# Thermodynamics of Metabolism

Metabolism is a the set of reactions occuring in cells that sustain life. Groups of reactions that accomplish a particular need are called metabolic pathwyas. One important metabolic pathway is glycolysis, in which the combustion of glucose, $C_6H_{12}O_6$, produces water and carbon dioxide:

$$C_6H_{12}O_6(s) + 6O_2(g) \rightarrow 6CO_2(g) + 6H_2O(l)$$

Characterize the themodynamic favorability of this reaction with respect to temperature. The standard state free energy of formation, standard state enthalpy of formation and the absolute entropy for glucose are shown here; you will find other necessary thermodynamic values in your textboook:

$$\Delta G_f^o = -910.52 \text{ kJ/mol}_{rxn} \qquad \Delta H_f^o = -1274.4 \text{ kJ/mol}_{rxn} \qquad S^o = 212.1 \text{ J/mol}_{rxn}\bullet\text{K}$$

*Answer*. The values of $\Delta H^o$ and $\Delta S^o$ for the reaction are

$$\Delta H^o = -2806 \text{ kJ/mol}_{rxn} \qquad \Delta S = 262 \text{ J/mol}_{rxn}\bullet\text{K}$$

The reaction, therefore, is favorable at all temperatures.

Imagine that a man weighing 60 kg eats a candy bar containing 60 g of glucose. Imagine, as well, that his body is a perfect calorimeter (not a good assumption, of course). Assuming the specific heat of his body is the same as that for water, calculate the change in the man's body temperature? In your experience as a consumer of candy bars, is your answer reasonable? Explain. If your answer isn't reasonable, provide at least one plausible explanation—other than the body is not a perfect calorimeter—for why the calculated $\Delta T$ is larger or smaller than expected.

*Answer*. Knowing that $\Delta H^o$ is $-2806$ kJ/mol$_{rxn}$, we first calculate the heat released when converting 60 g of glucose to carbon dioxide and water

$$q_{rxn} = \frac{-2806 \text{ kJ}}{\text{mol}_{rxn}} \times \frac{1 \text{ mol}_{rxn}}{\text{mol } C_6H_{12}O_6} \times \frac{1 \text{ mol } C_6H_{12}O_6}{180.2 \text{ g } C_6H_{12}O_6} \times 60 \text{ g } C_6H_{12}O_6 = -934.3 \text{ kJ}$$

We know that $q_{soln}$ is $-q_{rxn}$ so the body is absorbing 934.3 kJ of heat. To find the increase in temperature we solve as follows

$$q_{body} = 934.3 \text{ kJ} = mS\Delta T = (60{,}000 \text{ g}) \times (4.184\times10^{-3} \text{ kJ/g}\bullet{}^o\text{C}) \times (\Delta T)$$

giving a $\Delta T$ of 3.7°C. Of course, this answer is not reasonable as personal experience attests. The reason that the body's temperature doesn't rise this quickly is that the reaction doesn't take place with a single burst of released energy. Instead, the overall reaction proceeds through many steps with the energy leaking out bit-by-bit. And, of course, much of the released energy is used to accomplish useful chemical work and not to just heat up the body.

The first step in the glycolytic pathway is the transfer of a phosphate from adenosine-triphosphate (ATP) to glucose:

**Reaction I**: glucose + ATP $\rightarrow$ glucose-6-phosphate + ADP

Under standard state conditions and in the absence of ATP, glucose-6-phosphate is unstable and reacts with water to produce glucose and a free phosphate:

**Reaction II**: glucose-6-phosphate + $H_2O$ $\rightarrow$ glucose + phosphate

Additionally, for the hydrolysis of ATP under standard state conditions

**Reaction III**: ATP + $H_2O$ $\rightarrow$ ADP + phosphate

the free energy change is favorable.

$$\Delta G^{o}_{III} = -32.48 \text{ kJ/mol}_{rxn}$$

What prediction can you make concerning the sign of $\Delta G^{o}$ for Reaction II under standard state conditions? Explain.

*Answer*. We are told that glucose-6-phosphate is "unstable and reacts with water to produce glucose and a free phosphate." From this statement we know that the hydrolysis of glucose-6-phosphate is favorable and that $\Delta G^{o}_{II} < 0$.

Under standard state conditions, the sign of $\Delta G^{o}$ for Reaction I is unclear given the information provided above. Using Hess's law, what can you say about the value of $\Delta G^{o}_{I}$? State your answer as $\Delta G^{o}_{I}$ must be greater than…, or $\Delta G^{o}_{I}$ must be less than…, or $\Delta G^{o}_{I}$ is equal to… Hint: note that Reaction III is the sum of Reactions I and II.

*Answer*. We know that the $\Delta G^{o}_{III}$ for the conversion of ATP to ADP is $-32.48$ kJ/mol$_{rxn}$ and that $\Delta G^{o}_{II}$ for the hydrolysis of glucose is <0. Using Hess's law, we know that

reaction I + reaction II = reaction III

$$\Delta G_{I} + \Delta G_{II} = \Delta G_{III}$$

$$\Delta G_{I} + \Delta G_{II} = -32.48 \text{ kJ/mol}_{rxn}$$

$$\Delta G_{I} = -32.48 \text{ kJ/mol}_{rxn} - \Delta G_{II}$$

From this we can see that $\Delta G_{I}$ may be either favorable or unfavorable depending upon the value of $\Delta G_{II}$. For example, if $\Delta G_{II}$ is $< -32.48$ kJ/mol$_{rxn}$, then $\Delta G_{I}$ is unfavorable.

Another step in the glycolytic pathway is

fructose-1,6-diphosphate → dihydroxyacetone phosphate + glyceraldehyde-3-phosphate

for which $\Delta G^o$ is +23.8 kJ/$mol_{rxn}$ at a temperature of 298 K. Although this reaction is unfavorable under standard state conditions, we know it routinely occur in cells; thus, the concentrations of reactants and products in the cells must not be at their standard states values. What is the largest reaction quotient, Q, that will produce a favorable free energy change? Recall that Q is a measure of the relative amounts of products to reactants.

*Answer.* If the reaction occurs then ΔG must be less than zero. To find the relative ratio of products to reactants (Q), we recall that

$$\Delta G = \Delta G^o + RT\ln Q$$

$$0 = +23.8 \text{ kJ/mol}_{rxn} + (8.314\times10^{-3} \text{ J/mol}_{rxn}\bullet\text{K})(298 \text{ K})\ln Q$$

$$Q = 6.73\times10^{-5}$$

Thus, the value of Q must be less than $6.73\times10^{-5}$ for the reaction to be favorable.

The value of Q is approximately $10^{-4}$ in the cells of rats. What is the value of ΔG for this reaction under these conditions and what does this tell you about the favorability of this glycolytic pathway in rats? If you believe that the reaction is unfavorable, why might it still occur?

*Answer.* The typical ratio found in rats of approximately $10^{-4}$ suggests that the reaction is still not favorable as it is larger than the value calculated above. The value of ΔG under these conditions, however

$$\Delta G = +23.8 \text{ kJ/mol}_{rxn} + (8.314\times10^{-3} \text{ J/mol}_{rxn}\bullet\text{K})(298 \text{ K})\ln(10^{-4}) = 0.98 \text{ kJ/mol}_{rxn}$$

is only slightly unfavorable. A rat's body temperature, of course, is not 25°C, but is closer to 38°C, which might explain why the reaction is favorable. For example, at 311 K and assuming no change in $\Delta G^O$, we find that ΔG is slightly favorable

$$DG = +23.8 \text{ kJ/mol}_{rxn} + (8.314\times10^{-3} \text{ J/mol}_{rxn}\bullet\text{K})(311 \text{ K})\ln(10^{-4}) = -0.015 \text{ kJ/mol}_{rxn}$$

Of course, $\Delta G^O$ will change, but since we can guess that $\Delta H^O$ is positive and $\Delta S^O$ is positive for this reaction, an increase in temperature will make $\Delta G^O$ less positive and ΔG becomes even more favorable.