Optimization of kinetic parameters of non-linear models of complex reaction-diffusion networks applied to the study of molecular signaling and expression gene in biological systems

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The present work focus on the study of complex networks of biological systems like gene expression and molecular signaling networks to understand the pattern formation in living beings and the importance of that for the body functioning. The biological system chosen is the signaling network of the Toll pathway in the embryogenesis of Drosophila melanogaster, historically used as a model for genetic studies.

The Toll pathway is an important regulatory network in the dorsoventral axis patterning during embryogenesis. It has been shown that this pathway plays a critical role in the immune response to fungal infections. Also, homologues receptors to Drosophila's Toll has been found in other invertebrates and even in mammals.

Despite the growing variety of experimental methods to study signaling networks at molecular level, many physicochemical parameters are still not directly accessible. Dynamic models may help understand and test signaling networks in order to determine parameters that are needed to describe and model each part of the complex system. By fitting theoretical models to raw experimental data, it is possible to set parameters that lead to solutions compatible with the observed behavior in the experimental system.

Our strategy is based in regulatory network models capable of mimicking gene expression patterns. These Reaction-Diffusion Models describe protein synthesis and degradation, protein interactions with target genes and protein diffusion.

To make the study feasible, two computational tools were developed. The first one is a solving code written in MATLAB® that builds Nonlinear Partial Differential Equations from a user-defined network , and then solve it, given kinetic parameters and diffusion coefficients.

The second code uses the PDEs to perform the parameter optimization in the PDE trying to simulate as close as possible the experimental data. This code uses a Genetic Algorithms to search for good solutions.

Finally, after finding the best parameter set, it is possible to perform a dynamic study of the system, understanding the importance of each constituent element and its interactions; and making predictions through modifications in the model. The model can simulate mutations, competitive or inhibitors interactions in order to verify the role of these interactions in the global behavior. It contributes to understand networks signaling and immunological regulation networks.