A thermodynamic investigation of the glycolytic pathway

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The aim of system biology is the investigation and prediction of metabolic pathways using the metabolic flux analysis (MFA). The biggest disadvantage of this method is that huge underdetermined equation systems are usually obtained.

Thermodynamics might help with reducing the solution space by eliminating solutions that fulfill mass balances but violate the second law of thermodynamics. In this work, an algorithm called thermodynamic feasibility analysis (TFA) is applied to the glycolysis as an example for a metabolic pathway. This pathway was chosen because it is well understood and therefore poses a good model system for testing the method. An analysis of the feasibility of the glycolysis already exists but leads to the strange conclusion that, using the available literature data of the reactions, the whole glycolysis pathway is not feasible which is obviously wrong [1]. Reasons for this could be that the literature data was not determined under the conditions present in the cell or that the activity coefficients were neglected in the analysis. Therefore, new determinations and predictions of physical and thermochemical basis data of pure metabolites, reaction equilibria of single reaction steps, kinetic data and reaction heats under cell mimicking conditions (e.g. macromolecular crowding, ionic strength) are necessary. The reaction heats were quantified using an isothermal titration calorimeter doing multiple injection measurements under the influence of different cell-mimicking conditions. The improved thermodynamicdata can be used to establish a better TFA model which in future will include activity coefficients (using the ePC-SAFT equation of state), protonation and complexation of the metabolites, new $\Delta^R g^{0'}$ values and new calculated $\Delta^R g$ values.

Keywords isothermal titration calorimetry; TFA model; glycolysis

References

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