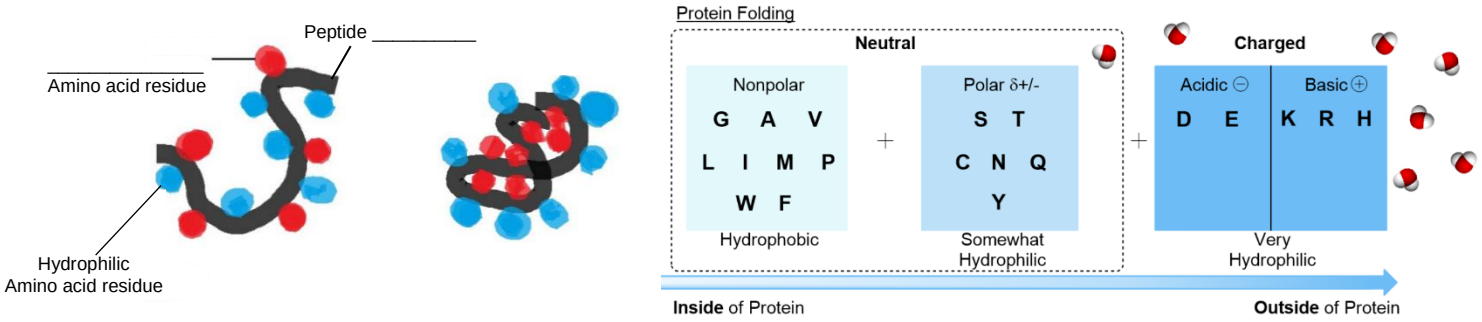
**CONCEPT:** PROTEIN FOLDING

●Protein folding has many different contributing factors but relies heavily on _____ interactions.

□ Recall: final protein conformation ultimately depends on its _____ level of structure.

□ Generally, folding leads to _____ amino acids on the interior & _____ amino acids on the perimeter.

**EXAMPLE:** Protein folding.




**PRACTICE:** Which of the following is the greatest contributor to spontaneous protein folding?

a) Decreased chain conformational entropy.
b) Increased chain conformational entropy.
c) Decreased entropy of the solvent due to folding.
d) Increased entropy of the solvent due to folding.

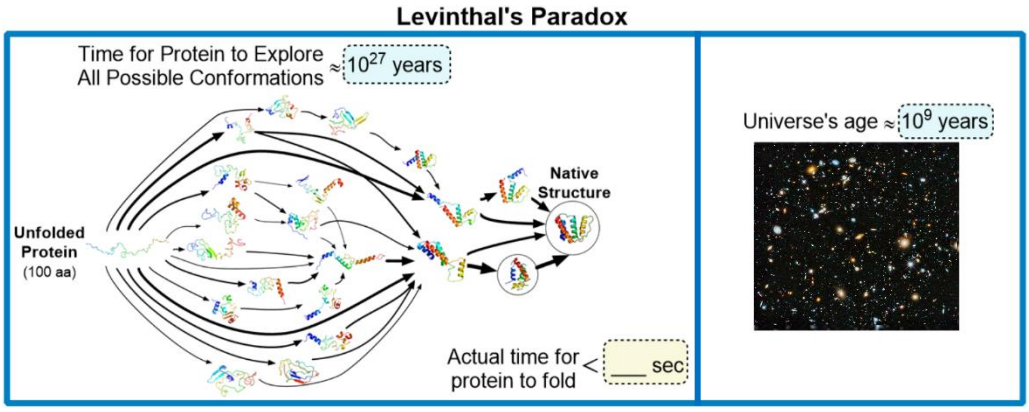
**Levinthal's Paradox**

●Cyrus Levinthal: disproved belief that protein folding is a random, "trial & error" process testing all possible conformations.

●Realized that would take too *long*: protein folding is *fast*, _____-random & must have predictable folding _____.

□ Cooperative, step-wise interactions between amino acids _____ up protein folding (folding short-cuts).

**EXAMPLE:**



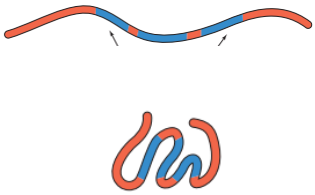

**PRACTICE:** Which of the following statements most accurately summarizes Levinthal's paradox?

a) A protein would essentially never find its native fold by sampling all possible conformations.
b) There are trillions of possible protein conformations, yet they strictly only adopt one.
c) With our current understanding of the laws of physics, we cannot explain protein folding.
d) Protein folding in nature occurs at a time scale many orders of magnitude longer than the age of the universe.

**CONCEPT:** PROTEIN FOLDING

**PRACTICE:** Draw each amino acid & determine which is most likely found in the blue regions of the folded protein below?

a) Asp. b) Glu. c) Ile. d) Gln.



**PRACTICE:** Which of the following occurs when myoglobin folds into its native conformation?

Myoglobin

a) Myoglobin adopts its lowest energy state form.
b) Most of the nonpolar, hydrophobic amino acid residues are found buried in myoglobin's core.
c) Most polar, charged, hydrophilic residues are found on the outside of myoglobin.
d) b and c.
e) All the above.

**PRACTICE:** In general, which option contains the major cooperative interactions driving spontaneous protein folding?

a) Hydrophobic interactions in the protein core & formation of hydrogen bonds in secondary structures.
b) Formation of salt bridges & disulfide bonds between R-groups that stabilize key interactions.
c) Reduced chain conformational entropy.
d) Restricting surrounding solvent molecules to have less rotational/conformational possibilities.