BCHE2030 Tutorial 4

Please change your participant name to the name on your student ID card, thanks!
For student changing group for the **first time, please indicate your original group next to your name so we can identify you for attendance, thank you.

Content

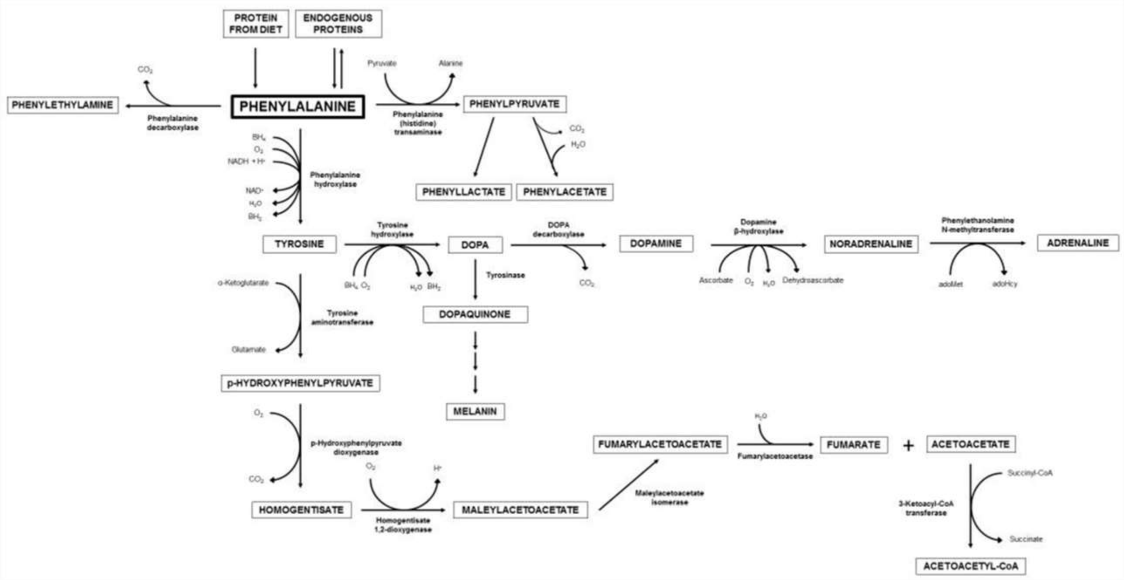
- ❑ Questions from students
- ❑ Quiz 1
- ❑ Protein Cooperativity
- ❑ Quiz 2
- ❑ Bioenergetic

What is causing the symptoms in PKU (mental retardation)? Is it phenylalanine or its metabolites?

1. PKU–defect in phenylalanine hydroxylase–enzyme becomes dysfunction
2. Cannot convert Phe to Tyr
3. Accumulate of Phe and its metabolites (phenylpyruvate)

⇒ In general, it is believed that human body is sensitive to Phe, and accumulation of Phe disrupts brain development

Additional info: Tyrosine is a precursor of several neurotransmitters.



Quiz 1 – Protein folding

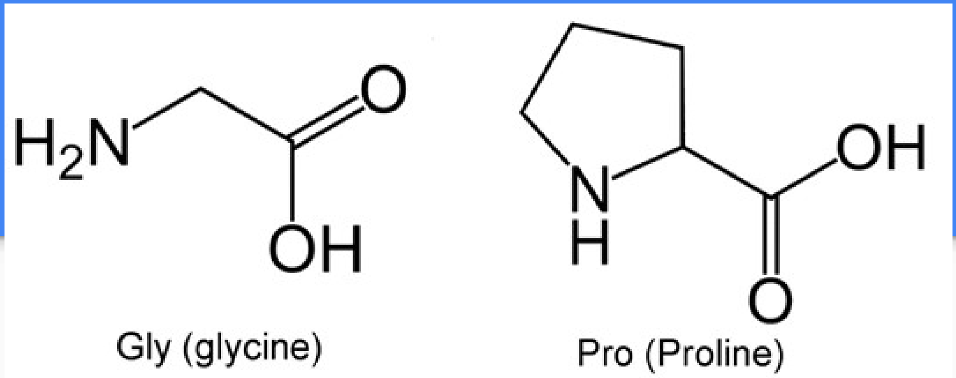
Which of the following is correct?

A. Proline is commonly found in beta-strand
B. Arginine is not commonly found in alpha-helix
C. Glycine is commonly found in alpha-helix
D. Alanine is not commonly found in alpha-helix

Hint: Amino acid which is too small or too bulky is not suitable for alpha-helix.

Try **integrate** what you have learnt so far!

Quiz 1 – Protein folding



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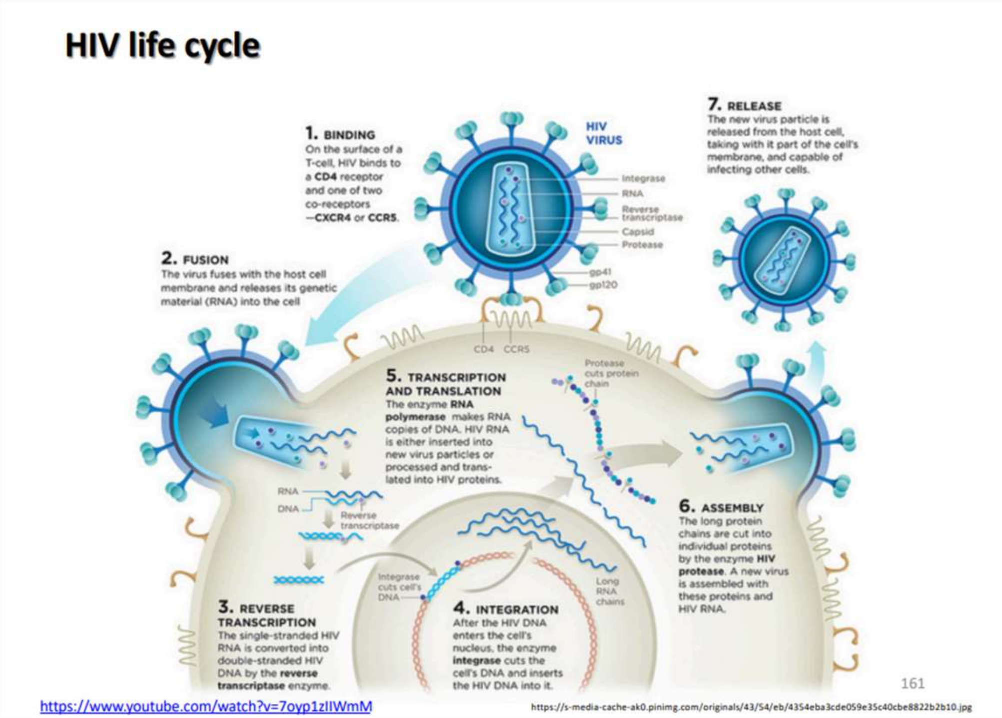
since two original RNA will be wrapped into the new systhesized virus eventually and export out of the host cell, there will not have RNA remain in the host cell, and so no new RNA can be synthesized, so actually just an in and out of virus, no net product of virus. Which i dont know how virus proliferate in host cell? Moreover, what the cell activity? The virus protein that can be continuously produced? or the virus RNA?



Virus infection is not simply in and out

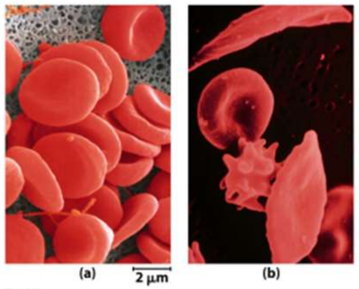
1. Translation and cleavage of polyproteins
2. transcription and replication of viral RNA genome(some will insert to host genome)
3. assemble and release out of host cells

host cell become factory of virus to synthesized their RNA genome with accessory protein. The cell activity(energy is consumed)will be disrupted until cell death

Normal hemoglobin also aggregate, but not as long as the length of aggregation of Hb S? So no issue is induced?

Sickle cell anemia

- sickle-cell hemoglobin (Hb S), which have a point mutation of Glu -> Val at residue position 6 of *β-globin* chain.
- Hb S can polymerize to form insoluble filaments that distort the shape of erythrocytes.



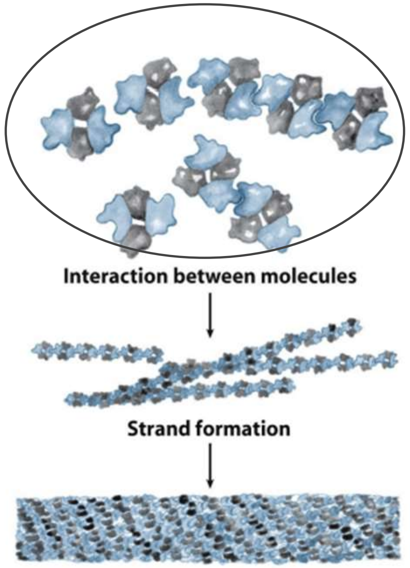


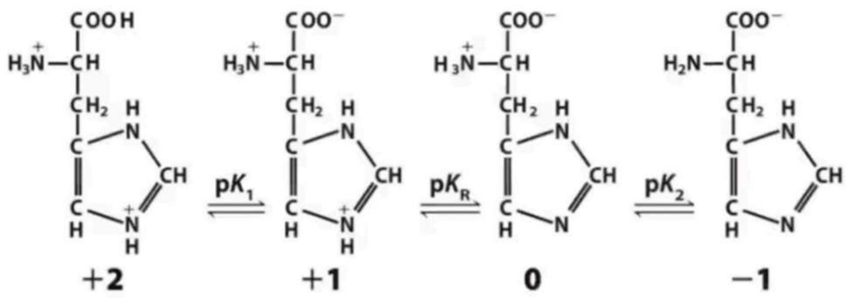
Figure 5-20b
Lehninger Principles of Biochemistry, Fifth Edition

In pH3, COOH should protonate, which present as COOH. NH3 of the backbone should deprotonate which has no charge and present as NH3. For the R group, it sould also deprotonate, which present as N. So it should be neutral, how come the answer is +1? i dont get it, what are the step for doing this kind of question?

What is the net charge of Histidine at pH 3.0?

pK_1 (-COOH) = 1.82
pK_2 ($-NH_3$) = 9.17
pK (R-group) = 6.0

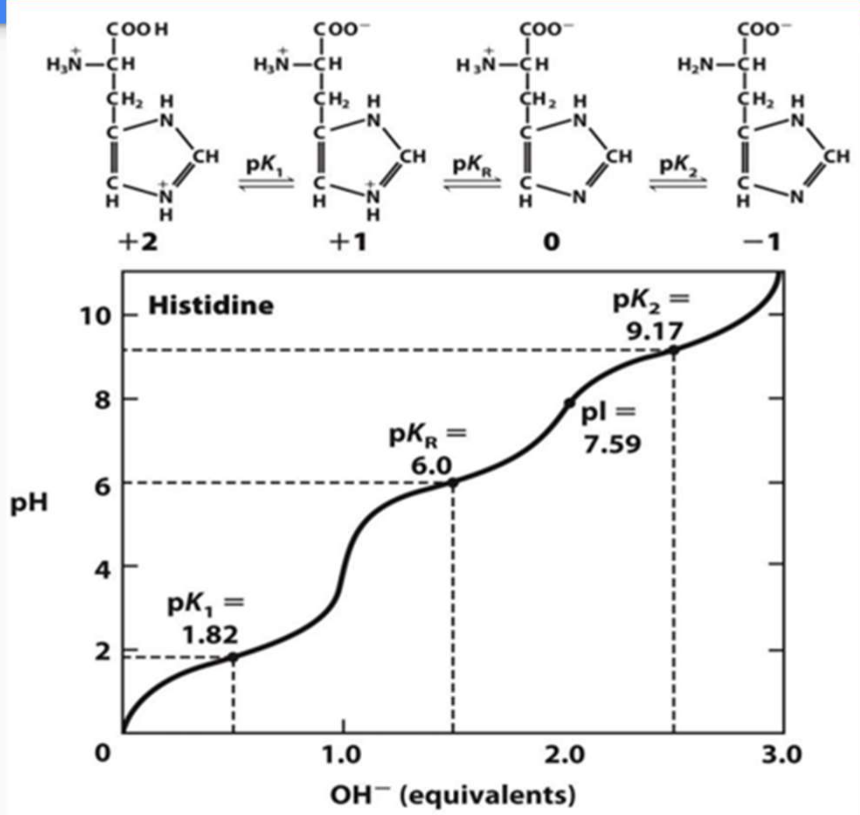
A. +2
B. +1
C. 0
D. -1



Charged groups in amino acids and pKa

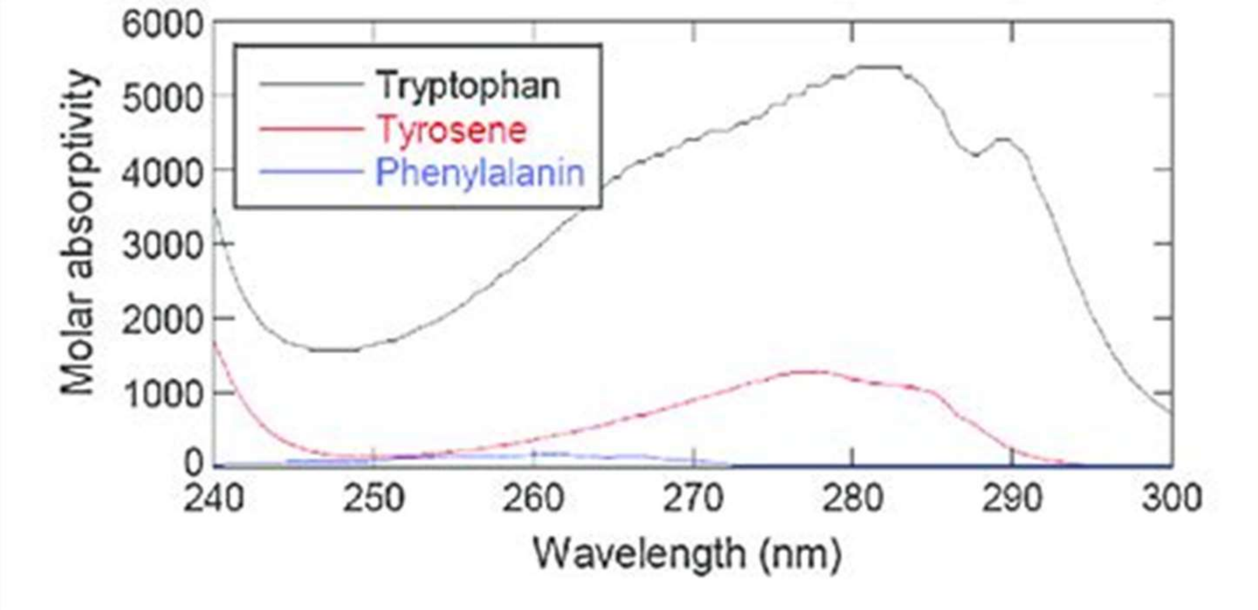
pH < pKa	protonated, accept hydrogen
pH > pKa	deprotonated, release hydrogen
pH = pKa	half protonated, half deprotonated

pH	amino group (9.17) (+1 or 0)	carboxyl group (1.82) (0 or -1)	R group (6) (+1 or 0)	overall charge
1	+1	0	+1	+2
3	+1	-1	+1	+1
6.5	+1	-1	0	0
12	0	-1	0	-1



I don't understand how aromatic ring absorb untraviolet, is that becuase of its shape or size? and its shape or size make it capable to absorb 280nm wavelenght of ultraviolet?

- UV absorption : excitation of electrons
- benzene: aromatic/conjugated double bonds → absorbs longer wavelengths
- addition groups render higher absorbance at 280nm

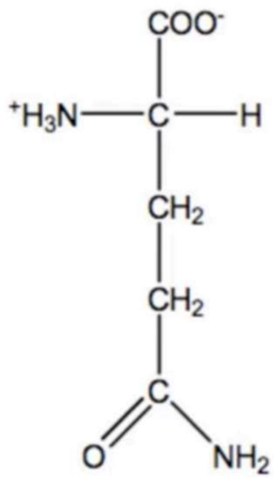


How to do this kind of question? And is the drawing of the amino acid provided always correspond to as the configuration of it at the pH of the question?

What is the net charge of this amino acid at pH7.5?

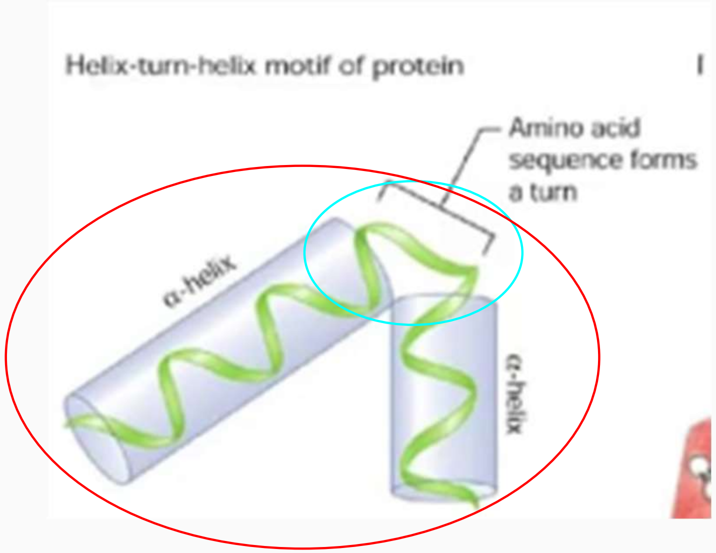
pK_1 (-COOH) = 2.17
pK_2 ($-NH_3$) = 9.13

A. Neutral
B. Positive
C. Negative



What is the difference between motifs and loops?

- loop: a region of a peptide which does not form alpha helix or beta strand
- motif: the ways of grouping alpha helices and/or beta strands

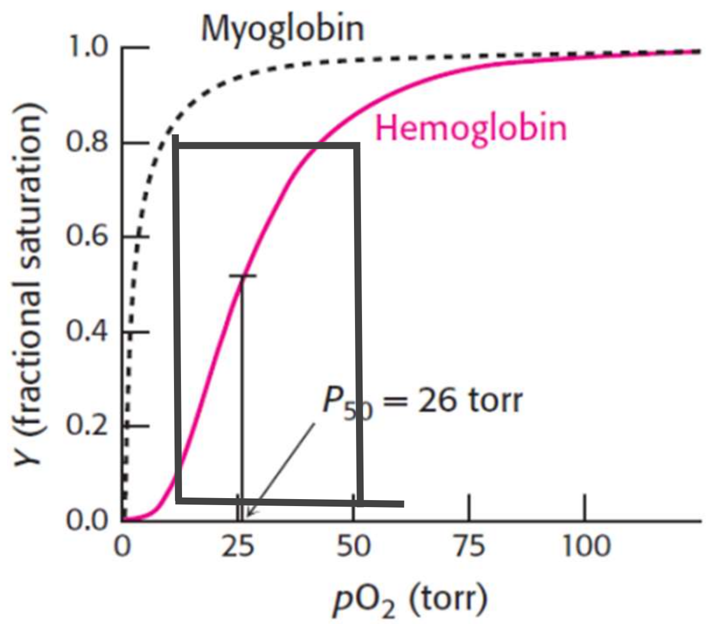


Protein Cooperativity

- multiple substrate binding sites (multiple subunits)
- sigmoidal curve
- binding of one substrate affects binding affinity of other substrates at other binding sites
- increase affinity (positive) / decrease affinity (negative)

Hemoglobin and Myoglobin

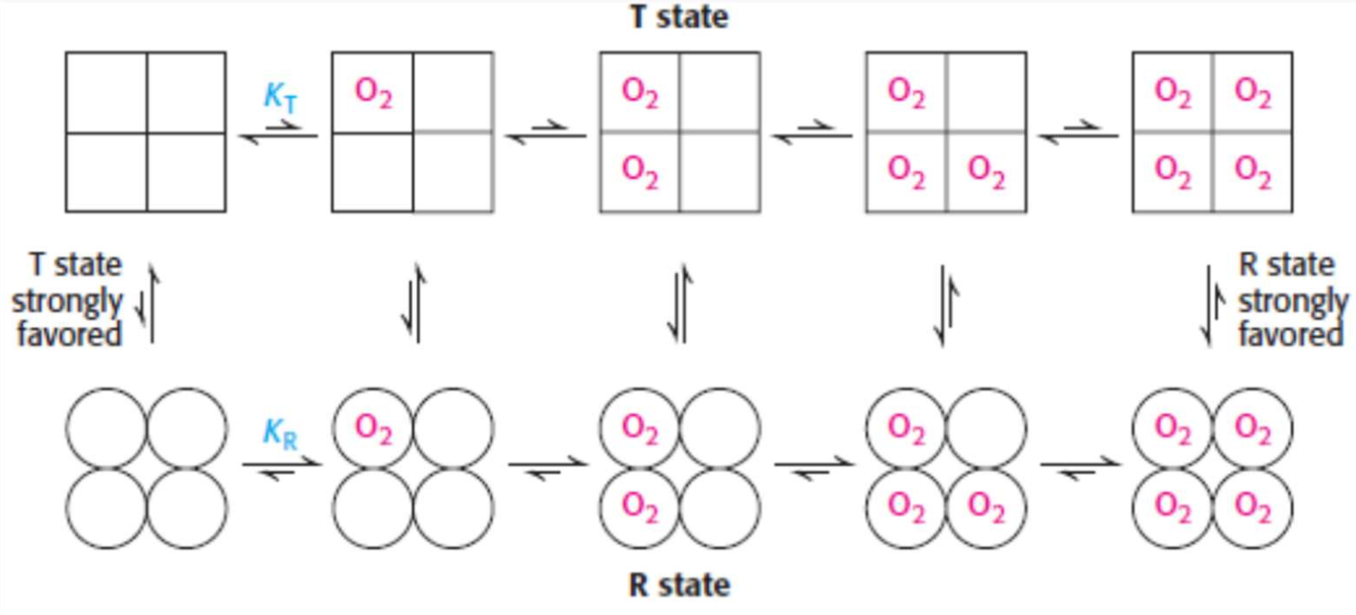
- 4 subunits vs single subunit
- myoglobin: no cooperativity
- Hemoglobin: low affinity at low oxygen<-> high affinity at high oxygen
- facilitate supply of oxygen to tissue/ accept oxygen at lungs



fractional saturation: fraction of possible binding sites that contains bound oxygen
PO_2: partial pressure of oxygen

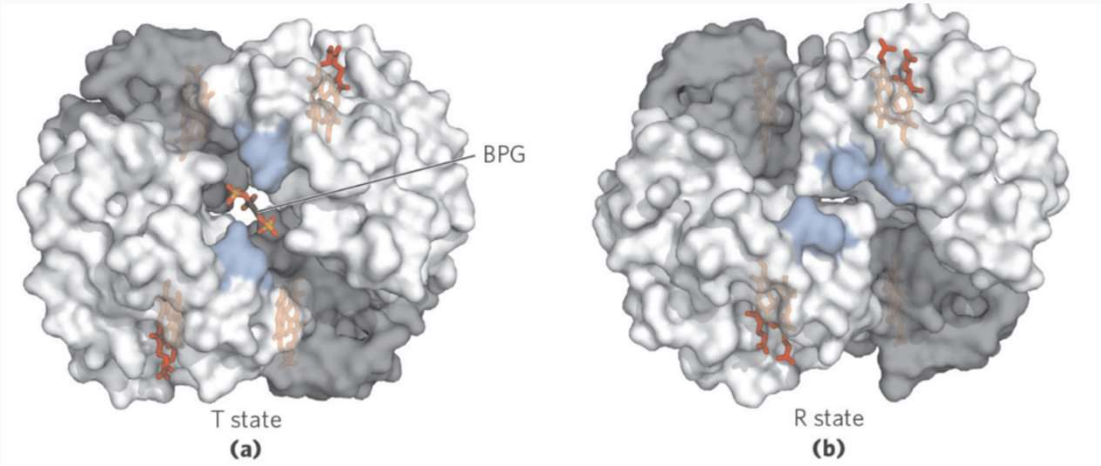
Mechanism of Hemoglobin Cooperativity

- Tense state: lower oxygen affinity
- Relax state: higher oxygen affinity
- Binding of oxygen promotes T → R state



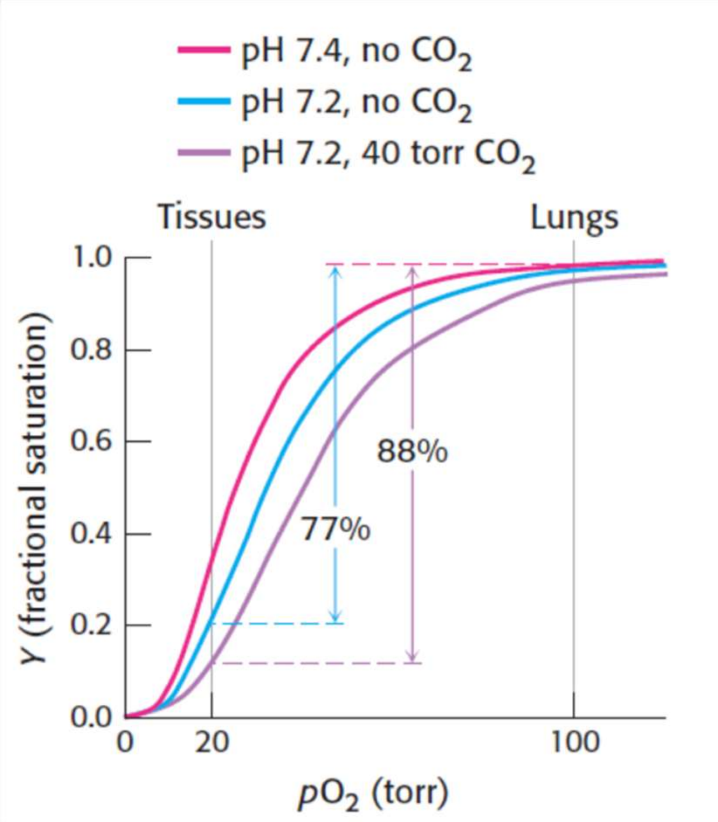
2,3-Bisphosphoglycerate (2,3-BPG)

- Hb-BPG + O2 <--> Hb-O2 + BPG
- Binds to the centre cavity
- Dissociate when Oyxgen binding
- His associated to Fe lifted → subunits closer



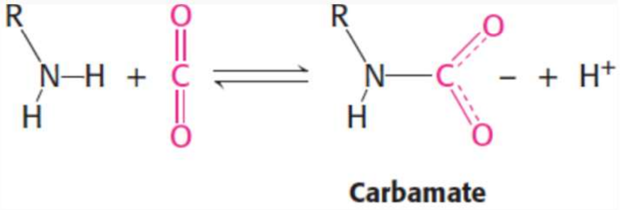
Bohr's Effect (pH)

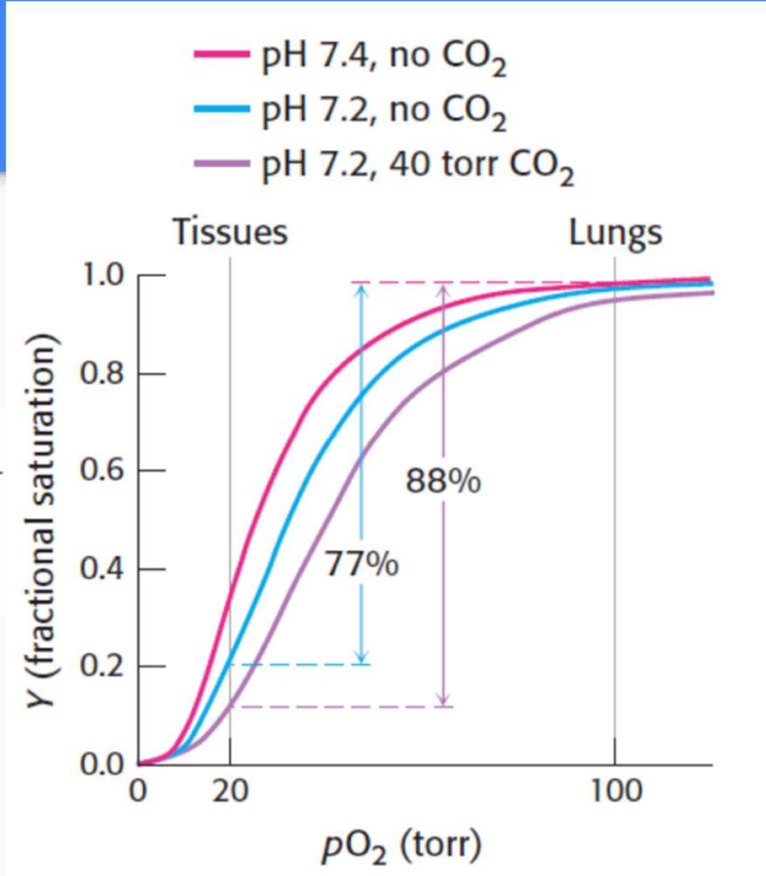
- pH and [CO2]
- acidic → lower affinity
- promotes interactions between subunits
- stabilizes T state



Bohr’s Effect (CO2)

- higher [CO2] → lower oxygen affinity
- formation of carbonic acid → more acidic
- formation of carbamate
  - oxygen dissociation
  - between Hb and CO2
- stabilizes T state





Quiz 2 - hemoglobin cooperative binding

Which of the following will increase the tendency of hemoglobin to **release** oxygen? (>2 answers)

A. BPG
B. BPG inhibitor
C. O_2
D. pH decreases from 7.4 to 6.4
E. pH increases from 6.4 to 7.4
F. CO_2

Quiz 2

Effects of CO_2:

1) CO_2 reacts with H_2O → H_2CO_3 (pKa ~ 3.5)

   High $[CO_2]$ → Low pH

2) direct chemical interaction between CO_2 and hemoglobin stimulates O_2 release

Which of the following will increase the tendency of hemoglobin to **release** oxygen? (>2 answers)

$$\text{Hb-BPG} + O_2 \;\text{<-->}\; \text{Hb-}O_2 + \text{BPG}$$

A. BPG

B. BPG inhibitor

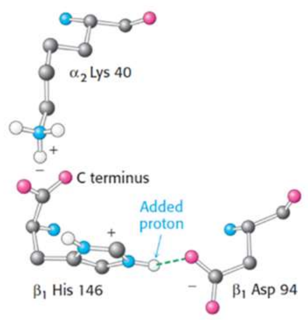
C. O2

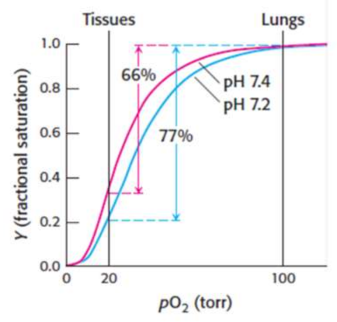
D. pH decreases from 7.4 to 6.4

E. pH increases from 6.4 to 7.4

F. CO2

- The O_2 affinity of hemoglobin decreases as pH decreases from 7.4
- Hemoglobin contains chemical groups for sensing changes in pH: e.g. His146 in β chain





Standard free-energy change, ΔG'°

$$\Delta G'^{o} = -RT \ln K'_{eq}$$

$$aA + bB \Leftrightarrow cC + dD$$

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

ΔG'° >0, reaction proceed backward
ΔG'° <0, reaction proceed forward
ΔG'°=0, at equilibrium

Keq > 1, more products than reactants are formed

Keq < 1, more reactants than products are formed

Actual free-energy change, ΔG

When ΔG=0 (equilibrium), [C][D]/[A][B]=keq

-> $\Delta G'^{o} = - RT \ ln \ K'_{eq}$

$$A + B \rightleftharpoons C + D$$

$$\Delta G = \Delta G'^{o} + RT \ ln \frac{[C]\,[D]}{[A]\,[B]}$$

By knowing actual free-energy change,

we can predict the direction of the reaction to progress

but not reaction rate

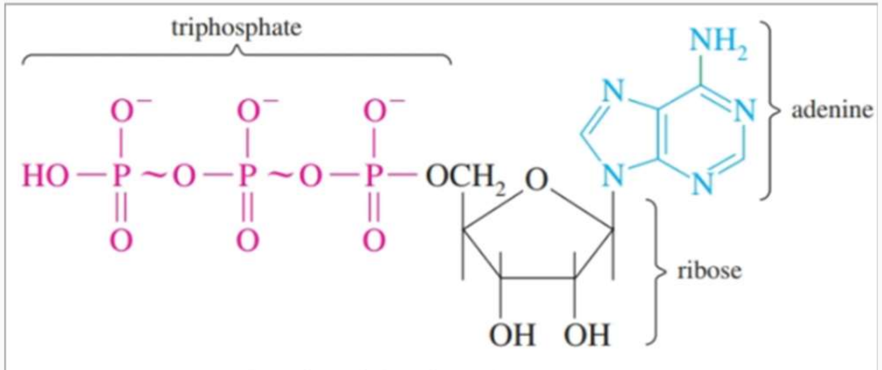
ΔG >0, reaction proceed backward
ΔG <0, reaction proceed forward
ΔG =0, at equilibrium

eg: given ΔG'° & [substrate] & [product], you can calculate ΔG

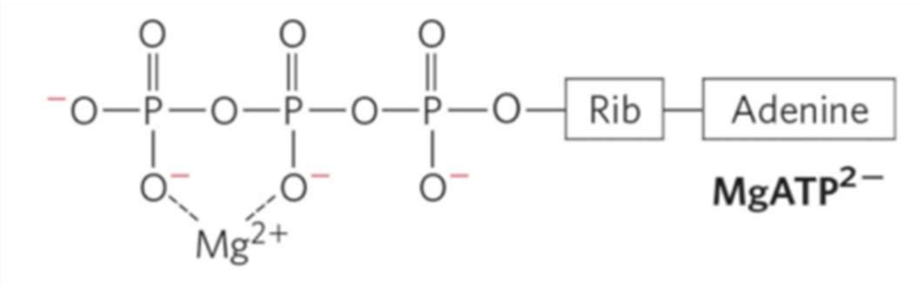
High energy compounds

ATP

- common energy currency
- Phosphate anhydride bond hold negative charge phosphate together (coiled spring)
- Mg2+ stablized ATP (with enzyme)



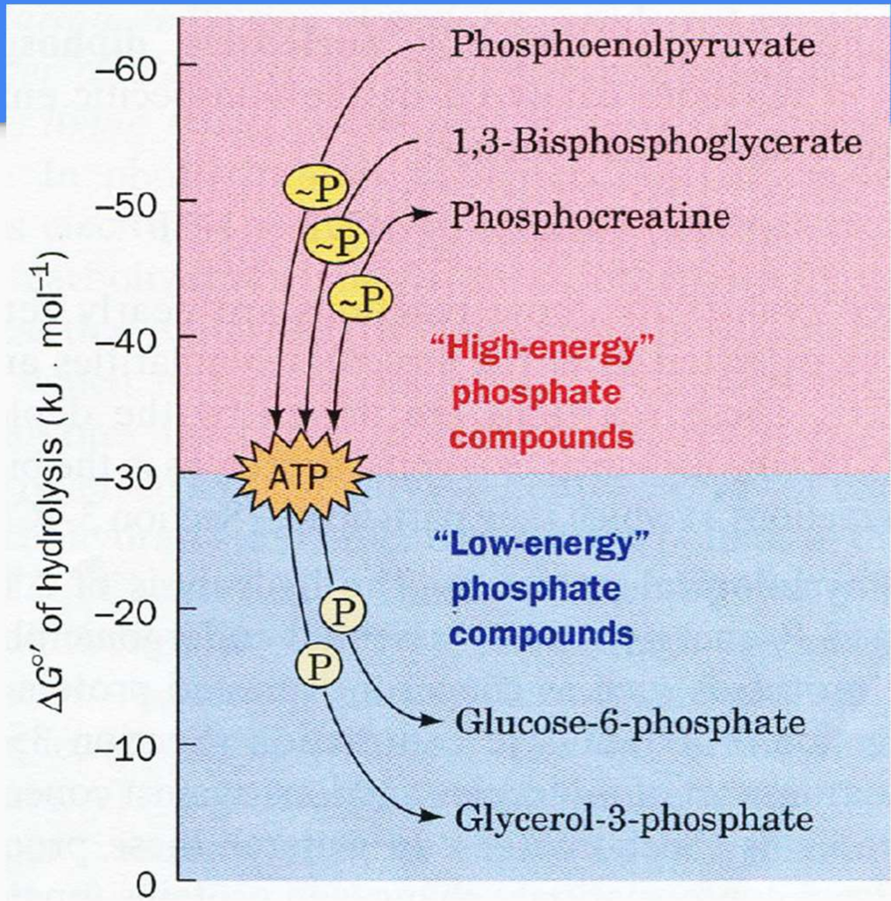
adenosine triphosphate (ATP)



ATP as energy currency

ATP serves as an energy conduit between "high energy" phosphate donors and "low energy" phosphate acceptors.

ATP can coupled with other reaction to make it overall ΔG<0 and thermodynamically favored



Source:BCHE3080

Rest & Exercise

$$ATP + creatine \rightleftharpoons Phosphocreatine + ADP$$

Rest:

[ATP] >> [ADP], reaction proceeds with net synthesis of phosphocreatine

High metabolic activity:

[ATP] is low, the equilibrium shifts to left so as to yield net synthes of

ATP