

Chapter 5

Actin Growth, Capping, and Fragmentation

The two ends of an actin filament have different polymerization rate constants. Below we explore the consequences of this fact in simple polymerization reaction, as well as in the presence of capping and fragmentation of the filaments.

5.1 Simple polymerization

Exercise 5.1.1 (Polymerization)

Consider a polymer with two distinct ends that we will denote as “pointed” (p) and “barbed” (b). Let $k_p^+, k_p^-, k_b^+, k_b^-$ be rate constants for monomer addition (+) and loss (-) at each end. Let $a(t)$ be the concentration of monomers that are available to polymerize.

- Write an equation for the rate of change of the monomer concentration. What is the “effective” net monomer on-rate? off-rate? Show that the same equation can be written in terms of constants $a_{\text{crit},b} = k_b^-/k_b^+$ and $a_{\text{crit},p} = k_p^-/k_p^+$. Interpret these constants.
- What is the equilibrium monomer concentration? We will refer to this as a_{crit} . Express this concentration in terms of $a_{\text{crit},b}$ and $a_{\text{crit},p}$.
- How would your answers to (a,b) change if there were N polymers, each with a barbed and a pointed end?
- Suppose the polymer is branched, so that it has 1 pointed and N barbed ends, how would your answers in (a,b) change then? Find a_{crit} when N is very large.

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- (e) Suppose the monomer size is δ . Find the rate at which the single linear polymer with “treadmill” (add monomer at one end and lose monomer at the same rate at the other end). We will refer to this as the “treadmilling velocity”.
- (f) Find values for the rate constants for actin, tubulin, and MreB and use these to estimate the critical concentration of each of these polymers. (See Table 1 in this chapter.)

5.2 Simple polymer length distribution

A number of papers have described size distributions of growing polymers. These include Edelstein-Keshet and Ermentrout [7], Ermentrout and Edelstein-Keshet [8] for actin polymers with and without fragmentation and end-capping by gelsolin. (Edelstein-Keshet and Ermentrout [5] also describe how such events would lead to spatial and length distributions of polymers in a 1D model of the cellular extension called the lamellipod.) Masel et al. [15] (and other papers by these authors) have modeled the growth and fragmentation of prion fibers. Nucleation, stabilization, and growth and breakage of yeast prion protein, Sup35 has also been modeled by Collins et al. [4], who found good fit between model and observed data. Finally, Craft et al. [3] investigated a model that was based on single monomer addition and loss from amyloid-beta fibers in the brain (with exchange of monomers from other compartments such as blood and cerebro-spinal fluid (CSF)).

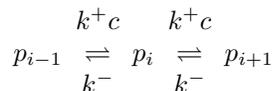
The simplest case to consider is filament growth by single monomer events. In such cases, it can be shown that the size distribution is exponentially decreasing in length. The initiation and extent of the lab phase of growth depends on the way that the first stable nuclei are formed.

Let

$p_i(t)$ = number of polymers having i monomer subunits at time t .

Let $c(t)$ be concentration of monomers. Polymers would consist of two or more monomers that are bound together. Now consider the growth dynamics of p_i , assuming that a single monomer is added or lost at increment.

The scheme we consider is as follows:



Transitions to the right involve an encounter between an existing polymer and a free monomer. According to the Law of Mass Action, the rate of such reactions is proportional to the concentration of reactants, i.e. to c and p_i . We use the notation k^+ to denote the constant of proportionality. Thus, the rate of adding a monomer to the growing polymer is k^+c per unit time. Transitions to the left are loss of monomer from a polymer, decreasing its size. We assume this happens at some constant rate, k^- . (Note that k^+ and k^- have different units, and that we consider these to be “effective rates” that incorporate both the pointed and barbed end kinetics.)

We could consider two different interesting situations: either (1) the free monomer concentration is held fixed artificially, or (2) it is used up and depleted by the polymerization reactions. We can represent both cases by an equation of the form

$$\frac{dc}{dt} = a_{\text{depl}}(k^- - k^+c)N_p$$

where in Case (1), $a_{\text{depl}} = 0$ for monomer that is held at a constant level, whereas in case (2), $a_{\text{depl}} = 1$. Here N_p is the total number of pieces. Note that

in case (2), the total amount of material (in all forms) is conserved.

Exercise 5.2.2 (The discrete polymer length distribution)

We first explore the equations of a model for the length distribution.

- (a) Motivate the following equation for the evolution of the number of polymers of size i :

$$\frac{dp_i}{dt} = k^+ c p_{i-1} - (k^+ c + k^-) p_i + k^- p_{i+1} \quad (5.1)$$

Here we assume that the integer i is larger than some value needed to start off the process. Rewrite this equation in terms of the critical concentration $c_{crit} = k^-/k^+$.

- (b) Let A be the total amount of monomer in all forms. How do we express A as a summation in terms of the polymer size distribution p_i and monomer concentration c ? Similarly, what is the total number of polymer pieces (sizes larger than 1 monomer) and what is their average length?
- (c) By regrouping terms in Eqn. (5.1), show that it can be written in an equivalent form,

$$\frac{dp_i}{dt} = \frac{1}{2}(k^+ c + k^-) [p_{i-1} - 2p_i + p_{i+1}] - (k^+ c - k^-) \frac{[p_{i+1} - p_{i-1}]}{2} \quad (5.2)$$

- (d) Eqn. (5.2) is a discrete convection-diffusion equation (in size space, i.e. with discrete size increments). What are the effective diffusion and transport rates?

Exercise 5.2.3 (Monomer held at a constant level)

We consider a steady-state length distribution in the case where the monomer level is held fixed.

- (a) Consider the steady state of Eqn. (5.1), i.e. set $dp_i/dt = 0$. In the case that the monomer c is constant, this leads to a so-called linear difference equation, which can be solved by a standard method. Make the substitution

$$p_i = Cr^i,$$

and find the possible values of r by simplifying and solving the resulting quadratic equation.

- (b) One of the solutions you found in (b) must be rejected, because it would correspond to an infinite amount of material. Which solution is the biologically reasonable one?
- (c) We now consider possible boundary conditions that prescribe how the whole polymerization reaction is started. In a paper about amyloid, Craft, Wein and Selkoe assume that the process starts off from dimers. These can lose monomer in only one way, compared with all larger polymers so that the effective reverse constant for dimers is $(1/2)k_r$, leading to the equation

$$\frac{dp_2}{dt} = ck_f p_1 - (ck_f + \frac{1}{2}k_r)p_2 + k_r p_3 \quad (5.3)$$

Use the previous results and the steady state assumption for this equation to show that in this case, the number of dimers at steady state is:

$$p_2 = Br^2 = 2c(c/c_{crit})$$

- (d) What is the average length of the polymers in this case?

Now suppose that monomers are being depleted when the polymers grow, $a_{depl} = 1$ (case(2)) so that monomers obey

$$\frac{dc}{dt} = (k_r - k_f c)N_p.$$

Directly from this equation, we note that monomer will be at steady state either if $N_p = 0$, i.e. no polymer exists, or else if $c = k_r/k_f = c_{crit}$ when the monomer level equilibrates at its critical concentration. We also use the following version of the polymer size distribution to draw conclusions about the time behaviour of the dynamics in the case that monomer is being depleted.

$$\frac{dp_i}{dt} = k_f (-c(p_i - p_{i-1}) + c_{crit}(p_{i+1} - p_i).) \quad (5.4)$$

Exercise 5.2.4 (Depleted monomer)

Consider Eqn. (5.4) at the beginning and near the end of the reaction.

- (a) Suppose initially, the monomer level is much higher than its critical concentration $c \gg c_{crit}$. Show that the size distribution appears to satisfy a (discrete) drift equation, i.e. the distribution just shifts to larger sizes without changing its shape.
- (b) Later on, monomer level is depleted. Show that as $c \rightarrow c_{crit}$, the polymer size distribution appears to satisfy a (discrete) diffusion equation. This means that the distribution grows broader, without changing its mean.

5.3 Continuous length distribution

Let $c(\ell, t)$ be the density of polymer of length ℓ , so defined that

$$\int_{\ell_1}^{\ell_2} c(s, t) ds$$

is the number of polymers with lengths $\ell_1 \leq \ell \leq \ell_2$.

Exercise 5.3.5 (Length Distributions)

- (a) Let δ be monomer size. Explain and motivate the equation

$$\frac{\partial c(\ell, t)}{\partial t} = k^+ a c(\ell - \delta, t) - (k^+ a + k^-) c(\ell, t) + k^- c(\ell + \delta, t).$$

- (b) Use Taylor series expansions up to second order to show that this equation can be put into the form of a drift-diffusion equation,

$$\frac{\partial c(\ell, t)}{\partial t} = D \frac{\partial^2 c}{\partial \ell^2} - v \frac{\partial c}{\partial \ell}.$$

How do the constants D, v depend on the parameters and the actin monomer concentration?

5.4 Simulating polymer length distribution in XPP

The following file can be used to experiment with the growth of a polymer size distribution.

```
# asizedis.ode
# polymer size distribution
# simple polymerization
# Mar 4, 2006

# xj= number of fibers of length j
# a= conc of monomers
# kf, kr = forward and reverse rate constants

par kf=10, kr=1, kinit=0.005, adepl=1
a(0)=20
sm99=x100
```

```

sm[98..2]=sm[j+1]+x[j+1]

#eqn for monomers:
# Set adepl=1 for constant total amt, 0 for fixed monomer level
a' = adepl*(-kf*a*(sm2-x100+x2)+kr*(sm2+x2))

# initialization from dimers
x1'= kinit*a*a+kr*x2-kf*a*x1
x[2..99]'= kf*a*(x[j-1]-x[j])+kr*(x[j+1]-x[j])
x100' = -kr*x100+kf*a*x99

#Computing the total number of fibers
Nf=sm2+x2+x1
aux Ntotal=Nf

# computing the total and mean length of fibers
p1=sum(2,100)of(i'*shift(x2,i'-2))+x1
aux Lttotal=p1
aux Lmean=p1/(Nf+1e-8)
@ bounds=10000000, meth=gear, dt=0.005, total=10
done

```

The other material in this chapter was not discussed in class. Feel free to either skip it or to independently discover it, with help if needed.

5.5 Length distribution at the leading edge of a cell

We now consider a spacial length distribution of actin filaments, assuming that most of the actively growing barbed ends are at the leading edge membrane of the cell. We consider what happens if some protein such as gelsolin cuts the filaments somewhere along their length. If this happens, generally the newly cut ends are not too useful in growing: gelsolin caps the barbed end of an actin filament, preventing it from adding monomers. (The pointed end is very slow-growing, or not growing at all).

We define the following notation:

$a(x, t)$	Concentration of actin monomers at position x and time t
$b_a(x, l, t)$	Density of active barbed ends of length l filaments at x
g	Concentration of actin filament chopper
$P(l)$	Filament cutting probability at distance l from an active barbed end

An active barbed end can undergo these transitions:

$$b_a(x, l, t) \begin{cases} \rightarrow b_a(x + \delta, l + \delta, t + dt) & \text{polymerization of barbed end} \\ \rightarrow b_a(x, l - \delta, t + dt) & \text{depolymerization of pointed end} \end{cases}$$

For simplicity, we will assume that the pointed ends have very slow kinetics, and we ignore their contribution to the growth or shrinkage of the filaments. We also ignore what happens to the capped filaments, as they get left behind and, soon, do not contribute to the density at the edge.

If the filaments are cut and then capped at the new barbed end, then

$$\frac{\partial b_a(x, l, t)}{\partial t} = v[b_a(x - \delta, l - \delta, t) - b_a(x, l, t)] \quad (5.5)$$

$$+ gP(l) \int_l^\infty b_a(x, s, t) ds$$

$$- gb_a(x, l, t) \int_0^l P(s) ds, \quad (5.6)$$

where v is the barbed end rate of polymerization and/or depolymerization, $P(l)$ is the probability that a filament is cut at a distance l away from its barbed end, x_{max} is the position of the leading edge of the cell.

Exercise 5.5.6 (Cut but not cap)

How would this equation change in the case where there is cutting but no capping?

We investigate Eqn. (5.6). We first transform the equations to a coordinate frame moving with constant velocity, v_b . The leading edge will now be "frozen" at $x = 0$ and Eqn. (5.6) will be independent of x so that $b_a(x, l, t) = \Lambda(x)B_a(l, t)$. We look at the length-dependent part, and approximate the finite differences using terms in a Taylor series expansion:

$$\frac{\partial b_a(l, t)}{\partial t} = -\frac{\partial}{\partial l} b_a v \delta + gP(l) \int_l^\infty b_a(s, t) ds - gb_a(l, t) \int_0^l P(s) ds. \quad (5.7)$$

Define the new variables

$$z(l, t) = \int_l^\infty b_a(s, t) ds,$$

$$F(l) = \int_0^l P(s) ds.$$

$z(l)$ is the density of active filament ends with filaments longer than l ; $F(l)$ is a cumulative probability that a filament will be broken at any position up to a distance l from its barbed end.

Exercise 5.5.7 (Analysis of the length distribution)

Here we will look for a steady state length distribution. By changing variables, we find a neat trick for solving the resulting ODE

- (a) Express Eqn. (5.7) in terms of z and $F(l)$.
- (b) Argue that $dz/dl = -b_a(l, t)$. Differentiate again and express d^2z/dl^2 in terms of $P(l)$, z , $F(l)$ and b_a .
- (c) Use the results to eliminate b_a from the equation for d^2z/dl^2 and show that you arrive at

$$\frac{d^2z}{dl^2} = -\frac{g}{v} \frac{d(Fz)}{dl}$$

- (d) Integrate this equation and use the fact that $b_a \rightarrow 0, z \rightarrow 0$ as $l \rightarrow \infty$ to establish that

$$z(l) = Z_o \exp\left(-\frac{g}{c} \int_0^l F(s) ds\right).$$

Now find $b_a(l)$.

Exercise 5.5.8 (Length-dependent cutting probability)

Investigate the following three possibilities for how the cutting probability depends on the position along the filament:

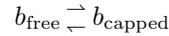
- (a) $P(l) = \text{constant} = p$.
- (b) $P(l) = ql$ is linearly increasing along the filament
- (c) $P(l) = (1 - \exp(-kl/z))$

5.6 The effect of capping

Because the barbed ends of actin filaments grow very quickly, there are proteins that bind to those ends and “cap them” to halt that growth. Capping proteins have a high affinity to barbed ends, and in a cell, they attach rapidly to actin filament ends that are not in a protected environment. (The proximity of the cell membrane provides a protected environment.) Here we explore the effect of capping proteins on the fraction of free barbed ends that are available to bind monomers.

Exercise 5.6.9 (Polymerization with capping)

Consider polymerization in the presence of a capping protein, and suppose that the “barbed ends” of actin filaments can be in either capped or uncapped form, with transitions:



Let $k_{\text{cap}}^B, k_{\text{uncap}}^B$ be the relevant rates of these transitions.

- (a) Show that the fraction of free barbed ends (at equilibrium) is

$$\eta_B = \frac{k_{\text{uncap}}^B}{k_{\text{cap}}^B + k_{\text{uncap}}^B}$$

- (b) Show that at equilibrium, this type of capping reaction leads to an actin treadmilling concentration of

$$a_{\text{tr}} = \frac{(k_p^+ a_{\text{crit,p}} + \eta_B k_b^+ a_{\text{crit,b}})}{(k_p^+ + \eta_B k_b^+)}. \quad (5.8)$$

- (c) Let N, N^u be the total number of actin filaments and the number that are uncapped. Use the definition of η_B to show that in the presence of uncapping,

$$\frac{d\eta_B}{dt} = k_{\text{uncap}}^B(1 - \eta_B)$$

5.7 Uncapping and Severing have similar effects

It was pointed out by Carlsson [2] that uncapping and severing have a functionally similar role as far as their effect on the fraction of uncapped barbed ends (η_B). Here we explore this assertion.

Exercise 5.7.10 (Severing and uncapping)

Suppose that filaments are cut at rate $k_{\text{sev}}\ell$ where ℓ =average filament length in

terms of number of subunits. Note that when filaments are cut, both the total number of filaments, N , and the number of uncapped filaments N^u increase.

Show that severing leads to a change in the fraction of free barbed ends as follows:

$$\frac{d\eta_B}{dt} = k_{\text{sev}}\ell(1 - \eta_B).$$

Observe that this is the same type of functional effect as uncapping, as found in Problem 5.5.9. What is the rate of change of η_B when both uncapping and severing take place?

In order to fully characterize the dynamics of the fraction of free barbed ends, η_B , we need to determine the average length of the actin filaments, ℓ . According to [2], it can be shown that

$$\ell = \sqrt{\frac{k_p^+(a_{\text{crit,p}} - a)}{k_{\text{sev}}}}$$

Exercise 5.7.11 (Average filament length and effective uncapping)

Carlsson assumes that the rate of change of the number of filaments is

$$\frac{dN}{dt} = k_{\text{sev}}\ell N - \frac{N}{\tau_{\text{depol}}},$$

where τ_{depol} is the depolarization time. Justify this equation. Then use it to establish the above formula. Use the speed of depolymerization of the filament (at its pointed end, assuming that its barbed end is capped).

With this result, find the effective uncapping rate when both severing and uncapping is present.

5.8 Severing and Capping Together

Exercise 5.8.12 (Severing and capping enhances polymerization)

- Proceeding from Eqn. 5.8, find the change in a_{tr} that occurs when the fraction of free barbed ends increases.
- Find the way that the fraction of free barbed ends changes when the uncapping rate changes.
- Show that in the presence of capping, the effect of severing the filaments is to increase the fraction of free barbed ends by

$$\Delta\eta_B = \frac{k_{\text{cap}}^B \sqrt{k_{\text{sev}}(a_{\text{crit,p}} - a_{\text{tr}})}}{(k_{\text{cap}}^B + k_{\text{uncap}}^B)^2}$$

- Use the results of parts (a-c) to argue that in the presence of capping, severing leads to enhanced polymerization. (Hint: note the signs of terms in braces. Show that the critical concentration of actin monomers decreases, enhancing polymerization, when there is some severing of filaments.)

5.9 Parameter Values

Table I. Actin related parameters

Symbol	Value	Meaning	Reference
δ	2.2 nm	filament length increment per monomer	[12]
L	$\simeq 10 \mu\text{m}$	length of lamellipod	[20]
k_b^+	$11.6 \mu\text{M}^{-1}\text{sec}^{-1}$	barbed-end monomer assembly rate constant	[16]
k_b^-	1.4sec^{-1}	barbed-end monomer off rate constant	[16]
k_p^+	$1.3 \mu\text{M}^{-1}\text{sec}^{-1}$	pointed-end monomer assembly rate constant	[16]
k_p^-	0.8sec^{-1}	pointed-end monomer off rate constant	[16]
γ_c	4sec^{-1}	barbed-end capping rate in cytoplasm	[19, 15]
γ	-- [sec^{-1}]	barbed end capping rate at leading edge	value unknown
n	-- [$\mu\text{M}^{-2}\text{sec}^{-1}$]	Arp2/3 nucleation rate	value unknown
L_n	$\sim 1 \mu\text{m}$	width of nucleation zone	speculative
D	$30 \mu\text{m}^2/\text{sec}$	diffusion coefficient of G-actin complexes	[1];
η	$100 \mu\text{M}^{-1}\mu\text{m}^{-2}$	conversion factor	[12]
F	$\sim 100 \text{pN}/\mu\text{m}$	membrane resistance force per unit edge length	[4, 5, 17, 8, 14]
$k_B T$	$\simeq 4.1 \text{pN} \cdot \text{nm}$	thermal energy	[13]
A	$\sim 250 \mu\text{M}$	total lamellipodial actin concentration	[15]
r	$\sim 1/(30 \text{sec})$	effective rate of actin filament disassembly	[15]

The material is based on: [7, 6, 9] and on Recent articles: [18, 3, 11, 2, 10]

Bibliography

AE Carlsson. Stimulation of Actin Polymerization by Filament Severing. *Biophysical Journal*, 90(2):413–422, 2006.

AE Carlsson. Disassembly of actin networks by filament severing. *New Journal of Physics*, 9, 2007.

Craft DL, Wein LM, Selkoe DJ. (2002) A mathematical model of the impact of novel treatments on the A beta burden in the Alzheimer’s brain, CSF and plasma. *Bull Math Biol.* 64(5):1011-31.

Collins SR, Douglass A, Vale RE, Weissmann JS (2004) Mechanism of prion propagation: amyloid growth occurs by monomer addition, *PLoS Biology*, 2: 1582–1590.

Edelstein-Keshet L, Ermentrout GB. (2001) A model for actin-filament length distribution in a lamellipod. *J Math Biol.* 43(4):325-55.

Edelstein-Keshet L, Ermentrout GB. (2000) Models for spatial polymerization dynamics of rod-like polymers. *J Math Biol.* 40(1):64-96.

Edelstein-Keshet L, Ermentrout GB. (1998) Models for the length distributions of actin filaments: I. Simple polymerization and fragmentation. *Bull Math Biol.* 60(3):449–75.

Ermentrout GB, Edelstein-Keshet L. (1998) Models for the length distributions of actin filaments: II. Polymerization and fragmentation by gelsolin acting together. *Bull Math Biol.* 60(3):477–503.

Flyvbjerg, H., Jobs, E., and Leibler, S. (1996) Kinetics of self-assembling microtubules: An "inverse problem" in biochemistry. *Proc. Natl. Acad. Sci.* 93: 5975–5979.

A. Gopinathan, K.C. Lee, JM Schwarz, and A.J. Liu. Branching, Capping, and Severing in Dynamic Actin Structures. *Arxiv preprint cond-mat/0703409*, 2007.

NS Gov. Theory of the length distribution of tread-milling actin filaments inside bundles. *Europhysics letters(Print)*, 77(6), 2007.

Masel J, Jansen VA (2001) The measured level of prion infectivity varies in a predictable way according to the aggregation state of the infectious agent. *Biochim Biophys Acta.*1535(2):164 –73.

Masel J, Jansen VA. (2000) Designing drugs to stop the formation of prion aggregates and other amyloids. *Biophys Chem.* 88(1-3):47-59.

Masel J, Jansen VA. (1999) The kinetics of proteinase K digestion of linear prion polymers. *Proc Biol Sci.* 266(1431):1927-31.

Masel, J., V. A. A. Jansen, and M. A. Nowak. (1999) Quantifying the kinetic parameters of prion replication. *Biophys. Chem.* 77:139-152.

Thomas D. Pollard. Rate constants for the reactions of ATP- and ADP- actin with the ends of actin filaments. *J Cell Biol*, 103 (6 pt 2):2747-2754, 1986.

D. A. Schafer, P B Jennings, and J A Cooper. Dynamics of capping protein and actin assembly in vitro: uncapping barbed ends by polyphosphoinositides. *J. Cell Biol.*, 135:169-179, 1996.

Bibliography

- [1] V C Abraham, V Krishnamurthi, D L Taylor, and F Lanni. The actin-based nanomachine at the leading edge of migrating cells. *Biophys J*, 77:1721–1732, 1999.
- [2] AE Carlsson. Stimulation of Actin Polymerization by Filament Severing. *Biophysical Journal*, 90(2):413–422, 2006.
- [3] AE Carlsson. Disassembly of actin networks by filament severing. *New Journal of Physics*, 9, 2007.
- [4] J Dai, M P Sheetz, X Wan, and C E Morris. Membrane tension in swelling and shrinking molluscan neurons. *J Neurosci*, 18(17):6681–6692, 1998.
- [5] J W Dai and M P Sheetz. Membrane tether formation from blebbing cells. *Biophys J*, 77(6):3363–3370, 1999.
- [6] L. Edelstein-Keshet and G.B. Ermentrout. Models for the length distributions of actin filaments: I. Simple polymerization and fragmentation. *Bulletin of Mathematical Biology*, 60(3):449–475, 1998.
- [7] L. Edelstein-Keshet and G.B. Ermentrout. A model for actin-filament length distribution in a lamellipod. *Journal of Mathematical Biology*, 43(4):325–355, 2001.
- [8] C A Erickson. The deformability of BHK cells in relation to locomotory behavior. *J. Cell Sci.*, 44:187–200, 1980.
- [9] G.B. Ermentrout and L. Edelstein-Keshet. Models for the length distributions of actin filaments: II. Polymerization and fragmentation by gelsolin acting together. *Bulletin of Mathematical Biology*, 60(3):477–503, 1998.
- [10] A. Gopinathan, K.C. Lee, JM Schwarz, and A.J. Liu. Branching, Capping, and Severing in Dynamic Actin Structures. *Arxiv preprint cond-mat/0703409*, 2007.
- [11] NS Gov. Theory of the length distribution of tread-milling actin filaments inside bundles. *Europhysics letters(Print)*, 77(6), 2007.

- [12] A. Mogilner and L. Edelstein-Keshet. Regulation of Actin Dynamics in Rapidly Moving Cells: A Quantitative Analysis. *Biophysical Journal*, 83(3):1237–1258, 2002.
- [13] C Peskin, G Odell, and G Oster. Cellular motions and thermal fluctuations: The brownian ratchet. *Biophys J*, 65:316–324, 1993.
- [14] N O Petersen, W B McConnaughey, and E Elson. Dependence of locally measured cell deformability on position of the cell, temperature and cytochalasin b. *Proc. Natl. Acad. Sci. USA*, 79:5327–5331, 1982.
- [15] T D Pollard, L Blanchoin, and R D Mullins. Molecular mechanisms controlling actin filament dynamics in nonmuscle cells. *Annu Rev Biophys Biomol Struct*, 29:545–576, 2000.
- [16] Thomas D. Pollard. Rate constants for the reactions of ATP- and ADP-actin with the ends of actin filaments. *J Cell Biol*, 103 (6 pt 2):2747–2754, 1986.
- [17] D Raucher and M P Sheetz. Membrane expansion increases endocytosis rate during mitosis. *J Cell Biol*, 144(3):497–506, 1999.
- [18] J. Roland, J. Berro, A. Michelot, L. Blanchoin, and J.L. Martiel. Stochastic severing of actin filaments by ADF/cofilin controls the emergence of a steady dynamical regime. *Biophysical Journal*, 2007.
- [19] D. A. Schafer, P B Jennings, and J A Cooper. Dynamics of capping protein and actin assembly in vitro: uncapping barbed ends by polyphosphoinositides. *J. Cell Biol.*, 135:169–179, 1996.
- [20] T M Svitkina, A B Verhovskiy, K M McQuade, and G G Borisy. Analysis of the actin-myosin II system in fish epidermal keratocytes: mechanism of cell body translocation. *J Cell Biol*, 139:397–415, 1997.