

How can a nucleosome motor measure DNA length?



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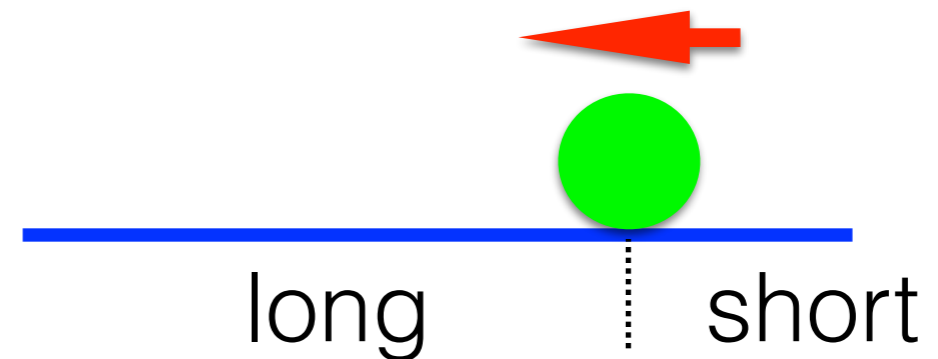
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acknowledgment



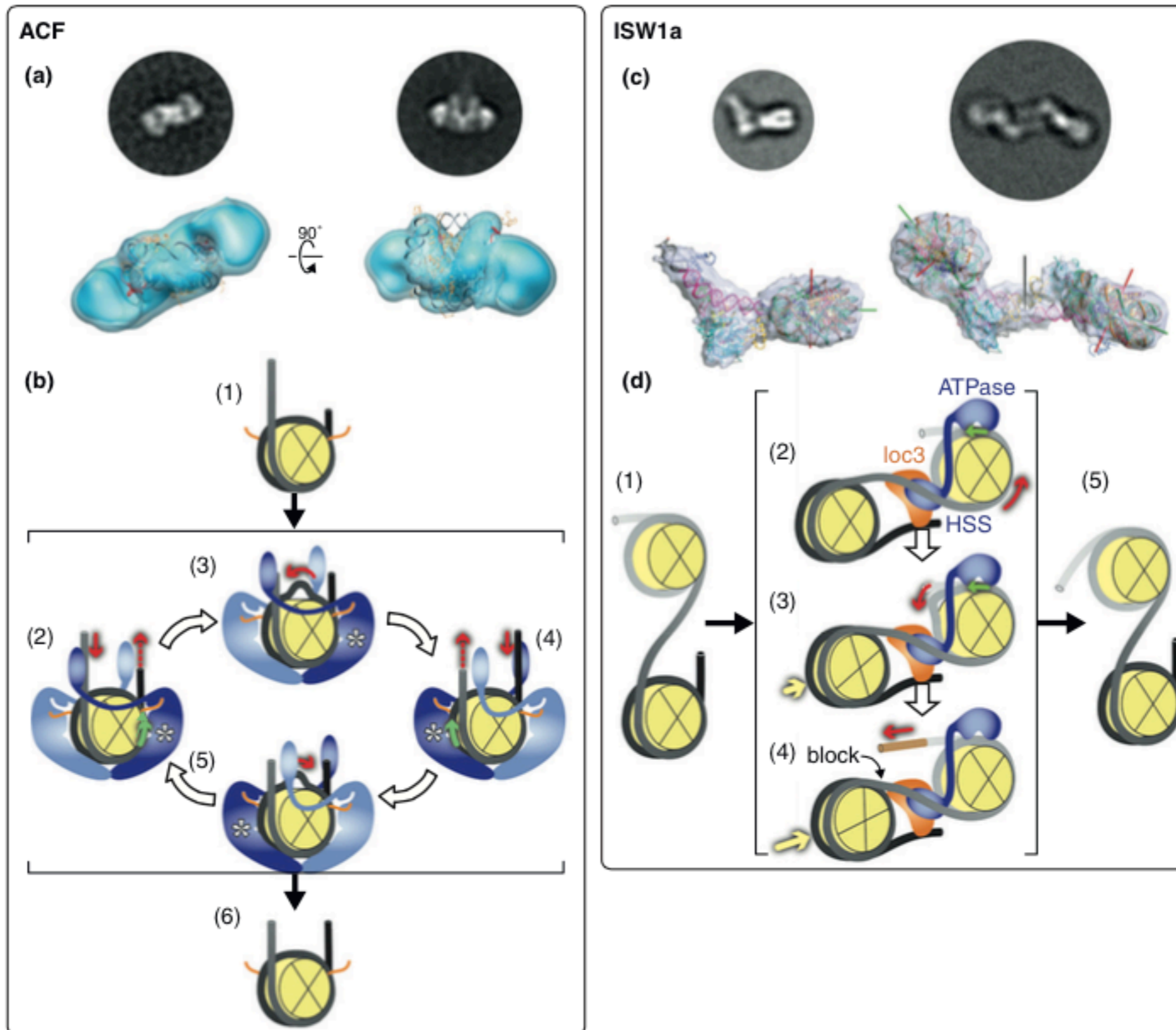
For discussion and support of this work, we thank Frank Jülicher and Max Planck Institute for Physics of Complex Systems, where the major part of this work was done.

the question



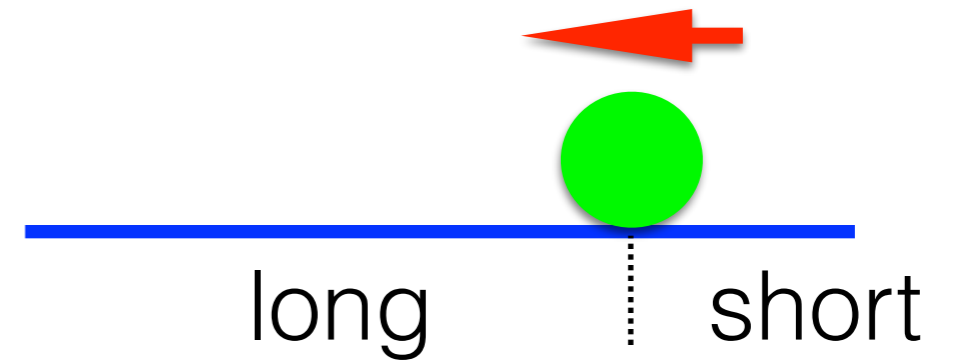
- A class of chromatin remodeling motors **translocates** the nucleosome **to the center** of DNA strand.
- How does it **sense** the **DNA length**?

ACF and ISW1a

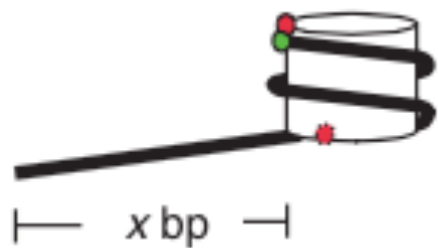


in vitro experiment

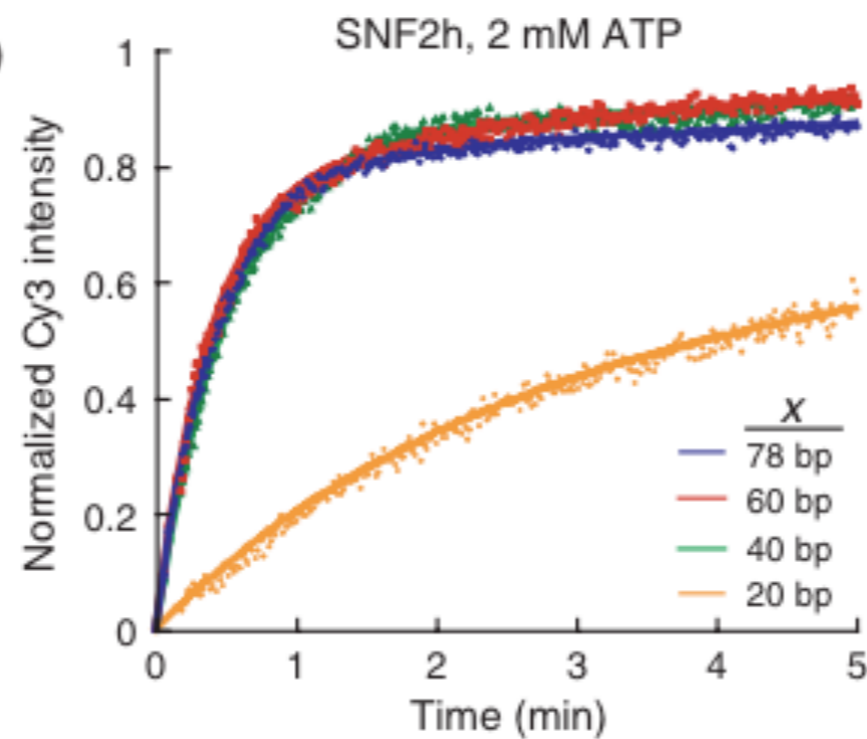
unquenching



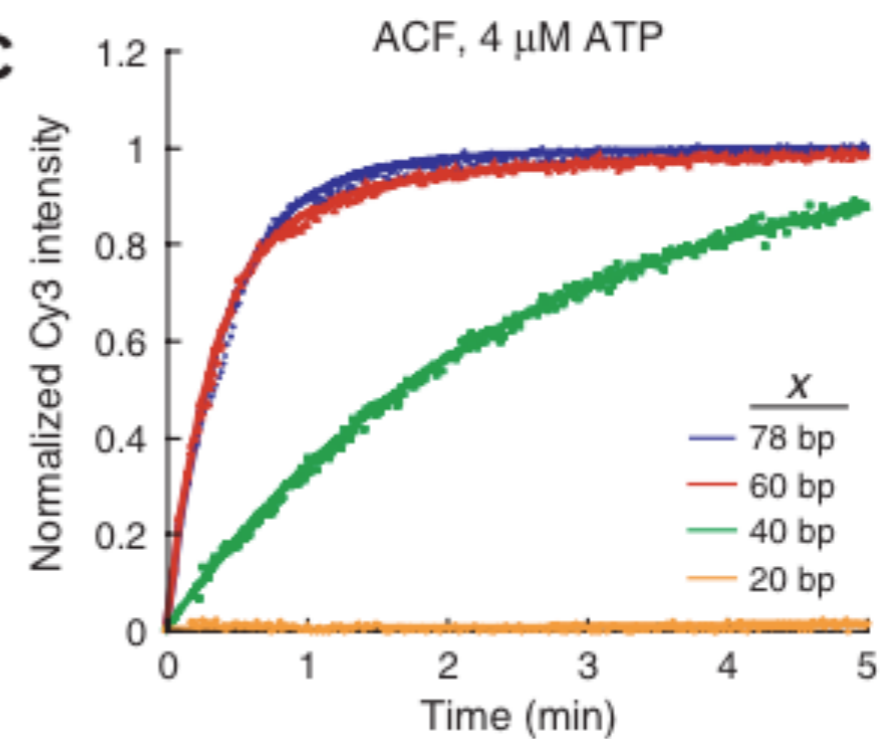
a



b

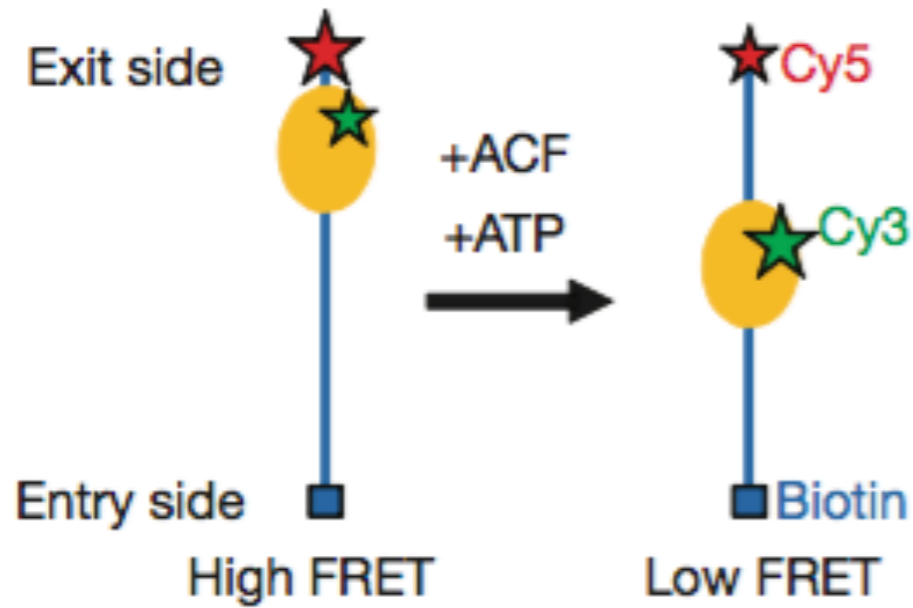


c

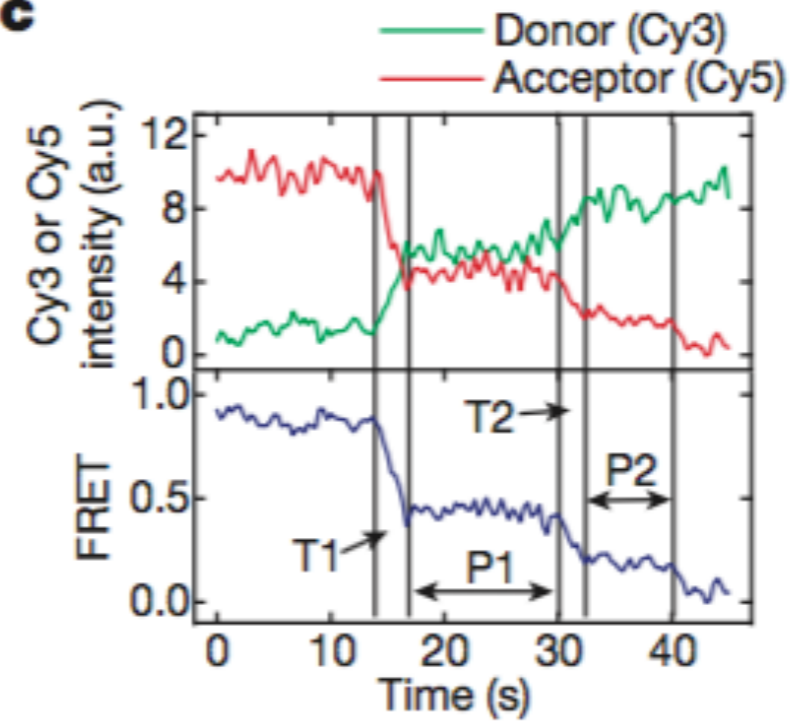


unit steps

a

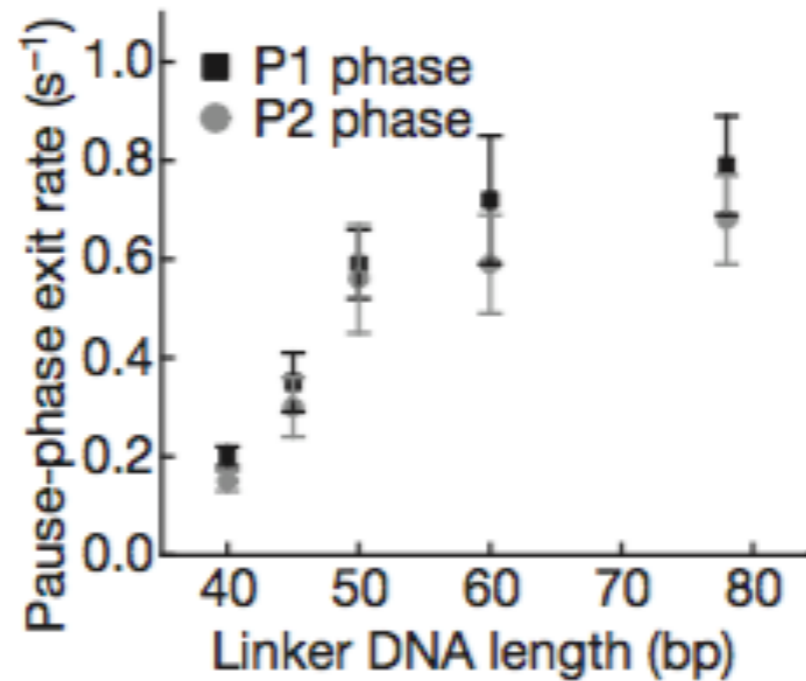
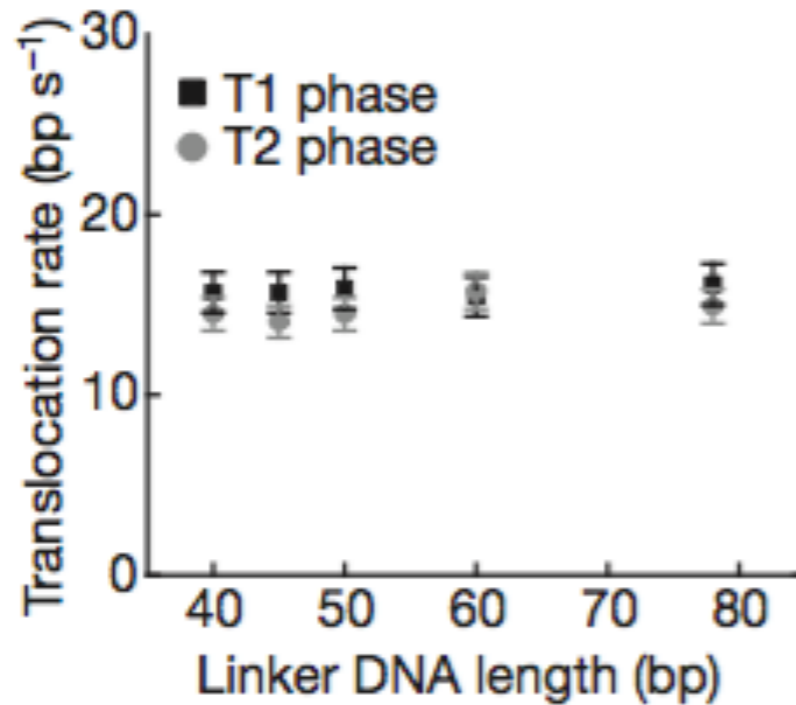


c



....

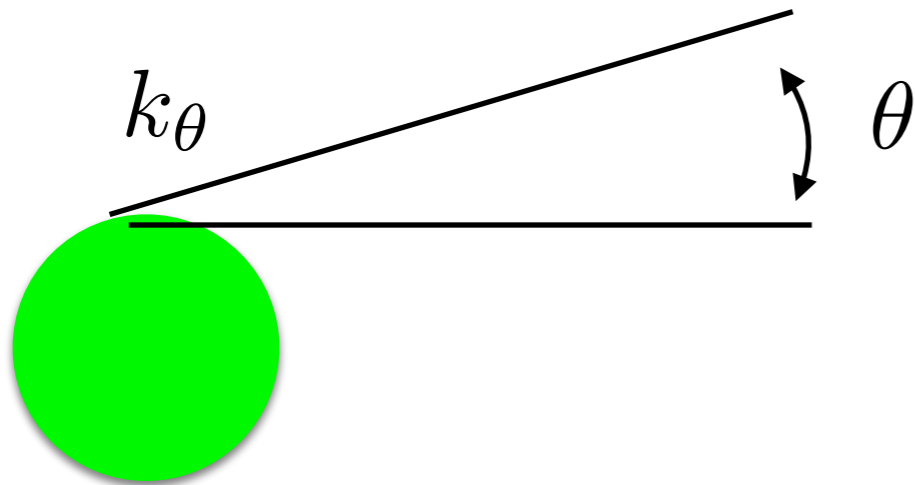
d



the assumptions

- The rate limiting step is DNA (un)binding, which depends on **fluctuation of DNA**.
- interaction between the motor and the chain can be described by **discrete steps**.
- the motor dimers have cooperative interaction between them

dominant mode of chain fluctuation



“breathing”* * Li, Bustamante, Widom 2000

approximated by a hinge.

angular fluctuation

**the spring that holds DNA determines
the amplitude of fluctuation in angle**

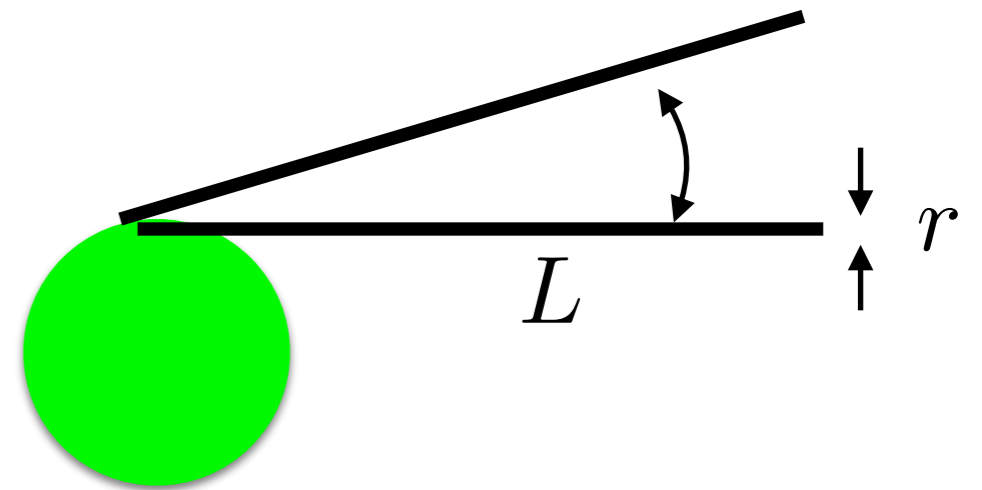
$$\frac{1}{2}k_\theta \langle \Delta\theta^2 \rangle \sim k_B T$$

length-independent

viscous drag on chain rotation

Rotational diffusion coefficient D_r is give by,*

$$\frac{\pi\eta L^3 D_r}{3k_B T} = \ln \frac{L}{2r} + \delta$$
$$\delta \approx -0.7 + \mathcal{O}\left(\frac{2r}{L}\right)$$



The Einstein relationship leads to the friction coefficient ζ_r ,

$$\zeta_r \approx \frac{\pi\eta L^3}{3} \frac{1}{\ln(L/2r) - 0.7}$$

* Tirado et al. 1984

rotational diffusion of nucleosome?

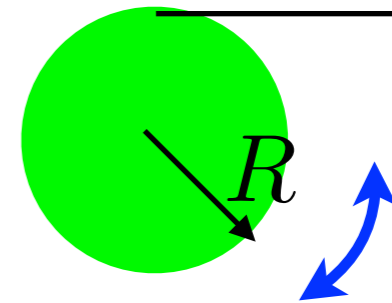
Approximate the nucleosome with a sphere,

L

$$\zeta_n = 8\pi\eta R^3$$

and

$$\frac{\zeta_n}{\zeta_r} = 24 \left(\frac{R}{L} \right)^3 \cdot [\ln(L/2r) - 0.7]$$



The mass of 1 MD leads to $R \approx 8$ nm. If $L=40$ nm,

$$\frac{\zeta_n}{\zeta_r} \sim 0.3$$

However, this is an underestimation of ζ_n because nucleosome is elongated in the direction it holds DNA.

fluctuation spectrum

Consider pivoting motion.

$$\zeta \frac{dy(t)}{dt} = -k y(t) + F(t)$$

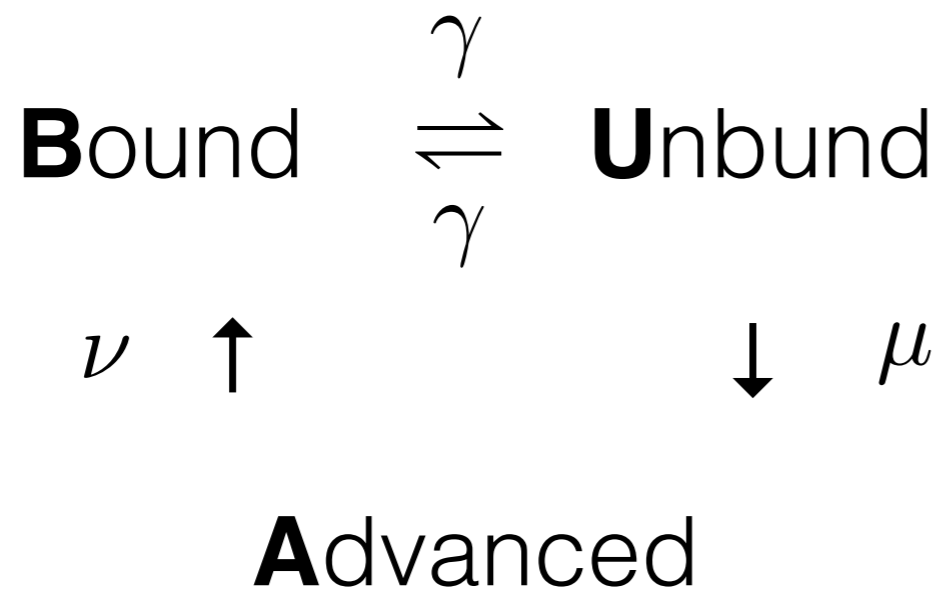
If random noise $F(t)$ is 'white,'

$$S_y(\omega) = \frac{2k_B T}{\zeta} \cdot \frac{1}{(k/\zeta)^2 + \omega^2}$$

with

$$\zeta_r \approx \frac{\pi \eta L^3}{3} \frac{1}{\ln(L/2r) - 0.7}$$

the model



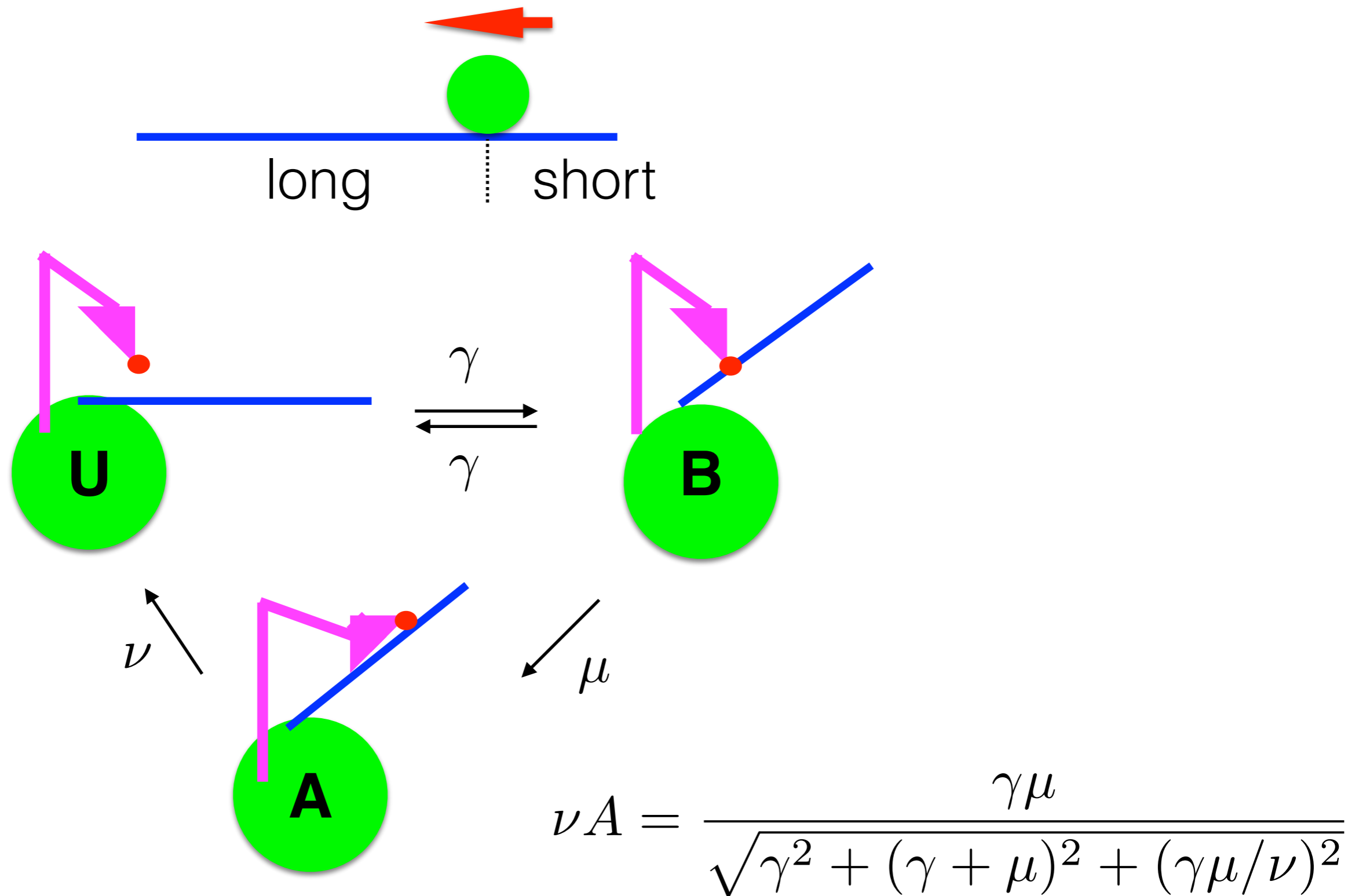
eigenvector

$$\begin{pmatrix} B \\ U \\ A \end{pmatrix} = \begin{pmatrix} \gamma + \mu \\ \gamma \\ \gamma\mu/\nu \end{pmatrix}$$

rotation rate of the motor:

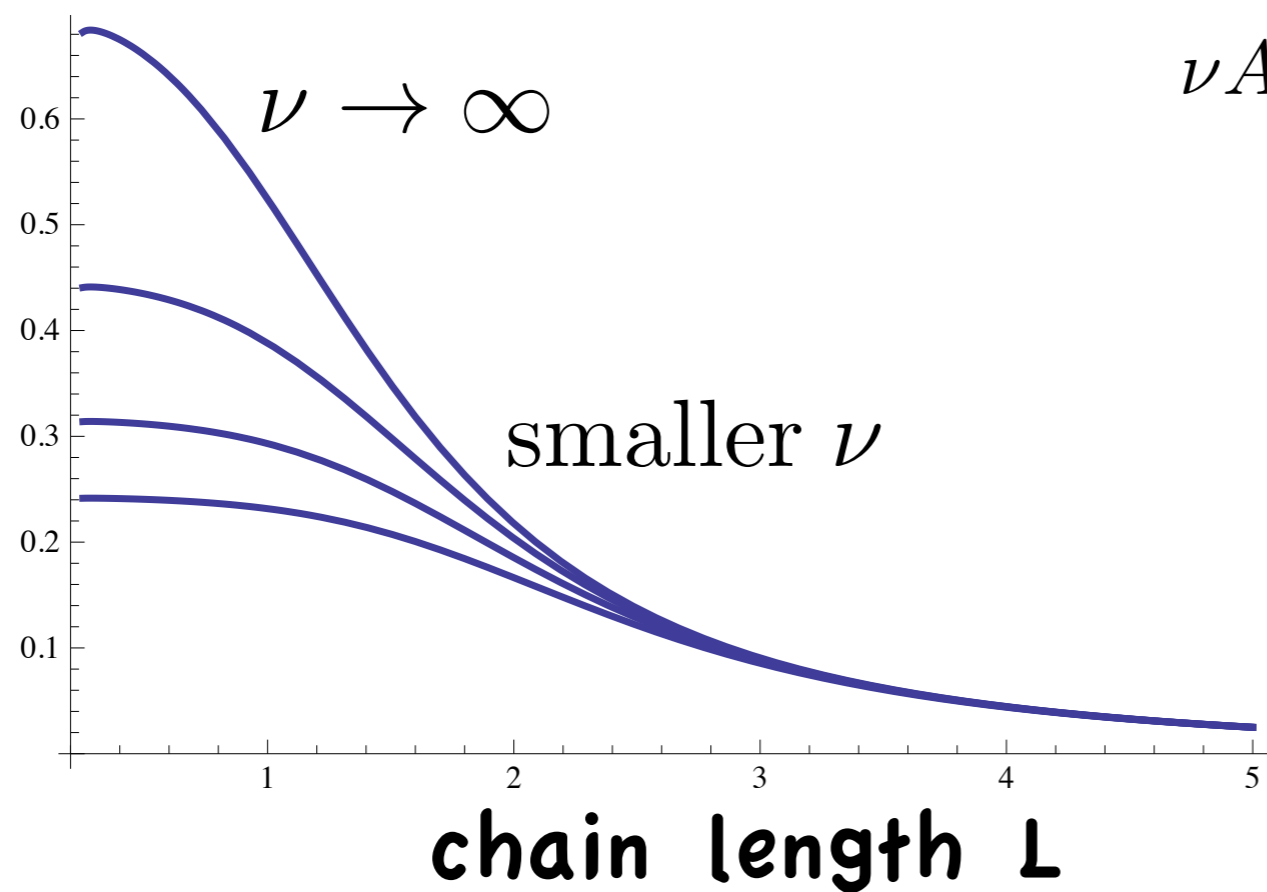
$$\nu A = \frac{\gamma\mu}{\sqrt{\gamma^2 + (\gamma + \mu)^2 + (\gamma\mu/\nu)^2}}$$

alternative assignment



length dependence of tugging

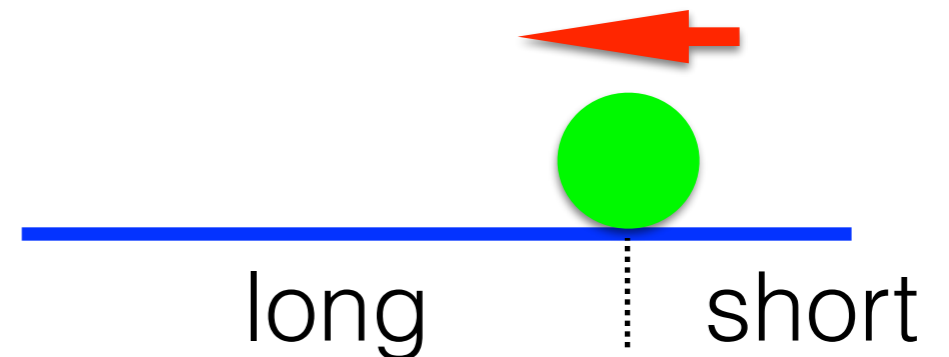
speed



$$\begin{cases} \mu = 1 \\ r = 0.1 \end{cases}$$

$$\nu A = \frac{\gamma \mu}{\sqrt{\gamma^2 + (\gamma + \mu)^2 + (\gamma \mu / \nu)^2}}$$

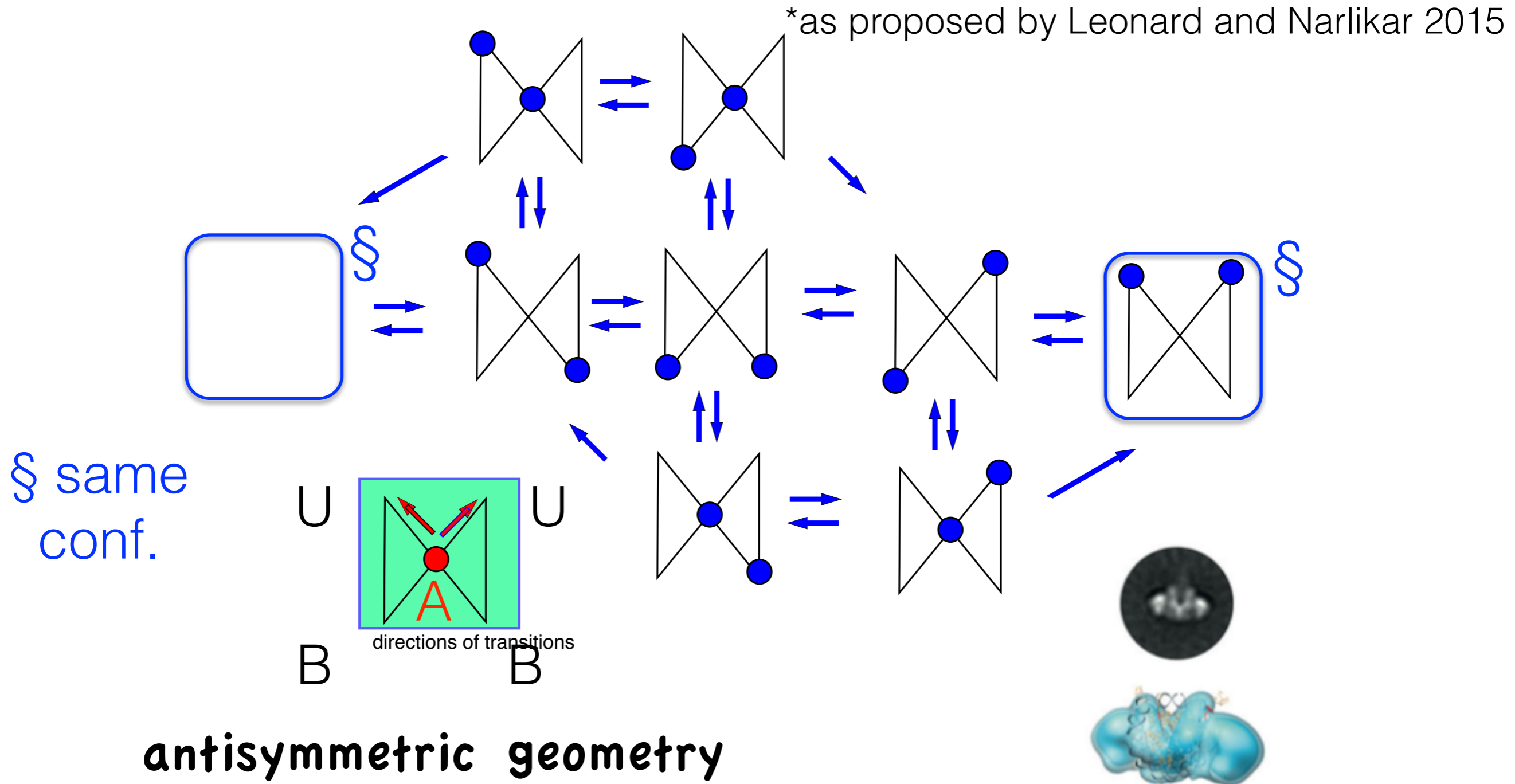
$$\gamma \sim (\ln(L/2r) - 0.7) / L^3$$



role of dimerization

the two subunits share a binding site
to avoid wasting energy*

*as proposed by Leonard and Narlikar 2015



is a protein arm stiffer than DNA?

assumed as if it is... is that true?

DNA does not have to be more flexible if:

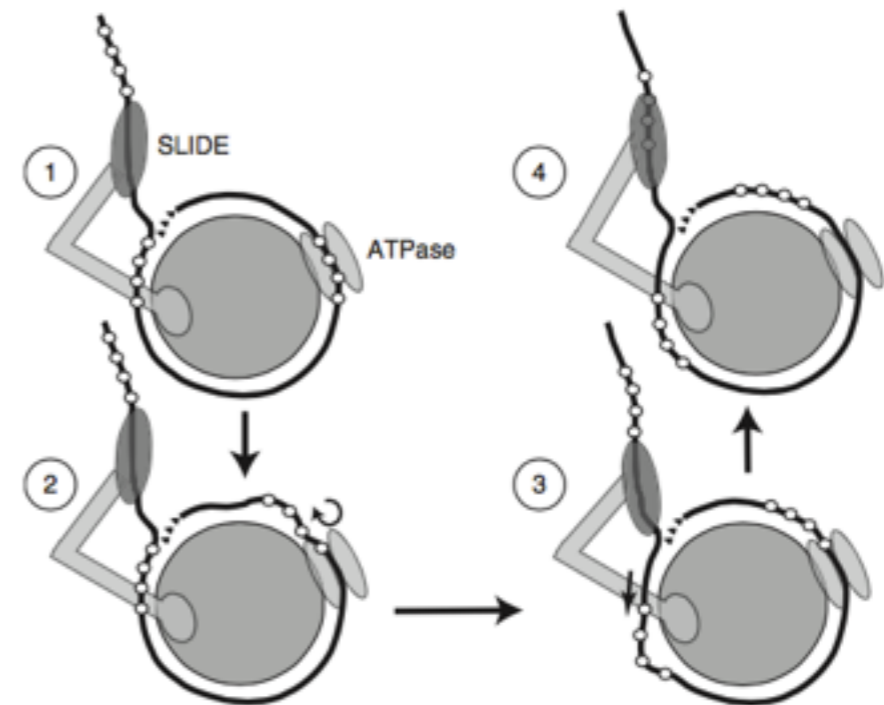
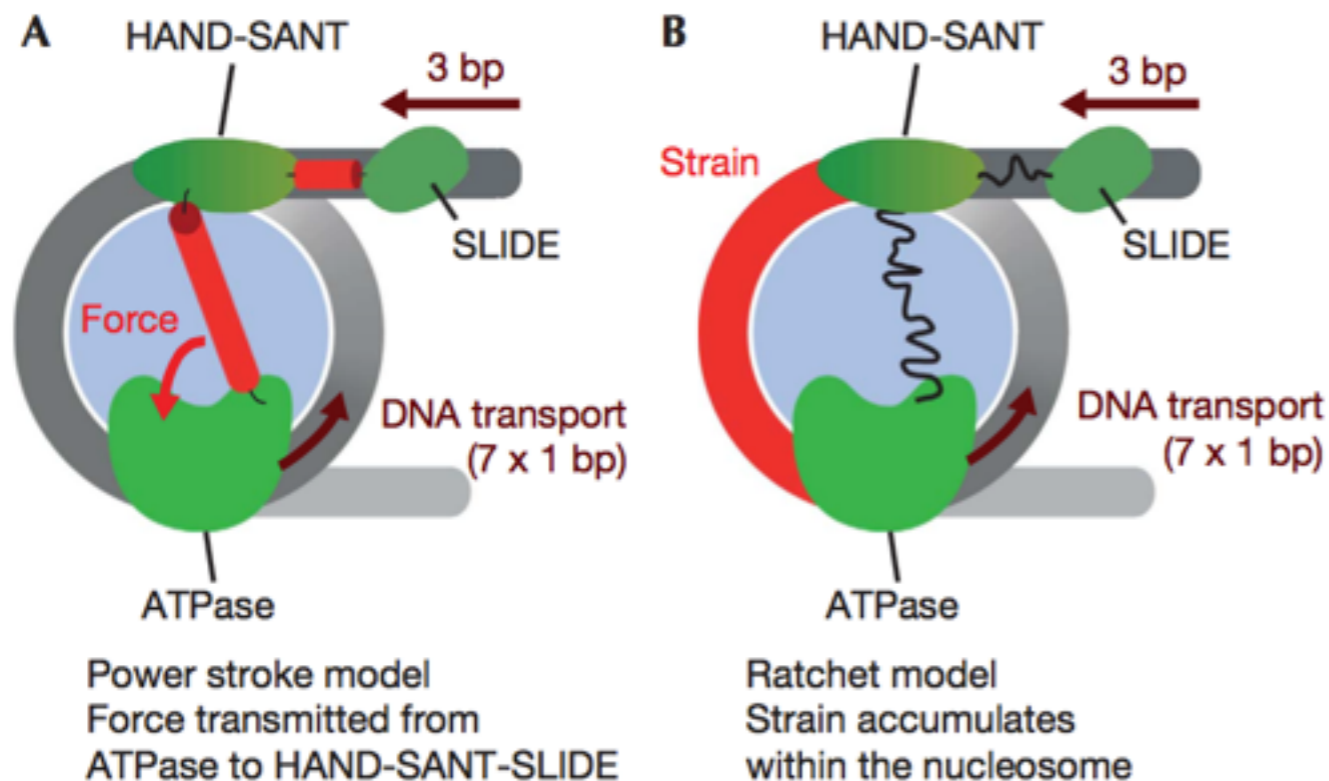
- the arm is shorter than saturation length
- its distribution is asymmetric with respect to DNA

sliding mechanism?

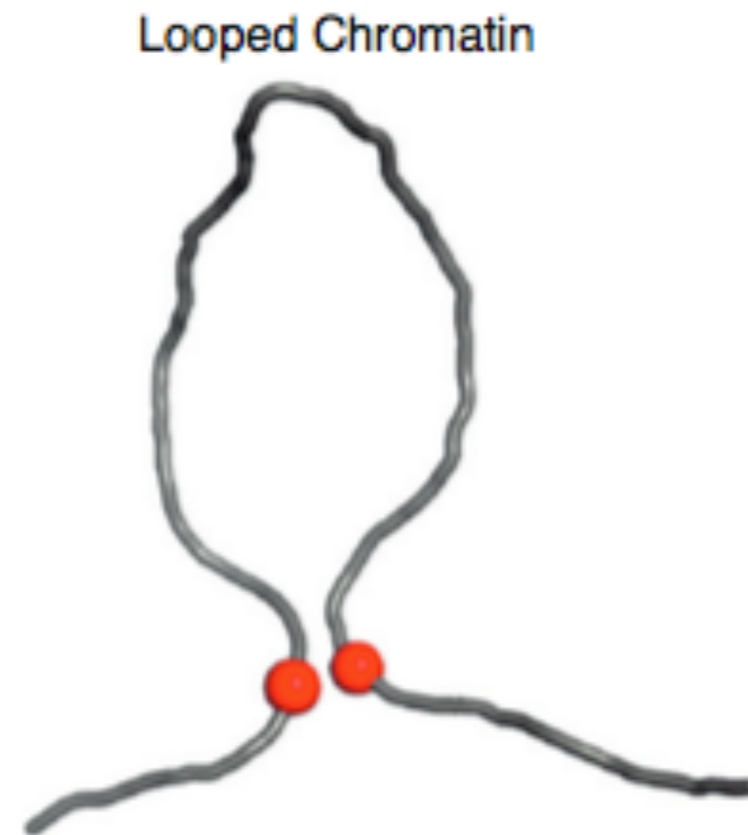
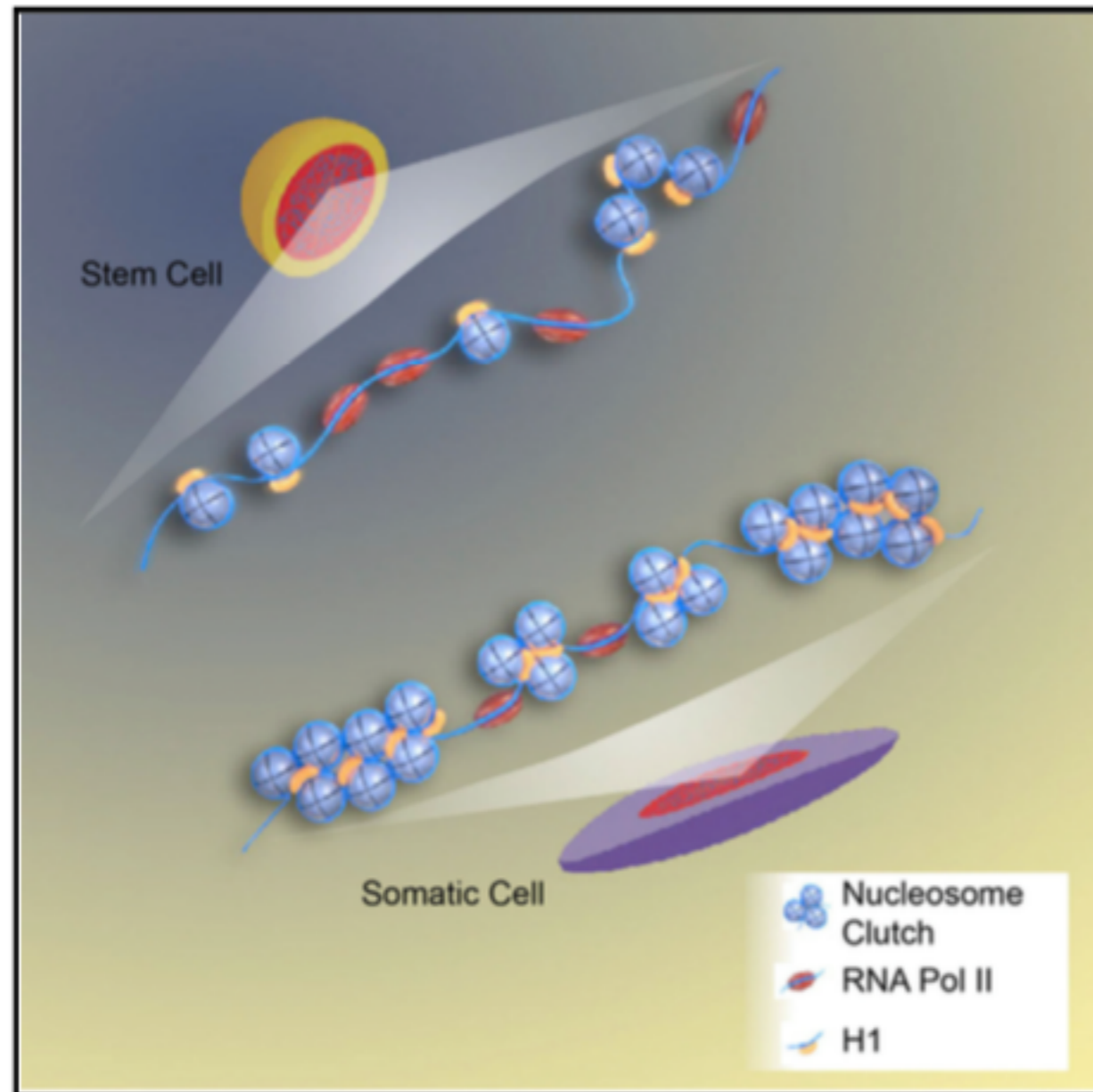
sliding mechanism is not addressed here.

addressed is how sliding is initiated.

compatible with various sliding mechanisms, e.g.



in vivo relevance ?



Ricci et al., 2015, Cell 160, 1145–1158

Fudenberg & Mirny 2012

conclusions

- A model for **sensing the length of DNA** strand is proposed.
- **Chain fluctuation** can serve as a sensing mechanism for ACF.
- Details need to be worked out for a more quantitative description.

Gràcies!