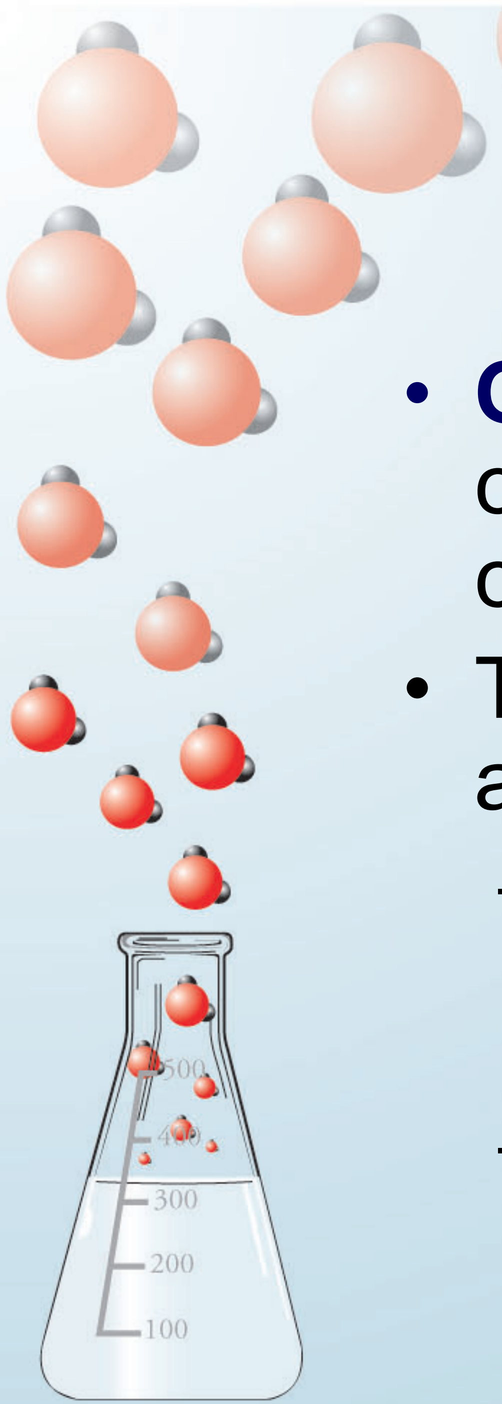
An Introduction to Organic Chemistry and Chemical Weapons

http://preparatorychemistry.com/Bishop_Book_atoms_15.pdf

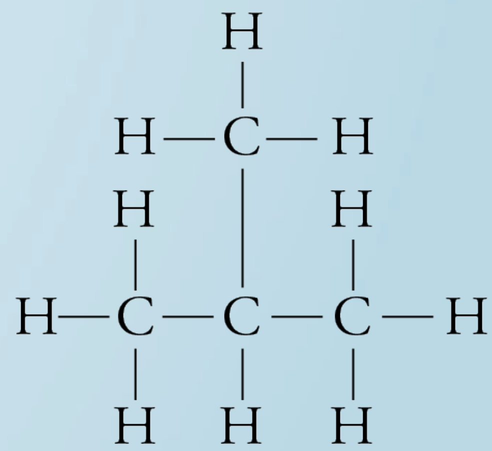


Organic Chemistry

- **Organic chemistry** is the chemistry of carbon-based compounds.
- There are two reasons why there are millions of organic chemicals.
  - Carbon atoms can form strong bonds to other carbon atoms and still form bonds to atoms of other elements.
  - There are many different ways to arrange the same atoms in carbon-based compounds.

Ways to Describe Organic Compounds

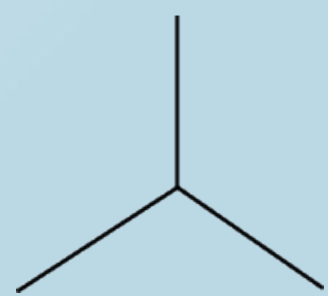
- Lewis structures



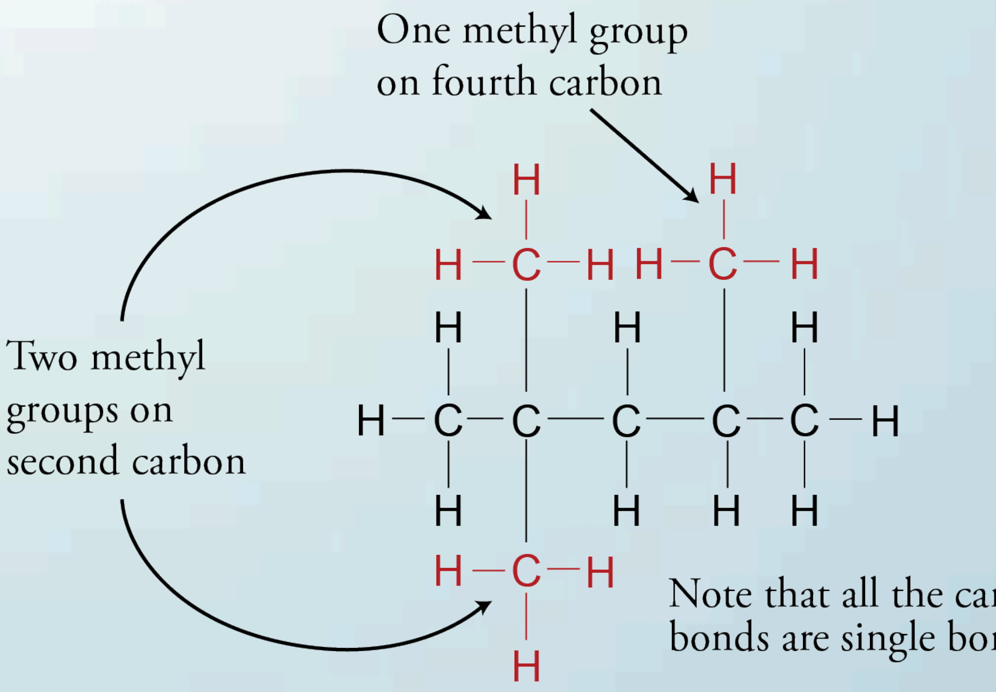
- Condensed Formulas

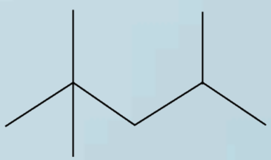
$CH_3CH(CH_3)CH_3$

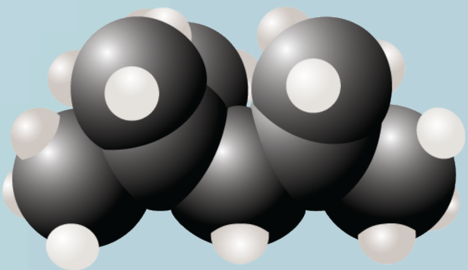
- Line Drawings



Alkanes - **Hydrocarbons (compounds composed of carbon and hydrogen) in which all of the carbon-carbon bonds are single bonds**

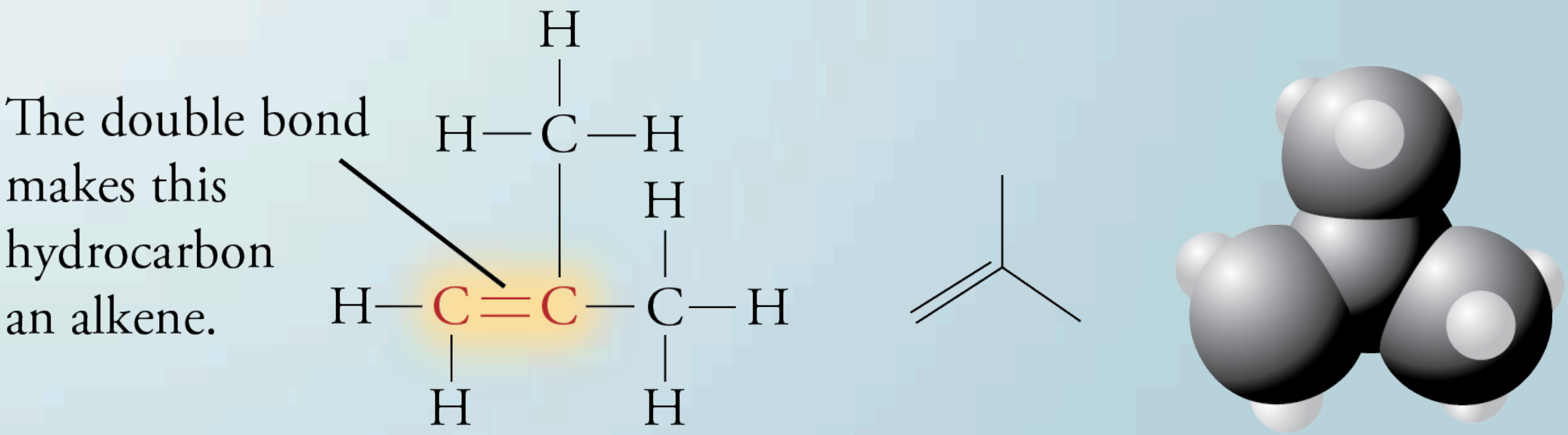






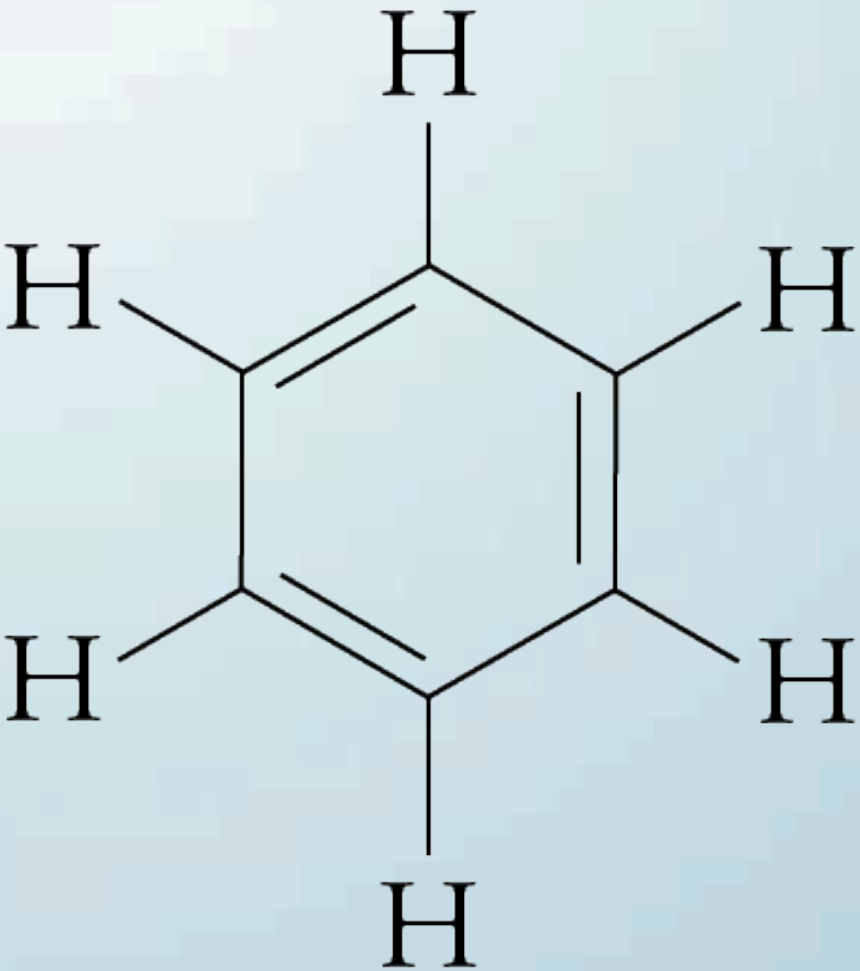
2,2,4-trimethylpentane, $CH_3C(CH_3)_2CH_2CH(CH_3)CH_3$

Alkenes - Hydrocarbons that have one or more carbon-carbon double bonds

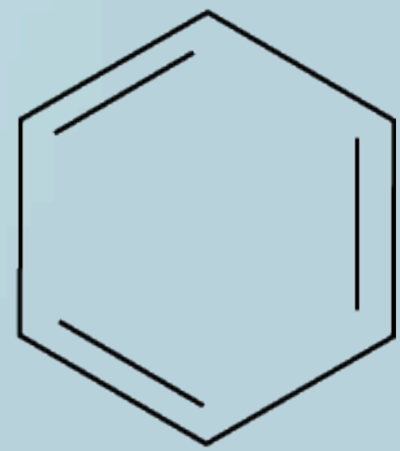


2-methylpropene (isobutene), $CH_2C(CH_3)CH_3$

Benzene

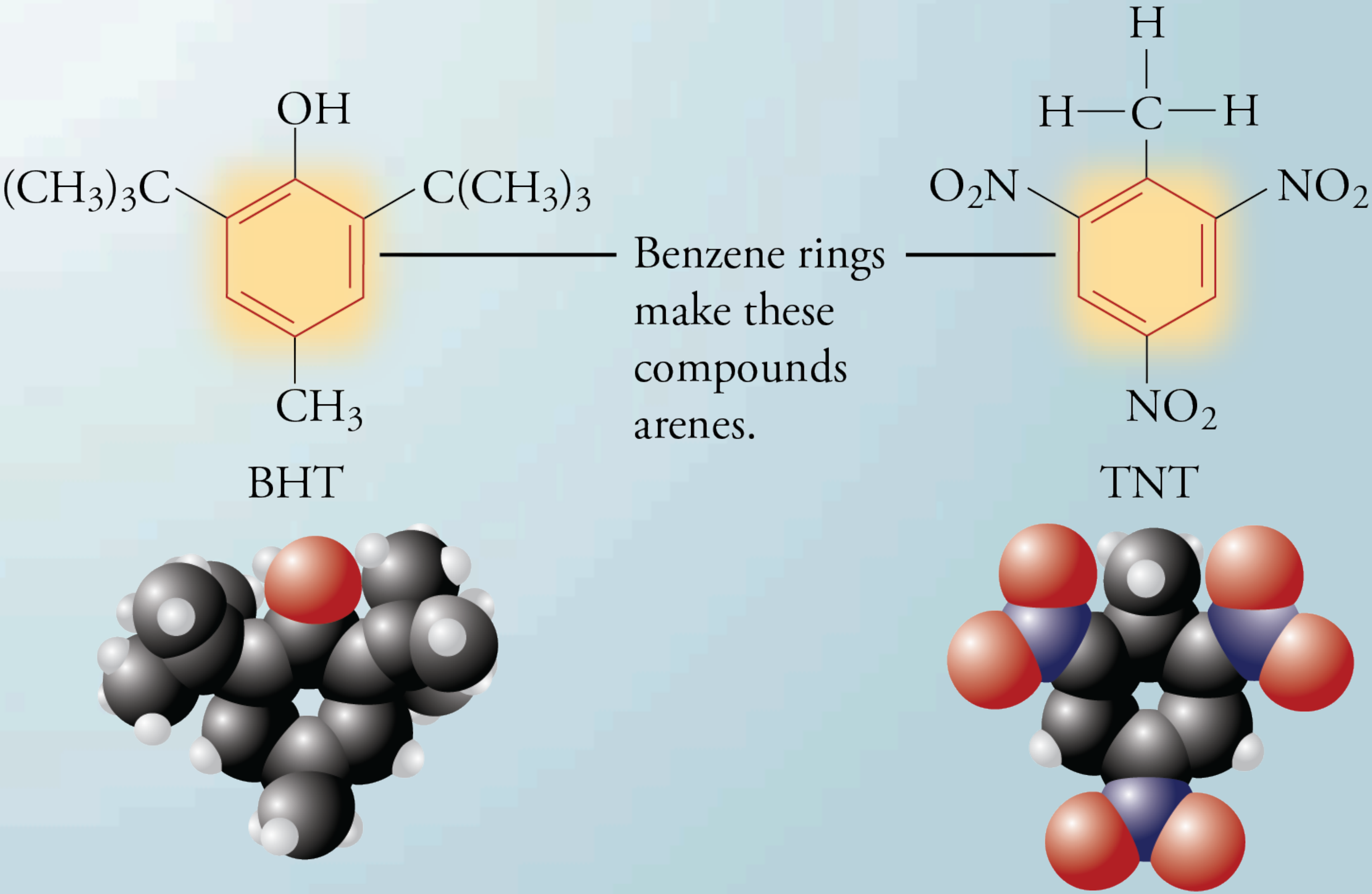


or

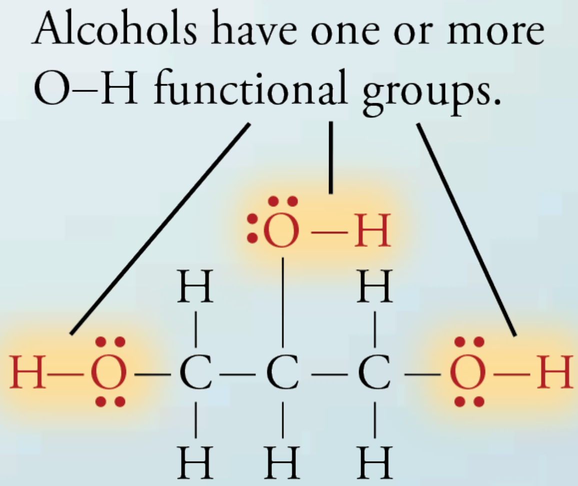


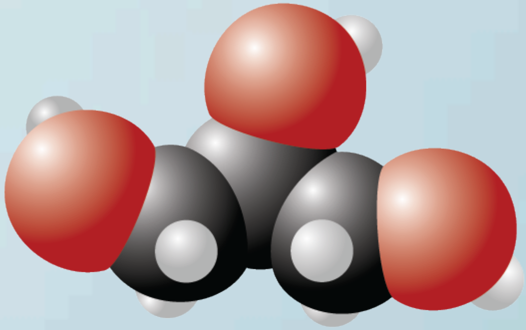
Benzene

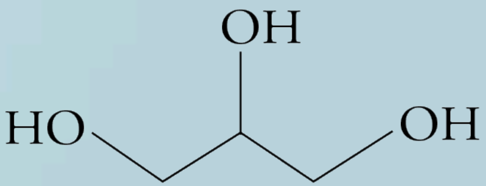
Arenes (or Aromatics) - Compounds that contain the benzene ring



Alcohols - compounds with one or more -OH groups attached to a hydrocarbon group







Glycerol, $HOCH_2CH(OH)CH_2OH$

Chemical Weapons (CW)

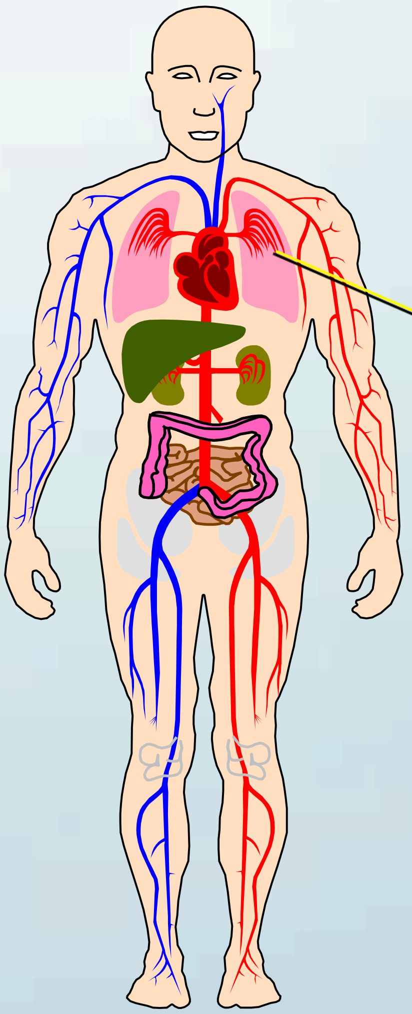
- Chemical weapons are “man-made, supertoxic chemicals that can be dispersed as a gas, vapor, liquid, aerosol (a suspension of microscopic droplets), or adsorbed onto a fine talcum-like powder to create *dusty* agents.” (Jonathan Tucker)

Special gas mask for dogs-1917

Classification of Chemical Weapons

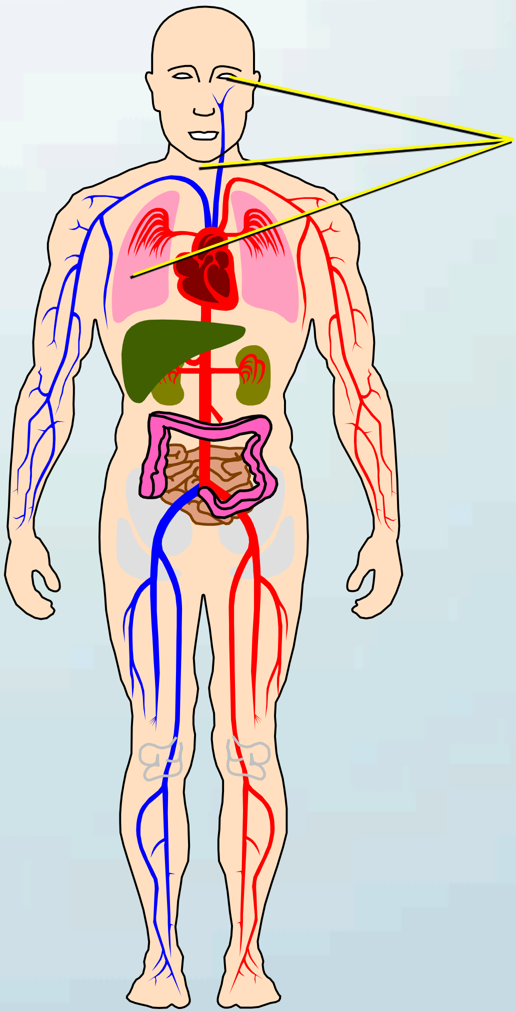
- **Lethal agents** – kill quickly with small quantities
  - Nerve agents (e.g. sarin and VX)
  - Blood agents (e.g. hydrogen cyanide)
- **Incapacitants**
  - Choking agents (e.g. chlorine or phosgene)
  - Blistering agents (e.g. sulfur mustard)
  - Tearing agents (e.g. CS)
  - Opiate-like agents (e.g. fentanyl)
  - Psychochemical Incapacitants (e.g. BZ)

Choking Agents



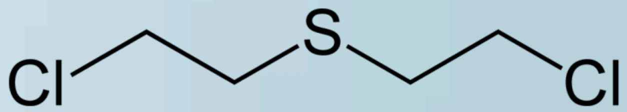
- Diphosgene, **phosgene**, **chlorine**, chloropicrin
- Mode of Action: Inhalation
- Physiological Effects
  - Agent inhaled into lungs
  - Fluid builds up in lungs & victim chokes on own fluid
  - “Dry land drowning”
  - Victim can die of oxygen deficiency
- Form When Disseminated: Gas
- Required Defensive Gear: Protective Mask

Blister Agents (Vesicants)

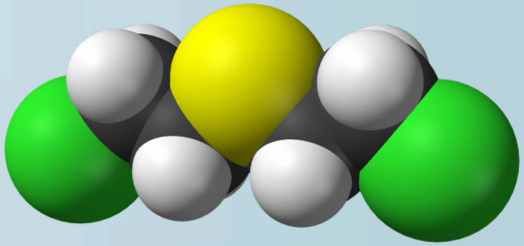


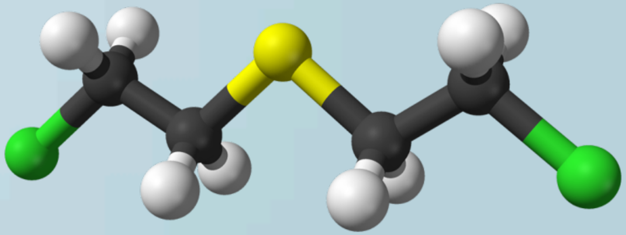
- **Sulfur mustard**, nitrogen mustard, phosgene oxime, Lewisite
- Mode of Action: Inhalation, Skin Contact
- Physiological Effects
  - Burns skin, mucous membranes, and eyes, causing large water blisters on exposed skin
  - Causes damage primarily to upper airways
  - Primarily used to cause medical casualties, but can be lethal when large amounts are inhaled
- Form When Disseminated: Liquid, Aerosol, Vapor, Dust
- Required Defensive Gear: Protective Mask & Clothing

Sulfur Mustard Gas, H or HD



- Although it was first made in the 19th century, it was developed by Haber and other German chemists to be used as a weapon.
- Called "mustard" because of its horseradish- or garlic-like smell.
- It is fat-soluble, so it dissolves in the oils in the skin, causing severe chemical burns and blisters.

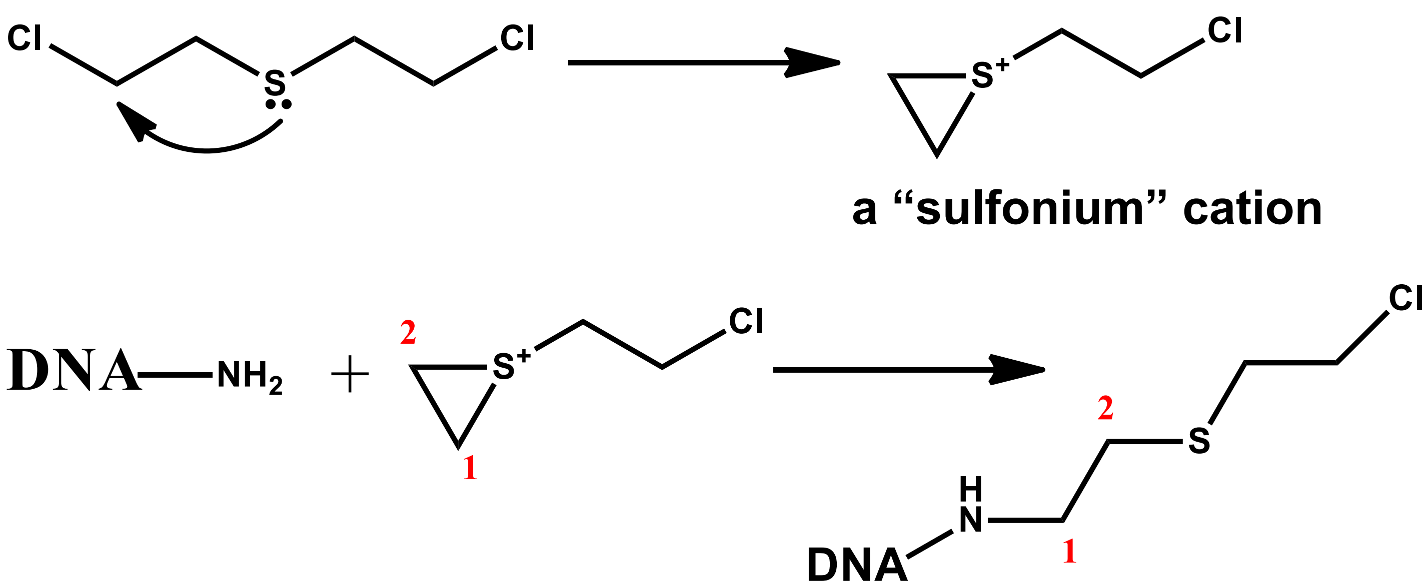




http://chemapps.stolaf.edu/jmol/jmol.php?model=ClCCSCCCl

Effect of Sulfur Mustard on DNA

Sulfur mustard forms a sulfonium ion, which attaches to the guanine nucleotide of DNA, disrupting cell division and function. This can lead to cellular death or cancer.

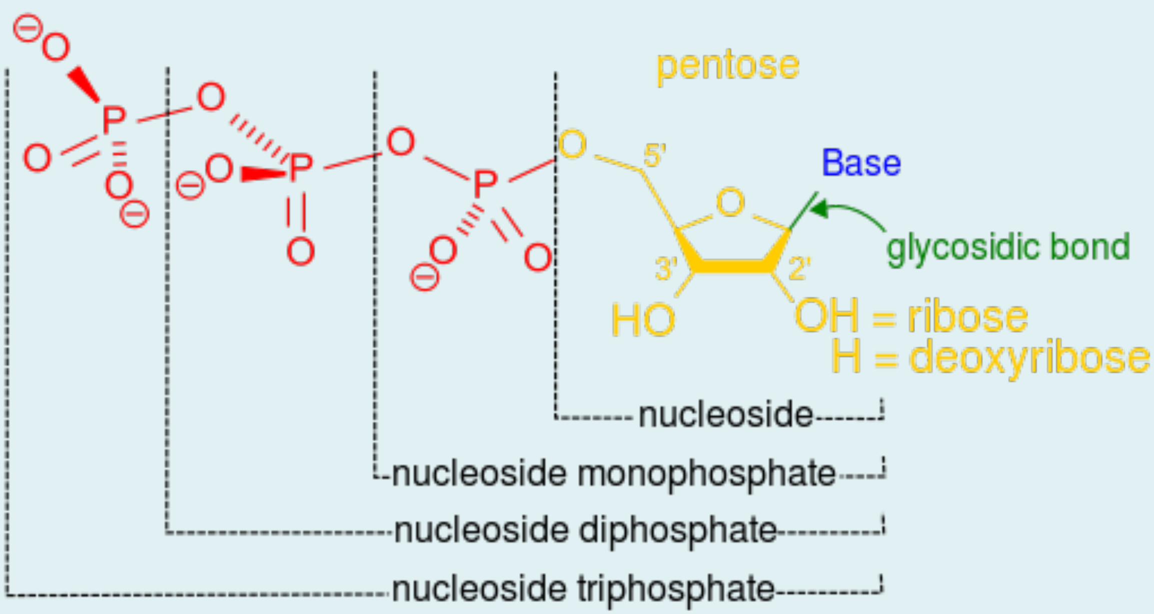


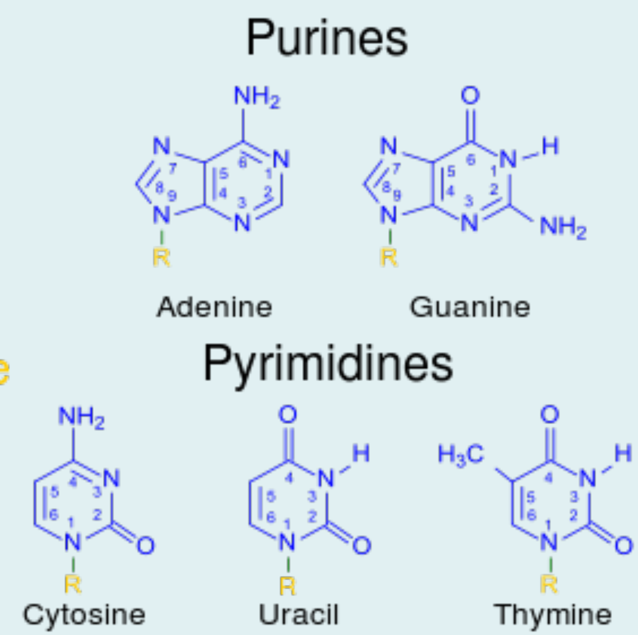
Nucleic Acids

- Encode and transmit genetic information.
- They include DNA (deoxyribonucleic acid) and RNA (ribonucleic acid).
- Nucleic acids were named for their initial discovery within the cell nucleus, and for the presence of phosphate groups (related to phosphoric acid).
- Found in all life forms.
- All living cells and organelles contain both DNA and RNA, while viruses contain either DNA or RNA, but usually not both.

Nucleotides

- Nucleic acids are polymers of repeating nucleotides, each of which contains a pentose sugar (ribose or deoxyribose), a phosphate group, and a nucleobase.

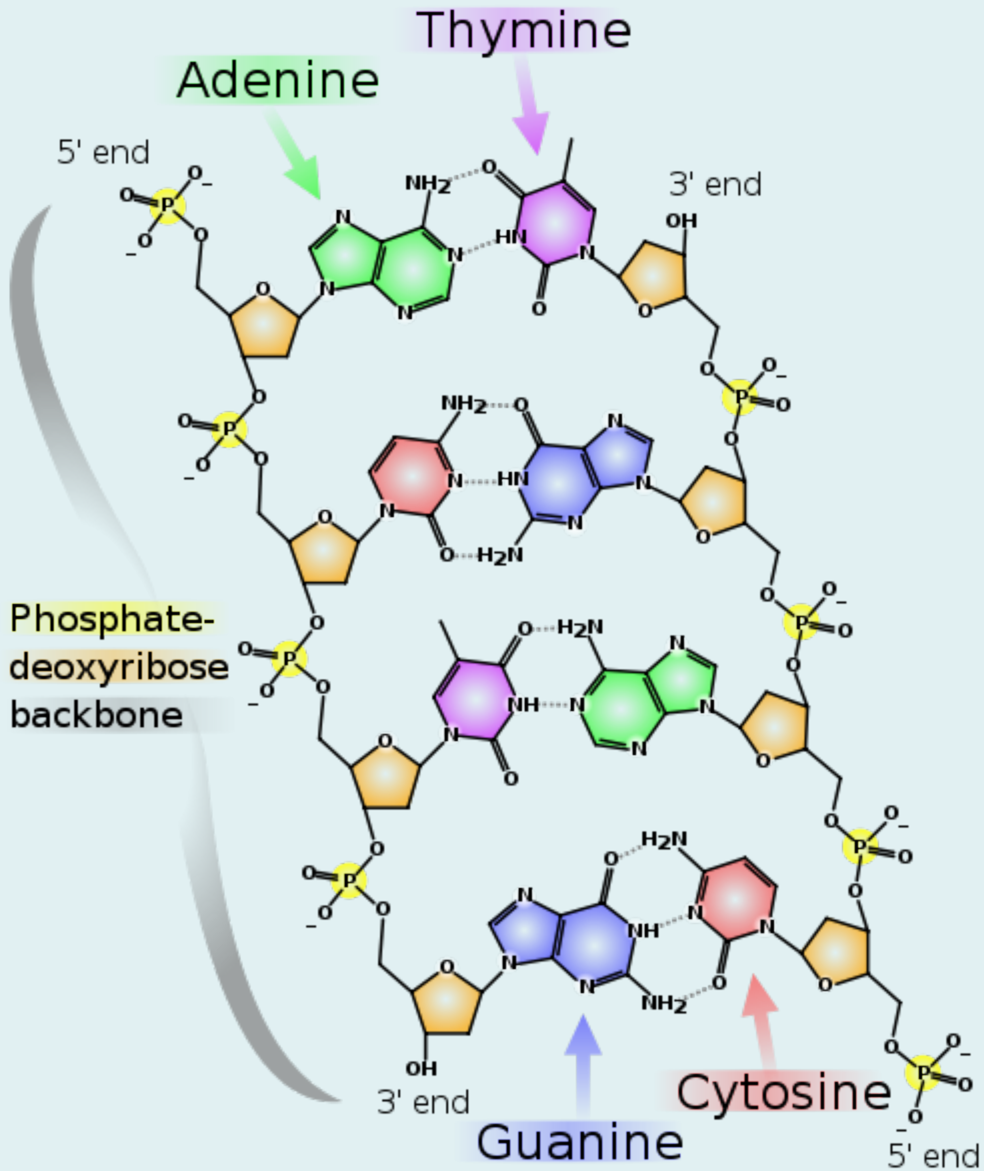




DNA, Deoxyribonucleic Acid

- **Deoxyribonucleic acid** (**DNA**) is a nucleic acid containing the genetic instructions used in the development and functioning of all known living organisms (with the exception of RNA viruses).
- The DNA segments carrying this genetic information are called genes.
- Double helix - two long polymers of repeating nucleotides.
- Backbones made of sugars and phosphate groups.
- Attached to each sugar is one of four types of molecules called nucleobases (informally called *bases*).
- Sequence of these four nucleobases encodes information and specifies the sequence of the amino acids linked together to form proteins.

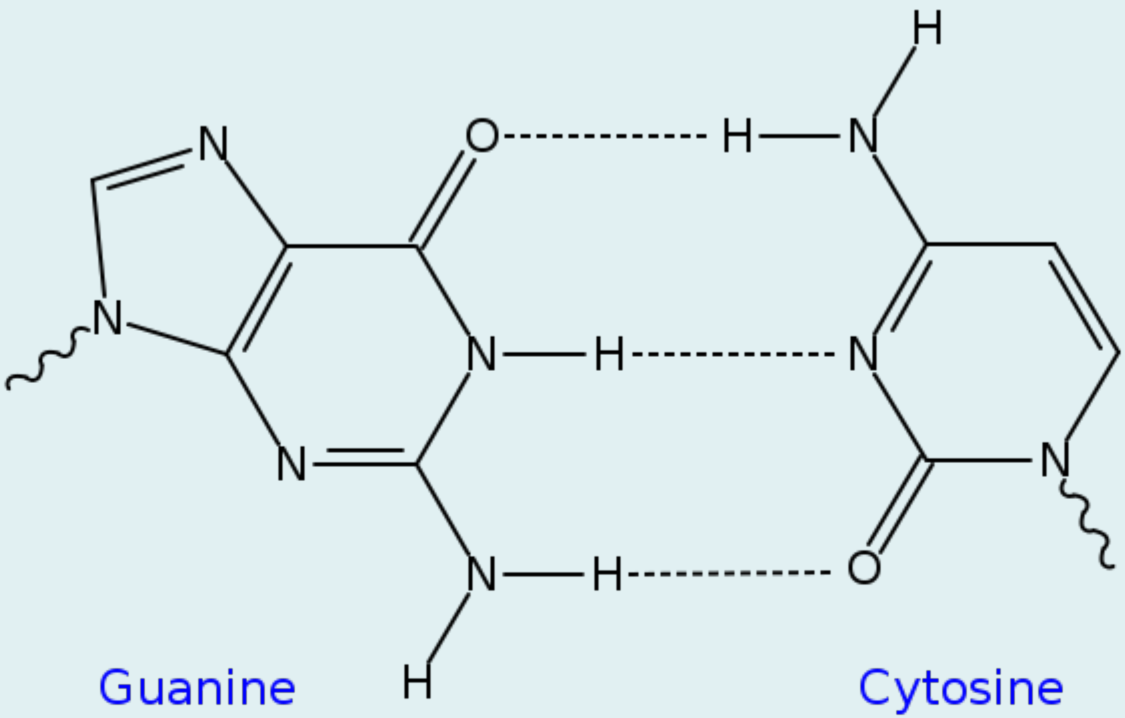
DNA



Thymine
Adenine
5' end
3' end
Phosphate-
deoxyribose
backbone
3' end
Cytosine
Guanine
5' end

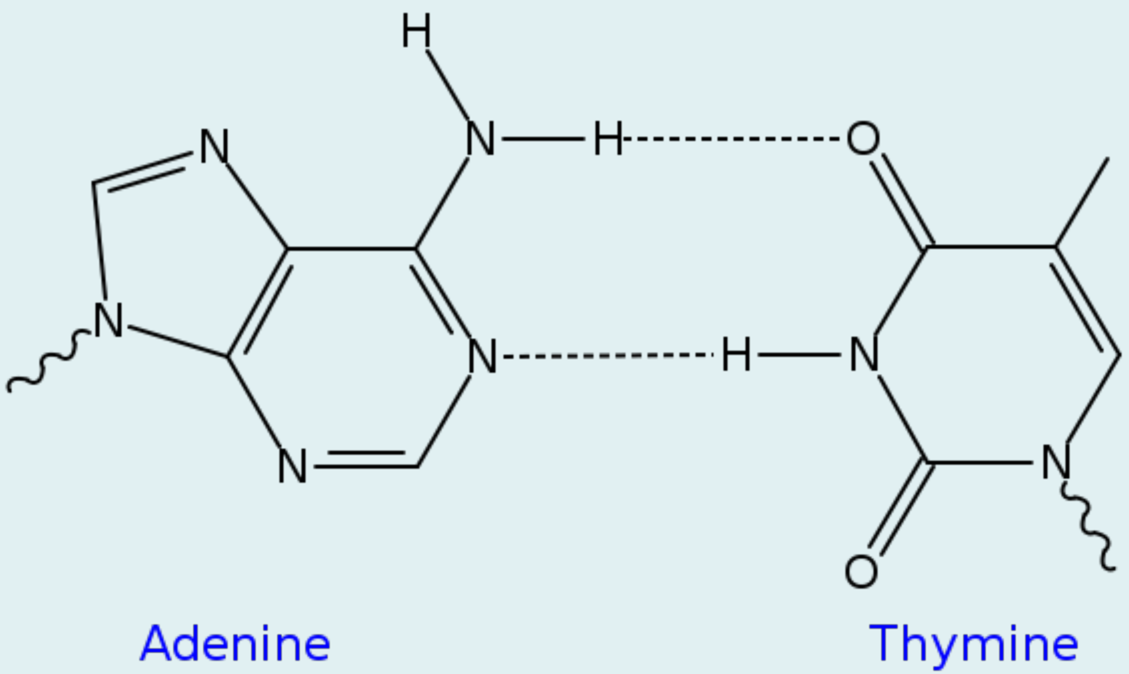
Base Pairing

- The guanine nucleobase links to the cytosine nucleobase by hydrogen bonds.

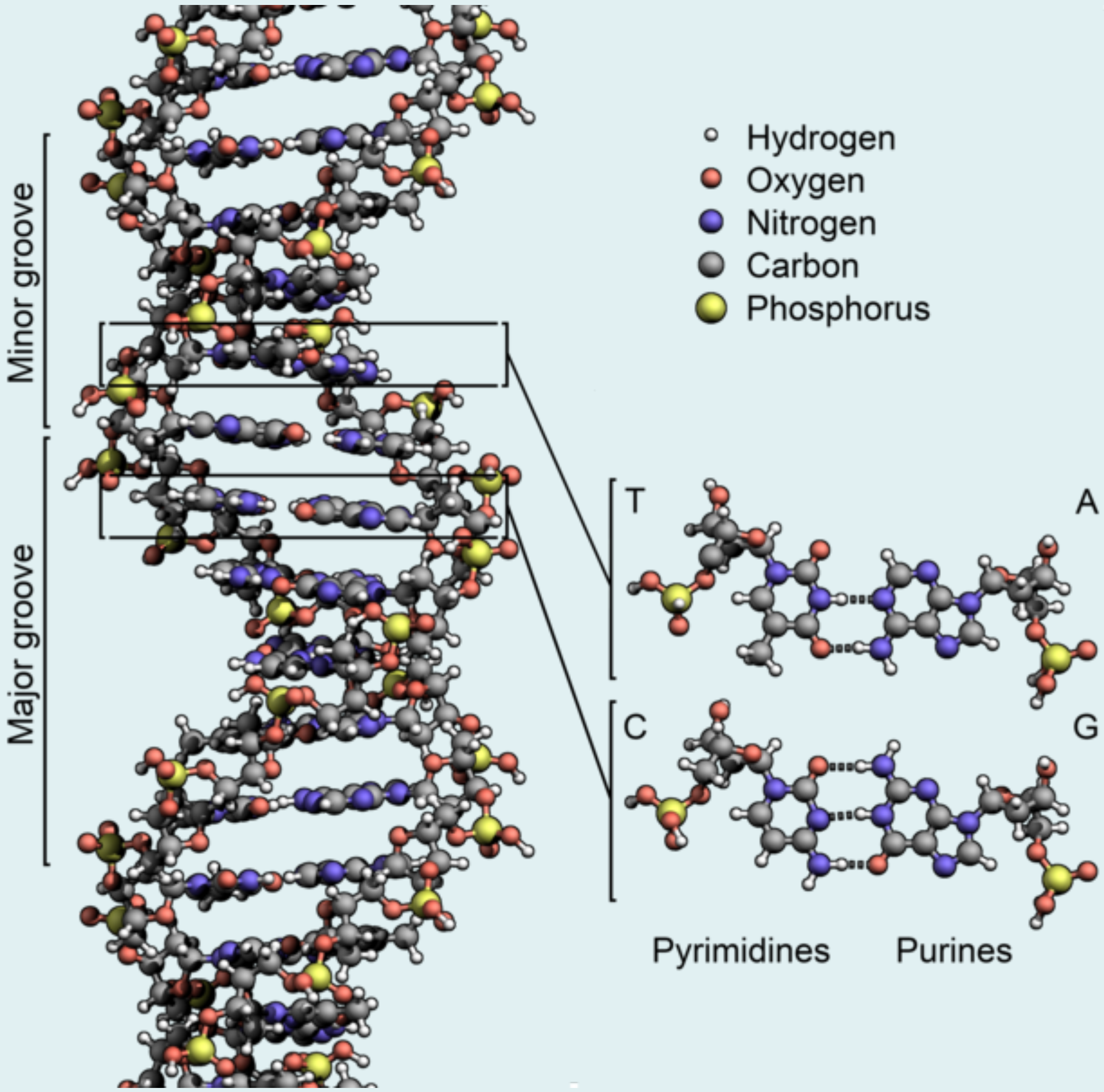


Base Pairing

- The adenine nucleobase links to the thymine nucleobase by hydrogen bonds.

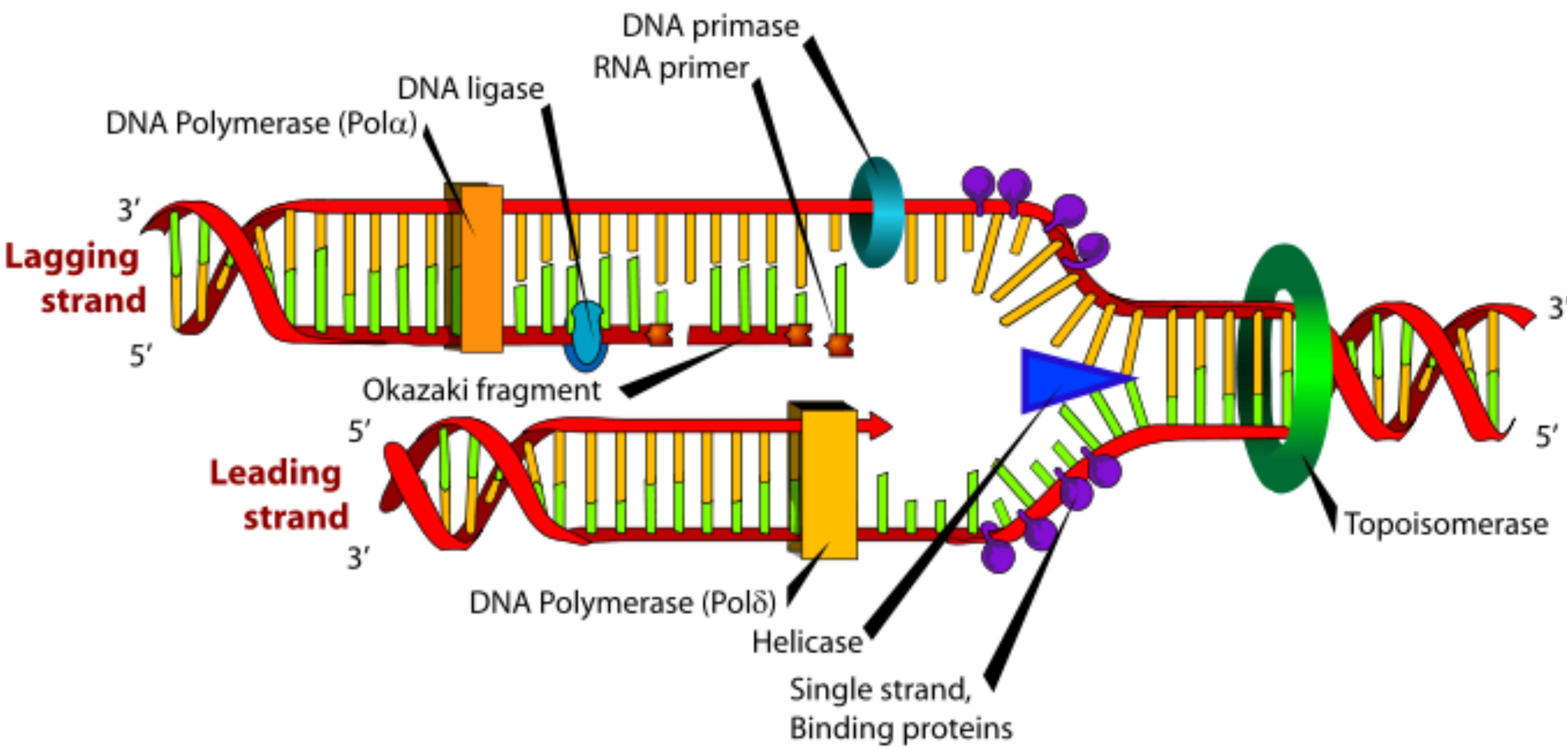


DNA Double Helix



DNA Replication

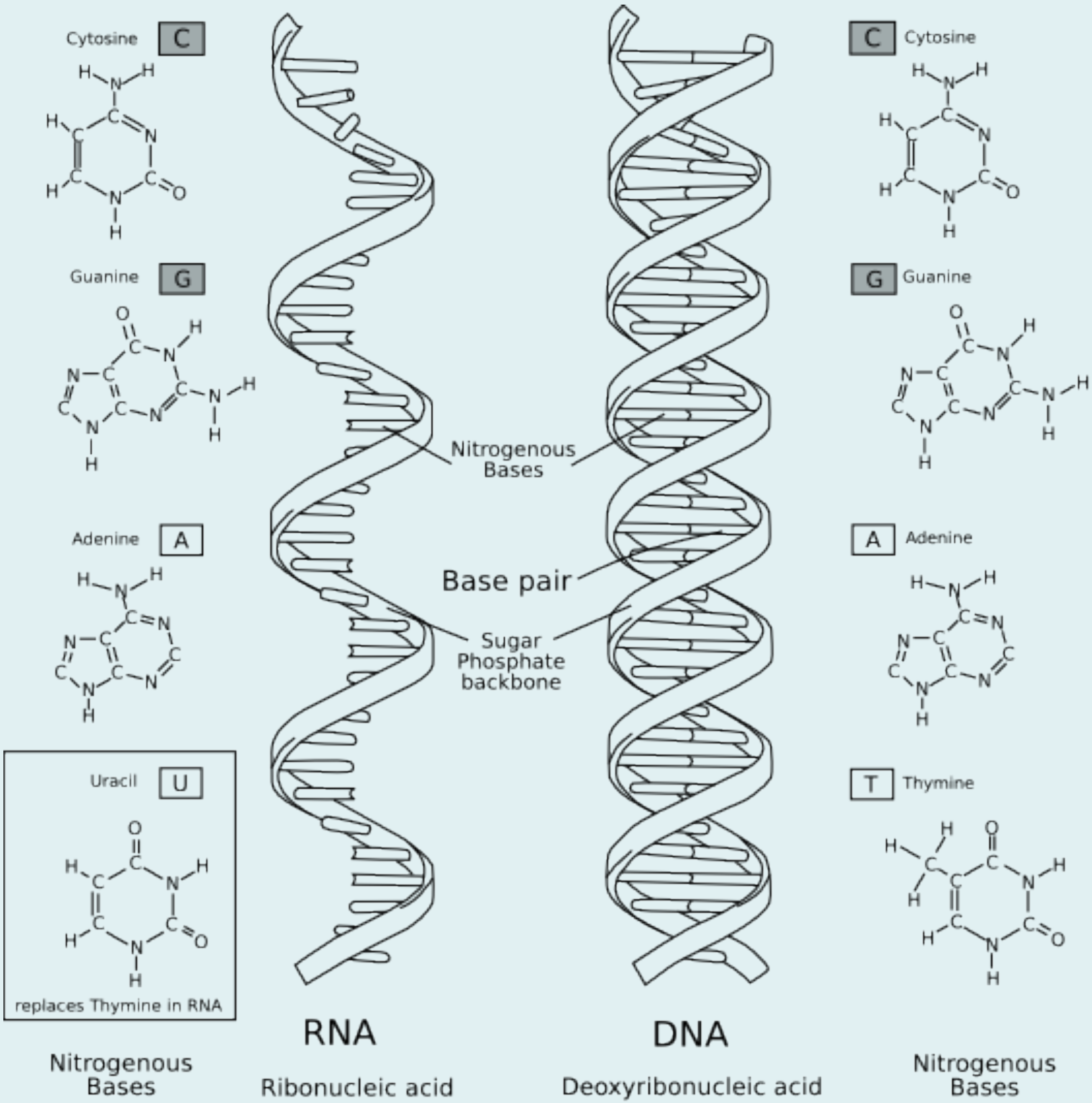
- One double-stranded DNA molecule produces two identical copies of the molecule.
- Occurs in all living organisms
- Basis for biological inheritance.



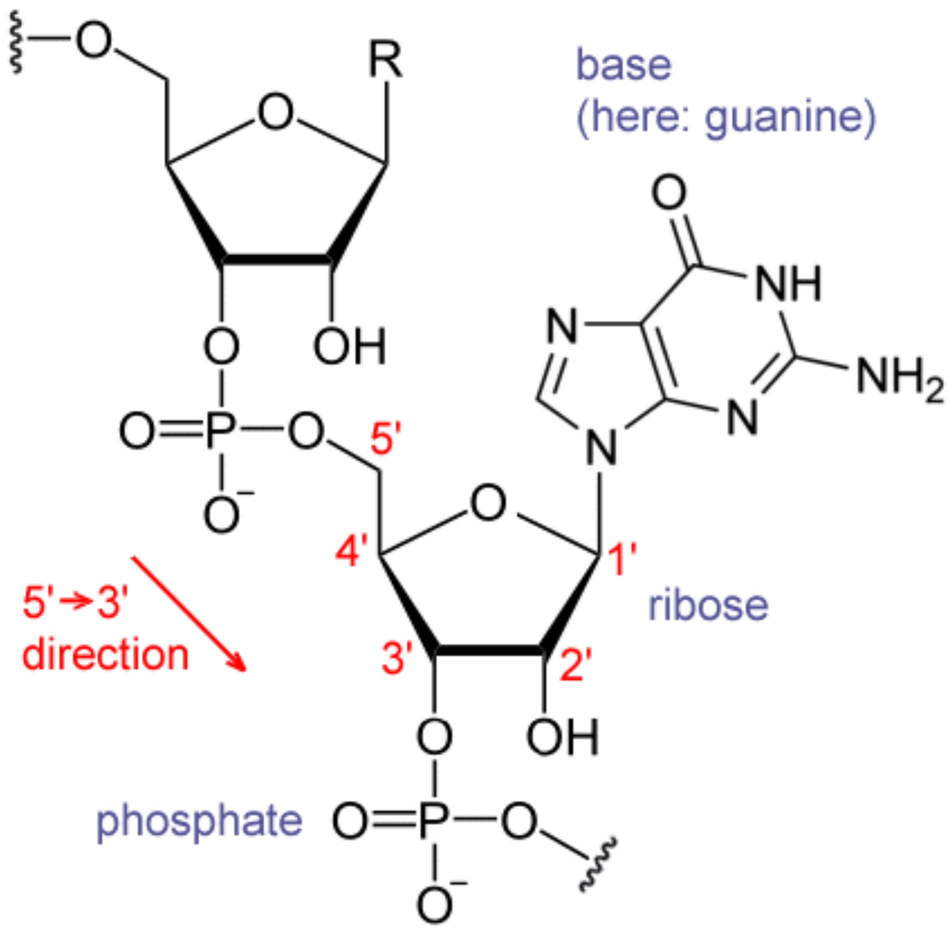
RNA, Ribonucleic Acid

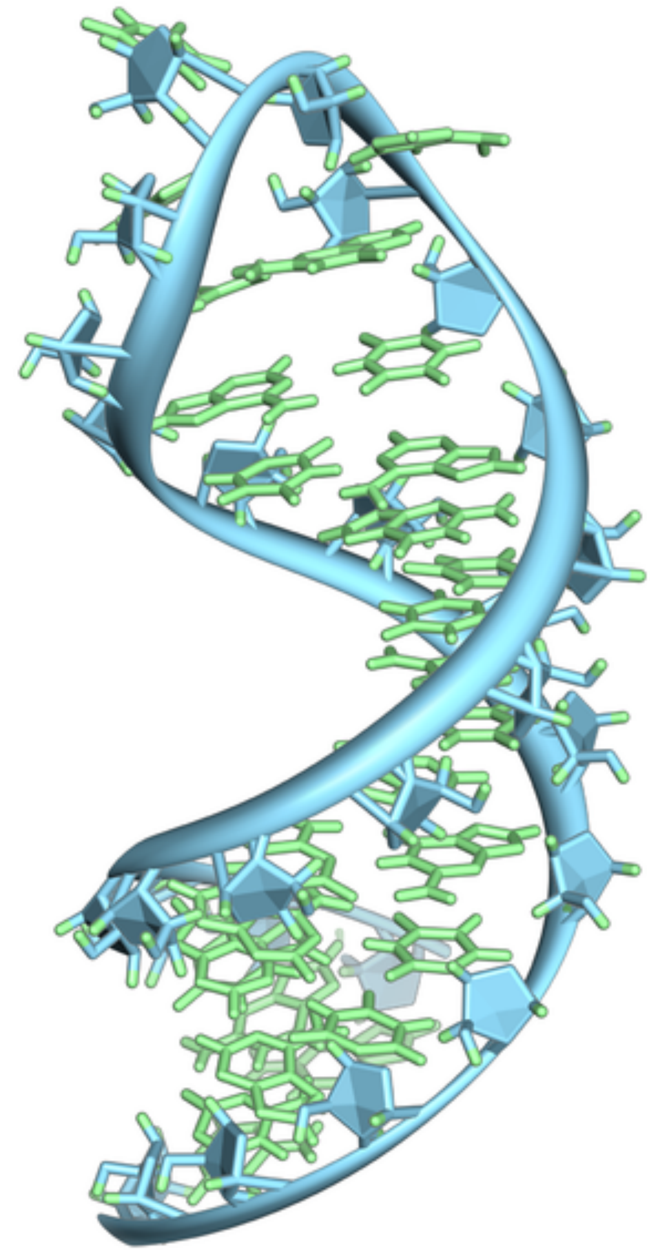
- All cellular organisms use messenger RNA (mRNA) to carry the genetic information that directs the synthesis of proteins.
- Many viruses use RNA instead of DNA as their genetic material.
- Transfer RNA (tRNA) molecules to deliver amino acids to the ribosome, where ribosomal RNA (rRNA) links amino acids together to form proteins.
- Differences from DNA
    - RNA contains the sugar *ribose*, while DNA contains the slightly different sugar *deoxyribose* (a type of ribose that lacks one oxygen atom)
    - RNA has the nucleobase uracil while DNA contains thymine.
    - Unlike DNA, most RNA molecules are single-stranded and can adopt very complex three-dimensional structures.

DNA and RNA


Cytosine
C
Guanine
G
Adenine
A
Uracil
U
replaces Thymine in RNA
Nitrogenous Bases
RNA
Ribonucleic acid
Nitrogenous Bases
Base pair
Sugar Phosphate backbone
DNA
Deoxyribonucleic acid
Cytosine
C
Guanine
G
Adenine
A
Thymine
T
Nitrogenous Bases

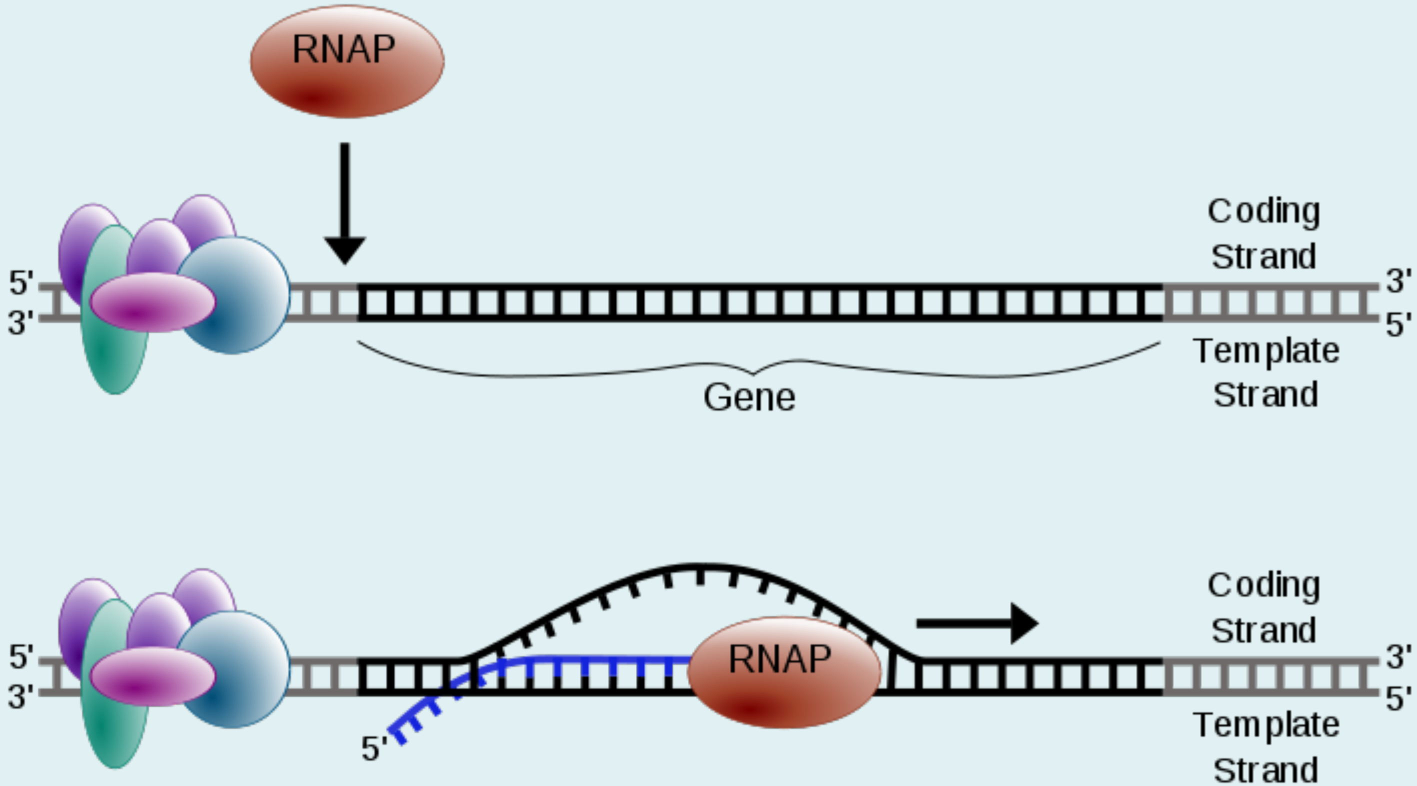
RNA



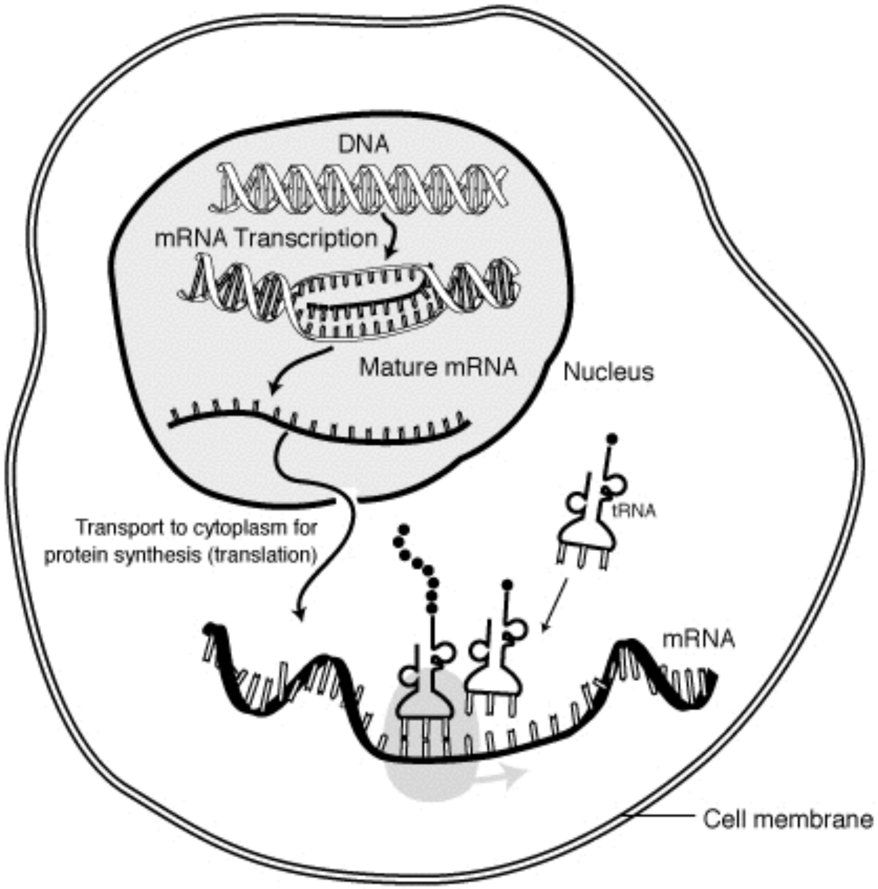


DNA to mRNA Transcription

- **Transcription** is the process of creating a complementary RNA copy of a sequence of DNA. (RNAP = RNA polymerase)



Protein Synthesis



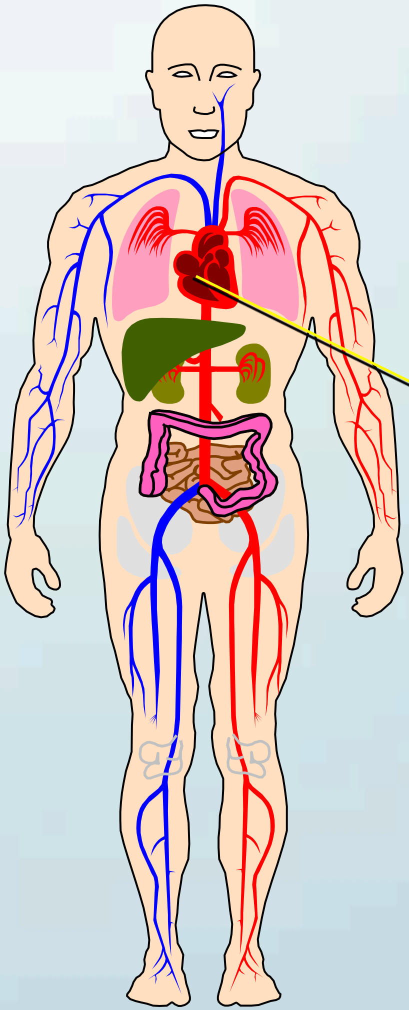
Genetic Engineering

- **Genetic engineering**, also called **genetic modification**, is the direct manipulation of an organism's genome.
- Introduction of foreign DNA or synthetic genes into the organism of interest.
- **Recombinant DNA** (rDNA) molecules are DNA sequences that result from bringing together genetic material from multiple sources, creating sequences that would not otherwise be found in biological organisms.
- It's possible because DNA molecules from all organisms share the same chemical structure; they differ only in the sequence of nucleotides.
- The foreign DNA is replicated along with the host DNA.

Genetic Engineering

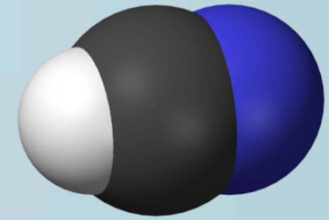
- The first organisms genetically engineered were bacteria in 1973 and then mice in 1974. Insulin-producing bacteria were commercialized in 1982 and genetically modified food has been sold since 1994.
- Uses
  - Medicines such as insulin and human growth hormone are now produced in bacteria.
  - Insect resistant and/or herbicide tolerant crops have been commercialized.
  - Genetically engineered plants and animals capable of producing biotechnology drugs more cheaply than current methods (called *pharming*) are being developed.

Blood Agents



- **Hydrogen cyanide**, cyanogen chloride, and arsine
- Mode of Action: Inhalation
- Physiological Effects of Cyanide
  - Destroys ability of tissues to utilize oxygen
- Form When Disseminated: Gas
- Required Defensive Gear: Protective Mask

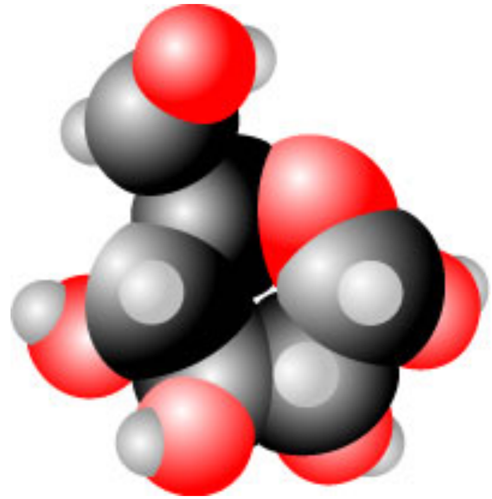
Hydrogen Cyanide, HCN

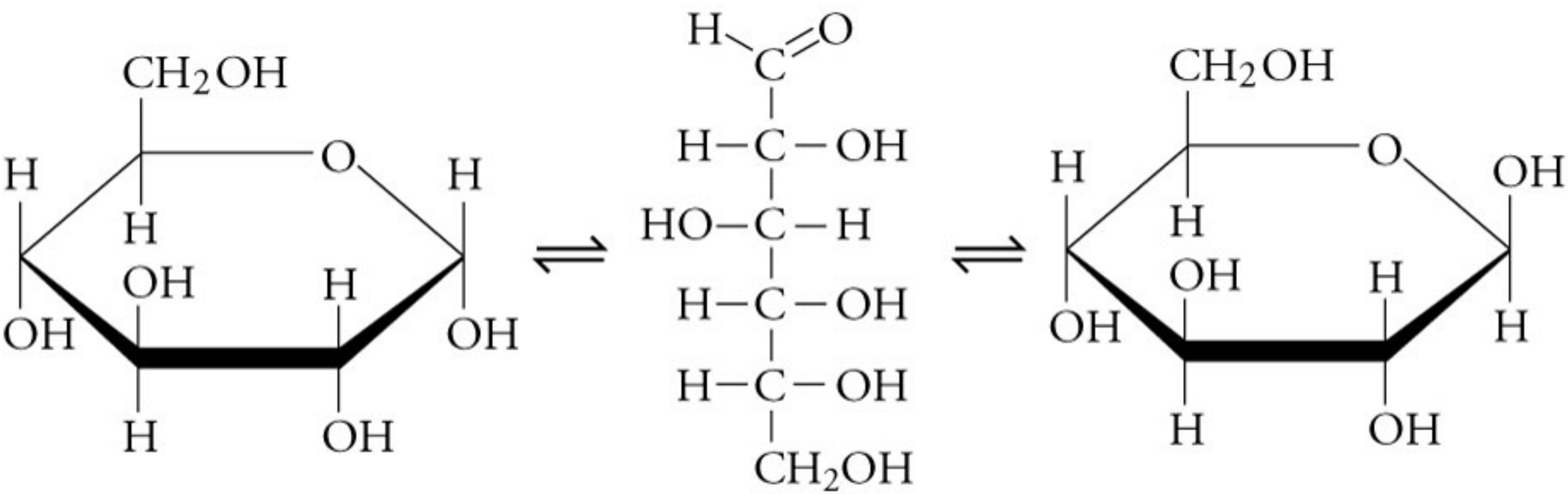


- Volatile liquid – boiling point 26 °C (79 °F)
- Used in industry to make many important chemicals
- Fatal at concentrations as low as 300 mg/m^3 in air.
- Schedule 3, Part A of the CWC
- Disrupts cellular respiration (the conversion of nutrients and oxygen into carbon dioxide, water, and energy) by inhibiting an enzyme (cytochrome oxidase) in mitochondria.
- Leads to dizziness, vomiting, loss of consciousness, and death
- Most made from the following reaction at 1200 °C over a platinum catalyst.

$$2CH_4 + 2NH_3 + 3O_2 \rightarrow 2HCN + 6H_2O$$

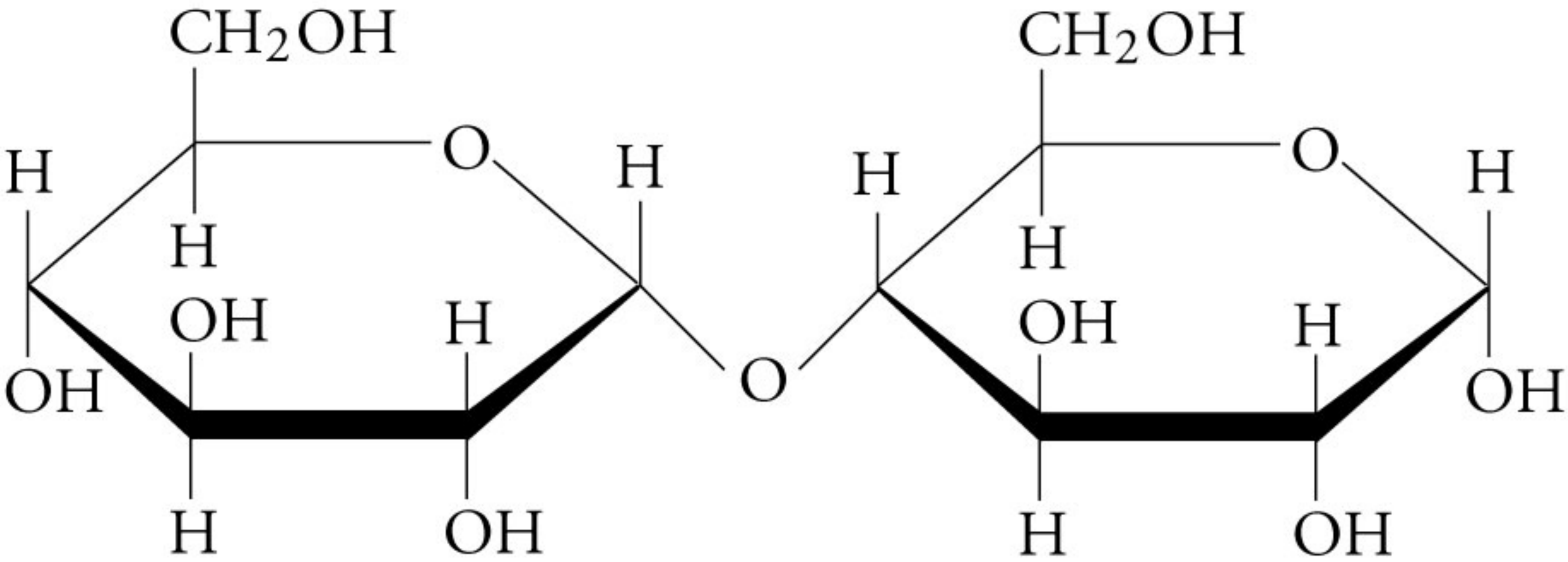
Glucose





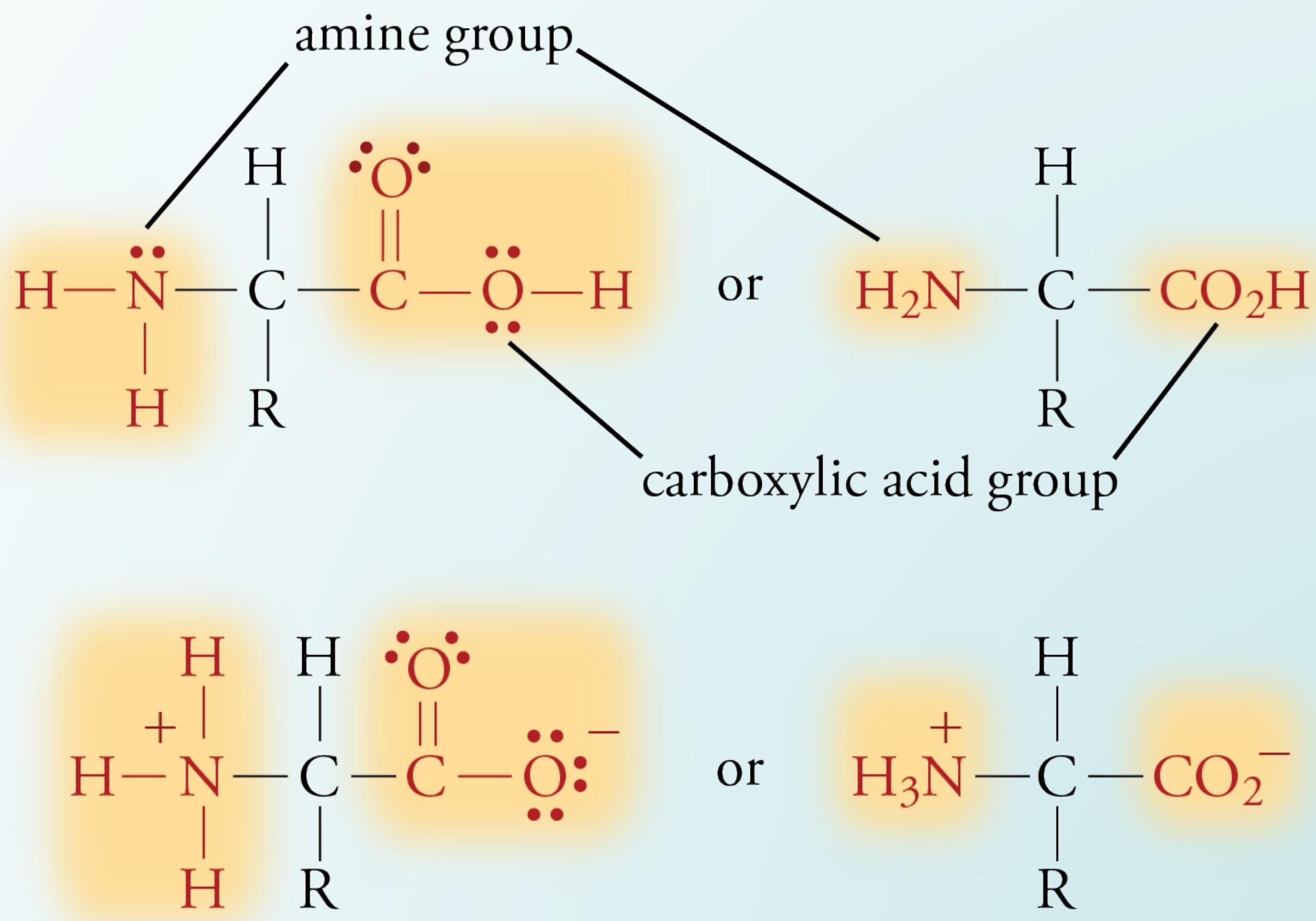
glucose

Maltose

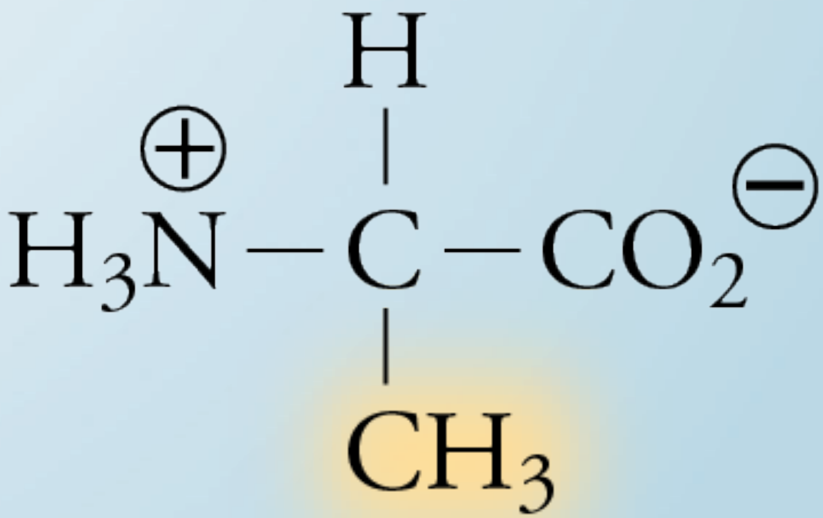


Maltose (glucose and glucose)

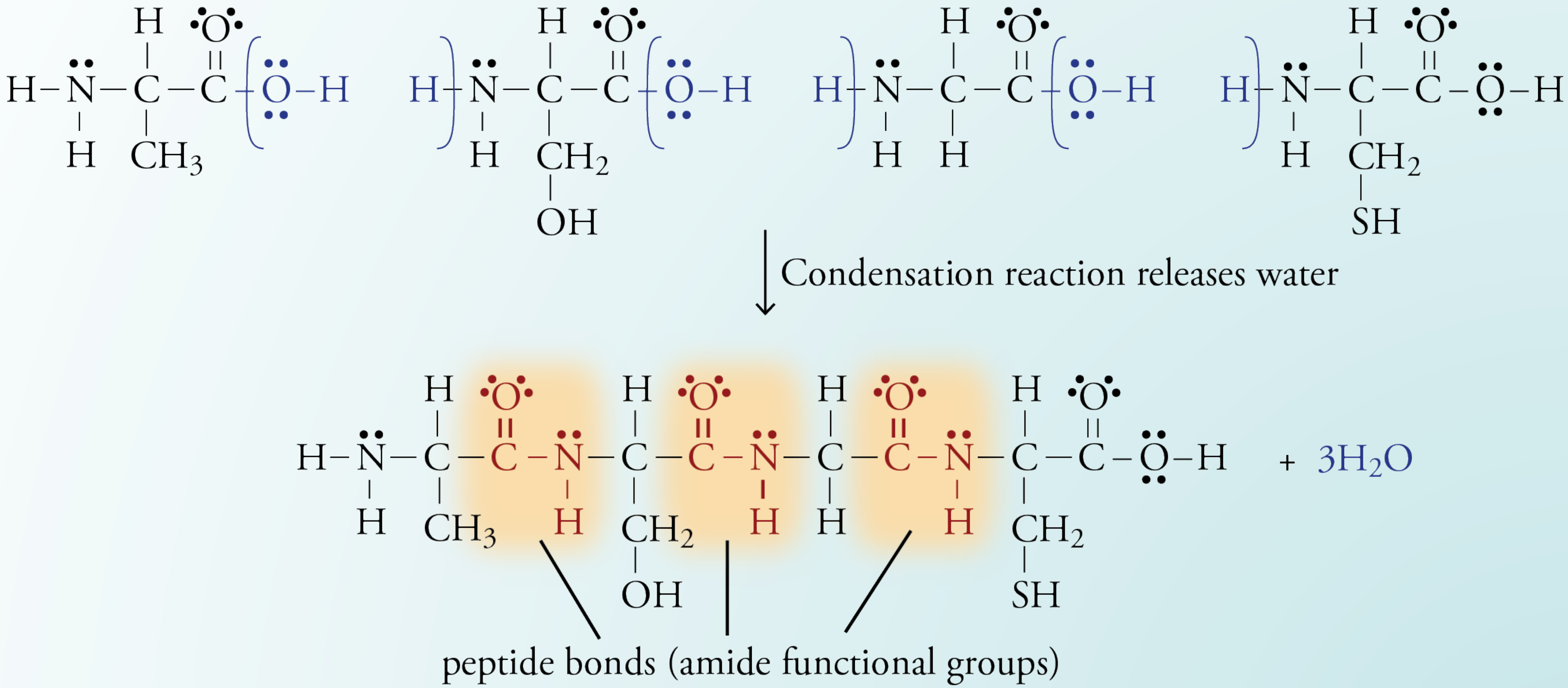
Amino Acids



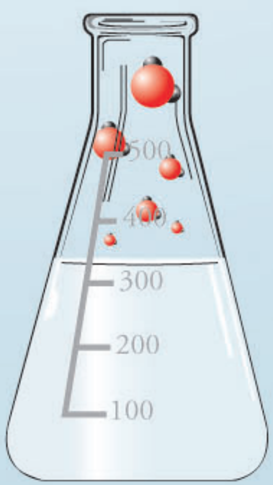
Alanine

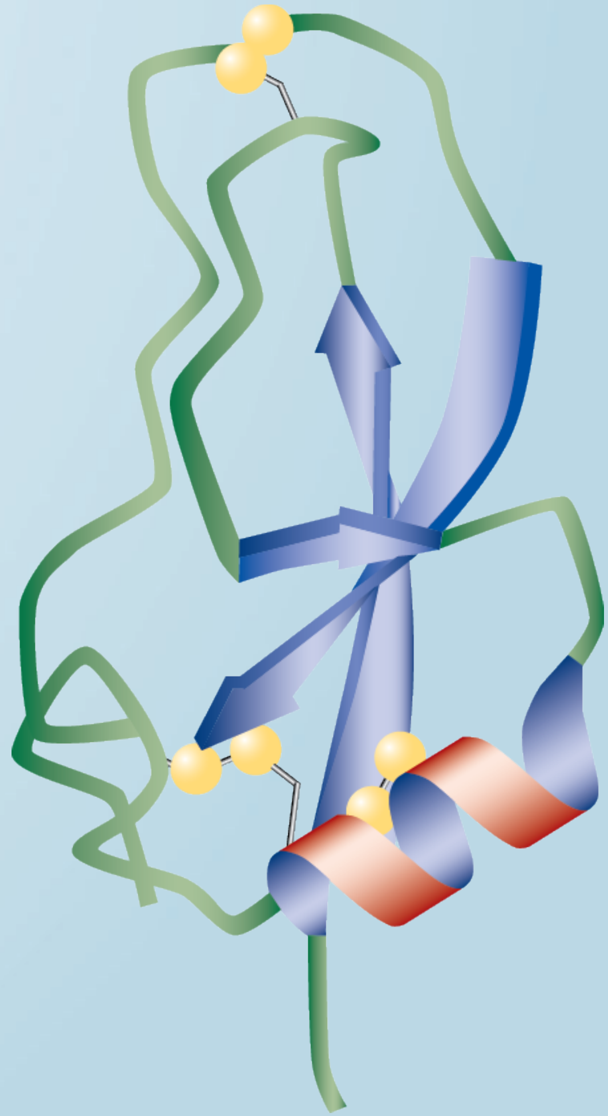


Formation of Ala-Ser-Gly-Cys



Protein - Bovine Pancreatic Trypsin Inhibitor (BPTI)



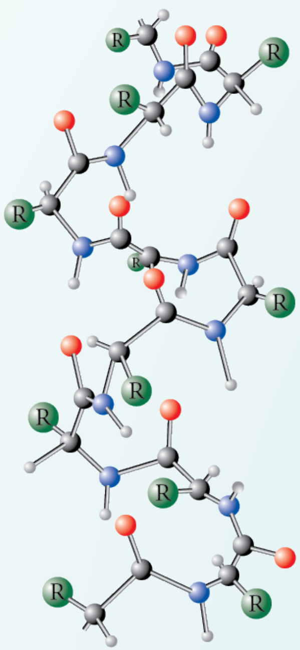


Primary and Secondary Protein Structures

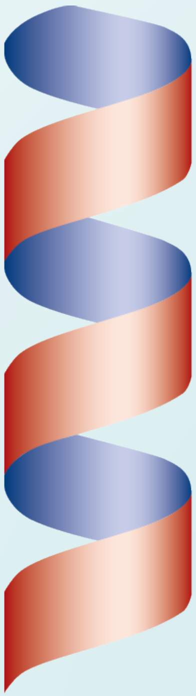
- ***Primary Structure*** = the sequence of amino acids in the protein
- The arrangement of atoms that are close to each other in the polypeptide chain is called the ***secondary structure*** of protein.
  - Three types
    - α-helix
    - β-sheet
    - irregular

α-helix - Secondary Structure

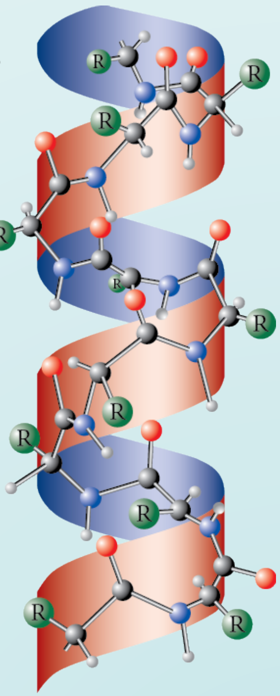
Ball-and-stick model of a portion of the α-helical secondary structure of a protein molecule



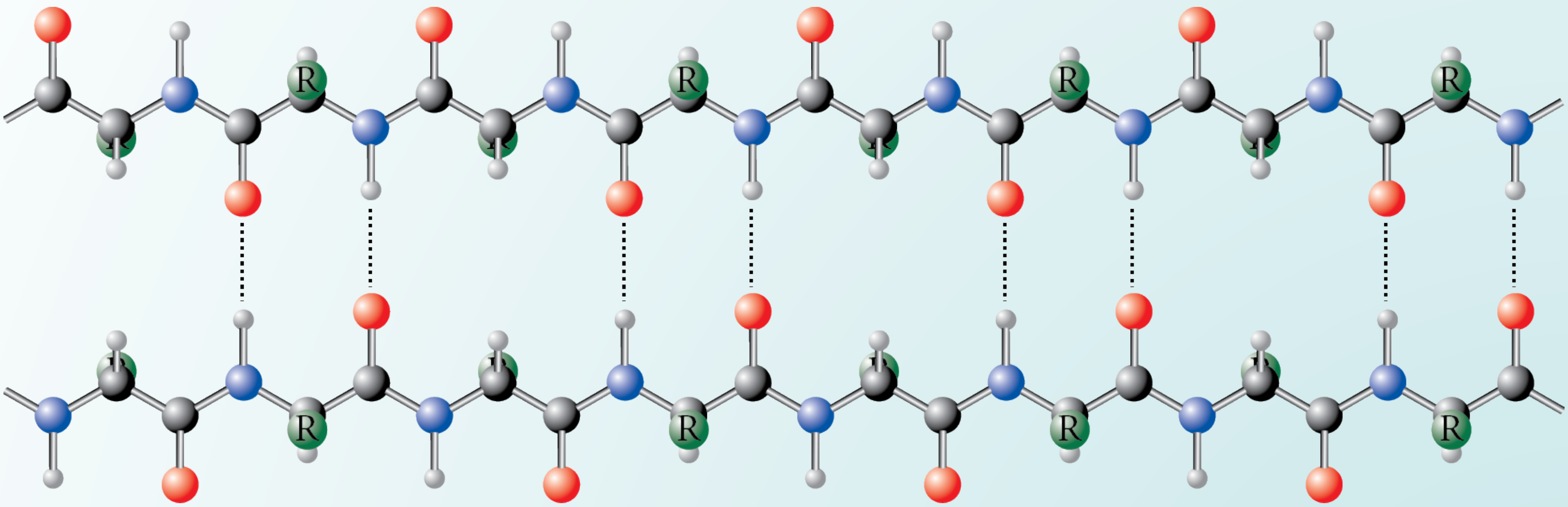
This ribbon model shows the general arrangement of atoms in a portion of the α-helical secondary structure of a protein molecule.



The two models superimposed



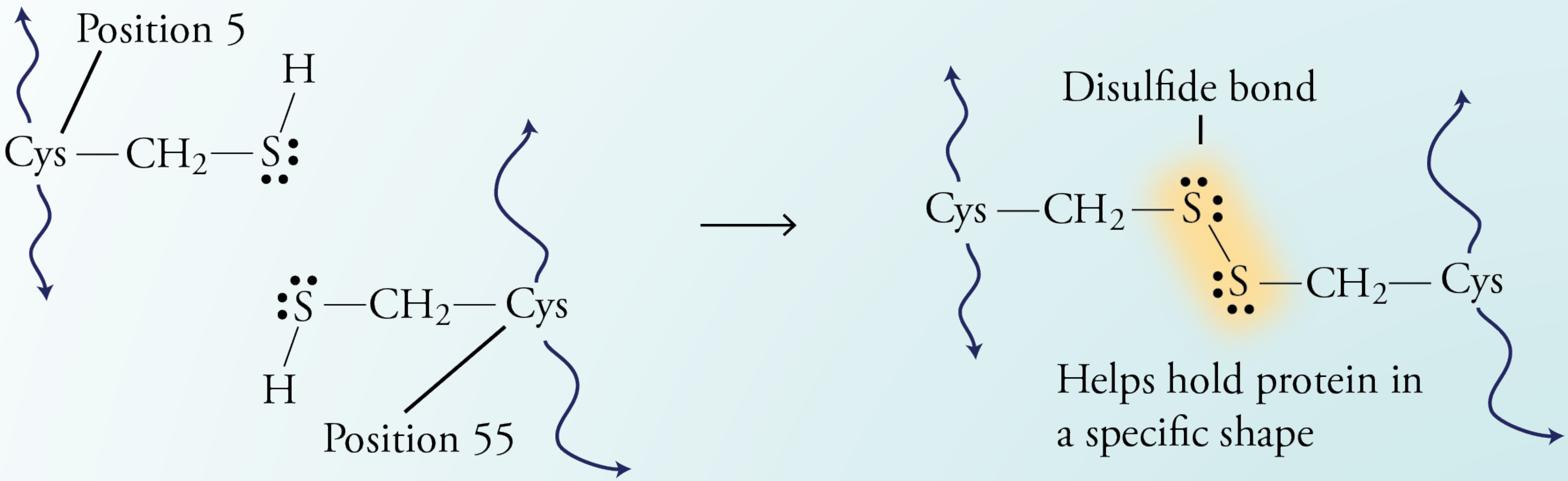
β-Sheet Secondary Structure



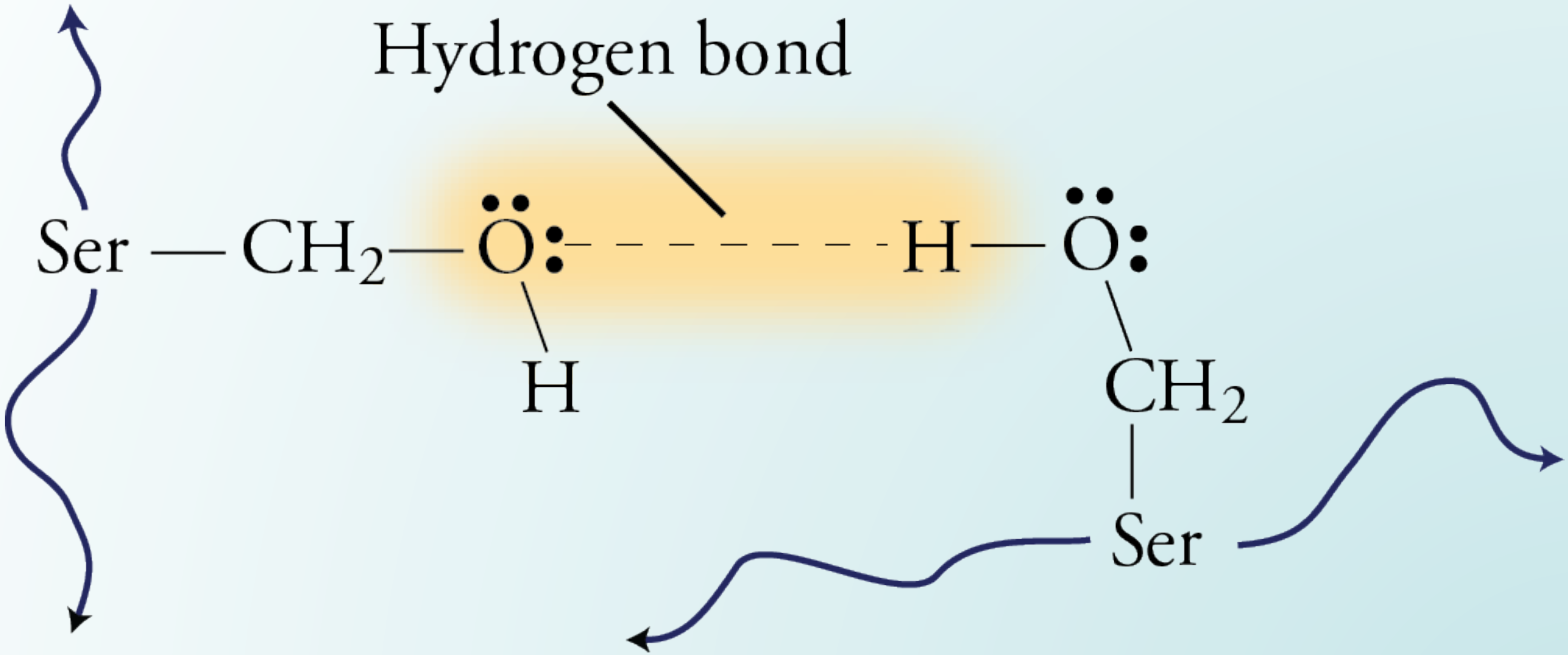
Tertiary Protein Structure

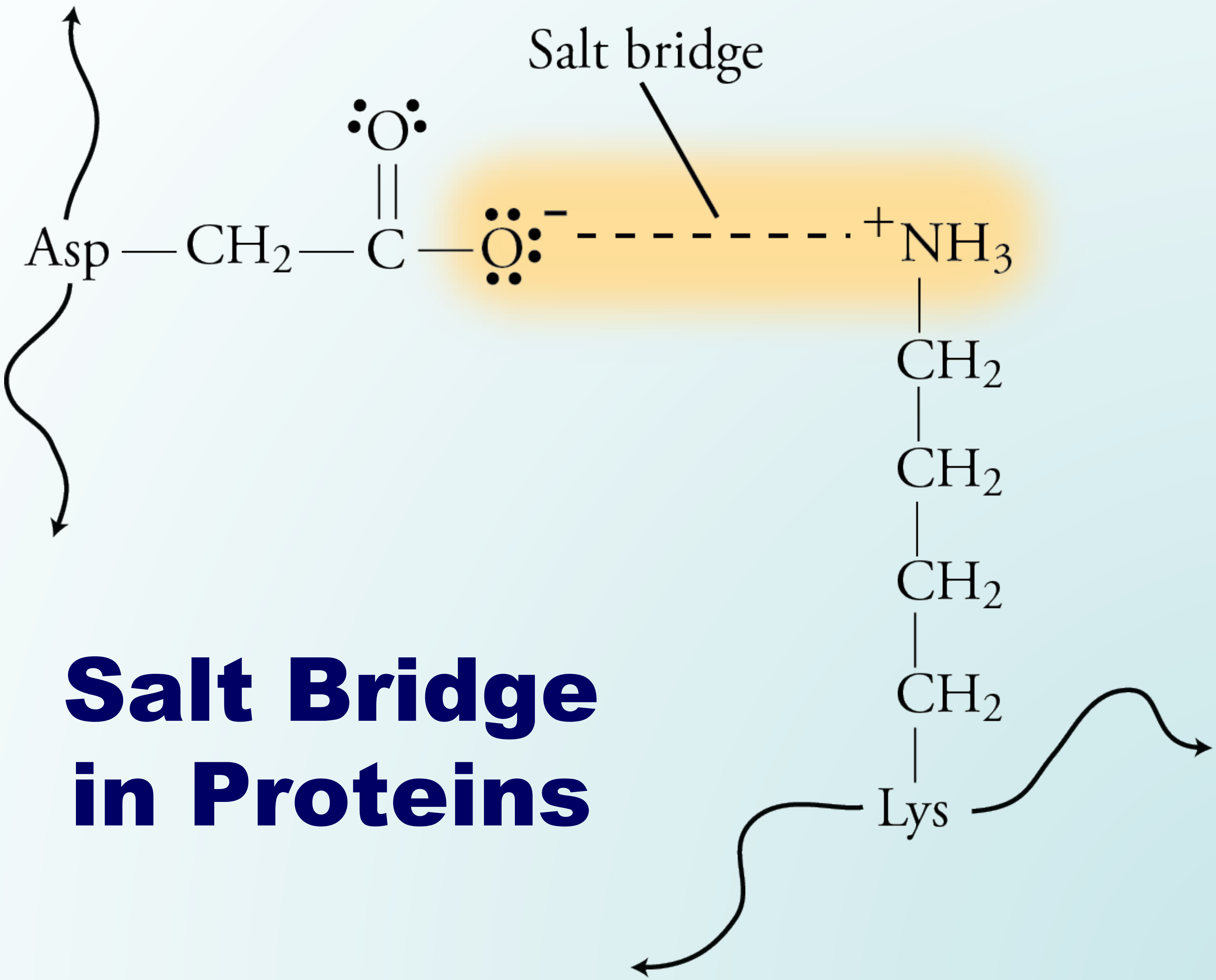
- The very specific overall shape of the protein called its ***tertiary structure***.
- The protein chain is held in its tertiary structure by interactions between the side chains of its amino acids.
  - Disulfide bonds
  - Hydrogen bonds
  - Salt bridges

Disulfide Bonds in Proteins



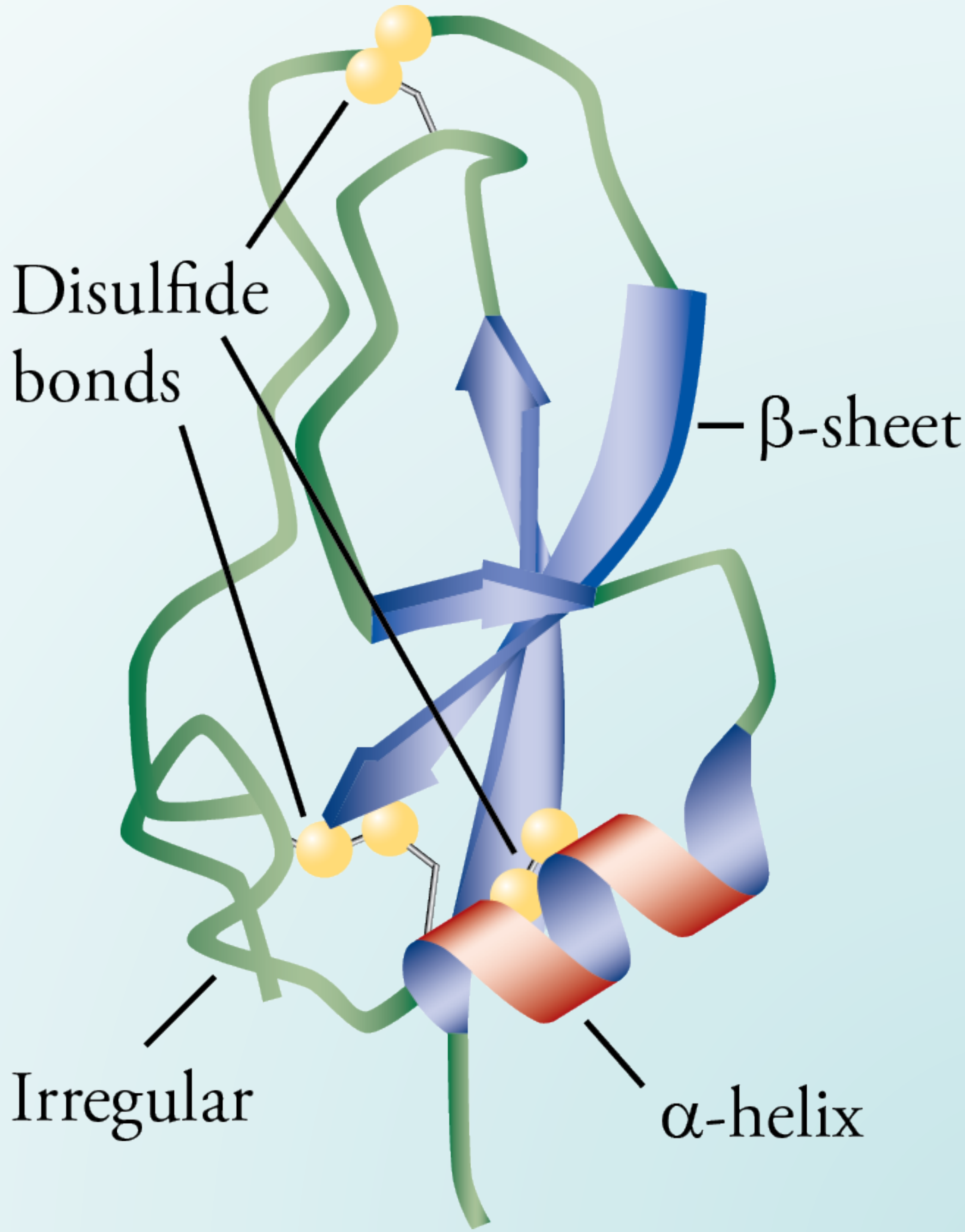
Hydrogen Bonding in Proteins



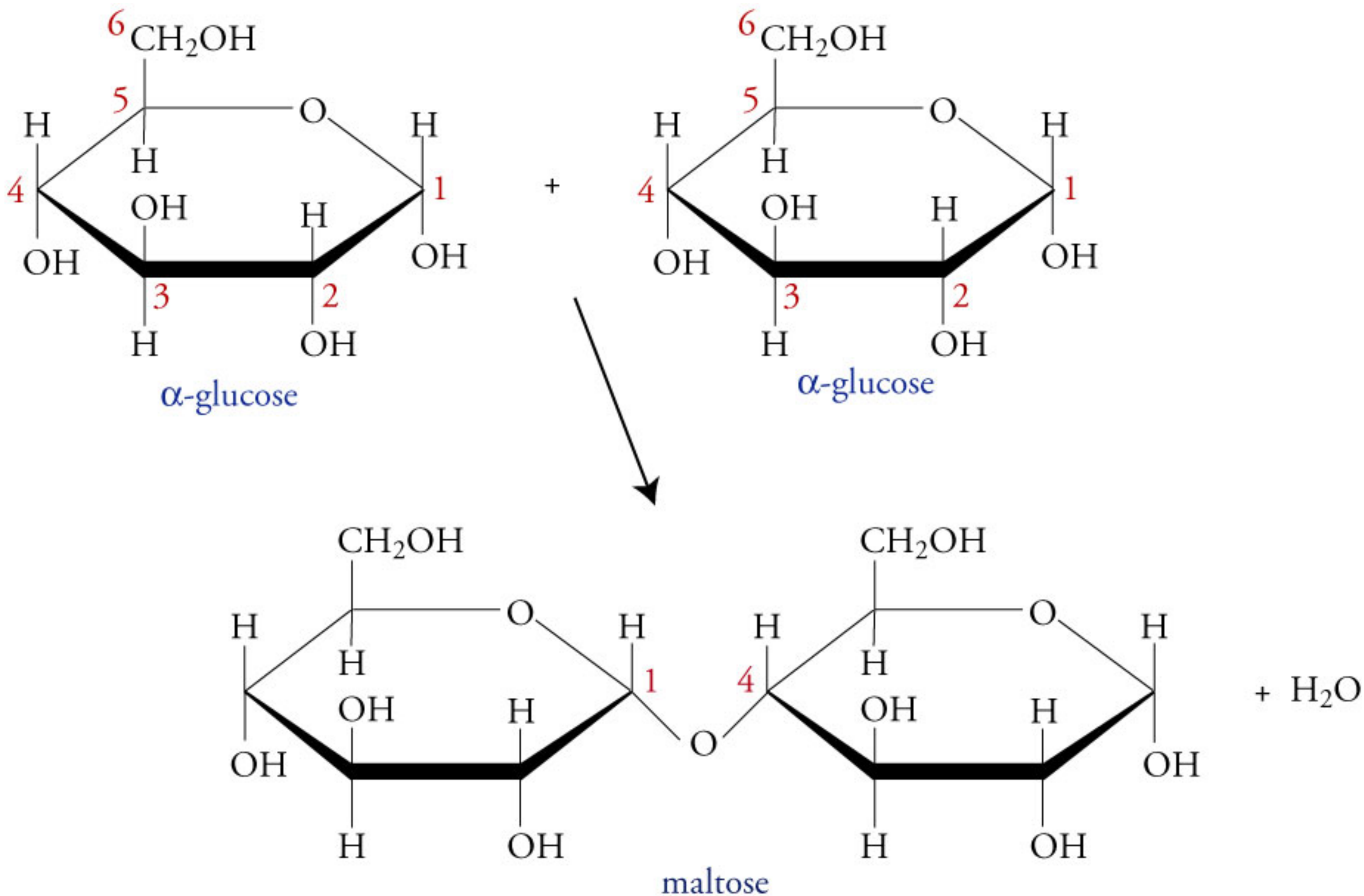


Salt Bridge in Proteins

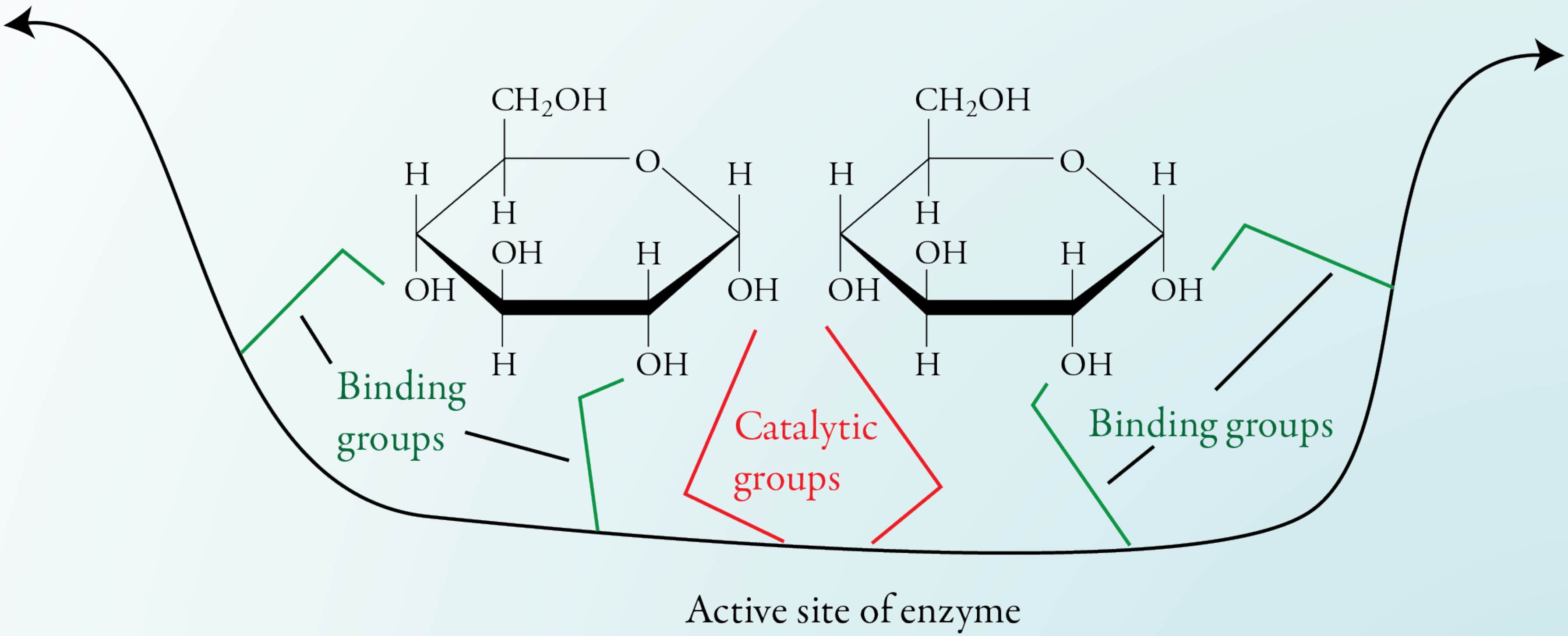
The Ribbon Structure of the Protein BPTI



The Formation of Maltose

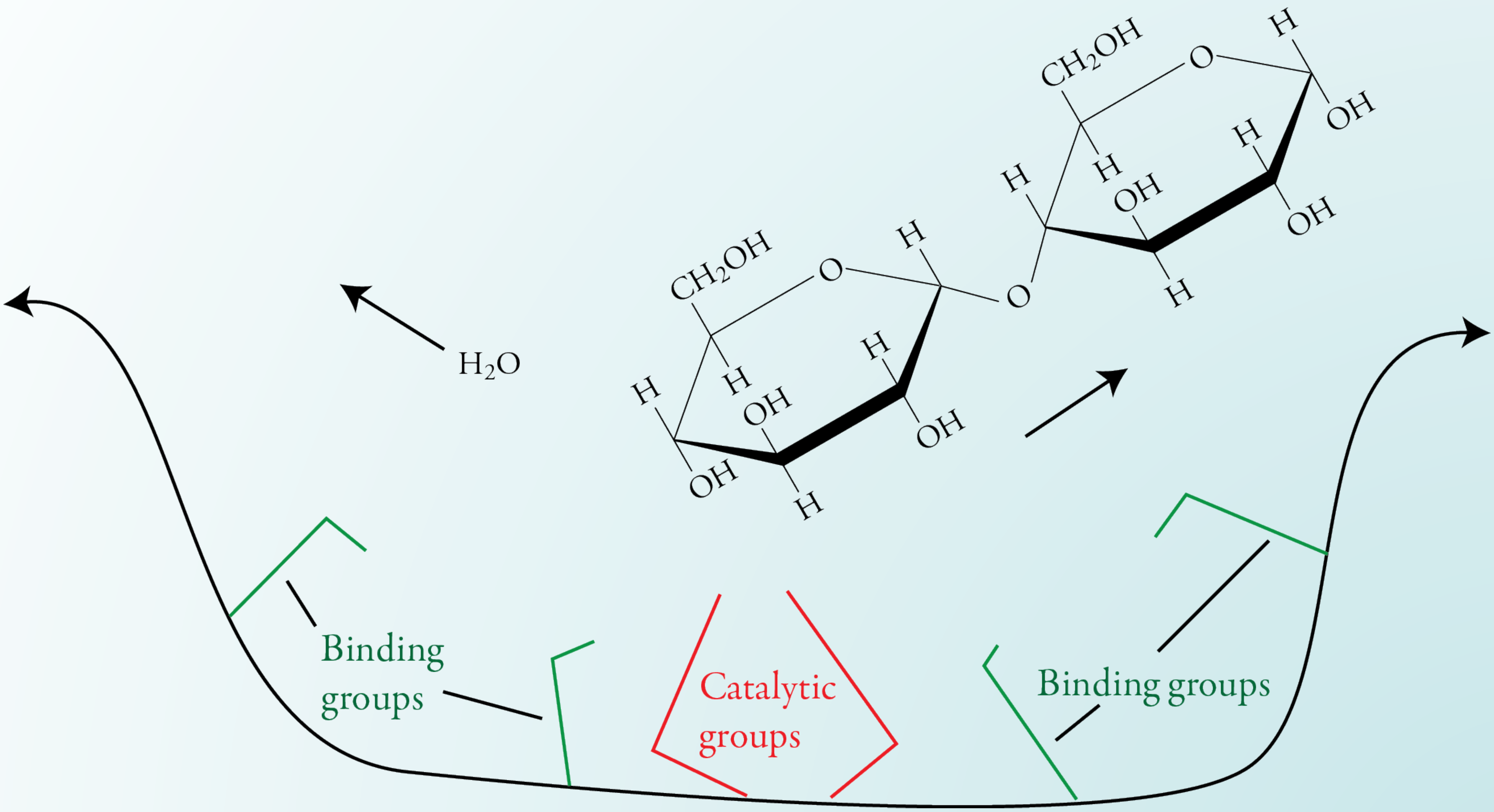


Maltose



CH2OH
O
H
H
OH
H
OH
OH
H
OH
CH2OH
O
H
H
OH
H
OH
OH
H
OH
Binding groups
Catalytic groups
Binding groups
Active site of enzyme

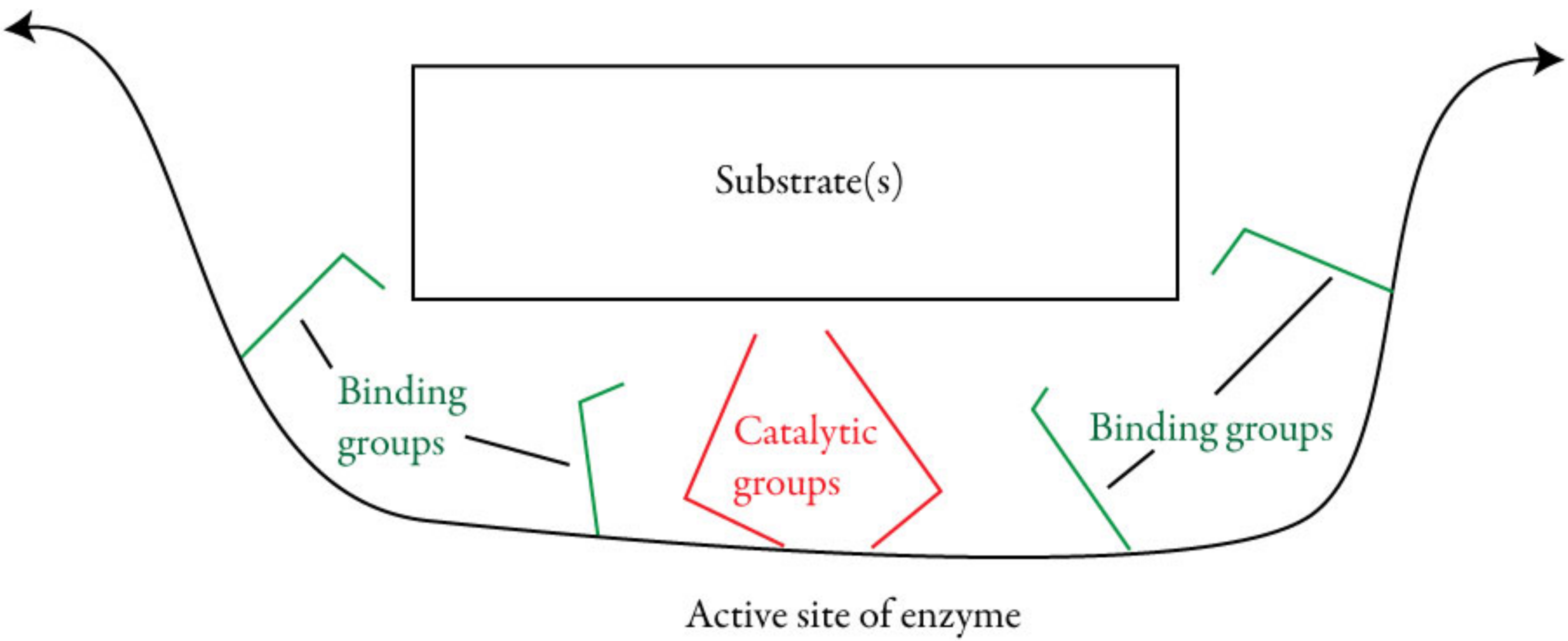
Maltose



CH$_2$OH
O
H
OH
H
H
OH
OH
H
OH
CH$_2$OH
O
H
O
H
H
OH
H
H
OH
OH
H
H_2O
Binding groups
Catalytic groups
Binding groups

Enzymes

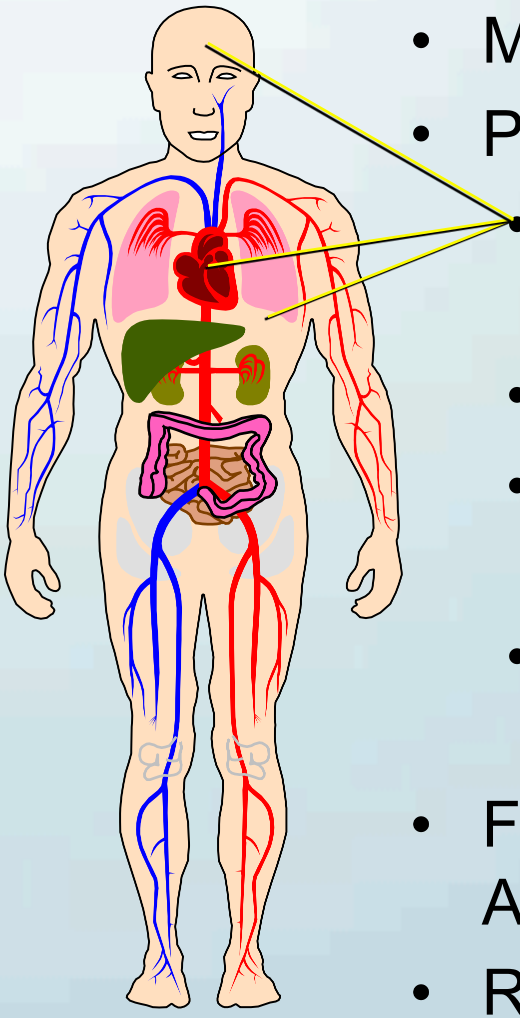
- ***Enzymes*** are naturally occurring catalysts, primarily composed of protein. ***Catalysts*** speed chemical changes without being permanently altered themselves.
- The chemicals that they act on are called ***substrates***.



Enzymes

- Very specific due to
  - Substrate shape – "Lock and Key"
  - Positions of binding groups, which attract substrates to the active site.
  - Positions of the catalytic groups that speed the reaction.
- Speed chemical reactions because
  - Provide a different path to products that has more stable intermediates and therefore requires less energy.
  - Give the correct orientation every time.

Nerve Agents



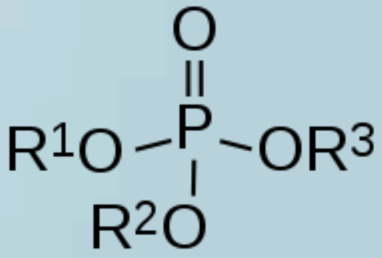
- **Tabun**, **sarin**, **soman**, cyclosarin, **VX**, Novichok
- Modes of Action: Contact, Inhalation
- Physiological Effects
  - Disrupt the mechanism by which nerves transfer messages to organs
  - Causes seizures and loss of body control
  - Exhausts muscles, including heart and diaphragm
  - Lethal dose can cause death from respiratory failure in five minutes
- Form When Disseminated: Liquid, Vapor, Aerosol
- Required Defensive Gear: Protective Mask & Clothing

Nerve Agents

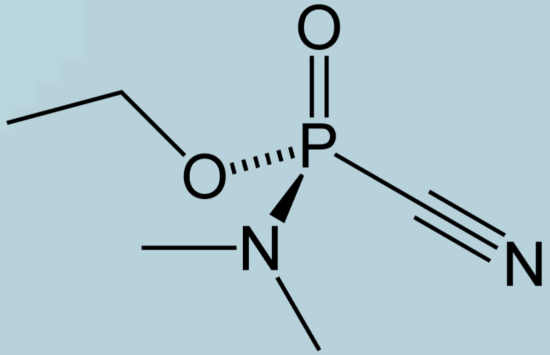
- Cause contraction of pupils, profuse salivation, convulsions, involuntary urination and defecation, and eventual death by asphyxiation as control is lost over respiratory muscles.
- U.S. and the Soviet Union developed and stockpiled large quantities of nerve agents in a chemical arms race that mirrored the nuclear arms race.

Nerve Agents

- Discovered accidentally by German chemists developing pesticides.
  - Germany had the world's most advanced chemical industry.
  - Searching for new organophosphate pesticides



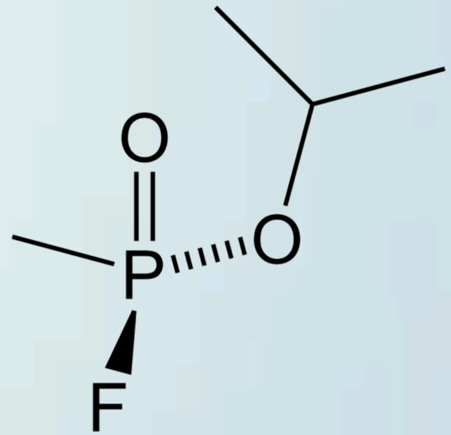
- Made many variations of the structure and tested them for potency.
- One compound found to be very dangerous and therefore considered "taboo" (tabu in German)…called Tabun.

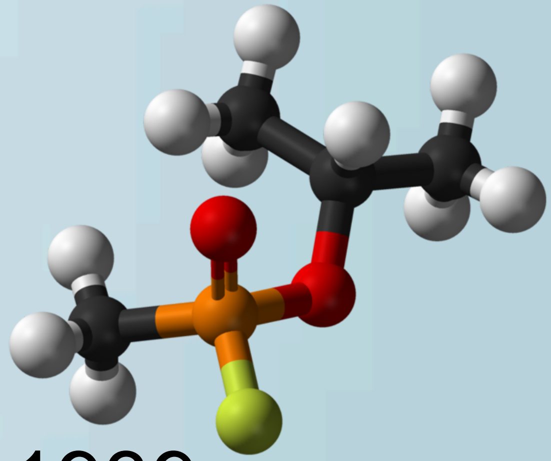


One Way to Do Science

- Trial-and-error based on previous experience.
- Steps taken by the German Gerhard Schrader working for the IG Farben chemical company and trying to make new pesticides.
  - Fluorine compounds are known to be toxic, so synthesized many different organic compounds with fluorine and tested them for toxicity to insects and safety for humans.
  - After no luck, tried adding first sulfur, then phosphorus, making a series of “organophosphate” compounds with promising characteristics.
  - To make the organophosphates more toxic, he added the cyanide group, which was known to be toxic, leading to tabun.
  - Noticed the adverse effects on himself after making it in the laboratory.

Sarin (GB)

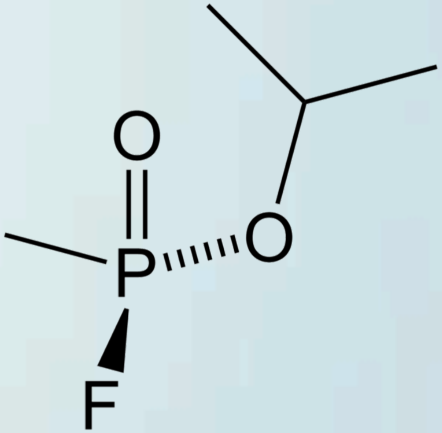


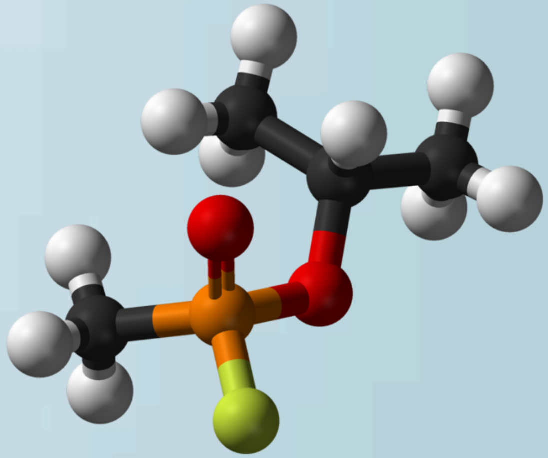


- Developed by the Germans in 1939
- Named for four scientists who were important in its discovery…**S**chrader and **A**mbros of IG Farben and **R**udiger and L**in**de or the German Army Ordinance Office
- Odorless
- Adopted as the standard nerve agent for the U.S. in 1948.

http://chemapps.stolaf.edu/jmol/jmol.php?model=FP%28%3DO%29%28OC%28C%29C%29C

Sarin (GB)

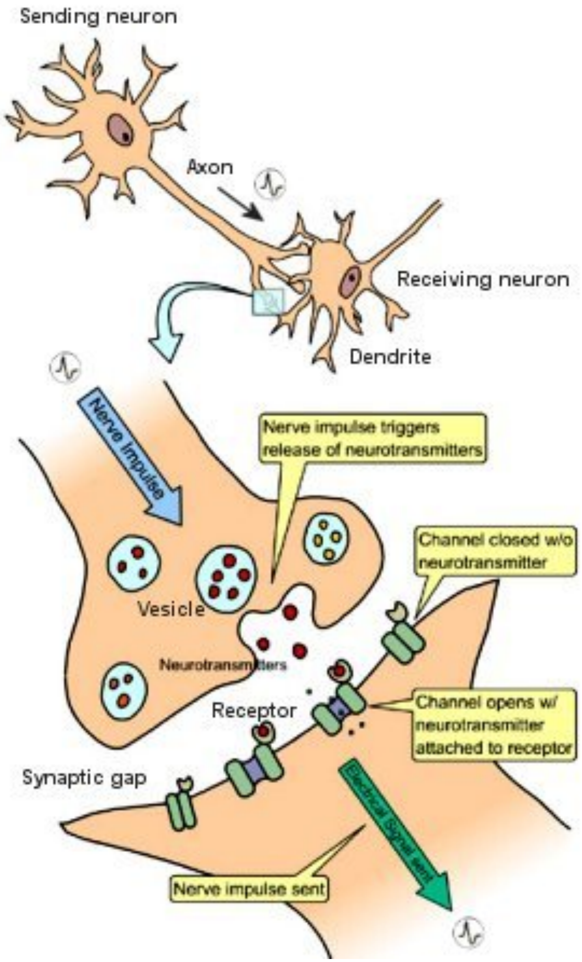




- If sarin does not have a high purity, it degrades fairly rapidly.
- Its shelf-life can be extended with stabilizers.
- Can be destroyed in a hydrolysis reaction with a water solution of sodium hydroxide.
- A very large amount of sarin has been made, but very little of it has been used.
- Iraq used sarin against Iran and the Kurds in the 1980s.
- Used in the Tokyo Subway attack by Aum Shinrikyo

Neurotransmitters

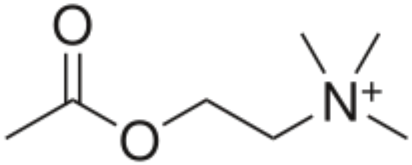
- Neurotransmitters cause nerve cells to fire.

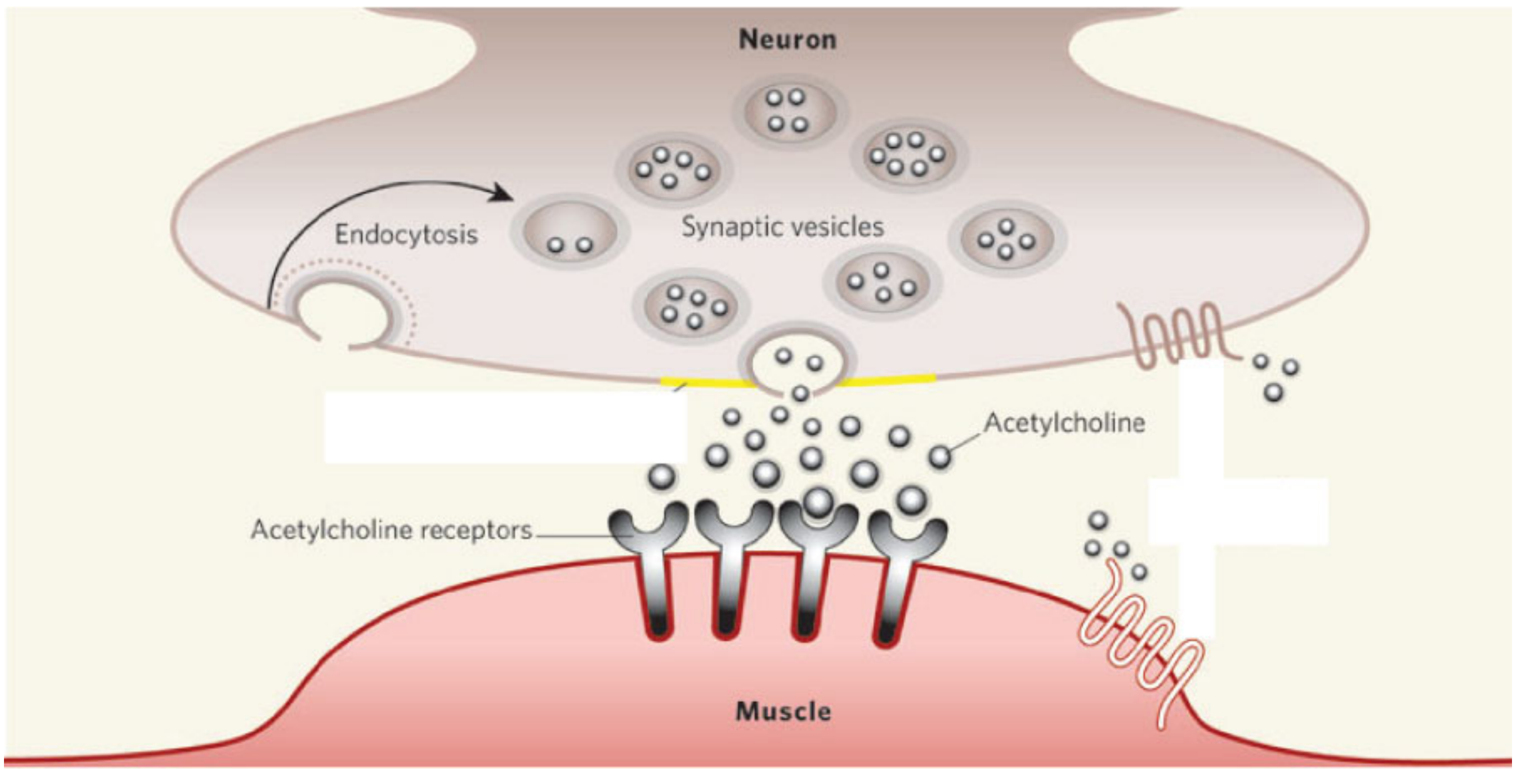


From http://universe-review.ca/R10-16-ANS.htm

Acetylcholine and Muscle Contraction

- Among other things, the neurotransmitter acetylcholine stimulates nerve cells that cause muscle contraction.





From Nature 436, 473-474 (28 July 2005)

Acetylcholine, Acetylcholinesterase, and Transfer of Nerve Information

- Normally, acetylcholine is broken down in the active site of an enzyme, acetylcholinesterase.
- Each enzyme molecule converts about 25,000 molecules of acetylcholine per second.
- Acetylcholine-acetylcholinesterase - like an on-off switch for muscles

Sarin and Acetylcholine-Acetylcholinesterase

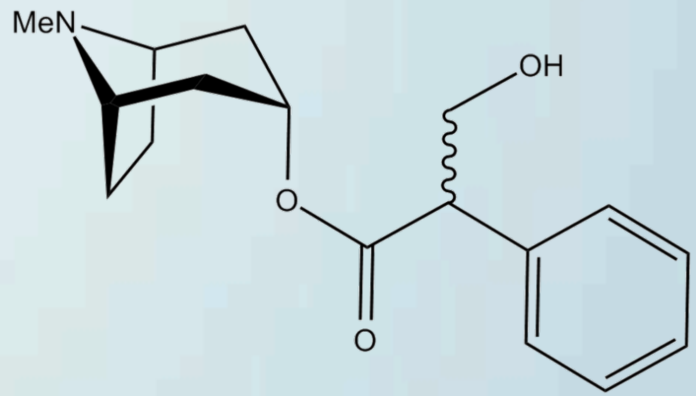
- Sarin forms a covalent bond to a serine side chain in the active site of acetylcholinesterase, deactivating it.
- If acetylcholinesterase is deactivated, the acetylcholine levels remain high, and the switch gets stuck in the “on” position.

http://preparatorychemistry.com/nerve_agent_sarin.html

Effects of Nerve Gases

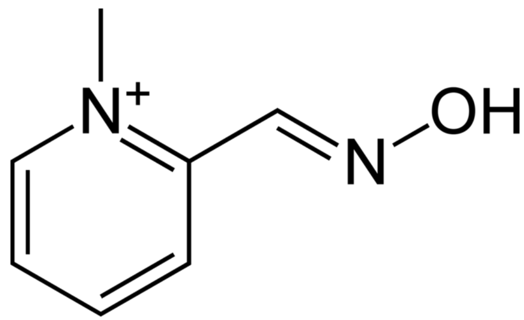
- For skeletal muscles: uncontrolled spasms, followed by paralysis
- For involuntary muscles: pupil contraction, excessive salivation, intestinal cramps, vomiting, and constriction of bronchial tubes
- For central nervous system: overstimulates the brain, causing seizures
- Causes glands to be overactive, secreting excess nasal mucus, saliva, and sweat
- Causes death by asphyxiation through constriction of bronchial tubes, suppression of the respiratory center of the brain, and paralysis of the breathing muscles

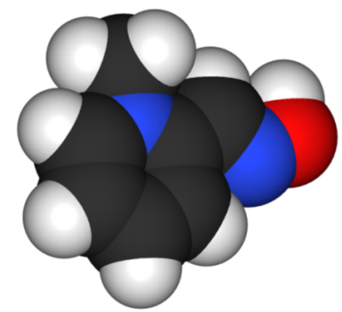
Nerve Gas Antidotes - Atropine



- Standard antidote for organophosphate poisoning
- Used in ancient Greece to dilate pupils (to make women's eyes prettier)
- Competes successfully with one type of acetylcholine receptors. This type of receptor is found in smooth muscles and glands.
- Helps relax muscles
- Stops the symptoms from nerve agent poisoning, *not* the cause

Nerve Gas Antidotes - PAM





- Pralidoxime (2-pyridine aldoxime methyl chloride,) or 2-PAM
- Removes the nerve agent from the active site of acetylcholinesterase, restoring the enzyme to more normal levels
- Too slow to work well alone
- Works best when administered with atropine, which acts more quickly, giving the slower-acting PAM time to work.
- Does not make it through the blood-brain barrier, so does not alleviate problems within the central nervous system. Alternatives are being developed.

Nerve Gas Antidotes

- Atropine and PAM can be administered with a pressurized syringe with a spring-loaded, recessed needle.
- A catch is released and when the syringe is pressed against the leg, the spring is released, pushing the needle through clothing and into the leg, releasing the antidote.