Modeling Cooperation Between Molecular Motors
Polymer Growth Against a Force

Christine Lind

University of Washington
Department of Applied Mathematics

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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
Where are Molecular Motors?

Muscle Cells & Neural Cells

Conventional Molecular Motors
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Conventional Molecular Motors

Myosin

Muscle Contraction

[Diagram showing muscle contraction process with sarcomere, thick filament (myosin filament), thin filament (actin filament), Z disc, Relaxation, Contraction]
Kinesin

Intracellular Transport
Conventional Molecular Motors

move along polymer tracks

▶ myosin - actin microfilaments
▶ kinesin - tubulin microtubules
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:
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


Rotaxane Molecule:

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

Probability of subtracting or adding a monomer:

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

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

⇒ Use this idea to create simulations!
Simulation with One Polymer

Polymer Length vs Time

\[ k_{\text{plus}} \cdot c = 4, \quad k_{\text{minus}} = 1, \quad dx = 1, \quad L(0) = 5, \quad t_{\text{max}} = 100 \]
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 Length and Gap Distance vs Time

$k_{\text{plus}}c = 4$, $k_{\text{minus}} = 1$, $w_{\text{plus}} = 2$, $w_{\text{minus}} = 1$, $t_{\text{max}} = 10,000$

- Moving Wall Position
- Polymer Length

- Gap Distance

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Polymer Model with a Moving Wall

Modeling the Gap Distance

- $\alpha$ - rate gap distance shrinks
  $\beta$ - rate gap distance grows
  \[ \alpha = k_+ c + w_+ \quad \beta = k_- + w_- \]

- $p(x, t)$: 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:
  \[ \Rightarrow p = p(x), \quad p_t = 0 \]
Polymer Model with a Moving Wall

Model the Steady-State Gap Distance

- Discrete Space $\Leftrightarrow$ Random Walk
  \[ p_i = \frac{\alpha}{\alpha + \beta} p_{i+1} + \frac{\beta}{\alpha + \beta} p_{i-1} \quad i > 0 \]
  \[ \frac{\beta}{\alpha + \beta} p_0 = \frac{\alpha}{\alpha + \beta} p_1 \quad \text{(B.C. for } i=0) \]

- Continuous Space Limit $\Leftrightarrow$ Brownian Motion
  \[ p_t = D p_{xx} + V p_x = 0 \quad x > 0 \]
  \[ D p_x + V p = 0 \quad \text{(B.C. for } x=0) \]
  \[ D = \lim_{\Delta x \to 0} \frac{(\alpha + \beta)(\Delta x)^2}{2} \quad V = \lim_{\Delta x \to 0} \frac{\alpha - \beta}{\Delta x} \]
Polymer Model with a Moving Wall

**Steady-State Gap Distance**

- **Discrete Space ↔ Random Walk**
  \[ p_i = \frac{\alpha - \beta}{\alpha} \left( \frac{\beta}{\alpha} \right)^i \]

- **Continuous Space Limit ↔ Brownian Motion**
  \[ p(x) = \frac{V}{D} e^{-\frac{V}{D}x} \]
Moving Wall Steady State Gap Distance

Gap Distribution (Moving Wall)

\[ k_{\text{plus}} \times c = 4, \ k_{\text{minus}} = 1, \ w_{\text{plus}} = 2, \ w_{\text{minus}} = 1, \ t_{\text{max}} = 10,000 \]

- Gap Distance Histogram
- Discrete Expected Distribution: \( (4/6)(2/6)^x \)
- Continuous Expected Distribution: \( (8/8)\exp(-8x/8) \)
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:
  - Motion is continuous in Space, Time
  - Initial Condition $\Rightarrow$ one possible trajectory

- Stochastic System:
  - Direction of motion, Time motion occurs - Random
  - Initial Condition $\Rightarrow$ many possible trajectories
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

\[ k_- + c \rightarrow k_+ \]

\[ w_- \rightarrow w_+ \]
Simulation with Many Polymers

Polymer Length and Gap Distance vs Time

$k_{\text{plus}}c = 4$, $k_{\text{minus}} = 1$, $w_{\text{plus}} = 2$, $w_{\text{minus}} = 1$, $t_{\text{max}} = 10,000$
More Complicated Polymer Model

Multiple Polymers Interacting with a Moving Wall

- The Polymers are *Identical*:
  - \( k_+ c_{p1} = k_+ c_{p2} = k_+ c \)
  - \( k_- p_1 = k_- p_2 = k_- \)

- Polymers do not *Explicitly* 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

Steady State Distribution for Gaps 1 & 2

\[ k_{\text{plus}} \cdot c = 4, \quad k_{\text{minus}} = 1, \quad w_{\text{plus}} = 2, \quad w_{\text{minus}} = 1, \quad t_{\text{max}} = 10,000 \]

- Calculated Histogram
- Expected Independent Distribution: \((4/6)(2/6)^x\)
Polymer Cooperation - 2D Random Walk

**Polymer Motion from Wall’s POV - Gap Distances**

Rates of motion are given by:

<table>
<thead>
<tr>
<th>polymer moves</th>
<th>wall moves</th>
<th>gaps</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_p$ - towards wall</td>
<td>$\alpha_w$ - towards polymer</td>
<td>shrink</td>
</tr>
<tr>
<td>$\beta_p$ - away from wall</td>
<td>$\beta_w$ - away from polymer</td>
<td>grow</td>
</tr>
</tbody>
</table>

(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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Diagram showing polymer 1 and polymer 2 distributions from the wall.
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Research to be Done

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