Project 3.15. Models of bacterial response to antibiotics

Supervisor: Dr hab. Anna Ochab-Marcinek/Co-supervisor: Dr Bartłomiej Wacław

ICP PAS Group: Dioscuri Centre for Physics and Chemistry of Bacteria

www: https://dioscuricentrebacteria.com/

Background:

The Dioscuri Centre for Physics and Chemistry of Bacteria invites applications for a PhD position in computer modelling of the response of intracellular bacteria to antibiotics.

Bacterial infections are often treated with antibiotics, but bacteria can rapidly develop resistance [1]. To find novel ways of treating infections, we need a better understanding of bacterial and human physiology, mechanisms of response and evolution of resistance to antibiotics. Mechanism-based, mathematical models can help here: by comparing model predictions with experimental data we can obtain an insight into processes that are difficult to probe directly. Data-driven models able to predict the dynamics of bacterial infections and treatment are also an important step towards the "in silico patient" – the Holy Grail of computational medicine.

Bacteria interact with host cells in many complex ways [2]. In particular, bacteria can invade and live inside animal cells. It is believed that changes in bacterial metabolism and reduced antibiotic concentration inside the animal cell help bacteria survive antimicrobial therapy. However, a quantitative characterization of these processes and their mechanistic modelling is rudimentary. In particular, existing models are based on laboratory experiments in which bacteria are cultured in standard media [3, 4] – an environment very different to that of the animal cell.

[1] Q. Zhang, et al., Science 333, 1764 (2011).
[2] A. L. Flores-Mireles, et al., Nat. Rev. Microbiol. 13, 269 (2015)
[3] P. Greulich, M. Scott, M. R. Evans, and R. J. Allen, Molecular Systems Biology 11, 796 (2015).
[4] N. Ojkic, et al., Antimicrob. Agents Chem, https://doi.org/10.1128/AAC.02487-19

Aim:

You will develop a computer model of how the bacterium E. coli growing in epithelial cells of the bladder responds to antibiotics used to treat urinary infections. You will include processes such as stress response, increased mutation rate, delay between the emergence of a mutation and phenotypic resistance, and others. The model will be parametrized using data from in-house experiments, and will help to build population-level models of urinary infections.

Requirements:

- Msc in mathematics, informatics, physics, chemistry, or bioengineering. Very good English. Very good programming skills (any language). Very good academic achievements and a strong motivation to learn the required biology. Strong interest in developing quantitative models inspired by data. Desired: previous experience in computer modelling, ability to work with people from diverse background.

- The candidate is expected to work closely with other modellers and experimentalists from the Dioscuri Centre and the Biophysical Chemistry group, and with theorists from the Department of Evolutionary Theory in MPI in Ploen, Germany. The project may involve regular visits to Ploen (a few weeks/year), participation in national and international conferences and in internal seminars/group discussions.
- In addition to submitting the application to the Warsaw4PhD doctoral school, candidates must submit a separate application for a position in the Dioscuri Centre. Further information on how to do this will be available on
- https://dioscuricentrebacteria.com/jobs/