ACTIVE BIOLOGICAL FLUIDS

Michael Shelley
Courant Institute of Mathematical Sciences, New York University, New York, NY 10012, USA

Summary I discuss the modeling and simulation of active fluids that arise in biological settings. One example concerns motile suspensions where the hydrodynamic coupling of many micro-swimmers creates fascinating self-generated collective dynamics. I show how these suspensions are modeled using continuum mechanics and large-scale simulation. I next discuss the migration and positioning of the male/female pronuclear complex in early embryo. Here, simulation of a fluid-structure interaction model reveals how immersed motor-proteins can pull on microtubules to center the complex in the cell, create observed streaming flows along microtubules, and rotate the complex into "proper position" for cell division.

INTRODUCTION

While engineering and materials sciences are the traditional disciplines concerned with complex fluids, modern biology has provided us with many new phenomena and complex fluids to study. Some of these biological fluids are *active fluids*, or compound fluids or suspensions whose microstructure is driven, either externally or internally, to move or change shape. This exerts stress on the surrounding fluid, creating flows and interactions with other suspended structures. One example is a bacterial bath where the swimming dynamics of many bacteria create a highly intermittent collective dynamics sometimes called “bacterial turbulence” (see [1] and references therein). These observations have led to the development of compound fluid models where the motile microstructure pumps energy into the macroscopic dynamics (see [2, 3] and references therein). Another active fluid is the cytoplasm of the cell where immersed motor proteins interact with biopolymers – microtubules or actin polymers – to mediate basic transport processes, such as those that lead to cell division [4]. Active fluids are increasingly studied in synthetic systems where suspended particles are driven by external fields – optical, magnetic, or electric – or through chemical reactions [5]. Related to this are active fluids synthesized from purified biological components such as tubelin and motor proteins. Some of these systems show fascinating dynamics such as the spontaneous formation of spindle structures [6] and complex fluid flows (Z. Dogic, private communication). I discuss the mathematical modeling and simulation of two such active fluid systems.

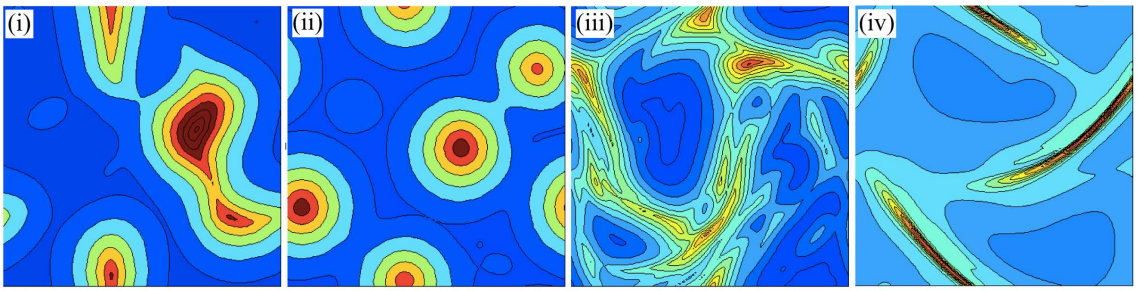

Figure 1. Results from coupling a kinetic theory for active suspensions of swimmers to a kinetic theory for swimmer response to a self-produced chemoattractant (from Lushi, Goldstein, & Shelley, submitted). (a): Swimmer aggregation in the absence of hydrodynamic interactions leads to a slowly coarsening field of high concentration regions. (b): Swimmer aggregation for hydrodynamically interacting “Puller” particles leads to a few isolated regions of high concentration. (c and d) Swimmer aggregation for hydrodynamically interacting “Pusher” particles destroys aggregation and leads to moving patchy (c) or moving bands (d) of swimmer high concentration.

Motile Suspensions

To study motile suspensions Saintillan and Shelley [7, 2] developed particle-based and continuum models of how self-propelled particles interact through a Newtonian fluid. The particle models are of rigid rods, immersed in a Stokesian fluid, actuated by a prescribed tangential stress on either the front (Puller) or rear (Pusher). Given a distribution of rod positions and orientations, the Stokes equations are solved using a fast solution methodology that yields the flow-field that moves and turns the particles. Our continuum models are similar to the kinetic theory of Doi for the dynamics of rigid rod suspensions. The system is described by a Fokker-Planck equation that evolves a distribution function whose configuration variables are rod center-of-mass position and orientation. Particles are driven by a background velocity field determined by the “active” stresses generated by swimming. The sign of this extra stress is determined by swimmer type, either Pusher (negative) or Puller (positive). We showed in these previous works that once above a critical concentration, Pusher suspensions, evolve through an alignment instability to a fully nonlinear dynamics with local orientational order, giant number fluctuations, and a stretch-fold dynamics that efficiently mixes the immersing fluid [7, 3, 2]. These results are similar to experiments in several aspects [1].

[a)] Corresponding author. E-mail: shelley@courant.nyu.edu.

We are currently extending the motile suspension models to account for other important effects. For example, Figure 1 shows long-time swimmer concentration fields when the swimmers evince a run-and-tumble dynamics whose frequency is modulated by a chemoattractant produced and advected by the swimmers themselves. This chemotactic response leads to swimming up the chemical gradient, and yields an elaborated version of the famous Keller-Segal model of aggregative chemotaxis that includes the effect of self-generated flows. We find that these active flows can fragment or destroy swimmer aggregation or limit concentration field coarsening. In other projects, we are studying how geometric confinement affects active flows, how local steric interactions at high swimmer concentration alters global flow dynamics, and how magneto-tactic responses yield peculiar concentration patterns of swimmers.

Active Fluids in the Cell

Active processes in cellular fluids play a central part in developmental biology. An important example is the migration and positioning of the male/female pronuclear complex in early embryo. Using *C. elegans* as a model system, we study how motor-proteins immersed in the cellular cytoplasm pull on microtubules (MTs) emanating from the complex and thus center the complex in the cell. "Proper" position and orientation of the complex precede the formation of the mitotic spindle and successful cell division [4].

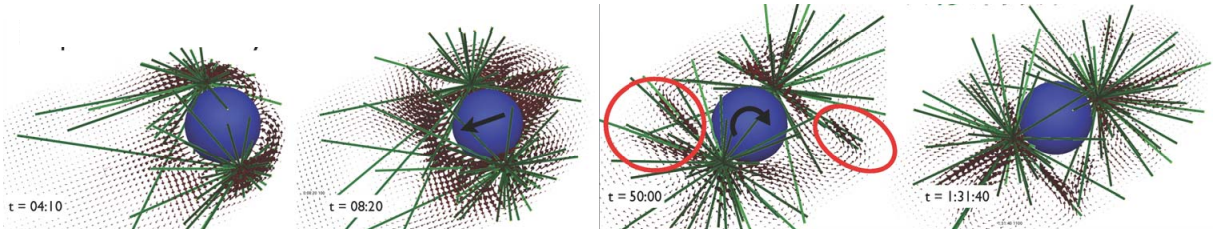

Figure 2. From a fluid-structure interaction model of pronuclear migration, the pronuclear complex is dragged across an ellipsoidally shaped cell by the action of cytoplasmically bound motor proteins. This creates a cytoplasmic velocity field (shown) associated with pronuclear motion, streaming flows along MTs, and rotation into proper position (Shinar & Shelley, in preparation; also see [8]).

In our model [8], a centrosome pair at the male pronucleus initiates stochastic MT growth. These MTs encounter motor proteins, distributed throughout the cytoplasm, that attach and exert a pulling force. The consequent pulling forces drag the pronucleus through the cytoplasm. On physical grounds, we assume that the motor proteins also exert equal and opposite forces on the surrounding viscous cytoplasm, here modeled as an incompressible Newtonian fluid constrained within an ellipsoidal eggshell. This naturally leads to streaming flows along the MTs.

Our computational method is based on an immersed boundary formulation that allows for the simultaneous treatment of fluid flow and the dynamics of structures immersed within (Shinar & Shelley, in prep.). Figure 2 shows simulation snapshots of the pronuclear complex (modeled as a sphere) with attached MTs as it translates and rotates. Also shown is the instantaneous cytoplasmic velocity field. Our simulations demonstrate that the balance of MT pulling forces and viscous nuclear drag is sufficient to move the pronucleus, while simultaneously generating minus-end directed flows along MTs that are similar to the observed movement of yolk granules toward the center of asters. Our simulations show pronuclear migration, and moreover, a robust pronuclear centration and rotation very similar to that observed *in vivo* [9]. We find also that the confinement provided by the eggshell significantly affects the internal dynamics of the cytoplasm, increasing by an order of magnitude the forces necessary to translocate and center the pronucleus.

References

[1] A. Sokolov, R. Goldstein, F. Feldchtein, and I. Aranson. Enhanced mixing and spatial instability in concentrated bacterial suspensions. *Phys. Rev. E.*, 80:031903, 2009.

[2] D. Saintillan and M. Shelley. Emergence of coherent structures and large-scale ows in motile suspensions. *J. Roy. Soc. Interface*, 9:571, 2012.

[3] C. Hohenegger and M. Shelley. Dynamics of complex bio-fluids. In M. Ben Amar, A. Goriely, M. Muller, and L. Cugliandolo, editors, *New Trends in the Physics and Mechanics of Biological Systems*. Oxford University Press, 2011.

[4] S. Reinsch and P. Gönczy. Mechanisms of nuclear positioning. *Journal of Cell Science*, 111:2283–2295, 1998.

[5] W. F. Paxton, K. C. Kistler, C. C. Olmeda, A. Sen, S. K. St. Angelo, Y. Cao, T. E. Mallouk, P. E. Lammert, and V. H. Crespi. Catalytic nanomotors: Autonomous movement of striped nanorods. *J. Am. Chem. Soc.*, 126:5, 2004.

[6] D. Needleman *et al.* Fast Microtubule Dynamics in Meiotic Spindles Measured by Single Molecule Imaging. *Mol. Bio. Cell*, 21:323, 2010.

[7] D. Saintillan and M. Shelley. Instabilities and pattern formation in active particle suspensions: Kinetic theory and continuum simulations. *Phys. Rev. Lett.*, 100:178103, 2008.

[8] T Shinar, M Mano, F Piano, and M Shelley. A model of cytoplasmically-driven microtubule-based motion in the single-celled *C elegans* embryo. *Proc. Natl. Acad. Sci. USA*, 108:10508, 2011.

[9] K. Kimura and A. Kimura. Intracellular organelles mediate cytoplasmic pulling force for centrosome centration in the *Caenorhabditis elegans* early embryo. *Proc. Natl. Acad. Sci.*, 108:137, 2011.