

## Homework 2. Make a small protein

The sequence of our small protein will be

**AAAAAAAAAAAAAAAAAAAAAAAA**

- 24 alanines.

We will fold it into a classic right-handed beta-alpha-beta unit (see TOPS drawing), using MOE.

- Step by step instruction follow. However, *your results may vary*.

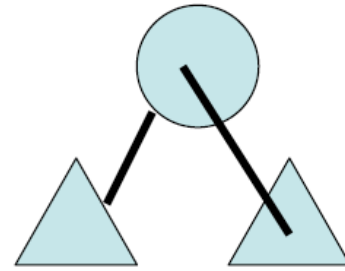


Figure 1

### Step 1 -- Synthesize

#### • **Edit/Build/Protein**

- select “**extended**” and click ALA 8 times.
- You now have a 8-residue beta strand.
- select “**helix**”. Click ALA 8 more times.
- select “**extended**” again and hit ALA 8 more times.
- Now you have a beta-alpha-beta unit, but it is not “folded”.

### Step 2 -- Fold

- Freeze the helix for the duration of this exercise. (Select helix. **Edit/Potential/Fix**, Invert selection, **Edit/Potential/Unfix**)

- Fold the two strands around the helix. Right-handed.
- Select residues 1-8  
Use meta-key to rotate the strand parallel to the helix axis. (see figure 2)
- Select residues 17-24  
• Use **meta-middlemouse** to rotate the strand parallel to the helix axis. Make it a right-handed  $\beta\alpha\beta$  unit.
- Try to rotate the strands so the the sidechains point in/out, and the oxygens/nitrogens point to each other, as they will when they make H-bonds. (see figure 3)
- \* In this view, strand 1 is on the right, connected to the helix (behind) at the top. This is right-handed.

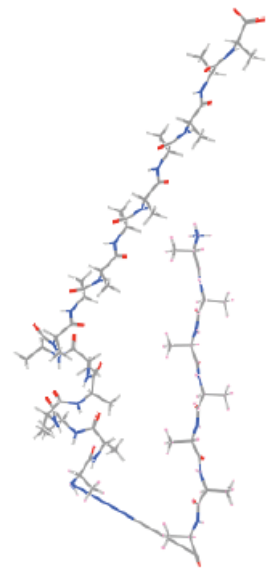


Figure 2

### Step 3 -- H-bonds

Use restraints to make H-bonds:

**Edit/Potential/Restrain**

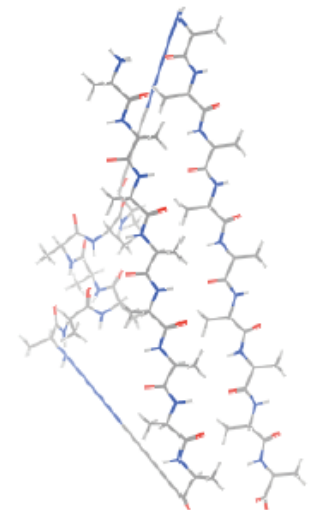


Figure 3

- Select “distance”. Set min, max target distances to 1.8 and 1.8.
- Set weight to 100
- Select O. Select H. Press Create.
- Do the same for O to N, but set the distance to 2.8, 2.8

O	N or H
1	19
19	3
3	21
21	5

## Step 4 -- Energy minimize

### Energy minimize.

- Compute/Structure preparation...
- GizMOE/Minimizer
  - Watch the stretched bonds relax to their ideal lengths.
  - Push and pull atoms by selecting and dragging with **meta-shift-middlemouse**. (meta is Alt or Command, depending on your system.)

*Note: selected atoms relax only after they are deselected.*

### To remove or modify a restraint

- **Window/Potential setup. Restraints**

- Find the one you want to delete or modify by looking at the atom names.

### Correct errors in the beta sheet.

Inevitably, energy minimization is not enough to find the ideal structure. Fix it by hand.

The beta-sheet should have its sidechains alternating sides, up-down-updown, when viewed from the side. To make a canonical parallel beta sheet:

- Drag the sidechains of 2, 4, 19, and 21 to the outside of the sheet, if they are not there already.
- Drag the sidechains of 1,3,5,18,20 and 22 to the inside of the sheet (the side that packs against the helix).
- Let the Minimizer relax them into place as you move them.

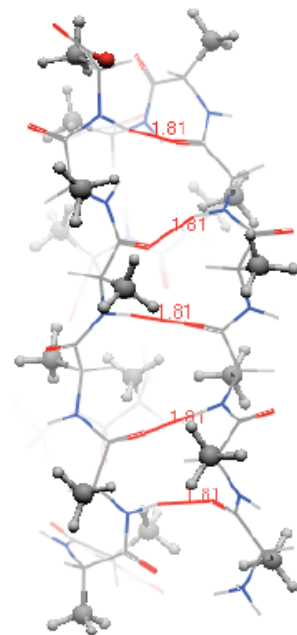
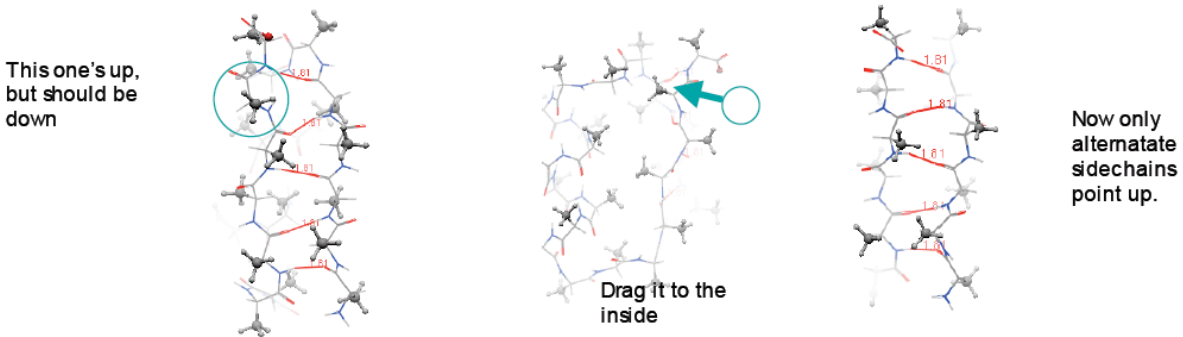


Figure 4

Figure 5



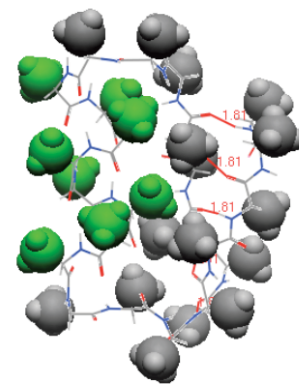
Make sure all residues are L-amino acids.

When dragging side chains, it is possible to convert L-amino acids to D-amino acids. There is no energy difference. Check chirality by eye (see Lecture 1 for how to do this.) If you find a D-amino acid, make it L by selecting the CB atom and swiftly dragging it directly through the CA atom to the other side. Then let the energy minimize.

### Knobs in holes packing

Select the side chains – **Selection/Protein/sidechain**

- Render them as spheres – (**Atoms** button. Pick spheres button.)
- *Push* and *pull* atoms so that beta sheet sidechains (knobs) fill the spaces between alpha helix sidechains (holes).



Helix sidechains (green) pack in the spaces between strand sidechains.

Figure 6

## Step 5 -- Save and submit

Make side chains ball-and-stick.  
Add a cartoon backbone.  
Save file as a MOE file (.moe)

Upload at  
<http://www.bioinfo.rpi.edu/bystrc/courses/biol4550/homework.html>  
Select Homework 2.

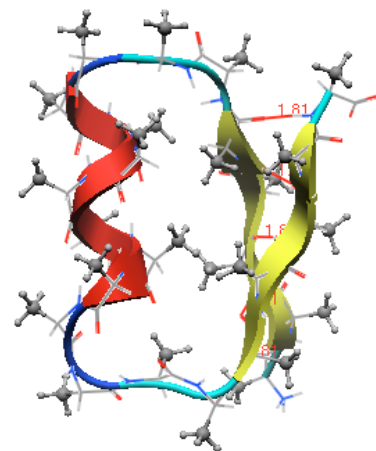


Figure 7