Protein Stability of a 21 Residue Alanine Based Peptide

Presented by

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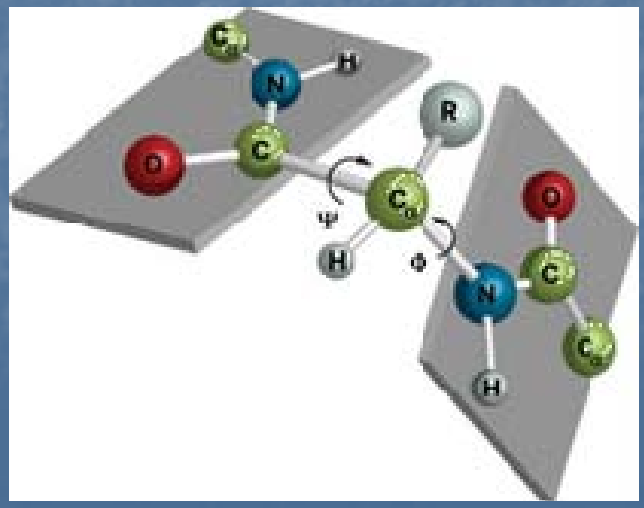
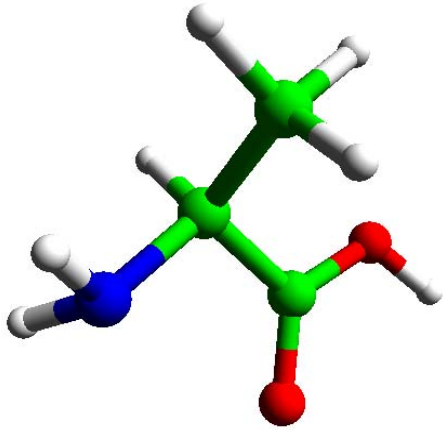
Biochemistry Background

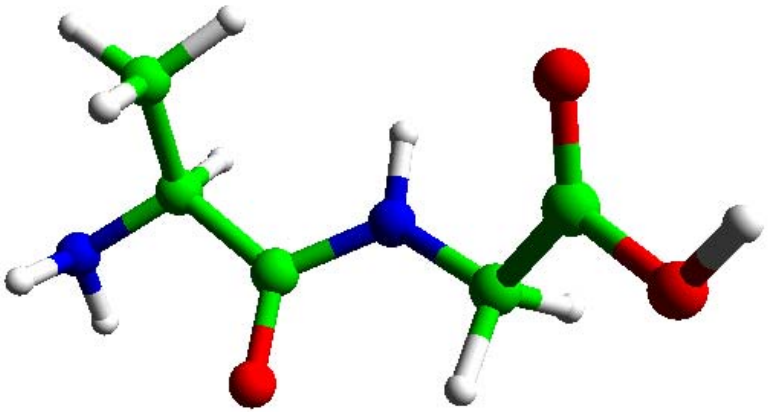
- Genes are used to make amino acids
  - The human genome is 3 billion DNA base pairs
  - Estimated 20,000-25,000 genes
- Amino acids are the basic building blocks of proteins
- Two major angles that biochemists are concerned with
  - Φ
  - Ψ



Protein Construction



Amino Acid



Peptide

-ALA-ALA-ARG-

Polypeptide

α-helix

The Problem

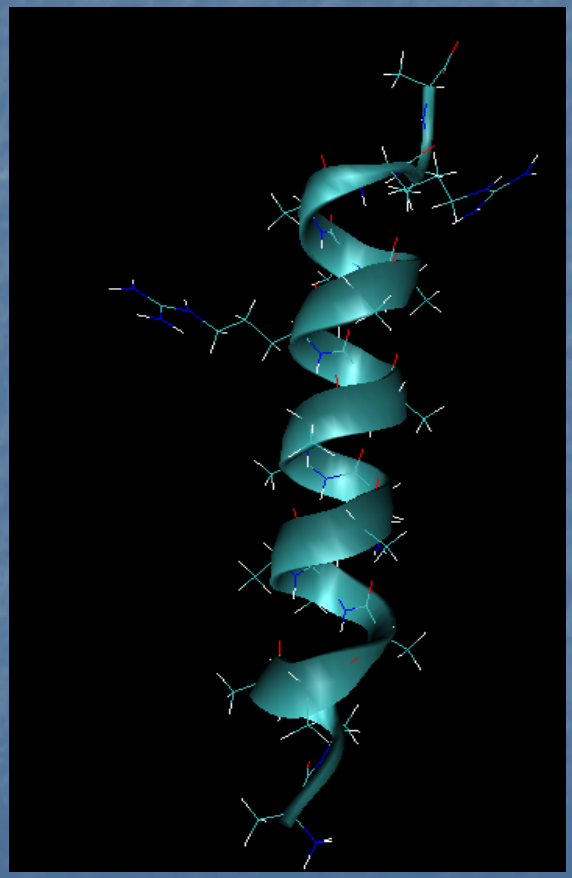
- The central dogma of biochemistry
  - How do proteins fold
  - How do external variants affect protein folding/stability
- Methods
  - Computational
  - X-ray crystallography
  - NMR spectroscopy
  - UV Raman
  - Fluorescence

Protein Folding/Stability

- Affected inter-molecular interactions
  - Amino acid hydrophobicity
  - Salt bridges
  - van der Waals forces
  - Ion-ion interactions
  - Hydrogen bonding
- Observed behaviors in salt solutions
  - Chloride destabilizes α-helices
  - Perchlorate stabilizes α-helices
  - Sulfate destabilizes α-helices

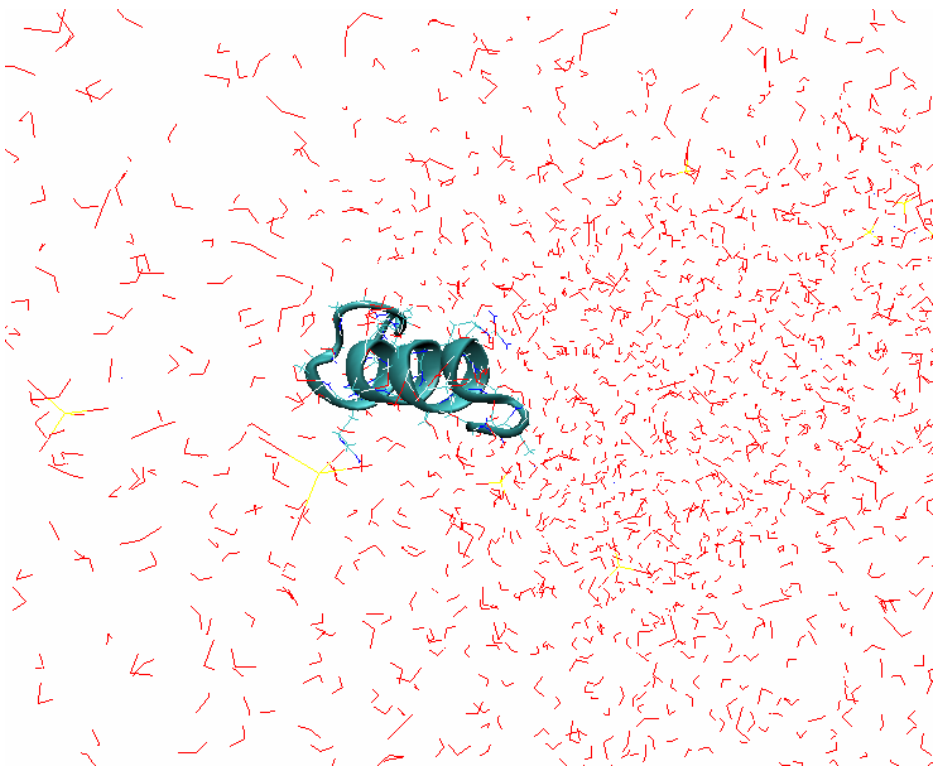
The peptide

- α-helical in structure
  - AAAAAAAARAAAARAAAARAA
- Melting temperature
  - 303K

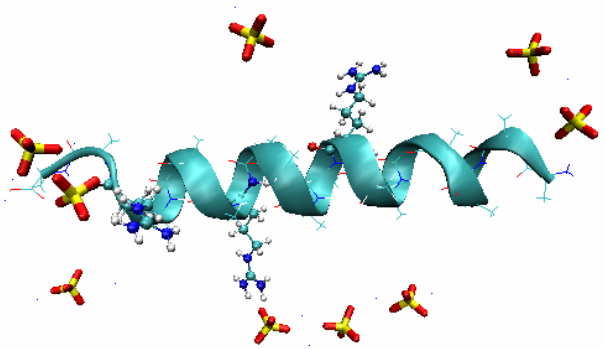


Molecular Dynamics

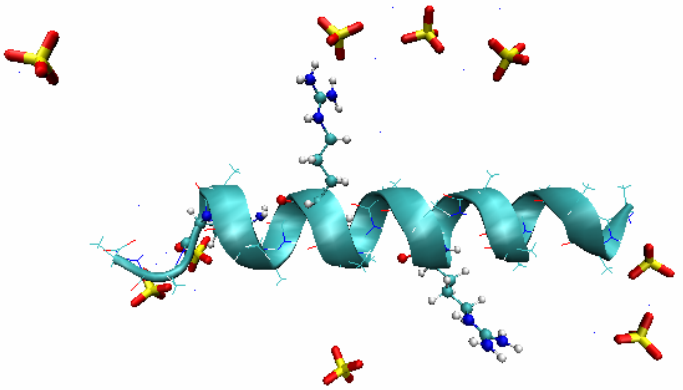
- Used AMBER 9
- System
  - 15 Sodiums added
  - 9 Sulfates added
  - 2338 molecules of Water
  - Temperature of 300K
  - Simulations ran for 70 ns
- Hardware
  - 8 Xeon processor cluster
  - 1 ns of simulation took 12 hours of clocktime to run



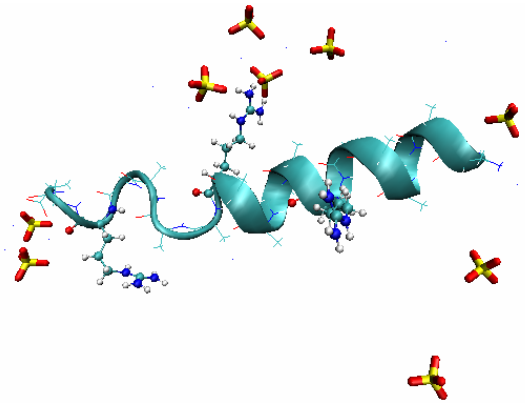
Preliminary Results



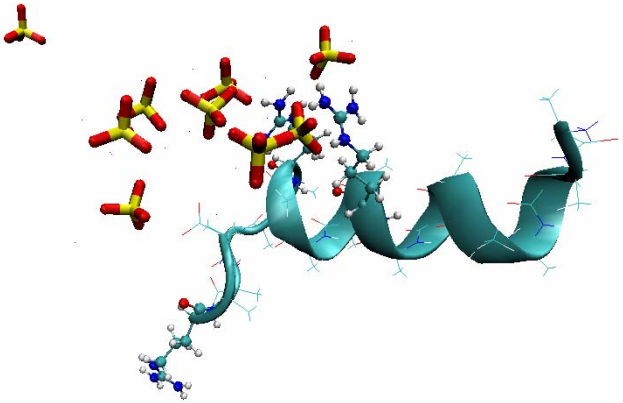
Initial helix



Equilibration



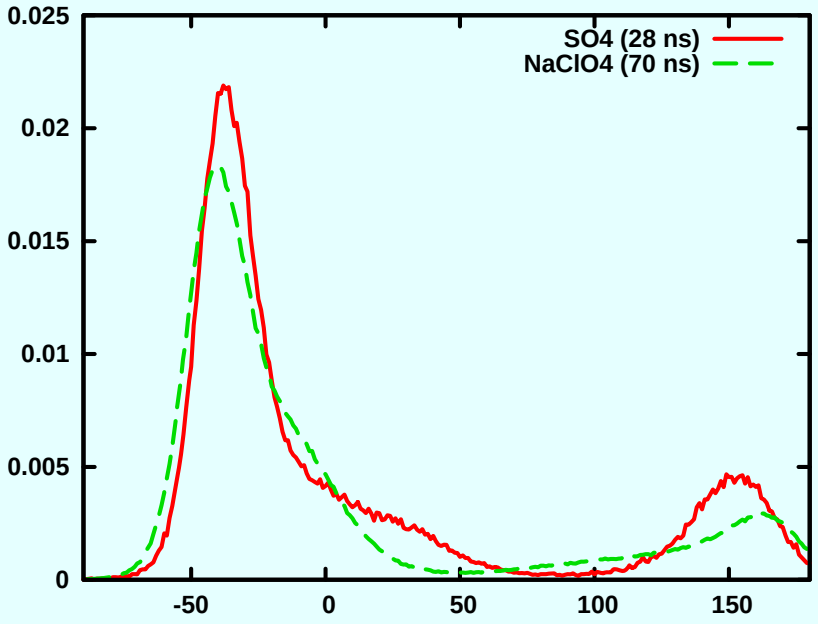
During Simulation



After 28 ns

Preliminary Conclusions

- Sodium Sulfate
  - Already unfolding after the equilibrations
  - Strong indicator of destabilization



- Phosphate and Acetate
  - Not unfolding after the equilibrations
  - Strong indicator of stabilization

Summary

- These simulations support previous experimental results
- They also support the trend of the Hoffmeister effect
- Based on results not discussed here, the change in solvent activity is the reason for stabilization

Thanks

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Questions