Coiled Coils

7.88J Protein Folding

Prof. David Gossard
September 24, 2003
PDB Acknowledgements

The Protein Data Bank (PDB - http://www.pdb.org/) is the single worldwide repository for the processing and distribution of 3-D biological macromolecular structure data.


PDB molecules and citations used in the “Coiled Coils” Lecture Notes for 7.88J - Protein Folding

PDB ID: 2ZTA


Pages: 3 (“Outline”), 14-15 (“GCN4 Leucine Zipper”)
Outline

• Review Key Features of Coiled Coils

• Examine a Particular Example
  – GCN4 Leucine Zipper (2ZTA)
Coiled Coils

- **Left-handed** spiral of right-handed helices
- May be parallel

or anti-parallel
2-Stranded Coiled Coils

- GCN4
- Tropomyosin
- Intermediate filament protein
- Lamin
- M-protein
- Paramyosin
- Myosin
Crick’s Models

- Geometry of Helix (Coil)

\[ x(t) = r_0 \cos(\omega_o \ t) \]
\[ y(t) = r_0 \sin(\omega_o \ t) \]
\[ z(t) = P \left( \frac{\omega_o \ t}{2\pi} \right) \]

\( \omega_o > 0 \) right-handed
Geometry of Coiled-Coil

\[
x(t) = r_0 \cos \omega_0 t + r_1 \cos \omega_0 t \cos \omega_1 t - r_1 \cos \alpha \sin \omega_0 t \sin \omega_1 t
\]

\[
y(t) = r_0 \sin \omega_0 t + r_1 \sin \omega_0 t \cos \omega_1 t + r_1 \cos \alpha \cos \omega_0 t \sin \omega_1 t
\]

\[
z(t) = p_0 (\omega_0 t) - r_1 \sin \alpha \sin \omega_1 t
\]

\[\alpha = \tan^{-1} \left( \frac{2 \pi r_1}{p_0} \right)\]


Features of Coiled Coil

- Heptad repeat in sequence
  \[ [a \ b \ c \ d \ e \ f \ g]_n \]
- Hydrophobic residues at “a” and “d”
- Charged residues at “e” and “g”

Figure adapted from Cohen, et.al., PROTEINS: Structure, Function and Genetics 7:1-15 (1990)
Significance of Heptad Repeat

• Hydrophobic residues at “a” and “d”
  – form hydrophobic core with other coil

• Charged residues at “e” and “g”
  – form ion pairs with oppositely charged residues on other coil
  – may distinguish parallel from anti-parallel coiled coils
Heptad Repeat in 3D

Hydrophobic residues

Charged residues

+/−  −/+
Hydrophobic Core is on Axis of Superhelix (~Straight)
Charged Residues Provide Stability, Registration

Charged residues “e” and “g”

Ion pairs between coils
“Knobs in Holes” Packing

Figure adapted from Crick, F. H. C. “The Packing of α-helices: Simple Coiled-coils.” *Acta Cryst.* 6 (1953): 689-697.
GCN4 Leucine Zipper (2ZTA)

• Parallel Coiled Coil
• Major helix pitch ~ 180 Å/turn
• 8 turns
• 31 residues

GCN4 Leucine Zipper (2ZTA)

- Residues contain heptad repeat

<table>
<thead>
<tr>
<th></th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARG1</td>
<td>MET2</td>
<td>LYS3</td>
<td>GLN4</td>
<td>LEU5</td>
<td>GLU6</td>
<td>ASP7</td>
<td>LYS8</td>
</tr>
<tr>
<td>VAL9</td>
<td>GLU10</td>
<td>GLU11</td>
<td>LEU12</td>
<td>LEU13</td>
<td>SER14</td>
<td>LYS15</td>
<td></td>
</tr>
<tr>
<td>ASN16</td>
<td>TYR17</td>
<td>HIS18</td>
<td>LEU19</td>
<td>GLU20</td>
<td>ASN21</td>
<td>GLU22</td>
<td></td>
</tr>
<tr>
<td>VAL23</td>
<td>ALA24</td>
<td>ARG25</td>
<td>LEU26</td>
<td>LYS27</td>
<td>LYS28</td>
<td>LEU29</td>
<td></td>
</tr>
<tr>
<td>VAL30</td>
<td>GLY31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Ion pairs
  - Lys$^{15}$ – Glu$^{20'}$
  - Glu$^{22}$ – Lys$^{27'}$
  - Glu$^{22'}$ – Lys$^{27}$
Crossing Angle $\sim 18^\circ$
Molecular Surface of GCN4
3D Demonstrations

• Tour of Heptad Repeat (3D Studio MAX)

• Tour of GCN4 (Swiss-PDB)
3 & 4-Stranded Coiled Coils

- 3-stranded
  - Gp17 (T7)
  - Fibrinogen (heterotrimer)
  - GCN4 mutant
- 4-stranded parallel
  - GCN4 mutants
- 4-stranded anti-parallel
  - Myohaemerythrin
  - Tobacco mosaic virus
  - Cytochrome c’
  - Apoferritin
3-Stranded Coiled Coil!? (parallel)

- Axial symmetry
- Hydrophobic core
- Ion pairs

Figure adapted from Cohen, C., and D.A. D. Perry, “α-helical coiled coils and bundles: How to design an α-helical protein.” PROTEINS: Structure, Function, and Genetics 7 (1990): 1-15.
4-Stranded Coiled Coil!? (parallel)

- Axial symmetry
- Hydrophobic core
- Ion pairs

Figure adapted from Cohen, C., and D.A.D. Perry, “α-helical coiled coils and bundles: How to design an α-helical protein.” PROTEINS: Structure, Function, and Genetics 7 (1990): 1-15.
Recall - GCN4

- Hydrophobic core:
  “a” (blue)    “d” (red)
  Val9      Leu5
  Asn16    Leu12
  Val23    Leu19
  Val30    Leu26

Harbury, P. B., Tao Zhang, Peter S. Kim, and Tom Alber.
Mutagenized Hydrophobic Core

- p-LI (X => Leu - volume-preserving)
  - “a”  “d”
  - Leu9  Ile5
  - Leu16  Ile12
  - Leu23  Ile19
  - Leu30  Ile26

- => tetramer (parallel) !!
Mutant p-LI

GCN4

P-LI
GCN4 p-LI

• Ion pairs/salt bridges
  – ‘e’ & ‘g’ (5/12)
    • GluB6 – ArgA1
  – ‘g’ & ‘b’ (4/8)
    • LysD8 – GluA10
  – ‘e’ & ‘c’ (5/8)
    • HisB18 – GluC20