RMSD from Ideal Protein Geometry

RMSD from ideal geometry for htADH structure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bonds (Å)</td>
<td>0.007</td>
</tr>
<tr>
<td>angles (°)</td>
<td>1.30</td>
</tr>
<tr>
<td>dihedrals (°)</td>
<td>23.60</td>
</tr>
<tr>
<td>impropers (°)</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Peptide Plane Reduces the Number of Parameters

Tortion angles

\( \phi \) PHI

\( \Psi \) PSI

Tortion kinemage: C1basics.kin
Ramachandran Plot to Evaluate Outliers of “Good Protein Geometry”

**Ramachandran plot from htADH**

- core (%) 91.3%
- allowed (%) 8.2%
- generously allowed 0.4%
- disallowed none

### Trp Cage Peptide Sequence

```
1  5  10  15  20
N L Y I Q W L K D G G P S S G R P P S
```

### Hydrogen Bonding Connection

- L²:O......W⁶:H
- Y¹:O......L¹:H
- L¹:O......K¹:H
- G¹⁰:O......G¹¹:H
- G¹¹:O......G¹²:H
- W⁶:HE1...R¹⁵:O
- L²:O......G¹⁰:H
- W⁶:O......G¹¹:H
Molecular Dynamic Simulation of a designed mini-protein (Trp-cage)

From the Duan lab
http://www.duanlab.ucdavis.edu/

The movie shown 2 slides ahead is 69.5 MB and can be downloaded here.
amphipathic α-helix

http://www.umass.edu/molvis/tutorials/hemoglobin/hbostruc.htm
Protein Folding

Richard Dawkins analogy (pg. 56 text) “Methinks it is like a weasel.”

Nucleation (2º struct.) vs. hydrophobic collapse (molten globule)
**Macromolecular Protein Crystallography**

- Purified Protein
- Build model and refine
- Solve Phase

---

**Diffraction**

- Light Microscope 400-700 nm
  - uses lens to focus diffracted light into an image
- X-ray crystallography uses X-rays of 0.154 nm (1.54 Å); no x-ray lens available. First structure solved 1959 by John Kendrew and Max Perutz of myoglobin and hemoglobin
- Need to know wavelength, for Cu sources its 1.54 Å
- Need to measure Amplitude of Diffracted Reflections
  - Intensity is proportional to $A^2$
- Need to estimate the relative phase
Proteins can form an ordered lattice

Growing Protein Crystals: by Vapor Diffusion

- Hanging drop method
  - Widely used
- Fast
- Simple
- Inexpensive
- Test for growth in a variety of conditions
Overview of X-ray Experiment

Protein crystal in a loop

X-ray Equipment in CBC at Delaware

RU-H3R
X-ray generator

Area Detector

Crystal mounted on a loop here
Zoom into a single reflection

Movie of a Data Collection
Active Site and Complete Model of IDH

2Fo – Fc map

\[ \rho(x, y, z) = \frac{1}{V} \sum_{h} \sum_{k} \sum_{l} |2F_o| - |F_c| e^{-2\pi i (hx + ky + lz - \alpha \text{calc})} \]

What does electron density look like at different limits of resolution?