Beginning Magnet Play

For this lab, we will be using "Zen Magnets" or similar extremely strong magnet spheres.
Our Goal is to see that self assembly derives naturally from physical law and that complex patterns can be made using repeating subunits following simple rules.
CAUTION: do not eat these. It is important that you not swallow one of these. It is ESPECIALLY important that you not swallow **TWO** of these.
Also, please try not to lose any of them. There will be a reward for any class that does not lose any beads.
First, just play with them for a few minutes. Make a long strand, wrap them around each other into tubes. Use the plastic card to separate beads or groups of beads. Have fun.

Figure 1: Zen Magnets

Make-believe proteins

As you read, proteins are long chains of amino acid (technically, amino acid residues because of the dehydration synthesis). Each amino acid residue consists of three "backbone" atoms that collectively make the chain. The atoms are N-C-C and are called the "Amine, α-carbon, and carbonyl carbon). Figure 2 has two amino acid residues, in this case, alanine and cysteine (a typical protein could have hundreds, and the largest protein has over 30,000). The particular sequence of amino acids in a protein is called its "**primary structure** (abbreviated 1° structure)." Stuck off each α-carbon is the side chain, often just called "R." Each amino acid is defined by what that side chain is (alanine has the CH_3, while cysteine has the CH_2-SH). They will be the components that provides actual function in the protein. But, today, we are going to ignore them. The interactions that mediate the first folding step in a protein occur along the backbone and don't depend *directly* on the side chain. In our first models, each bead will represent an amino acid residue (it will represent all three atoms), joined in a long chain.

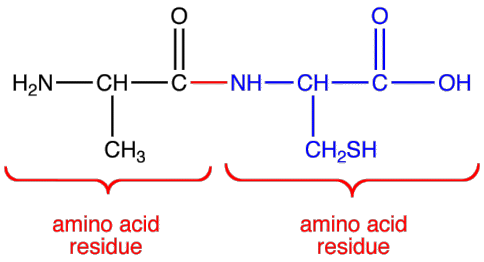


Figure 2, Ala-Cys dipeptide.

Notice that there is an amino end and a carboxyl end. That is important because it means that a protein chain has "polarity," or directionality. For our magnets, this will be the "South" and "North" ends of the chain.

The first levels of folding of a protein are mediated by hydrogen bonds between the amine of one residue (H-donor) and the carbonyl of another residue (the oxygen is the acceptor).
The magnetic fields will play the role of the hydrogen bonds, allowing interactions with the chain, to form complex structures.

How beads line up:

As noted, the strands have a polarity, with a "North" end and "South" end. You can line strands up either in a parallel or antiparallel direction. This will change the way they line up. In the first case (Figure 3) at right, the beads were simply folded back on themselves (video), and are therefore "antiparallel."
In figure 4 the beads were wrapped around so that both strands have "North" pointing the same way (Down).

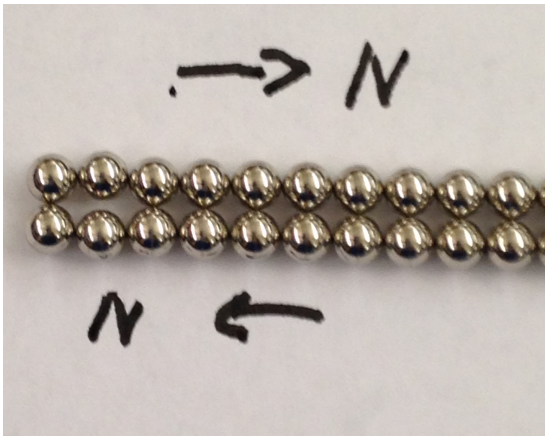


Figure 3: Antiparallel beads

Notice the difference in how the two sets of beads align. In the parallel arrangement, each bead links in between two beads on the other strand. The N end of each bead is near the S end of the bead on the strand next to it (Fig. 3). In the antiparallel form, they stack "bead on bead." This will turn out to be important when you start assembling structures.
While the analogy between N and S in a magnet and '+' and '-' in a hydrogen bond is not perfect, there are some important similarities. As we look at more structures, I want you to think about the implications of these constraints on how larger structures fit together.

Figure 4: Parallel beads

Beta sheets:

The first level of protein folding is called "**secondary structure"** (2° structure)**.** When a long protein chain folds, one simple form that it can take is a "beta sheet" (β-sheet, sometimes known as a β-pleated sheet, because of it's appearance). The strands of a β-sheet can be either parallel or antiparallel (See figure 5). For parallel

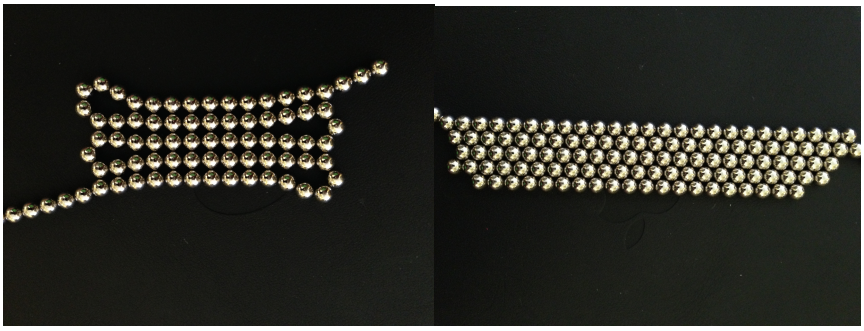


Figure 5: antiparallel (left) and parallel (right) sheets.

strands, there has to be some sort of connecting loop or other structure.

Simple Helix

Another simple self-assembling structure we can do this way is a helix. We can define a helix by how many subunits (beads) there are per turn. Start by making a couple of loops of a defined size (you pick it…maybe 8.5 beads per turn). Oh…you should make the helix "right handed." If you don't know what that means, ask me. Basically, it means that looking down the helix, the strand coils clockwise away from you.

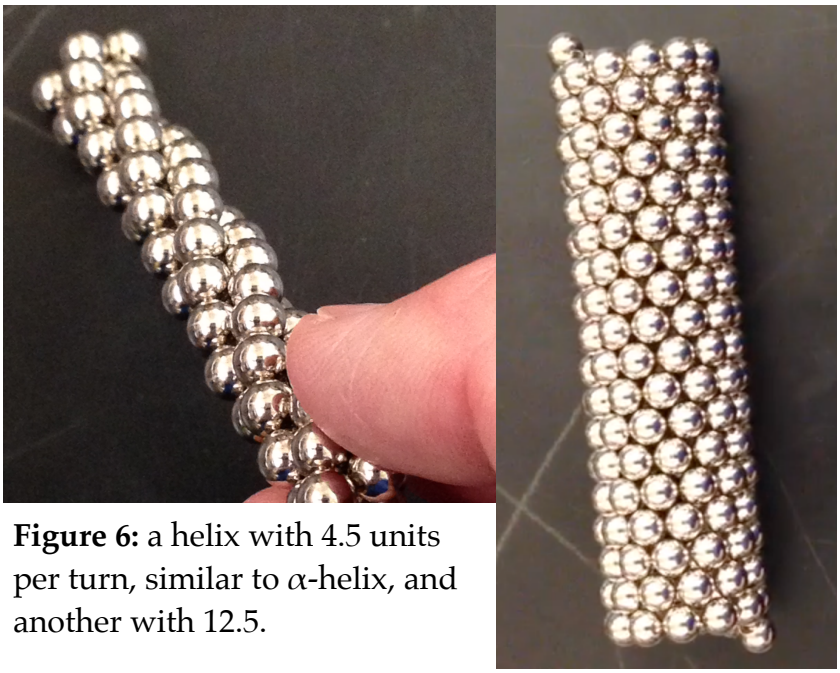


Figure 6: a helix with 4.5 units per turn, similar to α-helix, and another with 12.5.

Here is a link to a video of a "self-assembling" helix.

Do you understand now why I said "8.5," not "8" or "9?" Are the beads in parallel or antiparallel configuration? Also, do you see why I called it "self assembling?" Discuss what is driving that self assembly. On the scale of protein molecules, could hydrogen bonds drive a similar self assembly?

Figure 6 shows a helix that has only 4.5 beads per turn. It's a little hard to make. This is similar to the most common helix in protein structure, called an α-helix, which has about 3.6 amino acid residues per turn. Note: the more gentle spiral you see, also right handed, is the result of the ½ bead offset. It is not the primary helix to which I refer. That sort of pattern will be seen in protein structures, however.

The second helix in figure 6 has 12.5 beads per turn.

Notice any properties of the helix you made. How does, for example, changing the number of beads per turn change the properties of the helix?

A Real Protein:

Figure 7 is a representation of a protein. It is the coat protein from a virus called "Tobacco Mosaic Virus." This is a "ribbon diagram. The α helices are the spirals (obvious enough) and the β-strands…such as there are, are flat ribbons. There is only one small (two-strand) sheet in this particular protein. The arrows at the end of each β-strand point to the carboxyl end.

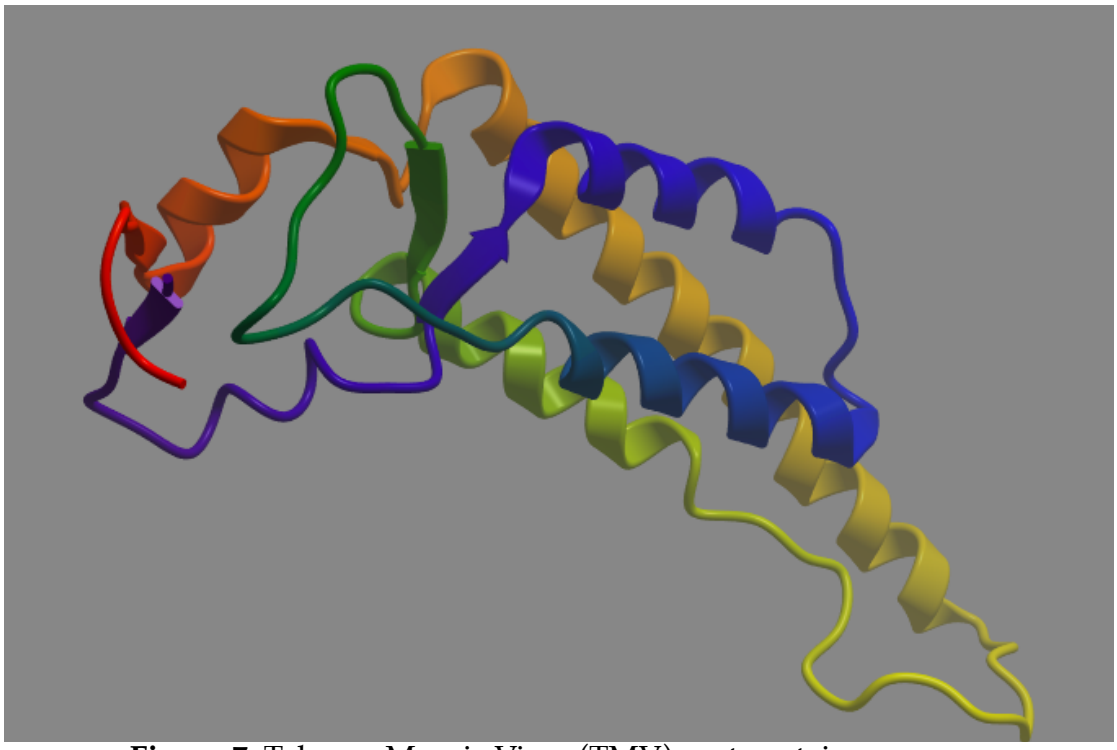


Figure 7. Tobacco Mosaic Virus (TMV) coat protein.

Are the two strands in that mini-sheet (the blue one and the green one) in the parallel or antiparallel orientation? For added positional information, the colors go through the visible spectrum from amino (violet) end to carboxyl (red) end (or "termini"). The green helix, therefore, is about in the middle of the protein. **Notice** there are lots of parts of the protein that are neither α-helix or β-sheet.

This just shows you the trace of the backbone…just the beads, if you will. On the next page, figure 8 shows the same angle in space-filling model, followed by "ball and stick," with the ribbons left in. You can see all the "side-chains." You can also see why we are leaving them out for now.

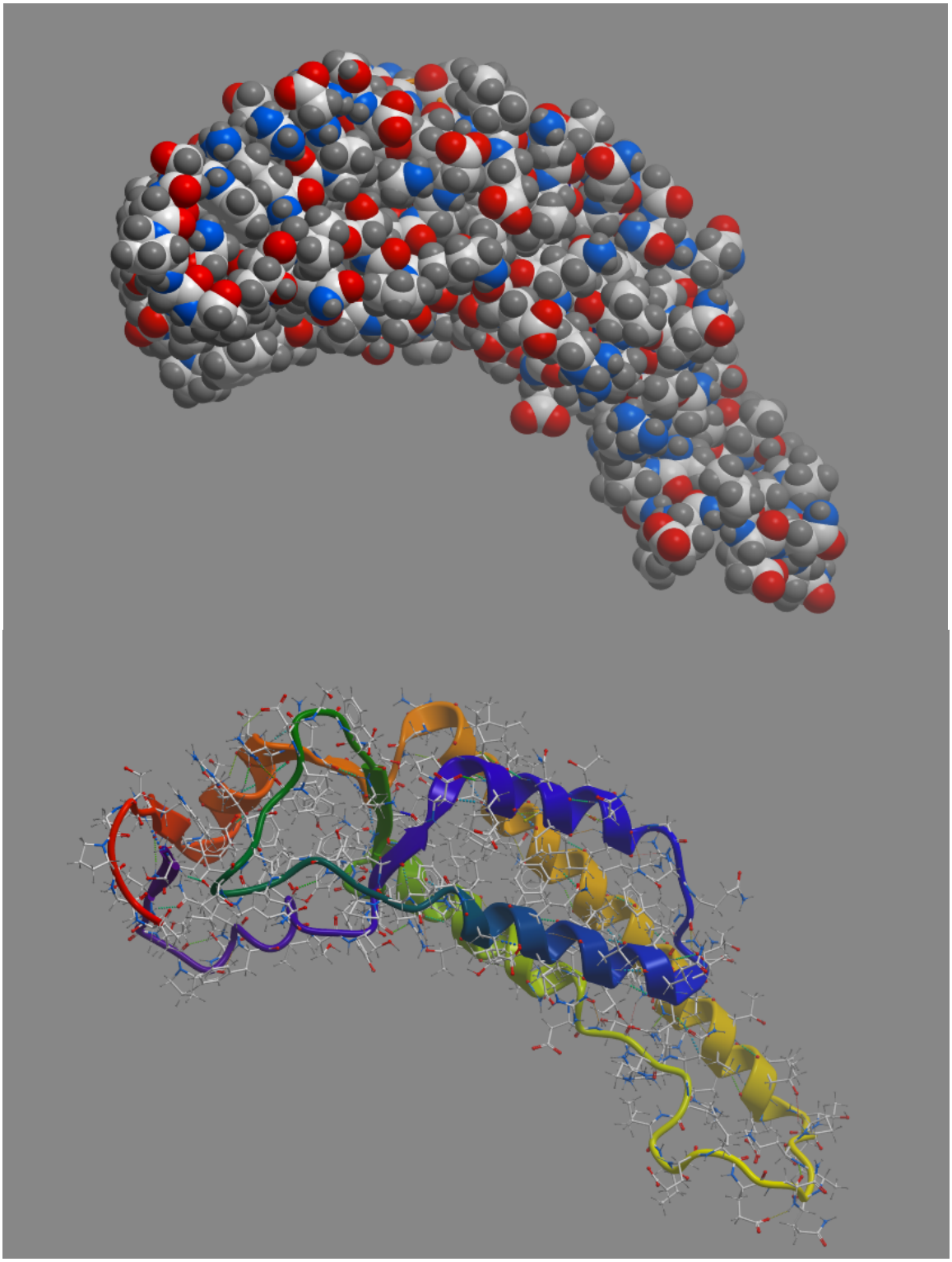


Figure 8: Space filling and "ball + stick" rendition of the TMV coat protein

Interactions among strands:

Here's where it gets a little interesting. I already told you, but, what is holding the two strands together in that mini-sheet?

In Figure 9, I've taken out the rest of the protein, left in the two little ribbons, but also added the stick drawings. You can see the side-chains. You'll learn to recognize them. But, notice the dotted lines between the red (carbonyl oxygen) and blue (amine)? Those are hydrogen bonds.

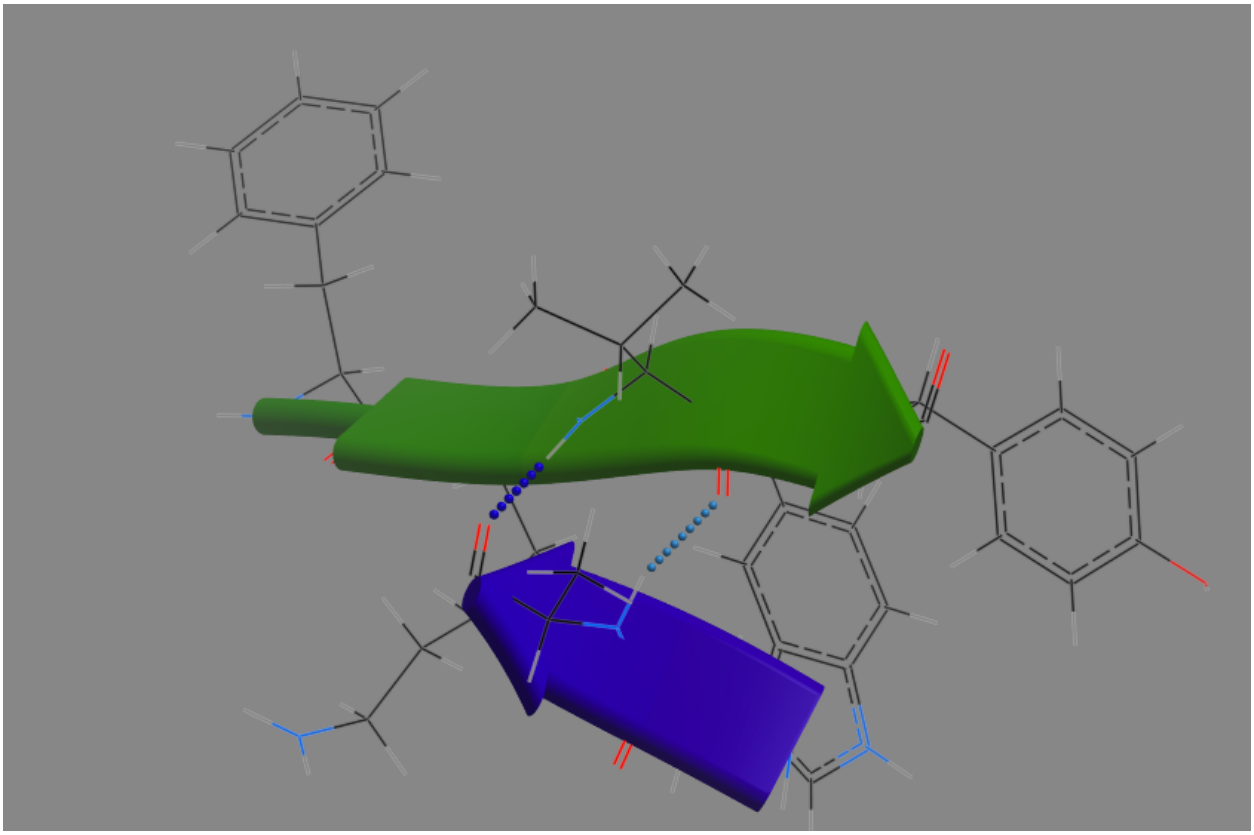


Figure 9.

Figure 10 on the next two pages presents several views of an α helix.

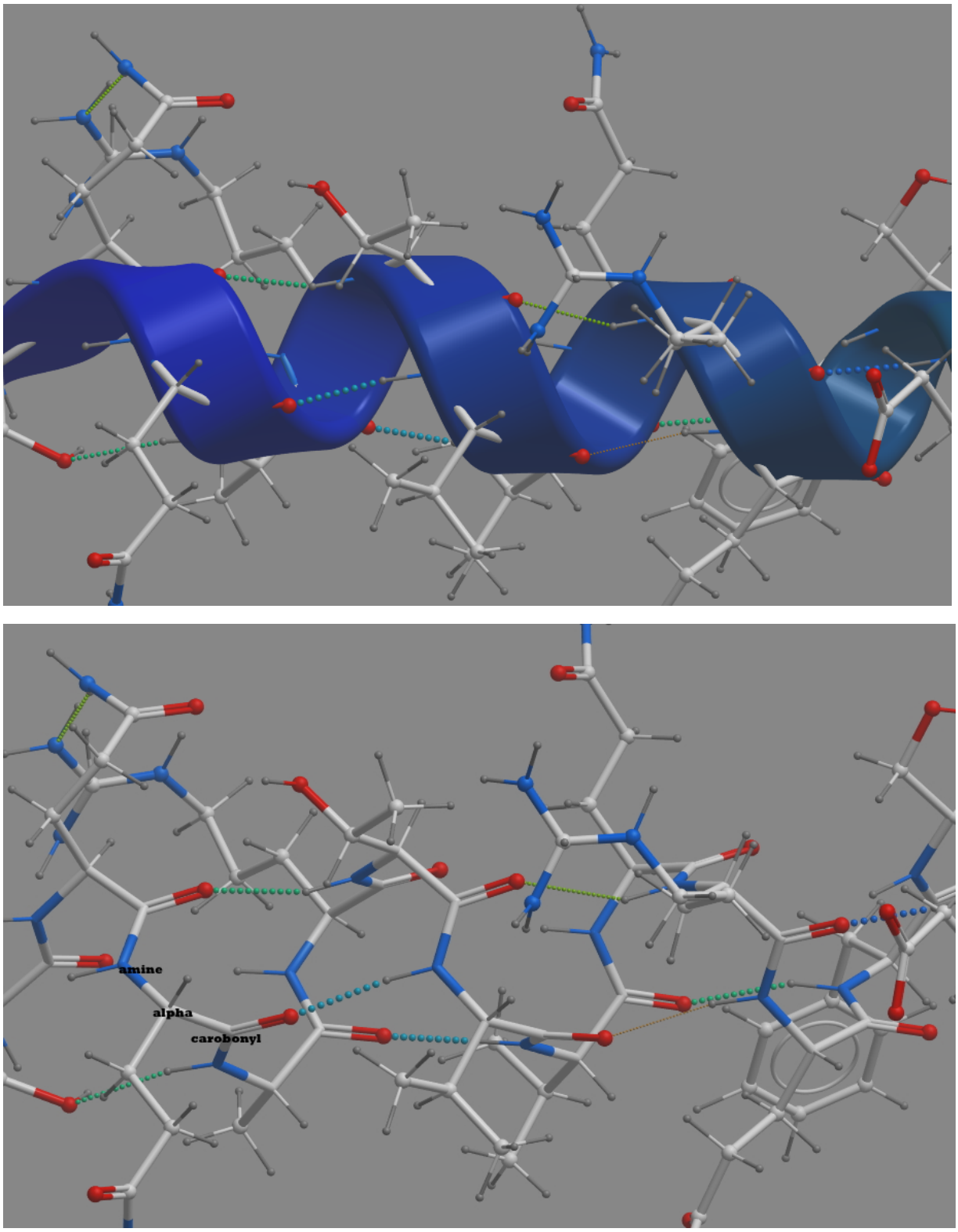


Figure 10 a and b: Hydrogen bonds in an α-helix. The ribbons in the top view help you see the helix. In the lower panel, going left-to-right, try to follow the blue nitrogen (amine), alpha carbon, carbonyl pattern as it spirals around.

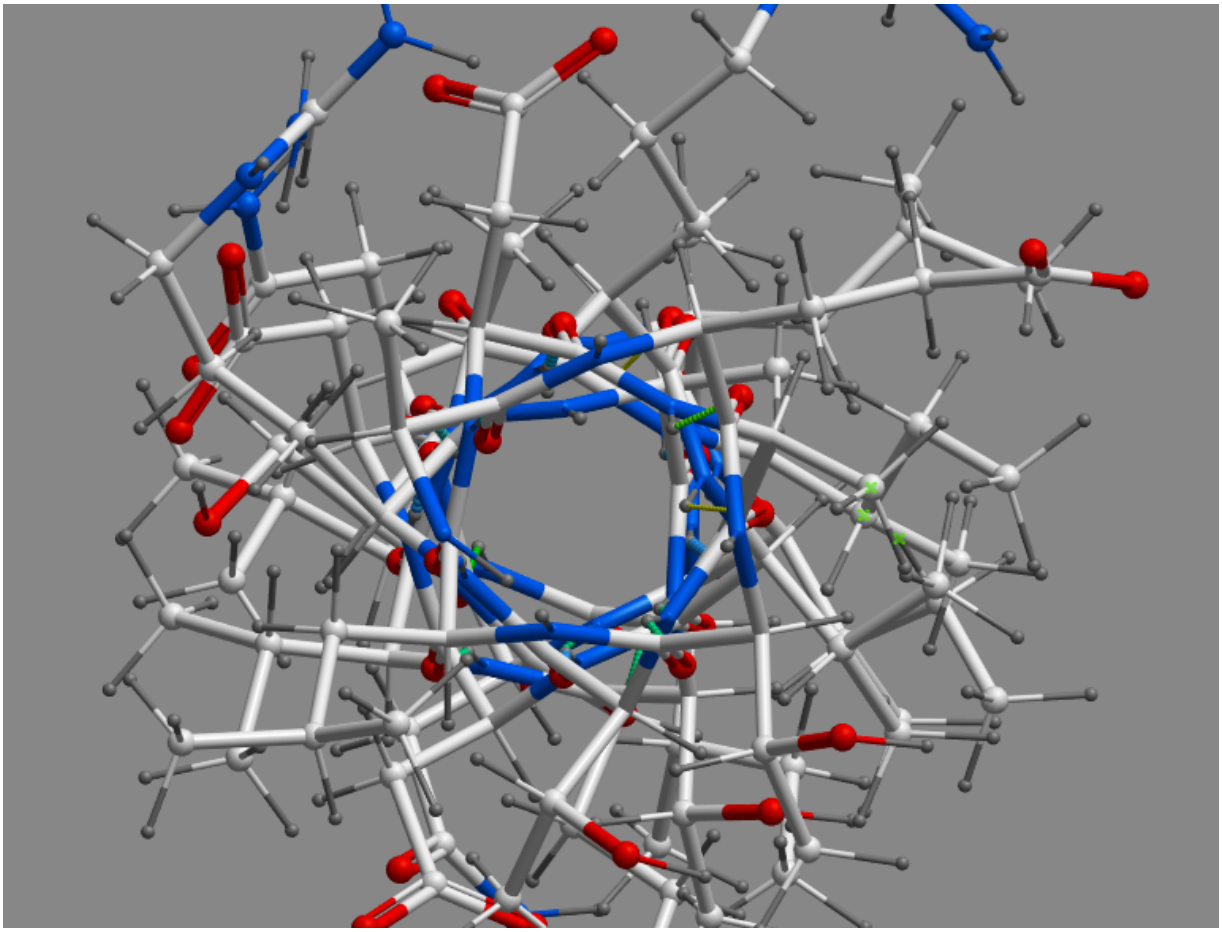


Figure 10c. Here is one more view of the same alpha helix as in 10b. Here we are looking up the center of the helix. The "tube" formed actually does not have even enough space for a water molecule (if it were in space-filling form, you would not see the tube at all). Notice that all of the "R" side chains are spoked off around the helix. These are the parts that convey important function and interactions—the functional groups that make each amino acid different.

Amphipathic helix:

Consider Figure 10c. Some side chains have oxygens (red) or nitrogens (blue) in them. They are polar or charged. The carbons (white) and hydrogens (gray) are non-polar.
Is the distribution of polar and non-polar side chains random around the helix? A helix with a polar side and a non-polar side is called "amphipathic."
Obtain a few colored magnet beads from me. In a chain, place one or two colored beads at regular spacing (say, beads 10 and 11, 20 and 21 etc.). Then make a helix with 10 beads per turn (or, that matches the spacing you chose). You can see a video of me doing this here.

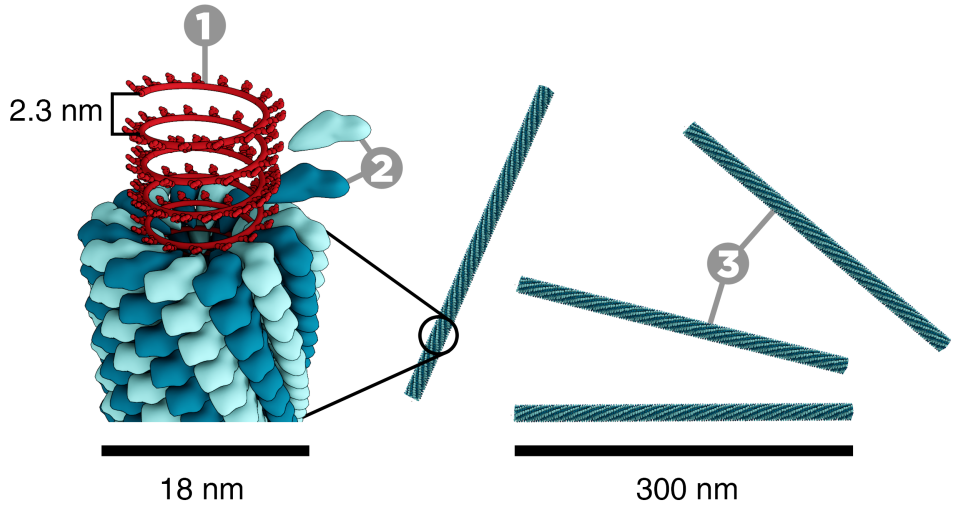
Building a Virus, or, Nature Repeats Itself

Once you've got the 2° structure, formed, the helices, sheets and other structures have to fold up into the finished protein. We call that tertiary (3°) structure. That requires interactions among the side-chains. That area in figure 10c that is non-polar interacts with a nearby helix along its non-polar face, for example. Our beads are not very good at modeling this. But, we can try a few things.

As I mentioned, the protein we have been observing is the TMV coat protein. To form the entire virus coat, many protein molecules need to assemble with each other. This also requires side-chain interactions. The assembly of individual proteins into larger structures is called "quaternary" (4°) structure. This can be just a few protein molecules that function together, or something huge like a virus particle.

To model this, we will pretend each bead now is a full protein molecule. It turns out that the helix, so easily built from repeating subunits with its "emergent" properties of being a rigid, hollow tube, is too useful not to repeat.

You should read this entry about TMV at Molecule of the Month. As we have discussed, a virus is some nucleic acid (in this case RNA) that encodes all the proteins of the virus, encapsulated in a box of some sort to allow it to gain entry into cells it infects and protect the nucleic acid when it is outside of cells.



As Professor Goodsell notes, there are 17 copies of the protein per ring (16 ⅓, once the offset occurs). Build a tube with 16.5 beads per turn.

Questions to Discussion for your ELN:

1. Is the hollow, rigid tube formed by the virus an "emergent property" not found in the underlying structure and sequence? Please use evidence to support your answer.
2. When you built a tube, you could make it arbitrarily long. That is, it was as long as you could make it with the number of subunits (beads) you had. TMV is 300nm in length. Why don't some grow longer? What keeps the length at 300nm? Propose an experiment to test your hypothesis.
3. Look at figure 10c. The distribution of polar and non-polar side chains clearly is not random around the helix. What significance does that have?
4. Check out this cleaned-up depiction of a similar view as in Fig. 10c. It's called a "helical wheel." Explain how the spacing of non-polar amino acids in the sequence below maps to the helix in figure 10c: Asp; ala; thr; Arg; Arg; Va; Asp; Asp; Ala; Thr; Val; Ala. You will need to look at a table of amino acids and their properties to answer this.