General Chemistry (CH101):
Chemistry around Us

Department of Chemistry

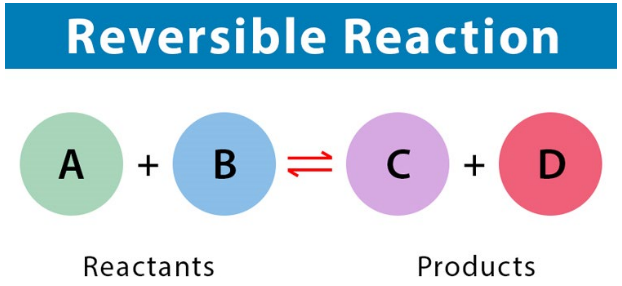
KAIST

©Phongphan Phongphan/Alamy Stock Images

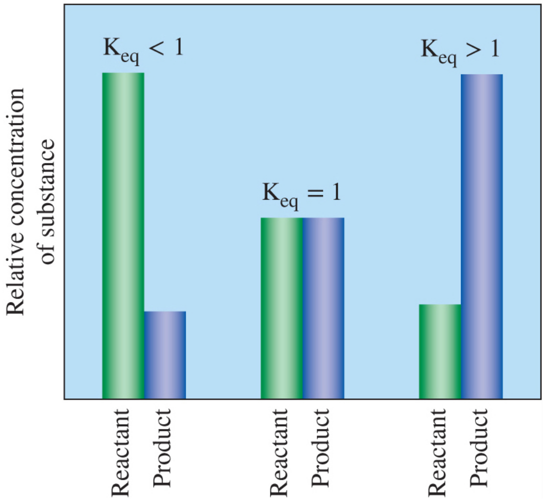
Health & Medicine

Chapter 12

A life spent fighting against equilibrium



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



- **Reversible**: Reactions in biochemistry are almost always reversible.

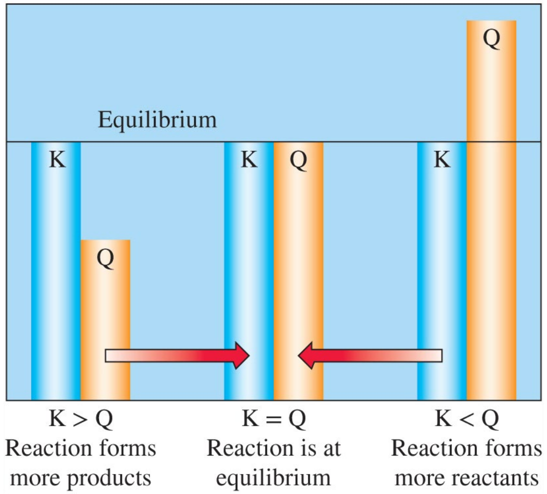
- **Equilibrium**: A balance of the products and reactants
  (a macroscopic level will appear static)

- **Equilibrium constant (K)**: The **stable ratio** of product to reactant concentrations

A life spent fighting against equilibrium

- **Equilibrium constant (K)**: The **stable ratio** of product to reactant concentrations

- **Reaction quotient (Q)**: The ratio of [products]/[reactants] **at a give point in time**



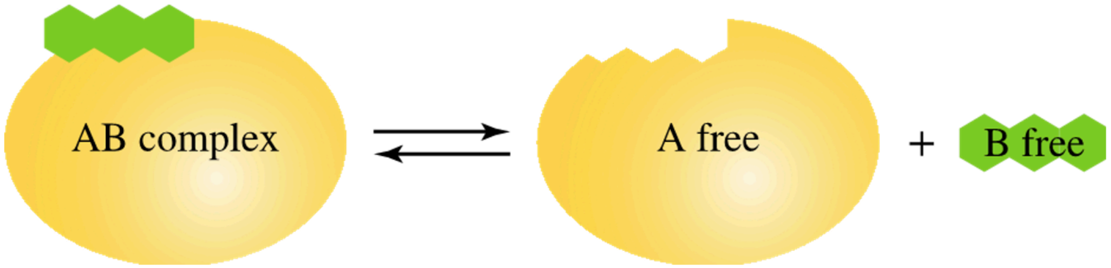
"Le Chatelier's principle"

Once an external stress alters a system in equilibrium
→ the system will seek to recover from the alteration

BUT!!! The equilibrium only tells us which direction it goes, not how quickly it goes

Kinetics vs Thermodynamics

https://youtu.be/RjFW3smI1fY



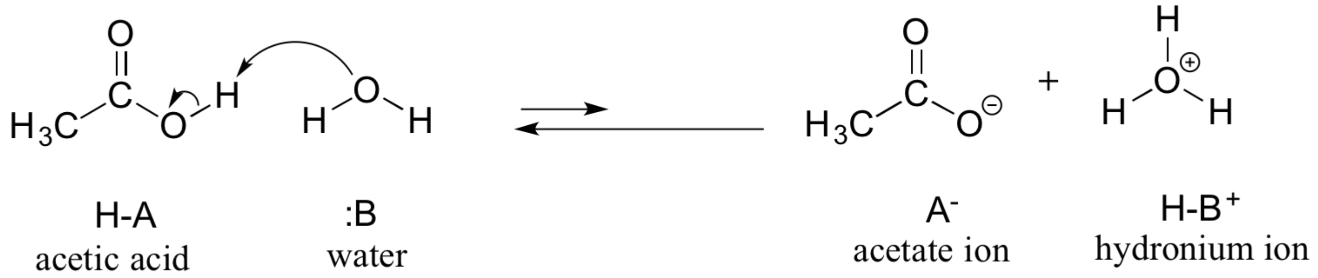
Your Turn 12.3 Finding Equilibrium in Binding

Epinephrine (better known as adrenaline) is a small organic molecule that binds to your cells at a specific site called the *β*-adrenergic receptor to give you that familiar heightened energy level. The release of epinephrine from the receptor has a K value 5×10^{-6}. For a solution of epinephrine with the *β*-adrenergic receptor, does the epinephrine prefer to stay bound or free?

Buffer system

= A system that responds only gradually or slightly to an external influence

→ **Buffers shield our bodies from large shifts in pH**



$$K_a = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH]} = 1.8 \times 10^{-5}$$ (K of acid = K_a)

Water is necessary for the reaction, but excluded from the expression for K

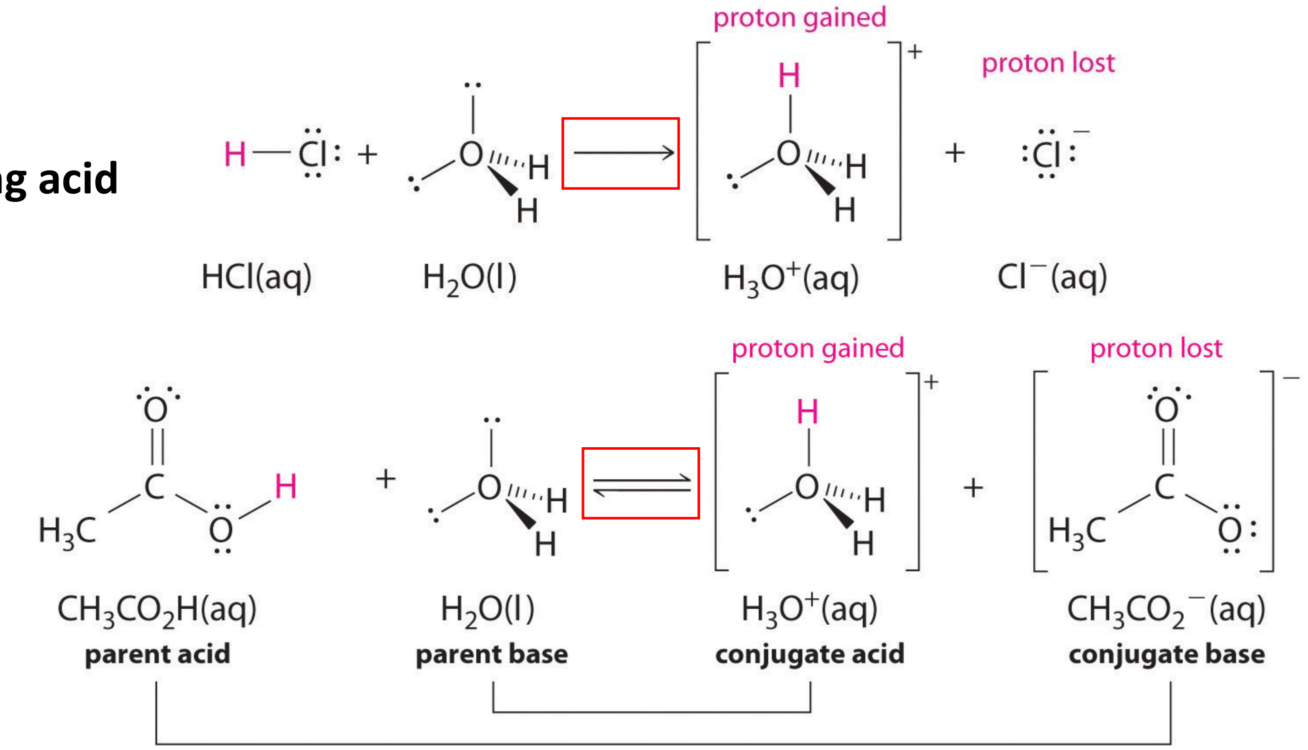
It presents in large excess, so its concentrations remain constant throughout the reaction

Acetic acid = **a weak acid** = The dissociated state is presents but **LESS FAVORED**

A magic of the weak acid

Strong acid

Weak acid



The conjugate base for weak acids
→ **It generates resistance(/preference)**

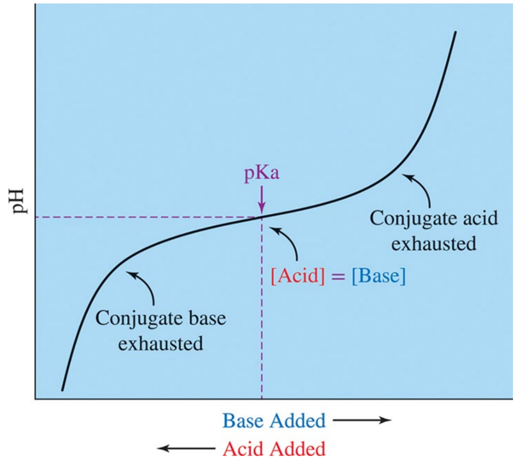
Practice 12.#

- Compare the two conditions

A. Addition of 0.05 mole of HCL to 1.0 L of pure water

B. Addition of 0.05 mole of HCL to 1.0 L of 0.1 M HF + 0.1 M F^- solution (pK_a = 3.14)

Importance of the buffer system



- A buffer has its own capacity
- A buffer is most useful when pH = pKa
- A buffer will resist against acids/bases up to ±1 pH

- Biological systems require the buffer systems → resist any local pH change
- Not all your systems use the same buffer/pH → your tissues have preferential pH
- Even within your cells, each compartment has different pH levels

Thus, we need to understand the chemical framework of biology to develop medicines!

Organic chemistry

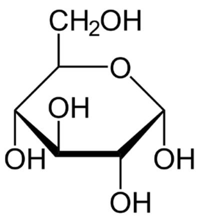
= study of carbon compounds

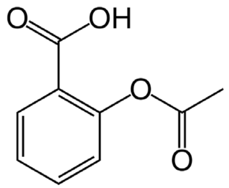
IUPAC (The international union of pure and applied chemistry)

→ a formal set of nomenclature rules (names of compounds)

(1) glucose = (2R,3S,4R,5R)-2,3,4,5,6-pentahydroxyhexanal

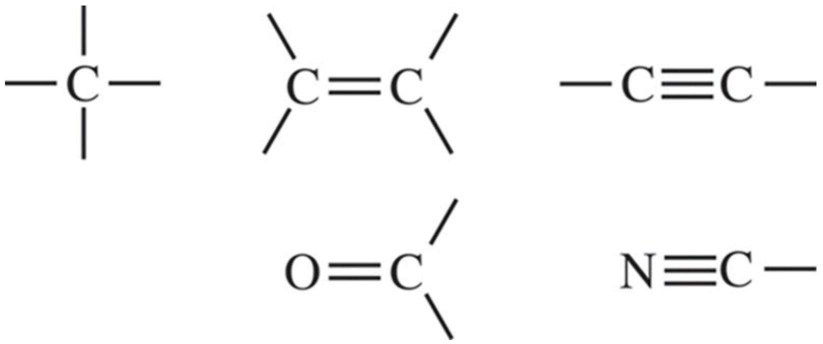
(2) aspirin = 2-acetoxybenzoic acid





Octet **rule**

→ each atom has a share in eight electrons (an octet)



- Carbon = four bonds

- Oxygen = two bonds

- Nitrogen = three bonds

*****nonbonding electrons***

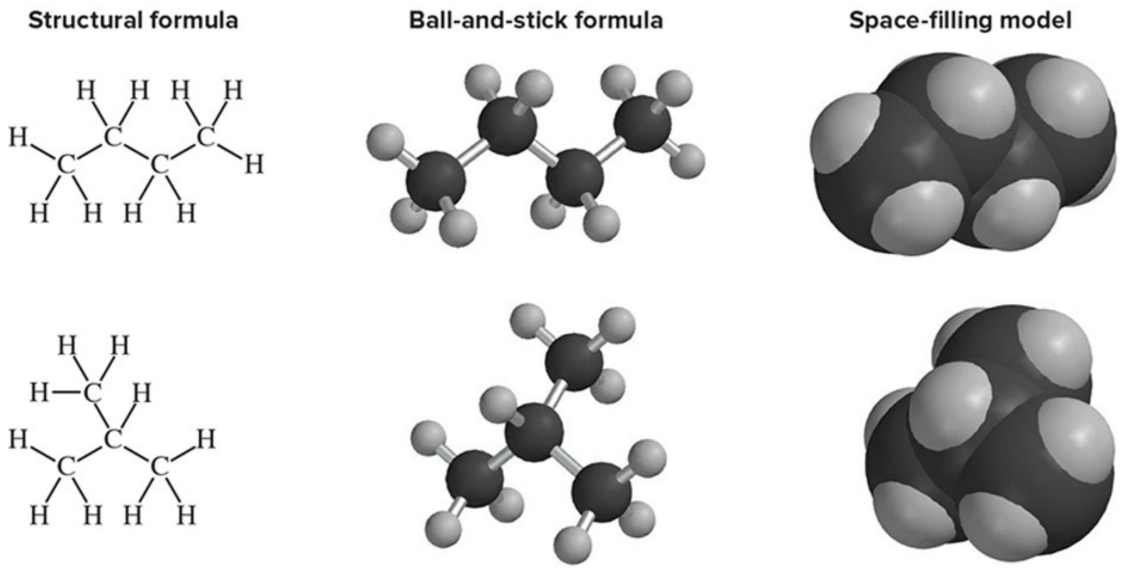
Practice With Lewis Structures

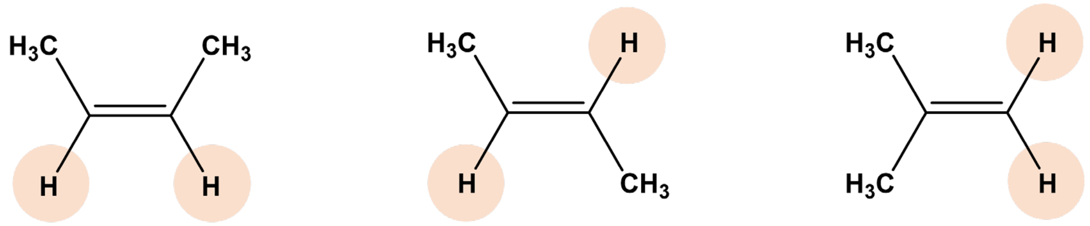
Your Turn 12.10 The Octet Rule.

- **a.** NH_3, ammonia
- **b.** N_2, nitrogen
- **c.** N_2H_2, diazene
- **d.** H_2O, water
- **e.** H_2CO (the C is the central ato m), formaldehyde
- **f.** CO_2, carbon dioxide
- **g.** CH_4, methane
- **h.** C_2H_2, acetylene
- **i.** C_2H_4, ethylene

Isomers

= the same chemical formula but different structures (and properties)





cis trans neither

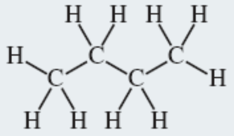
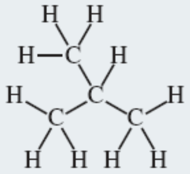
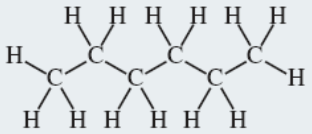
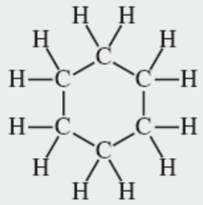
Your Turn 12.13 Practice with Isomers

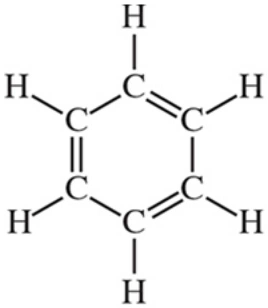
a. Are *n*-butane and isobutane isomers? Explain.

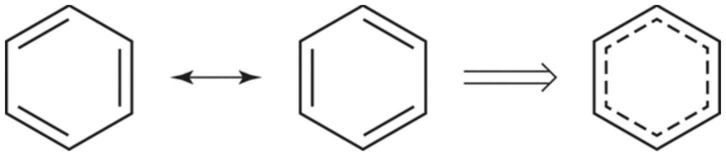
b. Are *n*-hexane and cyclohexane isomers? Explain.

c. Three isomers have the formula C_5H_{12}. For each, draw a structural formula, a cond ensed structural formula, and a line-angle drawing.

How to draw compounds

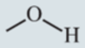
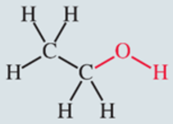
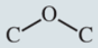
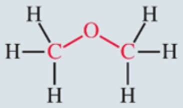
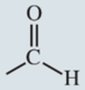
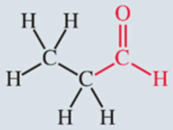
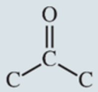
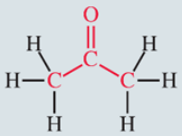
Compound	Chemical Formula	Structural Formula	Line-Angle Drawing
n-butane	C_4H_{10}		
isobutane	C_4H_{10}		
n-hexane	C_6H_{14}		
cyclohexane	C_6H_{12}		





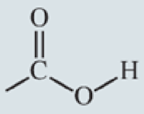
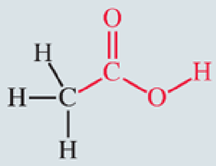
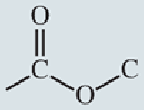
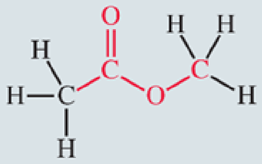
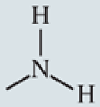
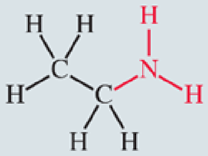
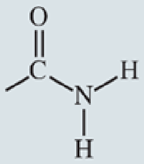
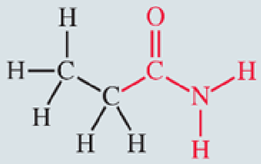
Functional groups

= impart characteristic physical and chemical properties to the molecules

		SPECIFIC EXAMPLES		
Functional Group	**Generic Formula**	**Name**	**Structural Formula**	**Condensed Structural Formula**
alcohol		ethanol (ethyl alcohol)		CH_3CH_2OH
ether		dimethyl ether		CH_3-O-CH_3 or CH_3OCH_3
aldehyde		propanal		$CH_3CH_2-\overset{\overset{O}{\|}}{C}-H$ or CH_3CH_2CHO
ketone		2-propanone (dimethyl ketone, acetone)		$CH_3-\overset{\overset{O}{\|}}{C}-CH_3$ or CH_3COCH_3

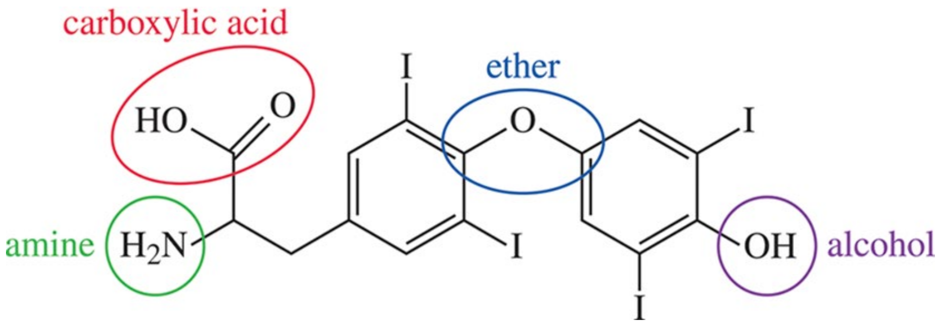
Functional groups

= impart characteristic physical and chemical properties to the molecules

carboxylic acid		ethanoic acid (acetic acid)		$CH_3-\overset{O}{\overset{\parallel}{C}}-OH$ or CH_3CO_2H or CH_3COOH
ester		methyl ethanoate (methyl acetate)		$CH_3-\overset{O}{\overset{\parallel}{C}}-OCH_3$ or CH_3COOCH_3
amine		ethylamine		$CH_3CH_2NH_2$
amide		propanamide		$CH_3CH_2-\overset{O}{\overset{\parallel}{C}}-NH_2$ or $CH_3CH_2CONH_2$

Functional groups

= impart characteristic physical and chemical properties to the molecules

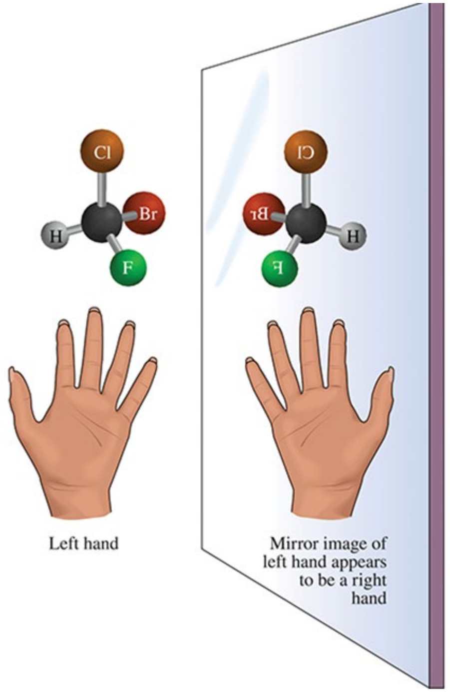


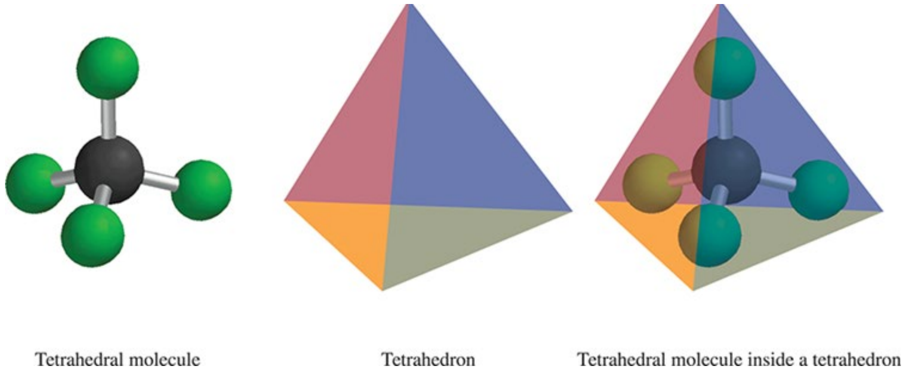
Based on the structure….

- **Acidity**
- **Polar** vs **nonpolar**
- **Solubility** (*"like dissolves like"*)

Chiral molecules (chirality)

= Optical isomers



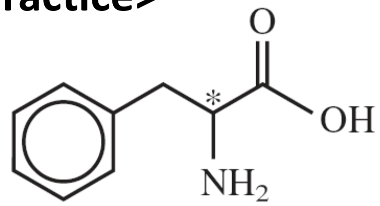


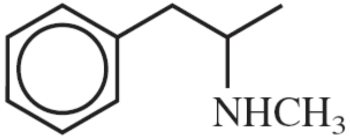
When four different groups are attached to a carbon atom

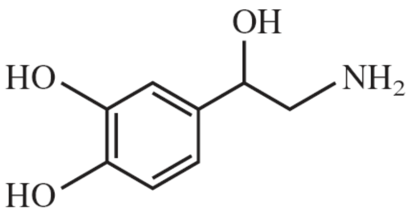
→ **nonsuperimposable**

Two hands are **nonsuperimposable**!

<Practice>



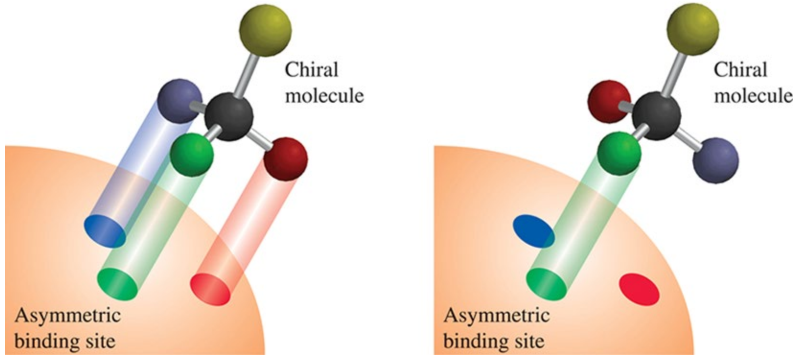




- $CH_3CH(OH)CH_2CH_3$

Chiral molecules (chirality)

= Optical isomers



Many biologically important molecules

= **chiral** (sugar, amino acids…)

→ They are sensitive to chirality

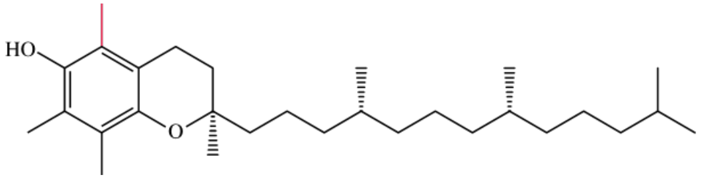
In the development of drugs, **the correct three-dimensional configuration is important!**

→ As their **"physical" properties** are often identical, it is **difficult to separate!!**

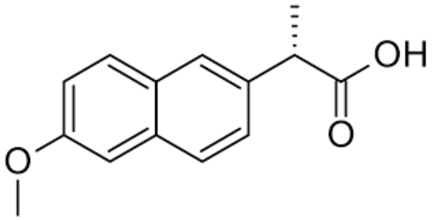
<u>= Medicinal chemist's task</u>

Racemic mixture = consisting of equal amounts of each optical isomer

- it can be either beneficial and dangerous



Vitamin E (mixture)
One isomer = fetal development
Another isomer = cancer prevention

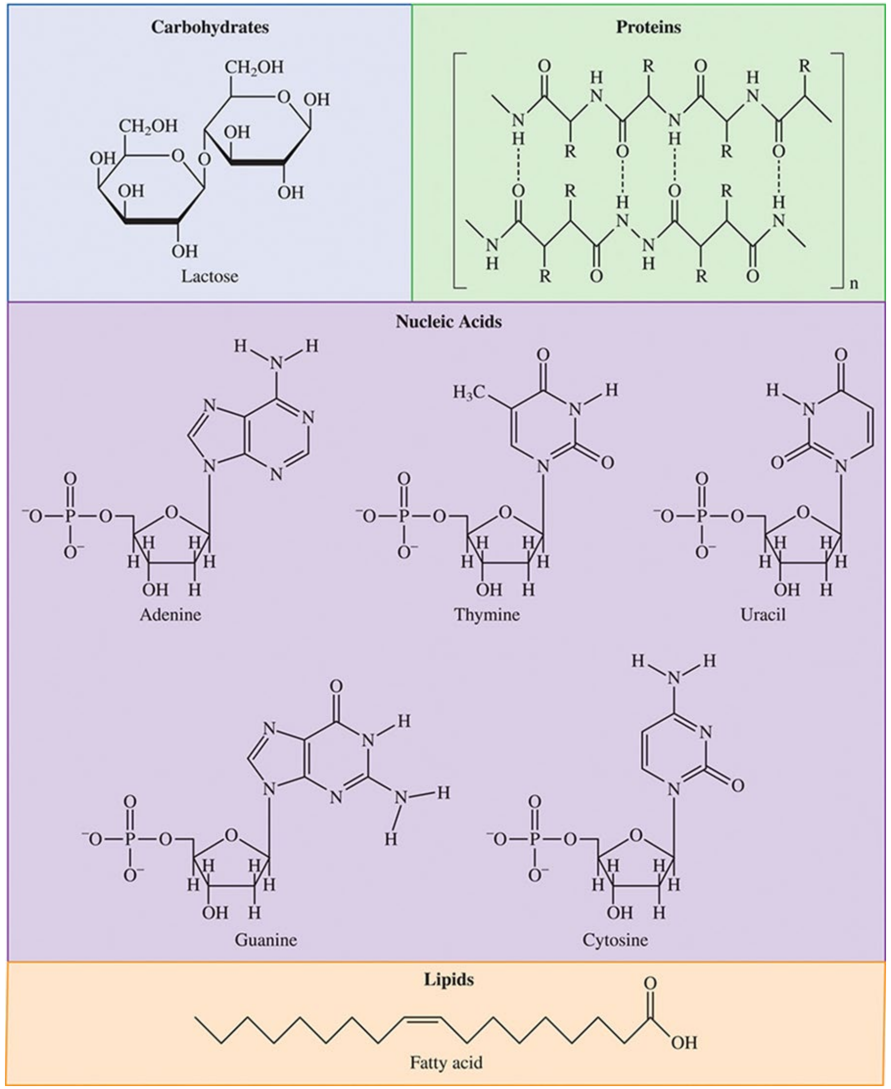


Naproxen
One isomer = pain reliever
The other isomer = liver damage

Four classes of macromolecules in life

Vital for energy storage, cellular structure, and signaling

Polymer of 20 different amino acids
→ diverse in structure and function



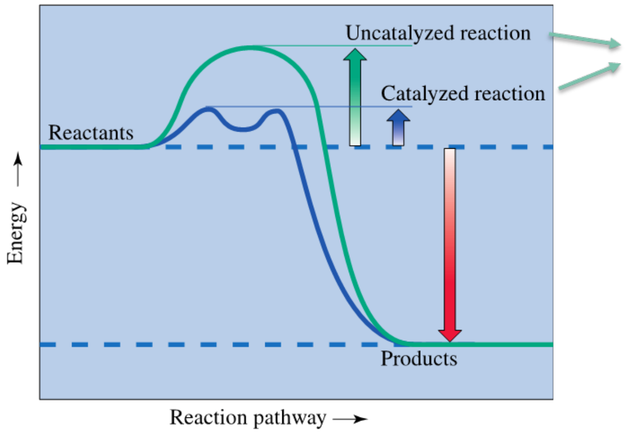
Polymer of nucleotides
=genetic information

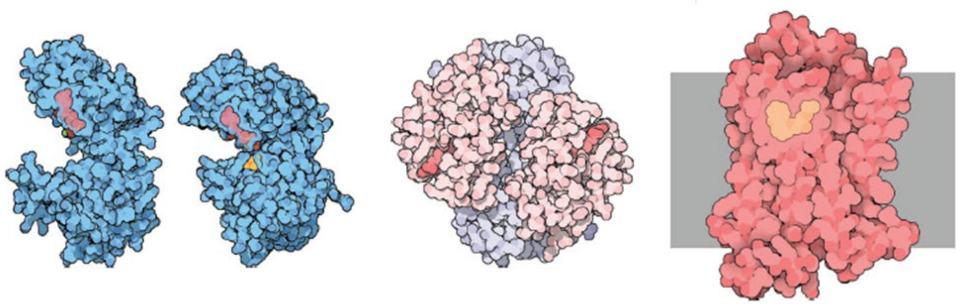
Provide Calories and cellular membrane

Respiration

Complete combustion of glucose to fuel your body

Activation energy is high → **Enzymes** are required



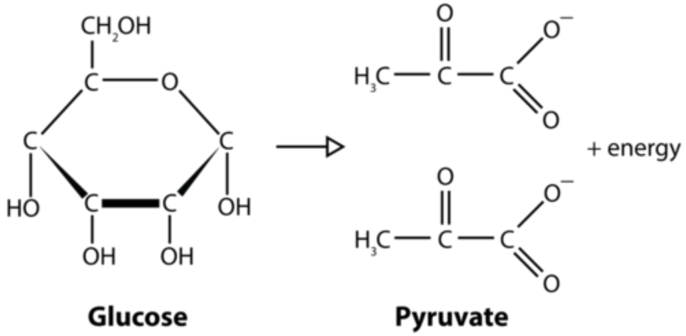


<u>= Biological catalysts</u>

Enzymes contain an **active site**
= selectively binds only specific reactants
→ Enabled by the specific shape and functional groups

Glycolysis

To break down glucose fuel (generating energy)



Stage 1 of glycolysis

When our muscle require energy immediately

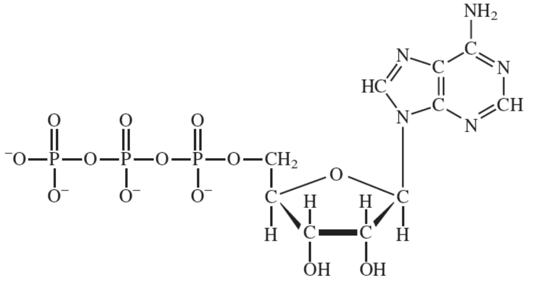
↓

Anaerobic respiration (absence of O_2)
=rapid but inefficient

Otherwise, aerobic condition
=slow but efficient

↓

1 glucose + O_2 → 32 ATP + CO_2

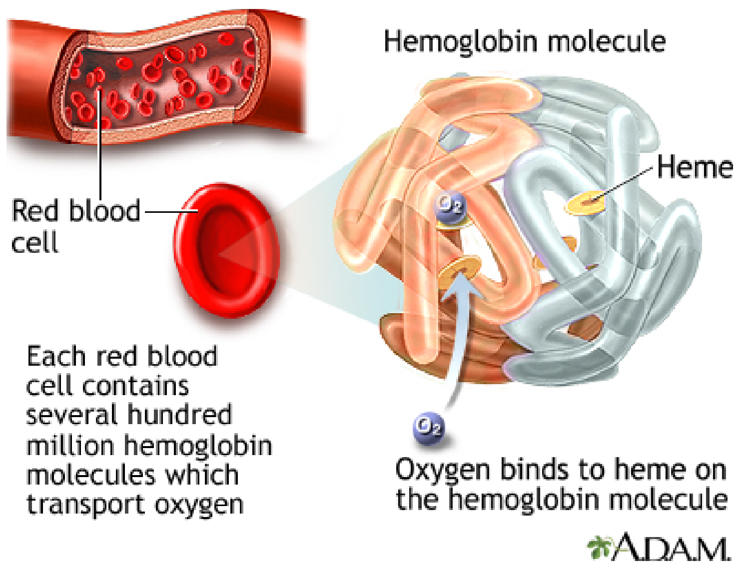


Universal chemical fuel

Hemoglobin

= A protein in red blood cells that carries oxygen

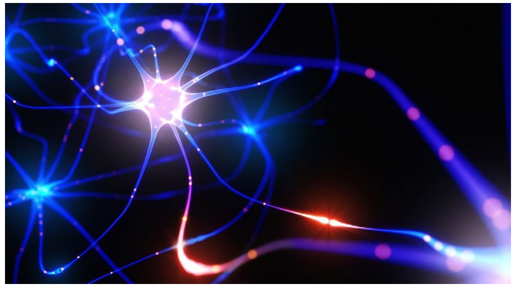
Respiration (which is ubiquitous) requires oxygen
→ The oxygen you inhale must be spread throughout your body



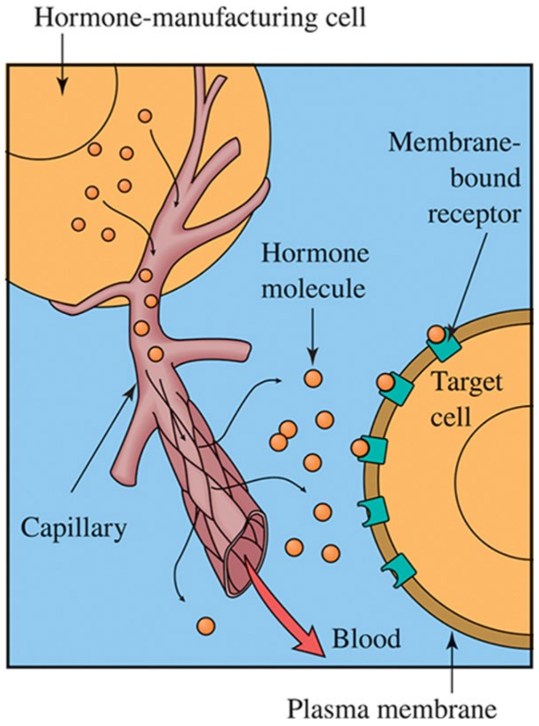
Heme contain iron that binds with oxygen
(Exposure of iron to oxygen = formation of rust!)

Chemical signaling process

Cells do not spontaneously use glucose
= It is triggered by a **signal**!



Electrical impulses
i.e., movement, breathing, heartbeats, reflexes



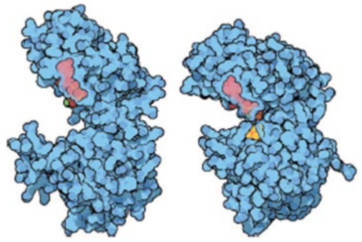
Chemical processes
Most of the body's signal

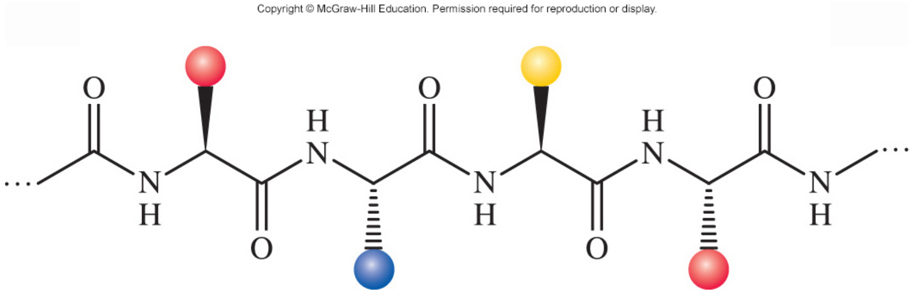
Hormones
= messenger compounds
= remain outside of the cells

Receptor
= embedded in the membrane
= like a doorbell for the cell

Hormone binds to receptor → change its shape → transport the information
→ a cascade of reactions inside of cells

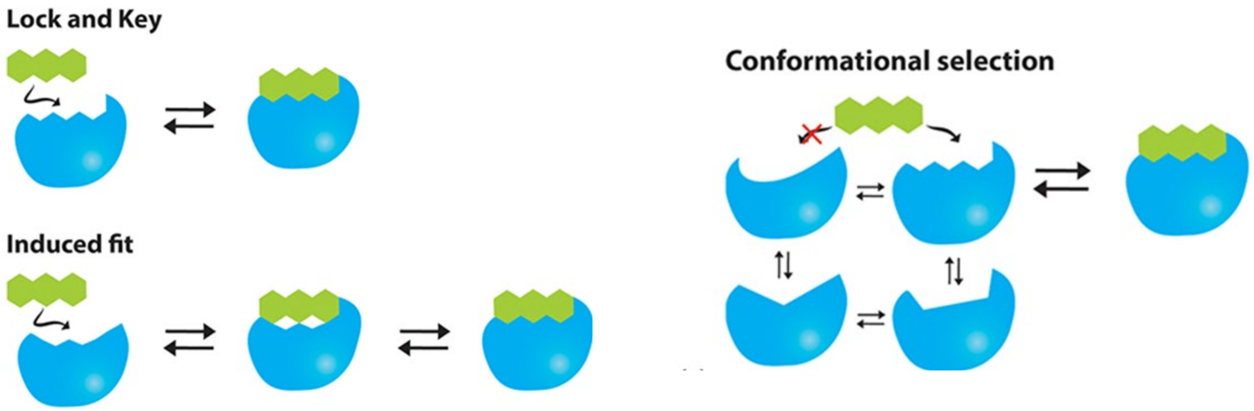
Protein-small molecule interactions





Structure of the binding pocket in proteins is determined by the functional groups (side chains) of amino acids!

<u>The same polyamide backbone with a diverse structures and functions</u>

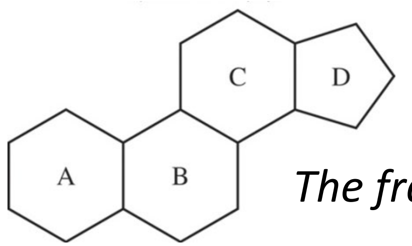


structure of protein has a limited range of motion

= high specificity

Steroids

Naturally occurring fat-soluble organic compounds
that share a common structure



17 carbon atoms arranged in four rings

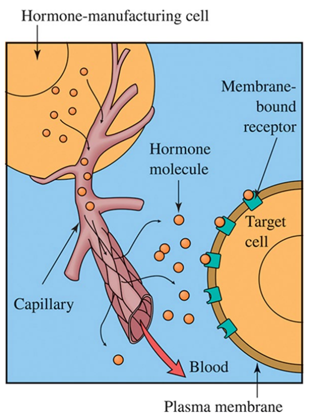
The framework appears to be flat but actually 3D in shape

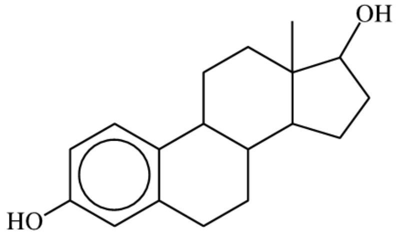
Table 12.4 Steroid Functions

Function	Example Molecules
Regulation of secondary sexual characteristics	estradiol (an estrogen), testosterone (an androgen)
Regulation of the female reproductive cycle	progesterone
Regulation of metabolism	cortisol
Digestion of fat	cholic acid
Component of cellular membranes	cholesterol
Stimulation of muscle and bone growth	gestrinone, trenbolone

Some differ only slightly in structure, but have radically different functions

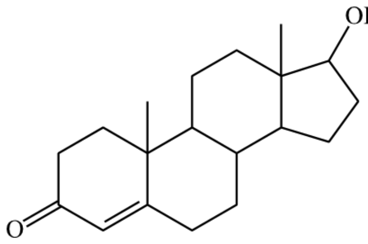
Steroids





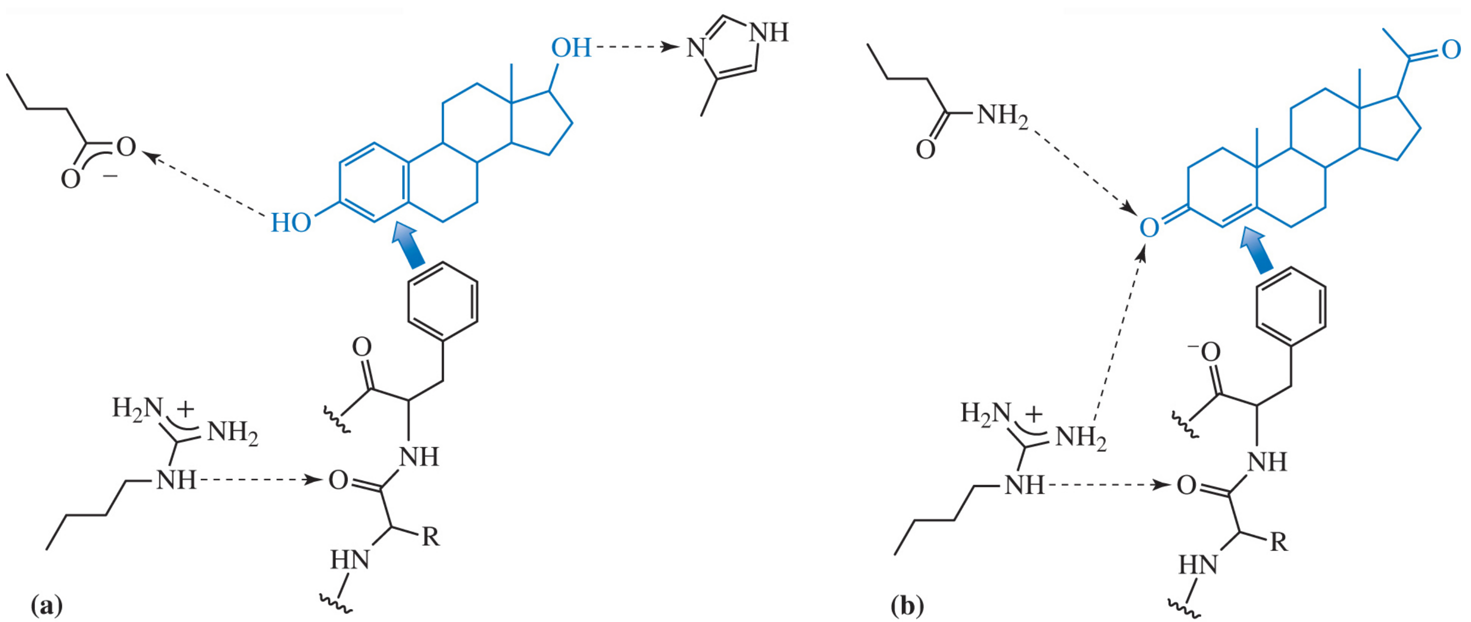
estradiol

(estrogen)



testosterone

Some differ only slightly in structure, but have radically different functions



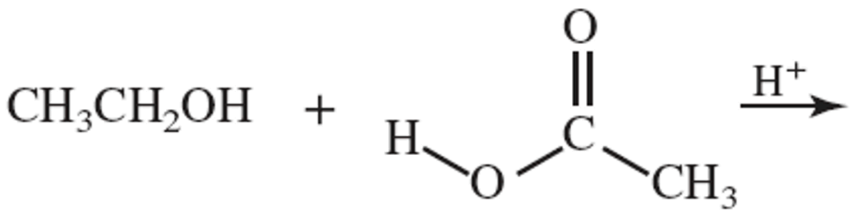
The first drug discovery

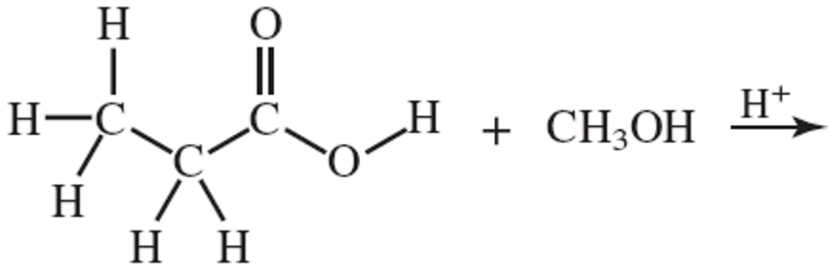
Aspirin: https://youtu.be/uRhkDN2WjzI

Penicilin: https://youtu.be/CNbnLgetqHs

Your Turn 12.26 Ester Formation

Draw structural formulas for the esters that form when these alcohol and acid pairs react.

a. 

b. 

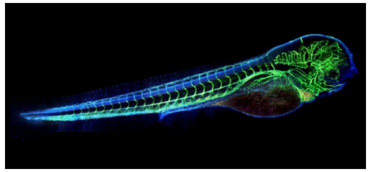
Difficulty?

Modern drug discovery

Drugs can be broadly classified into two groups

1. Drugs that produce **a physiological responses**
   (aspirin, anticancer drugs, morphine)

2. Drugs that **kill foreign invading organisms**
   (antibiotics, antifungal agents)



Cells always use the one that is best evolved to do the job

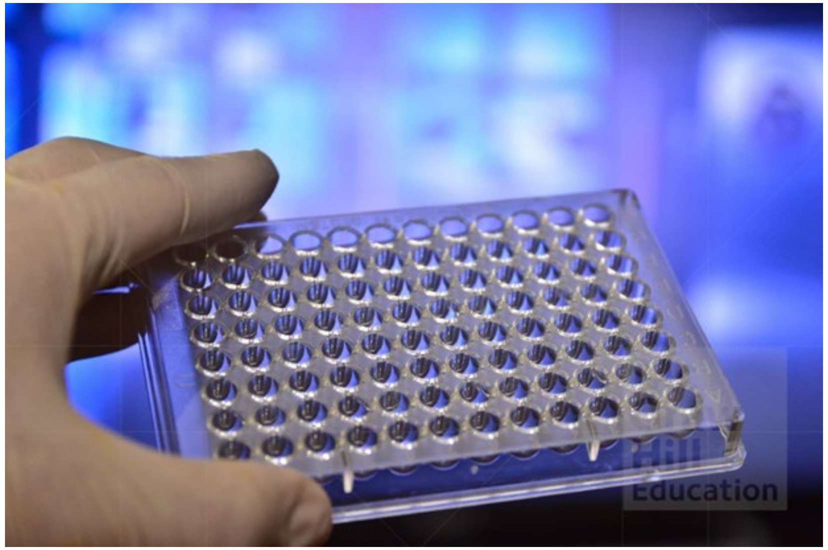
<Processes for the drug development>

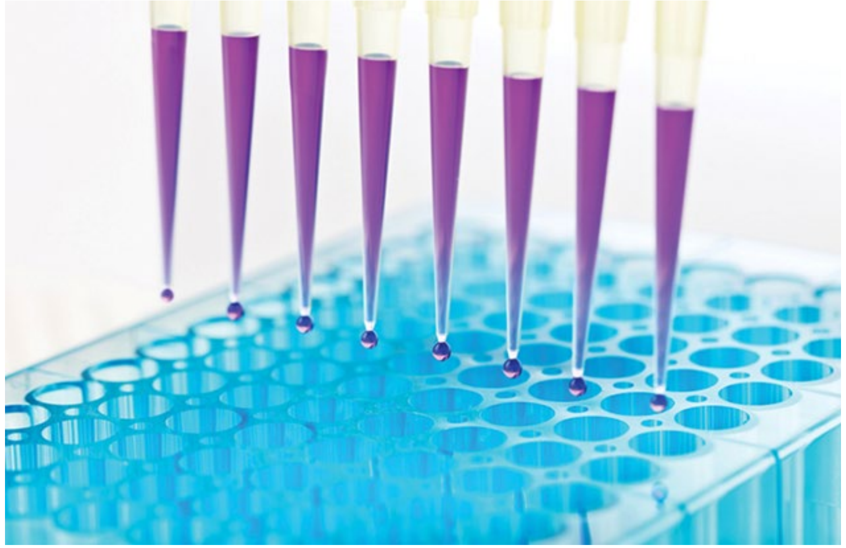
1. To find starting point: large library screening, design it based on 3D structure of the active site (pharmacophore)

2. Structure-activity relationship (SAR) study: The process of systematically changing the structure of a drug molecule with assessment of the resulting change

3. Evaluation: synthesized protein → cells → worms, zebrafish, and mice →→→ human

Modern drug discovery





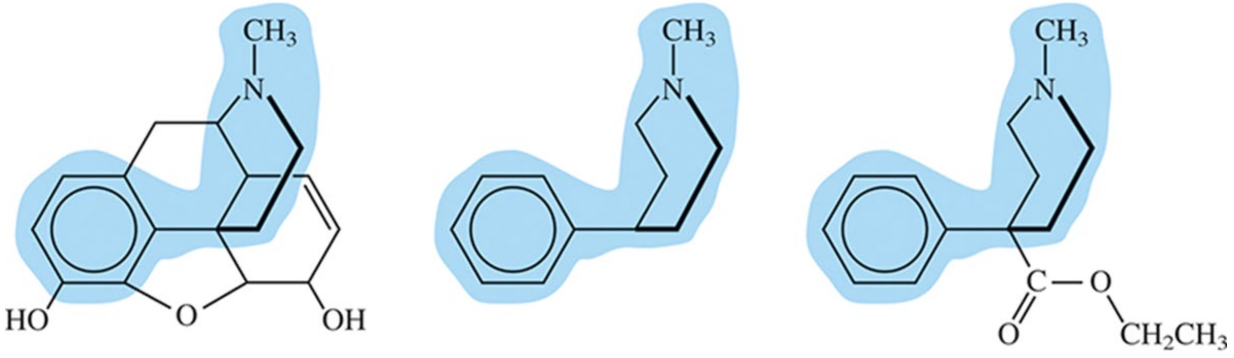
Combinatorial chemistry

Systematic testing large numbers of small molecular libraries

1. Many molecules can be created at a rapid rate
2. The cost of the procedure is much cheaper (than the synthesis)
3. Large libraries of bioactive lead compounds can be produced inexpensively

→ **Best way to find a lead compound by far**

Modern drug discovery

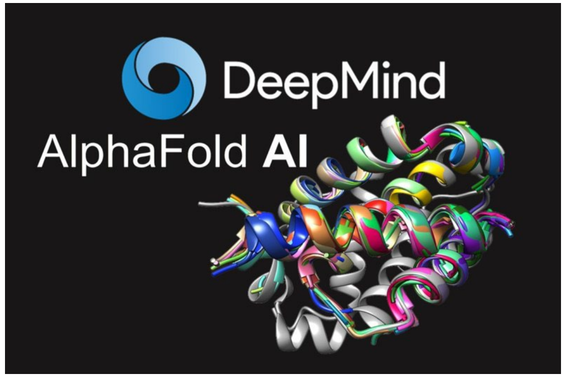


morphine | active area | Demerol

Highly addictive | Less addictive

Key = understanding of the structure of the binding site

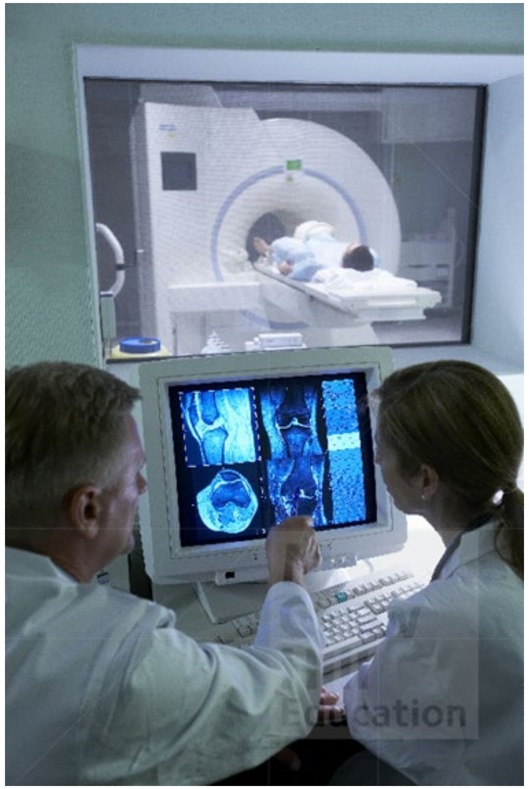
= The ideal search yields <u>functional groups</u> of the <u>proper polarity</u> in the <u>right places</u> **without any excess**!

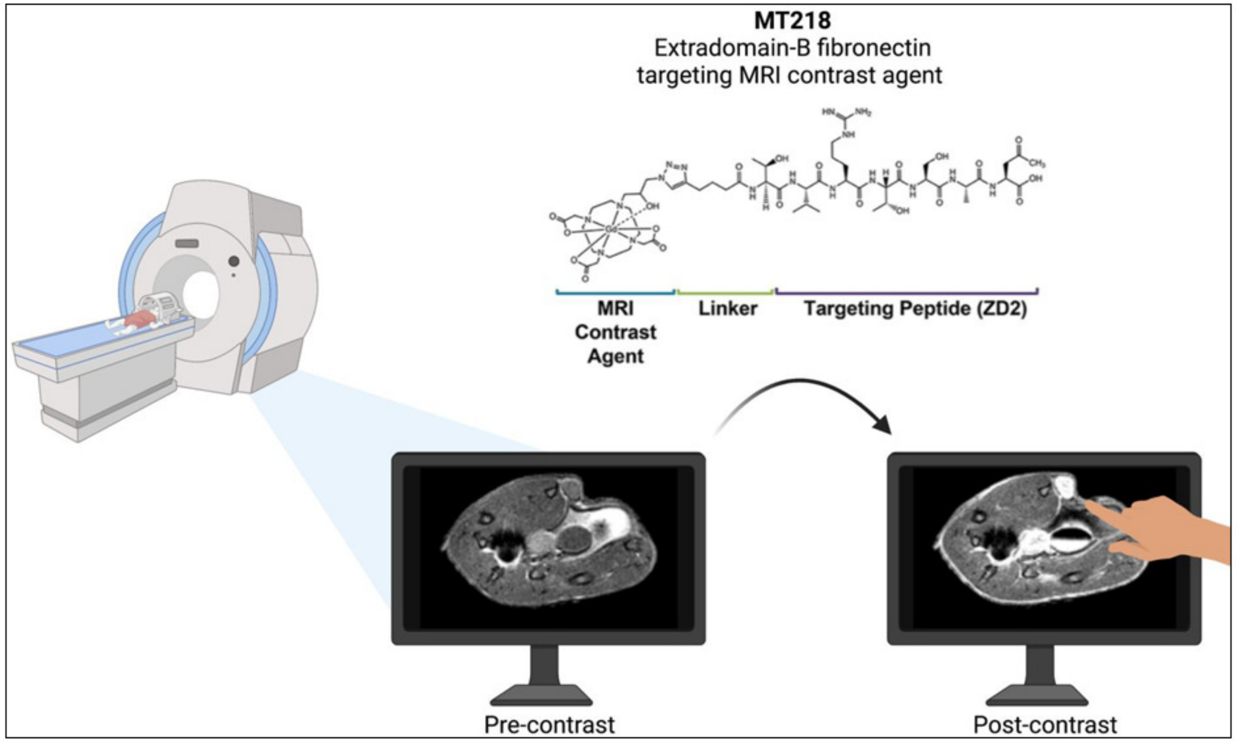


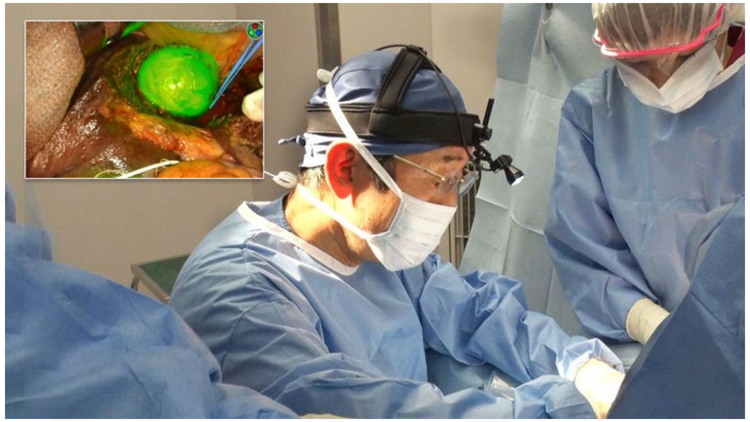
AI + computing process
= powerful tools

https://youtu.be/Kq6oNcd3d-U

Another type of chemicals for medicinal purpose







Seeing is believing!

- Discuss PEDs (Performance enhancing drugs). What are they? How do they work?
- Talk about the concept of image-guided surgery. Why is it so helpful?
- We’ve discussed the importance of synthetic chiral drugs. Discuss the importance of chirality in bio-molecules.
- Why are steroids beneficial to increase the size of muscles?