Analysis a Stiff Limit Cycle with CSP: Glycolysis in Saccharomyces cerevisiae

Panayotis D. Kourdis[1], Ralf Steuer[2], Dimitris A. Goussis[1]

[1]School of Applied Mathematics and Physical Sciences
National Technical University, Athens, Greece

[2]Institute of Theoretical Biology
Humboldt University, Berlin, Germany

Abstract

Complex mathematical models that describe a limit cycle behavior and are characterized by a wide spectrum of time scales are considered. Due to the action of the fast time scales, the limit cycle is constrained in a low dimensional subdomain of the phase space, where the solution evolves according to the slow time scales.

It is demonstrated that significant physical understanding can be acquired if the fast and slow dynamics are analyzed separately.

This type of analysis is applied on a 22-dimensional glycolysis model, by employing the Computational Singular Perturbation algorithm. It is shown that, due to fast dissipative time scales, the solution asymptotically approaches a 3-dimensional limit cycle; along the full length of which the characteristic time scale is of oscillatory nature. The motion around the limit cycle can be regulated by controlling the concentration of only three metabolites; i.e. [ATP], [G6P] and [FBP], which are associated to slow time scales.

In the talk, the dynamics of the problem will first be explored, the emphasis placed on the type of the developing time scales and their significance to the construction of a simplified model. The size of possible reduced order models that can be constructed and the accuracy these models provide will then be discussed. Next, the dynamics and the couplings among the variables of the problem on the manifold will be analyzed. Finally, the major features of the simplified model will be discussed.