On the Quasi-Stationary Dynamics of the MEK/ERK Signaling Pathway

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The main subject of cell signaling is an abstract notion of a pathway presented as a network of recurrent biochemical reactions partly connected by feedback loops. The considered in this article a MEK/ERK signaling pathway is a mitogen-activated protein kinase (MAPK) pathway, which exists in most, if not all eukaryotic cells, and is involved in various biological responses. For example it controls fundamental processes and is often deregulated in human cancer. In view of the great biological significance of this biochemical phenomenon the scientists consider different hypotheses, related to its reaction mechanism, which subsequently are accepted or rejected by theoretical or experimental verifications.

This work is focused on theoretical investigation of the MEK/ERK signal transduction dynamics. For the purpose, firstly we reduce dimensionality of the complete model of the pathway by applying a specific Quasi-Steady-State Approximation (QSSA) methodology. As a result of the QSSA procedure the complete model, presented by a system of seventeen ordinary differential equations is reduced to a system of eight ordinary differential equations. Next we concentrate on the quasi-stationary dynamics of the MEK/ERK signaling cascade. By solving the quasi-stationary system we obtain analytic relationships among the stationary and initial values of all MEK/ERK pathway components. The last ones can be considered as a direct connection among input (initial values) and output (stationary values) pathway signals. In addition, regulatory functions of a concrete signaling protein on the quasi-stationary pathway dynamics are established. The analytic results are supported by numerical simulations.