

Homework 2. Make a beta-alpha-beta unit

The sequence of our small protein will be

AAAAAAAAAAAAAAAAAAAAAAAAAAAA

- 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*.

Step 1 -- Make polyalanine

- Clear any selection
- **Edit | Build | Protein**
 - Set Geometry “**extended**” and click ALA 8 times.
 - Set Geometry “**helix**”. Set “append”. Click ALA 8 more times.
 - Set Geometry “**extended**” and click ALA 8 more times..
 - Now you have a beta-alpha-beta secondary structure, but it is not “folded”.

Step 2 -- Fold it by hand

- Freeze the **helix** for the duration of this exercise. (Select helix. **Edit | Potential | Fix, Select | Invert, Edit | Potential | Unfix**)
- Fold the two strands around the helix. Right-handed!
Select residues 1-8. Use **meta-key-middlemouse-drag** and **shift-meta-key-middlemouse-drag** to rotate and translate the strand so it is antiparallel to the helix axis. (see figure 2). Don't worry about the distorted bonds.
- Select residues 17-24. Use **meta-key-middlemouse-drag** and **shift-meta-key-middlemouse-drag** to rotate and translate the strand so it is parallel to the first strand . (see figure 3).
- Make sure it a **right-handed** $\beta\alpha\beta$ unit. (see Figure 1)
- Rotate the strands so the the side chains alternate in/out and they are aligned with each other. At the same time, point the backbone oxygens/ nitrogens towards each other, making parallel beta sheet H-bonds. (see figure 3)

Step 3 -- Restrain H-bonds

To restrain O—H distances:

Edit | Potential | Restrain

- Set “distance”. Set L, U = 1.8 , 1.9. Weight 50
- Select backbone O.
- Select backbone amide H.
- Press Apply. (“Create” in earlier versions of MOE)

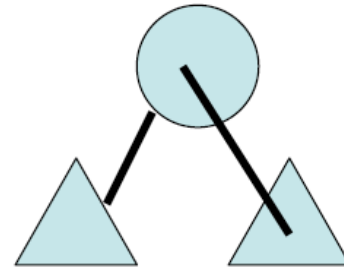


Figure 1

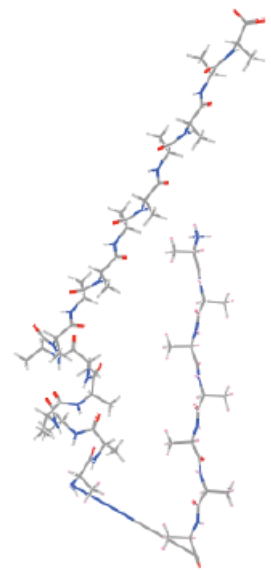


Figure 2

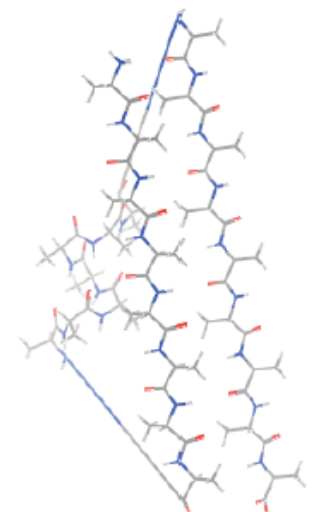


Figure 3

residue numbers for H-bonds	
C=O	N-H
1	19
19	3
3	21
21	5

Start with the restraints listed in this table. Fill in the rest yourself by applying the parallel beta strand rules (Lecture 17 slide 15).

0	1	2
1	0	0

0	1	0
1	0	-2

Step 4 -- Energy minimize

Energy minimize.

- Compute/Structure preparation...
- Hit **Minimize** (side panel)
 - Watch the stretched bonds relax to their ideal lengths...
- Check for bad geometry by eye (D-amino acids, *cis* peptide bonds. Non-planar peptide bonds)
 - To correct for bad geometry, push and pull atoms by selecting and **meta-shift-middlemouse-drag**. Then hit **Minimize**.

Or use 'gizmin.svl'

To remove or modify a restraint

- **Bottom bar | 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. You must **fix it by hand**, by selecting atoms and moving them by (**shift/meta**)-middlemouse dragging.

The beta-sheet should have its sidechains alternating sides, up-down-up-down, 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.

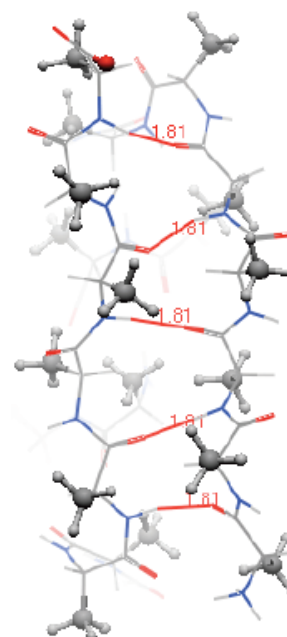


Figure 4

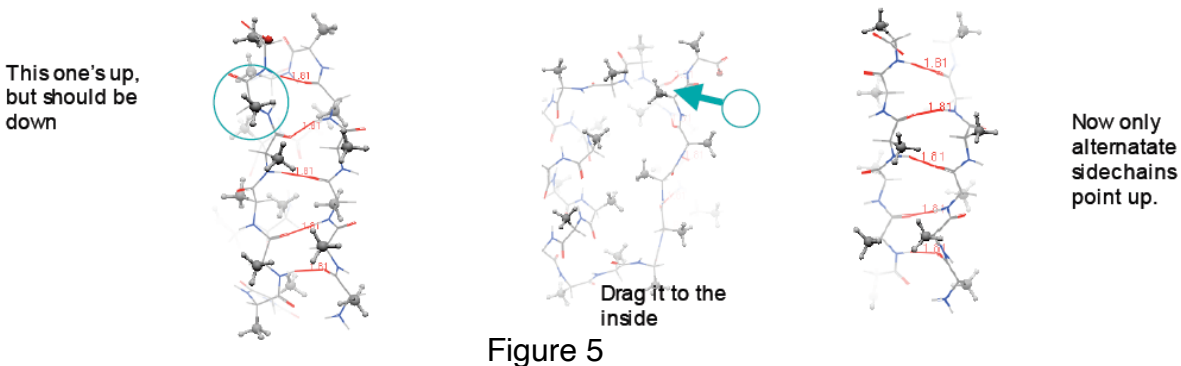


Figure 5

- Drag the sidechains of 1,3,5,18,20 and 22 to the inside of the sheet (the side that packs against the helix).
- Minimize. (or use gizmin)

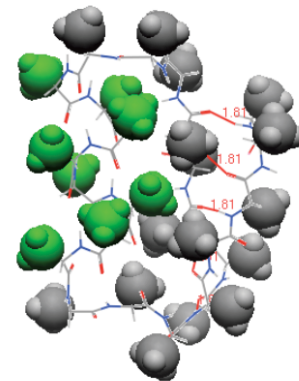
Make sure all residues are still L-amino acids! They were when you started.

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 spacefill.)
- *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.

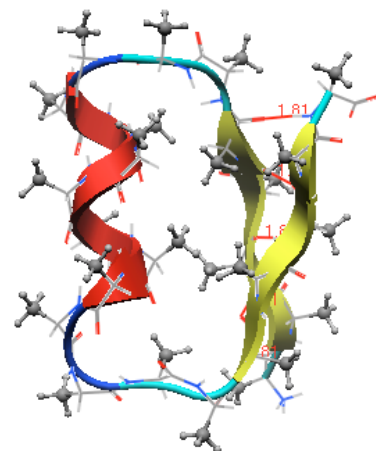


Figure 7