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# Analysis of Stochastic Polymerization Dynamics

Alisa Agafonova<sup>1</sup>, Azi Lipshtat<sup>2</sup>

<sup>1</sup>City College of New York, NY

<sup>2</sup>Department of Pharmacology and Systems Therapeutics,  
Mount Sinai School of Medicine, New York NY



## Abstract

Polymerization of actin filaments is the underlying mechanism of various biological processes such as cell growth and motility. In order to analyze the dynamics of the polymerization process and to examine possible stochastic effects, we have constructed deterministic and stochastic models. The deterministic models are analytically solved, providing the average length of the polymer as function of time and kinetic parameters. The stochastic model was simulated using Kinetic Monte Carlo (Gillespie) algorithm, and steady state length distribution was calculated using the Master Equation.

Analysis of the results revealed three phases of dynamics. Initial phase is characterized by formation of a distribution with increasing width. In the main phase the width of the length distribution decreases as function of time, and can be approximated by a power law. The final phase is a steady state distribution that can be analytically calculated. The width of the distribution is a quantitative measure of the system's stochasticity. These simple models can be extended by additional reactions in order to make them more realistic and to analyze more complex systems.

## Approach

Approaching polymerization as a stochastic process, we considered a system containing a large number of monomers, in which the rate of monomer detachment from the polymer is determined by the kinetic coefficient  $\beta$  only, while the rate of monomer attachment to the polymer depends on both the kinetic coefficient  $\alpha$  and the number of unattached monomers. The Master equation for this process illustrates the relationship between the rate of change of probability of finding a polymer with length  $L$  monomers, the kinetic coefficients, and the total number of monomers  $N$ .

$$\frac{\partial P(L)}{\partial t} = \alpha \cdot (N - L + 1) \cdot P(L - 1) + \beta \cdot P(L + 1) - \alpha \cdot (N - L) \cdot P(L) - \beta \cdot P(L)$$

The deterministic model for this system consists of two differential equations, where  $L$  is the average polymer length, and  $n_{available}$  is the number of unattached monomers.

$$\frac{\partial L}{\partial t} = \alpha \cdot n_{available} - \beta$$

$$\frac{\partial n_{available}}{\partial t} = \beta - \alpha \cdot n_{available}$$

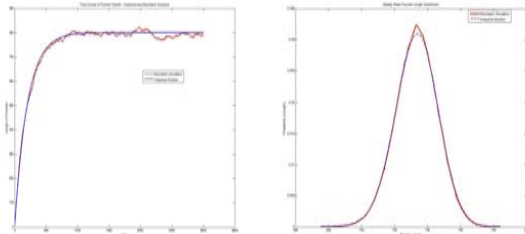
We solved the deterministic model analytically, and used Gillespie algorithm [1] to simulate the stochastic model.

## Results

Stochastic simulation of polymer growth is in agreement with the analytical solution of the deterministic approach to the problem:

$$L(t, \alpha) = \ell \times (1 - e^{-t \times \alpha})$$

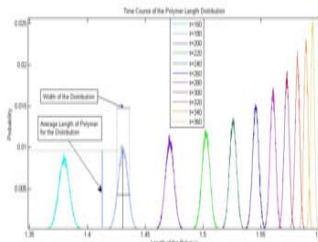
$\ell$  is the length of polymer at steady state  
 $\alpha$  is the Attachment Coefficient  
 $\beta$  is the Probability of detachment  
 $N$  is the Total Number of Monomers in the System



Steady state length distribution for stochastic simulation agrees with the analytical time independent solution for the Master Equation:

$$P(x) = P(1) \times \frac{(N-1)!}{x!} \times \left(\frac{\alpha}{\beta}\right)^{x-1}$$

In time-dependent stochastic models, the average length of the polymers changes with time, and the width of the distribution of lengths changes as well.



In order to quantify time-related developments in the distribution, we scaled each distribution down by its average length to obtain a Relative Width of Distribution:

$$RWD(t) = \text{Distribution Width}(t) / \text{Average Length}(t)$$

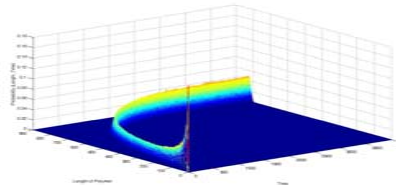
This is a measure for the stochasticity in the system.

## Reference

[1] Daniel T. Gillespie (1976), "A General Method for Numerically Simulating the Stochastic Time Evolution of Coupled Chemical Reactions", *Journal of Computational Physics* 22 (4): 403-434.

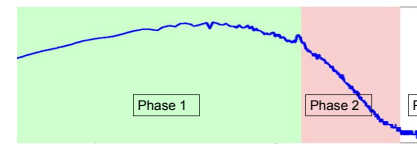
## Results

Three-dimensional stochastic representation of polymer growth ( $\alpha=0.002, \beta=0.75$ )



## Results

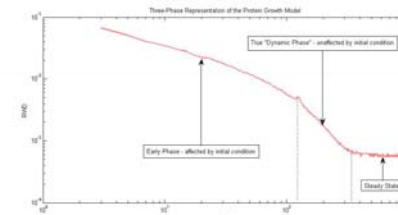
Time dependence of the length distribution width reveals three distinct phases in the stochastically simulated polymerization process:



### Phase 1: Initial Phase - growth is affected by initial condition

The initial condition is a seed of a single monomer. Since the model rules out polymers of length less than or equal to zero, in the early stages of the modeled polymer growth, the length distribution is narrower than it would be without this condition.

As the system gradually 'forgets' the initial condition, it begins to transfer to the next phase.



### Phase 2: Dynamic Phase

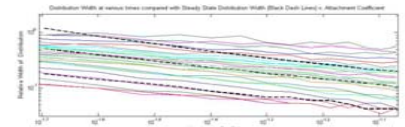
This is the phase we chose to study closely. The system behaves independently of initial condition. The part of the  $\log(RWD) \text{ v. } \log(\text{time})$  plot which corresponds to this phase fluctuates around a straight line, indicating a power law dynamics.

### Phase 3: Steady State Phase

Here the polymers' lengths are distributed around the steady state length in a time-independent distribution. This distribution agrees with the analytical solution of the Master Equation for the system.

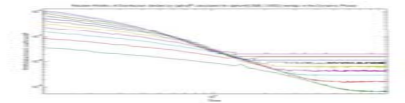
## Results

To investigate the model dynamics, we conducted simulations with various kinetic constants, but with fixed total number of monomers. Plotting the steady state RWD vs. polymerization coefficient  $\alpha$  on a log-log scale reveals a decreasing power law dependence, as predicted from analytical solution of the Master Equation (black dotted lines below). This indicates that stochasticity plays a more significant role under conditions of low polymerization rate (slow dynamics). These results hold true for the dynamics phase as well.

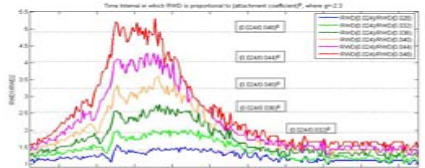


To test the hypothesis of a power law dependence on  $\alpha$ , with a constant exponent (independent of  $\alpha$ ), we calculated the temporal dependence by dividing the RWD by the assumed power law. For a broad range of values for  $\alpha$  (between 0.08 and 0.92), all the curves overlapped in the dynamic phase. This shows that the RWD can be described by a product of a temporal function  $f(t)$  and the power law:

$$RWD_{DynamicPhase} = C \cdot f(t) \cdot \alpha^\gamma \quad \gamma = -2.3$$

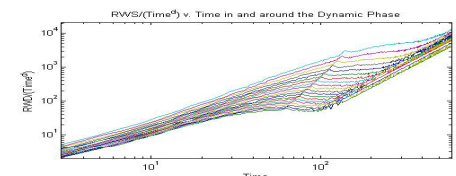


In agreement with the findings mentioned above, the ratio between RWD curves relating to different values of  $\alpha$  should be time independent, and fluctuate around  $(\alpha_1/\alpha_2)^\gamma$ .



## Results

$$RWD_{DynamicPhase} = C \cdot t^\delta \cdot \alpha^\gamma \quad \delta = -2.6, \gamma = -2.3$$



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