From Gene to Protein -- Transcription and Translation
Teacher Preparation Notes

By Dr. Ingrid Waldron and Dr. Jennifer Doherty, Department of Biology, University of Pennsylvania, Copyright, 2011[1]

Suggestions for Implementation

This activity is intended for students who have already learned about:

- the functions of proteins and DNA (key concepts and relevant learning activities are provided in "*Understanding the Functions of Proteins and DNA*", available at http://serendip.brynmawr.edu/exchange/bioactivities/proteins)
- proteins as polymers of amino acids
- DNA structure, replication, and the importance of the base-pairing rules (e.g. using the hands-on "*DNA*" activity, available at http://serendip.brynmawr.edu/sci_edu/waldron/#dna or the corresponding discussion/worksheet "*DNA*" activity, available at http://serendip.brynmawr.edu/exchange/bioactivities/DNA).
- the concept of genes

If you have already introduced transcription and translation, your students probably can complete this activity in two 50-minute periods. However, if you would like to use this activity to introduce these topics, a suggested sequence for four 50-minute periods is:

Period 1: Introduce the basic functions and processes of transcription and translation, and explain how transcription occurs (including the material on pages 1, 2 and the top of 3 of the student handout). Show an animation of transcription. We suggest the basic version of the animation of transcription of a gene produced by the Howard Hughes Medical Institute and available at: http://www.hhmi.org/biointeractive/dna/animations.html#dna-transcription_vo1.

Period 2: Have students model transcription and answer the questions (pages 3, 4 and the top of 5). If you have time, explain how translation occurs (pages 5-6) and show the basic version of the animation of translation http://www.hhmi.org/biointeractive/dna/animations.html#dna-translation_vo1.

Period 3: If you haven't finished explaining how translation occurs, explain translation. Have students model translation and answer the questions (pages 7-10).

Period 4: Discuss how different alleles affect phenotype, including sickle cell anemia, and have students answer the questions (pages 10-13). We also recommend showing and discussing the sickle cell anemia video available at http://www.hhmi.org/biointeractive/dna/DNAi_sicklecell.html.

In order for students to learn the process of transcription through this modeling activity, it is important for them to add each nucleotide one at a time, mimicking the actual activity of RNA polymerase. Some students will want to lay out all the mRNA nucleotides and tape them together all at once, which is more efficient in getting the task done, but less effective in modeling and understanding the real biological process. Similarly, during translation, the students should insert one tRNA with amino acid at a time, similar to the actual function of the ribosome. To encourage accurate modeling, we recommend that you cut out the 3 mm x 25 mm slots in the nucleus and ribosome pages and have your students insert the DNA and RNA molecules through these slots. Although the modeled process may seem rather long and tedious to some students, transcription and translation occur very rapidly in real cells. For example, RNA polymerase adds about 50 nucleotides per second to the growing mRNA molecule and a ribosome adds about 2-20 amino acids per second (in eukaryotes and bacteria, respectively).

We find that, at each step, you have to be very explicit in your instructions in order to prevent students from racing ahead in ways that undermine the learning goals. For example, in the transcription activity students should not tape the RNA nucleotides to the DNA nucleotides, since these are not linked by covalent bonds. (You may want to provide masking tape or low stick painters' tape to represent the weaker hydrogen bonds between complementary nucleotides.) You may want to make a transparency of the RNA polymerase, ribosome, and relevant molecules and use these on an overhead projector to demonstrate the proper procedures.

---

[1] These Teacher Preparation Notes and the related Student Handout are available at http://serendip.brynmawr.edu/sci_edu/waldron/.

To encourage students to actively synthesize their own basic understanding of transcription and translation, we strongly recommend assigning question 3 on page 5 and question 3 on page 13 of the Student Handout, perhaps as a homework assignment if you do not have time during the laboratory period. You may want to offer your students the option of providing their explanations as paragraphs or as diagrams. If you feel that these questions are too challenging for your students, you could provide a first sentence and the beginning of a second sentence to help your students get started. If your students have particular difficulty learning vocabulary, you may want to precede these questions with questions that ask for definitions of the terms listed (or perhaps a matching question in which you provide your preferred definitions for these terms).

If you want to emphasize learning how to use the standard chart of codons in mRNA and corresponding amino acids, you can substitute the chart from your textbook for the chart on the bottom of page 5 of the student handout. This would also provide the opportunity to discuss the function of the start and stop codons in initiating and terminating translation. Our preference is to use the simplified chart on page 5, so students can concentrate on understanding the process of translation, and then later practice using the standard codon chart in a separate activity such as "*From Gene to Polypeptide -- The Roles of the Base-Pairing Rules and the Genetic Code*" (available at http://serendip.brynmawr.edu/exchange/bioactivities/basepair). This discussion/worksheet activity reviews the information flow from a gene to a polypeptide, with an emphasis on understanding the roles of the base-pairing rules and the genetic code chart.

To request an answer key, write to iwaldron@sas.upenn.edu. .

Supplies needed

Use the templates shown, beginning on page 6 of these Teacher Preparation Notes, to make for each pair of students a page labeled Nucleus, a page labeled Ribosome, and a packet containing the following:

- DNA molecule on colored paper (cut the template in strips)
- Second Part of mRNA strip and 9 RNA nucleotides on a different color paper (each packet should have 1A, 2C, 3 G, and 3U)
- 6 tRNA molecules on same color paper as RNA nucleotides (cut each tRNA rectangle to include the three nucleotides and the words "amino acid" directly above these nucleotides; one of each type of tRNA per packet)
- 6 amino acids on a different color paper (one of each amino acid per packet)

The activity works best if the pages and pieces are printed on card stock or heavy paper.
Each pair of students will also need transparent tape.

Key Concepts for Students to Learn:

Genes influence our phenotype by determining the sequence of amino acids in proteins which determines protein structure and function which in turn influences our characteristics. For example, different versions of the gene for hemoglobin (normal vs. sickle cell alleles) result in the production of normal vs. sickle cell hemoglobin, and sickle cell hemoglobin can result in sickle cell anemia. The nucleotide sequence in a gene specifies the amino acid sequence in a protein by the molecular processes of transcription and translation.

nucleotide sequence in the DNA of a **gene**

→ nucleotide sequence in messenger RNA (mRNA)
transcription

→ amino acid sequence in a protein
translation

→ structure and function of the protein
(e.g. normal hemoglobin vs. sickle cell hemoglobin)

→ person's **characteristics** or **traits**
(e.g. normal health vs. sickle cell anemia)

Transcription is the process that copies the message in a gene into a messenger RNA (mRNA) molecule that will provide the instructions for making a protein molecule. The sequence of nucleotides in a gene in the DNA is copied into a corresponding sequence of nucleotides in the mRNA molecule. Each mRNA nucleotide is complementary to the corresponding DNA nucleotide (C pairs with G and A pairs with T (in DNA) or U (in RNA) in accord with the base-pairing rules). To make the mRNA molecule, the enzyme RNA polymerase adds the complementary nucleotides one-by-one to the growing mRNA molecule, using the base-pairing rules.

mRNA carries the genetic message from the nucleus to the ribosomes where proteins are synthesized. Each mRNA molecule codes for the sequence of amino acids in a polypeptide. The sequence of amino acids determines how the polypeptide folds to form a protein and determines the function of that protein.

Translation is the process that makes proteins. In the process of translation, the sequence of nucleotides in an mRNA molecule specifies the sequence of amino acids in a polypeptide. Each triplet codon in the mRNA codes for a specific amino acid in the protein. The ribosome adds amino acids one-by-one to the growing polypeptide in accord with the instructions from the codons in the mRNA molecule.

tRNA is needed for translation. Different types of tRNA bring the right amino acids for each position in the polypeptide as it is synthesized in the ribosomes. Each type of tRNA has an anti-codon with three nucleotides which are matched by the base-pairing rules to the three nucleotides in an mRNA codon; for each type of tRNA, there is a specific enzyme that recognizes the anti-codon and attaches the correct amino acid to the tRNA.

Transcription shares the following similarities with DNA replication: Both are carried out by a polymerase enzyme which adds nucleotide monomers one at a time, using the base-pairing rules to match each new nucleotide in the growing RNA or DNA polymer with the nucleotide in the DNA molecule that provides the instructions for transcription or replication, respectively. The primary differences are that a single gene is transcribed into an mRNA molecule, whereas the whole chromosome is replicated, transcription produces a single-stranded mRNA molecule whereas replication produces a double-stranded DNA molecule, the enzymes required are RNA polymerase and DNA polymerase, respectively, and thymine in DNA is replaced by uracil in RNA.

Background Biology and Suggestions for Discussion

To stimulate student interest, you may want to begin with the question "How can differences in the DNA molecules inside each cell cause differences in a person's appearance or health?" The examples discussed in this activity are the genes for albinism and sickle cell anemia, but the same principles apply to the effects of many other genes. A view of the human side of sickle cell anemia (including singer/actress Tionne T-boz Watkins) and an introduction to some current research on treatment of sickle cell anemia is available at http://videos.howstuffworks.com/hsw/18705-your-body-your-health-sickle-cell-disease-video.htm.

Transcription and Translation

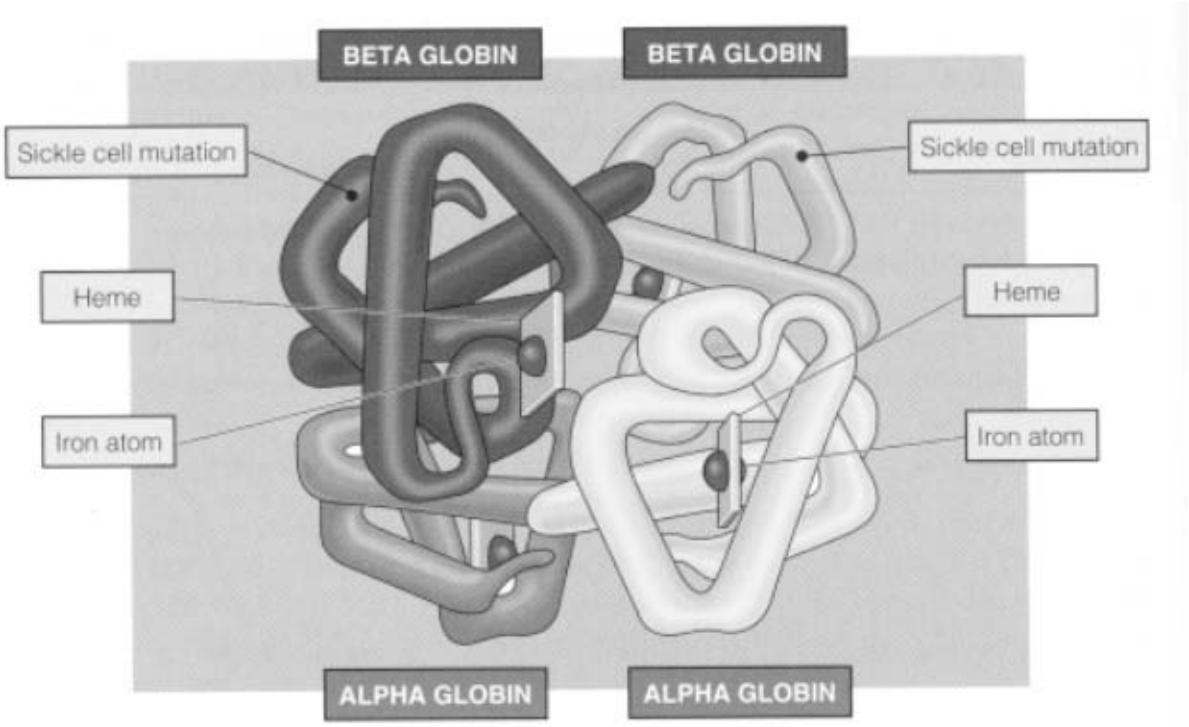
To ensure that students understand the basic processes of transcription and translation we have omitted many points, and you may want to include some of these if your students already have a good grasp of the basic processes. For example, the DNA strand we provide is the template strand for the beta globin polypeptide; the template strand (also called the anti-sense strand) is the DNA strand which is transcribed for a given gene. The other strand of the DNA double helix is called the coding or sense strand; it has the same nucleotide sequence as the RNA produced by transcription. If your students ask how the RNA polymerase is directed to transcribe the right strand of the DNA double helix, you can explain the role of the promoter in initiating transcription. Multiple different nucleotides enter and leave the RNA polymerase, but, for each DNA nucleotide only the complementary RNA nucleotide that can form hydrogen bonds with that specific DNA nucleotide will remain in place to be covalently bonded to the preceding RNA nucleotide.

Ribosomes consist of RNA and protein. The catalytic action to form the peptide bond between adjacent amino acids is provided by an RNA ribozyme within the ribosome. Ribosomes have three sites for tRNAs, including the sites we have shown in our model ribosome and a third site (to the left) where the tRNA that has lost its amino acid is located before it exits the ribosome. There are 40-45 different types of tRNA, with some types of tRNA able to match with two different codons that have the same first two nucleotides but differ in the third nucleotide (both are codons for the same amino acid).

Some students have difficulty understanding the function of the tRNA molecule. An analogy that may help them understand is as follows. Suppose a group of American tourists goes into a restaurant in China and each one wants to order his or her favorite Chinese dish. Suppose the tourists only speak English, and the cook only speaks Chinese. It will be very helpful to have a waiter who understands English and can speak Chinese, so he can serve as a translator. The tourists are equivalent to the mRNA which specifies which amino acids should be incorporated in the growing protein molecule, and the cook is equivalent to the cytoplasm which provides lots of different types of amino acids. The waiter is equivalent to the tRNA molecules which bring the right amino acids to the right locations.

Sickle Cell Hemoglobin and Sickle Cell Anemia

This activity discusses transcription and translation of the beginning of the gene for the beta globin polypeptide in the hemoglobin tetramer protein and ignores the gene for the alpha globin polypeptide. The alpha globin gene and polypeptides are the same in normal and sickle cell hemoglobin. You may want to explain that the lower solubility of nonpolar valine in the watery cytosol of the red blood cell (compared to the high solubility of ionic glutamic acid) contributes to the tendency of sickle cell hemoglobin to clump together in long rods inside the red blood cells. This difference in the solubility of amino acid 6 is crucial because amino acid 6 is on the outside of the hemoglobin molecule.



The last part of this activity summarizes the effects of the homozygous sickle cell allele, resulting in sickle cell anemia. Even in a person who has severe sickle cell anemia, most red blood cells are not sickled. Variation in the degree of clumping of sickle cell hemoglobin, sickling of red blood cells, and consequent symptoms is influenced by multiple factors, including oxygen levels in the blood, dehydration, and multiple genetic factors. Sickling crises that block the blood flow in some of the small blood vessels result in pain and organ damage. The causes of these crises are often unknown, but some sickling crises are triggered by infection which induces vomiting and diarrhea resulting in dehydration; dehydration increases the hemoglobin concentration in red blood cells and thus increases the tendency of sickle cell hemoglobin to clump into long rods, resulting in the sickling and other irregular shapes of red blood cells that cause blockage of the small blood vessels.

The severity of sickle cell anemia in different individuals varies from relatively mild sickle cell anemia with few sickling crises and nearly normal health and survival to severe sickle cell anemia with frequent sickling crises, significant organ damage and early death. The majority of people with sickle cell anemia have an intermediate severity. One factor that contributes to variation in the frequency of sickling crises is that some people with

sickle cell anemia spontaneously produce relatively high levels of fetal hemoglobin (which contains gamma globin instead of beta globin peptides), and fetal hemoglobin inhibits clumping of sickle cell hemoglobin. Hydroxyurea, which increases the production of fetal hemoglobin, is one treatment for sickle cell anemia. A good summary of the medical aspects of sickle cell anemia, including symptoms, diagnosis and treatment is available at http://www.mayoclinic.com/health/sickle-cell-anemia/DS00324.

An individual who is heterozygous for the sickle cell allele (sickle cell trait) almost always has no symptoms because each red blood cell contains both normal and sickle cell hemoglobin and the normal hemoglobin generally prevents clumping of the sickle cell hemoglobin. Athletic associations recommend testing for sickle cell trait and taking appropriate precautions to prevent extreme exertion and dehydration in order to reduce the small but significant risk of exercise-related sudden death. Harmful health effects of sickle cell trait are rare, and life expectancy is not detectable reduced. Individuals with sickle cell trait have less serious malaria infections because the malaria parasite doesn't grow as well in their red blood cells.

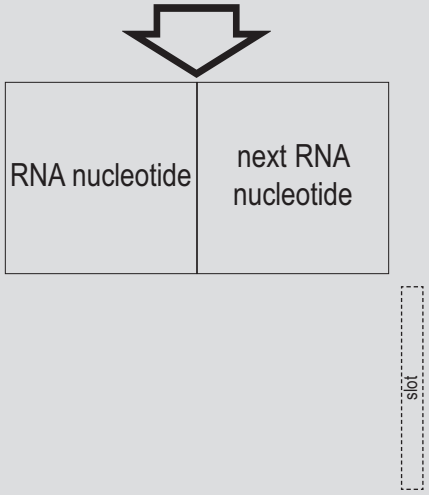
Related Activities

"*Molecular Biology: Major Concepts and Learning Activities*" (available at http://serendip.brynmawr.edu/exchange/bioactivities/MolBio). This overview reviews key concepts and learning activities to help students understand how genes influence our traits by molecular processes. Topics covered include basic understanding of the important roles of proteins and DNA, DNA structure and replication, and the molecular biology of how genes influence traits, including transcription, translation, and the molecular biology of mutations. To help students understand the relevance of these molecular processes, the suggested learning activities link alleles of specific genes to human characteristics such as albinism, sickle cell anemia and muscular dystrophy.

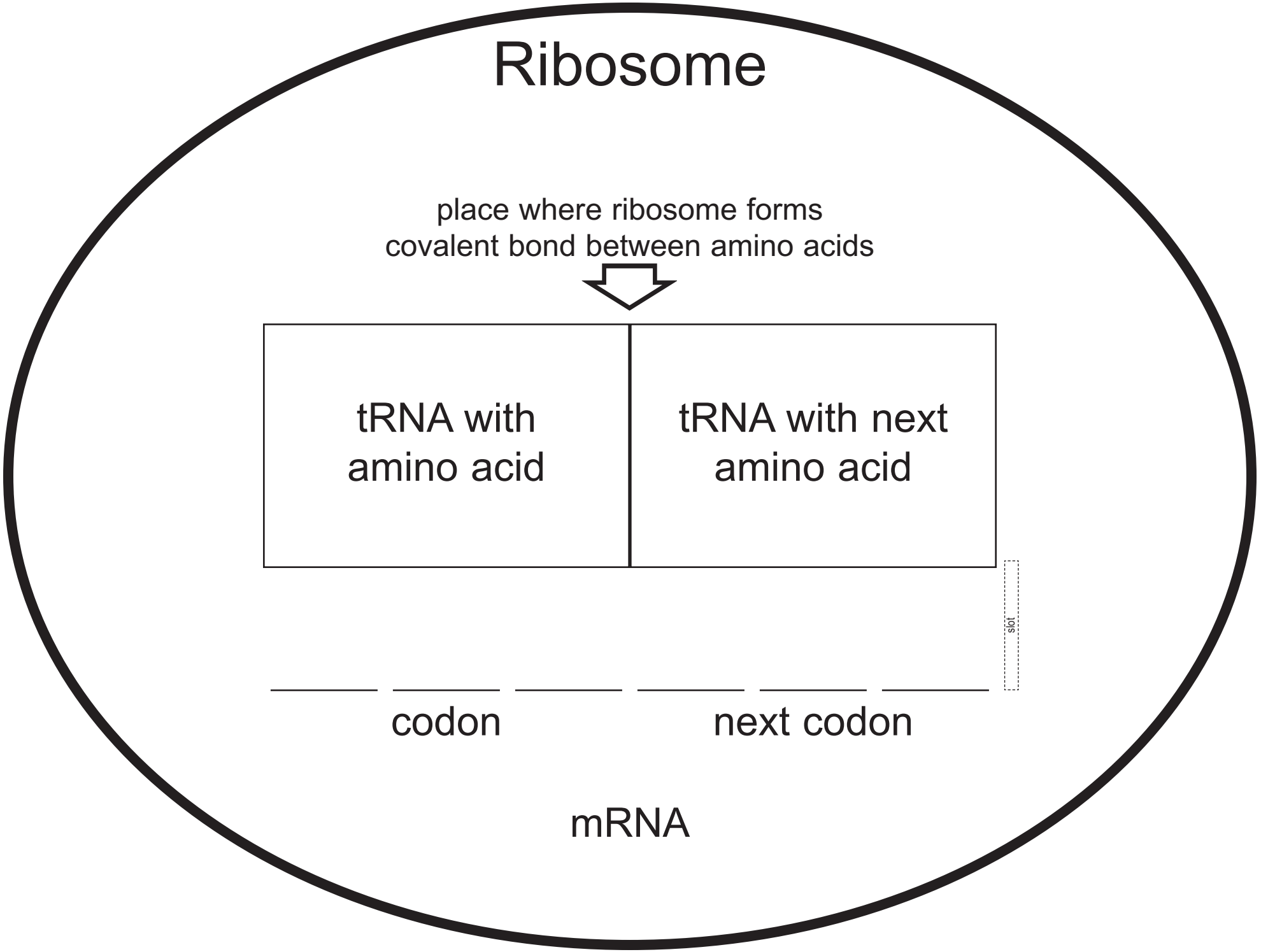
Nucleus

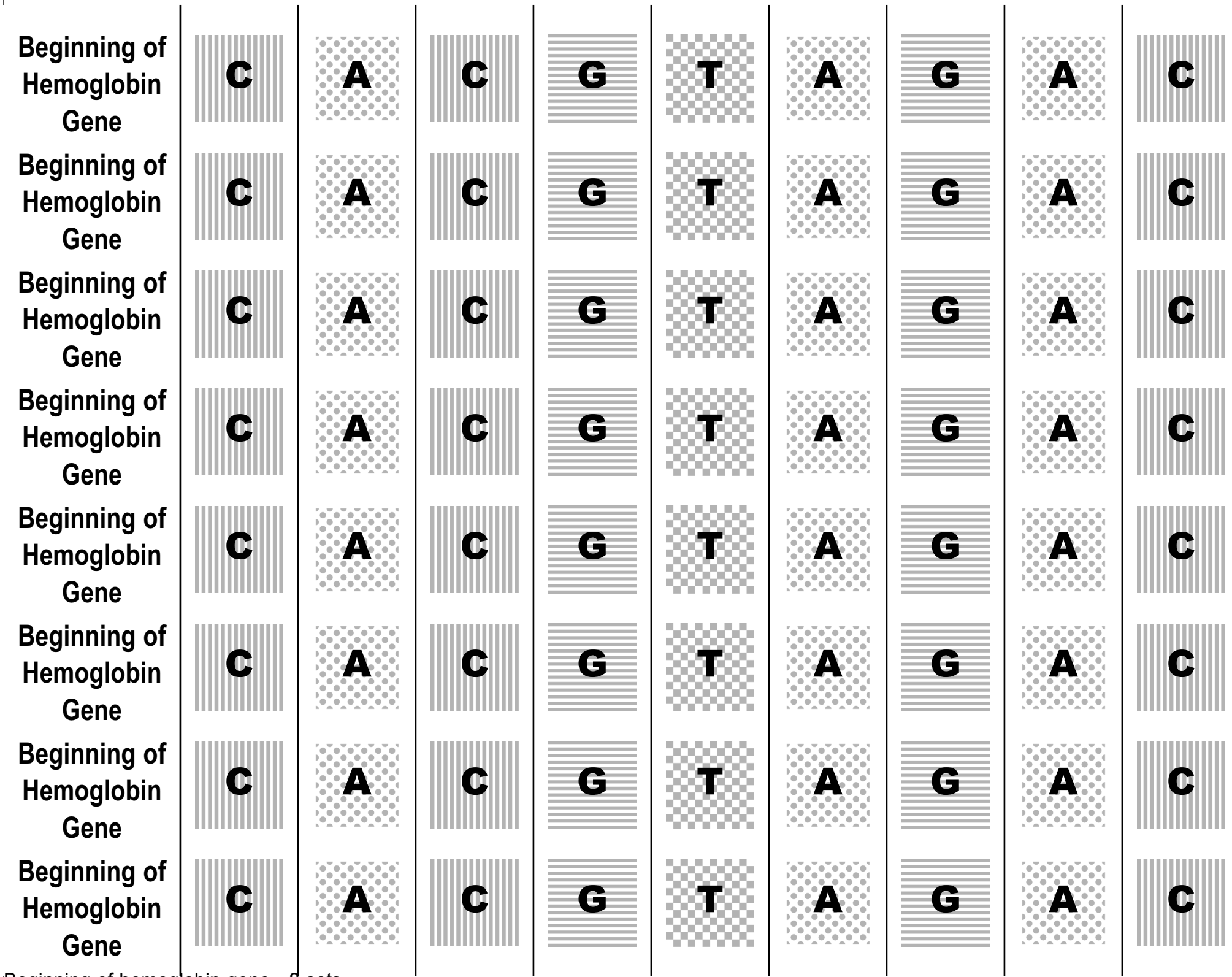
RNA polymerase

place where enzyme forms
covalent bond between nucleotides

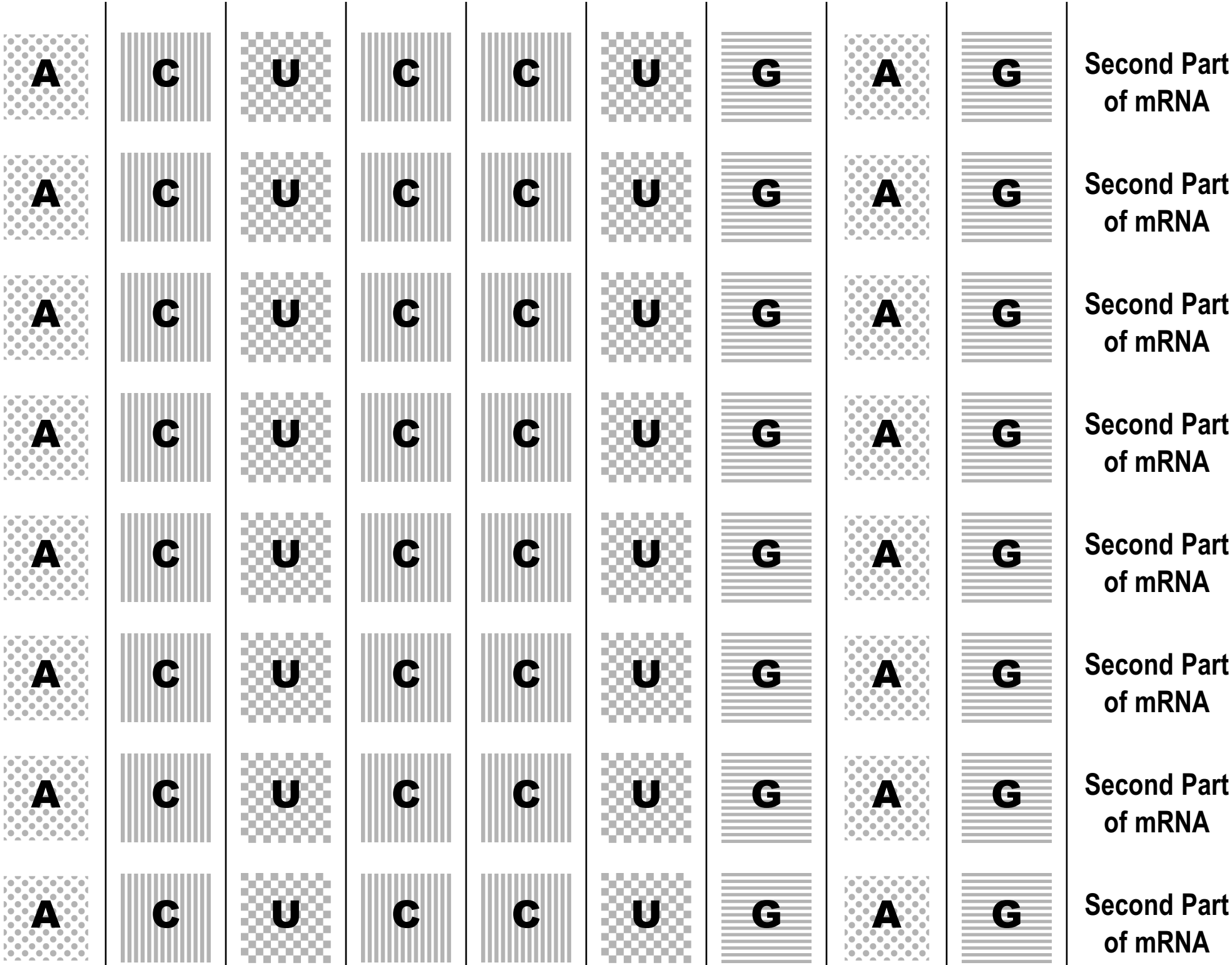


cytoplasm
around the nucleus

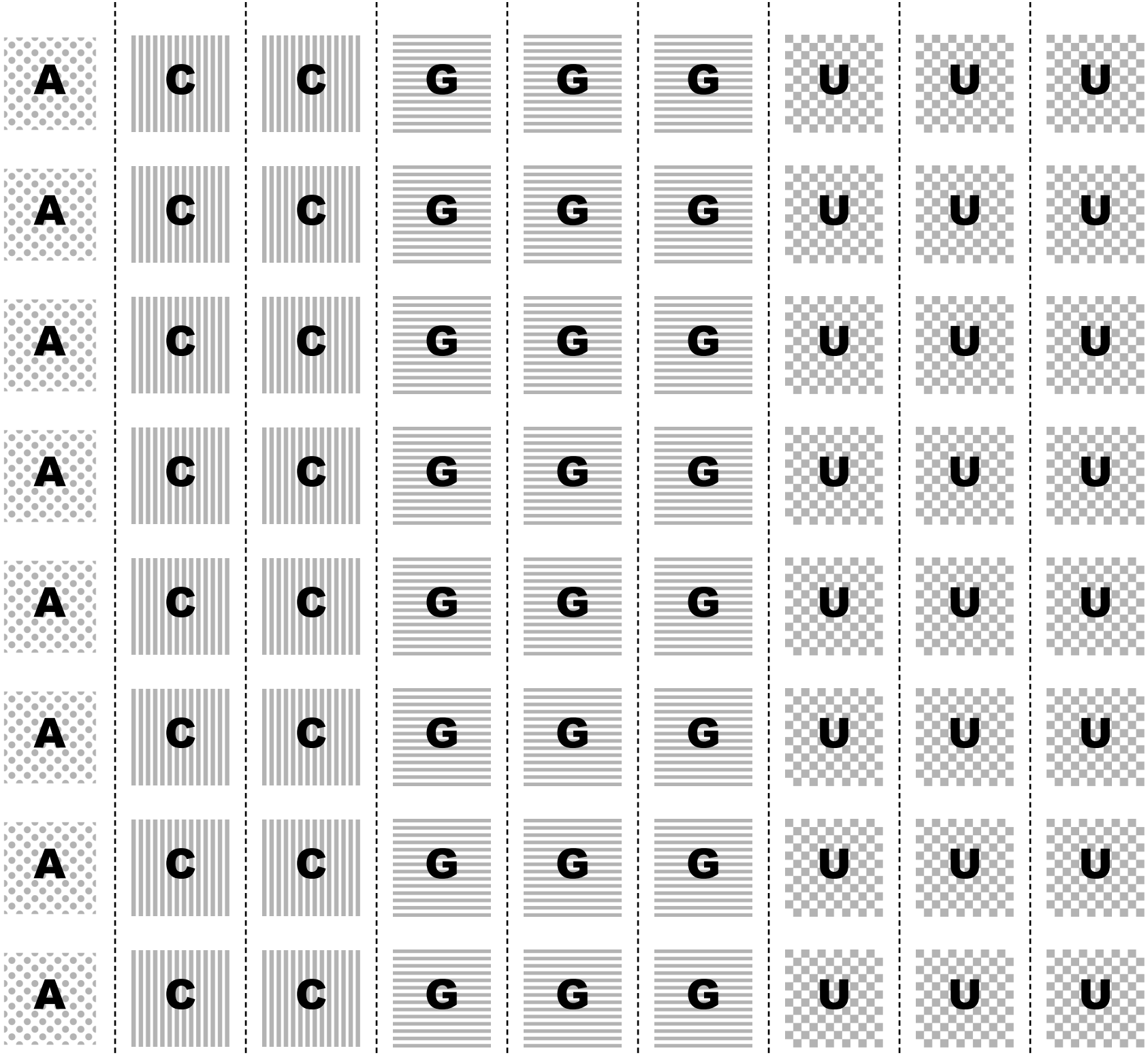

Ribosome
place where ribosome forms
covalent bond between amino acids
tRNA with
amino acid
tRNA with next
amino acid
slot
codon
next codon
mRNA



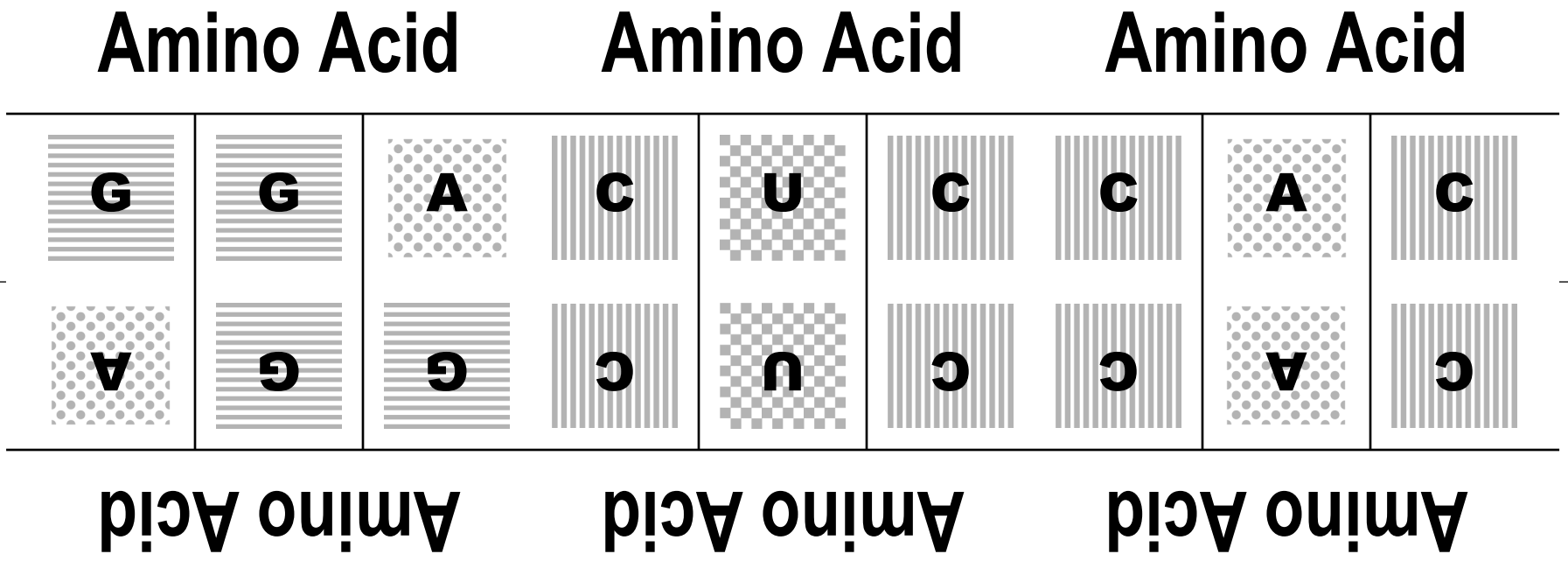
Beginning of hemoglobin gene - 8 sets

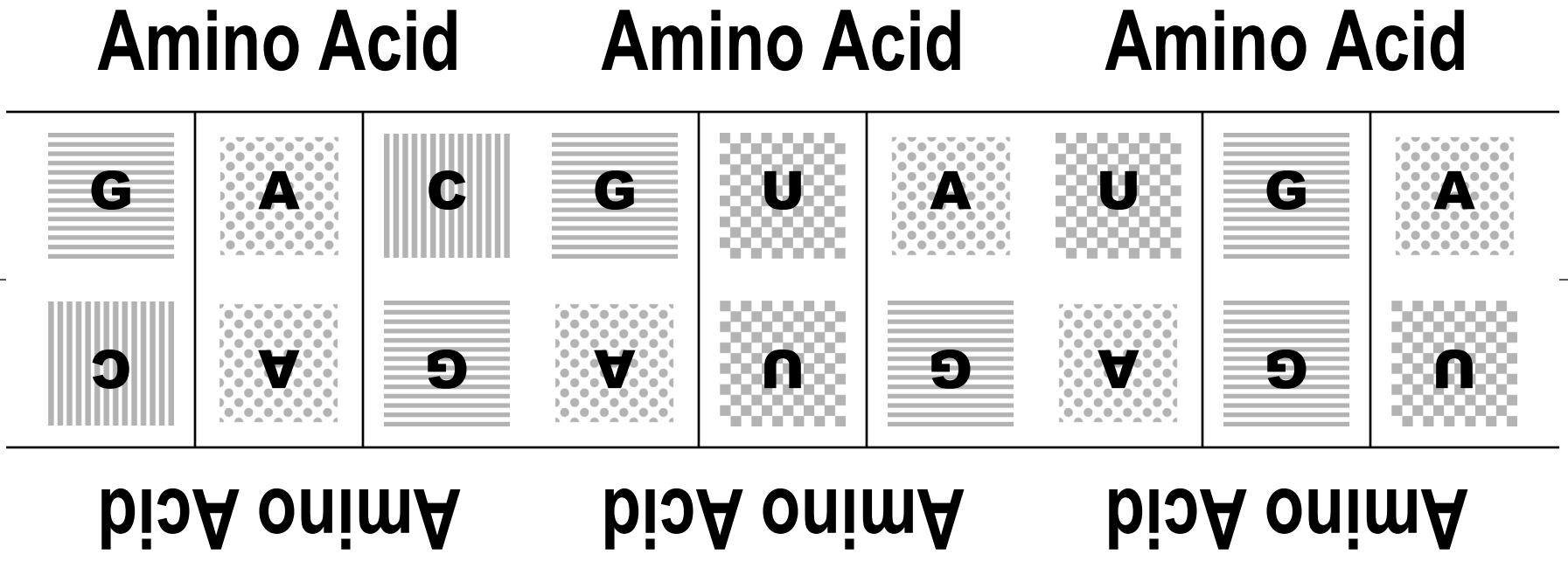


Second Part of mRNA - 8 sets



RNA neuclotides - 8 sets





tRNA molecules - 2 sets

Leucine	Histidine	Valine
Leucine	Histidine	Valine
Leucine	Histidine	Valine
Leucine	Histidine	Valine
Leucine	Histidine	Valine
Threonine	Proline	Glutamic Acid
Threonine	Proline	Glutamic Acid
Threonine	Proline	Glutamic Acid
Threonine	Proline	Glutamic Acid
Threonine	Proline	Glutamic Acid