Metabolism

- The overall process through which living systems acquire and utilize the free energy they need to carry out their various functions

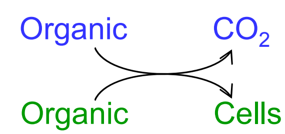
Metabolism

- Living systems couple *energy-releasing* nutrient oxidation to the *energy-requiring* processes required to maintain a living state
  - Performance of mechanical work
  - Active transport of solutes
  - Biosynthesis of complex molecules
  - Disposal of waste products

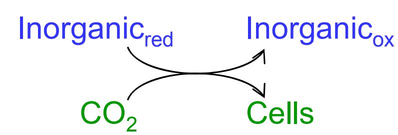
Classification of organisms

1. Classification on the basis of E source
   a) Phototrophs: obtain E from sunlight
   b) Chemotrophs: obtain E from oxidation of reduced compounds (organic or inorganic)
2. Classification on the basis of C source
   a) Autotrophs: use CO_2 as sole source of C
   b) Heterotrophs: Use reduced organic molecules as source of C

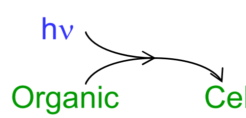
(1) chemoheterotroph



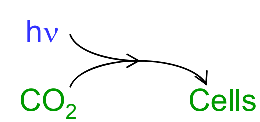
(2) chemoautotroph



(3) photoheterotroph

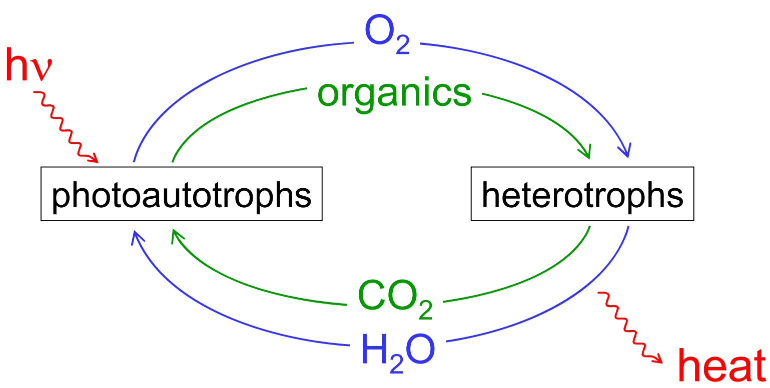


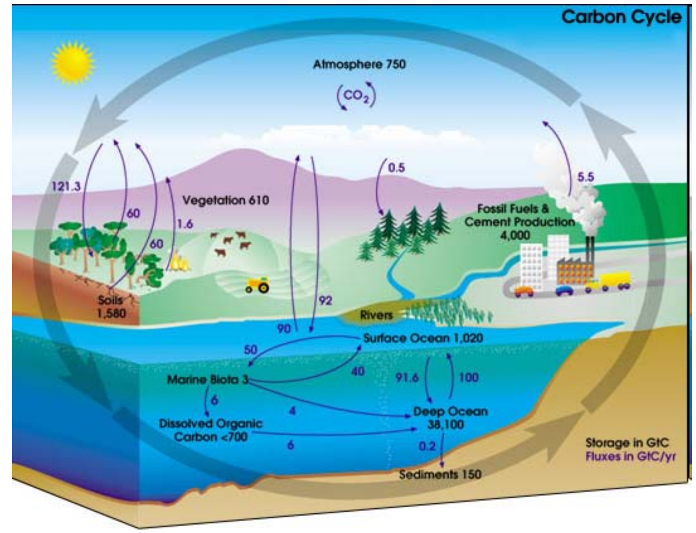
(4) photoautotroph



Biochemical cycling

- Living systems maintain relatively steady states
- Biogeochemical cycles are balanced: consumption = production
- Energy flow through biosphere is one way





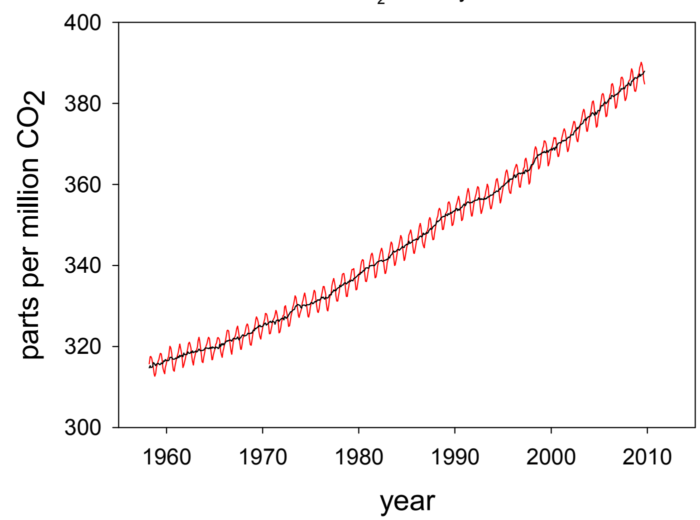
Credit: NASA picture, not protected by copyright
http://earthobservatory.nasa.gov/Library/CarbonCycle/carbon_cycle4.html

Global carbon cycling

source of carbon flux	carbon released to atmosphere (gigatons C/yr)	carbon removed from atmosphere (gigatons C/yr)
burning of fossil fuels	4-5	
oxidation and erosion of soil organic matter	61-62	
respiration of organisms	50	
deforestation	2	
incorporation into biomass via photosynthesis		110
diffusion into oceans		2.5
Net	117-119	112.5
Net increase in atmospheric C per year	+4.5-6.5	

data are from: http://www.oznet.ksu.edu/ctec/Carbon/carboncycle.htm

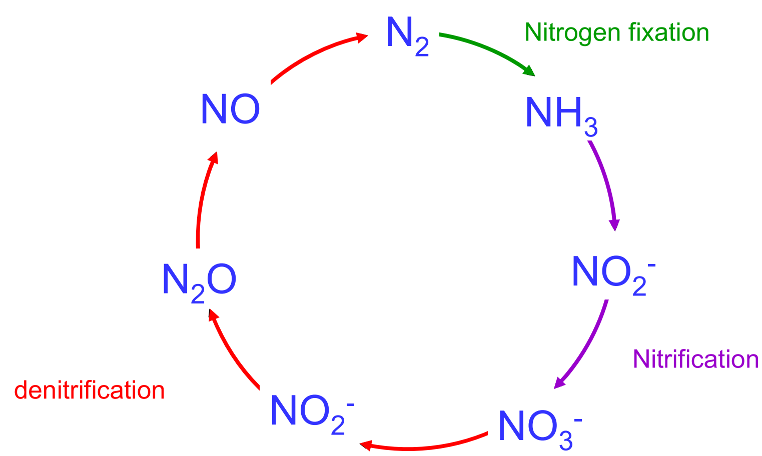
Mauna Loa CO_2 monthly mean data

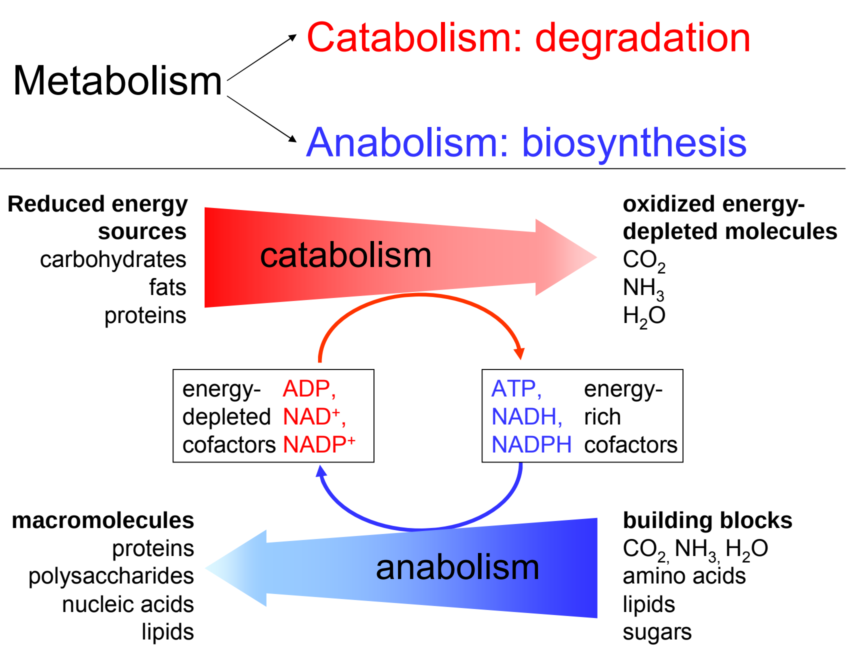


NOAA ESRL DATA, ftp://ftp.cmdl.noaa.gov/ccg/co2/trends/co2_mm_mlo.txt, Pieter Tans
http://www.esrl.noaa.gov/gmd/ccgg/trends/

Historic C cycle balance

Biochemical cycling: inorganic N

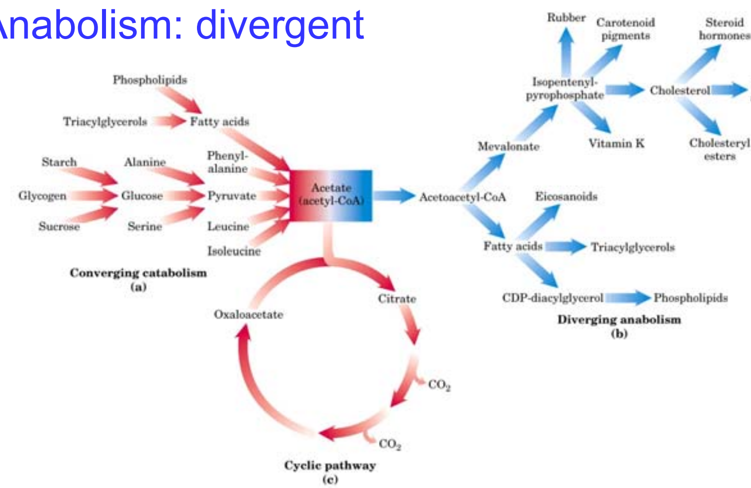




Some features of metabolic pathways

Catabolism: convergent → acetyl-CoA

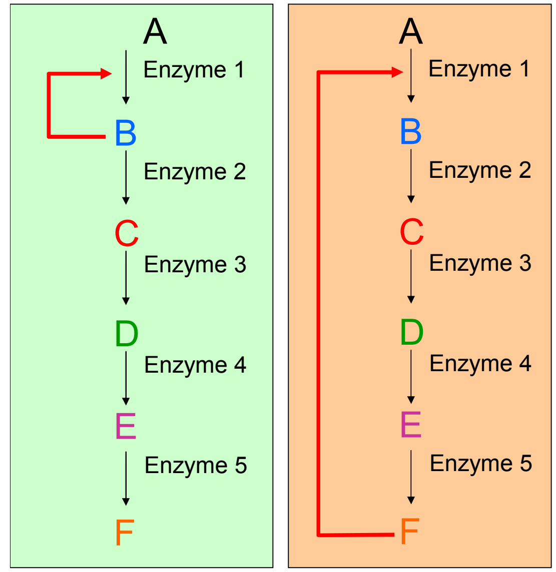
Anabolism: divergent



Some features of metabolic

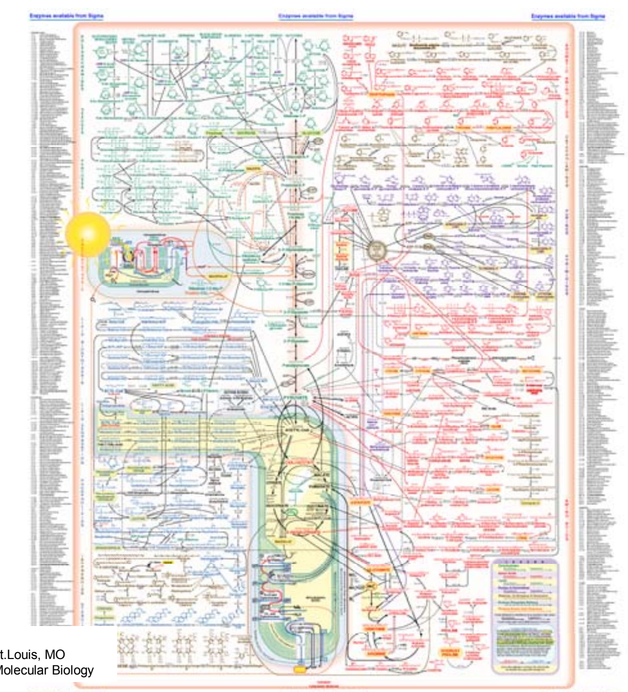
1. Metabolic pathways are "irrever
   - Occur with release of free energy
   - Go to completion
   - Have a direction
   - If two metabolites are metabolicall by a sequence of reactions, the pa to the 2nd must differ from the 2nd
2. Every metabolic pathway has an early "committed step"
3. Metabolic pathways are regulated
4. Metabolic pathways in eukaryotic cells occur in specific cellular locations

What kinds of inhibition are being illustrated here?



A. Feedback / product
B. Product / feedback
C. Feedback / Feedback
D. Product / product

The sheer number of metabolic pathways can at first glance seem a bit overwhelming……..



Designed by Donald Nicholson
Prepared and published by Sigma-Aldrich Co., St.Louis, MO

Four categories of enzymes (C. Walsh)

1. Group transfer reactions
2. Oxidations/reductions
3. Eliminations/isomerizations/rearrangements
4. Reactions that make or break C-C bonds

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International Enzyme Nomenclature

- Enzymes are assigned based on six classes of reactions that are a bit more confusing, yet allow more specific assignments

International Enzyme Nomenclature

Enzyme Nomenclature and Enzyme Commision Numbers

EC #	Class	# of sub-classes	Reactions catalyzed	Representative enzyme
1	oxidoreductases	22	Oxidation/reduction (e-transfer)	Alcohol dehydrogenase
2	transferases	9	Transfer of functional groups from one compound to another	hexokinase
3	hydrolases	13	Hydrolysis (group transfer to water)	chymotrypsin
4	lyases	7	Cleave C-C, C-O, C-N and other bonds by means other than (1) or (3)	Acetoacetate decarboxylase
5	isomerases	6	Changes within a single molecule; intramolecular rearrangement	Triose phosphate isomerase
6	ligases	6	Joining of two molecules forming new C-C, C-O, C-N, C-S bonds, using energy of NTP hydrolysis	Glutamine synthetase

International Enzyme Nomenclature

1. Group transfer

2. Oxidation/ reduction

3.Eliminations/ isomerizations

4. Reactions That make or Break C-C bonds

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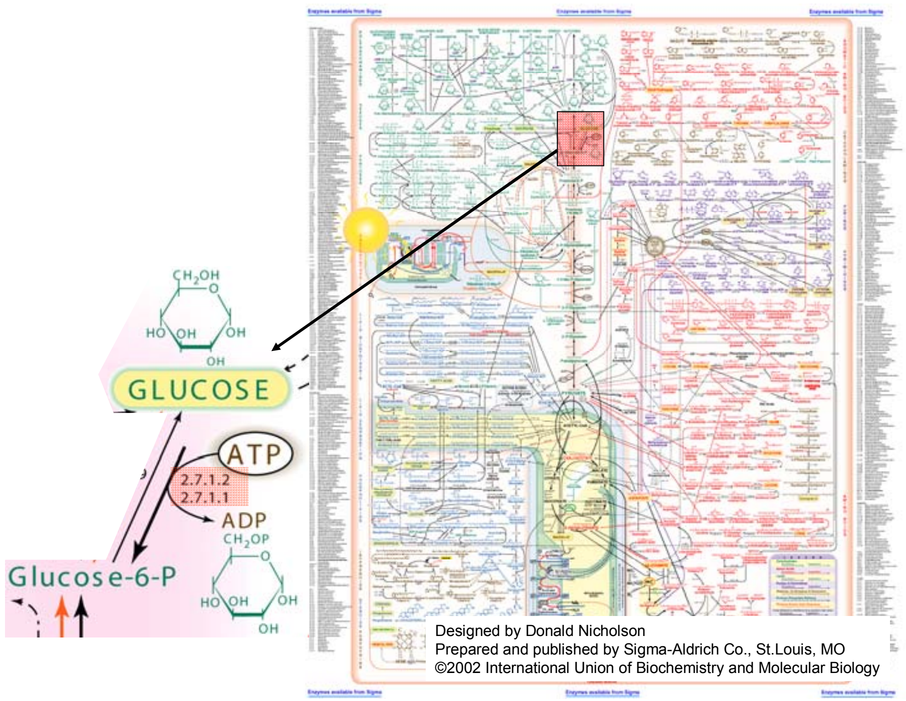
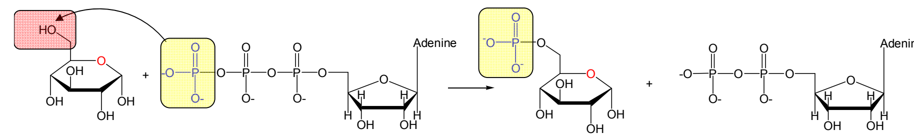
International Enzyme Nomenclature

- http://www.chem.qmul.ac.uk/iubmb/enzyme/
- Every enzyme can be assigned a unique four digit code based on six classes of enzymes
- e.g. "1.1.1.1" = alcohol dehydrogenase
- First digit: class of enzyme
- First three digits: classify reaction catalyzed
- Fourth digit: unique identifier for a particular enzyme
- Each enzyme is also assigned a systematic name describing the specific reaction catalyzed

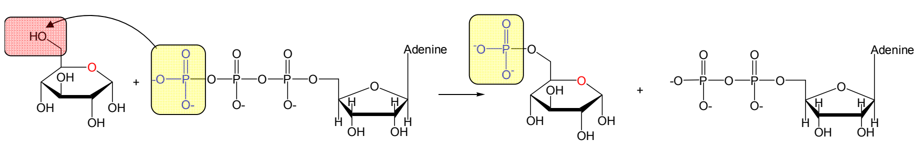


International Enzyme Nomenclature: Hexokinase EC 2.7.1.1



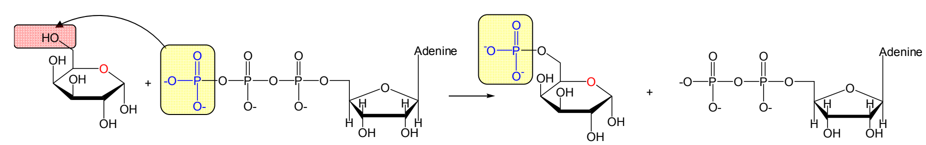
- 2.X.X.X: Transfer of a functional group
- 2.7.X.X: Phosphorus-containing functional group is transferred
- 2.7.1.X: Phosphotransferases with an alcohol group as acceptor
- 2.7.1.1: “hexokinase” is the specific enzyme: glucose is acceptor, ATP is donor
- Systematic name: ATP:D-hexose 6-phosphotransferase

International Enzyme Nomenclature: Glucokinase EC 2.7.1.2



- 2.X.X.X: Transfer of a functional group
- 2.7.X.X: Phosphorus-containing functional group is transferred
- 2.7.1.X: Phosphotransferases with an alcohol group as acceptor
- 2.7.1.1: “glucokinase” is the specific enzyme: glucose is acceptor, ATP is donor
- Systematic name: ATP:D-hexose 6-phosphotransferase
- Glucokinase is an “isozyme” of hexokinase

International Enzyme Nomenclature: Galactokinase EC 2.7.1.6



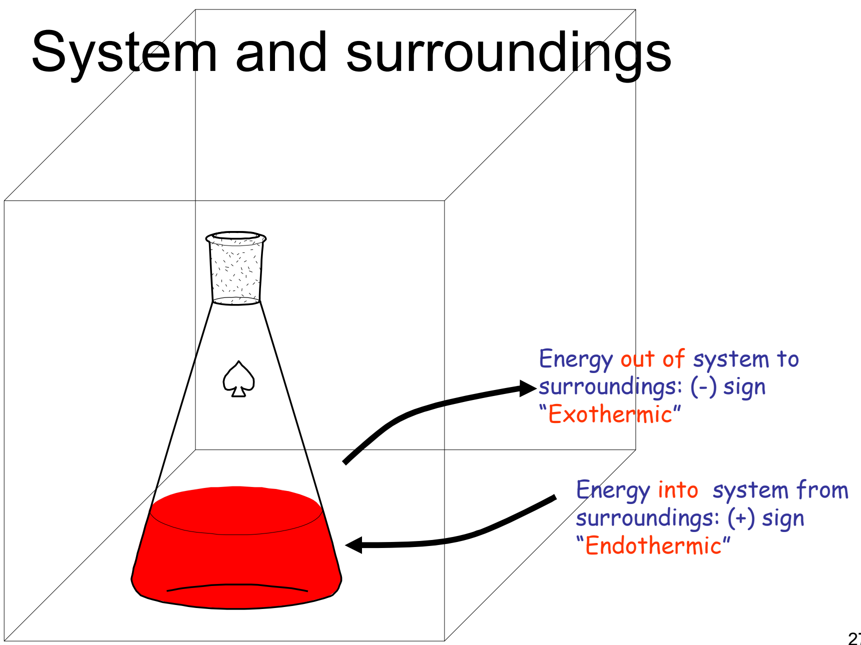
- 2.X.X.X: Transfer of a functional group
- 2.7.X.X: Phosphorus-containing functional group is transferred
- 2.7.1.X: Phosphotransferases with an alcohol group as acceptor
- 2.7.1.6: “galactokinase” is the specific enzyme: galactose is acceptor, ATP is donor
- Systematic name: ATP:D-galactose 6-phosphotransferase

To understand metabolic transformations, we need to understand the thermodynamics of the transformations

Bioenergetics

The quantitative study of energy transformations in living cells

System and surroundings



The first law of thermodynamics

The energy of the UNIVERSE is constant

The 2nd law of thermodynamics

The entropy of the UNIVERSE is increasing

Gibbs free energy

$$\Delta G = \Delta H - T\Delta S$$

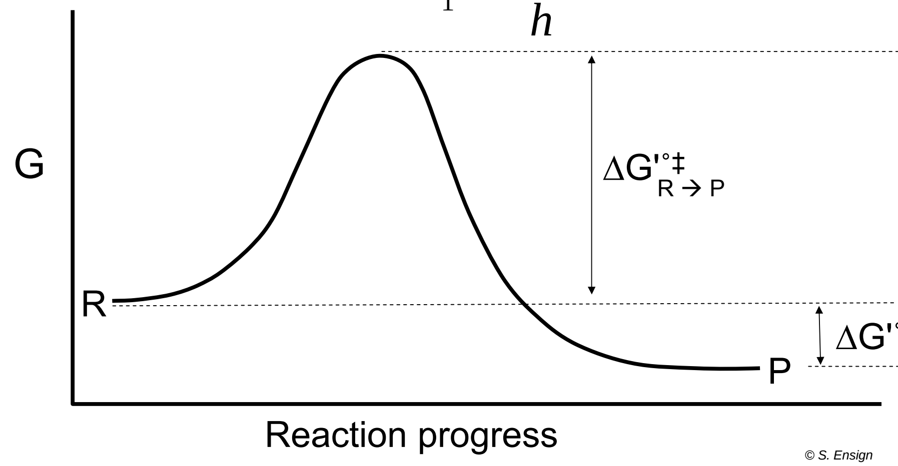
Exothermic ≠ Exergonic

Endothermic ≠ Endergonic

Chemical kinetics vs. thermodynamics

$$aA + bB \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} cC + dD \qquad K_{eq} = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

$$d[P]/dt = k_1[A]^n\,[B]^m \qquad k_1 = \frac{KT}{h} e^{-\Delta G^{\ddagger}/RT}$$



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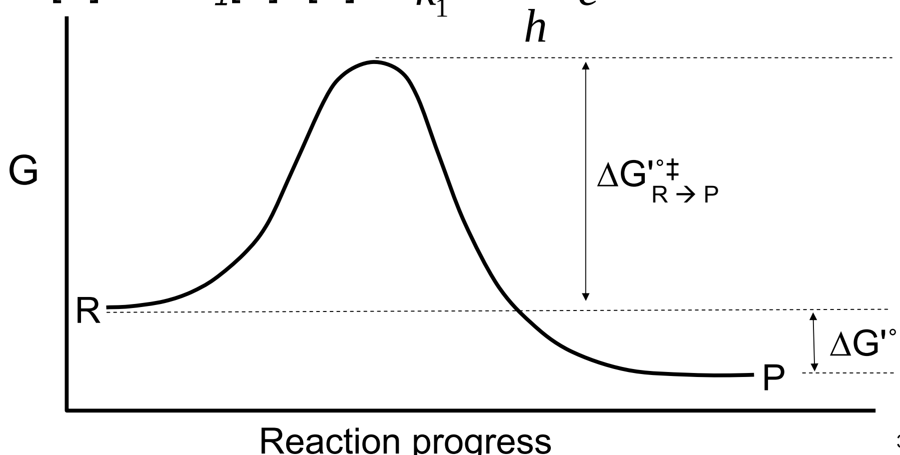
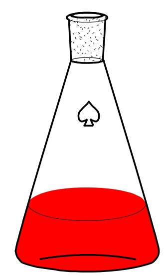


Standard state

1 M reactants and products, 1 atm. P for gaseous reactants and products, 25° C. $\Delta G = \Delta G°$

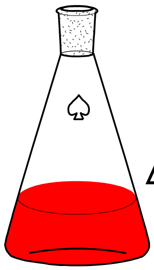


$$aA + bB \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} cC + dD$$

Nonstandard state

Nonstandard state: [reactants] and [products] $\neq 1$ M or 1 atm. P

$$aA + bB \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} cC + dD$$



$$\Delta G = \Delta G^{\circ} + RT \ln Q$$

"standard state"

"reaction quotient"

$$Q = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

Equilibrium

$$aA + bB \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} cC + dD$$

$$\Delta G = \Delta G^{\circ} + RT \ln Q$$

$$0 = \Delta G^{\circ} + RT \ln Q_{eq}$$

$$\Delta G^{\circ} = -RT \ln Q_{eq}$$

At equilibrium, Q = K_{eq}: $K_{eq} = \frac{[C]^c[D]^d}{[A]^a[B]^b}$

$$\Delta G^{\circ} = -RT \ln K_{eq}$$

Biochemical standard state

ΔG° values are additive