A Biological mechanism that utilizes intrinsic curvature of filaments.

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Acknowledgement: Prof. Dulal Panda (Bio-school, IIT Bombay)

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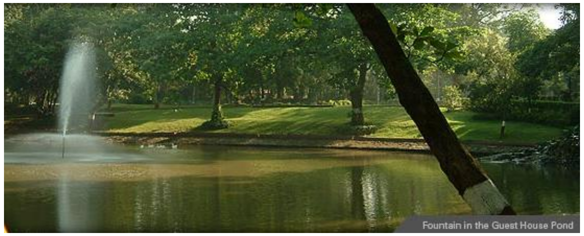


Outline

- Curved filaments

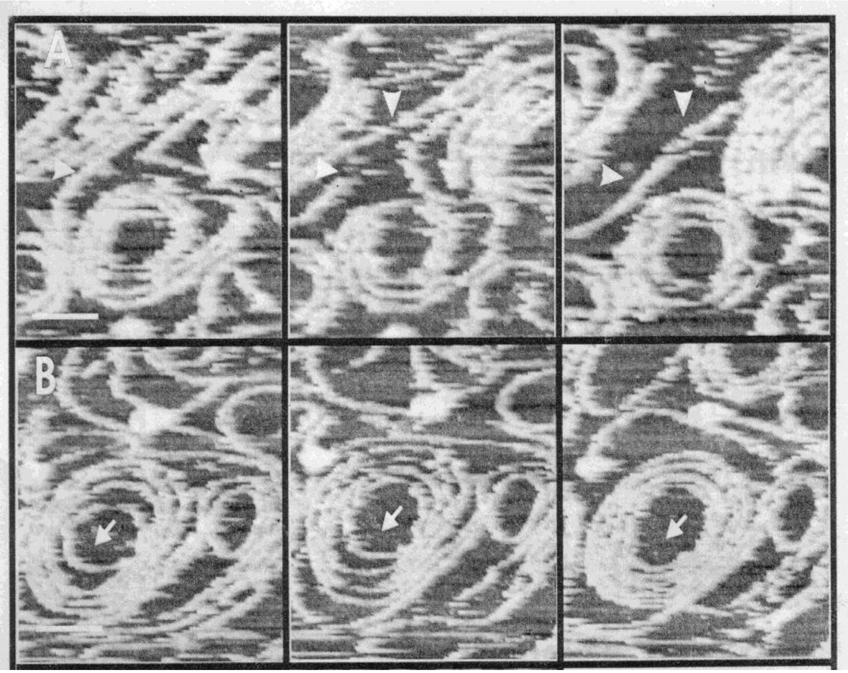
- Their Conformational properties

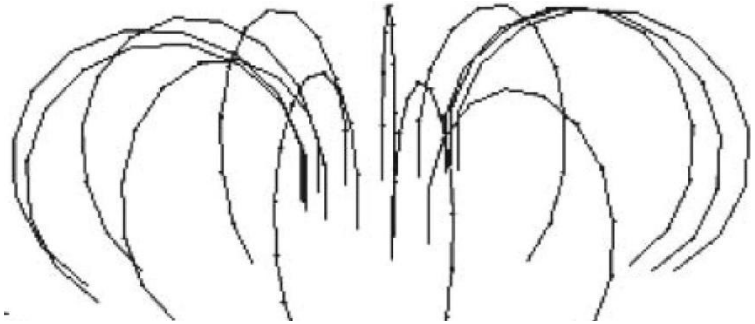
- Curved filaments in action:

  A mechanism for bacterial cell division.

Polymers with Intrinsic curvature

FtSz filaments (AFM Image)





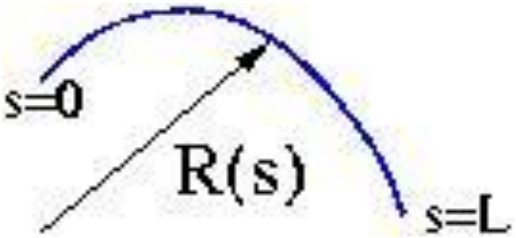
Tubulin filaments

Mingorance et al., J. Biol.Chem.(2005)

Filaments with Intrinsic curvature

Energy functional $H[\vec{R}(s)]$ for configuration $\vec{R}(s)$

$$\frac{H}{k_B T} = \frac{l_p}{2} \int_{s=0}^{L} [\kappa(s) - \tfrac{1}{R_o}]^2 ds$$

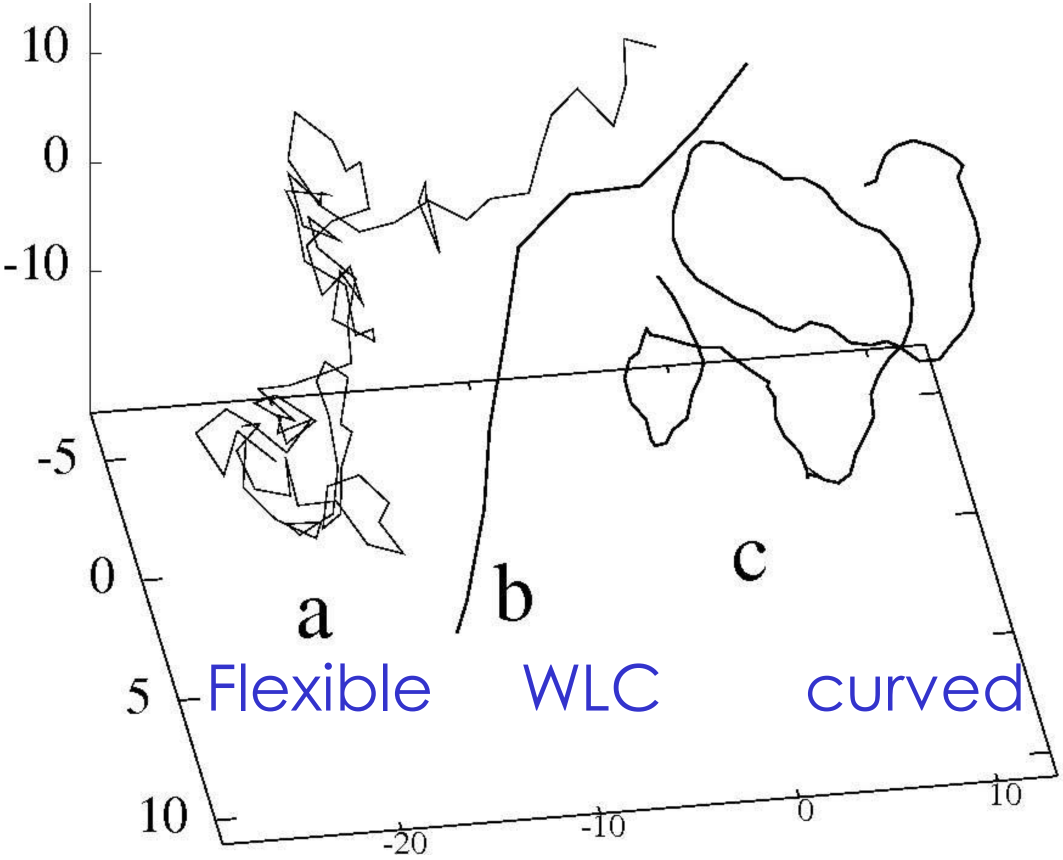


$\vec{\kappa}(s) = \frac{d^2\vec{R}(s)}{ds^2} = \frac{d\hat{t}(s)}{ds}$ = local curvature

$1/R_o$ = **Intrinsic curvature**

Shape of the polymer

(Monte-Carlo Simulation)



Flexible WLC curved

How to distinguish between a WLC and a curved polymer ?

Expect $$\langle \hat{t}(s).\hat{t}(s+r)\rangle \sim \cos(r/R_o)\exp(-r/\tilde{l}_p)$$

Dimensionless Ratios

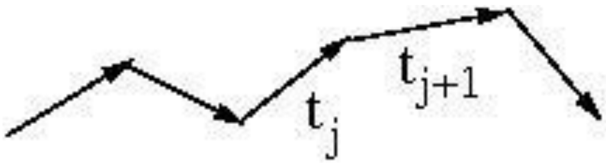
$$x = s/l_p$$

$$\frac{H}{k_B T} = \tfrac{1}{2} \int_{x=0}^{L/l_p} \left(\left| \frac{d\hat{t}(x)}{dx} \right| - \frac{l_p}{R_o} \right)^2 dx$$

Important parameters : l_p / L and l_p / R_o

Recall $$\vec{\kappa}(s) = \frac{d^2\vec{R}(s)}{ds^2} = \frac{d\hat{t}(s)}{ds}$$

Discretization



$$\frac{H}{k_B T} = \frac{1}{2}\sum_{i=1}^{N-1}\left(\frac{\left|\hat{t}_{i+1}-\hat{t}_i\right|}{\sqrt{\Delta}} - \frac{l_p\sqrt{\Delta}}{R_o}\right)^2$$

where $\Delta = \frac{L/l_p}{N}$

$$= \sum_{i=1}^{N-1}\left(\frac{\sqrt{1-\cos\theta_i}}{\sqrt{\Delta}} - \frac{l_p\sqrt{\Delta}}{\sqrt{2}R_o}\right)^2 = \sum_{i=1}^{N-1} h_i(\theta_i)$$

Depends on nearest neighbor angles only

↓

$$\boxed{\left\langle \hat{t}_i . \hat{t}_{i+k} \right\rangle = \left\langle \hat{t}_i . \hat{t}_{i+1} \right\rangle^k}$$

→ decays exponentially

$$\left\langle \hat{t}(s) . \hat{t}(s+r) \right\rangle = \exp(-r/\tilde{l}_p)$$

Effective persistence length

$$\tilde{l}_p = -\left(\tfrac{L}{N}\right) / \ln\left[\frac{\int d\Omega \cos\theta \, e^{-h(\theta)}}{\int d\Omega \, e^{-h(\theta)}}\right]$$

$\Downarrow$

$$\begin{aligned} & e^{-y^2}[2\sqrt{N}R_0(-L^2 l_p - 2LNR_0^2 + 2l_p N^2 R_0^2 + \exp\left[\tfrac{2l_p}{R_0}\right]^{-y_1^2}[L^2 l_p + 2l_p N^2 R_0^2 + 2LNR_0(l_p + R_0)]) \\ & \quad - e^{y^2}\sqrt{2\pi L l_p}(L^2 l_p + 3LNR_0^2 - 2l_p N^2 R_0^2)\{erf[y] - erf[y - y_1]\}]/[2l_p N^2 R_0^2(2\sqrt{N}R_0 e^{-y^2 - y_1^2}\{e^{y_1^2} - e^{\frac{2l_p}{R_0}}\} \\ & \quad + \sqrt{2\pi L l_p}\{erf[y] - erf[y - y_1]\})], \end{aligned}$$

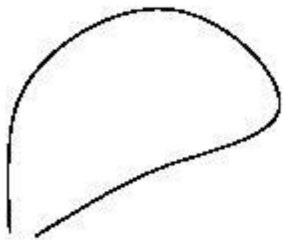
Continuum limit $(N \to \infty,\ \text{but L, R}_\text{o}\ \text{finite})$ $\tilde{l}_p \to l_p$

But short polymers (DNA) have finite unit length (bp).

So finite N is practically important.

Probability of loop formation

$$P_0 = \int_r P(r < a) \approx 4\pi a^3 P(\vec{r} = 0)$$



If loops are highly probable, then **P_o** vs **L** will

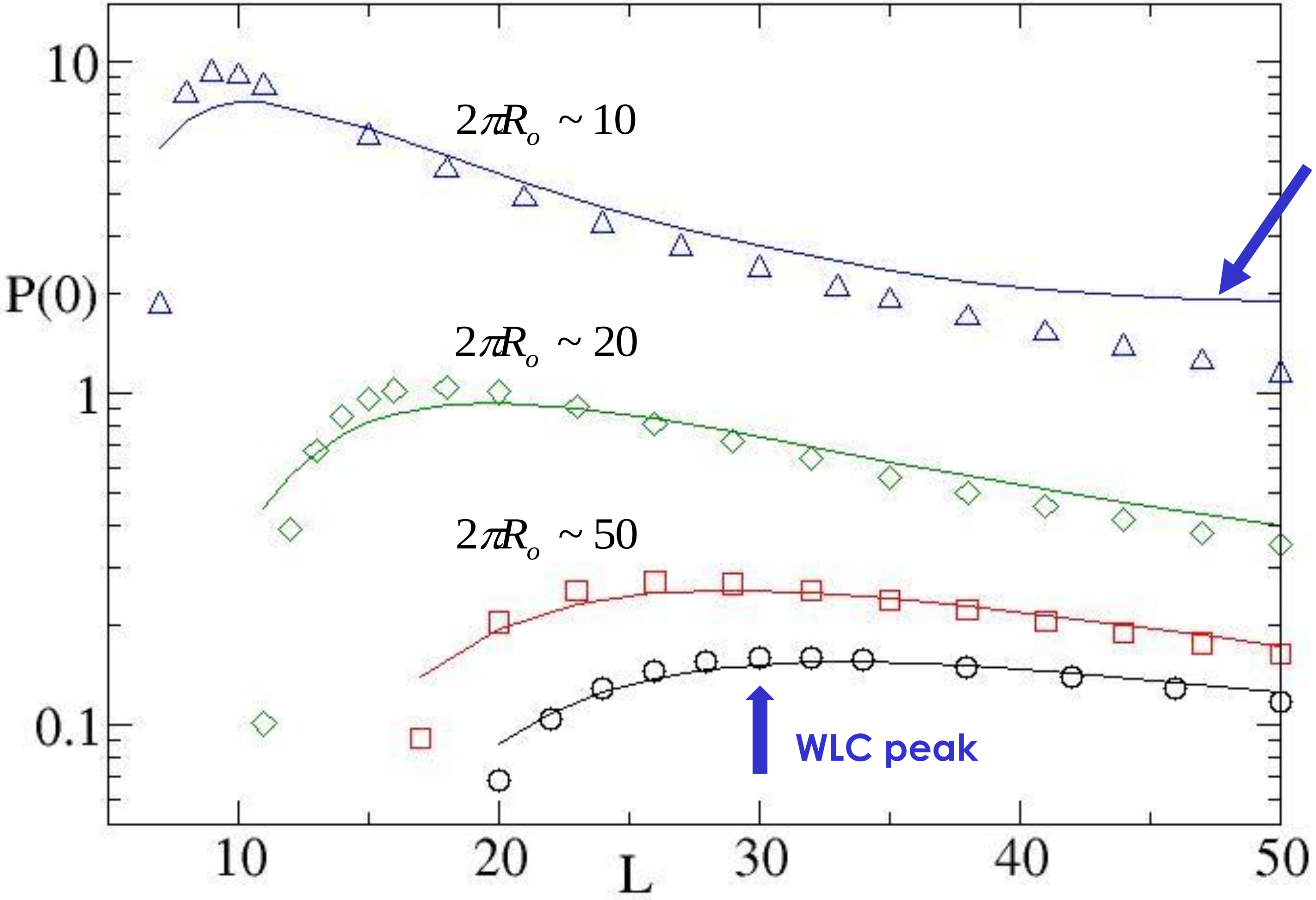
peak at $L = 2\pi R_o, 4\pi R_o, ..$

But, Monte-Carlo Simulation shows

peak actually shifts to $L < 2\pi R_o$

Rappaport and Rabin, Macromolecules **37**, 7847 (2004)

WLC peaks at L/ $l_p \sim 3$, Curved chain peaks at L/$2\pi R_o \sim 1$



Shimada & Yamakawa (1984)

S. Ghosh, K. Singh and A. Sain, PRE **80,** 051904 (2009)

Summary

Contrary to expectation the directional correlation decays exponentially.

Loop formation probability can distinguish between WLC and curved chain.

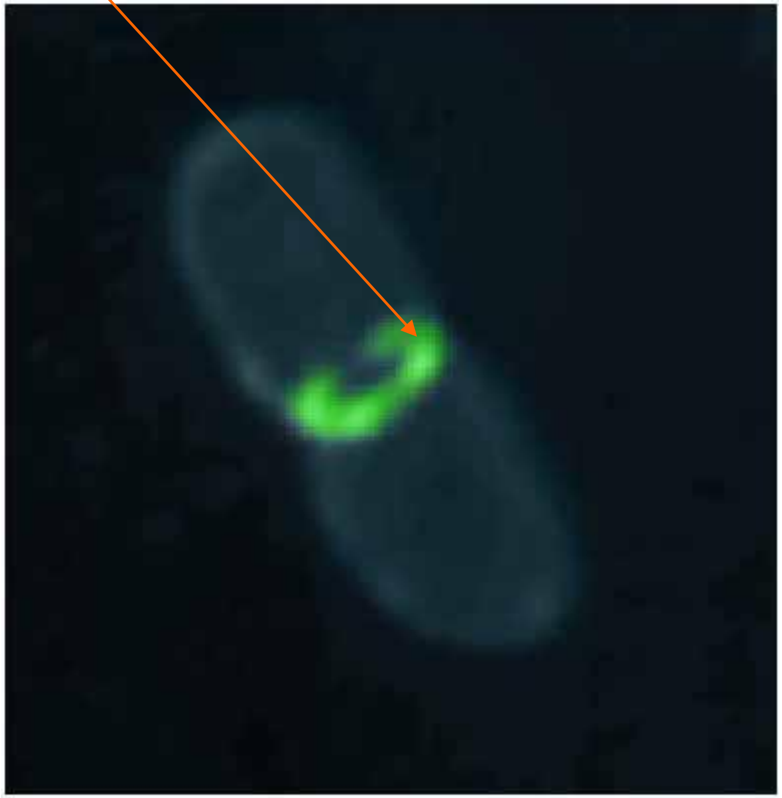
Cell division in bacteria

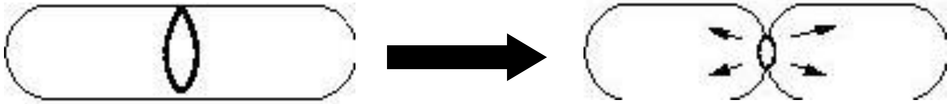
Contraction of the FtsZ ring divides the cell

E. coli

L ~ 3-4 μm

Dia ~ 1 μm

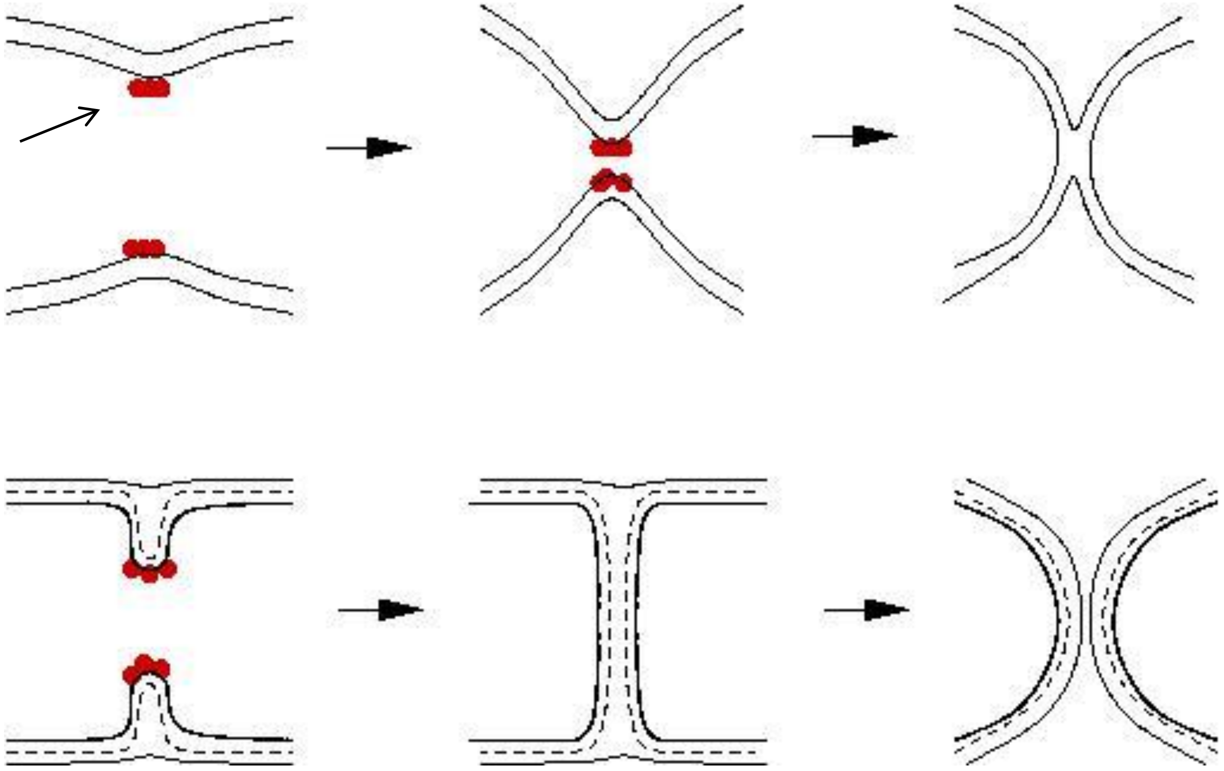




Contraction time ~ 10 min

What drives this contraction ?

Role of the cell wall



ring

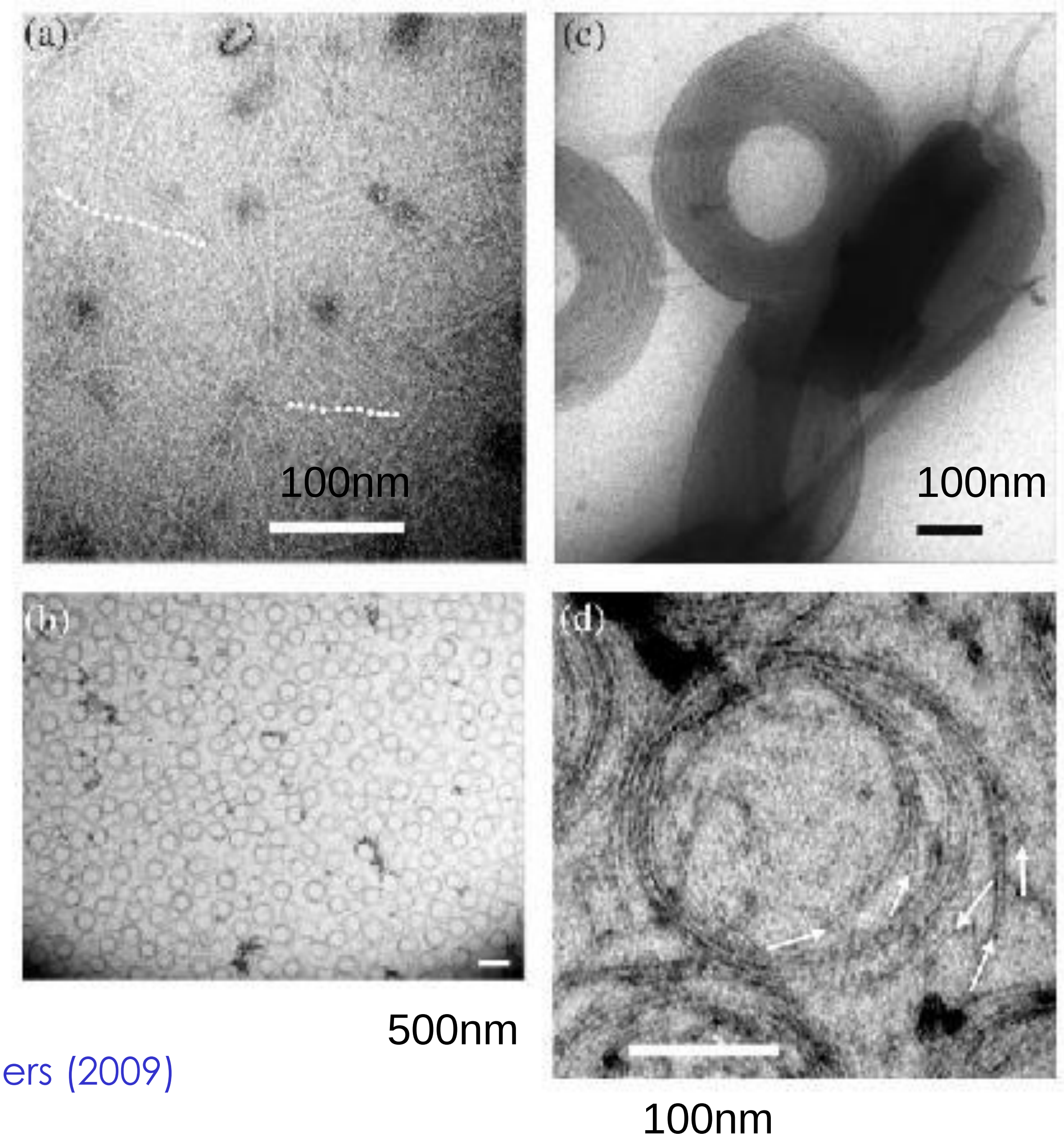
Caulobacter

E.coli

Mycoplasma (no cell wall)

In vitro polymerization and toroid formation via lateral attraction

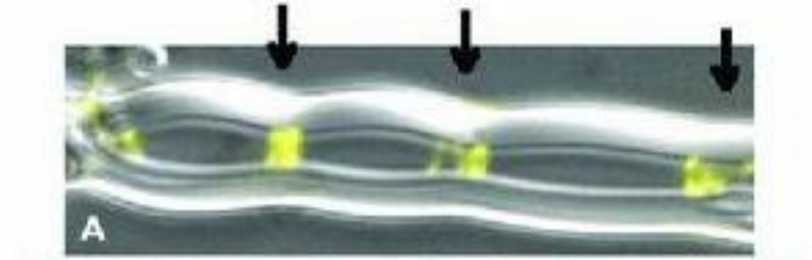
EM

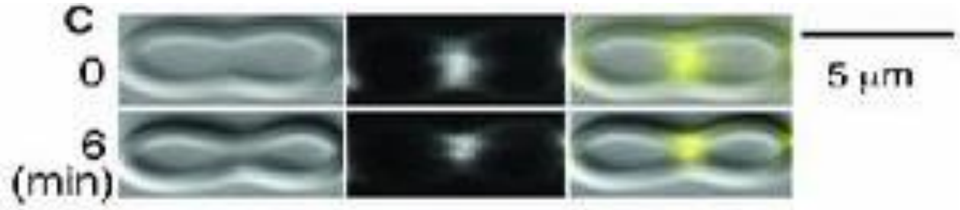


Popp et al, Biopolymers (2009)

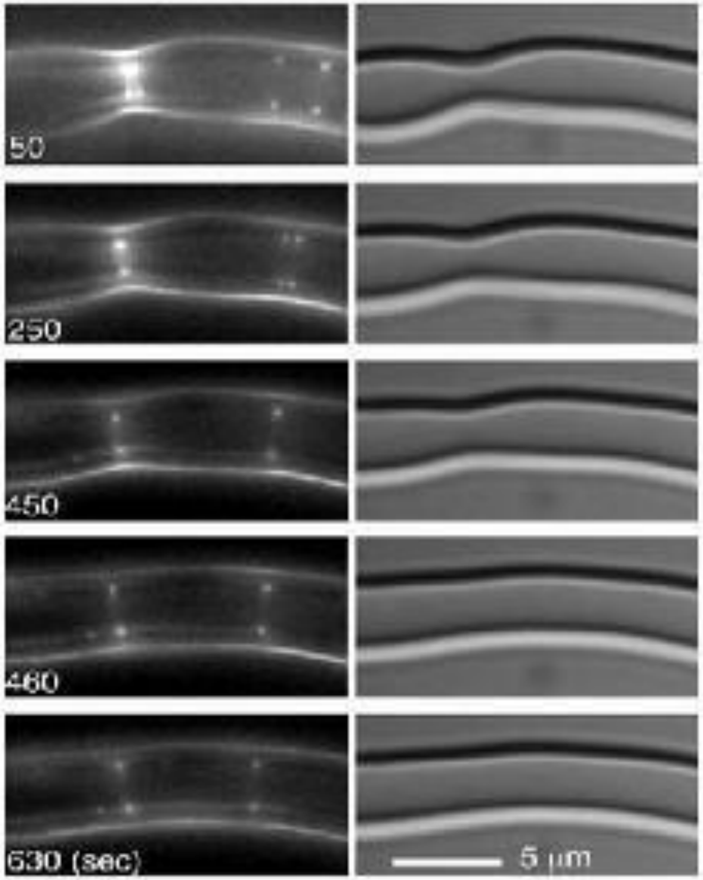
Reconstruction of artificial Z-rings

Z-ring inside
phospholipid tube !





Osawa et al., Science,2008



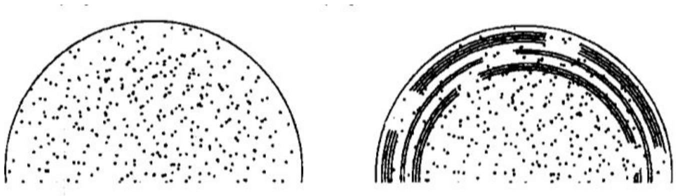
GTP hydrolysis needed for constriction

Lateral attraction between filaments

Z-ring formation in vivo:

FtsZ proteins ***polymerize***.

Monomers / Filaments anchor to the cell membrane.



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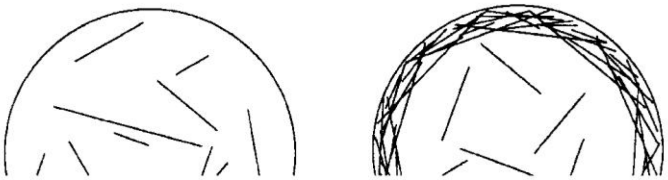


Stricker et al.,2002,PNAS

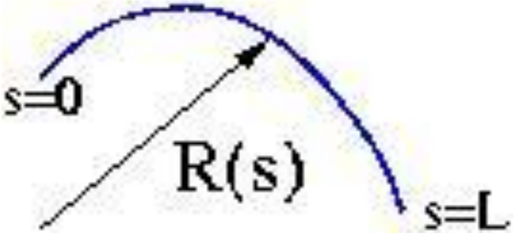
Structure of the ring is not resolved (filament width ~ 5nm)

May be a gel of short filaments.

Intrinsic curvature of FtsZ filaments

Energy functional $\boldsymbol{H}\,[R(s)]$ for configuration $R(s)$

$$\frac{H}{k_B T} = \frac{l_p}{2} \int_{s=0}^{L} \left[\frac{1}{r(s)} - \frac{1}{R_o}\right]^2 ds$$



$1/r(s) = |d^2\vec{R}(s)/ds^2|$ = local curvature

$1/R_o$ = Intrinsic curvature

In vitro Properties of FtsZ filaments

1) FtsZ units are attached to GTP or GDP (T or D)

2) GTP enhances

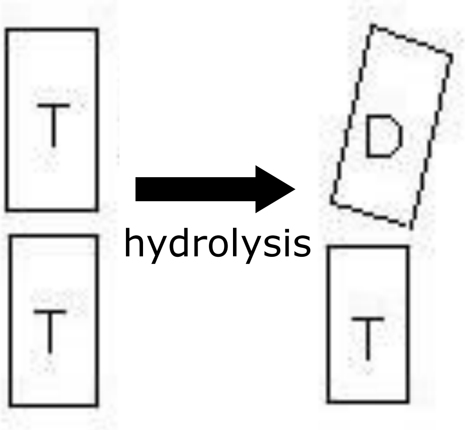
   a) polymerization ($-\sigma$)

   b) lateral bundling of filaments ($-\varepsilon$)

GDP does not.

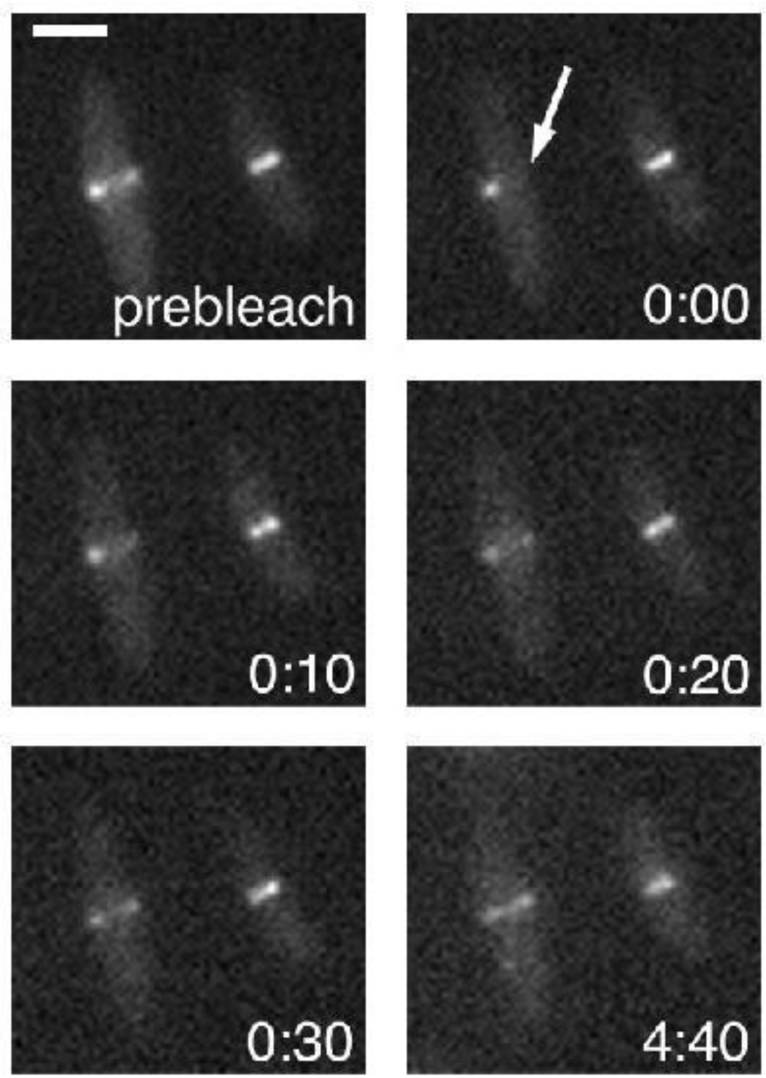
3) Hydrolysis: GTP → GDP+P

leads to filament bending ($+\eta$)



Z-ring is highly Dynamic

(It exchanges FtsZ with cytoplasm)



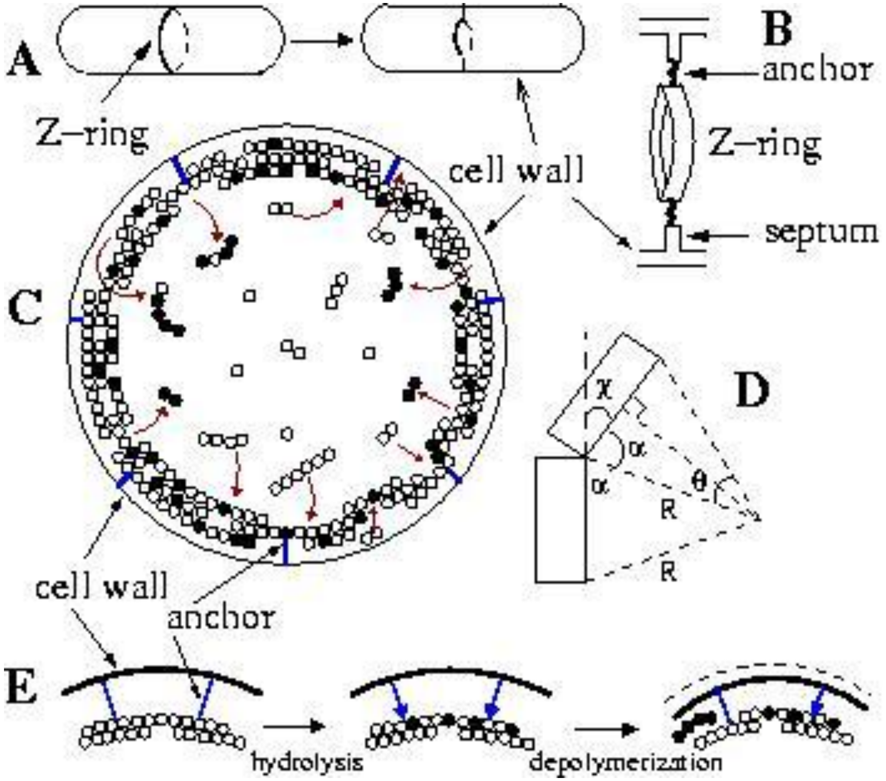
Turn-over of FtsZ units

(Fluorescent recovery after Photo-bleaching)

Half life $t_{1/2}$=8-30 sec

Stricker et al.,2002,PNAS

Our model of the ring (2-D cross section)



Discretization:

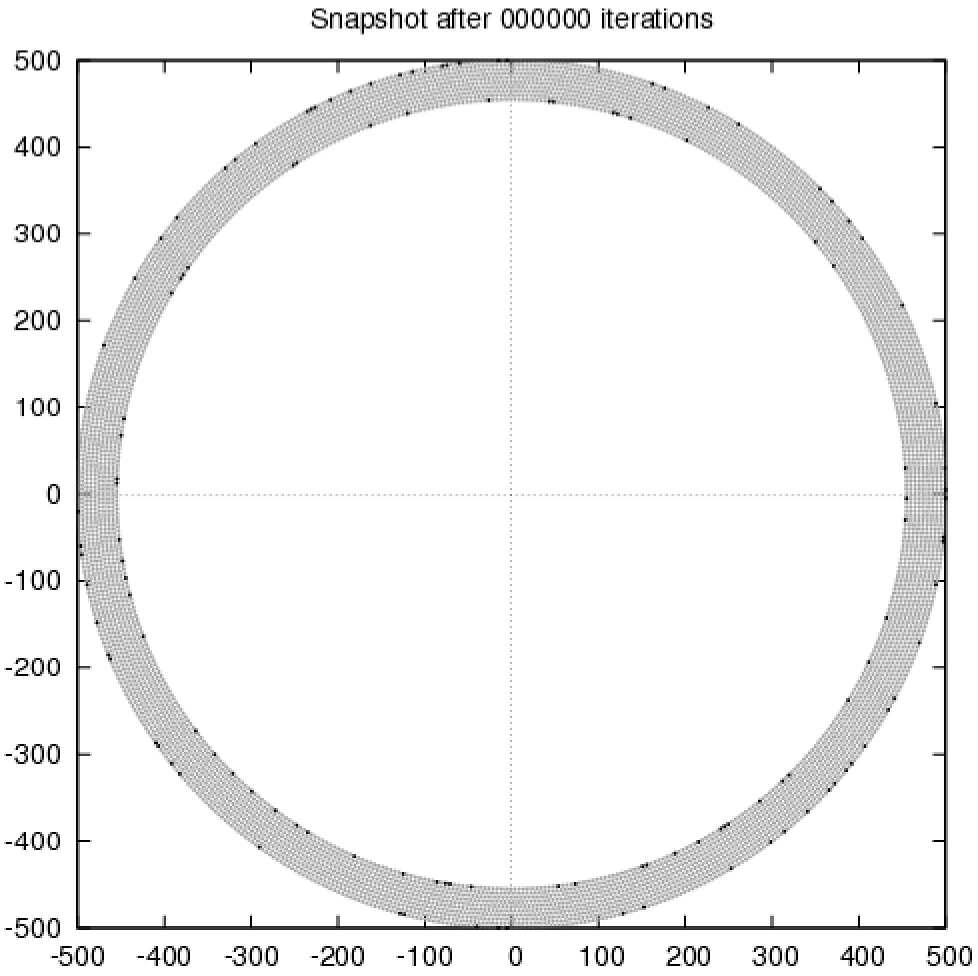
Each layer is a regular polygon with large number of sides of length= l (5nm). Bending angle= χ , Radius = R

$$l/R \sim \chi$$

Assumption: length distribution in cytoplasm is exponential

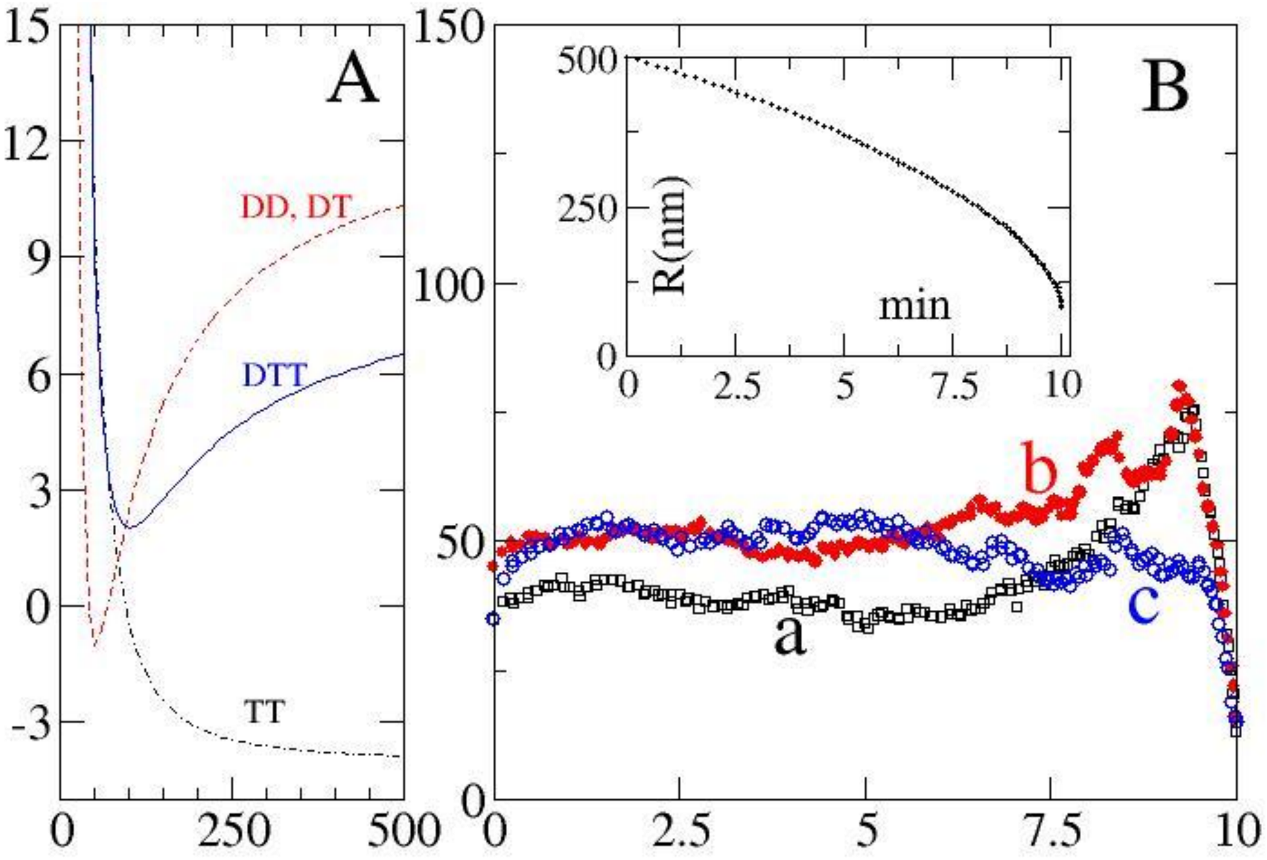
Results : self propelled contraction

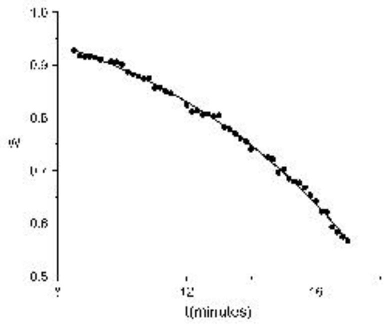
(Monte Carlo simulation)



B.Ghosh & A.Sain, PRL, **101**, 178101 (2008)

Thickness of the ring depends on rates.





Experiment

Reshes et al, BioPhys J.

(2008)

T-rich layers are stable but TD,DD segments at the exposed surface layers are unstable.

Having few layers is crucial for our mechanism.

Contractile force

Line tension

$$T = \frac{\mathrm{H(R)}}{2\pi\,\mathrm{R}} = \frac{\beta\, l_p}{2}\left(\frac{1}{r} - \frac{1}{Ro}\right)^2 \sim 10\,\mathrm{pN}$$

$l_p = 15\ \mu m$

$R_o = 50\ nm$

$$T_{\max}/\mathrm{R} = 0.02\,\mathrm{pN/nm}$$

Summary

A self propelled contraction mechanism for prokaryotes

Ingredients:

- Curved filaments
- poly/depolymerization of filaments
- GTP hydrolysis
- GTP/GDP dependent lateral attraction between filaments

Absence of straight to curved transition with hydrolysis.

FtsZ kinetics in the cytoplasm