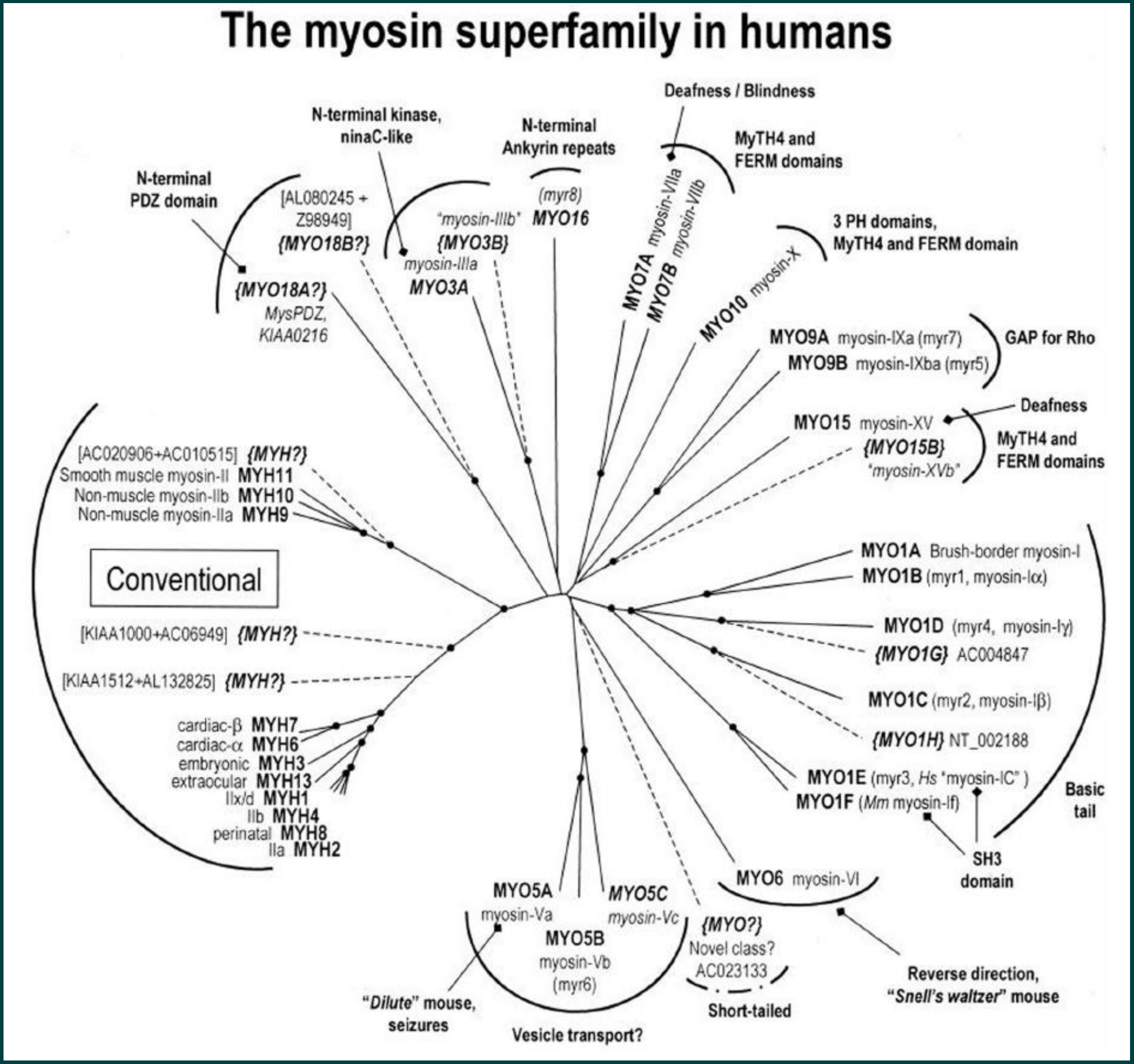
Nanonewton forces in mitotic spindle



microneedle in grasshopper spermatocytes
Nicklas, J. Cell Biol., 1983

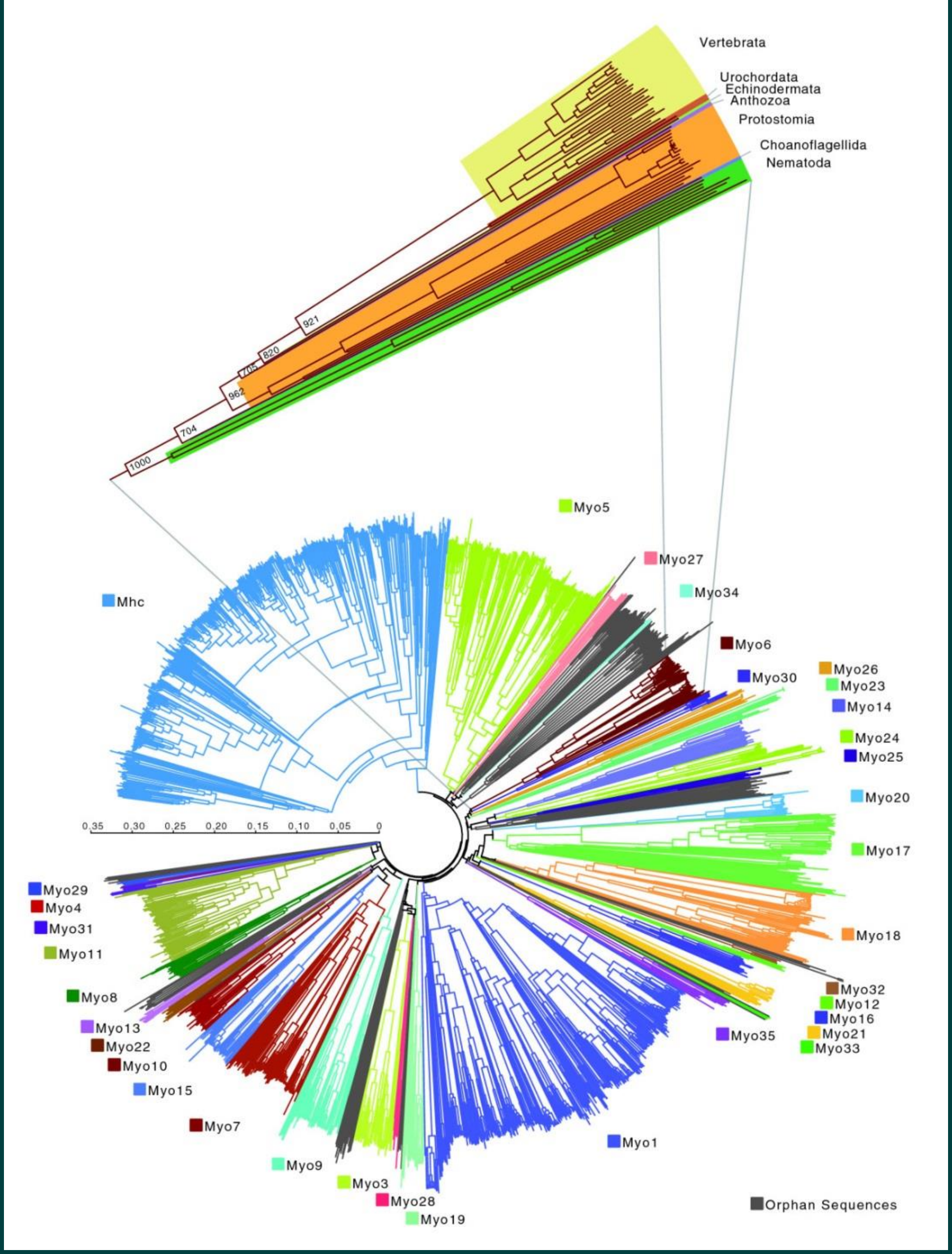
100 nN, but 1 nN is enough to overcome viscous resistance

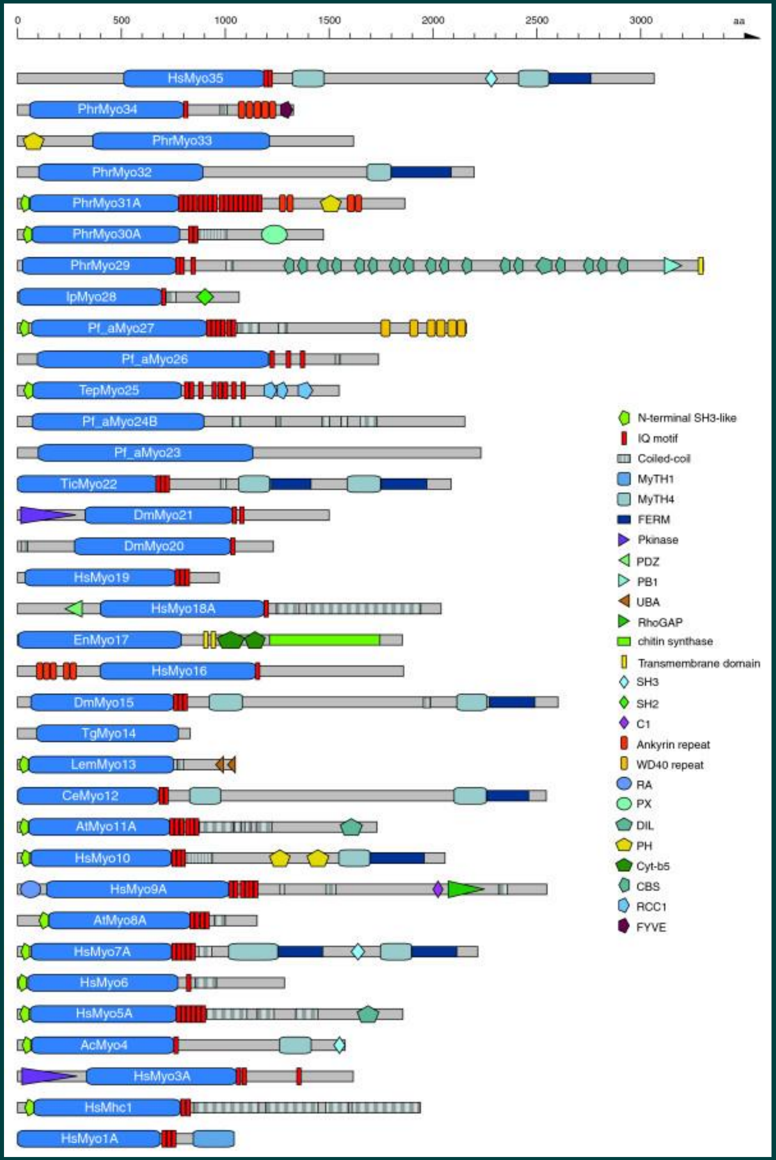
Myosin superfamily: actin-dependent translational motors



Batters et al., 2014

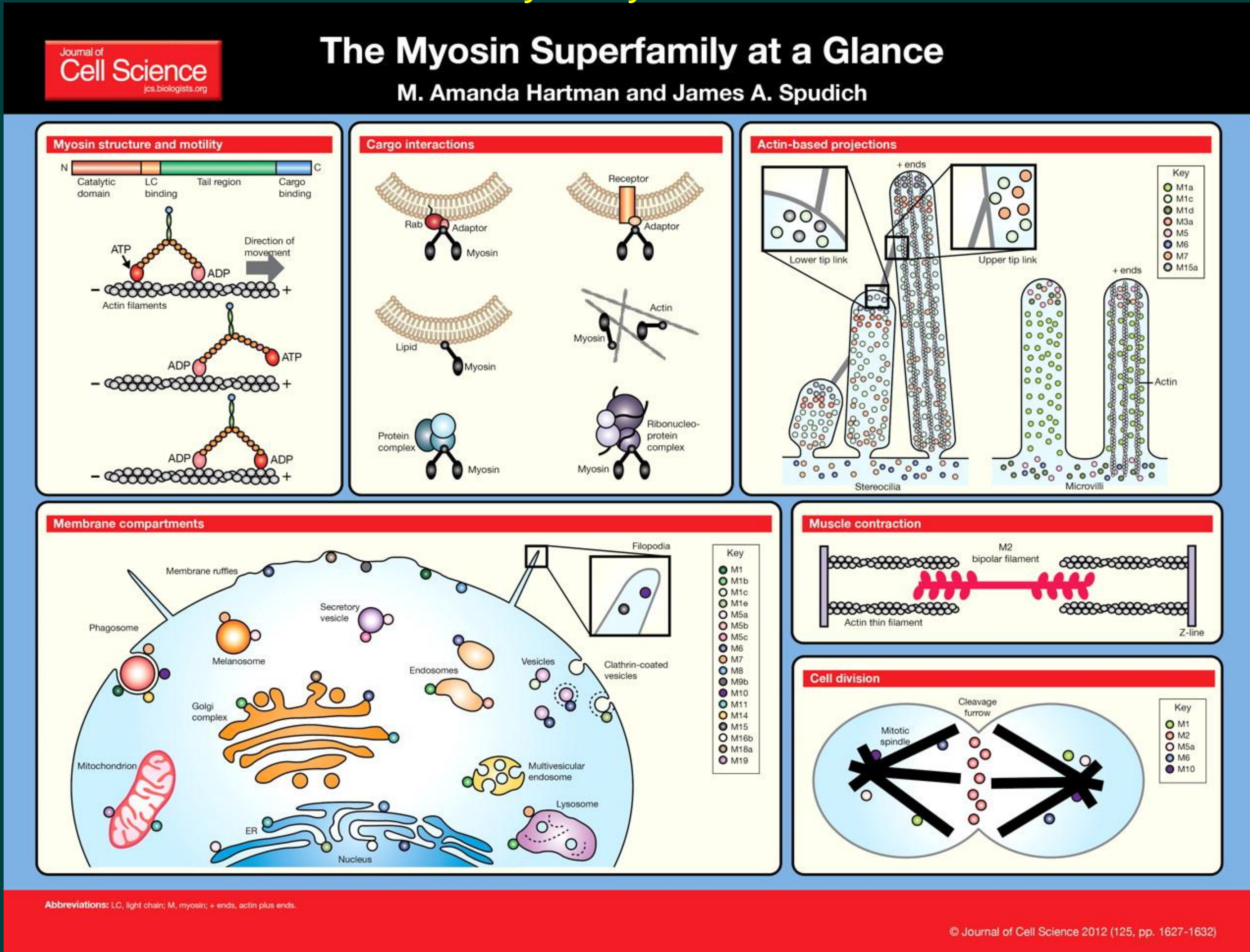
Filogenetic tree of myosin superfamily



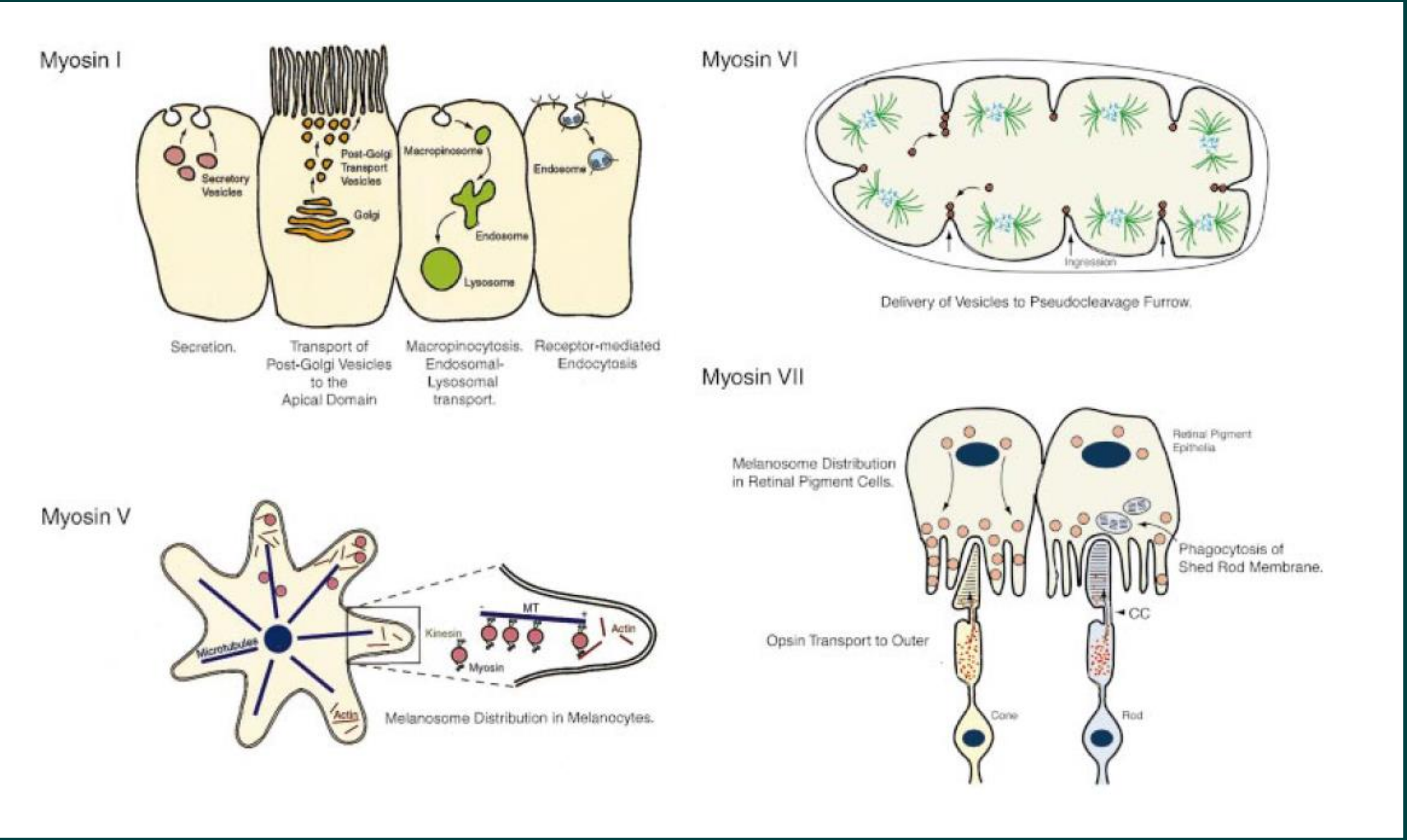


Odronitz and Kollmar, 2007

Summary of myosin functions

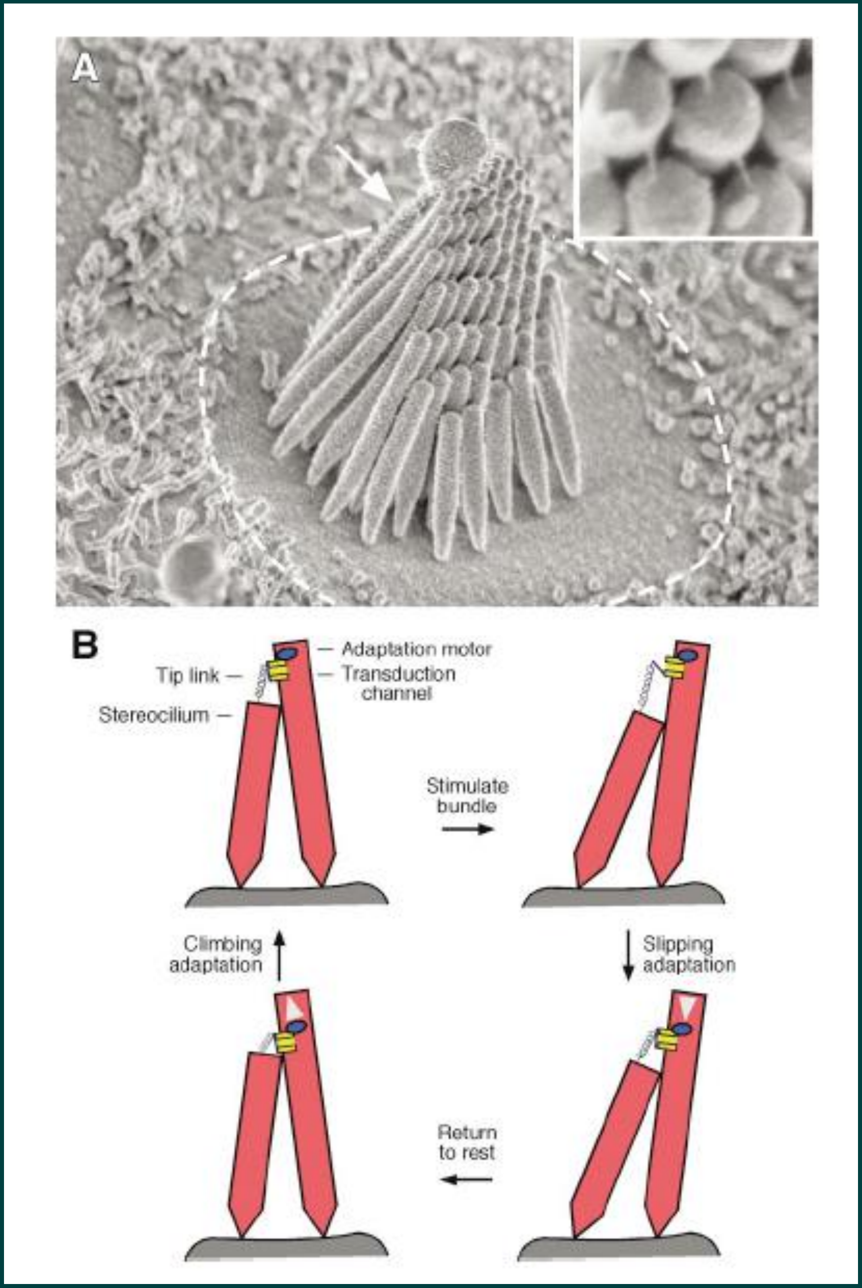


Unconventional myosins in membrane traffic

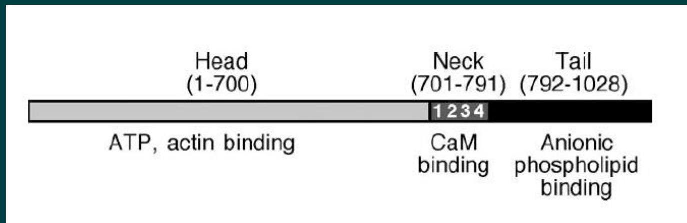


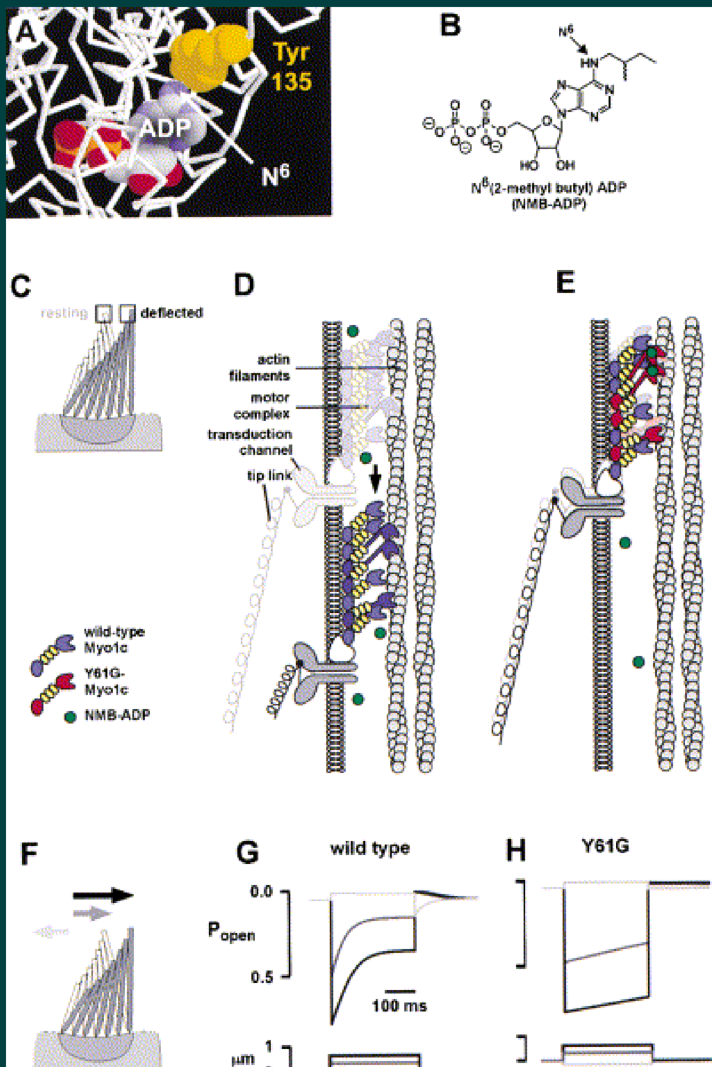
Tuxworth and Titus, Traffic, 2001

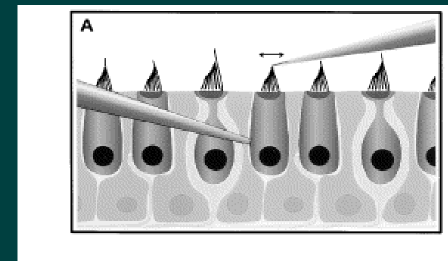
Adaptation motor

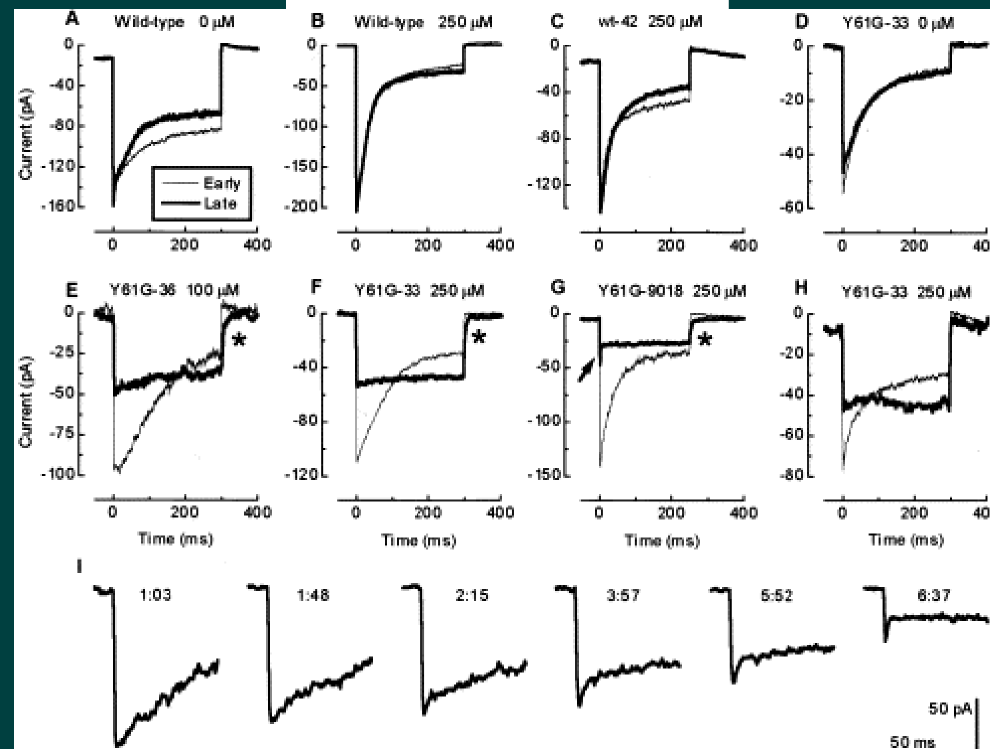


Myosin 1c in adaptation by hair cells









Holt et al., Cell, 2002

myosin II in the muscle

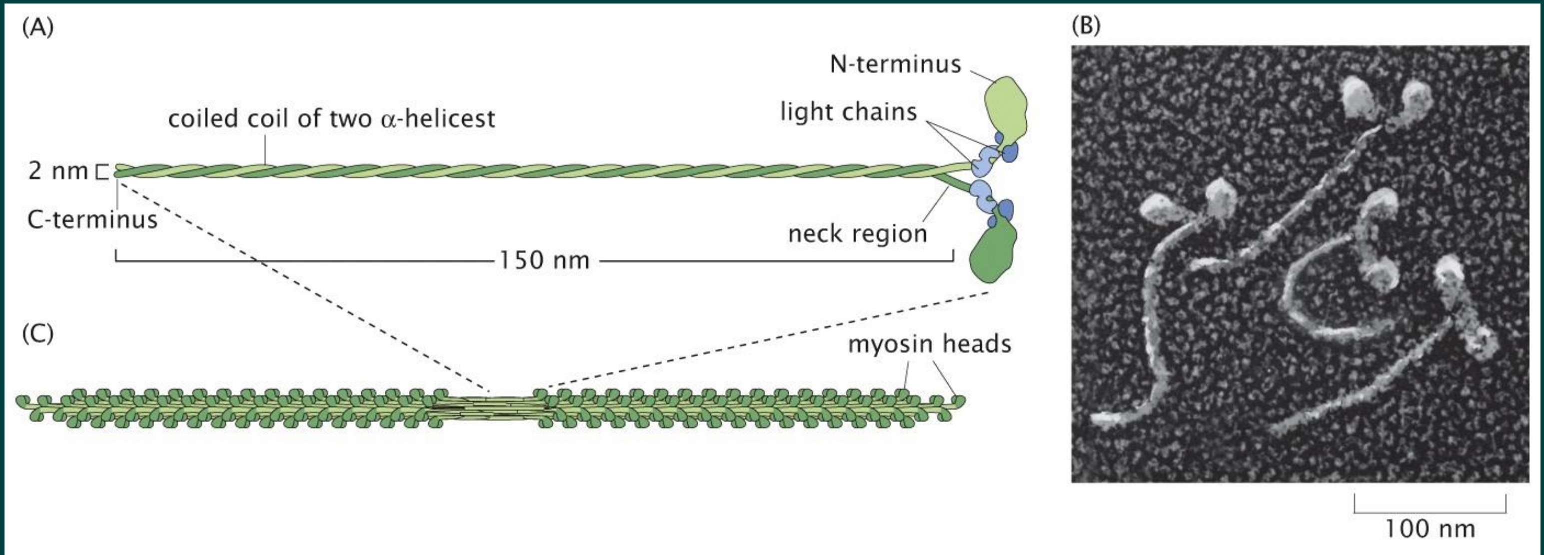


Figure 16.6 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

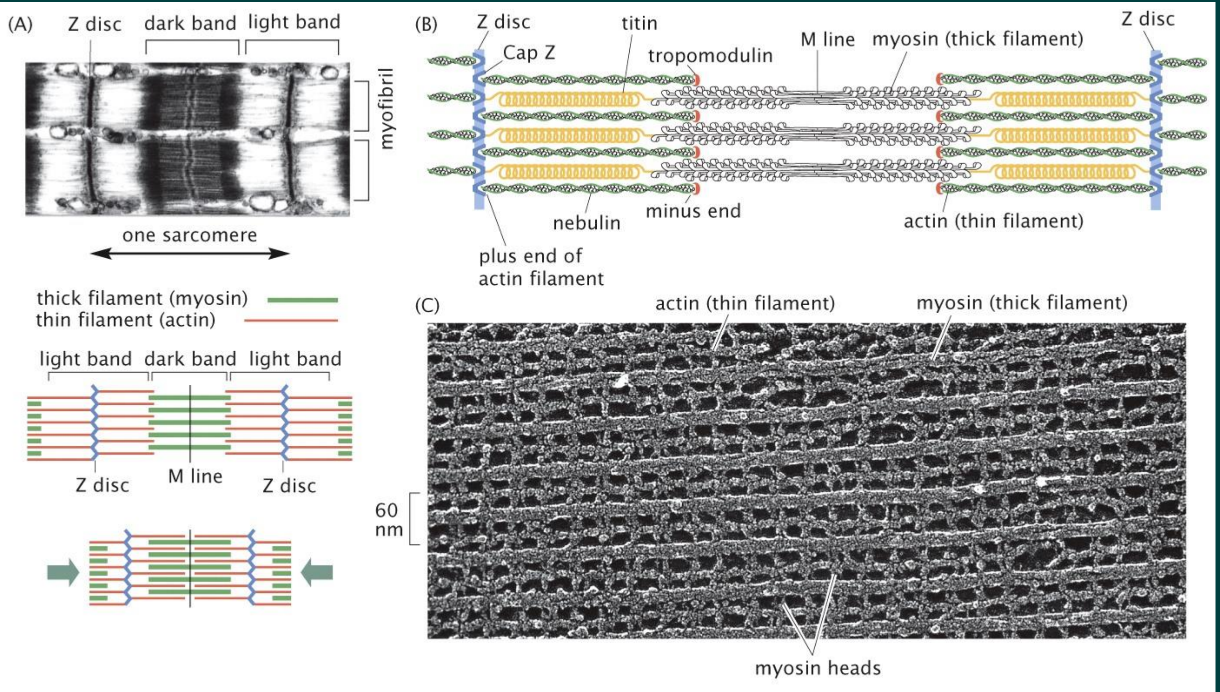
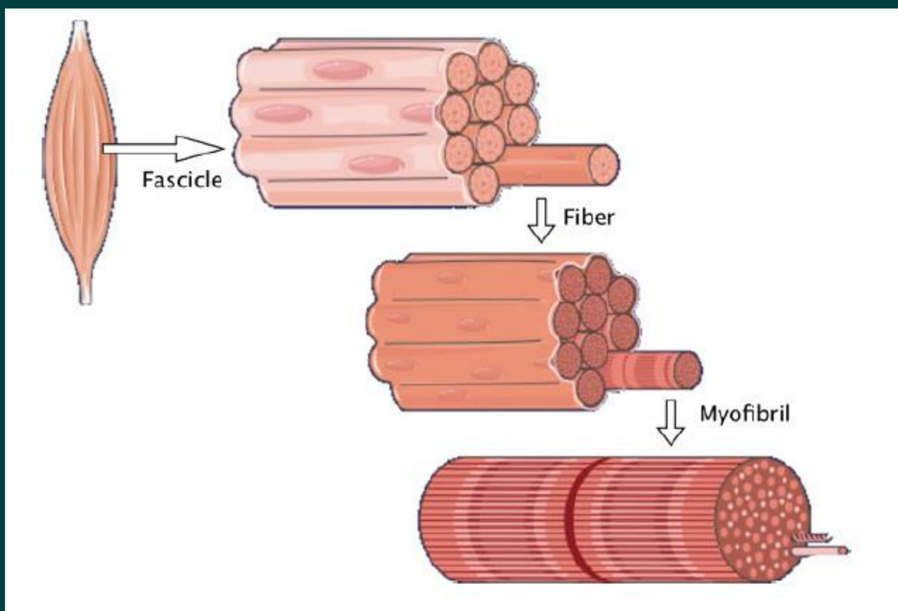
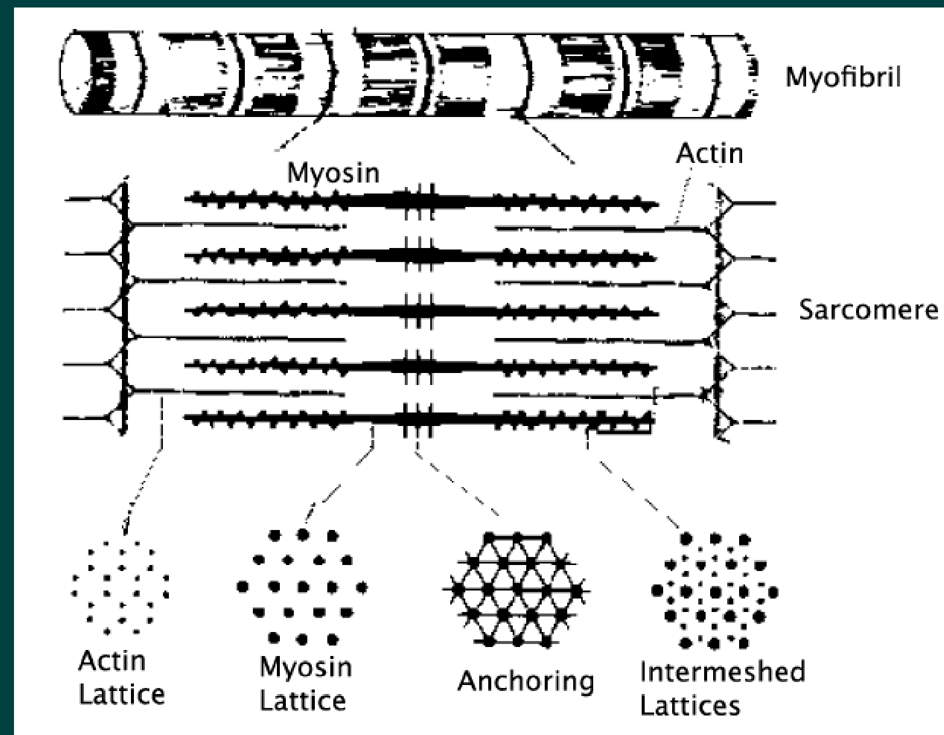


Figure 16.7 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Regular organization of contractile units in skeletal muscle





Williams, 2011

Muscle contraction is activated through release of Ca-ions from sarcoplasmic reticulum leading to a conformational change in troponin-tropomyosin complex making actin filaments accessible to myosin

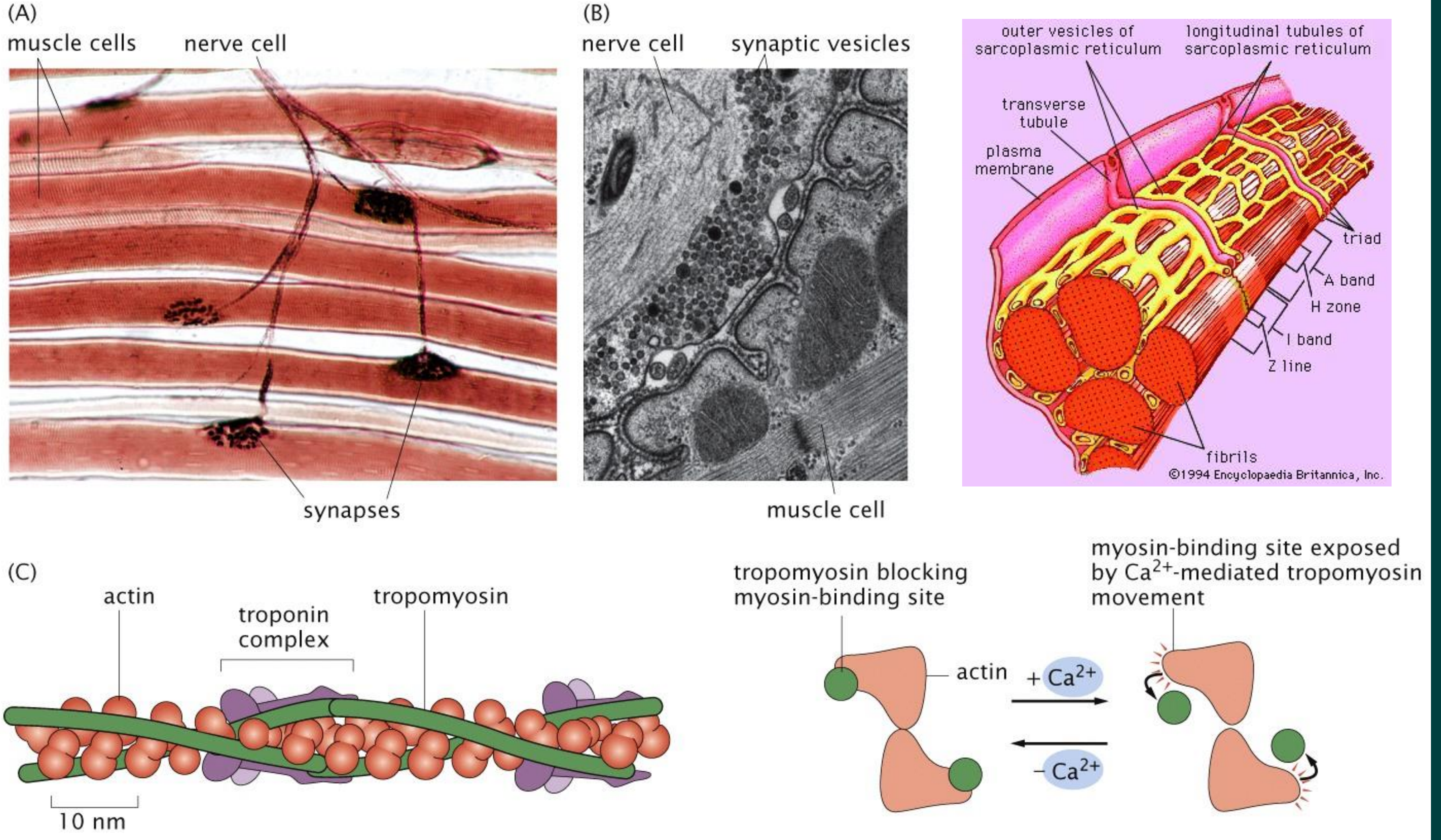
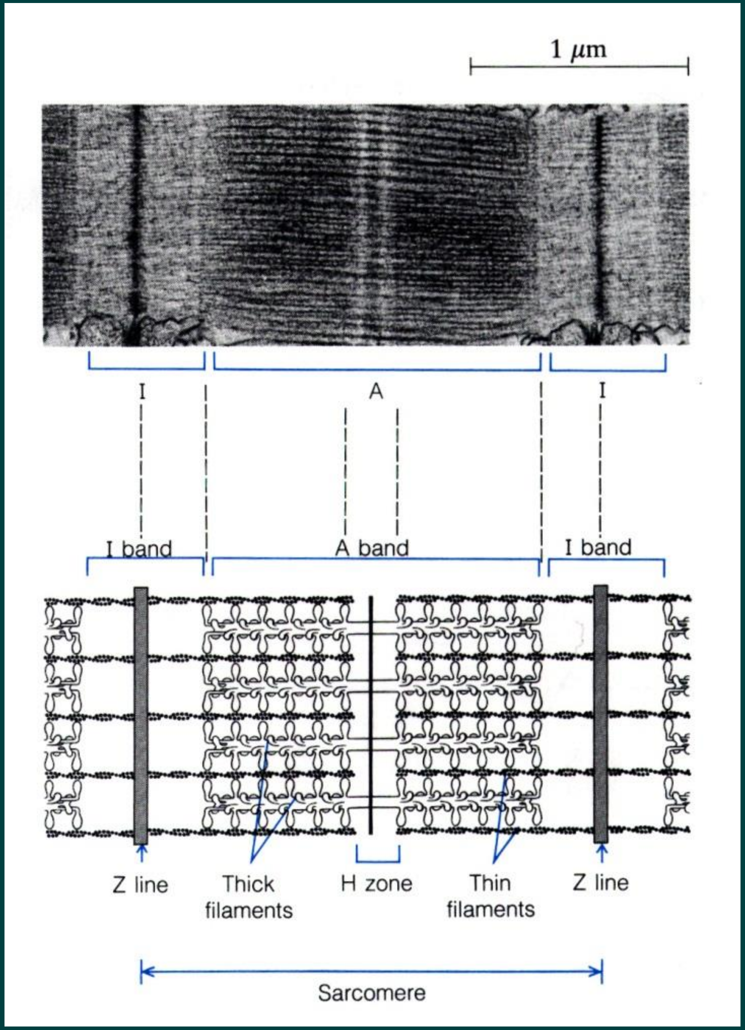
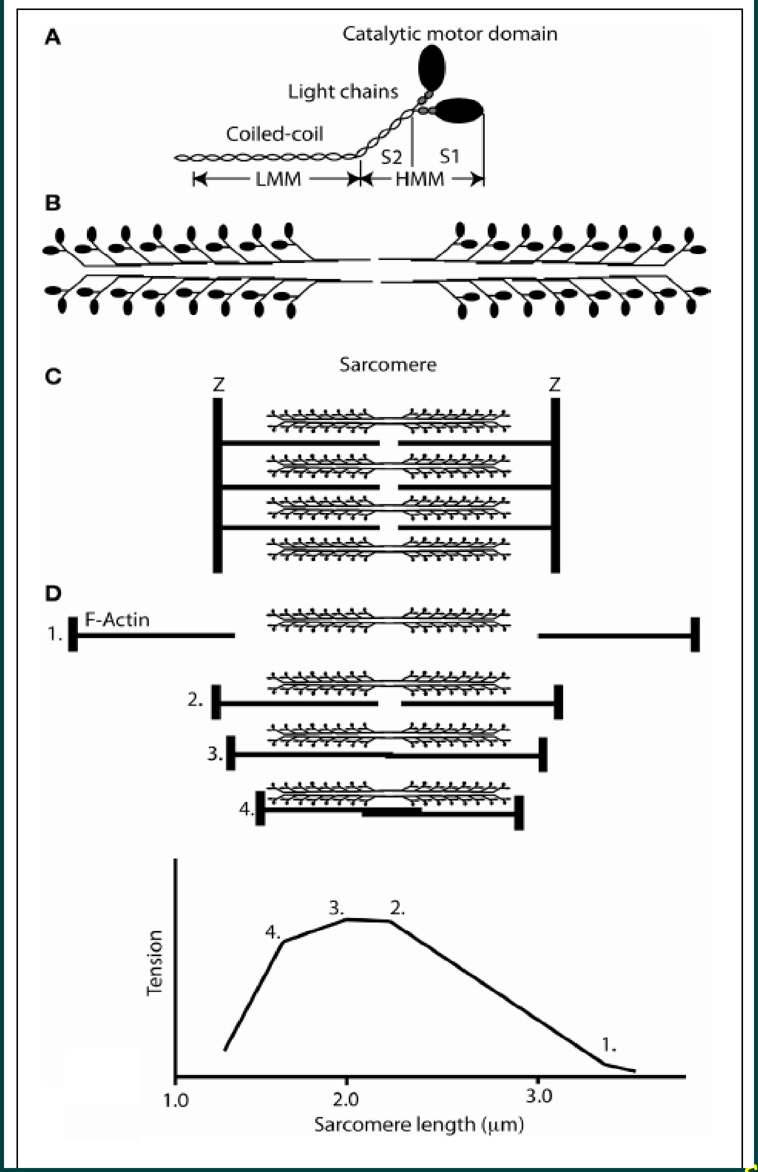


Figure 16.39 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Muscle contraction: sliding filament hypothesis
Huxley and Hanson, Huxley and Niedergerke, 1954

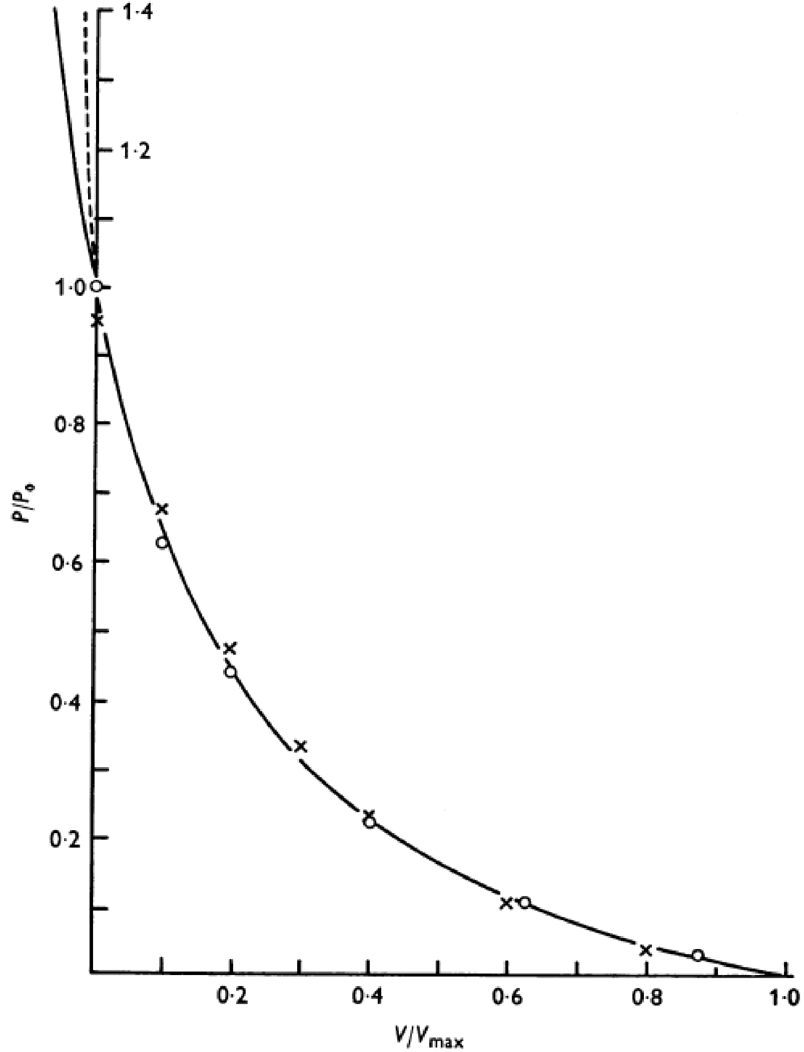




Linear force-velocity relation (an abstraction often used in modeling)

$F = F_0 \, (1 - V/V_{max})$

Force-velocity relationship for skeletal muscle is hyperbolic (Hill, 1938)



Text-fig. 1. Force–velocity relation. The degree of curvature of the relation varies between different preparations, and with temperature. Continuous line: Hill's (1938) relation,

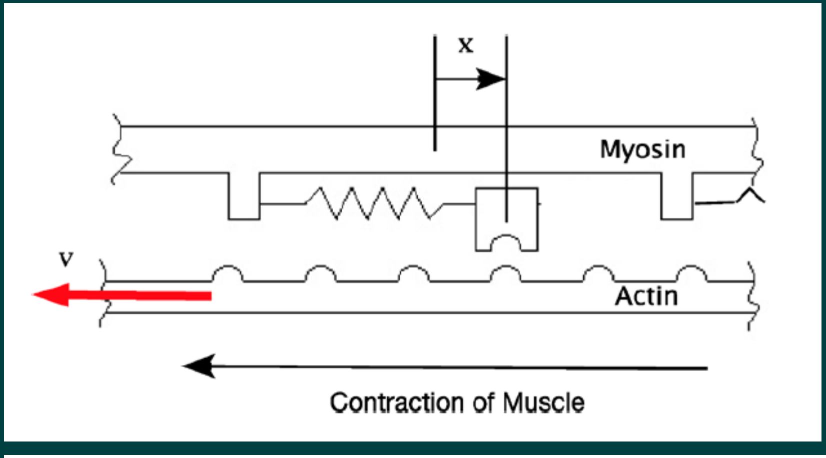
$$P/P_0 = (1 - V/V_{max})/(1 + (P_0/a)V/V_{max}),$$

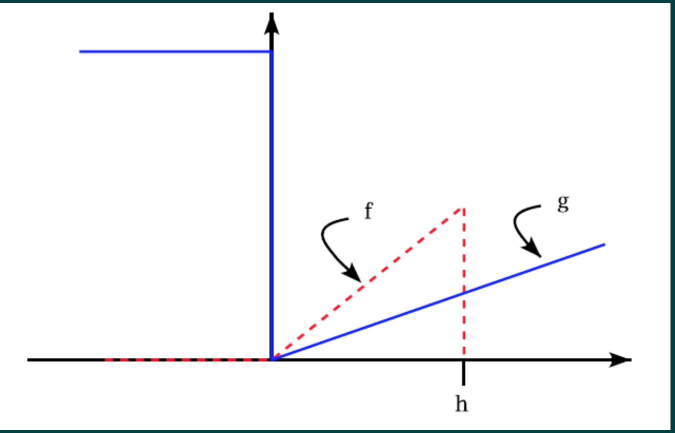
with $P_0/a = 4$, appropriate for frog muscle at 0° C.

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

A.F. Huxley, 1974

A.F. Huxley's model of muscle contraction: force and the probability to attach and detach depend on the cross-bridge deformation





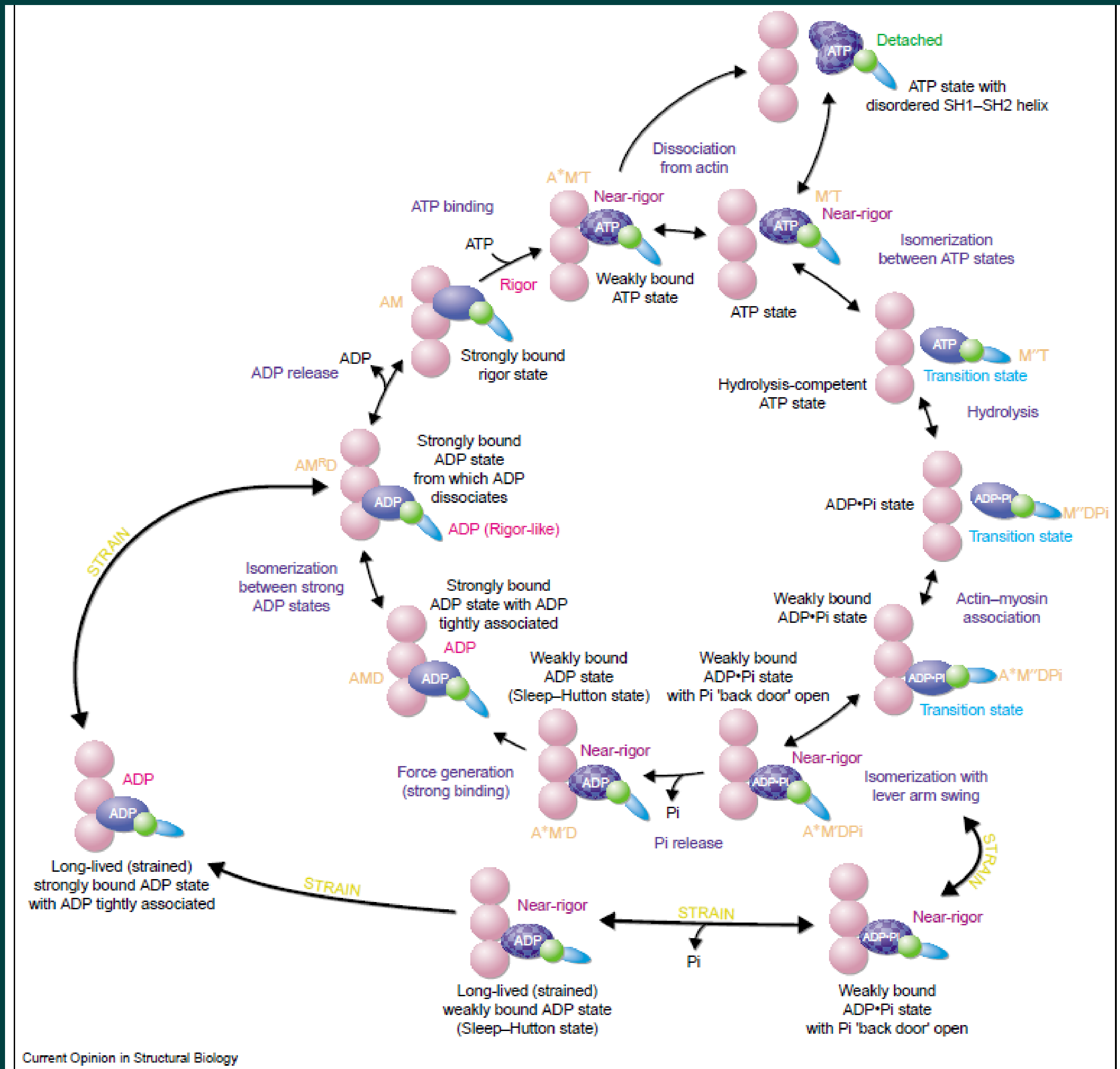
$$\frac{d}{dt}N((a,b),t) = \int_a^b \frac{\partial n}{\partial t}(x,t)\,\mathrm{d}x$$
$$= \int_a^b (F(x,t) - G(x,t))\,\mathrm{d}x + v(t)[n(b,t) - n(a,t)].$$

$$\frac{\partial n(x,t)}{\partial t} = F(x,t) - G(x,t) + v(t)\left(\frac{\partial n(x,t)}{\partial x}\right)$$

$$P(t) = \int_{-X}^{X} \mathcal{E}(x)\,n(x,t)\,\mathrm{d}x$$

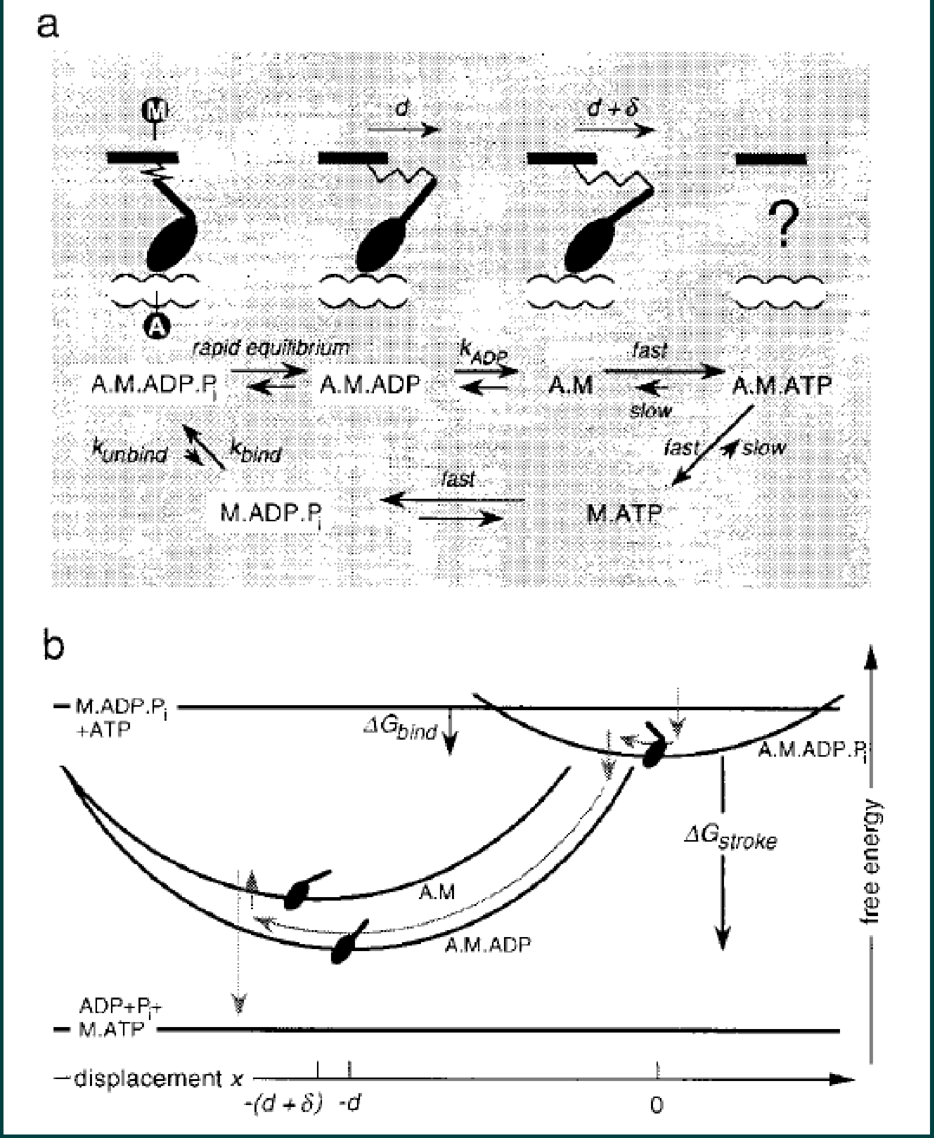
Williams, 2011

Huxley's model does not consider the complexity of myosin cycle of ATP-hydrolysis and power stroke



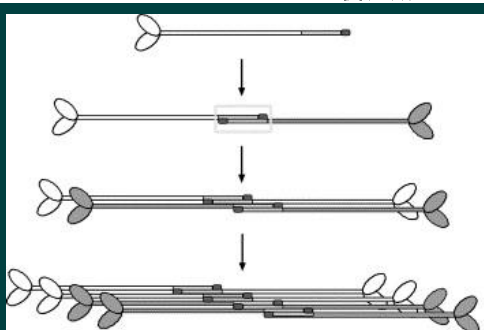
Houdusse and Sweeney, 2001

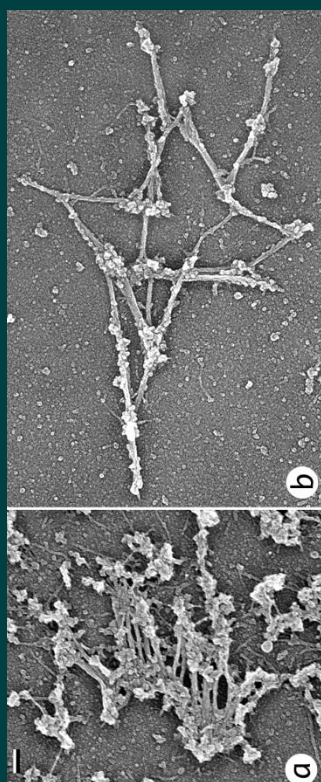
Molecular model taking into account myosin cycle

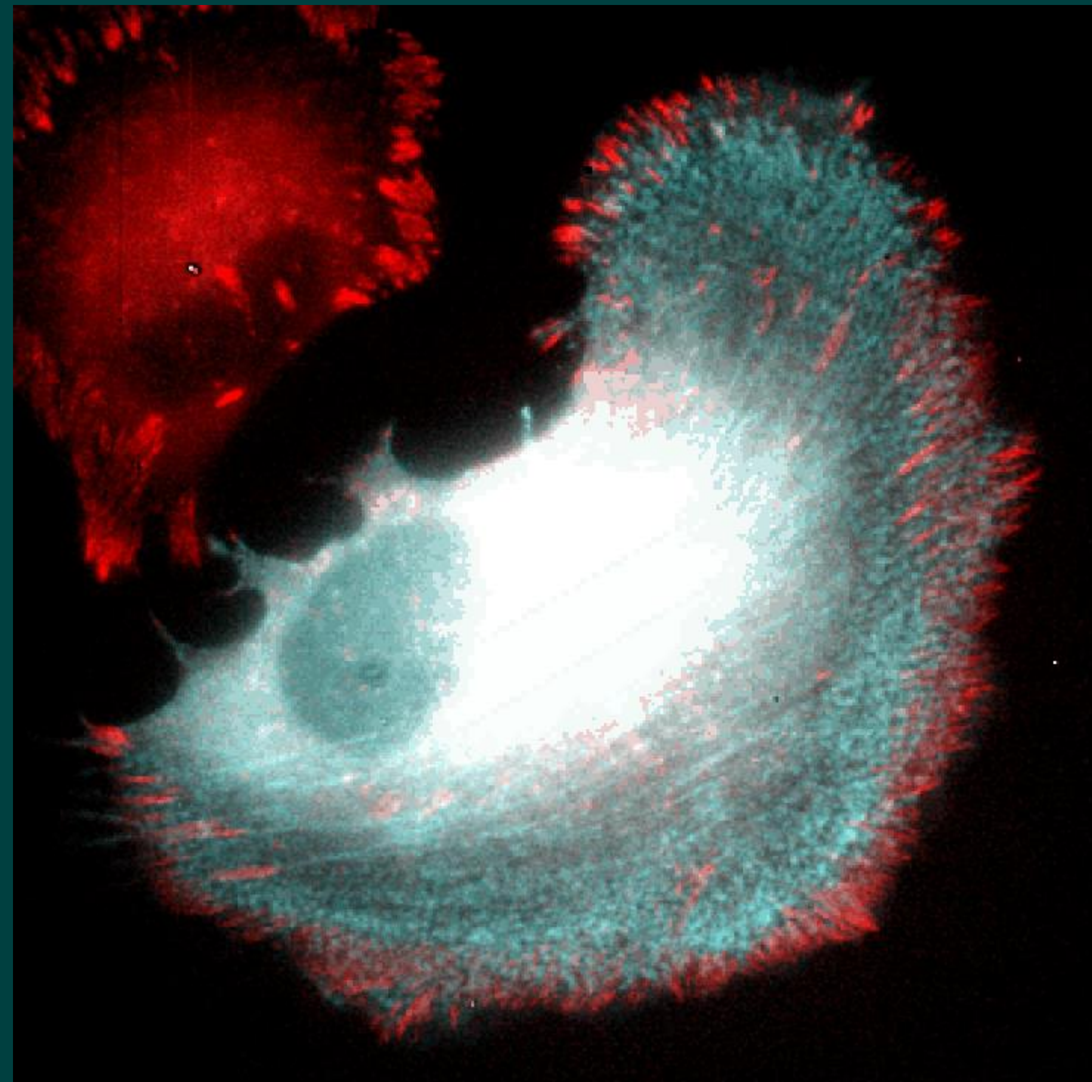


Duke, PNAS, 1999

Myosin II in non-muscle cells

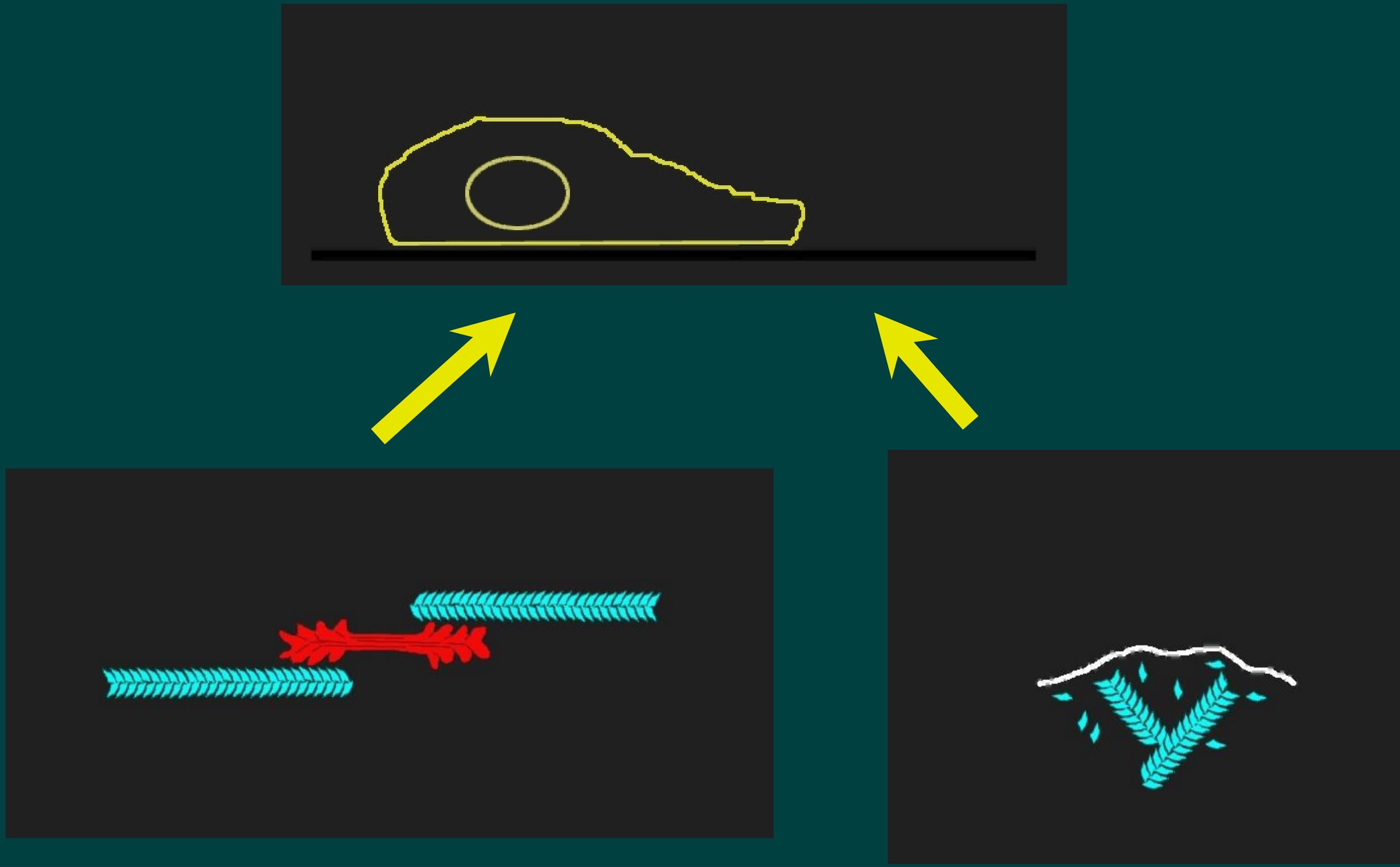






Verkhovsky et al., J. Cell Biol., 1995

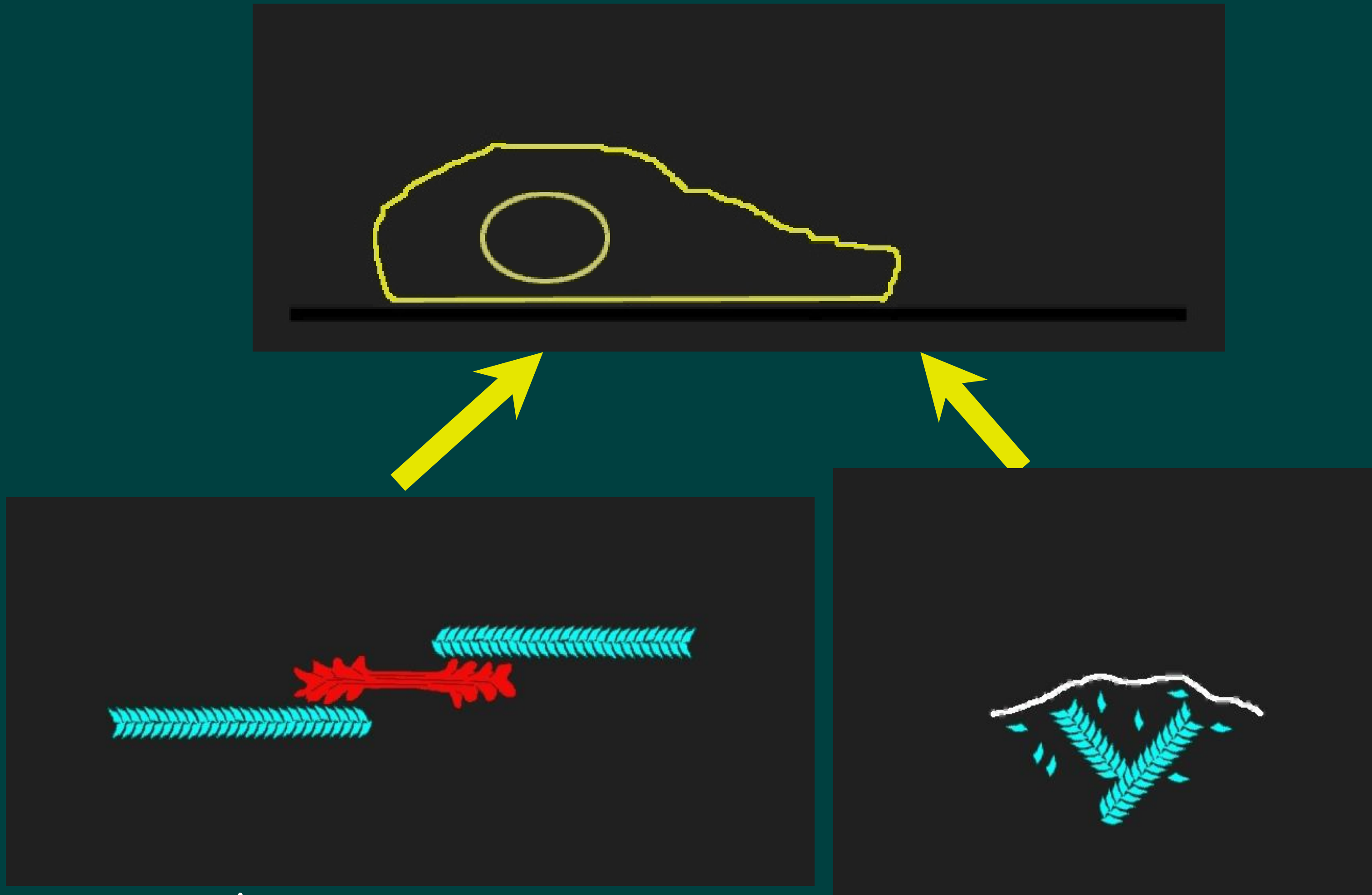
proposed role for myosin II in crawling cell motility



actin/myosin contraction
(analogous to muscle)

actin assembly

proposed role for myosin II in crawling motility



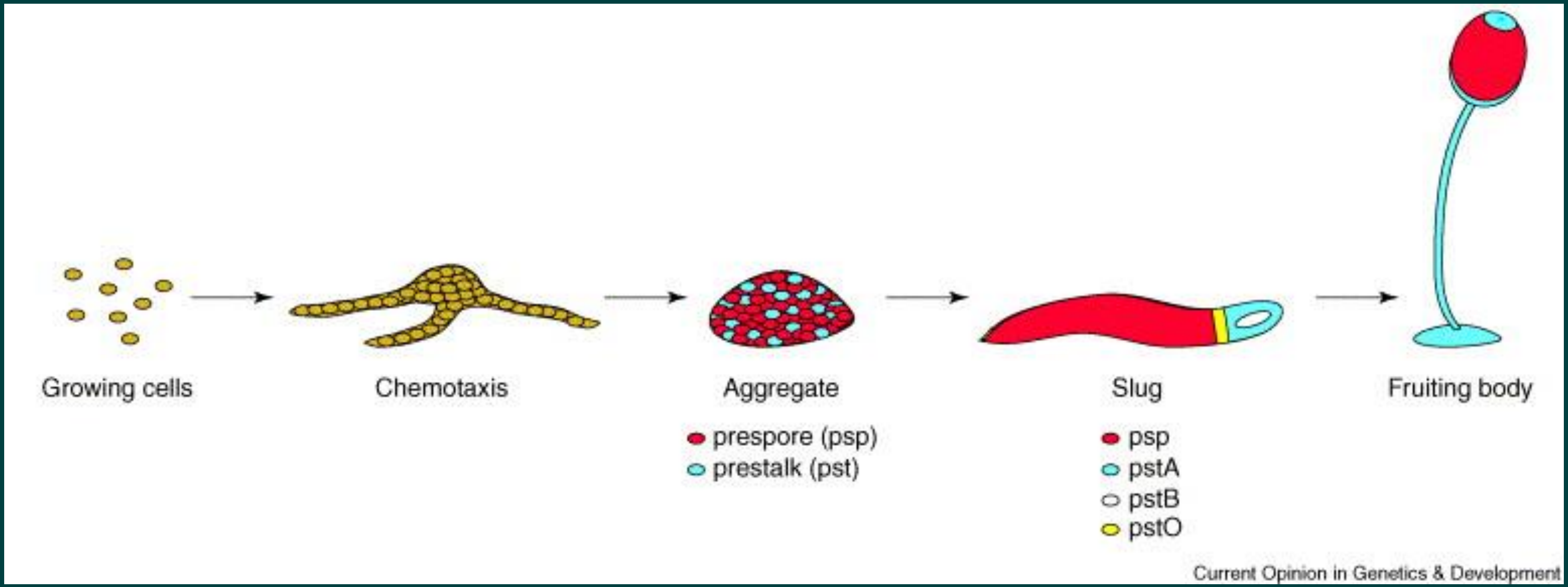
actin/myosin contraction

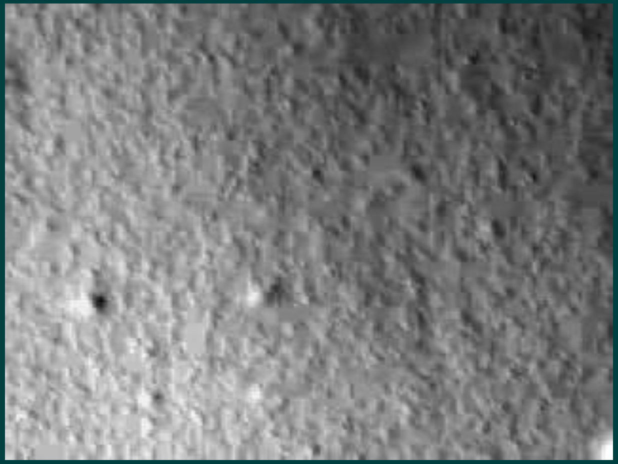
actin assembly

Is myosin II essential for retraction?

What is the contraction mechanism?

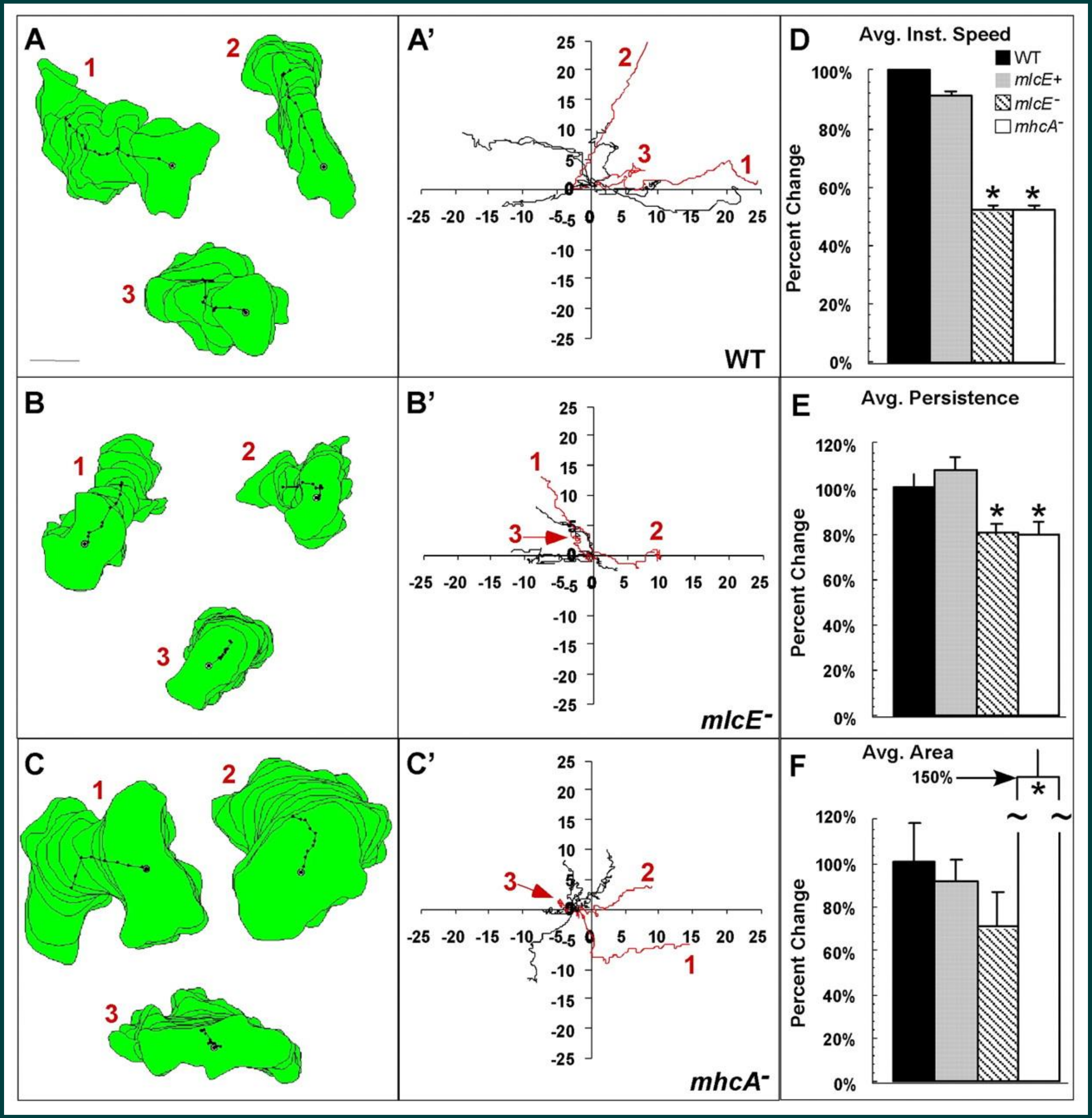
Dictyostelium : a model for motility and chemotaxis (accessible to genetic manipulation)





Myosin II mutants exhibit motility and chemotaxis, but do not form fruiting bodies

Motility in Dictyostelium myosin II mutants

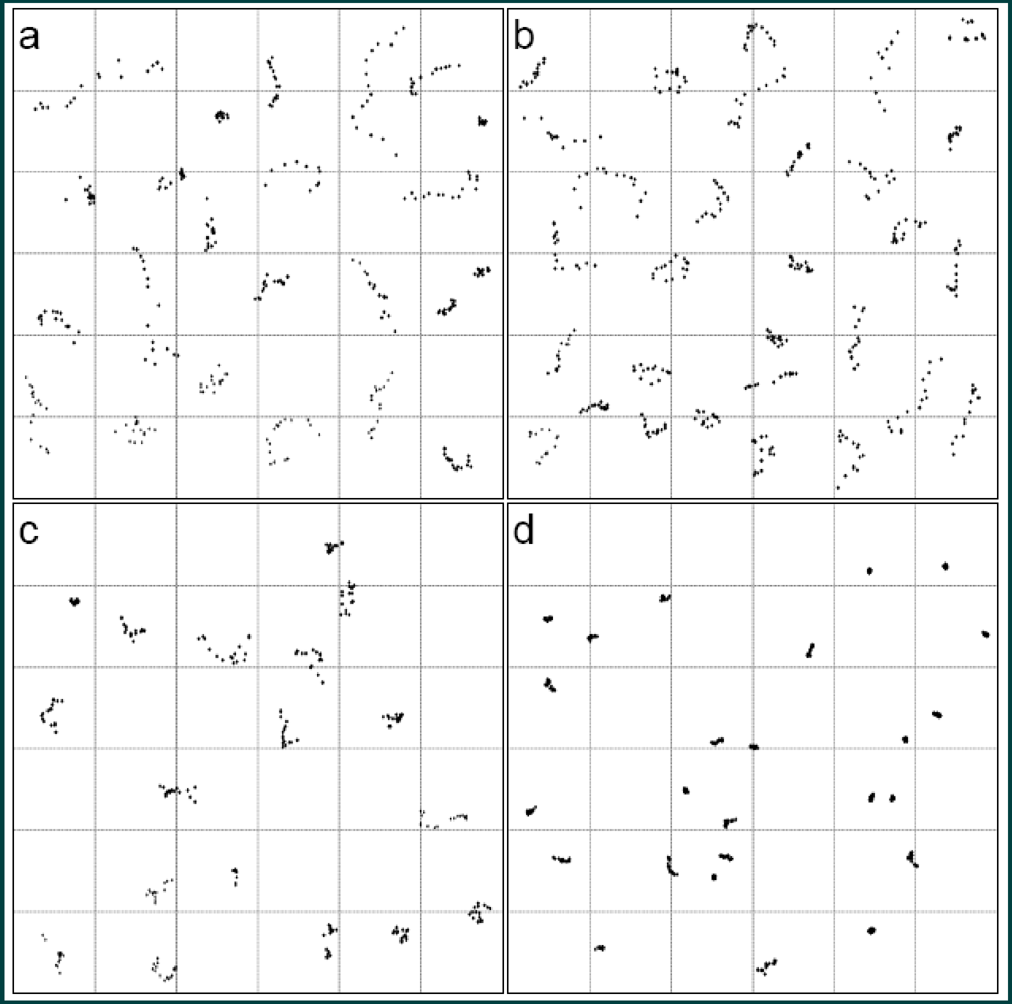


Lombardi et al., J. Cell Sci., 2007

Myosin II-null cells cannot move on strongly adhesive substrates

wild type

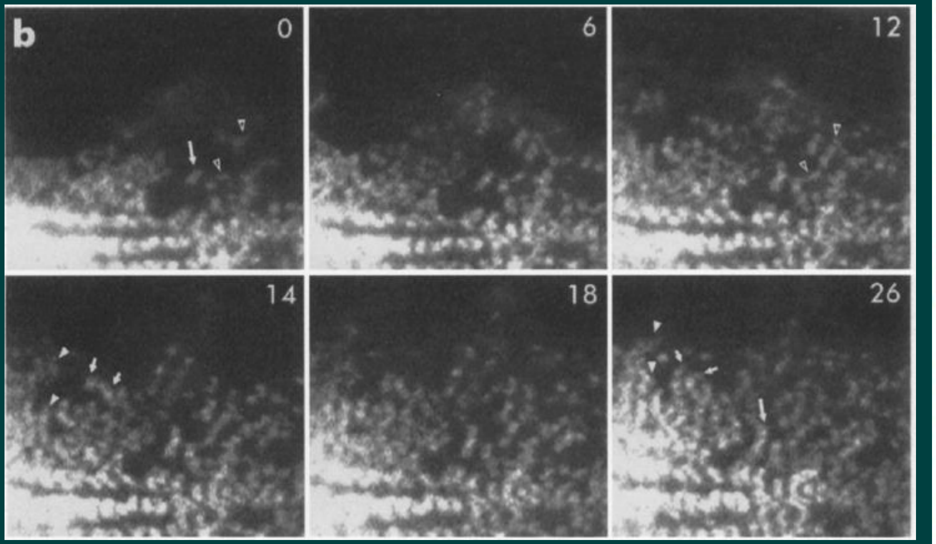
mhcA$^-$

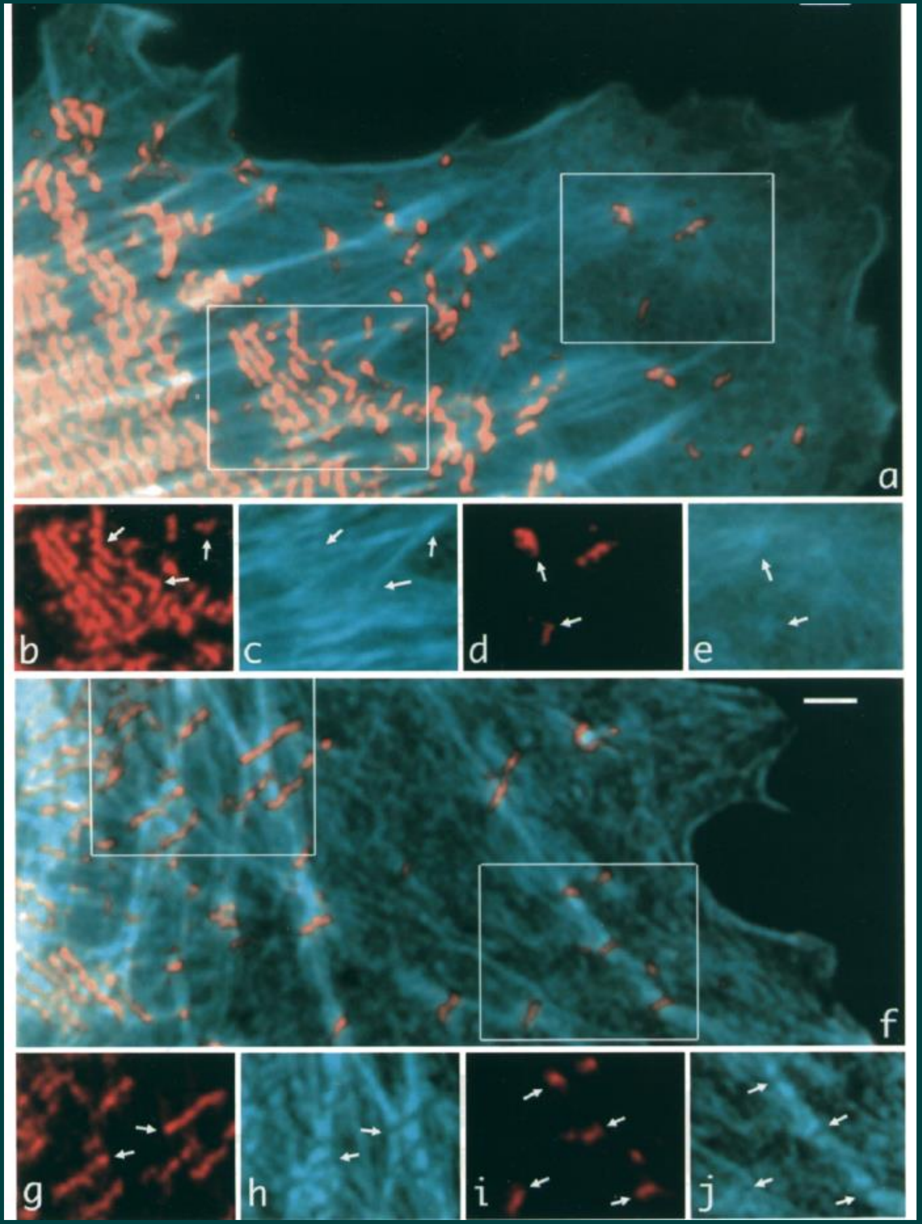


uncoated   polylysine-coated

Jay et al., J.Cell Sci., 1995

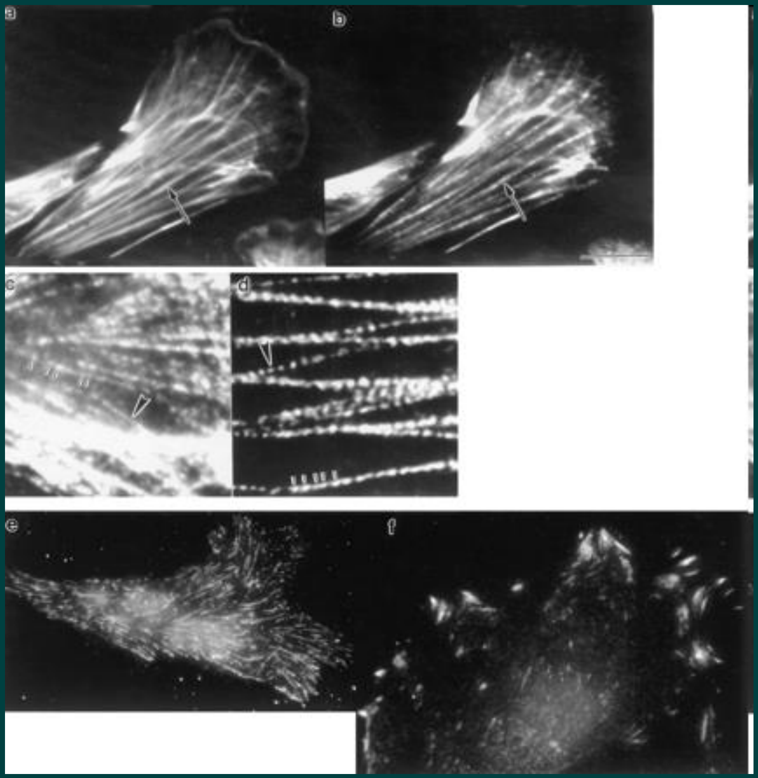
Myosin II organization in non-muscle cells (fibroblasts)

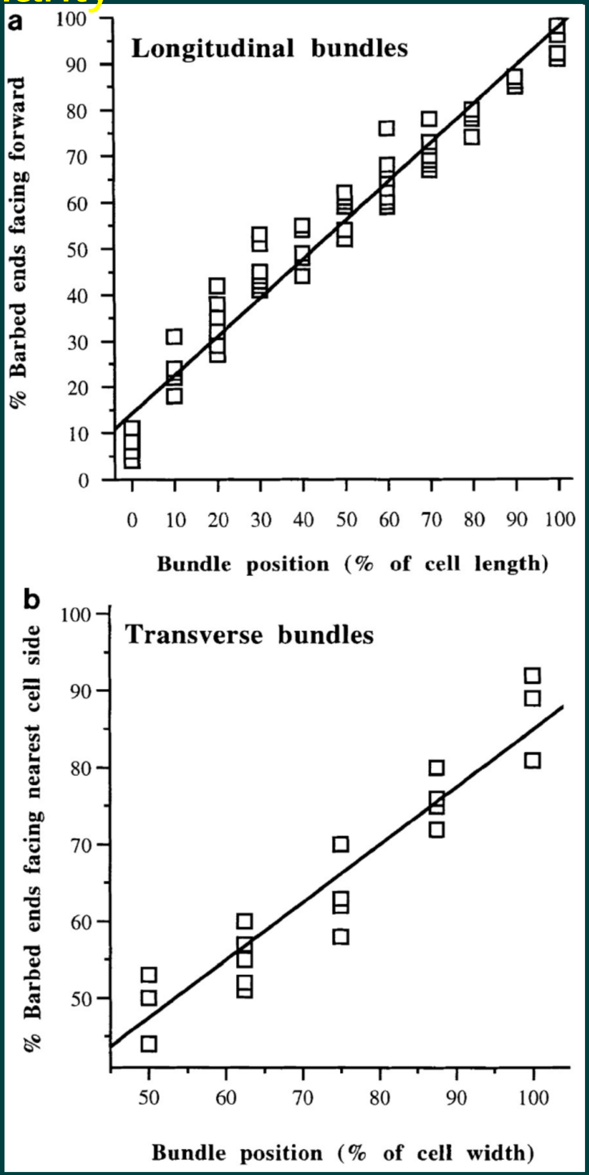




Verkhovsky et al, 1995

In migrating fibroblasts, actin filament bundles have irregular myosin II organization and graded actin filament polarity





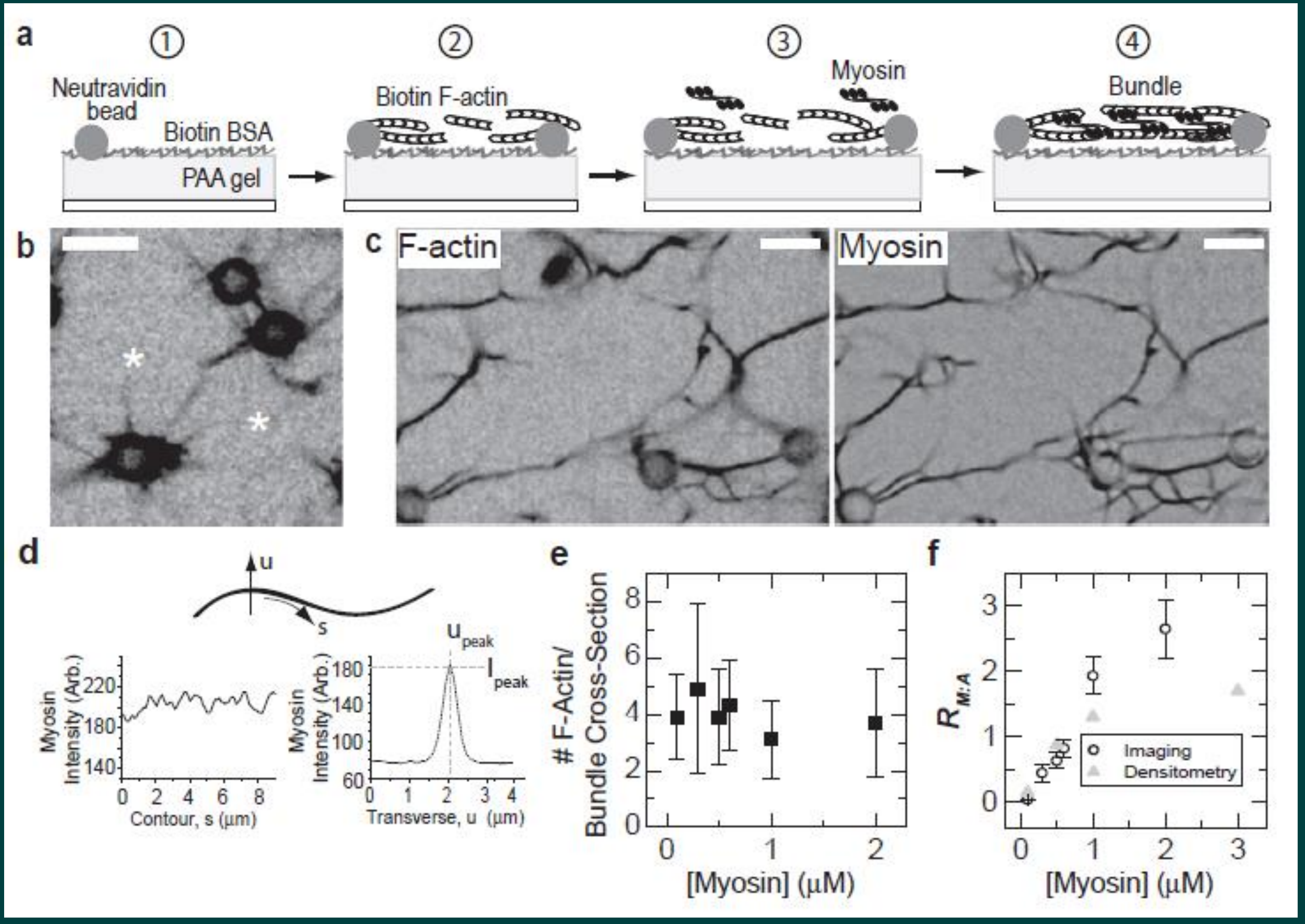
Cramer et al., JCB, 1997

How could actomyosin bundles contract in non-muscle cells if there is no regularly alternating actin polarity?

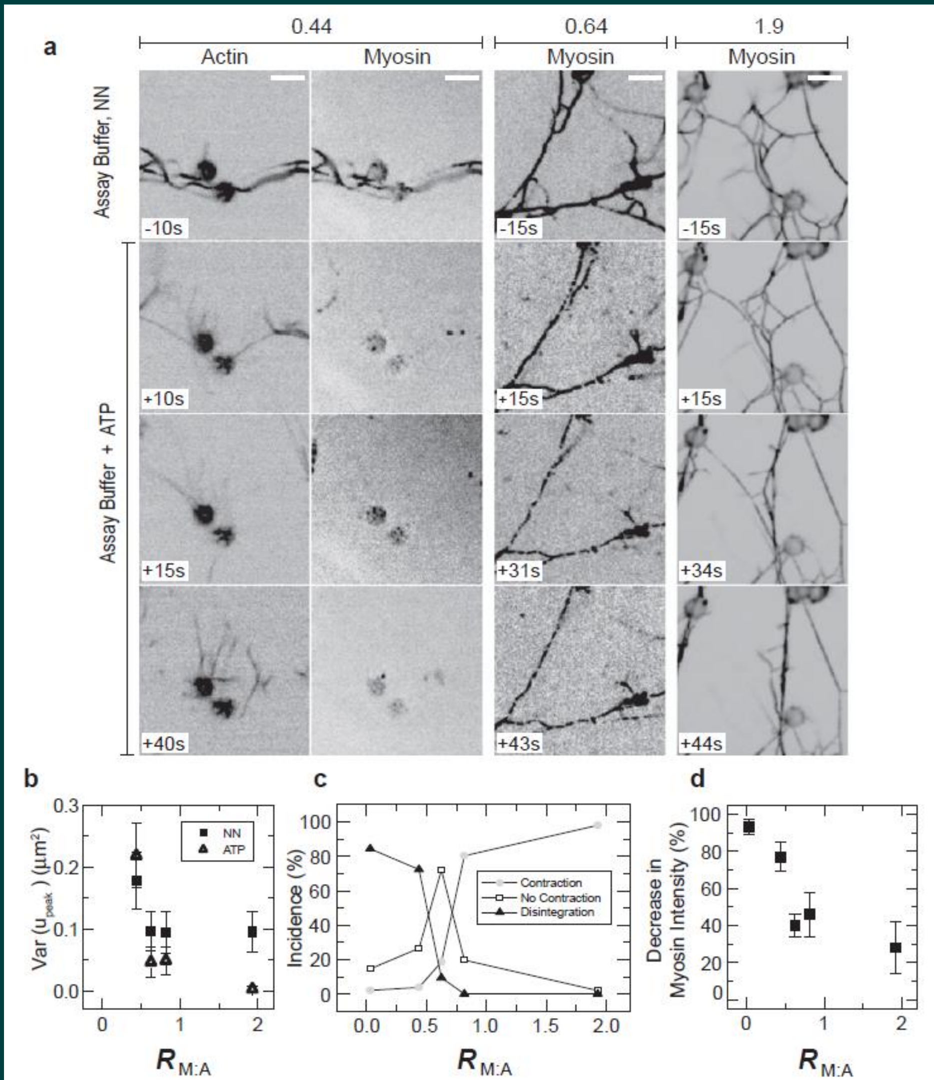
2698 Biophysical Journal Volume 100 June 2011 2698–2705

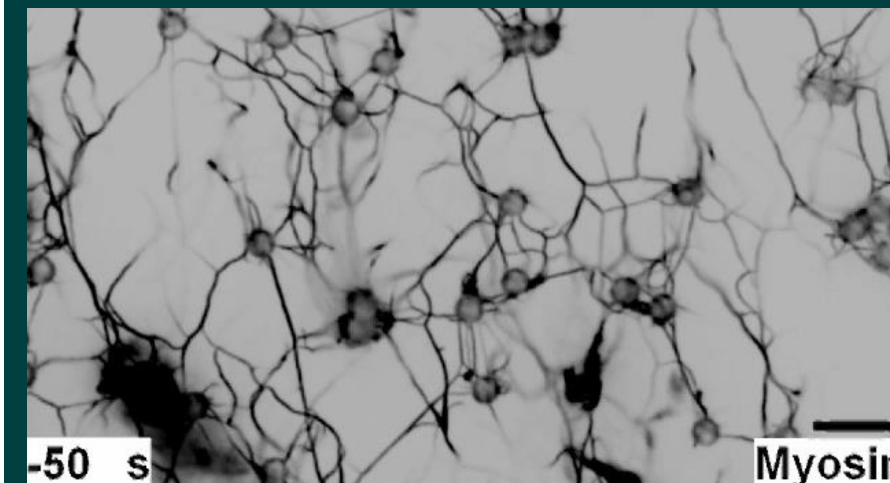
Reconstitution of Contractile Actomyosin Bundles

Todd Thoresen,[†] Martin Lenz,[†‡] and Margaret L. Gardel[†‡*]
[†]Institute for Biophysical Dynamics and [‡]James Franck Institute and Department of Physics, University of Chicago, Chicago, Illinois

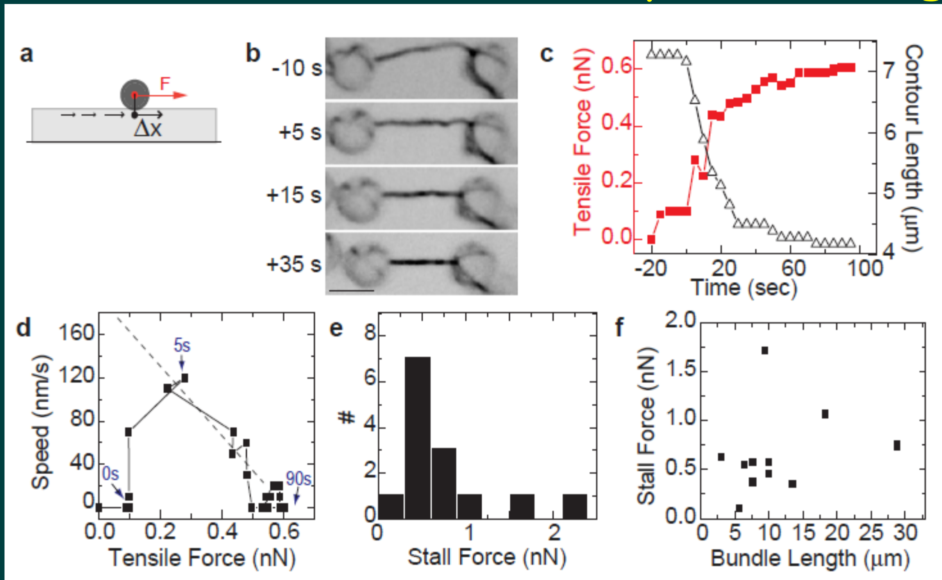


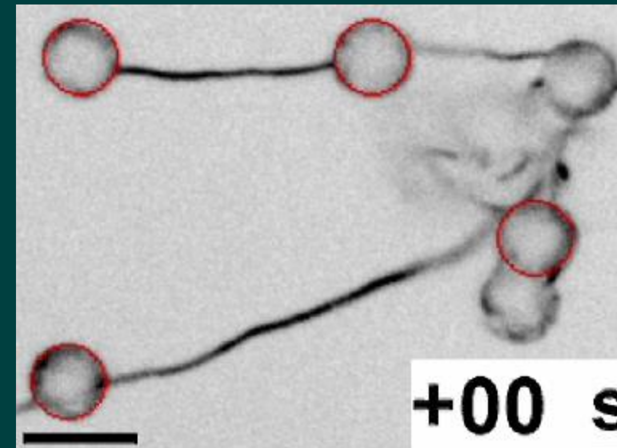
Reconstituted bundles contract

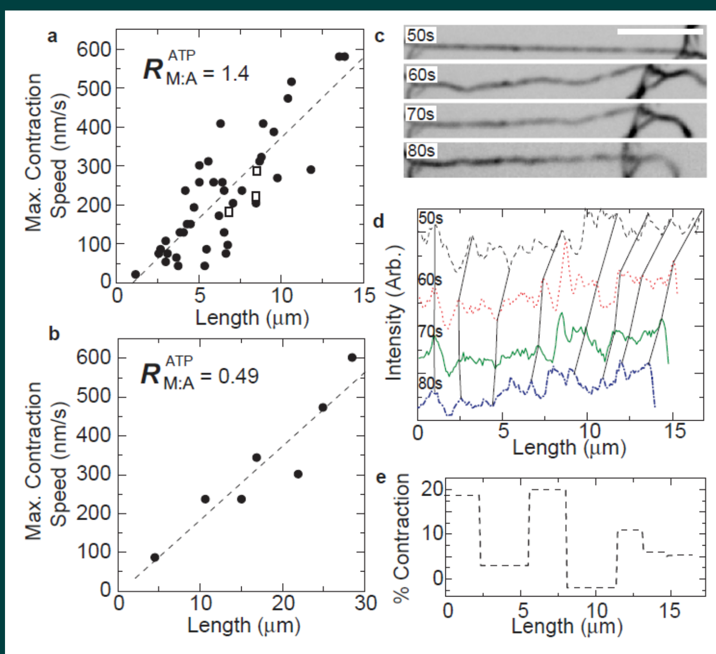


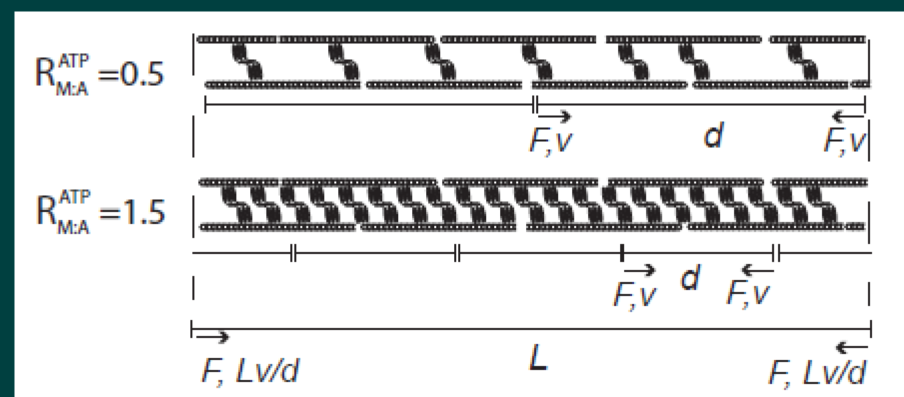


Force does not depend on length, velocity proportional to length







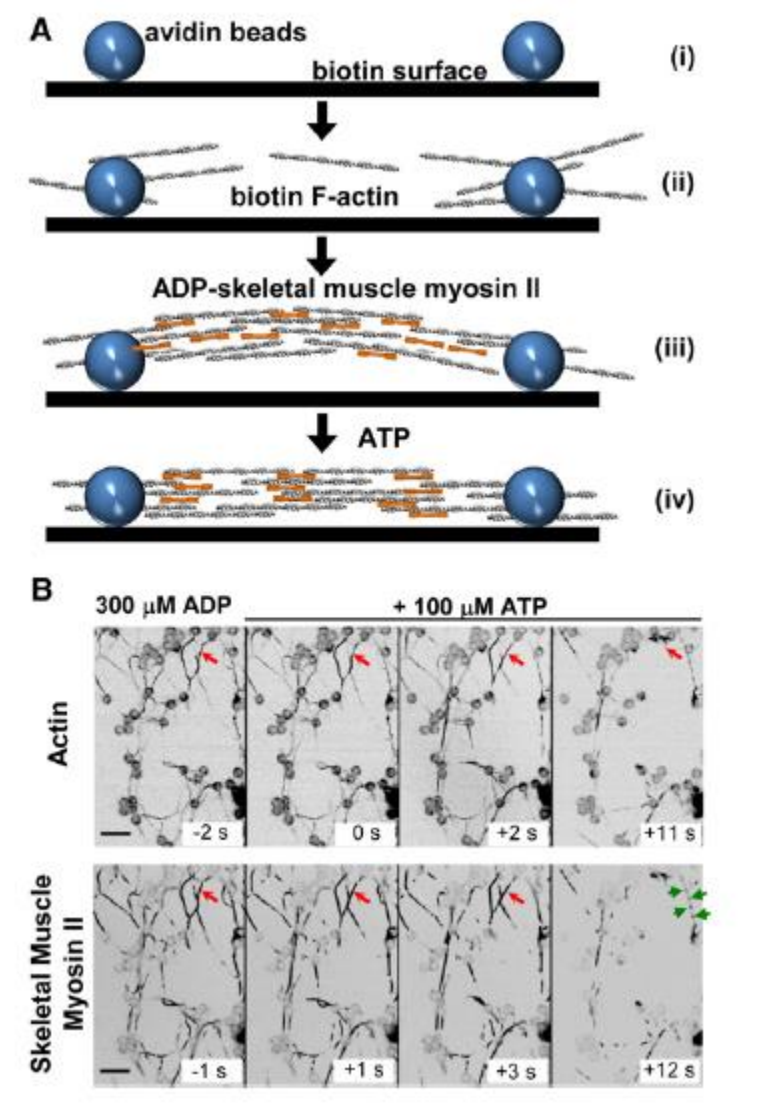


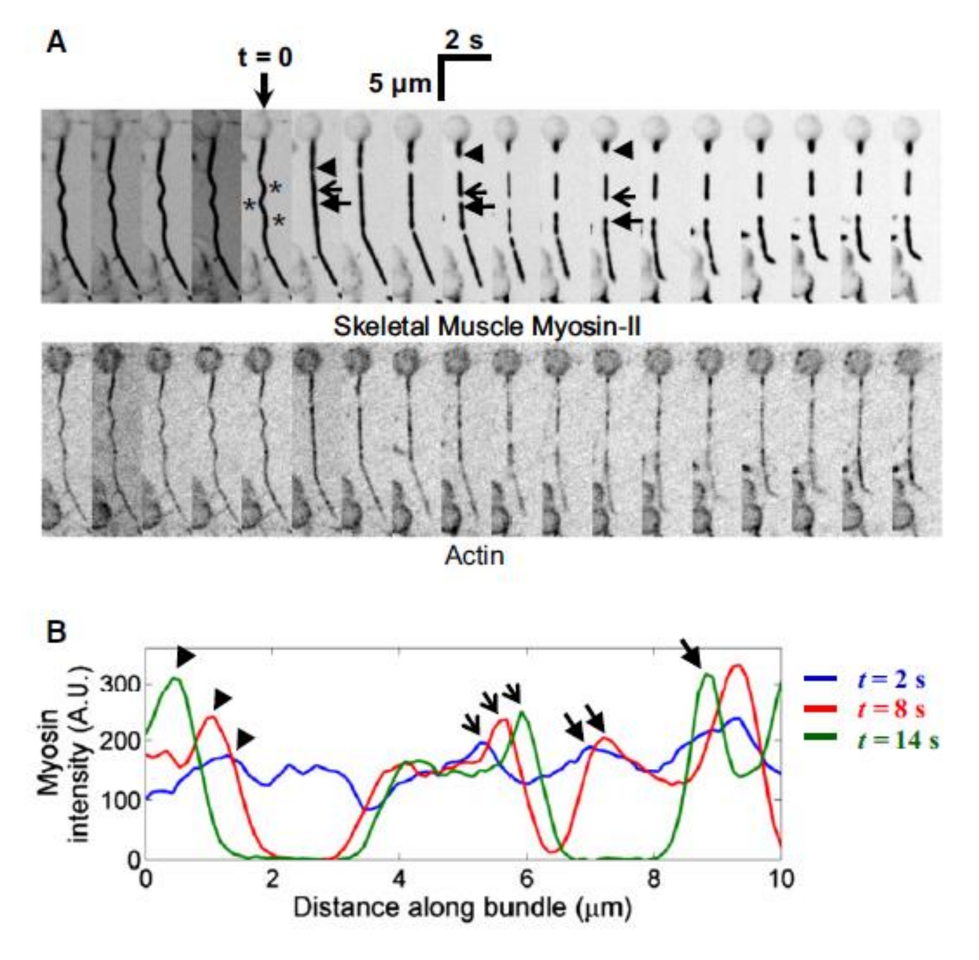
Biophysical Journal Volume 103 September 2012 1265–1274 1265

Self-Organization of Myosin II in Reconstituted Actomyosin Bundles

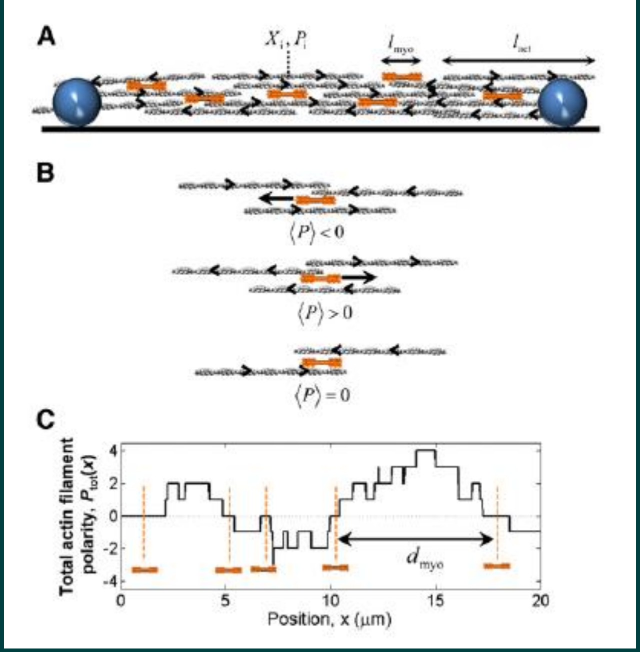
Matthew R. Stachowiak,[†] Patrick M. McCall,[‡§] Todd Thoresen,[‡¶] Hayri E. Balcioglu,[†] Lisa Kasiewicz,[†] Margaret L. Gardel,[‡§¶] and Ben O'Shaughnessy[†*]

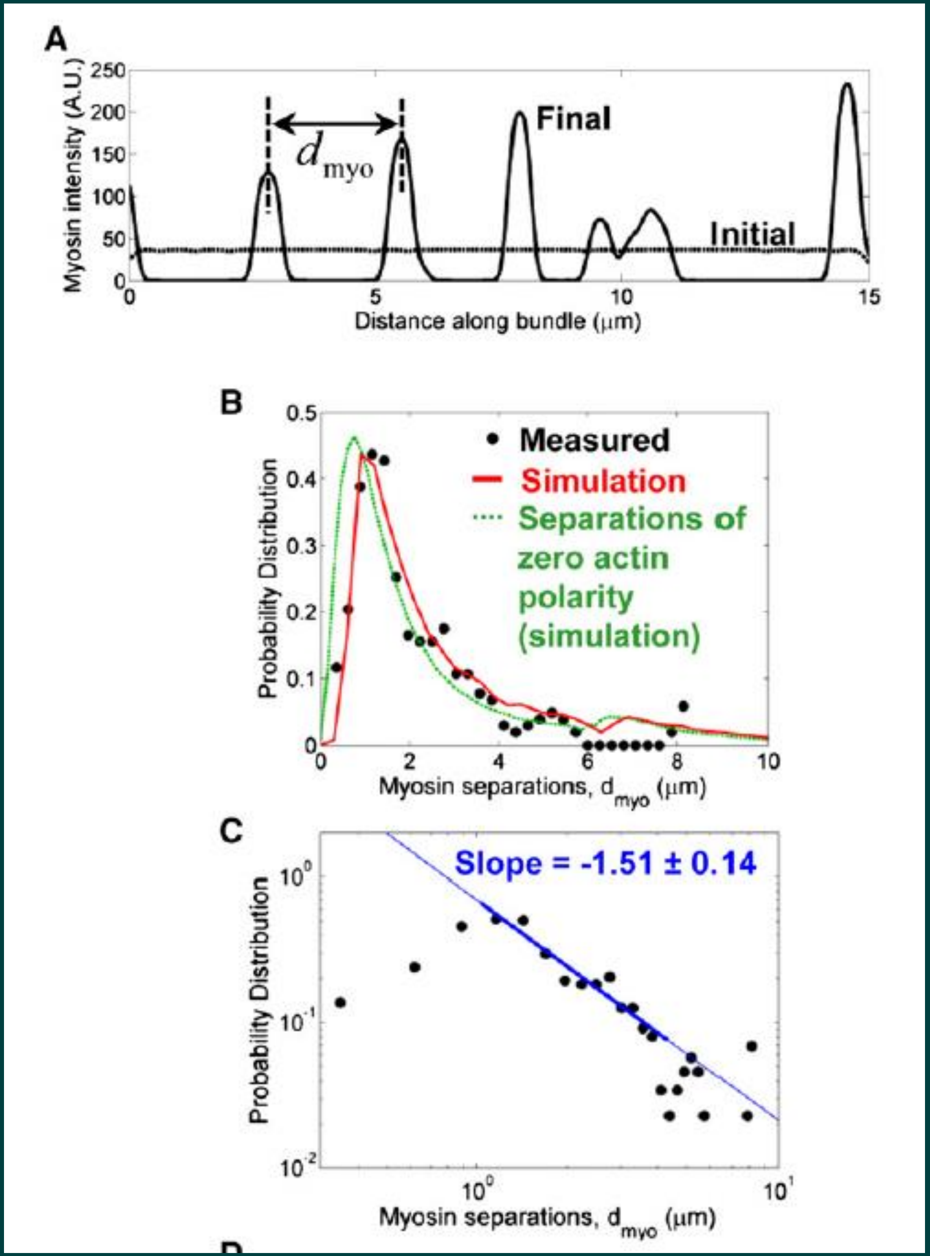
[†]Department of Chemical Engineering, Columbia University, New York, New York; and [‡]Department of Physics, [§]James Franck Institute, and [¶]Institute for Biophysical Dynamics, University of Chicago, Chicago, Illinois





myosin concentrates at zero actin polarity

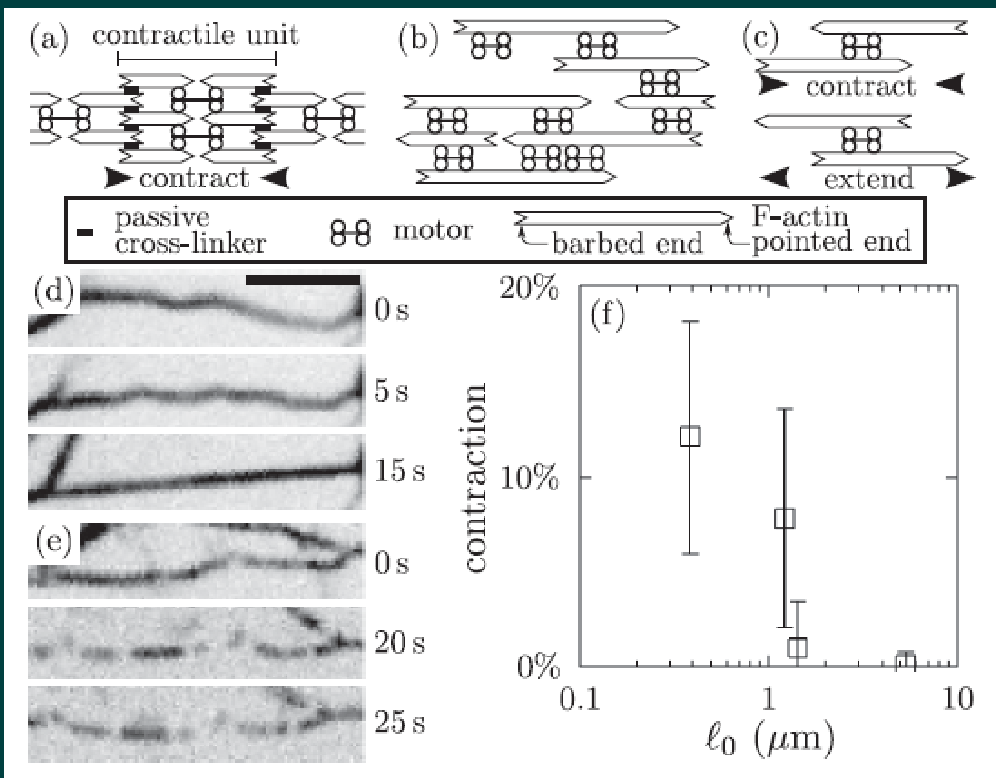


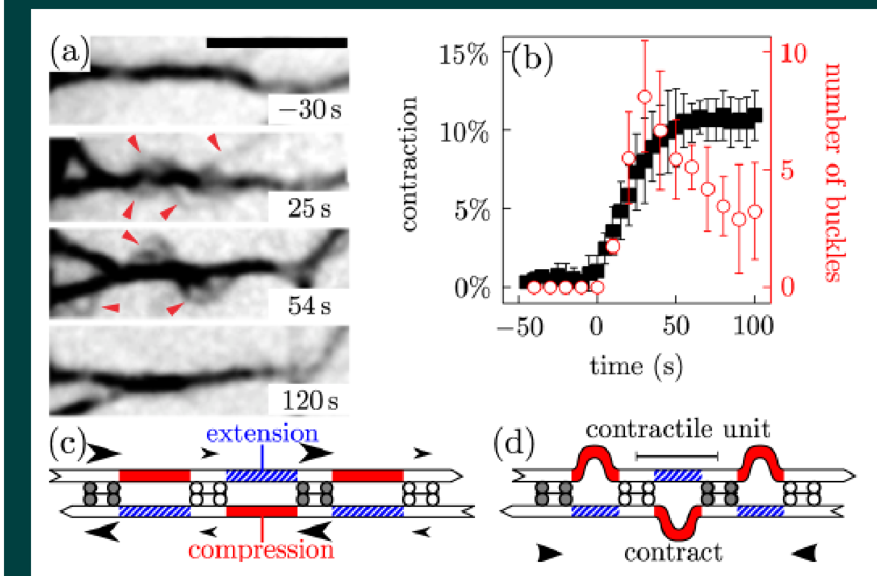


PRL 108, 238107 (2012) PHYSICAL REVIEW LETTERS week ending 8 JUNE 2012

Contractile Units in Disordered Actomyosin Bundles Arise from F-Actin Buckling

Martin Lenz,[1] Todd Thoresen,[2] Margaret L. Gardel,[1,2,3] and Aaron R. Dinner[1,2,4,*]





next time: how does it work in the cells?