Accurate Division in *E. coli*

E. Coli [www.deniskunkel.com]

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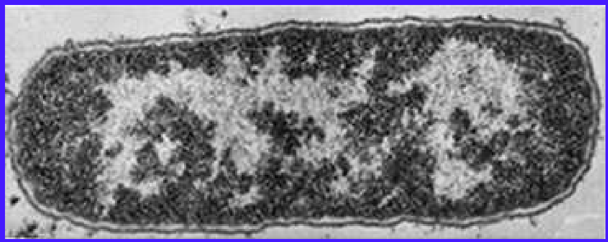
Length and Time-scales

- small rod (2-4µm in length, 1-1.5µm in diameter)
- divides accurately every hour



E. coli [Alberts *et al.*]

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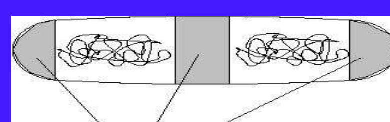
E. coli [Alberts *et al.*]

WHY HERE?

Qualitative Model

"Nucleoid Occlusion"

- midcell division
- minicell mutants
- no guillotining



[Res. Microbiol. **141**, p39 (1990).]

Qualitative Model

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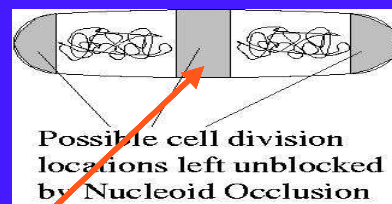


[Res. Microbiol. **141**, p39 (1990).]

How is midcell selected?

Experimental interactions:

MinC

- inhibits division
- recruited to membrane by MinD

MinD

- binds to membrane
- recruits MinE
- released by MinE

MinE

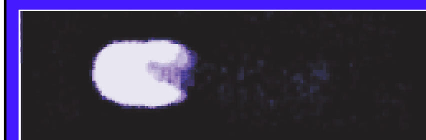
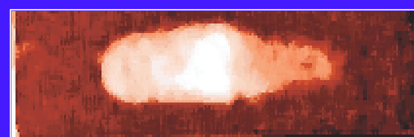
- recruited by MinD
- releases MinD

[labs of Larry Rothfield, Joe Lutkenhaus, Piet de Boer, and others]

Phenomenology:

MinC/MinD
- suppress division
- mostly at cell poles
- ~1600 copies per cell

MinE
- suppresses MinD
- mostly at midcell
- ~1600 copies per cell

[Hale, Meinhardt, de Boer, EMBO **20**, p1563 (2001).]

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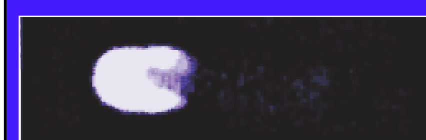
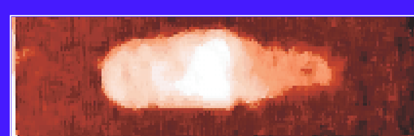



[Hale, Meinhardt, de Boer, EMBO **20**, p1563 (2001).]

Min Model:

Membrane

Bulk

Bulk MinD $\frac{\partial D}{\partial t}$

Membrane MinD $\frac{\partial d}{\partial t}$

Bulk MinE $\frac{\partial E}{\partial t}$

Membrane MinE $\frac{\partial e}{\partial t}$

Min Model:

DIFFUSION

- **all proteins diffuse along the bacterium**
- **no diffusion when membrane associated** ★

Bulk MinD $\frac{\partial D}{\partial t} = D_D \frac{\partial^2 D}{\partial x^2}$

Membrane MinD $\frac{\partial d}{\partial t} =$

Bulk MinE $\frac{\partial E}{\partial t} = D_E \frac{\partial^2 E}{\partial x^2}$

Membrane MinE $\frac{\partial e}{\partial t} =$

Min Model:

REACTION

- MinD goes onto membrane spontaneously, comes off due to MinE
- MinE goes onto membrane due to MinD, comes off spontaneously

Bulk MinD

$$\frac{\partial D}{\partial t} = D_D \frac{\partial^2 D}{\partial x^2} - \frac{\sigma_1 D}{1+\sigma'_1 e} + \sigma_2 e d$$

Membrane MinD

$$\frac{\partial d}{\partial t} = \quad + \ \ldots \ - \ \ldots$$

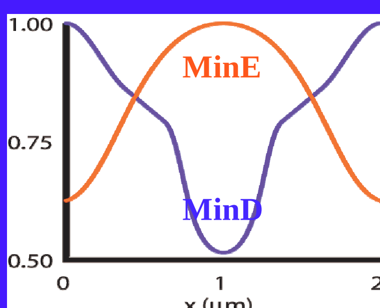
Bulk MinE

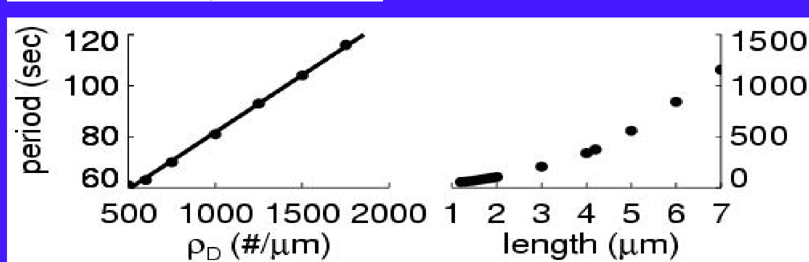
$$\frac{\partial E}{\partial t} = D_E \frac{\partial^2 E}{\partial x^2} - \sigma_3 E D + \frac{\sigma_4 e}{1+\sigma'_4 D}$$

Membrane MinE

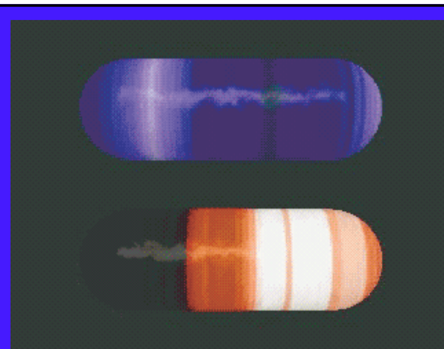
$$\frac{\partial e}{\partial t} = \quad + \ \ldots \ - \ \ldots$$

Results:

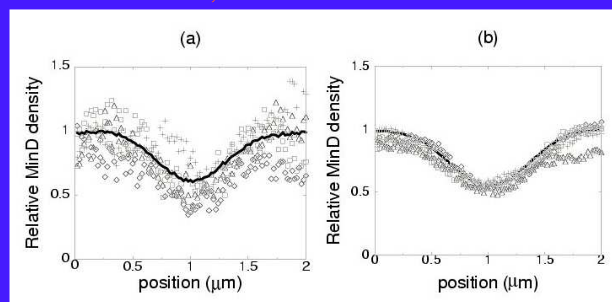




Shot-noise:



Number of MinD =200, number of MinD= 1500



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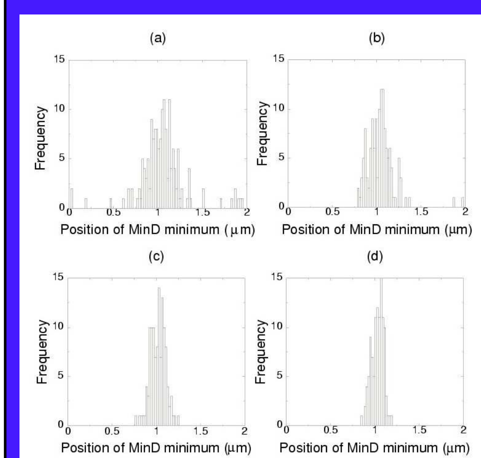
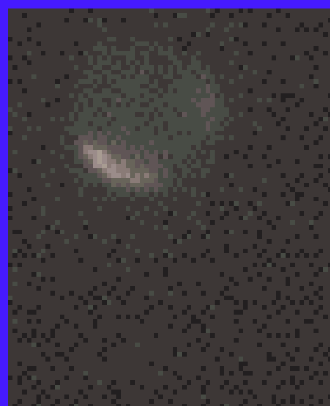


Number of MinD =200, 400, 800, 1500
for (a), (b), (c), (d)

more MinD leads to more precise midpoint positioning in every oscillation.

[Howard and Rutenberg, PRL **90**, p128102 (2003).]

Division of round cells:



[Corbin, Yu, and Margolin]

GFP-MinD in round *E. coli*

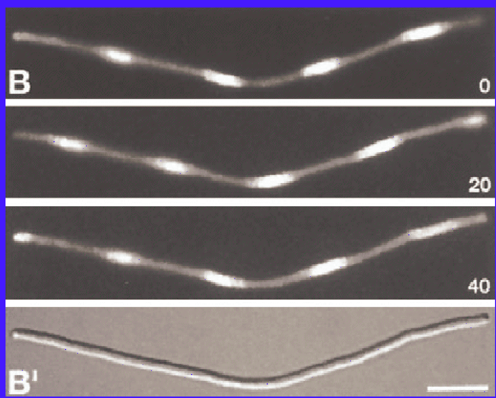
- oscillation axis wanders
- deformations lock axis

"Post-genomics"

- Quantitative model
- Dynamic compartmentalization:
  spatial regulation without organelles
- division accuracy imposes expression levels
- *in vivo* biochemistry

Tuning the model

- frequency tunable via time and parameter rescaling
- wavelength tunable via density and parameter rescaling



gfp-MinD
[Raskin and de Boer, PNAS **96**, p4971 (1999).]

5micron scale

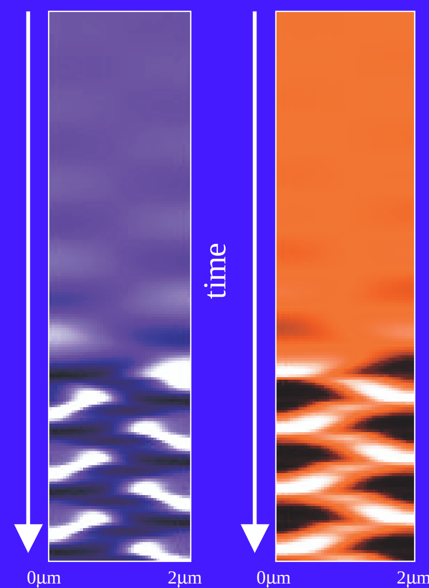
Min Models

paper	# parameters
Meinhardt, deBoer, PNAS, 98 (2001).	17
Wingreen, Huang, Meir, [01/2003, KITP biomolecular networks]	9
Kruse, Biophys J, 82 (2002).	6
Howard, Rutenberg, deVet, PRL **87**, (2001).	8

Linear Instability

- spontaneous oscillations
- exponential onset
- preliminary screening
- e.g.

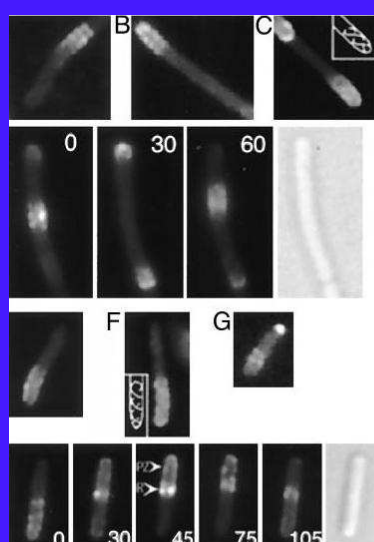
$$\frac{\partial D}{\partial t} = D_D \frac{\partial^2 D}{\partial x^2} - \frac{\sigma_1 D}{1+\sigma'_1 e} + \sigma_2 e d$$



Filaments:

MinD

MinE



Decorated or Assembled?

[Shih, Le, Rothfield PNAS **100**, p7865 (2003).]