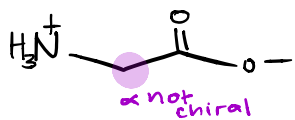


Proteins

amino acids = polymers
 oligopeptides = small chain of amino acids
 polypeptides = long chain of amino acids



(glycine)

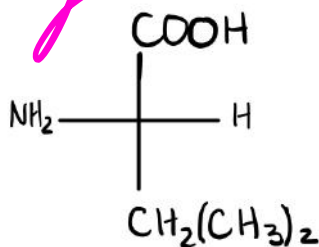


(valine)

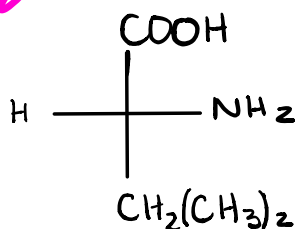
all amino acids are L configuration

Love
 Amino
 Acids

Fischer projection



L-Valine



D-Valine

* AMINO ACIDS *

- hydrophilic vs phobic
- naming
- structure
- aromaticity
- charge

Examples of amino acids:

Catalytic triad (chymotrypsinogen)

- serine
- histidine
- aspartate

Hemoglobin

- histidine (proximal bound to Fe^{2+})

α keto acid

- glutamate

Releases urea

- arginine

Ionizable amino acids + pKas

*COOH ~ 2

aspartate ~ 3

glutamate ~ 4

histidine ~ 6

cysteine ~ 8.18

*NH₃ ~ 9

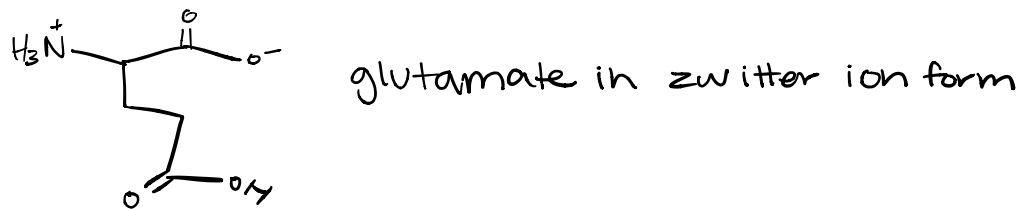
tyrosine ~ 10.07

lysine ~ 10.5

arginine ~ 12.48

Zwitter Ion

dipolar amino acid
where charges cancel
out.



*all amino acids without a charge are
zwitter ions at physiological pH.

pH > pKa

acids : -
bases : 0

pH < pKa

acids : 0
bases : +

Isoelectric point : where the molecule carries no charge. Or $pK_a = pH$.

isoelectric point is similar to equivalence point.

~ Isoelectric point for amino acids

neutral amino acids : take the average of amine + carboxyl pK_a

$$9 - 2 = 7/2 = 4.5 \sim \text{isoelectric point}$$

acidic amino acids : average of R group + carboxyl group

$$\begin{array}{l} \text{glutamate } pK_a = 4 \\ \text{COOH } pK_a = 2 \end{array} > 3 \sim \text{isoelectric point}$$

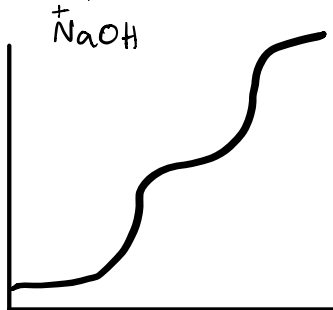
basic amino acids : average of R group + amine group

NaOH
+
Phenylalanine

$$\begin{array}{l} \text{Lysine } pK_a = 10.07 \\ \text{amine } pK_a = 9 \end{array} > 9.5 \sim \text{isoelectric point}$$

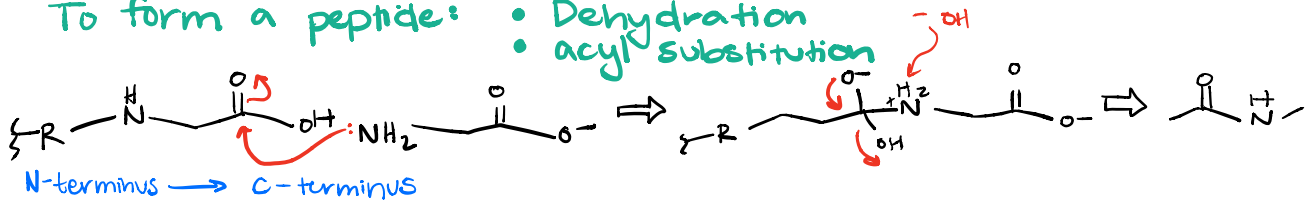


aspartic acid

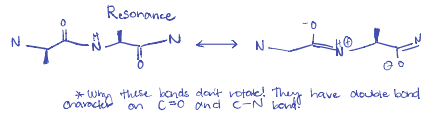


Amino Acid Rxn's

To form a peptide: • Dehydration
• acyl substitution

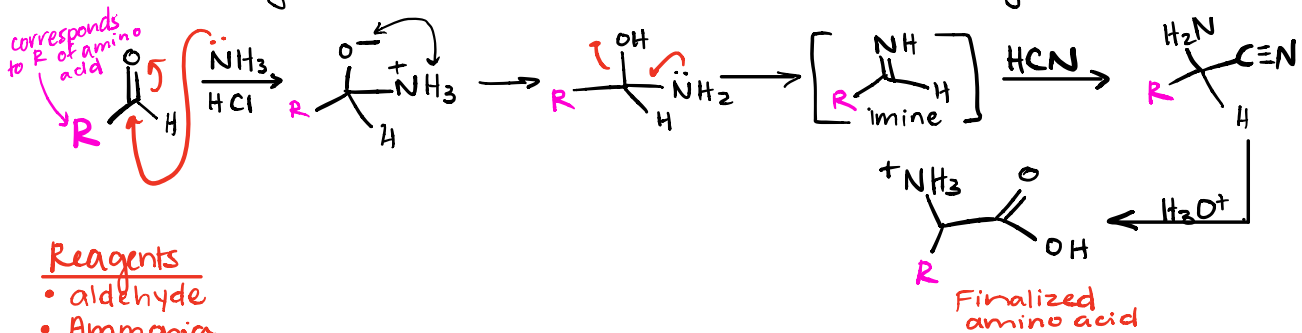


Protein Hydrolysis: • Trypsin
• Chymotrypsin



* arginine, lysine
* phenylalanine, tryptophan, tyrosine

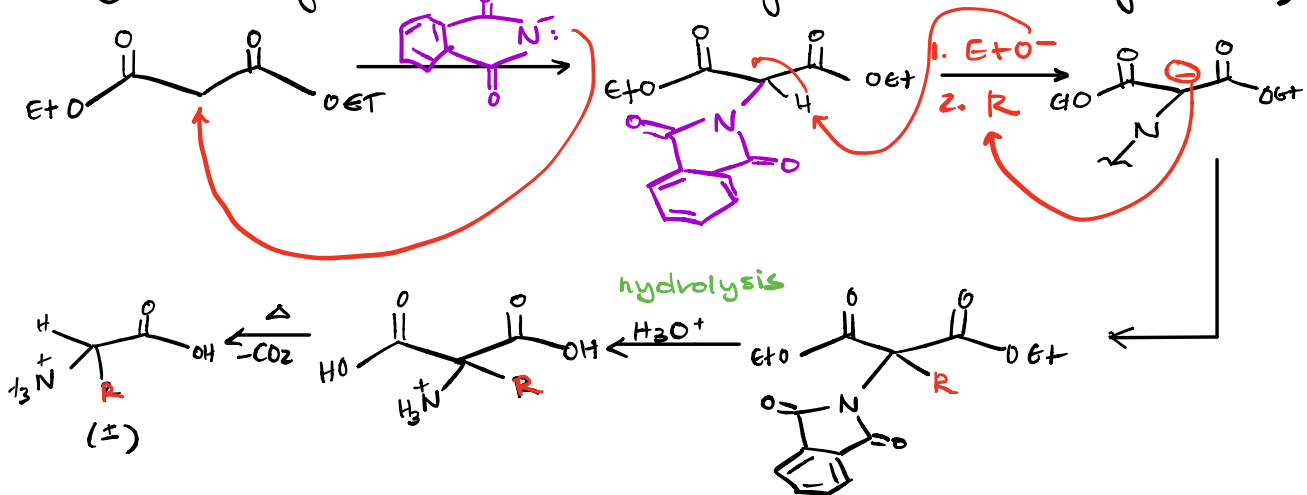
Strecker Synthesis: (How an amino acid is synthesized)



Reagents

- aldehyde
- Ammonia
- HCN
- H_3O^+

Gabriel Synthesis: (amino acid synthesis from acyl halide)



Which method of amino acid synthesis results in an optically active solution?

- I. Strecker Synthesis
- II. Gabriel Synthesis
- III. Trypsin Synthesis

- a. I only
- b. II only
- c. I, II, III
- d. None of the above

Which method of amino acid synthesis results in an optically active solution?

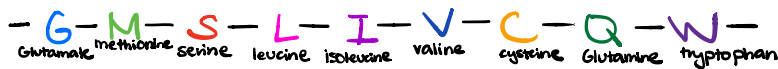
- I. Strecker Synthesis
- II. Gabriel Synthesis
- III. Trypsin Synthesis

- a. I only
- b. II only
- c. I, II, III
- d. None of the above

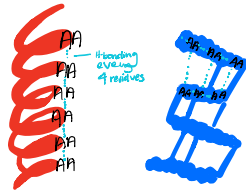
Both Strecker + Gabriel synthesis have planar intermediates which can have front and backside attacks. This results in a racemic mixture of enantiomers which is optically inactive. Trypsin synthesis = not a thing!

~ Protein Structure ~

1° amino acid sequence



2° 3-dimensional protein folding



ex: Keratin

ex: Fibroin

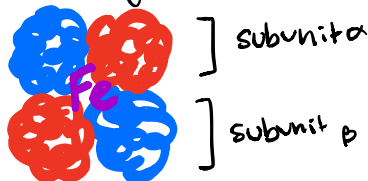
Proline = rarely in α -helix

3° Folded protein made of α -helices and Beta sheets

- molecular interactions:
- h-bonding
 - IMF (van der Waals)
 - Covalent bonding
 - ionic bonding (Na^+ bridges)
 - disulfide bonds
 - Proline turns

4° Multiple proteins come together

Hemoglobin



Positive cooperativity = ligand affinity increases with each ligand bound. i.e. first O_2 molecule to bind Hgb has relatively low affinity, but increases with O_2 #2, 3, and 4. ✓

Globule: *fully folded*



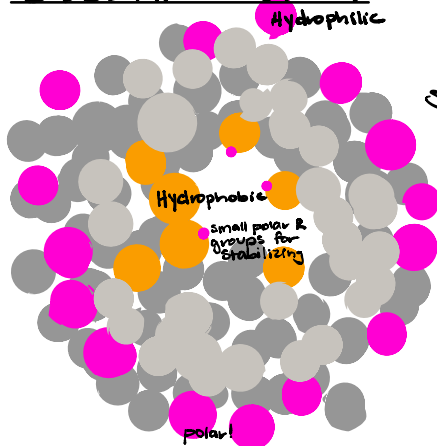
Molten globule: *partially folded*



Molten: *denatured protein*



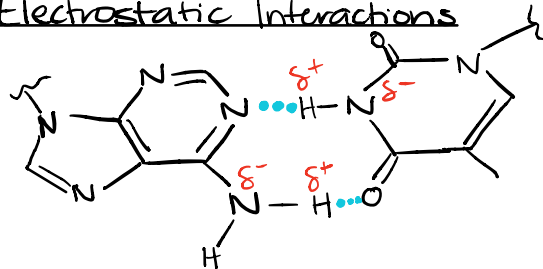
Globular Protein



Q: Are globular proteins soluble in water?

A: Yes, because the hydrophobic side groups are pointed inwards and hydrophilic are pointed outwards the globular proteins are water soluble.

Electrostatic Interactions

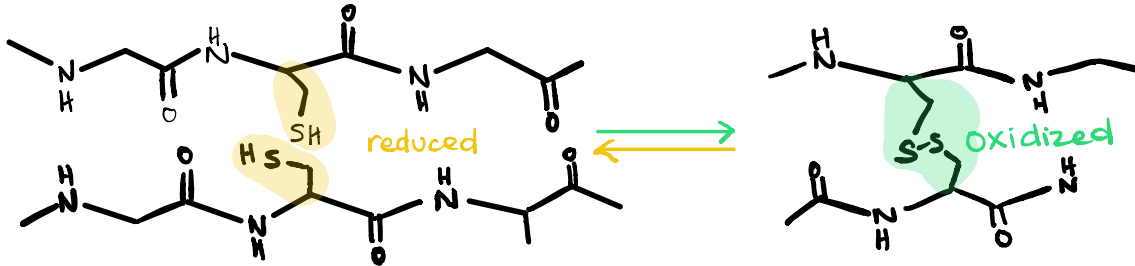


Q: Do electrostatic interactions improve or discourage protein folding?

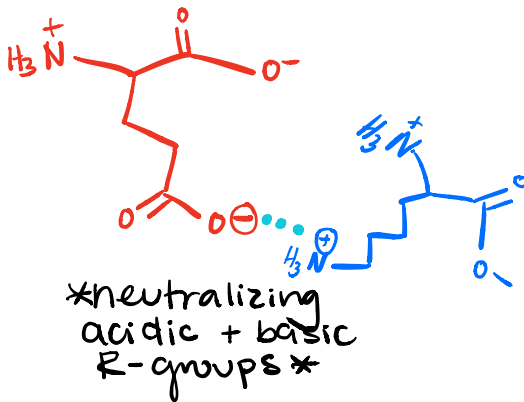
A: The electrostatic interactions improve protein folding and stabilize the protein itself.

• H-bonds are a form of electrostatic interaction

Disulfide Bridges

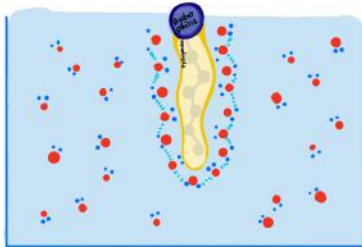


Salt Bridges



Q:

Solvation Layer



Hydration cage results in highly ordered H₂O molecules.

MCAT Question: If there were multiple hydrophobic molecules in solution, what would be the result of placing the molecules together?

- an increase in entropy
- an increase in enthalpy
- weaker hydrophobic interactions
- increased size in the water envelope

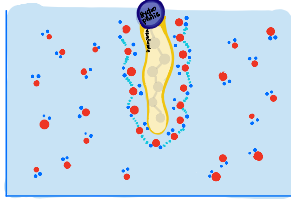
*** NOTE ***

Transitioning from solvation of non-polar regions to solvation of mostly polar globular proteins results in a net increase in entropy

↑ **NET increase in entropy:**
Major contributor to overall conformational stability of a folded protein.

A:

Solvation Layer

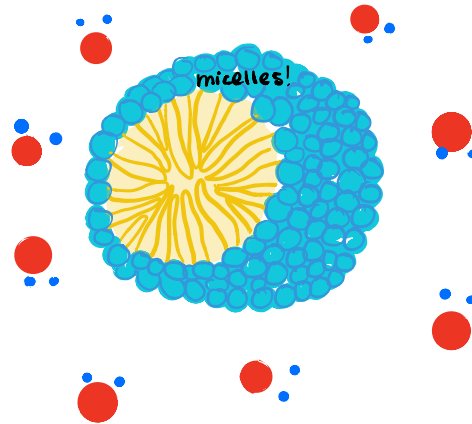


Hydration cage results in highly ordered H_2O molecules.

MCAT Question: If there were multiple hydrophobic molecules in solution, what would be the result of placing the molecules together?

- a. an increase in entropy
- b. an increase in enthalpy
- c. weaker hydrophobic interactions
↳ *not applicable*
↳ *stronger hydrophobic interactions*
- d. increased size in the water envelope
↳ *decreased size in water envelope*

* Multiple separated hydrophobic molecules would cause a serious decrease in entropy (due to decreased randomness of H_2O molecules.) If all the hydrophobic molecules were joined together we would increase entropy because there would only be one ordered H_2O layer. *

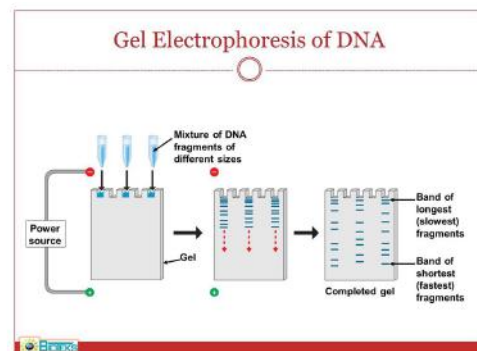


Denaturing Proteins

- acid
- Heat
- urea : H-bonds to (+) areas on proteins which disrupts 2° structure
- mercaptoethanol: reduces disulfide bonds
irreversibly

Protein Separation

- isoelectric point : where protein has no net charge. $pI = pH$
- Electrophoresis
- * coat proteins in universal negative charge (SDS-PAGE)

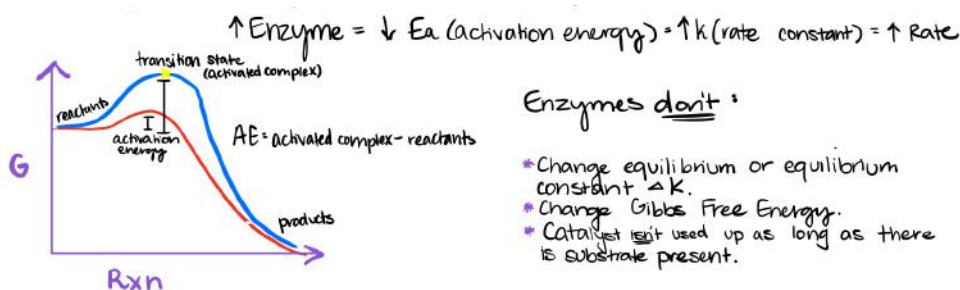


ENZYMES

Enzyme vs catalyst: both decrease activation energy of a reaction. Enzymes are organic. Neither are consumed during a reaction.

✓ Enzymes...

- ↑ rxn rate
- ↓ energy of activation
- do not change equilibrium or K_{eq}
- do not change % yield
- ↑ yield. (Kind of, just faster)



Classes:

Oxidoreductases: oxidize/reduce a species

- oxidase
- dehydrogenase
- hydroxylation

hydrolases: hydrolytically cleave substrate

- lipase
- amylase
- pepsin
- protease

transferases: move one group (methyl, phosphate) onto substrate.

- kinase
- phosphatase
- methylase

isomerase: change spacial orientation (make isomers)

- phosphohexose isomerase
- fumarase

Lyase: Non-hydrolytic cleavage or removal.

- synthase

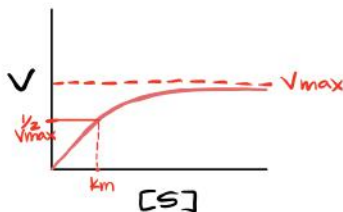
Ligase: Join substrates by condensation "addition reaction"

- synthetase

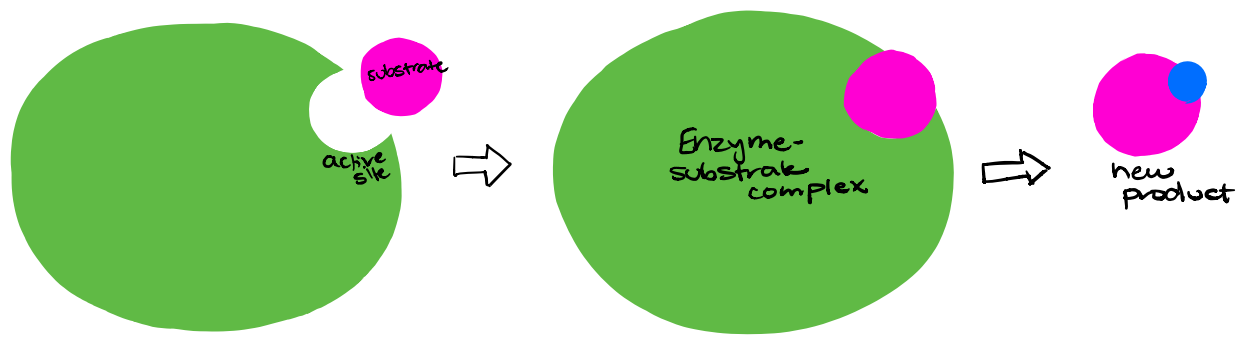
Kinetics:

Michaelis-Menten Plot

- * V_{max} = max ability of enzyme at given [enzyme]
- * K_m = M.M. constant is [substrate] at which $\frac{1}{2} V_{max}$ happens



↑ K_m = ↓ affinity (for substrate)



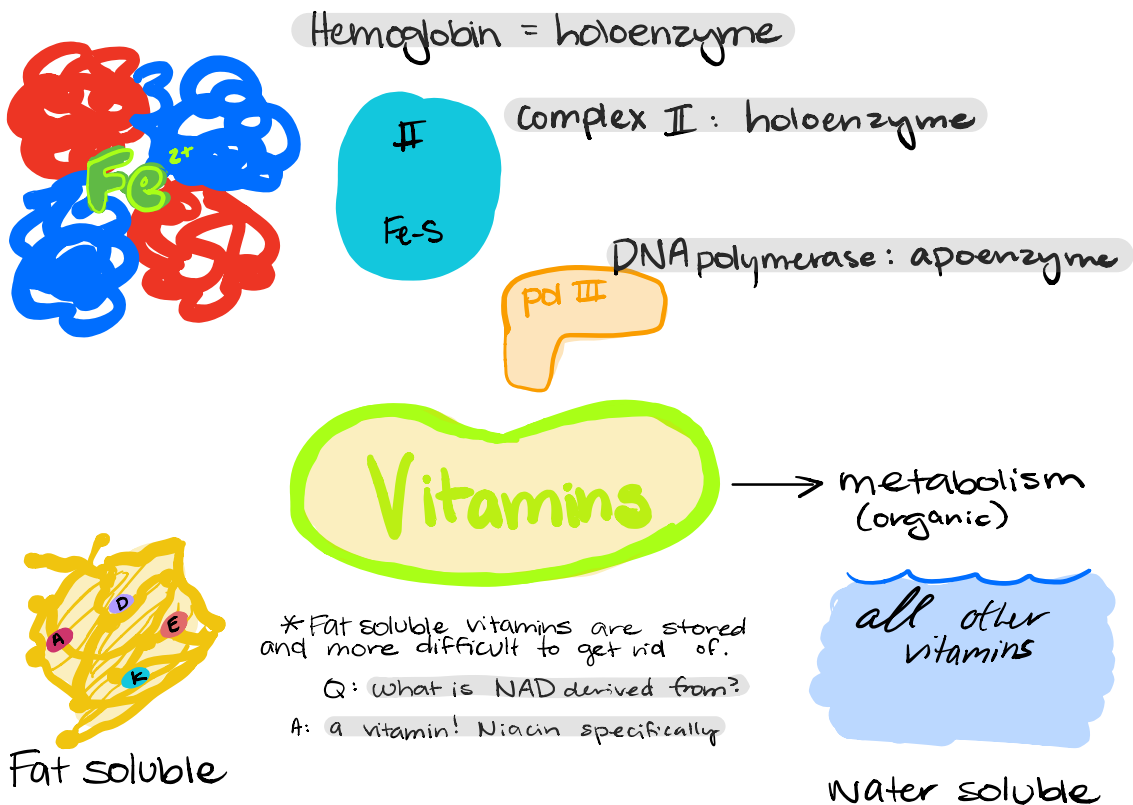
Enzyme Specificity Theories:

- Induced Fit * **Favored**
- Lock + Key * **largely dismissed**

Co Factors: **Pyridoxal Phosphate** (for Glycogen Phosphorylase)

Coenzymes: **Coenzyme Q** in ETC → carry electrons

Prosthetic groups: **Fe-S clusters** in complex II of ETC



Minerals

→ Bone formation/ion gradients/ O_2 transport
(inorganic)

Michaelis - Menten Kinetics

$$V_0 = \frac{V_{\max} [S]}{K_m + S}$$

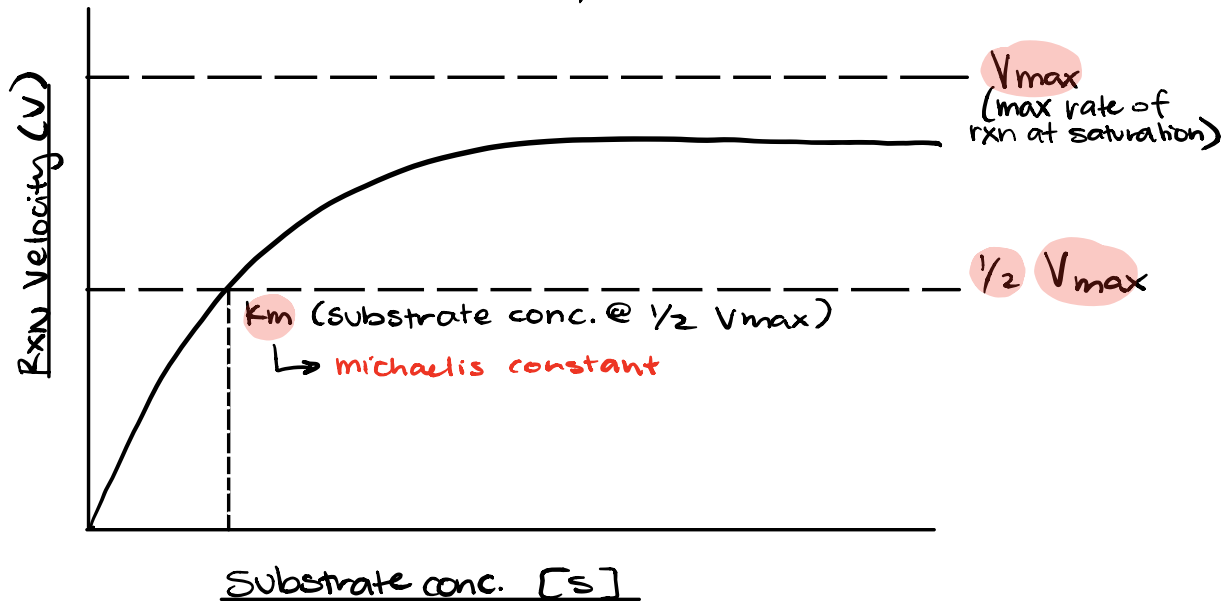
$$K_m + S = \frac{V_{\max} S}{V_0}$$

$$K_m = S_{1/2 V_{\max}}$$

$$K_m = \frac{k_2 + \frac{1}{k_1}}{k_1}$$

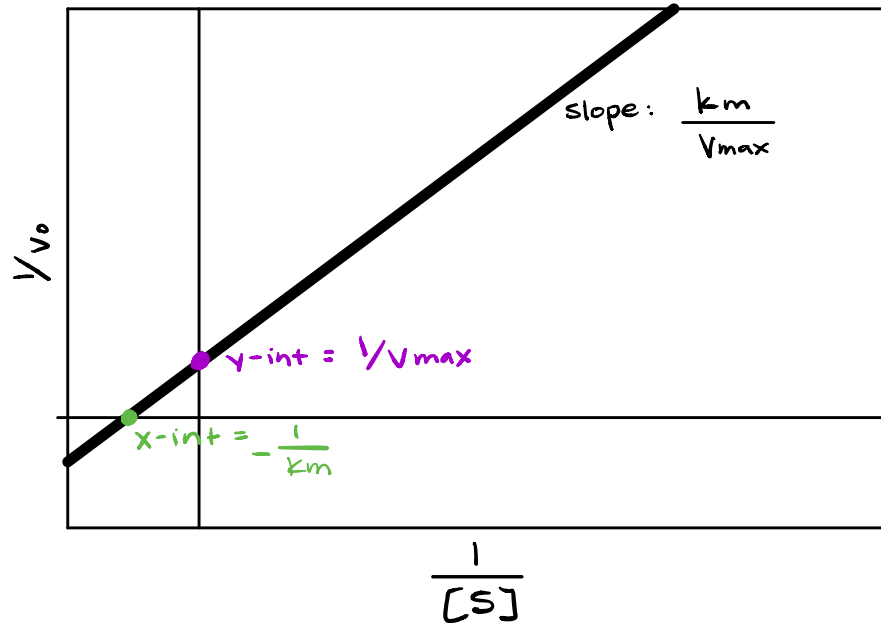
↓ $K_m = \uparrow$ binding affinity of an enzyme

$$K_m = [S] @ \frac{1}{2} V_{\max}$$

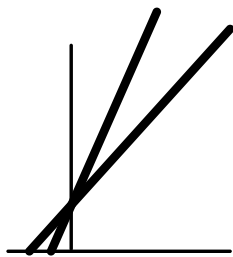


Line-Weaver Burke Plots

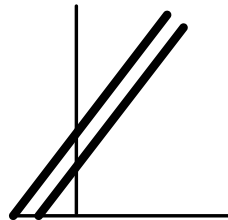
double reciprocal of Michaelis-Menten in order to linearize the data



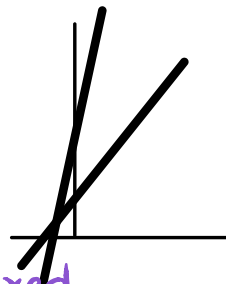
Types of Inhibitors



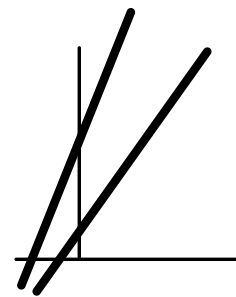
Competitive
 substrate + inhibitor compete for enzyme catalytic site
 $V_{\max}$: no change
 K_m : $\uparrow$



uncompetitive
 substrate binds first, then the inhibitor can bind
 $V_{\max}$: $\downarrow$
 K_m : $\downarrow$



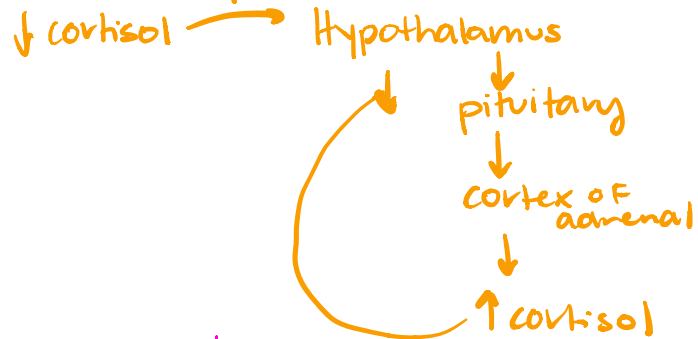
mixed
 either substrate or inhibitor may bind @ any time
 $V_{\max}$: $\downarrow$
 K_m : $\uparrow$ or $\downarrow$



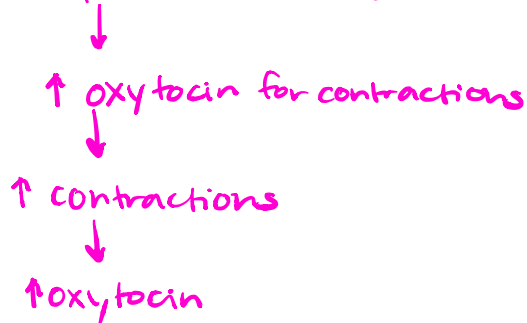
non-competitive inhibitor
 always binds enzyme but NOT @ active site.
 $V_{\max}$: $\downarrow$
 K_m : no change

Feedback Inhibition

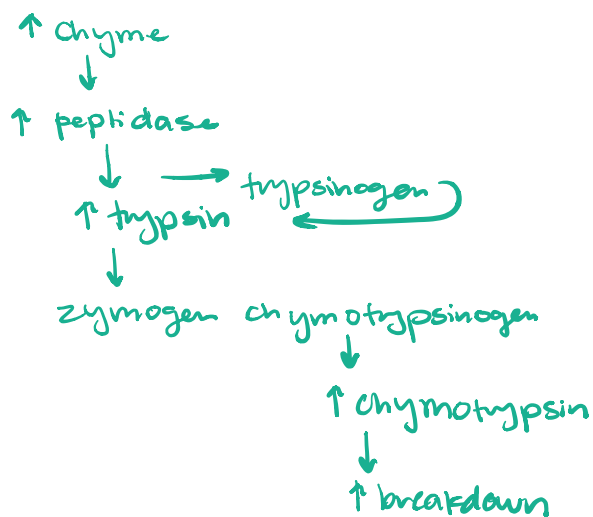
Negative Feedback: cortisol loop.



Positive Feedback: Amniotic sac breaks



Zymogens: enzymes that are inactive until acted on



Allosteric enzymes: change conformation upon binding

Hemoglobin! (as O_2 binds)

Mini Nomenclature break ☺

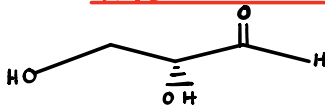
Monosaccharides : $(CH_2O)_n$

Polysaccharides: $C_n(H_2O)_x$

-ose = sugar
deoxy- = where an H replaced an -OH
Aldose = aldehyde
Ketose = ketone

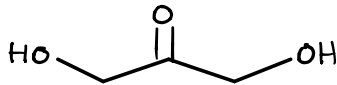
Sugars to know for the MCAT:

Monosaccharides



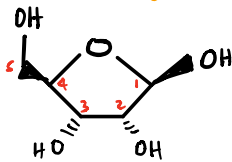
Glyceraldehyde

ex: glyceraldehyde-3-phosphate (glycolysis)



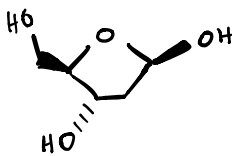
Dihydroxyacetone

ex: dihydroxyacetone phosphate (glycolysis)



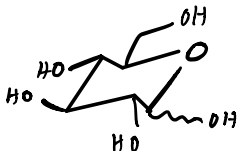
Ribose

ex: ribonucleic acid (RNA)



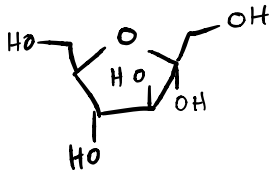
Deoxyribose

ex: deoxyribonucleic acid (DNA)



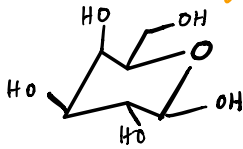
Glucose

ex: glucose ☺



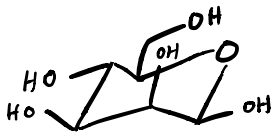
fructose

ex: phosphofructokinase



Galactose

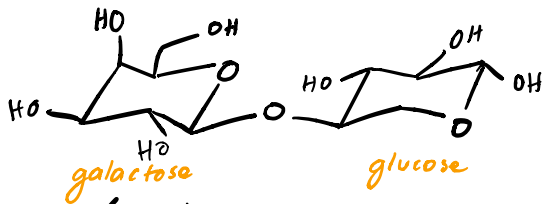
ex: UDP-galactose



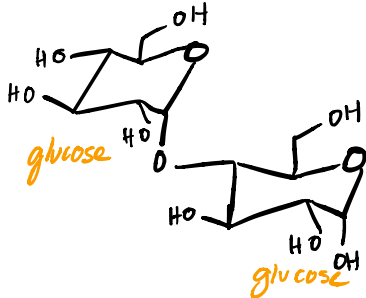
Mannose

ex: D-mannose

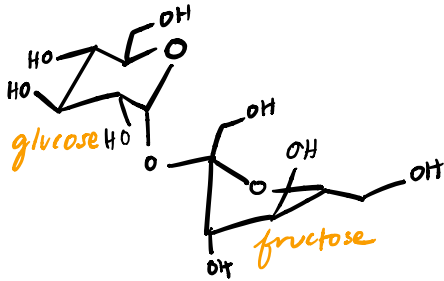
Disaccharides



Lactose



Maltose



Sucrose

Q: D5W is a 5% glucose solution used intravenously to treat patients with hyperkalemia. Which of the following disaccharides would be most likely used to create this solution?

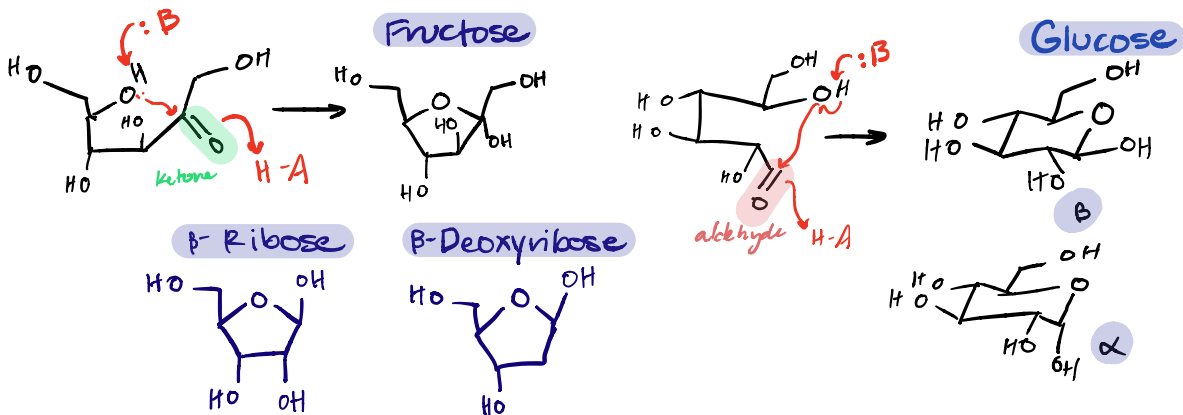
- I. Sucrose
 - II. Maltose
 - III. Lactose
 - IV. Galactose
- a. I and III
 - b. II and IV
 - c. II only
 - d. I only

A: D5W is a 5% glucose solution used intravenously to treat patients with hyperkalemia. Which of the following disaccharides would be most likely used to create this solution?

- I. Sucrose
 - II. Maltose
 - III. Lactose
 - IV. Galactose
- a. I and III
 - b. II and IV
 - c. II only
 - d. I only

The only information we have is that D5W is glucose. Therefore it is most logical to assume from our options Maltose is used (which is glucose-glucose.) Sucrose is glucose-fructose and Lactose is glucose-galactose.

* All human sugars are "D" as opposed to all human amino acids which are "L" conformation *

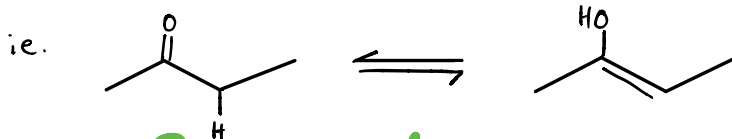


Reducing sugar - not attached at anomeric carbon + an aldehyde

Non-reducing sugar - attached at anomeric carbon

Tautomerism: isomers of a compound that only differ in the position of protons and electrons.

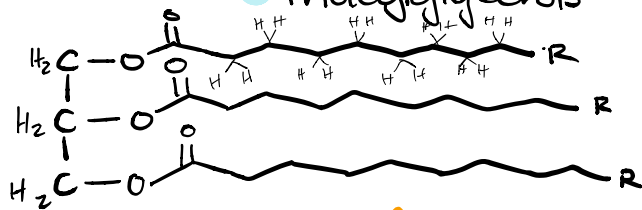
• hydride shifts •
Keto-enol tautomerism: Acid/Base catalyzed



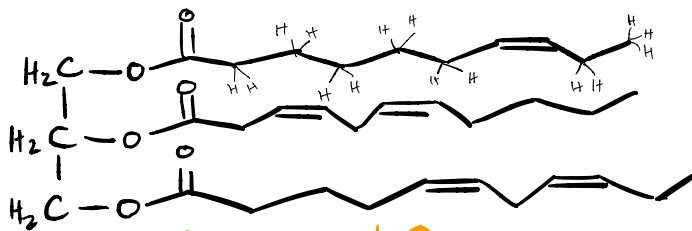
Lipids

- 1) Biomolecules
- 2) Hydrophobic

- Fatty acids — COOH Amphipathic
- Triacylglycerols — Esters Hydrophobic



Saturated → fully saturated with hydrogens, solid @ room temp. (Butter, oils)



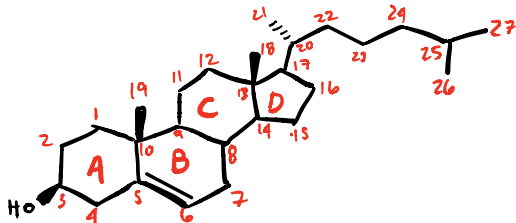
Unsaturated → Not fully saturated with hydrogen. Liquid @ room temp. Healthier

- Phospholipids — Esters Amphipathic

Saponification: Triglycerides react with KOH or NaOH

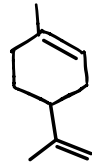
↓
Soap + glycerol

- Steroids - 4 membered ring



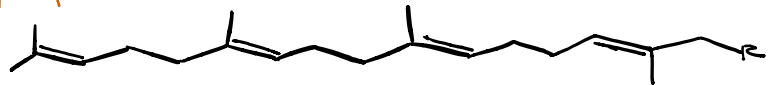
- Terpenes - $C_{10}H_{16}$ (unsaturated hydrocarbons)

ex:



D-limonene

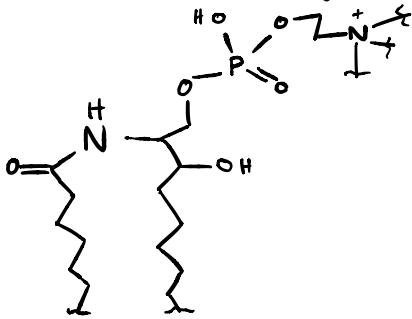
or



squalene

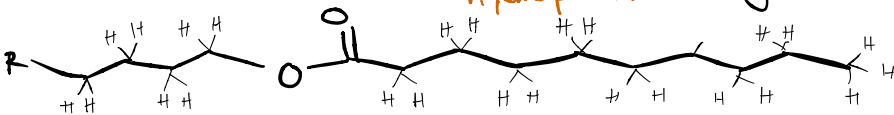
- Spingolipids (fatty acid derivatives of sphingosine - found in brain + nervous tissue)

Ampipathic



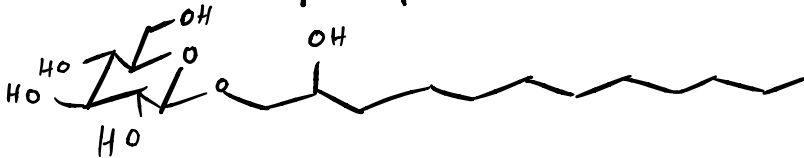
- Waxes - Ester + long chain alcohol + F.A.

Hydrophobic

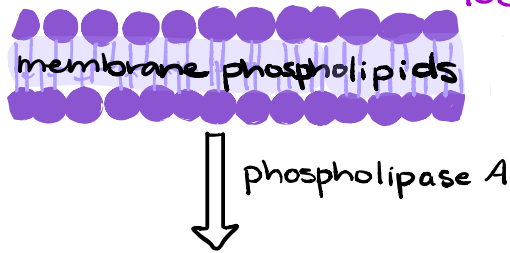


- Glycolipid

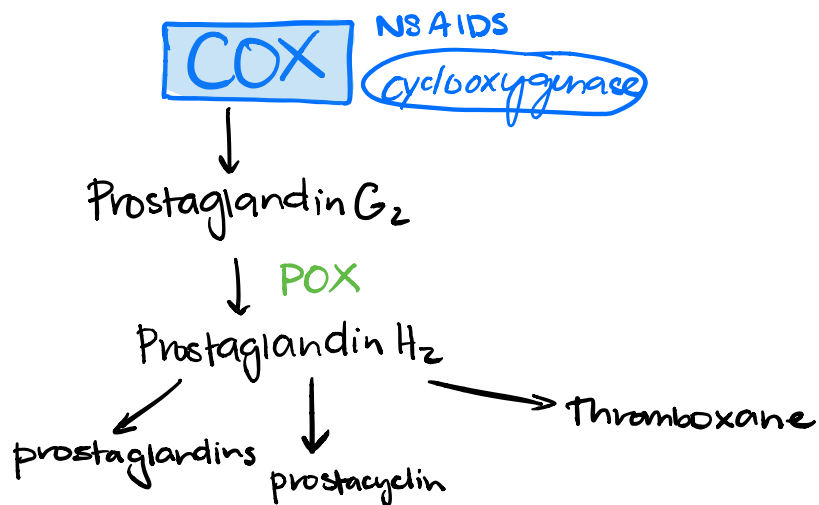
Ampipathic



- Prostaglandins — lipid mediators that act like localized hormones

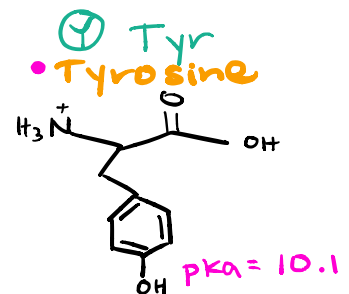
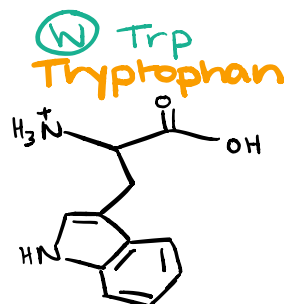
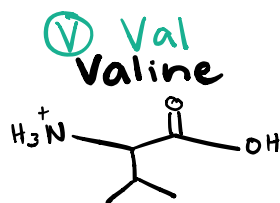
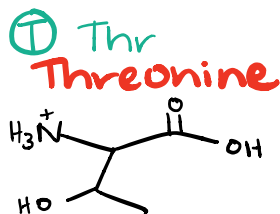
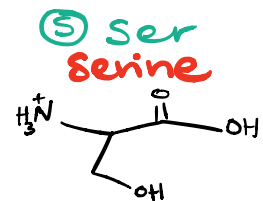
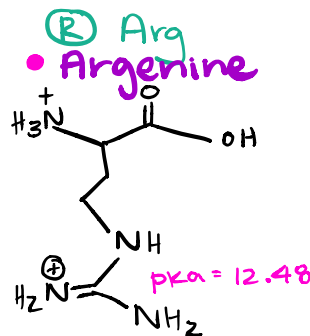
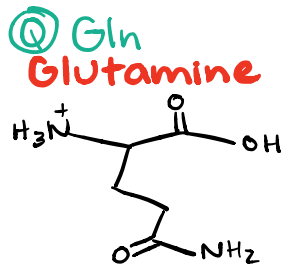
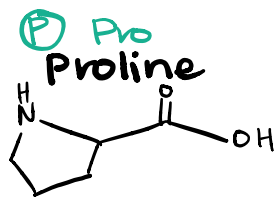
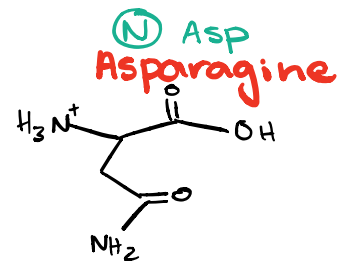
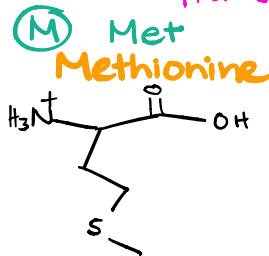
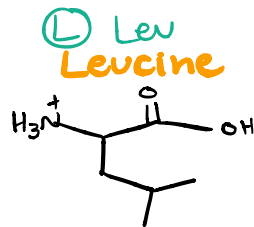
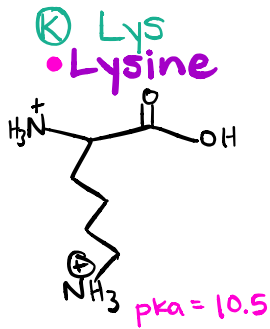
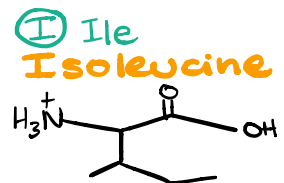
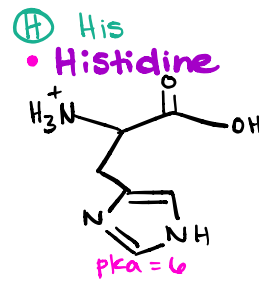
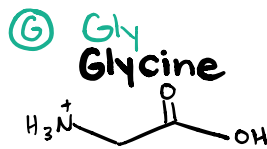
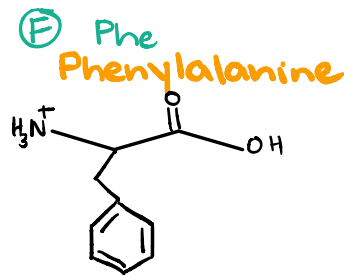
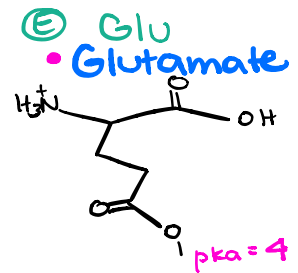
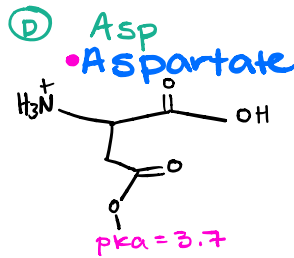
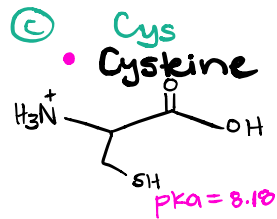


Arachidonic Acid



■ Hydrophobic (non-polar)	A, Y, W, V, I, L, M, F
■ Hydrophilic (polar)	Q, S, N, T
■ Negatively charged	D, E
■ Positively charged	K, H, R
■ ionizable	Y, C, H, E, R, K, D

Amino Acids



Bioenergetics → thermodynamics of biological systems

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

	+H	-H
+S	depends	-G Spontaneous
-S	+G not spontaneous	depends

Living Systems maintain a non-equilibrium state

Several steps in glycolysis have ΔG 's that are large and positive. How does the reaction still proceed forward?

- enzymes
- nutrients
- Reaction coupling

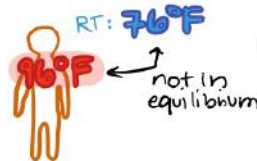


answer: c!
Reaction coupling drives glycolysis forward. Reactions rely on the products of previous steps.

Dynamic Steady State: (Homeostasis)

Living things maintain a constant steady internal environment.

↳ NOT in equilibrium with surroundings



Lowest possible entropy

EQUILIBRIUM ≠ STEADY STATE

Gibbs Free Energy

ΔG : no standard conditions

ΔG° : standard conditions

$\Delta G^{\circ'}$: physiological conditions (pH=7)

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

reaction quotient

variable & can be measured @ anytime during reaction.

Temp
gas constant

True/False Q's

- a) For Reaction X, $\Delta G = -30.78 \text{ kJ}$. For Reaction Y, $\Delta G = 22.5 \text{ kJ}$. It can be concluded that Reaction Y is closer to its equilibrium than is Reaction X,
- b) At equilibrium, $\Delta G^\circ = 0$
- c) At equilibrium $\Delta G = 0$
- d) For a given reaction at a given temperature, there are an infinite number of different ΔG° values associated with different ratios of products to reactants
- e) For a given reaction at a given temperature, there are an infinite number of different ΔG values associated with different ratios of products to reactants
- f) ΔG° represents the free energy change for a complete conversion of all reactants to products.

Answers

- a. **True** : ΔG tells us which direction the rxn needs to proceed to reach equilibrium.
- b. **False** $\Delta G^\circ = -RT \ln K_{eq}$ at equilibrium.
- c. **True**
 $\Delta G = 0$ at equilibrium
- d. **False**
 ΔG° is a set value and independent of concentrations.
- e. **True** ΔG can be calculated at any point
- f. **False**
 ΔG° = free energy associated with proceeding from standard conditions to equilibrium.

ΔG° and K_{eq}

@ Equilibrium...

$$Q = K_{eq}$$

$$\Delta G = 0$$

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

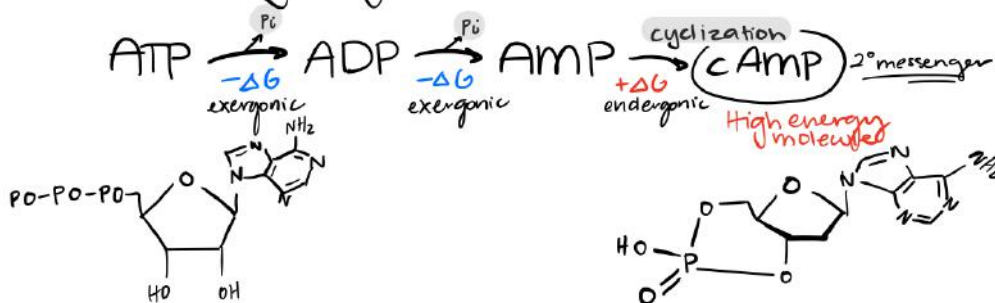
$$\text{Endergonic} = +\Delta G = \text{nonspontaneous}$$

$$\text{Exergonic} = -\Delta G = \text{spontaneous}$$

- if $K_{eq} = 1$ then $\Delta G^\circ = 0$
- if $K_{eq} = G$
- if $Q = 1$, $\Delta G = \Delta G^\circ$
- if $K_{eq} > 1$ then $\Delta G^\circ = (-)$

ATP

$$\text{ATP hydrolysis} = \Delta G^\circ = -30.5 \text{ kJ/mol} \ll 0$$



formation

Substrate level phosphorylation:



Phosphate comes from another molecule

• cytosol (glycolysis)

& mitochondrial matrix (GTP in CAC)

must be coupled to exergonic rxn

Oxidative Phosphorylation:

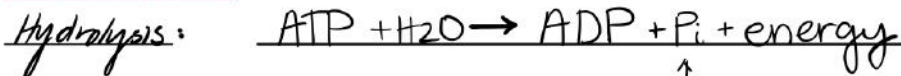


phosphate comes from free organic phosphate

• exclusively in mitochondrial matrix.

ie: ATP formed by ATP synthase.

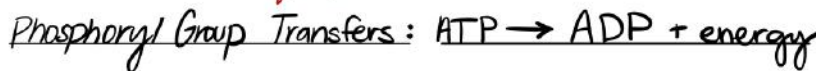
consumption



almost always coupled to another reaction

ie: cocking myosin head

↑
inorganic phosphate created



Phosphate gets transferred to another molecule.

ie: $\text{Glucose} + \text{ATP} \rightarrow \text{G-6-P} + \text{ADP}$

Phosphorylation using ATP

• MAJOR HUMAN BODY REGULATORY MECHANISM •

↳ turns enzymes / proteins / signaling molecules "off" or "on".

Phosphorylation

ATP is phosphate donor

kinase phosphorylates

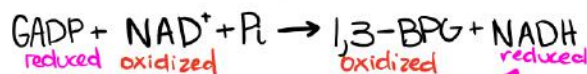
Dephosphorylation

dephosphorylates

phosphatase P_i

Biological Redox Reactions

step 6 (glycolysis)

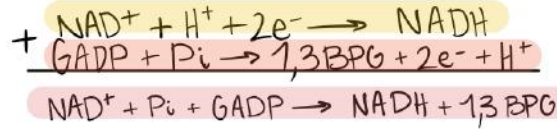


reduced oxidized

oxidized

reduced

1/2 reactions



when you see...

- NADH/NAD⁺
- NADPH/NADP⁺
- FADH₂/FAD
- FMNH₂/FMN
- Semi quinone
- Ubiquinone
- Cytochrome

think... REDOX

these are soluble electron carriers & there is always e⁻ transfer as they pass from one to another

Carbohydrate metabolism...

the sum of all chemical reactions in the body

* Respiration

An organic compound serves as the final electron acceptor in order to generate ATP.

fermentation or lactic acid
[anaerobic: O₂ is not final e⁻ acceptor
aerobic: O₂ is final e⁻ acceptor]

Humans do BOTH!

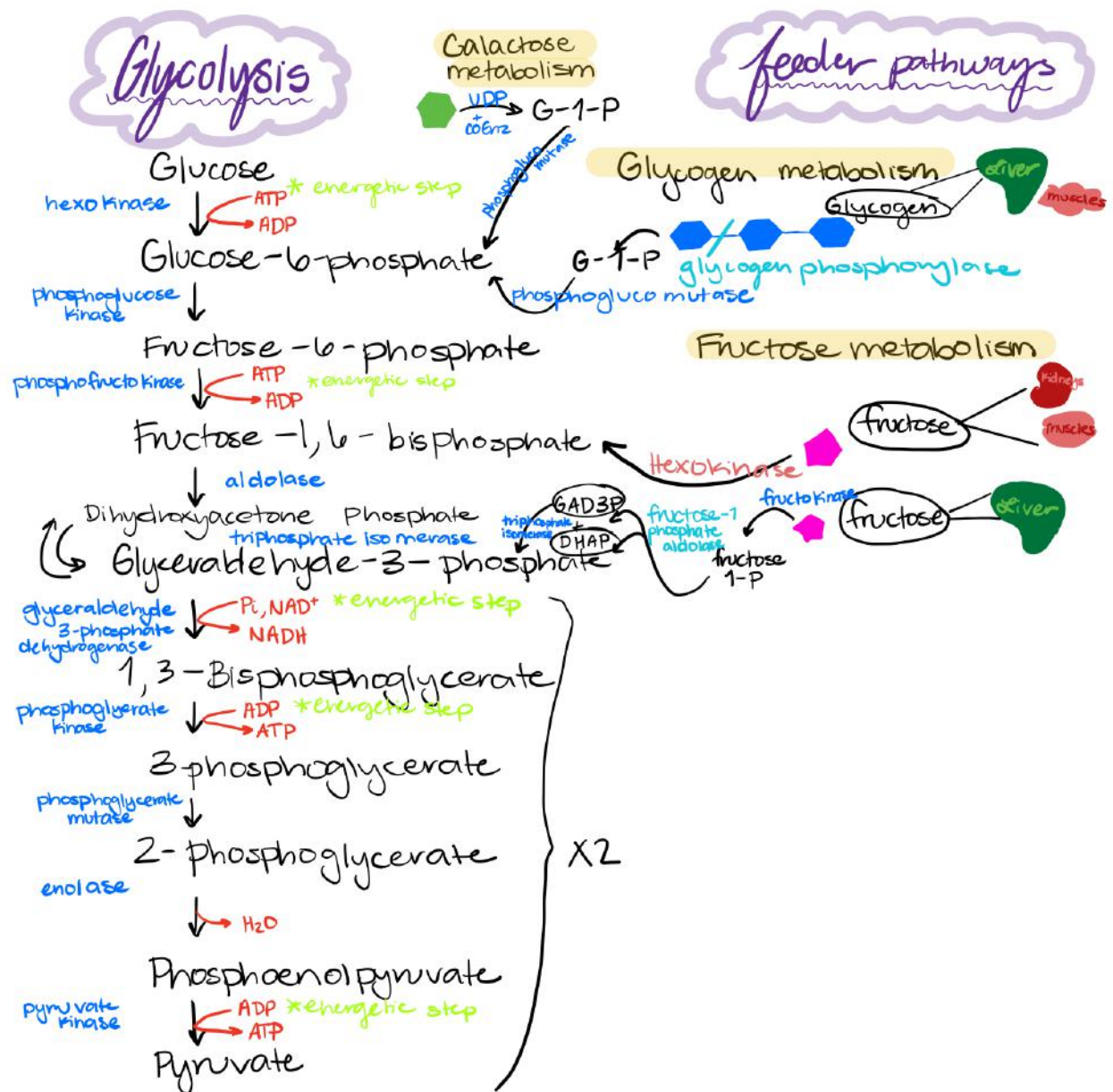
- Citric acid cycle
- electron transport

Obligate aerobes: organisms that can only use aerobic respiration

Obligate anaerobes: organisms that only use anaerobic respiration

Facultate aerobes: organisms that prefer aerobic respiration but can perform either aerobic or anaerobic.
humans

Facultate anaerobes: organisms that prefer anaerobic respiration but can do either.



NET:

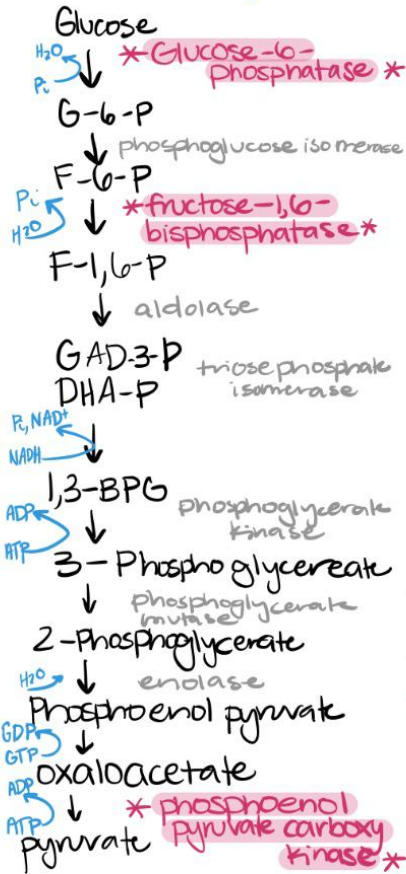
- 2 ATP
- 2 NADH
- 2 Pyruvate

Gluconeogenesis

- reverse glycolysis

Liver

done during fasting to increase blood sugar.



~ New Gluconeogenesis enzymes catalyze irreversible steps ~

Pyruvate Dehydrogenase Complex

pyruvate → acetyl-CoA



- ① PDH complex → acetyl-CoA
- ② lactate dehydrogenase → lactate
- ③ pyruvate carboxylase → oxaloacetate

fermentation

anaerobic glycolysis

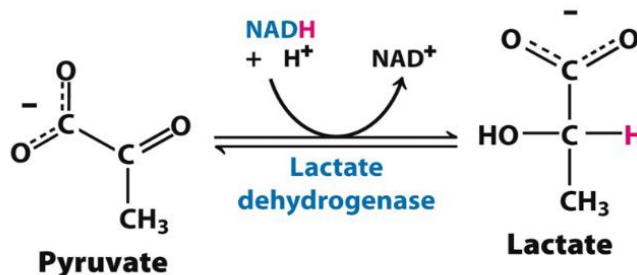
- bacteria
- animals during exercise
- erythrocytes

Ethanol fermentation: yeast + bacteria

→ ethanol is produced as is the final electron acceptor.

Lactic acid fermentation: animals

→ lactate is produced and is the final electron acceptor.



* fermentation regenerates NAD⁺ so glycolysis can continue *

Pentose Phosphate ... pathway ...

1) NADPH synthesis: "Reductive Biosynthesis" (fatty acids) & production of Glutathione (radical O₂ antioxidant).

2) Ribulose-5-phosphate: synthesizes nucleotides

Oxidative Phase

Glucose-6-P → 6-Phosphogluconate → Ribulose-5-P

* coupled w/ NADP⁺ → NADPH

Non-oxidative Phase

Ribulose-5-P → R5P ↔ Sugar Pool ↔ Glucose-6-P

Transketolase
Transaldolase

1 glucose = 2 NADPH = 4 glutathiones

The Citric Acid Cycle

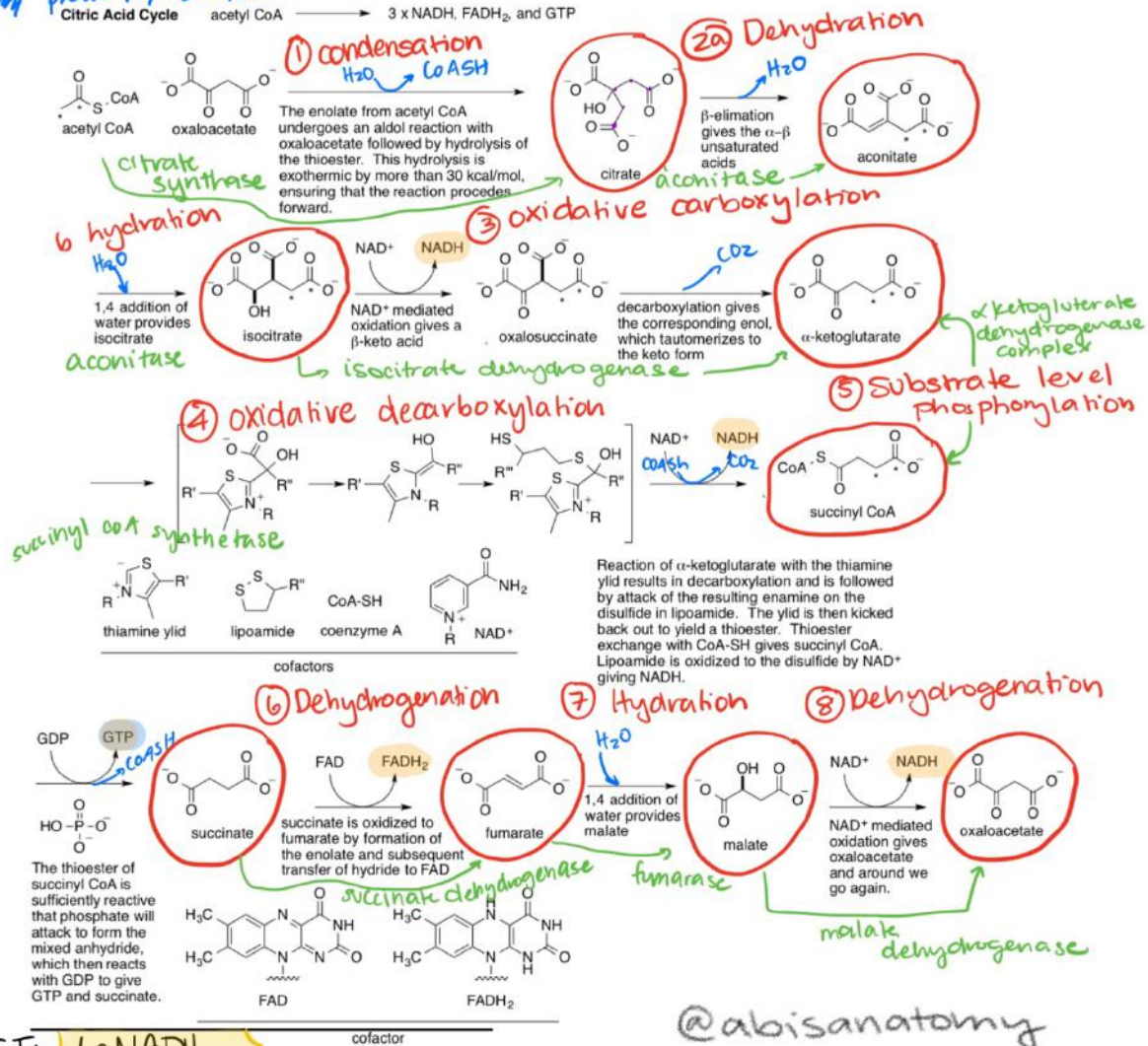
*Substrate level phosphorylation

intermediate

enzyme

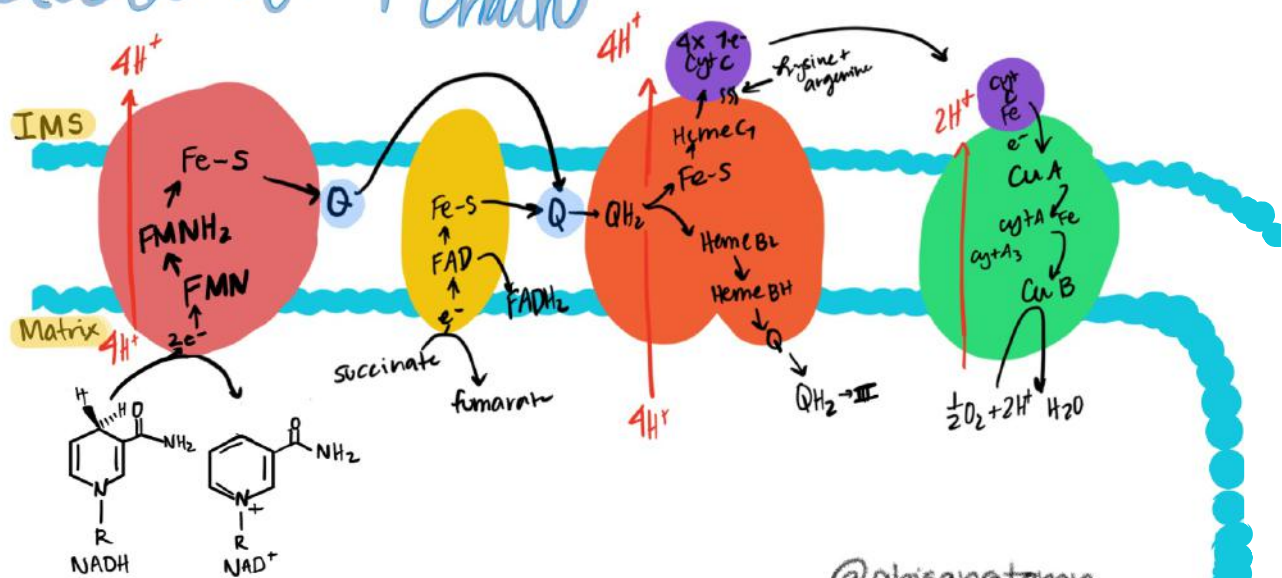
products/reactants

Citric Acid Cycle acetyl CoA $\rightarrow$ 3 x NADH, FADH₂, and GTP



@abisanatomy

Electron transport chain



@abisanatomy

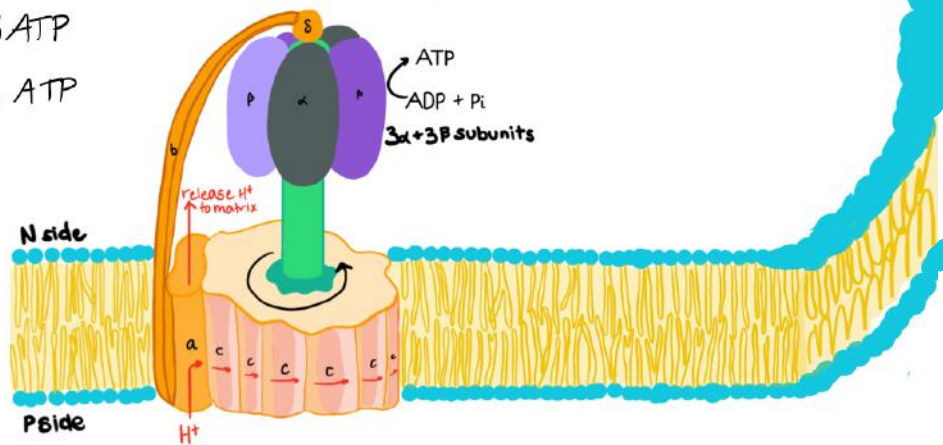
ATP Synthase

* Oxidative phosphorylation

Each NADH = 10 H⁺, 3 ATP

Each FADH₂ = 6 H⁺, 2 ATP

(FADH₂ bypasses complex I)



Total

NADH = 3 ATP

↳ in glycolysis = 2 ATP

FADH₂ = 2 ATP

Glycolysis

Citric Acid cycle

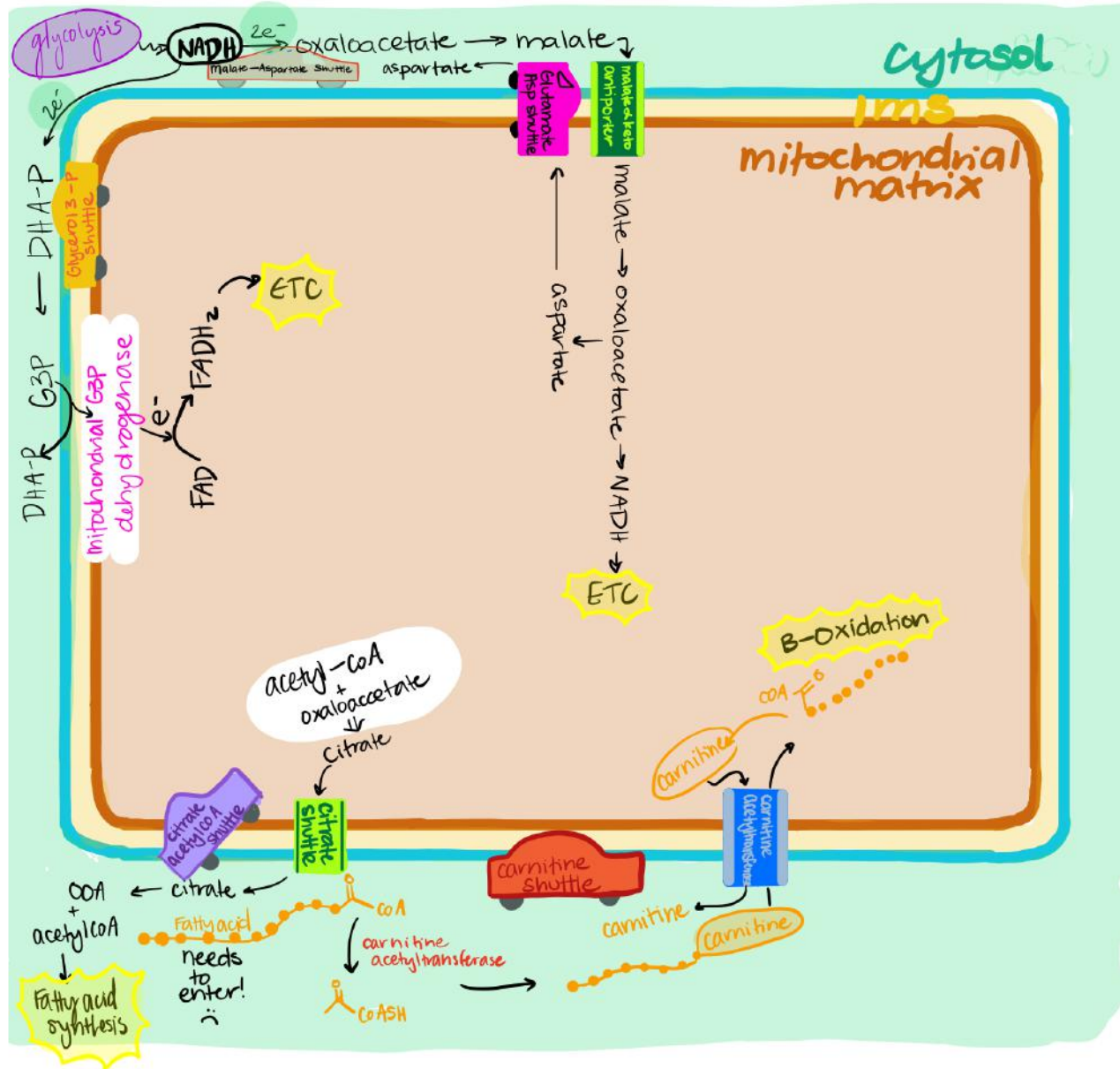
total

	NADH	FADH ₂	ATP
Glycolysis	2 (2 ATP)	0	2
Citric Acid cycle	8 (24 ATP)	2 (4 ATP)	2 (6 ATP)
total	10 (26 ATP)	2 (4 ATP)	4

= 36 ATP

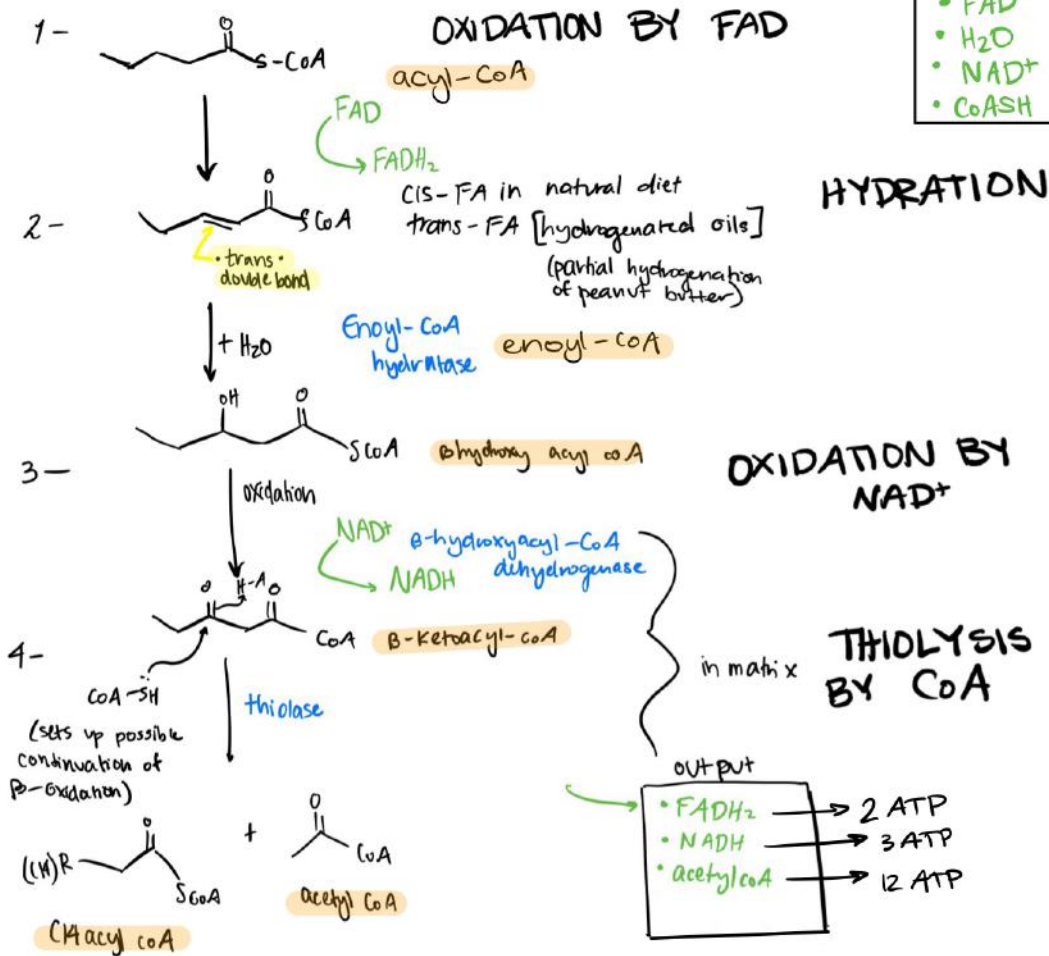
... Biochemical Shuttles ...

transport molecules across impermeable membranes



β-Oxidation

4 Basic steps of β-oxidation



* Note rules for odd vs even & saturated vs unsaturated

Ketone Bodies

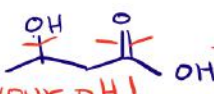
a family the liver will generate but cannot use when you watch your weight. [Fast]

↓ blood pH

(ketoacidosis)

acetone:  no energy is all alone

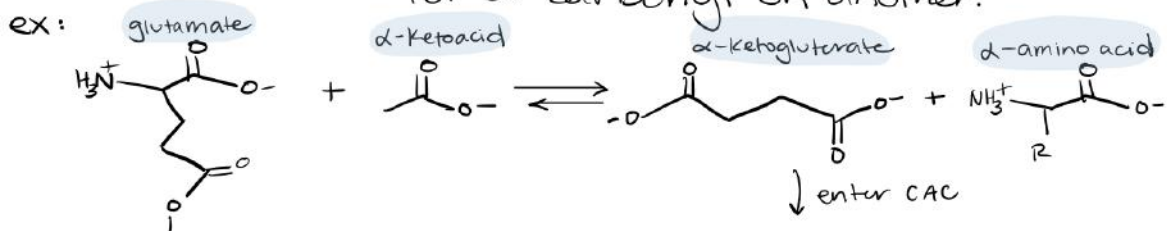
acetoacetate:  energy for Not  & 

3-hydroxybutyrate:  energy for NOT  & 
OH! OH! we decrease your pH!

Protein Metabolism

amino acids can be broken down by pyruvate or acetyl-coA and fed into citric acid cycle.

transamination: exchange of an amine group on one molecule for a carbonyl on another.



Suppose the following biomolecules were radioactively labeled... where would we see them in the greatest abundance?

- | | |
|--------------------------------------|--|
| a. pyruvate | the cytosol |
| b. oxaloacetate | the mitochondrial matrix |
| c. phosphofructokinase-1 | the cytosol |
| d. PDH complex | the mitochondrial matrix |
| e. phosphoenolpyruvate | the cytosol |
| f. glycogen synthase | the cytosol |
| g. pyruvate carboxylase | the mitochondrial matrix |
| h. α -ketoglutarate | the mitochondrial matrix |
| i. succinate dehydrogenase | inner mitochondrial membrane |
| j. ATP synthase | inner mitochondrial membrane |
| k. Fatty acids in β -oxidation | mitochondrial matrix |
| l. citrate | mitochondrial matrix |
| m. ketolysis | mitochondrial matrix but <u>NOT</u> of liver cells |

Regulation of metabolism

organism level

well-fed state (Postprandial) = hours after eating

- ↑ insulin levels ↓ glucagon levels
- ↑ anabolism (vs catabolism)
- ↑ glycogen synthesis (glycogenesis)
- ↑ fatty acid synthesis

Fasting state (Post-absorptive)

- ↑ glucagon levels ↓ insulin levels
- ↑ catabolism (vs anabolism)

immediate glycogenolysis

delayed gluconeogenesis

Starvation

- ↑↑ glucagon
- ↑↑ epinephrine
- ↑↑ gluconeogenesis
- ↑ fatty acid oxidation = ketoacidosis

tissue level



- ↑ glucose in well-fed state
- ↑ fatty acids when fasting
- No ketones



- ↑ glucose in well-fed state
- ↑ glucose when fasting
- ↑ ketones if starving



- ↑ glucose during well-fed state
- ↑ fatty acids when fasting



- ↑ Glucose in all states
- via anaerobic glycolysis

muscles



- ↑ fatty acids in well-fed state
- ↑ Fatty acids & ketones during fasting



- ↑ glucose during well-fed state
- ↑ fatty acids & ketone during fasting

fatty acid synthesis

- ★ Occurs in the cytosol of liver cells.
- ★ Constructs 16-carbon palmitic acid.