IQCB
Institute for Quantitative & Computational Biosciences

Under the Hood Seminar
September 4, 2024
10:30 AM

Lecture Hall (00.187) at BioZentrum I, Hanns-Dieter-Hüsch-Weg 15, 55128 Mainz

Prof. Dr. Rodrigo Mora

University of Costa Rica

Computational modeling of miRNA-transcription factor interactions

with applications to gene dosage compensation in cancer and genetic circuit bistability in macrophage phenotypic transitions

miRNAs are a type of small non-coding RNAs that can regulate gene expression. Sometimes regarded as simple regulators of gene-expression noise, in fact they can interact with transcription factors (TF) participating in the assembly of complex regulatory circuits including negative feedback loops, positive feedback loops, coherent feedforward loops, incoherent feedforward loops, miRNA clusters, and target hubs leading to non-linear, systems-level properties such as bistability, ultrasensitivity, and oscillations. Despite of multiple potential applications, the search for robust miRNA-based regulators has been limited by the paramount complexity of their regulatory networks. Thus, the identification of master key regulators for specific applications requires the aid of computational approaches. We present BioNetUCR, a biocomputational platform for the automatic construction of large-scale regulatory networks of miRNA-TF interactions and their corresponding mathematical models of ordinary differential equations for systems biology studies using COPASI. Two working examples will be presented for the application of BioNetUCR to bottom-down systems biology approaches. First, we have modeled the complex networks for a potential network of dosage compensation of gene expression in aneuploid cancer and identified a minimal model of MYC dosage compensation mediated redundantly by 3 miRNAs. These findings were experimentally validated with a novel experimental platform for the future design of therapeutic approaches against aneuploid cancer. Second, using an experimental model of human macrophage polarization, we generated multi-omic data for the construction and simplification of a miRNA-TF network

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potentially regulating macrophage phenotypic transitions. Here, we identified a minimal model with a switch-like behavior composed of 5 key genes where the property of bistability could be studied to identify ultrasensitivity and hysteresis of the potential transition trajectories between the steady states associated with different macrophage phenotypes. This has potential applications for the regulation of macrophage responses in cancer and inflammatory diseases.

The IQCB seminar series "Under the Hood" provides a forum for scientists at all career levels to present the technical side of their research. Talks are aimed at an audience interested in the methods, algorithms, and programs used to address a specific research question. "Under the Hood" talks stimulate lively discussions among researchers facing similar computational challenges in their research, lead to transfer of technical knowledge and ideas and promote collaboration.

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