Traveling wave like solutions to a singular model of kinase-receptor interaction on a sphere

B. Kazmierczak¹, T. Lipniacki¹

Short Abstract — We consider a Mc Kean type caricature of spatially-extended model describing mutual phosphorylation of cytosolic kinase molecules and membrane receptors on a sphere. The initial regulatory subsystem is a part of signal transduction mechanisms characteristic for immune receptors and Src family kinases and has been analyzed in [1]. We find a stationary front solution, analyze its stability and prove that its perturbation gives rise to traveling waves propagating towards one of the poles of the sphere.

Keywords — Signal transduction, B-cell activation, reactiondiffusion systems.

I. MOTIVATION

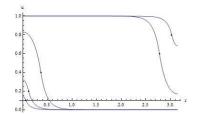
THE aim of the work is the analysis of the stability properties of stationary front solutions to a Mc Kean caricature of a spatially extended model of mutual interaction between cytosolic kinase molecules and membrane receptors. The starting point of our considerations is the model analyzed in [1], which in turn is a generalization of the models introduced in [2],[3] and [4]. It is assumed in these models 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 nonlinear Robin-type boundary conditions 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. Here we are interested in the situation when all the kinases live on the membrane of the cell. In fact, this corresponds to the assumption that the cytosolic kinases are only read-out transducers of the membrane activation phenomena.

II. RESULTS

We find an explicit expression for standing front solutions to the equations of the simplified model on the sphere. In fact, we consider the equation describing the diffusion of kinases on the membrane (by the Laplace-Beltrami operator) and the kinase-receptor interaction together with their

¹Institute of Fundamental Technological Research, Polish Academy of Sciences, Warsaw, E-mail: <u>bkazmier@ippt.gov.pl</u>

dephosphorylation by the phosphatases (by means of a nonlinear bistable piecewise continuous function). We prove that the standing front solutions can be expressed in terms of hypergeometric functions. Examples of such solutions for various parameters of the model, as a function of the polar angle, are shown below.



Profiles of the standing fronts for different values of the excitation parameter

We proved, among others, that the standing front solution $u_o(x)$ is unstable i.e., there exist initial data arbitrarily close to u_o such that the solution to the time dependent problem tends to one of the stable states approximately as a traveling wave.

CONCLUSION

We have found an explicit solution to a simplification of the model describing an interaction of B-cell receptors with membrane kinase molecules. We have considered the process of B-cell activation by analyzing the (in)stability of the stationary front and its dependence on the parameters of the model.

REFERENCES

[1] Crooks E, Kazmierczak B, Lipniacki T (2013) A spatially extended model of kinase-receptor interaction, *SIAM J Appl Math*, **73**, 374–400 [2] Kazmierczak B, Lipniacki T (2009), Regulation of kinase activity by diffusion and feedback. *J Theor Biol* **259**, 291-296.

[3] Kazmierczak B, Lipniacki T (2010) Spatial gradients in kinase cascade regulation, *IET Sys Biol* **4**, 348-355

[4] Hat B., Kazmierczak B, Lipniacki T (2011) B cell activation triggered by the formation of the small receptor cluster: a computational study. *PLoS Comp Biol* **5**, e1000448

Acknowledgements: This work was funded Foundation for Polish Science grant TEAM/2009-3/6.