IITB-Monash Research Academy

Indian Institute of Technology Bombay | MONASH University

An Indian-Australian research partnership

Project Title:	**Modelling subdiffusive motion of bacteriophage within mucus**	
Project Number	**IMURA0798**	
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Research Clusters:

Highlight which of the Academy's CLUSTERS this project will address? *(Please nominate JUST **one.** For more information, see www.iitbmonash.org)*	
1	*Material Science/Engineering (including Nano, Metallurgy)*
2	*Energy, Green Chem, Chemistry, Catalysis, Reaction Eng*
3	*Math, CFD, Modelling, Manufacturing*
4	*CSE, IT, Optimisation, Data, Sensors, Systems, Signal Processing, Control*
5	*Earth Sciences and Civil Engineering (Geo, Water, Climate)*
6	*Bio, Stem Cells, Bio Chem, Pharma, Food*
7	*Semi-Conductors, Optics, Photonics, Networks, Telecomm, Power Eng*
8	*HSS, Design, Management*

Research 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*
8	Design

The research problem

Mucosal surfaces are the primary zones where animals meet their environment, and thus also the main points of entry for pathogenic microorganisms. Within mucus, the predominant macromolecules are the large mucin glycoproteins. The amino acid backbone of these proteins is long, flexible and incorporates repeat hydrophobic regions alternating with blocks bearing extensive glycosylation. Thousands of variable, branched, negatively charged glycan chains extend outward from the protein core into the surrounding environment. The biophysical and biochemical properties of individual mucin chains determines the gel properties of the mucus layer.

Recent research has demonstrated that bacteriophages – viruses that infect and kill bacteria – adhere to the mucosal surfaces of diverse animals (Figure 1). Enrichment of bacteriophages (phages) in mucus occurs via binding interactions between mucin glycoproteins and Ig-like protein domains exposed on phage capsids. In particular, phage Ig-like domains bind variable glycan residues that coat the mucin glycoprotein of mucus. We characterised this bacteriophage adherence to mucus mechanism using high-speed microscopy and particle tracking. Bacteriophages are inert particles reliant on random Brownian motion, yet we demonstrated that mucus-adherent phages exhibit subdiffusive motion in mucin solutions. Subdiffusive motion was predicted to enhance phages encounter rates with bacterial hosts in mucus solutions, which provide increased antimicrobial affects and protection against bacterial infection and disease.

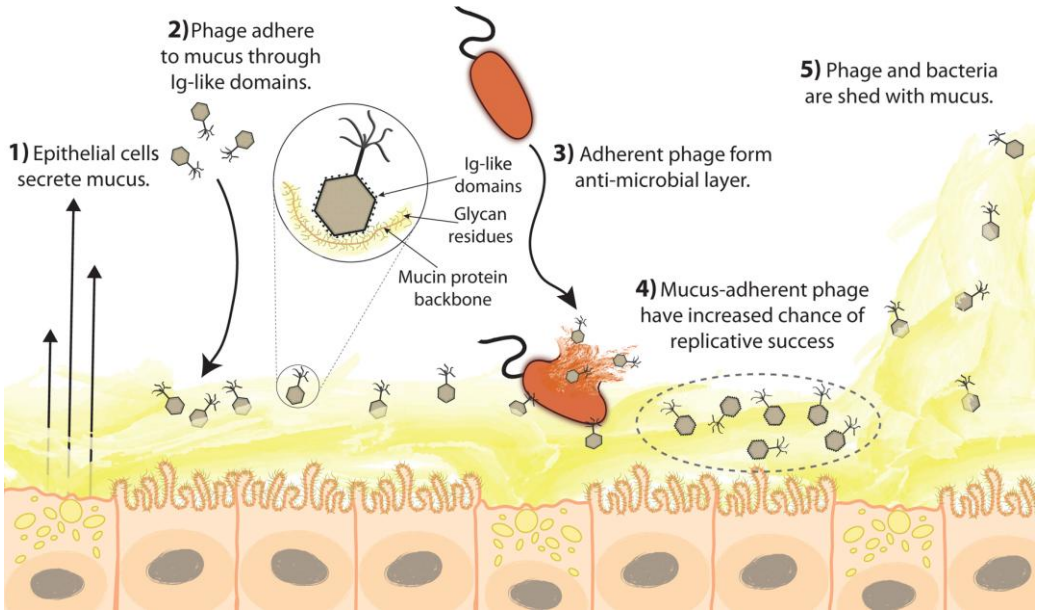

Figure 1. The Bacteriophage Adherence to Mucus (BAM) model.

The 3D organisation of the mucin network and phage adherence to mucus results in a complex biophysical process that leads to subdiffusive motion of the phage particles. Yet the subdiffusive mechanism remains unknown. The aim of this project is to simulate a mucus environment and the interactions of mucus-adherent and non-adherent phages with the mucus network. How these adherence mechanisms results in subdiffusive motion and how this motion increases the phages antimicrobial affects is an interesting and yet to be solved problem that has important implications for fundamental biology and biotechnology applications.

References:

Barr, JJ., Auro, R., Furlan, M., et. al., (2013) Bacteriophage adhering to mucus provide a non-host-derived immunity. *Proceedings of the National Academy of Sciences*. 110(26): 10771-6.

Barr, JJ., Auro, R., Sam-Soon, N., et. al., (2015) Subdiffusive motion of bacteriophage in mucosal surfaces increases the frequency of bacterial encounters. *Proceedings of the National Academy of Sciences*. 112(44): 13675-80.

Project aims

The aim of this project is to develop computational simulations based on polymer models, that enable the study of the 3D organisation and dynamics of a mucus layer, taking into account mucin glycoprotein bending, gelation and the presence of electrostatic interactions between negatively charge glycan polymers. We will then use this mucus simulation to study the mechanism of phage diffusion within this polymer environment and test how different phage-adherence to mucus mechanism influence the diffusivity of these particles. We have extensive high-speed particle tracking experimental data that will be used to compare with our simulations. The project supervisors combine expertise in phage experiments and particle tracking (Jeremy Barr), and theoretical analysis and computer simulations (Ravi Jagadeeshan). Though the project will be primarily computational in nature, the simulations will be guided by high-speed microscopy and biological data carried out by Jeremy Barr's group. Experimental data will be used to refine and tune computational models in order to obtain convergence between theory and experiment, and lead to the development of models that identify the mechanism of phage subdiffusion in complex biological environments.

Expected outcomes

The outcomes of the project will include:

1) The development of a simulation that can directly compute 3D organisation of a mucus environment given certain biological factors.
2) Simulate the diffusion of mucus-adherent and non-adherent bacteriophages within this mucus environment.
3) Understanding the mechanism of subdiffusion of bacteriophages within the mucus environment.

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

The project addresses an important question in the theme area of biology/biotechnology. Understanding the organisation of mucus environment and how mucus-adherent bacteriophages interact within this network will greatly help in our understanding of phage therapy and the microbiome.

Capabilities and Degrees Required

The following capabilities are essential:

1. Excellent training in mathematics and numerical methods (biology knowledge is not mandatory)
2. Proven experience with computer programming in high level languages
3. Ability to write and communicate fluently
4. Strong background in Engineering/Physics (Either M Sc in Physics or B Tech/BE in Mechanical/Chemical/Electrical Engg)

While the topic has a biological context, students without a background in physics or engineering will not be considered

Potential Collaborators

Select up to **(4)** keywords from the Academy's approved keyword list **(available at http://www.iitbmonash.org/becoming-a-research-supervisor/)** relating to this project to make it easier for the students to apply.

Modelling and Simulation, BioScience, Bio Medical Engineering, Pharmacology