Computational analysis of complex responses to drug treatment

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Most drugs act by binding with high affinity to specific proteins inside a cell, modulating this way its function. We often assume that the effect of a given drug is directly proportional to its concentration, but things can change when the targets of a given drug are nodes of nonlinear signalling cascades. In this very common situation, the architecture of the network strongly influences the efficiency of the drug, and the typical dose-response curve is no longer a simple sigmoidal.

We have shown previously that the effect of a drug does not only depend on its concentration or its affinity towards the target, and that also depends very strongly on the interaction that affect its target molecule. For instance, we have shown that some specific network architectures can induce a reduction or an increase in the sensitivity in a drug.

In the present project, the student will use mathematical modeling to study how different network motifs can induce complex dose-response curves, for instance, a drug can have little effect at low and high concentration, but show a very strong effect only at intermediate levels. This results will represent the first explanation of how the complex dose-responses observed for many drugs arise.

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Relevant Publications from the lab:

- The effects of Hh morphogen source movement on signaling dynamics

DG Míguez, A Iannini, D García-Morales, F Casares, Development 149 (23), dev199842 (2022)

- FGF2 modulates simultaneously the mode, the rate of division and the growth fraction in cultures of radial glia

M Ledesma-Terrón, N Peralta-Cañadas, DG Míguez, Development 147, dev189712 (2020)

- Analysis of actomyosin oscillatory dynamics using a coarse-grained model

M Hernández-Del-Valle, et al.,Frontiers in Physics 10, 881384 (2022)

- A Branching Process to Characterize the Dynamics of Stem Cell Differentiation DG Míguez, Scientific Reports 5, 13265 (2015)