Course 2851 Principles of Metabolism
Metabolism and endocrinology programme, Karolinska Institutet

Lecture 9

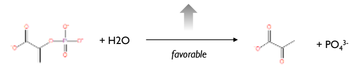
Energetics and enzyme catalysis

Roland Nilsson, Ph.D

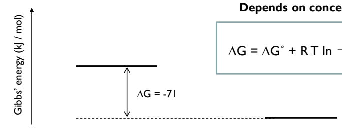
Department of Medicine, Solna
Center for Molecular Medicine
Karolinska Institutet

All reactions strive to minimize energy

Gibbs' energy difference: $\Delta G°= -71$ kJ / mol



Phosphoenolpyruvate (PEP) pyruvate



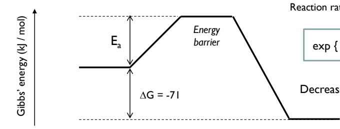
Depends on concentrations

$$\Delta G = \Delta G° + R\,T \ln \frac{\text{products}}{\text{substrates}}$$

Energy barrier of intermediates determine reaction rate

Gibbs' energy difference: $\Delta G°= -71$ kJ / mol

Phosphoenolpyruvate (PEP) pyruvate

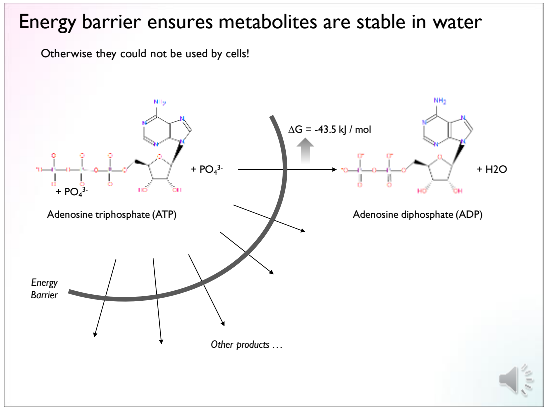


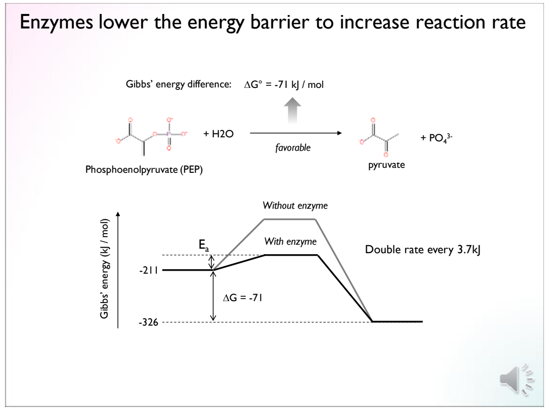
Reaction rate proportional to:

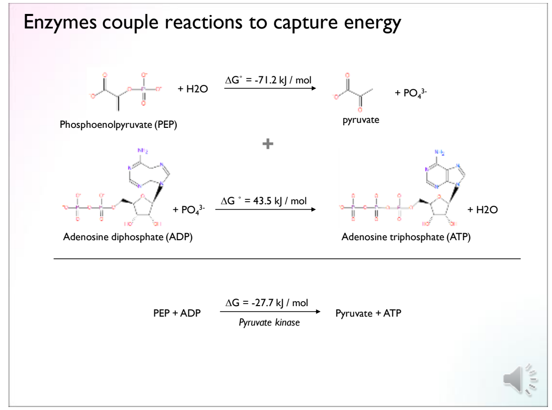
exp { -Ea / R T }

Decrease ½ every 3.7kJ

Example : Ea = 50 kJ → 10,000-fold decrease in reaction rate


Energy barrier ensures metabolites are stable in water
Otherwise they could not be used by cells!
ΔG = -43.5 kJ / mol
+ PO4 3-
+ H2O
Adenosine triphosphate (ATP)
Adenosine diphosphate (ADP)
Energy Barrier
Other products …

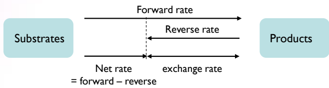

Enzymes lower the energy barrier to increase reaction rate
Gibbs' energy difference: ΔG° = -71 kJ / mol
+ H2O
favorable
+ PO4 3-
Phosphoenolpyruvate (PEP)
pyruvate
Without enzyme
With enzyme
Ea
Gibbs' energy (kJ / mol)
-211
-326
ΔG = -71
Double rate every 3.7kJ


Enzymes couple reactions to capture energy
+ H2O
ΔG° = -71.2 kJ / mol
+ PO4 3-
Phosphoenolpyruvate (PEP)
pyruvate
+
+ PO4 3-
ΔG° = 43.5 kJ / mol
+ H2O
Adenosine diphosphate (ADP)
Adenosine triphosphate (ATP)
PEP + ADP
ΔG = -27.7 kJ / mol
Pyruvate kinase
Pyruvate + ATP

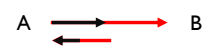
Activation energy is not the whole story!

Stryer: "*The ΔG provides no information about the rate of a reaction*" (p. 208, 6th ed)

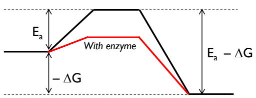
Actually, the ΔG provides no information about the **forward rate** of a reaction.
But most metabolic reactions are reversible!

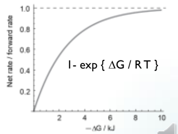


Enzyme catalysis



Forward *and* reverse rates increase

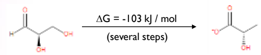




Tradeoff between reaction rate and ATP yield

Rate increases with ΔG, but high ATP yield lowers ΔG ...

Lower glycolysis maintains large ΔG

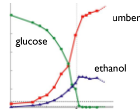


glyceraldehyde lactate

+ 1 ATP: ΔG = -59.7 kJ / mol
+ 2 ATP: ΔG = -16.2 kJ / mol

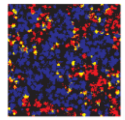
Bar-even et al, Nat Chem Bio 8:509-517, 2012.

Yeast diauxic shift



Brauer et al, Mol Biol Cell 16:2503–2517, 2005.

Microbial communities

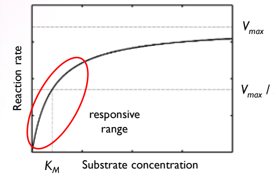


Glycolytic
Respiratory

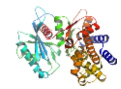
Pfeiffer et al, Science 292:504-507, 2001.

Michaelis-Menten kinetics

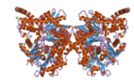
- Good phenomenological description of many enzymes



Glucokinase $K_M \approx 7$ mM



Hexokinase $K_M \approx 0.2$ mM



- K_M values can vary widely depending on chemical conditions

www.brenda-enzymes.org