PROJECT TITLE: Bacterial phenotypic adaptation to mechanical stress induced by nanoparticles at the single-cell level

Project Supervisor: Dr. Fabrice Gielen, Exeter, The Living Systems Institute

Project Enquiries: F.Gielen@exeter.ac.uk

Project keywords: microfluidics, single-cell biology, phenotypic plasticity, high-throughput assays, nanoparticles

Project description:

Physical stressors present in the environmental influence cell phenotypes and functions. The presence of nanoparticles in particular has been highlighted as a pressing environmental issue, contaminating soil and ground waters. How they effect individual bacteria in a population is not known, as is the timescale over which adaptation occurs. The project will focus on the interaction dynamics between bacteria (S. *aureus*, P. *aeruginosa*, E. *coli*) and model nanoparticles in micro-communities. The results will help illuminate how physical stresses influence cellular response at the single-cell level, and how this might impact ecosystem functioning and services.

The student will employ state-of-the-art microfluidic technologies to generate thousands of microbial microcultures. Growth will be quantified from high-resolution microscopy data using custom-made machine learning models that classify cellular morphologies in the presence and absence of nanoparticles. We will then use this information to plot fitness maps for the bacteria, track phenotypic changes over time and determine possible synergies using combinations of nanoparticles.

Candidate requirements:

This project would suit students interested in interdisciplinary research, with possible focus on either microbiology, microfluidics or machine learning aspects of the project. For the latter, they should ideally have some basic programming experience (e.g. with Python). Skills developed during the project include bacterial culture, microfluidics device fabrication and validation, setting up and training of deep learning models, advanced image analysis.

Background reading:

1. K. Matula *et al.*, Phenotypic plasticity of Escherichia coli upon exposure to physical stress induced by ZnO nanorods. *Sci Rep* **9**, 8575 (2019).
2. L. Howell, V. Anagnostidis, F. Gielen, Multi-Object Detector YOLOv4-Tiny Enables High-Throughput Combinatorial and Spatially-Resolved Sorting of Cells in Microdroplets. *Advanced Materials Technologies*, (2021).
3. A. Tiwari, N. Nikolic, V. Anagnostidis, F. Gielen, Label-free analysis of bacterial growth and lysis at the single-cell level using droplet microfluidics and object detection-oriented deep learning. *bioRxiv*, (2023).

Work Schedule:

Week 1: Background reading of relevant literature and lab inductions/training

Weeks 2-5: Core experimental work in laboratory (nanoparticle synthesis and miniaturised bacterial cultures)

Weeks 5-7: Image analysis and processing using deep-learning object detectors

Week 8: Writing of research report