Name: KEY

MCB 100A/ChemC130 Midterm 1 2010

Please write your name on the first page.

1. Find the letter below that best matches the following statements. Use a letter only once. **(20 pts.)**

A. GNRA tetraloop
B. amplifies X-ray scattering
C. reveal fluctuations or motions in DNA
D. two or more strands with one face exposed to solvent
E. usually 5 or more buried strands
F. R-factor
G. traps a nonphysiological structure
H. phylogenetic tree
I. multiple sequence alignment
J. BLAST
K. brings together different stems into a continuous helix
L. van der Waals interaction
M. jelly roll
N. ionic interaction
O. often recognized by hydrogen bonds from side chains in a helix
P. hydrogen bond
Q. NOEs
R. measure of quality of an NMR structure

i) **L** weakest attractive force
ii) **C** structures of DNA-protein complexes
iii) **I** a computational tool for identifying potential functional sites
iv) **E** parallel beta sheets
v) **R** rmsd
vi) **K** coaxial stacking
vii) **P** strength depends on angle as well as distance
viii) **B** crystal
ix) **J** makes pairwise comparisons of protein and nucleic acid sequences
x) **A** stabilizes the attached stem

2a. To expand the genetic code to efficiently incorporate new amino acids into proteins, Jason Chin and coworkers reported this week the creation of a new genetic code that is read in quadruplets instead of triplets (Neumann et al., *Nature*, Feb 14, 2010). List three fundamental modules of the translational machinery they would have to change to create cells that read a quadruplet code. **(9 pts.)**

ribosome
tRNA
aminoacyl tRNA synthetase
(mRNA)

2b. What is the maximum number of codons available in a quadruplet code? **(5 pts.)**

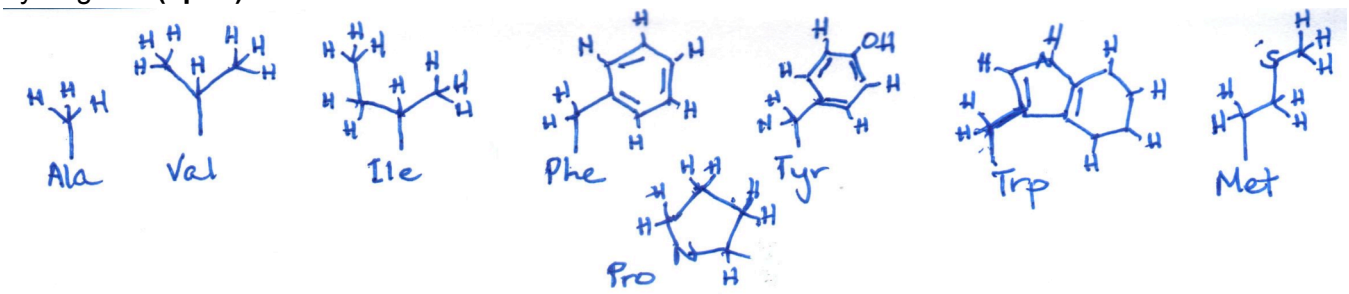
4 x 4 x 4 x 4 = 256

Name: KEY

2c. Why is it important or significant to expand the genetic code? Aren't the 20 biological amino acids enough to encode all the chemical diversity needed for protein structures? **(4 pts.)**

Nonbiological amino acids with new chemical groups can expand the functional range of proteins. Key practical examples include residues that increase stability or augment chemical reactivity. (New sensors might also be constructed using residues with novel fluorescence emission or regulatory properties. Residues with close structural relationships might enable systematic tests of mechanistic ideas.) Despite their diversity, the 20 biological amino acids are missing many chemical functionalities that would be useful to introduce at specific sites in proteins.

2d. Draw the chemical structures of two different (biological) hydrophobic side chains. Please include hydrogens. **(6pts.)**



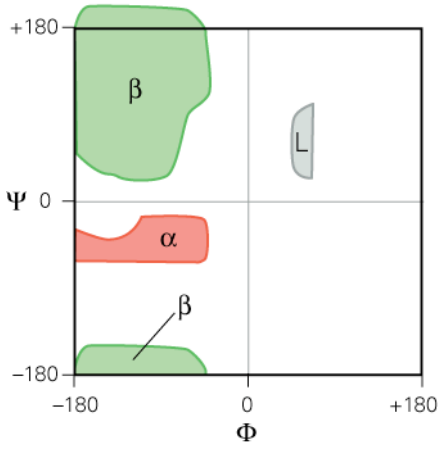
3a. What are two ways that nucleic acids coordinate metal ions? **(6 pts.)**

Inner sphere
Outer sphere
Diffuse

3b. Contrast the roles of these two kinds of coordination in stabilizing specific nucleic acid structures. **(6 pts.)**

Inner sphere: Direct bonds to the RNA stabilize specific 3D folds.
Outer sphere: Interactions bridged by water. Stabilizes double helices and other compact folds.
Diffuse: Flexible with several intermediary water layers. Shields negative charge repulsion of the phosphodiester backbone while preserving flexibility.

4a. Draw a Ramachandran diagram for a typical amino acid that is not glycine or proline. Label the axes and mark the regions of this diagram that correspond to α-helix and β-sheet. **(6 pts.)**



Name: KEY

4b. Do the residues in loops necessarily (always) populate different regions of the Ramachandran diagram compared to the residues in secondary structures? Why or why not? **(4 pts.)**

NO. The loop residues occur in the same regions of the Ramachandran diagram as residues in secondary structures, because these are the allowed regions. In secondary structures, sequential residues adopt similar dihedral angles, while sequential residues in loops populate different regions of the Ramachandran space.

4c. Define a side-chain rotamer. **(6 pts.)**

A favored side-chain "rotational isomer" that adopts a specific set of (low-energy) dihedral angles.

5a. In contrast to soluble proteins, membrane proteins can have a single, isolated, stable helix. What accounts for the stability of an isolated helix in the membrane but not in solution? **(6 pts.)**

Buried hydrophobic surface. The side chains in an isolated transmembrane helix are buried in a hydrophobic environment that stabilizes the helix. In contrast in solution, all the side chains are exposed to water and there is not enough buried hydrophobic surface to stabilize the helix.

5b. The hydrophobic tails of the mycolic acid outer layer of the *M. tuberculosis* cell wall are about 80 Å thick. How many residues would it take for an α-helix to span this unusual hydrophobic layer? **(4 pts.)**

80 Å/1.5 Å per residue = 53-54 residues

5c. What subset of β-sheet structures can span a membrane? Are these parallel, mixed or anti-parallel sheets? **(6 pts.)**

Anti-parallel β-barrels

6a. Why is the E-value produced by BLAST a more sensitive metric of sequence relatedness than % sequence identity? **(6 pts.)**

The E-value takes into account favored substitutions (as defined by a positive score in the substitution matrix) as well as identities. As a result, remote homologs with lower than 25% identity can produce a significant E-value that reveals relationships between more dissimilar sequences.

6b. List two patterns or principles of protein structure embodied in the environment classes used for 3D-1D profiles **(6 pts.)**

Weak secondary structural preferences of residues, hydrophobic residues buried, polar residues exposed, buried polar residues have polar neighbors