Today

Last lecture

Monday 4/28: no class

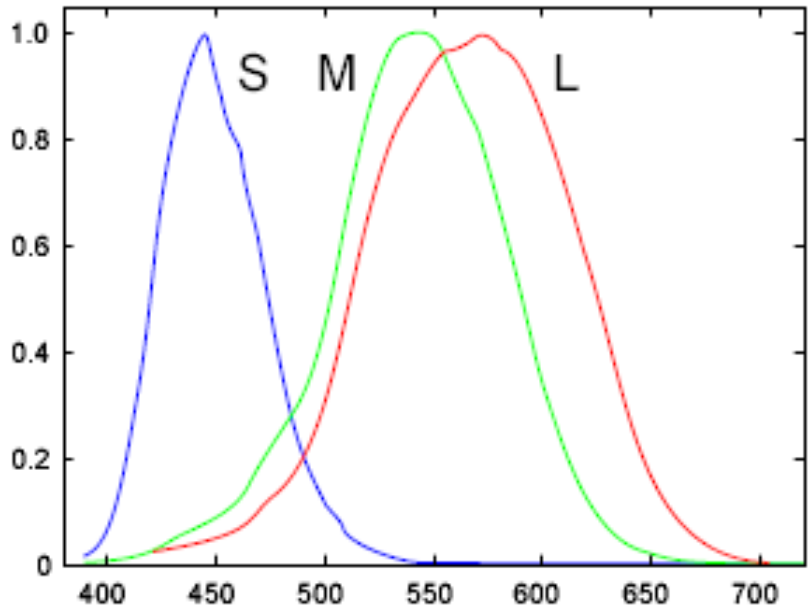
Wednesday 4/30: You present, morning in class, plus evening.

Friday May 2-Monday May 4th-Exam.

Would later be better?

May 9– Final paper due.

Cones & Color



Cone cells, which function best in relatively bright light, gradually become more sparse towards the periphery of the retina.
An average closer to 4.5 million cone cells and 90 million rod cells in the human retina.
Cones are able to perceive finer detail and more rapid changes in images, because their response times to stimuli are faster than those of rods.
Humans usually have three kinds of cones, with different photopsins, which have 3 different response curves, leading to trichromatic vision. People with **color** vision disorders usually have a deficiency or absence of **cone cells sensitive** to red or green wavelengths.

More on Color Vision

Cone type	Name	Range	Peak wavelength
S	β	400–500 nm	420–440 nm
M	γ	450–630 nm	534–545 nm
L	ρ	500–700 nm	564–580 nm

A range of wavelengths of light stimulates each of these receptor types to varying degrees. Yellowish-green light, for example, stimulates both L and M cones equally strongly, but only stimulates S-cones weakly. Red light stimulates L cones much more than M cones, and S cones hardly at all; blue-green light is the peak stimulant for rod cells. **The brain combines the information from each type of receptor to give rise to different perceptions of different wavelengths of light**.
The pigments present in the L and M cones are encoded on the X chromosome; defective encoding of these leads to the two most common forms of color blindness. The OPN1LW gene, which codes for the pigment that responds to yellowish light, is highly polymorphic (a recent study found 85 variants in a sample of 236 men).
Up to ten percent of women have an extra type of color receptor, and thus a degree of tetrachromatic color vision.

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
2. Nucleic acids
3. Fatty acids/Lipids
4. Sugars/polysaccharides/Carbohydrates

What does body/cell uses 4 molecules for?

1. Building blocks
2. Energy Source
3. Information

From Atoms to molecules to macromolecules to you!

What 3 elements make up 88% of body mass?

What 6 elements make up 99% of body mass?

What 4 elements make up 99% living weight of cell?:

Main food source of phosp? (meat, soda)

Formula?

Formula?

Formula?

Bones

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

Energy from Food

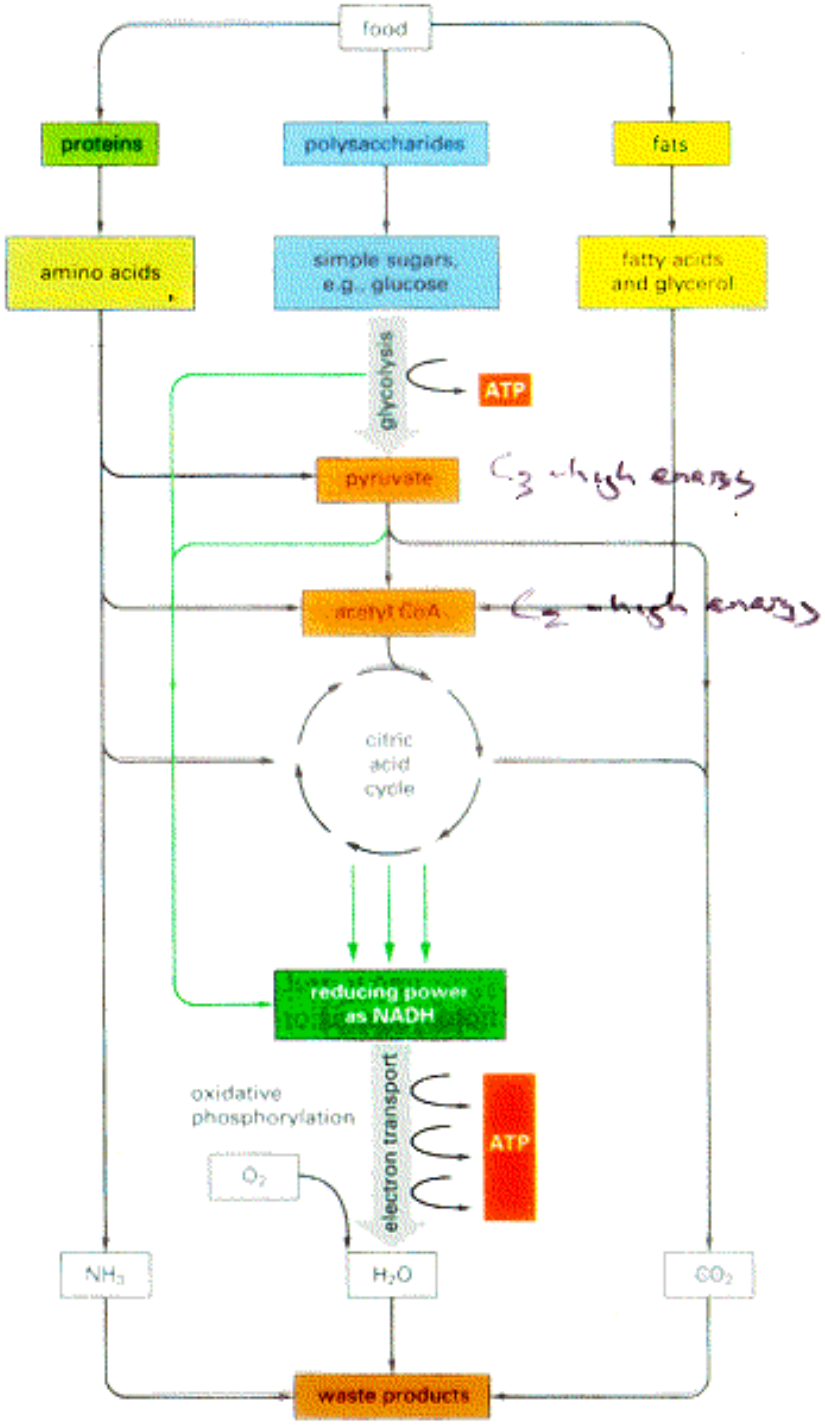
1. Breakdown of large macromolecules

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

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

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

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



Amino Acids

1. Building blocks

   -- Make proteins

2. Energy Source

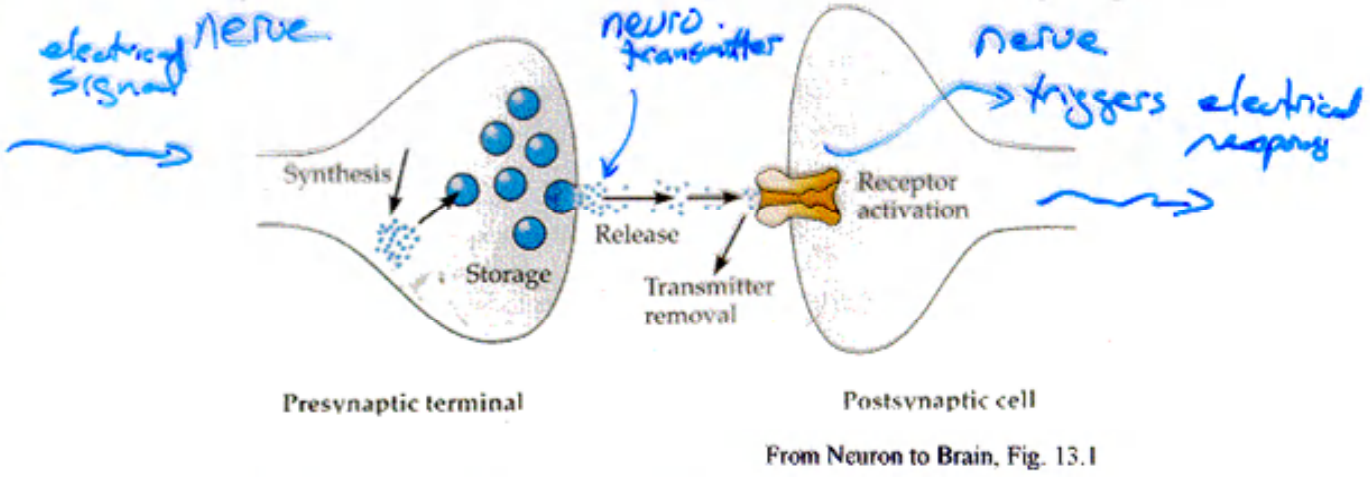
   -- Eat proteins

3. Information

   -- Signaling between cells/nerves

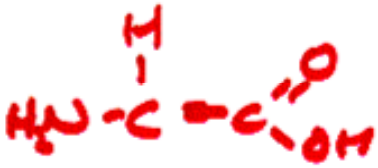
Amino Acids are used in Signaling.

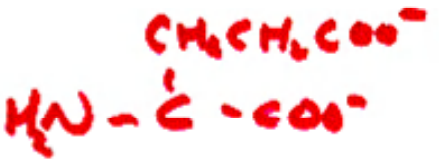
Mammalian central nervous system,
3 major transmitters act at direct chemical synapses:



From Neuron to Brain, Fig. 13.1

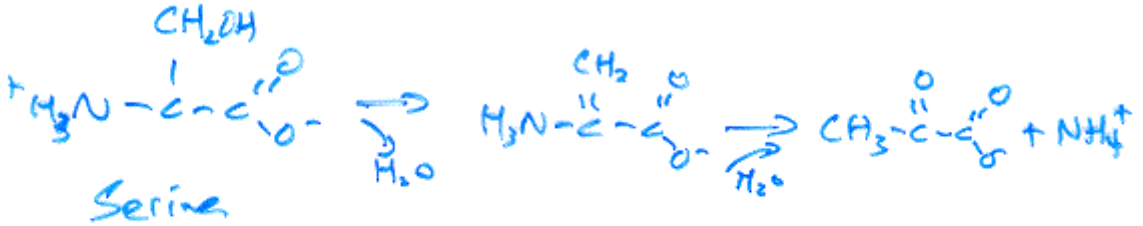
1. Glutamate, 2. Aminobutyric acid (GABA), 3. Glycine

Glycine 

Glutamate 

GABA: (made from glutamate)

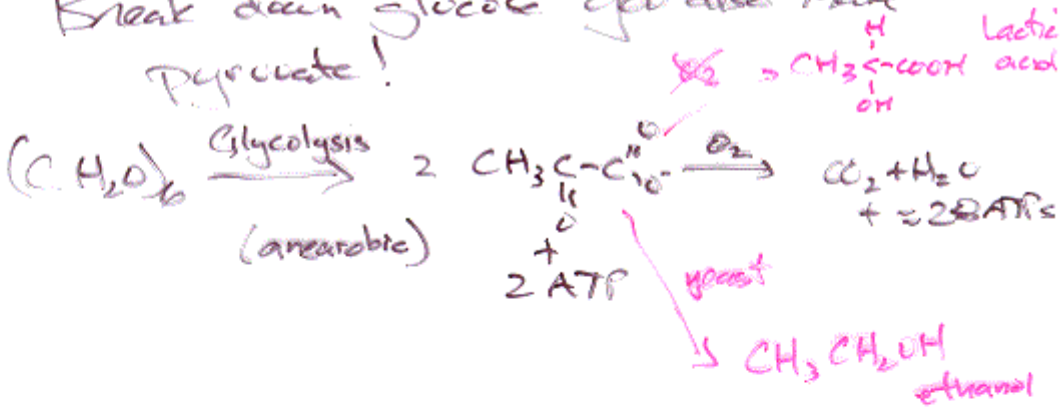
Example of a.a. breakdown



NH_4^+ ... → urea. (urine)

Common theme in energy utilization in body

Break down glucose you also make Pyruvate!



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.

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 40 ATPs

3. Information

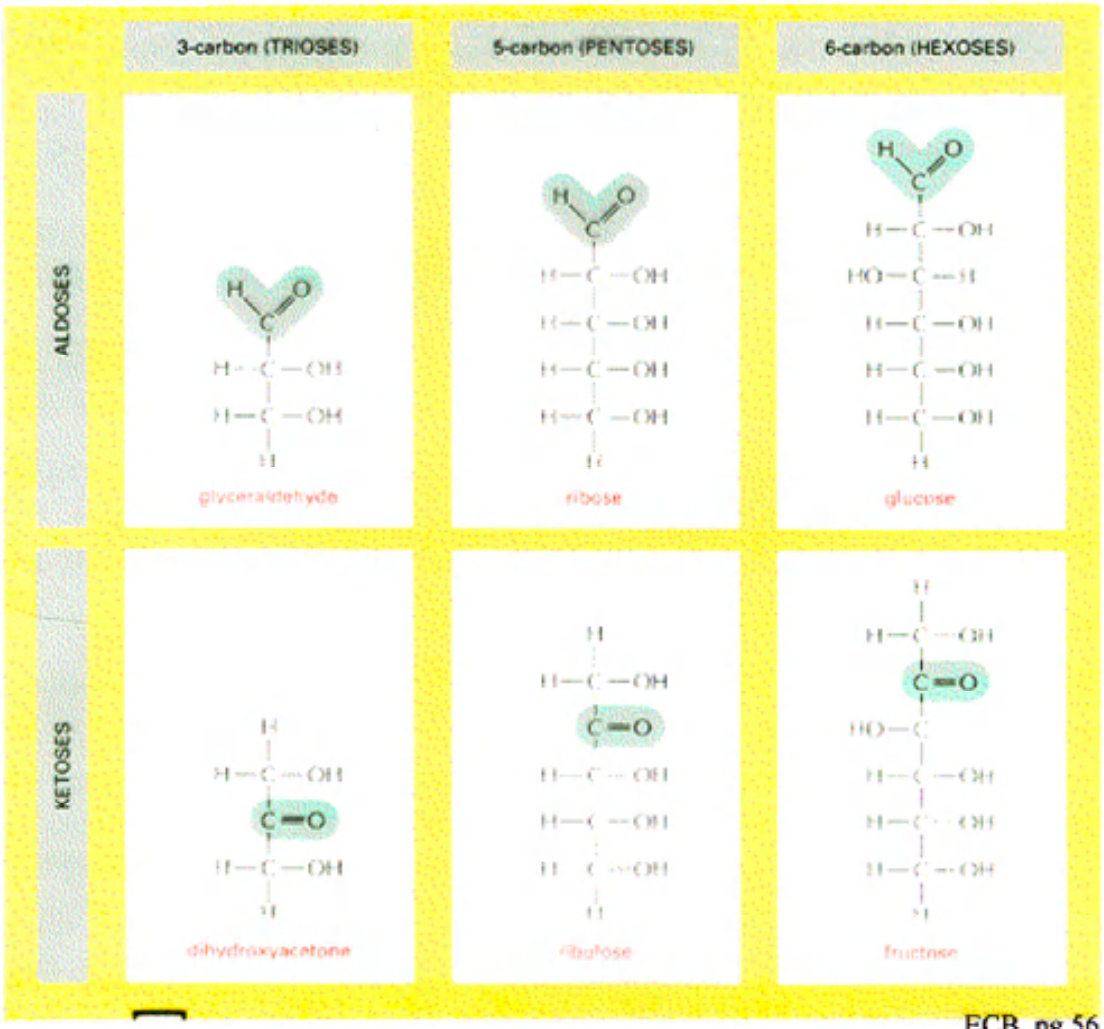
   -- A lot! Much information.

   Signaling that you are different than a pig.

Definition of Sugar ≡ carbohydrate ≡ saccharide

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

Polysaccharide = $(Monosaccharide)_m$



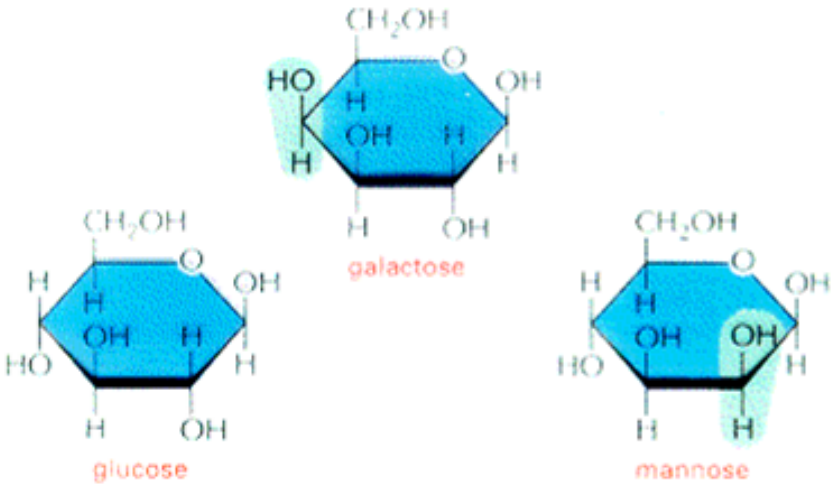
ECB. pg 56

Aldehyde: $R-C(=O)-H$

Ketone: $R_1-C(=O)-R_2$

Monosaccharides have isomers

Same chem. formula, different spatial arrangement.



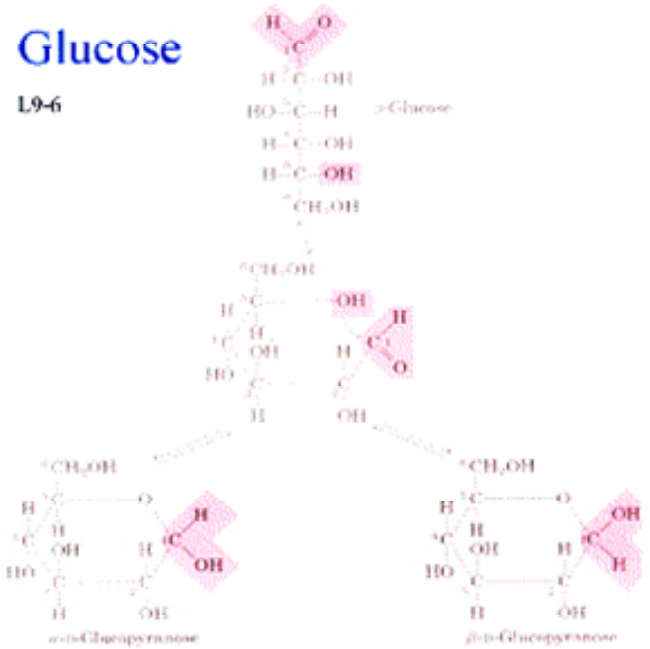
Small chem. differences but enzymes recognize isomers differently – significant biological effect.

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

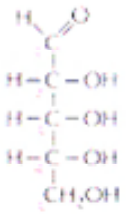
Sugars usually are in a ring-form.
Leads to two different linkages

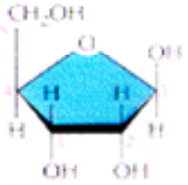
Glucose

L9-6



Ribose





ECB, pg56

RNA

ISOMERS

α AND β LINKS

The hydroxyl group on the carbon that carries the aldehyde or ketone can rapidly change from one position to the other. These two positions are called α and β.

β hydroxyl α hydroxyl

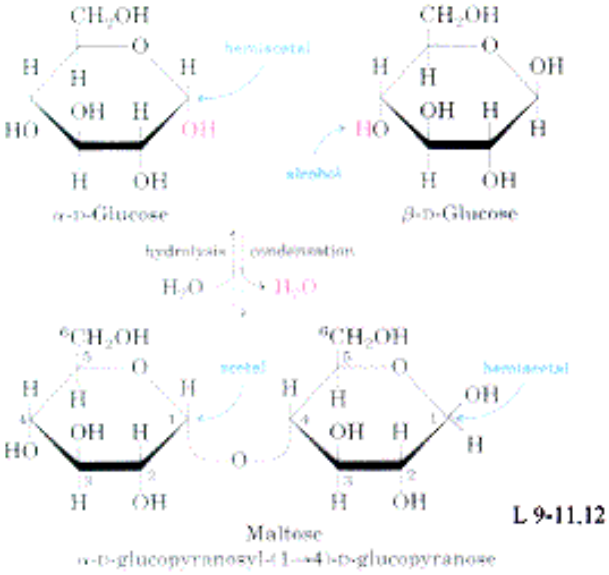
As soon as one sugar is linked to another, the α or β form is frozen.

α, β links determine shape/structure of polysaccharides: determine how sugars interact with enzymes (metabolism) and/or recognized (signaling).

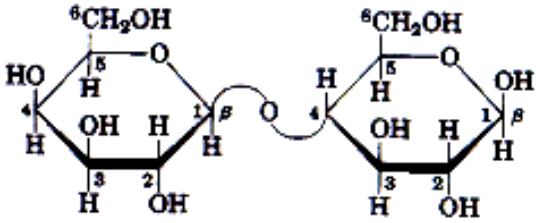
Sugars are used as energy sources.

Glucose… di-saccharides…

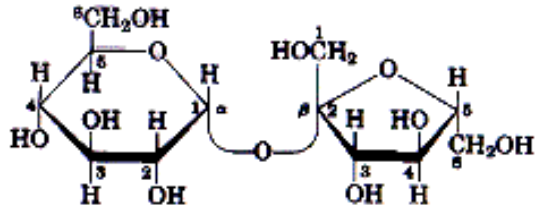
$(CH_2O)_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$ + Energy (36-38 ATPs)



L 9-11.12



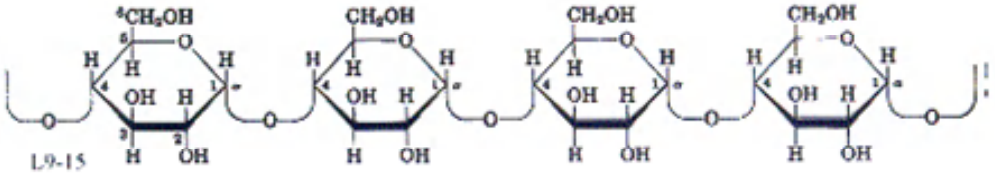
Lactose (β form)
β-D-galactopyranosyl-(1→4)-β-D-glucopyranose
Gal(β1→4)Glc



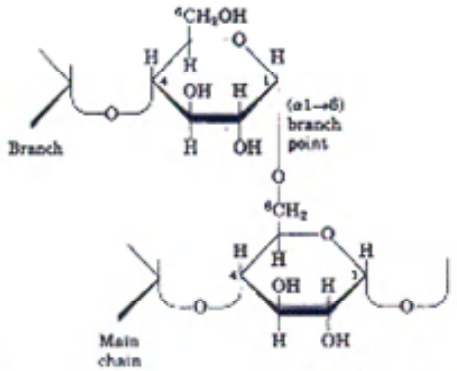
Sucrose
α-D-glucopyranosyl β-D-fructofuranoside
Glc(α1↔2β)Fru

Glycogen in bacteria, animals.

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



L9-15



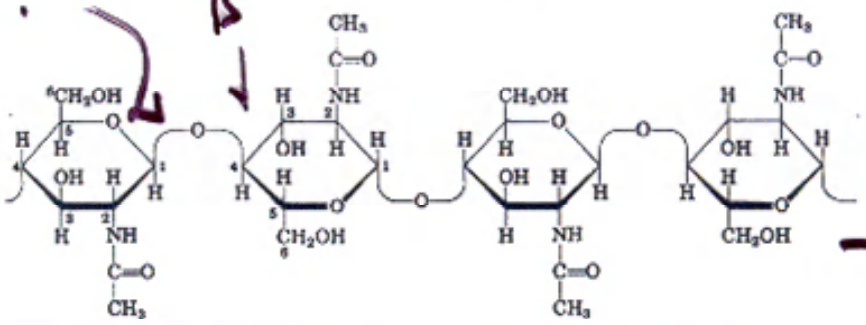
Why can eat (breakdown) both starch and glycogen?

Same π_1-K_4 bond
Enzymes break down

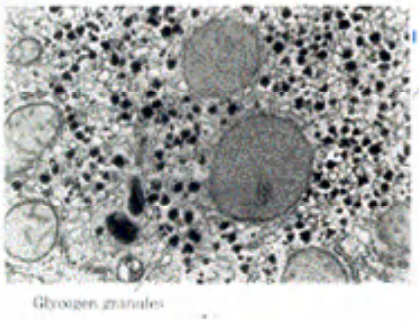
Cellulose (<15k) / Chitin (v. large)

B!

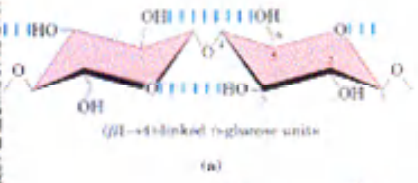
B



B-β bond conf. We do not have enzymes to cut

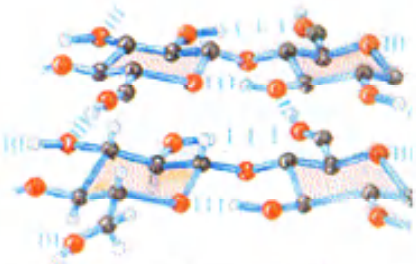


Glycogen granules



(a)

Wood Sheets →



Why can't we digest Cellulose?

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

Energy Transduction: Life is a slow burn.

Fire

wood - cellulose $C_6H_{10}O_5$

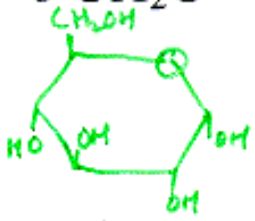
CH_2O

Carbohydrate $+O_2 \rightarrow$ 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 = 2×10^{-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.

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 life-saving 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.

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

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.

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

Fatty Acids/ Lipids

(Lipid– not dissolve in water)

1. Building blocks

   -- Make membranes.

2. Energy Source

   -- Eat fat (unsaturated, not saturated)

3. Information

   -- Signaling that you are different than a pig.

Definition of Fatty Acids

Defin: contain long hydrocarbon tails

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

e.s. palmatic acid

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

Diff. fatty acids

- diff lengths

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

- # of double bonds in chain

$CH_3-CH_2-CH_2-\cdots CH=CH-CH_2\cdots$

All single bond (saturated) ↳ as many H's as possible

Some double bonds - unsaturated.

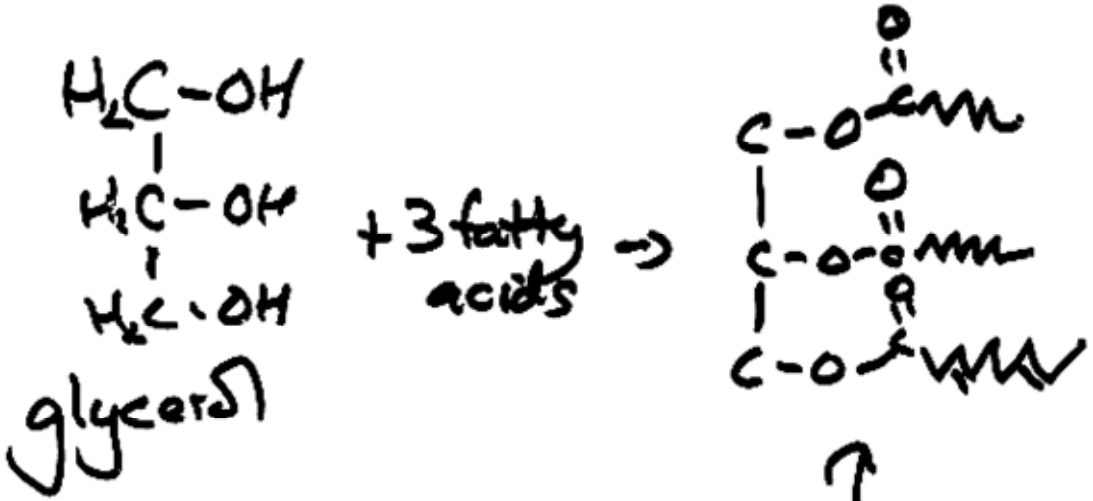
Unsaturated - "good" to eat.

Fatty Acids & Fat

Fatty acids are combined to make fat

Most common fat in our bodies

Triglycerides



glycerol

Fat

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

Form fat drops

Specialized cells - almost all fat drop (adipose cells)

Fat = Energy Source

Fat - energy

hydrocarbons - look a lot like gasoline,

$CH_3 - CH_2 - CH_2 - \ldots$

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

Energy from Food

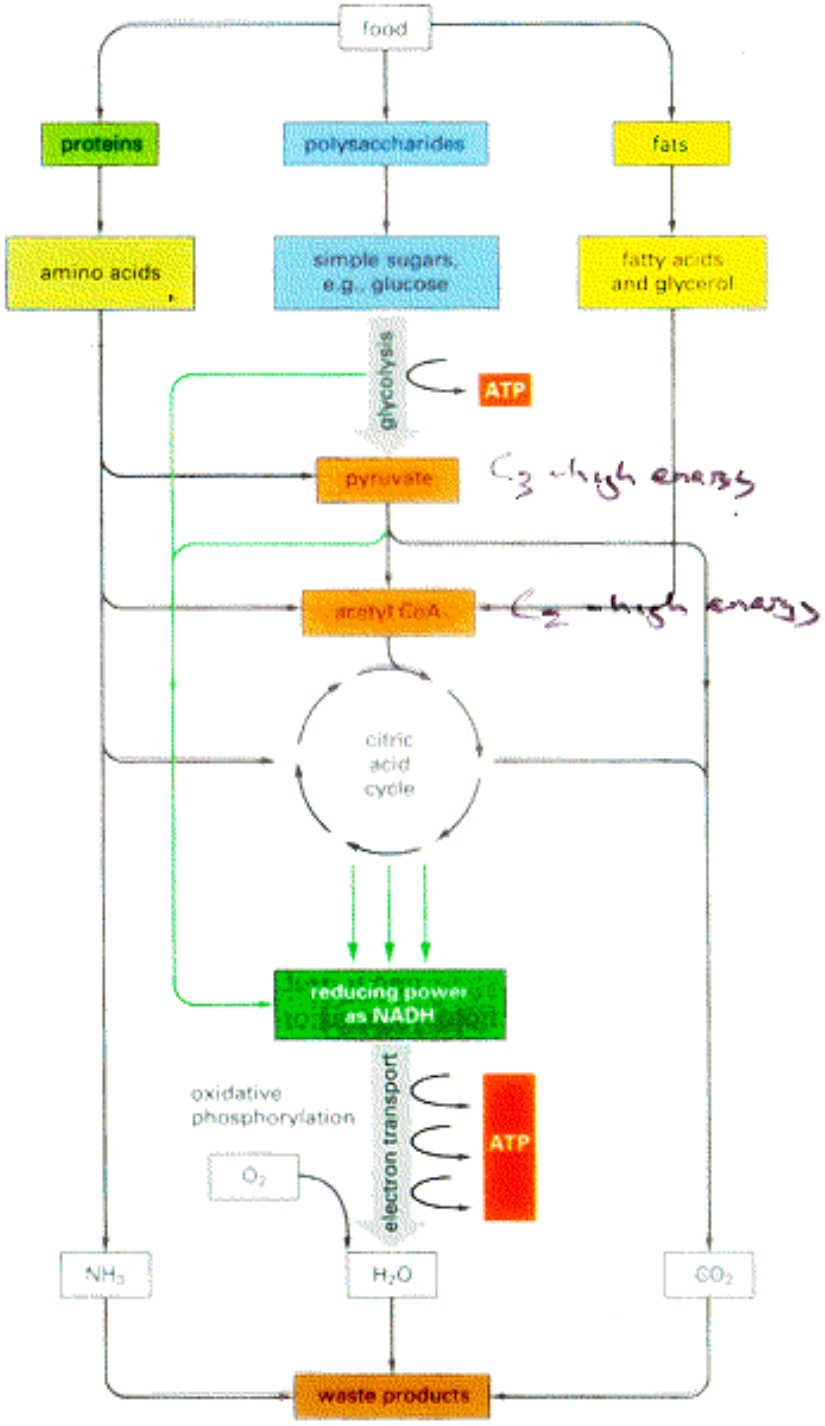
1. Breakdown of large macromolecules

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

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

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

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



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 fats) would need to be ~60% heavier

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

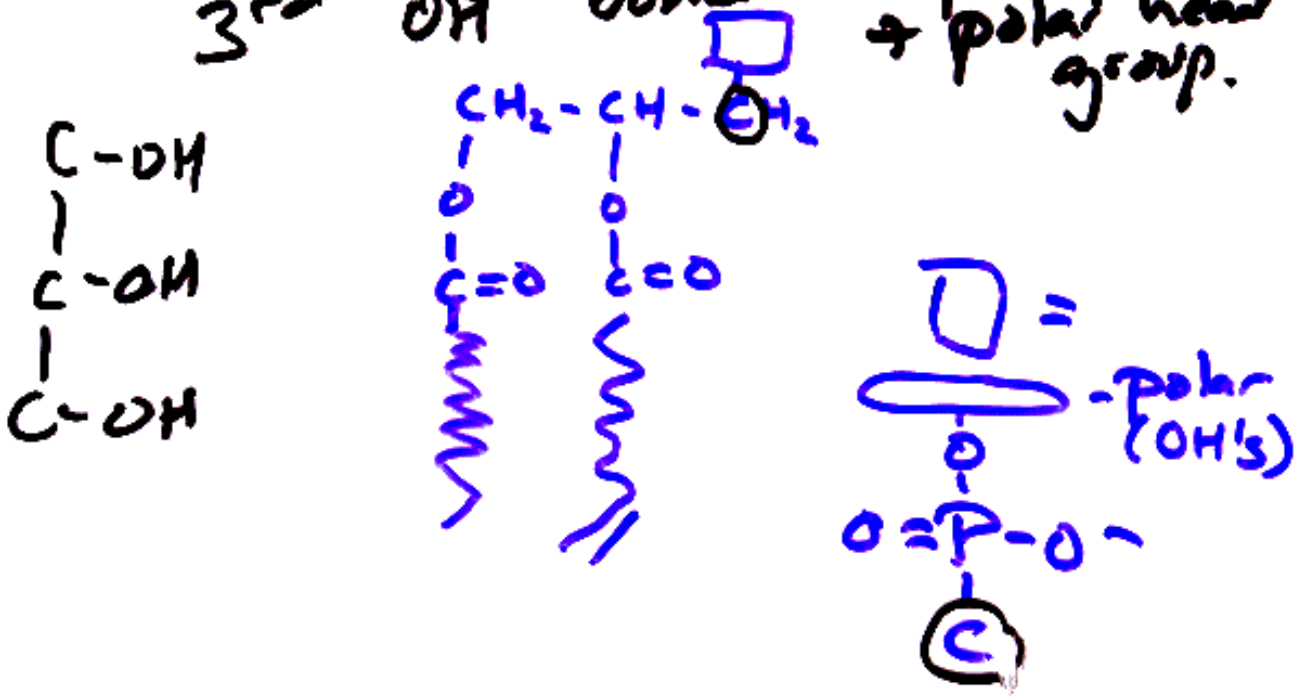
After meal, most of acetylcoA comes from glucose.

If eat more glucose than you can imm. use → make glycogen or use glucose to alt. make fat.

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

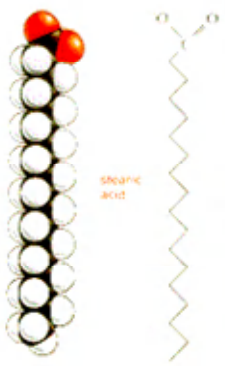
(lipid = compound which part/all does not dissolve in H_2O)

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



Fatty acids spontaneously form compartments i.e. membranes/cells.

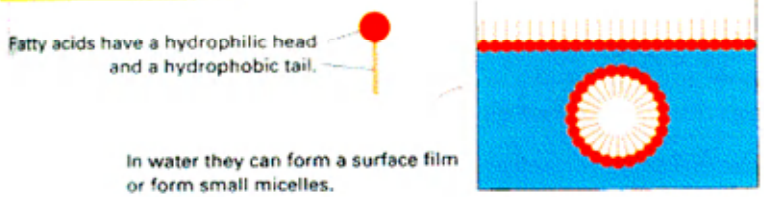
Hydrobophobic/hydrophilic effect in fatty acids.



Fatty Acid: (Carboxylic acids with long hydrocarbon chains)
Hydrophilic head, hydrophobic tail

[Lipid: Water insoluble molecules in cells: fats, steroids…]
Hydrophilic/Hydrophobic nature creates membranes/compartments.

LIPID AGGREGATES

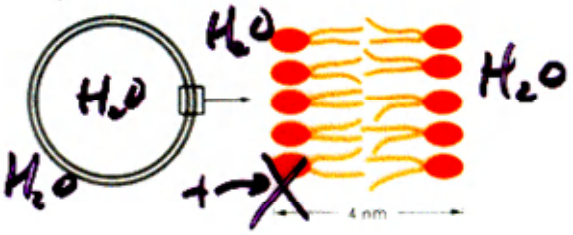


Their derivatives can form larger aggregates held together by hydrophobic forces:

Triglycerides form large spherical fat droplets in the cell cytoplasm.

Big mol. Cannot get through.

Phospholipids and glycolipids form self-sealing lipid bilayers that are the basis for all cellular membranes.



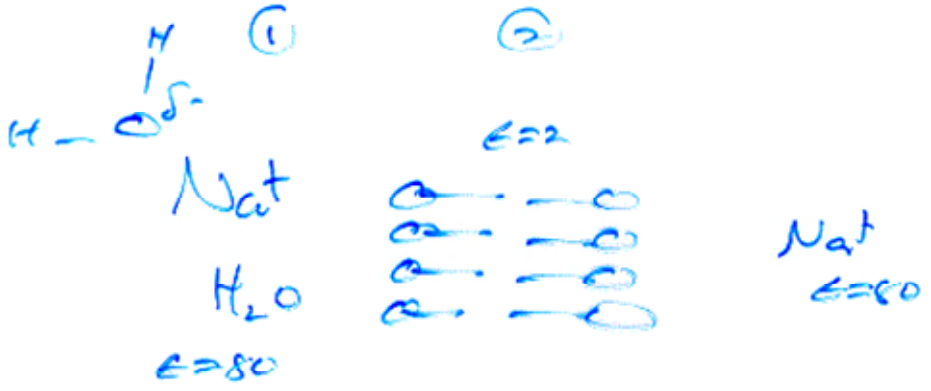
B. layer

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

Hydrophic core of cell membranes

→ low dielectric const. because not polarizable.

→ insulator



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!

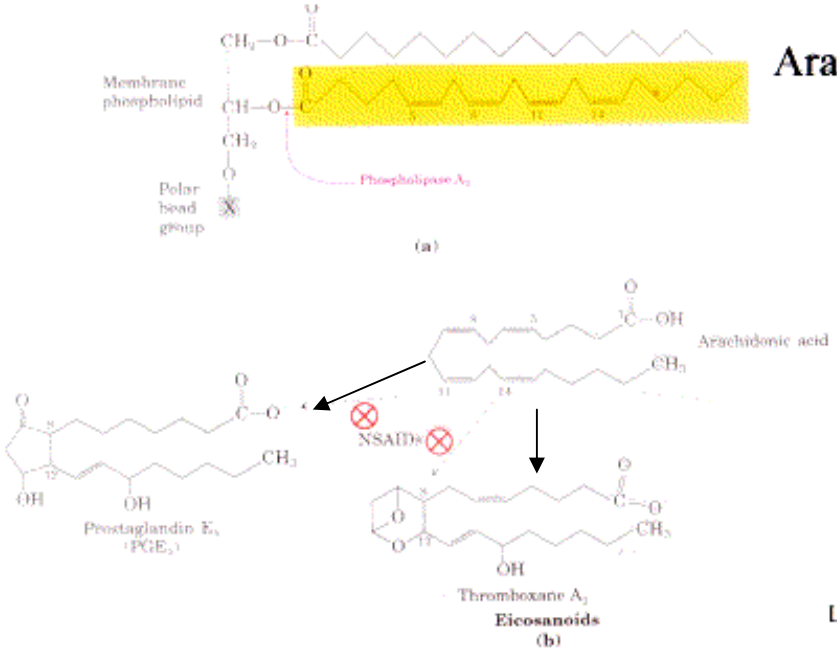
[ionic] inside cell + outside cell can be different

→ Used all the time

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

Nerve cell
$[Na^+]_{in}$ diff $[Na^+]_{out}$
Opening in membrane that allows Na^+ to flow

Fatty Acids are used as signaling precursors



Lehninger, Fig 11-16

Phospholipase A activated by hormonal signal.
Releases Arachidonic acid → Prostaglandins
by Prostaglandin H2 synthase (cyclooxygenase, or COX)
Produce fever, inflamation, pain, affect blood flow, sleep cycle….

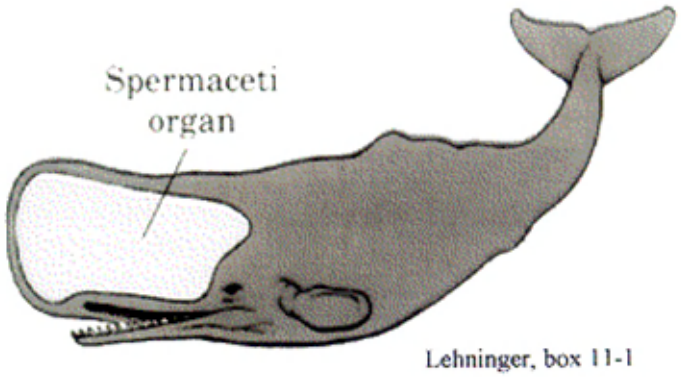
Thromboxanes, produced by platelets: blood clots, blood flow.

NSAIDS (aspirin, ibuprofen, acetaminophen are COX inhibitors.
Reduce swelling, pain, fever. Reduce chance of blood clots.

Big $$, Big lawsuits, pulled from shelves

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

US universities create bridges between physics and biology

[WASHINGTON] A number of leading US research universities are planning new institutes to bring physical and biomedical scientists together. This reflects a growing feeling that these fields should be linked more closely in both research and teaching.

One of the largest initiatives comes from Stanford University, where the Nobel-prizewinning physicist Steven Chu and biochemist James Spudich are spearheading a proposal for a research centre housing 50 faculty members, spanning disciplines from applied physics to clinical medicine.

Multidisciplinary research centres are also planned at the University of Chicago, which is setting up an 'interdivisional institute' straddling the biological and physical sciences, and the University of California at Berkeley, which is planning a building for its bioengineering department and some faculty members from molecular biology and several physical science departments.

In addition, Princeton University is due to announce plans this week for an interdisciplinary genomics institute in a new $40 million building connected to its molecular biology department.

About 10 of the 50 posts in the Stanford institute would be new positions. The proposal, which the university administration supports, calls for a new building of 200,000 square feet, which would make it one of Stanford's largest research centres.

University staff declined to estimate the project's cost. But the building alone would cost "tens of millions of dollars", according to Charles Kruger, dean of research.

Although some hurdles — including raising outside funds — remain to be cleared before the centre can receive formal approval from Stanford's board of trustees, its supporters expect the plan to go ahead, and hope to have the new building by 2002.

The project is currently called 'Bio-X', reflecting the desire to mix biologists with researchers from other disciplines, but without an explicit agenda of techniques to be used or problems to be solved.

"We just want to mix smart people together in an interdisciplinary environment, and let nature take its course," says Spudich. The new building will be between the medical school and the science departments, and Spudich hopes it will draw people in from the surrounding buildings.

The promise of the centre has already attracted one prominent new faculty member to Stanford. Princeton biophysicist Steven Block, a pioneer in the use of 'optical tweezers' to study molecular motors, has accepted a joint appointment in Stanford's applied physics and biology departments, starting in September.

Bio-X is motivated partly by the growing perception that a deeper understanding of complex biological systems will need a more quantitative type of biology that is closely integrated with the physical sciences.

Much of molecular biology already relies on experimental techniques invented by physicists, such as NMR and X-ray diffraction. But as biology becomes more data-rich, it increasingly requires the analytical and computational methods characteristic of the physical sciences.

At the same time, physicists are finding new problems in biology. For example, Chu, who won the Nobel prize for work on laser cooling of trapped atoms, now also works on the behaviour of single protein molecules.

The desire to bring together scientists from different disciplines stems from an awareness that traditional departments can be physical barriers to cross-fertilization. This is part of the thinking behind Princeton's new institute, planned to be built within two years, with about 12 faculty drawn from physics, chemistry, mathematics and engineering, as well as from biology.

Developmental geneticist Shirley Tilghman, the institute's director, says it will focus on what she calls "integrative biology" — the integration of many kinds of information to understand complex biological processes, such as interactions between cells or genes.

"Biology has thrived in the past 50 years by taking things apart and identifying their components," says Tilghman. "But there is a consensus in the field that the time is coming very soon to reverse the process" — to study how these components interact to form complex systems.

Chicago approved its interdivisional institute in June 1997, and two co-directors were appointed last year. A building of more than 200,000 square feet is planned, costing $110 million and due to be built by 2002. It will house not just the 24 faculty members of the new institute (half of whom will be new appointments), but also several existing departments and Howard Hughes investigators.

The new centres should each have an impact on graduate and undergraduate teaching, as well as research. "There is a growing feeling in the biological community that we need to be thinking hard about how to train the next generation of biologists," says Tilghman. She suggests that this training should include more mathematics, physics and chemistry.

Laura Garwin

France questions Israeli research deal

[JERUSALEM] Israeli officials have condemned a French-led effort to make Israel's participation in the European Union's fifth Framework research programme conditional on it implementing the 'Wye Plantation' agreement reached with the Palestinian Authority in October.

Pierre Lebovics, spokesperson for the French embassy in Tel Aviv, says that, although Israeli participation is desirable in principle, "it is clear that such participation has a political dimension, in the context of furthering the peace process and the implementation of the Wye accords".

But Orna Berry, Israel's chief scientist, describes France's stance as "a flagrant violation of professional integrity". She says she will refuse to co-ordinate Israel's participation in the Framework programme unless an agreement with Israel is signed by the European Union within two weeks.

Berry says that, if the matter is not resolved by mid-January, when the first calls for projects are issued, there will be little sense in Israel participating.

She argues that Israel's strong research community, and her own experience in working with the Palestinians and Jordan, can contribute to European research and development. "The right thing to do is to concentrate on what we have in common and not on what separates us." The issue will be taken up by Europe's Council of Ministers early this month.

Haim Watzman

Paul Selvin

"representative biophysicist"

Have a good rest of semester,
grad. student or other career!

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.