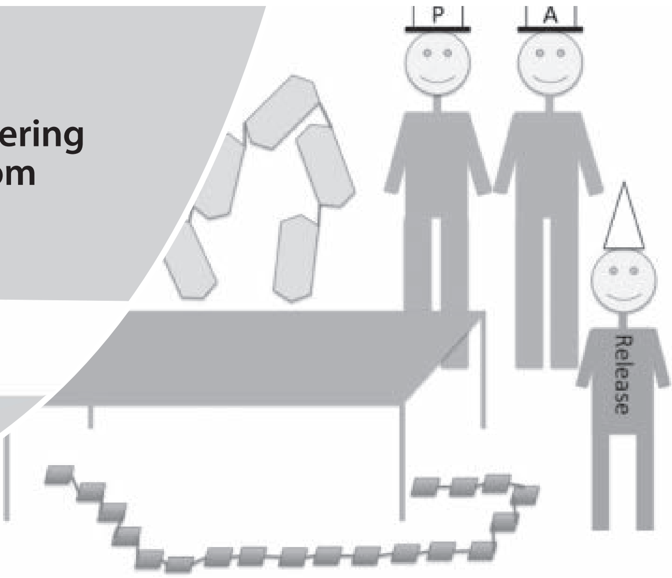
INQUIRY & INVESTIGATION

Time to Translate: Deciphering the Codon in the Classroom



RECOMMENDED FOR *AP Biology*

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Abstract

I describe and evaluate a fun and simple role-playing exercise that allows students to actively work through the process of translation. This exercise can easily be completed during a 50-minute class period, with time to review the steps and contemplate complications such as the effects of various types of mutations.

Key Words: *Eukaryotic translation; role-playing; genetic code; codons; anticodons.*

○ Introduction

Most students in introductory biology classes have difficulty visualizing complex subcellular processes (Chinnici et al., 2004; Nelson & Goetze, 2004). Although introductory textbooks provide beautiful diagrams showing the steps involved in translation as well as how the genetic code works, a review of these diagrams is just the beginning in my classroom. Through the role-playing exercise described here, students will read the genetic code, see the various characters involved in the process of translation, hear a description of the steps involved, and physically participate in deciphering the codons and carrying out the process to "translate" an mRNA to make a polypeptide. As suggested by Chinnici et al. (2004), this combination enhances learning.

Techniques that require active participation, whether through hands-on exercises with models (e.g., Templin & Fetters, 2002; Nelson & Goetze, 2004; Stavroulakis, 2005) or through role playing (e.g., Chinnici et al., 2004; Firooznia, 2007), help students visualize and better understand abstract concepts such as subcellular processes. In my introductory courses, I use various role-playing exercises to help students visualize more abstract topics, such as biochemical processes inside a cell, in a manner that is easier for most students to understand. In the exercise described here, students act as the ribosome and tRNA molecules to translate the codons of an mRNA to synthesize the corresponding polypeptide. This exercise can lead to improved understanding of the translation process, as shown through student responses to exam questions.

> *Most students in introductory biology classes have difficulty visualizing complex subcellular processes.*

○ Learning Objectives

To be able to explain:

- The three major steps of the translation process
- The significance and role of tRNA molecules
- The importance of codons and anticodons
- Hydrogen bonding between codons and anticodons
- The redundancy and unambiguity of the genetic code
- The point of the A and P sites in the ribosome
- The role of the release factor
- The relationship between the mRNA and the final polypeptide

○ Materials Required

- Party hats
- Posterboard
- Safety pins
- Pipe cleaners
- Scissors
- Stapler
- Velcro
- String

This exercise requires the willingness of the students to participate, and a few simple arts-and-crafts and party supplies (Table 1). Posterboard material is used to make the units that represent amino acids, as well as the nucleotides for the codons and anticodons cut into different shapes (see Figures 1 and 2). The nucleotides in the codons in the mRNA are attached together

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Table 1. Cast of characters.

Role	Actors or Props
The small ribosomal subunit	A table, or two chairs set side-by-side
The mRNA molecule (size depends on class size)	Nucleotides made of poster board joined together with safety pins, includes a cap and a poly-A tail
The A and P sites acting as the large ribosomal subunit	Two students with appropriately labeled party hats, A and P, together forming the large ribosomal subunit and designating the A and P sites in the ribosome
Individual tRNA molecules	Multiple students (based on class size) wearing an anticodon tied around their waist with string, and carrying the corresponding amino acids on their party hats
The release factor	1 student

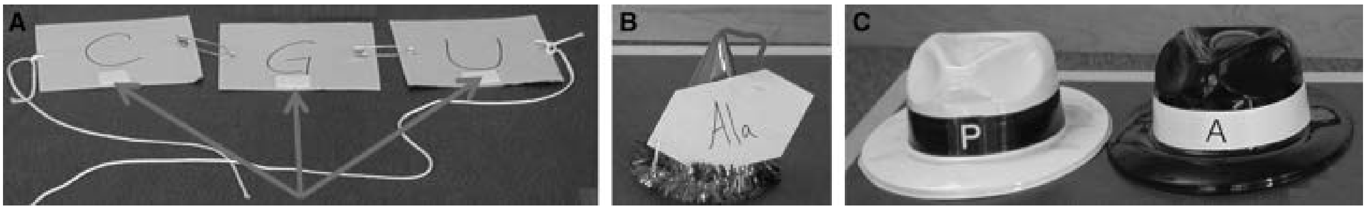

Figure 1. Symbols used in the exercise. (A) Sample tRNA anticodon (to be tied around the waist of the tRNAs), (B) corresponding amino acid (attached to a party hat for the tRNA), and (C) hats to designate A and P sites of the large ribosomal subunit. Arrows point to Velcro (white squares) on the nucleotides to be used for "hydrogen" bonding. Also note safety pins used for covalent bonds.

Figure 2. Part of the model mRNA attached to the small ribosomal subunit (the table). Poly-A tail and 5′ cap are not on the table. Arrows point to the Velcro (small white squares) on the nucleotides to be used for "hydrogen" bonding. The start codon is the first codon on the left.

by safety pins that represent covalent bonds, as are those in the anticodons for each tRNA. The nucleotides have Velcro on them to allow the anticodons to hydrogen-bond to the corresponding codons at the appropriate moment. If desired, the number of Velcro pieces could be set to match the number of hydrogen bonds for the A:U pair (2) versus the C:G pair (3). The student tRNAs wear the anticodons around their waists and will sit on the corresponding codon when the time comes. Party hats with pipe cleaners attached to them are used for the student tRNA molecules to carry their designated amino acids (Figure 1B). Other party hats with "A" (aminoacyl-tRNA) and "P" (peptidyl-tRNA) site labels (Figure 1C) are worn by two students to designate these sites in the ribosome. These two students together form the large ribosomal subunit. Either a standard table or two chairs put side-by-side can be used to act as the small subunit of the ribosome on which the mRNA lies (Figure 2). The length of the mRNA and the number of tRNAs involved can be modified according to class size. For example, to make a polypeptide with five amino acids, there will need to be an mRNA with five codons, two students as the large ribosomal subunit (designating the A and P sites), one student as the release factor, and five students as tRNAs.

○ The Activity

As we perform this activity in the class, the following events are acted out.

Initiation (Figure 3A)

1. The mRNA with its poly-A tail and cap is laid on the small ribosomal subunit (Figure 2).
2. The student acting as the initiator tRNA with the corresponding anticodon (worn around the waist) "attaches" to the start codon of the mRNA by sitting on the 5′AUG3′ sequence of the mRNA. The Velcro of the anticodon "hydrogen" bonds to that of the codon. The initiator tRNA carries methionine as the amino acid attached to its party hat.
3. This leads to the assembly of the ribosome as the large ribosomal subunit (the two students wearing the hats with the letters for the A and P sites) attaches to the mRNA–small subunit complex. The A- and P-site students stand behind the table or

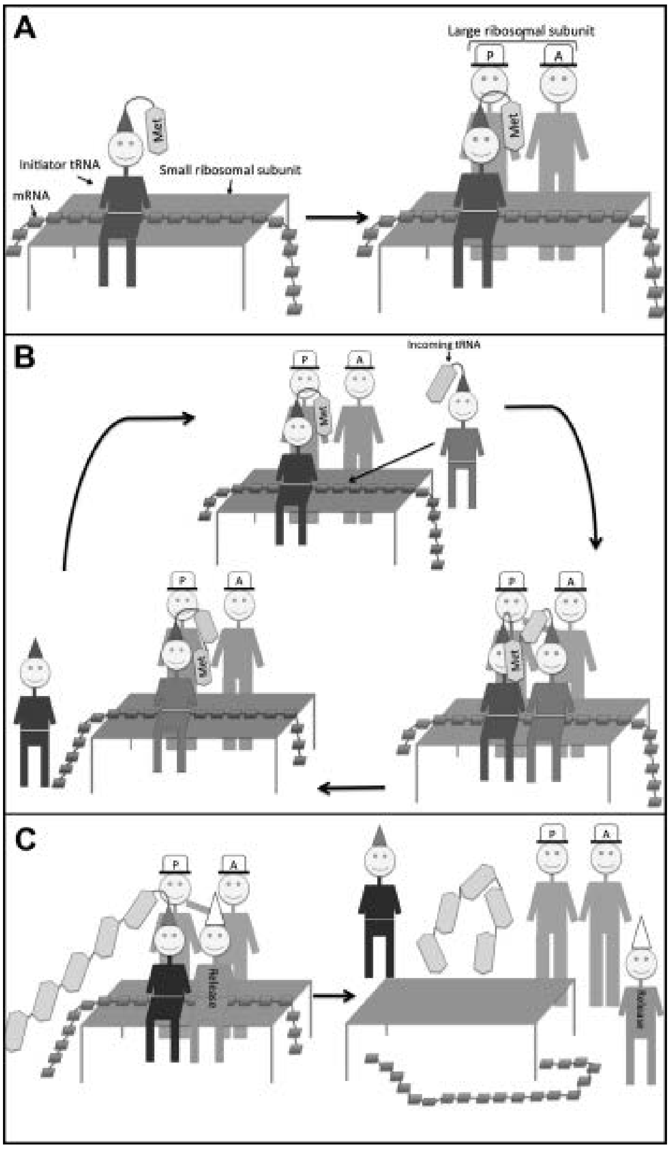

Figure 3. How the cast of characters is arranged during the three stages of eukaryotic translation: (A) initiation, (B) elongation, and (C) termination.

chairs representing the small ribosomal subunit and arch over the small subunit and the attached mRNA, with the initiator tRNA now clearly in the P site.

Elongation (Figure 3B)

1. The next tRNA with its anticodon complementing the codon of the mRNA in the A site enters the complex and sits on the mRNA codon on the table/chair under the "A" label. It has the appropriate amino acid on its party hat. The two students representing the large subunit attach the amino acid of this tRNA to the methionine of the initiator tRNA, using a safety pin to represent the covalent peptide bond forming between the two.
2. The students representing the large subunit now use a pair of scissors to cut the pipe cleaner that attaches the methionine to the party hat of the initiator tRNA student. The initiator tRNA is now released. The student representing the initiator tRNA, now without the methionine, gets up from the mRNA and leaves the ribosome assembly.
3. As the student tRNA in the A site slides over to the P site, the mRNA is carried over by one codon. This happens because of the Velcro acting as hydrogen bonds between the anticodon and codon.
4. The next student tRNA whose anticodon complements the new codon in the A site now enters the ribosome, bringing the next amino acid attached to the party hat that he or she is wearing.
5. The students representing the large subunit attach the new amino acid to the growing polypeptide using a safety pin and release the student tRNA in the P site by cutting the pipe cleaner attached to the amino acid attached to that student's party hat. The student tRNA in the P site then leaves the ribosome assembly. The growing polypeptide has been transferred from the first student tRNA to the second student tRNA.
6. The student tRNA in the A site now slides over, and the process continues until a stop codon is read in the A site.

Termination (Figure 3C)

1. There is a stop codon in the A site. There is no corresponding tRNA for this codon. At this point, the student acting as the release factor enters the A site. The students representing the large subunit and the release factor cut the growing polypeptide from the party hat of the last student tRNA in the P site by cutting the pipe cleaner that is the link between the hat and the joined amino acids, and release the polypeptide. To demonstrate that this reaction requires water, one could use a squirt or spray bottle in this step.
2. The last student tRNA leaves the P site. The ribosome disassembles.

Depending on the level of complexity desired in the class, the large ribosomal subunit could include a third student acting as the E site.

○ Review

Mid-activity Review

As we go through the activity, we review the following:

- What is accomplished in each of the three major steps of translation?
- What does each tRNA do?
- What are the A and P sites?
- How are the mRNA codons "read"?
- What is the role of the release factor?

Post-activity Review

Following the activity, we review the following:

- What happens if there is a mutation in one of the codons?
- What happens if an amino acid is missing in our diet?

Table 2. Comparison of student performance with different levels of participation in the activity on the two types of assessment questions used on the final exam.

Trial	Summer 2011			Fall 2011		
Total number of students	44			222		
Student group	A	P	N	A	P	N
Sample size	14	8	22	31	37	153
Type 1 question mean score ± SE (%)	80.7 ± 7.9	93.8 ± 4.2	72.1 ± 6.9	48.4 ± 5.1	38.4 ± 4.6	39.7 ± 2.4
Type 2 question mean score ± SE (%)	54.2 ± 8.0	42.5 ± 11.8	26.2 ± 6.7	54.0 ± 5.3	41.8 ± 5.3	45.4 ± 2.8
Trial	**Summer 2013**			**Fall 2013**		
Total number of students	69			230		
Student group	A	P	N	A	P	N
Sample size	16	17	36	70	63	97
Type 1 question mean score ± SE (%)	85.9 ± 6.8	74.0 ± 7.8	82.4 ± 4.8	80.8 ± 3.5	65.9 ± 4.4	74.3 ± 3.4
Type 2 question mean score ± SE (%)	53.9 ± 8.1	39.7 ± 4.7	35.1 ± 5.2	45.4 ± 3.4	35.4 ± 3.7	30.6 ± 3.0

Notes: N = none: students in lab sections in which the exercise was not used. P = passive: students in lab sections in which the exercise was used; the students observed the exercise. A = active: students in lab sections in which the exercise was used; each student acted as one of the characters.

○ Evaluation

The performance of the students who had learned about the process of translation through the standard methods of review with textbook diagrams and animations was compared with that of students who had been additionally exposed to this activity during four separate trials in the introductory biology course (Bio 10100) at The City College of New York, according to the guidelines by the Institutional Review Board. This introductory course is taught in a large lecture class with multiple laboratory sections, each with a maximum of 20 students. Regardless of the size of the class, all students in each trial attended the same large lecture class during which they learned about the process of translation through the standard methods of review with textbook diagrams. During each trial, the students in some lab sections were exposed to the activity described above while the students in other lab sections were not (control groups). The sample sizes are reported in Table 2. In fall 2011, because of scheduling conflicts, I was able to perform the exercise described above with the students in less than a third of the lab sections; thus, there are much larger differences in sample sizes among student groups for this trial. The activity was performed during a segment of the lab when the students were running a gel and there was free time in the lab to do something else.

The performance of students on two types of questions that dealt with the process of translation was compared. The two types of questions used were the following:

1. The nucleotide sequence of a DNA piece being transcribed is provided (sample below).

   5′… TTTCACCCCCT TT TCATCCGATA…3′

   3′…AAAGTGGGGGAAAAGTAGGCTAT…5′

   A messenger RNA molecule with complementary codons is transcribed from the template strand of this piece of DNA.

   a. Which strand, the top or the bottom, is the template strand?

   b. What is the nucleotide sequence of the mRNA corresponding to the coding sequence from start to stop?

   c. Label the 3′ and 5′ ends on the mRNA sequence you wrote in response to question b.

   d. Write the amino acid sequence of the polypeptide that would be produced from this mRNA if the ribosome starts translating from the start codon and stops at the stop codon.

2. Review the diagrams provided (taken from a standard textbook; show the three steps of translation). In your own words, describe the steps involved in eukaryotic translation: initiation, elongation, and termination.

These questions constituted ~20% of the final exam. The final exam includes ~20 questions that are a mixture of short-answer, essay, problem-solving, and multiple-choice questions. The final exam is not cumulative and focuses on the topics for the last quarter of the term. Transcription and translation are usually the second-to-last topic studied each term. However, in fall 2011, the class was behind schedule and transcription and translation were the last topic of the semester. The grades the students received for the questions were standardized to percentages for each question. The mean scores are presented in Table 2.

To determine whether participation level had any significant effect on student performance, the data were analyzed with a general linear model, using the statistical software MINITAB

(Minitab, State College, PA) with the final course grade as a covariate. The comparison was made among students who were not exposed to this exercise (student group = none), those who were active participants in the exercise (student group = active), and those who were passive participants and observed the exercise (student group = passive). If a significant effect was observed, pairwise comparisons were made using the Tukey-Kramer procedure. Gender and the number of semesters completed (including the semester during which the course was taken) were included as random factors in the analysis. The number of semesters completed ranged from 1 to >10 for current undergraduates, and there were several postbaccalaureate students. Neither gender nor number of semesters completed had any significant effect on the performance of the students in any trial for either question type ($P > 0.05$ for all).

Table 2 shows the mean scores for the two types of questions for students in all four trials. There were no significant differences among the students with different levels of participation in their performance on the first type of assessment questions during any of the four trials ($P > 0.05$ for all).

In both of the summer trials and in fall 2013, the mean scores for type 1 questions were very high, regardless of the level of participation in the exercise. Fall 2011 seems to be an outlier. The exercise does not include transcription, and part of the type 1 question is predicting the mRNA sequence, given a DNA sequence. However, reading the mRNA, finding the start and stop codons, and translating the mRNA codons are related to the exercise. It seems that students understand and can apply the concepts in type 1 questions rather easily. A possible explanation of the lower scores for type 1 questions in fall 2011 is that the class was behind schedule and that transcription and translation were the last topic studied during fall 2011. Perhaps there was not enough time before the final exam for the students to process the information or to practice how to predict mRNA sequences and the corresponding amino acids, given a DNA sequence.

The level of participation made a significant difference in the student responses to the type 2 questions in both summers and in fall 2013 ($P < 0.05$ for all). Pairwise comparisons for the data from these three trials show that the students who were active participants in the exercise performed significantly better than those who were in the lab sections that did not use this exercise ($P < 0.05$ for all three trials). The differences between the scores of the students who were passive participants and those of the other two groups of students are not statistically significant for the summer trials. However, in fall 2013, there was a statistically significant difference between the scores of the students who were passive participants and those in the lab sections that did not use this exercise ($p = 0.0167$), but not between passive and active participants. Because there are no statistically significant differences in performance between the active and passive participants, and because the passive participants performed significantly better than those not using this exercise in fall 2013, this suggests that observing the exercise seems to help the students understand the process and put it in their own words. It would be possible to either carry out the activity in small settings so that every student is an active participant, thus reaping the benefits of active participation, or redesign the activity so that small groups of students in the class perform the activity simultaneously, thus having every student actively participate in the activity. The lack of statistically significant differences among the scores for the three groups of students in fall 2011 is unexpected. The large difference in sample size for the three groups in this trial (Table 2) may be an important factor.

One interesting question that arose from this study is why the scores for type 2 questions are so low to begin with and why this in-class activity helps with improving performance in answering type 2 questions. The City College of New York (CCNY), the flagship college of The City University of New York, is an urban public university serving underrepresented minorities. The CCNY student demographics for fall 2013 were as follows: 51% female, 49% male; 30.9% Hispanic, 19.3% Black, 24.1 Asian/Pacific Islander, 18.4% White, 0.1% American Indian, 7.4% nonresident alien; 52% first in their family to attend college; 52% with less than $30,000 annual household income; 62.9% full-time, 37.1% part-time; and mean SAT verbal score 536. The majority of our students are graduates of low-performing public high schools in New York City. Additionally, many of our students are recent immigrants whose native language is not English. Thus, it is not surprising that writing about a subcellular process in their own words is a challenge for many of our students.

○ Conclusions

One of my goals in using such activities is to help students better visualize the subcellular processes and to move the students away from the conception of subcellular biology as being difficult. Students generally have positive reactions to such interactive exercises and consider them an indication of my enthusiasm for biology, despite their original hesitation to don the party hats and act as various macromolecules. I have found this activity, together with a review of the process, to be a helpful strategy to engage students in the learning process and to impress upon them the importance of the genetic code and the complementarity of the bases in the mRNA and tRNA. In addition, the significance of the redundancy of the genetic code, the effects of various types of mutations on the final polypeptide product, and the potential for damage due to mutations can easily be worked into this exercise. For example, there could be a mutation leading to the formation of a stop codon early in the mRNA sequence, and the translation process will come to an immediate halt, leaving many student tRNAs with nothing to do.

In conclusion, this is a simple, inexpensive, and creative way to involve students in learning about the important process of eukaryotic translation. This exercise can easily be implemented in both high school and introductory college biology courses and should make the learning of the translation process more fun and accessible to the average student. By adjusting the size of the mRNA and the number of tRNA molecules needed, all students in a small class can be active participants in the process. This in-class activity helps improve the ability of students to write in their own words what happens during the process of translation, a task that seems to be much more difficult than deciphering mRNA sequences and translating codons.

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