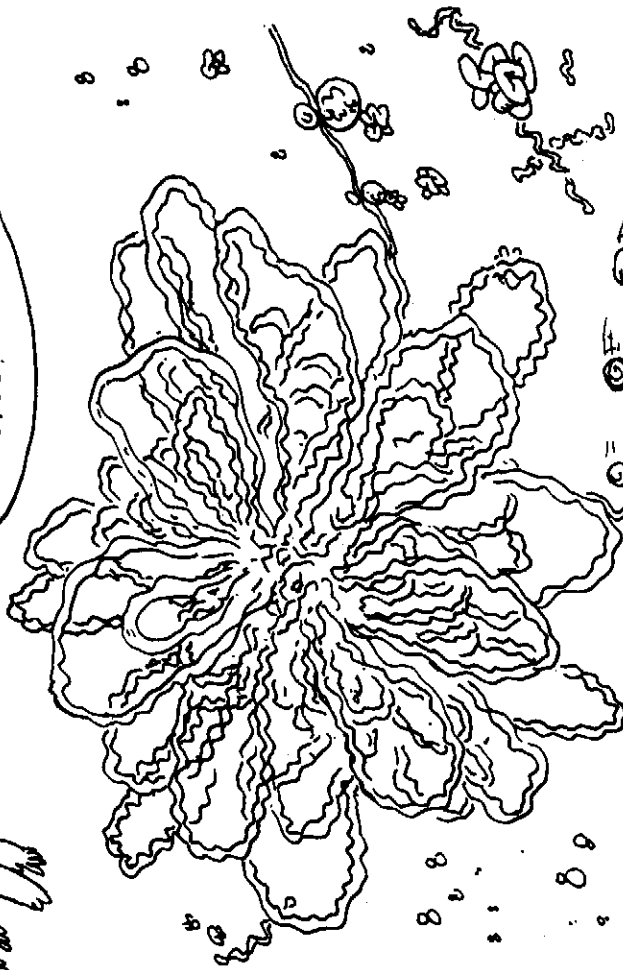
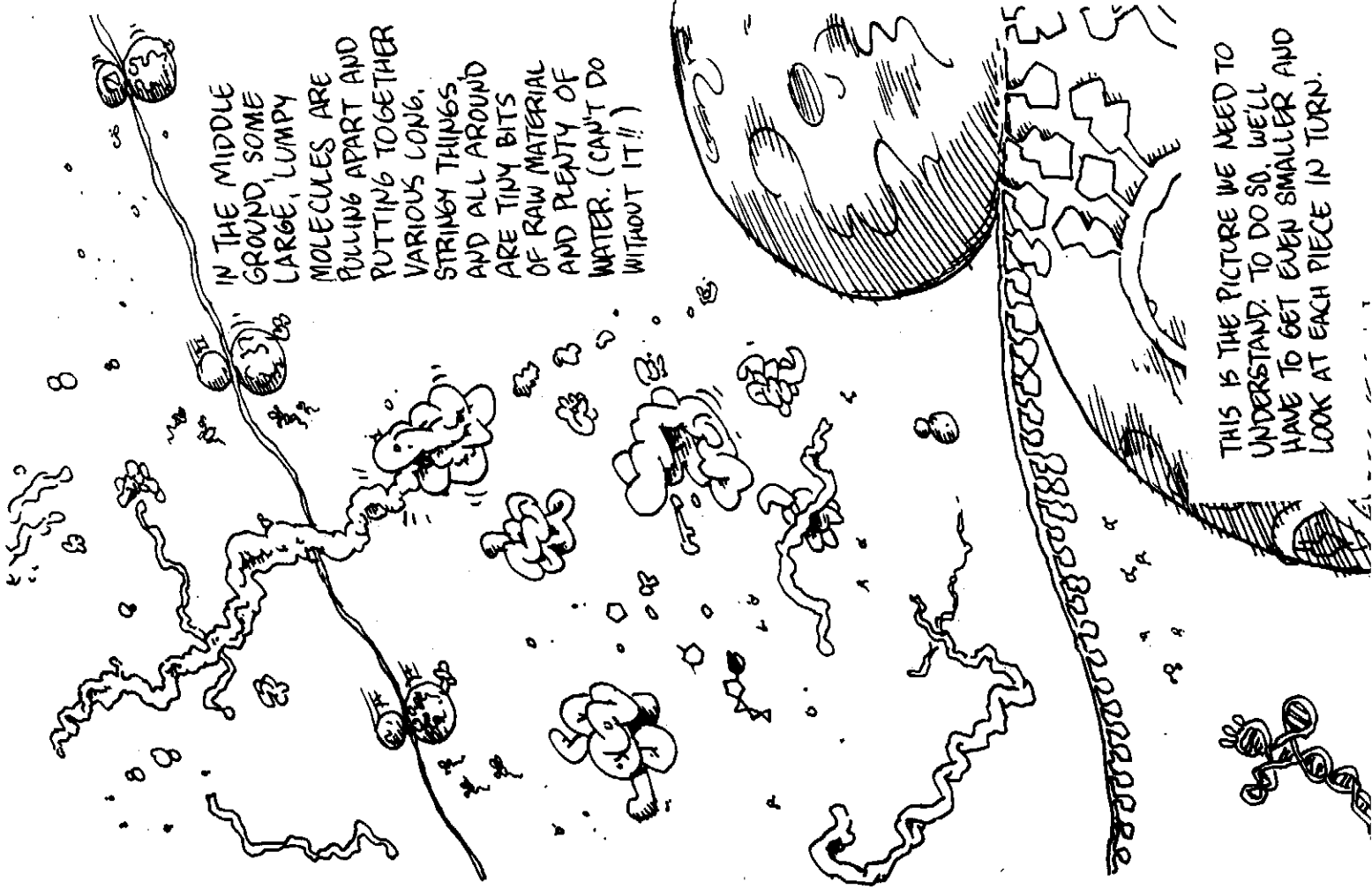




THIS IS THE VIEW FROM INSIDE THE BACTERIUM *E. COLI*! ALTHOUGH IT LOOKS PRETTY CONFUSING AT FIRST, WE CAN MAKE OUT A FEW OBVIOUS FEATURES!



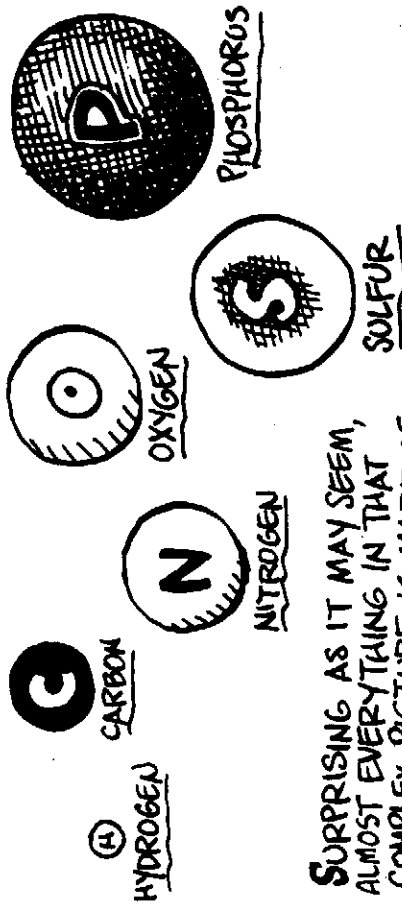
THAT TANGLED MASS IS THE SINGLE CHROMOSOME, CONTAINING THE GENETIC MATERIAL. TRAILING OFF THE CHROMOSOME ARE SOME LONG STRANDS WITH DOUBLE BALLS SLIDING ALONG THEM, THE SITE OF SOME ACTIVITY.



IN THE MIDDLE GROUND, SOME LARGE, LUMPY MOLECULES ARE PULLING APART AND PUTTING TOGETHER. VARIOUS LONG, STRINGY THINGS AND ALL AROUND ARE TINY BITS OF RAW MATERIAL AND PLenty OF WATER. (CAN'T DO WITHOUT IT!!)

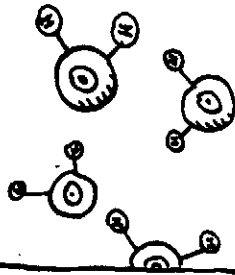
THIS IS THE PICTURE WE NEED TO UNDERSTAND. TO DO SO, WE'LL HAVE TO GET EVEN SMALLER AND LOOK AT EACH PIECE IN TURN.

# MACROMOLECULES



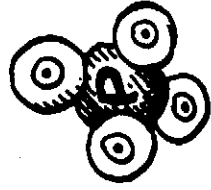
SURPRISING AS IT MAY SEEM, ALMOST EVERYTHING IN THAT COMPLEX PICTURE IS MADE OF JUST SIX DIFFERENT ELEMENTS.

IN THE CELL THESE ATOMS ARE JOINED TOGETHER TO FORM **MOLECULES**.

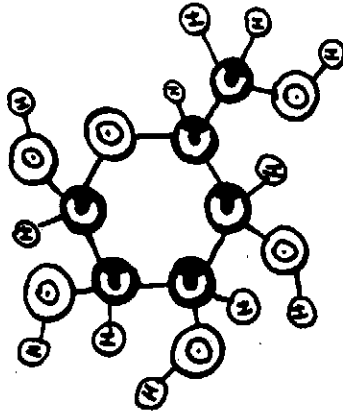


THE SIMPLEST AND MOST ABUNDANT BY FAR IS WATER,  $H_2O$ .

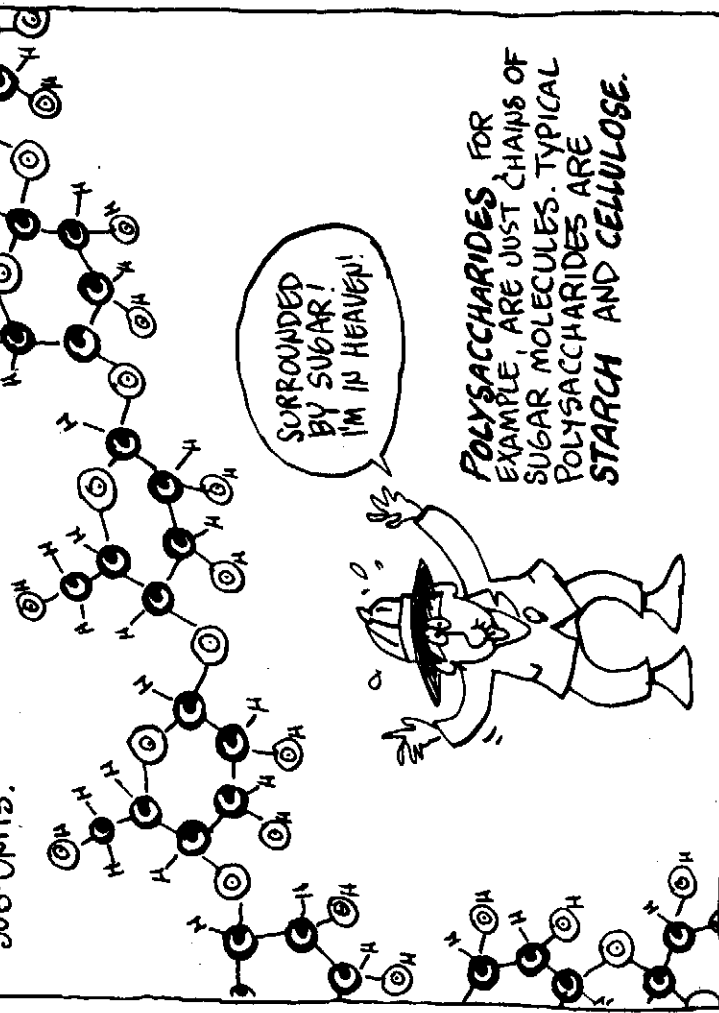
ANOTHER SMALL ONE IS THE PYRAMID-SHAPED **PHOSPHATE**,  $PO_4$ .



A BIT BIGGER ARE THE RING-SHAPED **SUGARS**. THIS ONE IS **GLUCOSE**,  $C_6H_{12}O_6$ .

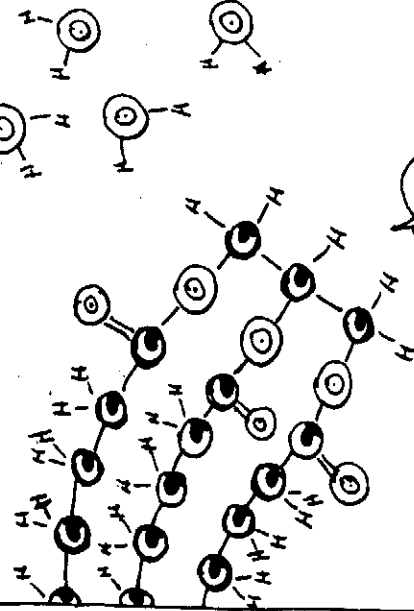


BUT MOST KINDS OF MOLECULES IN THE LIVING CELL ARE ENORMOUS, CONSISTING OF THOUSANDS OF ATOMS. THESE **MACROMOLECULES**, THOUGH LARGE, ARE GENERALLY MADE BY STRINGING TOGETHER MANY COPIES OF IDENTICAL SUB-UNITS.



SURROUNDED BY SUGAR! I'M IN HEAVEN!

**POLYSACCHARIDES** FOR EXAMPLE, ARE JUST CHAINS OF SUGAR MOLECULES. TYPICAL **POLYSACCHARIDES** ARE **STARCH** AND **CELLULOSE**.

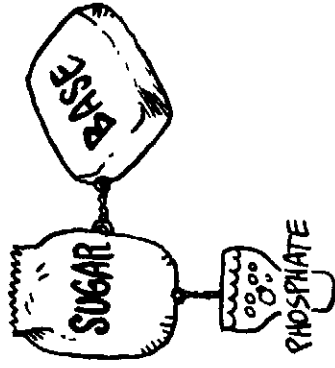


UGH!

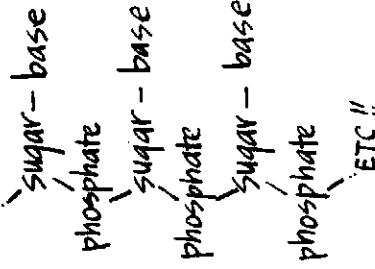
**LIPIDS** ARE A CLASS OF MORE COMPLEX MACROMOLECULES, HAVING AT LEAST ONE END WHICH IS REPELLED BY WATER. **LIPIDS** FORM A MAJOR COMPONENT OF CELL MEMBRANES AND INCLUDE THE ANIMAL FATS AND VEGETABLE OILS.

STILL MORE COMPLEX, BUT MOST IMPORTANT IN GENETICS, ARE THE NUCLEIC ACIDS AND PROTEINS... WATCH CLOSELY.

THE BUILDING BLOCKS FOR NUCLEIC ACIDS ARE CALLED NUCLEOTIDES. AN INDIVIDUAL NUCLEOTIDE ITSELF HAS 3 COMPONENTS: A SUGAR, A PHOSPHATE, AND A BASE, LIKE SO —

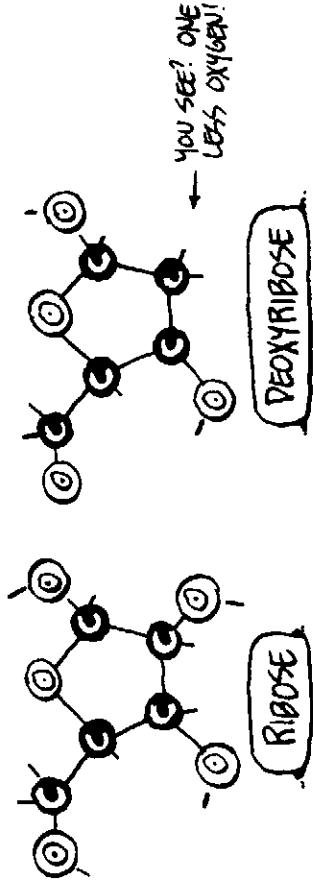


THESE ARE HOOKED TOGETHER TO MAKE A LONGWINDING SUGAR-PHOSPHATE "BACKBONE" WITH A SEQUENCE OF BASES STICKING OFF:

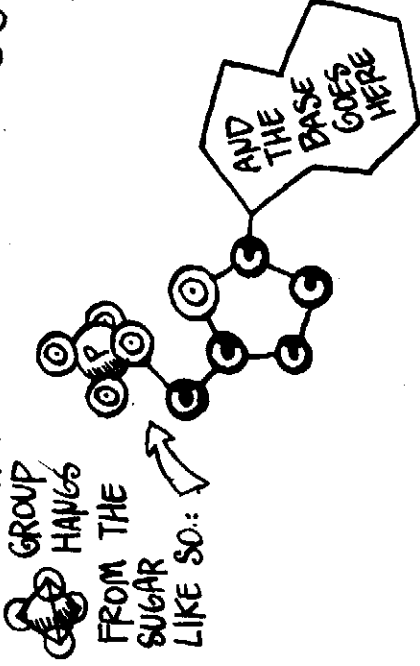


THIS MAY GO ON FOR MILLIONS OF NUCLEOTIDES!

THE SUGAR MAY BE ONE OF TWO KINDS, WHICH WE ILLUSTRATE HERE WITHOUT ALL THEIR PESKY HYDROGEN ATOMS. (THEY JUST CLUTTER UP THE PICTURE!)



THE PHOSPHATE GROUP HANGS FROM THE SUGAR LIKE SO:

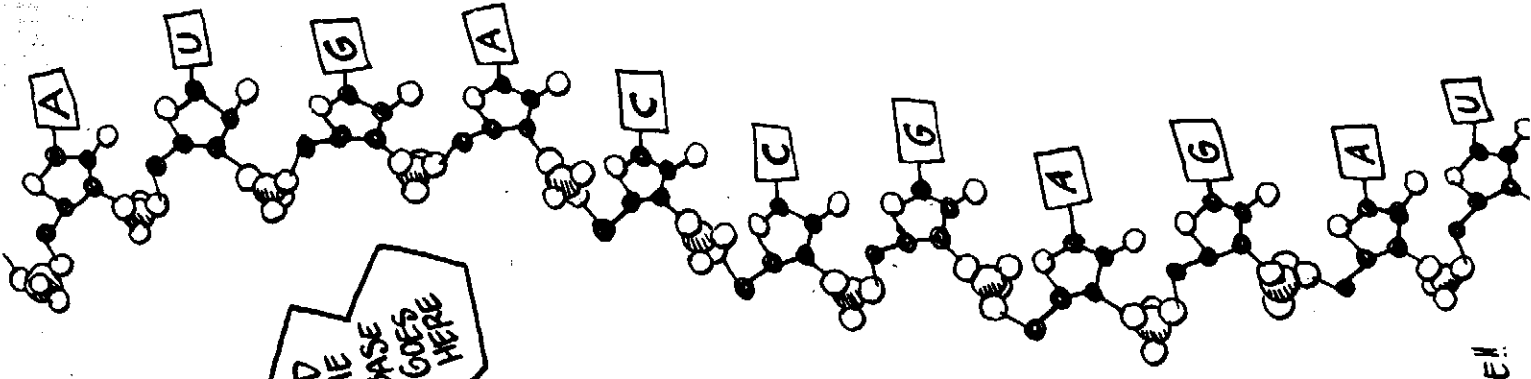


WE'LL TOUCH THE BASES LATER ..... FOR NOW WE'LL JUST SAY THERE ARE 5 KINDS, WITH THE NICKNAMES A, C, G, T, AND U.

IN ANY GIVEN NUCLEIC ACID MACROMOLECULE, ALL THE SUGARS ARE THE SAME.

NUCLEIC ACIDS WITH RIBOSE ARE CALLED RIBONUCLEIC ACID, OR RNA. THOSE WITH DEOXYRIBOSE ARE CALLED DNA (DEOXY-RIBONUCLEIC ACID, OF COURSE!).

IN BOTH DNA AND RNA, THE BASES MAY BE DIFFERENT FROM ONE NUCLEOTIDE TO THE NEXT, GIVING NUCLEIC ACIDS THE APPEARANCE OF MESSAGES IN SOME STRANGE MOLECULAR LANGUAGE!

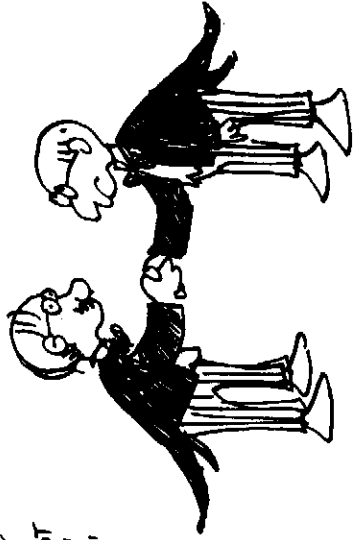


# PROTEINS

ARE THE MOST COMPLICATED MACROMOLECULES OF ALL. THE BIOLOGIST MAX PERUTZ SPENT 25 YEARS - MOST OF HIS CAREER - ANALYZING JUST ONE OF THEM: HEMOGLOBIN, THE PROTEIN THAT CARRIES OXYGEN THROUGH THE BLOODSTREAM. FOR THIS, PERUTZ RECEIVED THE NOBEL PRIZE IN 1962...

MAX, WHAT TOOK YOU SO LONG?

IT WOULD TAKE TOO MUCH TIME TO EXPLAIN...



YET IN A CERTAIN SENSE, PROTEINS ARE SIMPLE, TOO: LIKE OTHER MACROMOLECULES, THEY ARE LONG CHAINS OF SMALLER SUBUNITS.



ACTUALLY, HEMOGLOBIN IS TWO PAIR OF SUCH CHIMNS, WRAPPED UP IN A SYMMETRICAL TANGLE.

THE SUBUNITS OF PROTEIN MOLECULES ARE AMINO ACIDS, WHICH ARE NOT NAMED AFTER **IDI AMIN**, THE FORMER DICTATOR OF UGANDA.

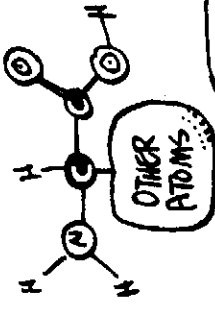
ABSURD!! OF COURSE THEY ARE!

TAKE IT FROM ME!



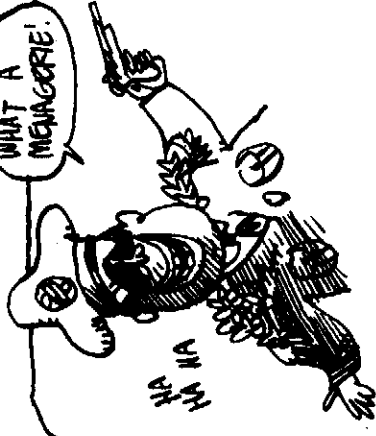
OH! O.K...

THE TYPICAL AMINO ACID LOOKS LIKE THIS:

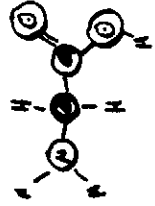


IT'S THAT CLUSTER OF "OTHER ATOMS" THAT COMPLICATES MATTERS...

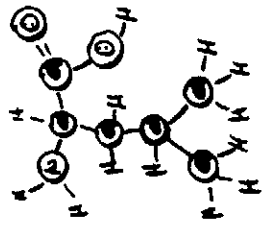
WHAT A MENAGERIE!



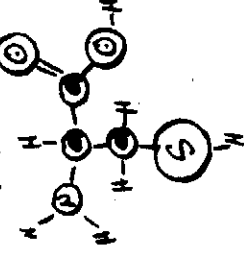
GLYCINE IS QUITE SIMPLE:



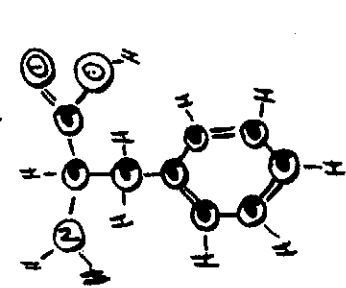
LEUCINE HAS A BRANCH:



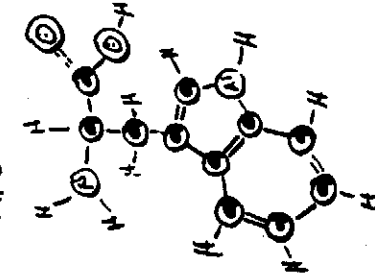
CYSTEINE CONTAINS SULFUR:



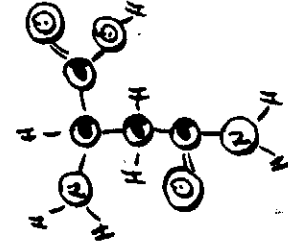
PHENYLALANINE HAS A RING:



TRYPTOPHAN HAS RINGS OF RINGS:



ASPARAGINE HAS EXTRA NITROGEN:



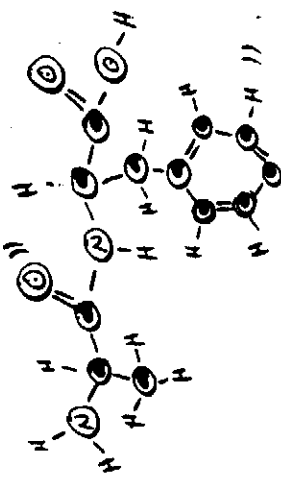
CONFUSED? HA HA HA HA



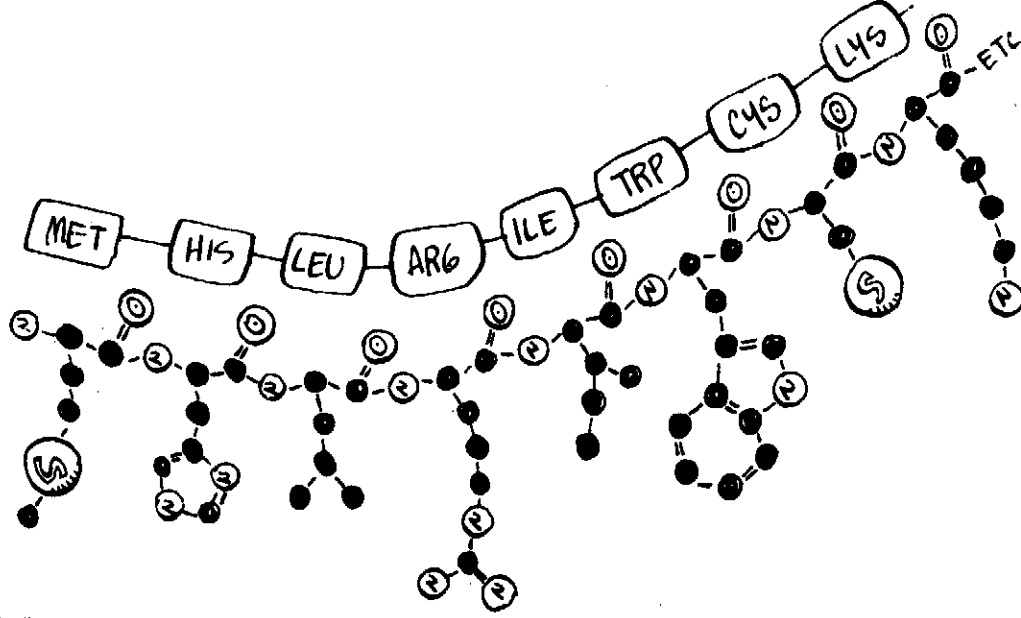
SO WERE THE CHEMISTS! HA HA HA HA

IN ALL, SOME 20 "STANDARD" AMINO ACIDS GO INTO PROTEINS:

AMINO ACID	ABBREVIATED AS:
GLYCINE	GLY
ALANINE	ALA
VALINE	VAL
LEUCINE	LEU
ISOLEUCINE	ILE
SERINE	SER
THREONINE	THR
ASPARTIC ACID	ASP
GLUTAMIC ACID	GLU
LYSINE	LYS
ARGININE	ARG
ASPARAGINE	ASN
GLUTAMINE	GLN
CYSTEINE	CYS
METHIONINE	MET
PHENYLALANINE	PHE
THYROSINE	TYR
TRYPTOPHAN	TRP
HISTIDINE	HIS
PROLINE	PRO



ANY TWO OF THEM CAN JOIN TOGETHER TO FORM A PEPTIDE... VERY PEPPY... ADD SOME MORE AND YOU GET A POLYPEPTIDE, OR PROTEIN CHAIN...



(HYDROGENS OMITTED!)

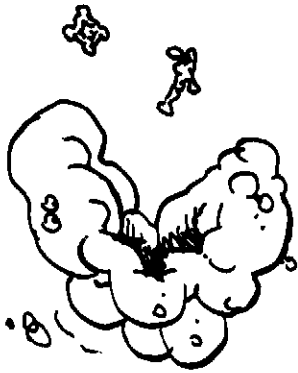
EVERY PROTEIN HAS A PRECISE NUMBER AND SEQUENCE OF AMINO ACIDS. MUTUAL ATTRACTIONS AMONG THEM CAUSE THE CHAIN TO COIL UP INTO A FAIRLY COMPACT, BUT FLEXIBLE SHAPE.

WHAT DO PROTEINS DO FOR A CELL? YOU PROBABLY THINK OF THEM AS SOMETHING THAT ENRICHES SHAMPOO... OR MAYBE YOU KNOW ABOUT THE PROTEIN IN FINGERNAILS, FEATHERS, AND HAIR... BUT ACTUALLY, MOST PROTEINS ARE SOMETHING ELSE AGAIN...

ENZYMES ARE PROTEINS WHICH TAKE APART OR PUT TOGETHER OTHER MOLECULES. EACH ENZYME IS RESPONSIBLE FOR JUST ONE SPECIFIC REACTION.

A TYPICAL ENZYME LIES IN WAIT FOR THE RIGHT MOLECULES TO COME AROUND.

THE ENZYME BINDS TO THE SMALL MOLECULES...

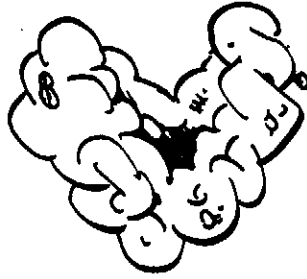


... AND COMBINES THEM...

... INTO A NEW MOLECULE WHICH IS RELEASED.



THE ENZYME ITSELF REMAINS UNCHANGED IN THE PROCESS.

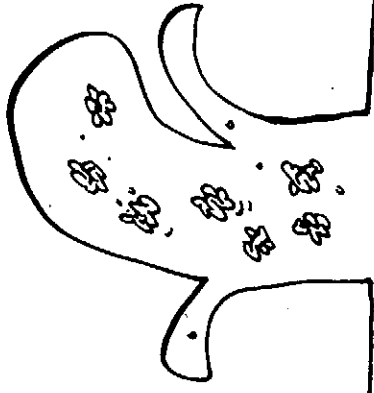


IN A SIMILAR WAY, **DIGESTIVE** ENZYMES BREAK DOWN LARGE MOLECULES. SEVERAL KINDS, FOR EXAMPLE, CHOP SUGARS OFF POLYSACCHARIDES !!

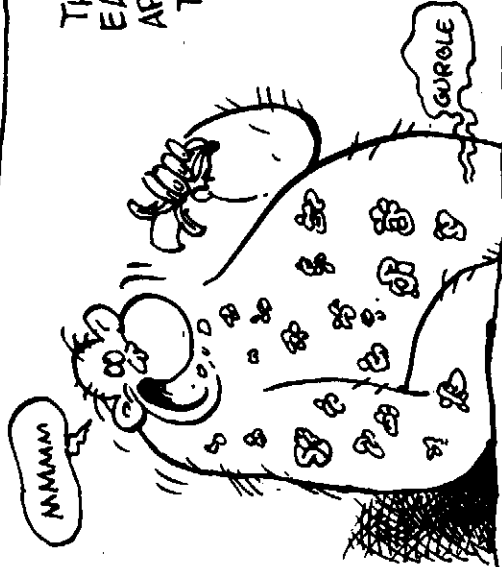


THESE PROTEINS ARE SO IMPORTANT BECAUSE VIRTUALLY EVERY ONE OF LIFE'S CHEMICAL REACTIONS IS DRIVEN BY SOME ENZYME.

WHEN CHEMICALS COME UP THROUGH THE ROOTS OF THE BANANA TREE, THE PLANT'S ENZYMES CONVERT THEM INTO THE CONSTITUENTS OF A BANANA...



THEN, WHEN THE GORILLA EATS THE BANANA, THE APES ENZYMES DIGEST THE FRUIT AND TURN IT INTO AN APE...



... AND LIKEWISE FOR E. COLI, WHICH HAS ITS OWN ENZYMES...!

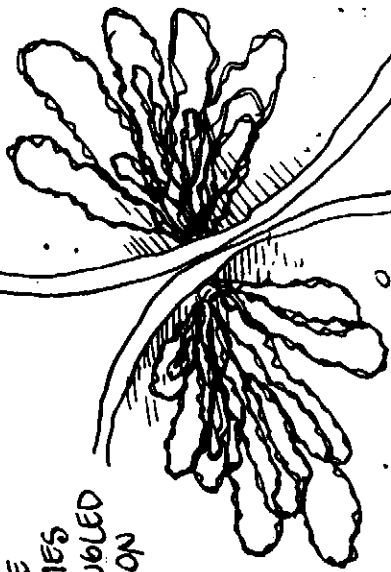
IN OTHER WORDS:

An organism is made by its enzymes.

AND WHAT DO YOU SUPPOSE MAKES THE ENZYMES?

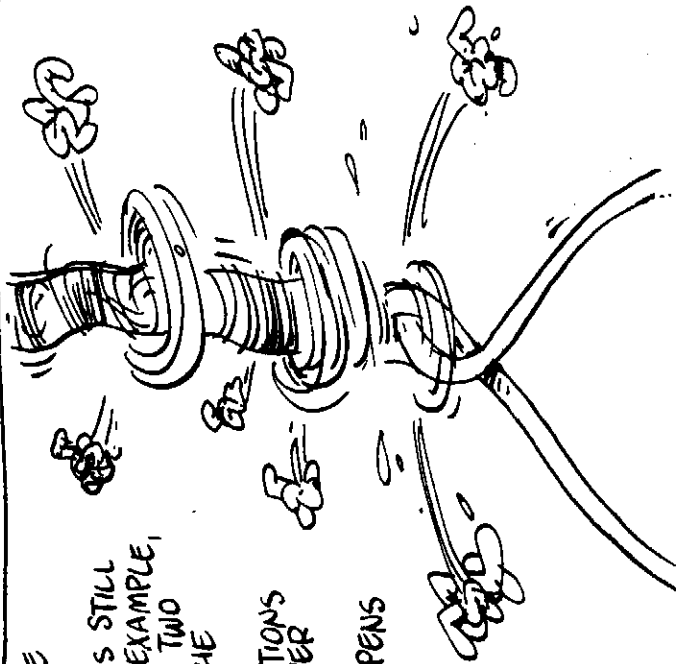


ONCE REPLICATED, THE TWO NEW CHROMOSOMES HAVE TO BE DISENTANGLED SO THAT CELL DIVISION CAN OCCUR.



'BYE, NOW!

THE PICTURE WE HAVE OF DNA REPLICATION IS STILL SKETCHY. FOR EXAMPLE, UNWINDING THE TWO STRANDS OF THE DOUBLE HELIX INVOLVES ROTATIONS AT SPEEDS OVER 8000 RPM. HOW THIS HAPPENS IS STILL NOT WELL UNDERSTOOD.



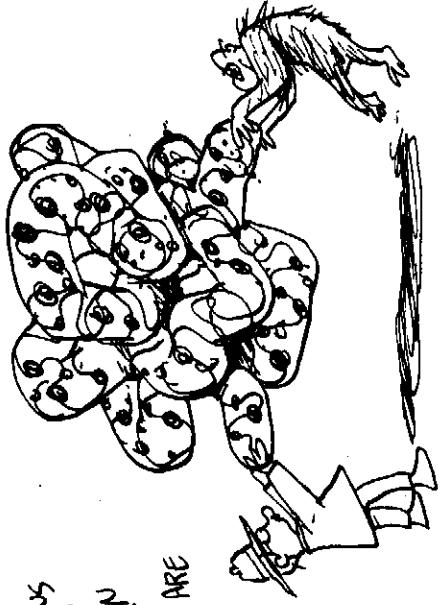
WHATEVER THE DETAILS, THE PRINCIPLE OF COMPLEMENTARITY IS THE KEY TO REPLICATION, AS WELL AS TO THE GENE'S SECOND MAIN FUNCTION:

MAKING ENZYMES!

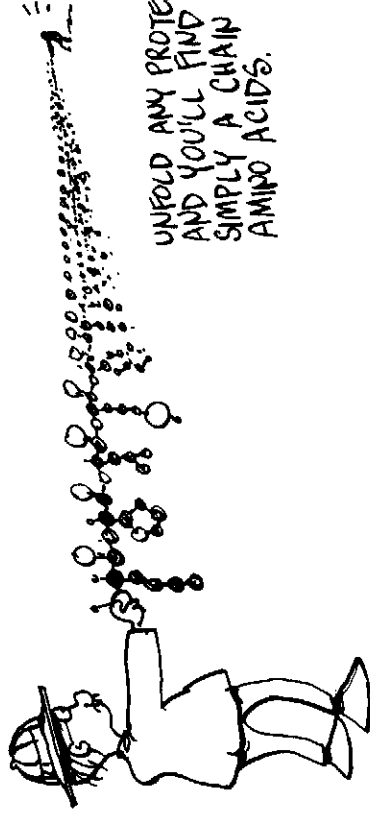
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# The MOLECULE is the MESSAGE

ENZYMES AND OTHER PROTEINS COME IN MANY SHAPES, BUT IN AN IMPORTANT RESPECT, THEY ARE ALL ALIKE.

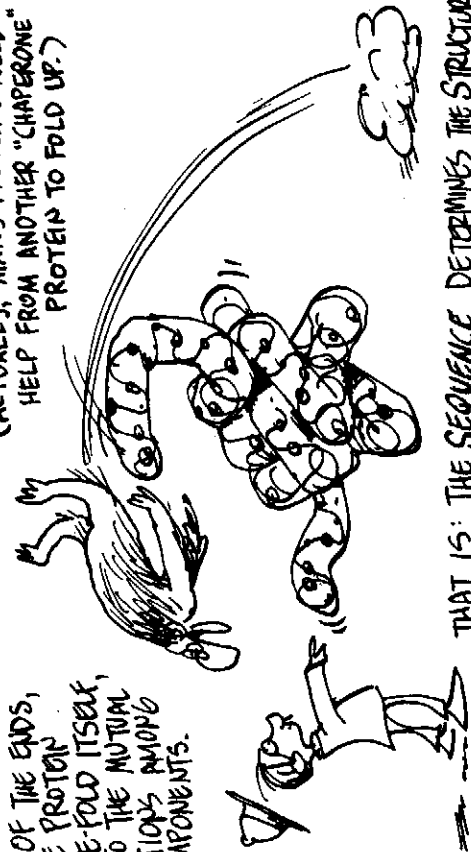


UNFOLD ANY PROTEIN, AND YOU'LL FIND ITS SIMPLY A CHAIN OF AMINO ACIDS.



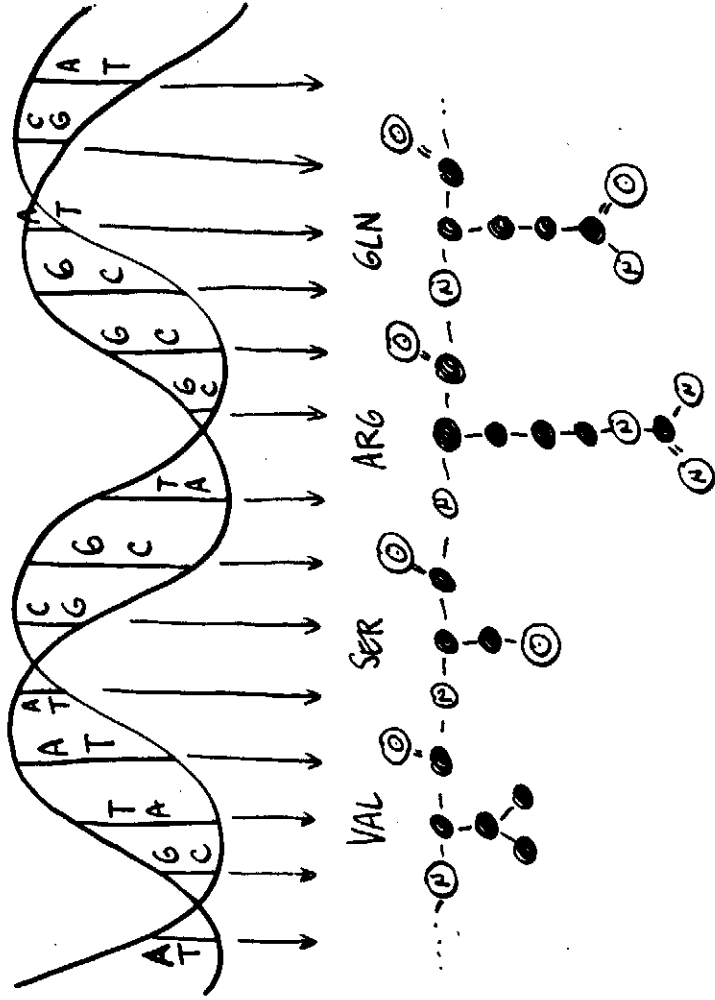
(ACTUALLY, MANY PROTEINS NEED HELP FROM ANOTHER "CHAPERONE" PROTEIN TO FOLD UP.)

LET GO OF THE ENDS, AND THE PROTEIN WILL RE-FOLD ITSELF, OWING TO THE MUTUAL ATTRACTIONS AMONG THE COMPONENTS.

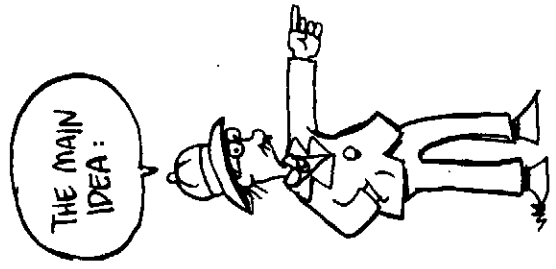


THAT IS: THE SEQUENCE DETERMINES THE STRUCTURE

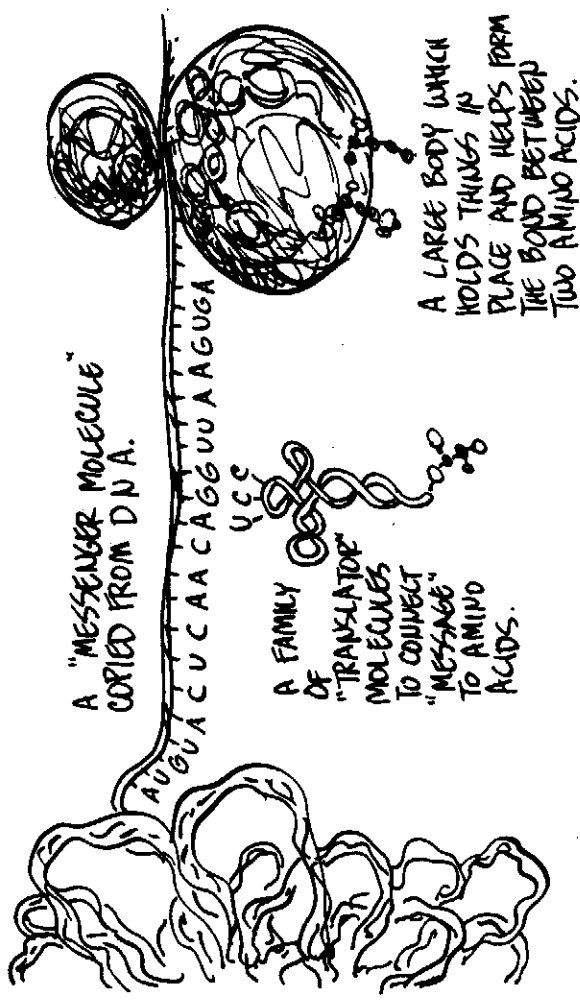
IN VIEW OF THE RELATIONSHIP BETWEEN GENES AND PROTEINS, THIS SUGGESTS THAT THE SEQUENCE OF D.N.A. MUST SOMEHOW PARALLEL OR REFLECT THE SEQUENCE OF THE PROTEIN.



The sequence of base pairs may be thought of as a series of "words" specifying the order of amino acids in each protein.



TO MAKE THE TRANSLATION FROM D.N.A. "WORDS" TO AMINO ACIDS, SOME SOPHISTICATED MOLECULAR MACHINERY COMES INTO PLAY...



A LARGE BODY WHICH HOLDS THINGS IN PLACE AND HELPS FORM THE BOND BETWEEN TWO AMINO ACIDS.





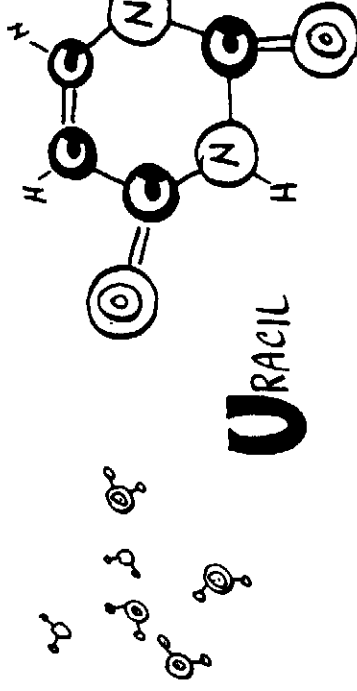
RNA — RIBONUCLEIC ACID — RESEMBLES DNA: A SUGAR-PHOSPHATE BACKBONE WITH A SERIES OF BASES ATTACHED.

THE DIFFERENCES:

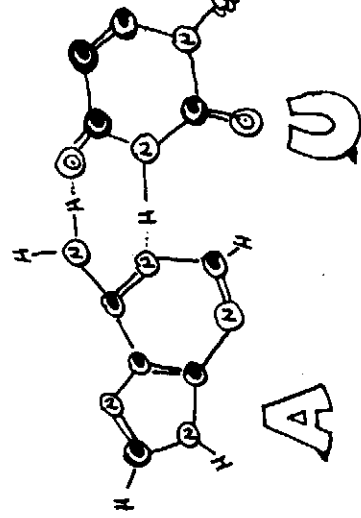


ITS SUGAR IS RIBOSE, RATHER THAN DEOXYRIBOSE; RNA IS USUALLY SINGLE-STRANDED; AND IT IS MUCH SHORTER — 50 TO 1000 NUCLEOTIDES, COMPARED WITH A MILLION OR MORE IN DNA!

AND FINALLY, WHILE THE BASES A, C, AND G ARE THE SAME AS IN DNA, RNA HAS IN PLACE OF T ANOTHER BASE CALLED URACIL ("U").



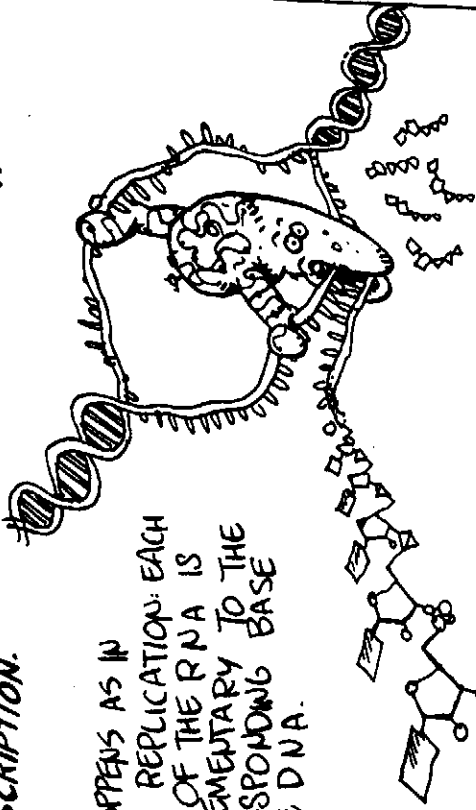
WHICH, LIKE THYMINE, IS COMPLEMENTARY TO ADENINE:



NOW LET'S SEE HOW RNA WORKS!!

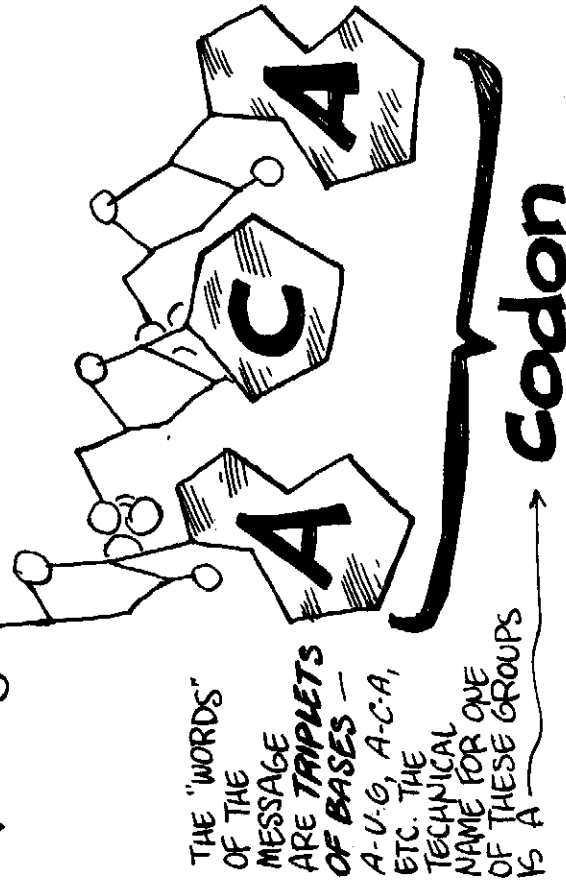


PROTEIN SYNTHESIS BEGINS WHEN A REGION OF DNA IS TEASED APART AND A MOLECULE OF RNA IS BUILT ALONG ONE STRAND BY AN ENZYME CALLED RNA POLYMERASE. THIS PROCESS IS CALLED TRANSCRIPTION.



IT HAPPENS AS IN DNA REPLICATION: EACH BASE OF THE RNA IS COMPLEMENTARY TO THE CORRESPONDING BASE ON THE DNA.

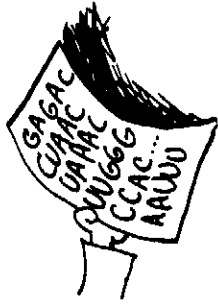
THIS RNA IS CALLED THE MESSENGER, OR mRNA, BECAUSE IT CARRIES THE GENETIC MESSAGE FROM THE DNA TO THE PROTEIN FACTORY.



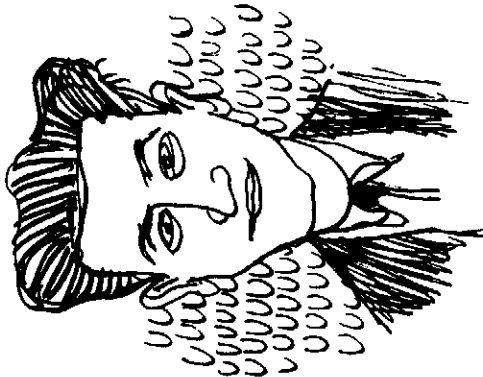
THE "WORDS" OF THE MESSAGE ARE TRIPLETS OF BASES — A-U-G, A-C-A, ETC. THE TECHNICAL NAME FOR ONE OF THESE GROUPS IS A

EACH 3-BASE CODON STANDS FOR A SINGLE AMINO ACID, AND THE WHOLE mRNA STRAND ENCODES A PROTEIN (OR SEVERAL PROTEINS). IT'S JUST LIKE A MESSAGE IN CODE —

# THE GENETIC CODE!



CRACKING THIS CODE BEGAN IN 1961, WHEN MARSHALL NIRENBERG WAS ABLE TO MAKE A SPECIAL mRNA, WHOSE ONLY BASE WAS URACIL, REPEATED OVER AND OVER. "POLY-U."



Phe-Phe-Phe-Phe-Phe  
FROM IT HE OBTAINED A PROTEIN CONSISTING ENTIRELY OF THE AMINO ACID PHENYLALANINE.

SO UUU WAS THE CODON FOR PHENYLALANINE...

NEXT THEY DECODED POLY-A, AND POLY-C, AND POLY-UG, POLY-UGU, ETC, ETC, UNTIL THE CODE WAS FINALLY BROKEN —

UUU → Phe  
AAA → Lys  
CCC →  
UGU →  
GUU →  
UUG → Leu

THE COMPLETE CODE TABLE FOLLOWS!

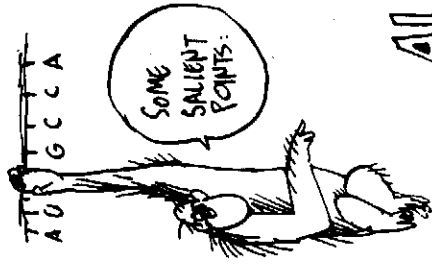


SECOND LETTER

THIRD LETTER

FIRST LETTER	U	C	A	G
U	UUU } PHE UUC } UUA } LEU UUG }	UCU } SER UCC } UCA } UCG }	UAU } TYR UAC } UAA } STOP UAG }	UGU } CYS UGC } UGA } STOP UGG } TRP
C	CUU } LEU CUC } CUA } CUG }	CCU } PRO CCC } CCA } CCG }	CAU } HIS CAC } CAA } GLN CAG }	CGU } ARG CGC } CGA } CGG }
A	AUU } ILE AUC } AUA } MET AUG }	ACU } THR ACC } ACA } ACG }	AAU } ASN AAC } AAA } LYS AAG }	AGU } SER AGC } AGA } ARG AGG }
G	GUU } VAL GUC } GUA } GUG }	GCU } ALA GCC } GCA } GCG }	GAU } ASP GAC } GAA } GLU GAG }	GGU } GLY GGC } GGA } GGG }
	U	C	A	G

FIRST LETTER



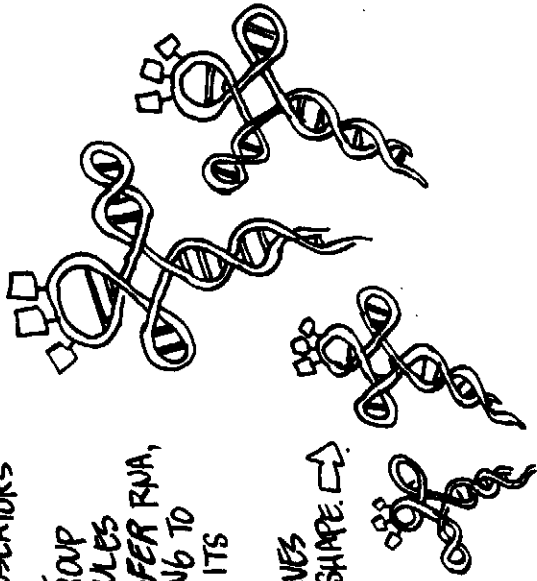
THE CODE IS REDUNDANT: WITH 64 POSSIBLE CODONS, BUT ONLY 20 AMINO ACIDS, THERE MUST BE "SYNONYMS," DIFFERENT CODONS WHICH ENCODE THE SAME AMINO ACID.

THERE ARE "STOP" SIGNALS. THREE CODONS DO NOT ENCODE ANY AMINO ACID AT ALL. THESE SERVE TO TERMINATE MESSAGES.

ALSO: THE CODE IS NON-OVERLAPPING. THE "WORDS" FOLLOW EACH OTHER WITHOUT GAPS OR OVERLAPS. WE'LL SEE SHORTLY HOW IT KNOWS WHERE TO START...

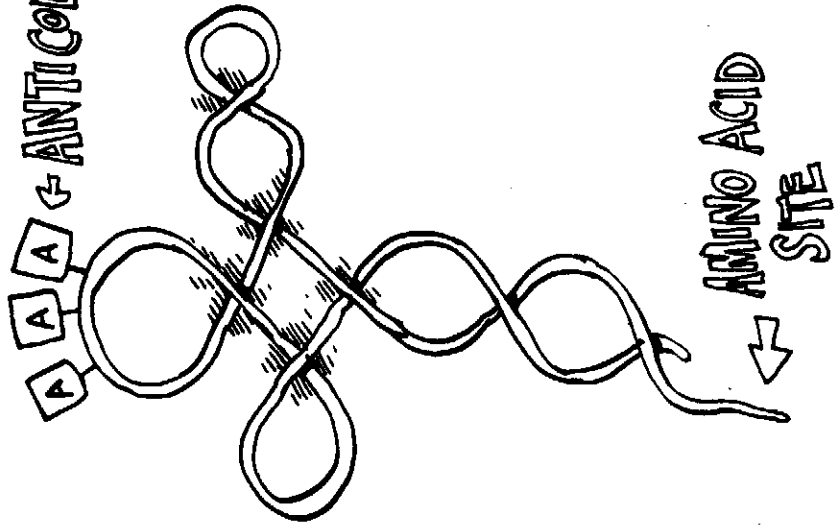


THE ACTUAL TRANSLATORS OF THE GENETIC CODE ARE A GROUP OF RNA MOLECULES CALLED TRANSFER RNA, OR tRNA. DURING TO PAIRING AMONG ITS BASES, tRNA'S TWIST THEMSELVES INTO THIS KEY SHAPE. →

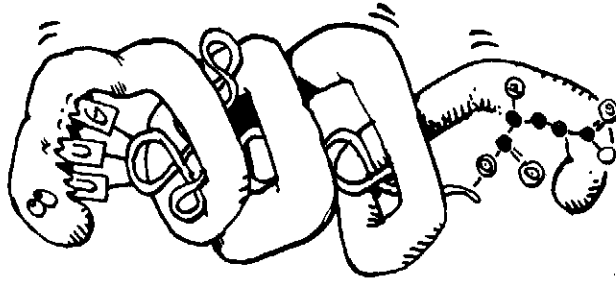


THE LOOP END OF tRNA HAS THREE UNPAIRED BASES. THIS "ANTICODON" MAY BIND WITH THE COMPLEMENTARY CODON OF mRNA. AT THE "TAIL" END OF tRNA IS A SITE FOR ATTACHING A SINGLE AMINO ACID.

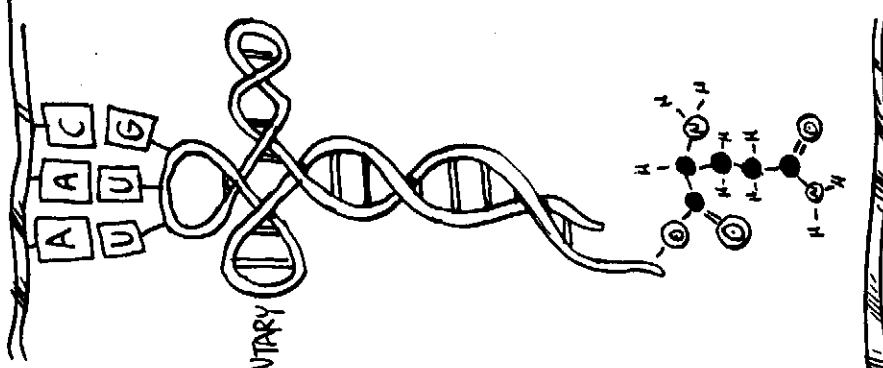
A A A ← ANTI CODON



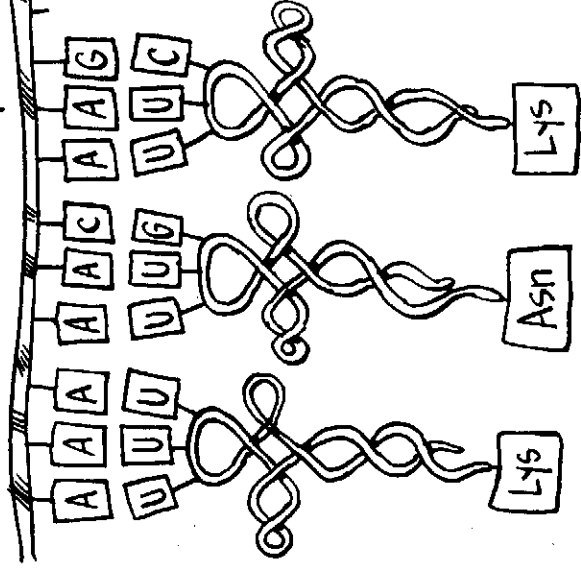
FOR EACH ANTICODON, THERE IS AN ENZYME WHICH RECOGNIZES IT AND ATTACHES THE APPROPRIATE AMINO ACID TO ITS tRNA.



ONCE THEY ARE LINKED, THE ANTICODON BINDS TO THE COMPLEMENTARY CODON OF MESSAGE.



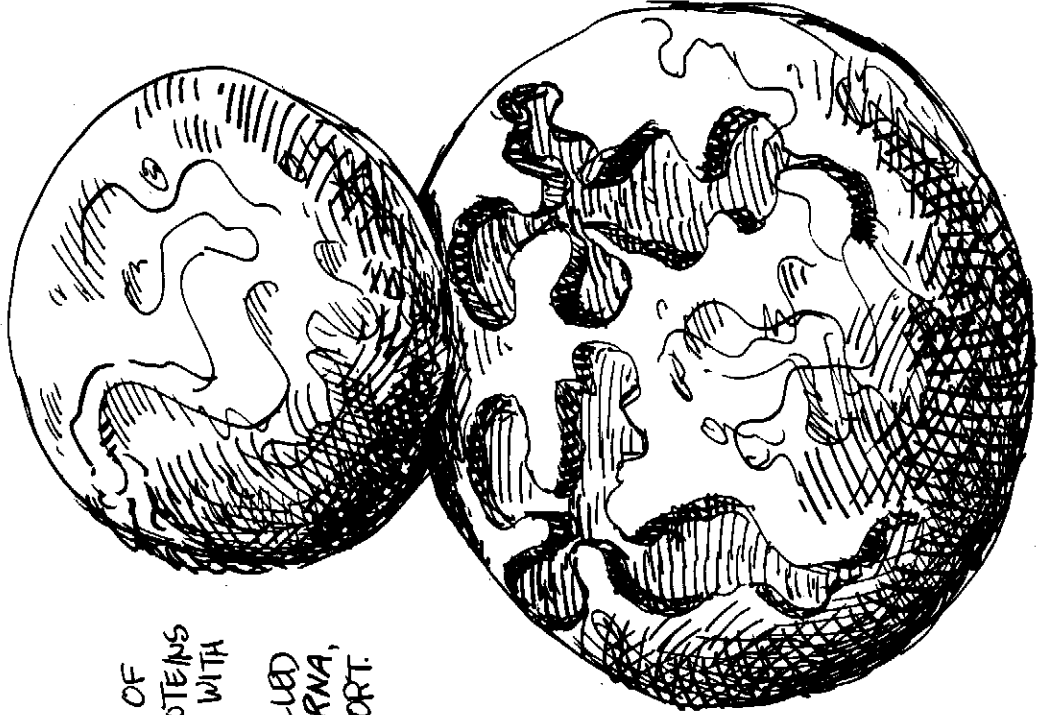
SCHEMATICALLY, THIS IS THE WAY A STRING OF BASES IS TRANSLATED INTO A SEQUENCE OF AMINO ACIDS. **HOWEVER,** THE CELL NEEDS ONE MORE PIECE OF EQUIPMENT TO MAKE IT WORK: THE RIBOSOME.



# HOW PROTEINS ARE MADE

THE FINAL INGREDIENT IN THE PROTEIN-MAKING APPARATUS IS AN OBJECT THAT HOLDS EVERYTHING IN PLACE.

THIS IS THE **RIBOSOME**, A DOUBLE BALL OF ABOUT 50 PROTEINS WRAPPED UP WITH R N A. THIS R N A IS CALLED **RIBOSOMAL RNA**, TRNA FOR SHORT.

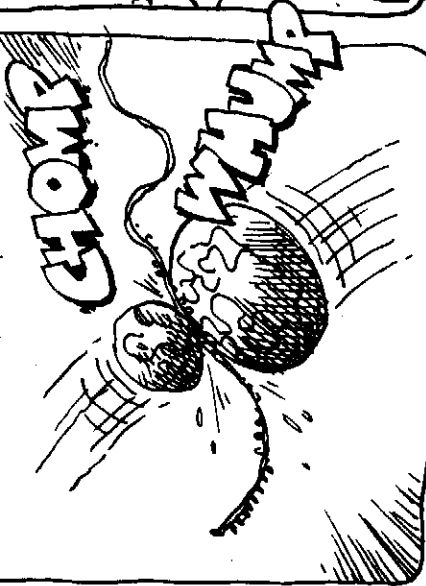


THE RIBOSOME HAS TWO SLOTS IN WHICH MOLECULES OF TRNA CAN FIT SNUGGLY.

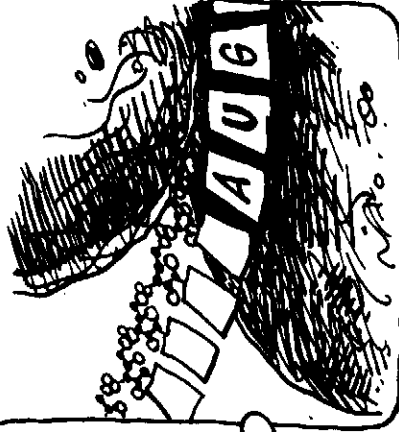
NOW TO MAKE A PROTEIN: WHEN THE mRNA READS OUT THE DNA SEQUENCE, IT ENTERS A SEA OF RIBOSOMES.



ONE HALF AT A TIME, A RIBOSOME BINDS ONTO THE mRNA.



THE BINDING SITE IS LOCATED AT OR NEAR THE CODON A-U-G.



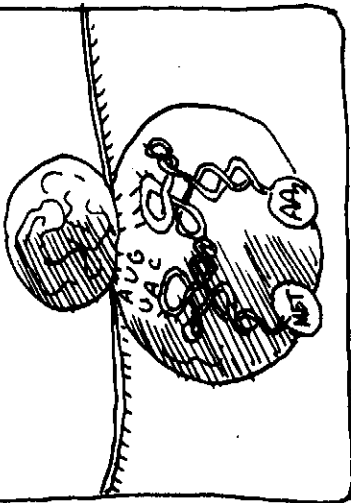
THUS, A-U-G IS ALWAYS THE FIRST 'WORD' OF EVERY MESSAGE.



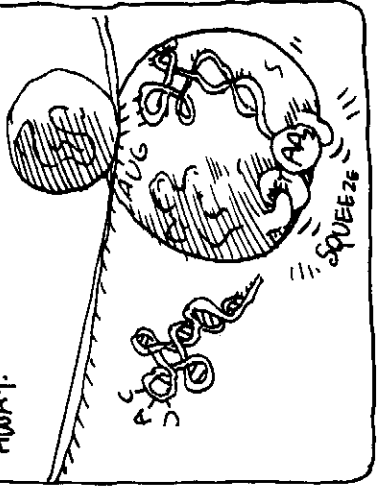
A-U-G AND THE NEXT CODON EACH BOND WITH COMPLEMENTARY TRNA'S, WHICH FIT INTO THE SLOTS ON THE RIBOSOME.



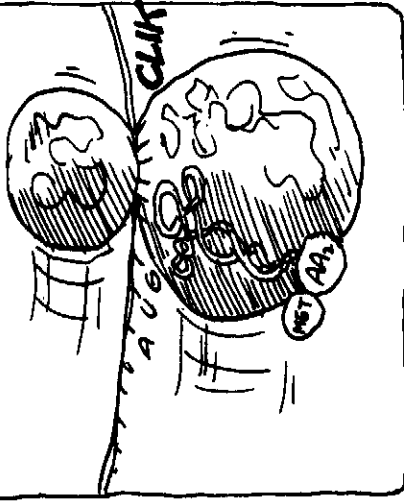
EACH tRNA CARRIES AN AMINO ACID (AA), THE FIRST ONE ALWAYS BEING METHIONINE, WHICH GOES WITH A-U-G.



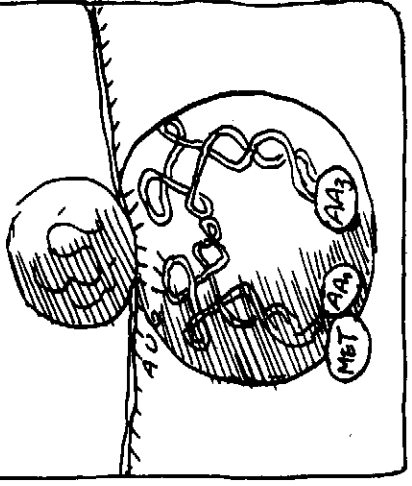
AN ENZYME IN THE RIBOSOME LINKS THE TWO AMINO ACIDS, AND THE FIRST tRNA FLOATS AWAY.



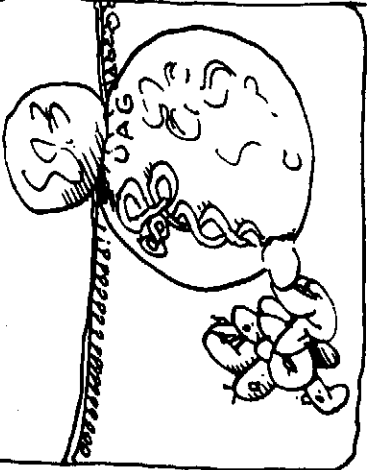
THE RIBOSOME THEN MOVES DOWN THREE MORE BASES.



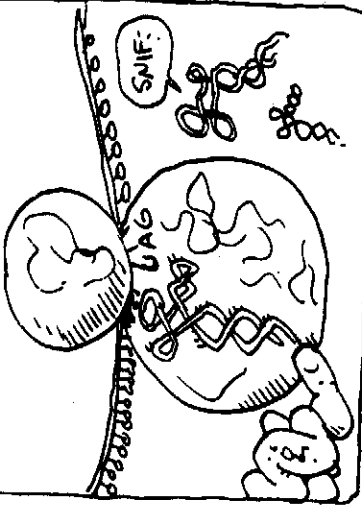
ANOTHER tRNA AND AMINO ACID BIND ON.



THIS PROCESS CONTINUES UNTIL THE RIBOSOME REACHES ONE OF THE "STOP" SIGNALS.



IT STOPS BECAUSE THERE IS NO tRNA WITH AN ANTICODON TO MATCH.

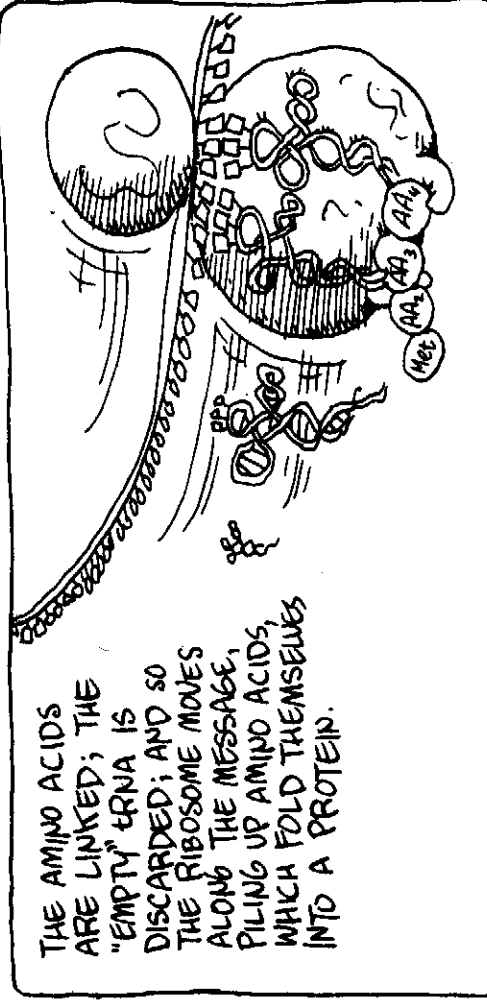


THE COMPLETED PROTEIN IS CLIPPED OFF BY ANOTHER RIBOSOMAL ENZYME.

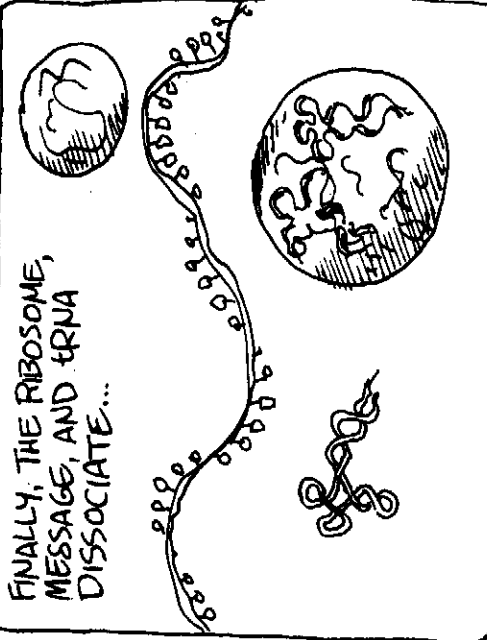


IT IS ALSO COMMON AT THIS POINT FOR THE PROTEIN TO BE TIDIED UP IN VARIOUS WAYS.

THE AMINO ACIDS ARE LINKED; THE "EMPTY" tRNA IS DISCARDED; AND SO THE RIBOSOME MOVES ALONG THE MESSAGE, PILING UP AMINO ACIDS, WHICH FOLD THEMSELVES INTO A PROTEIN.



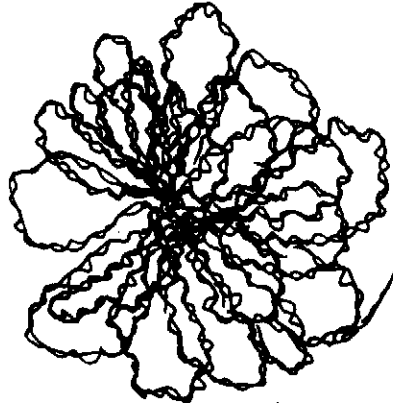
FINALLY, THE RIBOSOME, MESSAGE, AND tRNA DISSOCIATE...



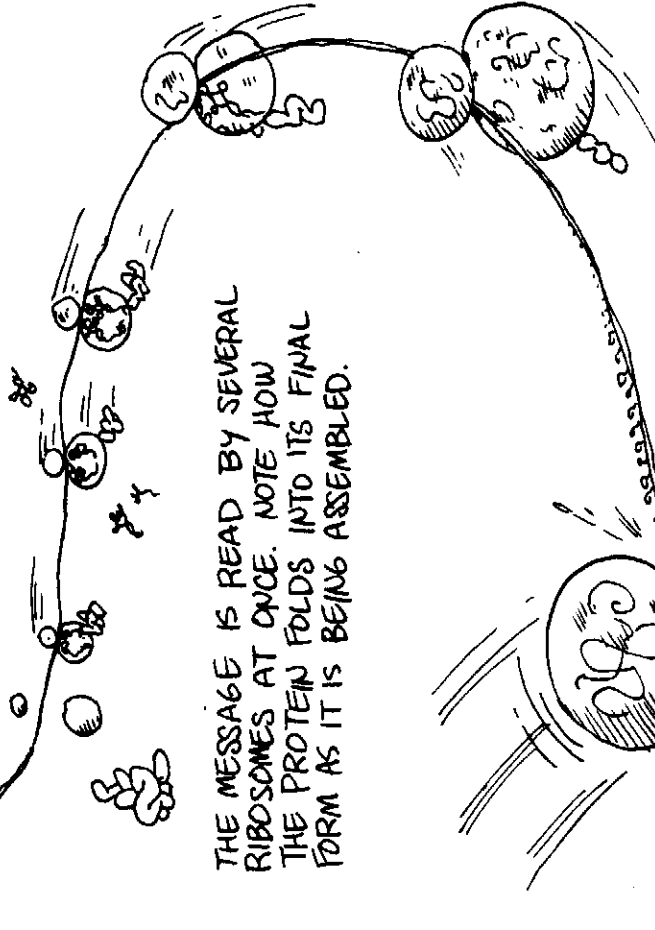
...AND THE NEW MACROMOLECULE GOES OFF TO DO ITS JOB: STRUCTURE, ENZYME, OR WHATEVER...



IN THE LIVING CELL, ALL THESE PROCESSES ARE GOING ON TOGETHER. THIS IS HOW IT LOOKS IN *E. COLI*.

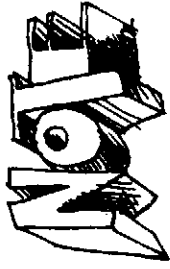


IN BACTERIA GENERALLY, PROTEIN-BUILDING BEGINS WHILE THE mRNA IS STILL BEING TRANSCRIBED FROM THE GENE.

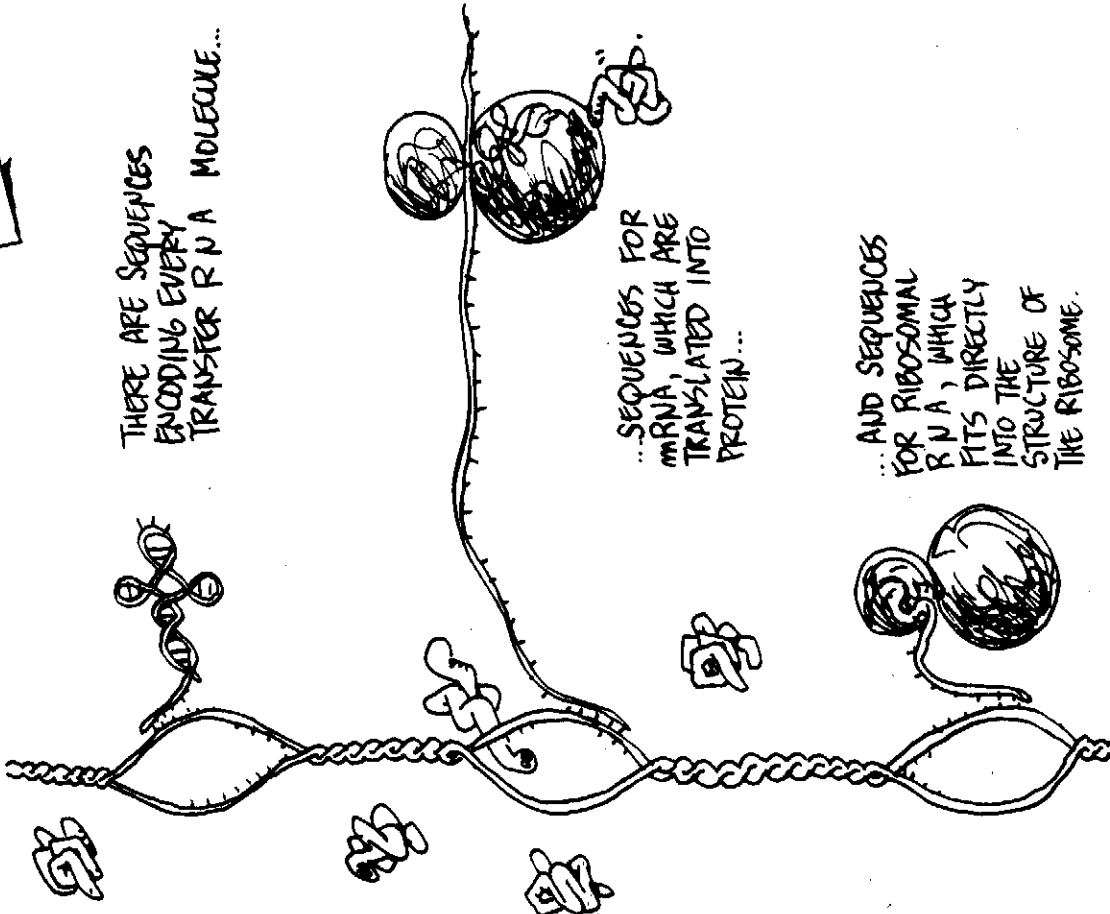


THE MESSAGE IS READ BY SEVERAL RIBOSOMES AT ONCE. NOTE HOW THE PROTEIN FOLDS INTO ITS FINAL FORM AS IT IS BEING ASSEMBLED.

AND NOW YOU UNDERSTAND HOW GENES WORK — IN *E. COLI* !!



FOR A MOMENT HOW MUCH WE'VE ALREADY FOUND ENCODED IN THE CHROMOSOME.



THERE ARE SEQUENCES ENCODING EVERY TRANSFER RNA MOLECULE...

...SEQUENCES FOR mRNA, WHICH ARE TRANSLATED INTO PROTEIN...

...AND SEQUENCES FOR RIBOSOMAL RNA, WHICH FITS DIRECTLY INTO THE STRUCTURE OF THE RIBOSOME.

TRULY, THE DNA IS THE BLUEPRINT OF ALL THE CELL'S ESSENTIAL PARTS.

BLUEPRINT! WHO'S THE ARCHITECT?

ASK MEDEL...

