

Coiled Coils

7.88J Protein Folding

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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.

Berman, H. M., J. Westbrook, Z. Feng, G. Gilliland, T. N. Bhat, H. Weissig, I. N. Shindyalov, and P. E. Bourne. "The Protein Data Bank." *Nucleic Acids Research* 28 (2000): 235-242.

(PDB Advisory Notice on using materials available in the archive: <http://www.rcsb.org/pdb/advisory.html>)

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

PDB ID: 2ZTA

JRNL reference: O'Shea, E. K., J. K. Klemm, P. S. Kim., and T. Alber. "X-ray structure of the GCN4 leucine zipper, a two-stranded, parallel coiled coil." *Science* 254 (1991): 539.

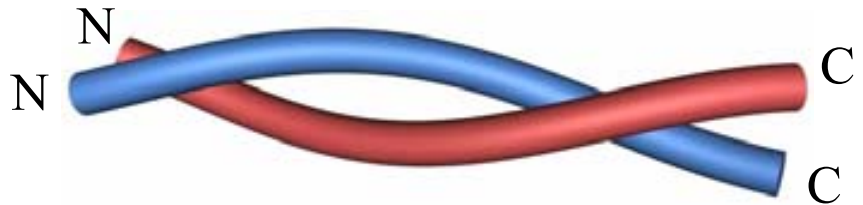
Pages: 3 ("Outline"), 14-15 ("GCN4 Leucine Zipper")

Outline

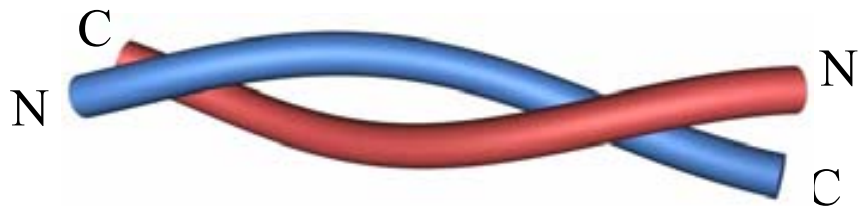
- Review Key Features of Coiled Coils
- Examine a Particular Example
 - GCN4 Leucine Zipper (2ZTA)

Coiled Coils

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

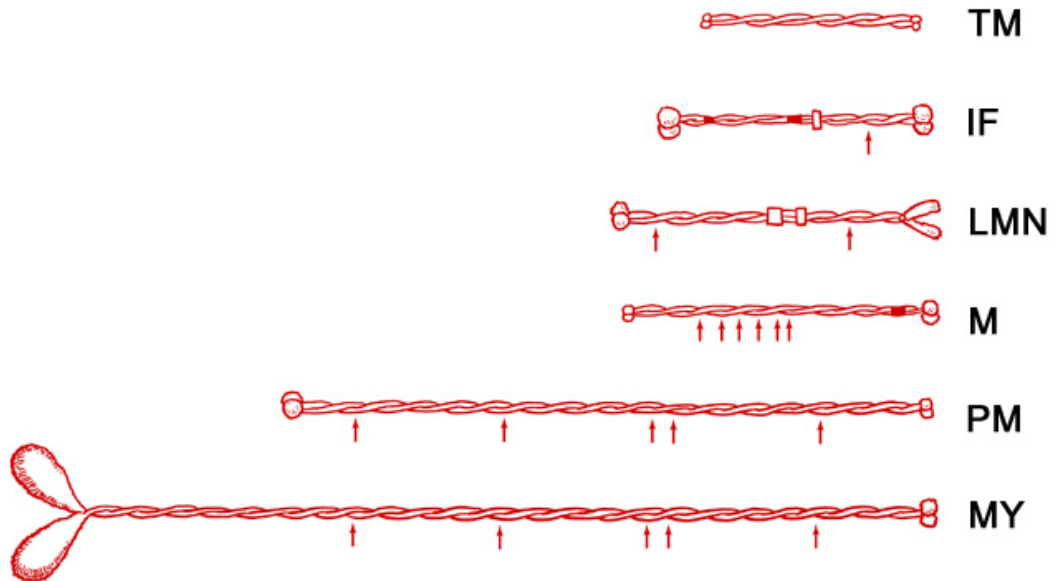


or anti-parallel



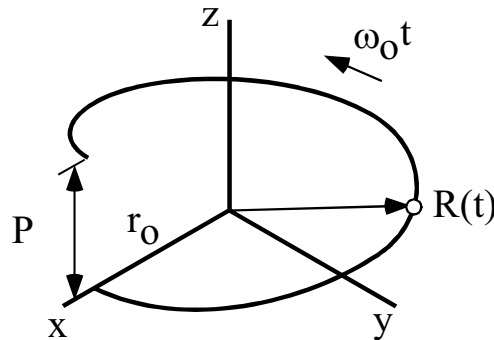
2-Stranded Coiled Coils

- GCN4
- Tropomyosin
- Intermediate filament protein
- Lamin
- M-protein
- Paramyosin
- Myosin



Crick's Models

- Geometry of Helix (Coil)



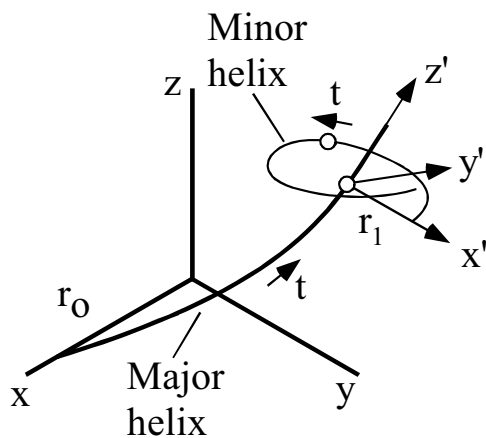
$\omega_0 > 0$ right-handed

$$x(t) = r_0 \cos(\omega_0 t)$$

$$y(t) = r_0 \sin(\omega_0 t)$$

$$z(t) = P (\omega_0 t / 2\pi)$$

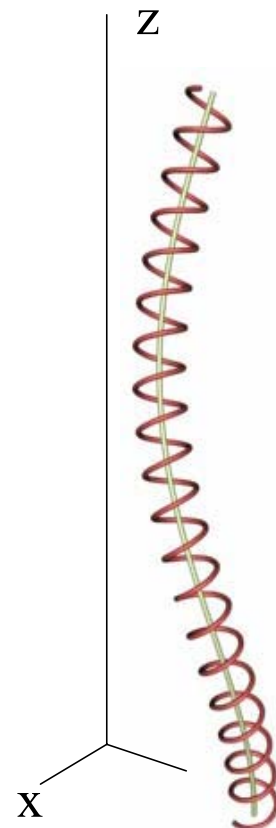
Geometry of Coiled-Coil



$\omega_0 < 0$ Major axis left-handed
 $\omega_1 > 0$ Minor axis right-handed

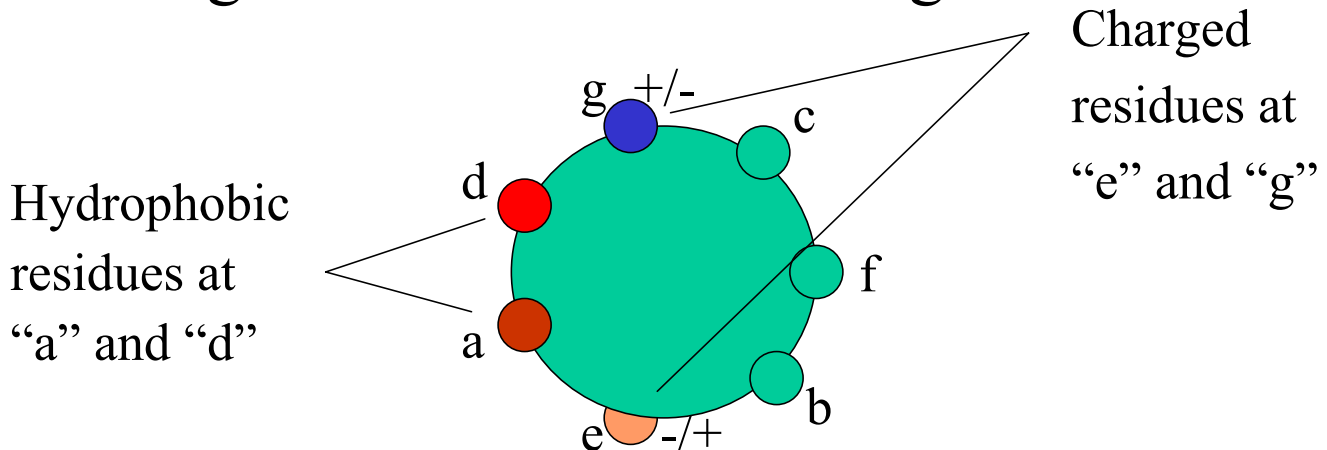
$$\begin{aligned}
 x(t) &= r_0 \cos \omega_0 t + r_1 \cos \omega_0 t \cos \omega_1 t - r_1 \cos \alpha \sin \omega_0 t \sin \omega_1 t \\
 y(t) &= r_0 \sin \omega_0 t + r_1 \sin \omega_0 t \cos \omega_1 t + r_1 \cos \alpha \cos \omega_0 t \sin \omega_1 t \\
 z(t) &= p_0(\omega_0 t) - r_1 \sin \alpha \sin \omega_1 t
 \end{aligned}$$

$$\alpha = \tan^{-1} (2\pi r_0 / p_0)$$



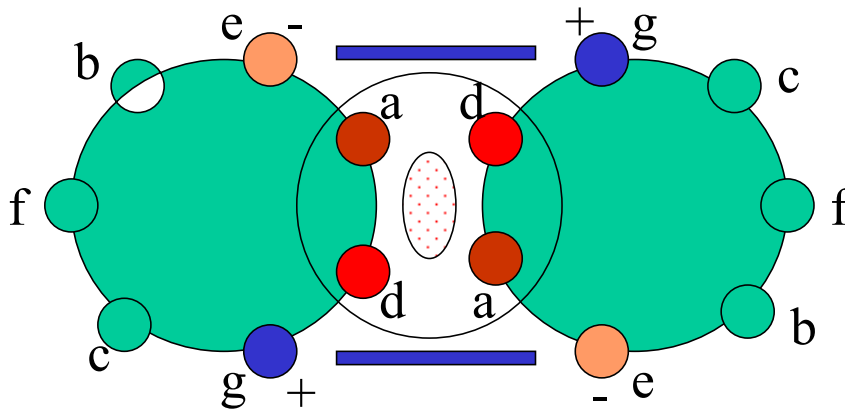
Features of Coiled Coil

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

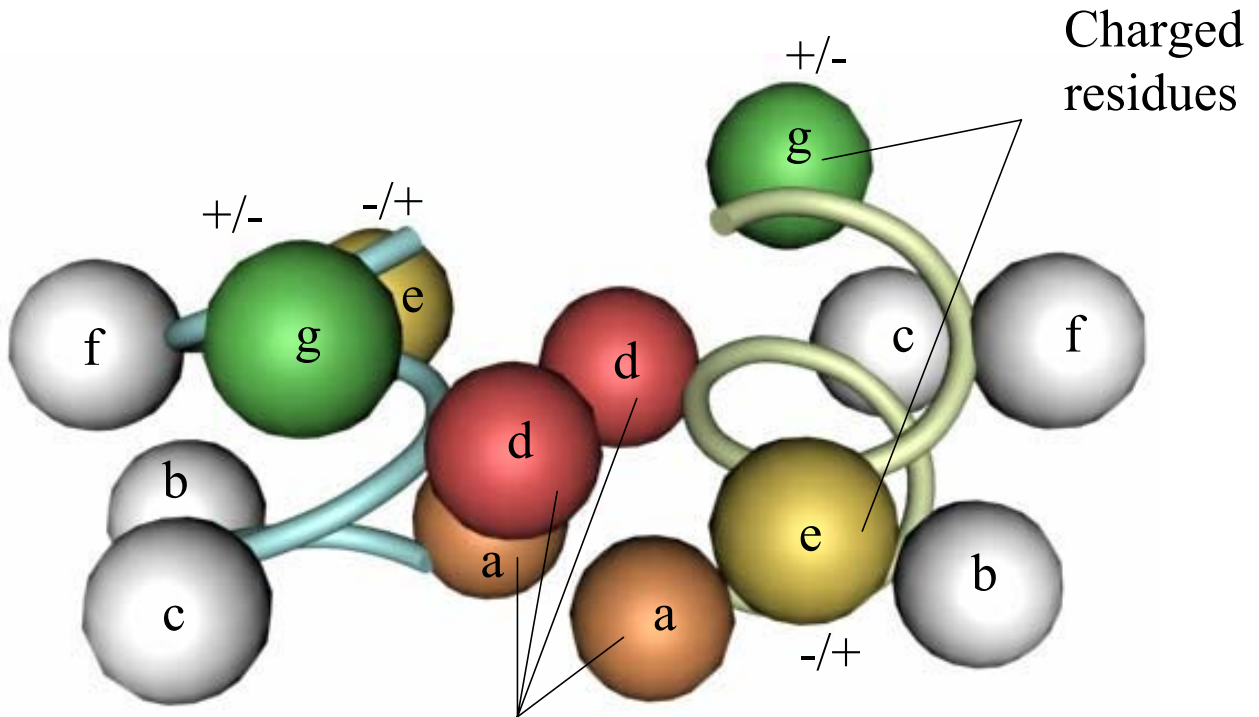


Significance of Heptad Repeat

- 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

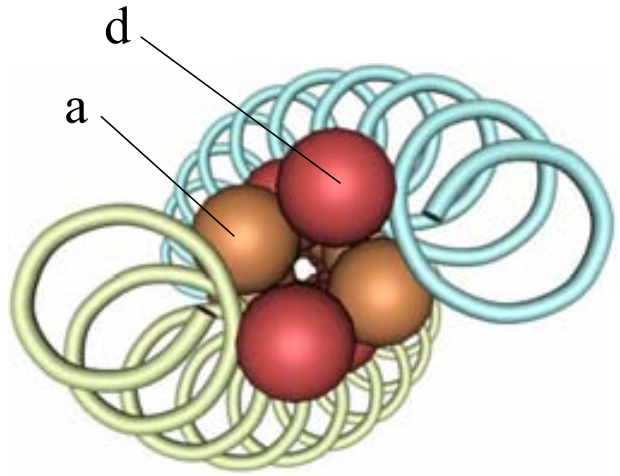
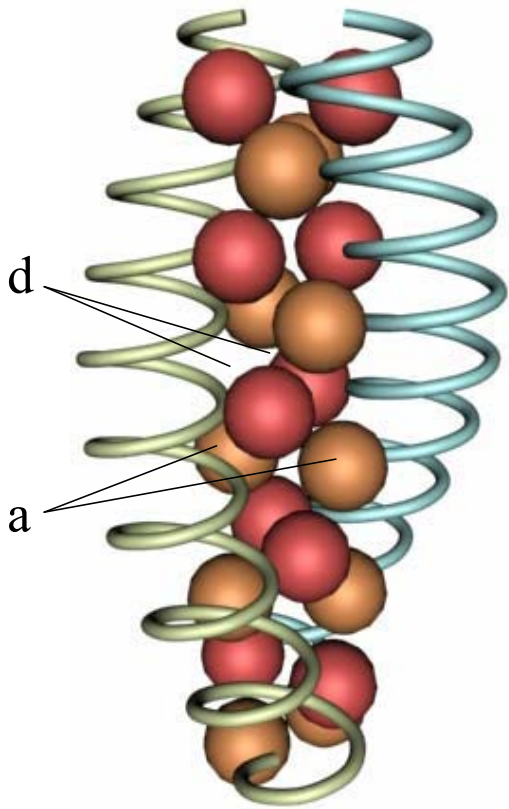


Heptad Repeat in 3D

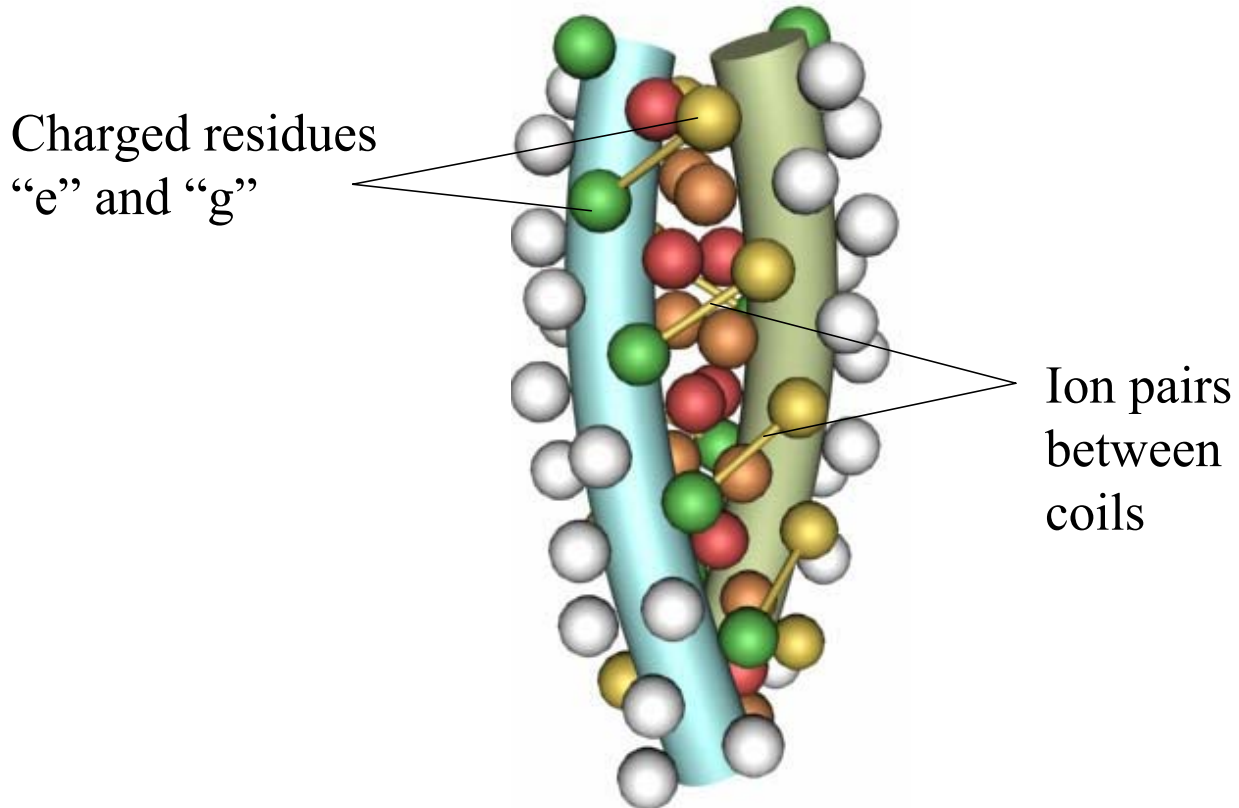


Hydrophobic residues

Hydrophobic Core is on Axis of Superhelix (~Straight)



Charged Residues Provide Stability, Registration



“Knobs in Holes” Packing

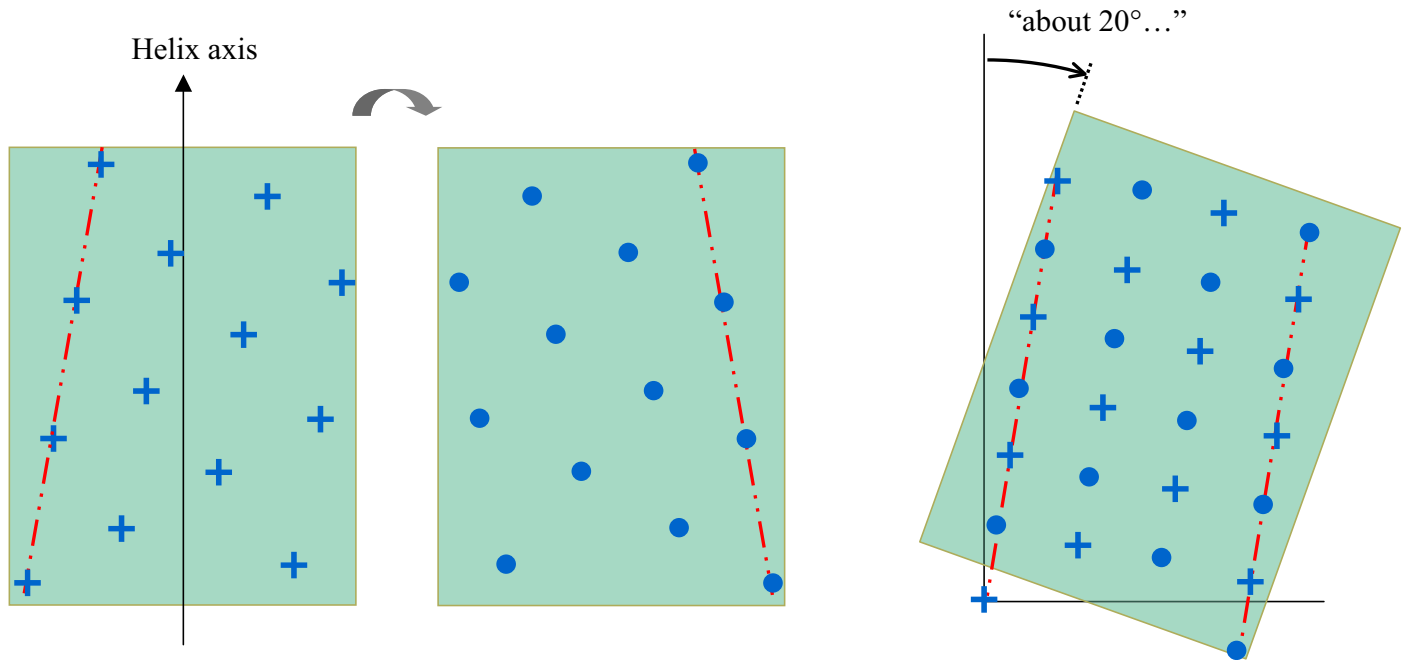
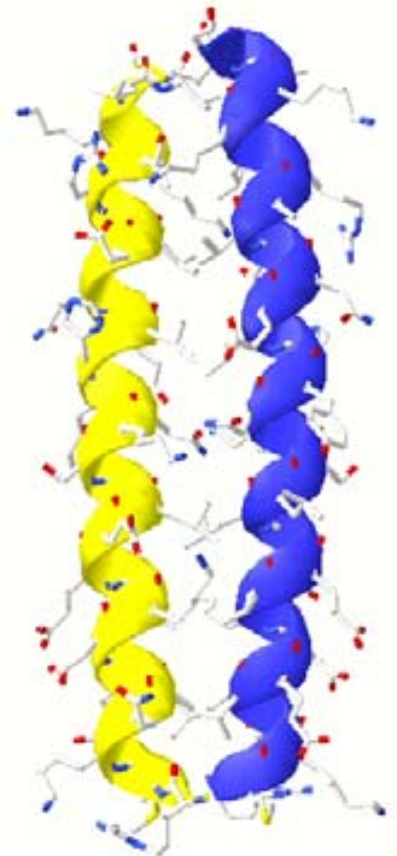


Figure adapted from Crick, F. H. C. “The Packing of α -helices: Simple Coiled-coils.” *Acta Cryst.* 6 (1953): 689-697.

GCN4 Leucine Zipper (2ZTA)

- Parallel Coiled Coil
- Major helix pitch ~ 180 A/turn
- 8 turns
- 31 residues

O'Shea, Erin, Juli D. Klemm, Peter S. Kim, and Tom Alber,
"X-ray Structure of the GCN4 Leucine Zipper, a Two-Stranded,
Parallel Coiled Coil." *Science* **254** (October 25, 1991): 539-544.

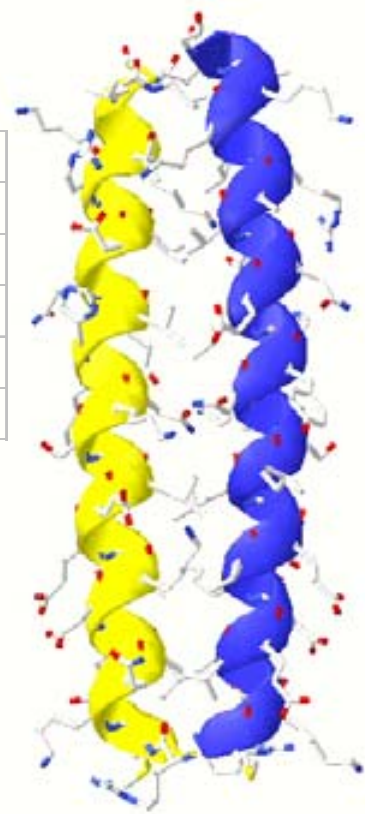


GCN4 Leucine Zipper (2ZTA)

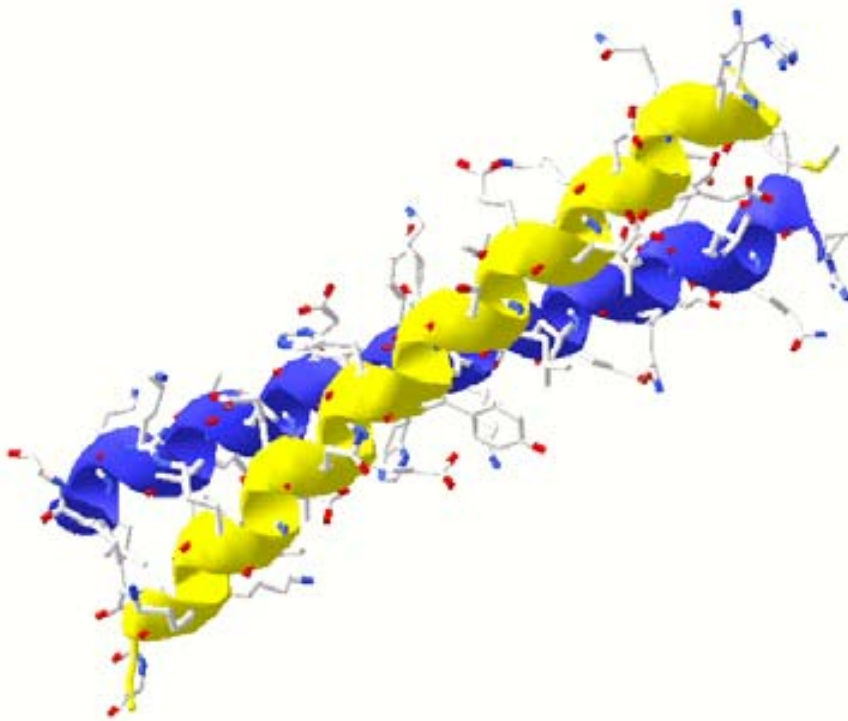
- Residues contain heptad repeat

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

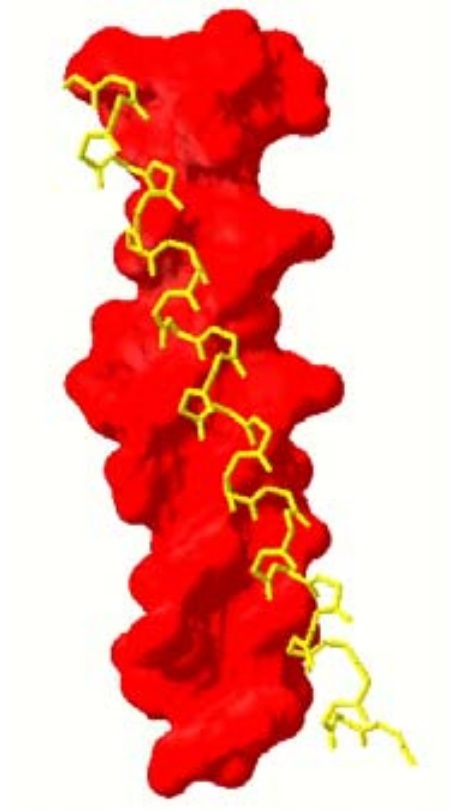
- Ion pairs
 - Lys¹⁵ – Glu^{20'}
 - Glu²² – Lys^{27'}
 - Glu^{22'} – Lys²⁷



Crossing Angle $\sim 18^\circ$



Molecular Surface of GCN4

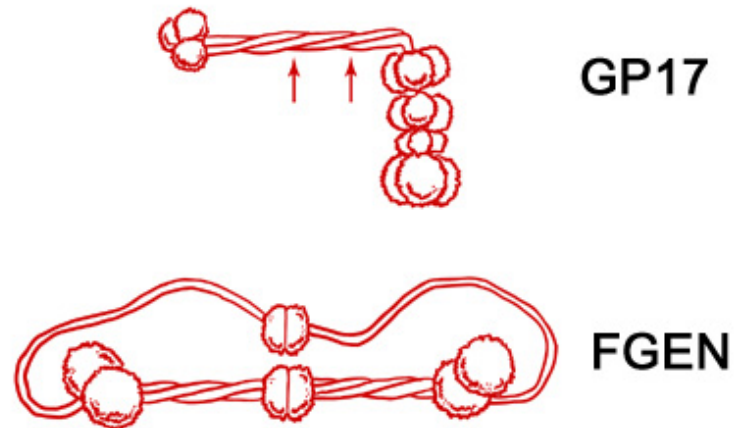


3D Demonstrations

- 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

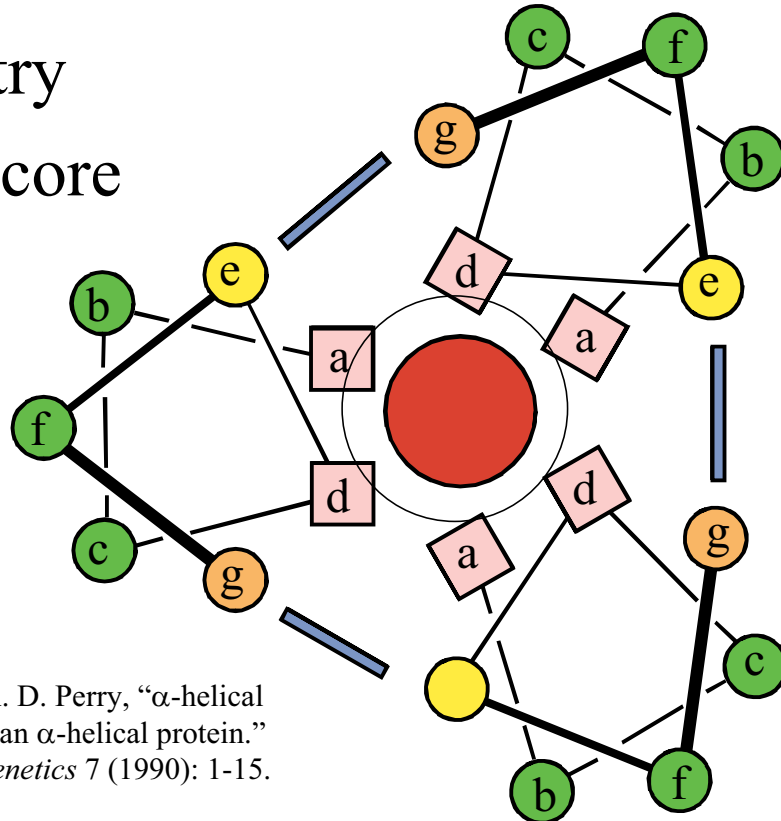


Figure adapted from Cohen, C., and D.A. D. Perry, "α-helical coiled coils and bundles: How to design an α-helical protein." *PROTEINS: Structure, Function, and Genetics* 7 (1990): 1-15.

4-Stranded Coiled Coil! (parallel)

- Axial symmetry
- Hydrophobic core
- Ion pairs

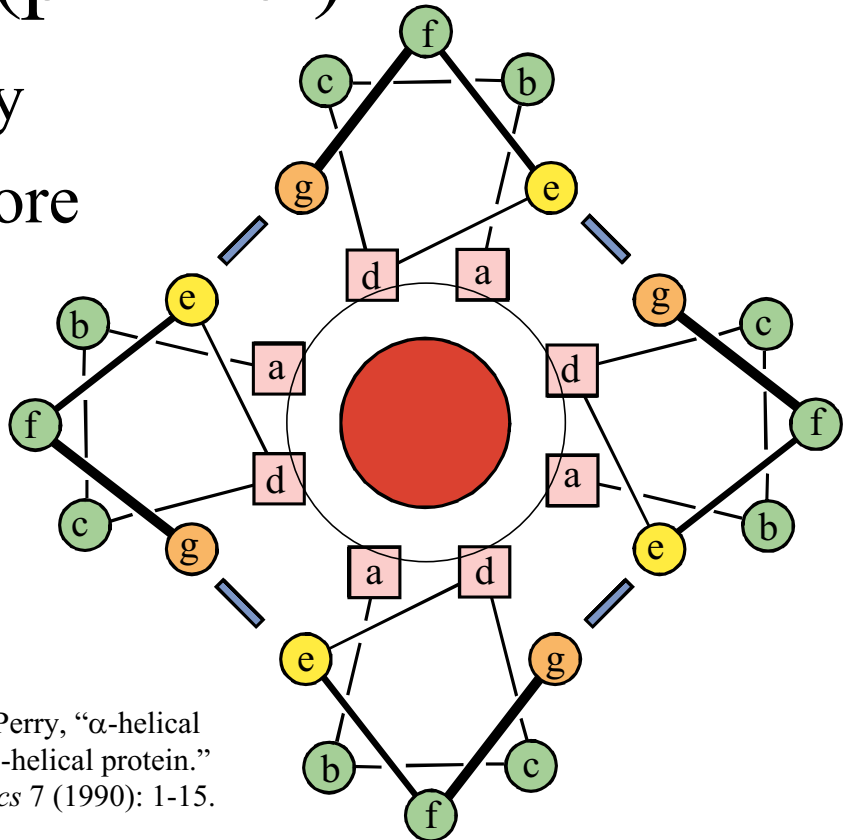


Figure adapted from Cohen, C., and D.A.D. Perry, "α-helical coiled coils and bundles: How to design an α-helical protein." *PROTEINS: Structure, Function, and Genetics* 7 (1990): 1-15.

Recall - GCN4

- Hydrophobic core:

“a” (blue) “d” (red)

Val9

Leu5

Asn16

Leu12

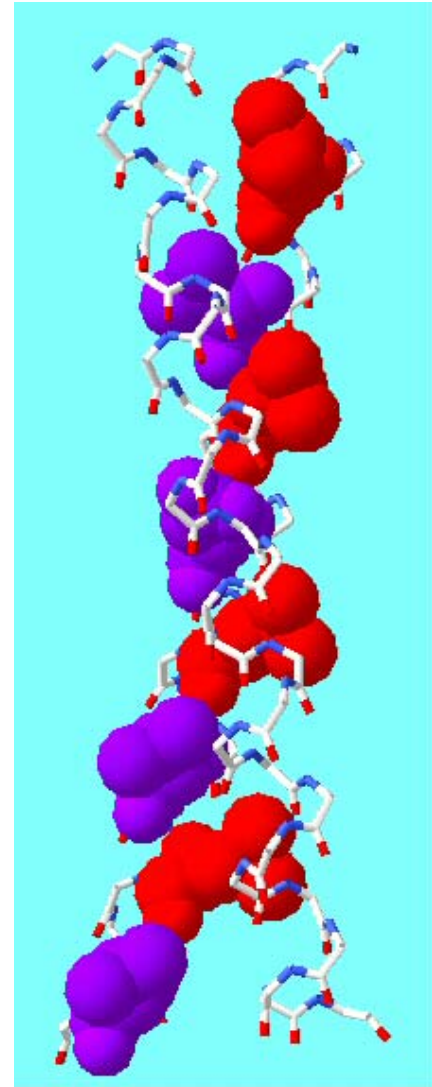
Val23

Leu19

Val30

Leu26

Harbury, P. B., Tao Zhang, Peter S. Kim, and Tom Alber.
“A Switch Between Two-, Three-, and Four-Stranded Coiled Coils
in GCN4 Leucine Zipper Mutants.” *Science* **262** (1993): 1401-1407.



Mutagenized Hydrophobic Core

- p-LI (X => Leu - volume-preserving)

“a” “d”

Leu9 Ile5

Leu16 Ile12

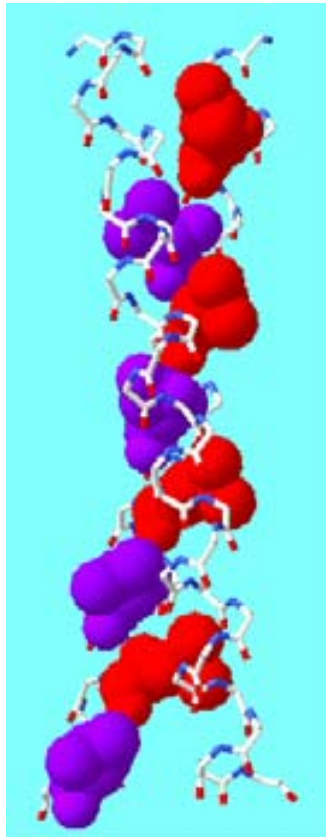
Leu23 Ile19

Leu30 Ile26

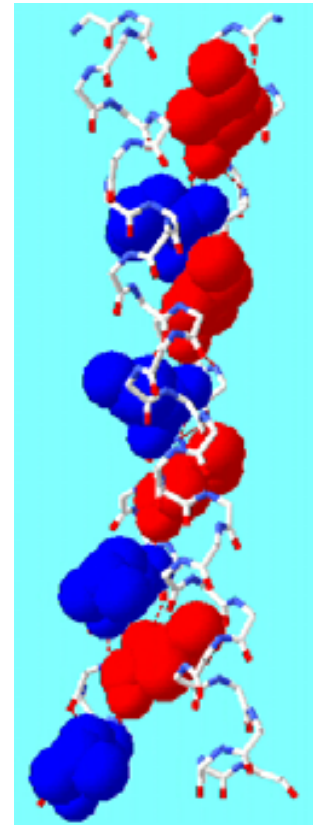
- => tetramer (parallel) !!

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

