Volume 4

Feynman Hughes Lectures

Biology, Organic Chemistry, and MicroBiology

October 1969 to May 1970

Notes taken & Transcribed by John T. Neer

Note: At the time of this lecture series in late 1969, Feynman was heavily involved in the particle physics and experimental research leading to his "parton" theory which complimented quark theory. Since the topics he set out to lecture on took him afield, the preparation and research he had to do to prepare the lectures became too time consuming and be had to give the lecture series up.
I decided to include what I had here even though they are incomplete and well dated now. My reason to include them is only to give the scientific community a look into the "dynamic range" of Feynman's inquistive nature. I have learned that Feynman most likely drew upon Seymour Benzer for insight into this series on microbiology and biophysics. Benzer had started out at as a physicist but with the discovery of the structure and nature of the DNA molecule he changed over to the emerging field of biophysics and genetics. As a CalTech colleague of Feynman, he apparently communicated with Feynman whose intellectual curiosity led him into this lecture series.

Those of us at the labs shared his curiosity in this emerging field even though Hughes Aircraft Company had nothing to do with this scientific pursuit. That could not be said, however, of the Howard Hughes Medical Institute (HHMI) that continues today to advance our medical and biological understandings. The ultimate sale of HAC in the mid 80's provided over $5B in "endowment" to the HHMI.

Feynman was always seeking to better understand nature and our world. This series of topics just demonstrates Feynman's interest to look outside of his known field of expertise. We should think about how our own professional focus can limit us in better understanding the interrelationships of all scientific endeavors. Today, that appreciation is reflected in multi-disciplinary study courses that represents non-linear teaching at all levels of educations. While we need very knowledgable specialists in a given field, we need well educated individuals who have developed an interest to see the interrelationships of physics to chemistry, biology, neuroscience, nanotechnology, etc$_e$
JTN comment Dec 2013

INTRODUCTION TO THE COURSE ON BIOLOGY

3 NOV. 69

TODAY, I WANT TO BE A NEW SUBJECT MATTER. I HAVE decided THE SUBJECT I WILL TALK ABOUT WILL BE BIOLOGY. THE LECTURES COULD GO ON forever BECAUSE THERE ARE SO MANY RELATED TOPICS, EG. biophysics, biochemistry, MOLECULAR BIOLIOGY, GENETIC, PHYSIOLOGY, ECOLOGY, THAT THE PROJECT IS ENVISION IS ENORMOUS. AGAIN I WILL BE GUIDED TO A LARGE EXTENT BY THE QUESTIONS YOU RAISE AND THE DIRECTION THEY LEAD ME.

TO FIND AN APPROPRIATE STARTING POINT IS AN IMPOSSIBLE JOB. THE SUBJECT MATTER differs from CHEMISTRY AND PHYSICS IN SOME SIGNIFICANT WAYS. ALL THE RELATED fields of BIOLOGY TO A GREAT EXTENT ARE INDEPENDENT. THE REASON for THIS IS BIOLOGY LACKS A BASIC FOUNDATION of FUNDAMENTAL LAWS; LAWS DEVELOPED BY THEORY AND PROVEN TO BE TRUE BY EXPERIMENT. WE WILL FIND VERY LITTLE MATHEMATICS AS WE GO THROUGH THE MATERIAL. BASIC ALGEBRA AND CALCULUS WILL SUFFICE. LACKING THIS UNDERLYING UNIFYING THREAD, AS IN PHYSICS, I HAVE FOUND IT MOST difficult TO ORGANIZE THE MATERIAL IN A MEANINGFUL WAY.

I HAVE TRIED TO ORIENT THE SUBJECTS ON A SCALE RANGING from THE VERY SMALL (THE ELECTRON, NUCLEUS, ATOM, MOLECULE REGIME) TO THE VERY LARGE SCALE WHERE MANY ~~BIOLOG~~ COMPLEX BIOLOGICAL SYSTEMS INTERACT IN A CLOSED ENVIRONMENT (THIS IS THE field of ECOLOGY). THUS I PLAN, SOONER or LATER, TO SPAN THE BIOLOGICAL SPECTRUM from THE SUBMOLECULAR LEVEL to THE GRANDIOSE ECOLOGICAL LEVEL. IT IS MY PLAN TO START AT THE MOLECULAR LEVEL AND WORK MY WAY up.

BIOLOGY, or more properly, CLASSICAL BIOLOGY IS BASED upon OBSERVATIONS AND EXPERIMENTS WITH LIVING ORGANISMS, ORGANS, AND CELLS. CLASSICAL BIOLOGY deALS WITH LIFE ON THE MULTICELLULAR AND SINGLE CELLULAR LEVEL; for BELOW THE ~~Pa~~ CELL LIFE IS NOT SAID TO EXIST. PLANTS AND ANIMALS ARE CATEGORIZED INTO SPECIES, GROUPS, PHYLLA, AND KINGDOMS. THE BASIS of CATEGORIZATION ARE COMMON TRAITS, FEATURES, RESEMBLANCES. THE TRICK TO UNDERSTANDING THE SUBJECT MATTER IS TO LEARN WHAT THE COMMON ELEMENTS ARE AMOUNG THE VARIOUS ORGANISMS.

Somewhat at odds with the ideas of classical biology is the more recent field of molecular biology. The new approach assumes that the chemical constituents, seprated from the cell and studied with sufficient subtlety and detail, react according to known chemical and physical laws in a manner which can account for life. It is proposed that life may even reside in a single cellular constituent. Thus molecular biology deals exclusively on the single cell level

Cells have been found to have several key common features:

(1). cellular chemical reactions are all govegned by catalysts

(2). Basic chemical process is to convert glucose to CO_2

(3). cell must be able to reproduce

The chemical reactions can be very complicated and involve many sequences each requiring a certain catalyst to make it go. However, all forms of life require the energy from the sun to sustain the chemical reactions and ultimately to sustain life. In plants the sun's energy is absorbed directly through the substance chlorophyll. Chlorophyll is subsequently broken down into a more stable chemical energy form. The chlorophyll, therefore, couples the sun's energy through photon excitation of its own atomic structure into a stable chemical-electric substance. The most common electro-chemical storage process is to use the energy of the excited electron to separate water, H_2O. Oxygen is released to the atmosphere while hydrogen joins other molecules.

The plants the absorb the energy from the sun; animals come along, eat the plants, and release the stored energy. The whole process represents one gigantic chemical factory. The catalysts, or enzymes, make the whole thing work but don't get consummed themselves. Enzymes are basically made of proteins and proteins represent the general construction unit of life.

Our study will begin by understanding those chemical reactions going on inside the cell and from there continue on.

I should mention the two great assumptions made in the field of biology:

(1). The environment of all living things is based on on the earth environment back to the birth of the planet about 4 billion years ago. As a consequence of this assumption it is postulated that the long history of evolution has led from the carbon molecule, to the single cell, and finally to the highly specialized multicellular body

(2). All phenomena associated with the happenings of a living being can be explained in physical-chemical terms. At one time it was felt that cells were not subject to the normal laws of natures and ~~HA~~ possessed strange qualities. Today the biologist strive for the physical-chemical explanation of the events he observes.

The first assumption limits the range of possibilities of how life on this planet originated. The possibility of being a transplanted society from another planet is not considered. That is not to say life does not ~~n~~ exist somewhere else in the universe. It would be impossible to assome that life on another planet would be like ours. It is almost incredible just understanding how it evolved here. Many accidents have occurred along the evolution path. Not only are there many other forms of life possible which may ~~be~~ rely on a carbon cycle but silicon could replace carbon and a large number of additional possibilities become possible. In fact it's almost inconceivable that atoms can acquire "consciousness" and many time it is necessary to resort to an explanation like "God did it."

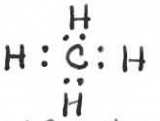
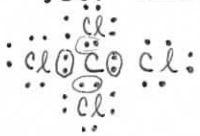
But we have learned to understand the key of life, DNA, and how it works. How it manages to duplicate itself while at the same time make the machinery for future reproduction has been a longtime mystery but now we ~~we~~ think we understand. Many times in the process of reproducing the

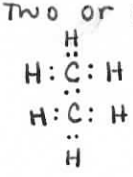
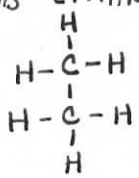
SHEET of INSTRUCTIONS GETS fouled UP AND THE COPY IS NO GOOD. SOMETIMES THE COPY IS REAL GOOD AND IT WORKS BETTER SO IT SURVIVES. BUT AS THE ORGANISM BECOME MORE COMPLEX EACH NEW CHANGE APPEARS TO BE for THE WORSE. IT IS ANALOGOUS TO THE LAW of ORGANIZATION IN TODAY'S SOCIETY: EVERY CHANGE LOOKS LIKE ITS for the WORSE.

ORGANIC CHEMISTRY.

I'LL BEGIN MY LECTURES BY FIRST CONSIDERING ORGANIC CHEMISTRY. PITY THE POOR GUY WHO HAS TO LEARN ALL THE MATERIAL IN ORGANIC CHEMISTRY JUST TO MAKE THE MILLIONS OF different COMPOUNDS. WE WON'T WORRY ABOUT HOW TO MANUFACTURE ORGANIC COMPOUNDS BUT RATHER CONCENTRATE ON WHAT THEY ARE AND WHY THEY ARE IMPORTANT TO BIOLOGY.

CARBON IS THE MOST IMPORTANT ELEMENT FOLLOWED BY OXYGEN, HYDROGEN, NITROGEN AND THEN ABOUT A DOZEN ~~OTH~~ LESSER ELEMENTS INVOLVED IN THE CHEMISTRY OF MAN. SOME OF THE OTHER KEY ELEMENTS ARE PHOSPHORUS, SULFUR, SODIUM, POTASSIUM, IODINE, IRON, CHLORINE AND MANGANESE. WE'LL START WITH CARBON

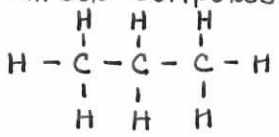
CARBON HAS 6 ELECTRONS 2 of which form THE CLOSED S-SHELL AND 4 VALENCE ELECTRONS. CARBON LIKES TO GAIN OR LOSE THESE four ELECTRONS IN ORDER TO GET TO A LOWER ENERGY STATE. ONE WAY TO DO ACHIEVE THE MINIMUM ENERGY STATE IS TO be surrounded by For hydrogen IONS H^+ AND THUS ACHIEVE A STABLE OCTET ARRANGEMENT. SYMBOLICALLY THIS IS DENOTED AS  where THE TWO PAIRED DOTS REPRESENT SHARED ELECTRONS which ARE IN TWO DIFFERENT SPIN STATES BUT OCCUPY THE SAME SPACE. CH_4 IS MORE COMMONLY KNOWN AS METHANE. WHEN ELECTRONS ARE SHARED LIKE THIS THE BOND IS CALLED A COVALENT BOND. THE OTHER WAY TO ACHIEVE A STABLE ELECTRON CONFIGURATION if for THE CARBON TO GIVE UP ITS 4 ELECTRONS, E.G. CHLORINE IS QUITE WILLING TO ACCEPT AN ELECTRON SO four CHLORINE ATOMS WILL NEUTRALIZE THE CARBON,  THIS TYPE of BONDING IS CALLED IONIC BONDING.

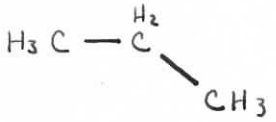
NOW THERE ARE A LOT of DIFFERENT SUBSTITUTION POSSIBLE WHEN CONSIDERING TWO or MORE CARBON ATOM SUCH AS ETHANE, C_2H_6 OR SYMBOLICALLY  ALTERNATELY DENOTED BY 

IN THIS MOLECULE THE HYDROGEN ATOMS CAN ROTATE FREELY ABOUT THE C-C bond. IN GENERAL ROTATION CAN OCCUR ABOUT A SINGLE BOND WHILE IT CAN'T ABOUT A DOUBLE BOND.

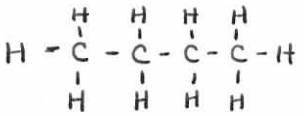
OTHER COMMON CARBON COMPONDS ARE

PROPANE : C_3H_8

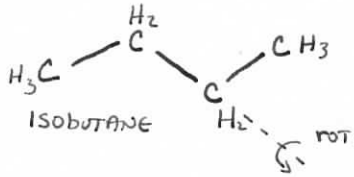




BUTANE : C_4H_{10}



NORMAL



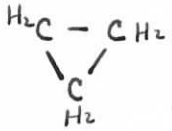
ISOBUTANE

AND CONTINUING THE SERIES THROUGH PENTANE, HEXANE, HEPTANE, OCTANE, ETC. THE FORMULAS OF ALL THESE HYDROCARBONS CONFORM TO THE TYPE $C_nH_{2(n+1)}$. AS YOU GET HIGHER AND HIGHER IN THE MOLECULAR WEIGHTS YOU COME TO THE WAXES. IN THESE SUBSTANCES THE CHAINS OF ATOMS BECOME SO INTERCONNECTED THAT MESS LOOKS LIKE A PLATE OF SPAGHETTI WITH ALL THE ENDS GLUED TOGETHER. COMPOUNDS WHICH ARE DERIVATIVES OF THE METHANE-ETHANE-PROPANE SERIES ARE CALLED SATURATED HYDROCARBONS BECAUSE THE CARBON VALENCES ARE ALL SATURATED WITH HYDROGEN.

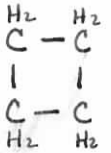
IN MANY COMPOUNDS CH_3 ACTS AS A LUMP TO REPLACE HYDROGEN; THE DERIVATIVES ARE SAID TO BELONG TO THE METHYL GROUP, E.G. CH_3Cl METHYL CHLORIDE IS ONE SUCH COMPOUND  .

ANOTHER MAJOR GROUPING of HYDROCARBONS IN SATURATED STRUCTURES ARE THE CYCLOALKANES, ALKANE STANDING for THE SATURATED BOND AND CYCLO DENOTING THE CLOSED STRUCTURE. SUCH EXAMPLES ARE :

CYCLOPROPANE C_3H_6



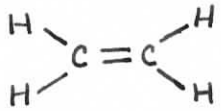
CYCLOBUTANCE C_4H_8



CYCLOPENTANE, HEXANE, HEPTANE, ETC.

ALKENES

ANOTHER MAJOR ~~of~~ CATEGORY of HYDROCARBONS ARE FORMED by DOUBLE BONDS AS OPPOSED TO THE SINGLE BONDS of THE ALKANES. THE CARBON ELECTRONS HAVE TWO VALENCE ELECTRONS AND ARE SAID TO BE UNSATURATED HYDROCARBONS. ALKENES ARE VERY REACTIVE AS COMPARED TO THE RELATIVELY DULL ALKANES. AN EXAMPLE of AN ALKENE IS ETHYLENE, C_2H_4,

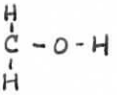


IN THE DOUBLE BOND STRUCTURE BOTH ELECTRON PAIRS ARE SHARED by THE TWO CARBON ATOMS. AN INTERESTING MEMBER of THIS GROUP IS BUTADIENE C_3H_8, $H_2C=\underset{H}{C}-\underset{H}{C}=CH_2$. IN THIS COMPOUND THE SHARED ELECTRON CAN RUN BACK AND FORTH ALONG THE CARBON CHAIN JUST LIKE A WIRE.

ALCOHOLS

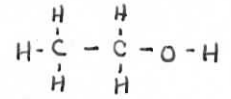
ALCOHOLS ARE HYDROXYL DERIVATIVES (OH) OF ALKANES. METHYL ALCOHOL IS A COMMON COMPOUND of THIS GROUP

CH_3OH :

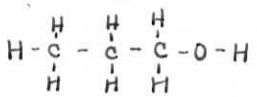


OTHER COMPOUNDS ARE HIGHER ORDER MULTIPLES of THIS BASIC STRUCTURE, E.G.

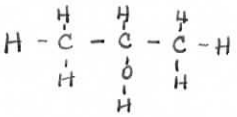
ETHYL ALCOHOL (LIQUOR) :



PROPYL ALCOHOL
$n\text{-}C_3H_7OH$

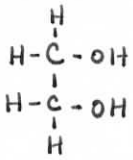


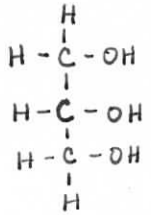
ISOPROPYL ALCOHOL
$i\text{-}C_3H_7OH$



GENERAL FORM: ROH
where R SYMBOLIZES CH_3, H, ETC.

THESE COMPOUNDS ARE ALL CHARACTERIZED by A STRAIGHT-CARBON CHAIN. IN ADDITION TO THE SINGLE HYDROXYL GROUP THERE IS ANOTHER ASSOCIATED WITH SUBSTITUTING TWO OH'S AS IN THE CASE of

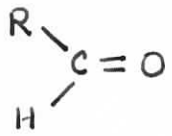




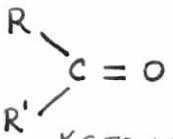
GLYCERIN

CARBONYL COMPOUNDS

Compounds formed with double bonded oxygen are called carbonyl and are of two types: Aldehydes and Ketones.

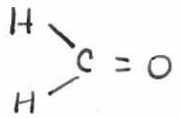


Aldahyde

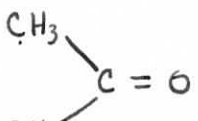


Ketone

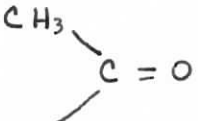
Two examples of Aldahydes and Ketones are



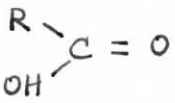
formaldahyde



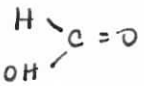
Acetone



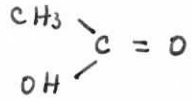
Acetaldehyde

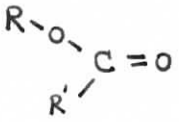
An interesting class of substances belonging to this category is the carboxyl group, 

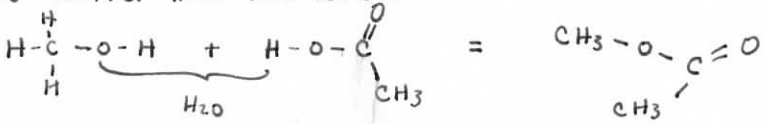
When R=H the compound is formic Acid, a pungent smelling liquid in ants,

formic Acid 

Also if $R=CH_3$ we get Acetic Acid, sour liquid in vinegar,

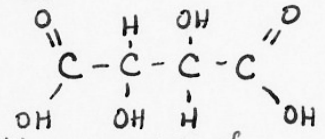


A derivative of the carboxylic Acids, a carbonyl compound, is called an ester. The general form of an ester is  and is formed by combining an alcohol with an Acid forming water and the ester



Esters have a characteristic fruity flavor and give many flowers and fruits their fragrance.

ASYMMETRIC CARBON COMPOUNDS

AN INTERESTING ACID IS TARTARIC ACID, 

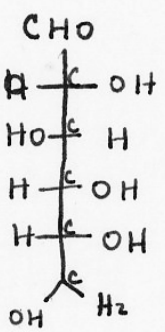
WHEN POLARIZED LIGHT SHINES ON THE COMPOUND THE PLANE of POLARIZATION becomes rotated. MANY COMPOUNDS DISPLAY THIS PROPERTY AND ALL HAVE IN COMMON A SYMMETRY which is REFLETED IN A MIRROR. TO DISTINGUISH COMPOUNDS which ROTATE THE PLANE of POLARIZATION TO THE RIGHT OR THE LEFT THE TERMS dextro (d) AND LEVO (l), RESPECTIVELY, ARE USED.

SUGARS

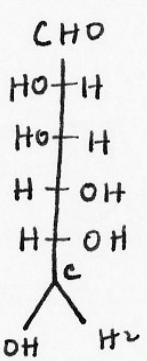
I'd NOW LIKE TO GET INTO A brief DESCRIPTION of SUGARS because from SUGARS WE CAN MOVE INTO biochemistry AND THEN biology. SUGARS SERVE IN TWO MAJOR CAPACITIES IN NATURE. TO ANIMALS SUGARS CONSTITUTE NOT ONLY A SOURCE of ENERGY BUT ALSO A BASIC BUILDING BLOCK IN CELL STRUCTURE. GLUCOSE IS THE BASIC SUGAR UNIT IN ANIMALS AND THE DIGESTIVE PROCESS WORKS TO BREAK DOWN THE MORE COMPLEX SUGARS TO THIS SIMPLE UNIT. IN ~~ANIMALS~~ PLANTS SUGARS PROVIDE A STORAGE PLACE for THE ENERGY Absorbed IN THE PHOTOSYNTHESIS PROCESS. ALSO, LIKE IN ANIMALS, THE MORE COMPLEX SUGARS form STRUCTURAL MATERIALS LIKE CELLULOSE IN PLANTS

THE SIMPLEST SUGARS ARE THE MONOSACCHARIDES. These SUGARS ARE CHARACTERISTICALLY COMPOSED of FIVE or SIX CARBON ATOMS AND ARE KNOWN AS PENTOSES AND HEXOSES. THE GENERAL FORMULA for SUGARS IS $C_n H_{2n} O_n$. ~~AND~~ More complex SUGARS such AS disaccharide, TRISACCHARIDES, ETC CAN d be formed from THE MONOSACCHARIDES. SUGARS ARE BASICALLY STRAIGHT CHAIN MOLECULES which DISPLAY AN ASYMMETRY. Four COMMON MONOSACCHARIDES APPEARING IN NATURE ARE

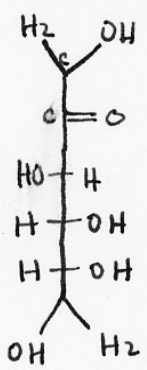
D-GLUCOSE



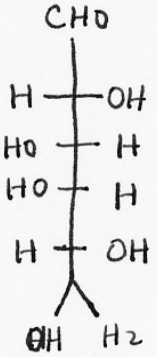
D-MANNOSE



D-FRUCTOSE



D-GALACTOSE

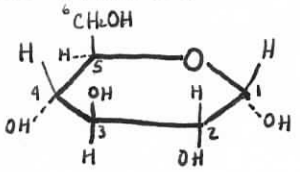


BIOCHEMISTRY

LAST TIME WE TALKED ABOUT SUGARS AND OTHER CARBON COMPOUND AS WE WERE LEARNING ABOUT THE GENERAL SUBJECT of ORGANIC CHEMISTRY. I WOULD LIKE TO CONTINUE ON BY DISCUSSING ONLY THOSE CHEMICAL PROCESSES WHICH ARE IMPORTANT IN BIOLOGICAL SYSTEMS.

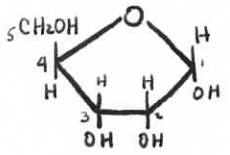
WE WERE DISCUSSING SUGARS BECAUSE of THEIR IMPORTANCE IN BIOLOGY. I WOULD LIKE TO SHOW YOU A LITTLE BETTER WAY TO REPRESENT THESE COMPLEX MOLECULAR STRUCTURES. THE STRUCTURE for D-α-GLUCOSE, MORE COMMONLY, DEXTROSE, IS SHOWN IN THIS QUASI-THREE DIMENSIONAL DRAWING

DEXTROSE

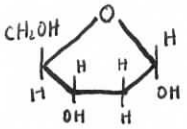


THE VERTICES of THE POLYGON ARE THE SITES of THE CARBON ATOMS (NOTE THE NUMBERING) EXCEPT WHERE THE OXYGEN ATOM OCCURS.

THE PENTOSE SUGAR, RIBOSE, HAS A SIMILAR STRUCTURE



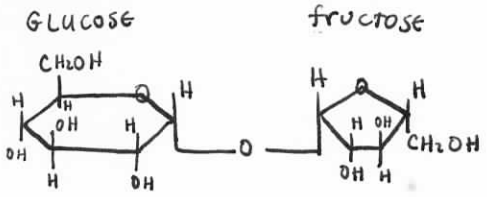
AND 2-DESOXYRIBOSE IS GIVEN BY:



HERE THE OXYGEN ON THE 2nd CARBON ATOM HAS BEEN REMOVED.

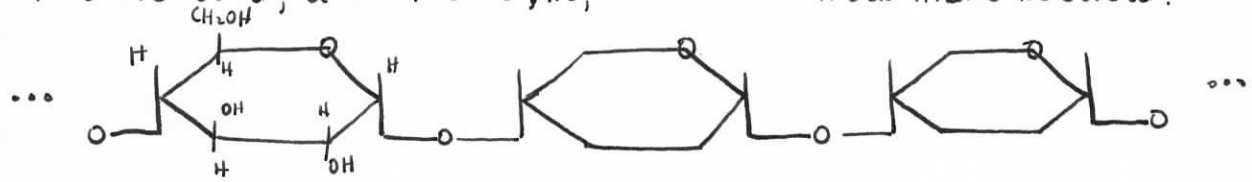
THE LIST of MONOSACCHARIDES APPEARING IN NATURE IS NOT VERY LONG. A few of THE COMMON MONOSACCHARIDES ARE THE: TETROSES, ARITHROSE; PENTOSES, PETROSE, ARABINOSE, XYLOSE, RIBOSE; HEXOSES, D-GLUCOSE, MANNOSE, GALACTOSE, FRUCTOSE, ASORBOSE, TALOSE

DISACCHARIDES CAN BE FORMED FROM MONOSACCHARIDES BY WHAT IS CALLED A GLYCOSIDIC BOND BETWEEN THE CONSTITUENT SUGARS. SUCROSE IS formed BY COMBINING FRUCTOSE AND GLUCOSE:

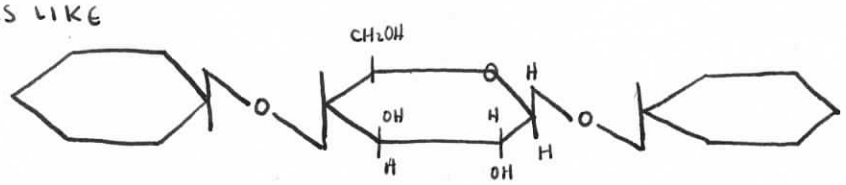


OTHER COMMON DISSACCHARIDES ARE LACTOSE (FOUND IN MILK), MALTOSE (IN STARCH), CELLOBIOSE (CELLULOSE). THE PROCESS OF DIGESTION INVOLVES SPLITTING THE GLYCOSIDIC (OXYGEN) BOND AND PUTTING THE HYDROGEN BACK. THUS SUCROSE IS REDUCED TO GLUCOSE AND FRUCTOSE. THE ENZYME THAT REDUCES SUCROSE IS CALLED INVERTASE. THE SUFFIX "ASE" DENOTES AN ENZYME WHILE THE PREFIX DENOTES ONLY WHAT IT DOES.

WE HAVE ALREADY MENTIONED THAT SUGARS SERVE AS A FOOD STORAGE DEVICE AND THE COMMON FORM IS STARCH. STARCH IS JUST A TREMENDOUS CHAIN OF GLUCOSE SUGARS TIED TOGETHER BY THE GLYCOSIDIC BOND, α (1-4) BOND, I.E, THE 1 AND 4 CARBON ATOMS ARE BONDED:

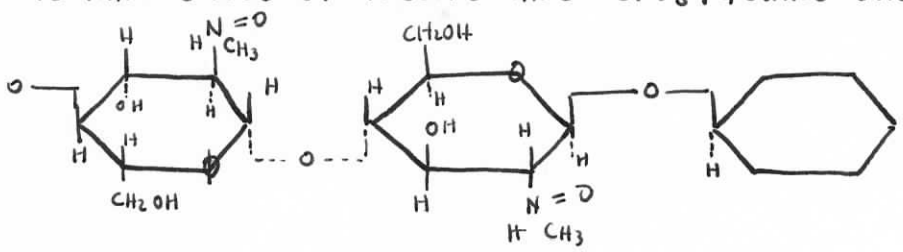


STARCH IS THEREFORE A POLYSACCHARIDE. ANOTHER COMMON POLYSACCHARIDE IS CELLULOSE. CELLULOSE IS THE BASIC STRUCTURAL TOOL OF PLANTS. CELLULOSE IS MADE FROM GLUCOSE SIMILAR TO STARCH BUT DIFFERENT IN THE BONDING. THE BOND IS CALLED A β(1-4) BOND. AND LOOKS LIKE



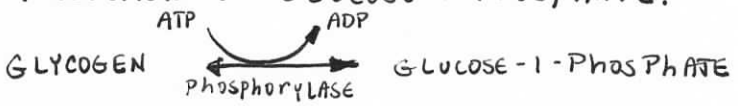
IT IS THIS SEEMINGLY INNOCENT VARIATION IN BONDING THAT DETERMINES WHAT IS EDIBLE AND IT ISN'T FOR MAN AND ALL OTHER ANIMALS. TERMITES, ON THE OTHER HAND, HAVE WITHIN THEIR GUT A BACTERIA CAPABLE OF DESTROYING THE β(1-4) BOND AND THUS PERMITTING THEM EAT WOOD. JUST THINK IF WE COULD DEVELOPE AN ENZYME TO DESTROY CELLULOSE, LIKE A COW, THERE WOULDN'T BE A FOOD PROBLEM TODAY.

CHITIN IS ANOTHER POLYSACCHARIDE, SIMILAR TO CELLULOSE; IT FORMS THE HARD SHELL OF INSECTS AND CRUSTACEANS LIKE LOBSTERS.

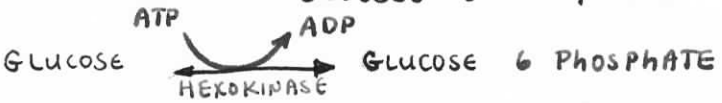


CARBOHYDRATE METABOLISM

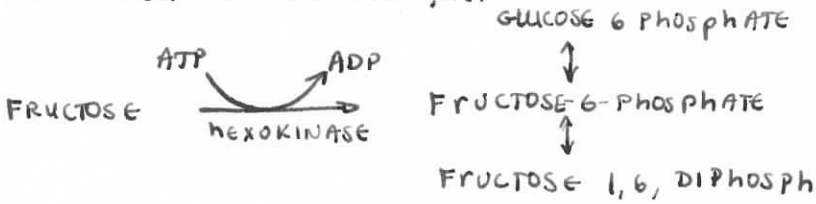
ONE CHEMICAL REACTION OF INTEREST IS THE REDUCTION OF POLYSACCHARIDES INTO THE SIMPLE MONOSACCHARIDES. THIS IS THE ACT OF DIGESTION. THE FIRST STEP IN THE PROCESS IS PHOSPHOROLYSIS OF THE POLYSACCHARIDE WITH THE PRODUCTION OF GLUCOSE-1-PHOSPHATE.



AN ALTERNATE BUT EQUALLY PROBABLE REACTION • INVOLVES GLUCOSE WHICH IS CONVERTED INTO GLUCOSE-6-PHOSPHATE



THE FIRST REACTION OCCURS COMMONLY IN ANIMALS AND IN HIGHER PLANT TYPES WHILE THE SECONDS IS FOUND BASICALLY IN MICROORGANISMS. DURING THE RESTING PERIOD OF ORGANISMS GLUCOSE IS THE CHIEF SUGAR PRODUCT OF GLYCOGEN, BUT IN PERIODS OF MUSCULAR ACTIVITY FRUCTOSE 6 PHOSPHATE APPEARS IN PREDOMINANCE. FREE FRUCTOSE DOES NOT ARISE AS A PRODUCT OF METABOLISM BUT WHEN PRESENT IN THE DIET CAN PARTICIPATE IN THE SYSTEM SIMILAR TO GLUCOSE, I.E.



THE CONVERSION OF ATP INTO ADP LIBERATES STORED ENERGY OBTAINED FROM THE SUN THROUGH PHOTOSYNTHESIS. IT IS NOT AN ENZYME BUT RATHER A REACTANT WHICH SUPPLIES THE ENERGY TO RUN THE REACTIONS UP HILL.

PHOTOSYNTHESIS

EVERY PLANT AND ANIMAL ON EARTH DEPENDS, ULTIMATELY, ON THE ENERGY FROM THE SUN TO SUSTAIN LIFE. THE ENERGY TRANSFER, HOWEVER, TAKES PLACE IN ONLY ONE SPECIFIC PLACE IN PLANTS CALLED PLASTIDS. IN THE PLASTIDS CARBON DIOXIDE IS EXTRACTED FROM THE AIR COMBINED WITH WATER AND INORGANIC SALTS FROM THE SOIL TO FORM THE BASIC CARBOHYDRATES NECESSARY FOR LIFE TO CONTINUE. FOR THE COMPLEX SUGARS TO BE FORMED THE ENERGY FROM THE SUN IS REQUIRED. THE BASIC PHOTOSYNTHESIS PROCESS CAN BE REPRESENTED BY THE FOLLOWING FORMULA,

$$n CO_2 + n H_2O \xleftrightarrow{h\nu} (CH_2O)_n + nO_2$$

HERE THE SUN'S ENERGY, $h\nu$, IS CARRIED BY A PHOTON. THE EXACT WAY IN WHICH THE PHOTON IS ABSORBED AND CONVERTED INTO A USEFUL FORM IS RATHER COMPLEX, NOT TOO WELL UNDERSTOOD, AND WILL BE DISCUSSED LATER. IT IS INTERESTING TO OBSERVE A LOG BURNING FOR THERE YOU SEE THE ABOVE PROCESS IN REVERSE. THE CO_2 AND H_2O IS RELEASE LEAVING BEHIND A SMALL PILE OF ASHES, THE INORGANIC SALTS, AND GIVING OFF HEAT IN THE FLAMES WHICH IS JUST THE REEMISSION OF THE ABSORBED ENERGY FROM THE SUN. IN ANIMALS AND PLANTS THE REVERSE PROCESS IS CONTROLLED TO RUN VERY SLOWLY SO AS TO PRODUCE WARMTH, ACTION, RESPONSES, ETC. THE PLANTS GO THROUGH THE REVERSE PROCESS AT NIGHT.

PHOTOSYNTHESIS OCCURS THROUGH TWO BASIC PROCESSES: ONE THAT WORKS IN SUN LIGHT AND ONE THAT WORK IN THE DARK. THE LIGHT PHASE INVOLVES THE PHOTO ELECTRON TRANSFER BETWEEN PHOTON ENERGY AND A HIGH ENERGY CHEMICAL SUBSTANCE ATP. ATP IS AN INORGANIC COMPOUND WHICH SERVES AS THE BASIC DRIVING FORCE (ENERGY SOURCE) TO A LARGE NUMBER OF CHEMICAL REACTIONS. ATP IS MADE THROUGH A PROCESS CALLED PHOSPHORYLATION IN WHICH HYDROGEN IS DRIVEN OFF (ESTERIFICATION) BY THE SUN'S ENERGY AND LEAVES BEHIND ATP AND WATER. ATP, OR ADENOSINE TRIPHOSPHATE, IS CALLED A REDUCING AGENT. IN ADDITION TO ATP A SECOND REDUCING AGENT IS FORMED IN A SIMILAR MANNER; IT IS CALLED NICOTINAMIDE ADENINE DINUCLEOTIDE TRIPHOSPHATE, NADPH.

DURING PHOTOSYNTHESIS NADP BECOMES NADPH BY THE ADDITION of TWO HYDROGEN ATOMS. ONE hydrogen BINDS DIRECTLY TO THE MOLECULE WHILE THE OTHER LOSES ITS ELECTRON AND IS RELEASED AS A PROTON (H^+). IT IS NADPH which SUPPLIES THE "reducing power" for THE fixATION of CARBON dioxide. THE TWO BASIC REACTIONS CAN BE SUMMARIZED AS

$$n' \text{ ADP} + n' P_i + n h\nu \longrightarrow n' \text{ ATP}$$

$$2\text{NADP} + 2H^+ + 4h\nu \longrightarrow 2\text{NADPH}$$

where THE PROTONS ARE GENERATED from THE REACTION

$$2H_2O \longrightarrow O_2 + 4e^- + 4H^+$$

P_i represents A high ENERGY Phosphate Group PO_3. FINALLY WHEN CO_2 IS PRESENT THE PHOTOSYNTHESIS UNDERGOES THE SECOND MAJOR REACTION. WE CAN SUMMARIZE IT AS

$$2\text{NADPH} + 2H^+ + CO_2 \longrightarrow 2\text{NADP} + H_2O + CH_2O$$

THE NET REACTION CAN BE WRITTEN AS

$$CO_2 + H_2O \longrightarrow CH_2O + O_2$$

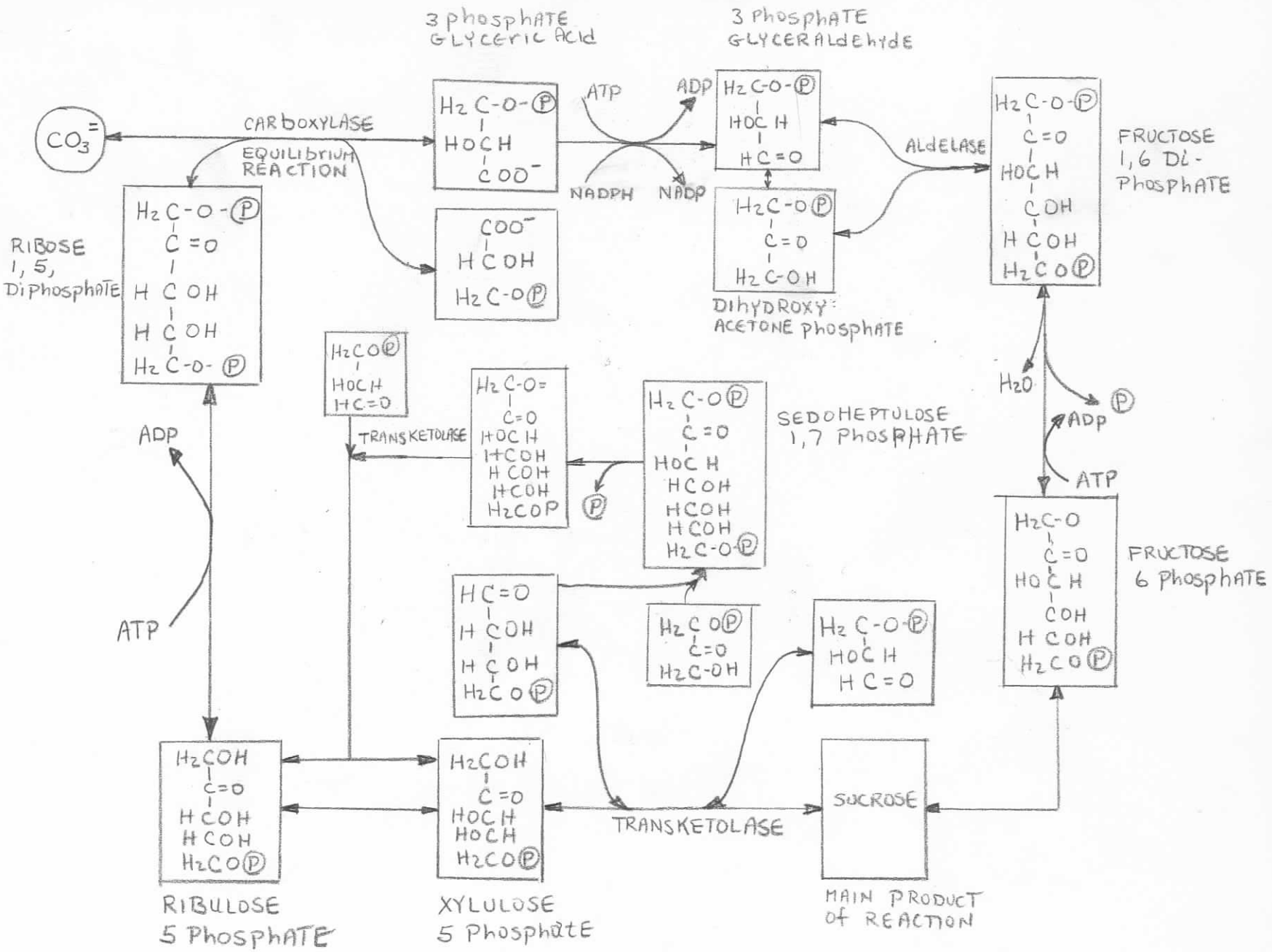
FIXATION of CARBON

I NOW WANT TO TALK ABOUT CONVERSION of CARBON INTO SUGAR. THIS REACTION ONLY OCCURS AT KNIGHT. THE BASIC REACTION GOES LIKE

$$CO_2 + 2\text{NADPH} + 3\text{ATP} + 3H_2O \longrightarrow \tfrac{1}{6}\text{hexose} + 2\text{NADP}^+ + 3\text{ADP} + 3P_i$$

THE ACTUAL REACTION IS MUCH MORE COMPLEX THAN THIS REACTION INDICATES. THE REASON for THE ADDITIONAL COMPLEXITY IS THAT SUGAR IS A MUCH higher ENERGY STATE THAN CO_2 AND H_2O SEPARATELY. IN order TO form A SUGAR AN ADDITIONAL ENERGY CORRESPONDING TO ABOUT 12 LIGHT PHOTONS IS REQUIRED for THE REACTION TO GO. QUANTUM MECHANICALLY THE SIMULTANEOUS UNION of 12 PHOTONS IS STATISCALLY IMPROBABLE, NOT IMPOSSIBLE THOUGH. THUS NATURE MUST PURSUE A CLEVER COURSE IN order TO ACQUIRE THE NECESSARY ENERGY. THE NEXT PAGE Shows THIS COMPLEX PATH.

CARBON FIXATION IN PHOTOSYNTHESIS



IN words THE PRECEEDING CYCLE IS THIS. FIRST, CO_2 IS ADDED TO THE 5-CARBON RIBULOSE diPHOSPHATE, MAKING AN INTERMEDIATE 6-CARBON COMPOUND which QUICKLY SPLITS IN TWO, FORMING THE 3-CARBON GLYCERAL PHOSPHATE. THIS REACTION IS IN EQUILIBRIUM AND CAN GO EITHER WAY. If THERE IS MORE CO_2 PRESENT THE REACTION WILL BE forced TO form MORE ~~GLYCERA~~ GLYCERYL PHOSPHATE. A SERIES of REACTIONS INVOLVING SEDO HEPTULOSE PHOSPHATE AND OTHER COMPOUNDS THEN PUTS TWO GLYCERYL PHOSPHATES TOGETHER TO For THE 6-CARBON GLUCOSE PHOSPHATE. MEANWHILE RIBULOSE Di-PHOSPHOSPHATE IS REGENERATED AND IS READY TO TAKE ON ANOTHER CO_2 MOLECULE. THE CYCLE IS REPEATED 6 TIMES UNTIL SUCROSE IS formed. POWER TO RUN THIS REACTION IS SUPPLIED by BOTH ATP AND NADPH.

IN THIS CYCLE NATURE BEGINS WITH A PENTOSE (RIBULOSE) breaks IT INTO A TRIOSE by first forming A HEXOSE. THEN SHE HAS TO STRUGGLE TO PUT THE TRIOSES BACK TOGETHER TO form A PENTOSE. SINCE 3 AND 5 ARE NOT ~~MULTI~~ PRIME MULTIPLES THE COURSE PURSUED represents NOTHING MORE THAN A STRUGGLE WITH ARITHMETIC. HOWEVER, AFTER THE FIFTH CYCLE PENTOSE IS formed AGAIN SO ON THE SIXTH A LITTLE EXTRA COMES OUT- THAT LITTLE bIT EXTRA IS WHAT RUNS LIFE. AND ALL THAT had TO GO IN WAS CO_2, H_2O AND ENERGY!

SUBSTANCES of LIFE

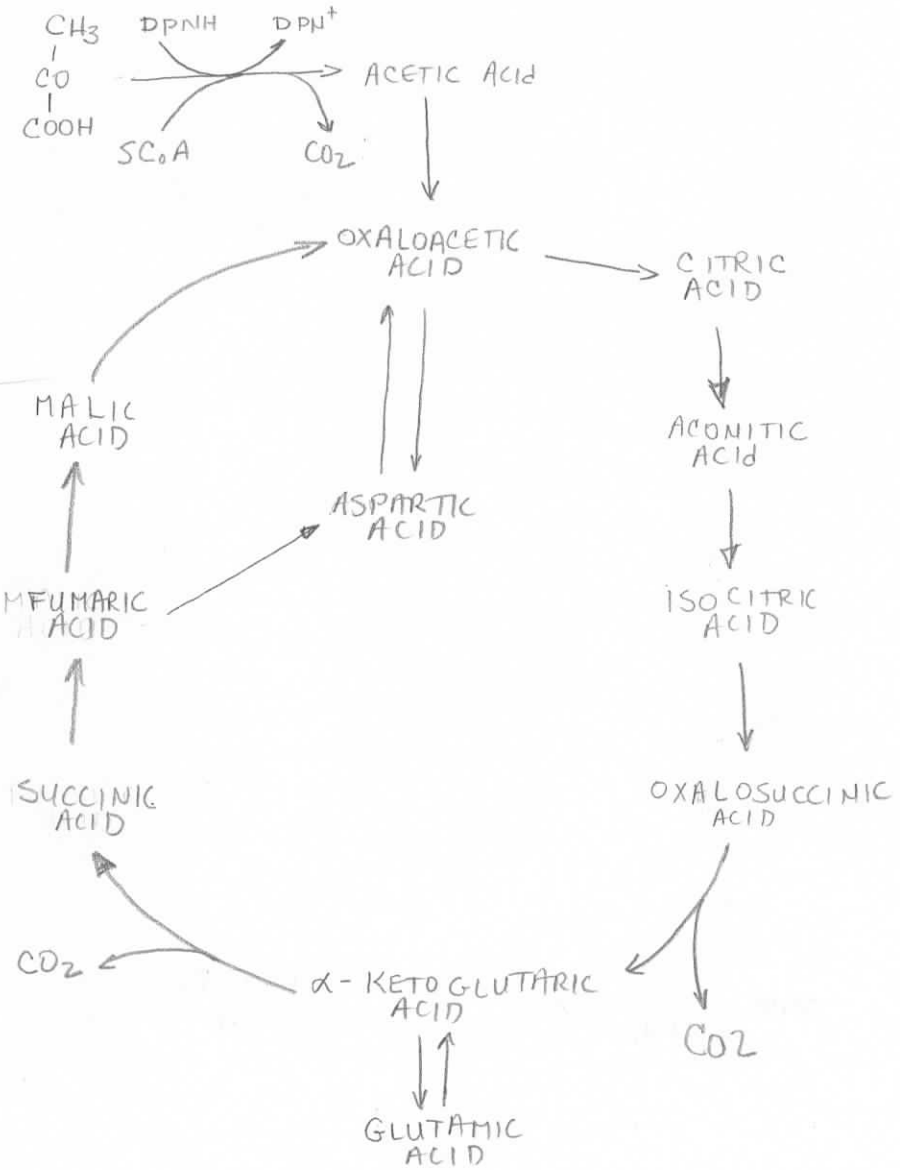
WE HAVE BEEN TALKING ABOUT CARBON COMPOUNDS AND specifically CARBOHYDRATES for THE PAST few LECTURES. THERE ARE OTHER SUBSTANCES COMMON TO ALL LIVING THINGS WHICH I WANT TO GO INTO. I CAN LIST THE SUBSTANCES IN THE FOLLOWING CATEGORIES

- CARBOHYDRATES
- FATS
- PROTEINS
- NUCLEIC ACID (RNA, DNA)
- OTHERS, EG, PROSTHETIC GROUPS (NON-ENZYMES), HORMONES, VITAMINS, PIGMENTS, ALKALOIDS

So FAR WE HAVE ESTABLISHED A BASIC UNDERSTANDING of how THESE KINDS of MOLECULES UNDERGO CHANGE. HUNDRED, THOUSAND, EVEN MILLIONS of TINY LITTLE STEPS ARE OFTEN INVOLVED WHEN GOING FROM ONE form TO ANOTHER. EACH STEP IS CAREFULLY CONTROLLED BY A PARTICULAR ENZYMES. WE LOOKED AT THE CARBON fixATION PROCESS IN SOME DETAIL AND observed THE COMPLEXITY of THE WHOLE REACTION. THE final PRODUCT of THAT REACTION, GLUCOSE, IS LATER USED THROUGHOUT THE body for VARIOUS PURPOSES. IN THE MUSCLES THE GLUCOSE IS CONVERTED INTO A LACTIC ACID, PYRUVIC ACID, IN THE ABSENCE of OXYGEN. THE PYRUVIC ACID IS SUBSEQUENTLY BROKEN DOWN INTO CARBON dioxide AND WATER. IN THE PROCESS A LOT of ENERGY IS RELEASED IN THE form of DNP^+ WHICH IN TURN IS reduced TO $DPNH$. THE reduction PROCESS RELEASES CHEMICAL ENERGY WHICH IS THEN CONVERTED INTO MECHANICAL ENERGY. ON THE NEXT PAGE THE WHOLE REACTION IS OUTLINED. THIS IS CALLED THE KREBS CYCLE or THE CITRIC ACID CYCLE, CRITIC ACID BEING ONE of THE KEY PRODUCTS formed ALONG THE WAY. AGAIN THE COMPLEXITY of THE CYCLE IS APPARENT.

THE KREB CYCLE TAKES PLACE IN THE MITOCHONDRIA, PART of THE CELL. ENZYMES CONTROL THE WHOLE REACTION AS WE MIGHT EXPECT. BECAUSE ENZYMES, I.E. PROTEINS, PLAY SUCH A KEY ROLE IN BIOLOGY THEY ARE PERHAPS THE MOST INTERESTING TO DISCUSS. FOR THAT REASON I AM GOING TO QUICKLY DISCUSS FATS BECAUSE THERE ISN'T TOO MUCH TO SAY ABOUT THEM - THEY ARE NOT TOO INTERESTING.

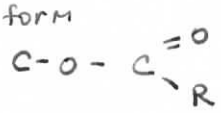
KREBS CYCLE


CH3
CO
COOH
DPNH
DPN+
SCoA
CO2
ACETIC Acid
OXALOACETIC ACID
CITRIC ACID
ACONITIC Acid
ISOCITRIC ACID
OXALOSUCCINIC ACID
α-KETOGLUTARIC ACID
CO2
GLUTAMIC ACID
CO2
SUCCINIC ACID
FUMARIC ACID
MALIC ACID
ASPARTIC ACID

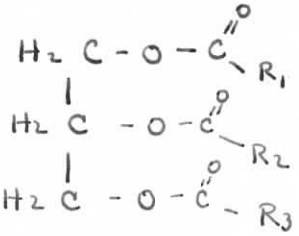
FATS

FATS ARE INVOLVED IN LIVING THINGS PRIMARILY AS AN ENERGY SUPPLIES BUT SERVE A SECONDARY ROLE AS A STRUCTURAL SUBSTANCE. FATS ARE STORED IN FORMS WHICH ARE LESS OXYDIZED THAN SUGARS; THEY ARE THUS HARDER TO BREAK DOWN AND UTILIZE. THE NUMBER OF CARBON ATOMS ASSOCIATED WITH FATTY MOLECULES IS OFTEN TIMES ENORMOUS. THERE ARE HOWEVER IN MOST LIVING THINGS ONLY A SMALL NUMBER OF FATS COMPARED TO THE INFINITE POSSIBILITIES. IN THE COURSE OF EVOLUTION FOR SOME REASON THE NUMBER OF FATS WAS LIMITED TO ABOUT 6.

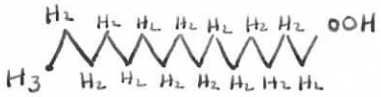
THE SIMPLEST FAT IS A TRIPLE ALCOHOL. ALCOHOL IS AN ESTER HAVING THE GENERAL FORM



FAT IS COMPOSED OF THREE SUCH ESTERS

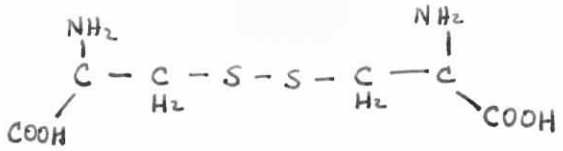


IN ORDER TO DESCRIBE FATS ALL THAT IS NEEDED IS TO DESCRIBE THE VARIOUS R'S. A TYPICAL EXAMPLE IS PALMITIC ACID WHICH HAS AN $R = CH_3(CH_2)_{14}COOH$. THE MOLECULE IS LAID OUT IN A STRUCTURE SOMETHING LIKE



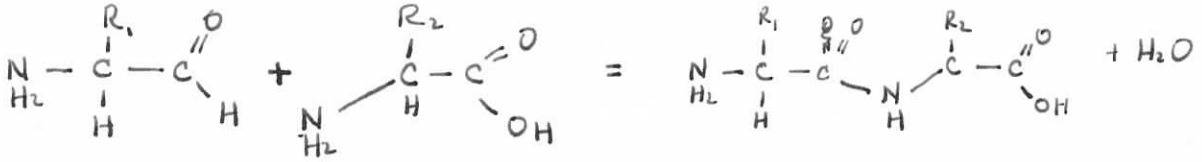
STERIC ACID IS ANOTHER EXAMPLE OF A FAT $R = CH_3(CH_2)_{16}COOH$. This FATTY ACID CONSISTS of 18 CARBON ATOMS WHILE PALMITIC ACID HAS 16 CARBONS. ALMOST ALL FATS OCCURRING IN NATURE CONSIST of 16 AND 18 CARBONS. THERE ARE VERY FEW 14, 20 AND 22 CARBON FATS OCCURRING NATURALLY. Of COURSE MORE COMPLEX FATS CAN BE SYNTHESIZED IS DESIRED. THE OTHER NATURAL FATS ARE OLEIC, LINDEIC, AND LINOLEIC. UNSATURATED FATS ARE OILY AND ARE MADE UP of OLEIC ACID WHILE SATURATED FATS ARE SOLID.

IN THE PREVIOUS TABLE SEVERAL INTERESTING RADICALS ARE WORTH BRIEFLY MENTIONING. CYSTEIN, ONE OF THE SULFUR GROUP, IS VERY REACTIVE FORMING WHAT IS CALLED A SULFUR BRIDE. THIS BRIDGE MAKE IT POSSIBLE TO MAKE MOLECULAR LOOPS OUT OF LONG CHAINS. THE BONDING LOOKS LIKE



PROLINE, WHEN PRESENT, PUT KINKS IN THE PROTEIN CHAIN. THE KINKS OCCUR AT fixed ANGLES WHICH DEPEND ON THE ELECTRICAL FORCES.

THE PEPTIDE BOND IS ANOTHER WAY IN WHICH AMINO ACIDS CAN JOIN TOGETHER TO form MORE COMPLEX PROTEINS. IN THIS BOND THE CARBOXY IONS JOINS WITH THE AMMONIUM ION OF ANOTHER ACID AND IN THE PROCESS RELEASES WATER. AN EXAMPLE OF THIS BONDING IS THE FOLLOWING



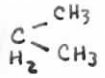
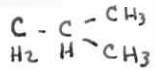
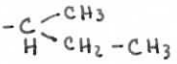
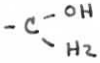
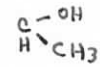
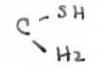
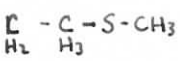
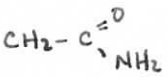
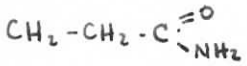
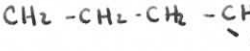
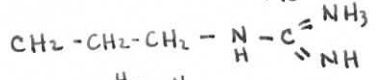
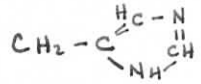
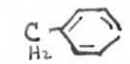
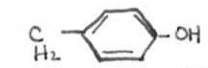
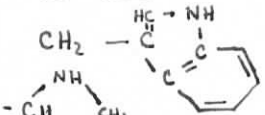
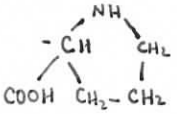
PROTEINS form BY THIS BONDING PROCESS ARE CALLED PEPTIDES.

WHILE ALL 20 AMINO ACIDS ARE ESSENTIAL for LIFE, IT IS NECESSARY THAT THEY ALL APPEAR IN A PERSON DIETS. IT IS POSSIBLE TO MANUFACTURE THE MISSING ACIDS FROM EIGHT FUNDAMENTAL AMINO ACIDS. THESE ACIDS AND THE MINIMUM DAILY INTAKE REQUIRED IS

Acid	LYS.	TRP	PHE	THR	VAL	MET	LEU	ILU
INTAKE, $\frac{GM}{DAY}$	.08	.25	1.1	0.5	.8	1.1	1.1	.07

WHILE MAN NEEDS THIS MINIMUM INTAKE, PLANTS ARE MORE PREPARED FOR SURVIVAL SINCE THEY CAN MANUFACTURE ALL THE BASIC 20 PROTEINS. THUS IT IS THAT WE EAT PLANTS AND OTHER ANIMALS TO OBTAIN OUR OWN SUBSISTENCE.

THE AMINO ACIDS COMMONLY OCCURING IN PROTEINS

NAME	ABBREV.	RADICAL R	HYDROPHOBIC 0 = LIKE H_2O 1 ≠ LIKE H_2O	CHARGE 0 NEUTRAL
1. GLYCINE	GLY	H	0	0
2. ALANINE	ALA	CH_3	0	0
3 VALINE	VAL		0	0
4 LEUCINE	LEU		0	0
5 ISOLEUCINE	ILU		0	0
6 SERINE	SER		1	0
7 THREONINE	THR		1	0
8 CYSTEIN	CYS		?	
9 METHIONINE	MET		0	0
10 ASPARTIC ACID	ASP	CH_2-COOH	1	−
11 ASPARAGINE	ASN		1	0
12 GLUTAMIC ACID	GLU	CH_2-CH_2-COOH	1	−
13 GLUTAMINE	GLN		1	0
14 LYSINE	LYS		1	+
15 ARGININE	ARG		1	+
16 HISTIDINE	HIS		1	+
17 PHENYLADANINE	PHE		0	0
18 TYROSINE	TYR		1	0
19 TRYTOPHAN	TRP		0	0
20 PROLINE	PRO		0	0

PROTEIN

PROTEINS ARE ESSENTIAL CONSTITUENTS OF ALL LIVING CELLS. They are found in all sorts of special things like hair, beaks, muscle, tendon and all the enzymes. There is a tremendous variety of protein molecules even within the same species differences or specialization arise, e.g. antibodies of different people can react negatively

While the variety of proteins is theoretically limitless there are only a small finite sub group appearing in nature. The major building blocks of proteins are amino acids. Amino acids are organic compounds having at least one amino group and one carboxyl group. The amino group is commonly attached to the carbon atom in the carboxyl group. The general formula for the proteins is

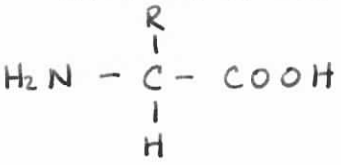
R represents ~~are~~ any one of a great variety of structure. Categorizing proteins is actually just a listing of the various radical groups. When R is an acid then we are dealing with an amino acid. E.G. If R = H then the protein glycine is formed.

Now there is a variety of amino acids from which all naturally occuring proteins are made. There are twenty of these amino acids which are basic to all living things. The names and characteristics of these 20 amino acids is given on the next page. The electric charge on the amino acid influences the properties markedly. The charge arise from the base - acid structure of the ~~acids~~ amino acids.

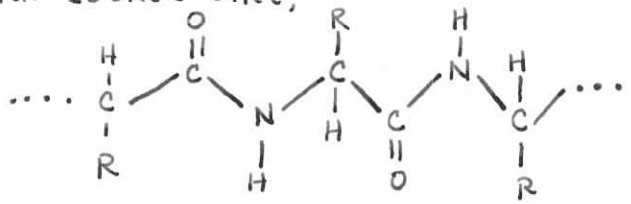
2/2/70

PROTEIN STRUCTURE

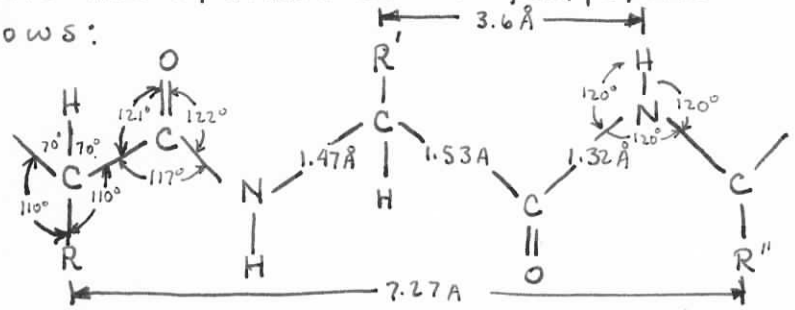
PROTEINS ARE MADE UP OF 20 AMINO ACIDS WHICH ARE ARRANGED IN LINEAR SEQUENCE ALONG A POLYPEPTIDE CHAIN. RECALL THE TYPICAL CHARACTER OF THE AMINO ACID WAS



WHERE R IS ONE OF TWENTY AMINO ACID RESIDUES. THE RESULTING CHAIN THEN LOOKED LIKE,



THROUGH X-RAY ANALYSIS TECHNIQUES THE STRUCTURE OF AMINO ACIDS HAS BEEN IDENTIFIED. THE ESSENTIAL FEATURE OF THE PEPTIDE LINKAGE IS ONE OF A PLANAR CONFIGURATION. THE DIMENSIONS AND SPACINGS OF THE POLYPEPTIDE CHAIN IS GIVEN AS FOLLOWS:

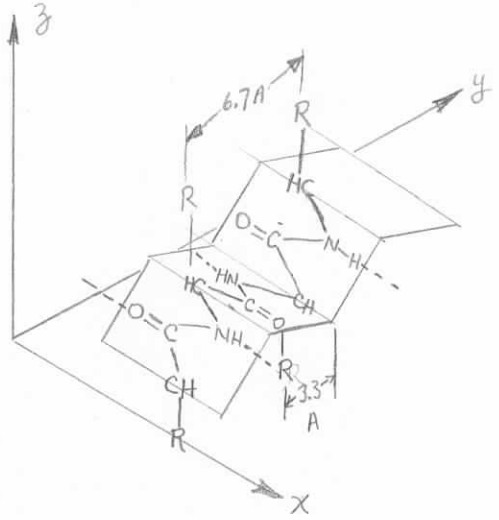


THE BOND SPACINGS AND ANGLES ARE DETERMINED BY ENERGY CONSIDERATIONS ONLY. THE MOST STABLE CONFIGURATION IS PLANAR OR NEAR PLANAR. FOR THE EXTENDED POLY PEPTIDE CHAINS AS SEEN ABOVE THE REPETITION OF THE BOND ANGLES AND SEPARATIONS PLUS THE MINIMUM ~~EEL~~ ENERGY CONSTRAINT SUGGESTED A HIGHLY SYMMETRIC STRUCTURE. PAULING SUGGESTED A HELICAL STRUCTURE AND HE WAS RIGHT. ~~HO~~ HOWEVER THERE WAS NO REASON ~~TO~~ TO SUPPOSE THAT THERE MUST BE AN INTEGRAL NUMBER OF AMINO ACIDS PER TURN OF THE HELIX. THUS WHILE THE BASIC HELICAL STRUCTURE IS PRESERVED THE HELIX IS SOMEWHAT COMPLICATED.

OF THE MANY POSSIBLE STRUCTURES OF AMINO ACIDS ONLY ~~TWO~~ THREE SURVIVE: NAMELY TWO TYPES OF PLEATED SHEATS AND ONE HELIX, CALLED THE α-HELIX.

The PLEATED SHEETS AND α-HELIX

The TWO PLANAR CONFIGURATIONS of POLYPEPTIDE CHAINS ARE CALLED The PLEATED SHEETS AND β-KERATIN. The PLANAR GROUP C-CONH-C IS LINKED TOGETHER ABOUT A TETRAHEDRAL CARBON ATOM. ONE WAY SUCH AN ORIENTATION COULD OCCUR IS The FOLLOWING:

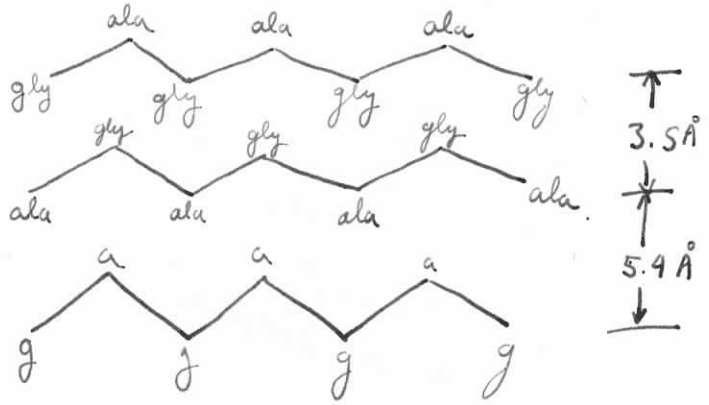


β-SHEET (RESIDUES HANG UP AND DOWN).

HYDROGEN BONDS ARE SHOWN DASHED

The PLEATED ARRANGEMENT SHOWN HERE GIVES RISE TO A LAYERING ARRANGEMENT WHEN The CHAINS are STACKED TOGETHER. The CHAINS MAY be EITHER PARALLEL or ANTI-PARALLEL SEQUENCES of AMINO ACIDS. THERE ARE A NUMBER of POSSIBLE ARRANGEMENTS of AMINO ACIDS EACH GIVING RISE TO A DIFFERENT SUBSTANCE.

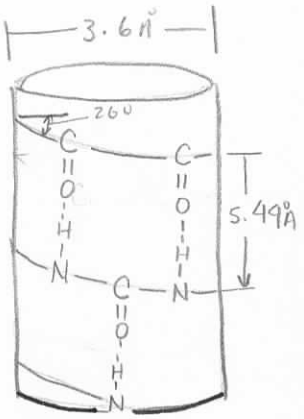
For EXAMPLE INSECT fibres LIKE SILK IS A PLEATED SHEET MADE of ALTERNATING AMINO ACID GROUPS (GLY-SER-GLY-ALA-GLY-ALA) The BASIC STRUCTURE RESULTING IS



THE α-HELIX

The SYSTEM of PLANAR GROUPINGS THAT MAKE UP POLYPEPTIDE CHAINS MAY be ROTATED ABOUT THE α-CARBON ATOMS. If THE ROTATION FROM PLANE TO PLANE IS CONSTANT A HELIX RESULTS. IN THE HELICAL STRUCTURE THE C=O AND N-H GROUPS PARTICIPATE IN HYDROGEN BONDING WHICH ARE THE INTRA CHAIN BOND. THE DIMENSIONS of THE HELIX ARE:

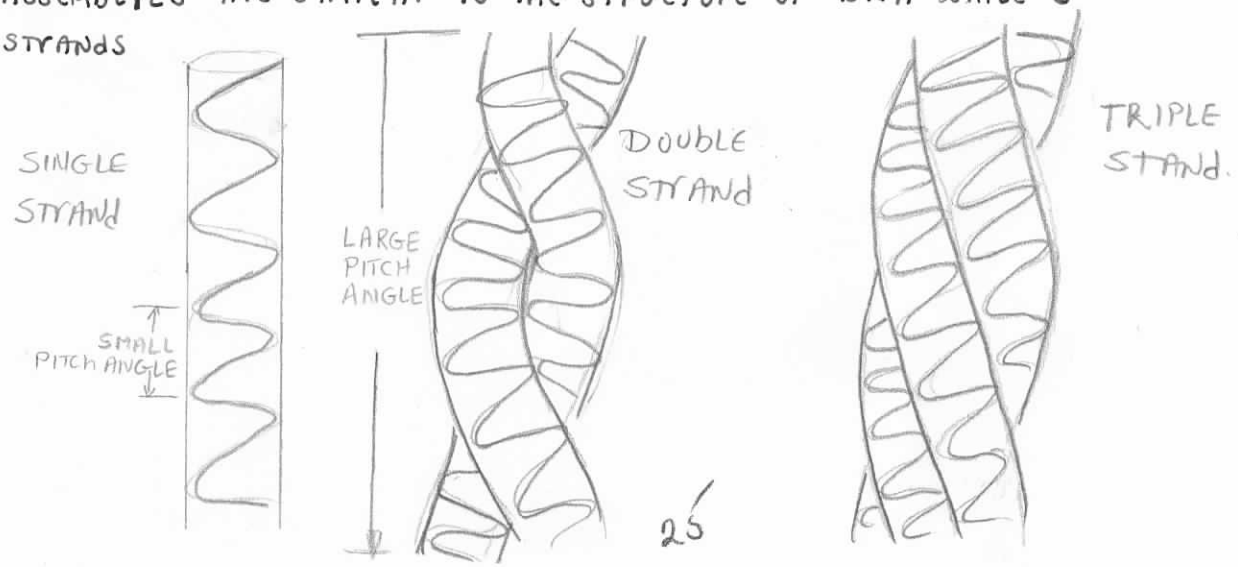
ROTATION BETWEEN RESIDUES	97.2°
RESIDUES PER TURN	3.69 A
TRANSLATON PER RESIDUE	1.47 A
N-H DIRECTION FROM AXIS	12°
HELIX RADIUS	1.81 A
N-H-O ANGLE	10°
PITCH	5.44 A



The NUMBER of RESIDUES PER TURN IS NOT INTEGRAL SO IT IS POSSIBLE TO FIND 48 RESIDUES IN 13 TURNS, 11 RESIDUES IN 3 TURNS, 15 RESIDUES IN 4 TURNS or 18 RESIDUES IN 5 TURNS. THE repeat DISTANCE of 1.5 A AXIALLY WAS PREDICTED AND FOUND IN HAIR, MUSCLE FIBER AND HEMOGLOBIN. HOWEVER NOT ALL GLOBULAR PROTEINS ARE MADE UP IN PART of α-HELICES.

α-KERATIN

The α HELIX UNITS form LONG THIN FIBERS which CAN IN TURN WRAP AROUND EACH OTHER ~~THE~~ TO form ROPE-LIKE STRUCTURES of VARIOUS STRAND NUMBERS. TWO STRANDS ASSEMBLYES ARE SIMILAR TO THE STRUCTURE of DNA WHILE 3 STRANDS



AS THE α-HELIX STRANDS WIND AROUND EACHOTHER THEY FORM HELICES WITH LARGER PITCH ANGLES TYPICALLY ON THE ORDER OF 200 TO 400 A WITH A DIAMETER OF 10Å. IT IS POSSIBLE THAT AS MANY AS SIX OF HELICAL α-HELICES MAY BE WOUND AROUND ONE STRAIGHT HELIXE TO GIVE A SEVEN-STRANDED CABLE.

THE STRUCTURE OF α-KERATIN BEGINS THEN WITH THESE STRANDED CABLES CALLED PROTOFIBRILS COMING TOGETHER TO FORM WHAT IS CALLED A ~~MA~~ MICROFIBRIL. THE MICROFIBRIL SRUCTURE LOOKS LIKE

WHERE 9 PROTOFIBRILS SURROUND TWO CENTRALLY ORIENTED PROTOFIBRILS. FURTHER BUNDING OF MICROFIBRILS INTO CORTICAL CELLS (MACROFIBRILS) AND SUBSEQUENT LUMPING OF CORTICAL CELLS INTO WOOL FIBER OR HAIR.

THE 9-2 COMBINATION IS VERY COMMON TO A LOT OF LIVING THINGS. THE WHIP LIKE TAILS OF SPERM, THE FLAGELLA, ARE BASICALLY 9-2 STRUCTURES. THUS IT IS THAT THE PROTEIN KERATIN IS BASICALLY COMMON TO SCALES OF FISH, HAIR, FEATHERS, HORNS, ~~HOOFS~~, BEAKS, CLAWS, AND FINGER NAILS. SKIN IS STRONG BECAUSE IT HAS A LOT OF KERATIN.

COLLAGEN

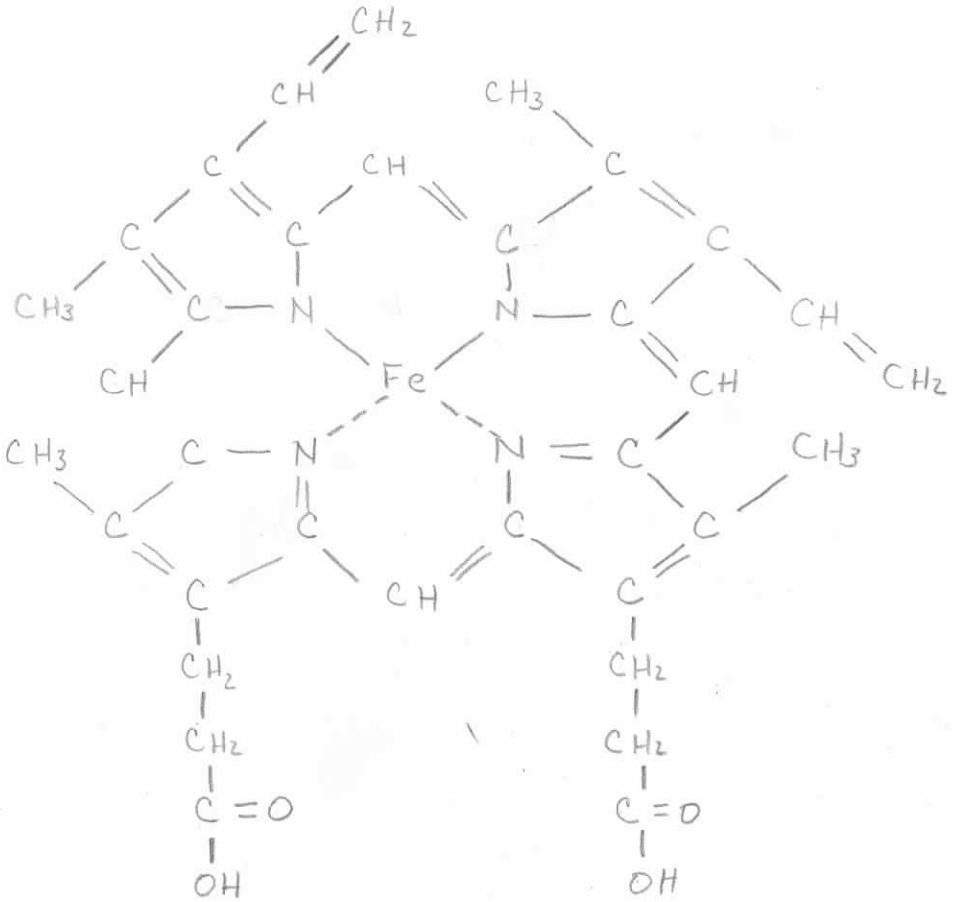
ANOTHE PROTEIN BUILDING BLOCK IS COLLAGEN. THIS FIBROUS MATERIAL IS FOUND IN CARTILAGE, LIGAMENTS, TENDONS AND IN THE CLOTTING MATERIAL FIBRINOGEN. THE BASIC COLLAGEN STRUCTURE CONSISTS OF A 3-STRAND PROTOFIBRIL WITH A LEFTHANDED PITCH. THE LENGTH OF THE PROTOFIBRIL IS ABOUT 2800Å WITH A DIAMETER OF ABOUT 10 Å. THE FIBROUS MATERIAL IS WOUND TIGHT DUE TO THE PRESENCE OF HYDRO PROLENE WHICH THROWS A LOT OF KINKS IN THE WINDINGS.

2-2-(51)

GLOBULAR PROTEINS

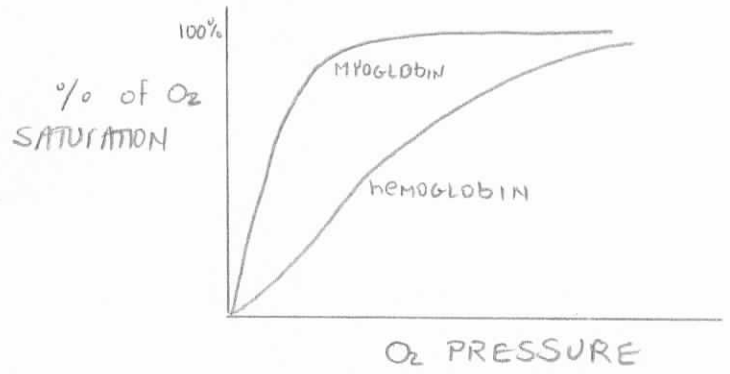
ANOTHER BASIC PROTEIN STRUCTURE IS THE GLOBULAR PROTEIN. THESE BALL LIKE STRUCTURES ~~HA~~ EXHIBIT A TREMENDOUS VARIETY AND AND THEREFORE QUITE INTERESTING TO STUDY. EXAMPLES OF GLOBULAR PROTEINS ARE HEMOGLOBIN, CYTOCHROM C AND LYSOZYME. THE INTERESTING THING ABOUT GLOBULAR PROTEINS IS THAT THEY HAVE BEEN THOROUGHLY ANALYZED AND THE AMINO ACID SEQUENCES ARE KNOWN EXACTLY; EVEN THE SPATIAL STRUCTURE IS WELL KNOWN.

HEMOGLOBIN, FOR INSTANCE, CONSISTS OF TWO CHAINS OF α AND β HELICES. MYOGLOBIN IS SIMILAR TO HEMOGLOBIN BUT ACTS AS AN OXYGEN STORAGE COMPARTMENT RATHER THAN AN OXYGEN CARRIER LIKE HEMOGLOBIN. MYOGLOBIN IS FOUND MAINLY IN THE MUSCLE TISSUE. THE COMMON ELEMENT TO BOTH OF THESE PROTEINS IS HEME. THE FORMULA FOR HEME IS $C_{34}H_{32}O_4N_4Fe$ AND THE STRUCTURE LOOKS LIKE:



THE RING STRUCTURE AND THE IRON ATOM IS CALLED A PORPHIN RING.

ONE OF THE CHEMICAL PROPERTIES OF HEMOGLOBIN AND MYOGLOBIN OF INTEREST IS THEIR OXYGEN CARRYING CAPABILITY. PLOTTING THE % of OXYGEN SATURATION VERSUS OXYGEN PRESSURE THE RESULTING CURVES ARE

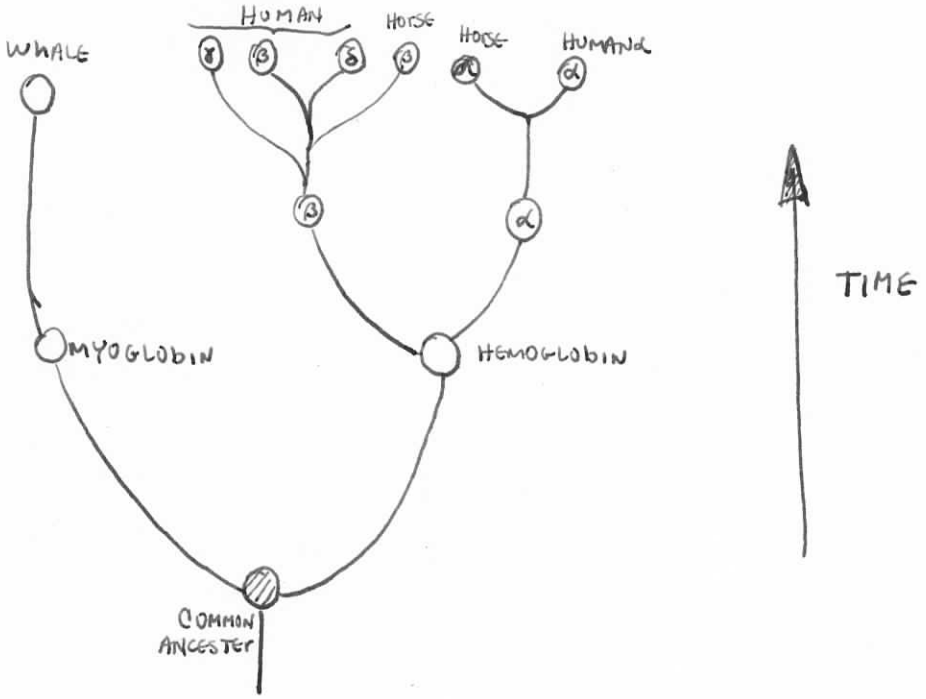


BECAUSE O_2 IS BOUND TO HEMOGLOBIN IN A MORE COMPLICATED MANNER THAN MYOGLOBIN THE CURVES ARE DIFFERENT.

HEMOGLOBIN IS MADE UP OF ACTUAL 4 PEPTIDE CHAINS: α, β, δ AND γ CHAINS. THE LATTER γ CHAIN IS REFERRED TO AS FETAL HEMOGLOBIN WHICH WORKS TO PICK UP O_2 FROM THE MOTHER'S BLOOD. BECAUSE OF VARIATIONS IN DIFFERENCES SPECIES THE α, β, δ AND γ CHAINS ARE CONSIST OF VARIOUS AMINO ACIDS. THUS HEMOGLOBIN CAN BE USED LIKE CYTOCHROME C TO CONSTRUCTH AN EVOLUTIONARY TREE. THE FOLLOWING TABLE LISTS THE VARIATIANS IN AMINO ACID RESIDUES

	HORSE α	HUMAN α	HORSE β	HUMAN β	HUMAN δ	HUMAN γ	WHALE MYO.
	141	141	146	146	146	146	153
HORSE α	0	18	84	86	87	87	118
HUMA α	18	0	87	84	85	89	115
HORSE β	84	87	0	25	26	39	119
HUMAN β	86	84	25	0	10	39	117
HUMAN δ	87	84	26	10	0	41	118
HUMAN γ	87	85	39	39	41	8	121
WHALE MYO	118	115	119	117	118	121	0

WE CAN LEARN FROM THIS TABLE THAT THE α AND β CHAINS SEPARATED IN EVOLUTION BEFORE THE HORSE AND HUMAN PHYSICALLY SEPARATED IN AN EVOLUTIONARY SENSE. THE ASSUMPTION MADE IN DRAWING THIS CONCLUSION IS THAT IN TIME MORE AMINO ACIDS MUTATE AND ACCUMULATE. OF COURSE THIS IS NOT STRICTLY TRUE BUT IT DOES PERMIT US TO DRAW THE NICE 'EVOLUTIONARY TREE'!



2/23/70

CYTOCHROME C

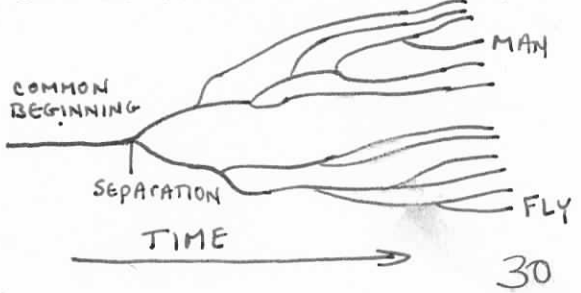
ONE ENZYMATIC PROTEIN which we have discussed before is CYTOchrome C. This ENZYME APPEARED IN The CArbon fixATION CYCLE. IT's BASIC STRUCTURE IS NOT KNOWN TOO WELL BUT ITS CHEMISTRY AND FUNCTION CAN be described.

THIS ENZYME APPEARS IN ANEROBIC REACTIONS (i.e., Those NOT INVOLVING ~~REACTION~~ OXYGEN). The PRIMARY PURPOSE of The ENZYME IS TO SPEED up The REACTION BY SERVING AS AN ELECTRICAL bridge TO PASS ELECTRONS down The REACTION CHAIN. IN ESSENCE ITS PRESENCE ACTS TO LOWER The path RESISTANCE AND MAKES The whole PROCESS GO FASTER.

INTERNAL TO The PROTEIN IS AN IRON ATOM WHICH SUPPLIES The NECESSARY ELECTRON AS IRON MAKES A TRANSITION FROM Fe^{++} TO Fe^{+++}. The IRON ITSELF APPEARS IN The CENTER of A porphyrin RING. There ARE A TOTAL of 105 AMINO Acids IN CYTOchrome C. The AMINO Acid PATTERN of CYTOchrome C HAS been worked OUT for A NUMBER of SPECIES AND The differences NOTED. ~~The~~ BECAUSE NONLETHAL CYTOchrome C MUTATIONS ARE RARE TRACING The DIFFERENCES from ONE SPECIES TO ANOTHER PROVIDES INTERESTING EVOLUTIONARY DATA.

IT HAS been found THAT The GREATER The SEPARATION of The SPECIES IN The EVOLUTIONARY SCHEME, The GREATER The NUMBER of differences IN CYTOchrome C. FOR EXAMPLE, The CYTOchrome C of MAN differs from THAT of The rhesus MONKEY BY ONLY ONE AMINO ACID, IN The ENTIRE CHAIN. BETWEEN MAN AND The TUNA fish There ARE 28 differences, AND of A YEAST CELL There ARE 48 differences.

BY OBSERVATION IT HAS been THEORIZED THAT The RATE of CYTOchrome C MUTATION IS ABOUT ONCE EVERY 10^6 YEARS. USING This ASSUMPTION EVOLUTIONARY TREES CAN be drawn which SUGGEST The ~~GREEN~~ GENERAL TREND of EVOLUTION; E.G.



THE STRUCTURE of NUCLEIC ACID POLYMERS - DNA AND RNA

WE HAVE YET TO DISCUSS THE WHOLE INTERESTING SUBJECT of NUCLEIC ACIDS. THE ESSENTIAL INGREDIENTS for NUCLEIC Acids ARE SUGAR, Phosphoric Acid, AND PURINE or PYRIMIDINE bASES. of ALL THE POSSIBLE COMBINATIONS of THESE CHEMICAL SUBSTANCES ONLY Four bASIC building bLOCKS ARE ATTACHED TO THE SUGAR - Phosphoric STRUCTURE. DEPENDING ON THE CHARACTER of THE SUGAR AND ON THE PRESENCE of URACIL IN PLACE of THYMINE TWO KINDS of NUCLEIC Acids ARE SEPARATED - RIBONUCLEIC (RNA) ACID AND DEOXYRIBONUCLEIC Acid (DNA).

THE STRUCTURE of THE NUCLEIC Acid HAS A COMPONENT UNIT which IS QUITE ANALAGOUS TO AN AMINO ACID IN A PEPTIDE CHAIN - which IS -

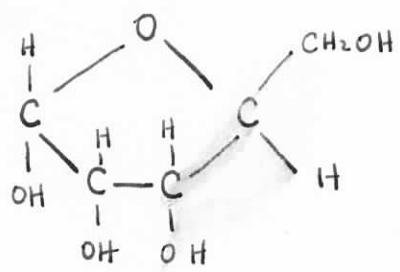
BASE - SUGAR - PhosPhATE

THE LINKAGE of THESE UNITS IS by THE phosphATE TO TWO SUGARS IN A STEPWISE PATTERN

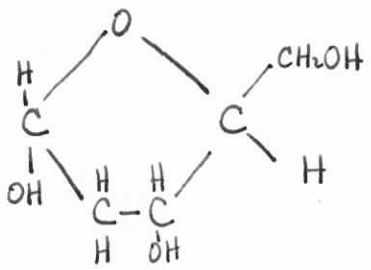
BASE - SUGAR
|
PhosPhATE
|
BASE - SUGAR
|
PhosphATE

THE COMBINATION of THE SUGAR WITH THE PhosPhATE form WHAT IS CALLED A NUCLEOTIDE. IT IS LONG CHAINS of THESE NUCLEOTIDES THAT MAKE UP DNA AND RNA.

THE TWO BASE STRUCTURES ATE RIbOSE AND DEOXYRIbOSE; THE LATER ribOSE MISSING ONE OXYGEN



RIBOSE

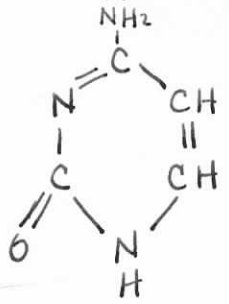


DEOXYRIBOSE

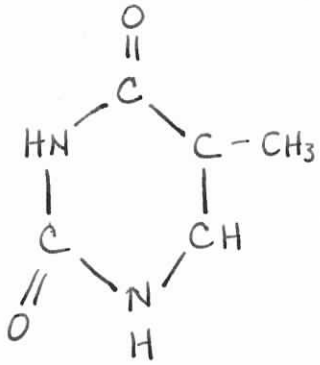
THE 5 IMPORTANT BASES FALL INTO TWO CATEGORIES – PYRIMIDINE or PURINE :

PYRIMIDINES

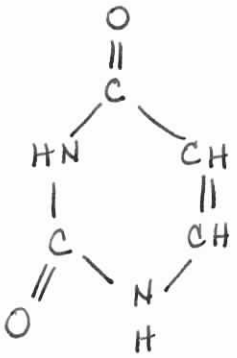
CYTOSINE (C)



THYMINE (IN DNA) (T)

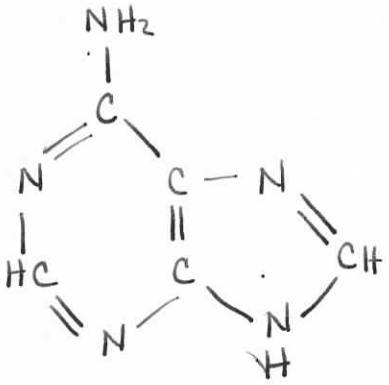


URACIL (IN RNA) (U)

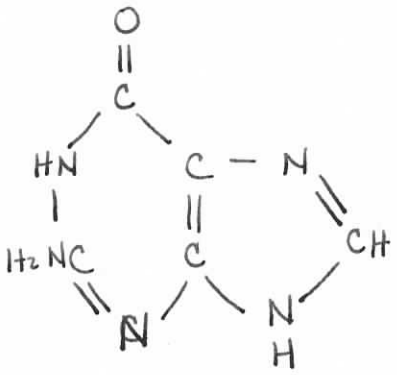


PURINES

ADENINE (A)



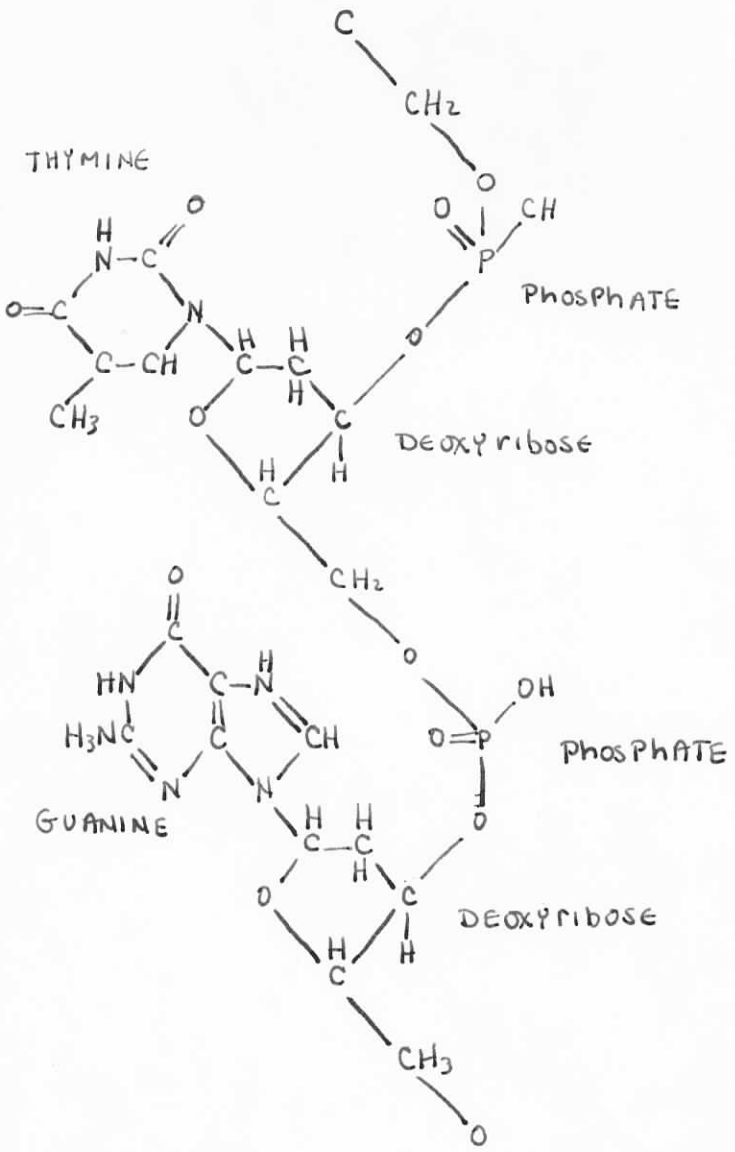
GUANINE (G)



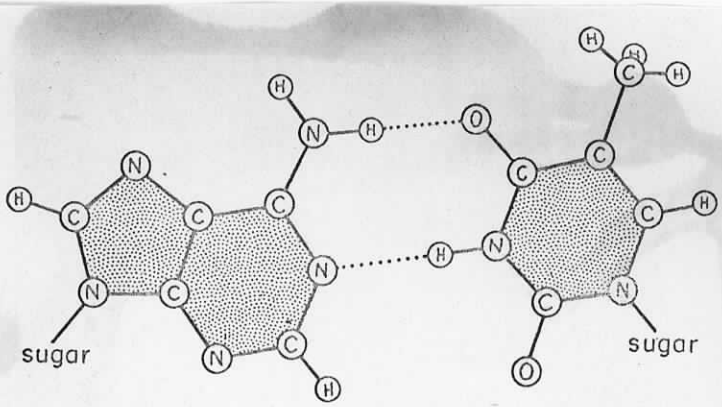
DNA

THE NUCLEIC ACID IS, ~~ONE~~ PERHAPS, THE SINGLE MOST IMPORTANT CHEMICAL SUBSTANCE IN THE LIVING CELL. FOUND PREDOMINANTLY IN THE NUCLEUS THE LONG NUCLEOTIDE CHAIN HAVING MOLECULAR WEIGHTS IN THE MILLIONS. THE GREATEST OF DNA IS IN ITS ABILITY TO REPRODUCE ITSELF. THE METHOD OF REPRODUCTION IS BETTER UNDERSTOOD BY LOOKING AT THE SPECIFIC STRUCTURE OF DNA.

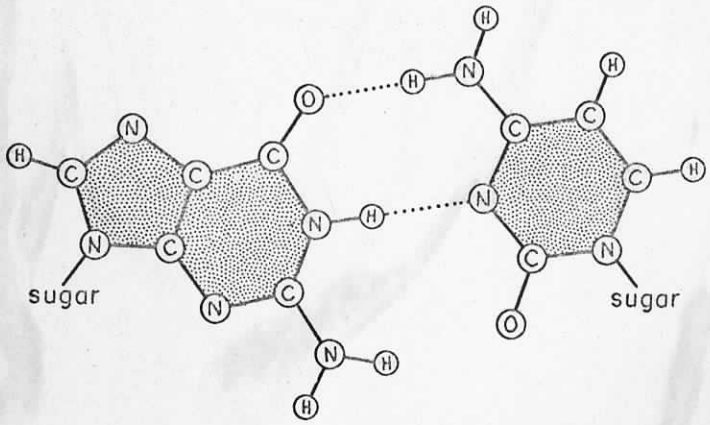
THE DETAILS of THE COUPLING BETWEEN BASE, SUGAR, AND phosphATE IS GIVEN IN THE FOLLOWING REPRESENTATIVE ARRANGEMENT



THE BASES ARE ARRANGED SO THAT THE form hydrogen bonds BETWEEN THE FACE of AN NH GROUP AND THE NEGATIVE FACE of C=O GROUP ; FOR GUANINE AND CYTOSINE THERE ARE 3 BOND POINTS AND for ADENINE AND THYMINE ONLY TWO. THIS BONDING GIVES RISES TO A DOUBLE HELICAL ARRANGEMENT where TWO INTERTWINED CHAINS of DNA form A highly STABLE STRUCTURE. AN IMPORTANT POINT IS THAT BASE BONDING ONLY OCCURS BETWEEN GUANINE AND CYSTOSINE AND BETWEEN THYMINE AND ADENINE. THE BONDING IS SHOWN ON THE NEXT PAGE:



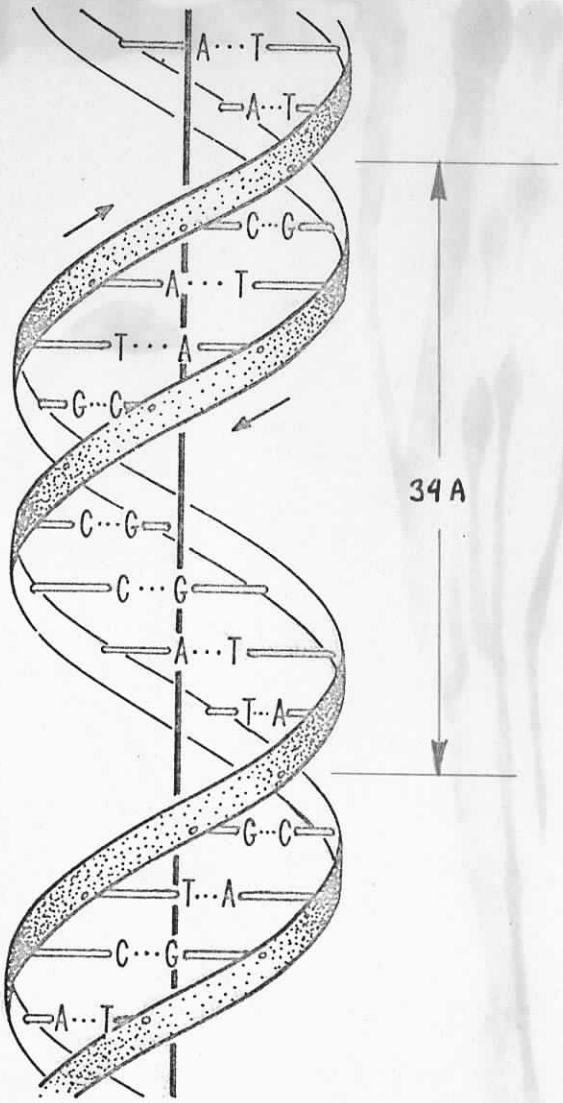
adenine thymine



guanine cytosine

The adenine-thymine and guanine-cytosine base pairs used to construct the double helix (hydrogen bonds are dotted). The formation of a third hydrogen bond between guanine and cytosine was considered, but rejected because a crystallographic study of guanine hinted that it would be very weak. Now this conjecture is known to be wrong. Three strong hydrogen bonds can be drawn between guanine and cytosine.

THE RESULTANT DOUBLE HELIX LOOKS LIKE THE FOLLOWING SCHEMATIC :



A schematic illustration of the double helix. The two sugar-phosphate backbones twist about on the outside with the flat hydrogen-bonded base pairs forming the core. Seen this way, the structure resembles a spiral staircase with the base pairs forming the steps.

DNA REPRODUCTION

THE DOUBLE SPIRAL STRUCTURE of DNA has very PRACTICAL and INTERESTING PROPERTIES CONCERNED WITH INFORMATION STORAGE AND REPLICATION of GENETIC MATERIAL. I WANT TO first DISCUSS THE DUPLICATION PROCESS THEN I'LL DISCUSS THE NATURE of THE GENETIC CODE.

IN THE PRESENCE of AN ENZYME CALLED DNA ase THE hydrogen BONDS ARE SPLIT STARTING AT ONE END OF THE CHAIN. THE DNA MOLECULAR, LIKE A ZIPPER, STARTS TO PEEL OPEN EXPOSING THE MILLIONS of LINKS, I.E. BASES. BECAUSE THE DNA MOLECULE IS IN A BATH of THE NUCLEOTIDES CONSISTING of A, G, T, U AND C THE EXPOSED BASES ARE PAIRED UP WITH THE APPROPRIATE BASE, I.E. G TO C AND T TO A. THE NEW NEUCLEOTIDE hydrogen bond TO THE TEMPLATE. THUS THE PROCESS CONTINUES UNTIL TWO IDENTICAL DNA MOLECULES ARE formed. THUS TO SYNTHESIZE DNA you NEED TO START WITH SOME DNA MIX IN SOME NUCLEOTIDES AND ATP, TTP, GTP, or GTP AND Add A LITTLE DNA ase.

THE RATES of REACTION ARE INTERESTING TO EXAMINE. IN THE BACTERIUM E. COLI 8×10^{-15} GM of DNA IS SYNTHESIZED IN 50 MINUTES. THIS EQUIVALENT TO 5×10^{3} NUCLEOTIDES BEING FASTENED IN PLACE PER SECOND. BASED ON RANDOM COLLISION CONSIDERATIONS IT IS CONCLUDED THAT THE SYNTHESIS MUST OCCUR AT LEAST 10 PLACES SIMULTANEOUSLY. A MORE REASONABLE ASSUMPTION WOULD BE THAT ABOUT 100 ENZYME SYSTEMS ARE ENGAGED IN NUCLEOTIDE POLYMERIZATION AT A TIME, I.E., EACH CITE HANDLING 50 NUCLEOTIDE PER SECOND. ON A TIME BASES IT IS ESTIMATED THAT EACH BASE IS LAID down CORRECTLY IN ABOUT 2×10^{-13} SEC. CONSIDERING THE DISTANCE BETWEEN NEIGHBORING NUCLEOTIDES, ABOUT 3.4 Å, IS BEING TRAVERSED IN 2×10^{-13} SEC, THE RESULTING VELOCITY of 1.7×10^{5} cm/sec PRODUCES AN ~~UNEER~~ UNREALISTIC ENERGY JUMP of 9×10^{9} eV. THUS IF THE process of DNA SYNTHESIS WVOLVES A CONTINUOUS BOMBARDMENT by four NEGLEOSIde TRIPHOSPHATES, WITH A CHANGING SPECIFIC SELECTION, THE SPEED of CHANGE REQUIRED TO AVOID SELECTION of THE WRONG BASE IS SO FAST THAT IT CANNOT be ACHIEVED by A PHYSICAL TRANSLATION of EITHER THE PRIMER or THE ENZYME.

ALSO WORTH NOTING IS THAT THE DNA CHAIN CANNOT UNCOIL AS IT IS BEING SPLIT APART BECAUSE THIS UNCOILING WOULD REQUIRE 30° PER BASE of ROTATION. TO DO THIS IN 2×10^{-13} SEC. REQUIRES AN ANGULAR VELOCITY O 2.5×10^{12} rad/SEC AND A ROTATIONAL ENERGY of 2×10^{5} eV. THUS IT IS CONCLUDED THAT MULTIPLE ~~SA~~ CITES of DNA REPLICATION MUST OCCUR SIMULTANEOUSLY.

If DURING REPRODUCTION ONE BASE GETS SCREWED UP AND DOES NOT CONFORM TO THE four FUNDAMENTAL BASE TYPES, THEN A MUTATION HAS OCCURRED. ONE ANOMALOUS BASE PAIR IN SEVERAL MILLION IS SUFFICIENT TO CHAIN THE ENTIRE MESSAGE ON THE DNA MOLECULE. If THE CELL CONTINUES TO LIVE AND THE DNA REPLICATE THE NEW TEMPLATE THE MUTATION IS NON-LETHAL.

GENETIC CODE

So far we have talked about the structure of DNA but we haven't said too much about how it really accomplishes all of its wonderful work, i.e., of providing the architectural plans for making specific protein molecules. In order to build a protein the DNA molecule must specify which block, amino acid, goes in place at a particular time in the construction. Since there are 20 basic amino acids the plans must be specific. If there were 20 different basic units in the DNA molecule, the problem would not be so difficult to understand. However we know that there are only 4 nucleotide bases which can vary. Thus it becomes necessary to define a code; consisting of 4 letters and capable of uniquely specifying ~~four~~ 20 different amino acids.

After some thought it is realized that if the 4 letters; A, T, G and C, are taken three at a time then there are 64 (4x4x4) different combinations possible. Thus a nucleotide triplet is a word in the code specifying ~~The~~ a particular amino acid. In addition to the 20 amino acids, there are redundant words to stop, i.e., to terminate a "sentence" of amino acids. Presently it is not known if there are any start words. But given the 64 combinations and roughly 21 necessary words the code can be specified as follows

First Amino Acid ↓	Second Amino Acid → U	C	A	G
	3rd A.A.			
U	Phe U or C Leu A or G	Ser (all)	Tyr, U or C X A or G	Cys U or C X A Trp G
C	Leu U, G, A, C	Pro (all) ~~Hydro~~	His U or C Gln A or G	Arg All
A	ILeu U, C, A Met G	Thr (all)	Asn U or C Lys A or G	Ser U, C Arg A, G
G	Val (all)	Ala (all)	Asp U or C Glu A or G	Gly, All

X denotes stop

NOTE THE CODE IS NOT TOO SENSITIVE TO THE THIRD BASE. IN MANY CASES ANY ONE OF THE 4 BASES WILL PRODUCE THE SAME AMINO ACID. THUS THE CODE HAS A NUMBER OF DEGENERACIES. AS AN EXAMPLE OF THE CODE, A SEGMENT OF THE DNA MOLECULE MIGHT READ

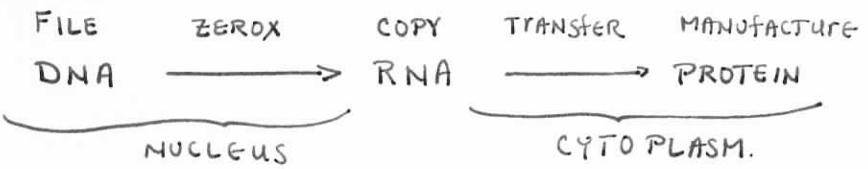
/AGT/CCA/GGT/TAA

WHICH IS SERINE - PROLINE - GLYSINE - STOP

AT PRESENT THE CHEMICAL RELATIONSHIP OF THE LETTERS, I.E, NUCLEOTIDES, TO THE AMINO ACIDS IS NOT KNOWN. PERHAPS THE CHEMICAL PROPERTIES OF THE VARIOUS AMINO ACIDS SUGGEST WHY SOME ARE DOUBLE CODED AND OTHERS ARE NOT, ALSO THE QUESTION OF HOW THE CODE EVOLVED IS OPEN. IT IS KNOWN THAT THE CODE IS UNIVERSAL THROUGHOUT THE SIMPLEST AND MOST COMPLEX PLANTS AND ANIMALS. THEREFORE, THE CODE MUST NOT HAVE EVOLVED BEYOND A ITS MOST EARLY FORM.

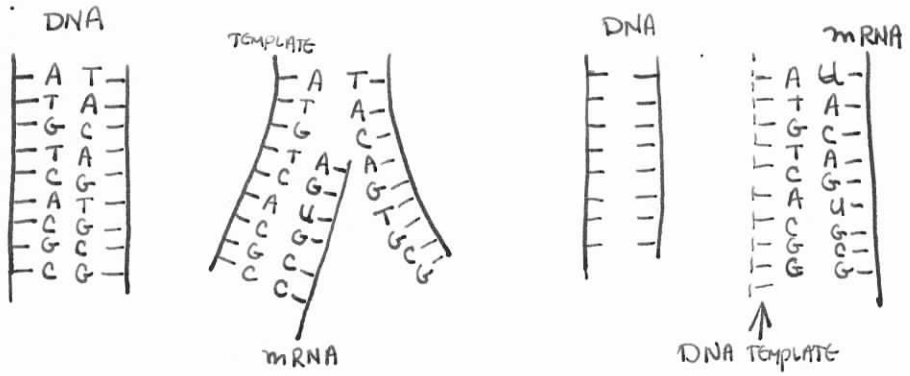
PROTEIN SYNTHESIS

NOW WE WOULD LIKE TO UNDERSTAND HOW PROTEINS ARE ACTUALLY SYNTHESIZED USING THIS CODE. FIRST THE DNA DOES NOT MAKE THE PROTEIN DIRECTLY. THE DNA MOLECULE IS ONLY THE BLUEPRINT. OUTSIDE OF THE NUCLEUS IN THE CELL CYTOPLASM IS THE PROTEIN MANUFACTURING FACTORY. TO GET THE DNA BLUEPRINT TO THE FACTORY A MESSENGER IS REQUIRED - THIS IS RNA. CONCEPTUALLY THE STEPS ARE THE FOLLOWING



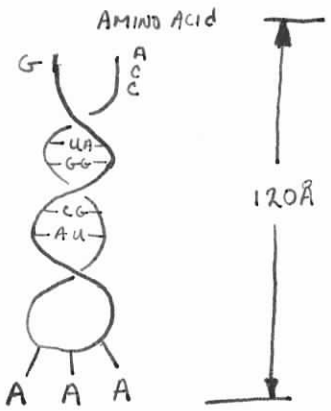
NOW WE HAVE TO KEEP OUR WITS BECAUSE THERE IS NOT JUST ONE RNA MOLECULE BUT INSTEAD THREE SEPARATE TYPES: MESSENGER, TRANSFER AND RIBOSOMAL RNA. MESSENGER RNA, MRNA, AS THE NAME IMPLIES HAS THE DNA MESSENGE ON IT. IT IS A SINGLE STRAND MOLECULE AND IS IDENTICAL TO ONE HALF OF THE DNA MOLECULE FROM WHICH IT WAS FORMS - DIFFERING ONLY IN THE PRESENCE OF THE BASE URACIL INSTEAD OF THYMINE AND THE ADDITIONAL OXYGEN IN THE SUGAR. THE MRNA IS MUCH SMALLER THAN THE DNA MOLECULE

THUS IT ONLY CARRIES PART OF THE TOTAL DNA MESSAGE. THE mRNA TRANSCRIBES THE DNA INFORMATION DURING A READING PERIOD WHEN THE DNA SPLITS IN TWO LIKE IT IS GOING TO DUPLICATE ITSELF BUT DOESN'T. THE READING PROCESS LOOKS LIKE THE FOLLOWING



THE RIBOSOMAL RNA IS NOT WELL UNDERSTOOD AT THE PRESENT. IT IS INVOLVED IN THE RIBOSOMES, PART OF THE CELL WHERE PROTEIN IS MADE. RIBOSOMES ARE ABOUT 200 Å IN SIZE AND ARE THROUGHOUT THE CYTOPLASM. RRNA IS A RELATIVELY PERMANENT STRUCTURE

TRANSFER RNA, TRNA, IS IMPORTANT IN THE PROTEIN SYNTHESIS PROCESS BECAUSE ATTACHED TO ONE END OF THE TRNA IS ONE OF 20 AMINO ACIDS. ALSO A PART OF THE TRNA IS A TRIPLET "CODE" OF 3 BASES WHICH ARE CAPABLE OF ESTABLISHING A FIRM RELATIONSHIP WITH THREE COMPLEMENTARY BASES ON THE mRNA. THIS LATTER FEATURE MAKES IT POSSIBLE TO ASSIGN THE APPROPRIATE AMINO ACID A PLACE IN THE POLYPEPTIDE CHAIN AS IT IS MADE. THUS THERE ARE 20 DIFFERENT KINDS OF TRNA. THE STRUCTURE OF TRNA CONSISTS OF ABOUT 80 BASES, FORMING A HAIRPIN WHICH IS TWISTED TO FORM A SMALL DOUBLE HELIX WITH A GREAT DEAL OF COMPLEMENTARY BASE PAIRING WITHIN ITSELF.



THE PARTICULAR AMINO ACIDS ARE ATTACHED TO TRNA THROUGH A SERIES OF STEPS EACH STEP BEING CONTROLLED BY A PARTICULAR ENZYME. THE SCHEME CURRENTLY PROPOSED IS AS FOLLOWS:

$$AA + ATP \xrightarrow{\text{ENZYME}} E(AMP\text{-}AA) + PP + \cdot$$

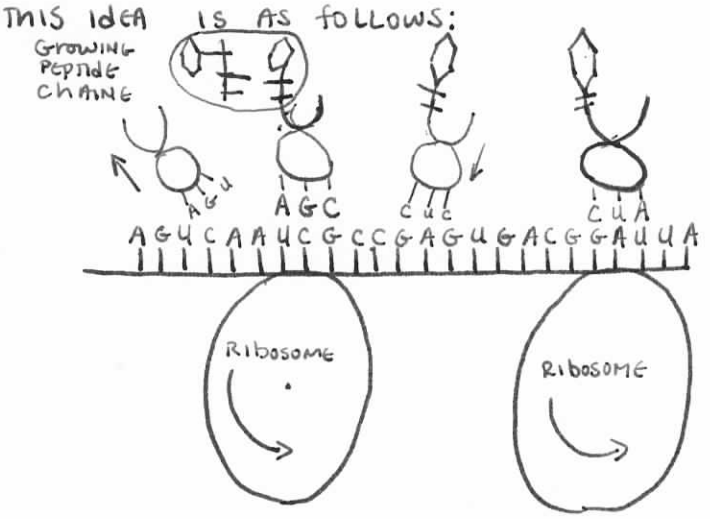
$$E(AMP\text{-}AA) \rightarrow TRNA\text{-}AA + E + AMP$$

$$TRNA\text{-}AA \rightarrow AA \text{ IN PROTEIN}$$

where AA = AMINO ACID
ATP = ADENINE TRIPHOSPHATE
AMP = ADENINE MONO PHOSPHATE
P = TRIPHOSPHOSPHATE
E = ENZYME

THE FIRST STEP OF THE REACTION IS ACTIVATION, THE SECOND IS ATTACHMENT TO RNA TO FORM THE TRNA COMPLEX, AND THE LAST STEP IS TRANSFER TO THE RIBOSOME. THE SPECIAL ENZYME INVOLVED IN THE REACTION ESTABLISHES WHICH AA WILL BE ATTACHED TO WHICH TRNA. THUS THE ATTACHMENT BETWEEN TRNA AND EACH AMINO ACID IS QUITE SPECIFIC. THE TRNA ACTS AS AN "ADAPTOR" BETWEEN THE TEMPLATE, mRNA, AND THE AMINO ACID.

PROTEIN SYNTHESIS BEGINS WHEN THE mRNA COMES NEAR A RIBOSOME AND GETS ATTACHED. ONCE THIS HAPPENS THE TRNA CAN ATTACH TO THE mRNA AT THE APPROPRIATE ~~TRIPLET~~ NUCLEOTIDE TRIPLET WHILE THE AMINO ACID HANGS off THE OTHER END. THE RIBOSOME MOVES ON ONE "NOTCH" AND ANOTHER TRNA COMES INTO PLACE, THUS POSITIONING ANOTHER AMINO ACID WITH ITS RESPECTIVE AMINO GROUP AND CARBOXYL GROUP BOTH HELD READY for THE UNION AND formation of THE PEPTIDE BOND. A SCHEMATIC REPRESENTATION OF THIS IDEA IS AS FOLLOWS:



~~MORE~~

TYPICAL PROTEIN MOLECULE FORMATION OCCURS AT A RATE of ONE EVERY 10 SECOND PER RIBOSOME. THIS RATE SUGGESTS THAT MORE THAN ONE RIBOSOME IS WORKING ON A mRNA AT ONE TIME. IN FACT IT IS POSSIBLE THAT mRNA IS READING DNA ON ONE END AND CONSTRUCTING PROTEINS ON THE OTHER.

MUTATION

The ordering of the amino acids in a polypeptide chain is extremely important. If for any reason the code messes up and produces a wrong amino acid, the final product will not be what was expected. In the case of leukemia, there are 12 different types each differing by one amino acid from the normal hemoglobin. The amino acid changes occur in both the α and β chains. The mutations are well understood and representative amino acid changes are:

	Amino Acid Number					
Chain	6	16	30	57	58	65
α		Lys → Asp	Glu → Gln	Gly → Asp	His → Tyr	Asn → Lys
β	Glu → Val, Glu → Lys					

The β chain mutation is responsible for sickle-cell anemia.

If the genetic code is examined to see how likely these mutations are, we find that all but one is accomplished by changing one base, e.g.

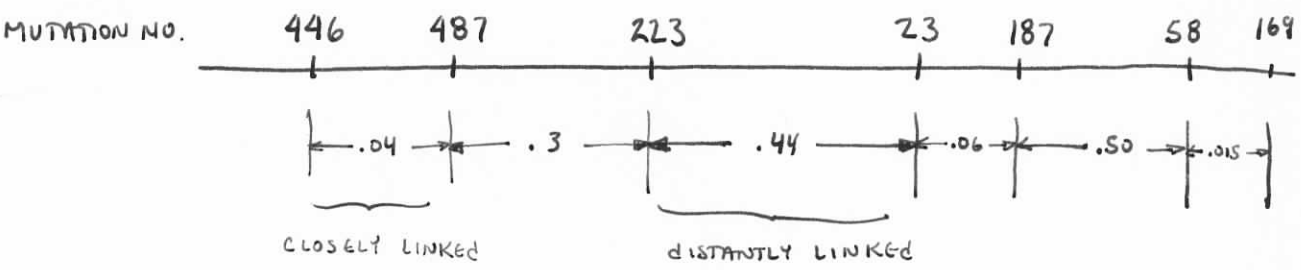
Amino Acid	Glu	→ Gln
code	GAA	→ CAA

The two base change is Lys to Asp; this mutation is less likely to occur than the one base pair mutation.

Out of the study of mutations the concept of genetic map order and mutation distance has evolved. As an example the bacteria E. coli can undergo several different types of mutations of tryptophane - each mutation corresponding to a different amino acid change. By ordering the mutations it is found that some seemed to be more strongly linked than other. That is to say when one mutation occurs most likely the other will too. This suggests that the gene carrying the mutations are

IN CLOSE PROXIMITY. SOME MUTATIONS ARE WEAKLY LINKED IMPLYING A GREATER SEPARATION DISTANCE ON THE DNA MOLECULE. THE FOLLOWING GRAPH IS REPRESENTATIVE of THE ORDERING AND MAPPING IDEA:

AMINO ACid	11	13	19	47	49	30	71
NORMAL	TYR	Leu	Thr	GLy	GLy	GLy	SER
	↓	↓	↓	↓	↓	↓	↓
MUTETED	CYS	ARG	ILEU	ARG	VAL	ASp	Leu



GENETIC

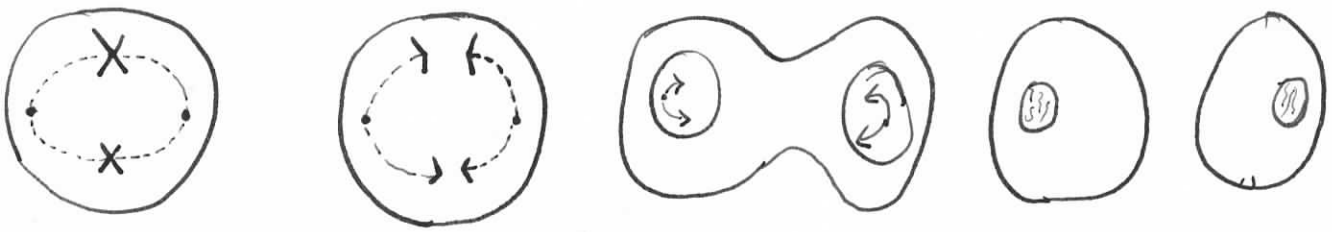
GENETICS IS THE STUDY of GENES. GENES ARE SEGMENTS of INFORMATION ON THE DNA MOLECULE for MANUFACTURING A PARTICULAR ~~AMINO Acid~~ POLYPEPTIDE CHAIN, I.E A PROTEIN. THE DNA IS THE CHROMOSOME SO A GENE IS PART of THE CHROMOSOME ONE FASCINATING SUBJECT IS CELL DIVISION AND THE PROCESS of INFORMATION TRANSfer. THE CELL DIVISION IS CALLED MITOSIS AND CENTRAL TO THE DIVISION IS DOUBLING of THE CHROMOSOMES. IN MAN THERE ARE NORMALLY 46 CHROMOSOMES. THE 46 IS DOUBLED TO 92 THEN THE CELL DIVIDES. THE PROCESS IS SOMETHING LIKE THE FOLLOWING.

THE CHROMOSOMES ARE ARRANGED IN THE NUCLEUS IN PAIRS. EACH of THE 23 PAIRS DIFFERS IN SIZE AND SHAPE FROM THE OTHERS. THE CHROMOSOMES ARE ATTACHED TOGETHER BY A STRUCTURE CALLED THE CENTROMERE. TWO REPRESENTATIVE PAIRS MAY LOOK LIKE THE FOLLOWING

DURING THE NORMAL PHASE of THE CELL LIFE THE STRUCTURAL DETAIL of THE CHROMOSOME PAIRS CANNOT BE DISTINGUISHED.

IN THE FIRST STAGE OF MITOSIS, CALLED THE INTERPHASE, THE CHROMOSOMES SPLIT, I.E. THE DOUBLE HELICES REPLICATE. THEN THE CHROMOSOMES CONTRACT BECOMING SHORTER, FATTER, AND VISIBLE TO THE MICROSCOPE. THIS MARKS THE SECOND STAGE CALLED THE PROPHASE. THERE ARE NOW 4 DNA MOLECULES ATTACHED TO ONE CENTROMERE. THE DNA HALVES CALLED CHROMATIDS CONTRACT LIKE A COILED SPRING. WHEN THE CHROMATIDS HAVE FINISHED CONTRACTING, THE third PHASE, THE METAPHASE, BEGINS. THE CHROMOSOMES NOW LOOK LIKE

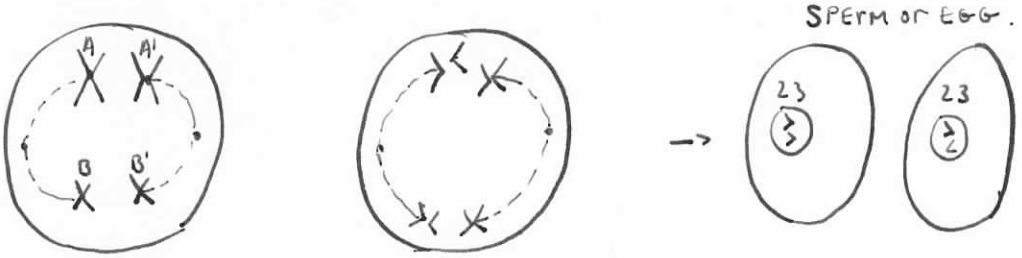
IN THE METAPHASE A NEW STRUCTURE CALLED THE SPINDLE APPEARS. THE SPINDLE IS A LONG-CHAIN PROTEIN MOLECULE. THE SPINDLES ATTACH TO THE CENTROMERES AT ONE END AND TO TWO "POLES" of THE NUCLEUS AT THE OTHER. THE POLES ARE LOCATED AN THE EQUATOR of THE NUCLEUS. THE CENTROMERES, THE MECHANISM of CHROMOSOME MOVEMENT, POSITIONS THE CHROMATIDS ALONG THE SPINDLES IN PREPARATION of THE DIVISION PROCESS. WHEN ALL 43 CHROMASOMES ARE IN ONE PLANE, THE DIVISION PHASE, THE ANA PHASE PHASE BEGINS. THE CENTROMERES DIVIDE SO THAT EACH CHROMATID HAS ITS OWN CENTROMERE. THE SPINDLES CONTRACT PULLING THE TWO HALVES TO OPPOSITE CORNERS of THE NUCLEUS. WHEN THE CHROMATIDS ARE TIGHTLY PACKED NEAR THE POLES, THE NUCLEUS AND CELL DIVIDES IN THE TELOPHASE. THE SPINDLES THEN DISAPPEAR AND THE TWO CELLS BECOME NORMAL. THE SEQUENCE of EVENTS IS OUTLINED BELOW:



MEIOSIS

MITOSIS IS NOT THE ONLY form of NUCLEAR division. DURING SEXUAL REPRODUCTION THE CHROMOSOME NUMBER DOES NOT INCREASE. If IT DID AFTER EACH DIVISION THERE WOULD BE 46 more CHROMOSOMES. AFTER 3 DIVISIONS THERE WOULD BE 184 CHROMOSOMES AND 23,332 AFTER 10 DIVISIONS. THUS ANOTHER division PROCESS MUST BE WORKING WHICH KEEPS ~~A~~ CONSTANT NUMBER of CHROMOSOMES. FOR MAN TWO CELLS A SPERM AND EGG UNITE TO form A SINGLE NEW CELL CALLED A ZYGOTE which CONSISTS of THE desired 46 CHROMOSOME AGAIN IN 23 PAIRS. THUS SOMEHOW THE SPERM AND EGGS GET rid of 23 CHROMOSOMES. THE DECISION AS TO which HALF of THE 23 PAIRS IS EXCLUDED IN THE SPERM AND EGG IS PURELY RANDOM.

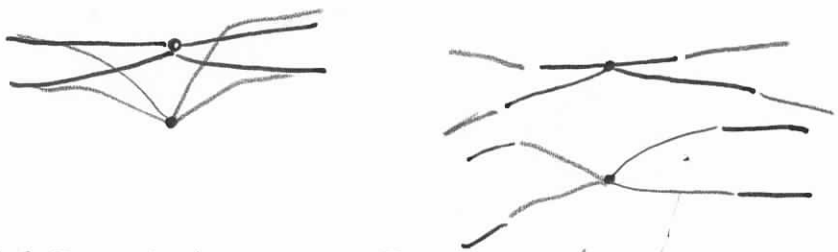
WHEN THE CHROMOSOMES DOUBLE AND THE CENTROMERE IS ATTACHED TO THE SPINDLE, THE PARTS ARE PULLED APART DIFFERENTLY



SPERM or EGG.

THE 23 REMAINING CHROMATIDS IN EACH NUCLEUS EVENTUALLY die off.

WHEN THE SPERM AND EGG COME TOGETHER IN PAIRS THERE ARE 2^{23} (8,388,608) POSSIBLE COMBINATIONS. of CHROMOSOMES. THUS THE CHANCE of ANY SINGLE SPERM or EGG CONTAINING ONLY PATERNAL or MATERNAL ~~CHROMOSOMES~~ IS NEGLIGIBLE. FURTHER diversity IS afforded through CROSSOVER LINKAGE IN CHROMOSOMES PRIOR TO DIVISION. WHEN 2 PAIRS of CHROMOSOMES ARE IN CLOSE PROXIMITY THEY ~~CHA~~ CAN EXCHANGE GENES



MEIOSIS THUS ASURE COMPLETE MIXING of THE GENETIC INFORMATION

The following pages are the original real time notes taken during the lectures. As Feynman was having a harder time prepring for the lectures given the developments in the theoretical and experimental physics world, the lectures started to reach a stopping point.

As mentioned before, these raw notes are the working material I started with to transcribe them into a more representive and presentable form. They are crude and maybe be of limited value to the readers very familiar to the subject matter. That said, their value remains in capturing the topics of interest Feynman had as be explored another part of science and nature that was not part of his CalTech program.

In my own case I found the transcription time and effort to become challenging as work demands were increasing. At the time I was working on the Intelsat IV satellite program and we were in integration andd testing preparing for the first launch toward the end of 1970/early '71. It was Intelsat IV that carried the live video of Nixon's historic visit to China. As I was helping prepare for launch, several colleagues transported the critical ground station over to China and prepared it for the video relay. Today we take for granted such global communications but 40+ years ago it was "magic" as Sir Arthur Clarke called it.

4×10^4 base pairs $\times \frac{1 \text{ amino acid}}{10^2 \text{ base pairs}} \times 46 \times 3 = 1.84 \times 10^6$

3/23/70

46 chromosomes each big piece DNA coming in 23 apparent ~~cells~~ pairs

characteristics of heredity

suppose ~~on~~ A certain protein makes red flower in pea plant. gene = line of information tell how make enzyme and suppose R gene in complementary pair. If no ~~on~~ R gene in both ~~cells~~ chromosomes appear white

A +R +R

B | |

C | |

D

R + + NO R + + NO

A' A"

R + + R R + + NO R + - + NO NO + + NO

Red Red' red' white

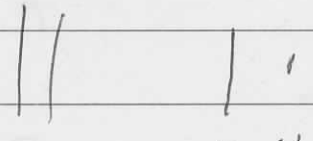
if red' more like red than white. then red is dominant and white is recessive.

when ~~red~~ read A' and A" ~~on~~ concentration of R and NOR dictates what characteristic protein. E.g. R + NOR → 1/2 strength so get mixture. ∴ number recessive genes unknown.

strong link genes closed together.

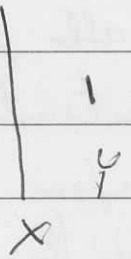
Sex determination.

in man have sex determining chromosomes which may not be the same



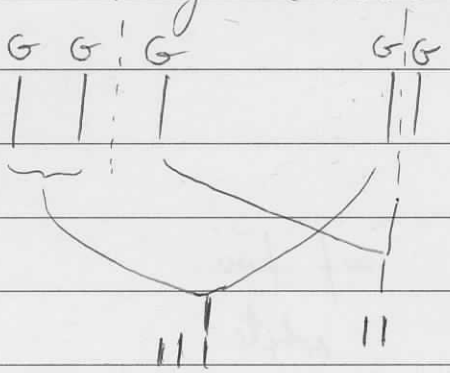
XX female

X Y male



Sex linked inheritance - haemophilia

3 chromosomal chromosomes 666 or 111 instead of 2 = Mongolock idiot. prior reference to Down Syndrome



deleted B

Sex mutation - nothing happens at maturity

XX Y

X O female body - die in miscarriage usually

XX O female

X YY - no unusual physical difference - 5% in institution

XXX (XX) - normal body feable mined

take verbal things no failure but can't retain

magic. (feature of mental ability impaired

3/30/70

We have just discussed kinetics and 2 genes of each kind in higher animals. Haven't discussed Controls or evolution.

- Control -

at least 4 different ways to control reaction.

(1) Chem. Kinetics - Thermodynamics

(2). Allostery - enzyme changes its affinity in different circumstances)

(3). MRNA amount is controlled, i.e. controlling rate of destruction after read

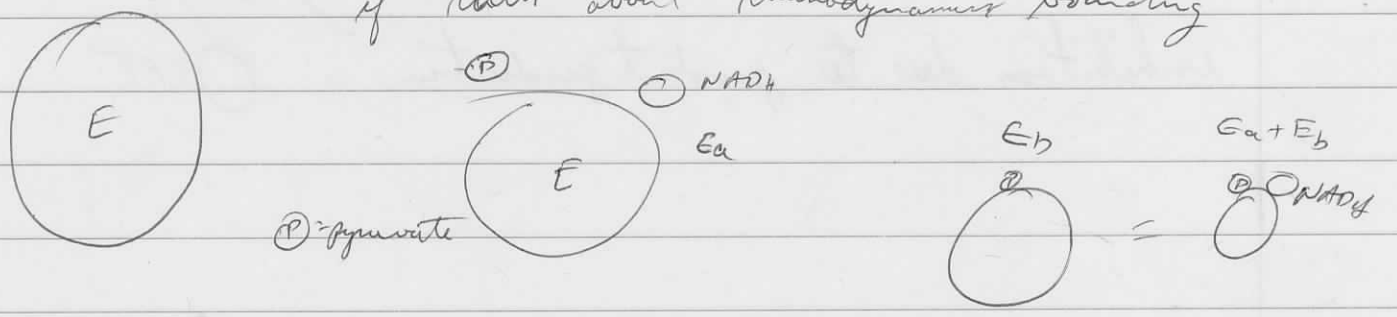
(4). Control of reading of DNA

Enzymatic reactions, E.g. enzyme

pyruvate + NADH $\rightarrow$ lactic acid + NAD

for this to work NADH must bind first and lactic is first to leave. NADH is in short supply.

if talk about Thermodynamics bonding

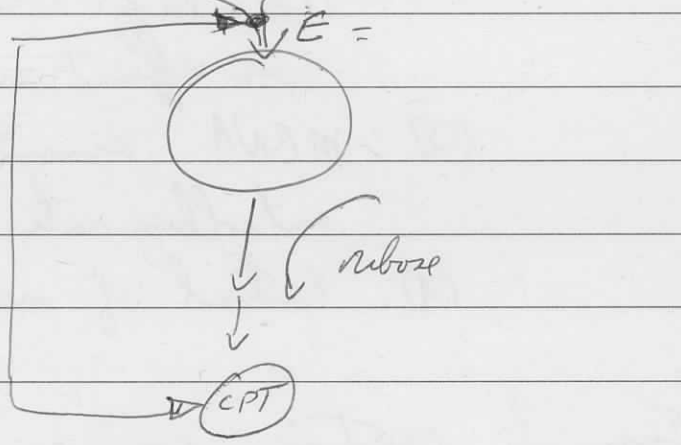


suppose certain binding energy, E_A and E_B. Bind as $e^{-(E_A+E_B)/kT}$ more like to bind (P) after NADH already bound to E. Means supply lot enzyme using " and in short supply. if P is ~~about~~ present increase probably to form E+P+NADH. which is bound tighter than if

if bound separately. Binding directly affected by (P)

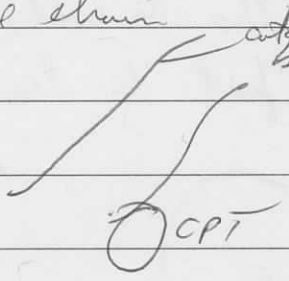
(2) Allosteric

in manufacture of CPT start with asp and carbamyle



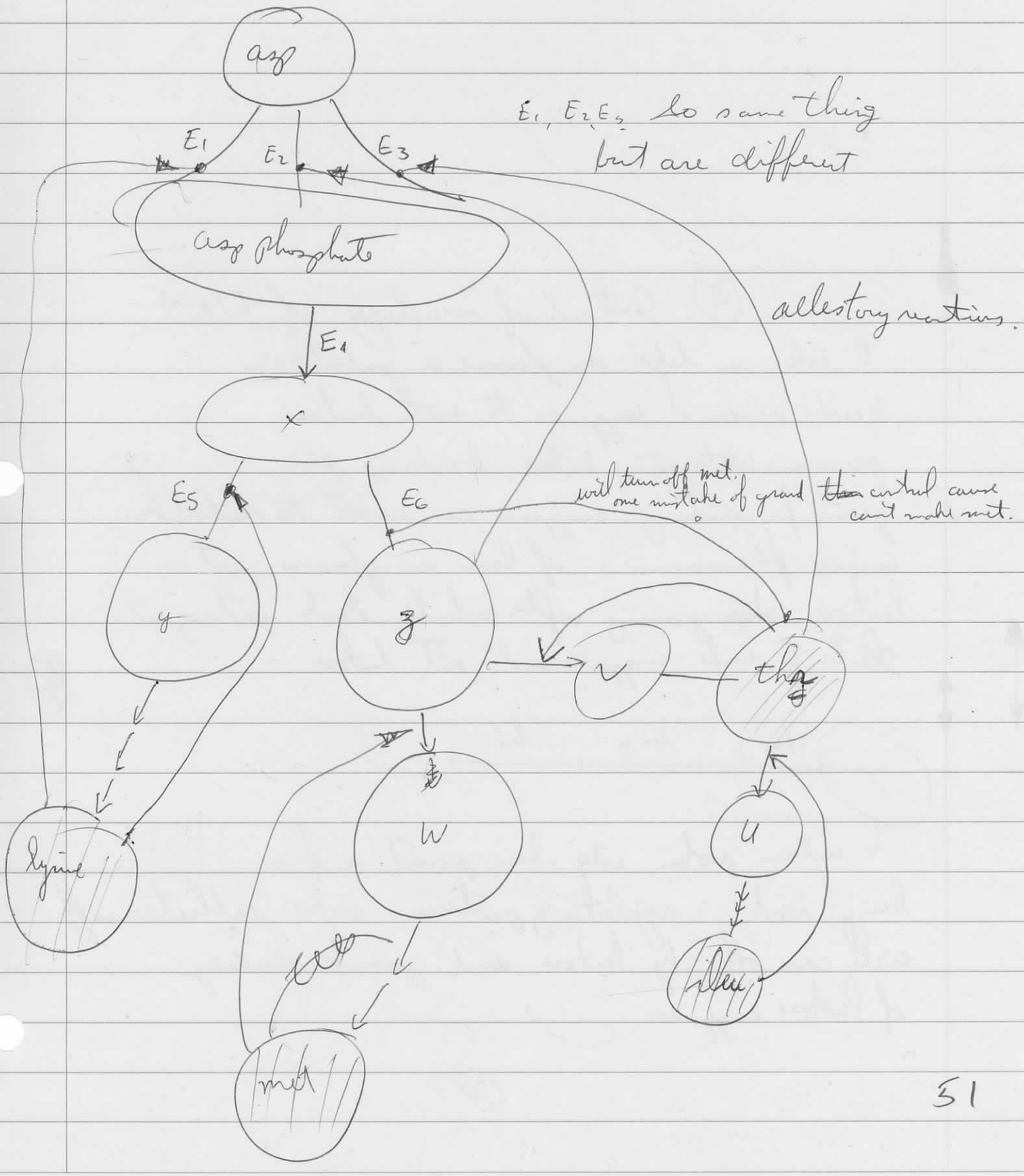
feedback controls quantity of E which makes it go

CPT attached to neighboring polypeptide chain which distorts catalytic site



inhibition due to product production

Production of various amino acids
aspartic and like food stuff for making ~~of~~ other
amino acids.



$E_1, E_2 E_3$ do same thing
but are different

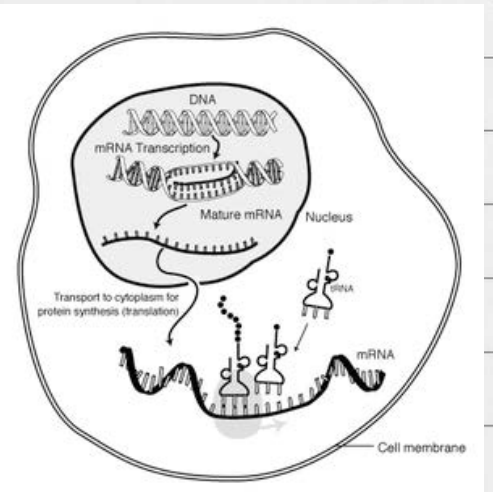
allestory reactions.

will turn off met.
one mistake of grand ~~the~~ cortical cannot
can't make met.

(3) MRNA - amount

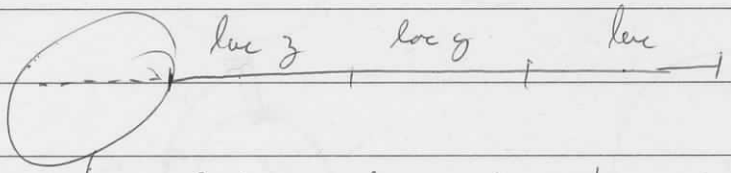
mRNA, messenger RNA

control amount enzyme manufactured.
not known too well



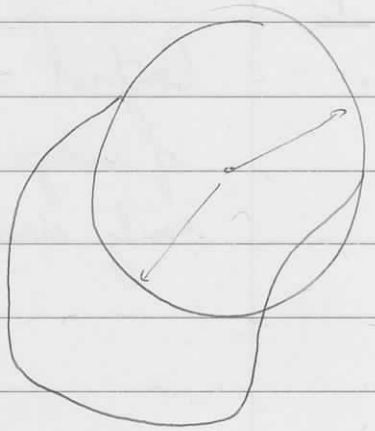
(4) Control of reading of RNA

E. Coli can live on glucose or galactose.
need enzymes to eat lactose,
permease lets in, lactose, breaks up, plus —
genes for making enzyme are next to each other
cause phenomena: if lives on glucose put in
lactose stops growing after while start eating it.
starts to make enzymes and eat lactose



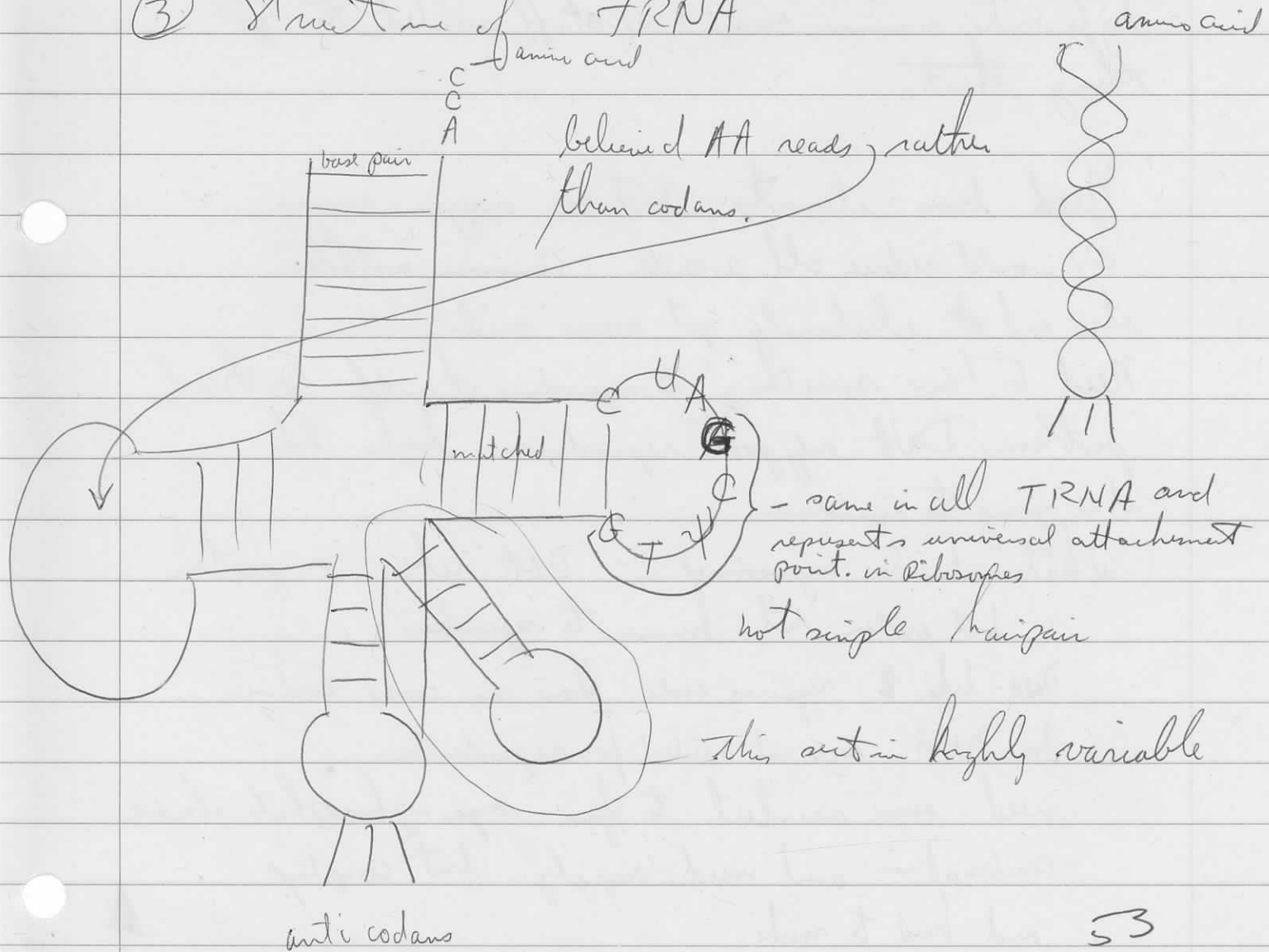
certain protein sits here prevent. s from
being read. = regulating protein. works allosterically
will come off by lactose and permits reading
of lactose enzymes.

① Chromosome for bacteria is a circle and seen in electron microscope



② in Bacteria start of reading protein is peculiar. ~~Starts to read~~ from amino and end. Acetate end attaches to met and form chain then enzyme cuts along and cuts off met-met.

③ Structure of TRNA



1

Control leads to subject of development of embryo. How cells differentiation in early development.

How did all begin

do we start with cells etc no must be answer. try to make minimum amount of stuff needed to get thing start.

Need basic elements but no oxygen cause O2 would reduce all a. acids. Ammonia, methane etc and electricity. get amino acid.
Need to have something to reproduce itself. Central problem. DNA only part reproduces. looks like it is going to reproduce
What molecule reproduced - DNA like or protein
but protein that known to reproduce.
DNA-like requires code. How can code evolve.
In DNA code not needed for reproduction.
need some accident to form sugar-phosphate-base combination and need supply. but complex and hard to make.

4/20

$\varphi = \frac{\pi}{\delta}$

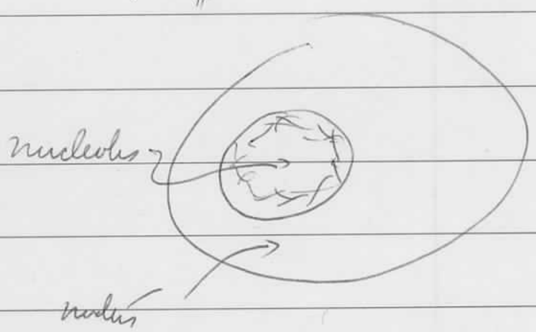
$\tau = \frac{\partial}{\pi}$

Mitosis - Retina - Muscles.

Last time Cell structure

nucleus, nucleolis

nuclear membrane in 2 layers



special Cells

Retina

sensitive to light. Cones cells have outer and inner segment

light must reach outer surface comes in wrong

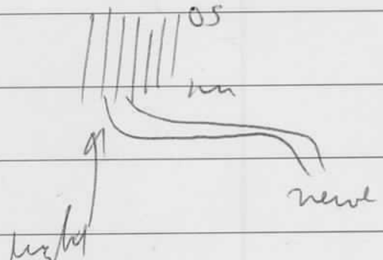
in Octopus eye inverted.

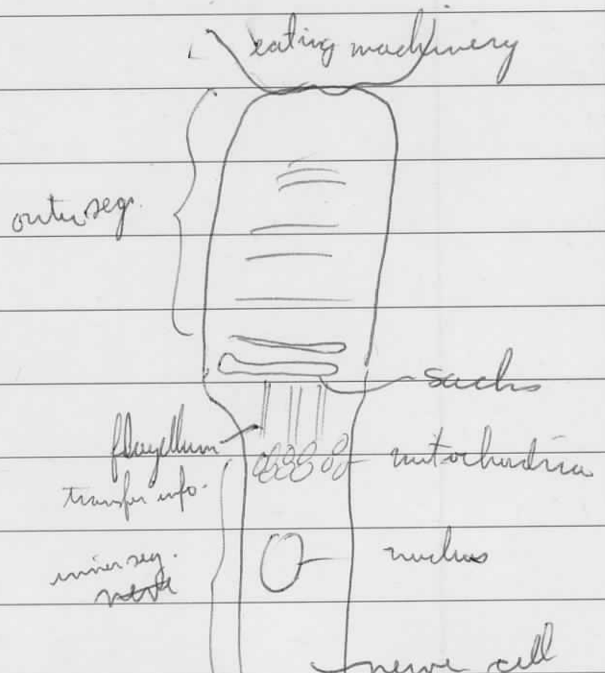
cells come in rods and cones

enzymes obsin involved. (visual purple)

flagellum may pass information somehow.

1/10 relaxation time need 4-5 photons.





Antibody Reaction

Happens in mammals. Aim or purpose to fight disease
If large protein molecule enters bloodstream then
after time ~~substance~~, antibody, is produced which
attach to molecule and agglomerate, i.e. lumps together
Antigen generates antibody,
"Foreign stuff
If put in rabbit protein develops antigen will not
coagulate different protein. very little crossover
almost taylor made
everyone is chemically individual

Where is made- lymph node and Spleen make
plasma cells. There is precursor cell, various
immature plasmacytoblasts which start to divide
and produce machinery to make protein and secrete
into blood.

If antigen is injected into newborn won't make
antibody right latter won't produce antibody latter.
~~Before no good but~~ Must inject protein divide
make antibody won't attack your own must know
everything Goddamn incredible

How does know ~~not~~ to produce right antibody
If have more 1 antigen get more 1 antibody. Antigen
excites plasma cell
to chromosome info to make all antibody but wanted
on this information

structural versin - from DNA

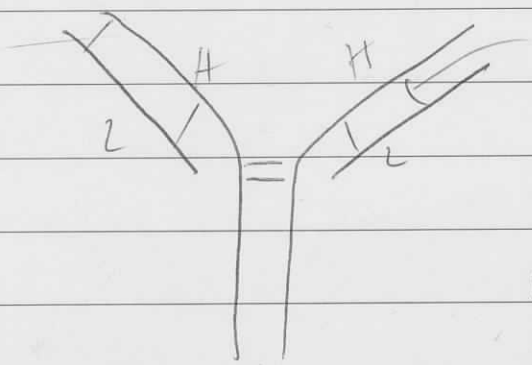
at newborn suppose antibody

antigen kills cell precursor to antibody latter

speaks cells. I.E. so won't kill off own ~~so~~ protein

Auto antibody production do opposite

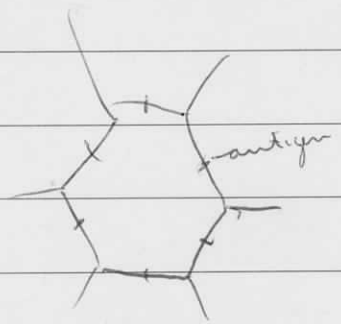
x g1



sulphur bridges

antibody Segments

variable



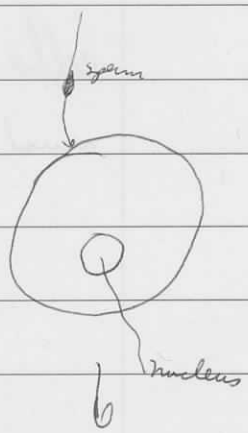
how precursor know what antigen to produce.

4/27/70

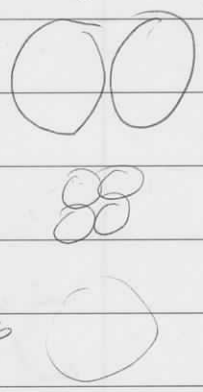
Fertilization Cell division

after sperm hits egg membrane

lot RNA stored in egg it is not synthesized by DNA is and rapidly divides in ~ hour and division continues



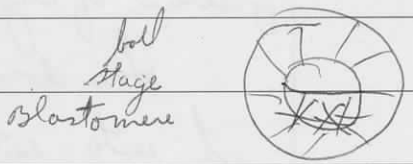
Ball stage start asymmetric division and indentation starts and forms gastrula and forms endo, ecto, meso derm

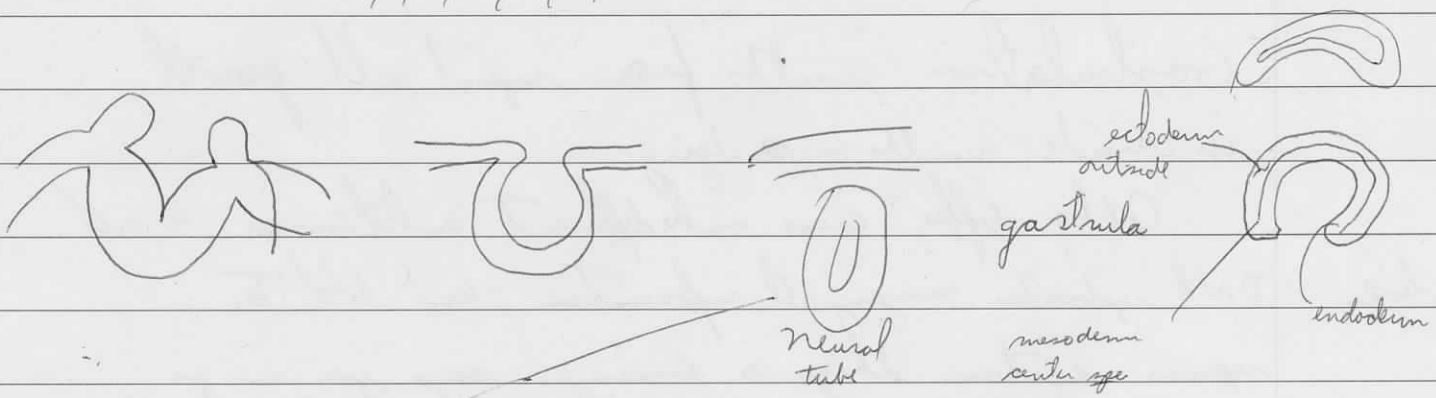


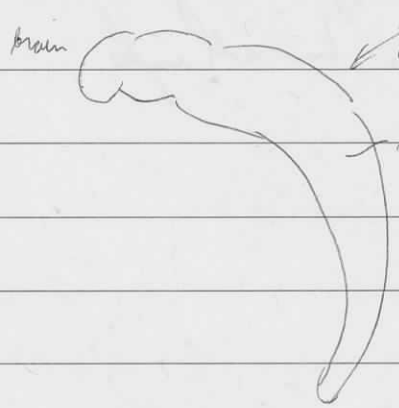
mesoderm = muscle,

ectoderm -> nerve

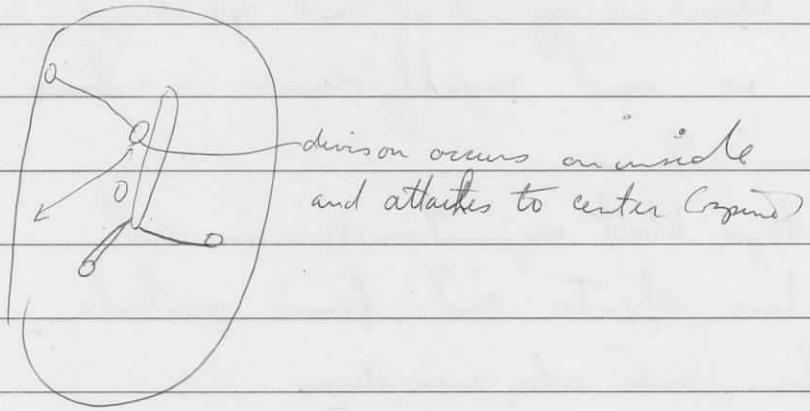
Neural tube







cells can move in fetus, germ cells migrate
neural tube



Cell different nit in
in what way are cells different chemically
and how do arise. don't want make muscles in brain
Pattern of Organization
How does fact cell is in certain place turn
it into certain thing.

Gastrulation results from rapid cell growth
in inside results in bulging.

Cells differ cause make different substances. As cell
divides DNA replicates carrying all information, and told to
repress certain things a message says "you are a
pancreas cell". But goes as repressor have all info.

$x + y = \$9$ $1.2y + y = 9$

$x = 1.2y$ $y = 9/2.2 = 4.1$

$x = \$1.20$ $x = 4.9$

$y = \$1$

may be some loss of info in adult cell. Tadpole can replicate nucleus from intestine and fertilized egg new frog developed

parthenogenesis

How do cells differ if all have same DNA - Must be suppressors which come from cytoplasm. from frog experiment ovule develops like egg not intestine.

TRNA produced in blastomere.

Control from cytoplasm.

When does certain particular protein developed which level determines growth pattern.

Sc American

How cells move around -

eg. central nervous system

Cells seek out correct morphology or spatial location

5/4/70

From cytoplasm comes controller to tell cell what part to read.

Animal metamorphus

when larva develops there ~12 imaginal disks ↑ remains in undifferentiated cells like islands all over larval. Enzymes digests itself into food except for disc which start to divide & grow as expense of fluid. Leg disks, head has 6, rear end, wing

How nerve cells grow?

do nerve fibers grow like topsy or is it organized. Brain is organized. When things need to be very specific they are like the eye.

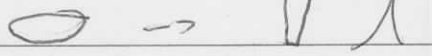
How does nerve know where to go? Special protein for each position rather than gradient.

Slim mold — Social Amoebe

after eat all food goin together 10 to 10^5

eventually form spor mass at top

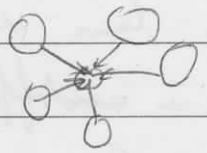
forms hollow tube.

How do come together? emit 

substance and attracts eachothe

Cyclic AMP and blow away.

to green area:



Epinephrin (adrenalin) supplies energy fast.