

**Project title:** The mechanics of biofilm morphogenesis

**Supervisor:** Dr Nuno Miguel Oliveira

**Department:** DAMTP and Veterinary Medicine

**E-mail address:** [nmdso2@cam.ac.uk](mailto:nmdso2@cam.ac.uk)

### **Project Description:**

Bacteria most often grow as surface-attached communities called biofilms that are critical for their impacts on us, ranging from chronic infections and antibiotic resistance to biofouling, bioremediation and nutrient cycling (Kolter and Greenberg 2006, Oliveira et al. 2015). This realization fostered the study of biofilm growth, the expectation being that, if we know how biofilms develop, we are better equipped to manipulate these cell collectives, promoting the growth of those that are beneficial, while limiting those that are deleterious. Biofilm growth can be described as a developmental process akin to what we find in multicellular organisms where cells experience a range of chemical stimuli and surface-specific mechanics to which they respond to throughout biofilm morphogenesis (O'Toole et al. 2000, Persat et al. 2015). However, microbiology has predominantly focused on how bacterial cells respond to their chemical world and our understanding of bacterial mechanobiology remains very limited. The mechanics of biofilm growth in particular is poorly understood partially because it is hard to measure the forces that bacteria experience during community development. This problem has recently been circumvented in our lab by the use of bioluminescent bacteria that literally light up when they are mechanically stimulated. We have recently discovered that mechanical cues such as fluid shear trigger light emission in bacteria (Birwa SK, Goldstein RM, Oliveira NM. In preparation) and, therefore, we can now use bacterial bioluminescence as a probe to describe and understand the mechanics of biofilm morphogenesis. As bacterial cells grow in biofilms, they exert forces on the surface, and onto each other, that can be quantified by measuring their light emission over time.

The summer student is expected to analyse experimental data where bacteria were grown on different stiffness substrates, which generate different biofilm morphologies and light patterns. From these patterns, and with a suitable calibration curve of force versus light intensity, the student will be able to reconstruct the forces generated during biofilm morphogenesis with high precision for the first time. In addition to this characterization, it is

expected that the student develops a mathematical model that can capture and help to explain the key patterns observed experimentally. This modelling will hopefully make predictions that can be tested next. The bibliography presented below provides relevant works on the available mathematical models that students can use to describe the system, namely those rooted on mechanical instability theory and viscoelastic theory (e.g., Fei et al. 2020, Matoz-Fernandez et al. 2020, Yan et al. 2019). For this part of the project, the student will work closely with of a final-year PhD student (Mr George Fortune), who is an expert in fluid dynamics and theoretical approaches for biofilm growth (Fortune G, Oliveira NM, Goldstein RE. In preparation). The ideal candidate should be familiar with quantitative and image analysis, programming, fluid mechanics and pattern formation. The project duration is 8 weeks and can be conducted remotely if needed. While the focus of the project is on quantitative analysis and mathematical modelling, students wishing to obtain their own experimental data and further explore the system empirically are welcome. Experimental work might be possible depending on pandemic-related restrictions at the time.

### **Bibliography:**

- Birwa SK, Goldstein RM, Oliveira NM. Bacteria bioluminesce in response to fluid shear. In preparation. Draft available upon request.
- Fei C, et al (2020) Nonuniform growth and surface friction determine bacterial biofilm morphology on soft substrates. *PNAS* 117(14):7622-7632.
- Fortune GT, Oliveira NM, Goldstein RA. Biofilm growth under elastic confinement. In preparation. Draft available upon request.
- Kolter R, Greenberg EP (2006) Microbial – The superficial life of microbes. *Nature* 441:300-302.
- Matoz-Fernandez DA, et al (2020) Wrinkle patterns in active viscoelastic thin sheets. *PRR* 2:013165.
- Oliveira NM et al. (2015) Biofilm formation as a response to ecological competition. *Plos Biol* 13(7).
- O’Toole G, et al. (2000) Biofilm formation as microbial development. *Annu Rev Microbiol* 54:49-79.
- Persat A, et al (2015) The mechanical world of bacteria. *Cell* 161(5):988-997.
- Yan J, et al (2019) Mechanical instability and interfacial energy drive biofilm morphogenesis. *eLife* 8:e43920.