IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	Modeling and simulations of the mechanics of autonomous cell migration across surfaces in response to chemical signals	
Project Number	**IMURA0623**	
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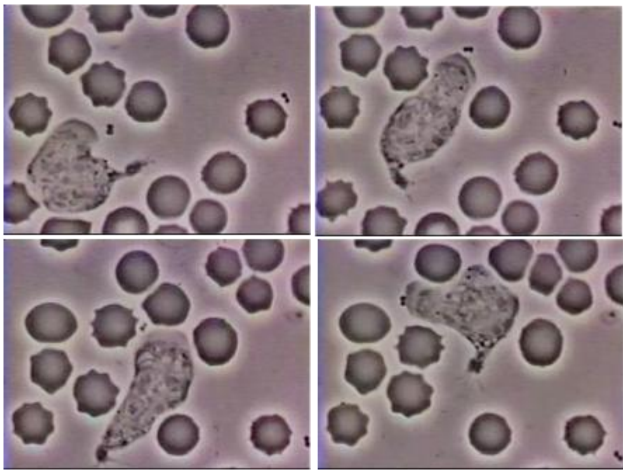
Research Academy Themes:

Highlight which of the Academy's Theme(s) this project will address?
(Feel free to nominate more than one. For more information, see www.iitbmonash.org)

1. Advanced computational engineering, simulation and manufacture
2. Infrastructure Engineering
3. Clean Energy
4. Water
5. Nanotechnology
6. Biotechnology and Stem Cell Research
7. Humanities and Social Sciences

The problem: Microfluidics is currently at an impasse. The original dream was that small, efficient and cheap devices could be built for a wide range of applications such as medical diagnostics and synthesis of speciality chemicals by shrinking fluid handling processes to small scales. A typical microfluidic device today requires a host of desktop accessories --- pumps, valves, tubing, electronic controllers --- for powering and controlling fluid flow within a miniature pipe network: it is a "chip-in-a-lab", rather than a "lab-on-chip" that everyone wants.



The images above are from a movie (see [http://biochemweb.net/neutrophil.shtml)](http://biochemweb.net/neutrophil.shtml)showing a white blood cell (WBC) chasing a small infectious bacterium. The dark nearly circular objects are red blood cells. The internal cytoskeleton of the WBC continually rearranges itself to change the cell's shape and power its crawling on the glass slide.

In sharp contrast, biological cells can perform an incredible range of precisely controlled activities without all that paraphernalia. Consider, for instance, neutrophils. Normally, these white blood cells in the blood stream are in an unactivated state and passively roll around with the flow. As soon as they detect chemicals signalling a wound or a site of a bacterial invasion in the body, they switch on, crawl through tissues at very high speeds to reach the site of the breach to begin fighting bacteria. The adjoining figure shows a crawling neutrophil chasing and consuming a small bacterial cell. Can we build autonomous soft microfluidic devices that can mimic such behaviour?

The solution: Our goal in this project is to demonstrate with computer simulations the minimal requirements to create such devices. We aim specifically to build on the considerable insight from experiments studying the migration behaviour of neutrophils on flat surfaces. It is observed in these studies that the presence of a chemical signal causes the internal cytoskeleton within a neutrophil to polarize. These cells then begin to migrate in the direction of the chemical signal by developing extending pseudopods at the front and retracting them at the back. The surface forces exerted by the cells have also been carefully measured. The stage is now set to combine the knowledge of the biochemical sensory and regulation network with the mechanics of the forces exerted by the cytoskeleton and the cell membrane to predict the motion of such cells across surfaces.

The outcomes: The mathematical model and simulations in this project will lay the foundation for a mechanical understanding of how cells such as neutrophils move. Techniques for harvesting components of cells and reconstituting them within vesicles already exist. Experiments have also demonstrated how such artificial "cells" can be internally powered. The results of our simulations will provide clues for the ingredients required design and guide experimental fabricationof novel self-contained soft microfluidic robots that will detect a chemical signal and crawl towards it. The project will be a launch-pad for a research career in the exciting new area of active matter and living fluids, and provide in-depth training in cutting-edge concepts and techniques inbiophysical modelling and simulations.

How will the project address the Goals of the above Themes?

As indicated in the description, the project is about computational biophysics and will use techniques from computational fluid dynamics and continuum mechanics (CFD). These simulations will lead to insight that could enable the development of novel microfluidic applications. The project thus addresses the goals of the theme of "advanced computational engineering, simulation and manufacture".

Capabilities and Degrees Required

Essential requirements:

- Undergraduate degree or masters in physics or mechanical/ chemical/ civil engineering
- Interest in theory, mathematical modeling and computer simulations

Preferred:

- Experience in theory or mathematical modelingor computer simulations of physical phenomena

Potential Collaborators

Sameer Jadhav, Chem. Eng., IIT-B

Please provide a few key words relating to this project to make it easier for the students to apply.

Active matter, cytoskeleton, surface migration, neutrophil, chemotaxis, amoeboid motility