Pipe Cleaner Protein Modeling C. Kohn, Waterford WI

Name: Hour Date:

Date Assignment is due: Why late? Score: + ✓ -
 Day of Week Date If your project was late, describe whyThe function of a protein is determined by its shape, and the shape of the protein is determined by its amino acids. Because proteins are smaller than microscopic, we would have a pretty hard time doing a hands-on lab on this topic. However, we can explore proteins in an indirect way through modeling.

Everything in science is done with models – the scientific method itself is about modeling complex ideas into simpler formats so that we can better understand them. Scientific models may also help us to do things that would otherwise be impossible. For example, there is no way that we could have sequenced the 6 billion bases in the human genome without prior experience with simpler organisms like nematodes with genomes smaller than our own.

A model is a substitute for the actual thing we are studying, but it is also similar to what it represents. It tends to follow the same rules as the actual object, and it provides us with a simpler idea of a more complex process so that we can better understand it.

In this case, you will be using pipe cleaners, beads, and cut up straws to model how proteins fold, and how mutations affect the shape of proteins. Each person will be responsible for completing their own sheet, normal protein, and mutated protein.

**There are 3 basic laws of protein folding:**

1. **Hydrophobicity** – hydrophobic (*water hating*) amino acids will always try to get to the inside of a protein.
	1. Because our bodies are mostly water, hydrophobic amino acids basically try to ‘hide’ in this kind of environment.
	2. On the other hand, hydrophilic (*water loving*) amino acids try to get further into the water because they love it so much – they’re kind of like the 7-year-old version of yourself when you stayed at a hotel with a pool – you wanted to be in the water and moved towards it.
		1. Hydrophilic amino acids will try to move as far away from the center of the protein as they can.
2. **Charge** – amino acids can have one of three charges – positive, negative, or neutral
	1. Like opposite sides of a magnet, positively and negatively charged amino acids try to move toward each other
	2. Like the same pole of a magnet, amino acids with similar charges (positive and positive, or negative and negative) will try to move as far apart from each other as they can.
	3. Neutral amino acids remain largely unaffected
3. **Cysteine** **Bonds** – cysteine amino acids are sort of the like obnoxious couple in the lunch line – they just can’t bear to be apart! Cysteine amino acid pairs will move toward each other and form solid bonds whenever they can.

**To represent this, we will use colored beads. Read the hints and tips below before getting started.**

1. Hydrophobicity – yellow beads will represent hydrophobic amino acids; purple beads will represent hydrophilic amino acids. As such, all yellow beads should be as far inside the protein as they can, and purple beads should be on the outside whenever possible.
2. Charge – blue beads will be a positive charge and red beads will be the negatively charged amino acids (we won’t bother with neutral amino acids). Red and blue beads near each other should form a bond (if they can); similarly colored blues or reds should be as far apart as possible.
3. Cysteine bonds – we’ll use green to represent the amino acids cysteine; green beads should form pairs whenever they can.
4. Some amino acids may have multiple beads! For example, Arginine is both positively charged (blue) and hydrophilic (yellow). As such, you would use both a blue and yellow bead together to represent this amino acid.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity**  |  | **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity**  |
| Alanine | Ala | A | Neutral | Hydrophobic  |  | Leucine | Leu | L | Neutral | Hydrophobic  |
| Arginine | Arg | R | **Positive** | *Hydrophilic* |  | Lysine | Lys | K | **Positive** | *Hydrophilic* |
| Asparagine | Asn | N | Neutral | *Hydrophilic* |  | Methionine | Met | M | Neutral | Hydrophobic  |
| Aspartic acid | Asp | D | **Negative** | *Hydrophilic* |  | Phenylalanine | Phe | F | Neutral | Hydrophobic  |
| Cysteine | Cys | C | Neutral | *Hydrophilic (G)* |  | Proline | Pro | P | Neutral | Hydrophobic  |
| Glutamine | Glu | Q | **Positive** | *Hydrophilic* |  | Serine | Ser | S | Neutral | *Hydrophilic* |
| Glutamic acid | Gln | E | **Negative** | *Hydrophilic* |  | Threonine | Thr | T | Neutral | *Hydrophilic* |
| Glycine | Gly | G | Neutral | Hydrophobic  |  | Tryptophan | Trp | W | Neutral | Hydrophobic  |
| Histidine | His | H | **Positive** | *Hydrophilic* |  | Tyrosine | Tyr | Y | Neutral | Hydrophobic  |
| Isoleucine | Ile | I | Neutral | Hydrophobic  |  | Valine | Val | V | Neutral | Hydrophobic  |

1. Be sure to have a cut up straw in between each amino acid so that you know where one ends and the next begins! You may need multiple pipe cleaners to fit all of your amino acids!
2. You will begin by creating the mRNA strand of a gene (transcription). Remember that for every…
	1. G in DNA you would add a C in mRNA
	2. C in DNA you would add a G in mRNA
	3. T in DNA you would add a A in mRNA
	4. A in DNA you would add a U in mRNA
	5. 5’ in DNA, you would add a 3’ in mRNA, and vice versa
3. From your mRNA strand, you will need to create codons; remember that a codon is a group of 3 bases that codes for a specific amino acid. Your codons are read in the 5’ 🡪 3’ direction (hint: it might be right to left!).
4. You will then need to convert your codons into amino acids in the 5’ 🡪 3’ direction (translation).
5. Once you have your order of amino acids, you will need to find your respective beads and assemble them onto a pipe cleaner. Again, be sure to separate each bead by a cut up straw! (TERM is not an amino acid but a command; it will not have a bead). NOTE: some amino acids have two beads! (e.g. Arg is blue AND purple!).
6. Finally, you will need to fold your protein. Start by moving your purple to the outside and your yellow to the inside. Then connect your opposite charges and cysteine amino acids (wrap them around each other using the pipe cleaner). Your finished protein should have an ‘outer shell’ of hydrophilic and charged amino acids with an inner center of hydrophobic amino acids.
7. When you are done, you will also have to create a second protein from the same gene which has been mutated.

DNA Strand (the second side of this strand has been omitted for easier reading)

3’ TAC-TTA-CGA-TGG-TAC-ACG-CAA-TCT-ATA-CTC-AAA-TAT-AGG-ACC-TTG-ACG-TCG-AAT-CTC-CAC-TGT-ACC-TTG-AAC-CTG-ACT 5’

mRNA Strand (written in codons):

5’-AUG-AAU-

Amino Acid Sequence (*Hint: it may help to write the color of the bead above each amino acid or highlight with markers).*

MET-ASN-

Now create your protein using the chart below

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity**  |  | **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity**  |
| Alanine | Ala | A | Neutral | Hydrophobic  |  | Leucine | Leu | L | Neutral | Hydrophobic  |
| Arginine | Arg | R | **Positive** | *Hydrophilic* |  | Lysine | Lys | K | **Positive** | *Hydrophilic* |
| Asparagine | Asn | N | Neutral | *Hydrophilic* |  | Methionine | Met | M | Neutral | Hydrophobic  |
| Aspartic acid | Asp | D | **Negative** | *Hydrophilic* |  | Phenylalanine | Phe | F | Neutral | Hydrophobic  |
| Cysteine | Cys | C | Neutral | *Hydrophilic* |  | Proline | Pro | P | Neutral | Hydrophobic  |
| Glutamine | Glu | Q | Positive | *Hydrophilic* |  | Serine | Ser | S | Neutral | *Hydrophilic* |
| Glutamic acid | Gln | E | **Negative** | *Hydrophilic* |  | Threonine | Thr | T | Neutral | *Hydrophilic* |
| Glycine | Gly | G | Neutral | Hydrophobic  |  | Tryptophan | Trp | W | Neutral | Hydrophobic  |
| Histidine | His | H | **Positive** | *Hydrophilic* |  | Tyrosine | Tyr | Y | Neutral | Hydrophobic  |
| Isoleucine | Ile | I | Neutral | Hydrophobic  |  | Valine | Val | V | Neutral | Hydrophobic  |

Once you have finished your protein, compare yours with another student’s protein. They should look similar. If your protein has 2 green cysteines, three positive blue amino acid beads, and one negative red amino acid bead, your protein is probably correct. The DNA strand below shows a deletion frameshift mutation. The mutated mRNA strand is completed for you. Complete the amino acid sequence for the mutated mRNA and then create the mutated protein. Pay special attention to how the elimination of a single base changes the entire strand.

 Original DNA

3’ TAC-TTA-CGA-TGG-TAC-ACG-CAA-TCT-ATA-CTC-AAA-TAT-AGG-ACC-TTG-ACG-TCG-AAT-CTC-CAC-TGT-ACC-TTG-AAC-CTG-ACT 5’

Mutated mRNA

Note: the mRNA is shown as it would be read by a ribosome.
Mutated Amino Acid Sequence

MET-ASN-

5’ AUG-AAU-GCU-ACC-AUG-UGC-GUU-AGA-UAU-GAG-UUU-AUA-UCU-GGA-ACU-GCA-GCU-UAG-AGG-UGA-CAU-GGA-ACU-UGG-ACU-GA\_- 3’