Thermodynamics of Glycolysis

New standard Gibbs energy of reaction values for glycolysis reactions determined from equilibrium measurements combined with activity coefficients

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For many organisms, glycolysis is a central metabolic pathway that provides energy and synthesis of precursors for further biosyntheses. The reaction equilibria of the single glycolytic reaction steps was investigated in this work to gain new thermodynamically-consistent standard data. The availability of such new data allows applying systems-biology tools for future investigations of the feasibility of the pathway, or parts of it, in a cell or even in a bioreactor.

Within glycolysis, one mole of glucose is converted in ten reaction steps to two moles of pyruvate. For this, two moles of adenosine diphosphate (ADP), phosphate (P_i) and nicotinamide adenine dinucleotide (NAD^+) are required, finally yielding two moles of each of the products adenosine triphosphate (ATP), the reduced form of NAD^+ (NADH), H^+ and water. The net gain of two moles ATP and two moles NADH makes glycolysis so important for the energy production of a cell.

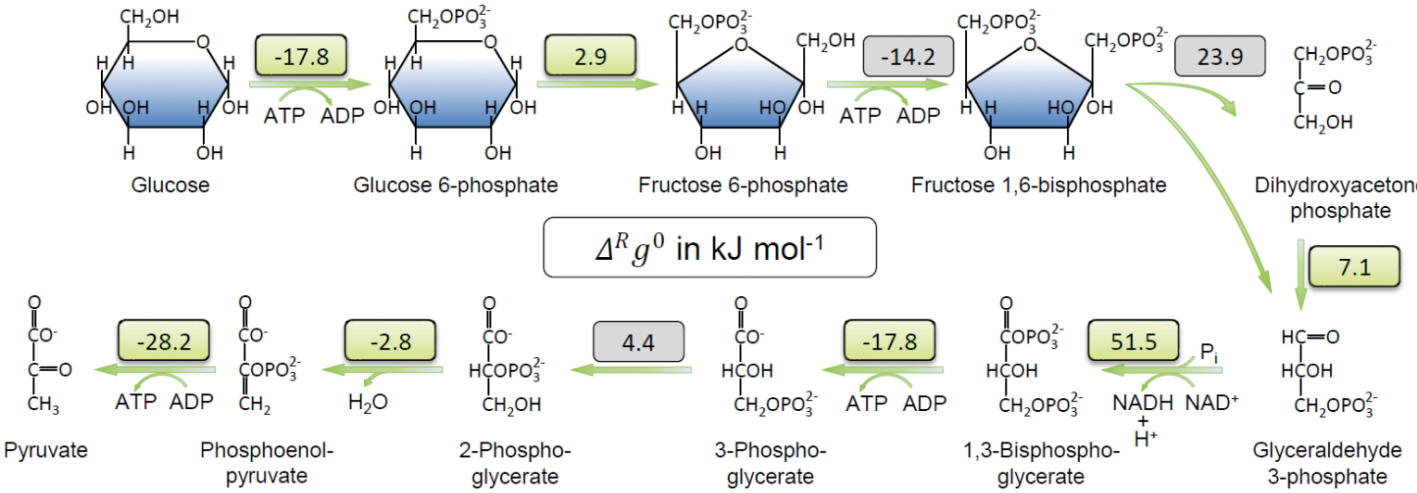

Figure 1: New (green) standard Gibbs energy of reaction values $\Delta^R g^0$ for the ten reaction steps of the glycolytic pathway at 298.15 K and 1 bar.

This energy gain depends on the reaction conditions. Therefore, researchers have investigated the feasibility of glycolysis at reaction conditions in a cell or in a bioreactor. Such feasibility analyses require a thermodynamically correct standard Gibbs energy of reaction $\Delta^R g^0$. This can be calculated from the activity-based thermodynamic equilibrium constant K_a:

$$\Delta^R g^0 = -RT \ln(K_a) = -RT \ln(K_{exp} K_\gamma) \qquad \text{(Eq. 1)}$$

K_a is calculated in this work from the ratio of the product and reactant concentrations K_{exp} and the ratio of the activity coefficients of products and reactants K_γ. K_{exp} is accessible by equilibrium measurements of the single reaction steps and analysis of the concentrations. K_{exp} depends on the reaction conditions chosen for the measurements, i.e. temperature, pressure, and the composition of the media. This includes concentration and type of buffers, salts or other co-solutes and even the concentration of the substrates. In literature, the concentration-dependent K_{exp} values were used instead of K_a to determine standard Gibbs energies of reaction. However, this is not correct as K_{exp} values are valid at very specific conditions only. This leads to misinterpretations of feasibility analyses. In this work K_{exp} was remeasured for the ten reaction steps; further, K_{exp} values were combined with K_γ values obtained from the thermodynamic model ePC-SAFT yielding the activity-based K_a value and thus consistent $\Delta^R g^0$ values. These new $\Delta^R g^0$ values were determined for all glycolytic reactions shown in Figure 1. This contributes to the full thermodynamic description of the glycolytic pathway at any desired conditions.

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Publications:
T. Greinert, K. Baumhove, G. Sadowski, C. Held, Biophysical Chemistry 258, 106330 (2020).

T. Greinert, K. Vogel, A.I. Seifert, R. Siewert, I.V. Andreeva, S.P. Verevkin, T. Maskow, G. Sadowski, C. Held, Biochimica et Biophysica Acta – Proteins and Proteomics 1868, 140365 (2020).

T. Greinert, K. Vogel, J.K. Mühlenweg, G. Sadowski, T. Maskow, C. Held, Fluid Phase Equilibria, 112597 (2020).