Gepasi - Numerical simulation and optimization of biochemical kinetics

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Computer simulations of the kinetics of biochemical systems have been carried out since the first computers were available to academics. Nevertheless, this field has not expanded as widely as one would have expected, especially if we compare it to the growth of computer use in other areas of science (such as visualization of chemical structures). This slow progress is mostly to blame on the lack of availability of user-friendly simulation software. Without such programs, most biochemists cannot afford to invest enough time to learn the underlying mathematics and write a computer program to simulate their system of interest. General mathematical software such as *Mathematica* (Wolfram Research), even though capable of carrying out all the necessary numerical procedures, has the disadvantage of requiring the user to know which numerical methods to apply and also to overcome a language barrier. The ideal simulator should thus turn the process of defining a model into an easy task for the average biochemist and should be able to produce a simulation without requiring the user to supply technical details of the numerical methods. This should be achieved without sacrificing power for ease of use. *Gepasi* has been designed exactly to address these points, and we hope it will help contribute to making quantitative modeling of metabolic processes a common procedure both in research and education.

Optimisation methods attempt to *minimize* or *maximize* a function by adjusting the values of a set of parameters of that function. In biochemical kinetics, the functions that one is interested in optimizing are always results of a full steady state or time course simulations, therefore the optimization methods have to be coupled with a simulator. In the new version of *Gepasi* I have implemented a way of coupling optimization methods to the simulation engine that allows numerical optimization to be carried out easily. This was done in such a way that many optimization modules can be plugged in the program and the user can select any of these to minimize or maximize *any* system variable or indeed any function of them. One is not just limited to optimizing concentrations and fluxes, but also control coefficients, mass action ratios, and indeed any function of the variables including implicit functions. This capability is very useful for:

a) rational metabolic engineering, to design pathways with properties of interest;
b) evolutionary studies of metabolism, to investigate paths towards optimal states;
c) exploration of high dimensional parameter space, to overcome limitations related with models containing large number of parameters; and
d) parameter estimation, to fit models to experimental measurements.

Gepasi version 3.21 is available over the web at http://www.ncgr.org/gepasi/gepasi.html.