PhD Position
Signal Amplification via Engineered Competition in Bacteria

Topic profile

theory/math

wet-lab

Tags

#synthetic biology

#genetic circuits

#bacterial conjugation

Supervision

Matthias Függer

CNRS Researcher at ENS Paris-Saclay

Thomas Nowak

Professor at ENS Paris-Saclay

Context

In the past few decades, synthetic biology has laid considerable focus on the re-programming of cells as computing machines, e.g., via genetic circuits and molecular control mechanisms. A central problem in this setting is to maintain a consistent state of circuit values among the bacteria. The problem of maintaining a consistent state among agents has been studied in distributed computing for decades in different contexts, e.g., for replicated state machines and mobile networks. Starting from a mathematical computing model, analysis of a system's behavior has led to correctness proofs and performance bounds of proposed solutions, also shedding light on how protocol parameters influence the quality of the outcome [1].

We are looking for

Prerequisites are a Master degree in a relevant subject (e.g., biology or computer science). We expect a curious, driven attitude and interest to combine wet-lab and modeling work.

The team

You will be part of an interdisciplinary research team at Laboratoire Méthodes Formelles in the ENS Paris-Saclay, near Paris, working at the interface between computer science and synthetic biology.

Research

We use engineered competition to boost the relative population of one bacterial type over another for differential signal amplification. An initial mixed population of 60% bacteria of type `Yes` and 40% of type `No` being amplified into a population of, say, 95% of type `Yes` and 5% of type `No` makes downstream computations based on these signals less complex and more robust [2]. As such, this form of signal amplification is a relaxed variant of the distributed consensus problem. A simple yet effective algorithm to achieve signal amplification is to introduce the single inter-bacterial reaction $\text{Yes} + \text{No} \to \emptyset$ that removes opposing bacteria. We will implement this mechanism by DNA communication of a genetic circuit part via bacterial conjugation [3]. The always present duplication and death reactions make the mathematical analysis challenging and non-standard. They do, however, actually introduce robustness to noise for our algorithm due to the fact that constant duplication keeps some high-variance stochastic effects caused by low population counts from occurring.

References

[1] Cho et al. *Distrib. Comput.*'21. URL

[2] Aoki et al. *Nature*'19. URL

[3] Marken, Murray. *Nature Comm.*'23. URL

You are interested or would like to join us?

Please mail your questions or, in case you would like to apply, a short statement of interest and a curriculum vitae to Matthias Függer (mfuegger@lmf.cnrs.fr) and Thomas Nowak (thomas@thomasnowak.net). Applications until the end of April 2024 will receive full consideration.