Spatially extended model of kinase-receptor interaction

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***Short Abstract* — We consider a spatially-extended model describing mutual phosphorylation of cytosolic kinase molecules and membrane receptors. The analyzed regulatory subsystem is a part of signal transduction mechanisms characteristic for immune receptors and Src family kinases. It couples differential equations defined in a domain and on its boundary via nonlinear Robin boundary conditions. Assuming a spherically symmetric framework, our approach is to consider an auxiliary problem in which a uniform Dirichlet boundary condition is imposed on the external boundary of the spherical shell instead of the Robin boundary condition. This method allows us to find the stationary spherically-symmetric solutions, both stable and unstable.**

***Keywords* — Regulatory pathways, signal transduction, reaction-diffusion systems.**

I. Motivation

THE aim of the work is the analysis of the spatially extended model of mutual interaction between cytosolic kinase molecules and membrane receptors. We consider a generalization of the models introduced in [1],[2] and [3]. It is assumed that non-active kinase molecules are activated by active receptors on the boundary and diffuse freely in the cytosol. The stream of activated kinase molecules resulting from their phosphorylation by the surface receptors can be modelled by the nonlinear Robin-type boundary condition in which the diffusional flux of activated kinase, according to the law of mass action, is proportional to the product of the concentration of active receptors and the concentration of non-active kinases. The activated receptors as well as the activated kinases may be dephosphorylated by the action of phosphatases, in general of different kinds. The fact that there exists a finite amount of phosphatases is taken into account by introducing the Michaelis-Menten kinetics to model the process of active kinase deactivation.

II. Results

We construct spherically-symmetric stationary solutions to the equations of the model. As we mentioned, dephosphorylation of kinases is in general a nonlinear process of Michaelis-Menten type, so unlike the linear model considered in [1], the solutions cannot be found explicitly. We prove that such solutions exist and study their stability. The idea of taking into account the nonlinear Robin boundary conditions consists of considering an auxiliary elliptic problem with Dirichlet boundary conditions. This method is elementary and its application is not confined to the considered system. We also prove that similarly to the usual reaction-diffusion system with co-operative coupling, our system obeys the sub- and supersolution property. This property allows us to conjecture about the existence of a non spherically-symmetric stationary solution to the system in a spherically-symmetric regions (spherical shells). Under the assumptions that the kinases are not cytosolic but live on the cell membrane, then we may consider the membrane model. This model is described by a system of reaction-diffusion equations on a surface of a (unit) sphere. Under certain additional assumptions, we are able to find to the stationary solution to the system having the form of a standing front. We can determine the stability of the stationary solution as a function of the model parameters. Finally, we prepare a mathematical background for similar models based on the cytosolic-membrane interaction, by proving existence theorems for more general systems of equations.

III. Conclusion

We have designed and analyzed mathematically models of receptors interaction with both cytosolic and membrane kinase molecules. In the spherically symmetric cytosolic case, we have found a method of finding branches of stationary solutions, both stable and unstable. In the "membrane" case, we have also an analytical form of the standing wave solution and found its stability.

References

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