

**Subject**

Deciphering biochemical signalling by means of information theory

**Supervisors, contact, place of research**

dr hab. Michał Komorowski (m.komorowski@symbiosig.org tel. 228261281 w. 449), IPPT PAN, Pawińskiego 5b

**Project Description**

Biochemical signalling is a key mechanism to coordinate an organism in all aspects of its function. In multicellular organisms like the human body trillions of cells, of multiple different cell types communicate with each other by releasing a thousand types of molecules such as hormones, growth factors, cytokines, or chemokines. Aberrations in signalling processes may have detrimental consequences whereas therapeutic interventions in signalling have led to numerous success stories of modern pharmacology. Mathematical methods of information theory and probabilistic dynamical modelling constitute natural tools to describe how information flows in signalling pathways and how stimuli are encoded in activities of the pathway's effectors. Specifically, the information-theoretical notion of channel capacity expresses the overall amount of information that can flow through a given system. A system for which the information capacity is equal to  $C$  bits can, based on Shannon's coding theorem, be interpreted as having signalling fidelity sufficient to derive  $2^C$  distinct responses from different levels of stimuli. The main goal of the project will be to improve our understanding how cellular signalling processes can derive a variety of distinct outputs from complex inputs, and how these mechanisms can be harnessed to induce therapeutically useful behaviour. Current tools of information theory are applicable for very small systems only and have therefore limited use in modelling of biological systems. To overcome this limitation a novel analytical and computational tools of mathematical information theory are required, which are suitable to reflect the complex biochemistry of signalling processes. We will make use of concepts developed in our group as reported in papers listed below.

**Bibliography**

1. An information-theoretic framework for deciphering pleiotropic and noisy biochemical signaling Tomasz Jetka, Karol Nieniałtowski, Sarah Filippi, Michael PH Stumpf, Michał Komorowski, Nature communications, 2018, <https://doi.org/10.1038/s41467-018-07085-1>.
2. The Limited Information Capacity of Cross-Reactive Sensors Drives the Evolutionary Expansion of Signaling, Michał Komorowski and Dan S Tawfik, Cell systems, 2019, <https://doi.org/10.1016/j.cels.2018.12.006>
3. Information-theoretic analysis of multivariate single - cell signaling responses, Tomasz Jetka, Tomasz Winarski, Karol Nieniałtowski, Sławomir Błoński, and Michał Komorowski PLOS Computational Biology, 2019, <https://doi:10.1371/journal.pcbi.1007132>

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