TECHNISCHE UNIVERSITÄT DARMSTADT

Automated Design of Genetic (Logic) Circuits

Pro seminar · Project seminar · Bachelor thesis · Master thesis

Fachbereich 18
Elektrotechnik und Informationstechnik
Bioinspirierte Kommunikationssysteme

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Electrical Engineering and Information Technology
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October 2020

"Cells navigate environments, communicate and build complex patterns by initiating gene expression in response to specific signals. Engineers need to harness this capability to program cells to perform tasks or build chemicals and materials that match the complexity seen in nature" [1].

Many cellular regulatory mechanisms are encoded on the level of DNA as regulatory motifs, such as promoters, repressors, oscillators, etc. A genetic circuit (be it of natural or artificial origin) interconnects these building blocks to realize a logical or otherwise mathematical function of available biochemical quantities. In artificial circuits, we also desire to implement functionality not present in natural circuits in any or only highly modified form. A continuously increasing complexity of the desired functions, however, leads to a continuously increasing difficulty of even finding working implementations, especially since the spatial and temporal requirements of more and more of these functions exceed the capabilities of single cells.

To unlock complex, controlled metabolic dynamics distributed over cell populations, we need to find ways to coordinate the implementation of these functions automatically using as much available information as possible. To tackle our part of this giant task, we concentrate on finding assemblies of available intermediate functional building blocks (e.g. logic gates [2]) to implement larger building blocks realizing more complicated functionality (e.g. state automators [3], transceivers for inter-cell communication [4]). We want to do this in accordance to some criteria of optimality, such as reliability, robustness, resource efficiency, etc.

Unfortunately, the considerably stochastic biochemical environment present in cells - and its diversity across cells - makes it expensive to find such assemblies, which can be considered acceptable with respect to those optimality criteria. In contrast to electrical circuit design, we therefore often need to perform this optimization on a significantly more detailled level with a larger functional variety of the involved building blocks. This can e.g. involve a detailled temporal, structural and statistical analysis [5]. The choice of an appropriate level of detail is then again very specific to the scope of the assembly in question.

Below are **currently open questions**, I want to address specifically:

- "Variational Inference for Parameters of Genetic Logic Gates from Whole-Circuit Measurements"

Otherwise, you are **always free to bring in your own ideas** and expertise.

Useful knowledge:

- Mathematical optimization
- Boolean logic circuits and circuit verification
- Statistical inference

For further information, please contact Nicolai Engelmann.

References

[1] Jennifer Brophy and Christopher Voigt. Principles of genetic circuit design. *Nature methods*, 11:508–520, 04 2014.

[2] Alec Nielsen, Bryan Der, Jonghyeon Shin, Prashant Vaidyanathan, Vanya Paralanov, Elizabeth Strychalski, D. Ross, Douglas Densmore, and Christopher Voigt. Genetic circuit design automation. *Science*, 352:aac7341–aac7341, 04 2016.

[3] Lauren Andrews, Alec Nielsen, and Christopher Voigt. Cellular checkpoint control using programmable sequential logic. *Science*, 361:eaap8987, 09 2018.

[4] A. Marcone, M. Pierobon, and M. Magarini. Parity-check coding based on genetic circuits for engineered molecular communication between biological cells. *IEEE Transactions on Communications*, 66(12):6221–6236, 2018.

[5] Tobias Schladt, Erik Kubaczka, Nicolai Engelmann, Christian Hochberger, and Heinz Koeppl. Genetic circuit design automation involving structural variants and parameter statistics. *IWBDA 2020 Proceedings*, 11:19–20, 07 2020.