October 2002

# Dynamics of Polymerization of Macromolecules with Multiple Binding Sites

Ian J. Laurenzi
*University of Pennsylvania*

Scott L. Diamond
*University of Pennsylvania*, sld@seas.upenn.edu



Copyright 2002 IEEE. Reprinted from *Proceedings of the Second Joint Engineering in Medicine and Biology Society/Biomedical Engineering Society Conference 2002 (EMBS/BMES 2002)*, Volume 3, page 2204.
Publisher URL: http://ieeexplore.ieee.org/xpl/tocresult.jsp?isNumber=22474&page=14

# Dynamics of Polymerization of Macromolecules with Multiple Binding Sites

**Abstract**
In Nature, there are many examples of biological polymerizations in which the monomers possess multiple binding sites. Under certain circumstances, such branched polymerizations may produce a large macroparticle that constitutes a significant fraction of the monomers. In this paper, we show that the polymerizations of antibodies with antigens and the polymerization of fibrin are of this type. We then present the results of stochastic simulations for the time-evolutions of these processes, and characterize their gel transitions. Finally, we relate the innate fluctuations of these processes to the gel transition, and demonstrate the necessity of using a stochastic approach to quantify polymerization kinetics.

**Keywords**
moments, colored noise, gelation

Proceedings of the Second Joint EMBS/BMES Conference
Houston, TX, USA • October 23-26, 2002

# Dynamics of Polymerization of Macromolecules with Multiple Binding Sites

I. J. Laurenzi, S. L. Diamond
Institute for Medicine and Engineering, University of Pennsylvania, PA, USA

*Abstract* - **In Nature, there are many examples of biological polymerizations in which the monomers possess multiple binding sites. Under certain circumstances, such branched polymerizations may produce a large macroparticle that constitutes a significant fraction of the monomers. In this paper, we show that the polymerizations of antibodies with antigens and the polymerization of fibrin are of this type. We then present the results of stochastic simulations for the time-evolutions of these processes, and characterize their gel transitions. Finally, we relate the innate fluctuations of these processes to the gel transition, and demonstrate the necessity of using a stochastic approach to quantify polymerization kinetics.**
***Keywords*** **- Moments, Colored Noise, Gelation**

## I. INTRODUCTION

The aggregation-fragmentation equation [1, 2]

$$\dot{c}_k(t) = \tfrac{1}{2}\sum_{i+j=k}\left[K(i,j)c_i c_j - F(i,j)c_{i+j}\right] - \sum_{j=1}^{\infty}\left[K(k,j)c_k c_j - F(k,j)c_{k+j}\right] \quad (1)$$

is a deterministic population balance equation that describes the time evolution of the concentration of $k$-mers, $c_k(t)$. In (1), the quantities $K(i,j)$ and $F(i,j)$ are called the aggregation and fragmentation rate kernels, respectively, and represent rate constants for the following chemical reactions:

$$A_i + A_j \xrightarrow{K(i,j)} A_{i+j} \qquad A_{i+j} \xrightarrow{F(i,j)} A_i + A_j \quad (2)$$

Although (1) has been used successfully in descriptions of the kinetics of polymerization processes [2], it has shortcomings that constrain its use: it accounts for only one type of monomer (ie. not co-polymerization), it is exceedingly difficult to solve analytically, and it fails to account for statistical fluctuations of $c_k(t)$ resulting from the random nature of chemical reaction. Recently, the last of these considerations has been observed to be of great significance as $t$ becomes large and in cases where $K(i,j)$ and $F(i,j)$ produce a gel transition [3, 4].

Fortunately, there is an alternative to (1) that obviates all of these potential problems. The stochastic approach to chemical kinetics accounts for statistical fluctuations and may readily account for multiple types of monomers when realized as a Monte Carlo (MC) simulation technique [3, 4, 6]. In this paper, we employ MC simulation to study the time-evolution of multi-functional polymerization processes such as the polymerization of fibrin and co-polymerization of multi-functional antigens with bi-functional antibodies.

## II. METHODOLOGY

The stochastic approach to chemical and aggregation kinetics and MC simulation algorithm have been detailed elsewhere [3, 4, 5, 6]. In brief, the aforementioned kernels $K(i,j)$ and $F(i,j)$ are employed to construct probability distributions for the time until the next aggregation or fragmentation event, and which event it will be. These distributions are sampled by MC in order to sequentially choose a time step and reaction event. After updating the time, the populations of the species ($k$-mers) involved in the chosen event are modified, and a new event and time step are chosen.

## ACKNOWLEDGMENT

This work was supported by National Institutes of Health grant HL 56621 and National American Heart Association grant 96-6670. SLD is an Established Investigator of the National American Heart Association.

## REFERENCES

[1] M. v. Smoluchowski, "Vensuch einer mathematischen theorie der koagulation kinetic kolloider losungen." *Z. Phys. Chem.*, vol. 92, pp. 129 –168, 1917.
[2] P. J. Blatz and A. V. Tobolsky, "Note on the kinetics of systems manifesting simultaneous polymerization-depolymerization phenomena." *J. Phys. Chem.*, vol. 49, pp. 77-80, 1945.
[3] I. J. Laurenzi, J. D. Bartels, and S. L. Diamond, "A general algorithm for the exact simulation of multicomponent aggregation processes." *J. Comput. Phys.* (in press).
[4] I. J. Laurenzi, S. L. Diamond, "Kinetics of reversible aggregation with multiple conservation laws" (submitted for publication).
[5] D. T. Gillespie, "A general method for numerically simulating the stochastic time evolution of coupled chemical reactions." *J. Comput. Phys.*, vol. 22, pp. 403– 434, 1976.
[6] I. J. Laurenzi, S. L. Diamond, "Monte carlo simulation of the heterotypic aggregation kinetics of platelets and neutrophils", *Biophys. J.*, vol. 77, pp. 1733–1746, 1999.