Activity: Decoding a molecular message

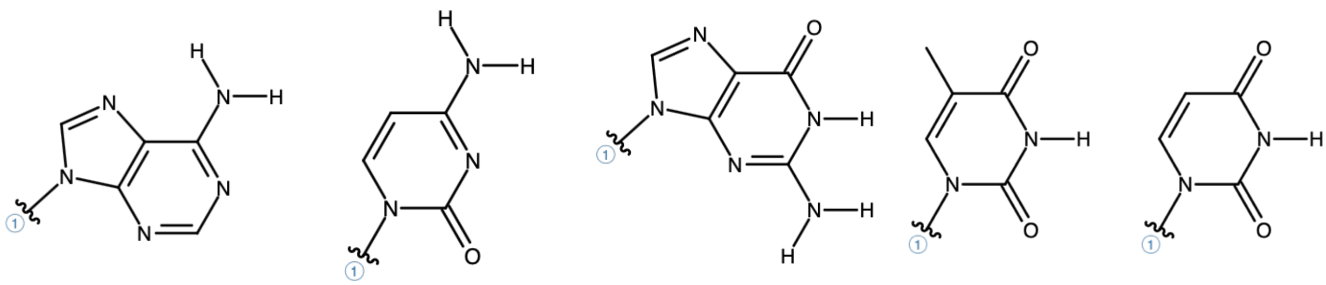
In this activity, you will identify complementary nucleobase pairs and model replication, transcription, and translation.

Background

Nucleic acid structure

Deoxyribonucleic acid, or **DNA,** is a biopolymer that stores genetic information. It is made of nucleotide units consisting of a nucleobase, a sugar (deoxyribose), and phosphate. Neighboring nucleotides within the polymer chain bond together by alternating phosphates and sugars. The nucleobases branch off this "backbone" and stick to nucleobases on a second backbone through hydrogen bonding. There are four canonical **nucleobases** in DNA: adenine (A), cytosine (C), guanine (G), and thymine (T). DNA in cells has two chains of nucleotides hydrogen-bonded to each other and is said to be "double stranded." The two strands twist around each other, forming the famous "double helix" structure.

Cells contain another nucleic acid polymer called ribonucleic acid, or **RNA**. RNA is also made of nucleotides, but the sugar is ribose instead of deoxyribose, and uracil (U) is used instead of thymine.



Adenine **C**ytosine **G**uanine **T**hymine **U**racil

Genetic code

DNA stores genetic information in the form of **codons**, triplets of nucleobases that correspond to specific **amino acids**. Some amino acids are encoded with a single three-base sequence (e.g., methionine), while other amino acids have as many as six codons (e.g., leucine). A few codons can also tell the cellular machinery to "start" or "stop" making proteins. The complement to a codon is called an **anticodon**.

Procedure

Part I: Match Nucleobase Pairs

1. Get a set of nucleobase cards. A complete set of 10 cards includes two copies of each of the 5 canonical nucleobases, one with the connection to the DNA/RNA backbone on the lower left, and the mirror image with the connection on the lower right. These mirror images are just two different views of the *exact same structure* to make pairing easier (in step 2).
2. Look at the structures of the nucleobases and use your knowledge of molecular shape, bond polarity, and hydrogen bonding to determine which "left side" nucleobases are most likely to form pairs with which "right side" nucleobases. Make at least one pair for each nucleobase.
3. Sketch the *unique* nucleobase pairings in your notebook (i.e., pair XY is the same as pair YX, but pair XZ is different; you'd sketch XZ and *either* XY or YX).
4. Draw dotted lines to show hydrogen bonding between atoms of "left side" nucleobases and "right side" nucleobases in each of your sketches.
5. Check your nucleobase pairs with your instructor. Revise your pairings and sketches as needed before moving on to Part II.

Part II: Model DNA Replication

1. Using your final pairings from Part I, copy the table below into your notebook and complete the empty rows. The "complement" is the other half of the nucleobase pair. Keep in mind that the DNA nucleobases are ACGT and the RNA nucleobases are ACGU.

Nucleobase	A	C	G	T	U
DNA complement					
RNA complement					

2. Get a DNA sequence strip from your instructor. Leave the center folded lengthwise for now, and (using the table from step 1) check that the row labeled "Template DNA" is the complement of the row labeled "Coding DNA." These two rows represent the two strands of DNA that form the famous double helix shape.

During DNA replication, specialized proteins called helicases "unzip" the two strands from each other. You will be the helicase.

3. Unzip the DNA by unfolding the length of the paper.
4. As DNA replicates, complementary nucleotides match up with each strand. You will replicate just one strand. In the row labeled "Replication," write the DNA complement for the nucleobase written above it in the "Coding DNA" row. (Refer to the table from step 1.)
5. If DNA replication is successful, the new strand should match the original complementary strand exactly. Check that your "Replication" row matches the "Template DNA" row.

Part III: Model DNA Transcription

During DNA transcription, specialized proteins "unzip" a segment of DNA and fit complementary RNA nucleotides (called "messenger RNA" or mRNA) into place. You will unzip and translate the entire sequence provided.

1. In the row labeled "mRNA," write the RNA complement for the nucleobase written below it in the "Template DNA" row. (Refer to the table from Part II step 1.)
2. If DNA translation is successful, the new RNA strand should match the original complement to the DNA strand, but with uracil (U) in place of thymine (T). Check that your "mRNA" row matches the "Coding DNA" row, with all T's replaced by U's.

Part IV: Model RNA Translation

During RNA translation, the mRNA produced by transcription is read by a molecular machine called a ribosome. The ribosome helps other RNA molecules (called "transfer RNA" or tRNA) find their complements on the mRNA strand. The tRNA molecules carry amino acids with them, which the ribosome covalently bonds together to make a protein chain. You will act as the ribosome.

1. Get a set of 64 tRNA cards from your instructor. Each card includes an anticodon and a 1-letter abbreviation for an amino acid.
2. Starting from the left, mark a vertical line every three bases. The areas between these vertical marks are the codons. For example, A A C|G U C|C C C has the codons AAC, GUC, and CCC.
3. Find the tRNA card with the RNA sequence that *complements* the first codon (*not* the card that matches the sequence). You are holding the tRNA card correctly if the letters are oriented the same way on the card as on the DNA sequence strip.
4. Write the 1-letter abbreviation for the amino acid on the tRNA card above the "mRNA" row on the DNA sequence strip. For example, the UUG tRNA card says N (for asparagine).
5. Read the next the next codon (nucleobases 4-6), find the tRNA card with the complement, and record the amino acids. Continue with this process with the remaining codons.
6. Read the entire amino acid sequence to find a hidden message. Record this message in your notebook. Note that there are 26 letters in the English alphabet but only 20 common amino acids, so some letters may be substituted, and some messages may use abbreviations.

Activity: Decoding a molecular message

Time required

- **Preparation:** about 1 hour the first time. Subsequent preparation is 5-10 minutes to make new DNA sequence strips.
- **Implementation:** about 1 hour

Safety

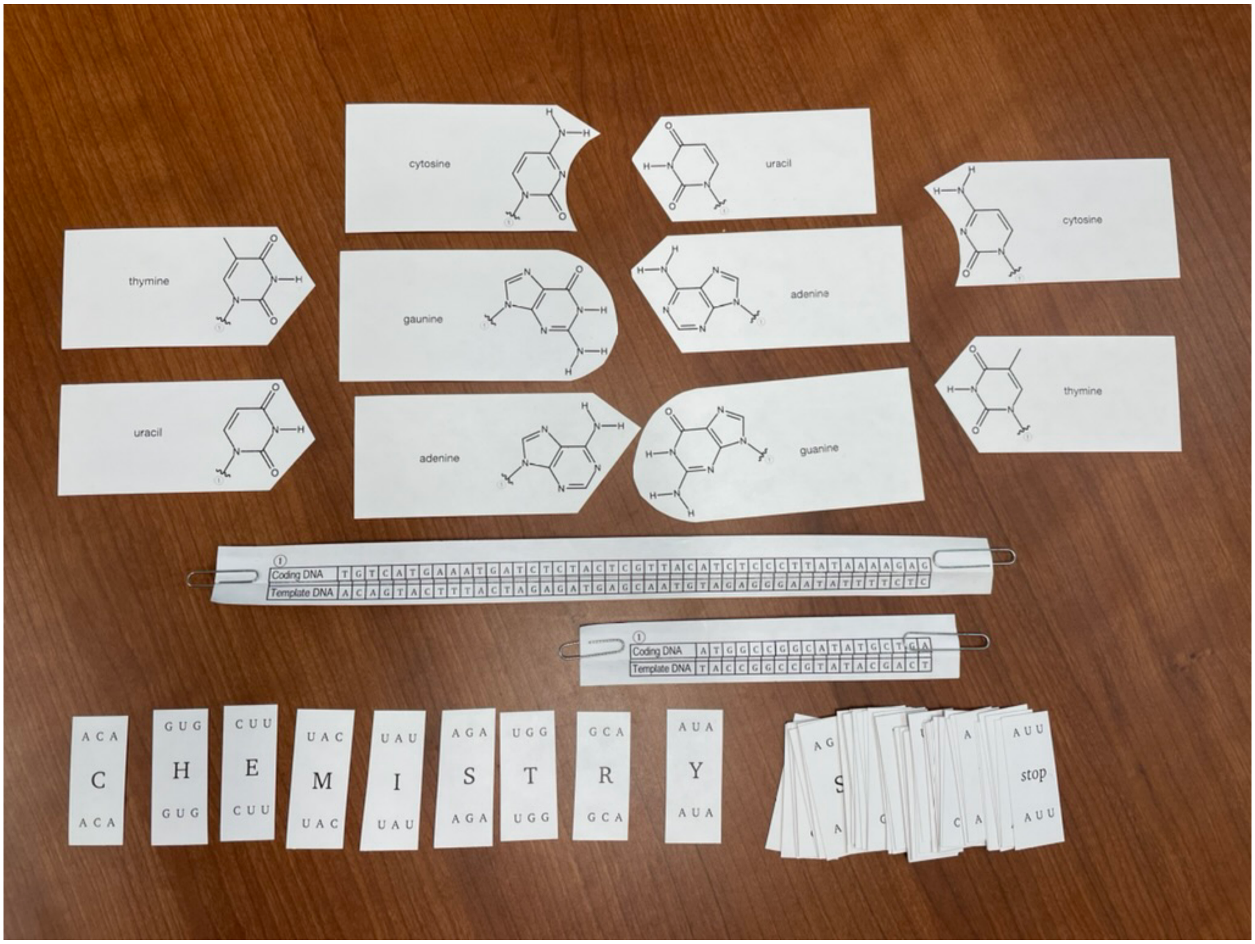
This activity does not require hazardous materials or equipment.

Materials & Equipment

- Supplemental files (nucleobase cards, tRNA cards, DNA sequence strips)
- Computer with printer
- Cardstock (letter size; max. 3 sheets per group)
- Printer paper (letter size; ½ sheet per group + 2 sheets per student)
- Tape
- Paper cutter (recommended)
- Scissors
- Sandwich bags or small boxes (1 per group)
- Sharpened pencil with working eraser (1 per group)
- Notebooks, note sheets, or whiteboards for recording observations (recommended)

Preparation

1. Print the nucleobase cards on cardstock, cut the page horizontally in five strips (1 strip per mirrored pair of nucleobases), and then cut the pairs apart, angling or curving around the shape of the molecular structure.
2. Print the DNA sequence strips on letter size printer paper (landscape orientation). Cut the strips apart with a paper cutter. Each numbered sequence strip has two segments: one long, and one short. Either instruct students to begin with the long strip or join the strips together: trim the right edge off of the long segment and tape it over the wide column of the short segment. Avoid taping over the empty squares.
3. Fold each DNA sequence strip in half lengthwise. Then fold back the top and bottom rows of the strip (Coding DNA and Template DNA) so that the DNA sequence strip can be set on a table with only the top and bottom rows visible.
4. Print the tRNA cards on cardstock (2 single-sided pages per set). Cut the cards apart with a paper cutter.
5. Assemble an activity kit for each group:
    - Nucleobase cards (set of 10)
    - 1 DNA sequence strip (or 1 long strip and 1 short strip)
    - tRNA cards (set of 64; could be shared between 2 groups, if needed)
    - 1 pencil (unless students provide their own)
    - 1 bag/box to hold materials



The components of an activity kit

Implementation

Split the class into small groups (3-5 students). Each group needs an activity kit, a copy of the student instructions, and a space to work together.

It helps to have a place for the students to sketch the nucleobase structures and their complements and generate a summary table of nucleobases (in Part I: Match Nucleobase Pairs). Lab notebooks, note sheets (see supplemental files), or even a small whiteboard can work, depending on your needs and resources.

You may want to check groups' tables of nucleobases at the end of Part I (Match Nucleobase Pairs) before allowing them to proceed to Part II (Model DNA Replication).

Activity Design Considerations and Limitations

Message length: A sequence of about 20 amino acids is long enough to convey a simple message without becoming too tedious to decode by hand. All of the DNA sequences in the provided Excel file contain 20 characters followed by a "stop" codon (63 base pairs).

Amino acid letters: There are 26 letters in the English language, but only 20 standard amino acids. O and U are used for less common amino acids whose codons are usually interpreted as stop codons. B, J, X, and Z are used as to indicate multiple possible amino acids in a particular position. The messages I have created use Q in place of O and V in place of U because they are visually similar. None of the included messages use B, J, X, or Z.

tRNA cards: The tRNA cards have the anticodons printed twice because it makes them a little easier to identify when spread on a table, and because students kept rotating the cards and matching the wrong anticodon (e.g. matching AUC with GAU instead of UAG). They can match the tRNA sequence on the top or bottom of the card so long as all the letters in the mRNA and tRNA sequences are oriented in the same direction.

Extension: Student-Generated Sequences

The activity could be extended further to have students generate and encode their own short messages for other groups to decipher.

In the Message Generator Excel file, change the font color of the DNA sequences to white or transparent before printing to get "empty" DNA sequence strips. Assemble them as before.

Each group can work in reverse (amino acids → tRNA → mRNA → template DNA → coding DNA) or use an inverse DNA codon table to skip from the amino acid symbols directly to an appropriate DNA sequence. (Note: Pick *just one* DNA sequence per amino acid.) They write their new sequence in the empty Coding DNA row for another group to decipher (coding DNA → template DNA → mRNA → tRNA → amino acid message).

Extension: Directionality

DNA and RNA polymerases work only in the 5′ to 3′ direction. You could label the strand ends, start midway through the sequence, and work from 5′ to 3′, mimicking Okazaki fragments during DNA replication. This concept was outside the scope of the class I was teaching and could create additional confusion, so I did not include it in the student instructions.

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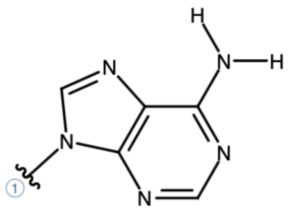
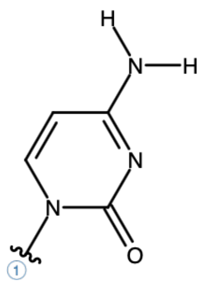
Part I: Match Nucleobase Pairs

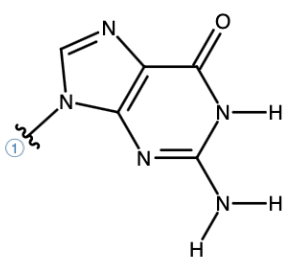
Sketch one complementary nucleobase for each of the nucleobases below. Then draw dotted lines to show hydrogen bonding between atoms on each pair of nucleobases.



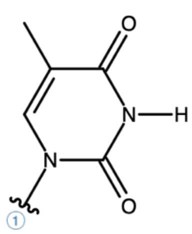
Adenine



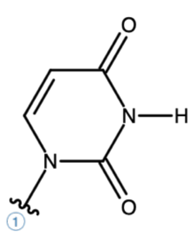
Cytosine



Guanine



Thymine



Uracil

Part II: Model DNA Replication

Using your final pairings from Part I complete the table below. The “complement” is the other half of the nucleobase pair. Keep in mind that the DNA nucleobases are ACGT and the RNA nucleobases are ACGU.

Nucleobase	A	C	G	T	U
DNA complement					
RNA complement					

Part IV: Model RNA Translation

What was your hidden message?

Note: There are 26 letters in the English alphabet but only 20 common amino acids, so some letters may be substituted, and some messages may use abbreviations.