Molecular Modeling Homework 4 (2020) -- protein design

Due Friday Apr 17

Open"**messedup.moe**" from the course web site. Delete the template 2gb1 and the target sequence, and keep the model.

Design it as best you can using any and all tools within MOE.

You can make as many mutations as you like, you can move side chains and backbone atoms, but *no deletions or insertions*. Add as many waters as you think you need. You may model loops. You may run homology modeling (no indels!). You may energy minimize. You may use molecular dynamics. No particular method is required. Please use only MOE. Do not use, for example, the SwissModel server, or EGAD, or Rosetta, or any other modeling tools. Just MOE.

Your structure will be graded as follows: You will get 100 points to start, then lose points as follows:

1. Buried polar void space bigger than a water that does not contain a water..... -1 each

2. Buried hydrophobic void space bigger than a water, whether or not it contains a water.....-1 each

3. Deep pockets bigger than a leucine side chain..... -1

4. Buried (i.e. solvent excluded) hydrogen bond donor that is not within H-bonding distance of a hydrogen bond acceptor or a water..... -1 each

5. Buried (i.e. solvent excluded) hydrogen bond acceptor that is not within H-bonding distance of a hydrogen bond donor or a water..... -1 each

6. Buried charged group (Arg, Lys, Glu, Asp sidechains) that is not within H-bonding distance of an oppositely charged group.....-2. each

7. Highly exposed solitary hydrophobic side chain ..... -1 each

8. Solvent exposed hydrophobic surface patch involving 3 side chains ..... -1 each

9. Solvent exposed hydrophobic surface patch involving four or more side chains..... -2 each

10. D-amino acid .....-1 each

11. cis-peptides ..... -1 each

12. Planarity over 4 kcal/mol ..... -1 each

13. Bond lengths over 4 kcal/mol ..... -1 each

14. Backbone angles in disallowed region ..... -1 each

15. Positive backbone phi angle not at a Glycine residue ..... -1 each

16. Rotamers over 5 kcal/mol ..... -1 each

17. Side chains packed too tightly ..... -1 (only counted once)

18. Like charges within H-bond distance on the surface ..... -1. each

19. Like charges within H-bond distance, buried ..... -2 each

20. Atom clashes ..... -1 each

21. Non-canonical hydrogen bonding in a beta sheet..... -1 (counted once)

22. Non-canonical hydrogen bonding in the middle of an alpha helix..... -1 (counted once)

23. Glycine residue in alpha helix ..... -1 each

24. Proline residue in alpha helix ..... -1 each

25. Waters not hydrogen bonded to anything ..... -1 each

Save the final MOE file and upload to the Homework server as Homework 4. Due Apr 17.