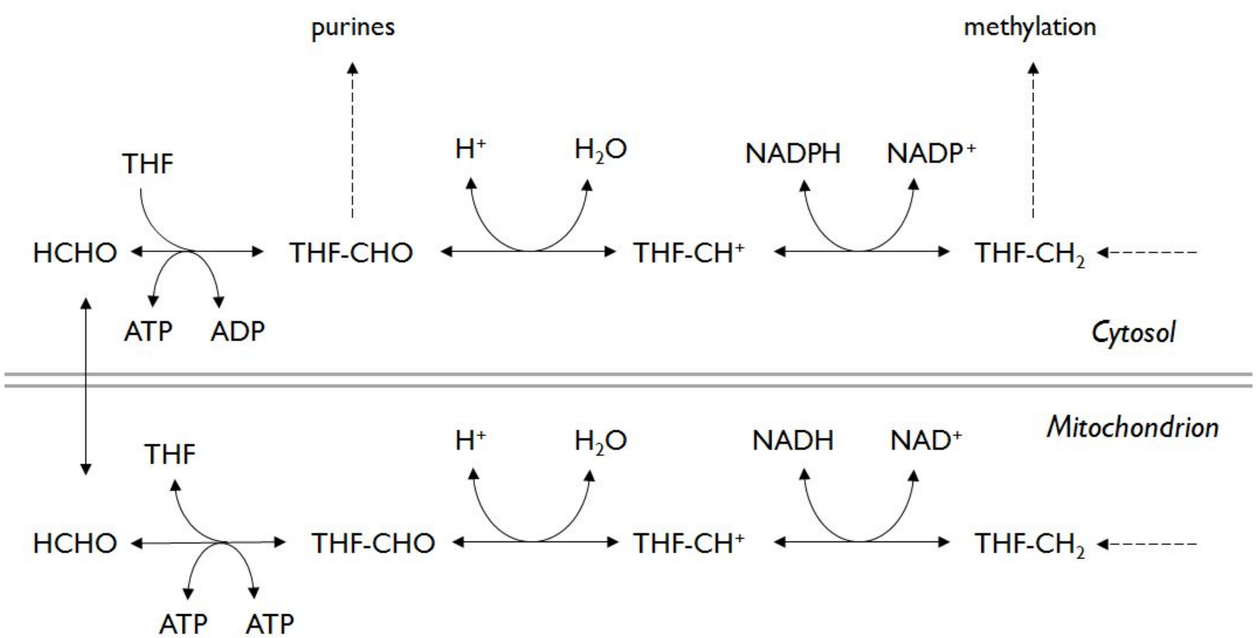
Seminar 5

Compartmentalization

1. Below is a schematic of "one-carbon" metabolism, which is compartmentalized into mitochondria and cytosol since the tetrahydrofolate cofactor (THF) cannot cross the membrane. Instead, formate (HCHO, left) exchanges between the two compartments and connects the pathways. What classes of enzymes are involved? In what direction should reactions proceed? Are some irreversible? The major products of the system are THF-CHO (formyl-THF) and THF-CH2 (methylene-THF), uses for purine synthesis and methylation. How should the pathway operate to produce this products efficiently? Why might the compartmentalization be beneficial?



Transport

2. The actual Gibb's energy difference ΔG of a reaction or process $A \rightarrow B$ depends on the concentrations of A and B as $\Delta G = \Delta G° + R\,T\,\ln([B] / [A])$. What is the Gibb's energy difference of transport of a nutrient against a 1000-fold concentration gradient? Can such transport be driven by ATP hydrolysis? What is the maximum gradient that could be maintained by a 100% efficient ATP-driven pump? What do you think is the maximum gradient in practise?

3. The insulin-dependent glucose transporter GLUT4 is passive and has K_M around 5 mM. What does a Michaelis-Menten constant mean for a passive transporter? Does the value make sense physiologically?

4. The transport of glucose by GLUT4 followed by phosphorylation by hexokinase (ΔG = -17 kJ / mol) is considered to "trap" glucose in cells. If this system was allowed to go to equilibrium, what would the ratio $[\text{glucose-6P}]_{in} / [\text{glucose}]_{in}$ be? What about $[\text{glucose}]_{in} / [\text{glucose}]_{out}$?

5. The Na/K ATPase maintains inside-outside ratios of approx $[Na]_{in} / [Na]_{out} = 0.1$ and $[K]_{in} / [K]_{out} = 40$, at an electric potential difference of ΔV = -50 mV. At these conditions, the ATPase pumps 3 Na^+ out and simultaneously 2 Na^+ inward against their gradients; this process has ΔG = 37 kJ/mol. The ΔG for transport of Na+ ions back into the cell is about 11 kJ/mol. What gradient can be achieved by a Na^+-driven nutrient transporter? Why would cells choose Na-coupled transport of nutrients rather than ATP-driven?