

SUPPORTING MATERIAL

A. Numerical Method for Growth Rates.

Here we describe the numerical method we used in the main text to calculate the growth rate curves of Figs. 3 and 4. Consider an ATP-actin monomer that polymerizes at the filament tip at time $t = 0$. We define the return probabilities ψ_t^T , ψ_t^P , and ψ_t^D to be the probability that this monomer is once again at the tip after time t as ATP-actin, ADP-Pi-actin, or ADP-actin, respectively. The total depolymerization rate of this monomer at time t is

$$F_t = v_{\bar{T}}\psi_t^T + v_{\bar{P}}\psi_t^P + v_{\bar{D}}\psi_t^D . \quad (1)$$

The dynamical equations obeyed by the return probabilities are

$$\begin{aligned} \frac{d}{dt}\psi_t^T &= -(k_{\bar{T}}^+c + v_{\bar{T}} + r_H)\psi_t^T + k_{\bar{T}}^+c \int_0^t dt' \psi_{t-t'}^T F_{t-t'} e^{-r_H(t-t')} , \\ \frac{d}{dt}\psi_t^P &= -(k_{\bar{T}}^+c + v_{\bar{P}} + r_{Pi})\psi_t^P + r_H\psi_t^T + k_{\bar{T}}^+c \int_0^t dt' \psi_{t-t'}^P F_{t-t'} e^{-r_{Pi}(t-t')} \\ &\quad + k_{\bar{T}}^+c \int_0^t dt' \psi_{t-t'}^T F_{t-t'} \frac{r_H}{r_{Pi} - r_H} \left(e^{-r_H(t-t')} - e^{-r_{Pi}(t-t')} \right) , \\ \frac{d}{dt}\psi_t^D &= -(k_{\bar{T}}^+c + v_{\bar{D}})\psi_t^D + r_{Pi}\psi_t^P + k_{\bar{T}}^+c \int_0^t dt' \psi_{t-t'}^D F_{t-t'} + k_{\bar{T}}^+c \int_0^t dt' \psi_{t-t'}^P F_{t-t'} \left(1 - e^{-r_{Pi}(t-t')} \right) \\ &\quad + k_{\bar{T}}^+c \int_0^t dt' \psi_{t-t'}^T F_{t-t'} \left(1 - \frac{r_{Pi}}{r_{Pi} - r_H} e^{-r_H(t-t')} + \frac{r_H}{r_{Pi} - r_H} e^{-r_{Pi}(t-t')} \right) . \end{aligned} \quad (2)$$

Here the non-integral terms on the right-hand sides represent change of tip status due to polymerization, depolymerization, hydrolysis, and phosphate release events at time t . The integral terms represent rates of reappearance of the monomer at the tip, weighted by factors accounting for the probability of hydrolysis or phosphate release during the time interval since the last appearance at the tip. For example, the first term on the right-hand side of the first equation represents the rate of change of the probability of finding the ATP-actin monomer at the tip due to (i) polymerization of another monomer on top of it, (ii) depolymerization of the monomer itself, or (iii) hydrolysis of the ATP nucleotide bound to the monomer at the tip. The integral term on the right-hand side represents reappearance events of the ATP-actin unit at the tip given that it got buried inside the filament due to a polymerization event at time t' , an event that occurred with rate $k_{\bar{T}}^+c$. Factor F represents the rate of reappearance of the buried monomer at the tip due to depolymerization of all the monomers that were added on top of it. The factor $e^{-r_H(t-t')}$ is the probability that the ATP-actin monomer in question is not hydrolyzed while being buried.

Now the filament growth rate is given by

$$j = \begin{cases} v_{\bar{D}} \left[1 - \int_0^\infty dt (\psi_t^D + \psi_t^P + \psi_t^T) \right] & (j < 0) \\ k_{\bar{T}}^+c - \int_0^\infty dt F_t & (j > 0) \end{cases} . \quad (3)$$

Carrying out a Laplace transformation, $t \rightarrow E$, $F_t \rightarrow f_E$, and $\psi_t \rightarrow \Psi_E$ one has from Eq. 3

$$j = \begin{cases} v_{\bar{D}} \left[1 - \Psi_0^D - \Psi_0^P - \Psi_0^T \right] & (j < 0) \\ k_{\bar{T}}^+c - f_0 & (j > 0) \end{cases} \quad (4)$$

while from Eq. 2 one obtains

$$\Psi_E^T = 1 / \left(E + v_{\bar{T}} + r_H + k_{\bar{T}}^+c(1 - f_{E+r_H}) \right) ,$$

$$\begin{aligned}\Psi_E^P &= \frac{r_H + k_T^+ c r_H (f_{E+r_H} - f_{E+r_{P_i}}) / (r_{P_i} - r_H)}{E + v_{\bar{P}} + r_{P_i} + k_T^+ c (1 - f_{E+r_{P_i}})} \Psi_E^T, \\ \Psi_E^D &= \frac{(r_{P_i} + k_T^+ c (f_E - f_{E+r_{P_i}})) \Psi_E^P + k_T^+ c (f_E - r_{P_i} f_{E+r_H} / (r_{P_i} - r_H) + r_H f_{E+r_{P_i}} / (r_{P_i} - r_H)) \Psi_E^T}{E + v_{\bar{D}} + k_T^+ c (1 - f_E)}\end{aligned}\quad (5)$$

Eliminating all Ψ in the Laplace transformation of Eq. 1 after using Eq. 5 one obtains the following recursive relationship involving the function f alone:

$$f_E = \mathcal{R}[f_{E+r_H}, f_{E+r_{P_i}}], \quad (6)$$

where

$$\mathcal{R}[f_{E+r_H}, f_{E+r_{P_i}}] = \frac{-b_1 + \sqrt{b_1^2 - 4b_2 b_0}}{2b_2}. \quad (7)$$

Here the symbols b_0 , b_1 , and b_2 are functions of E , f_{E+r_H} and $f_{E+r_{P_i}}$ as follows:

$$\begin{aligned}b_0 &= A_{0,2} E^2 + A_{0,1} E + A_{0,0}, \\ b_1 &= A_{1,3} E^3 + A_{1,2} E^2 + A_{1,1} E + A_{1,0}, \\ b_2 &= A_{2,2} E^2 + A_{2,1} E + A_{2,0},\end{aligned}\quad (8)$$

where

$$\begin{aligned}A_{0,2} &= -(r_H - r_{P_i}) v_{\bar{T}} k_T^+ c, \\ A_{0,1} &= (v_{\bar{D}} r_H - r_{P_i} v_{\bar{T}} + r_H (-v_{\bar{P}} + v_{\bar{T}})) (k_T^+ c)^2 f_{E+r_{P_i}} + (r_H v_{\bar{P}} - v_{\bar{D}} r_{P_i}) (k_T^+ c)^2 f_{E+r_H} \\ &\quad - (r_H - r_{P_i}) k_T^+ c (r_H v_{\bar{P}} + v_{\bar{T}} (v_{\bar{D}} + v_{\bar{P}} + r_{P_i} + 2k_T^+ c)), \\ A_{0,0} &= -v_{\bar{D}} (r_H - r_{P_i}) (k_T^+ c)^3 f_{E+r_{P_i}} f_{E+r_H} \\ &\quad - (r_H (v_{\bar{P}} - v_{\bar{T}}) + r_{P_i} v_{\bar{T}}) k_T^+ c + v_{\bar{D}} ((r_H)^2 - r_{P_i} v_{\bar{T}} + r_H (-r_{P_i} + v_{\bar{T}} + k_T^+ c)) (k_T^+ c)^2 f_{E+r_{P_i}} \\ &\quad + (r_H v_{\bar{P}} k_T^+ c + v_{\bar{D}} (r_H (v_{\bar{P}} + r_{P_i}) - r_{P_i} (v_{\bar{P}} + r_{P_i} + k_T^+ c))) (k_T^+ c)^2 f_{E+r_H} \\ &\quad - (r_H - r_{P_i}) k_T^+ c (k_T^+ c (r_H v_{\bar{P}} + v_{\bar{T}} (v_{\bar{P}} + r_{P_i} + k_T^+ c)) + v_{\bar{D}} (r_H (v_{\bar{P}} + r_{P_i}) + v_{\bar{T}} (v_{\bar{P}} + r_{P_i} + k_T^+ c))), \\ A_{1,3} &= r_H - r_{P_i}, \\ A_{1,2} &= -(r_H - r_{P_i}) k_T^+ c (f_{E+r_{P_i}} + f_{E+r_H}) + (r_H - r_{P_i}) (v_{\bar{D}} + r_H + v_{\bar{P}} + r_{P_i} + v_{\bar{T}} + 3k_T^+ c), \\ A_{1,1} &= (r_H - r_{P_i}) (k_T^+ c)^2 f_{E+r_{P_i}} f_{E+r_H} - (r_H - r_{P_i}) (v_{\bar{D}} + r_H + v_{\bar{T}} + 2k_T^+ c) k_T^+ c f_{E+r_{P_i}} \\ &\quad - (r_H - r_{P_i}) (v_{\bar{D}} + v_{\bar{P}} + r_{P_i} + 2k_T^+ c) k_T^+ c f_{E+r_H} \\ &\quad + (r_H - r_{P_i}) (v_{\bar{P}} v_{\bar{T}} + r_{P_i} v_{\bar{T}} + 2v_{\bar{P}} k_T^+ c + 2r_{P_i} k_T^+ c + 3v_{\bar{T}} k_T^+ c + 3(k_T^+ c)^2 \\ &\quad \quad + v_{\bar{D}} (r_H + v_{\bar{P}} + r_{P_i} + v_{\bar{T}} + k_T^+ c) + r_H (v_{\bar{P}} + r_{P_i} + 2k_T^+ c)), \\ A_{1,0} &= (r_H - r_{P_i}) (v_{\bar{D}} + k_T^+ c) (k_T^+ c)^2 f_{E+r_{P_i}} f_{E+r_H} \\ &\quad + (-v_{\bar{D}} (r_H^2 - r_{P_i} v_{\bar{T}} + r_H (-r_{P_i} + v_{\bar{T}} + k_T^+ c)) \\ &\quad \quad + k_T^+ c (-r_H^2 + r_H (v_{\bar{P}} + r_{P_i} - 2v_{\bar{T}} - k_T^+ c) + r_{P_i} (2v_{\bar{T}} + k_T^+ c))) k_T^+ c f_{E+r_{P_i}} \\ &\quad + (v_{\bar{D}} (-r_H (v_{\bar{P}} + r_{P_i}) + r_{P_i} (v_{\bar{P}} + r_{P_i} + k_T^+ c)) \\ &\quad \quad + k_T^+ c (r_{P_i} (v_{\bar{P}} + r_{P_i} + k_T^+ c) - r_H (2v_{\bar{P}} + r_{P_i} + k_T^+ c))) k_T^+ c f_{E+r_H} \\ &\quad + (r_H - r_{P_i}) (v_{\bar{D}} (r_H (v_{\bar{P}} + r_{P_i}) + v_{\bar{T}} (v_{\bar{P}} + r_{P_i} + k_T^+ c)) \\ &\quad \quad + k_T^+ c (r_H (2v_{\bar{P}} + r_{P_i} + k_T^+ c) + (v_{\bar{P}} + r_{P_i} + k_T^+ c) (2v_{\bar{T}} + k_T^+ c))), \\ A_{2,2} &= r_{P_i} - r_H, \\ A_{2,1} &= (r_H - r_{P_i}) k_T^+ c (f_{E+r_{P_i}} + f_{E+r_H}) - (r_H - r_{P_i}) (r_H + v_{\bar{P}} + r_{P_i} + v_{\bar{T}} + 2k_T^+ c), \\ A_{2,0} &= -(r_H - r_{P_i}) (k_T^+ c)^2 f_{E+r_{P_i}} f_{E+r_H} + (r_H - r_{P_i}) (r_H + v_{\bar{T}} + k_T^+ c) k_T^+ c f_{E+r_{P_i}} \\ &\quad + (r_H - r_{P_i}) (v_{\bar{P}} + r_{P_i} + k_T^+ c) k_T^+ c f_{E+r_H} - (r_H - r_{P_i}) (v_{\bar{P}} + r_{P_i} + k_T^+ c) (r_H + v_{\bar{T}} + k_T^+ c).\end{aligned}\quad (9)$$

We remark that Eq. 7 is the solution of a quadratic equation; which of the two solutions of the quadratic is meaningful is easily checked by demanding $f < 1$ in the $E \rightarrow \infty$ limit.

Now for any given monomer concentration c , with the boundary condition $f_E \rightarrow 0$ as $E \rightarrow \infty$, we started from a large enough E value and evolved Eq. 6 towards $E = 0$ to obtain f_0 , $f_{r_{\text{Pi}}}$, and $f_{r_{\text{H}}}$. Substituting these values in Eq. 5 we further obtained Ψ_0^{T} , Ψ_0^{P} , and Ψ_0^{D} . Thus, given f_0 , Ψ_0^{T} , Ψ_0^{P} , and Ψ_0^{D} we evaluated $j(c)$ using Eq. 4. It was shown that this method converges to a unique solution provided one starts the evolution from large enough E , retaining a sufficient number of significant digits.

B. Preaveraging Approximation: Calculation of Growth Rates.

Here we present the method we used to calculate cap sizes and growth rates based on a preaveraging approximation. As discussed in the main text, compared with the exact calculations, this method gives different results for the cap size below c_{crit} , but provides very good approximations to growth rates. We denote $\phi_{\text{T}}(n)$, $\phi_{\text{P}}(n)$, and $\phi_{\text{D}}(n)$ the probability that the n^{th} monomer away from the tip binds ATP, ADP-Pi, or ADP, respectively. Consider first the tip, i. e. $n = 1$. One has (1)

$$\frac{d}{dt}\phi_{\text{T}}(1) = k_{\text{T}}^+c[\phi_{\text{P}}(1) + \phi_{\text{D}}(1)] + [v_{\text{P}}^- \phi_{\text{P}}(1) + v_{\text{D}}^- \phi_{\text{D}}(1)]\phi_{\text{T}}(2) - v_{\text{T}}^-[\phi_{\text{P}}(2) + \phi_{\text{D}}(2)]\phi_{\text{T}}(1) - r_{\text{H}}\phi_{\text{T}}(1) . \quad (10)$$

The first term on the right-hand side represents change of tip status into ATP-actin due to polymerization of ATP-actin at an ADP-Pi-actin or ADP-actin tip. The second term represents change of tip status into ATP-actin due to (i) depolymerization of ADP-Pi-actin or ADP-actin at $n = 1$, and (ii) exposure of ATP-actin, previously buried at position $n = 2$. Within the preaveraging approximation, the joint probability of ADP at $n = 1$ and simultaneously ATP at $n = 2$, for example, is approximated as a product of probabilities: $\phi_{\text{DT}}(1, 2) \approx \phi_{\text{D}}(1)\phi_{\text{T}}(2)$ in Eq. 10. Similarly, the third term on the right-hand side represents depolymerization of ATP-actin while the last term is change due to hydrolysis.

For ADP-Pi-actin one has similarly

$$\frac{d}{dt}\phi_{\text{P}}(1) = [v_{\text{T}}^- \phi_{\text{T}}(1) + v_{\text{D}}^- \phi_{\text{D}}(1)]\phi_{\text{P}}(2) - \left\{ v_{\text{P}}^- [\phi_{\text{T}}(2) + \phi_{\text{D}}(2)] + k_{\text{T}}^+c + r_{\text{Pi}} \right\} \phi_{\text{P}}(1) + r_{\text{H}}\phi_{\text{T}}(1) . \quad (11)$$

The analogous equations for $n > 1$ are (1)

$$\begin{aligned} \frac{d}{dt}\phi_{\text{T}}(n) &= k_{\text{T}}^+c[\phi_{\text{T}}(n-1) - \phi_{\text{T}}(n)] + [v_{\text{T}}^- \phi_{\text{T}}(1) + v_{\text{D}}^- \phi_{\text{D}}(1) + v_{\text{P}}^- \phi_{\text{P}}(1)][\phi_{\text{T}}(n+1) - \phi_{\text{T}}(n)] - r_{\text{H}}\phi_{\text{T}}(n) \\ \frac{d}{dt}\phi_{\text{P}}(n) &= k_{\text{T}}^+c[\phi_{\text{P}}(n-1) - \phi_{\text{P}}(n)] + [v_{\text{T}}^- \phi_{\text{T}}(1) + v_{\text{D}}^- \phi_{\text{D}}(1) + v_{\text{P}}^- \phi_{\text{P}}(1)][\phi_{\text{P}}(n+1) - \phi_{\text{P}}(n)] \\ &+ r_{\text{H}}\phi_{\text{T}}(n) - r_{\text{Pi}}\phi_{\text{P}}(n) \quad (n > 1) \end{aligned} \quad (12)$$

The rate of change of the ADP-actin probabilities are determined from $\phi_{\text{T}}(n) + \phi_{\text{P}}(n) + \phi_{\text{D}}(n) = 1$. Starting from an arbitrary nucleotide profile and using long filaments, we evolved numerically Eqs. 10-12 for a long enough time to allow the profile to reach its steady state [note that an analytical solution is also possible since Eq. 12 is linear, except for the tip terms (1)]. The growth rate and the cap size were calculated from

$$N_{\text{cap}} = \sum_{n=1}^{\infty} \phi_{\text{T}}(n) + \phi_{\text{P}}(n), \quad N_{\text{cap}}^{\text{ATP}} = \sum_{n=1}^{\infty} \phi_{\text{T}}(n), \quad j = k_{\text{T}}^+c - v_{\text{T}}^- \phi_{\text{T}}(1) - v_{\text{P}}^- \phi_{\text{P}}(1) - v_{\text{D}}^- \phi_{\text{D}}(1) . \quad (13)$$

C. Analytical Calculation of Length Diffusivity as a Function of Concentration.

Here we prove that $D_\infty(c)$ in Fig. 6 has a sawtooth shape in the special case $v_{\text{P}}^- = v_{\text{T}}^-$ and $r_{\text{Pi}} \rightarrow 0$. Consider first shrinking barbed ends, $c < c_{\text{crit}}$. For long times, $t \gg t_{\text{cap}}$, apart from fluctuations in the size of the steady-state ATP/ADP-Pi cap, fluctuations in tip displacement are due to fluctuations in how far the ADP core has shrunk. Let us call $u(\tau|t)$ the probability that in time t the filament is uncapped for a total time τ . The probability that N monomers have been lost during this time is

$$p(N, t) = \int_0^\infty d\tau u(\tau|t) \mathcal{P}(N, v_{\text{D}}^- \tau), \quad \mathcal{P}(N, x) \equiv x^N e^{-x} / N!, \quad (14)$$

where the Poisson distribution, \mathcal{P} , describes the probability distribution of the number of depolymerized ADP-actin monomers during the total uncapped period. Let us evaluate u by noting that the average value of τ and its second moment are given by

$$\langle \tau \rangle = t S_\infty, \quad \langle \tau^2 \rangle = 2S_\infty \int_0^t dt' \int_{t'}^t S(t'' - t') dt'', \quad (15)$$

for long enough times. Here $S(t)$ is a return probability, namely the probability that the tip is uncapped at time t , given that it was uncapped at $t = 0$, and $S(t) \rightarrow S_\infty$ for $t \rightarrow \infty$. To prove Eq. 15, define $\xi(t''|t')$ to be a random variable that is zero (unity) when the tip is capped (uncapped) at time t'' , given it was uncapped at t' . One has $\langle \tau^2 \rangle = \int_0^t \int_0^t dt' dt'' \langle \xi(t'|0) \xi(t''|0) \rangle = 2 \int_0^t dt' \int_{t'}^t dt'' \langle \xi(t'|0) \rangle \langle \xi(t''|t') \rangle$. Noting that $S(t) = \langle \xi(t|0) \rangle$ one recovers Eq. 15.

Now the exact result for S is (2)

$$S(t) = e^{-(k_{\text{T}}^+ c + v_{\text{T}}^-) t} [I_0(2tx) + y^{-1/2} I_1(2tx) + (1-y) \sum_{j=2}^{\infty} y^{-j/2} I_j(2tx)], \quad y \equiv k_{\text{T}}^+ c / v_{\text{T}}^-, \quad x \equiv (k_{\text{T}}^+ c v_{\text{T}}^-)^{1/2}, \quad (16)$$

where I_j are modified Bessel functions. Using $S_\infty = 1 - c/c_{\text{crit}}$ one obtains for long times $\langle \tau \rangle = t(1 - c/c_{\text{crit}})$ and $\langle \tau^2 \rangle_c = (t/v_{\text{T}}^-)$ where $\langle \rangle_c$ denotes second cumulant. Thus relative fluctuations in τ become small for long times and u becomes Gaussian, $u(\tau|t) \approx \text{const.} \exp[-(\tau - \langle \tau \rangle)^2 / (2 \langle \tau^2 \rangle_c)]$. Substituting u in $p(N, t)$ of Eq. 14 and performing the integration one obtains

$$D_\infty(c) = \begin{cases} (v_{\text{D}}^-/2)[1 + (2v_{\text{D}}^-/v_{\text{T}}^- - 1)c/c_{\text{crit}}] & (c < c_{\text{crit}}) \\ (k_{\text{T}}^+ c + v_{\text{T}}^-)/2 & (c > c_{\text{crit}}) \end{cases}, \quad (17)$$

which is the sawtooth curve plotted in Fig. 6. Notice that D_∞ decreases for smaller concentrations since at $c = 0$ one must recover the Poissonian fluctuations of a pure depolymerization process for which $D_\infty = v_{\text{D}}^-/2$. In Eq. 17, the $c > c_{\text{crit}}$ expression represents the fluctuations of a polymerization process of identical subunits (3) (since in the limit considered here the cap is never lost above c_{crit}).

References

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