Students should be able to….

**Protein Structure Fundamentals**
1. Sketch the chemical structure of the 20 naturally-occurring amino acids and write the correct one- and three-letter abbreviations.
2. List hydrophobic, charged, and polar amino acids, and identify other structural and chemical amino-acid properties.
3. Describe structural characteristics of α-helices, β-sheets, and fold architecture.
4. Calculate atom coordinates from torsion angles and vice-versa.
5. Implement a computer algorithm to convert torsion space to Cartesian space and vice-versa.

**Molecular Visualization**
6. Find molecular structures in the Protein Data Bank.
7. Measure geometric quantities (distances, angles, dihedrals) using PyMOL.
8. Create pictures using color and various molecular and protein representations (lines, sticks, surface, cartoon) to present structural features clearly.
9. Use PyRosetta to measure and alter protein structure (in internal or Cartesian coordinates).

**Molecular Energies and Forces**
10. Describe the molecular forces which determine protein structure.
11. Calculate van der Waals energies, electrostatic energies, solvation energies and hydrogen bonding energies from atomic coordinates using simple pair-wise energy models.
12. Explain the physical basis of the components of a molecular energy function and alternate model formulations.
13. Calculate free energies from probability distributions, and vice-versa.
14. Derive forces from energy expressions and vice-versa, and project those forces onto relevant protein coordinate systems.
15. Use PyRosetta to calculate various components of energy on atoms, residues, or biomolecules.
16. Test different score function components or weighted combinations using PyRosetta.

**Ab-initio Structure Prediction (Protein Folding)**
17. Explain the fundamental challenges of protein structure prediction.
18. Describe the use of protein fragments for building protein backbones.
19. Describe the use of knowledge-based potentials, and be able to create such potentials from probability distributions.
20. Explain a Metropolis Monte Carlo search strategy.
21. Implement a Metropolis Monte Carlo algorithm.
22. Use standard PyRosetta protocols to optimize protein structure.
23. Use robetta.org to obtain predicted protein structures and interpret results.

**High-resolution refinement**
24. Explain or implement a Monte Carlo-plus-minimization algorithm.
25. Explain concepts such as the free energy funnel, and interpret structure prediction results to identify failures in sampling or scoring.
26. Use various standard PyRosetta Movers to manipulate protein structure.
**Side-chain packing**
27. Explain the assumptions, observations and conditions justifying the use of rotamer libraries.
28. Identify rotameric classes of protein side-chains, and calculate side-chain positions and internal energies from rotamer statistics.
29. Explain the dead-end elimination algorithm and stochastic packing algorithms (Monte Carlo simulated annealing), including their practical use and limitations.
30. Estimate the size of conformation or design space to be searched under the rotamer approximation.
32. Integrate side-chain packing with small and shear moves and minimization in PyRosetta refinement protocols.

**Design**
33. Define the computational protein design problem(s).
34. Describe the current capabilities and limitations of computational protein design, particularly through the use of examples.
35. Explain various algorithms and approaches for computational protein design.
36. Use PyRosetta to optimize protein sequence.
37. Write custom PyRosetta protocols to simultaneously optimize protein structure and sequence.

**Docking**
38. Describe the major approaches to docking (grid based, FFT, Monte Carlo) and their advantages and disadvantages.
39. Justify the rigid-backbone assumption in docking (and identify when it is valid).
40. Use conformer selection and induced fit binding theories to justify flexible docking methods.

**Loop modeling**
41. Identify the importance of loop modeling.
42. Describe the loop modeling and loop closure problems.
43. Identify the major categories of loop modeling approaches and the advantages and disadvantages of each.
44. Describe the cyclic coordinate descent approach and identify its advantages and limitations.
45. Describe the kinematic closure approach and identify its advantages and limitations.

**Fold tree**
46. Interpret the propagation of conformational change across a fold tree
47. Design a fold tree and move map for an arbitrary structure prediction or design problem.
48. Use a job distributor object to collect multiple structures using multiple computers.

**Design for Function**
49. Explain the challenge of creating protein function and the successes achieved.
50. Explain the fold-before-function hypothesis.
51. Explain the underlying hypotheses and the successful methods used for enzyme design, protein interface design, vaccine design, and symmetric multi-protein design.
52. Explain the ideas of negative design or multistate design.

**Non–Amino-Acid Residues**
53. Describe several biological functions for metals, organic cofactors/vitamins, and non–amino-acid biopolymer residues.
54. List three types of degrees of freedom that must be considered for alternative residue types.
55. Explain the extra challenges in sampling ring conformations.
56. Interpret and write Rosetta topology (.params) and patch files.
Membrane Protein Modeling
57. Describe the importance of membrane proteins, including examples.
58. List the challenges in membrane protein structure determination (be able to explain membrane mimetics).
59. List the challenges in membrane protein structure prediction.
60. Explain hydrophobicity scales, how trans-membrane span prediction is accomplished and the physical basis.
61. Describe how various experimental data can be used to constrain membrane protein structure prediction.
62. List future challenges involving membrane protein structure prediction and design.

Coding
63. Follow standard Python coding conventions.
64. Write loop and conditional statements.
65. Organize code into functions and classes.

PyRosetta
66. Critically interpret results from any of the PyRosetta calculations mentioned above.
67. Write a PyRosetta program to predict or design a structure (or some combination) for a specific biomolecular engineering application.

Applications
68. Interpret a current paper in the literature, identifying the contribution to the field, the novelty of the methods, and assessing the validity of the results.
69. Explain the findings from the projects and recent papers presented in class.

Students are responsible for all assigned readings posted on the course website (not including references, although those may help with details and the larger context of the topics).