Model Reduction based on dynamic sensitivity analysis: A systems biology case of study

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1. Objective

The complexity of dynamic mathematical models due to large number of parameters is a major obstacle for their effective use in optimization and control processes. Furthermore, the experimental estimation of a large number of parameters is often an unfeasible task. Therefore, model reduction represents a key step to eliminate unimportant parameters and to uncover the most important control pathways of the models. Several techniques for parameter model reduction exist, including methods based on sensitivity analysis. Herein, the complex *E. coli* dynamic model [1] describing the carbon central metabolism which has 25 species participating in 30 reactions and with 116 parameters was used to study a model reduction strategy based on univariate analysis of the Euclidean norm to consider the effect to all metabolites. Additionally, two different model reduction strategies based on the local sensitivity and global sensitivity analysis were compared.

2. Results

Of all the 116 parameters from the complex model analyzed, 41 (35.3%) parameters were rejected without significant changes on the model prediction. Further 24 (20.7%) parameters were found to have significant influence on the systems, although their overall sensitivity (OSj) was low, and as such were also not considered in the model reduction. Although the metabolically structured model was affected by the model reduction, the dynamics of the network are generally well represented. By comparing the simulation results of the original and the reduced model, it can be showed that species trajectories did not change considerably with time (Figure 1).

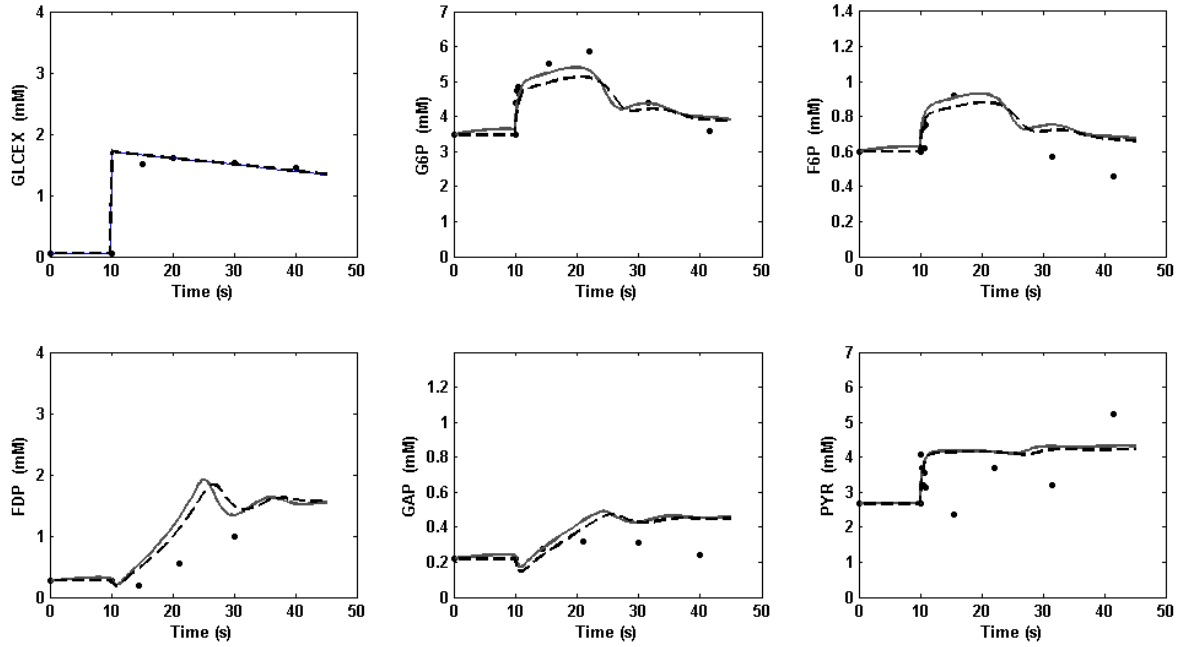

Figure 1. Comparison between experimental (symbols) and simulated data (gray solid line: reduced model based on local sensitivity and black dashed line: original model) of GLCEX (extracellular glucose), G6P (glucose-6-phospate), F6P (fructose-6-phospate), FDP (fructose-1,6-bisphosphate), GAP (glyceradehyde-3-phosphate) and PYR (pyruvate) variation with time in *E. coli*, after a glucose pulse. For GLCEX the lines are overlapped.

3. Conclusions

The dynamic sensitivity analysis with multiple variables is qualified as a promising tool for the complex model structure reduction and is shown to be capable of satisfactorily describing the dynamics of the original *E. coli* model. The kinetic model parameters can be rejected from the rate expressions with very limited effect on the overall model.

Keywords model reduction, dynamic *E. coli* model, dynamic sensitivity analysis

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References

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