Today

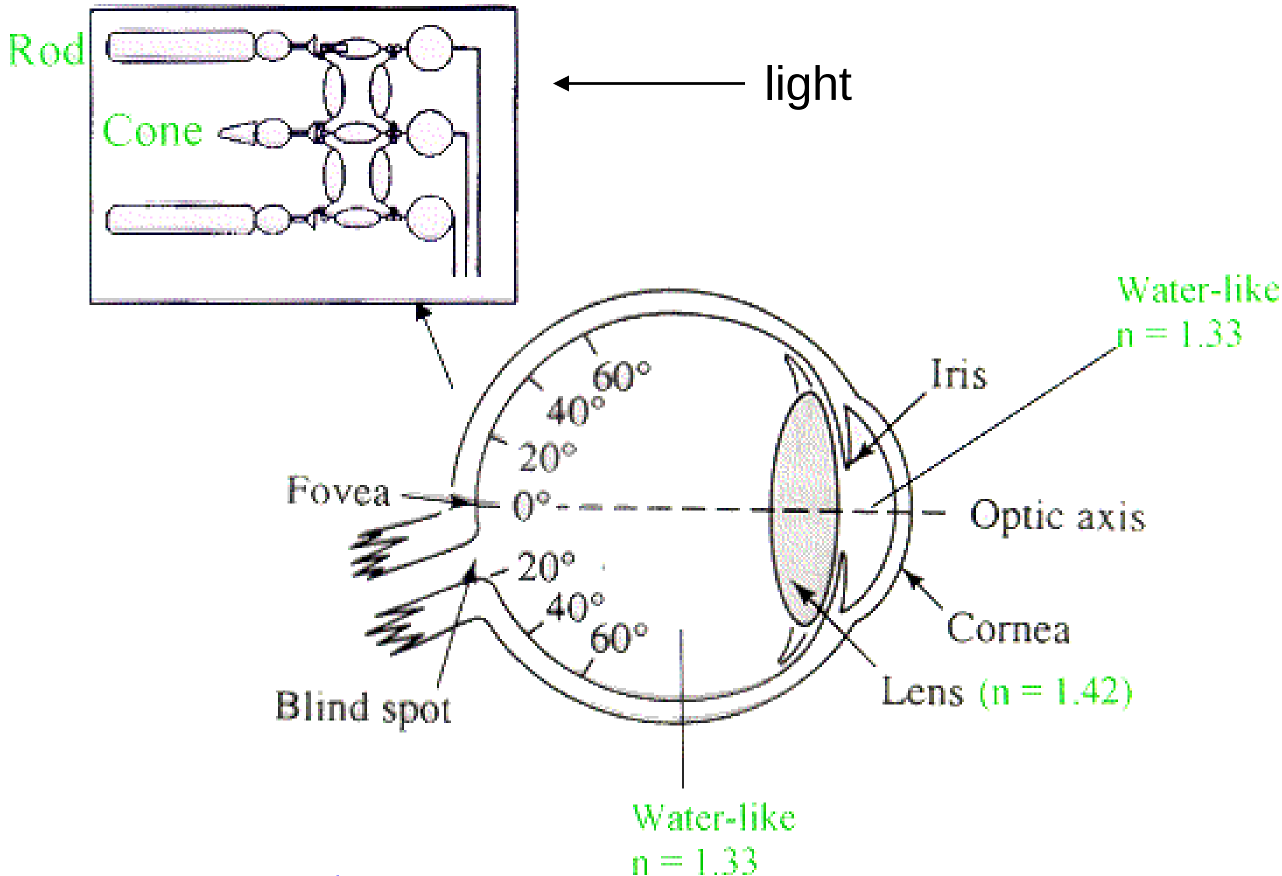
Forgot to post Vision. Now done.
Homework due this Wednesday (sorry!)

Today– <u>not</u> part of homework.

Finish up Vision (quickly): Cones vs. Rods

Fats, Sugars, Food you need to survive.

Basic Structure of the Eye



Things to notice:

Image formation:

1. **Two lenses, not one! One fixed, one variable**
   Big index mismatch at cornea/air; some at lens.
2. **Image distance is fixed.**
3. **Normal eye: object at ∞, focussed on retina with lense relaxed.**

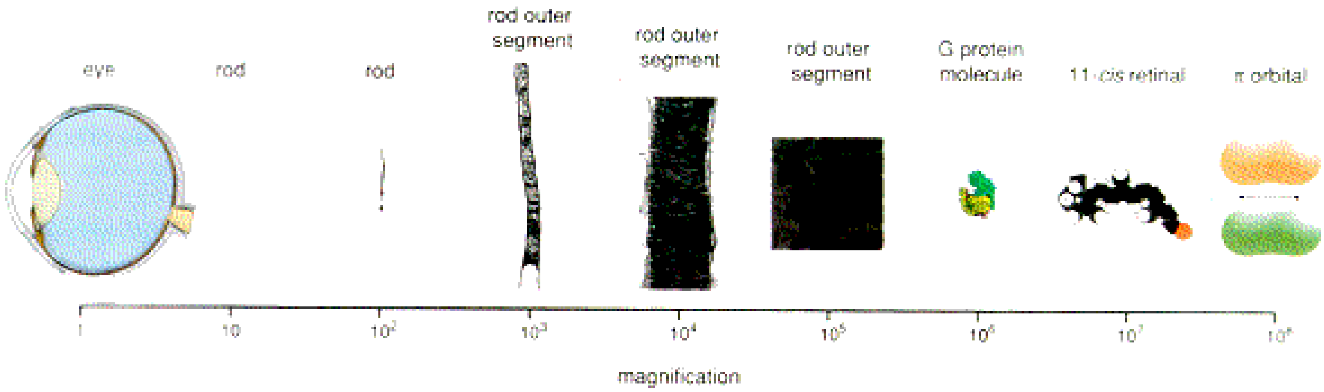
Light (and color) detection:

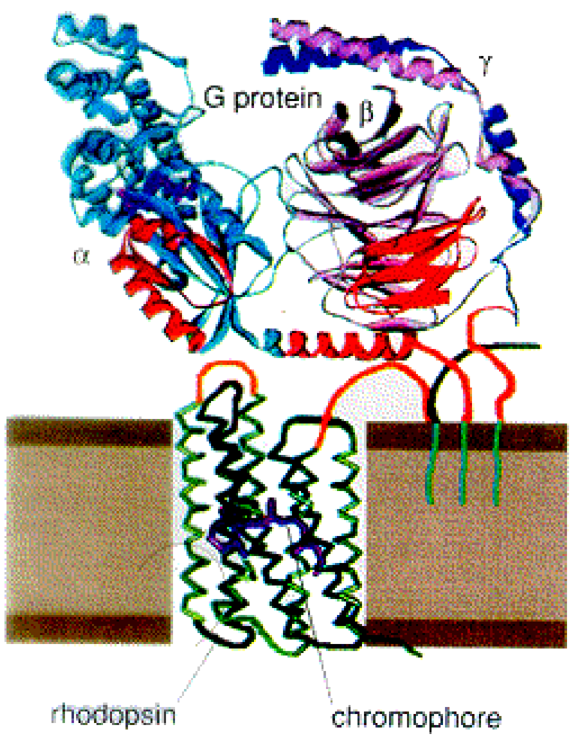
4. **Sensitivity of retina = function position**

5. **Rods and Cone Backwards!**

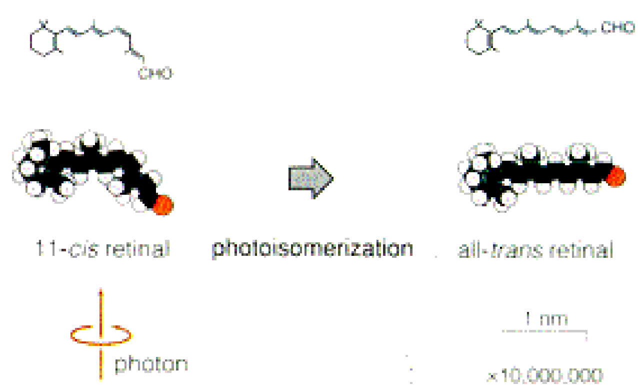
Molecular Biology of Vision

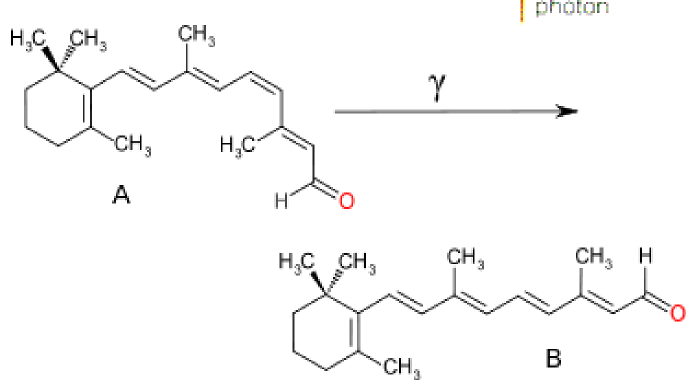
Photon abs → retinal cis→trans …ion channel close.



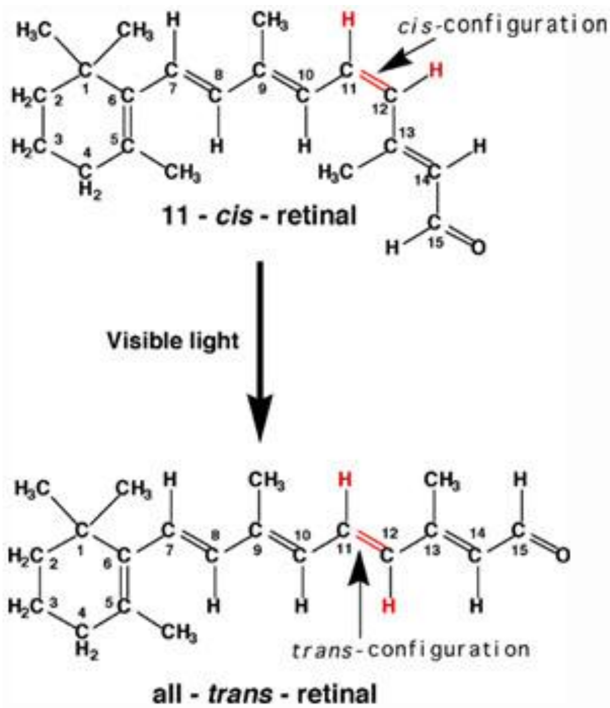


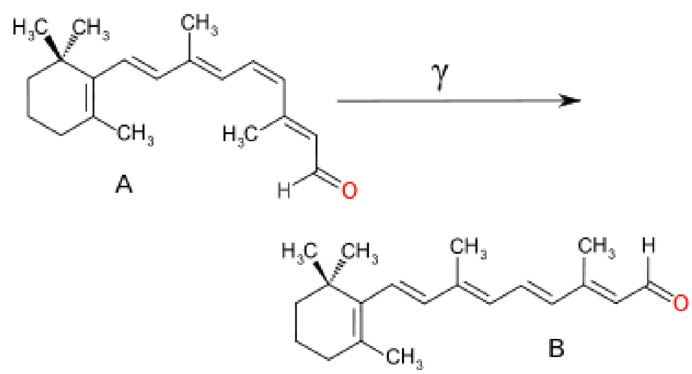
1. Photon absorbed: 3 femtosec.
2. Retinal: cis → trans: 200 fs.
3. Strain on protein Opsin. Opsin changes shape: ¼ → ½ msec.
4. Activates G-protein.





Cis→ trans - retinal



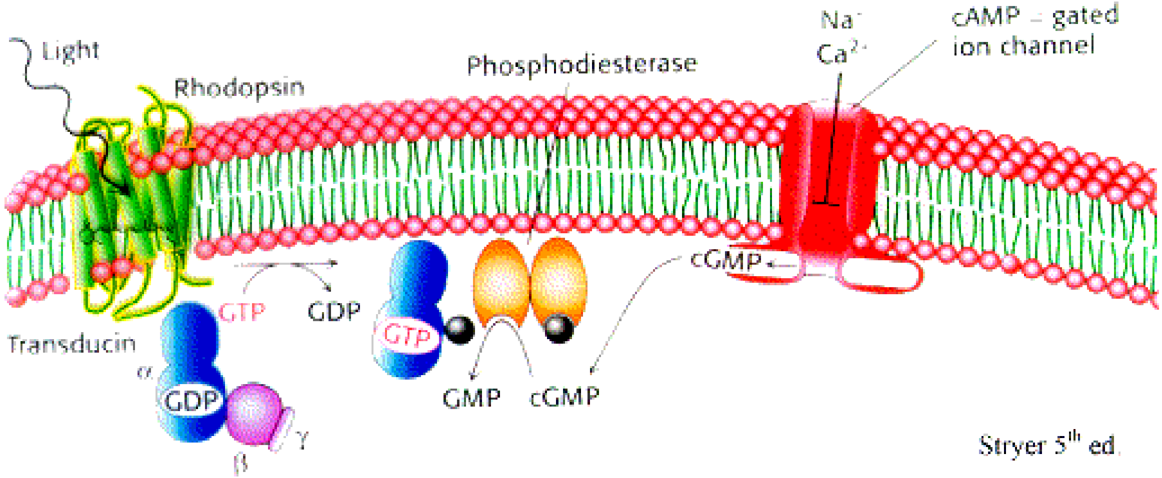


- Rhodopsin molecules contain a protein called **opsin** plus a derivative of vitamin A called 11-*cis*-retinal. In the dark, 11-*cis*-retinal fits nicely into the folds of the surrounding opsin. When light hits the rhodopsin, the 11-*cis*-retinal becomes *all-trans*-retinal and no longer fits into the cavity of opsin. The opsin and the *all-trans*-retinal separate. [Ultimately, the all-*trans*-retinal molecule is expelled from the protein, yielding free opsin plus free all-*trans*-retinal.] The change in rhodopsin conformation is eventually transmitted to the nerve cells in the eye and then the brain. The stereoisomerism of retinal is thus an important part of the vision process. Note that only one of the five double bonds is affected in this transformation, but when this one changes from cis to trans, the shape of the entire molecule changes. An enzyme later catalyzes the change of *all-trans*-retinal back to 11-*cis*-retinal so that it can once again bind opsin and wait for the next exposure to light.

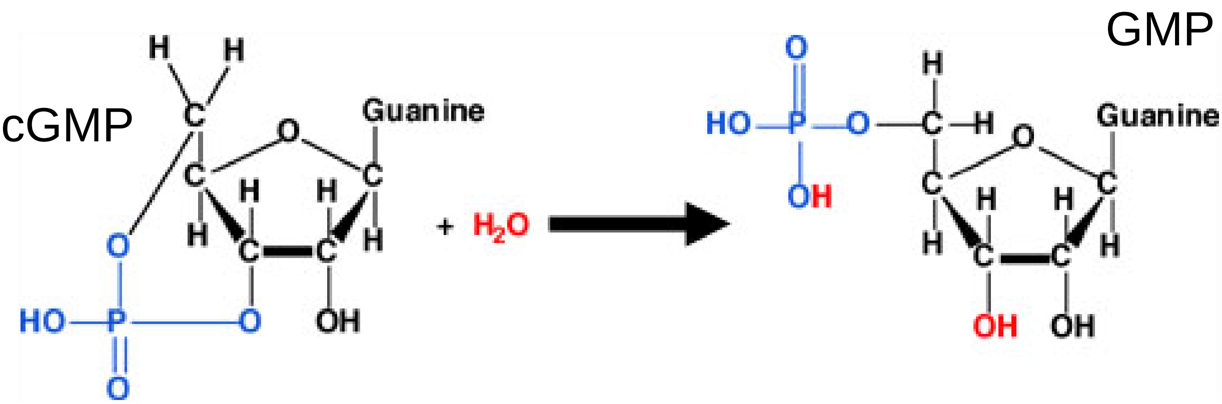
http://www.chemistry.wustl.edu/~edudev/LabTutorials/Vision/Vision.html

http://www.brookscole.com/chemistry_d/templates/student_resources/0030012910_kotz/oscience/ch11/carbon4.html

Biochemical Cascade con't



5. G-protein activates Phophodiesterase, which decreases cyclic GMP concentration.



6. cGMP required to <u>open</u> Na^+ channels. Therefore Ligand-gated Na^+ and Ca^{2+} close.

Notice that ion channel is Metabotropic—change in response goes through a secondary messenger

7. Action Potential <u>decreases</u>

Vision is odd: Light levels cause a secession of action potentials. In dark, rod cells are working the hardest!

Rod/Cone cells use up huge amounts of oxygen.

(I think more oxygen than any other cell.)

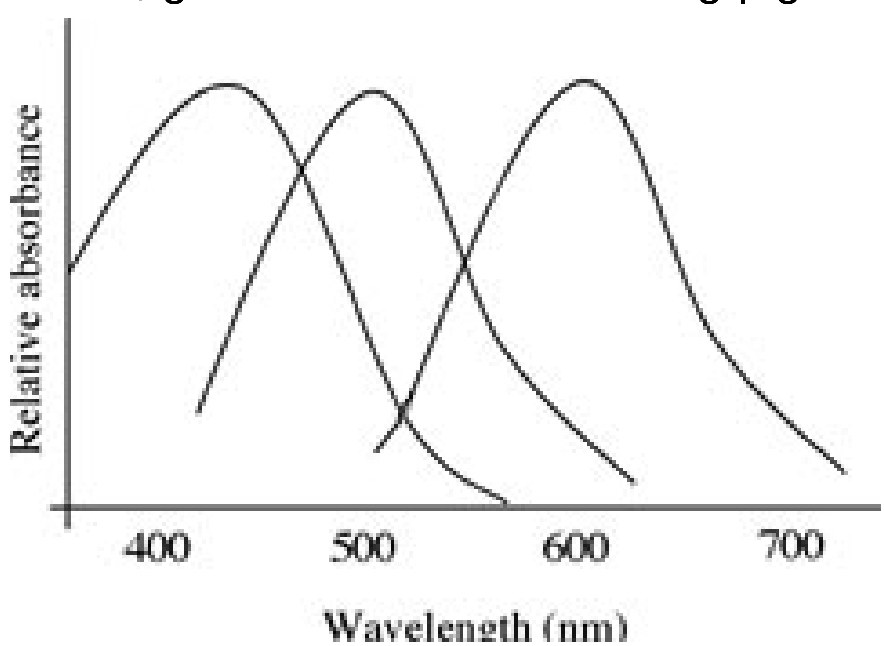
http://www.chemistry.wustl.edu/~edudev/LabTutorials/Vision/Vision.html#Signal

Color Vision—Cone Cells

Color vision in the cone cells operates by essentially the same process as the monochrome vision in the rod cells. However, whereas the eye only has one type of rod cell, the eye has three different types of cone cells. The differences between the three types of cone cells, allow us to distinguish colors.

Every color in the visible spectrum can be made by a mixture of the three primary colors recognized by the three types of cone cells. Each type of cone cell contains a different protein bound to 11-*cis*-retinal and has its own characteristic absorption spectrum, corresponding to the particular pigment protein that it contains.

Goldfish red-, green- and blue-absorbing pigments



Only a few amino acids differ in retinal which is sensitive to blue, green & red.

http://www.chemistry.wustl.edu/~edudev/LabTutorials/Vision/Vision.html#Signal

Rods and Cones

Sharpness & Sensitivity

Rods are very sensitive to light
—seeing about a single photon.
Cones are not as sensitive
— but are useful for differentiating color
— create sharper images.

Why is this?

Brain reads from optic nerve,
which differentially takes signals from rods and cones.

Each cone connects to a single nerve.
Brain can tell exactly where light came from,
i.e. extremely sharp image.

Each rod may share a nerve with 10,000 other rods.
Less sharp. Yet more sensitive (?).

Thus, our ability to view images depends on the brain determining the location of the photoreceptor cell that passes an impulse to any given nerve fiber.

http://www.chemistry.wustl.edu/~edudev/LabTutorials/Vision/Vision.html#Signal

Color Perception Diff. Animals

• Perception of color is achieved in **mammals**.
In most primates closely related to humans there are **three** types of cone cells, although up to 10% of women have tetrachromacy!
• Nocturnal mammals: less-developed color vision.
• Honey- and bumblebees have trichromatic color vision, which is insensitive to red but sensitive in ultraviolet to a color called *bee purple*.
•Tropical fish and birds, may have more complex color vision systems than humans. In the latter example, tetrachromacy is achieved through up to four cone types, depending on species.
•Many other primates and other mammals are dichromats, and many mammals have little or no color vision. Marine mammals: a single cone type and are thus monochromats.
•Pigeons are likely pentachromats.
Many invertebrates have color vision. *Papilio* butterflies apparently have tetrachromatic color vision despite possessing six photoreceptor types. The most complex color vision system in animal kingdom has been found in **stomatopods** with up to 12 different spectral receptor types which are thought to work as multiple dichromatic units.

Wikepedia

Evolution: herbivore primates

Search for flowering plants

From Atoms to molecules to macromolecules to you!

3-6 elements make up majority of you.

About 3 dozen organic compound

-- precursors of almost all biomolecules

Body (Cell) uses 4 types of small molecules

1. Amino acids– make up proteins
2. Nucleic acids—DNA, RNA
3. Fatty acids/Lipids-- membranes
4. Sugars/polysaccharides/Carbohydrates— structural, food

What does body/cell uses 4 molecules for?

1. Building blocks
2. Energy Source
3. Information

Primarily made of 4 small molecules

1. Sugar :

2. Fatty acid :

3. Nucleotide

4. Amino acids

H2CHRCOOH: R= 1 or 20 side groups

Atoms combine to make small molecules & macromolecules of cell

Table 2-1 The Approximate Chemical Composition of a Bacterial Cell

	Percent of Total Cell Weight	Number of Types of Each Molecule
Water	70	1
Inorganic ions	1	20
Sugars and precursors	1	250
Amino acids and precursors	0.4	100
Nucleotides and precursors	0.4	100
Fatty acids and precursors	1	50
Other small molecules	0.2	~300
Macromolecules (proteins, nucleic acids, and polysaccharides)	26	~3000

Alberts, Mol Biol Cell

Minimal Requirements of Food

A complete diet must supply the elements; carbon, hydrogen, oxygen, nitrogen, phosphorus, sulfur, and at least 18 other inorganic elements. The major elements are supplied in carbohydrates, lipids, and protein. In addition, at least 17 vitamins and water are necessary. If an essential nutrient is omitted from the diet, certain deficiency symptoms appear.

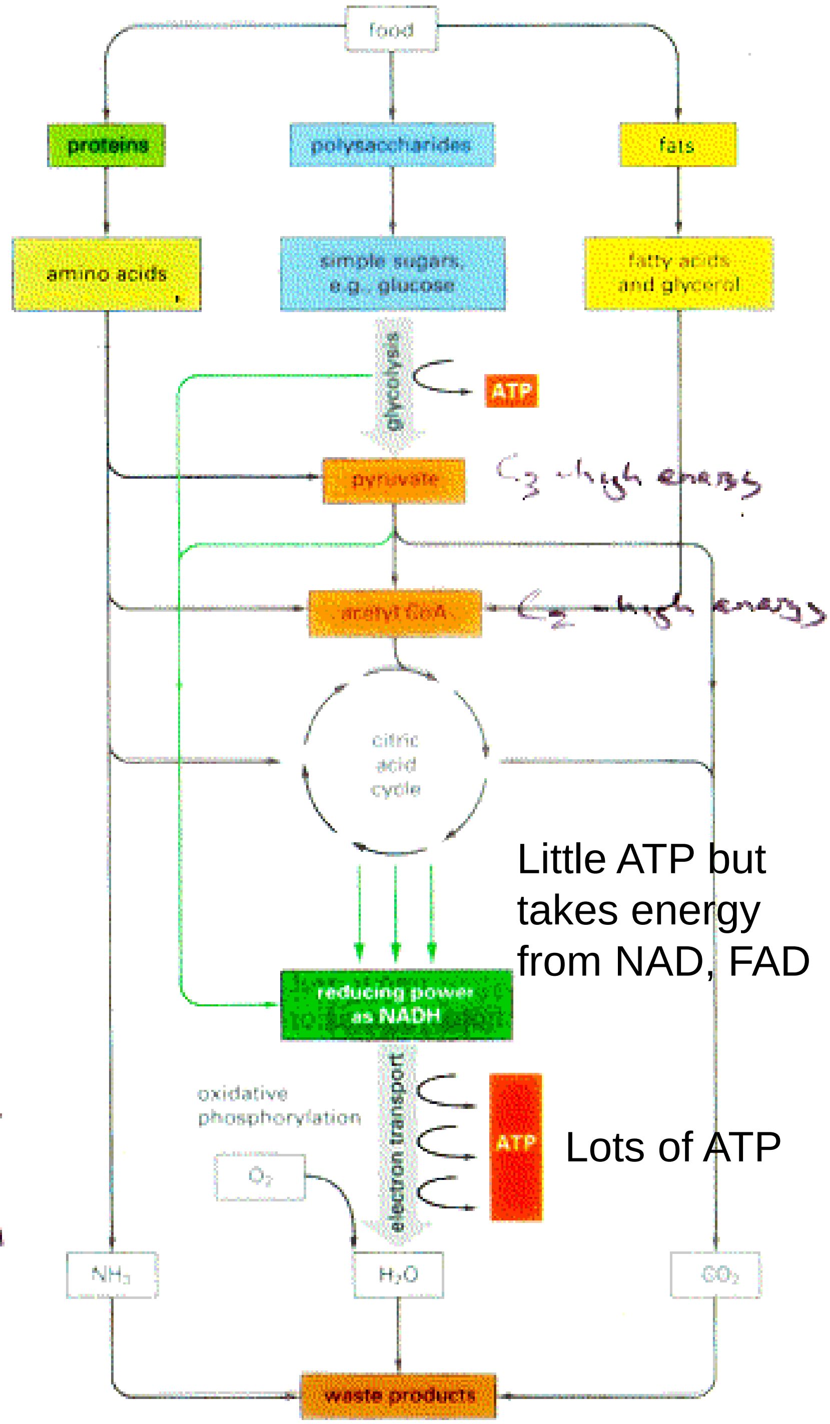
http://www.elmhurst.edu/~chm/vchembook/5900verviewmet.html

Energy from Food

1. Breakdown of large macromolecules

2. Breakdown of simple subunits to pyruvate, acetyl CoA plus limited ATPs.

Citric acid/Krebs cycle. Compplete oxidation of Acetyl CoA to $H_2O + CO_2$ and large amouns of ATPs



Pyruvate $CH_3-C(=O)-COO^-$

Acetyl CoA $CH_3C(=O)-CoA$

1 Glucose → ≈ 30 ATP

Amino Acids

1. Building blocks

    -- Make proteins

2. Energy Source

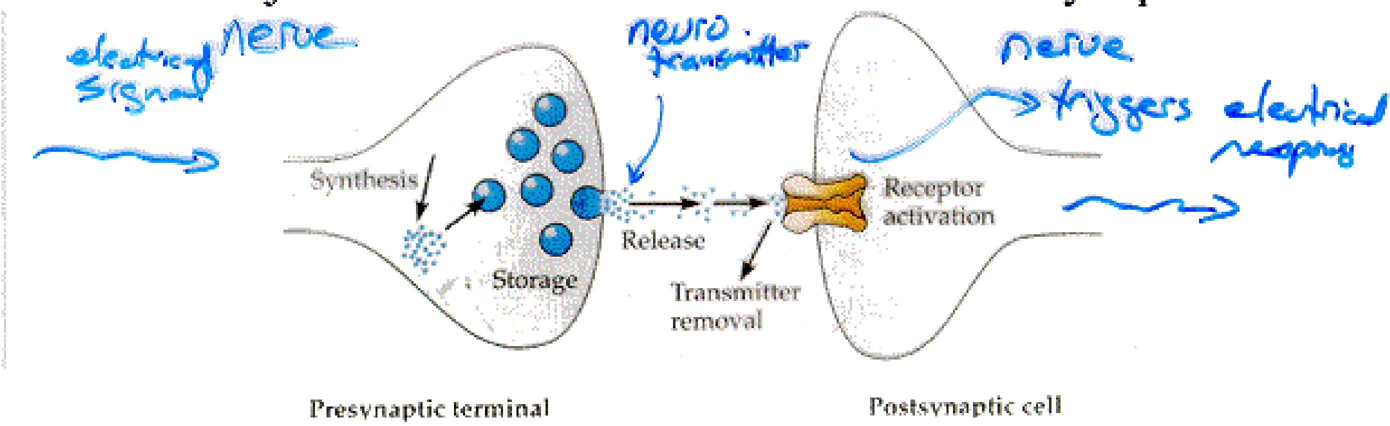
    -- Eat proteins

3. Information

    -- Signaling between cells/nerves

Amino Acids are used in Signaling.

Mammalian central nervous system,
3 major transmitters act at direct chemical synapses:

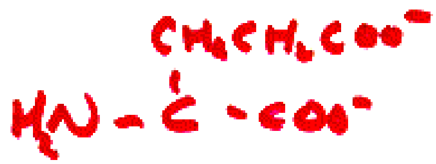


From Neuron to Brain, Fig. 13.1

1. Glutamate, 2. Aminobutyric acid (GABA), 3. Glycine

Glycine

Glutamate



GABA: (made from glutamate)

Amino Acids are used as energy source

Surplus a.a. beyond that needed to make proteins
are broken down (burned)
[a.a. can't be stored, not excreted]

Amino acids broken down into
Pyruvate (high energy 3-carbon compound) + **urea**
(amine-containing waste)

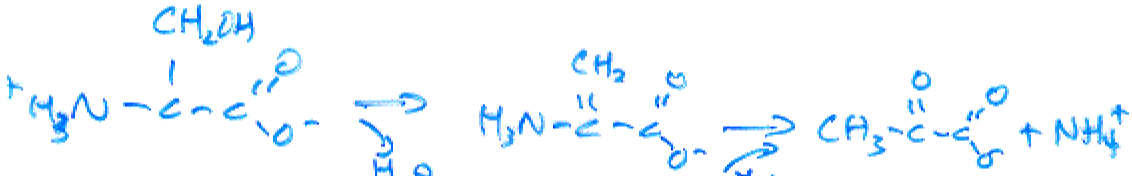
Eat proteins → indiv. a.a. in stomach
Body takes a.a. → makes own proteins
extra a.a. → used up / burned to
create ATP...
+ waste.

urea → waste.

Pyruvate

3-carbon high energy
compound.

Example of amino acid breakdown



Serine

$NH_4^+ \ldots \rightarrow$ urea (urine)

Common theme in energy utilization in body

Break down glucose you also make pyruvate!

$(CH_2O)_6 \xrightarrow[\text{(anaerobic)}]{\text{Glycolysis}} 2\ CH_3C(=O)-COO^- + 2\ ATP \xrightarrow{O_2} CO_2 + H_2O + \approx 28\ ATPs$

$\rightarrow CH_3CH(OH)-COOH$ Lactic acid

yeast $\rightarrow CH_3CH_2OH$ ethanol

Energy from proteins (a.a.) + from sugar both end up as pyruvate which is then broken down to yield most of ATP you get out.

Proteins, sugar → Pyruvate→ ATP

Sugars = Carbohydrates

1. Building blocks

   -- Make complex sugars… glucose, glycogen (polymer of glucose

   Holds your cells together--Extra-cellular space filled with sugars

   Cellulose (if a plant)

2. Energy Source

   -- Eat Hershey's chocolate!

   Glucose makes 30-40 ATPs

3. Information

   -- A lot! Much information.

   Signaling that you are different than a pig.

Carbohydrates

Energy Transduction: Life is a slow burn.

Fire

wood - cellulose C, H, O.

CH$_2$O

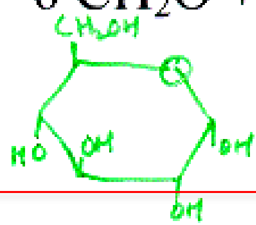
Carbohydrate + O$_2$ → products.

P.E. chem bonds → released into heat (random K.E)

Life is a slow burn.

$$6\ CH_2O + O_2 \rightarrow 6\ CO_2 + H_2O + \text{energy}$$

convert. electrochemical energy of carbohydrate into P.E. of proton gradient → ATP.



30-40

Glucose Energy = 30ATP at 20-25 kT/ATP
= 600-750kT = 2 x 10^{-18}J

Explains:

a. Why we breathe in oxygen

b. Why we breathe out CO$_2$.

c. Why some animals (gerbils, kangaroo rats, camels) can go for long time w/o external water.

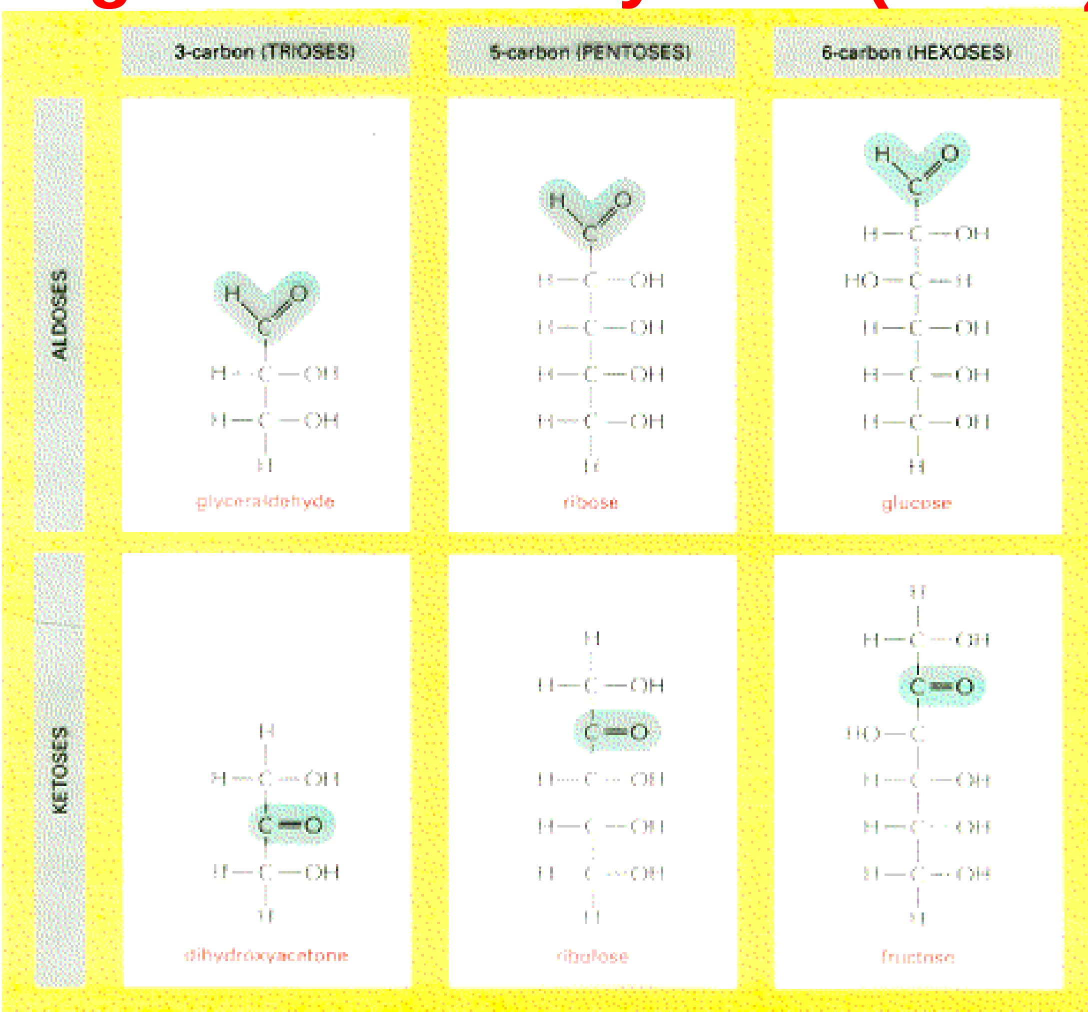
d. We are reverse plants.

Definition of Sugar ≡ carbohydrate ≡ saccharide

Monosaccharide: $(CH_2O)_n$ $n = 3\text{-}8$
2 or more OH groups;
(Precursor or) Sugar contains, C=O (aldehyde, ketone).

Polysaccharide = $(\text{Monosaccharide})_m$

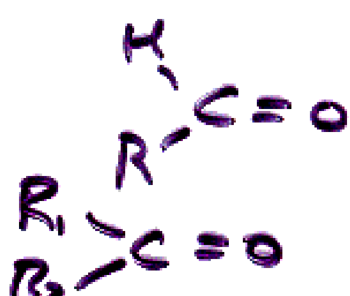
Sugar is a carbohydrate (C + H_2O)



ECB. pg 56

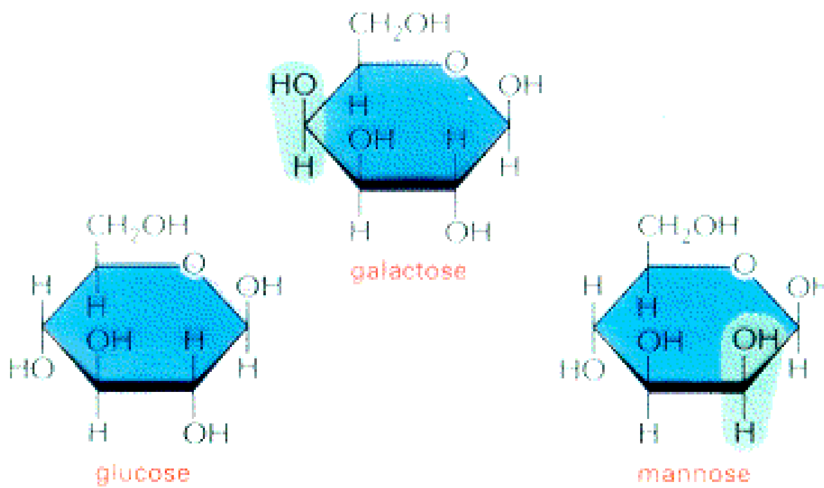
Aldehyde:

Ketone:



Monosaccharides have isomers

Same chem. formula, different spatial arrangement.



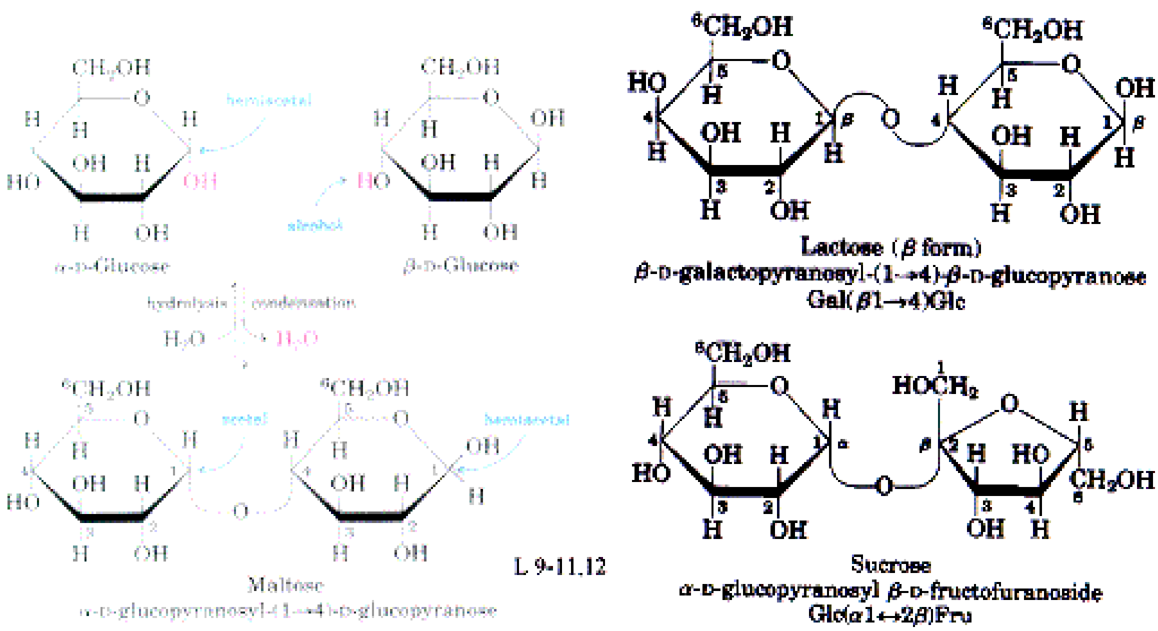
Small chem. differences but enzymes recognize isomers differently – significant biological effect.

# of possible polysaccharides increased enormously. Info. content high.

Sugars are used as energy sources.

Glucose… di-saccharides…

$(CH_2O)_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$ + Energy (36-38 ATPs)

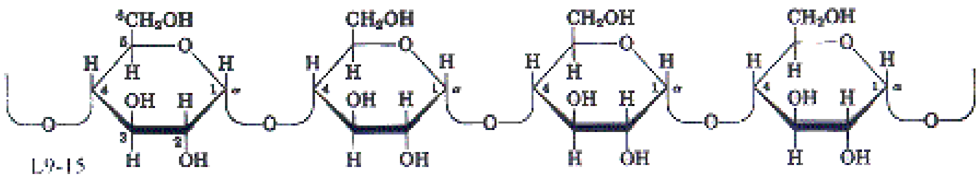


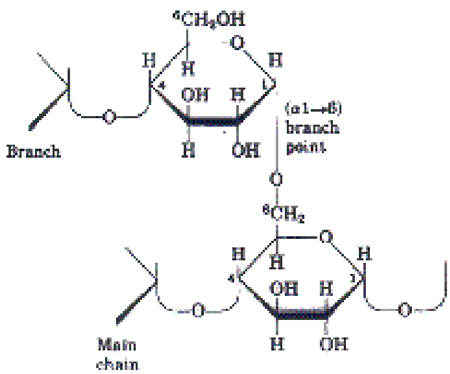
Sucrose & Lactose broken down into Glucose then into Pyruvate and then into ATP as energy.

Glycogen in bacteria, animals.

Linear + branched (every 8-12 units) glucose, up to 50k.

With Enzyme can digest!





Why can eat (breakdown) both starch and glycogen?

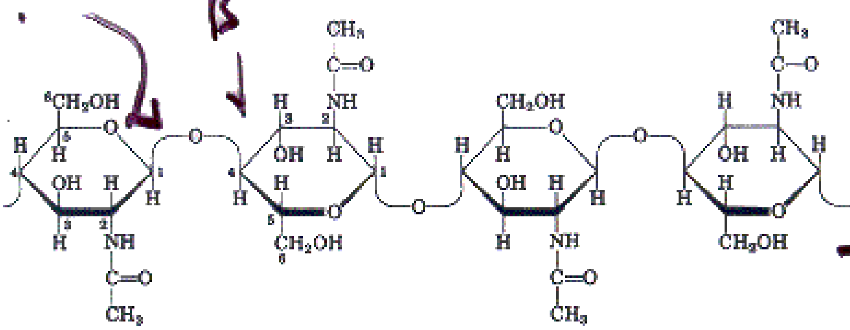
Same $\alpha_1 - \alpha_4$ bond
Enzymes break down.

If no Enzyme can't digest!

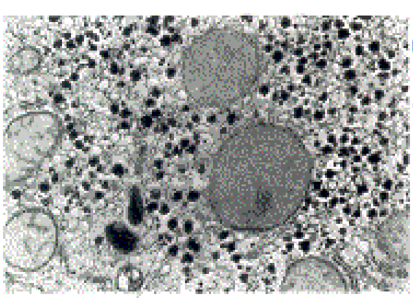
β!

Cellulose (<15k) / Chitin (v. large)

β

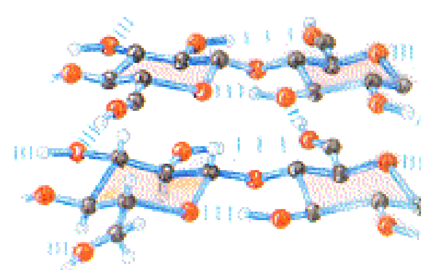


β-β bond conf.
we do not have enzymes to cut



Glycogen granules

Wood sheets.



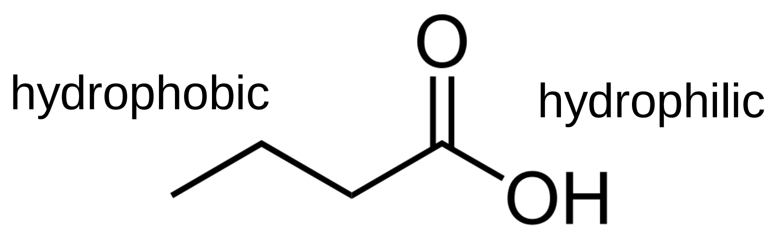
Why can't we digest Cellulose?

We can't eat cellulose
... but other animals can.

Fatty Acids/ Lipids

(Lipid– not dissolve in water)

Carboxylic acid with an aliphatic tail



1. Building blocks

-- Make membranes.

2. Energy Source

 -- Eat fat

3. Information

 -- Signaling that you are different than a pig.

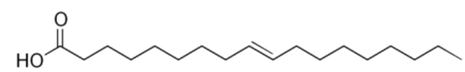
Definition of Fatty Acids

Def'n: contain long hydrocarbon tails.

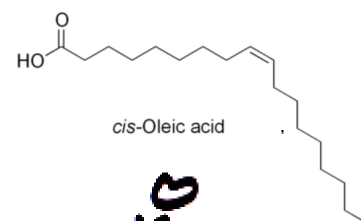
- end in $C(=O)O^-$ (carboxylate group)

e.g. palmatic acid

$CH_3-(CH_2)_{15}-C(=O)O^-$



trans-Oleic acid



cis-Oleic acid

Diff. fatty acids

- diff lengths

$CH_3-(CH_2)_n-C(=O)O^-$

- # of double bonds in chain

$CH_3-CH_2-CH_2\sim\sim CH=CH-CH_2\ldots$

All single bond (saturated)

↳ as many H's as possible

Some double bonds

- unsaturated.

Unsaturated - "good" to eat.

Fatty Acids & Fat

Fatty acids are combined to make fat

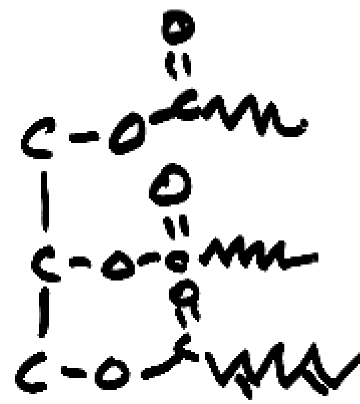
Most common fat in our bodies

Triglycerides

H_2C-OH
$|$
H_2C-OH
$|$
H_2C-OH

glycerol

+ 3 fatty acids →



Fat

Can have 2 or 3 diff. fatty acids on one fat.

Form fat drops

specialized cells – almost all fat drops (adipose cells)

Fat = Energy Source

Fat - energy

hydrocarbons - look a lot like gasoline,

$CH_3 - CH_2 -- CH_2 ---$

octane ⇒ 8 c

Burn for energy

2x useable energy/g than glucose
6x " " " " glycogen

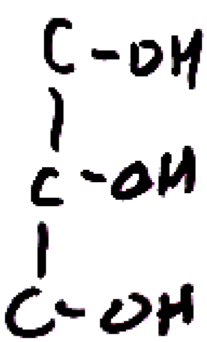
Break down fats
↳ 2-carbon intermediate
(acetyl co-enzyme)

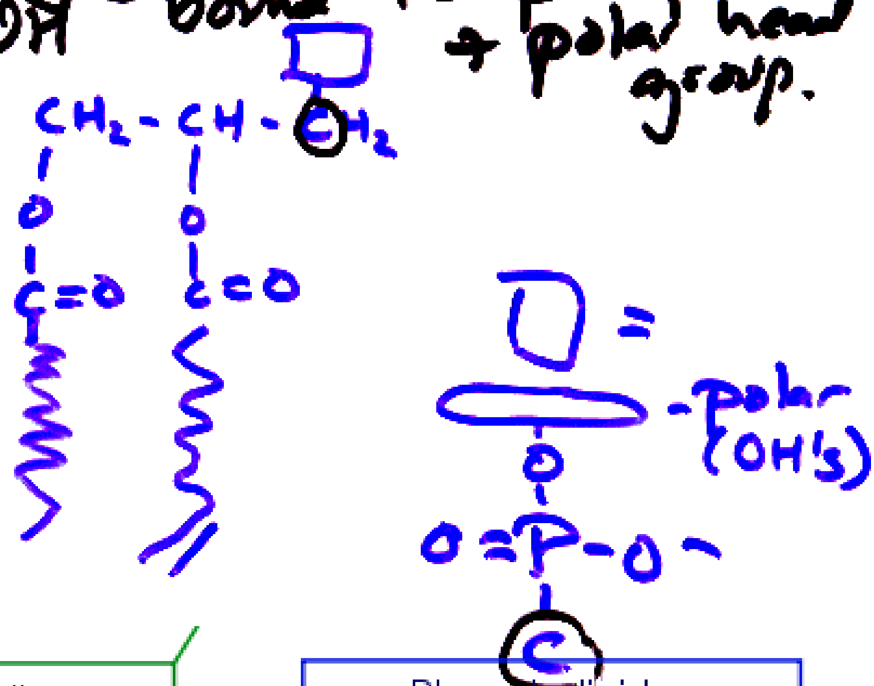
→ intermediate sent into Kreb

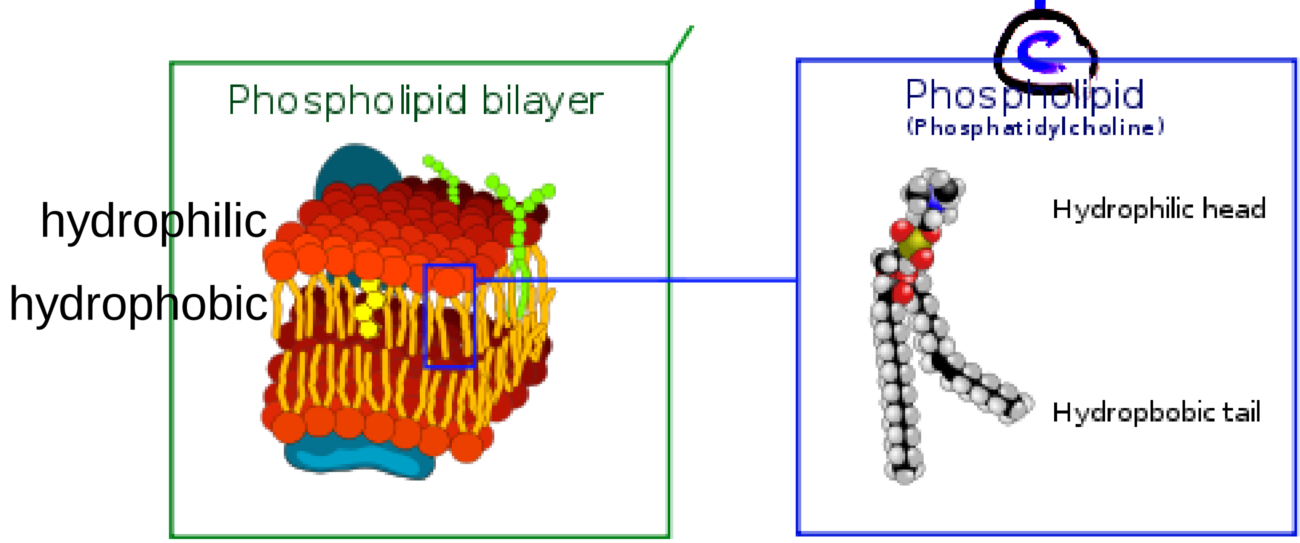
Fatty acids combine to make phospholipids
→ which make up membranes.

(lipid = compound which part/all does not dissolve in H_2O)

Like triglycerides except 3rd OH bond to phosphate + polar head group.







Lipids—low dielectric constant, excludes Ions, used a lot.

Hydrophic core of cell membranes

→ low dielectric const. because not polarizable.

→ insulator

① ②

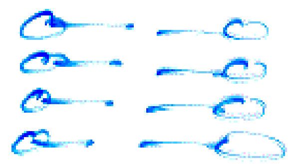
H
|
H — O δ^-

$\epsilon = 2$

Na^+

H_2O

$\epsilon = 80$



Na^+

$\epsilon = 80$

Energy of Na^+ in H_2O is much lower (ϵ_1/ϵ_2) in H_2O than in dielectric.

Charges cannot get through cell membrane!

[ionic] inside cell + outside cell can be different

→ Used all the time

Na^+
K^+
Ca^{++}
H^+

nerve cell

$[Na^+]_{in}$ diff $[Na^+]_{out}$

Opening in membrane that allows Na^+ to flow

Sugars are used as signals

Recognition of cells

Signal where to send glycoproteins

Science, 4 Jan 2002, pg 25

XENOTRANSPLANTATION

Cloned Pigs May Help Overcome Rejection

The cloning of Dolly the sheep nearly 5 years ago raised the hopes of transplant scientists looking for an endless supply of lifesaving organs. It was a key step toward creating a line of identical animals genetically engineered so their organs could be used in people. Now, a team led by researchers at the University of Missouri, Columbia, has made another major advance—the creation of four cloned piglets that lack one copy of a gene that causes pig organs to be rejected by the human immune system.

"This is something that's been eagerly awaited," says immunologist Jeffrey Platt of the Mayo Clinic in Rochester, Minnesota, an expert in xenotransplantation, or animal-to-human transplants. The work, published online this week by *Science* (www.sciencexpress.org), brings researchers halfway to their goal of producing live pigs lacking both copies of the gene. It puts the Missouri group ahead of a pack of companies, one of which has just welcomed the birth of knockout pigs, that are pursuing the same goal.

Pigs are the most promising species for organ transplants because they are physiologically similar to humans and, unlike nonhuman primates, are in plentiful supply. But progress in the field has been slow for two reasons—the fear of new viruses being transmitted from pigs to humans and the almost certain rejection of the transplanted organ.

Pigs produce a sugar, a link between two galactoses, on the surface of their endothelial cells that humans and Old World monkeys do not make. Primates' immune systems recognize this sugar as a foreign antigen and attack the pig cells, leading to "hyperacute rejection" and organ failure.

Researchers have addressed the problem by endowing transgenic pigs with protective proteins to counter the immune response, which has allowed the organs to function in primates for months rather than days. But the only complete solution is thought to be a pig lacking the gene for the enzyme galactosyltransferase that makes the sugar. Cloning technology raises the possibility of disrupting, or knocking out, this gene in cultured cells, then inserting the nucleus of the modified cells into an empty pig egg to create embryos.

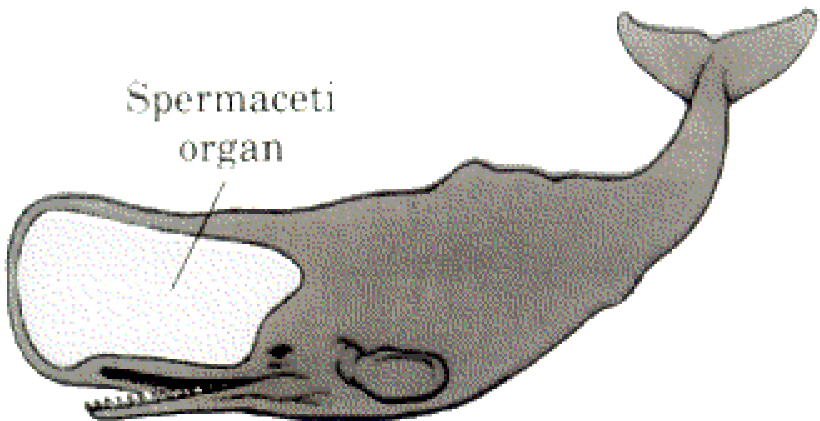
The first cloned pigs were created in 2000 (*Science*, 18 August 2000, pp. 1118 and 1188). Now, animal scientist Randall Prather and his team at Missouri, along with collaborators at Immerge BioTherapeutics Inc. in Charlestown, Massachusetts, have knocked out the galtransferase gene in fetal cells used to make cloned piglets.

Handling rejection. This piglet lacks one copy of a sugar-producing gene that makes humans reject pig organs.

cell produces proteins
need to know where to target protein within cell
attach sugar to protein = glycoprotein
helps signal / "address" where to send protein

Sperm Whales: Fatheads of the Deep

4 tons of Fat used as variable floating device



Lehninger, box 11-1

Sperm whale head

1/3 total body weight
90% of head = 4 tons (3,600 kg) of blubber
= unsaturated fat (triglycerides) & wax

Normal whale body temp: 37°C fat = liquid.
Whale dives (1-3 km; 2 miles!), lays in wait to eat squid.
Cold water, more dense; fat freezes, becomes more dense.

Evolved to have right composition
of chain lengths/ saturation so at all depths,
whale is ≈ same density as water

Class evaluation

1. What was the most interesting thing you learned in class today?

2. What are you confused about?

3. Related to today's subject, what would you like to know more about?

4. Any helpful comments.

Answer, and turn in at the end of class.

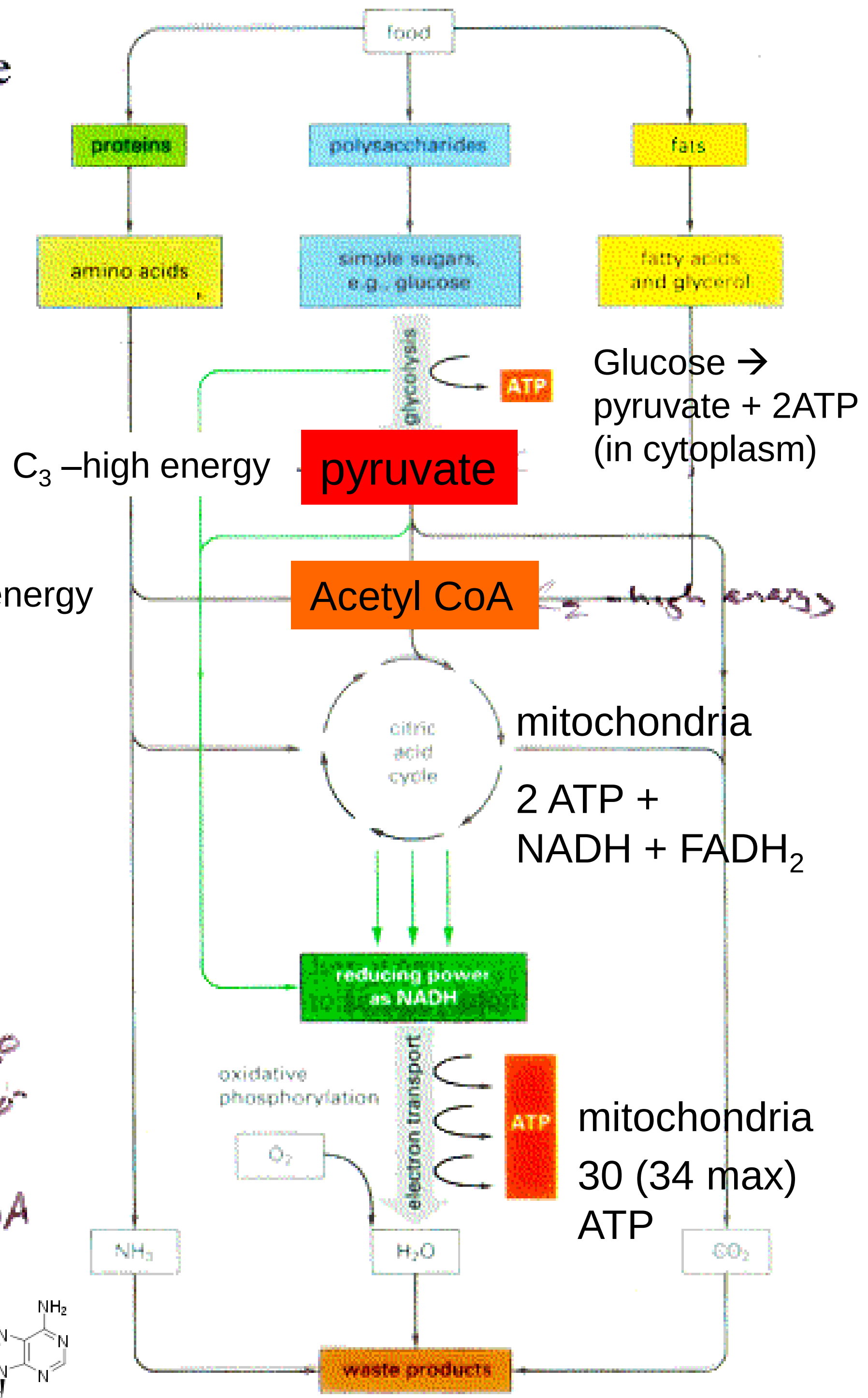
Energy from Food

1. Breakdown of large macromolecules

2. Breakdown of simple subunits to pyruvate, acetyl CoA plus limited ATPs.

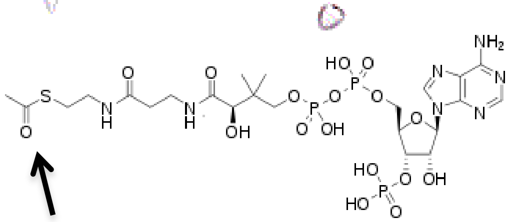
C_2 –high energy

Citric acid/Krebs cycle. ~~Compplete~~ Complete oxidation of Acetyl CoA to $H_2O + CO_2$ and large amouns of ATPs



Pyruvate $CH_3-\underset{\displaystyle O}{\overset{\|}{C}}-C{\overset{O}{\underset{O^-}{}}}$

Acetyl CoA $CH_3-\underset{\displaystyle O}{\overset{\|}{C}}-CoA$



Acetyl-Coenzyme A

The three major carbohydrate energy producing reactions are glycolysis, the citric acid cycle, and the electron transport chain.

Animated Glycolysis

http://www.johnkyrk.com/glycolysis.html

Multiple steps to get ATP and reduced NADP (NADPH) to enter the (Citric acid =) Krebs cycle in mitochondria to get more ATP.

If you were a biochemist, you'd have to know all of the steps! Aren't you lucky that you don't have to know them!

Interesting Details about Energy Storage

Energy storage:

Ave. human stores enough fat
to last ~month
∴ stores enough glycogen
to last ~day

If stored only glycogen
(no fat) you'd need to
be ~60% heavier

After overnight fast most of
acetyl coA that enters Kreb
cycle comes from fat (rather
than glucose, glycogen

After meal, most of acetylcoA
comes from glucose.
If eat more glucose than you can imm.
use → make glycogen or use glucose
to ult. make fat.