Undergraduate Mathematical Sciences Seminar

Modeling Cooperation Between Molecular Motors
Polymer Growth Against a Force

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Outline

Introduction

Conventional Molecular Motors
Polymerization as a Molecular Motor
Why Do We Care?

Current Research

Preliminary Model Set-Up
Polymer Growth Simulations
More Complicated Systems

Future Research

Materials

What are Molecular Motors?

Protein molecules in the cell that:

- generate force
- cause transport

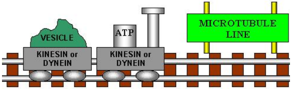
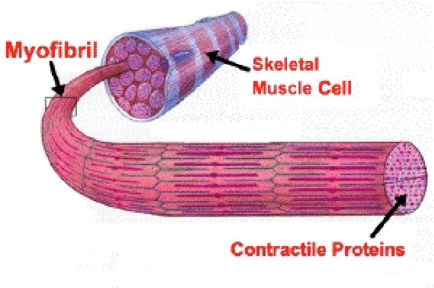
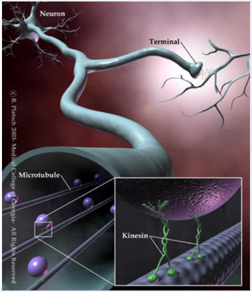


Image (c) MedicalEngineer.co.uk & V F Murphy 2004

Where are Molecular Motors?

Muscle Cells & Neural Cells





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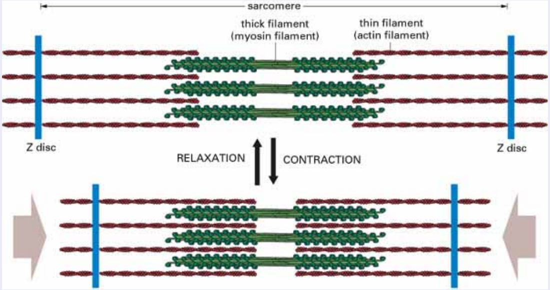
Conventional Molecular Motors

Myosin

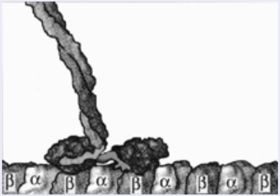
Muscle Contraction



Conventional Molecular Motors

Kinesin

Intracellular Transport

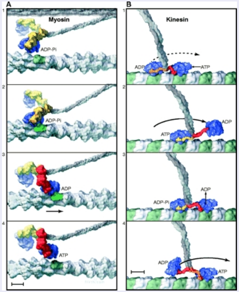


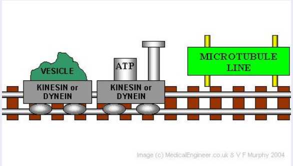
Conventional Molecular Motors

Conventional Molecular Motors

move along polymer tracks

- myosin - actin microfilaments
- kinesin - tubulin microtubules





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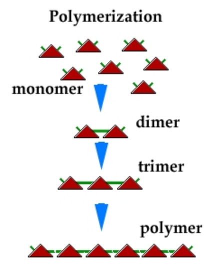
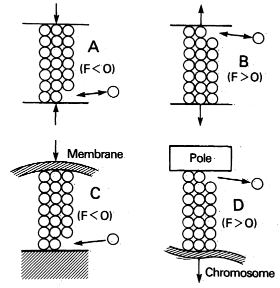
Polymerization as a Motor

Another way to cause motion/transport

- POLYMERIZATION-or-DEPOLYMERIZATION !
- (adding or subtracting monomers)

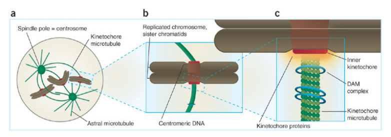


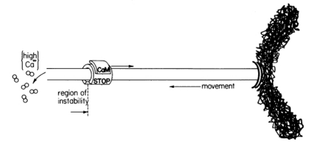


Polymerization as a Motor - Biological Examples

Chromosome Transport During Anaphase

Depolymerization of Spindle Pulls Sister Chromatids Apart:

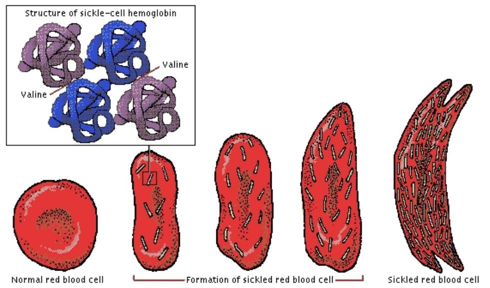


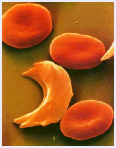


Polymerization as a Motor - Biological Examples

Cell Membrane Deformation

Sickle Hemoglobin Polymerization creates Sickle Cells:





Why Do We Care About Molecular Motors?

Molecular Motors are Special Because:

- Chemical Energy ⇒ Mechanical Energy
  - DIRECTLY! (not via heat or electrical energy)
- Highly Efficient
  - 6 times more efficient than a car
- Models for Molecular Motors ⇒ Nano-Engineering of Future
  - Nano-mechano-chemical Machines
  - Tiny Robots!

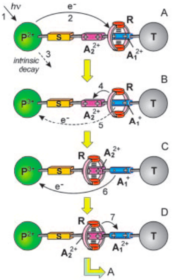
Artificial Nanomotors

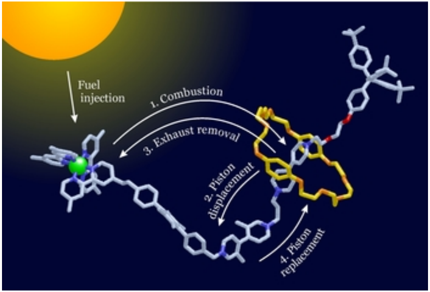
Rotaxane

Vincenzo Balzani et. al. “Autonomous artificial nanomotor powered by sunlight” *PNAS* Vol. 103 No. 5 January 31, 2006.

Rotaxane Molecule:

- ≈ 5 nm long (nm $= 10^{-9}$ meters)
- powered by sunlight (photons)
- operates at 1000 Hz ⇔ 60,000 rpm car engine





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- Preliminary Model Set-Up
- Polymer Growth Simulations
- More Complicated Systems

Future Research

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Basic Polymer Model

How does Polymerization Work?

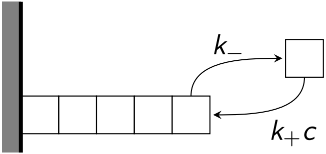
Rate Constants:

k_+: second order rate constant of adding a monomer

k_-: first order rate constant of subtracting a monomer

c: concentration of monomers in surrounding solution

Position of the end of the polymer can be modeled as a 1-D biased random walk.



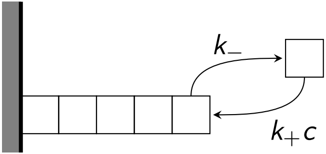
Basic Polymer Model

How does Polymerization Work?

$P_n(t)$: probability length is n at time t

Differential Equation for Polymer Length:

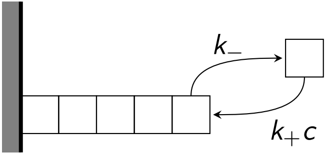
$$\frac{dP_n(t)}{dt} = k_+ c P_{n-1}(t) + k_- P_{n+1}(t) - (k_+ c + k_-) P_n(t)$$



Basic Polymer Model

How does Polymerization Work?

- Deterministic System:
  - Motion is continuous in Space, Time
  - Initial Condition ⇒ one possible trajectory
- Stochastic System:
  - Direction of motion, Time motion occurs - Random
  - Initial Condition ⇒ many possible trajectories



Basic Polymer Model

Stochastic System: Continuous-Time Random Walk

Number of Events in time t is modeled as a Poisson Process with rate:

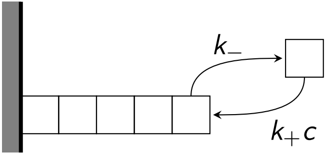
- $\lambda = k_+ c + k_-$

Times between Events have an Exponential Distribution with rate λ.

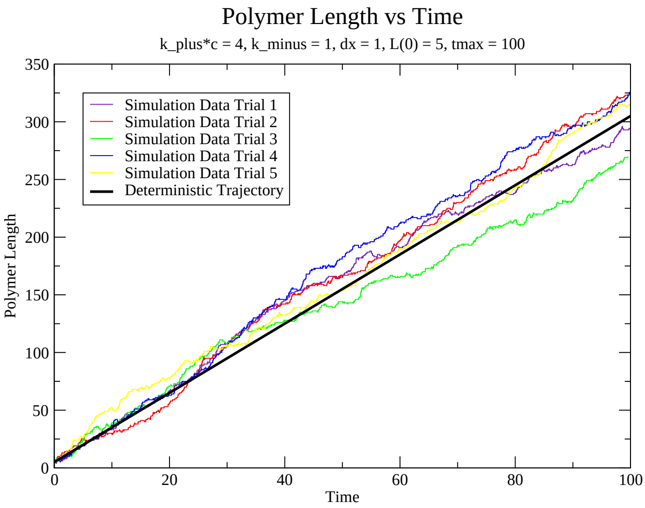
Probability of subtracting or adding a monomer:

- $P(-) = \frac{k_-}{k_- + k_+ c} = \frac{k_-}{\lambda}$
- $P(+) = \frac{k_+ c}{k_- + k_+ c} = \frac{k_+ c}{\lambda}$

$\Rightarrow$ Use this idea to create simulations!



Simulation with One Polymer



Polymer Model with a Moving Wall

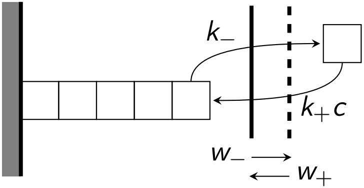
Polymer Interacting with a Moving Wall

Let w be the position of the moving wall.

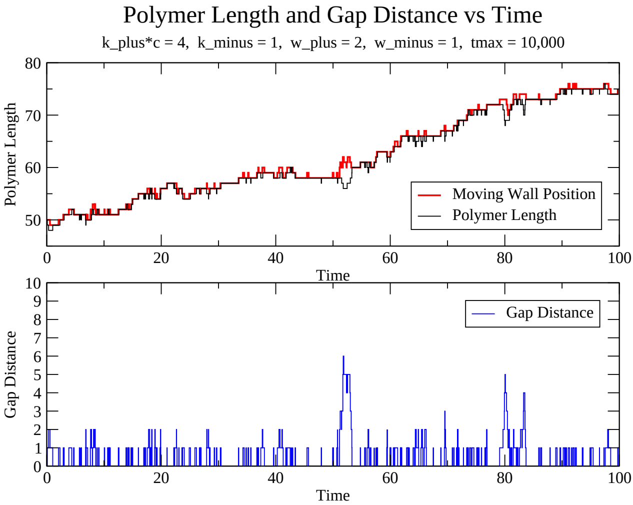
- w_+ - rate that the wall moves towards the polymers
- w_- - rate the wall moves away from the polymers

Additional Constraint, if $w - x < \Delta x$:

- monomer cannot be added.
- wall cannot move towards the polymer.



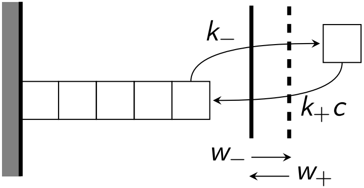
Simulation with One Polymer and a Moving Wall

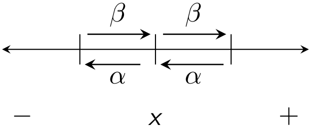


Polymer Model with a Moving Wall

Modeling the Gap Distance

- α - rate gap distance shrinks
  β - rate gap distance grows
  $\alpha = k_+ c + w_+ \qquad \beta = k_- + w_-$
- $p(x,t)$: probability that the gap distance is x at time t
- $p_t(x,t) = \alpha p(x+\Delta x, t) + \beta p(x-\Delta x, t) - (\alpha+\beta) p(x,t)$
- Solve for Steady-State:
  $\Rightarrow p = p(x), \qquad p_t = 0$





Polymer Model with a Moving Wall

Model the Steady-State Gap Distance

- Discrete Space ⇔ Random Walk

$$p_i = \frac{\alpha}{\alpha+\beta} p_{i+1} + \frac{\beta}{\alpha+\beta} p_{i-1} \qquad i > 0$$

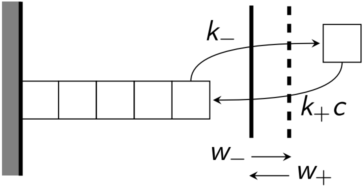
$$\frac{\beta}{\alpha+\beta} p_0 = \frac{\alpha}{\alpha+\beta} p_1 \qquad \text{(B.C. for i=0)}$$

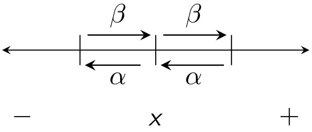
- Continuous Space Limit ⇔ Brownian Motion

$$p_t = Dp_{xx} + Vp_x = 0 \qquad x > 0$$

$$Dp_x + Vp = 0 \qquad \text{(B.C. for x=0)}$$

$$D = \lim_{\Delta x \to 0} (\alpha+\beta) \frac{(\Delta x)^2}{2} \qquad V = \lim_{\Delta x \to 0} (\alpha-\beta)\Delta x$$

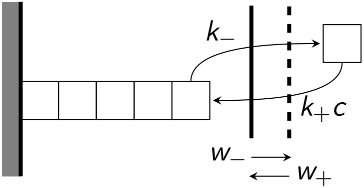


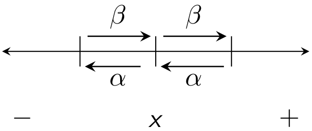


Polymer Model with a Moving Wall

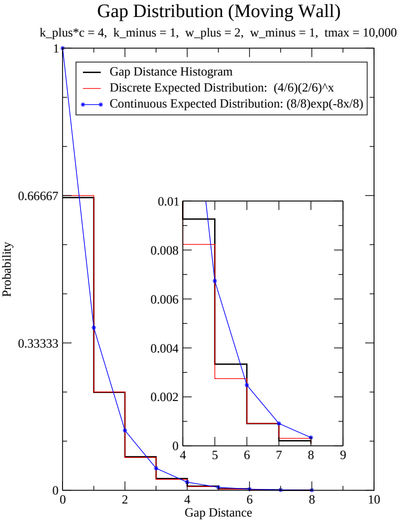
Steady-State Gap Distance

- Discrete Space ⇔ Random Walk
  $\Rightarrow p_i = \frac{\alpha-\beta}{\alpha}\left(\frac{\beta}{\alpha}\right)^i$
- Continuous Space Limit ⇔ Brownian Motion
  $\Rightarrow p(x) = \frac{V}{D} e^{-\frac{V}{D}x}$





Moving Wall Steady State Gap Distance



More Complicated Polymer Model

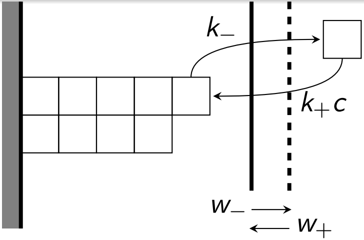
Multiple Polymers Interacting with a Moving Wall

Build upon the basic model and simulations to study a more interesting system:

- N Polymers

Gap distances between each polymer and the wall can be modeled as an N-D biased random walk.

- Special Case: N=2



More Complicated Polymer Model

Multiple Polymers Interacting with a Moving Wall

- Deterministic System:
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  - Initial Condition ⇒ one possible trajectory
- Stochastic System:
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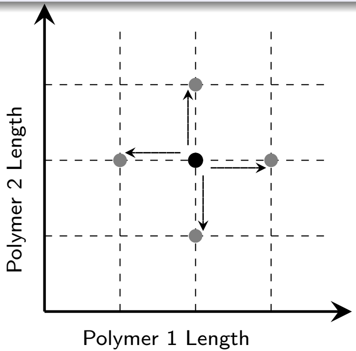
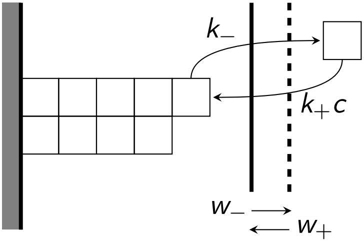


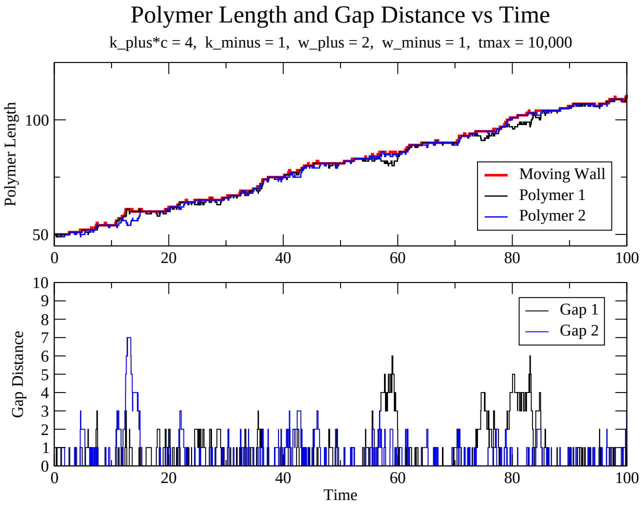
Polymer Growth Simulations

Multiple Polymers Interacting with a Moving Wall

- Gillespie-type Algorithm Generates:
  - Position of each Polymer Tip
  - Position of the Moving Wall
- Simulations can be used to:
  - Investigate the System
  - Compare with Theoretical Results



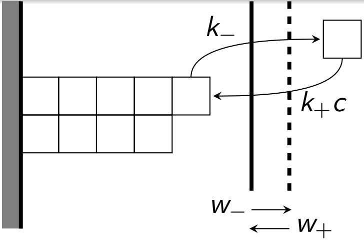
Simulation with Many Polymers



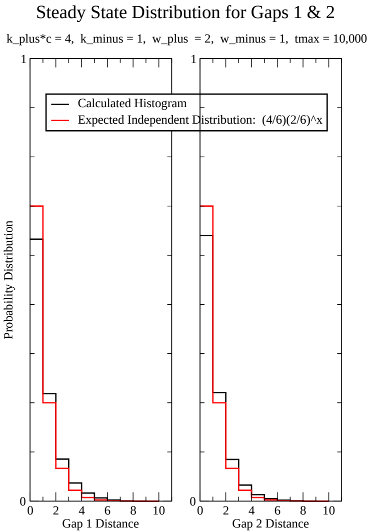
More Complicated Polymer Model

Multiple Polymers Interacting with a Moving Wall

- The Polymers are *Identical*:
  - $k_+ c_{p1} = k_+ c_{p2} = k_+ c$
  - $k_{-p1} = k_{-p2} = k_-$
- Polymers do not *Explicity* Interact
- Are the Polymers *Independent*?
  - *Independent* $\Rightarrow p_i = \frac{\alpha - \beta}{\alpha} \left(\frac{\beta}{\alpha} \right)^i$



Steady State Gap Distribution for 2-Polymer System



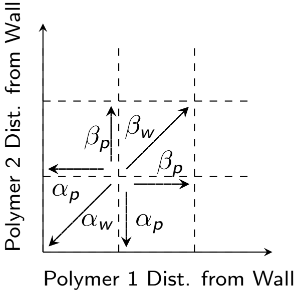
Polymer Cooperation - 2D Random Walk

Polymer Motion from Wall's POV - Gap Distances

Rates of motion are given by:

polymer moves	wall moves	gaps
α_p - towards wall	α_w - towards polymer	shrink
β_p - away from wall	β_w - away from polymer	grow

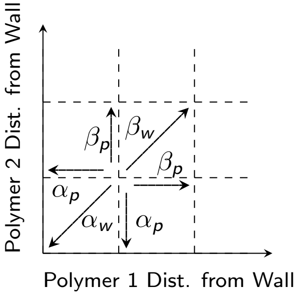
(Origin represents both polymers touching the wall)



Polymer Cooperation - 2D Random Walk

$p(x, y, t)$ - gap 1 distance is x , gap 2 distance is y, at time t

- PDE for Gap Distance Probability
  - $p_t = D_1 (p_{xx} + p_{yy}) + 2D_2 p_{xy} + V (p_x + p_y)$
- No-Flux Boundary Conditions:
  - $J_1(0, y) = D_1 p_x + D_2 p_y + Vp = 0$
  - $J_2(x, 0) = D_1 p_y + D_2 p_x + Vp = 0$
- Solve for Steady-State Solution



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Future Research

Research to be Done

- Finish analysis of 2-Polymer Model
- Generalize to N-Polymer Model
    - Gap Distances ⇒ N+1-D PDE for $p(x_1, x_2, \dots, x_N, t)$
    - N spatial, 1 time
- Mathematical & Biophysical Analysis of N-Polymer Model
- Study Density Function for an N-Polymer Model
    - Gap Distances ⇒ 2-D PDE for $c(x, t)$
    - 1 space, 1 time

Questions?

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Selected References

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Selected References

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Press Release:
http://newsroom.ucla.edu/page.asp?RelNum=6778