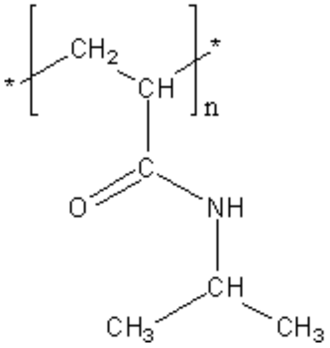
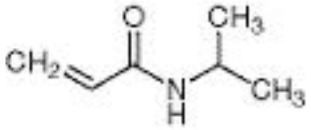
120111 Quiz 1 Morphology of Complex Materials

1) Proteins are the seminal model for molecular hierarchy. The primary structure is a sequence of amino acids.
   a) Give the generic chemical structure for an amino acid and a protein molecule (a tripeptide).
   b) Label the a-carbon, the b-carbon and the N and C termini of the protein.
   c) Show what parts of the structure are coplanar (sheet-like).
   d) Indicate the two bond angles used to make a Ramachandran plot giving the Greek letter for the angles and an English spelling of the letter, e.g. p and pi.
   e) What values of these angles are forbidden? Why?

2) Poly N-isopropylacrylamide (PINPAm) is a synthetic polymer that is said to display some features of proteins such as a chain collapse transition at about 30°C that is reminiscent of protein folding.



PNIPAm



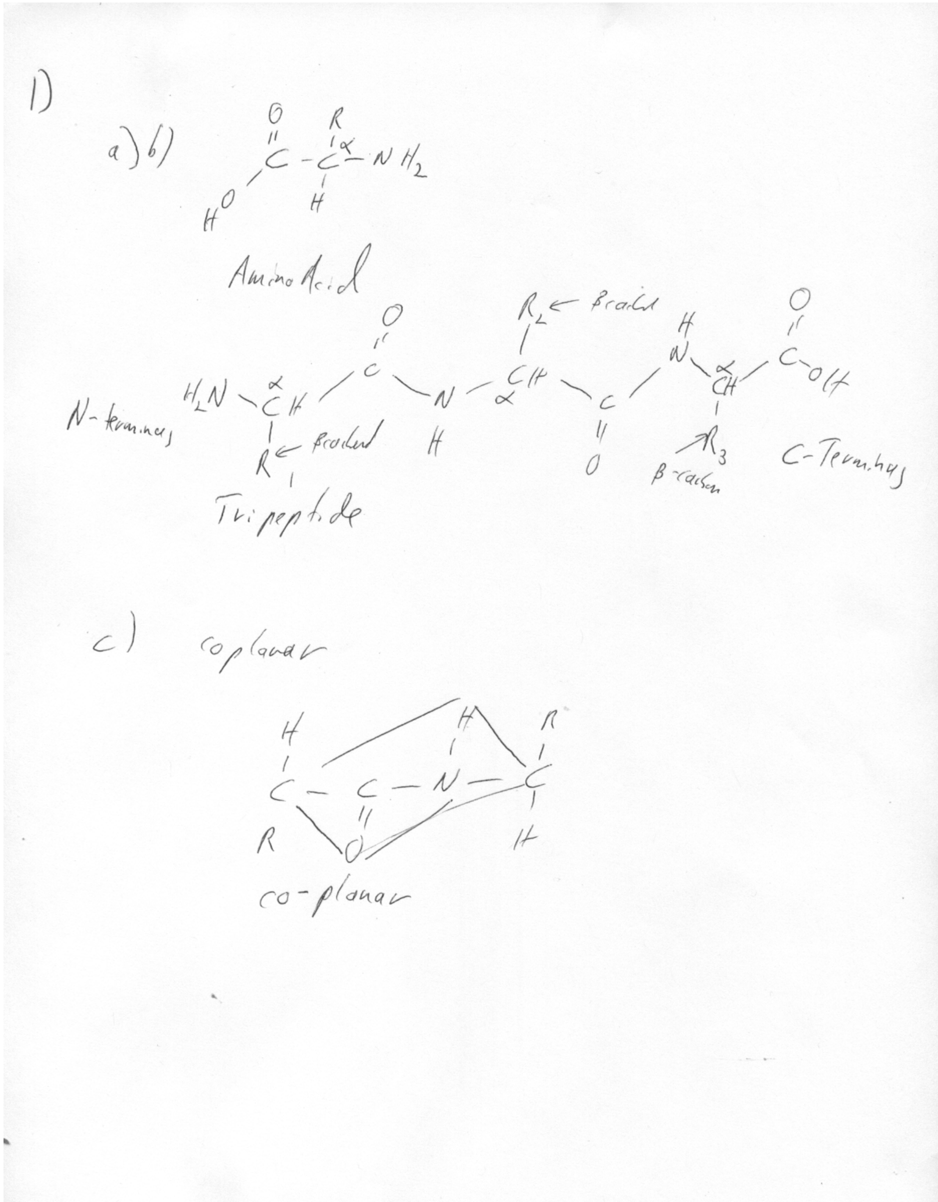
N-IPAm

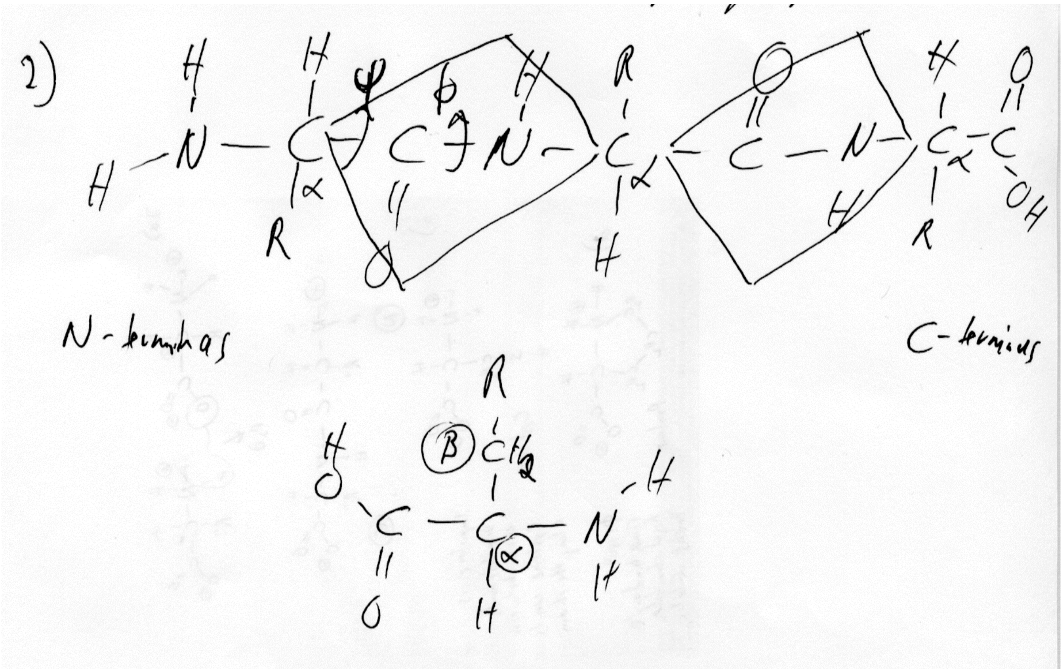
   a) What (or which) amino acid(s) do you think that the PINPAm repeat unit resembles?
   b) Does PINPAm display a "card-like" unit? Explain
   c) Can PNIPAm hydrogen bond? Could it form β-sheet like structures?
   d) Can you describe a possible mechanism for PNIPAm to form a dense globular structure? (That is a structure where bonding within a single chain causes collapse of the random coil.)
   e) The monomer for this polymer (N-isoproplyacrylamide) (N-IPAm) is extremely toxic. Why do you think this molecule might be toxic?

3) The change in Gibbs free energy for folding is composed of a change in enthalpy (associated with bonding) and a change in entropy (randomness of the chain): $\Delta G = \Delta H - T\Delta S$
   a) A drop in G must occur for a spontaneous process. Explain how spontaneous folding is possible in terms of thermodynamics.
   b) Consider another spontaneous process, crystallization of water. Use the Gibbs equation to explain this process and compare it with protein folding.
   c) Explain how dissociation of water from a protein during folding could lower the free energy and drive folding.
   d) What is a disulfide bond and which amino acids are involved in this bond?
   e) What other kinds of specific enthalpic interactions are involved in protein folding?

Answers: **081001 Quiz 1 Morpholgy of Complex Materials**

1)





$\phi = \psi = 0^\circ$ is forbidden

& also $\phi = 0$ or $\psi = 0$ due to steric constraints

2) a) If the terminal isopropyl group were an alpha carbon the amino acid might be similar to alanine. You could also view it as similar to valine.

b) Yes the amine and carboxylic group would form a card like planar group with the two neighboring carbons. So the structure is a card with rotation of the isopropyl group about the central carbon and rotation of the card about the main chain. Hydrogen bonding between the cards is possible.

c) It can hydrogen bond but it would not be able to form a sheet like structure since it is the side groups that could hydrogen bond either with each other or with other chains.

d) If the side groups hydrogen bonded with each other the chain could collapse on itself and form a structure similar to a globular structure in proteins. It is unlikely that it would be as densely packed as a native state protein but it could show some similarities.

e) The monomer can hydrogen bond so it can interfere with hydrogen bonding in proteins and might disrupt enzymatic activity of proteins. It could also interfere with DNA and RNA structures. The unsaturated vinyl group (double bond) could lead to free radicals that might be somewhat toxic, especially with its affinity for enzymes and nucleic acids.

3) a) Spontaneous folding is possible despite the huge loss in conformational entropy, that is TΔS is negative and very large, since there are many enthalpic interactions that sum to a larger negative ΔH.

b) Crystallization of water also involves a large loss in translational entropy of the water atoms which are constrained in the crystal. The enthalpy drop with crystallization overcomes this loss in translational entropy at the equilibrium melting point where $\Delta G = 0$, $T_m = \Delta H/\Delta S$.
c) In protein folding water that is locked to the polar and hydrogen bonding groups of the protein are freed up so that they can obtain a large amount of translational entropy. This is a positive change in ΔS so it favors folding.
d) Cystine is the amino acid that can form disulfide bonds, -S-S- linkages in a protein. These disulfide bonds serve to guide protein folding.
e) The main types of specific interactions that lead to a drop in enthalpy and free energy are disulfide bonds, hydrogen bonds, hydrophobic/hydrophilic interactions and polar interactions.