Teacher Preparation Notes for "From Gene to Protein – Transcription and Translation"[1]

In this hands-on activity students learn how a gene provides the instructions for making a protein, and how genes can cause albinism or sickle cell anemia. Simple paper models are used to simulate the molecular processes of transcription and translation. This activity can be used to introduce students to transcription and translation or to reinforce student understanding. In addition, students evaluate the advantages and disadvantages of different types of models included in this activity.

This activity typically requires two to four 50-minute periods, depending on your students and whether they are already familiar with transcription and translation (see pages 3-4 for additional information).

This activity is intended for students who have been introduced to:

- the structure and function 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)
- DNA replication and the base-pairing rules (key points are presented in the discussion activity, "DNA", available at http://serendip.brynmawr.edu/exchange/bioactivities/DNA or the hands-on activity, "DNA", available at http://serendip.brynmawr.edu/sci_edu/waldron/#dna).

Learning Goals

Genes influence our phenotype by the following sequence of steps:

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 (in accord with the base-pairing rules, C pairs with G and A pairs with T (in DNA) or U (in RNA)). 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 protein. The sequence of amino acids determines the structure and function of the protein.

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[1] By Drs. Ingrid Waldron and. Jennifer Doherty, Department of Biology, University of Pennsylvania, 2014. These Teacher Preparation Notes and the related Student Handout are available at http://serendip.brynmawr.edu/sci_edu/waldron/. We thank Amy Dewees, Jenkintown High School, Erica Foley and Lori Spindler for helpful suggestions and NancyLee Bergey, University of Pennsylvania School of Education, Holly Graham, Central Bucks High School South, and Mr. Ippolito, Port Chester High School, for sharing helpful activities which provided us with many useful ideas.

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 protein. 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 protein in accord with the instructions from the codons in the mRNA molecule.

tRNA molecules are needed for translation. Different types of tRNA bring the right amino acids for each position in the protein as it is synthesized by the ribosome. 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.

A comparison between transcription and DNA replication shows:

Similarities	Differences
- Both transcription and replication are carried out by a polymerase enzyme which adds nucleotide monomers one at a time. - Both use 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.	- 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. - Thymine in DNA is replaced by uracil in RNA.

Different types of models serve different purposes for learning about and understanding how genes influence characteristics, including the molecular processes of transcription and translation. Like all models, the models presented in the Student Handout involve simplifications which help to clarify important points, but also limit the accuracy of the models as representations of the actual complex biological processes.

In accord with the Next Generation Science Standards (http://www.nextgenscience.org/next-generation-science-standards), students will:

- gain understanding of Disciplinary Core Ideas LS3.A and LS3.B, Inheritance and Variation of Traits, including "Genes chiefly regulate a specific protein, which affect an individual's traits." and "DNA carries instructions for forming species characteristics."
- engage in Science Practices, including "Evaluate merits and limitations of two different models of the same… process…" and "use multiple types of models to provide mechanistic accounts and/or predict phenomena, and move flexibly between model types…".

Supplies needed

For each pair of students, use the templates shown beginning on page 9 of these Teacher Preparation Notes to make:

- a page labeled Nucleus and a page labeled Ribosome[2] (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 so that initially only the beginning of the DNA or RNA molecule can be seen; for the ribosomes, you may want to make the

[2] The nucleus and ribosome pages can be reused in multiple classes, especially if they are printed on card stock or heavy paper. We are interested in the possibility of laminating all items used in this simulation, so that everything could be reused in multiple classes. We haven't actually tried this, so if you try lamination, please send us feedback about how well or poorly this worked (iwaldron@sas.upenn.edu). Thank you!

slots slightly longer so the part of the mRNA molecule that students produce by taping together nucleotides will fit through.)

- the following disposable items[3]:
  - DNA molecule on colored paper (cut the page in strips)
  - Second Part of mRNA strip and 9 RNA nucleotides on a different color paper (each pair of students will need 1A, 2 C, 3 G, and 3 U)
  - 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 for each pair of students)
  - 6 amino acids on a different color paper (one of each amino acid for each pair of students)
- transparent tape

Depending on your students, you may want to prepare a packet with all the supplies for each pair of students or you may want to dole out supplies as needed for each step in the simulation and have the 9 RNA nucleotides, the 6 tRNA molecules and the 6 amino acids for each student pair in three separate coin envelopes.

Suggestions for Implementation

We recommend the following sequence:

1. To stimulate student interest and get your students thinking about the topic, you may want to begin with the probe question "How can differences in DNA molecules cause differences in a person's appearance or health?" The examples discussed in this activity are the genes for albinism (top half of page 1 of the Student Handout) and sickle cell anemia (page 11).
2. Introduce the basic functions and processes of transcription and translation (using the information on page 1 of the Student Handout). Have students answer questions 1-3, and discuss their answers.
3. Explain how transcription occurs (using the material on page 2 of the Student Handout, including questions 4-5). Show the basic version of the animation of transcription of a gene produced by the Howard Hughes Medical Institute (http://www.hhmi.org/biointeractive/dna-transcription-basic-detail). This animation provides a dynamic simulation of the basic process of transcription and also illustrates the amazing rapidity of the process; RNA polymerase adds about 50 nucleotides per second to the growing mRNA molecule.
4. Have students model transcription by carefully following the instructions on page 3 of the Student Handout; try to make sure that each pair of students carries out each step accurately in order to ensure accurate understanding of the process of transcription.
5. Have students answer questions 7-9 and discuss their answers.
6. Explain how translation occurs (pages 4-5 of the Student Handout) and show the basic version of the animation of translation (http://www.hhmi.org/biointeractive/translation-basic-detail). (A ribosome adds about 2-20 amino acids per second, in eukaryotes and bacteria, respectively.)
7. Have students model translation by carefully following the instructions on pages 6-8 of the Student Handout.
8. Have students answer questions 16-21 and discuss their answers.
9. Discuss how different alleles result in different versions of a protein which in turn can result in different characteristics (e.g. albinism vs. not) (page 10 of the Student Handout). Have students answer questions 22-26 and discuss their answers. During the discussion, we recommend showing the sickle cell anemia video (http://www.hhmi.org/biointeractive/sickle-cell-anemia).
10. Introduce the concept of a model and have students work in pairs to answer question 27 to evaluate the advantages and disadvantages of the different types of models included in this activity. Discuss their answers.

[3] The DNA molecule, second part of mRNA strip, and tRNA molecules may be reusable in multiple classes, especially if they are printed on card stock or heavy paper.

If you plan to use this activity to introduce transcription and translation, this sequence will probably require four 50-minute periods. Alternatively, if your students already have a basic understanding of transcription and translation, you may be able to complete this activity in two 50-minute periods.

We recommend that you have your students work in pairs to model transcription and translation and also to answer the questions.

To use this modeling activity to facilitate student understanding of how transcription takes place, 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 mimic the actual function of the ribosome by bringing in one tRNA with amino acid at a time. Using the slots in the nucleus and ribosome pages helps to encourage students to do the modeling correctly.

To help your students understand why RNA polymerase adds nucleotides one at a time and ribosomes add amino acids one at a time, you may want to point out that a typical protein has hundreds of amino acids. Have your students think about the problems that would arise if natural selection or a molecular biologist tried to design a ribosome that could simultaneously arrange and bond together the whole sequence of amino acids in a protein, especially considering that there are many thousands of different types of proteins in a cell. Similarly, have your students think about the problems of trying to design an enzyme that could simultaneously arrange and join together the whole sequence of nucleotides in an mRNA molecule.

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 might want to provide masking tape or low stick painters' tape to represent the weaker hydrogen bonds between complementary nucleotides.)

For the simulation, it is important to make sure that one student in each pair is acting as the cytoplasm and the other student is acting as the RNA polymerase or ribosome. If appropriate, you may want to require your students to check off each arrow indicating a step in the simulation and also answer any questions *before* moving on to the next step. To demonstrate the proper procedures, you may want to project images of the nucleus, ribosome, and relevant molecules.

To encourage students to actively synthesize their own basic understanding of transcription and translation, we strongly recommend assigning question 9 on page 4 and question 21 on page 9 of the Student Handout, perhaps as a homework assignment if you do not have time during the class periods. If you feel that these questions will be challenging for your students, we have several suggestions to help your students meet this challenge.

- Immediately before the students answer question 9, you may want to show the video at http://www.hhmi.org/biointeractive/dna-transcription-basic-detail to refresh students' memory of the overall process of transcription. Similarly, immediately before students answer question 21, you can show the video at http://www.hhmi.org/biointeractive/translation-basic-detail.
- You could provide a first sentence and the beginning of a second sentence to help your students get started.
- You may want to rearrange the word list from its current alphabetical order into a suggestive sequence or clusters of related concepts.
- If your students have particular difficulty learning vocabulary, you may want to precede questions 9 and 21 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).

To ensure that students develop a good understanding of the basic processes of transcription and translation, this activity omits many complexities (e.g. proteins may have more than one polypeptide; introns, exons and splicing). If your students already have a good grasp of the basic processes, you may want to include some of these points. For example, if you want to emphasize learning how to use the standard chart of codons in mRNA and corresponding amino acids, you can replace the chart on the top of page 5 of the Student Handout with the codon chart from your textbook or from the activity described at the end of this paragraph. 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 of the Student Handout, 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" (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.

Background Biology and Suggestions for Discussion

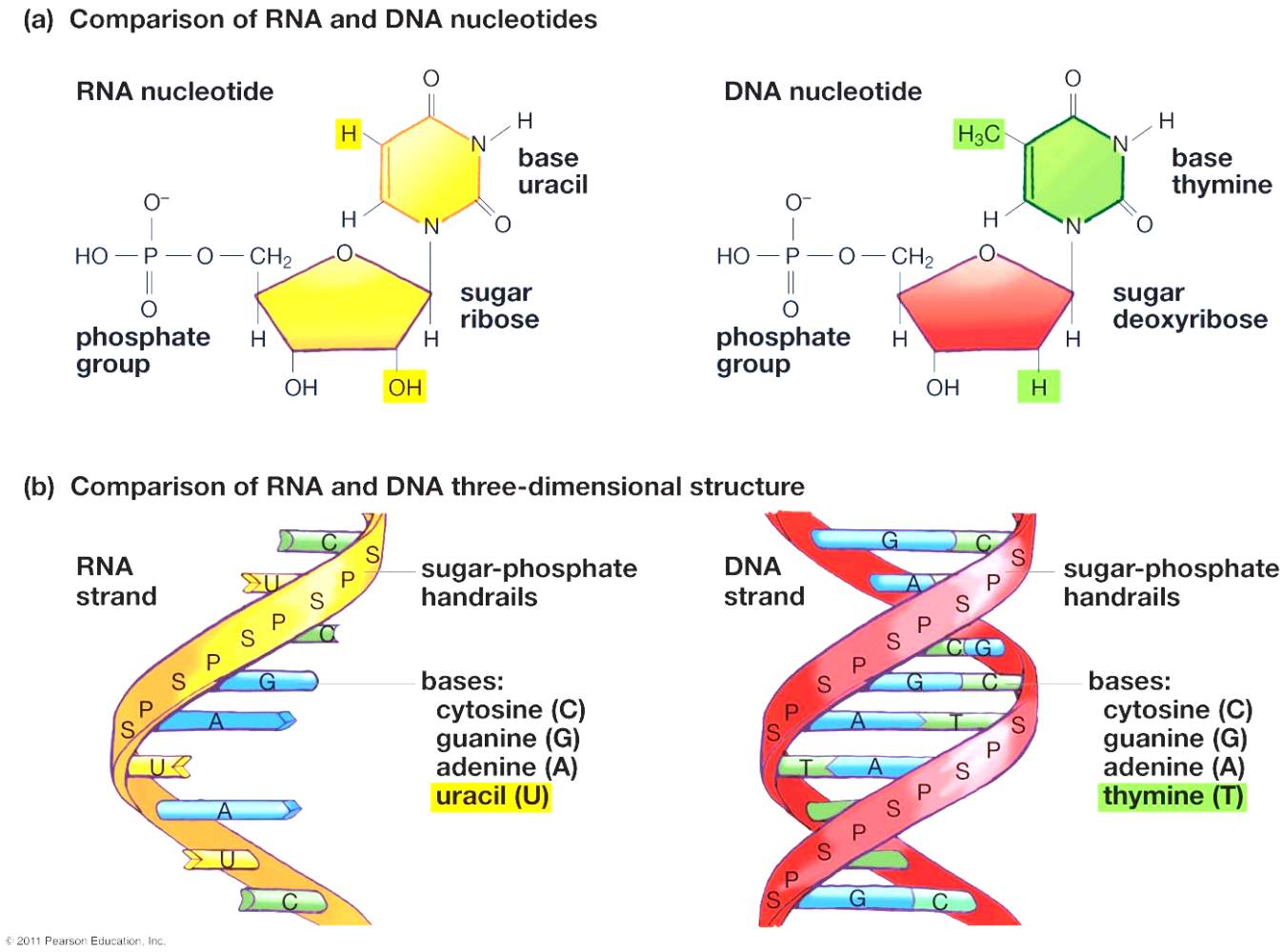
The basic points and information to be included in discussing the questions in the Student Handout are provided in the answer key, available upon request to iwaldron@sas.upenn.edu. Additional relevant background information is provided in the following sections, primarily to give you information that may be helpful for responding to student questions.

The type of albinism discussed in the introduction to this activity is called oculocutaneous albinism, because the melanin deficiency results in vision problems as well as pale skin and hair color. This type of albinism is due to a defect in the tyrosinase enzyme which catalyzes the first step in the production of melanin (http://ghr.nlm.nih.gov/gene/TYR).

Transcription and Translation

If your students are somewhat hazy about nucleic acid structure and the base-pairing rules you may want to use the figure shown on the next page to remind them of key background information for understanding the discussion of the base-pairing rules on page 2 of the Student Handout.

The DNA strand we provide is the template strand (i.e. the DNA strand that is transcribed) for the beta globin polypeptide of the hemoglobin protein. The other strand of the DNA double helix is called the non-template or sense strand; it has the same nucleotide sequence as the RNA produced by transcription (except of course **T** in DNA is replaced by **U** in RNA). 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. This would also provide the opportunity to mention that the rate of transcription of specific genes varies in different types of cells, corresponding to the differences in specific types of proteins in different types of cells (e.g. hemoglobin abundant in red blood cells and the enzyme for making melanin abundant in melanocytes in the skin).



(from Krogh, Biology: a Guide to the Natural World)

The bonds within each strand are covalent bonds. In contrast, base pairing involves weaker hydrogen bonds which are more readily broken as occurs during transcription and translation. During transcription, multiple different nucleotides enter and leave the RNA polymerase, but, for each DNA nucleotide only the complementary RNA nucleotide that has the right shape and charges to form multiple hydrogen bonds with that specific DNA nucleotide will remain in place to be covalently bonded to the preceding RNA nucleotide.

The enzyme that binds each tRNA to the appropriate amino acid forms a covalent bond between the tRNA and amino acid.[4] Inside the ribosome there is a ribozyme (RNA enzyme) that simultaneously breaks this covalent bond and forms a new covalent peptide bond between this amino acid and the previous amino acid in the growing polypeptide chain; thus, this ribozyme, transfers the amino acid from the tRNA to the growing polypeptide chain. 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.

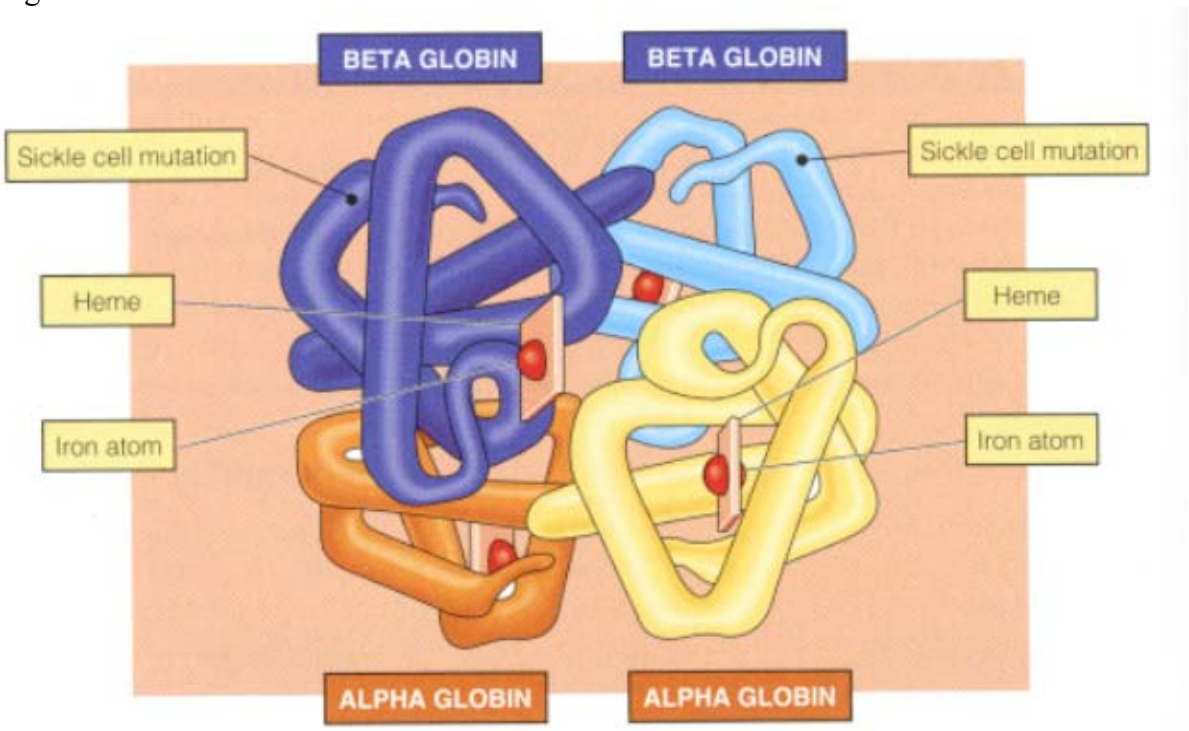
There are 40-45 different types of tRNA, with some types of tRNA able to match with two different codons that have the same first two nucleotides but differ in the third nucleotide (both are codons for the same amino acid). Some students have difficulty understanding the function of the tRNA molecule. An analogy that may help them understand is as follows. Suppose a group of American

[4] A simulation of this enzyme in action is available at http://www.phschool.com/science/biology_place/biocoach/translation/addaa.html

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 which position in the growing protein molecule, and the cook is equivalent to the cytoplasm which provides the 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 section of the activity discusses transcription and translation of the beginning of the gene for the beta globin polypeptides in the hemoglobin tetramer protein and ignores the gene for the alpha globin polypeptides. 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.



This section of the activity summarizes the effects of homozygous sickle cell alleles, resulting in sickle cell anemia. Even in a person who has severe sickle cell anemia, most red blood cells are not sickled most of the time. Variation in the degree of clumping of sickle cell hemoglobin into rods, 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 an infection that induces vomiting and diarrhea which can result in dehydration; dehydration increases the concentration of hemoglobin 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, for athletes with sickle cell trait, 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.

In discussing question 26, you may want to point out that our bodies are made up of roughly 100,000 different types of proteins and each protein is made up of hundreds or thousands of amino acids, so there is a great deal of opportunity for variation in genes, proteins and characteristics. In addition, there are inherited differences in the regulation of the amount of expression of various genes, and this is another important source of variation in human characteristics.

Evaluating Models

Thinking about and discussing their answers to question 27 will help students to understand that different types of models can serve different purposes. Discussion of question 27 also provides the opportunity to illustrate how models help us to understand complex phenomena by focusing on basic features of the phenomena and ignoring other complexities; however, the simplifications incorporated in models can also limit the accuracy of our understanding of complex biological phenomena. Answering this question should also help to reinforce basic biological principles students have learned in this activity.

The key does not include suggestions for how to improve the models, because we have already incorporated all the suggestions we could think of. Obviously, we anticipate that many or most students will not have suggestions for improvements in these models, but if you or your students do develop suggestions for improvements, please send them to iwaldron@sas.upenn.edu. Thank you!

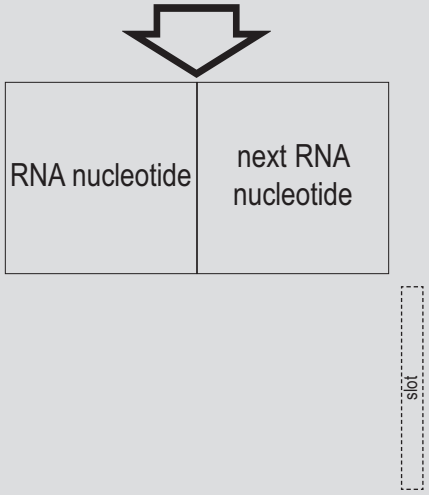
Related Activities

"Molecular Biology: Major Concepts and Learning Activities" (available at http://serendip.brynmawr.edu/exchange/bioactivities/MolBio) is an overview that reviews key concepts and learning activities. 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. Several potential follow-up activities are suggested, including ″The Molecular Biology of Mutations and Muscular Dystrophy″ (available at http://serendip.brynmawr.edu/exchange/bioactivities/mutation).

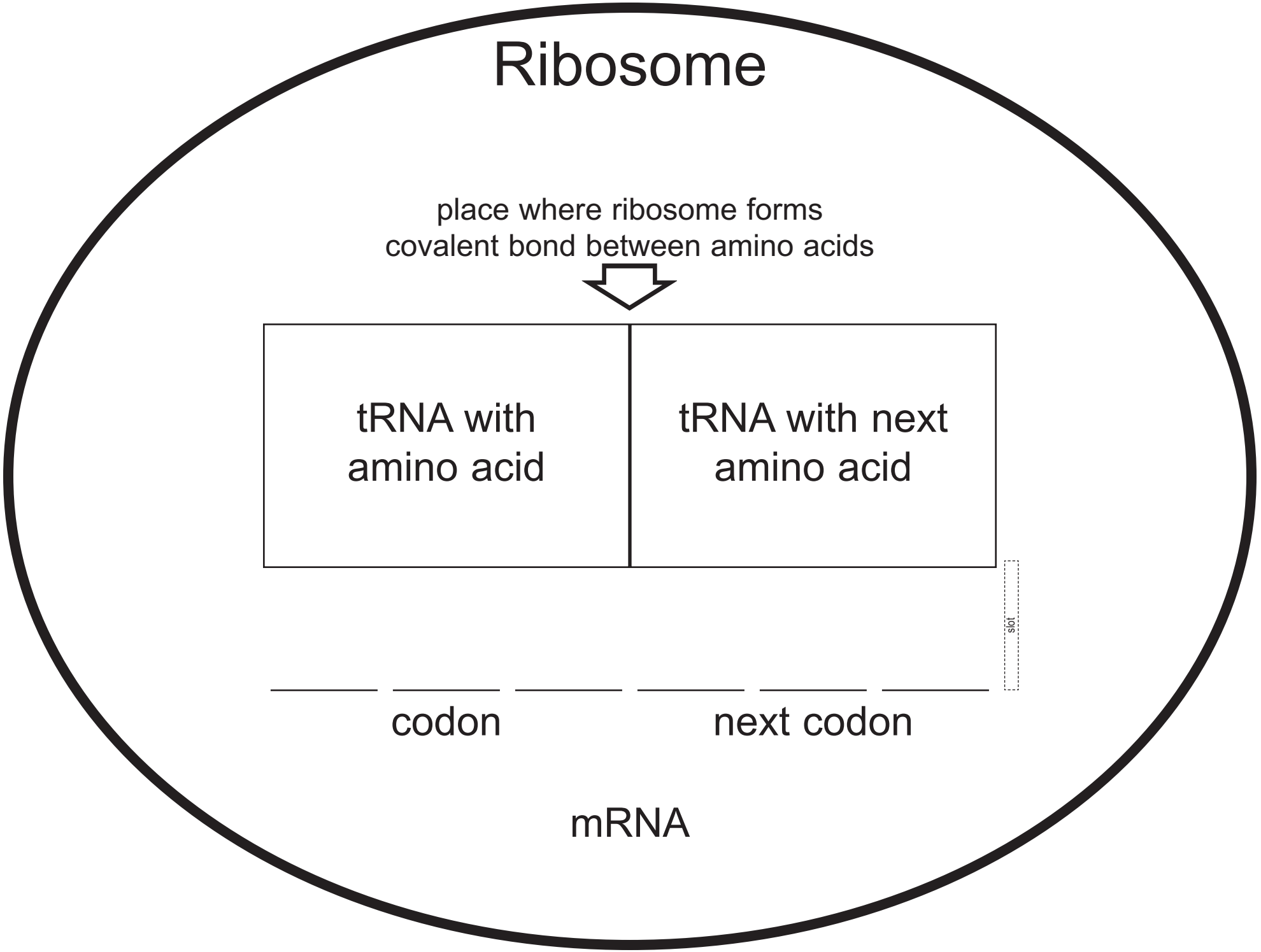
Nucleus

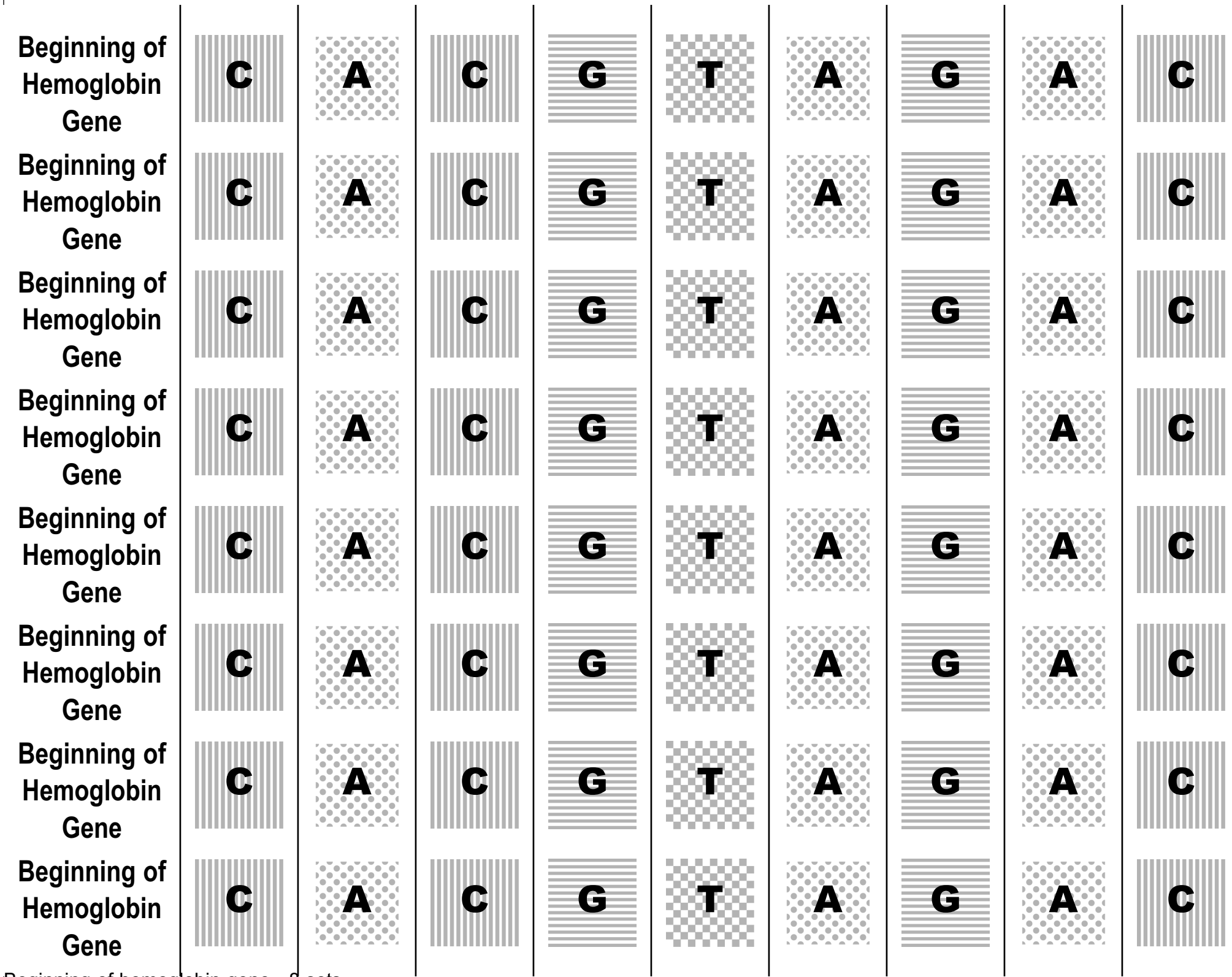
RNA polymerase

place where enzyme forms
covalent bond between nucleotides

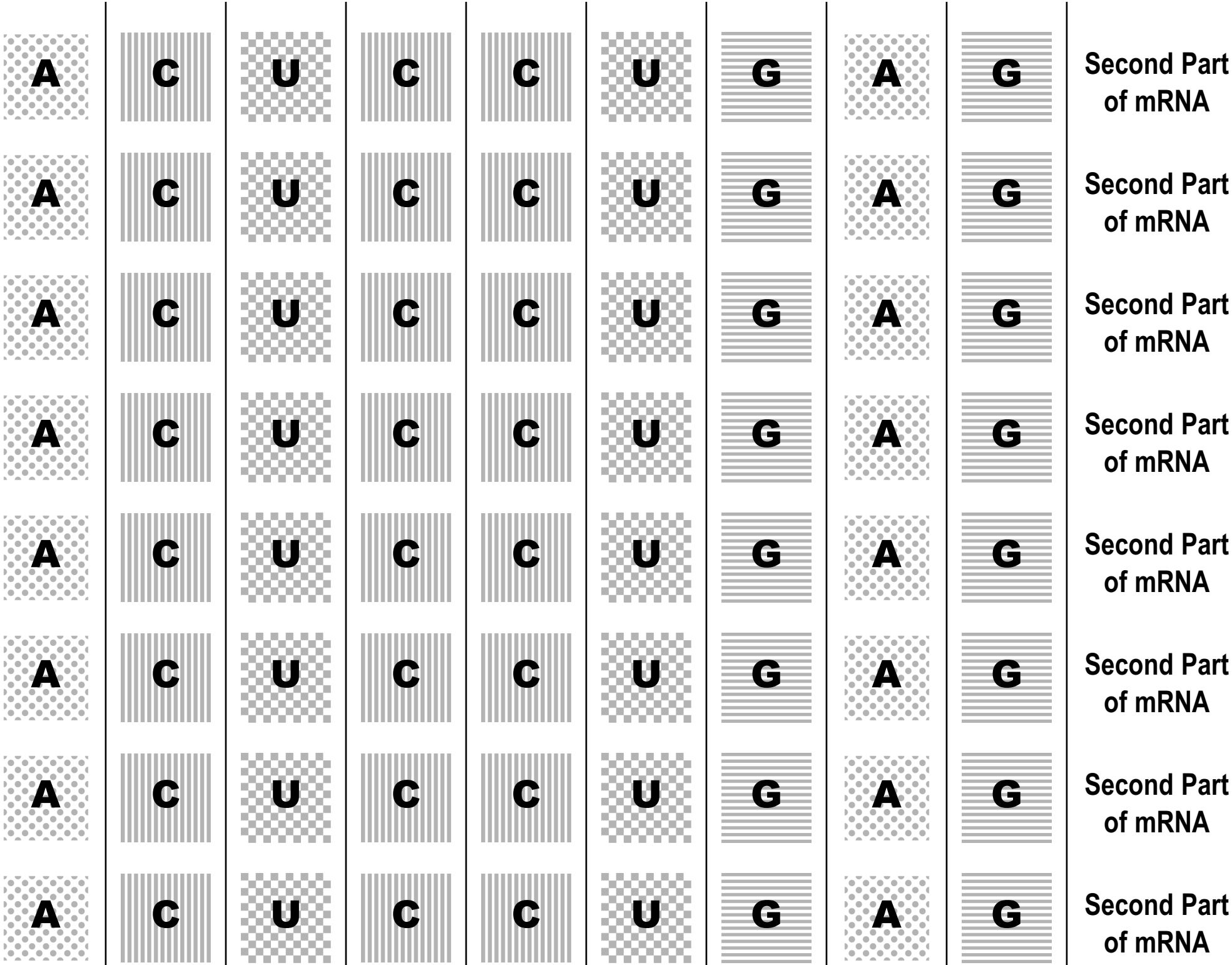


cytoplasm
around the nucleus

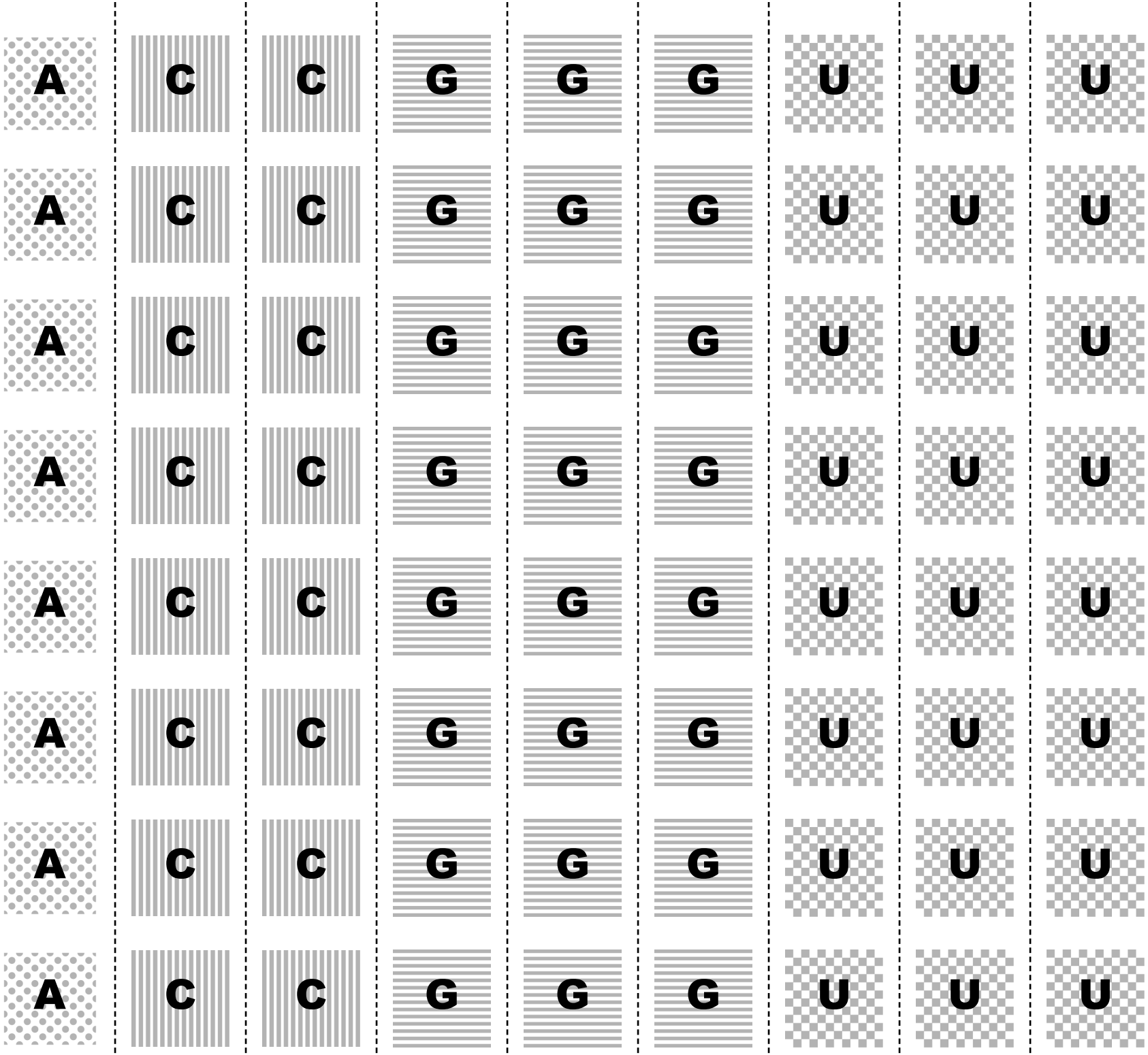

Ribosome
place where ribosome forms
covalent bond between amino acids
tRNA with
amino acid
tRNA with next
amino acid
slot
codon
next codon
mRNA



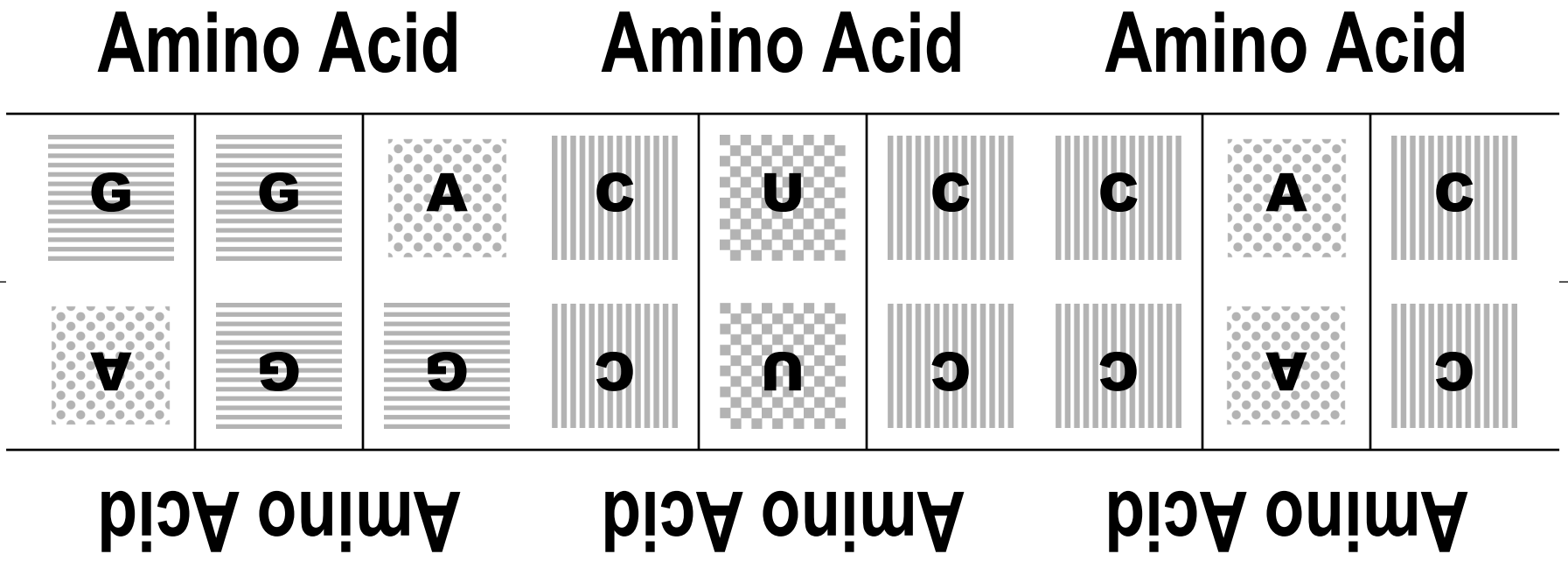
Beginning of hemoglobin gene - 8 sets

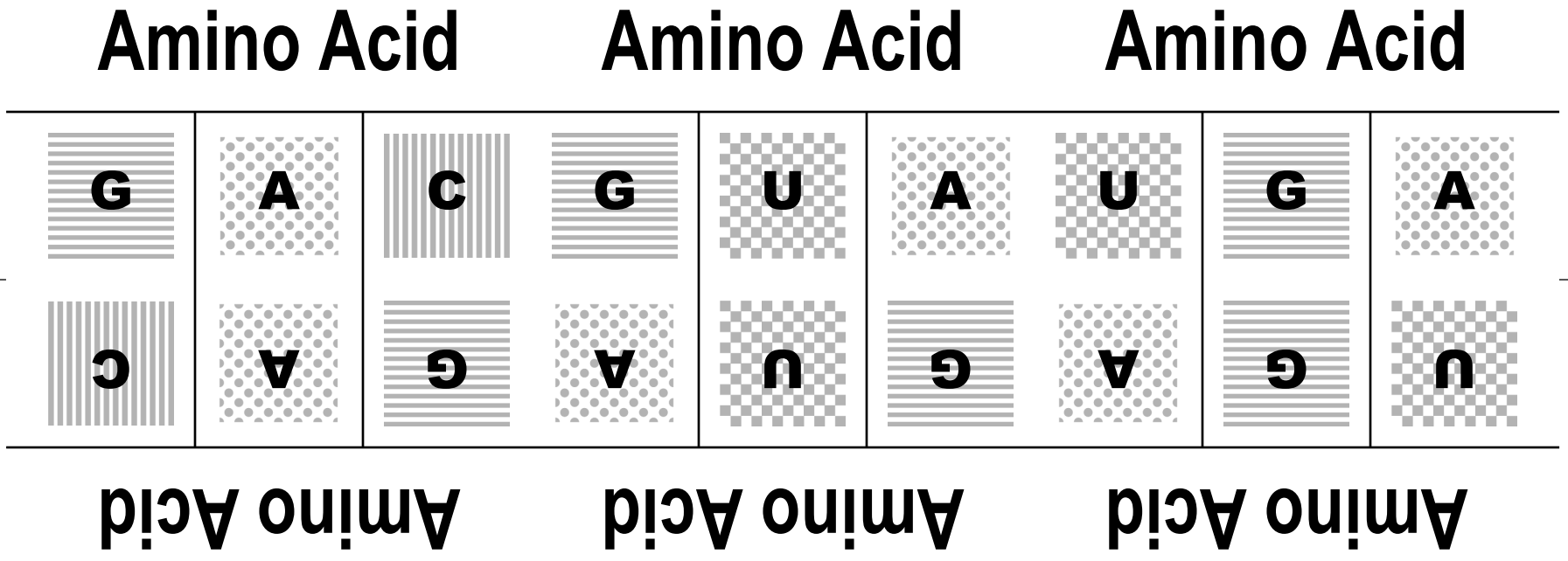


Second Part of mRNA - 8 sets



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