

Molecular Literacy for All

$C_6H_{12}O_6$ to CO_2 : Glycolysis & Citric Acid
Cycle

Why, to write down the stuff
and people of every day,
must poems be dressed up in gold,
in old and fearful stone?

[...]

I want poems stained
by hands and everydayness.

Sweetness, Always
Pablo Neruda

Session 8

Today's Outline

Breaking Bread

- Yeast: Man's Best Microscopic Friend
- Glycolysis
- Citric Acid Cycle

Carbonyls: Keys to the Kingdom

- Nucleophiles and Electrophiles
- Carbonyl Chemistry
- Glycation of Hb_{A1c}
- Amadori Rearrangement

Be Careful What You Crave For


- Alkylation: A Dark History
- Alkylation: A Bright Future

Questions from Session 7

- Why does COVID-19 disable our sense of smell?
 - Some viruses disable sense of smell by triggering congestion. COVID-19 can disable sense of smell without nasal obstruction
 - ACE2 and TMPRSS2 genes encode the enzymes that are targeted by SARS-CoV-2 to enter the cell. These genes are found in sustentacular cells and basal cells.
 - There must be an indirect mechanism for taste & smell deactivation, but that mechanism is not yet known.

STARCH

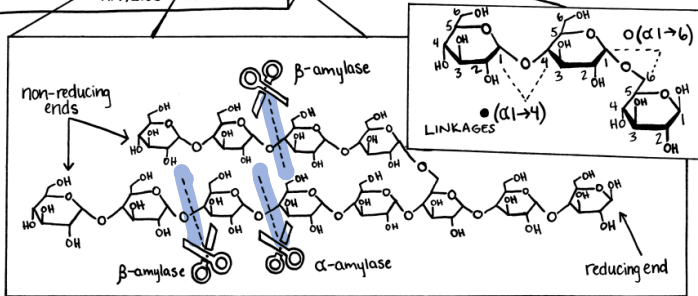
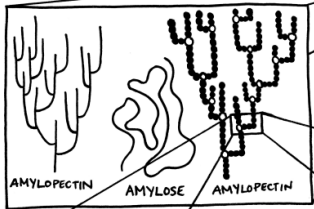


- alpha linked polymer of glucose
- most abundant biomolecule after cellulose
- $\uparrow 60^{\circ}\text{C}$ helix unravels in water
- helical structure 



- layered like an onion
- starts from a single glucose and branches out

- Amylopectin - highly branched polymer of glucose
- Amylose - long unbranched polysaccharide chain

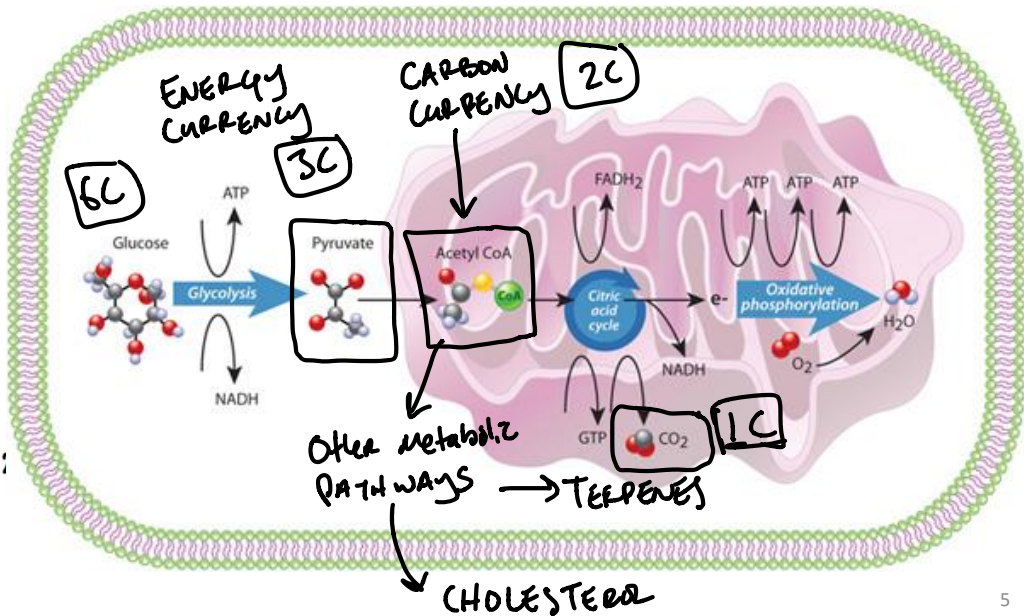
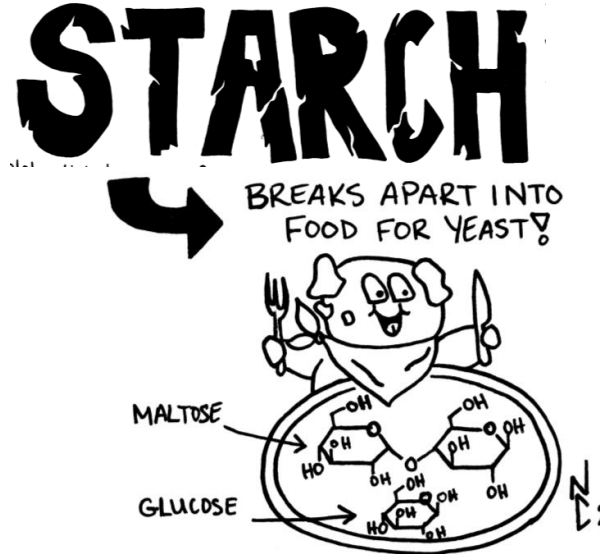


Breaking Down Starch



- Amylase enzymes catalyze the hydrolysis of starch into smaller sugars
- Alpha-amylase (α -amylase)
 - randomly breaks ($\alpha 1\rightarrow 4$) glycosidic linkages
 - but not near branchpoints or non-reducing ends
- Beta-amylase (β -amylase)
 - breaks ($\alpha 1\rightarrow 4$) glycosidic linkages near non-reducing ends

Yeast – Man’s Best Microscopic Friend



Crash Course in History of French Wine

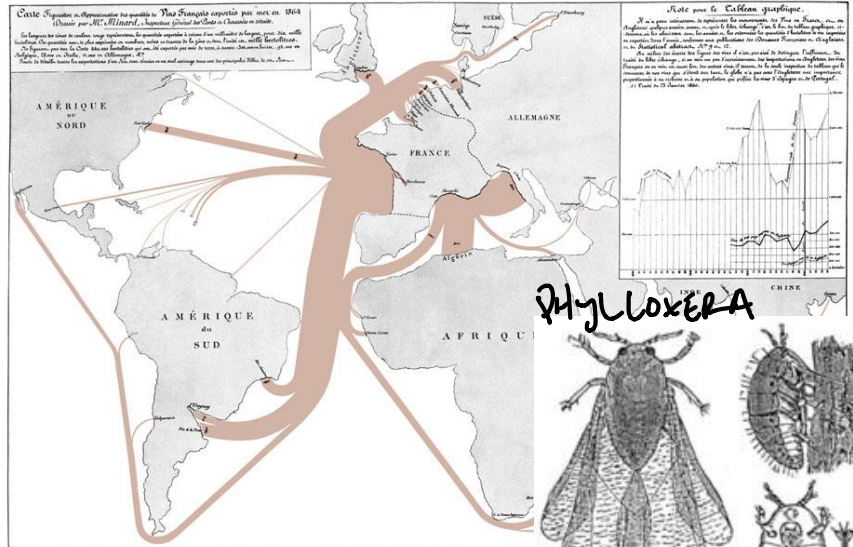


"Day of 21 January 1793 the death of Louis Capet on the Place de la Révolution" – French engraving.



As Minister of the Interior, Jean-Antoine Chaptal played an important role in helping the French wine industry recover from the French Revolution.

CHAPTALIZATION → ADDING SUGAR TO WINE



Charles Joseph Minard, *Tableaux Graphiques et Cartes Figuratives de M. Minard*, 1845-1869, a portfolio of his work held by the Bibliothèque de l'École Nationale des Ponts et Chaussées, Paris.

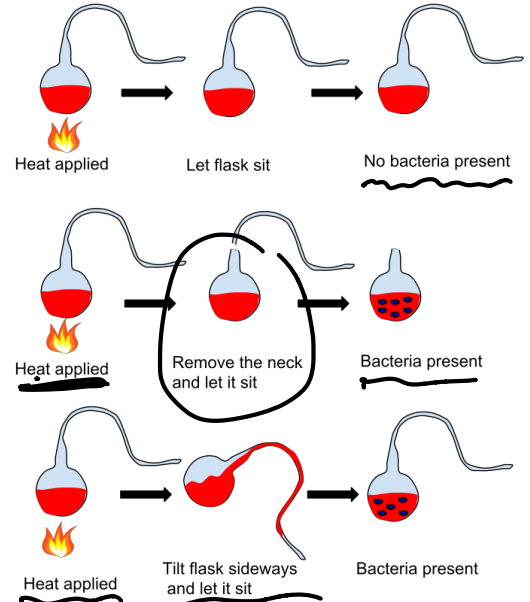
By the mid-1800's, French wine industry reaches a golden age. The golden age soon collapses as a result of various diseases.

Louis Pasteur to the Rescue

MIASMA

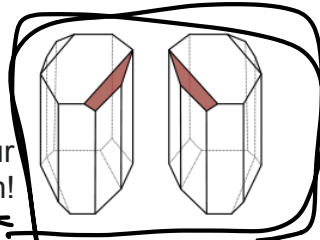


In 1850's, Louis Pasteur makes significant progress toward the germ theory of disease.

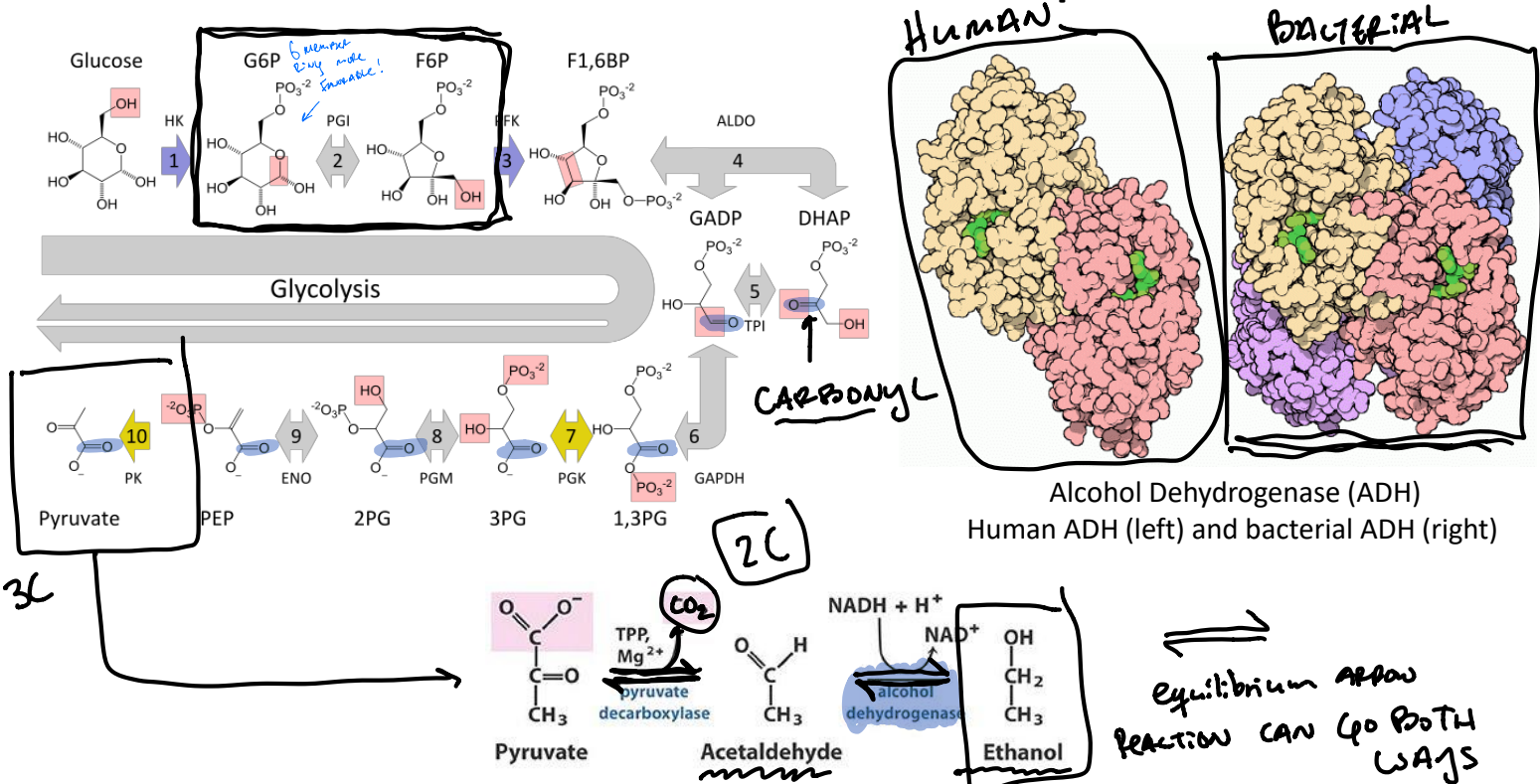


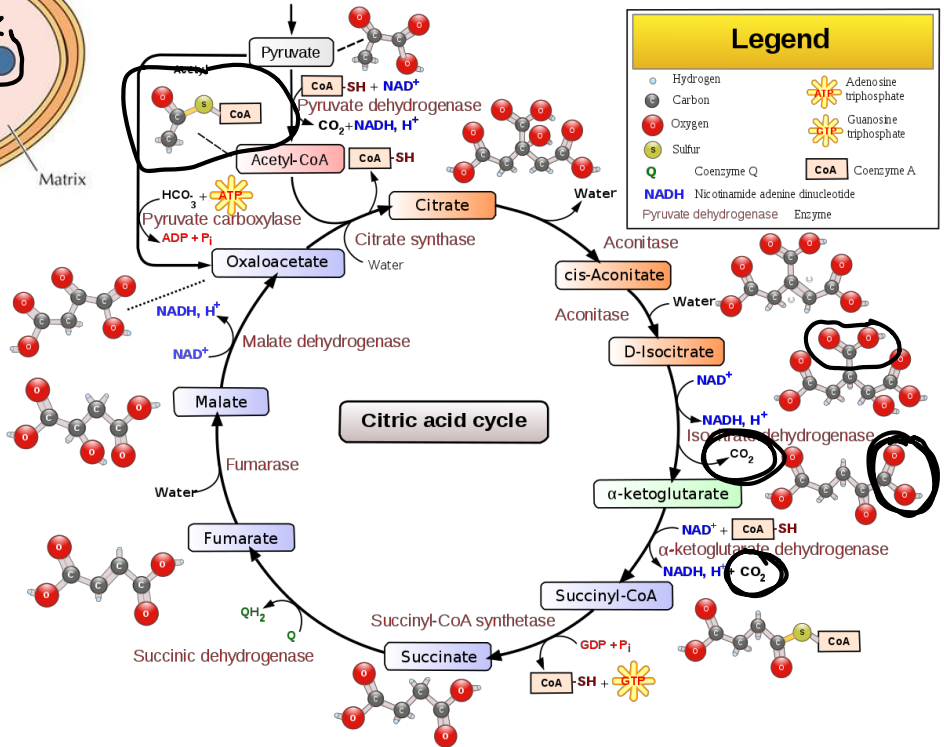
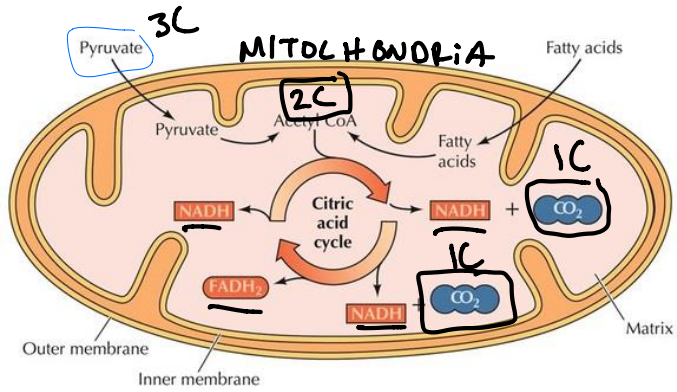
Patents process of wine pasteurization in 1865.

Pasteur made contributions to our understanding of racemization!



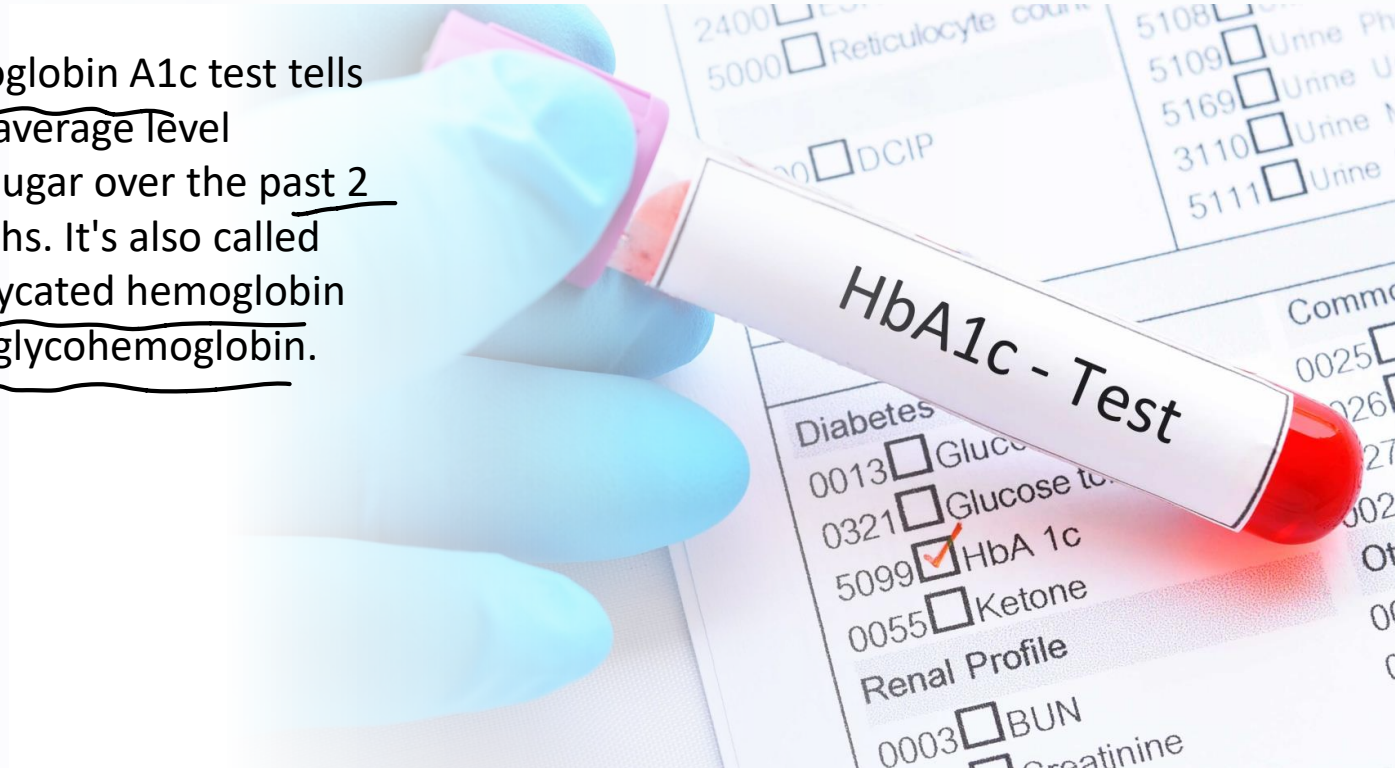
Yeast – Man’s Best Microscopic Friend





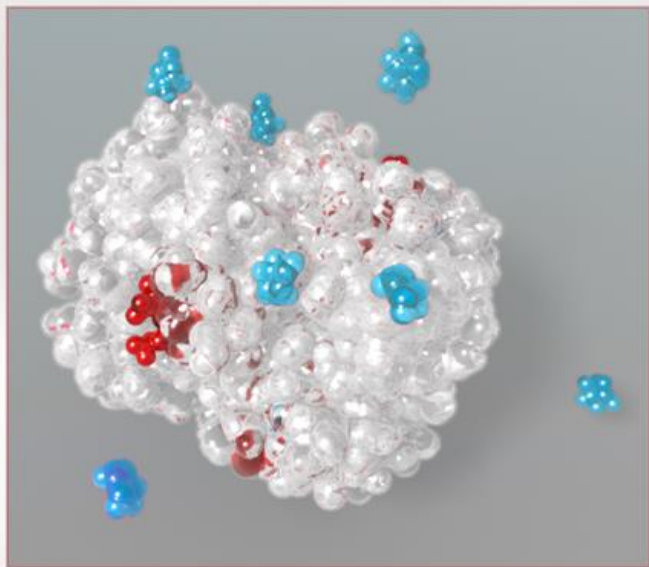
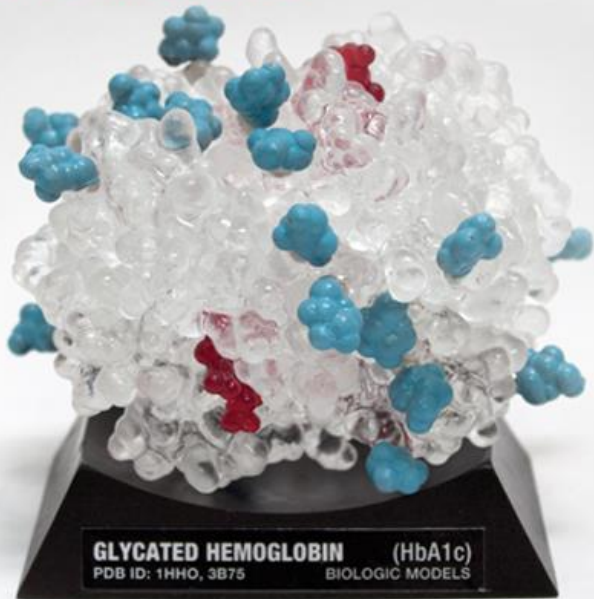
Testing blood sugar – HbA1c

The hemoglobin A1c test tells you your average level of blood sugar over the past 2 to 3 months. It's also called HbA1c, glycated hemoglobin test, and glycohemoglobin.

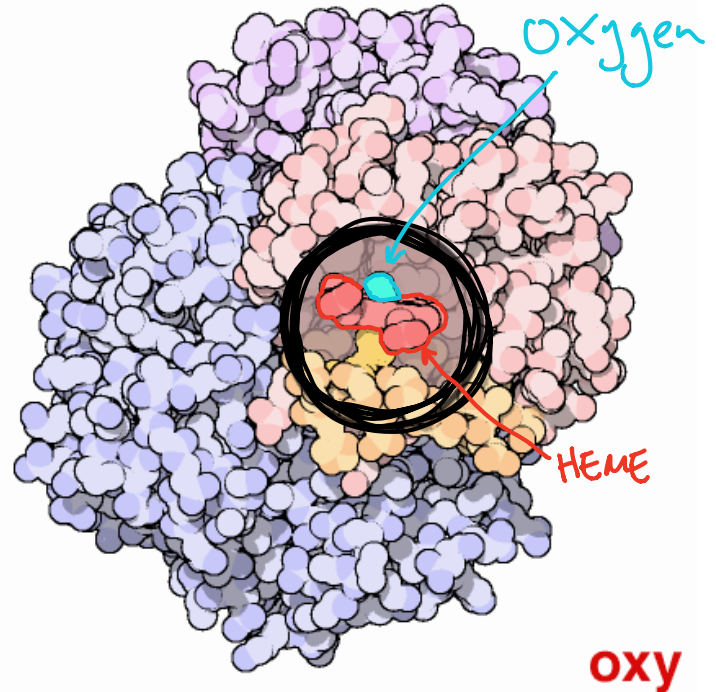
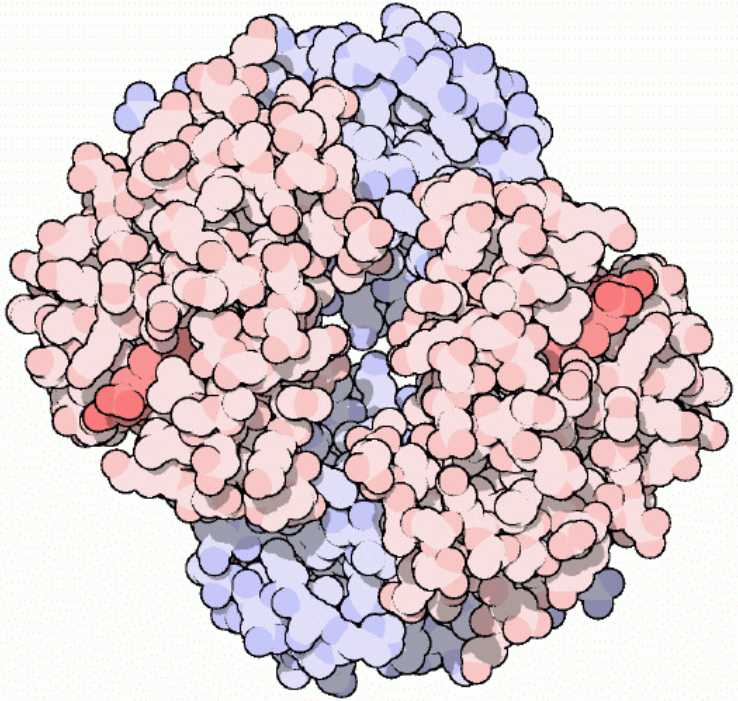


Glycated Hemoglobin HbA1c

PDB ID: 1HHO, 3B75



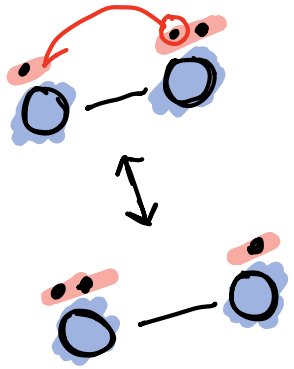
Hemoglobin – Molecule of the Month



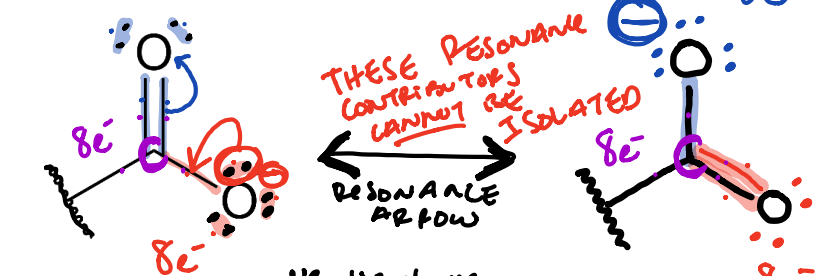
\rightleftharpoons EQUILIBRIUM ARROW
 THESE MOLECULES CAN BE ISOLATED

Resonance

ELECTRONS MOVE ONLY!

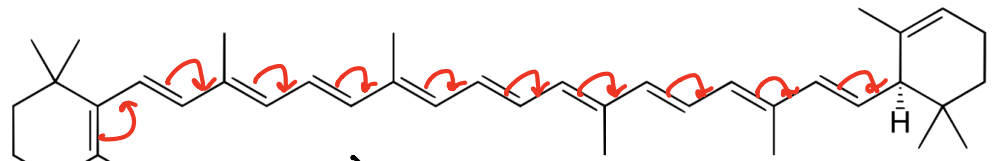
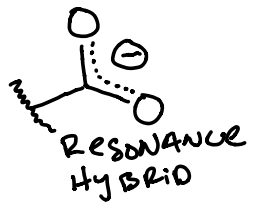


3 e⁻
2 center
resonance

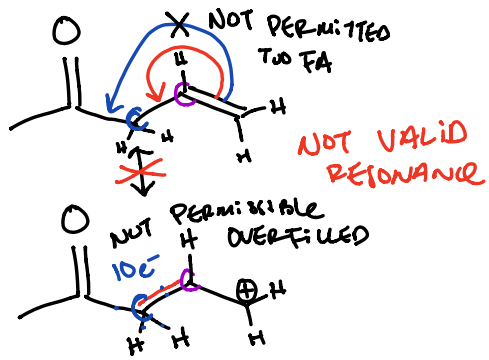
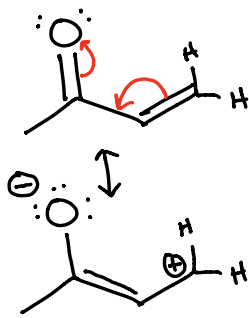


THESE RESONANCE CONTRIBUTORS CANNOT BE ISOLATED
 RESONANCE ARROW
 CARBOYLATE ^{negative charge}
 CARBOXYLIC ACID

RESONANCE ARROW



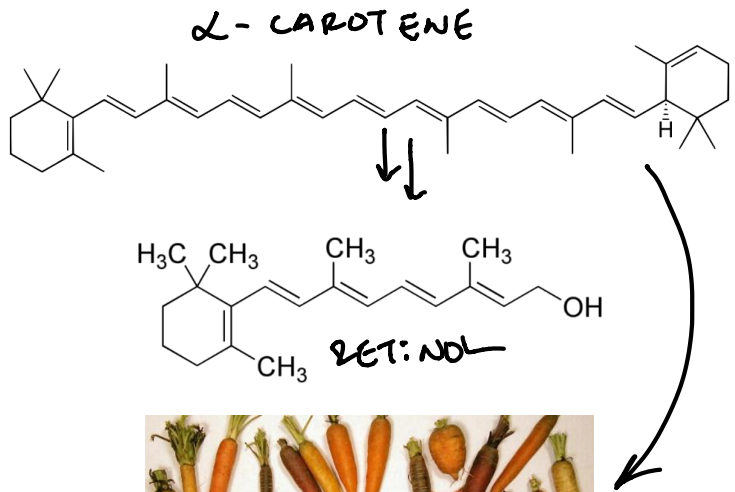
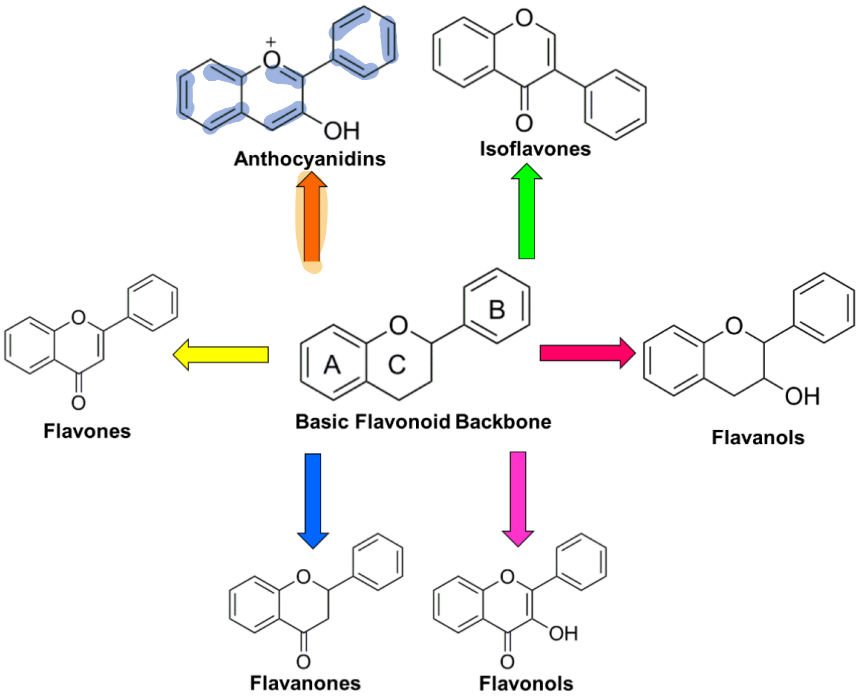
CONJUGATED PI SYSTEM



RED CABBAGE
EXPERIMENT

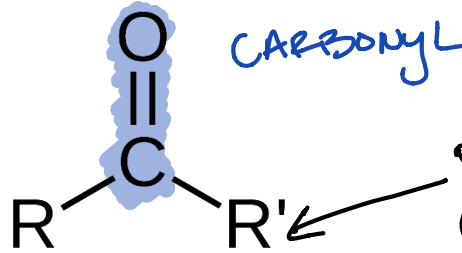
pH AND COLOR CHANGE!!

Colorful Conjugated Systems



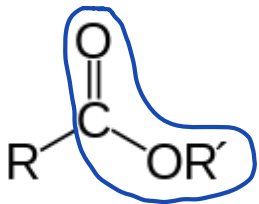
Carbonyls: Keys to the Kingdom

TRANSFERABILITY
of functional
groups allows us
to predict chemical
properties !!

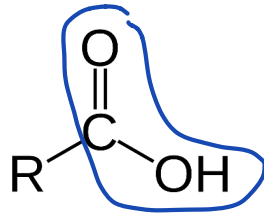


Residual R
CAN BE CARBONYL
OR Hydrogen
amide

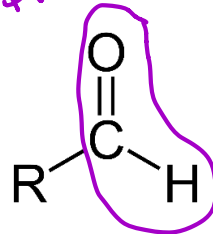
ketone
fructose



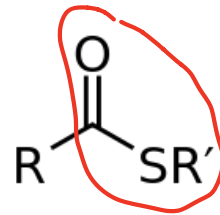
ESTER
STORING FATS



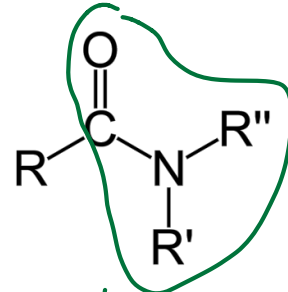
CARBOXYLIC
ACID



ALDEHYDE
glucose



THIOESTER
acetyl-CoA

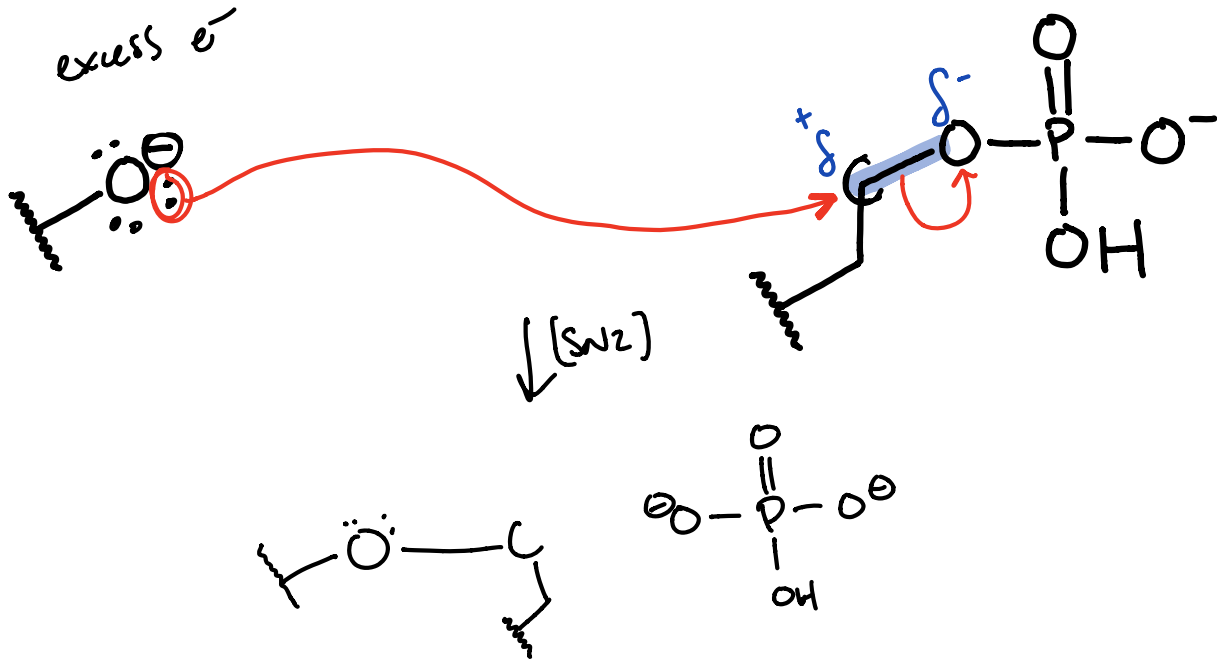


in proteins

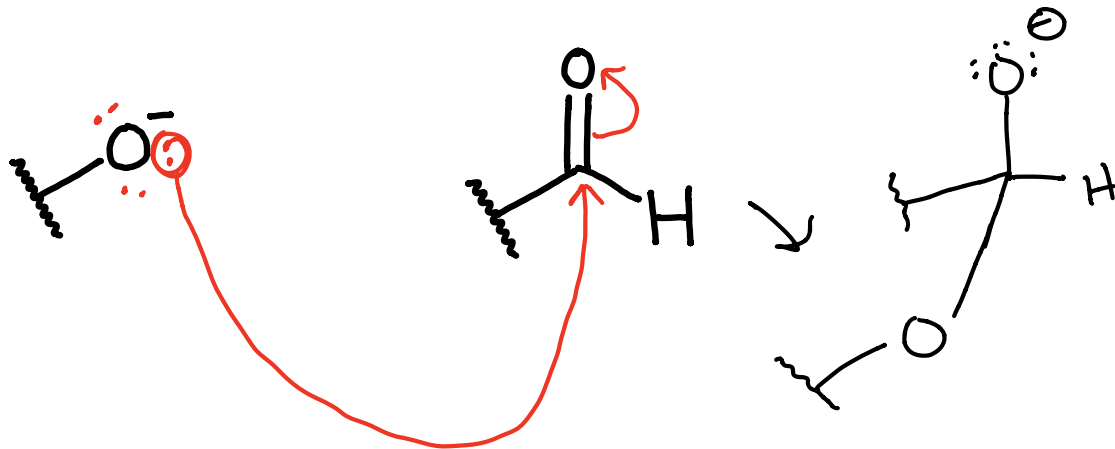
Nucleophiles vs Electrophiles

Seeker of nucleus

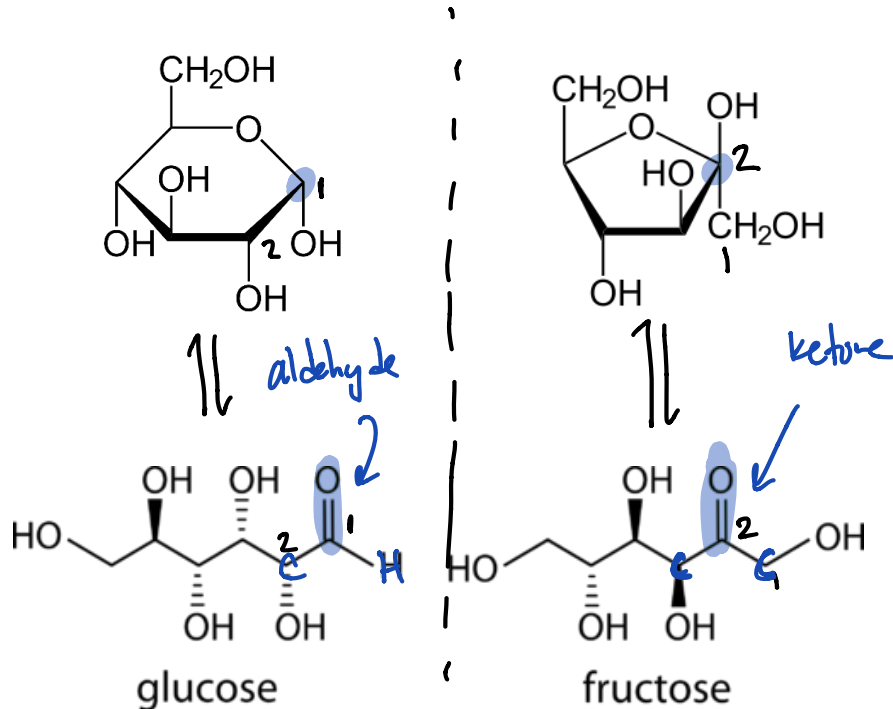
Seeker of electrons

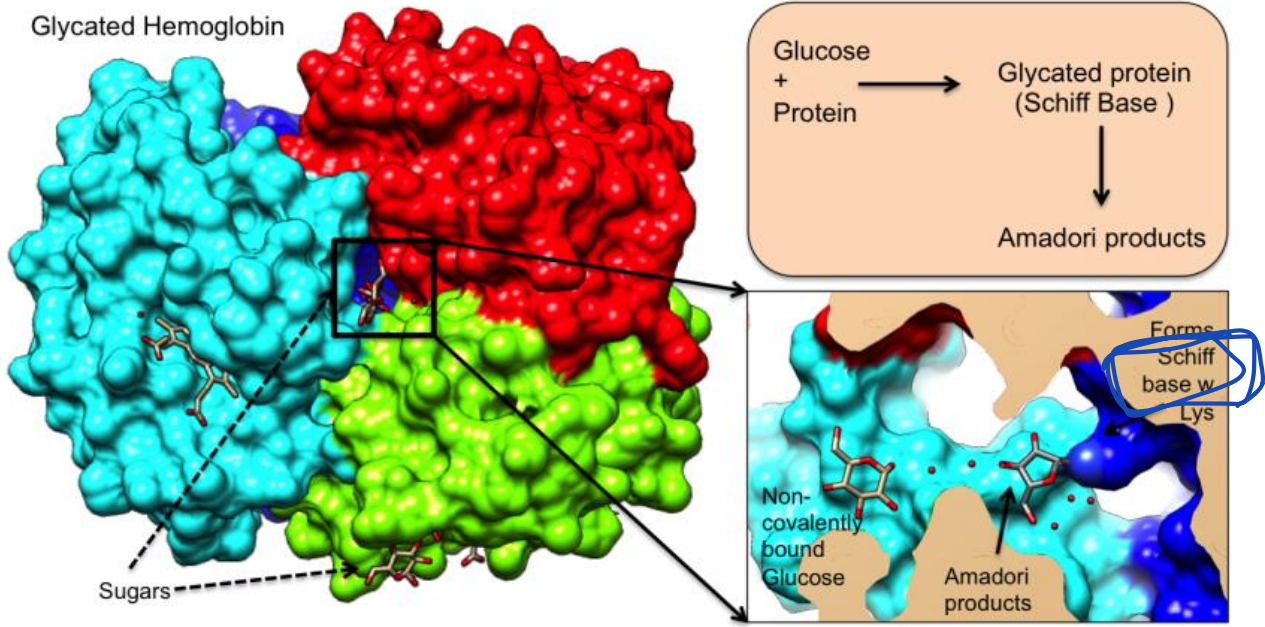


Attacking Carbonyls



Anomeric Carbon





HbA1c MOLECULAR MARKER

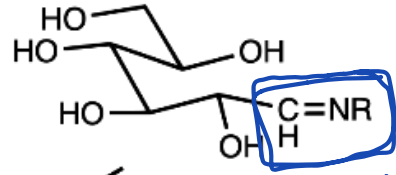
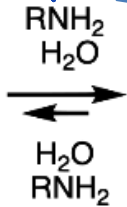
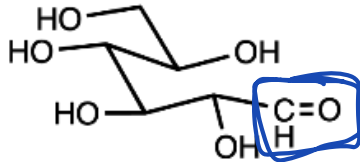
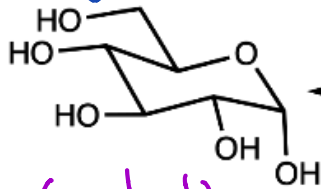
Hemoglobin Glycation

glucose

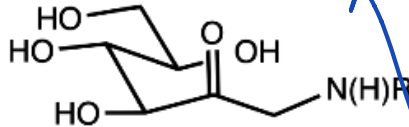
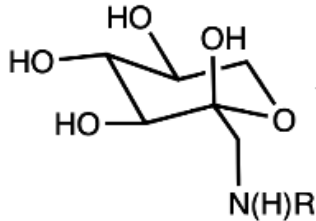
More Glucose
More glycosylated Hemoglobins!

Lys

Hemoglobin amino group



High Concentration
of Glucose
Drives the
Reaction

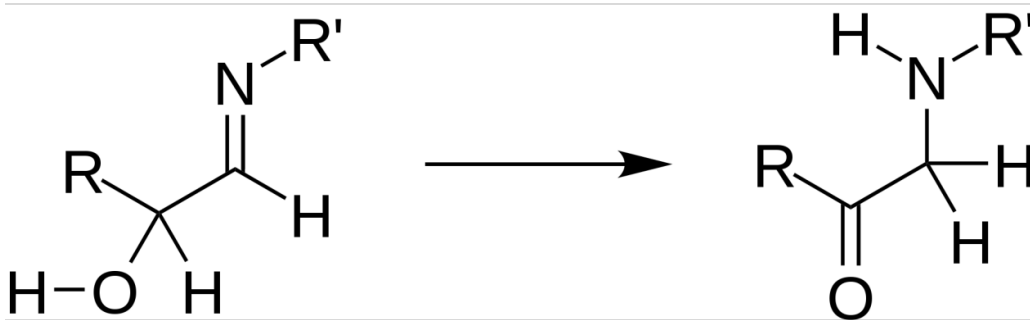


Schiff base

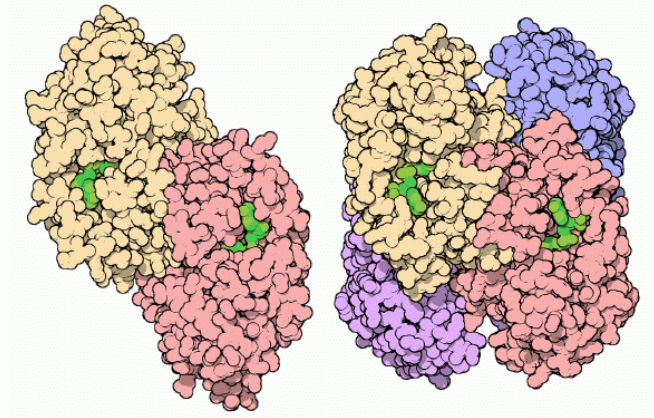
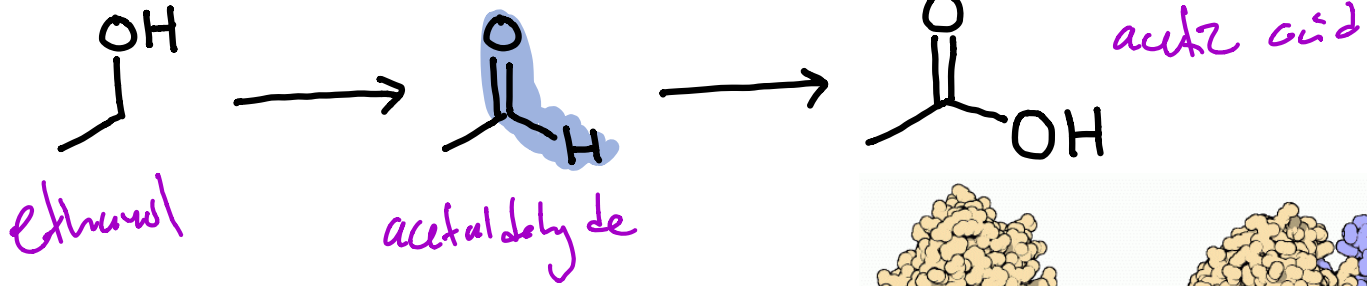
Advanced
Glycation
End products

Amino
Reaction

Amadori Rearrangement

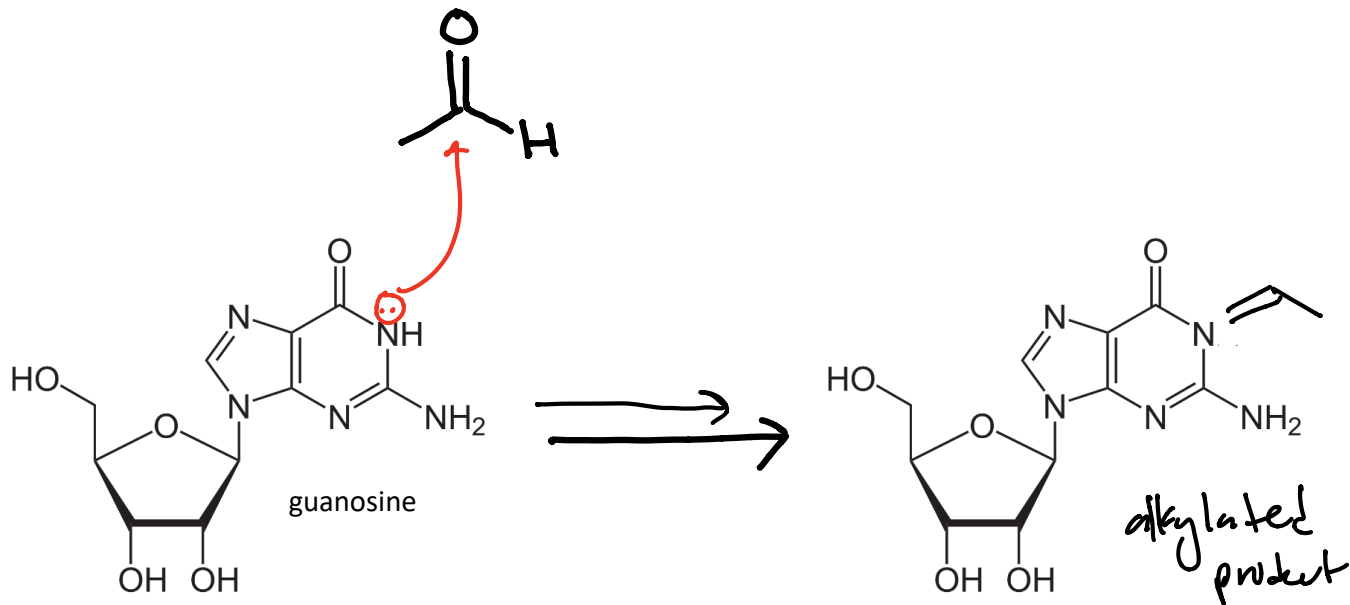


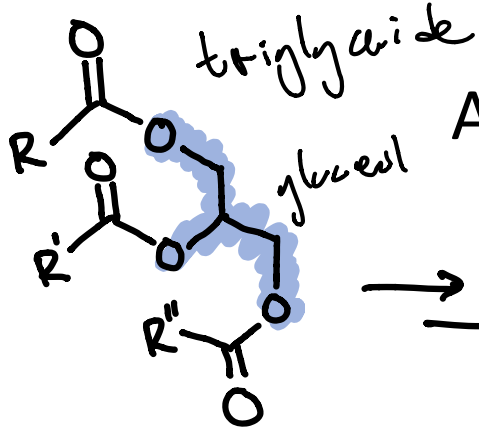
Alcohol Metabolism



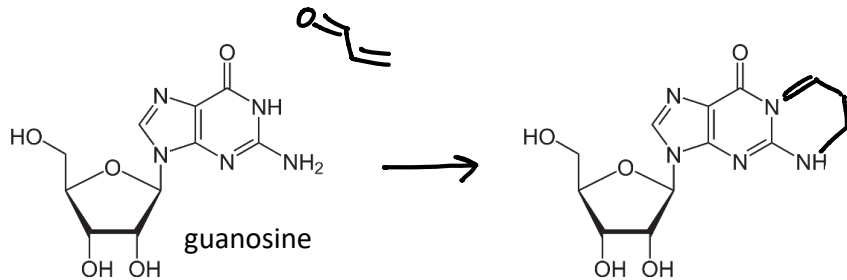
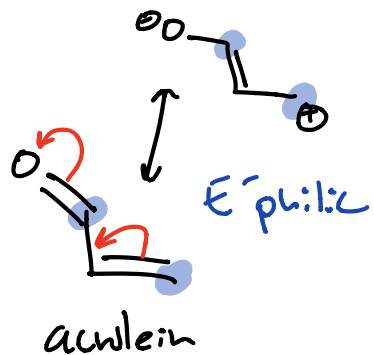
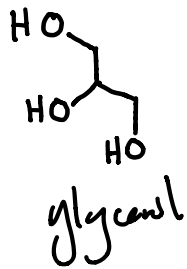
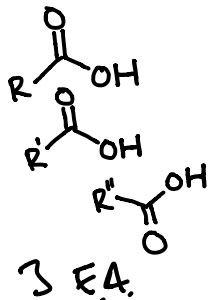
Human ADH (left) bacteria ADH (right)

Aldehyde Alkylation





Acrolein Alkylation



Discovering Sulfur Mustard



In 1860, Francis Guthrie isolates the compounds and records its irritating properties, especially in tasting.



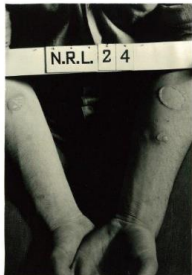
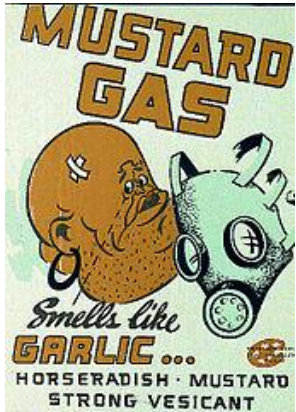
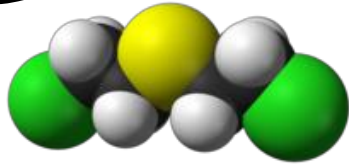
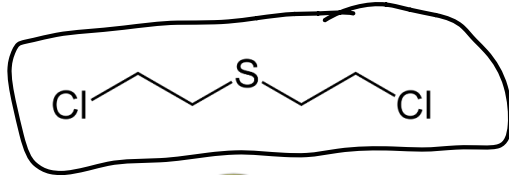
Also in 1860, Albert Niemann synthesizes and records blistering-effect of mustard



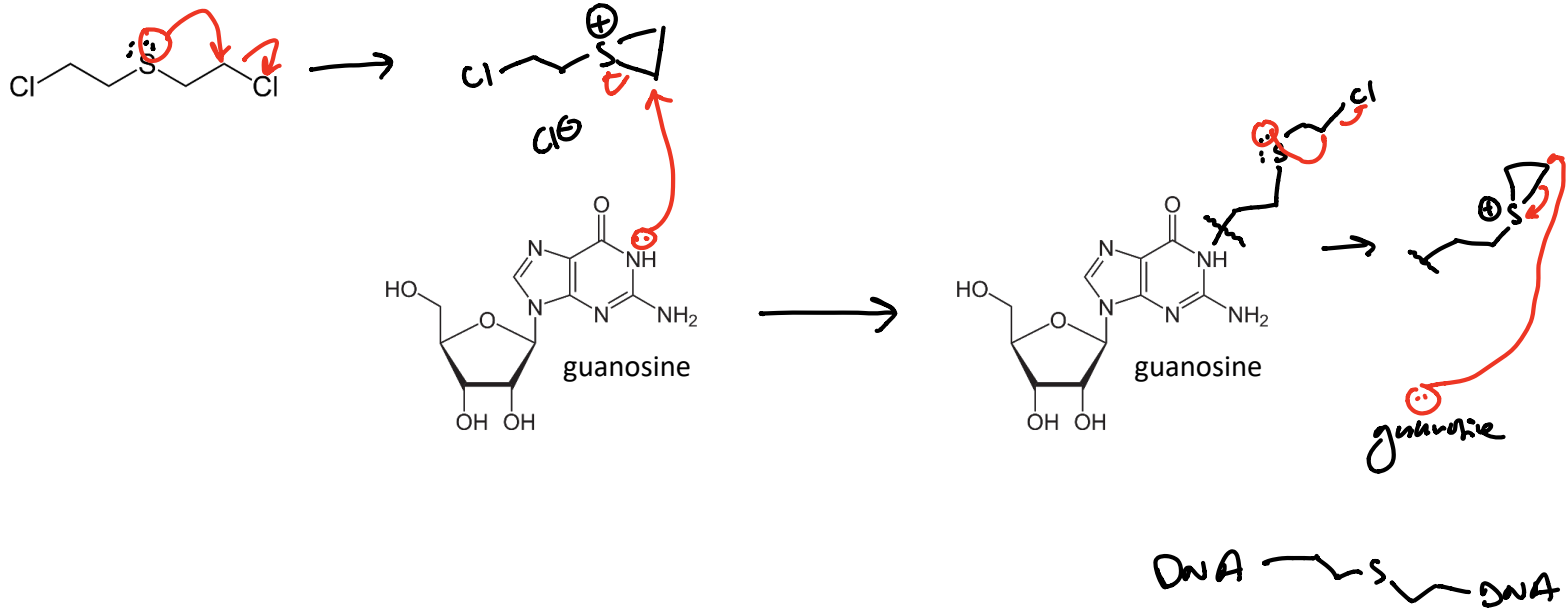
In 1886, Viktor Meyer produced sulfur mustard in high yield

Militarizing Sulfur Mustard

First use in 1917, Battle of Ypres.
Sometimes this chemical is called yperite.

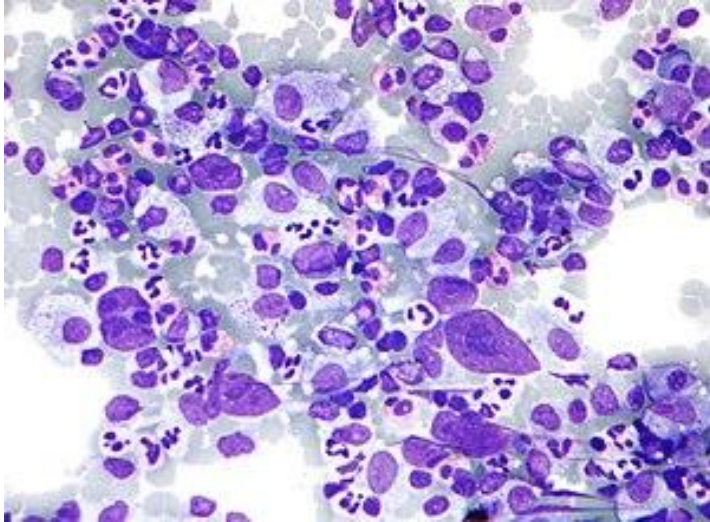


Chemical Mechanism of Sulfur Mustard

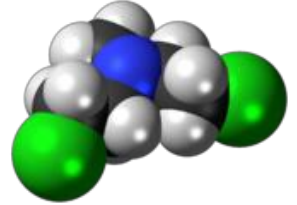
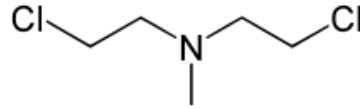


REASON BY ANALOGY!
The first cancer chemotherapy drug

TRANSFERABILITY



Hodgkin lymphoma (HL) is a type of lymphoma in which cancer originates from a specific type of white blood cells called lymphocytes.



In 1919, it became apparent that people exposed to mustard gas had decreased white blood cell counts.

In 1946, research on nitrogen mustards was declassified. Chloromethine became the first chemotherapy drug to be used in clinics.

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