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Office Hours:	
Monday 10:00	Tuesday 9:15
Wednesday 11:15	
Thursday By appt	Friday 2:00

and now the fun begins				
Functio rganic c	nal Gr hemis	oups - One of the reasons why stry is a prerequisite for the clas	, SS	
st for re	view -	- recognize each of the followin	ıg.	
Functional Group	Structure	Notes		
Hydroxyl	R—O—H	Hydroxyl groups are common to all classes of biological molecules. The participate in numerous reactions including esterifications, dehydrations, and oxidations.		
Carbonyl (aldehydes and ketones)	R-C-H	The polar carbonyl group participates in numerous biochemical reactions. Frequently carbonyl carbons are subjected to nucleophilic attack by hydroxy or amino groups.		
Carboxyl	R−C−0 <sup>-</sup>	Carboxyl groups are weak acids. They are common functional groups and participate in the formation of several other groups, including esters and amides.		
Ester	R <sup>1</sup> -C-O-R <sup>2</sup>	Esters are the result of a hydroxyl and carboxylic acid reacting with one another. Esters are commonly found in many lipids.		
Sulfur analogs				
Thiol	R—S—H	Thiol groups can be thought of as hydroxyl analogs. They are found in the amino acid cysteine.		
Disulfide	R—S—S—R'	Disulfides result from the reaction of two thiol groups together. Disulfide reducing agents cleave the disulfide and restore the two thiols.		
Thioester	R <sup>1</sup> -C-S-R <sup>2</sup>	Thioesters have a large negative free energy of hydroylsis.		



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- Covalent bonds hold atoms together so that molecules are formed
- Weak forces profoundly influence the structures and behaviors of all biological molecules
- Weak forces create interactions that are constantly forming and breaking under physiological conditions
- Energies of weak forces range from 0.4 to 30
  kJ/mol





























# University Thermodynamics Defined

#### Thermodynamics is the study of energy.

It can provide information about how and why a reaction can occur.

It can also provide information about the conditions required for a reaction to occur.

In biochemistry – we want to understand how the equilibria impacts... well... everything:

 reactions at different conditions (mostly reactants and temps), folding of macromolecules, binding...





Entropy (S) representing the quality of energy and the disorder in any system.

The entropy of a system increases in disorder and randomness.

Without added work, systems proceed from ordered to disordered

Natural processes move towards an equilibrium (minimum pot. energy)—energy flows spontaneously to be diffused, spread out (increase in entropy—a measure of disorder and randomness)

Change in entropy:  $\Delta S > 0$ , favorable reaction



## Third Law of Thermodynamics

The entropy of a perfect crystalline system at 0 K is 0.

Not really going to use this law, as most biological/biochemical processes entropy changes are more useful than absolute entropies.





Standard Free Energy (G°)					
Gibbs Free Energy under standa	ard cond. (1 ati	m, 25°C, 1 M)			
• We use standard state to ask at these conditions (1M) will					
the reaction proceed in the direction written?					
Compound and Hydrolysis Reaction	$\Delta G^{\circ}$ (kJ/mol)				
Phosphoenolpyruvate $\rightarrow$ Pyruvate +P <sub>i</sub>	-62.2				
1,3-bisphosphoglycerate $\rightarrow$ 3-phosphoglycerate+P	-49.6				
Creatine phosphate $\rightarrow$ Creatine + P <sub>i</sub>	-43.3				
Acetyl phosphate $\rightarrow$ Acetate + P <sub>i</sub>	-43.3				
Adenosine-5'-triphosphate $\rightarrow$ ADP+P <sub>1</sub>	-35.7	$\Delta G^{\circ}$ = pH 7.0			
Adenosine-5'-triphosphate $\rightarrow$ ADP+P <sub>i</sub> (with excess Mg <sup>2+</sup> )	-30.5	20 -pii /.0			
$Adenosine\text{-}5'\text{-}diphosphate \rightarrow AMP + P_i$	-35.7				
Pyrophosphate $\rightarrow P_i + P_i$ (in 5 mM Mg <sup>2+</sup> )	-33.6				
$Adenosine-5'\text{-triphosphate} \rightarrow AMP + PP_1 (excess Mg^{2*})$	-32.3				
Uridine diphosphoglucose $\rightarrow$ UDP+glucose -31.9					
Acetyl-coenzyme A → Acetate+CoA -31.5					
S-Adenosylmethionine $\rightarrow$ Methionine + adenosine -25.6					
$Glucose-1$ -phosphate $\rightarrow$ $Glucose+P_1$ -21.0					
Glycerol-3-phosphate $\rightarrow$ Glycerol+P <sub>1</sub> -9.2					
Adenosine-5'-monophosphate $\rightarrow$ Adenosine + P <sub>1</sub> -9.2					





















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What common theme to you see in this table?	TABLE 3.3      Free Energies of Hydrolysis of Some High-En        Compound and Hydrolysis Reaction	ergy Compo ∆G°' (kJ/mol)	unds* Structure
	Phosphoenolpyruvate $\longrightarrow$ pyruvate + P <sub>i</sub>	-62.2	Figure 3.12
mportant:	1,3-Bisphosphoglycerate $\longrightarrow$ 3-phosphoglycerate + P <sub>i</sub>	-49.6	Figure 3.10
. High energy	Creatine phosphate $\longrightarrow$ creatine + P <sub>i</sub>	-43.3	Figure 13.21
phosphate	Acetyl phosphate $\longrightarrow$ acetate + P <sub>i</sub>	-43.3	Figure 3.10
compounds are a	Adenosine-5'-triphosphate $\longrightarrow$ ADP + P <sub>i</sub>	$-35.7^{\dagger}$	Figure 3.9
TEMPORARY	Adenosine-5'-triphosphate $\longrightarrow$ ADP + P <sub>i</sub> (with excess Mg <sup>2+</sup> )	-30.5	Figure 3.9
method of energy	Adenosine-5'-diphosphate $\longrightarrow$ AMP + P <sub>i</sub>	-35.7	Figure 3.9
storage	Pyrophosphate $\longrightarrow$ P <sub>i</sub> + P <sub>i</sub> (in 5 mM Mg <sup>2+</sup> )	-33.6	Figure 3.8
i nese compounds	Adenosine-5'-triphosphate $\longrightarrow$ AMP + PP <sub>i</sub> (excess Mg <sup>2+</sup> )	-32.3	Figure 10.14
are not randomly	Uridine diphosphoglucose	-31.9	Figure 22.14
degrading-	Acetyl-coenzyme A $\longrightarrow$ acetate + CoA	-31.5	page 616
substantial	S-adenosylmethionine	-25.6‡	Figure 25.28
<i>activation energy</i> <i>required</i> for phos. hydrolysis	$Glucose-1$ -phosphate $\longrightarrow$ glucose + $P_i$	-21.0	Figure 7.13
	$Sn$ -Glycerol-3-phosphate $\longrightarrow$ glycerol + $P_i$	-9.2	Figure 8.5
	Adenosine-5'-monophosphate $\longrightarrow$ adenosine + P <sub>i</sub>	-9.2	Figure 10.11









What are the Chara	cteris	stics o
TABLE 3.3 Free Energies of Hydrolysis of Some High-En	ergy Compo	unds*
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# ATP – sits in the middle!

Phosphorylation of ATP by a kinase is called substrate level phosphorylation.

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> This process uses a higher energy compound than ATP to make ATP i.e.(phosphate group transfer from a high transfer potential to a lower (ATP) transfer potential compound)

- important to note other compounds have higher group transfer potential...















## **Energy Coupling**

- A spontaneous reaction can drive a nonspontaneous reaction
- The free energy change of coupled reactions are additive
- Some enzyme-catalyzed reactions are interpretable as two coupled half-reactions, one spontaneous and the other non-spontaneous.
- At the enzyme active site, the coupled reaction is kinetically facilitated, while the individual halfreactions are prevented. The free energy changes of the half-reactions may be summed, to yield the free energy of the coupled reaction.









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Phosphoglucomutase catalyzes the reaction in which a phosphate group is transferred from the C-1 of glucose to the C-6 of glucose (G1P  $\rightrightarrows$  G6P).

A student incubates a 0.2 M solution of glucose-1-phosphate overnight with a small amount of the enzyme.

At equilibrium the concentration of glucose-1-phosphate is 9.0 ×  $10^{-3}$  M and the concentration of glucose-6-phosphate is 19.1 ×  $10^{-2}$  M.

Calculate the equilibrium constant (Keq) and the standard state free energy ( $\Delta G^{\circ i})$  for this reaction at 25°C.

0°C + 273 = 273K

R=8.315 J·K<sup>-1</sup>mol<sup>-1</sup>

























Case 2) when the pH is above or below 1 pH unit of the pKa



Calculate the pH of a mixture of 250 mM acetic acid and 100 mM Na acetate. The pKa of acetic acid is 4.75.





What is the concentration of base and acid you need to add to make a 50 mM solution of lactate buffer at pH 4.0? The MW of Lactic acid is 91 amu and sodium lactate is 102 amu. -- What is the pH of the buffer if an

enzyme reaction produces 20 mM H<sup>+</sup>?





# Biological buffering of blood

There are three major contributors to regulating the pH of blood. Bicarbonate, phosphate and proteins

Blood pH Must be Kept Close to 7.4

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- Hydrogen ion is extremely reactive and effects many molecules which regulate physiological processes
- Blood pH is set at a slightly alkaline level of 7.4 (pH 7.0 is neutral)
- A change of pH of 0.2 units in either direction is considered serious
- Blood pHs below 6.9 or above 7.9 are usually fatal if they last for more than a short time











# Acidosis and Alkalosis

#### Metabolic Conditions lead to both acid and alkali conditions

- Metabolic acidosis results from an increase in loss of bicarbonate (such as diarrhea) or overproduction of acids (ketosis, anaerobic metabolism)
- Metabolic alkalosis results from Conditions that lead to a reduced amount of fluid in the body, like vomiting or excessive urination due to use of diuretic drugs, or excess bicarbonate ingestion.

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# Acidosis and Alkalosis

### There can also respiratory reasons for either condition:

- Respiratory acidosis results from hypoventilation which is manifested by the accumulation of CO<sub>2</sub> in the blood and a drop in blood pH.
  - Central Nervous System Depression (Sedatives, CNS disease, Obesity Hypoventilation syndrome)
  - · Lung Disease (emphysema, pneumonia)
  - Musculoskelatal disorders (Myasthenia Gravis, Polio)



- · Liver cirrhosis
- Anxiety

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University Compensation			
Disturban	ce	Response	Expected Change
RESPIRATORYA	CIDOSIS		
<u> </u>	Acute	↑ [HCO <sub>3</sub> -]	1 mmol/L/10mmHg increase in PaCO <sub>2</sub>
	Chronic	↑ [HCO <sub>3</sub> -]	4 mmol/L/10mmHg increase in PaCO <sub>2</sub>
RESPIRATORY ALKALOSIS			
	Acute	↓ [HCO <sub>3</sub> -]	2 mmol/L/10mmHg decrease in PaCO <sub>2</sub>
	Chronic	↓ [HCO <sub>3</sub> -]	4 mmol/L/10mmHg decrease in PaCO <sub>2</sub>
METABOLIC ACI	DOSIS	↓ PaCO <sub>2</sub>	1.2 x the decrease in [HCO3 <sup>-</sup> ]

#### Adjusting levels - Compensation University an Diego In reality the kidneys regulate the bicarbonate concentration. If there is too little bicarbonate, the kidneys filter and excrete H<sup>+</sup>, causing a shift in the equilibrium to increase bicarbonate. -If there is too much bicarbonate, kidneys will excrete it. The carbon dioxide is replaced by metabolism (Food -> H<sub>2</sub>O and CO<sub>2</sub>) Changes in breathing can increase or decrease the CO<sub>2</sub>

Breathe too fast and what happens. Decrease the breathing rate and alter the pH as well. (think of the last time you got sick and

threw up) The pH problem (either metabolic or resp) cannot be compensated by the same means. i.e. if you have a lung disease you can not compensate by breathing faster - it just isn' t possible.



### Respiratory & metabolic pathways compensate for pH changes

### **Respiratory** acid-base imbalances

- nronic ventilatory failure Would expect acidosis conditions
- Kidneys will retain HCO3 in blood
- Renal compensation if HCO3<sup>°</sup> and pH readings are higher than expected for PCO2 level
- Would expect alkalosis condition Kidneys will excrete HCO
- Renal compensation if HCO3<sup>-</sup> and pH readings lower than expected for PCO2 level.

#### Metabolic acid-base imbalances

- Increased ventilatory rate and depth Respiratory compensation when PaCO<sub>2</sub> decreases to bring pH in normal range.
- Decreased ventilatory rate and depth