Collective Force Generation by Multiple Bio-filaments and Molecular Motors


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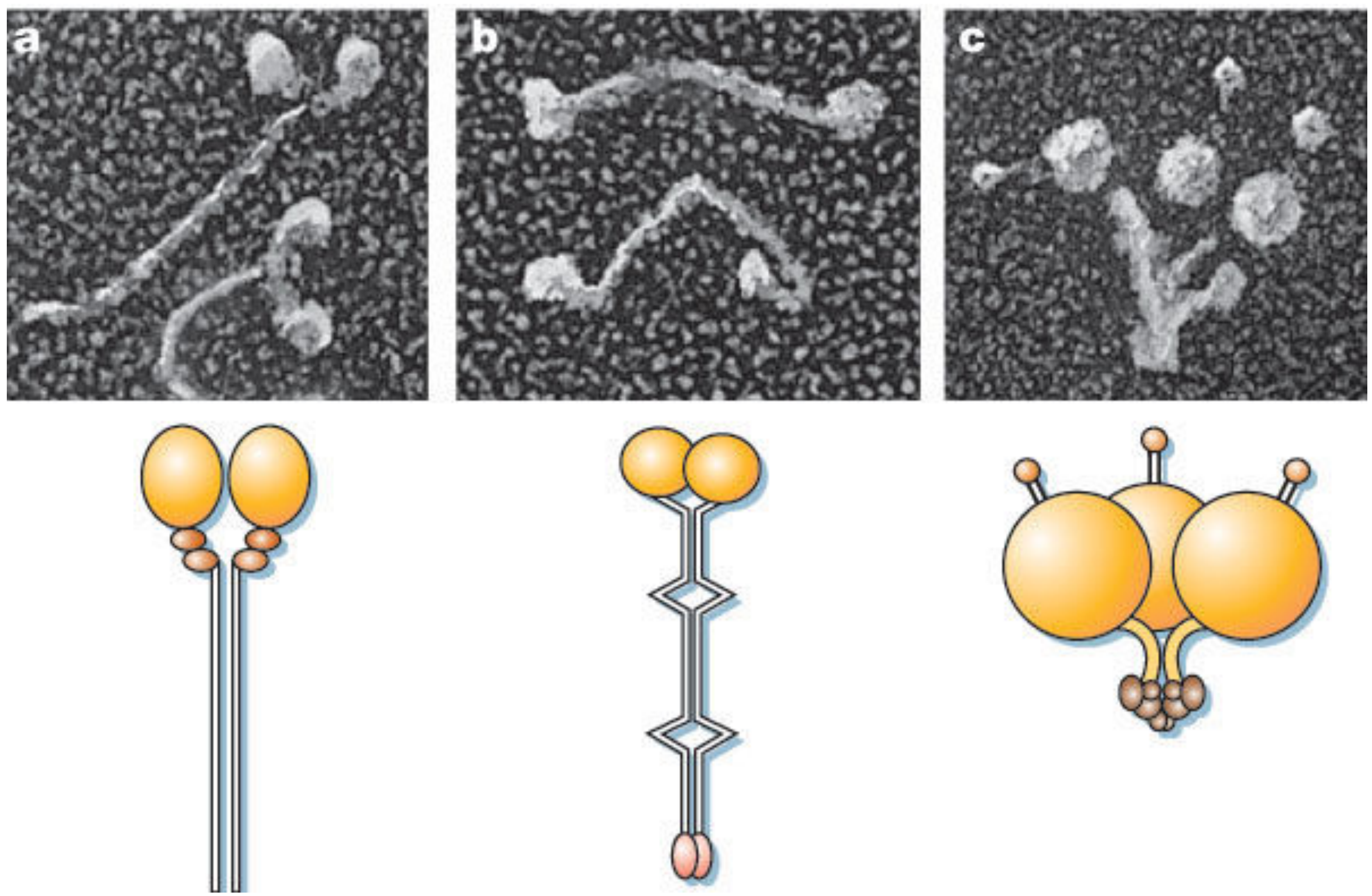
Molecular motors

Most forms of movement in the living world are powered by tiny protein machines.

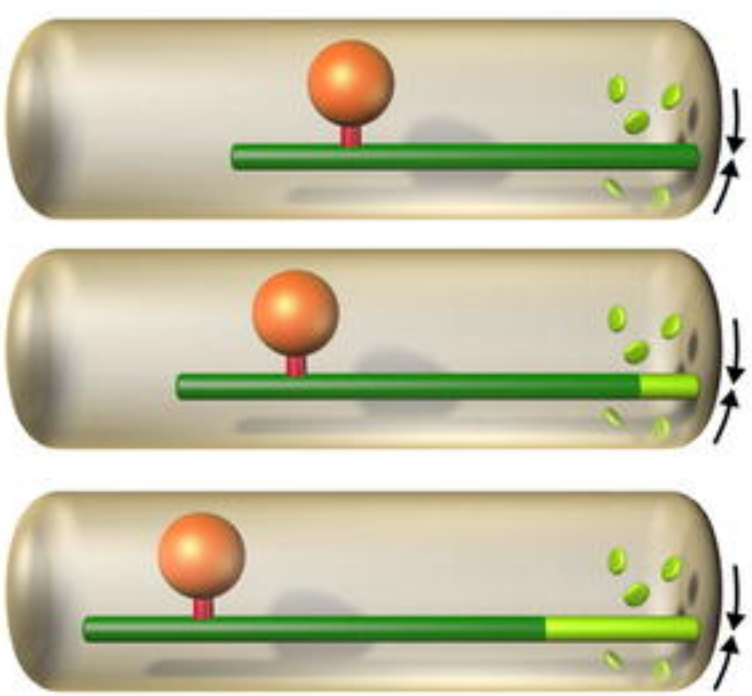


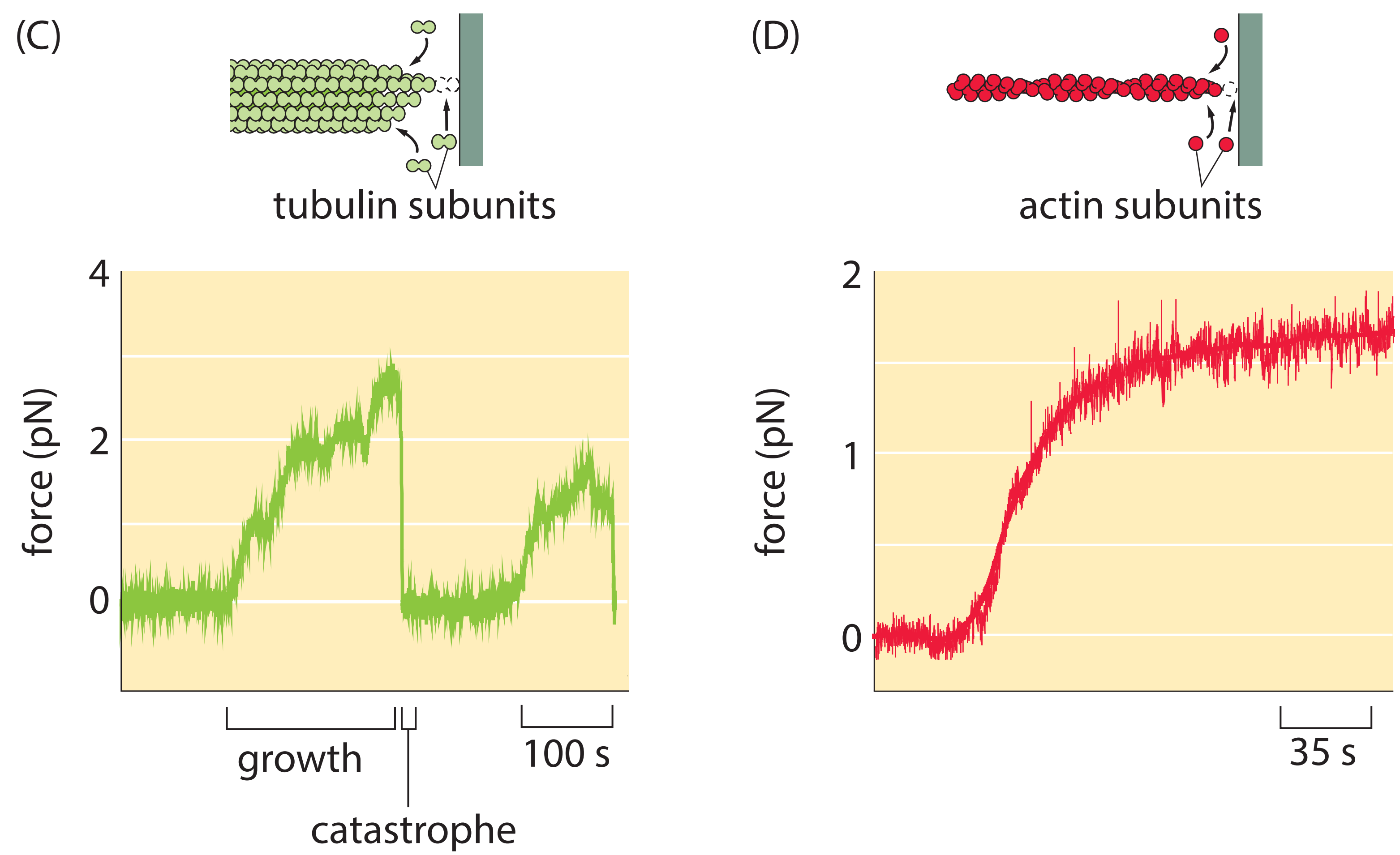
Myosin II conventional kinesin ciliary dynein

Manfred Schliwa,Nature ,2003

Bio-filaments

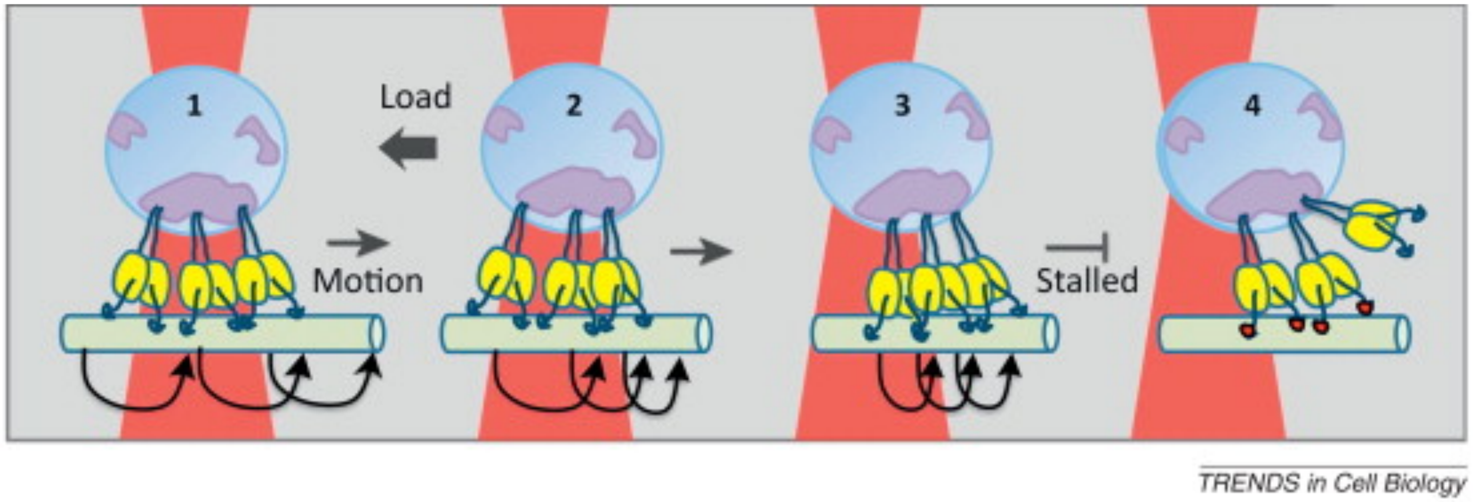
Simplest Nano-machine, utilize chemical energy of polymerization to generate significant amount of force





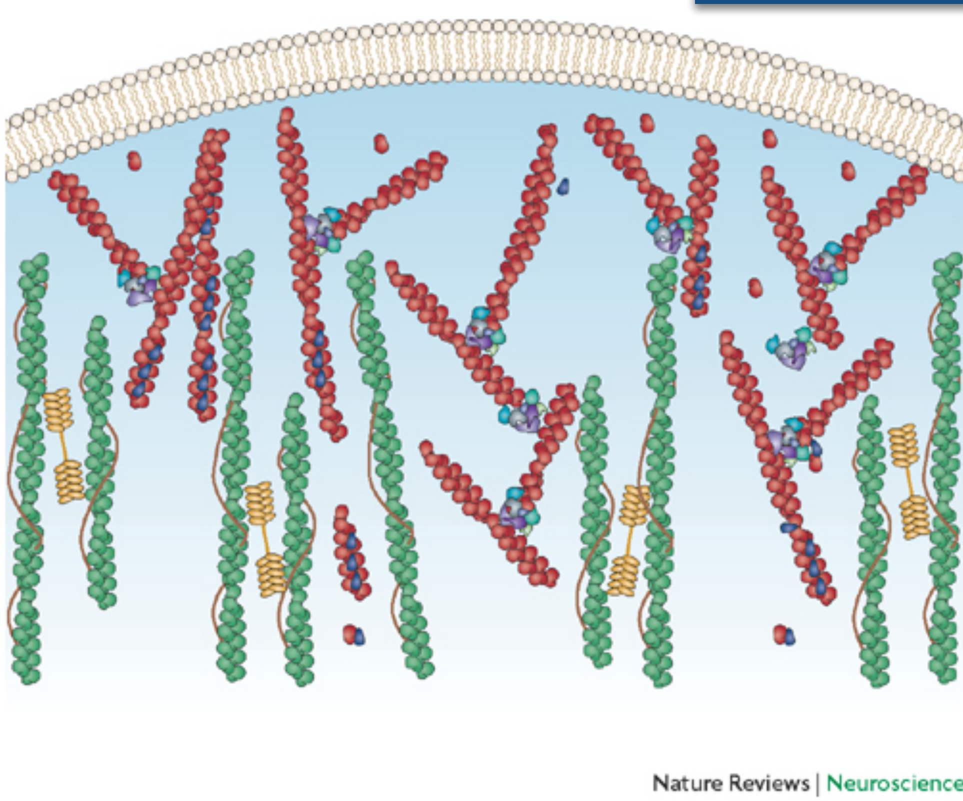
Iva Tolic, 2008, EBJ

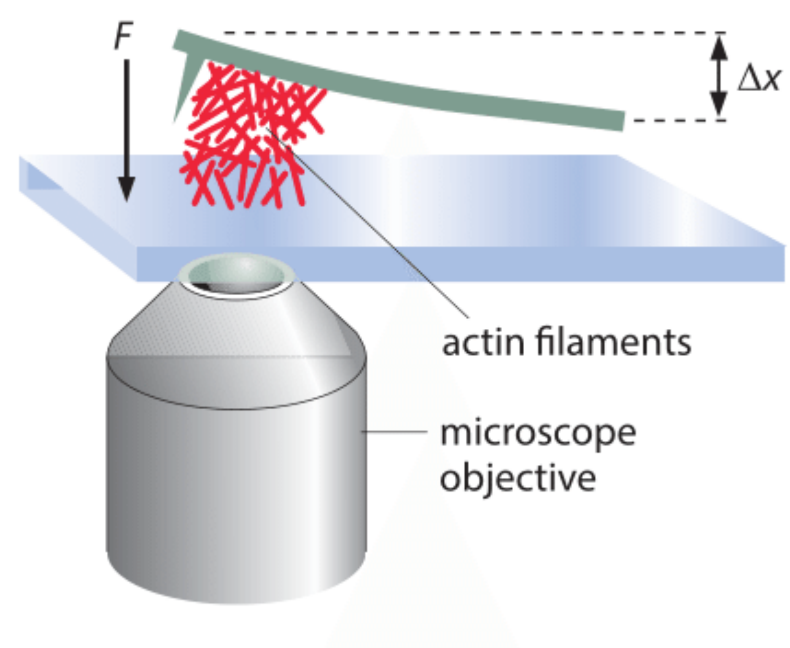
Multiple motor working in coordination



Roop Mallik et. al., Trends in Cell Biology,2013

Multiple bio-filament at work





S. H. Parekh et al., Nat. Cell Biol. 7:1219, 2005

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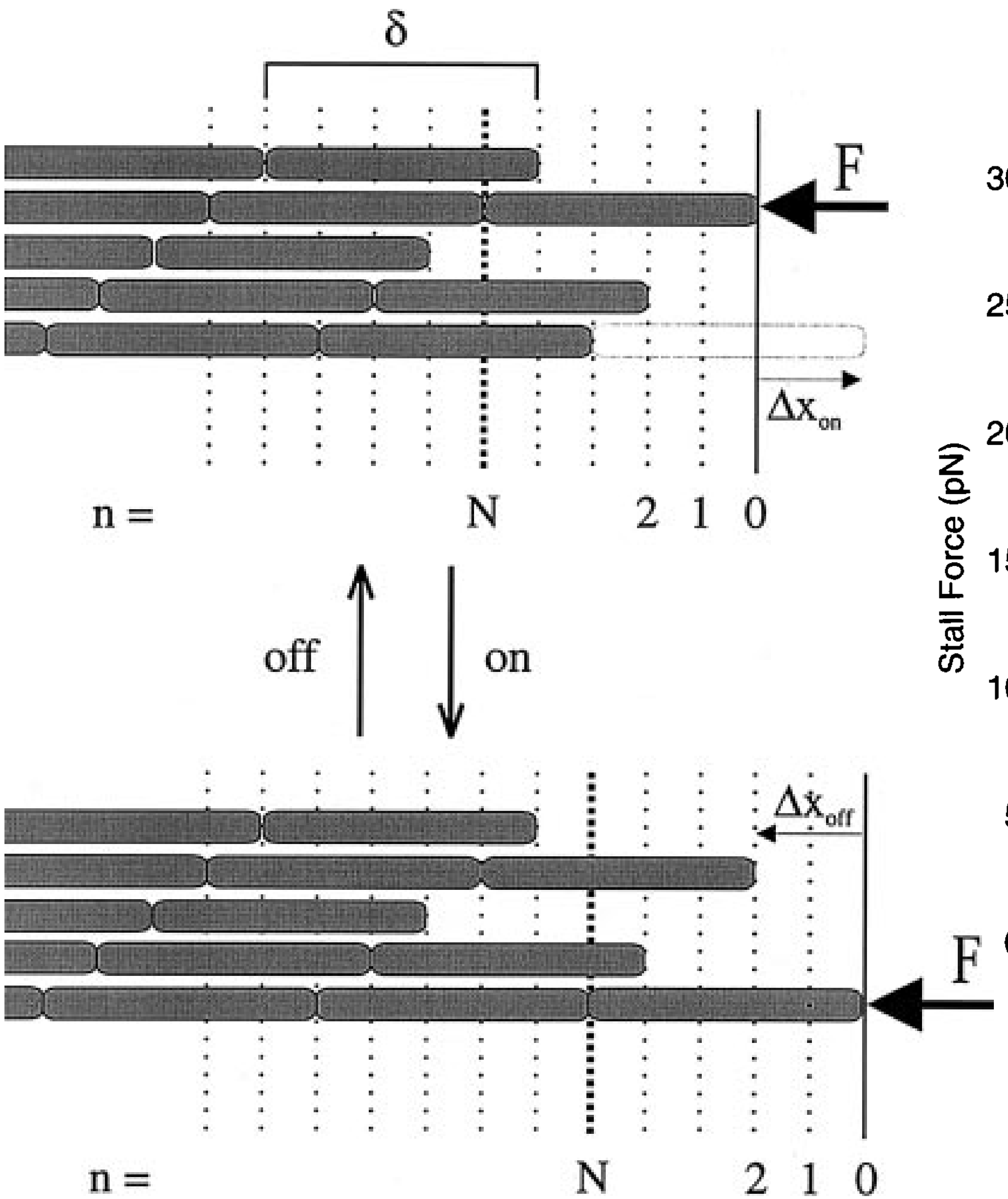
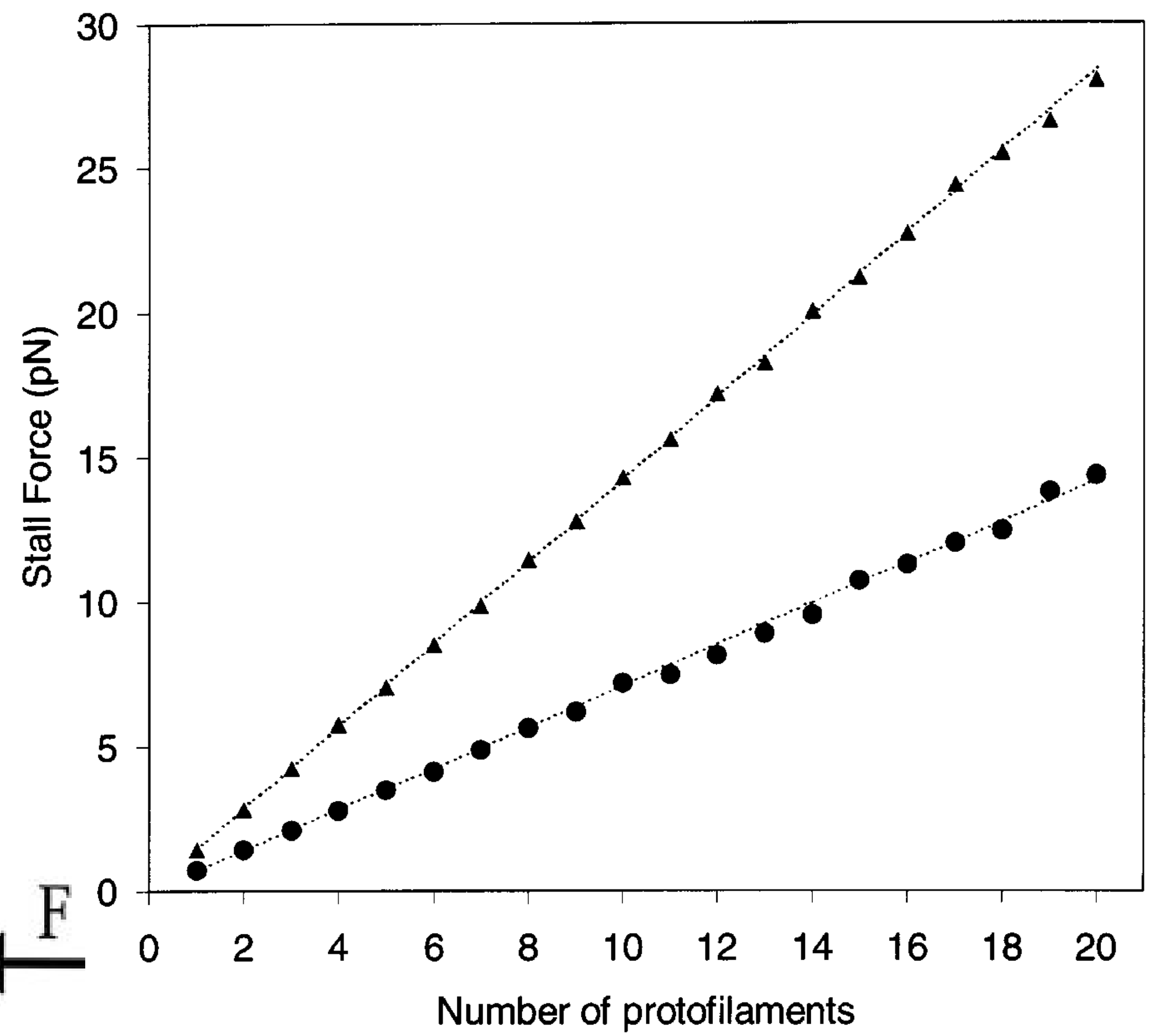
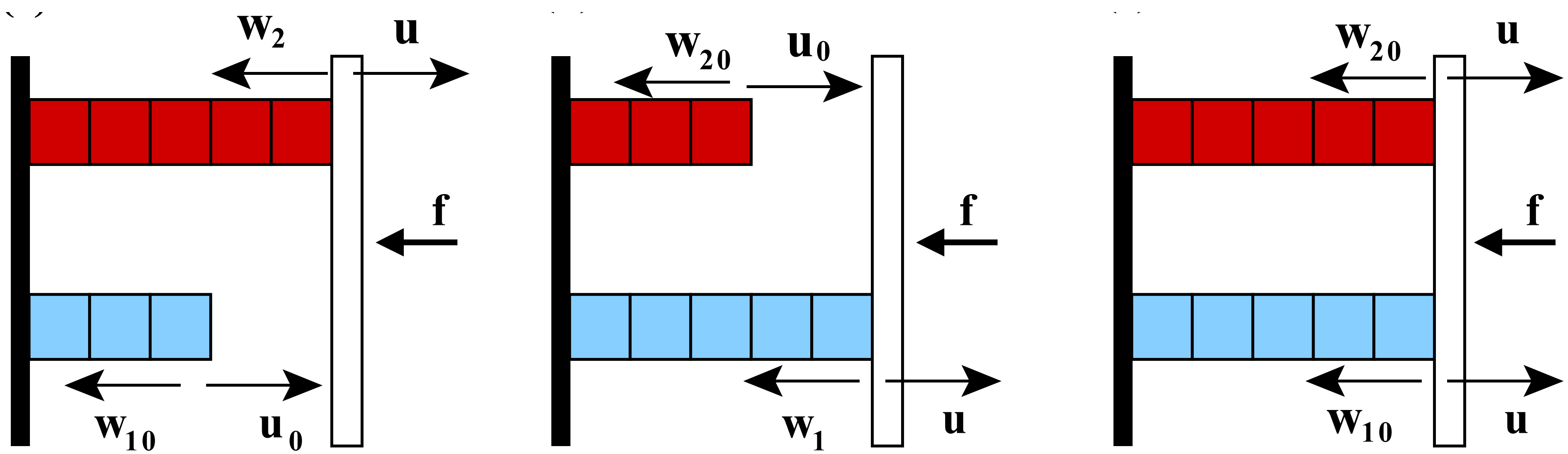
Stall force generated by multiple filament

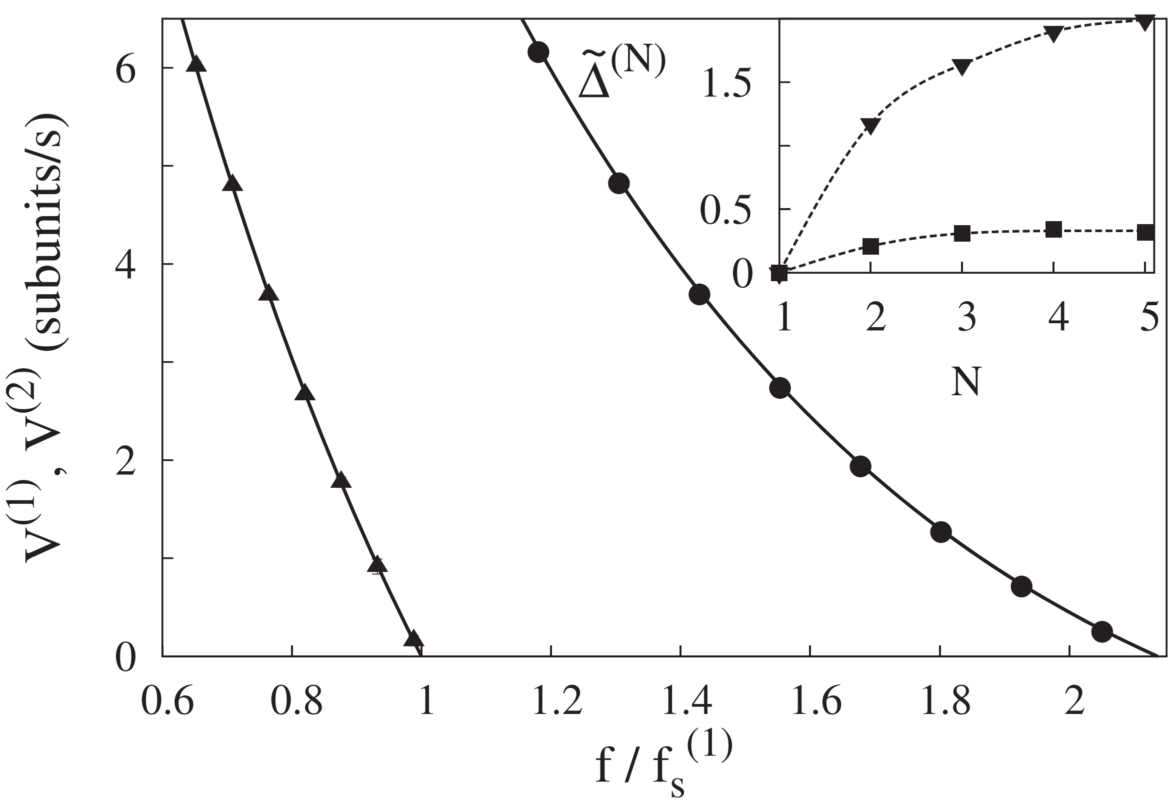




G. Sander van Doorn et al. , Eur Biophys J , 2000

Stall force generated by multiple filament

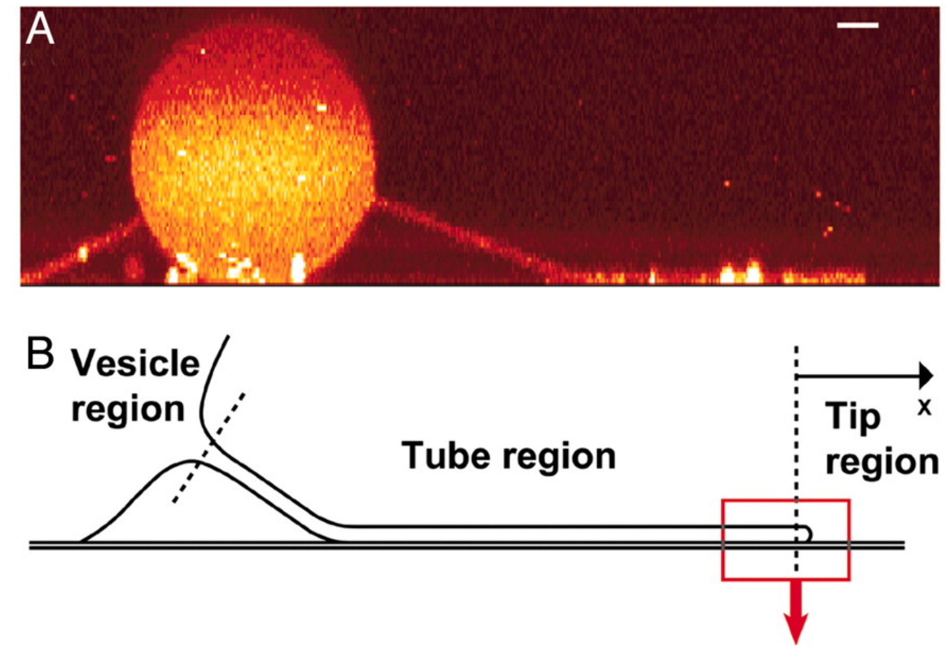




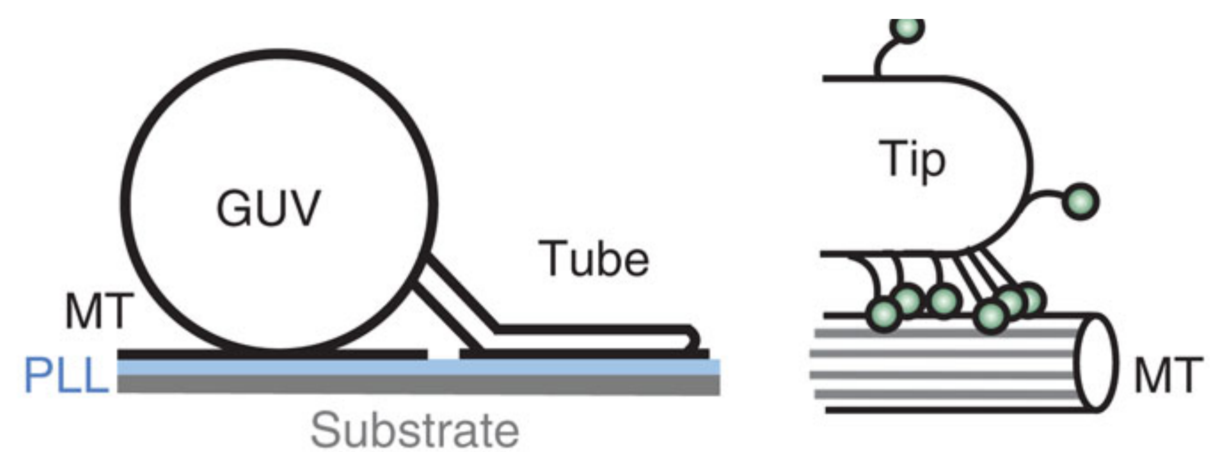
Dipjyoti Das et al, NJP, 2014

Cooperative force generation by single-headed KIF1A motors

- Team work of single-headed KIF1A motors to extract membrane tubes from giant unilamellar vesicles.

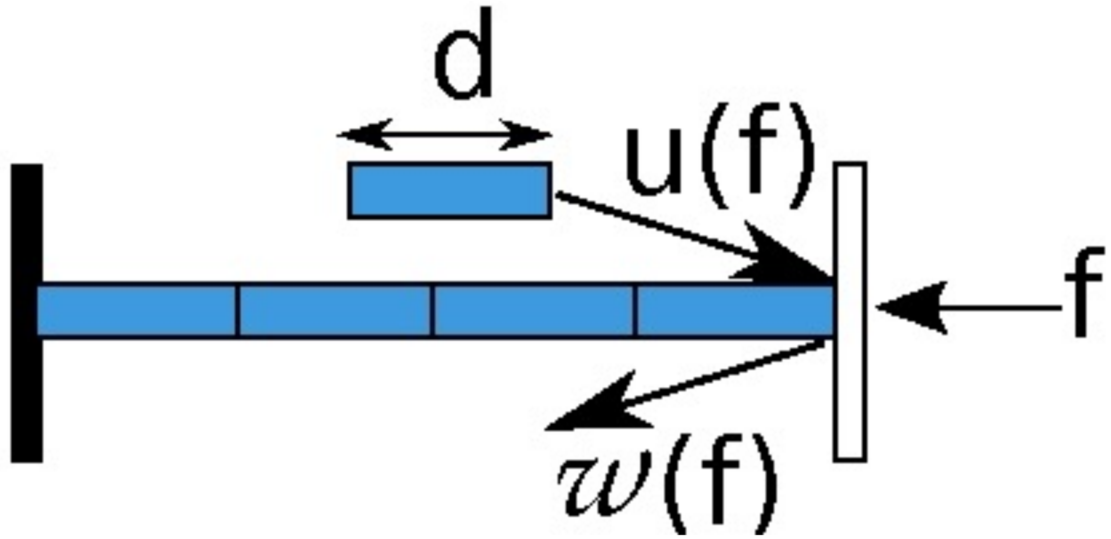


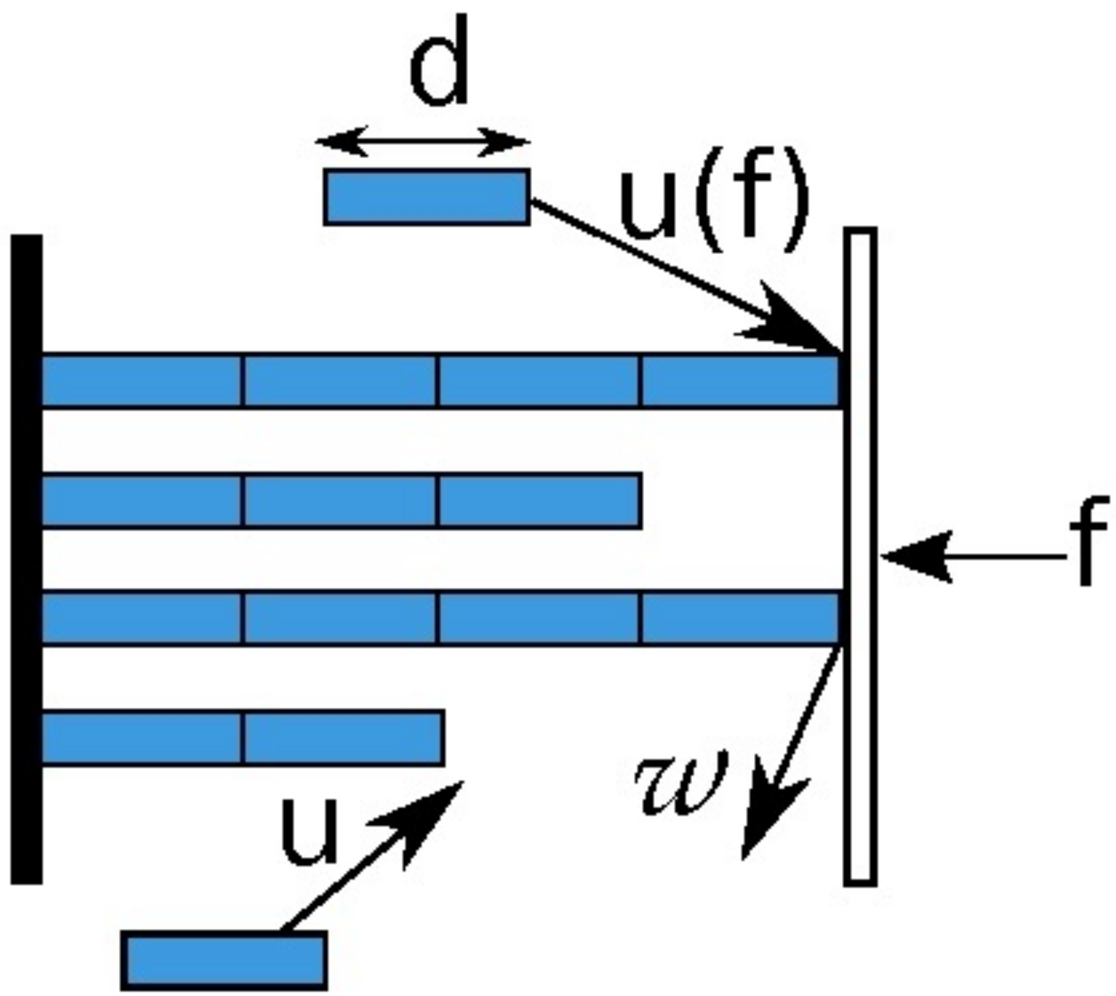
- ~15 KIF1A motors can extract tubes in similar conditions to conventional kinesin, despite having a stall force 60 time smaller.



Casademunt, *Nature Communications* (2015)

Simple kinetic model for bio-filaments





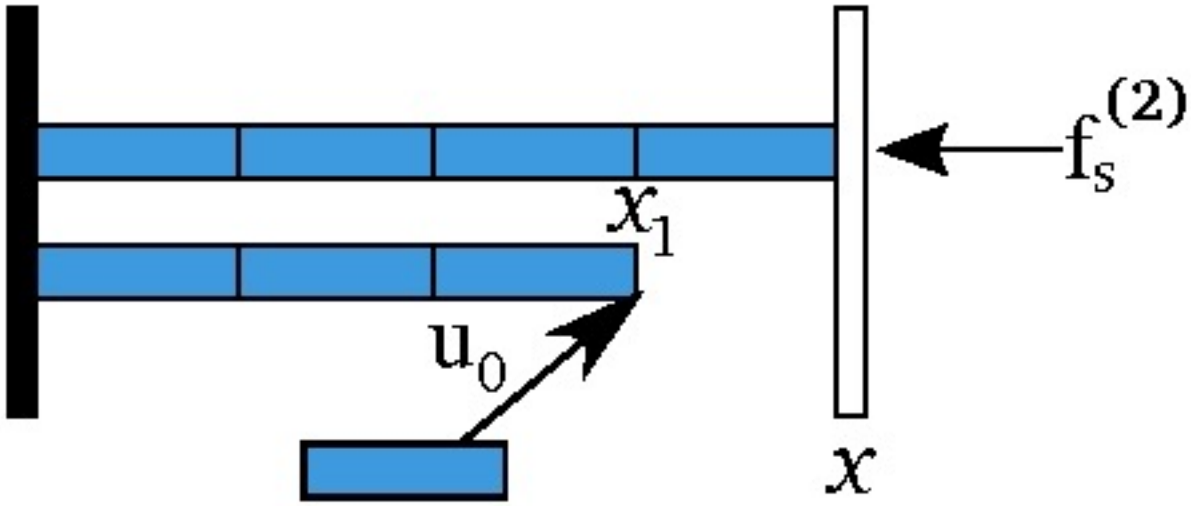
Derivation for stall formula using textbook stat mech.

- System is at equilibrium at stall
- Probability distribution of the wall-position for single filament

$$P(x) = \frac{1}{Z} e^{\beta f_s^{(1)} x} e^{\beta \epsilon x}$$
$$= \frac{1}{Z} e^{\beta (f_s^{(1)} - \epsilon) x}$$

Here,

$$\epsilon = ln\left(\frac{u}{w}\right)$$



$P(x)$ is expected not to depend on

$$f_s^{(1)} = \epsilon$$

T.Bameta et al PRE (2017)

Probability distribution of the wall-position for two filament system

$$P(x) = \frac{1}{Z} e^{\beta f_s^{(2)} x} e^{\beta \epsilon} \left(2 \sum_{x_1=0}^{x} e^{\beta \epsilon x_1} - e^{\beta \epsilon x} \right) \sim e^{\beta (f_s^{(2)} - 2\epsilon) x}$$

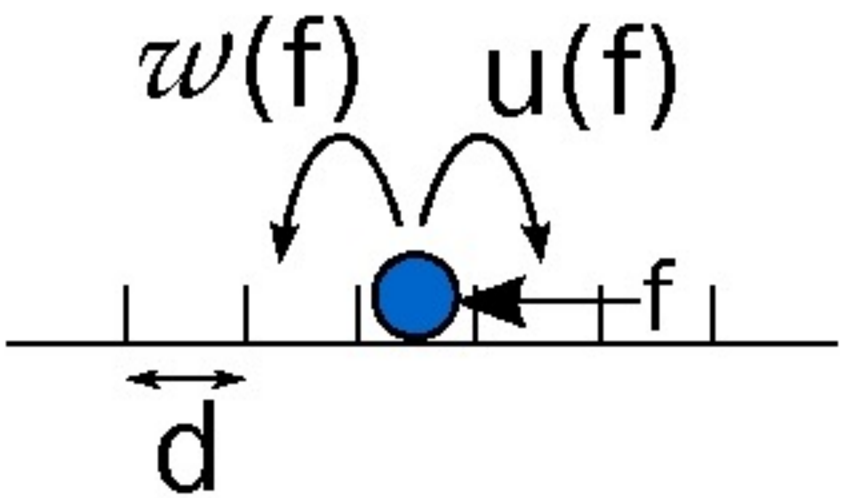
$P(x)$ is expected not to depend on x

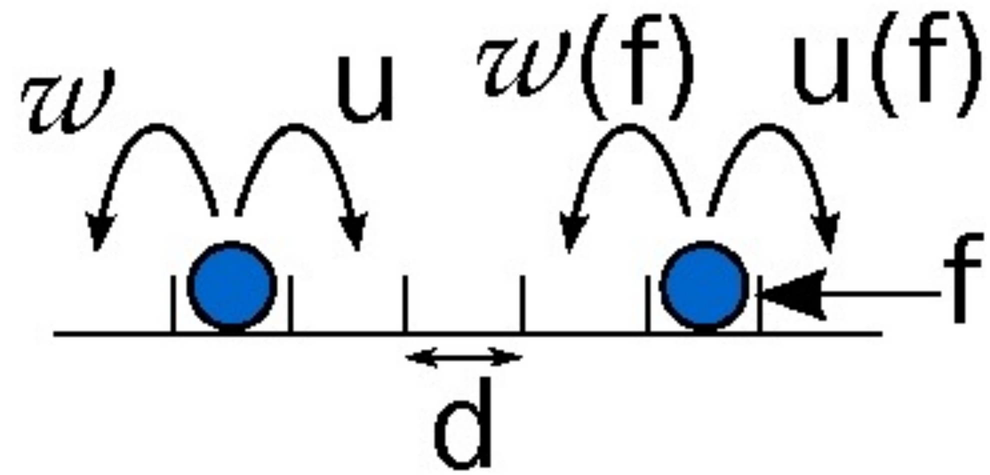
$$f_s^{(2)} = 2\epsilon = 2 f_s^1$$

This argument can be easily extended to $N > 2$

$$f_s^{(N)} = N f_s^{(1)}$$

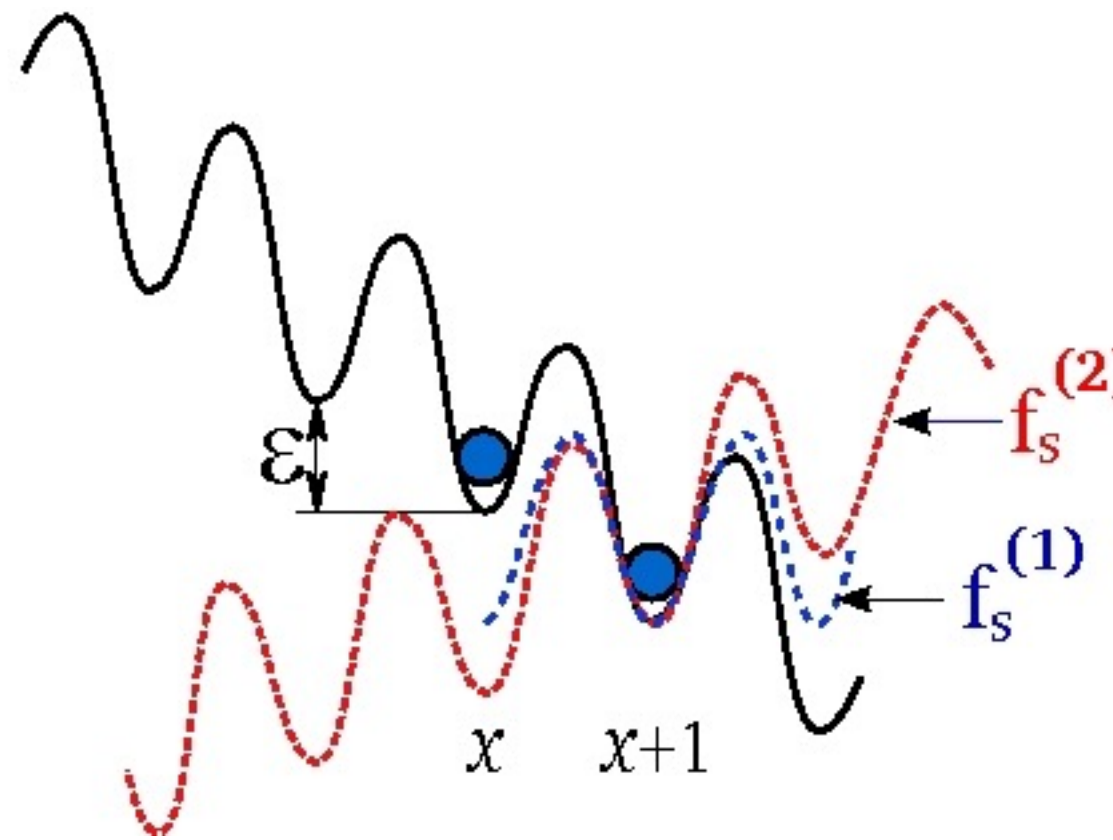
Simple kinetic model for molecular motors





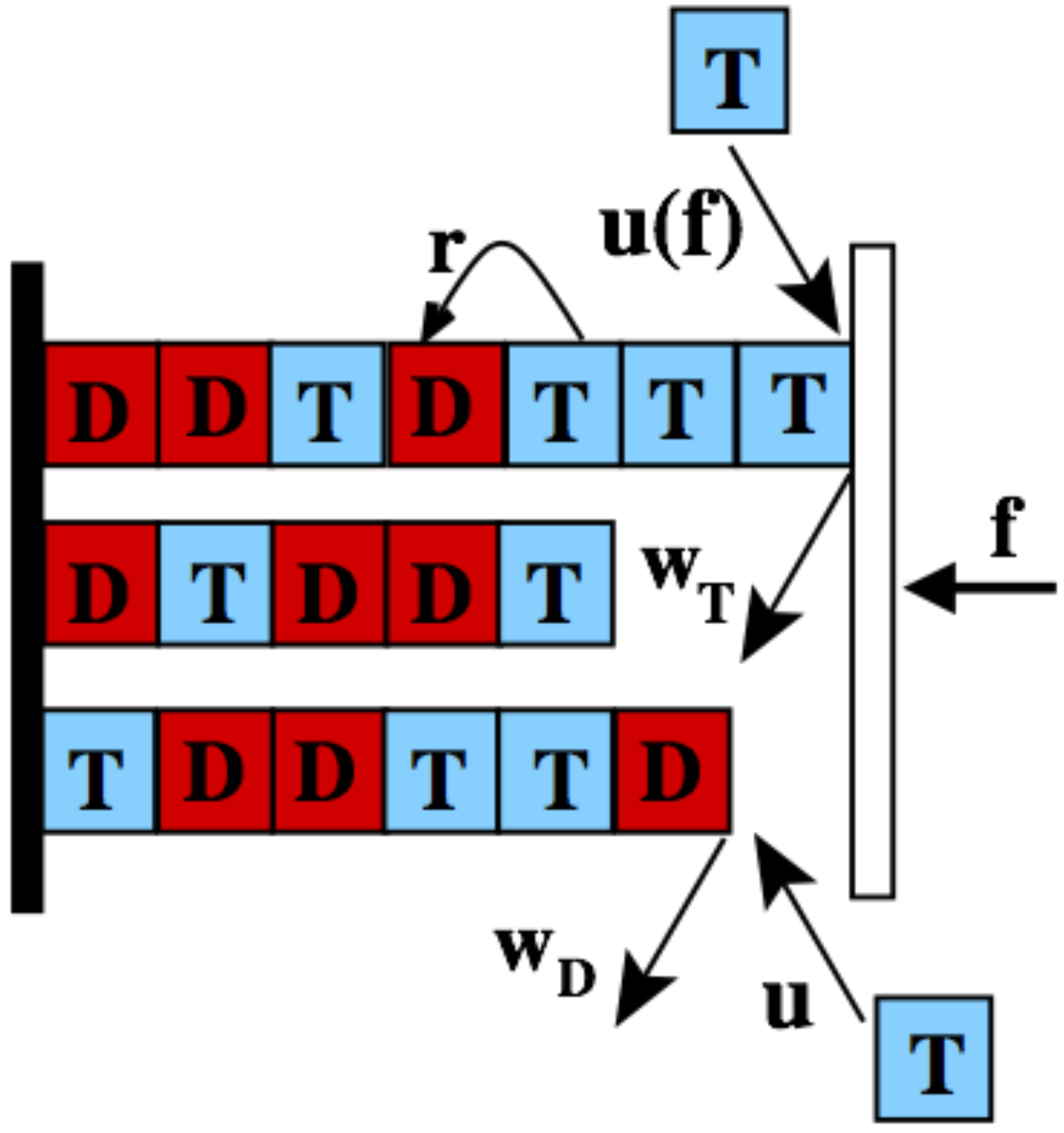
$$P(x) = \frac{1}{Z} e^{-\beta f_s^{(2)} x} e^{\beta \epsilon x} \Big(\sum_{x_1=0}^{x-1} e^{\beta \epsilon x_1} \Big)$$

$$\sim e^{-\beta (f_s^{(2)} - 2\epsilon) x}, \text{ for large } x.$$



Stall force is additive for simple models

Random hydrolysis model



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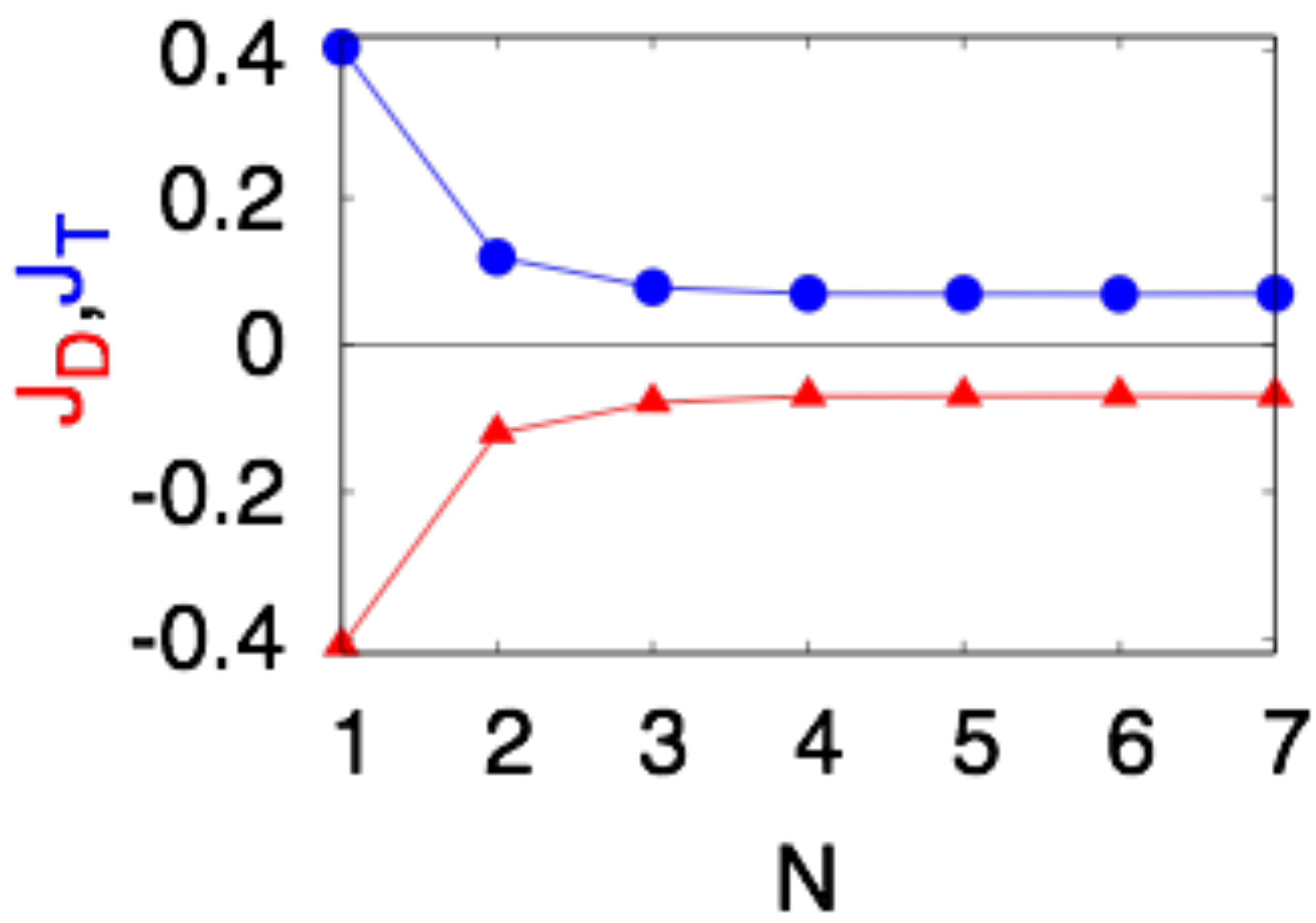
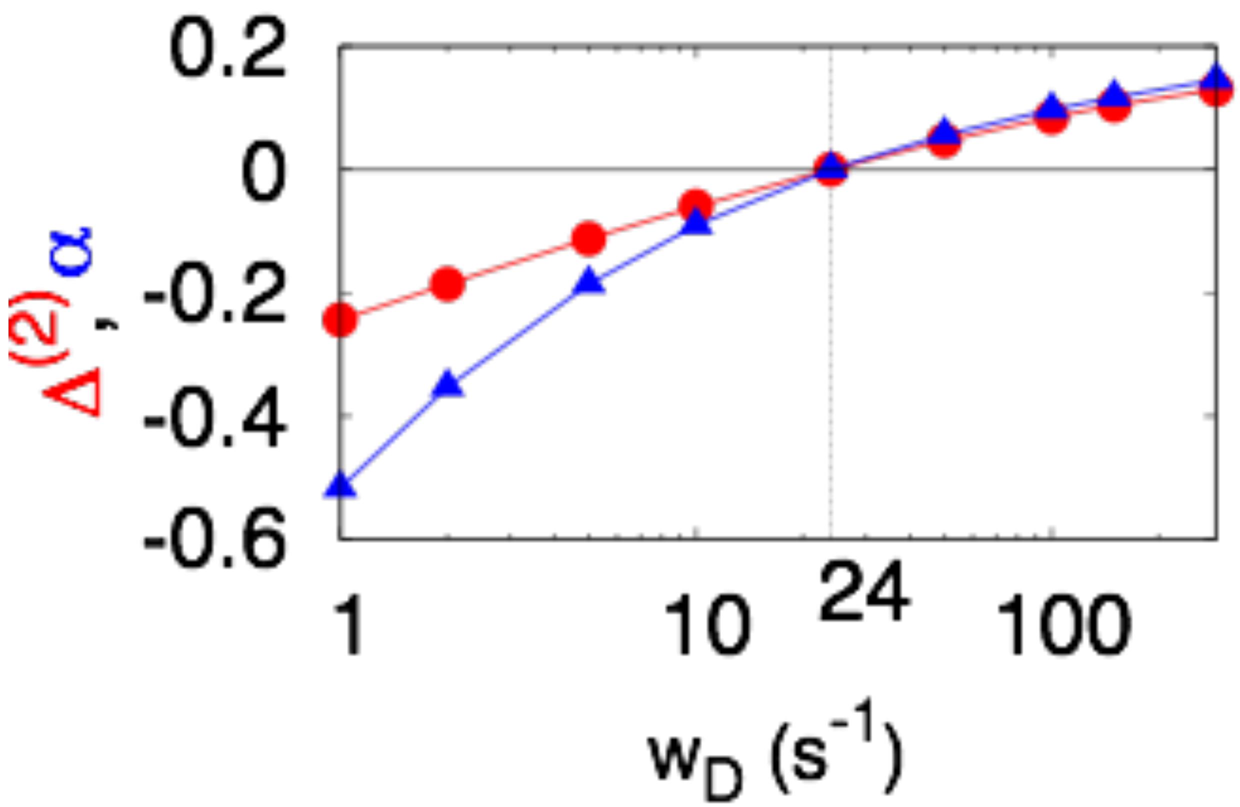
Random hydrolysis model



System with larger number of filament is closer to equilibrium

T.Bameta et al PRE *(*2017)

Random hydrolysis model



$$\Delta_2 = f_s^{(2)} - 2f_s^{(1)}$$

$$\alpha = F_{poly} - W_{poly}^{max}$$
$$= ln\left(\frac{u}{W_T}\right) - f_s^{(1)}$$

$u = k_0 c, k_0 = 3.2\ \mu\text{M}^{-1}s^{-1},$
$c = 100\mu\text{M}, w_T = 24s^{-1},$
and $r = 0.2s^{-1}$

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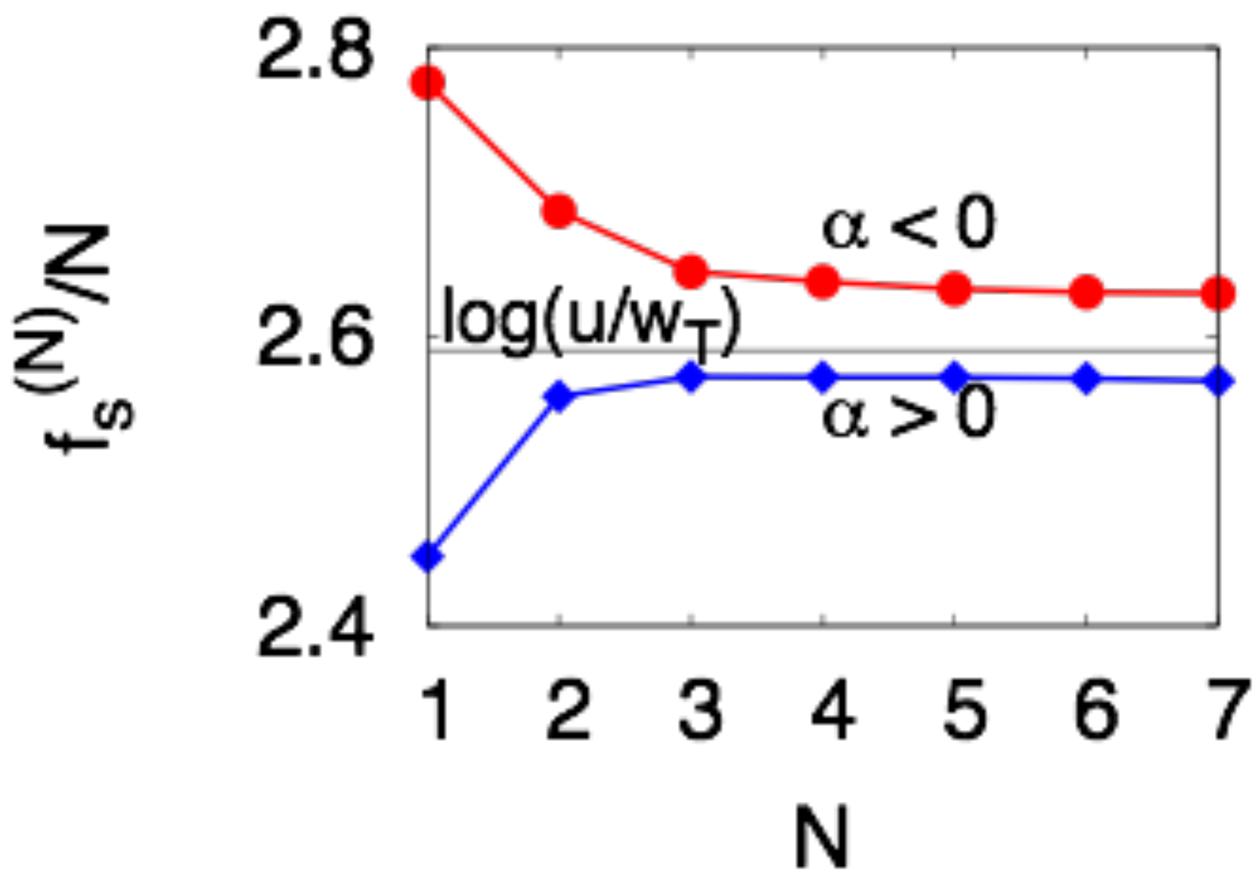
Random hydrolysis model



$$\alpha > 0 \quad \left(w_D = 290 s^{-1}\right)$$
$$\alpha < 0 \quad \left(w_D = 5 s^{-1}\right)$$

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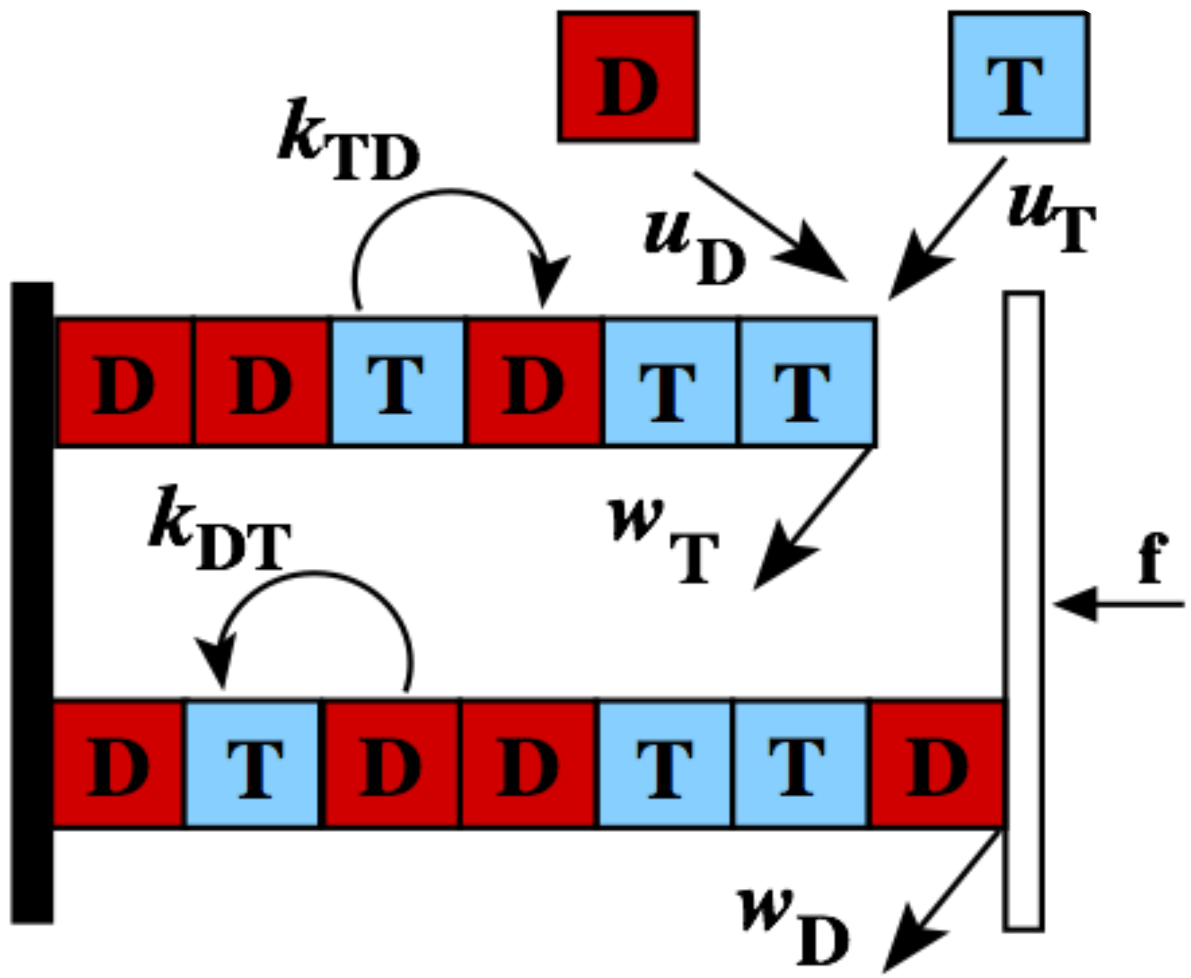
Stall forces are non-additive for biologically relevant non-equilibrium models

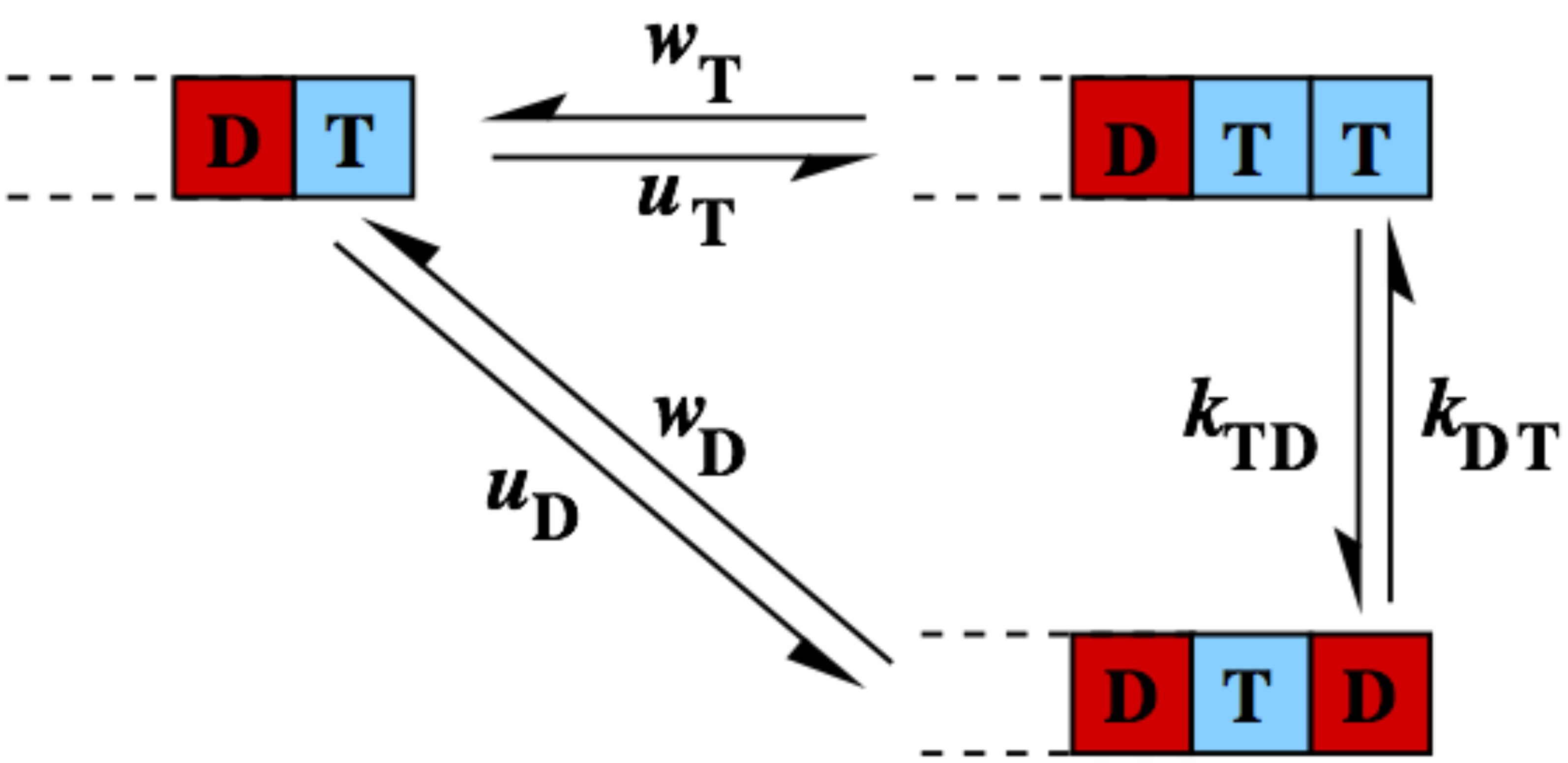
Conjectured connection between:

detailed balance $\leftrightarrow$ thermal equilibrium $\leftrightarrow$ stall force additivity

Reversible hydrolysis model

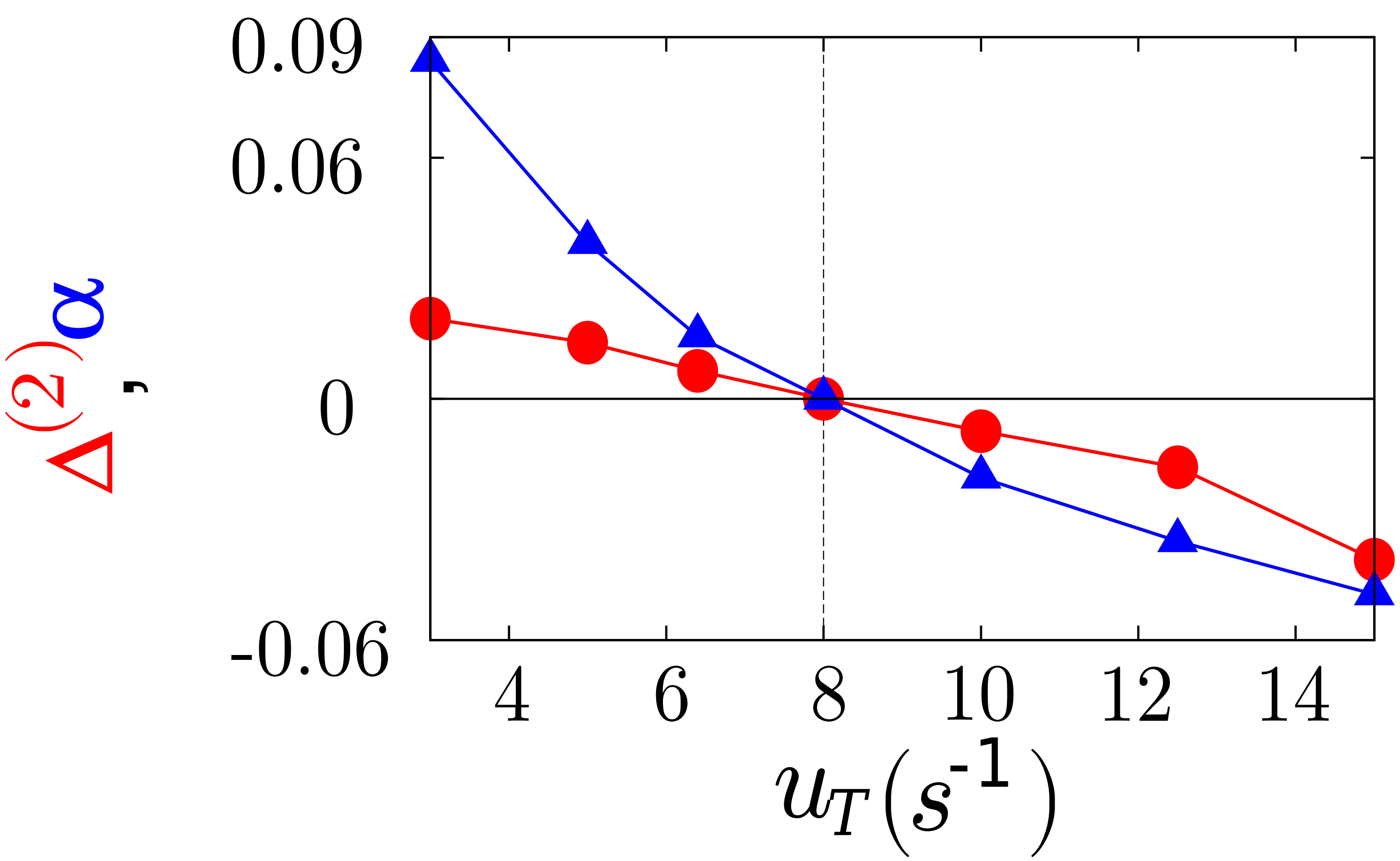


Reversible hydrolysis model



$$\frac{u_T}{w_T}\frac{k_{TD}}{k_{DT}}\frac{w_D}{u_D} = 1$$

Reversible hydrolysis model

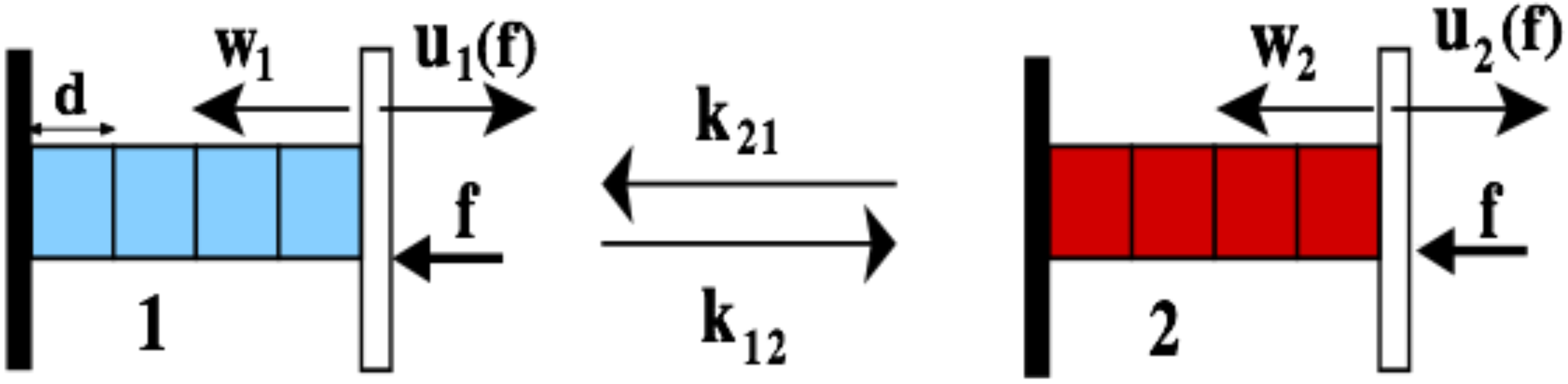


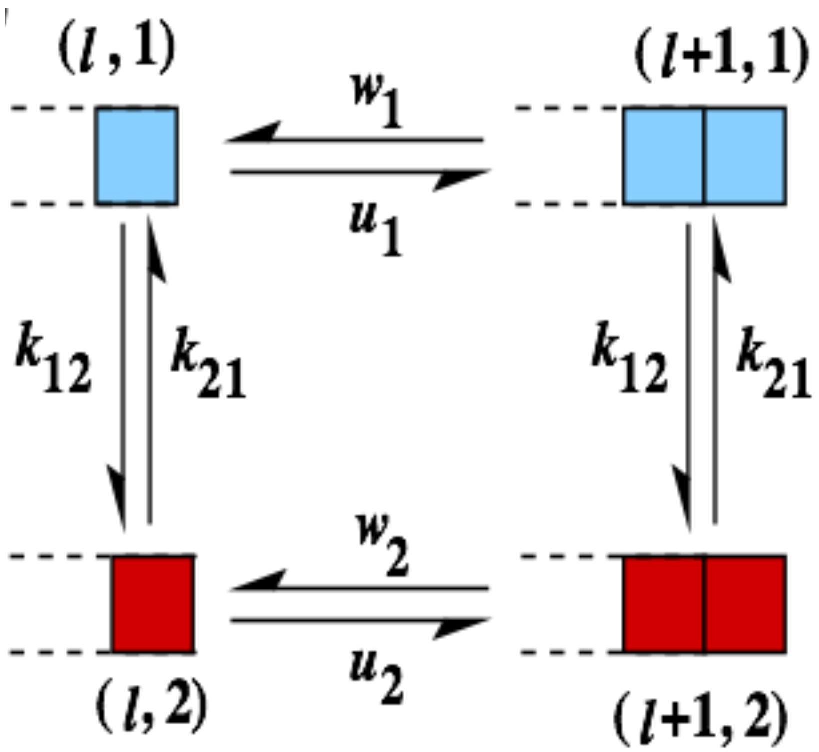
$w_T = 2s^{-1}, k_{TD} = 0.3s^{-1},$
$k_{DT} = 0.4s^{-1}, u_D = 3s^{-1},$
and $w_D = 1s^{-1}$

$$\alpha = ln\left[\left(\frac{u_T}{w_T}\right) + \left(\frac{u_D}{w_D}\right)\right] - f_s^{(1)}$$

from the equilibrium condition at $\Delta^{(2)} = 0$ at $u_T = 8s^{-1}$

A toy model for filaments





$$u_1 k_{12} w_2 k_{21} = k_{12} u_2 k_{21} w_1$$

$$\Longrightarrow \quad \frac{u_1}{w_1} = \frac{u_2}{w_2}$$

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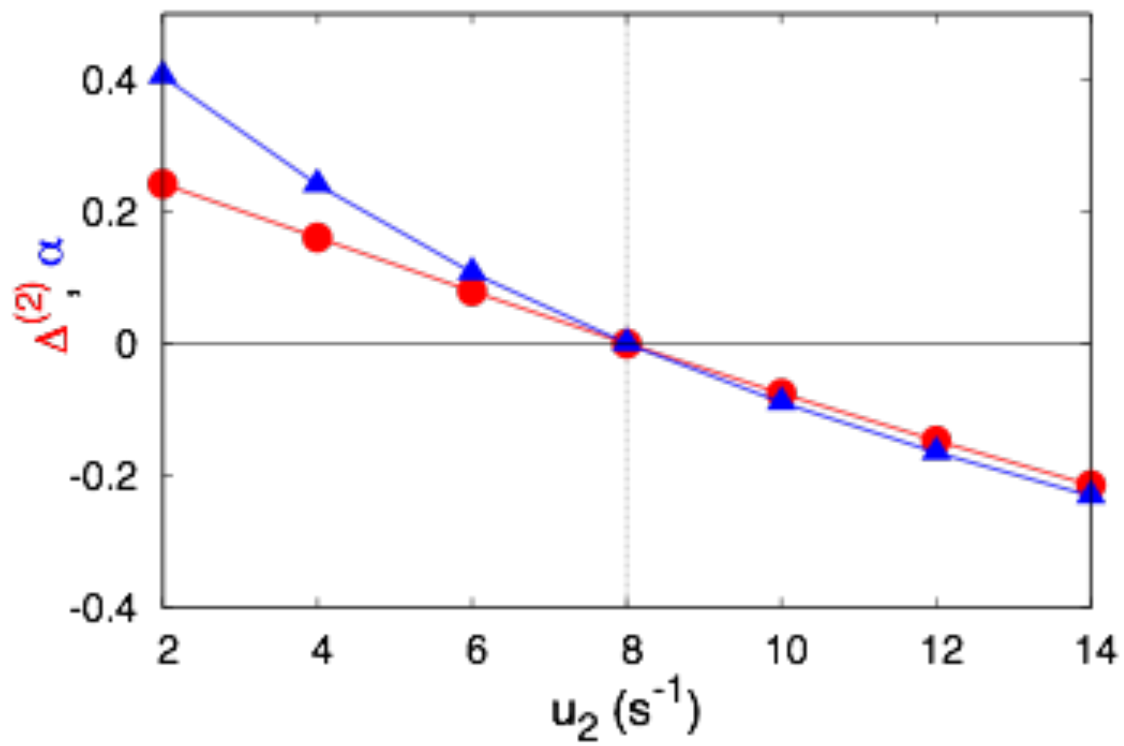


$$\alpha = [P_1 \ln(u_1/w_1) + P_2 \ln(u_2/w_2)] - f_s^{(1)}$$

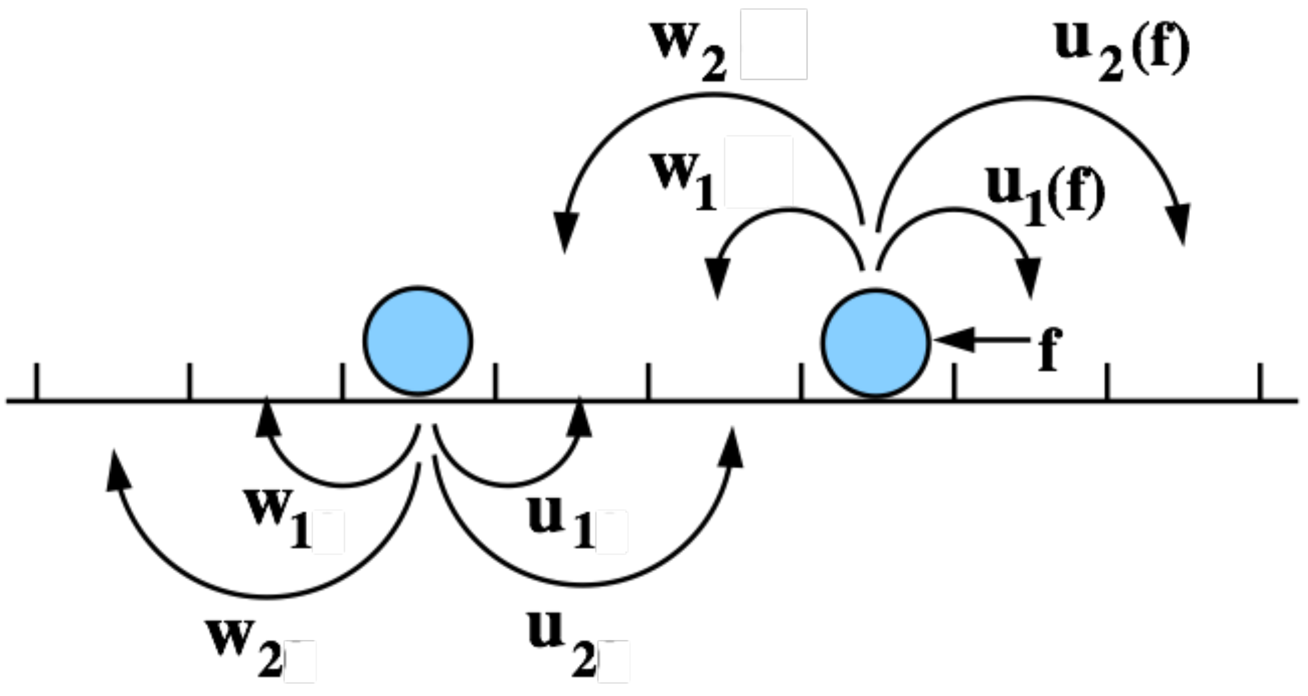
where, $P_1 = k_{21}/(k_{12}+k_{21})$ and $P_2 = k_{12}/(k_{12}+k_{21})$

$k_{12} = 0.5\ s^{-1}$, $k_{21} = 0.5\ s^{-1}$, $w_1 = 0.1\ s^{-1}$, $u_1 = 1\ s^{-1}$, and $w_2 = 0.8\ s^{-1}$

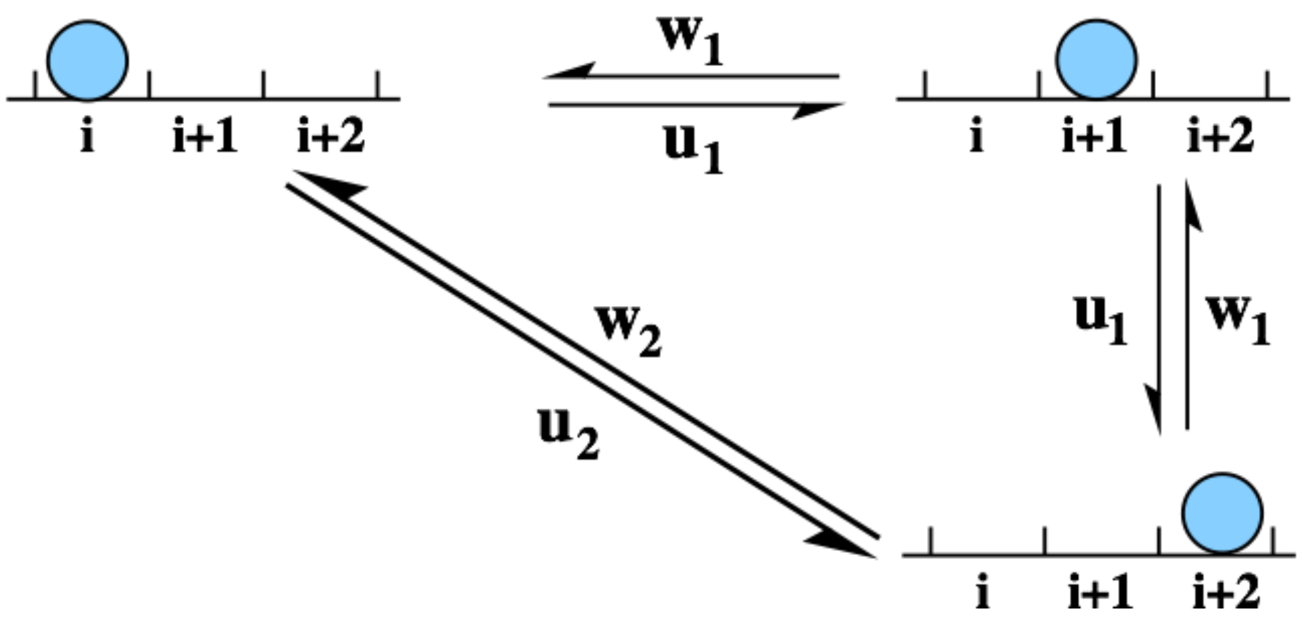
from the equilibrium condition $\Delta^{(2)} = 0$ at $u_2 = 8s^{-1}$

Motor Models

Multiple step-size motor

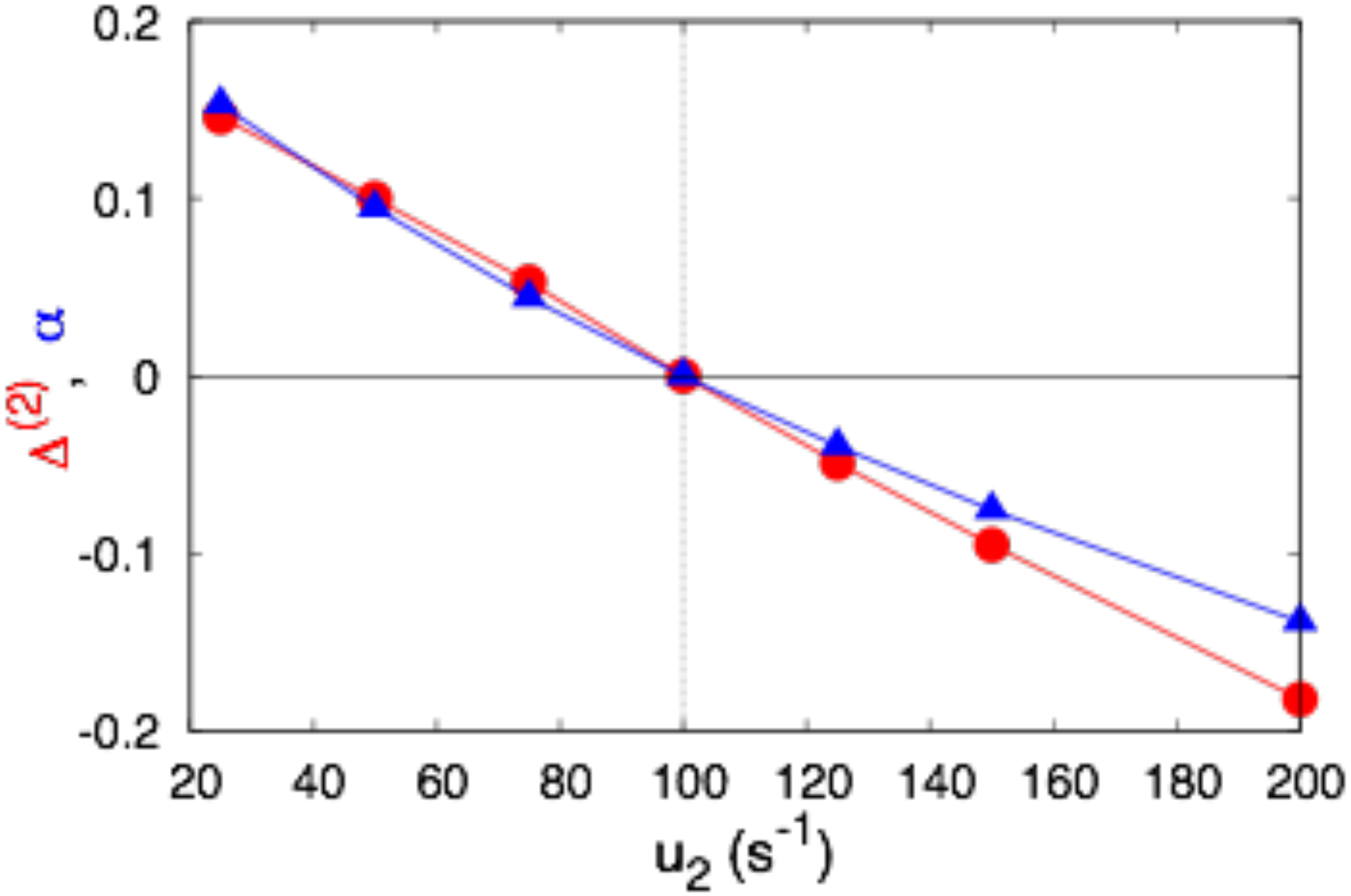


Multiple step-size motor



$$\frac{u_2}{w_2} = \left(\frac{u}{w}\right)^2$$

Multiple step-size motor

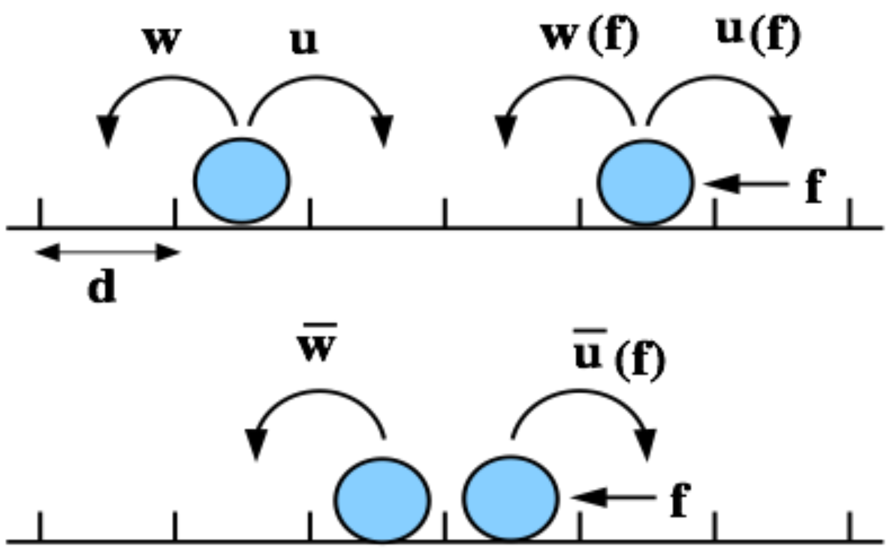


$$\alpha = ln\left(\frac{u_1}{w_1}\right) - f_s^{(1)}$$

$$u_1 = 80s^{-1}, w_1 = 8^{-1}, \text{ and } w_2 = 1s^{-1}$$

from the equilibrium condition at $\Delta^{(2)} = 0$ at $u_2 = 100s^{-1}$

Biased random walk model for many motors



$$f_s^{(2)} = ln\left(\frac{u\bar{u}}{w\bar{w}} + \frac{w}{u} - \frac{\bar{u}}{\bar{w}}\right)$$

$$\frac{u}{w} = \frac{\bar{u}}{\bar{w}} \implies f_s^{(2)} = 2f_s^{(1)}$$

Campas et al. PRL 2006

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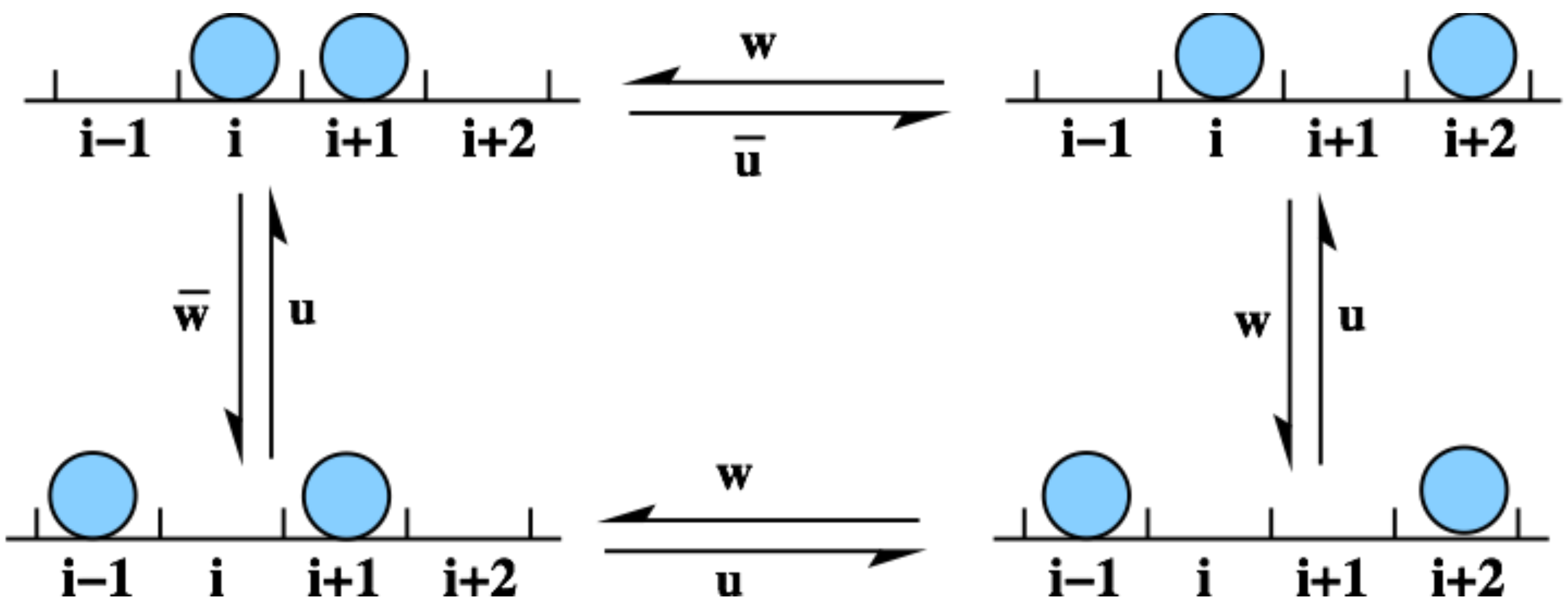
Biased random walk model for many motors

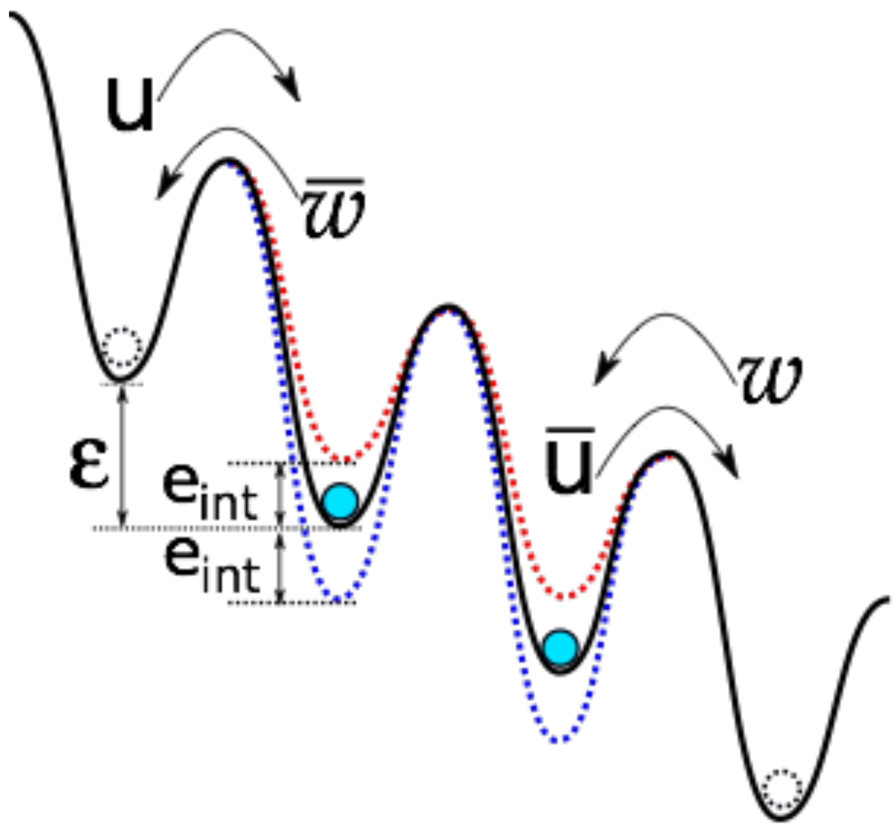


$$u.\bar{u}.w.w = \bar{w}.u.u.w$$

$$\Longrightarrow \quad \frac{u}{w} = \frac{\bar{u}}{\bar{w}}$$

Biased random walk model for many motors

Using energy landscape



$$\frac{u}{\bar{w}} = e^{\epsilon - e_{int}}$$

$$\frac{\bar{u}}{w} = e^{\epsilon + e_{int}}$$

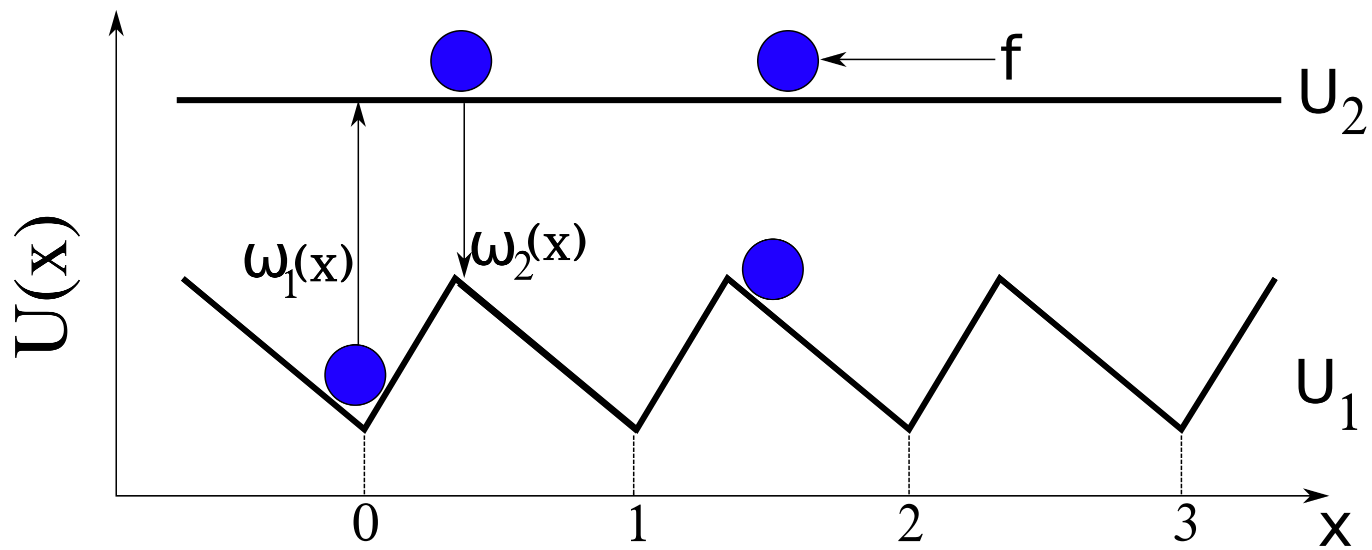
Without any interaction

$$\frac{u}{w} = e^{\epsilon}$$

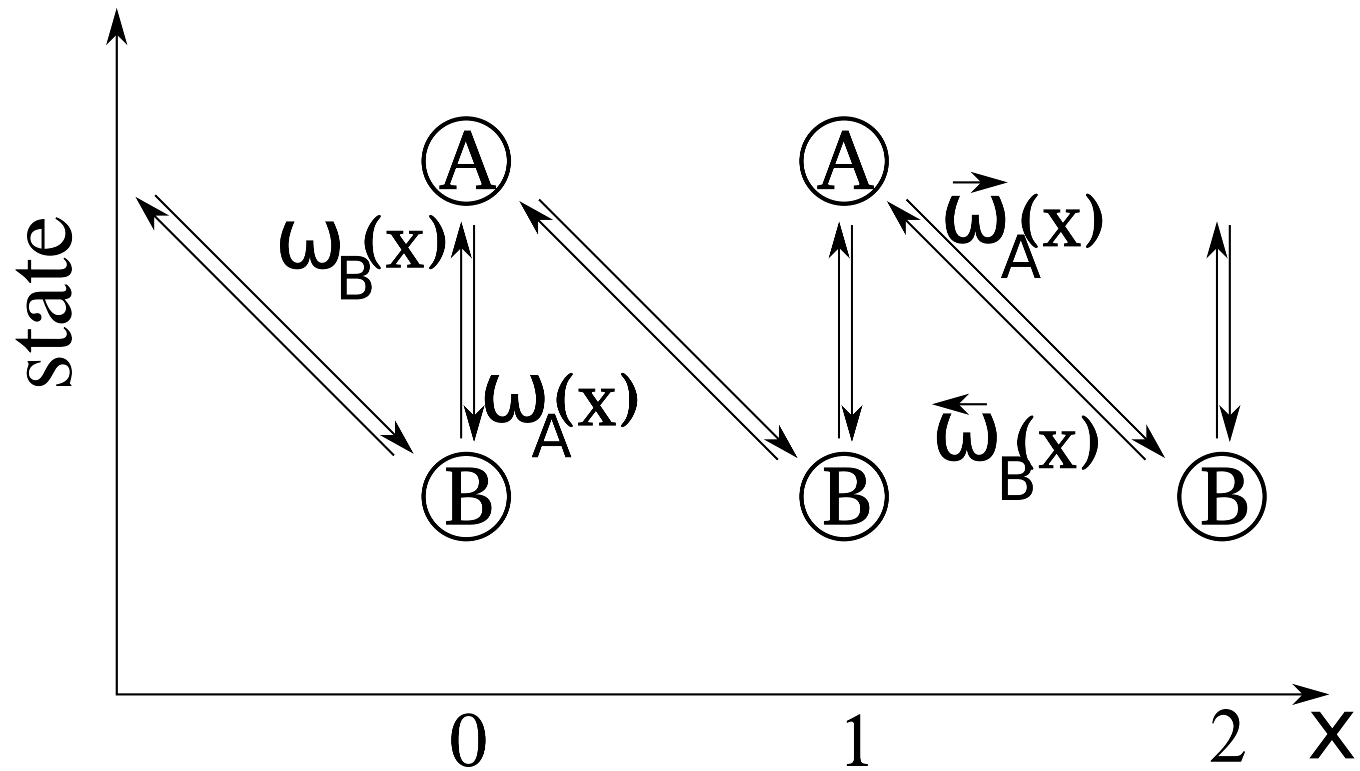
rearranging equations

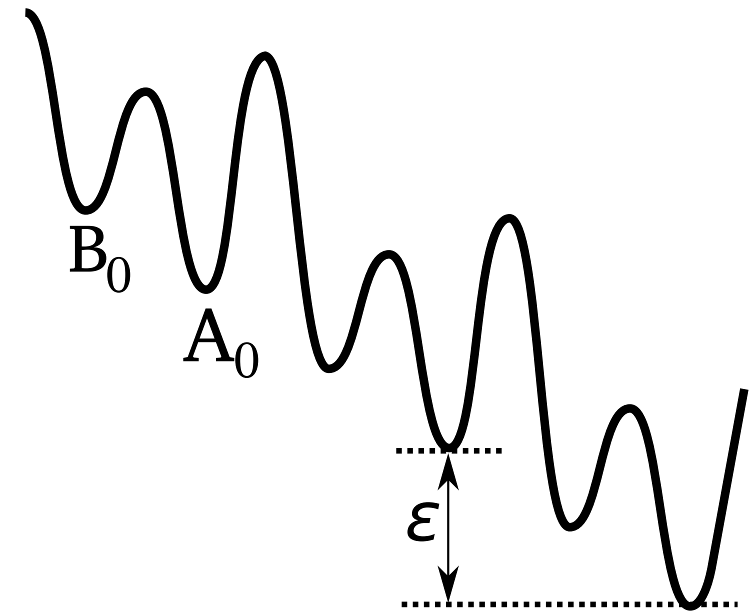
$$\frac{u}{w} = \frac{\bar{u}}{\bar{w}}$$

Two-state Brownian ratchet (BR) model

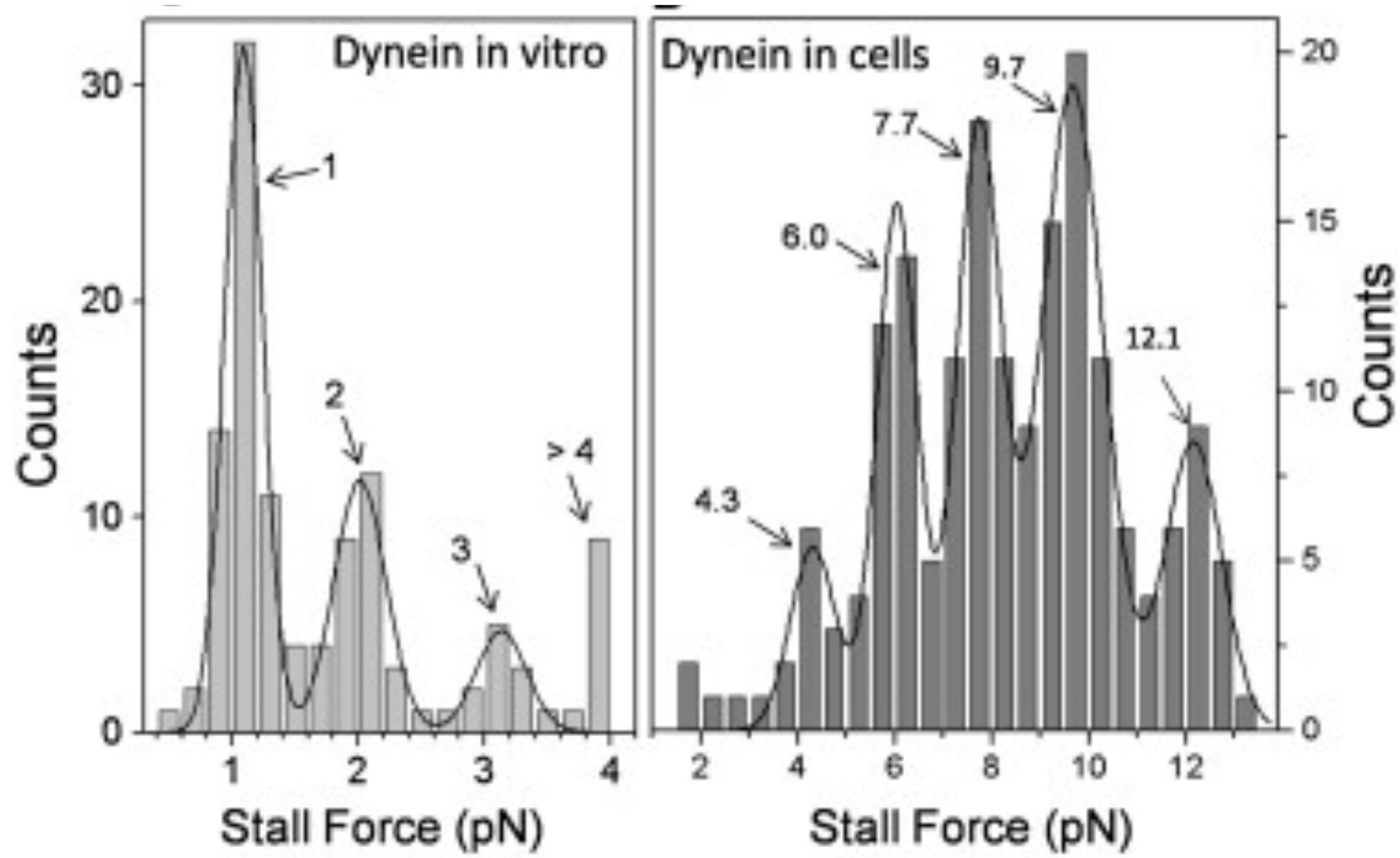


Always gives enhanced cooperativity for steric interaction





Always show force additivity, no matter how many intermediate steps are present



In vivo dynein attache to Microtubule in pair.

Is it possible that dynein are not attaching to the MT in pair but cooperating in such a way that generates twice the force?

A.K. Rai et.al. Cell, 2013

Conclusion

- Provides a simple description for stall force for “biased random walk” type collective motion using equilibrium arguments.
- In the presence of detailed balance for rates, stall forces for multiple filaments/motors are always additive.
- Lack of detailed balance almost always result in non-additivity of stall forces.
- In case of only one path one potential land scape, one will always get stall force additivity no matter how much intermediate steps are introduced.
- Works reasonable well for non-processive motor, as long as as long as the number of motors clustered behind the leading motor remains large enough
- Extremely broad

Collaborators

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Dibyendu Das

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