Multiscale Analysis of Pattern Formation in Biological Systems

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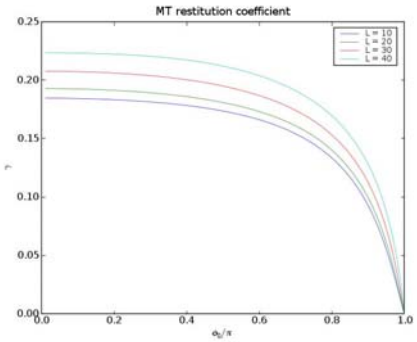
Summary

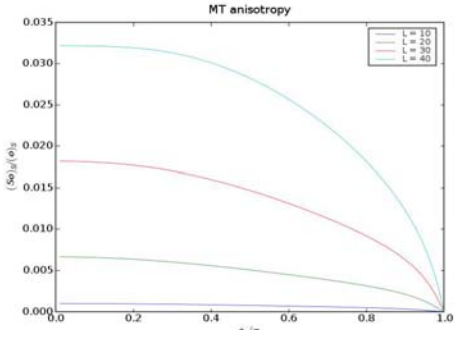
How do random mixtures of molecular components organize themselves into large-scale cellular structures? Can we model this process mathematically, can we simulate it computationally, and what can we learn about the process of self-organization? We address these questions by studying a system of microtubules and molecular motors. Specifically, we develop a multiscale mathematical framework for studying pattern-formation in these and other complex systems.

Microtubules are the building block of the cellular cytoskeleton; they are also responsible for the separation of genetic material in cell division. Recent experiments have shown that a biological system of microtubules and molecular motors can sustain a variety of large-scale 2-D structures (e.g., asters, vortices). Underlying this phenomenon is a multiscale process, where nonlinear interactions on a microscopic scale result in the emergence of coherent structures on the macroscopic scale.

To study this process, we are developing a mathematical framework based on a master equation on the mesoscopic scale. The equation describes the evolution of the density of microtubules as a function of position and angular orientation. The interaction kernel is determined by the molecular interactions on the microscopic scale. Macroscopic spatiotemporal structures are identified through dimension reduction from the mesoscopic scale. All three scales interact strongly, resulting in macroscopically observable patterns of self-organization.

Since receiving funding in April 2006, we have analyzed aspects of the microscopic interactions between semi-flexible tubules modeled as elastic rods subject to a moving singular force. Simulation of the governing partial differential equation shows that the effective bending stiffness decays as the fourth power of the length of the tubule. This is reflected in a length-dependent mean restitution coefficient (Fig. 1), which characterizes the degree to which tubules are aligned after their interaction with the motor. The mean anisotropy of restitution (Fig. 2) reveals further differences in the behavior depending on the tubule length. These





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results have motivated our search for bifurcations during transition from rigid to flexible rods of varying lengths.

At the mesoscopic level we have developed a simulation of the stochastic process underlying the master equation. An equivalent formulation in terms of stochastic differential equations was simulated using the Monte-Carlo method. The results revealed transitions from disordered states to aster and vortex patterns, as observed in experiments.

These patterns are a result of the competition between diffusion and alignment processes. Different longitudinal, transversal, and rotational diffusion coefficients parameterize the phase space of possible patterns.

Studying this parametric dependence led us to the discovery of a previously unobserved cluster state (Fig. 3).

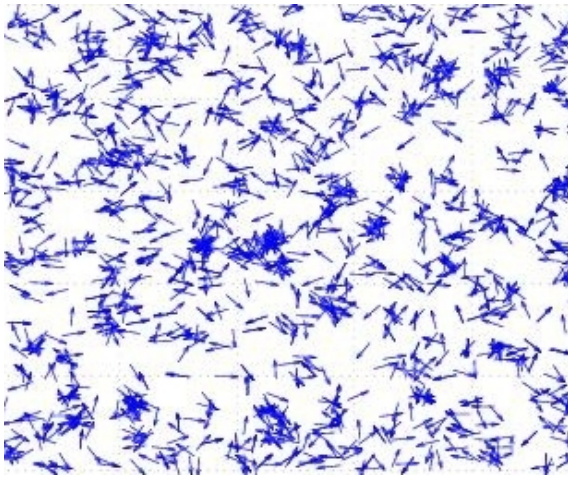

Figure 3 Cluster state evolved from disorder.

The stochastic simulation study promises to be a useful guide in our planned analysis of the governing stochastic dynamics and the dependence of emerging patterns on microscopic analysis. At the same time, the master equation (the corresponding nonlinear Fokker-Planck operator) makes the system amenable to PDE-based analysis, which we are beginning now.

In particular, we are interested in isolating the controlling features of the microscopic behavior (flexibility, relative diffusion strengths, distribution of lengths, etc.) that would enable us to control the type of observable patterns and transitions between them.

Our experimental work focusing on the physics of the problem has revealed that similar mechanisms of inelastic interaction may govern formation of transient patterns in populations of mobile bacteria. It appears that low Reynolds number Stokes flows resulting from the motion of bacteria result in their interaction through the fluid and subsequent alignment. This work promises to be an unexpected application of our formalism to complex systems other than of molecular origin. Moreover, it illustrates the universality of our approach and the particular models based on the master equation formalism. We plan to pursue this line of research further and compare our results to traditional fluid-particle interaction models.

This project is a successful collaboration between the Materials Science Division and the Mathematics and Computer Science Division at Argonne and involves joint supervision of graduate students.

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