Additivity of Maximum Force Generated by Multiple Filaments or Motors

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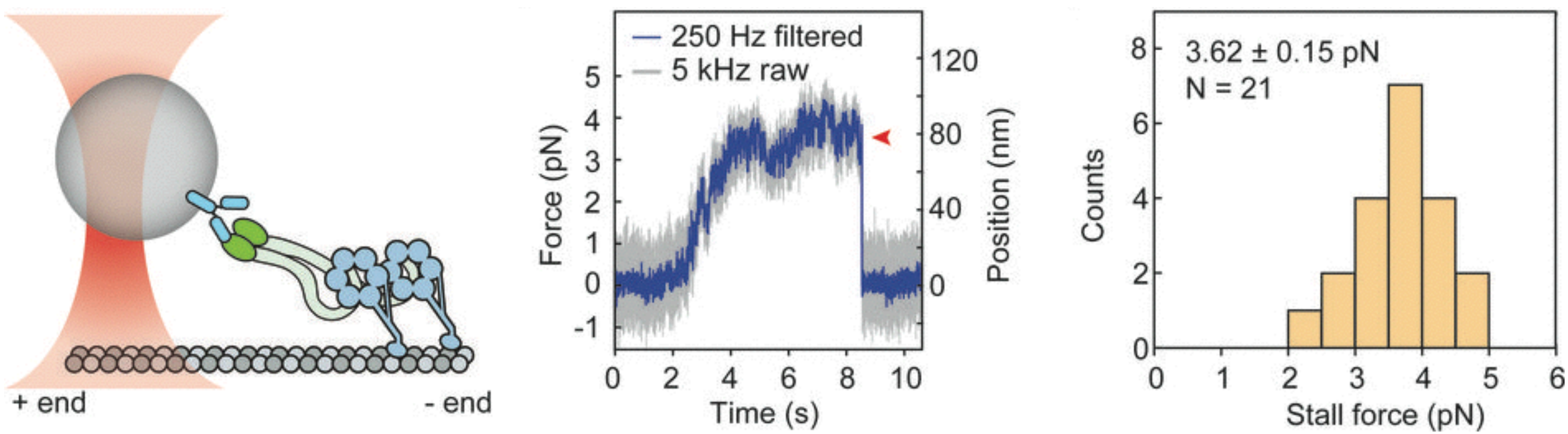
Force generation by Molecular motors

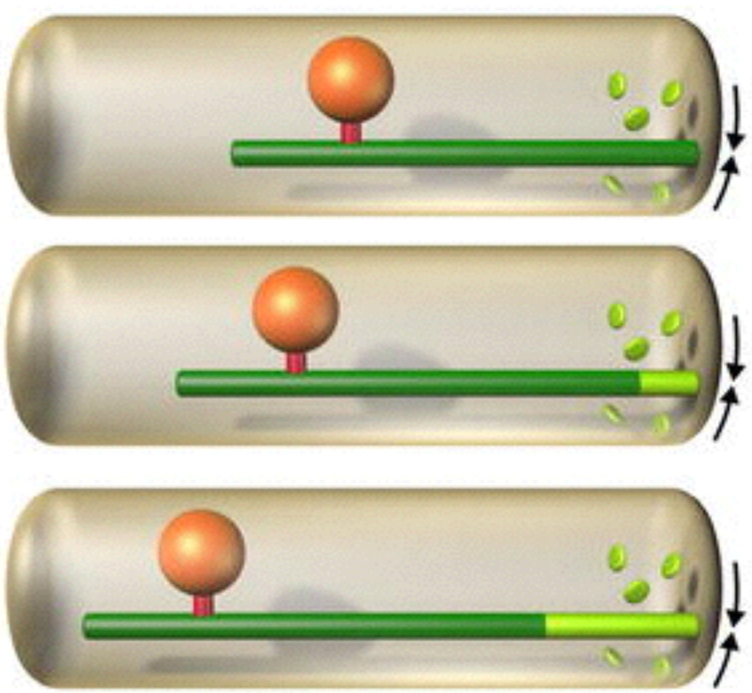
Most forms of movement in the living world are powered by tiny protein machines.

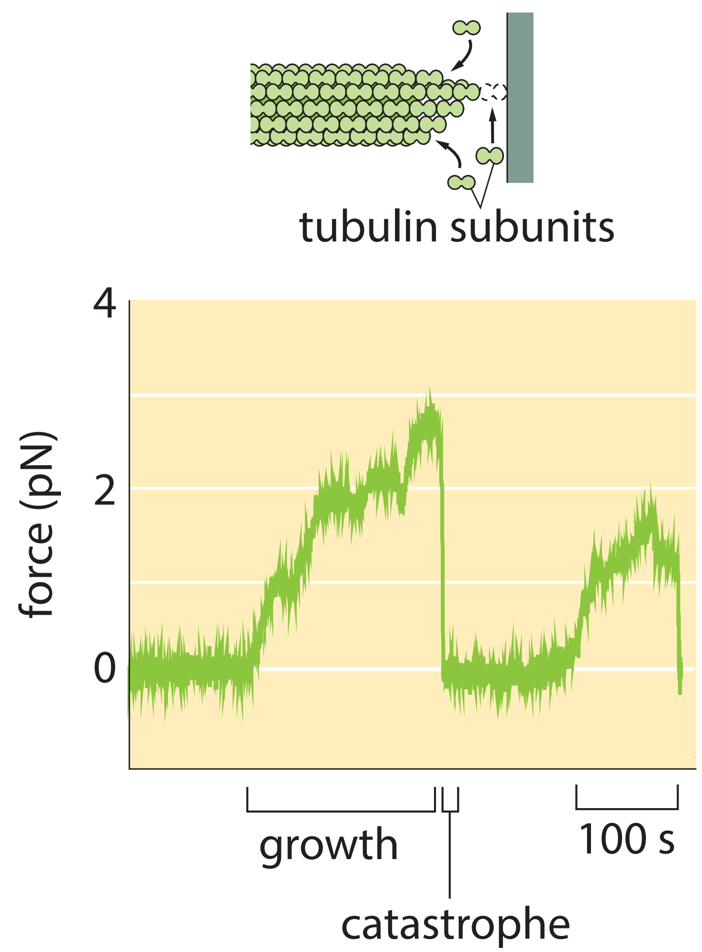


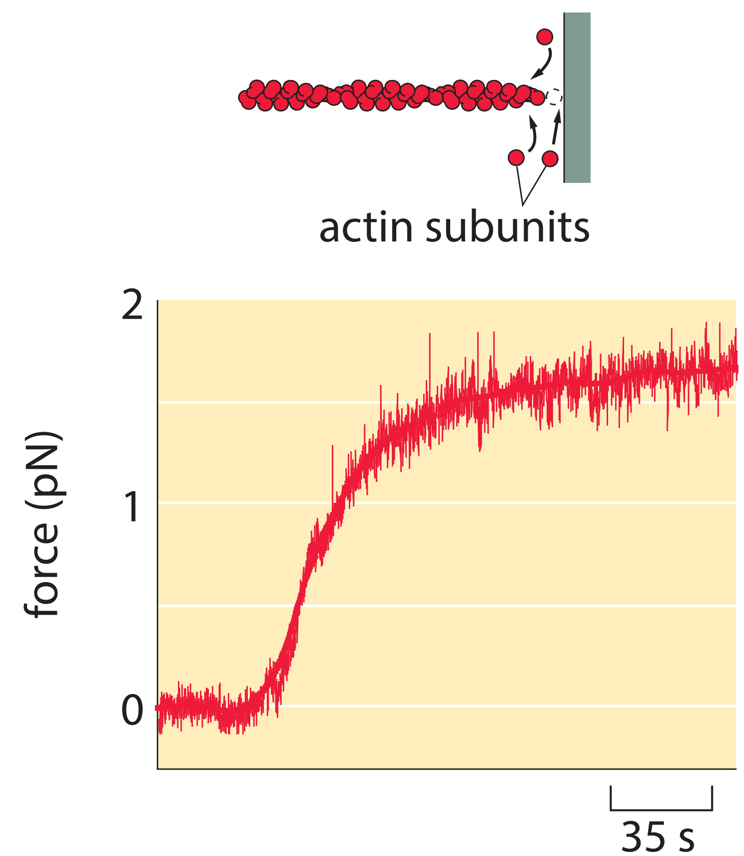
Nature Cell Biology **18**, 1018–1024 (2016)

Force generation by Bio-filaments

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



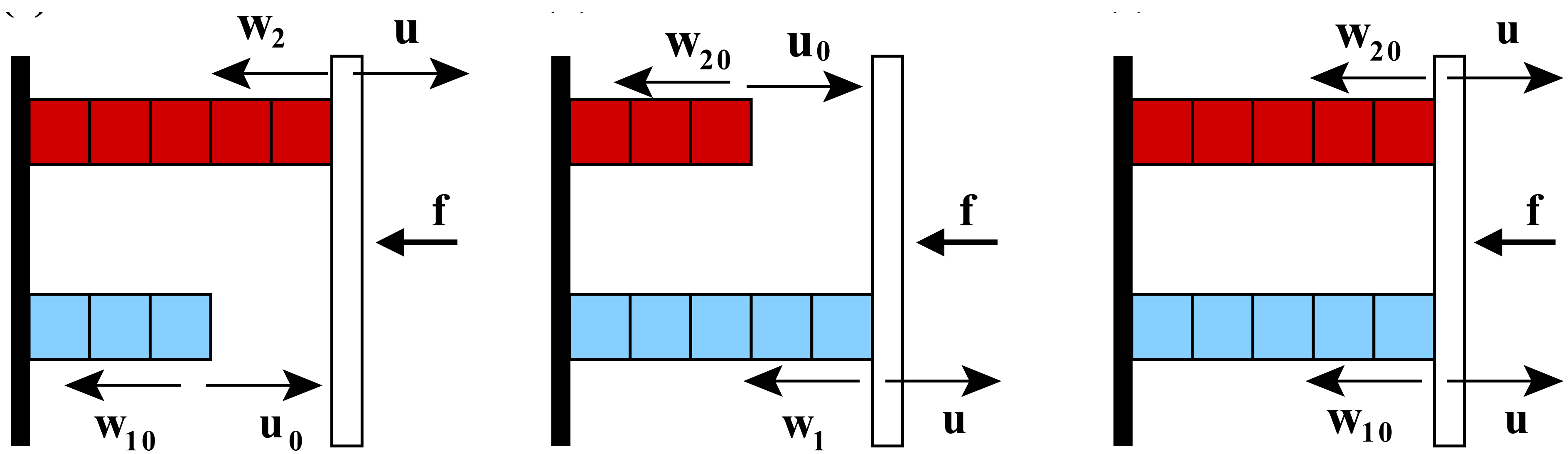


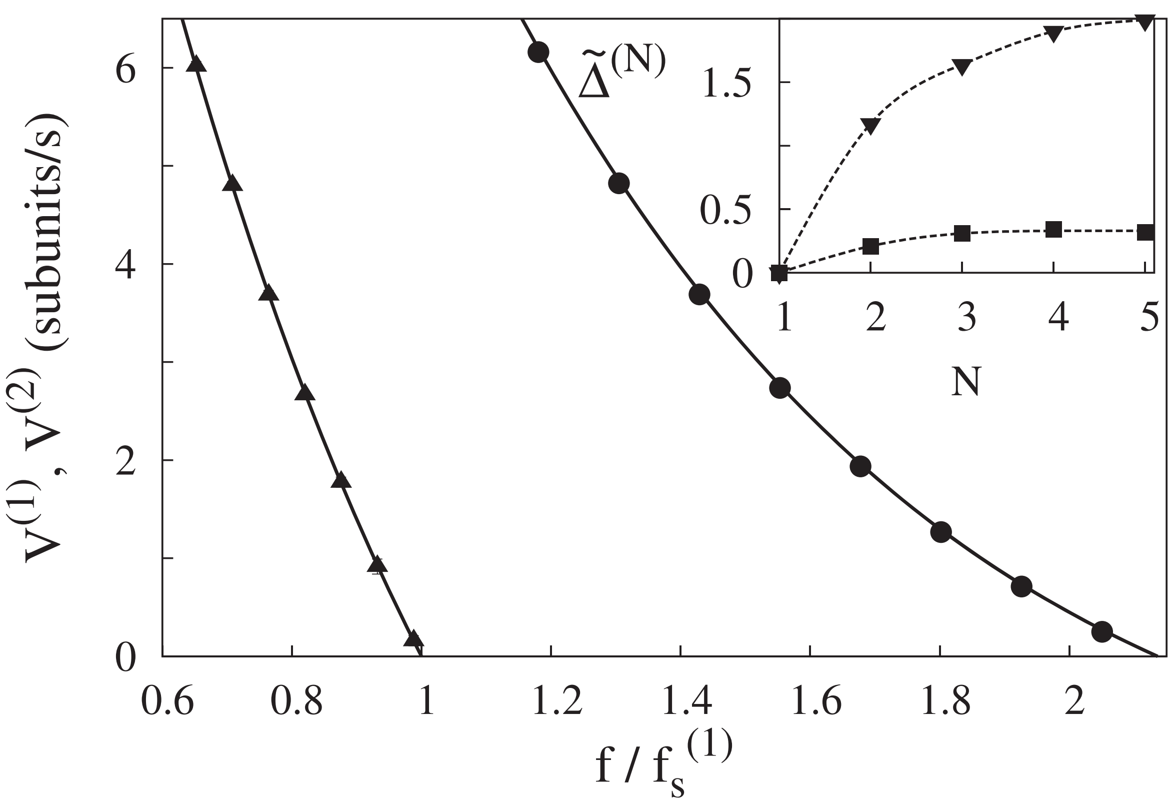


Iva Tolic, 2008, EBJ

How stall force scales with number of filaments/motors?

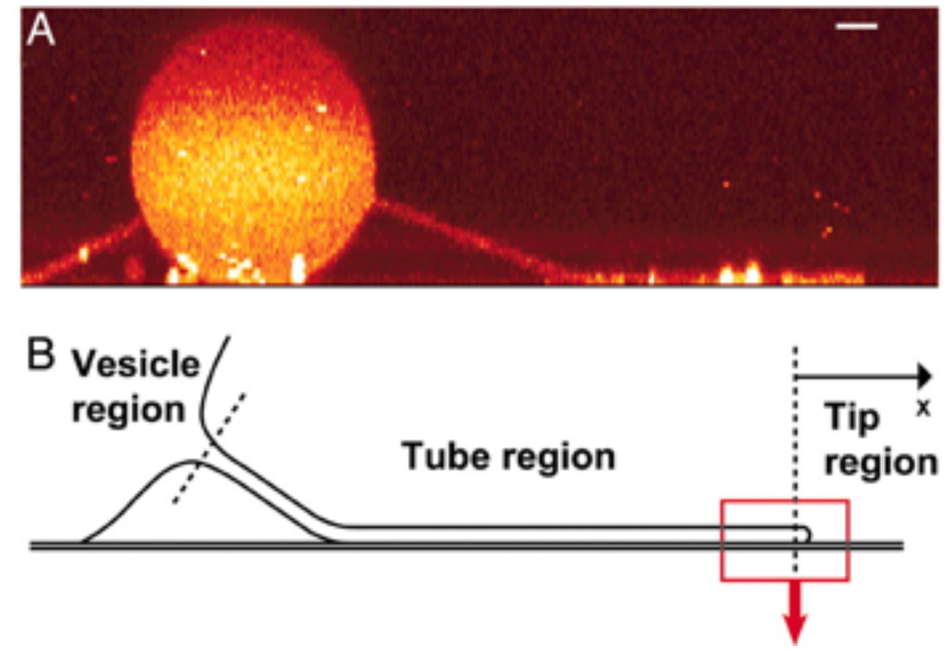
Stall force generated by multiple filament



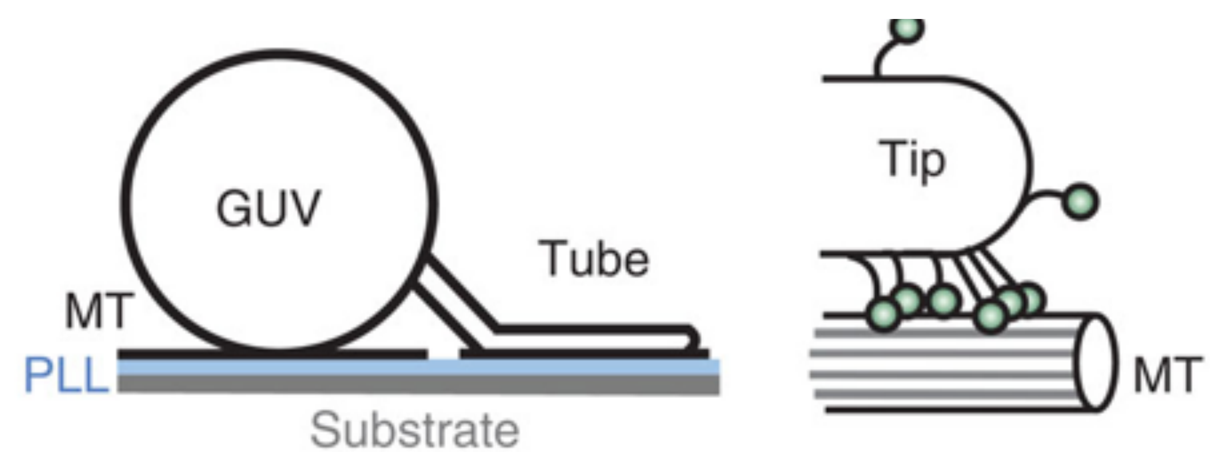


Dipjyoti Das et al, NJP, 2014

Cooperative force generation by single-headed KIF1A motors

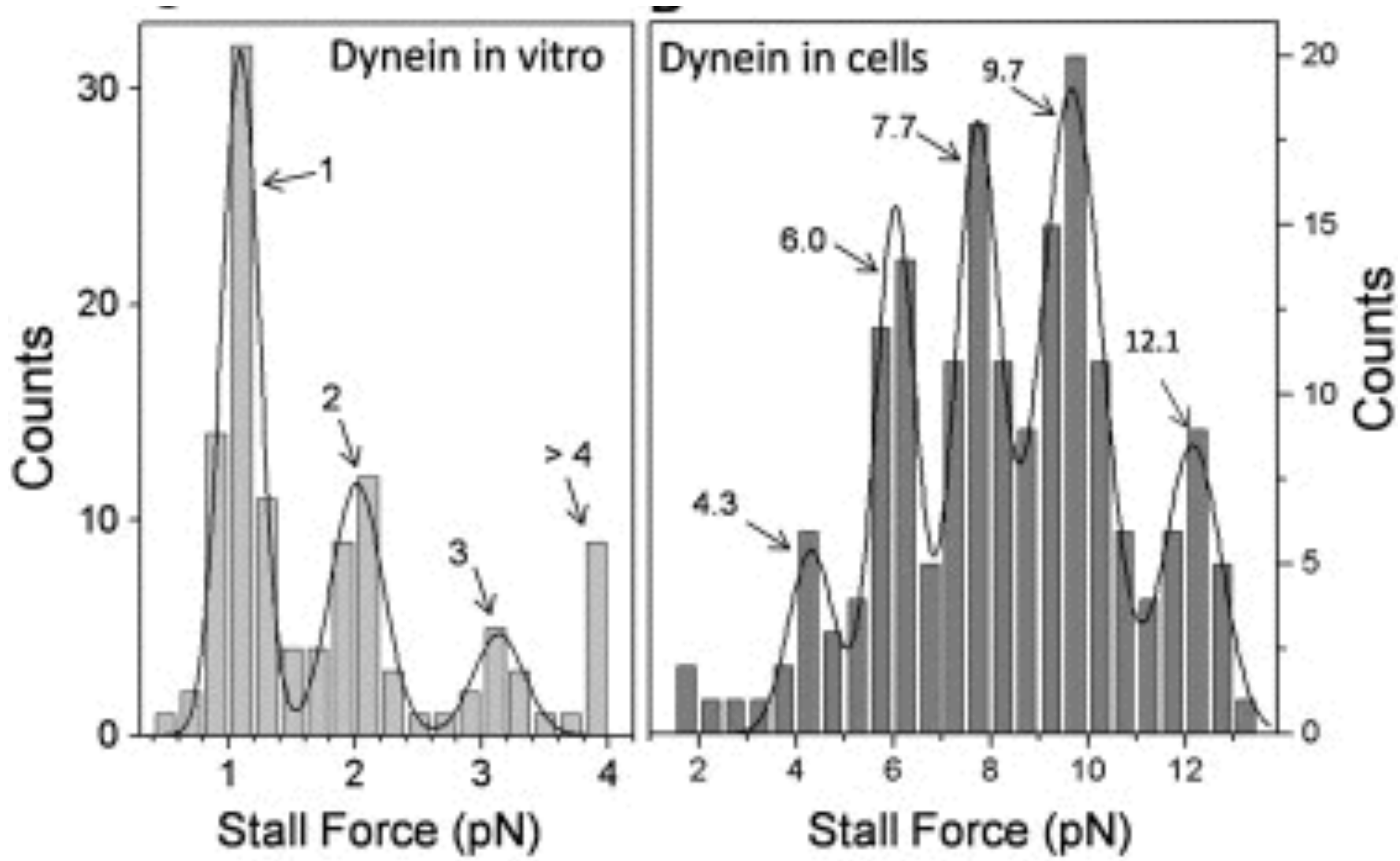


- Team work of single-headed KIF1A motors to extract membrane tubes from giant unilamellar vesicles.



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

Casademunt, *Nature Communications* (2015)

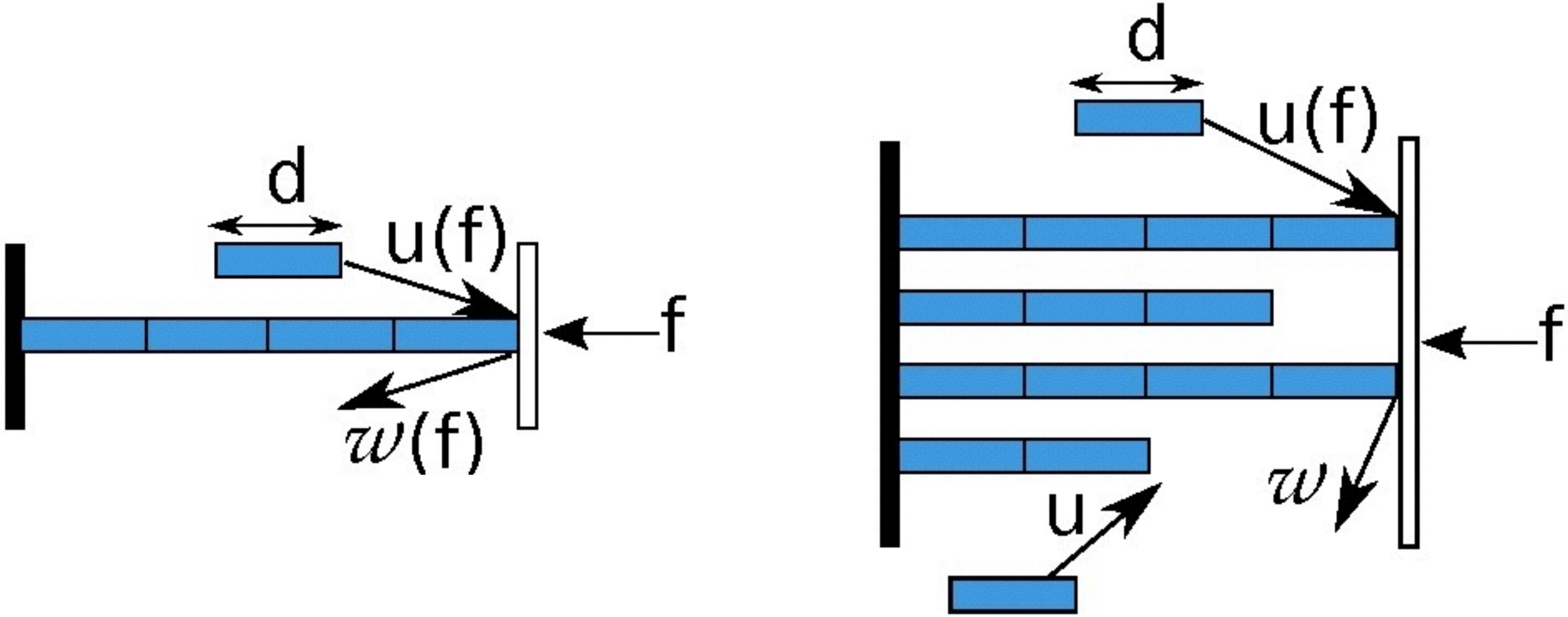


In vivo dynein attache to Microtubule in pair.

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

Roop Mallik et al, Cell 2013

Simple kinetic model for bio-filaments



Editors' Suggestion

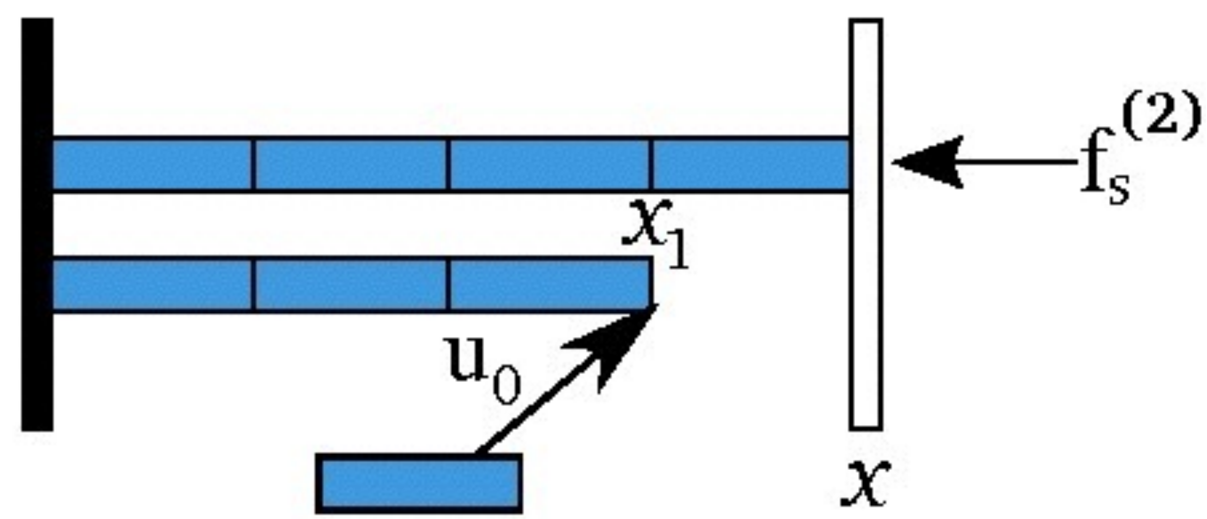
Sufficient conditions for the additivity of stall forces generated by multiple filaments or motors

Tripti Bameta, Dipjyoti Das, Dibyendu Das, Ranjith Padinhateeri, and Mandar M. Inamdar

Phys. Rev. E **95**, 022406 – Published 13 February 2017

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

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

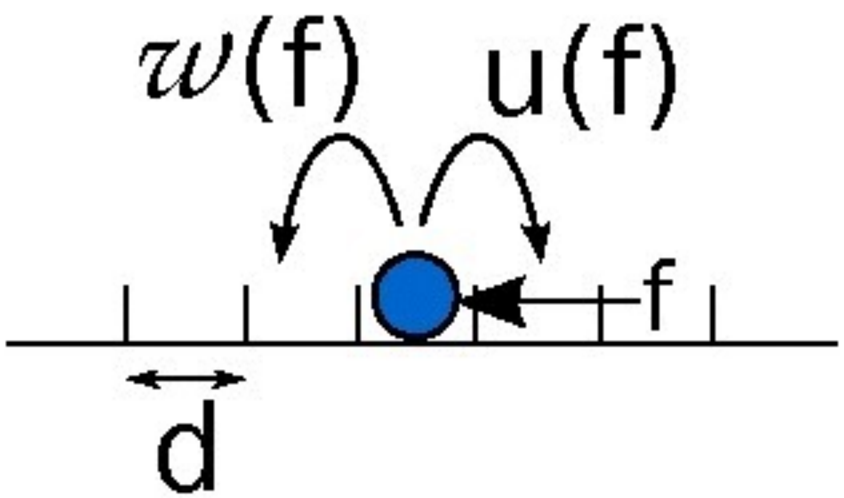
$P(x)$ is expected not to depend on x

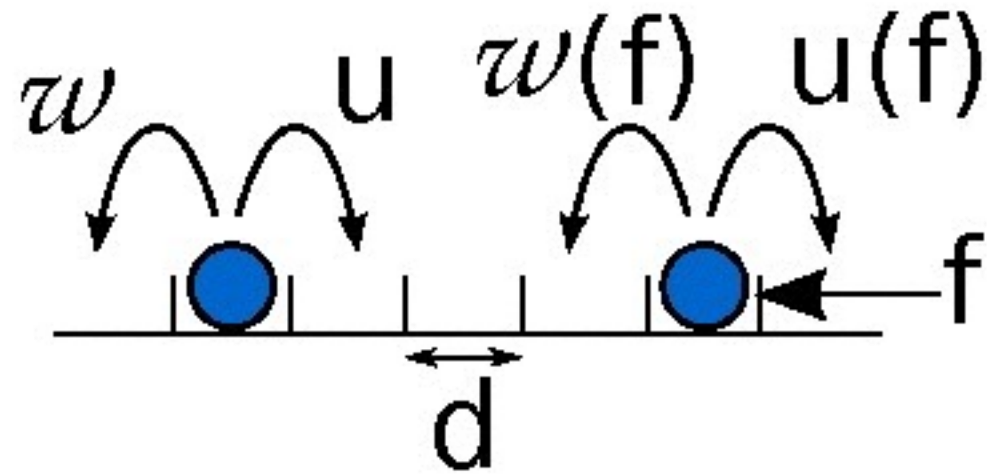
$$f_s^{(2)} = 2\epsilon = 2 f_s^1$$

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

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

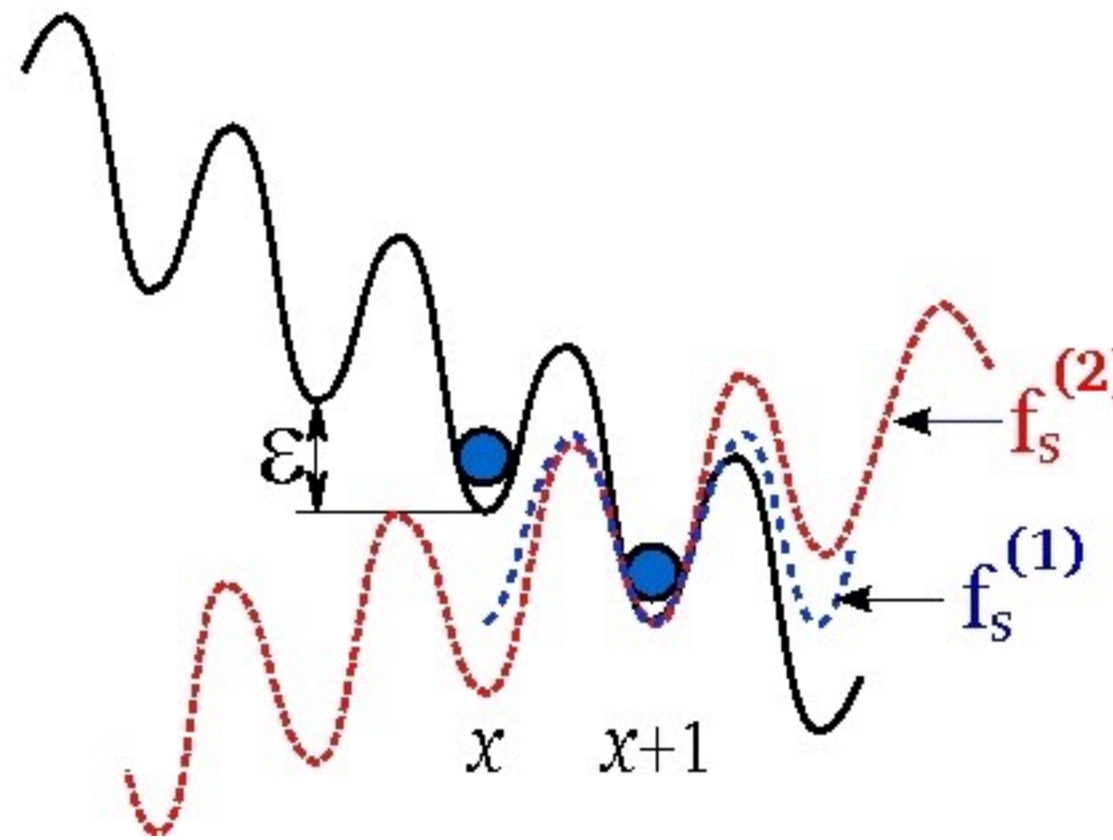
Simple kinetic model for molecular motors





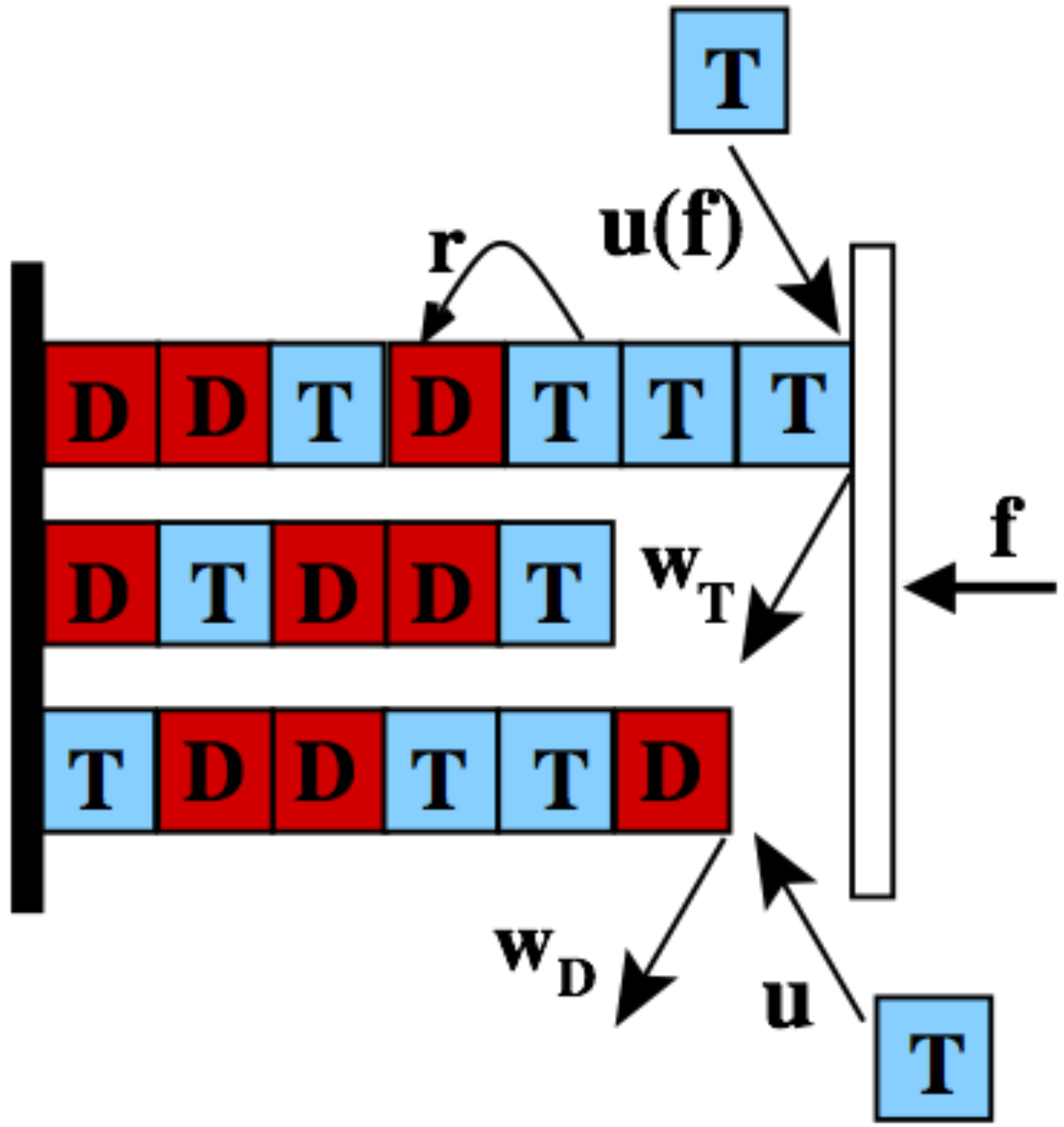
$$P(x) = \frac{1}{Z} e^{-\beta f_s^{(2)} x} e^{\beta \epsilon x} \Big(\sum_{x_1=0}^{x-1} e^{\beta \epsilon x_1} \Big)$$

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

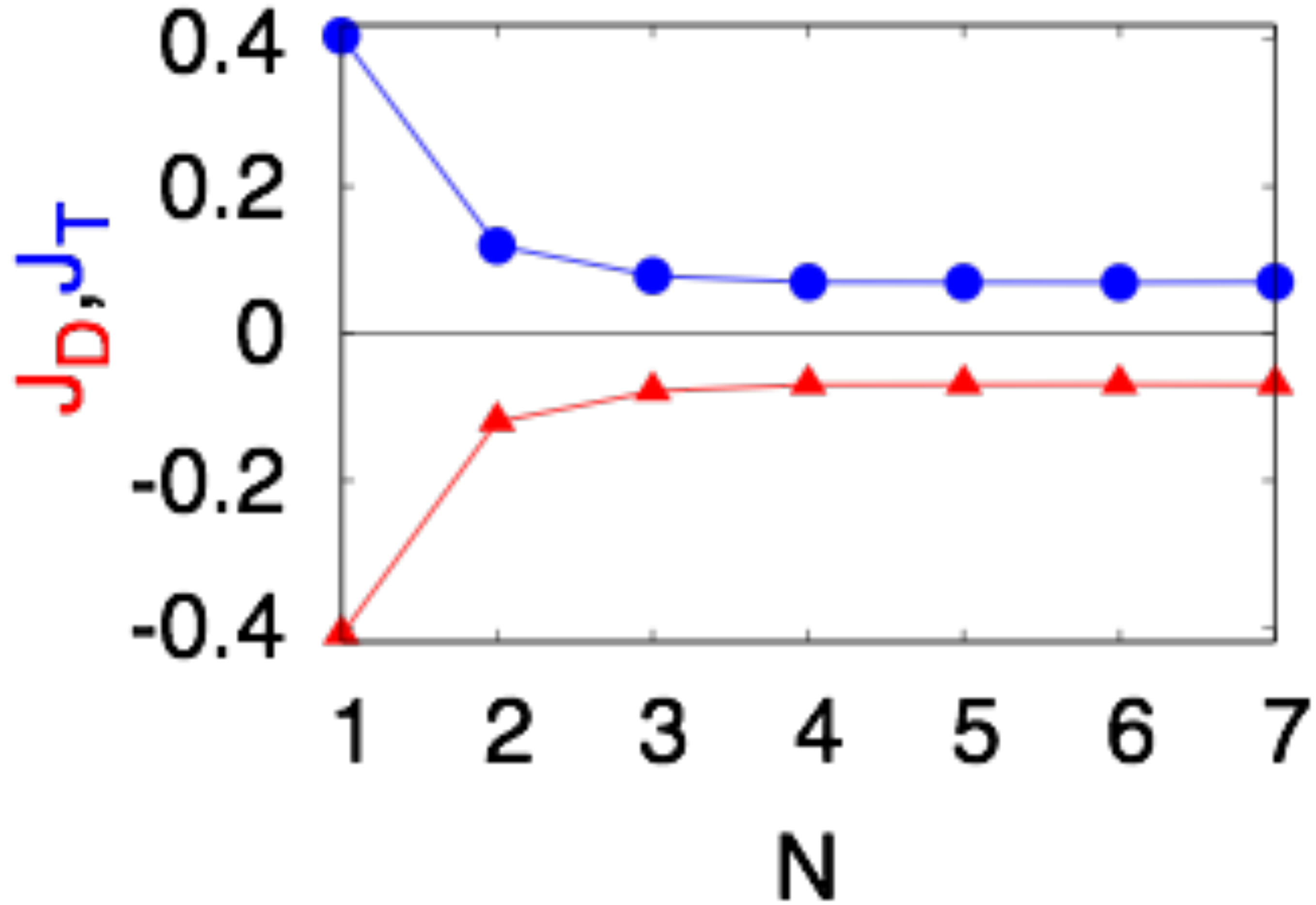


Stall force is additive for simple models

Random hydrolysis model



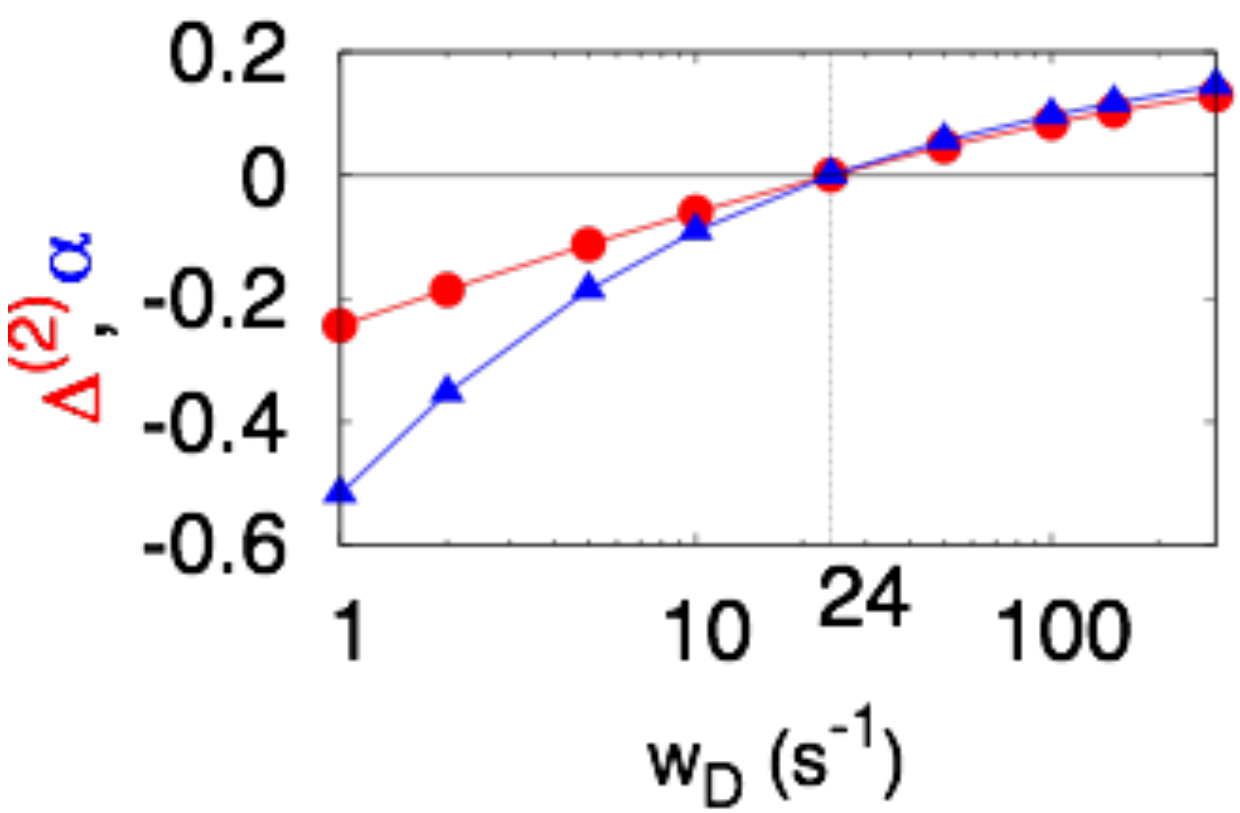
Random hydrolysis model



System with larger number of filament is closer to equilibrium

T.Bameta et al PRE *(*2017)

Random hydrolysis model



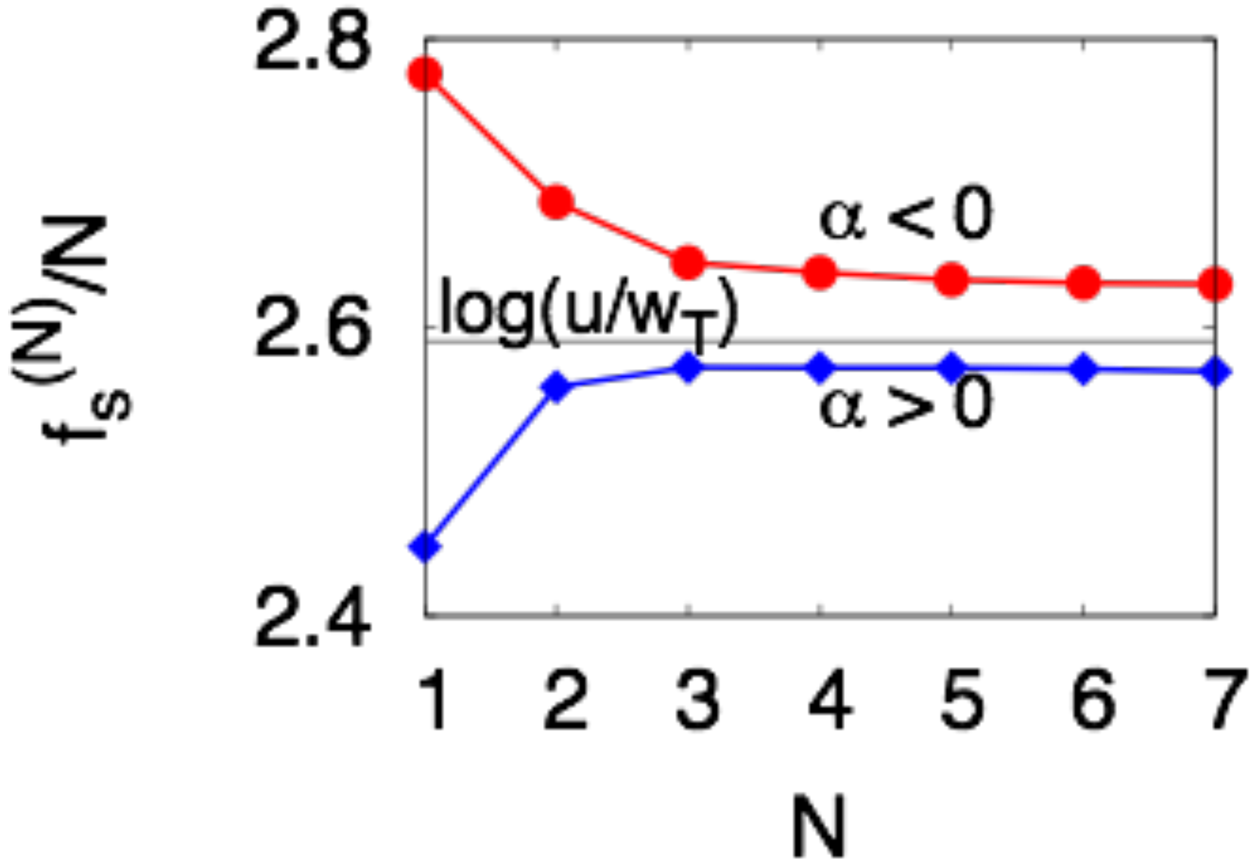
$$\Delta_2 = f_s^{(2)} - 2f_s^{(1)}$$

$$\alpha = F_{poly} - W_{poly}^{max}$$

$$= ln\left(\frac{u}{W_T}\right) - f_s^{(1)}$$

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

Random hydrolysis model



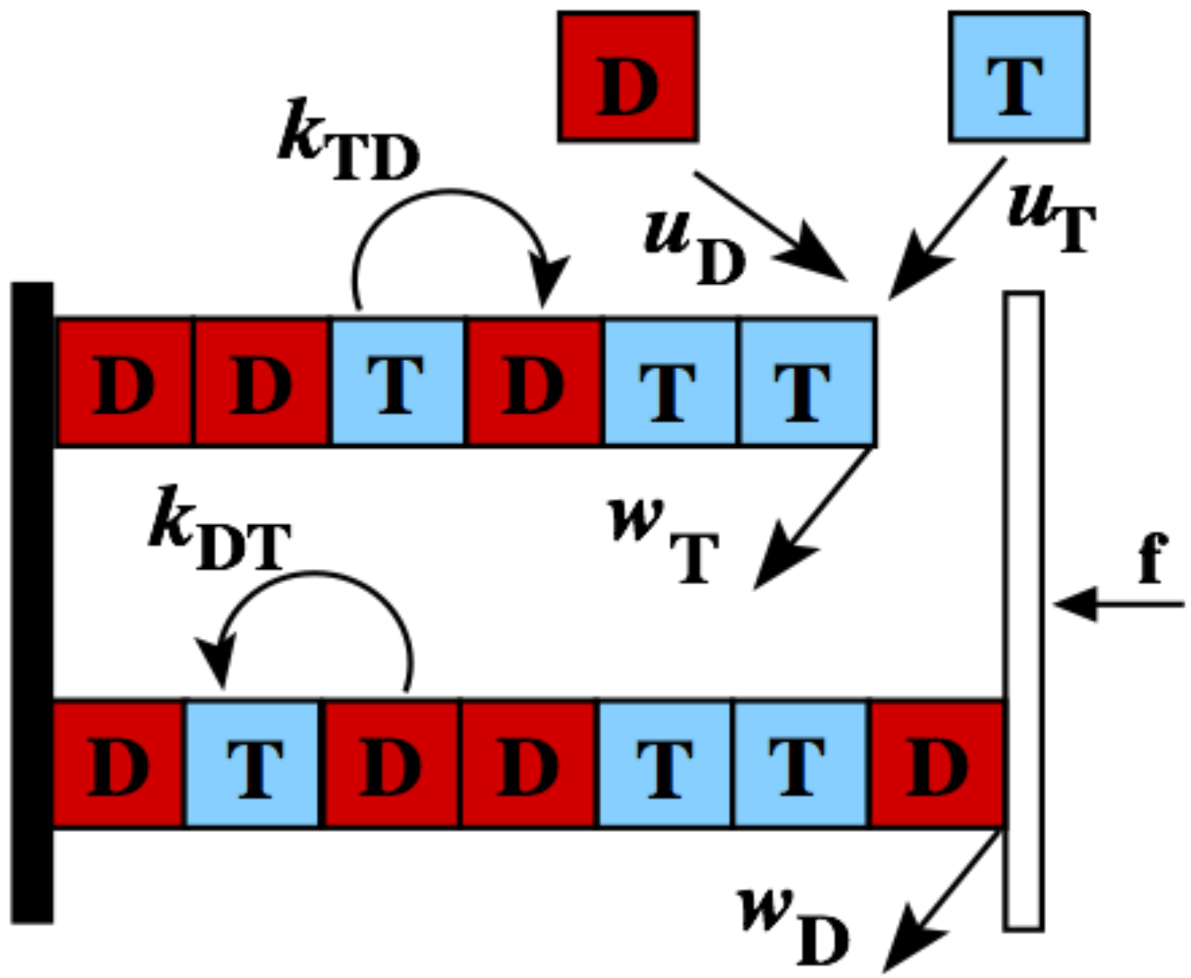
$$\alpha > 0 \quad \left(w_D = 290 s^{-1}\right)$$

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

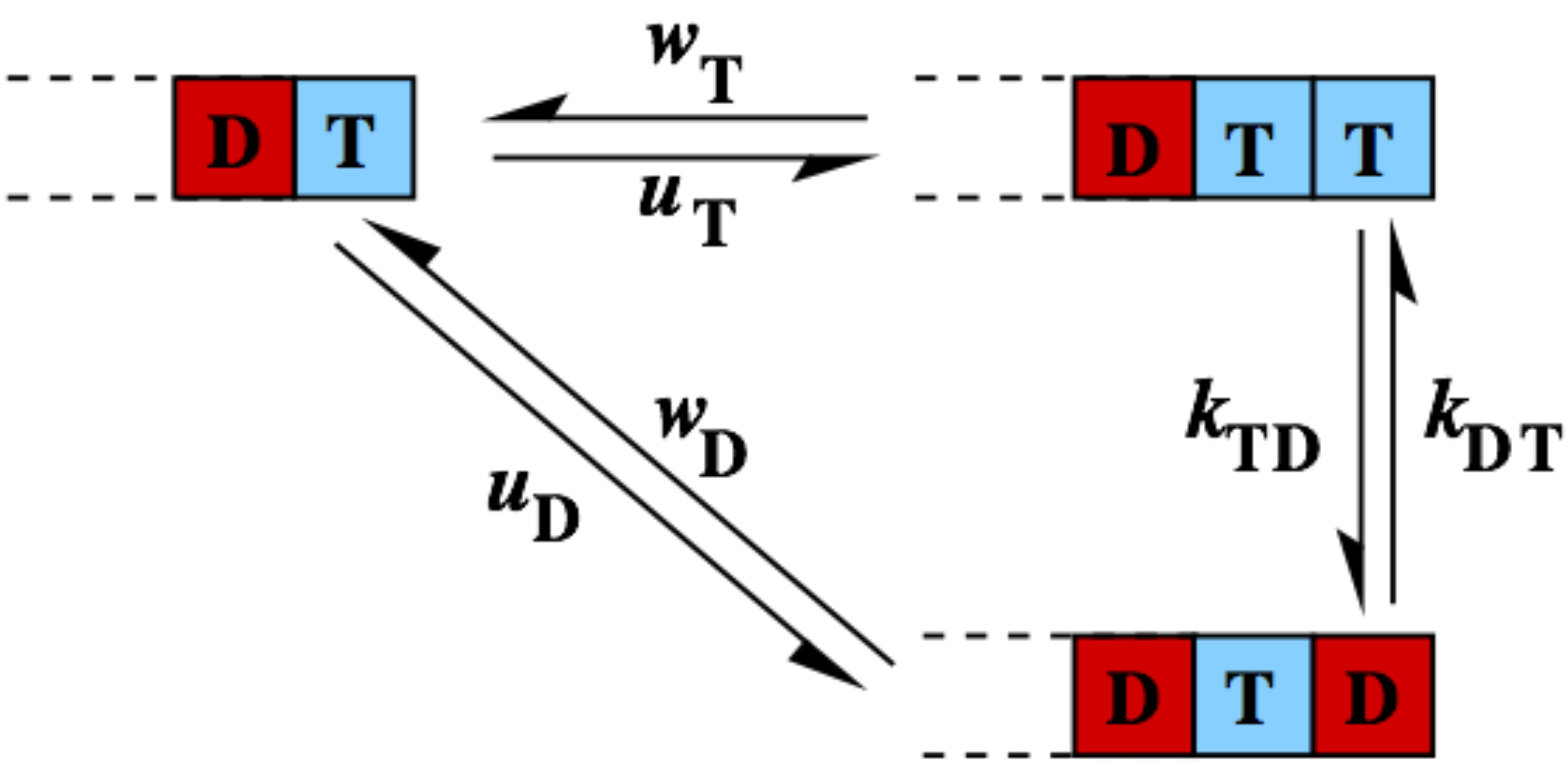
Stall forces are non-additive for biologically relevant non-equilibrium models

detailed balance ↔ thermal equilibrium ↔ stall force additivity

Reversible hydrolysis model

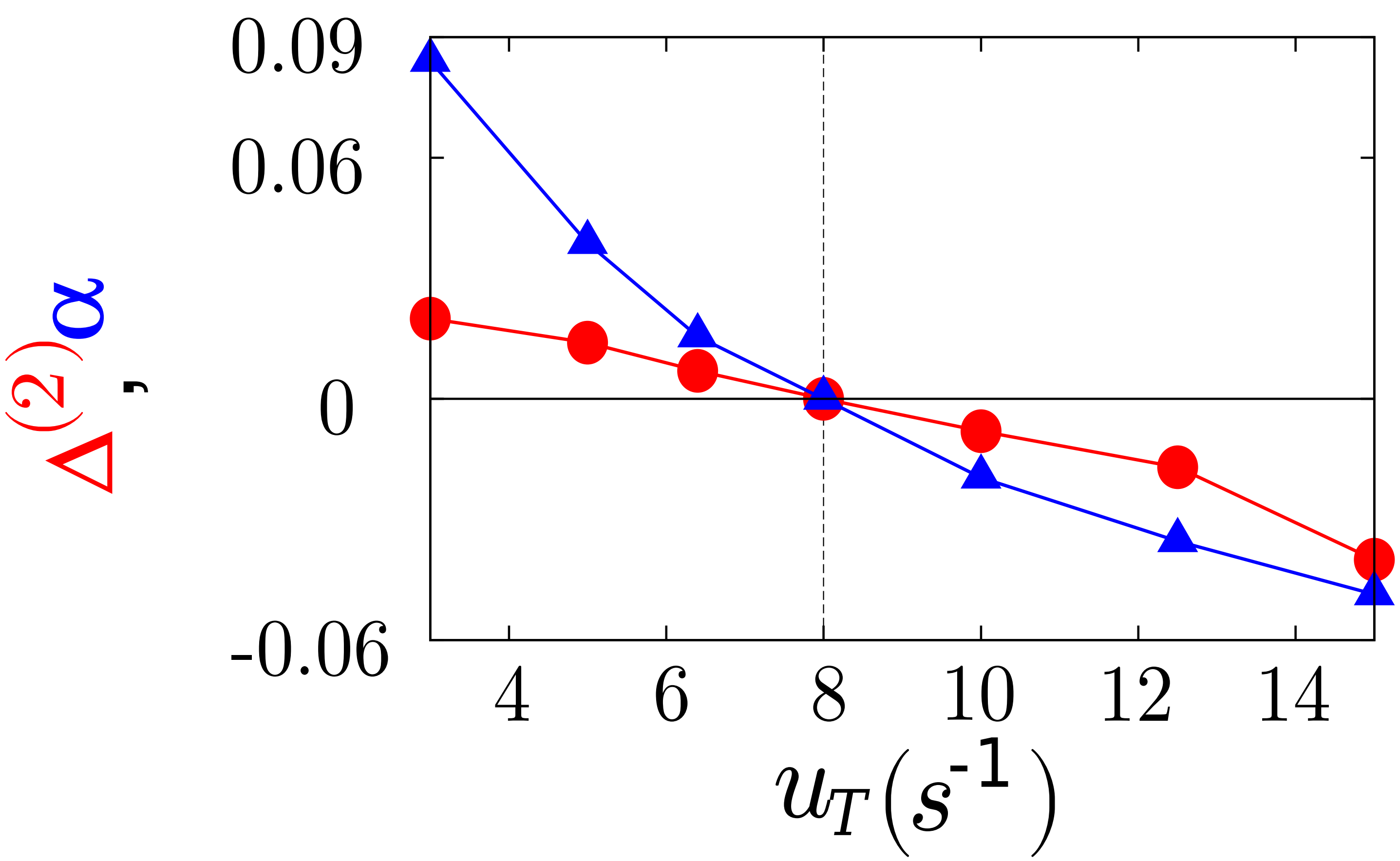


Reversible hydrolysis model



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

Reversible hydrolysis model

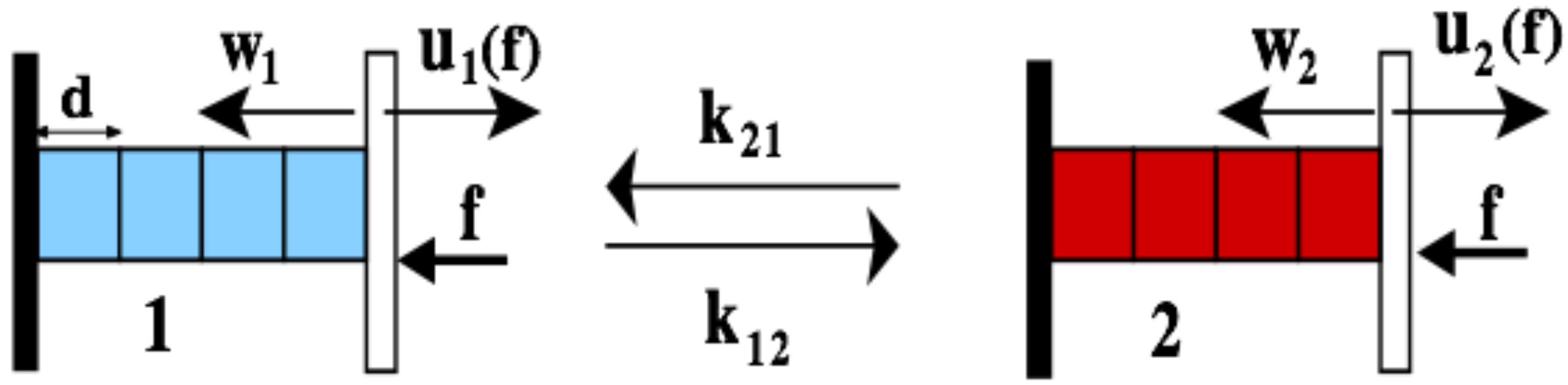


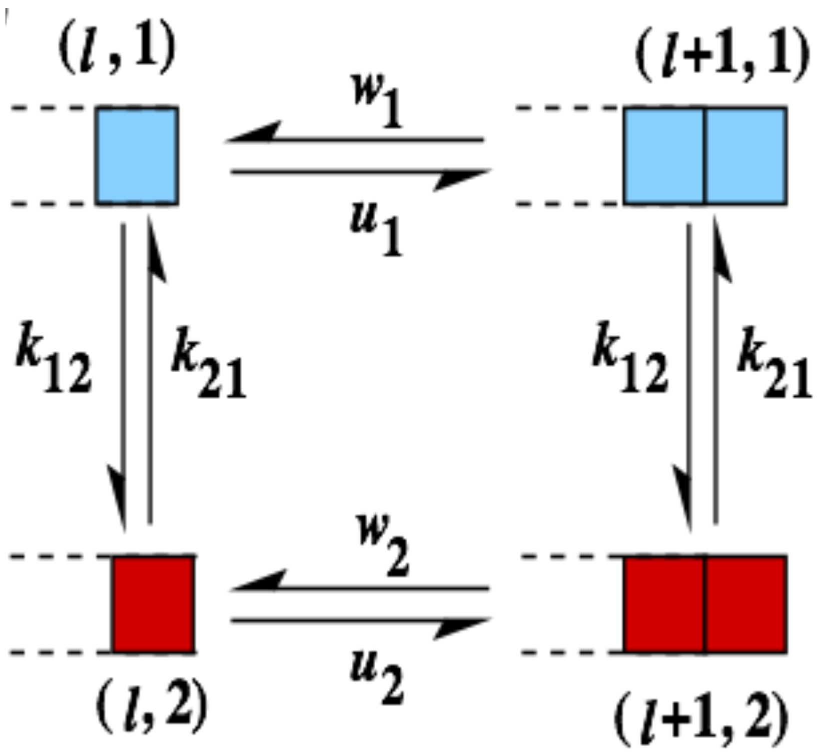
$$w_T = 2s^{-1}, k_{TD} = 0.3s^{-1},$$
$$k_{DT} = 0.4s^{-1}, u_D = 3s^{-1},$$
and $w_D = 1s^{-1}$

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

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

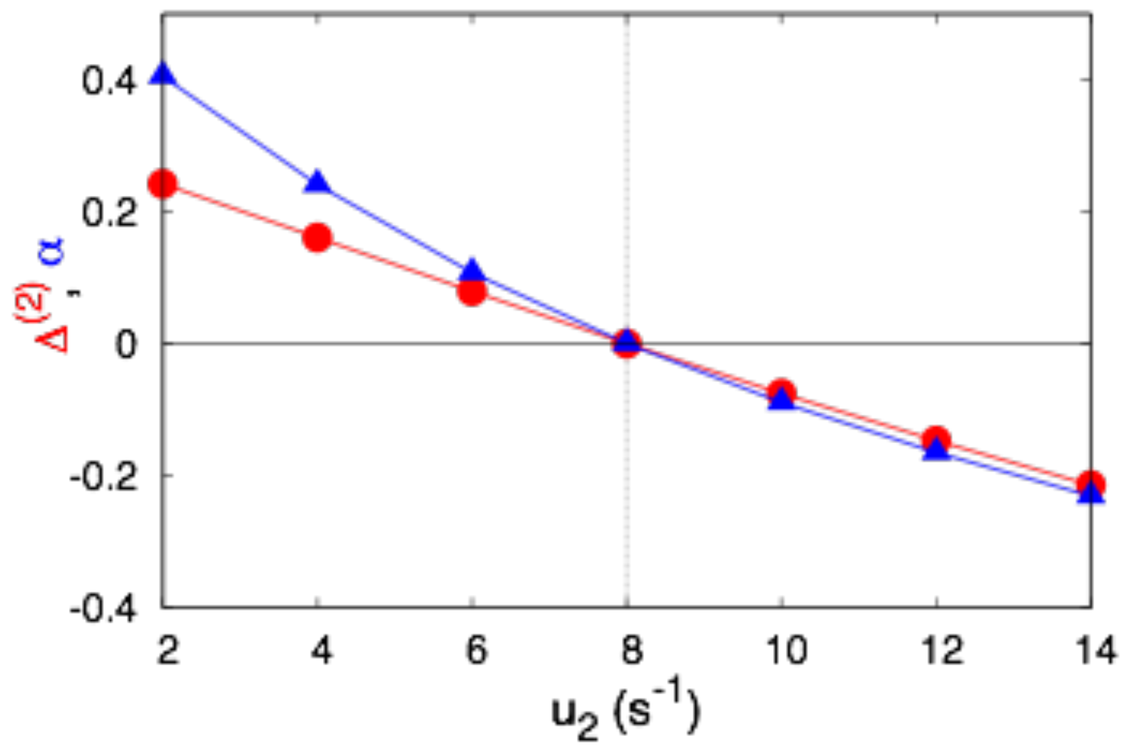
A toy model for filaments





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

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



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

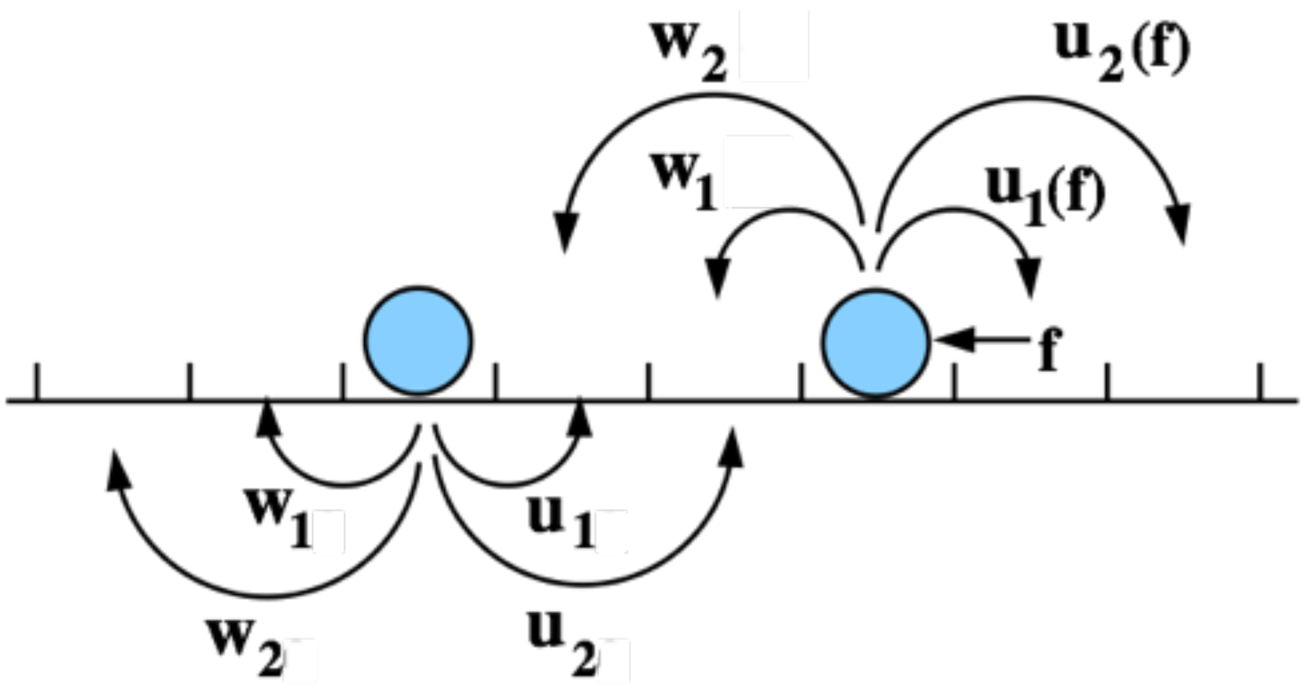
where, $P_1 = k_{21}/(k_{12}+k_{21})$ and
$P_2 = k_{12}/(k_{12}+k_{21})$

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

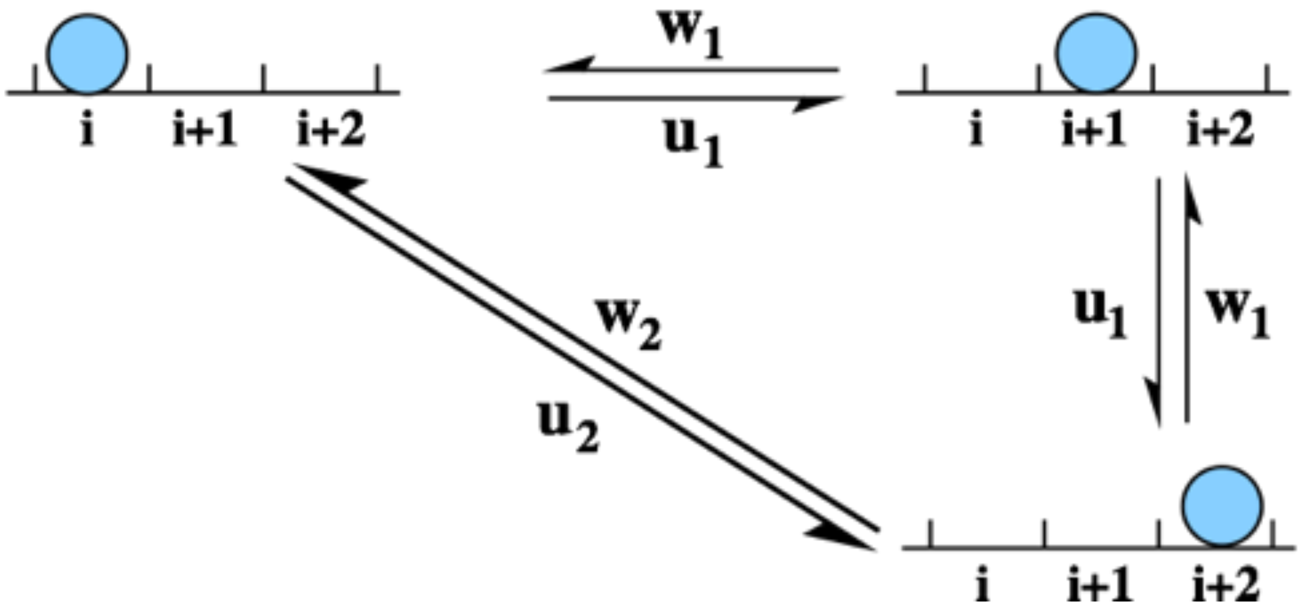
from the equilibrium condition $\Delta^{(2)} = 0$ at $u_2 = 8s^{-1}$

Motor Models

Multiple step-size motor

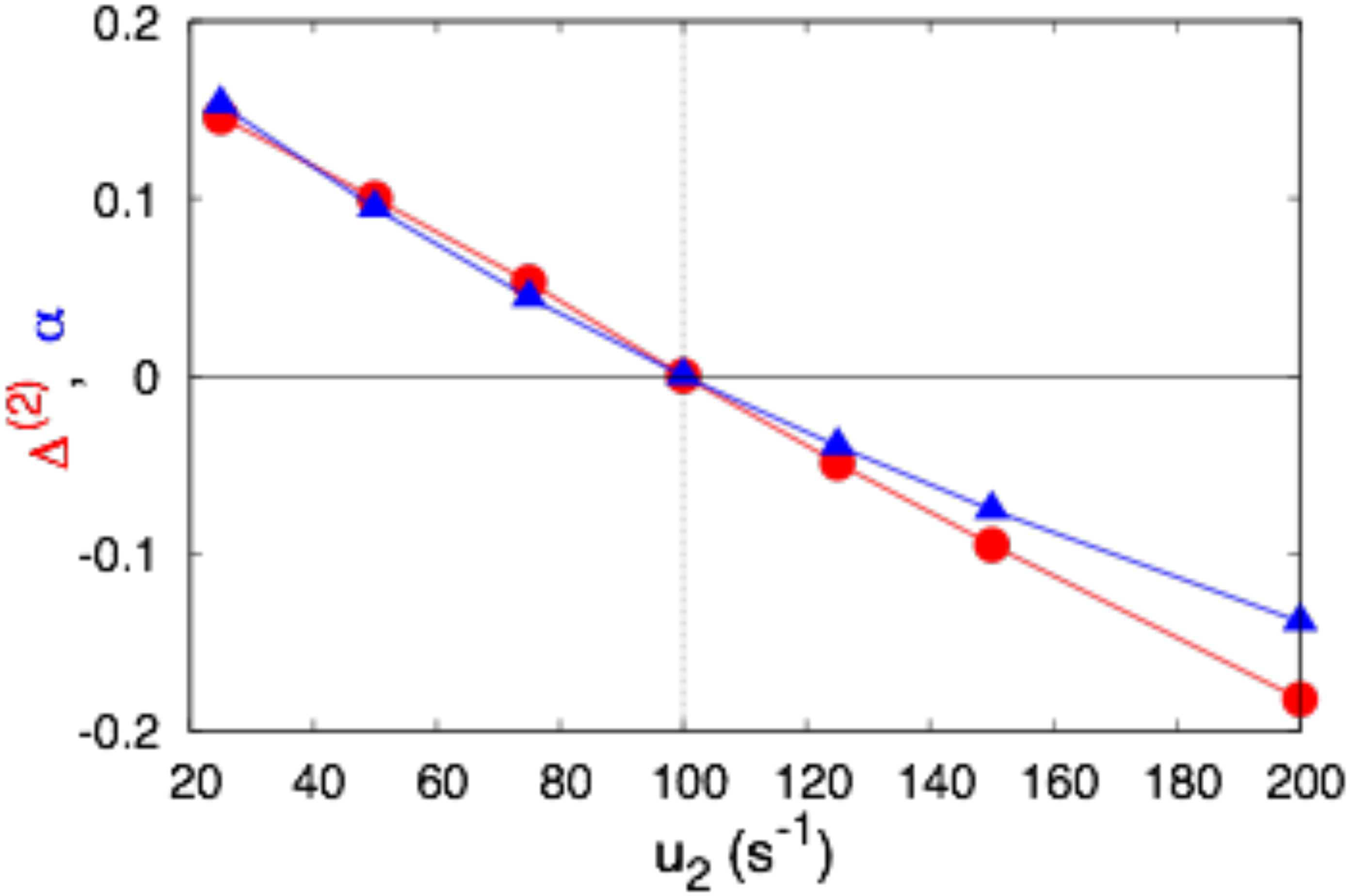


Multiple step-size motor



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

Multiple step-size motor

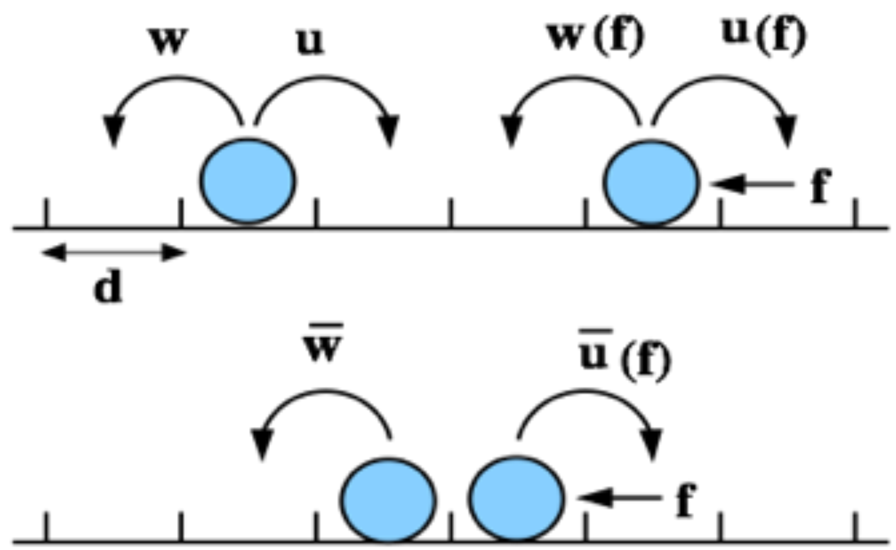


$$\alpha = ln\left(\frac{u_1}{w_1}\right) - f_s^{(1)}$$

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

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

Biased random walk model for many motors



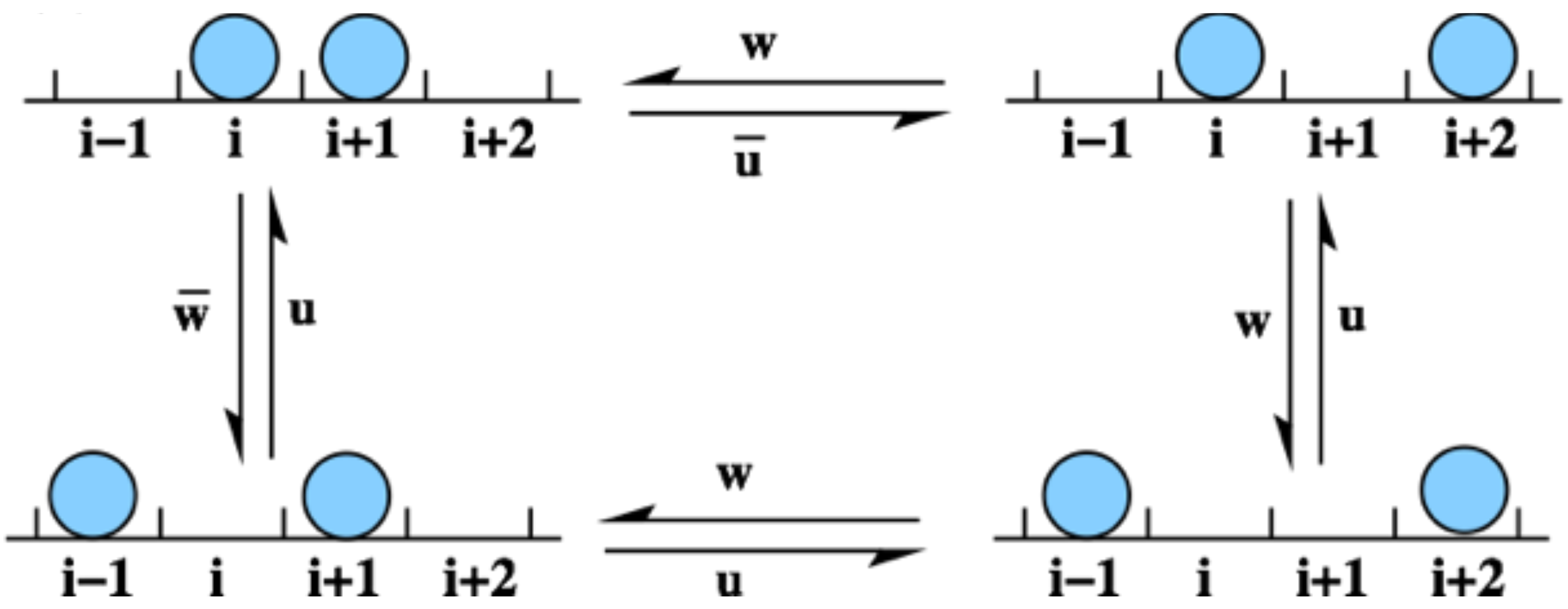
$$f_s^{(2)} = ln\left(\frac{u\bar{u}}{w\bar{w}} + \frac{w}{u} - \frac{\bar{u}}{\bar{w}}\right)$$

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

Campas et al. PRL 2006

मौलिक विज्ञान प्रकर्ष केन्द्र

Biased random walk model for many motors

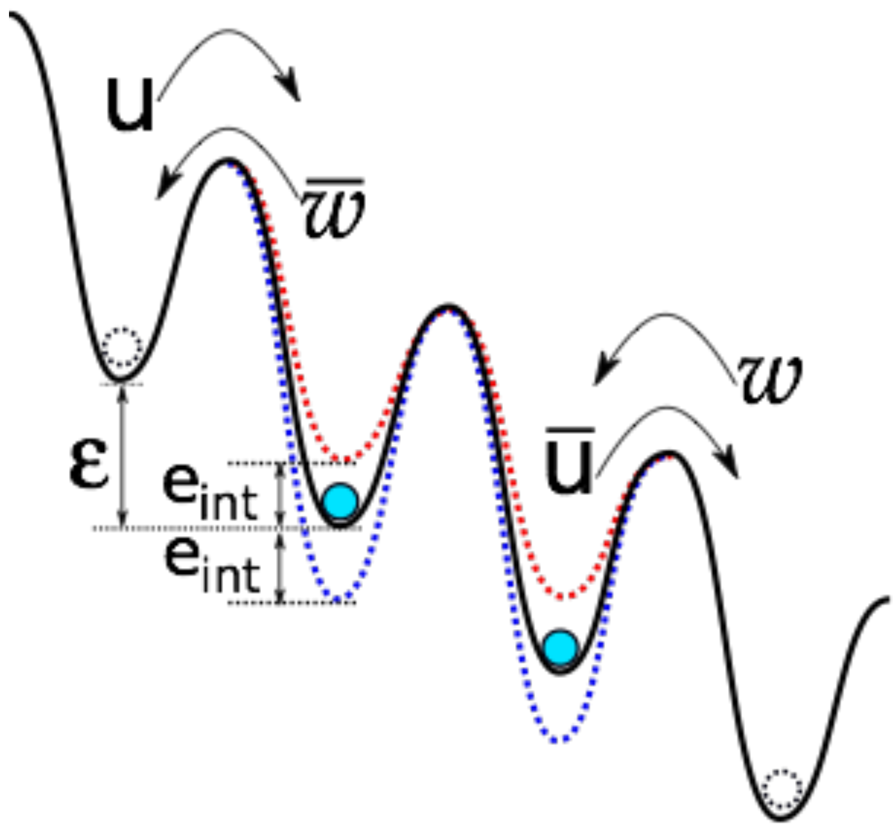


$$u.\bar{u}.w.w = \bar{w}.u.u.w$$

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

Biased random walk model for many motors

Using energy landscape



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

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

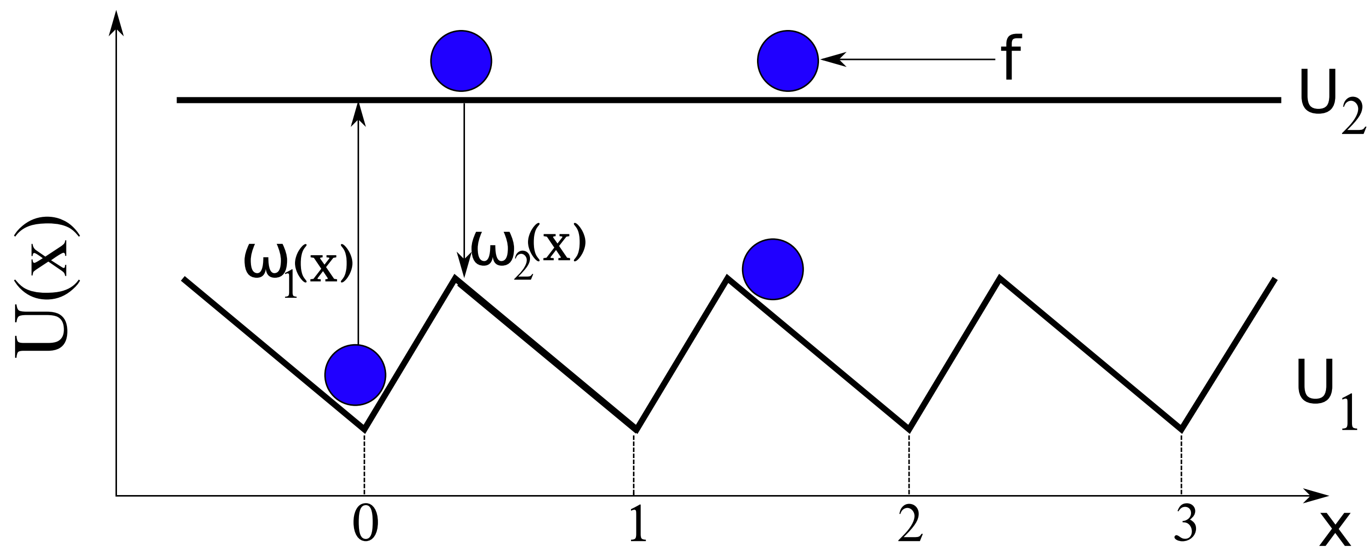
Without any interaction

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

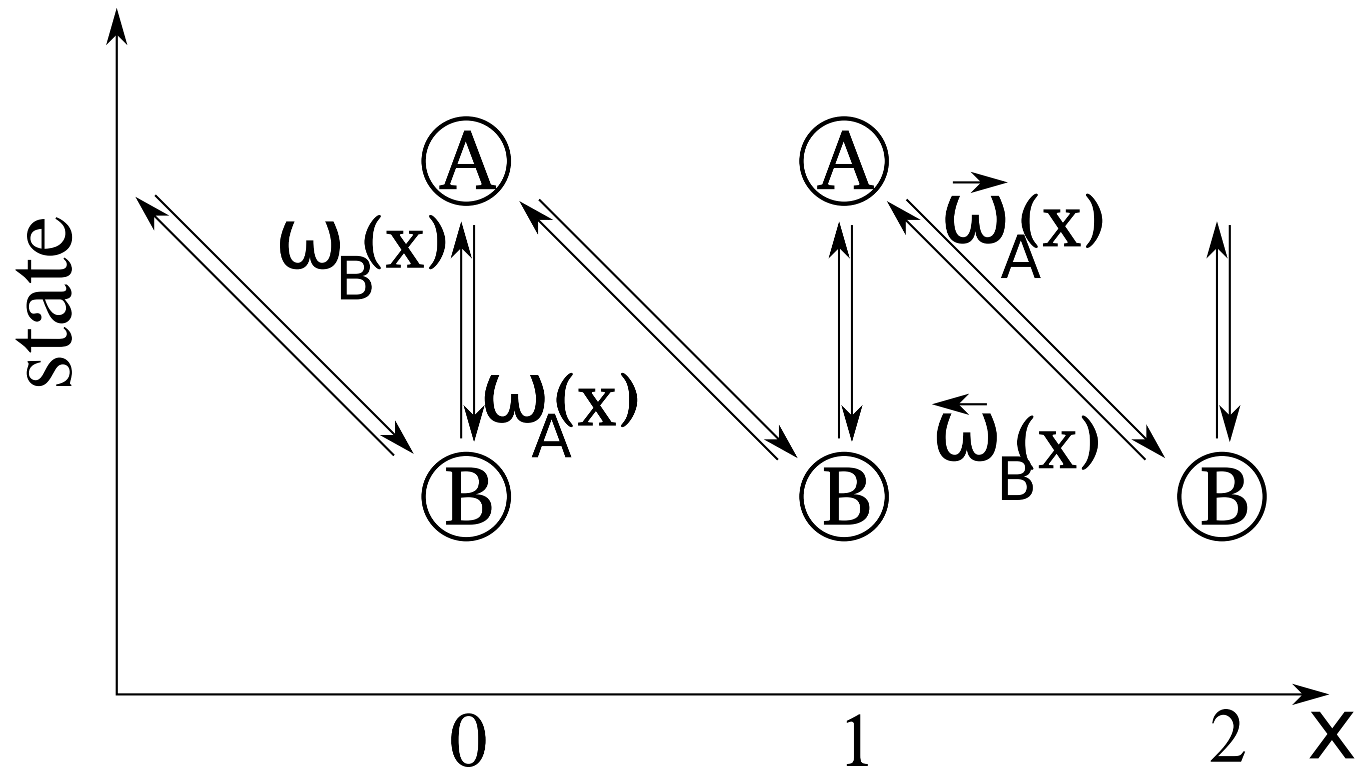
rearranging equations

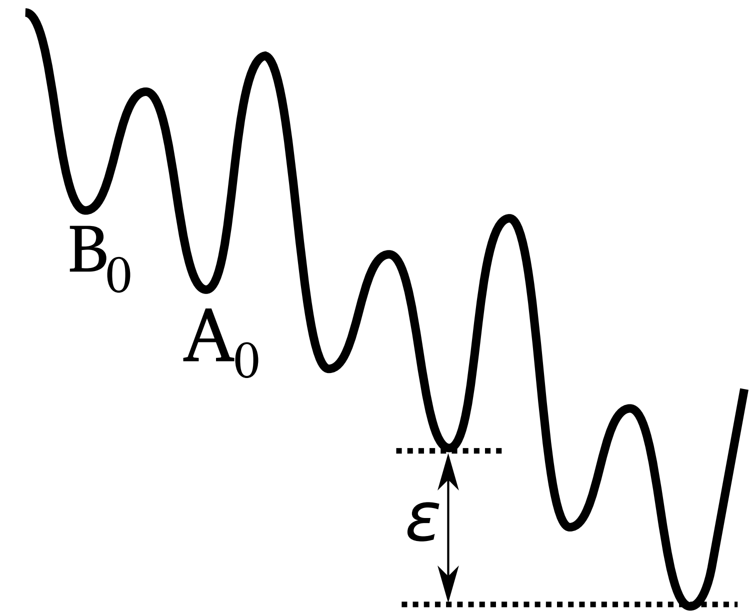
$$\frac{u}{w} = \frac{\bar{u}}{\bar{w}}$$

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

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.

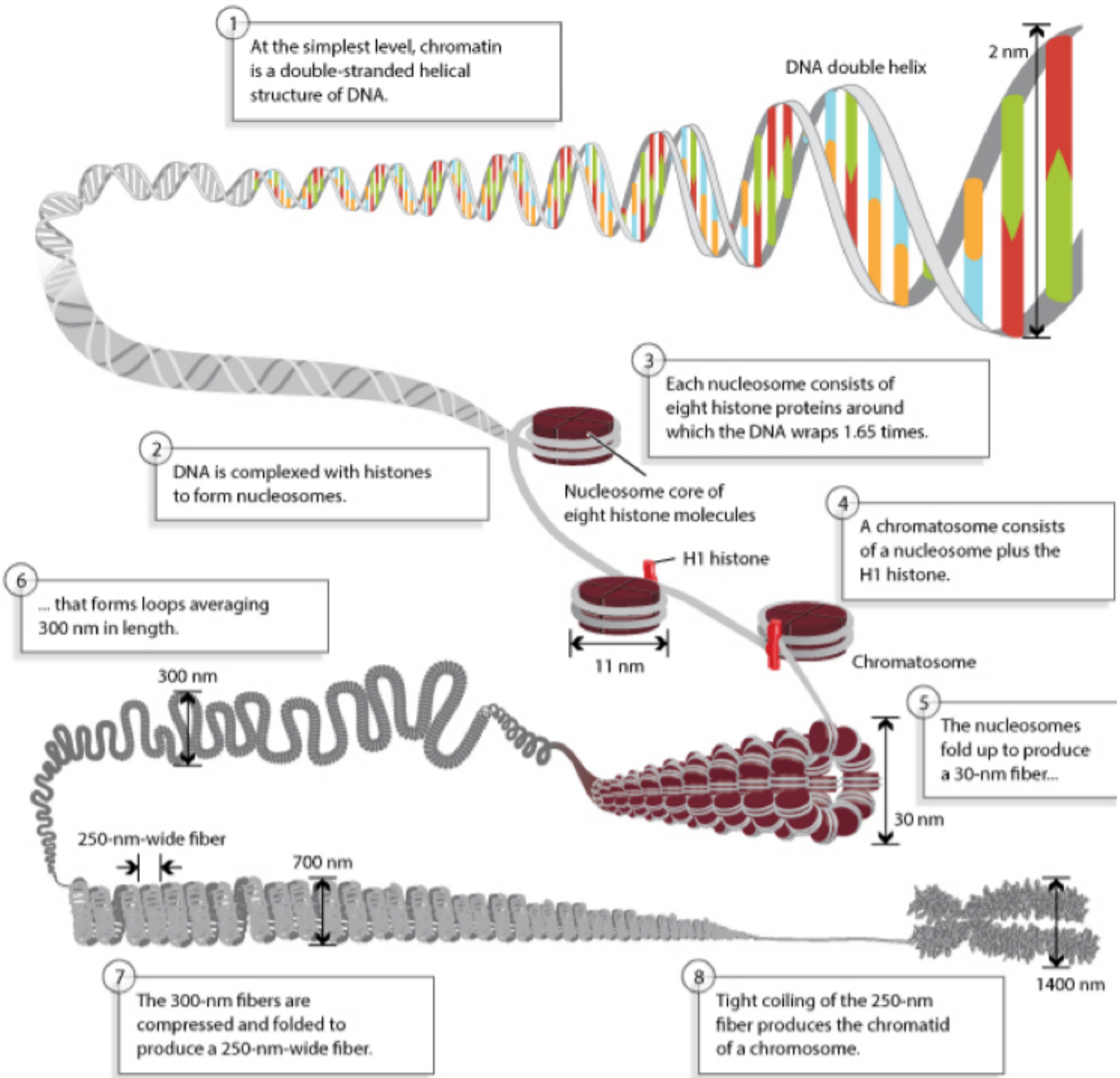
- Lack of detailed balance almost always result in non-additivity of stall forces.

- 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

Mother-daughter information transfer through the coupling of replication fork movement and nucleosome dynamics



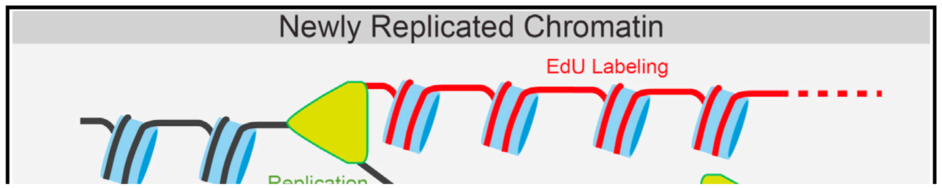
1
At the simplest level, chromatin is a double-stranded helical structure of DNA.
DNA double helix
2 nm
2
DNA is complexed with histones to form nucleosomes.
3
Each nucleosome consists of eight histone proteins around which the DNA wraps 1.65 times.
Nucleosome core of eight histone molecules
H1 histone
4
A chromatosome consists of a nucleosome plus the H1 histone.
11 nm
Chromatosome
6
... that forms loops averaging 300 nm in length.
300 nm
5
The nucleosomes fold up to produce a 30-nm fiber...
30 nm
250-nm-wide fiber
700 nm
1400 nm
7
The 300-nm fibers are compressed and folded to produce a 250-nm-wide fiber.
8
Tight coiling of the 250-nm fiber produces the chromatid of a chromosome.

Article

Cell

Transcriptional Regulators Compete with Nucleosomes Post-replication

Graphical Abstract



Authors

Srinivas Ramachandran, Steven Henikoff

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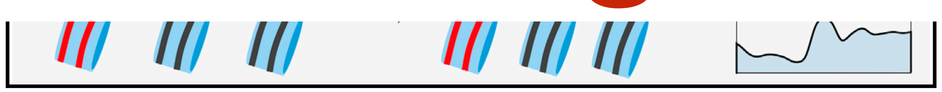
Nucleosome positioning inheritance after replication is absolutely necessary in certain gene



Highlights

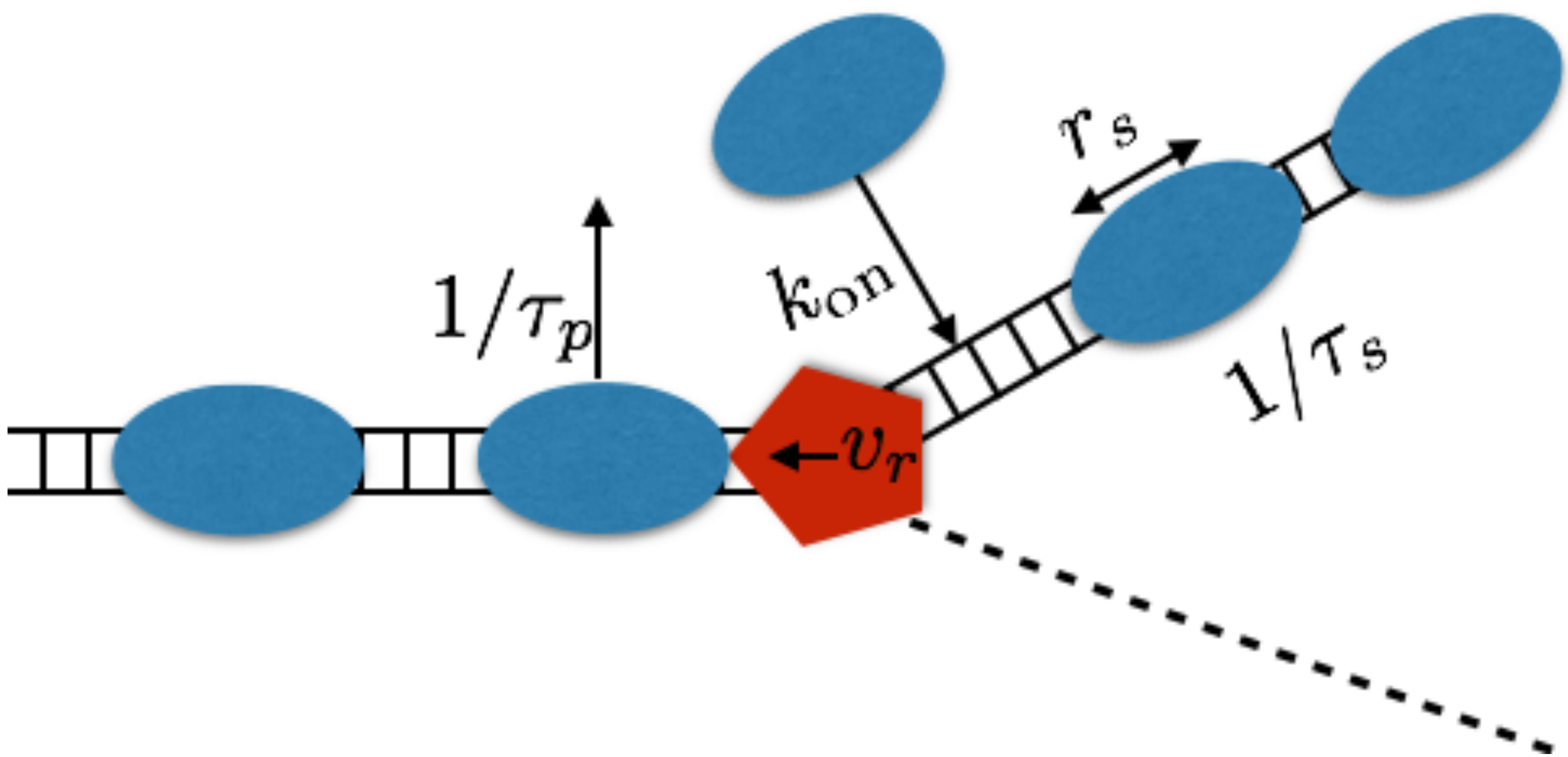
- MINCE-seq maps the nascent chromatin landscape within minutes of replication
- Nucleosomes replace transcription factors at active sites post-replication
- Nucleosome positions are conserved at inactive sites behind the replication fork
- Nucleosome gains correlate with the local abundance of transcriptional activators

Accession Numbers

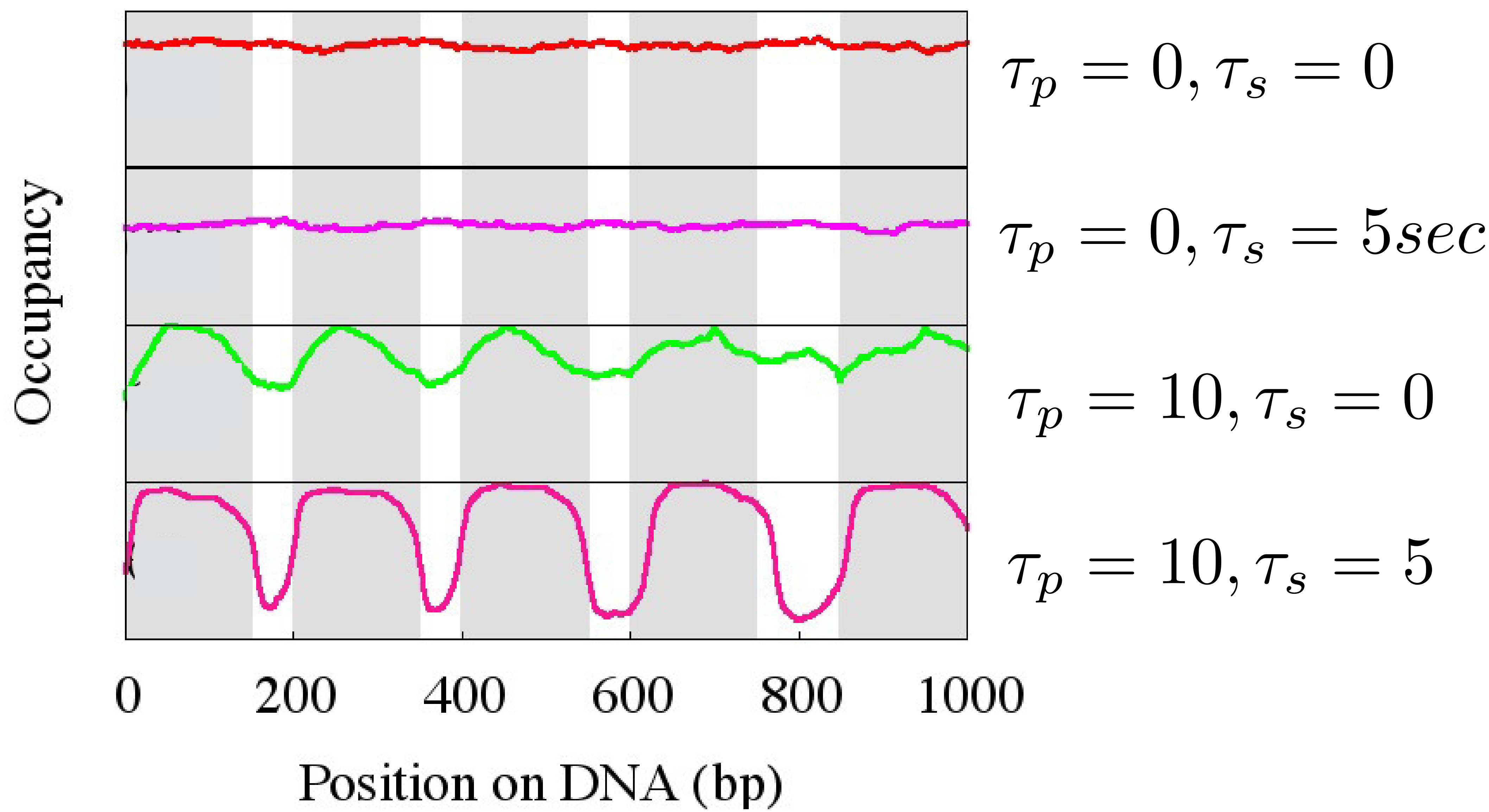
GSE76120

Is there any physical phenomenon that will help information about nucleosome positioning to be transferred from mother to daughter?

Model

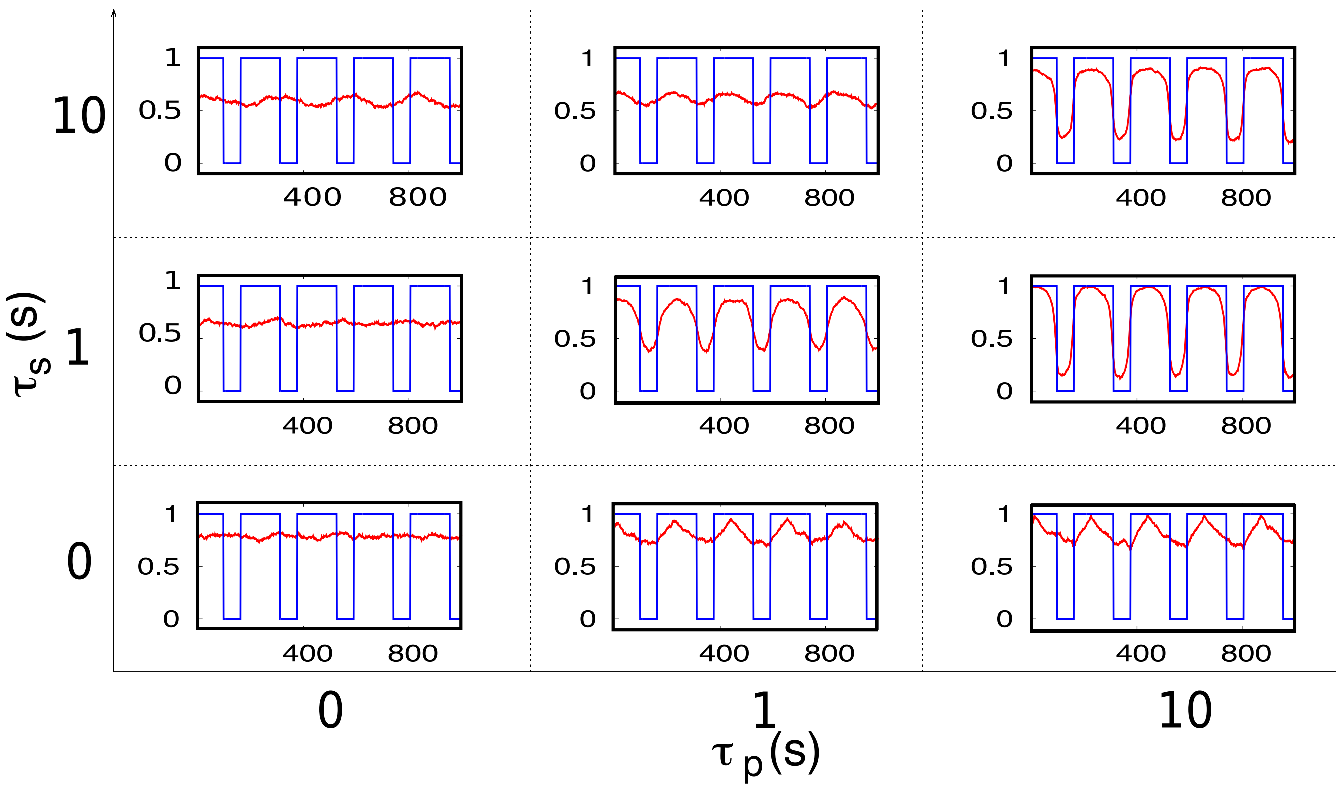


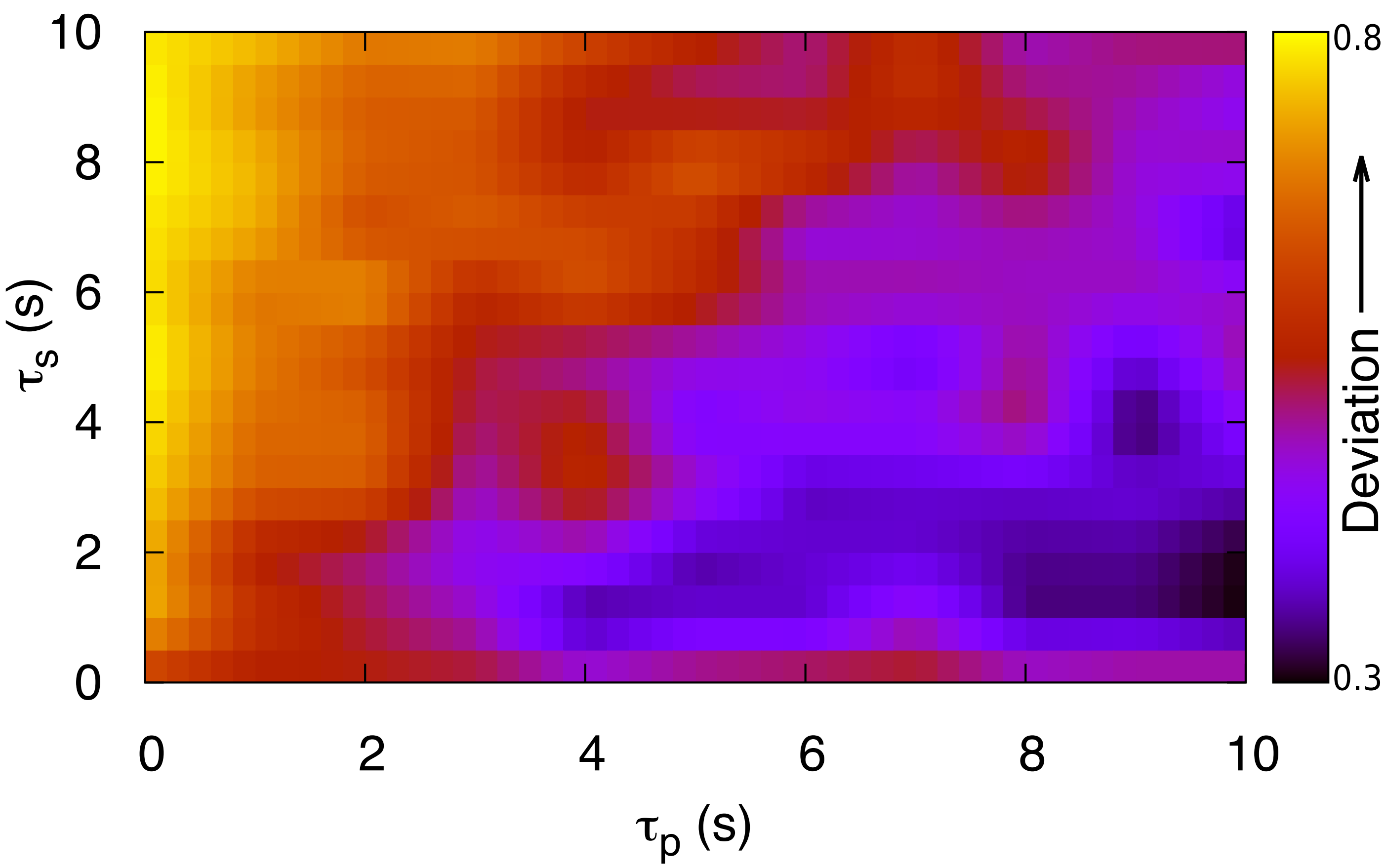
Results



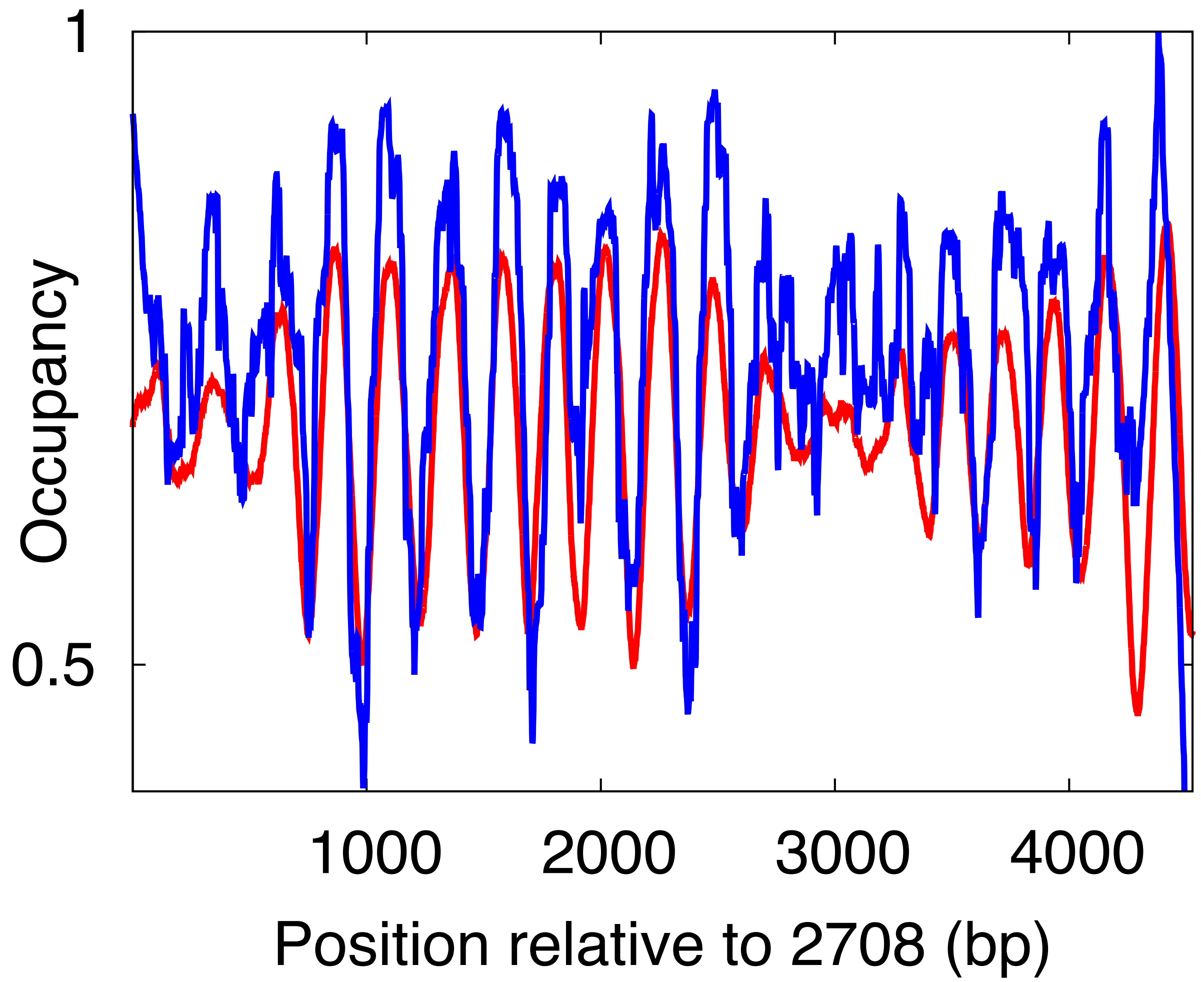
Occupancy
$\tau_p = 0, \tau_s = 0$
$\tau_p = 0, \tau_s = 5sec$
$\tau_p = 10, \tau_s = 0$
$\tau_p = 10, \tau_s = 5$
0
200
400
600
800
1000
Position on DNA (bp)

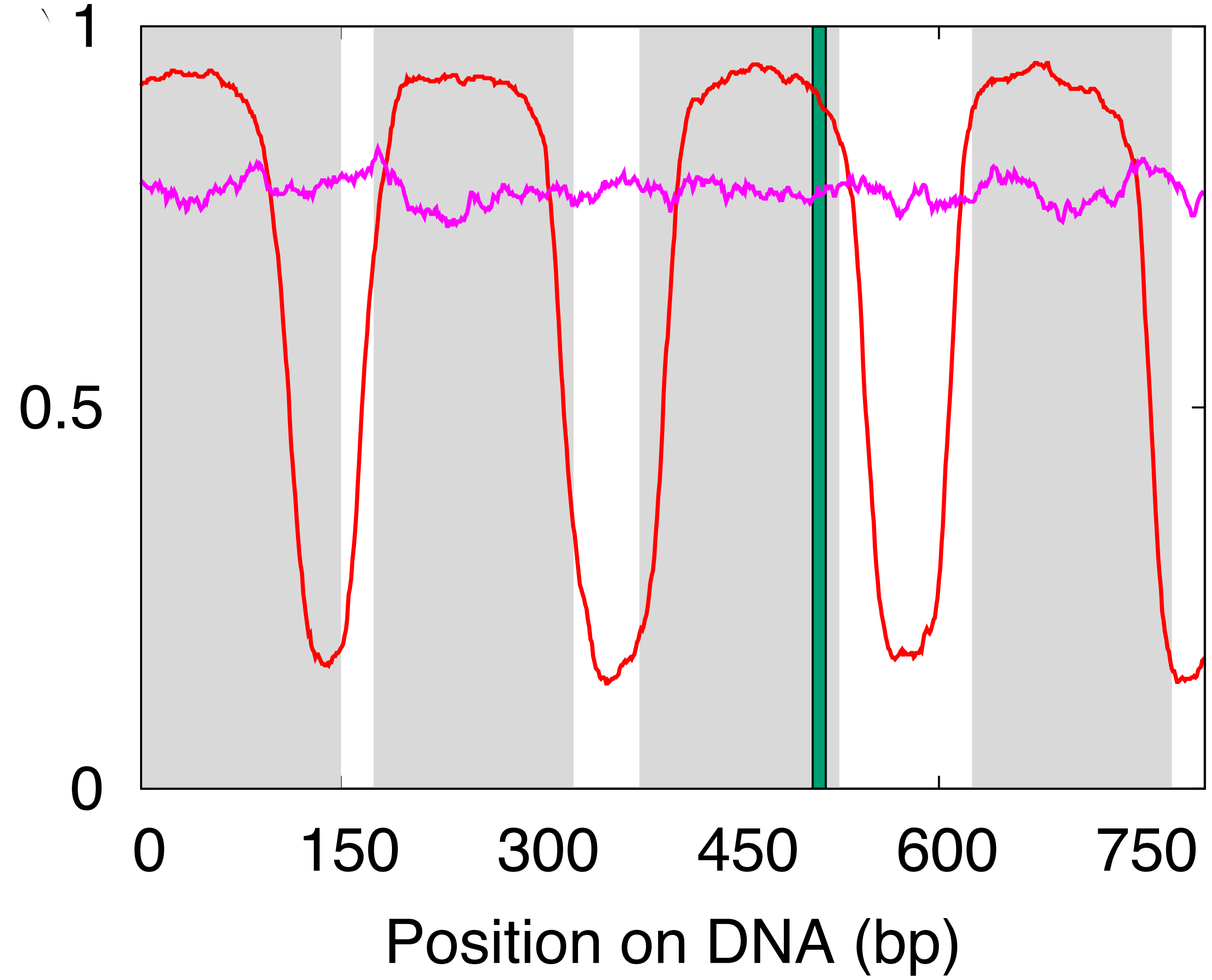
Deviation



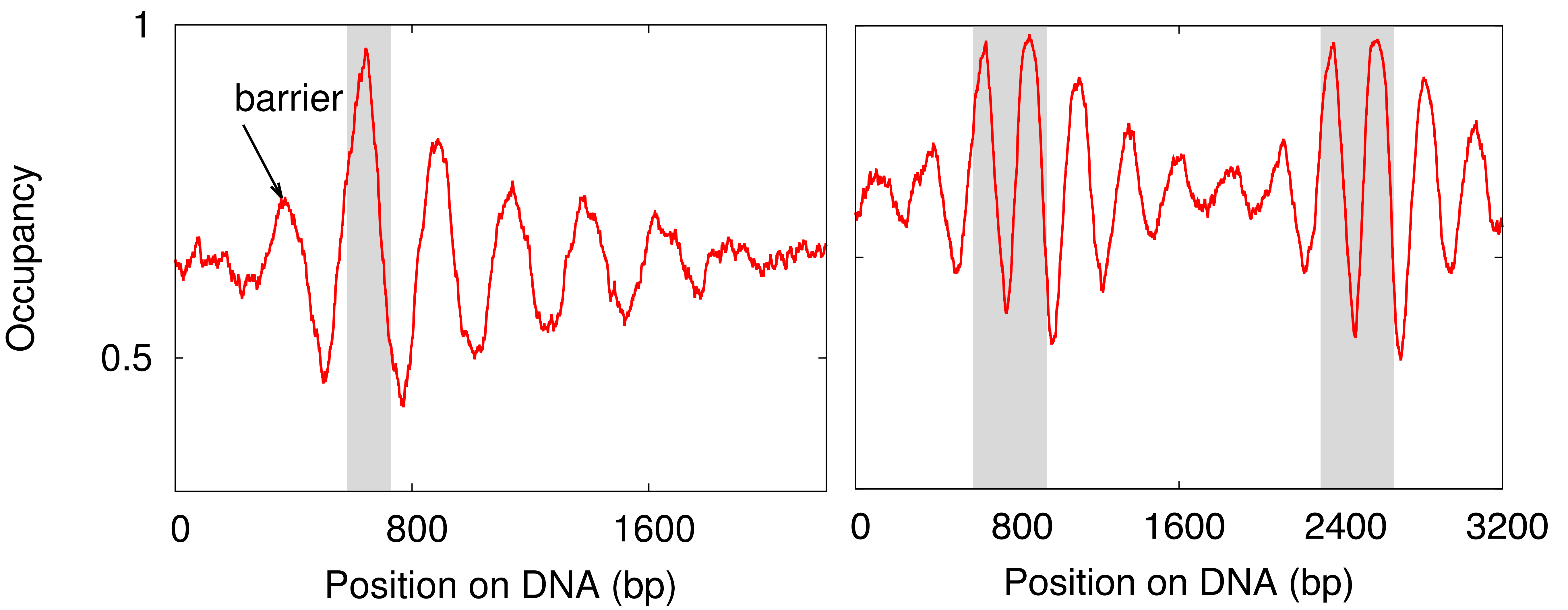


$$\chi = \sqrt{\frac{1}{L}\sum_{i=1}^{L}(m_i - d_i)^2}$$





Heterogeneous nucleosome organization inherited in daughter



Strongly positioned mother nucleosome gives strongly positioned daughter nucleosome

Summery

- First step towards theoretically understanding of a possible mechanism for nucleosome positioning transfer.
- Nucleosome positioning inheritance at “inactive” gene region can be produced.
- It is necessary to consider that not all the nucleosomes are well positioned and fork does not pause at all nucleosome site.
- Our results do not imply that, with pausing, the inheritance is perfect. There is some finite amount of deviation which requires further modification specially in active genes .