Diffusion, and How it is Used or How Stupid Organisms Do Math

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Introduction

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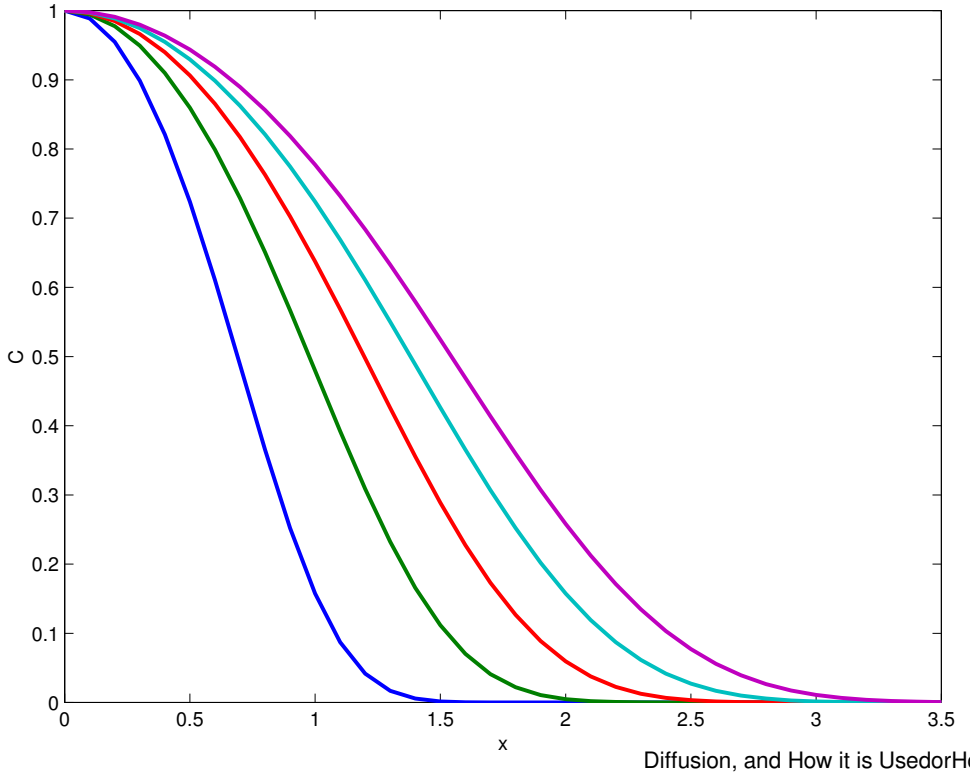
leading to the Diffusion Equation

$$\frac{\partial C}{\partial t} = \frac{\partial}{\partial x}(D\frac{\partial C}{\partial x}).$$

Basic Consequences - I

Diffusion in a tube fed by a reservoir

$$C(x,t) = f(\frac{x^2}{Dt})$$



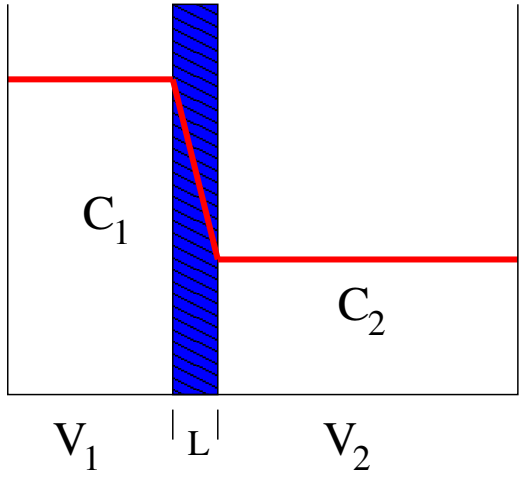
Basic Consequences - II

Diffusion time:$t = \frac{x^2}{D}$ for hydrogen ($D = 10^{-5}$cm^2/s).

x	t	Example
10 nm	100 ns	cell membrane
1 μm	1 ms	mitochondrion
10 μm	100 ms	mammalian cell
100 μm	10 s	diameter of muscle fiber
250 μm	60 s	radius of squid giant axon
1 mm	16.7 min	half-thickness of frog sartorius muscle
2 mm	1.1h	half-thickness of lens in the eye
5 mm	6.9 h	radius of mature ovarian follicle
2 cm	2.6 d	thickness of ventricular myocardium
1 m	31.7 yrs	length of sciatic nerve

Basic Consequences - II

Diffusion across a membrane



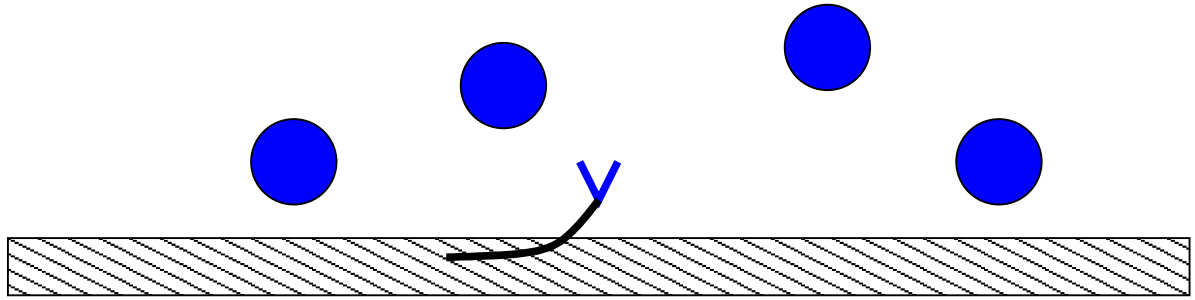
$$J = \frac{AD}{L}(C_1 - C_2)$$

then

$$\frac{d}{dt}(V_1 C_1) = \frac{AD}{L}(C_2 - C_1), \qquad V_1 C_1 + V_2 C_2 = (V_1 + V_2) C_0$$

Carrier Mediated Diffusion

Problem: If glucose only moves down its gradient, there must always be more glucose in the blood than in cells, or else cells will lose their glucose.



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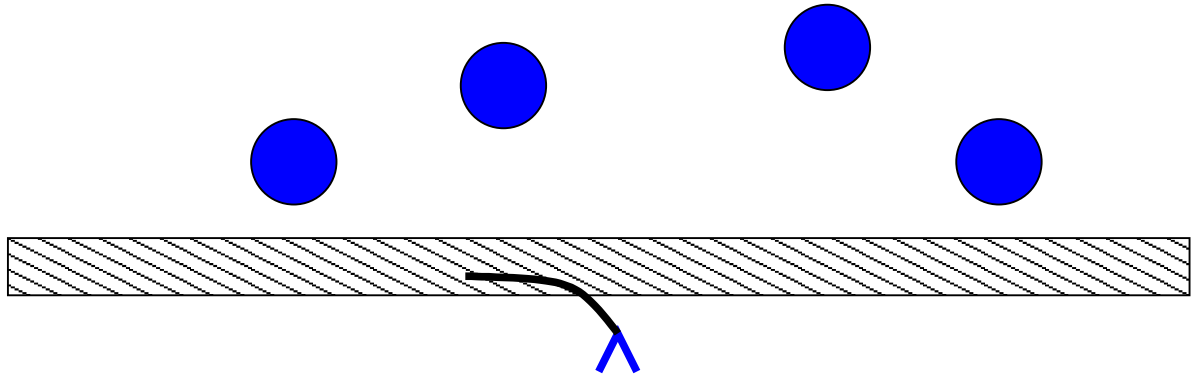

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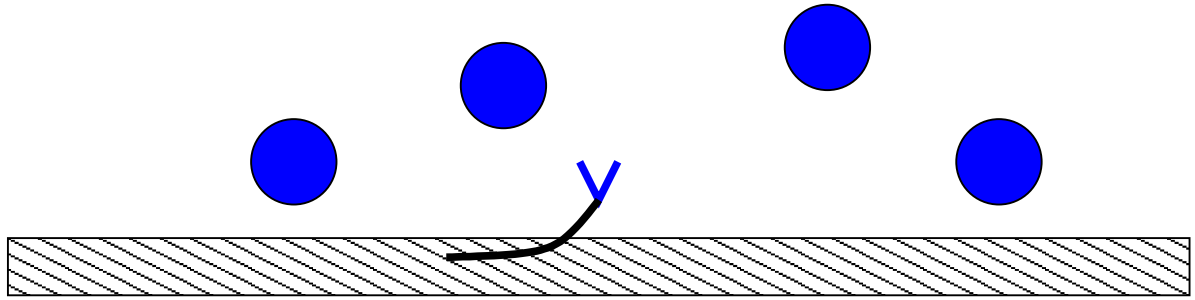

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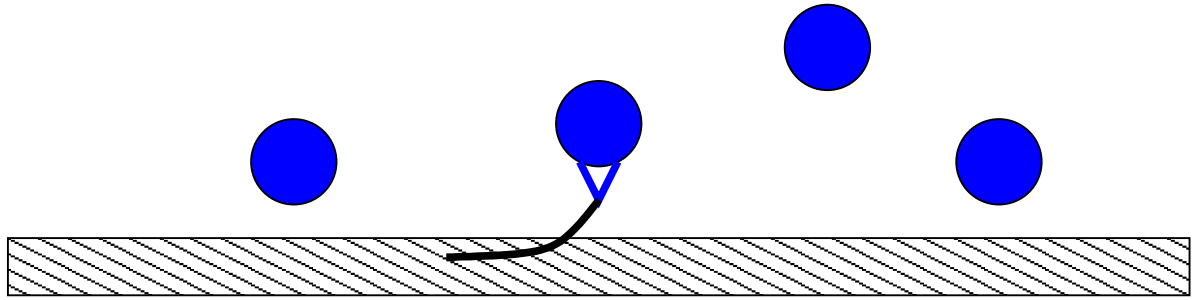

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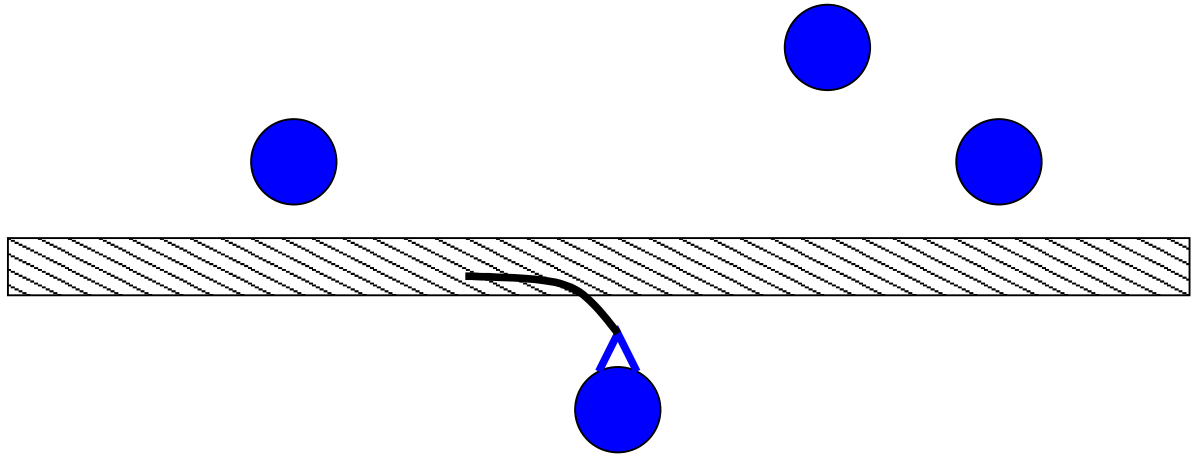

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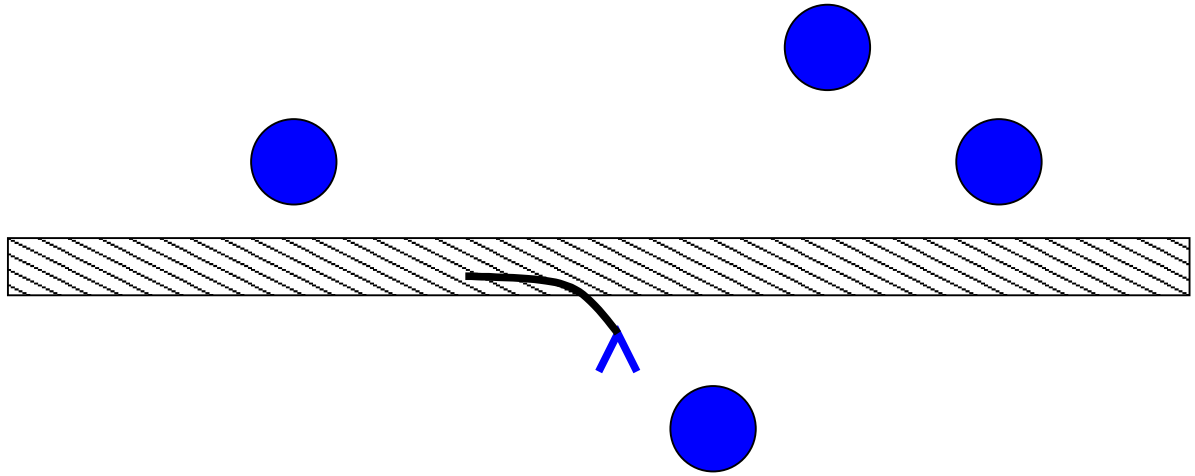

For this system,

$$J = J_{max} \frac{g_e - g_i}{(g_e + K)(\frac{g_i}{K} + 1)}$$

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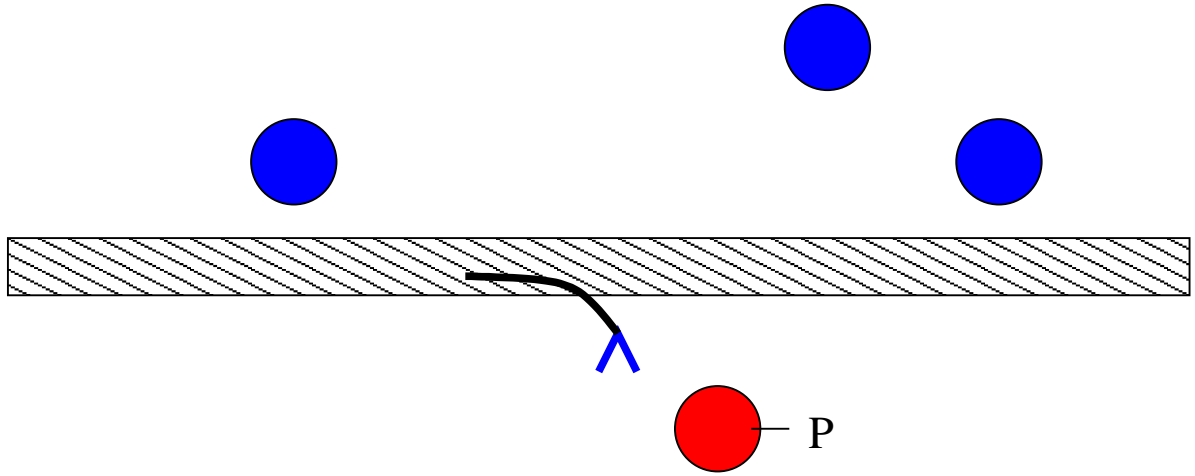
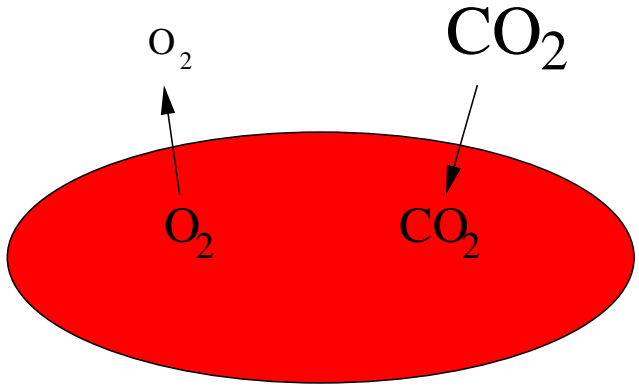


Solution: Immediately phosphorylate internal glucose, setting $g_i = 0$ so that

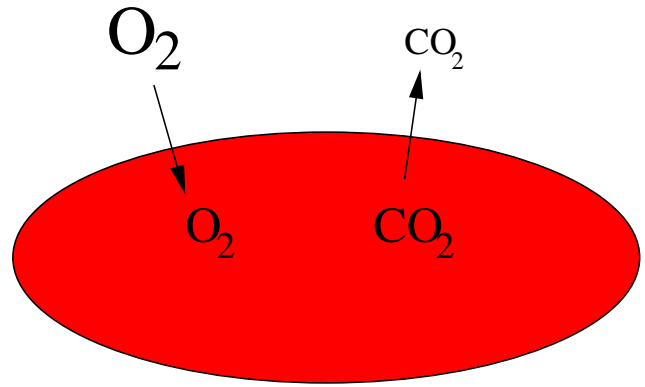
$$J = J_{max} \frac{g_e}{g_e + K}$$

Oxygen and Carbon Dioxide Transport

Problem: If oxygen and carbon dioxide move into and out of the blood by diffusion, their concentrations cannot be very high (and no large organisms could exist.)



In Tissue



In Lungs

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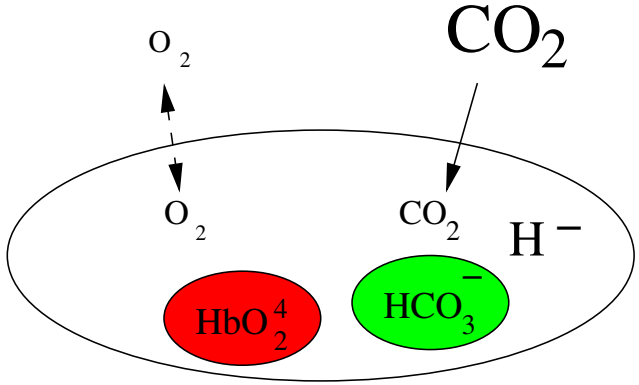

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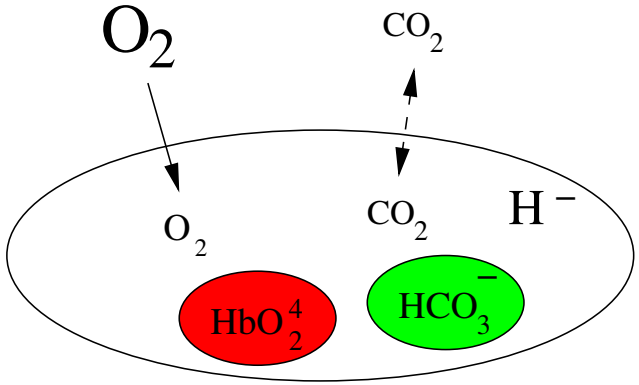

In Lungs

Chemical reactions that help enormously:

$$CO_2 + H_2O \rightleftarrows HCO_3^+ + H^- \qquad Hb + 4O_2 \rightleftarrows Hb(O_2)^4$$

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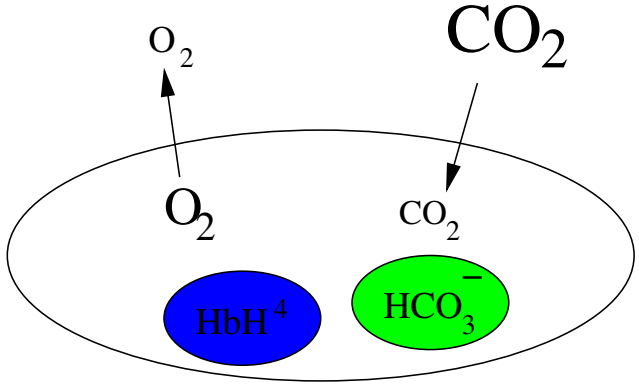

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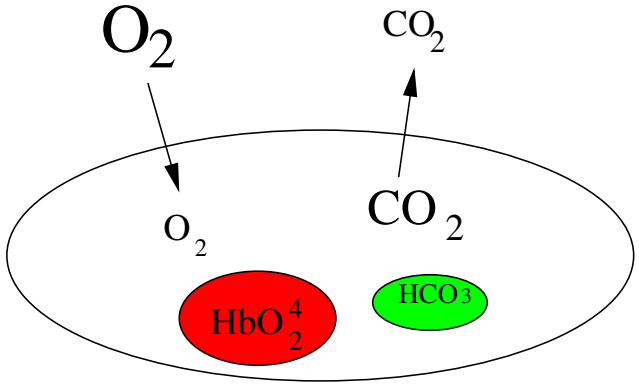


In Lungs

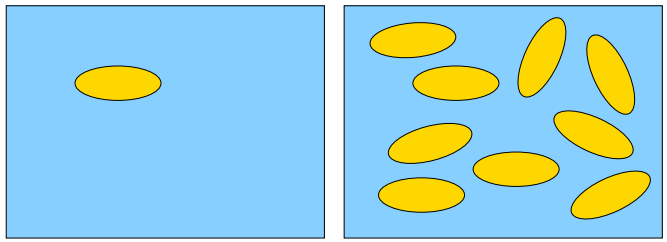
Chemical reactions that help enormously:

$$CO_2 + H_2O \rightleftarrows HCO_3^+ + H^- \qquad Hb + 4O_2 \rightleftarrows Hb(O_2)^4$$

Hydrogen competes with oxygen for hemoglobin binding.

Quorum Sensing

Quorum sensing: The ability of bacteria to respond to their population size. Question: How do bacteria conduct a census?



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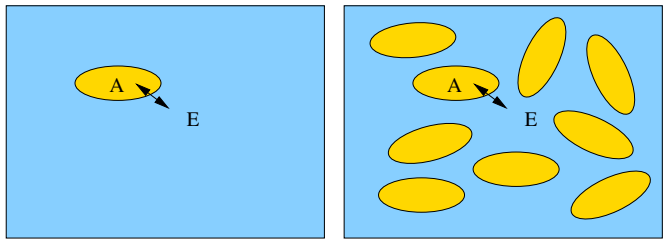
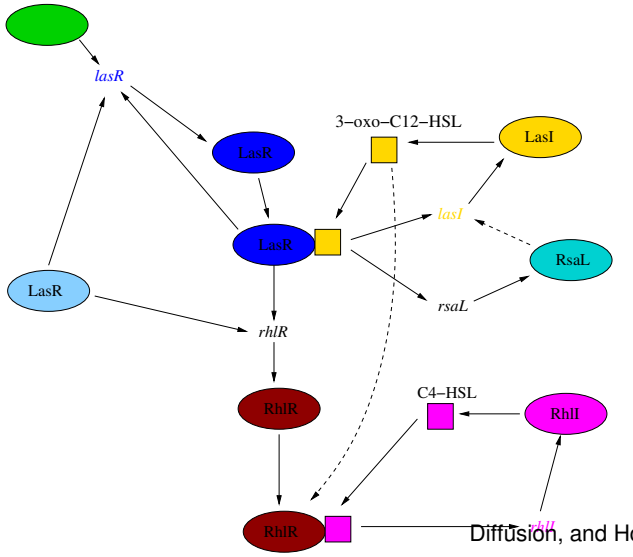
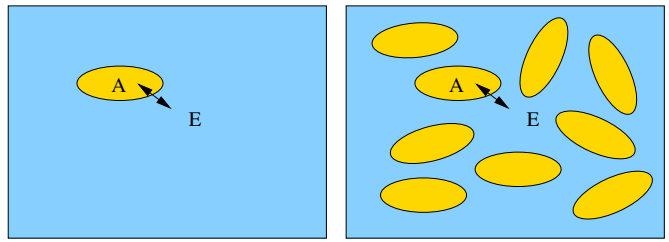


Solution: Autoinducer (HSL)- a freely diffusing chemical with auto-catalytic (positive feedback) production.



Quorum Sensing-II



$$\frac{dA}{dt} = F(A) + \delta(E - A)$$

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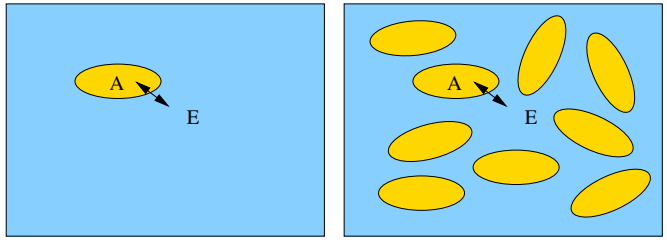
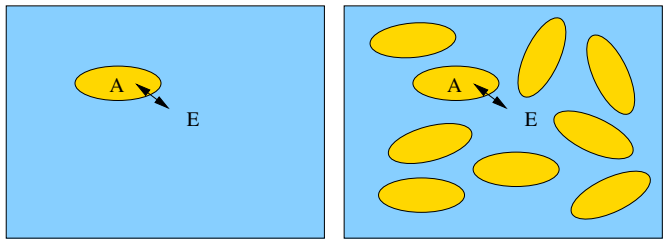


$$\boxed{\frac{dA}{dt}} = F(A) + \delta(E - A)$$

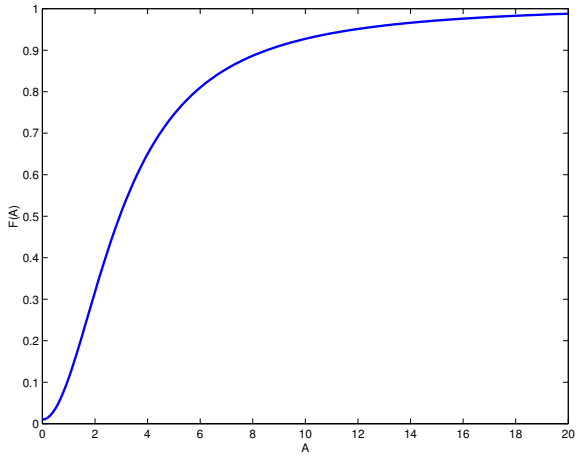
rate of change of A,

Quorum Sensing-II



$$\frac{dA}{dt} = \boxed{F(A)} + \delta(E - A)$$

production of A, production rate,



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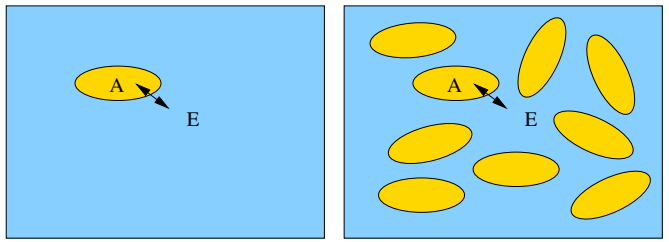
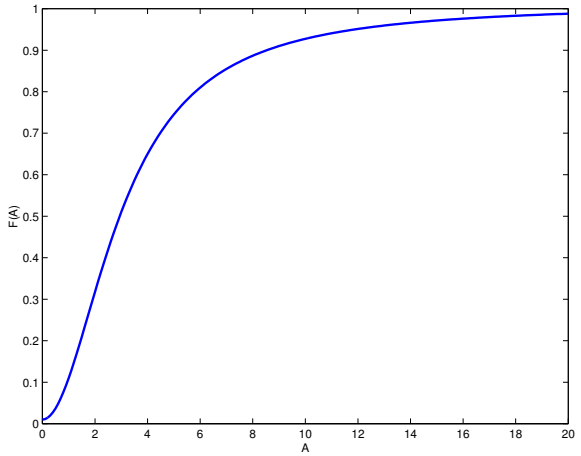


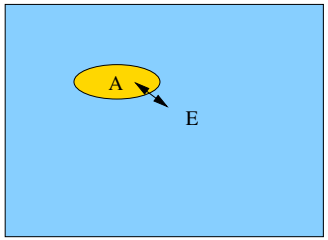
$$\frac{dA}{dt} = F(A) + \boxed{\delta(E - A)}$$

production of A, production rate, diffusive loss .



Quorum Sensing-III

Extracellular Autoinducer E:



$$\frac{dE}{dt} = - k_E E + \delta(A - E)$$

.

Quorum Sensing-III

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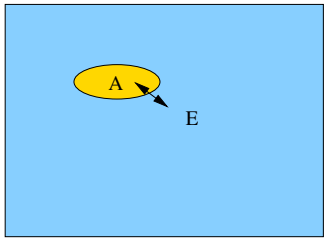

$$\boxed{\frac{dE}{dt}} = -\ k_E E\ +\ \delta(A - E)$$

rate of change of E, .

Quorum Sensing-III

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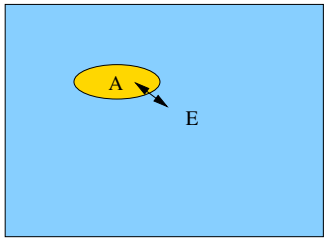
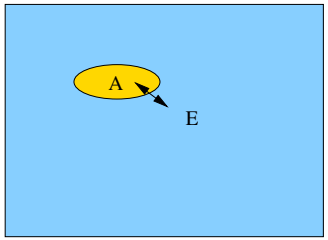


$$\frac{dE}{dt} = -\boxed{k_E E} + \delta(A - E)$$

rate of change of E, degradation rate, .

Quorum Sensing-III

Extracellular Autoinducer E:

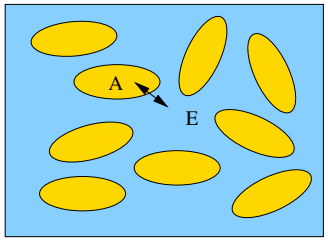


$$\frac{dE}{dt} = - k_E E + \boxed{\delta(A - E)}$$

rate of change of E, degradation rate, diffusive source, .

Quorum Sensing-III

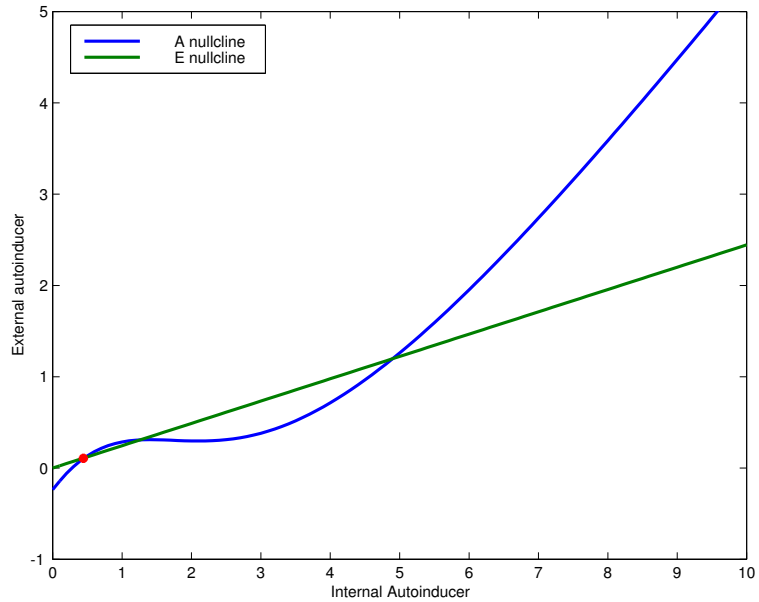
Extracellular Autoinducer E:



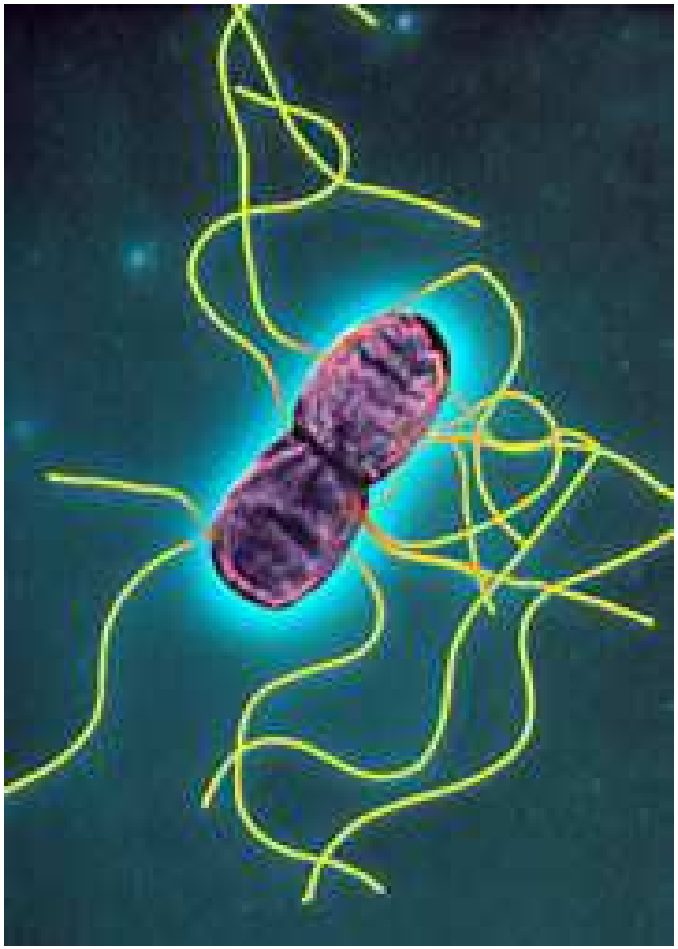
$$\boxed{(1-\rho)}\left(\frac{dE}{dt}+K_E E\right)=\boxed{\rho}\,\delta(A-E)$$

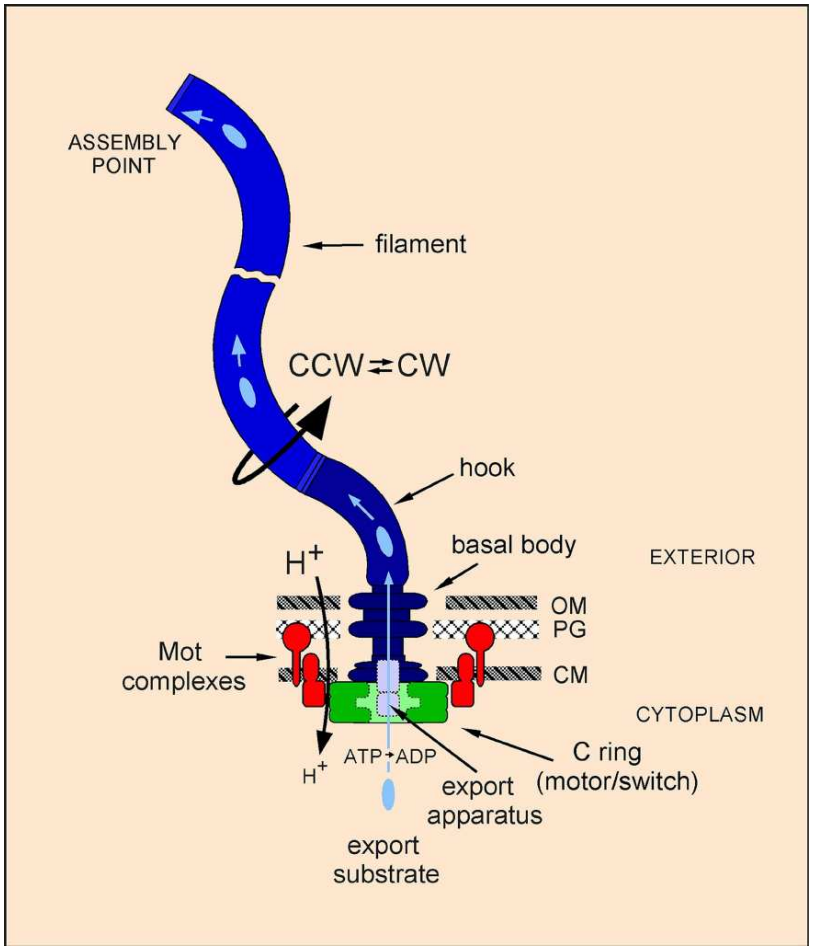
rate of change of E, degradation rate, diffusive source, density dependence .

Quorum Sensing-IV



Length Detection





Observations

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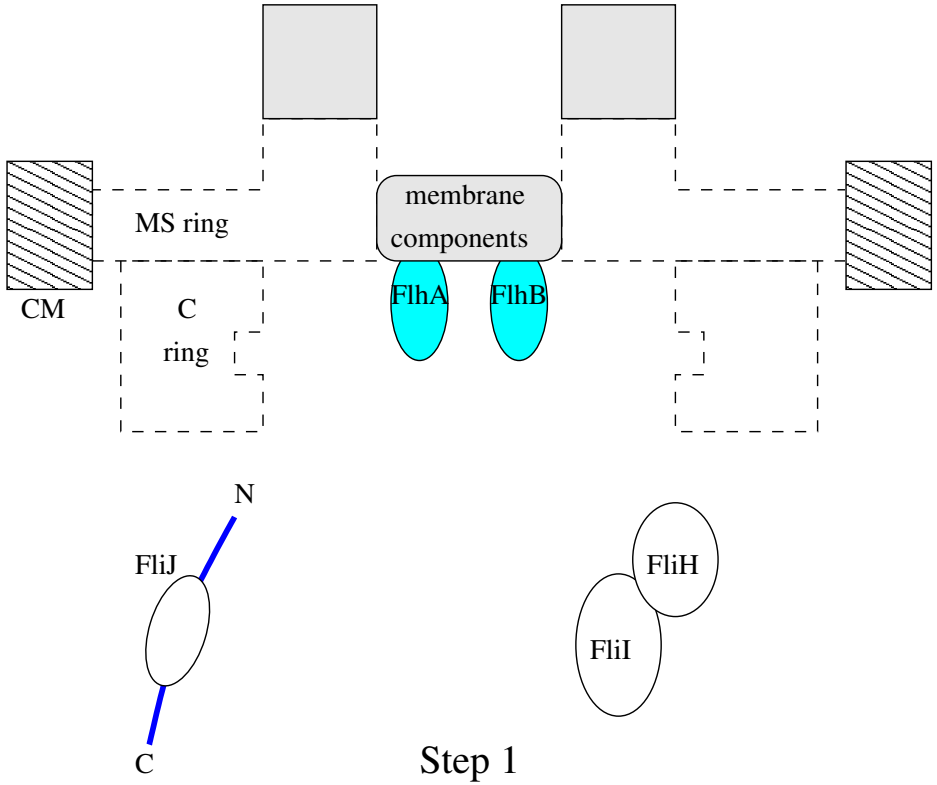
Question: How does the bacterium "know" how long its flagella are?

How Do Flagella Grow?

Stage 1: Secretion of Flagellin (FliC)



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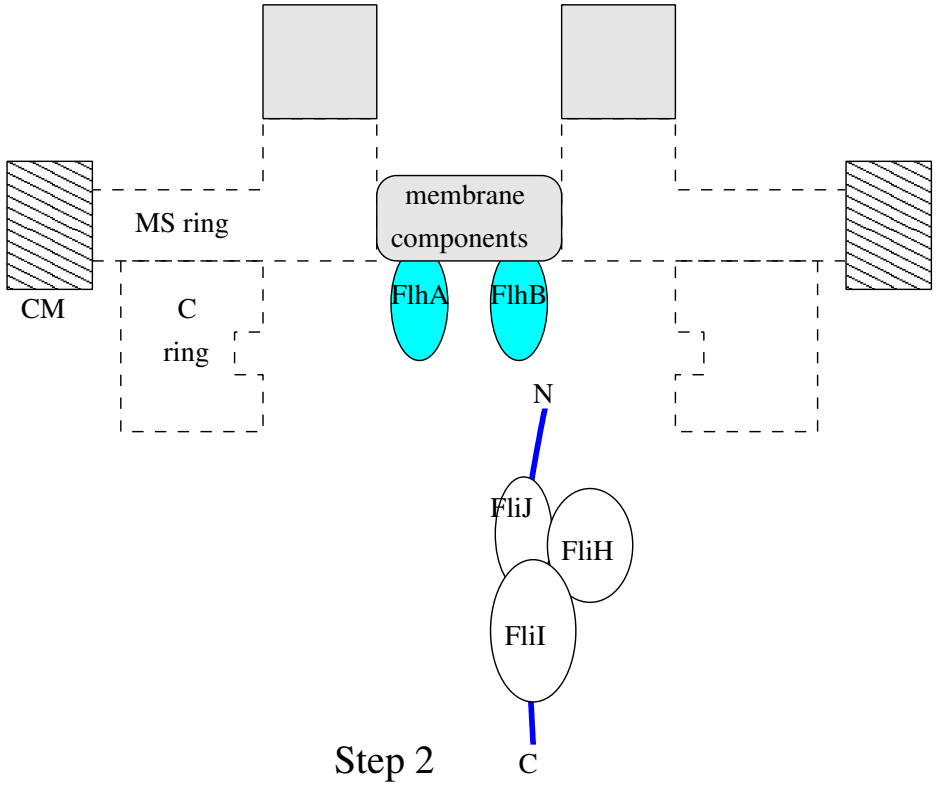

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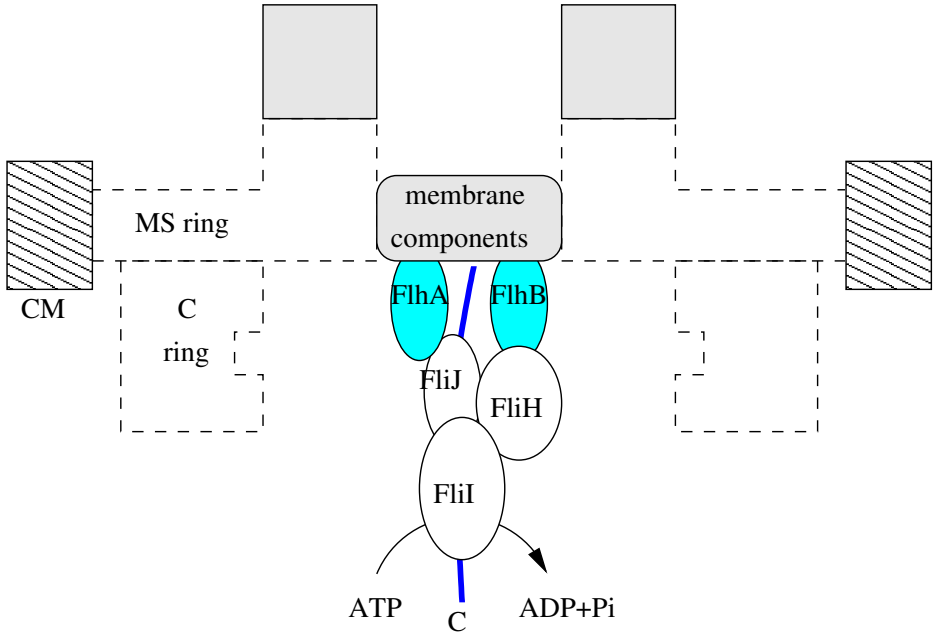

Step 3

How Do Flagella Grow?

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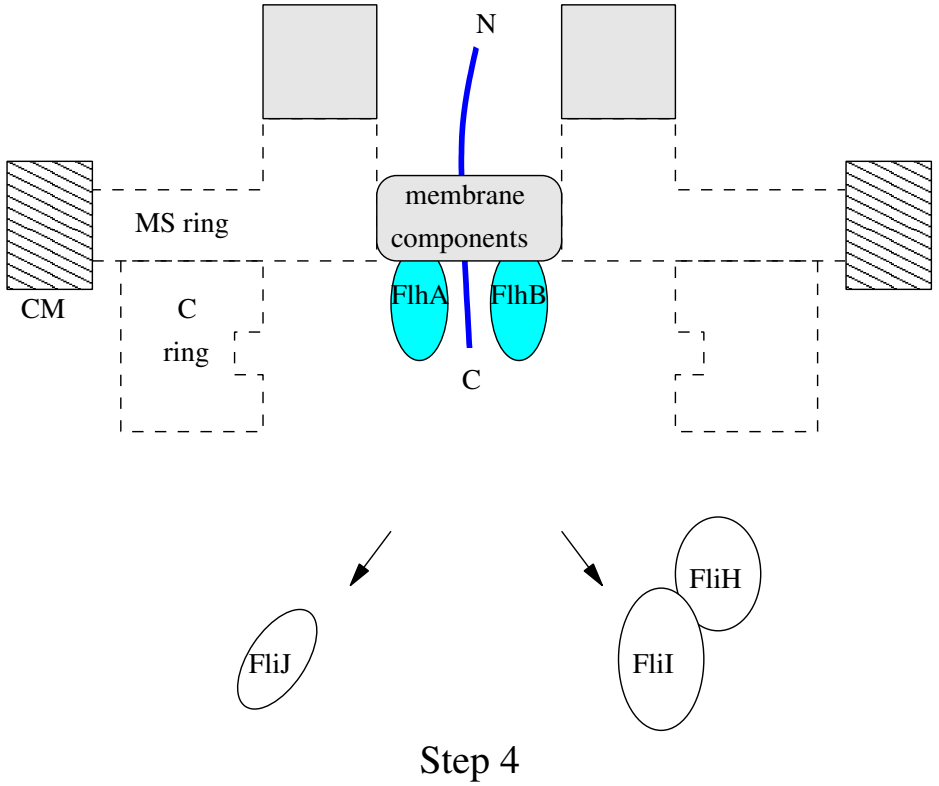
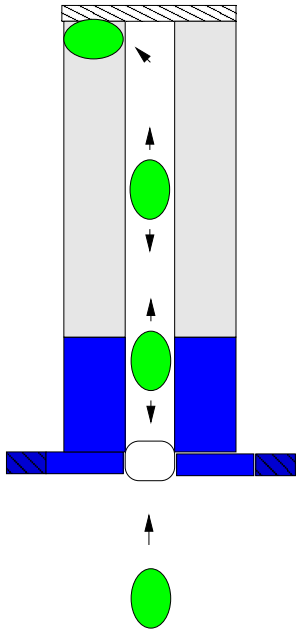


Step 4

How Do Flagella Grow?

Stage 2: Diffusion and polymerization



A good approximation

$$J \approx \frac{1}{K_J + \frac{L}{D}} \approx \frac{D}{L} \text{ for large } L(\text{length dependence!})$$

Length Detection

The protein FlgM has three important properties:

- It is secreted during filament growth;
- It inhibits its own production (negative feedback);
- It inhibits the production of Flagellin.

Tracking Concentrations

FlgM (M):

$$\frac{dM}{dt} = \text{rate of production} - \text{rate of secretion}$$

Flagellin (F):

$$\frac{dF}{dt} = \text{rate of production} - \text{rate of secretion}$$

Filament Length (L):

$$\frac{dL}{dt} = \beta \frac{F}{M+F} J$$

Tracking Concentrations

FlgM (M):

$$\frac{dM}{dt} = \frac{K_*}{K_M + M} - \alpha \frac{F}{F + M} J$$

Flagellin (F):

$$\frac{dF}{dt} = \frac{K_*}{K_M + M} - \alpha \frac{M}{F + M} J$$

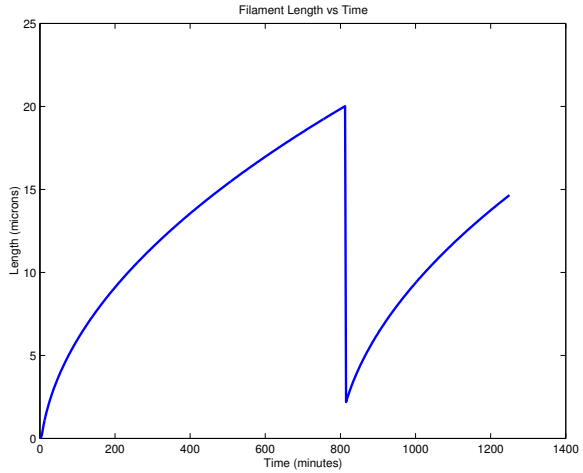
Filament Length (L):

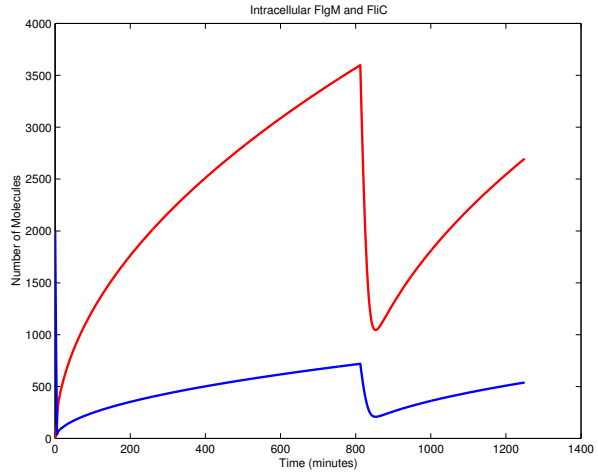
$$\frac{dL}{dt} = \beta \frac{F}{M + F} J$$

with

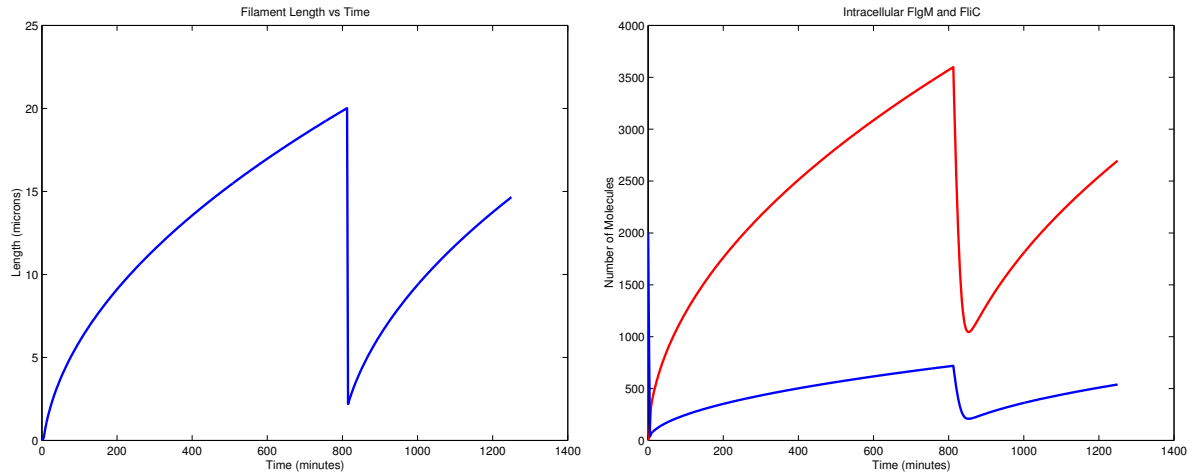
$$J = \frac{1}{K_J + \frac{L}{D}}$$

Filament Growth



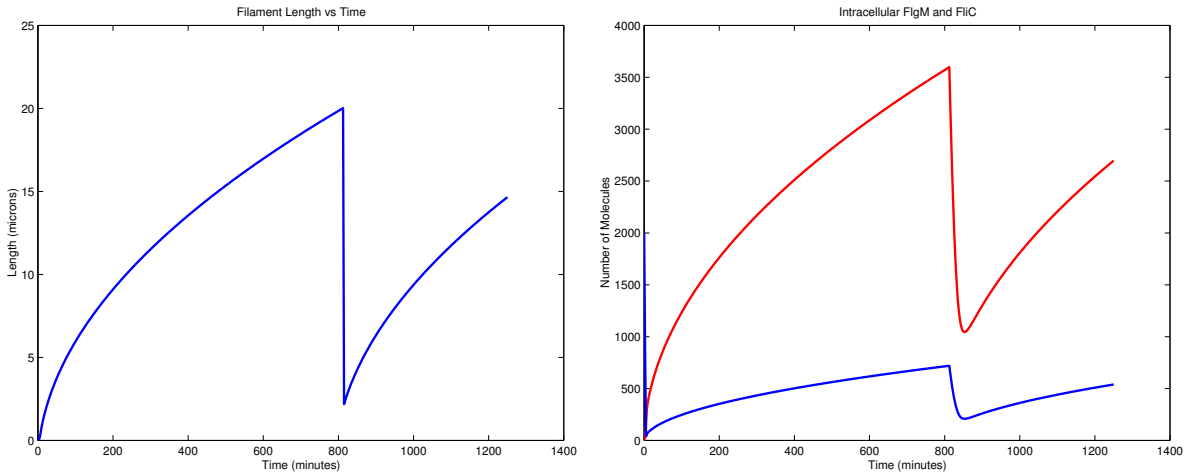


Filament Growth



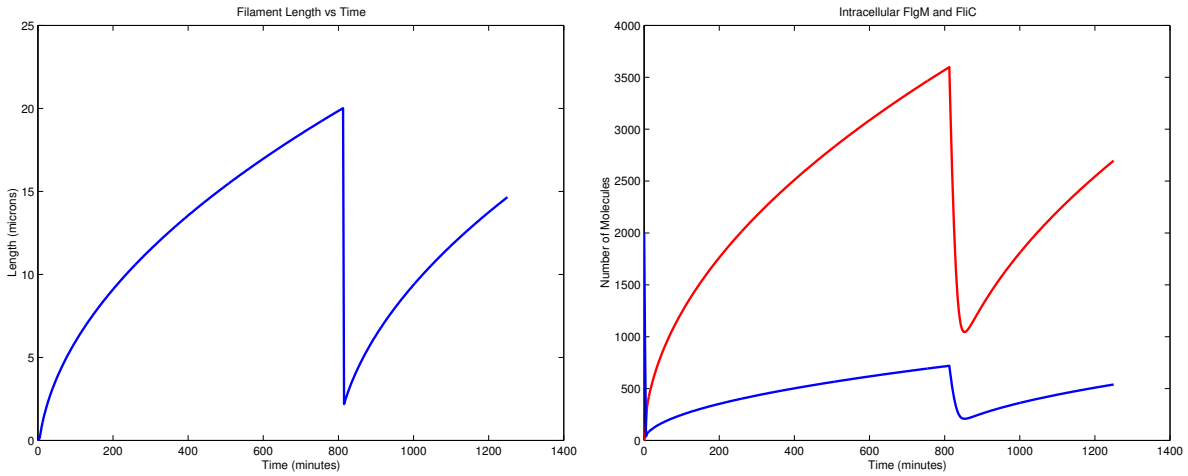
- FlgM concentration is initially large. When secretion begins, FlgM concentration drops, producing FliC and more FlgM.

Filament Growth



- FlgM concentration is initially large. When secretion begins, FlgM concentration drops, producing FliC and more FlgM.
- As filament length grows, secretion slows, FlgM concentration increases, shutting off FliC and FlgM production.

Filament Growth



- FlgM concentration is initially large. When secretion begins, FlgM concentration drops, producing FliC and more FlgM.
- As filament length grows, secretion slows, FlgM concentration increases, shutting off FliC and FlgM production.
- If filament is suddenly shortened, secretion suddenly increases, reinitiating the grow phase.

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The End