

MOLECULAR GENETICS COLORING

THE DOUBLE HELIX

This plate illustrates the double helix structure of DNA proposed by Watson and Crick and widely accepted today as correct. To allow a better view of the parts of the molecule, the spaces between base pairs has been greatly exaggerated. The upper end of the illustration is highly diagrammatic and shows the overall relations of the parts, while the lower portion shows the structural formula with all of the individual atoms and their bonds.

Color the headings Simplified Structure and Uprights/Backbone, titles D and P, and the associated structures in the upper portion of the plate. Use light colors for D and P.

The structure of the DNA molecule is often compared to that of a ladder that has been twisted. The *deoxyribose* and *phosphate groups* alternate continuously the whole length of the molecule and form the “uprights” of the ladder (sometimes called the “backbone”).

Color the heading Rungs/Base Pairs, titles A, T, C, G, and H, and their associated structures in the upper portion of the plate. Use light colors for A, T, C, and G.

The base pairs occupy the position of the “rungs” of the ladder, although in the actual molecule they are tightly packed on top of one another as no ladder rungs ever would be. The particular sequence of the four different bases constitutes a “code” in which specific hereditary information is recorded. The method by which that code is translated to specify the exact sequences of amino acids to be used in making the cell’s proteins will be covered in the next few plates.

The helix shown here, called the “B-form,” is the most stable and therefore the most common structure for DNA. In recent years it has been discovered that local regions of DNA may form a slightly more open helix, called the A-form, and in some cases a very different, left-handed helix, called the Z-form. (The significance of these alternate forms is not known.)

The average length of DNA in a human chromosome is about 140 million base pairs, or 14 million turns of the

helix. If laid out in a straight line, it would be about 4.8 centimeters long (just under 2 inches).

Color the heading Structural Formula and the remainder of the plate.

The structural formula shows more clearly which atoms are attached to which. Those details may or may not be important to you, depending on your reasons for studying this plate, but they are important to the cell because any deviation will result in some kind of mutation or even the death of the cell.

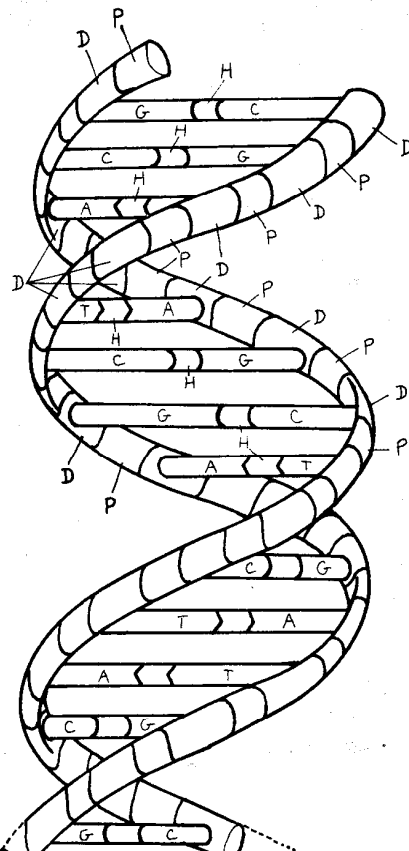
To clarify the exact interconnections of the various atoms, this view shows the base pairs and the ribose subunits rotated 90 degrees from their actual orientation in the molecule. You will note that each base is attached to carbon number 1 of its deoxyribose molecule. To facilitate discussions of the structure of DNA, this carbon atom is designated as carbon 1’ (“one prime”) to distinguish it from the carbon atom number 1 of the base. The phosphates, then, are attached to carbons 3’ and 5’.

Note also that the directions of the sugar and phosphate uprights or backbones are “antiparallel”; that is, the chain on one side runs in the opposite direction to the chain on the other side. On one side, the 5’ carbon of each ribose connects by way of a phosphate group to the 3’ carbon of the ribose above. On the other side, the 5’ carbon of each ribose connects by way of a phosphate group to the 3’ carbon of the ribose below. Thus the chains progress in the direction 5’ to 3’ up the helix on one side and 5’ to 3’ down the helix on the other side. At each end of the DNA molecule, then, one strand will end with a 3’-OH and the other will end with a 5’-phosphate.

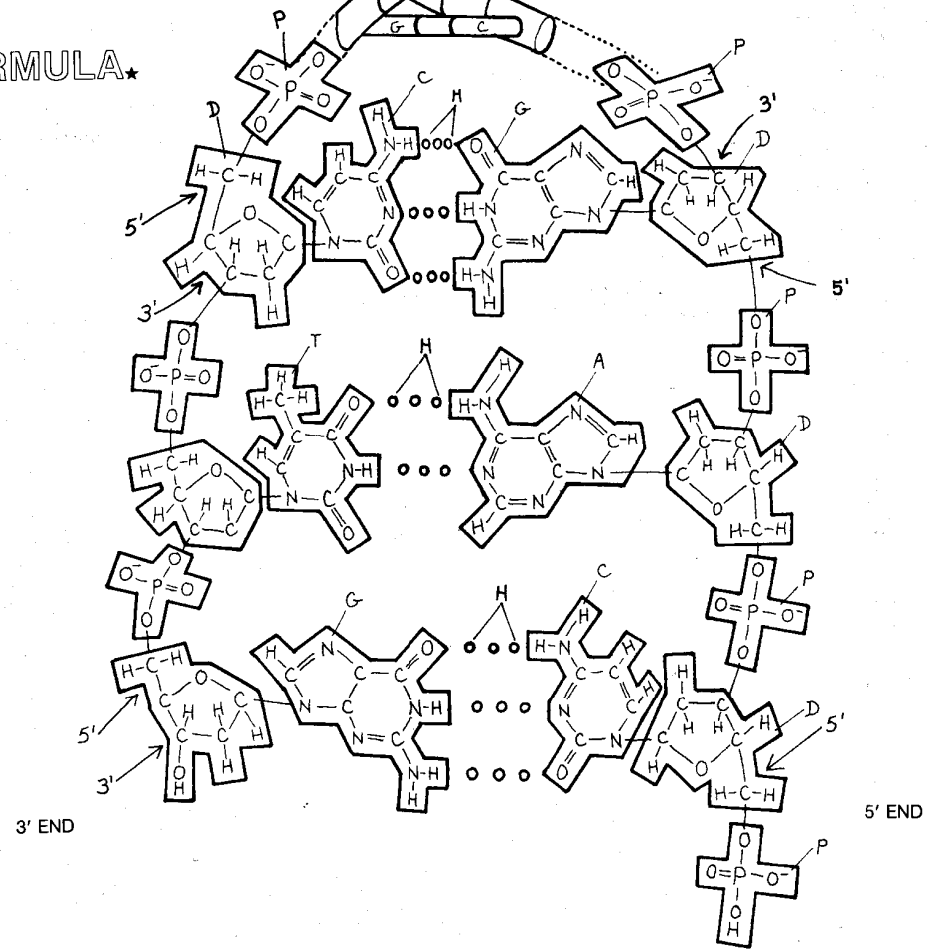
In 1958 Watson, Crick, and Wilkins received the Nobel Prize in physiology and medicine for this discovery of the structure of DNA. It was an extremely important achievement because, as Watson and Crick pointed out in their paper announcing the discovery, not only could such a structure carry genetic information coded in the varying sequence of the bases, but there was also an obvious mechanism by which the molecule could be self-replicating, so that exact copies could be supplied for each daughter cell in cell division.

THE DOUBLE HELIX.

SIMPLIFIED STRUCTURE★
 UPRIGHTS/BACKBONE★
 DEOXYRIBOSE,
 PHOSPHATE,
 RUNGS/BASE PAIRS★
 ADENINE, A
 THYMINE, T
 CYTOSINE, C
 GUANINE, G
 HYDROGEN BOND, H



STRUCTURAL FORMULA★



DNA REPLICATION

This plate shows how the structure of DNA provides a method of exact replication. Although we cannot actually see these events at the molecular level, experiments with radioactive tracer atoms have provided very strong support for the idea that the events occur as illustrated in this plate.

Color the first seven titles and the corresponding structures in the upper portion of the plate only, using the same colors as in the previous plate.

The upper portion of the plate shows the DNA molecule in the double helix form prior to replication. The two strands of this "parent" DNA are held tightly together by *hydrogen bonds* between the bases in each pair.

Color the heading Unzipping and Replication, titles B, E, and F, and the structures in the center portion of the plate. Use a very light color for B.

For replication to occur, the two strands of the parent DNA must separate in much the same fashion as the two halves of a zipper unzip, exposing the bases in an unpaired condition. An enzyme, *DNA polymerase*, adds new nucleotides from the surrounding nucleoplasm to form "daughter" strands of DNA. Since the formation of the chemical bonds joining the nucleotides requires an input of energy, the cell must provide the nucleotides in the form of nucleoside triphosphates (base + sugar + three phosphates). Two of the three *phosphates* are *hydrolyzed* to provide the energy to add the nucleotide remaining to the growing daughter strand.

Since only *adenine* fits *thymine* and has opposite electrical charges in the correct places, only adenine is inserted into the growing daughter strand wherever a thymine is present in the parent strand, and vice versa. Similarly, only *guanine* is inserted into the growing daughter strand wherever a *cytosine* is present in the parent strand, and vice versa. This assures that each daughter strand is exactly complementary to the parent strand on which it is assembled and is an exact duplicate of the opposite parent strand. The two complete DNA molecules that result when the entire process is completed are exact duplicates of the original DNA molecule.

Molecules of DNA polymerase move along the parent strands, assembling new daughter strands as they go. They always assemble the new strand in the 5' to 3' direction, forming a covalent bond between the phosphate of the new nucleotide and the 3' oxygen atom of the deoxyribose on the growing end of the strand. This means that replication is in opposite *directions* on the two sides of the molecule. One strand, called the leading strand (left side of the plate), is assembled in a direction toward the "replication fork" (point of unzipping). The other strand, called the lagging strand (right side in the plate), is assembled in a direction away from the replication fork and must be done in segments. The segments are then connected by a different enzyme, DNA ligase, which also repairs DNA when it is damaged. Actually, numerous replication forks are started simultaneously at various points along a chromosome, usually in pairs running in opposite directions, so the leading strand also ends up being made in segments and needing DNA ligase to join the segments together.

Color the heading Duplicate Strands and the remainder of the plate.

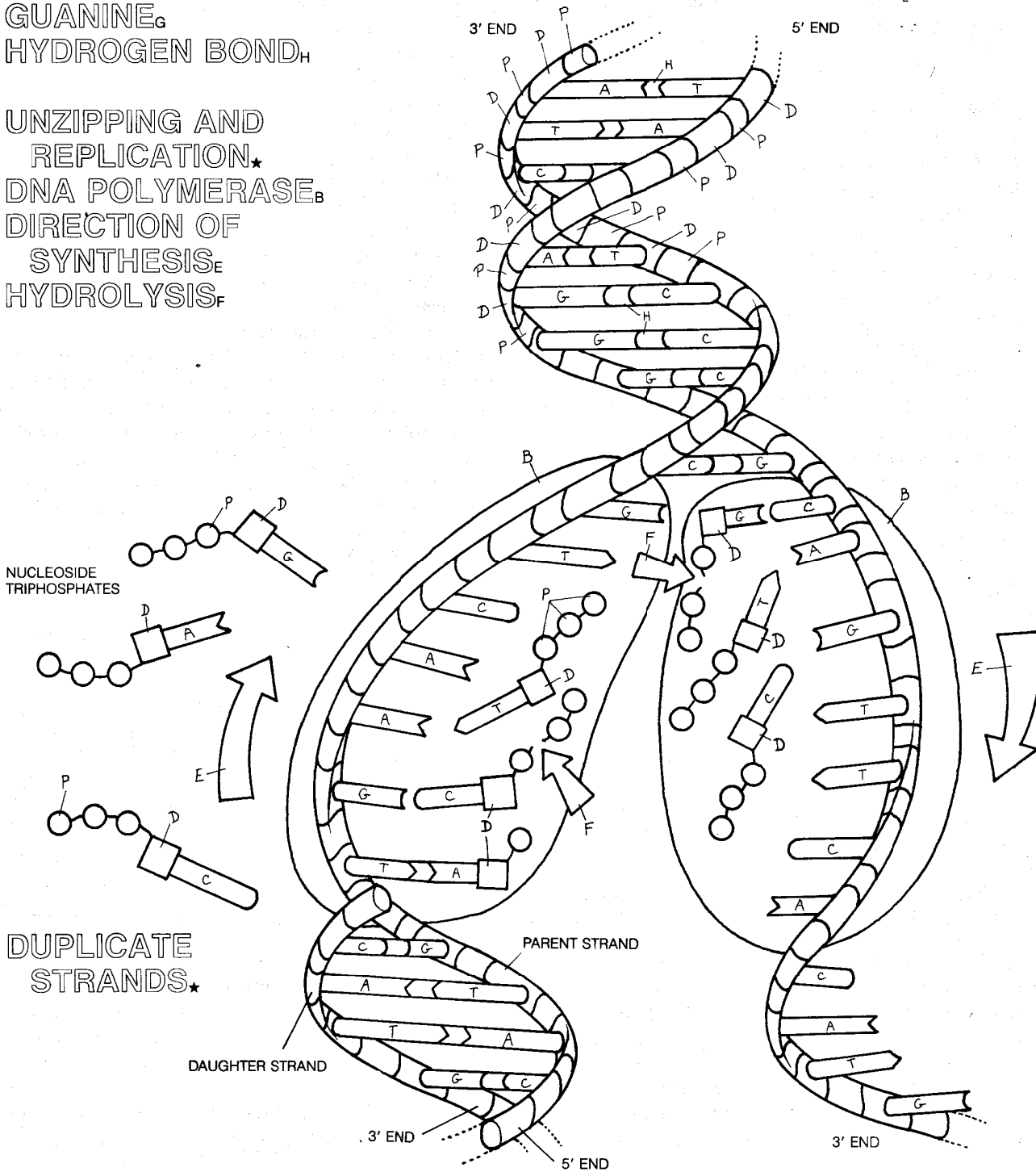
The consequence of all these steps is that two exact duplicate strands of DNA are produced, each of them consisting of one of the original parent strands and a new daughter strand. The cell can now undergo cell division and provide each daughter cell with a complete copy of this DNA molecule.

In recent years one of the intriguing discoveries (not illustrated) has been that while one part of the DNA polymerase molecule functions as a polymerase, attaching nucleotides, another portion of the same molecule acts as an "exonuclease" (nucleotide-cutting-out enzyme) and performs a "proofreading" function. It is estimated that about one time in 10,000 to 100,000 the wrong base is added to a growing DNA strand. Somehow the exonuclease portion of the DNA polymerase molecule recognizes nearly all such mistakes and removes each erroneous base as fast as it is added so that another attempt to add the correct one can be made. The result is that there is an estimated error rate of only one in one billion base pairs copied.

DNA REPLICATION.

DEOXYRIBOSE,
 PHOSPHATE,
 ADENINE,
 THYMINE,
 CYTOSINE,
 GUANINE,
 HYDROGEN BOND_H

UNZIPPING AND
 REPLICATION,
 DNA POLYMERASE,
 DIRECTION OF
 SYNTHESIS,
 HYDROLYSIS_F



DNA TRANSCRIPTION

The process in which the hereditary code carried by DNA is used by the cell to control protein synthesis has turned out to be quite complex. It involves three different types of a slightly different nucleic acid, called RNA, and two sequential processes known as transcription and translation.

Color the headings DNA and RNA and titles and structures D, T, R, and U. Use the D and T colors from the previous plates and light colors for R and U.

RNA (ribonucleic acid) is made up of numerous nucleotides assembled in exactly the same way as in DNA except that RNA is mostly single-stranded and mostly not in the form of a helix. It differs in composition in that the sugar component is *ribose*, rather than *deoxyribose*, and that the base *thymine* is replaced by *uracil*, a different, though quite similar, molecule. The other three bases are the same as in DNA: adenine, cytosine, and guanine.

Color the heading Transcription and titles P, A, C, G, H, B, and E. Use the established colors from the previous plates for P through H and a very light color for B. Color the associated illustration.

The first step in utilizing the DNA code is the process of transcription. In transcription, the DNA unzips, just as if it were going to be replicated (Plate 83), except that instead of DNA polymerase attaching to it, a different enzyme, called *RNA polymerase*, attaches, synthesizing a molecule of RNA instead of a molecule of DNA. Only one side of the DNA molecule is transcribed. This is assured by the fact that RNA polymerase is not attracted to just any stretch of DNA but only to certain DNA base sequences, called "promoters." Promoters are sequences of bases that do not determine protein structure but serve only to convey the message "RNA polymerase, start here."

The transcription process is essentially identical to replication. The differences are that the complementary daughter strand is being assembled with ribonucleotides instead of deoxyribonucleotides and that the RNA daughter strand does not remain attached to the parent DNA strand. Instead it separates from the DNA, and the DNA then zips back together. The RNA migrates out of the nucleus of the cell to the cytoplasm.

Three different classes of RNA are made in this way. The most abundant class is called messenger RNA (abbreviated mRNA) because it carries the message of what

amino acids are to be put together in what sequence to make the cell's proteins. The second class is ribosomal RNA (rRNA), which is an important component of the ribosomes, the organelles that actually accomplish the synthesis of the cell's proteins. The third class is called transfer RNA (tRNA) because it transfers the amino acids to the ribosome for assembly into proteins. The RNA molecule being synthesized in the center of this plate could belong to any of the three classes of RNA. They are all alike except in length and the sequence of bases. Messenger RNA varies in length according to the number of amino acids in the protein for which it carries the code, but it is typically from 900 to 1500 nucleotides in length. It is mostly linear, although it can fold back on itself, and a few short sections may form a helix where the bases are complementary.

Ribosomal RNA takes only certain specific lengths, approximately 120, 1500, and 3000 nucleotides in prokaryotic cells and approximately 120, 160, 2000, and 5000 in eukaryotic cells. It is extensively folded back and forth upon itself, because it forms a framework for the attachment of a number of protein molecules to form the somewhat globular ribosome, which is slightly more than half rRNA by weight and slightly less than half protein.

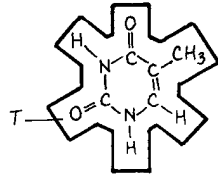
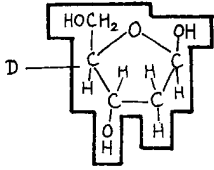
Color the heading Transfer RNA, title F, and the remainder of the plate.

Transfer RNA deserves some special attention because of its peculiar structure. There must be at least one different kind for each amino acid (actually a few more than that), all are about 80 nucleotides in length, all end in the sequence CCA (cytosine, cytosine, adenine) on their 3' ends, that end always serves as the attachment point of the amino acid to be transferred, and all tRNAs are folded into a complex "hairpin" structure with most of the molecule in helix form but three loops of unpaired bases.

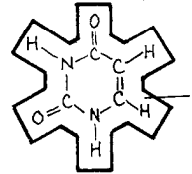
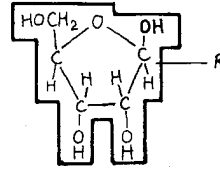
The center loop has a set of three unpaired bases known as the "*anticodon*" (see next plate), which serves as a "recognition code" and assures that that particular tRNA is attracted only to a particular complementary set of three bases on the mRNA, known as a "codon." The unpaired bases on one of the other loops serve to attach the tRNA to the ribosome, and the bases on the third loop serve as a recognition code for the specific aminoacyl-tRNA synthetase enzyme that attaches a particular amino acid to a particular tRNA molecule. The correct protein will be synthesized only if each of these recognition codes is correct.

DNA TRANSCRIPTION.

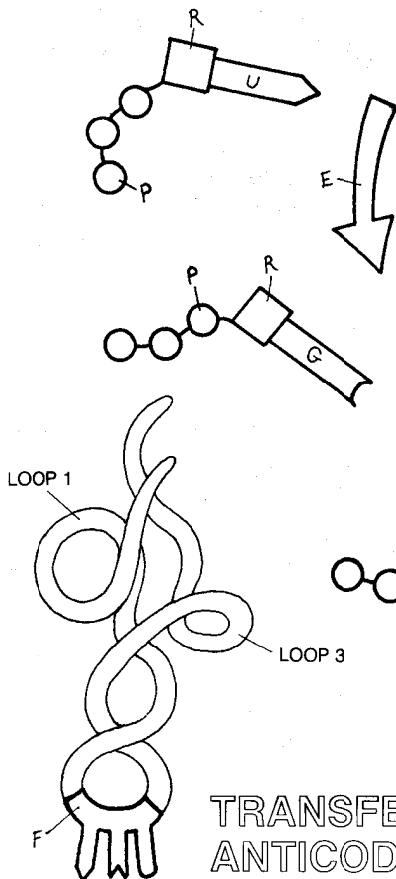
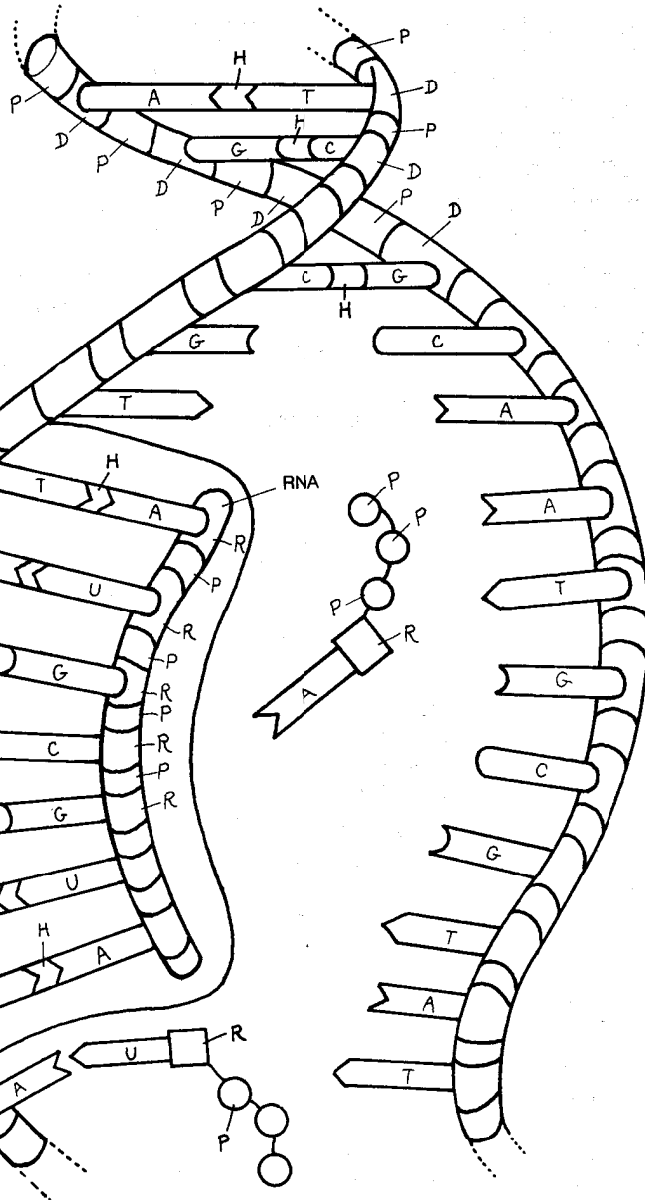
DNA★
DEOXYRIBOSE,
THYMINET



RNA★
RIBOSE,
URACILU



TRANSCRIPTION★
PHOSPHATEP
ADENINEA
CYTOSINEC
GUANINEG
HYDROGEN BONDH
RNA POLYMERASEB
DIRECTION OF
TRANSCRIPTIONE



TRANSFER RNA★
ANTICODONF

PROTEIN SYNTHESIS: TRANSLATION

After the process of transcription, messenger RNA migrates out of the nucleus of the cell and into the cytoplasm. There the genetic code is "translated" by a ribosome into a specific amino acid sequence in the synthesis of a protein (or at least the polypeptide portion if it is a complex protein).

Color titles and structures B and D.

Each set of three bases on a messenger RNA molecule constitutes a *codon* for one amino acid. Each codon is "recognized" by a complementary *anticodon* on a transfer RNA molecule, which brings the correct amino acid into position for addition to the polypeptide being synthesized.

Color the headings Ribosome, Phases of Translation, and Initiation, titles E through L, and the associated illustrations. Use very light colors for H, I, J, and K.

The ribosome is roughly half protein and half ribosomal RNA, organized into *small* and *large subunits*. The subunits are separate from one another except when translating messenger RNA. The large subunit has two separate binding sites for tRNA, known as the *P* (peptidyl) *site* and the *A* (aminoacyl) *site*.

The initiation phase begins with the binding of the *mRNA* to the small subunit of a ribosome. Next the first *tRNA*, with its amino acid, binds to the *mRNA*. Then the large ribosomal subunit binds, doing so in such a way that the first tRNA ends up bound to the *P* site.

The first codon of every *mRNA* is always AUG (adenine, uracil, guanine), and therefore the first tRNA to bind is always one with the anticodon TAC (thymine, adenine, cytosine), which is complementary to the AUG codon. The tRNA with that anticodon always has the amino acid *methionine* attached to it, so methionine is always the first amino acid in the new polypeptide chain. (In prokaryotic cells, the closely related N-formyl methionine is used.) The methionine is often removed later.

Color the heading Elongation, titles M, N, O, and J', and the associated illustration.

Immediately following initiation, the process of elongation begins, with the binding of a second tRNA, carrying its specific amino acid, to the second binding site on the ribosome, known as the *A* site. (Remember, each kind of tRNA carries only one particular amino acid of the 20 used in protein synthesis.) The *A* site is immediately adja-

cent to the *P* site, so the tRNA binding to it is always the one that has an anticodon that is complementary to the very next three bases (codon) on the *mRNA* molecule. In this plate, the second codon is GCU, which will bind only with the tRNA having the anticodon CGA, which always carries the amino acid *alanine*. The fact that the second codon is GCU will thus assure that the second amino acid in the chain being formed will be alanine and not one of the other 19 amino acids used to make proteins.

Once the tRNA is in place, an enzyme (peptidyl transferase) detaches the first amino acid, methionine, from its tRNA on the *P* site and joins its carboxyl end to the amino group of the amino acid (alanine) attached to the tRNA on the *A* site to form a *peptide bond* (Plate 18). Then the first tRNA is released from the *P* site to go back out into the cytoplasm for another amino acid molecule to be attached to it. The ribosome moves exactly three bases along the *mRNA*, moving the second tRNA to the *P* site (shown), taking along with it what is now a dipeptide (composed of two amino acids).

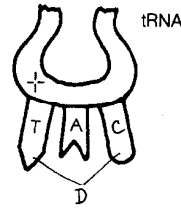
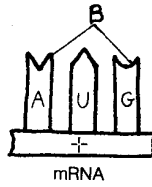
The elongation process then repeats over and over. A third tRNA with an anticodon (AAA in this illustration) complementary to the third codon (UUU) binds to the *A* site. The dipeptide constructed so far is transferred by the enzyme from the second tRNA on the *P* site to the third amino acid (on the tRNA at the *A* site) to form a tripeptide. Because the tRNA with the anticodon AAA always carries the amino acid *phenylalanine*, the fact that the third codon is UUU assures that the third amino acid will be phenylalanine. The same process repeats over and over until the entire polypeptide specified by the *mRNA* is complete.

Color the heading Termination, title P, and the remainder of the plate.

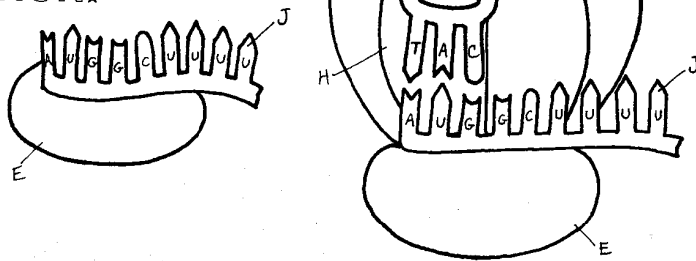
As will be seen in the next plate, three particular *mRNA* codons do not code for particular amino acids but serve as termination codons (also commonly called *stop codons*). When one of them, such as UGA shown here, reaches the *A* site, it attracts a protein called *release factor* instead of a tRNA. This causes the peptidyl transferase enzyme to break a water molecule to obtain a hydroxyl group, add that hydroxyl group to the end of the polypeptide chain to make a complete carboxyl group there, and release the completed polypeptide. The ribosome then separates into two subunits. The *mRNA* may bind to several more ribosomes and make several more copies of the polypeptide, but before long it is broken down by an enzyme, ribonuclease.

PROTEIN SYNTHESIS: TRANSLATION.

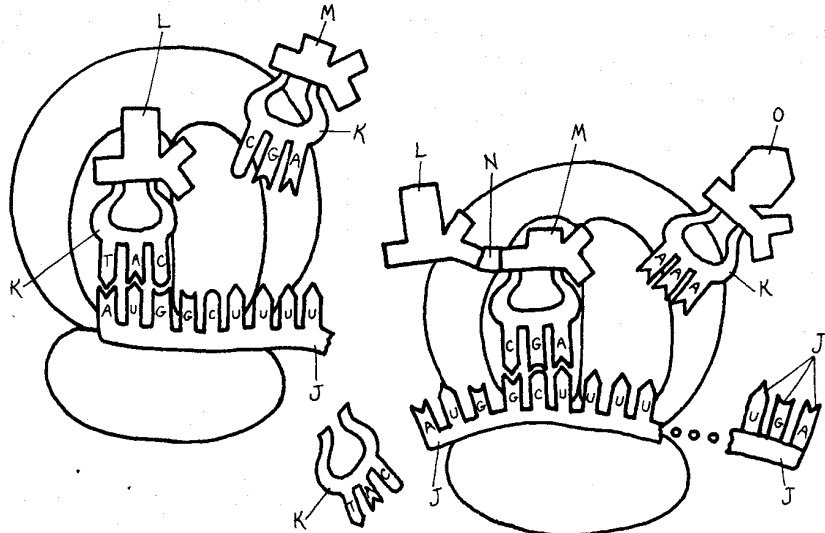
CODON_B
 ANTICODON_D
 RIBOSOME_E
 SMALL SUBUNIT_F
 LARGE SUBUNIT_F
 P SITE_H
 A SITE_I



PHASES OF TRANSLATION.
 INITIATION.
 mRNA_J
 tRNA_K
 METHIONINE_L



ELONGATION.
 ALANINE_M
 PEPTIDE BOND_N
 PHENYLALANINE_O
 STOP CODON_{J'}



TERMINATION.
 RELEASE
 FACTOR_P

