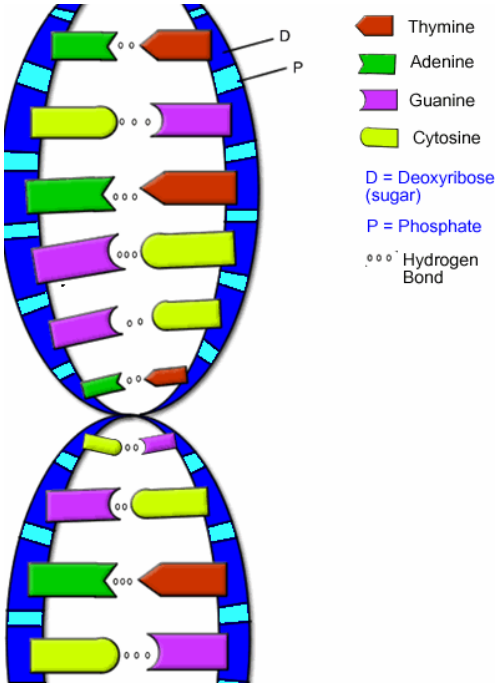
Protein synthesis (Primer)

Central Dogma of Molecular Biology states that information flow from

DNA ➔ RNA ➔ protein

DNA is made of phosphonucleotides (phosphoate + sugar + base)

Genetic information is encoded in a string of DNA bases (A,C,G,T)



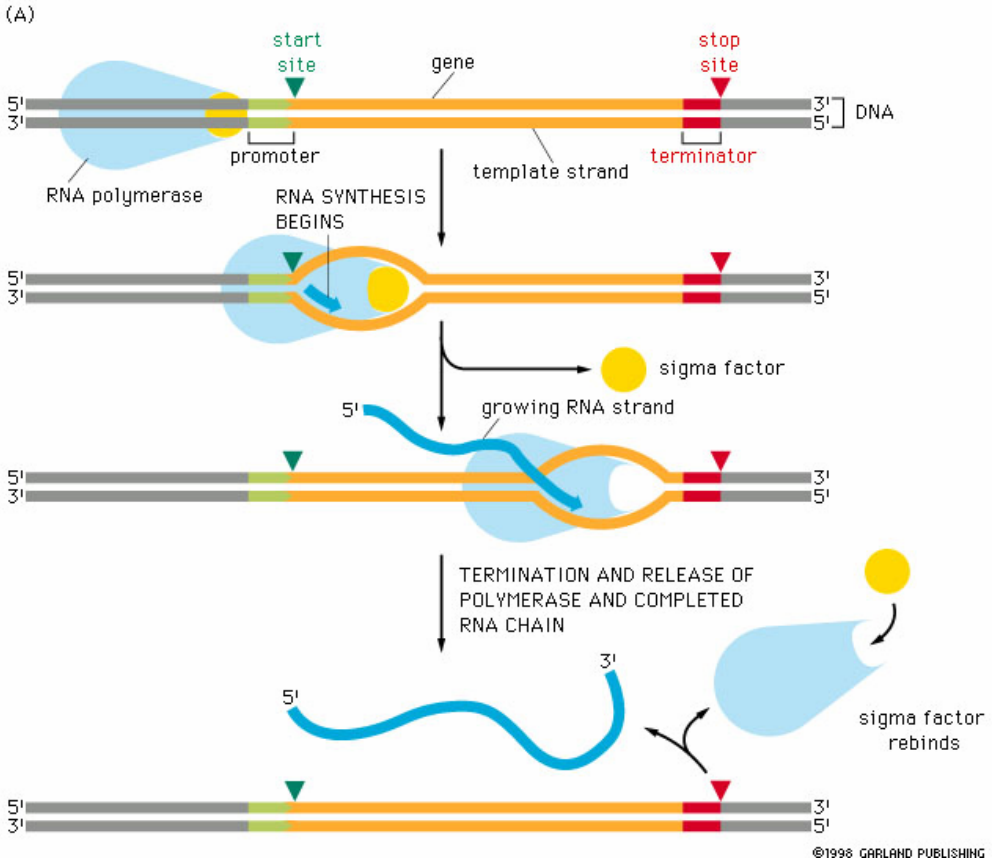
Hydrogen bond mediated base pairing (A**T, C**G)

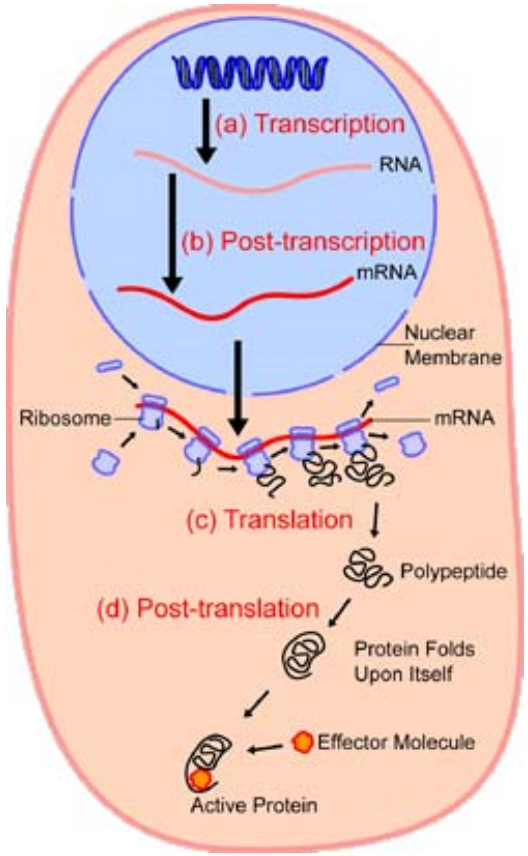
- protects DNA bases from chemical damages
- allows repair using the undamaged strand as template recombination

Three DNA bases are ultimately translated to one amino acid

Transcription

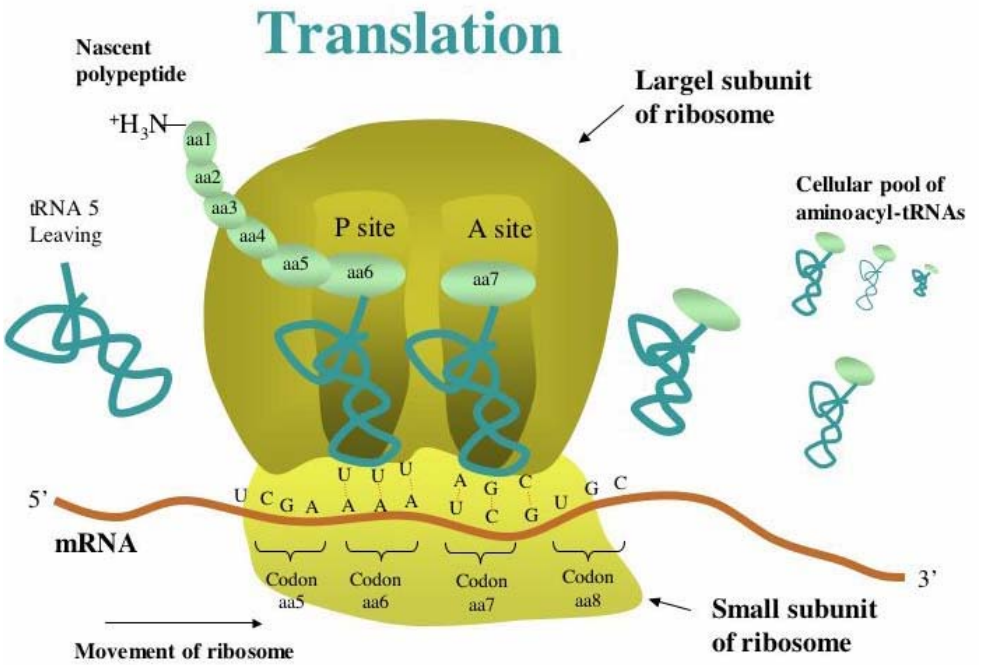
The first step in protein synthesis is copying the genetic information stored in DNA to messenger RNA in a process called **transcription**

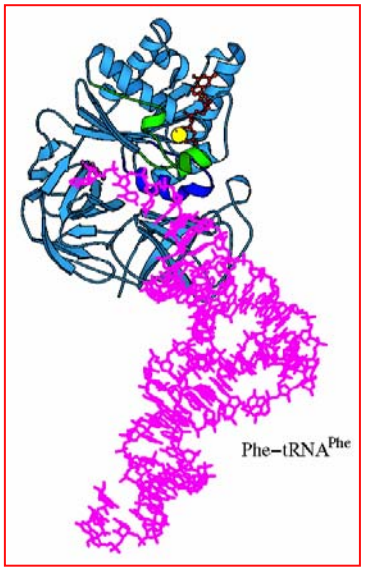




mRNA then undergoes editing, including **base insertion, base deletion and base modifications** --Smith et al, RNA 3, 1105 (1997)

mRNA leaves the nucleus and enters the cytoplasm (in eukaryotes), where ribosome, aminoacyl tRNA ("charged" or "loaded" tRNA) come together to synthesizing a polypeptide chain. This process is called **translation**





Synthesis is done, what next?

Once synthesized, proteins must first fold to stable conformations in order to function, ...

although there are also intrinsically disordered proteins

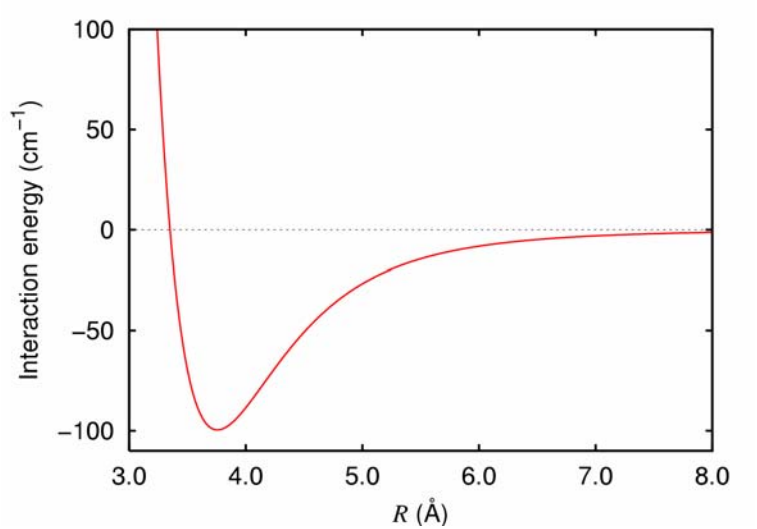
Hansen and Woody, J Biol Chem 281, 1853 (2006)

The folding of a peptide chain minimizes the total free energy of the system, which is a combination of

- entropy change in
  - » solvent molecules (usually water)
  - » protein (both main chain and side chain)
  - » disulfide
- enthalpy
  - » van der Waals contact (hydrophobic effects)
  - » hydrogen bonding interaction (intramolecular as well as protein-water)
  - » electrostatic interaction
  - » disulfide

van der Waals interaction

- Arise from interactions from transient fluctuating dipole moments
- Attractive at long distances, repulsive at short distances
- Also called London dispersion force, it is usually modeled using 12-6 Lennard-Jones potential



$$E = \frac{A}{r^{12}} - \frac{B}{r^{6}} = \varepsilon\left[\left(\frac{r_m}{r}\right)^{12} - 2\left(\frac{r_m}{r}\right)^{6}\right]$$

for C-C pair, $\varepsilon \sim 0.05 - 0.2$ kcal/mol,

$r_m \approx$ 3.5 - 4 ang

Optimal distance between 2 non-interacting atoms is the bottom of the potential energy function.

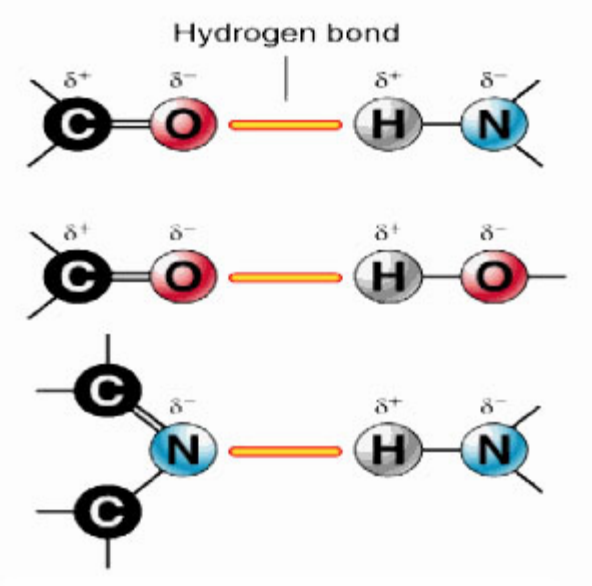
Atom	Radius (Å)
Hydrogen	1.20
Carbon	1.7
Nitrogen	1.55
Oxygen	1.52
Fluorine	1.35
Phosphorus	1.9
Sulphur	1.85
Chlorine	1.8

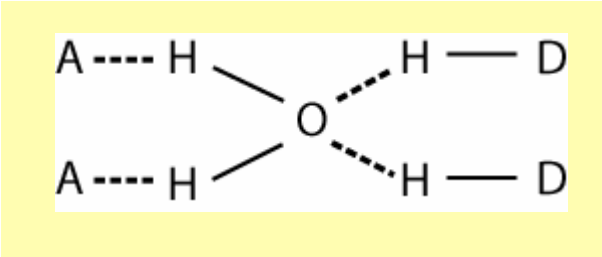
Hydrogen Bond

A sharing of a hydrogen by two electronegative heavy atoms

The hydrogen is covalently attached to one of the two heavy atoms (donor) and interacts electrostatically with the electron lone pair of the other heavy atom (acceptor)

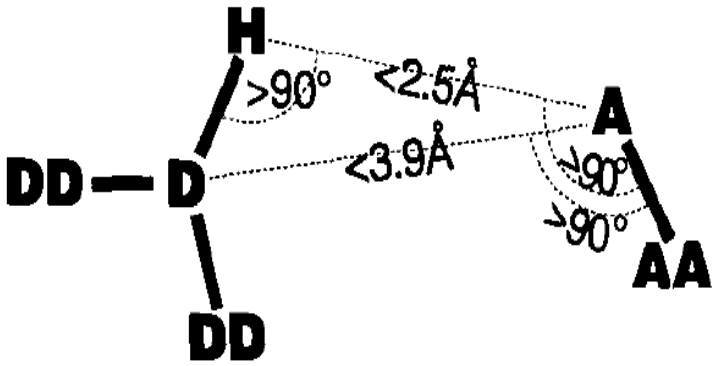
In proteins, hydrogen bonds typically occur as N—H *** O = C (68%), although other combinations are possible and sulfur and carbon atoms can also participate in a hydrogen bond



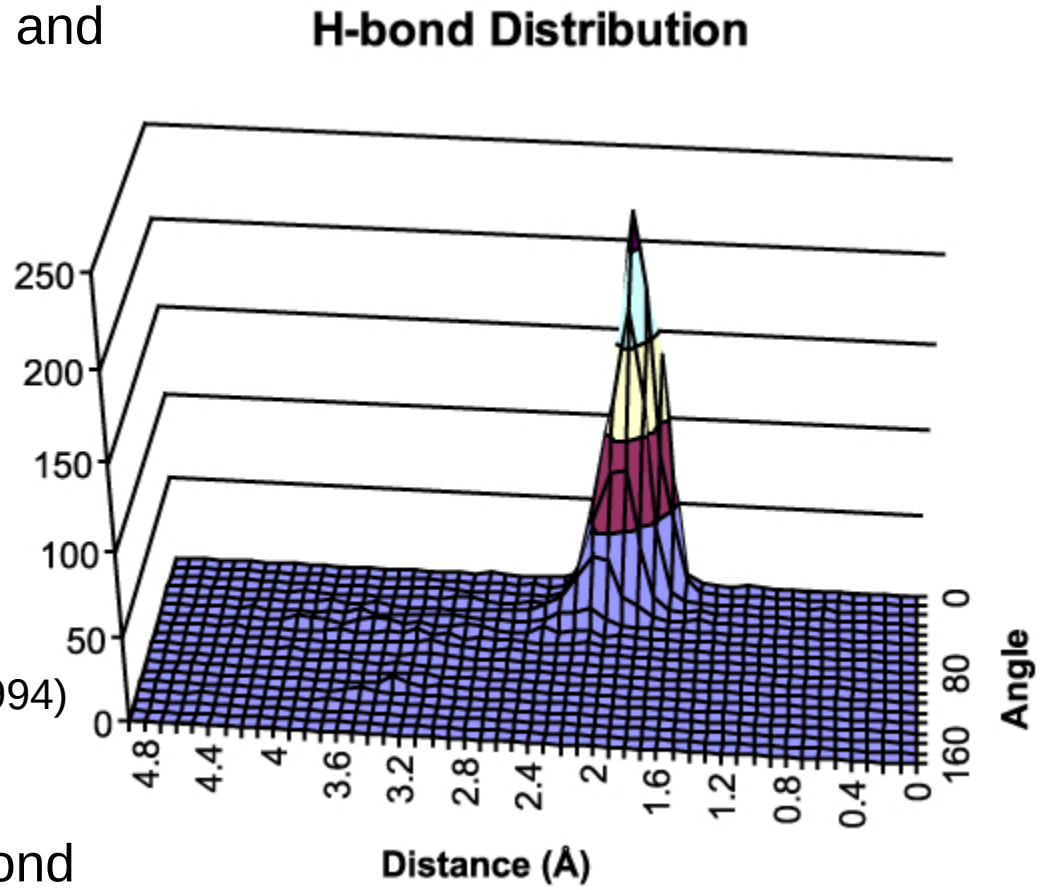


Distribution of hydrogen bonds

Hydrogen bonds are directional and defined by geometry



McDonald & Thornton, JMB, 238, 777 (1994)



stabilization by one hydrogen bond
$\Delta G \sim -0.6$ kcal/mol

Pace et al, Faseb J 10, 75 (1996)

Park & Saven, Proteins, 60, 450 (2005)

Electrostatic interaction

Coulombic interaction between positively and negatively charged side chains

Also called salt bridges, contributes to the stability of protein structure

$$E_{elec} \propto \frac{q_1 q_2}{\varepsilon r_{12}}$$

where epsilon is the dielectric constant
N.B. this epsilon is different from the epsilon in van der Waals force

Epsilon = 80 in water, whereas epsilon ~ 4 in lipid (or inside the protein core)

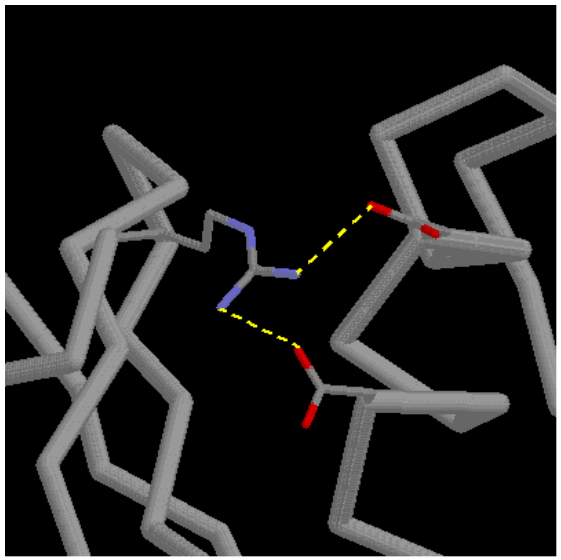
Hence, salt bridges exposed to the solvent is not as energetically significant as salt bridges shielded from the solvent

e.g. salt bridge on barnase

Asp12/Arg110 =1.25 kcal/mol

Asp8/Arg110 pair = 0.98 kcal/mol

Horovitz, et al JMB 216, 1031 (1990)



Secondary structure

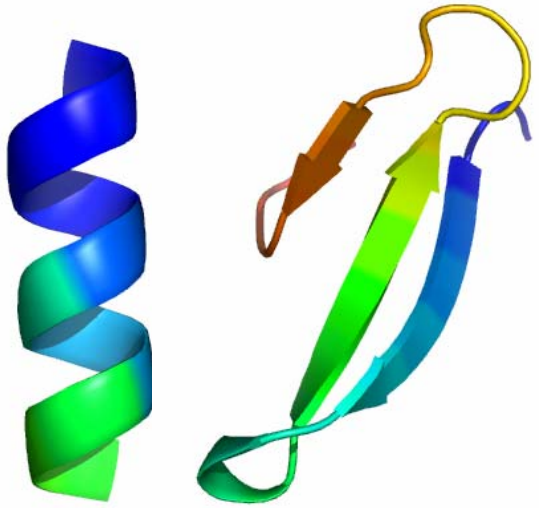
Recurring patterns of main chain conformations stabilized by hydrogen bonds

There are two types of secondary structure, i.e. **alpha-helix** and **beta-sheet**, characterized by different hydrogen bonding patterns

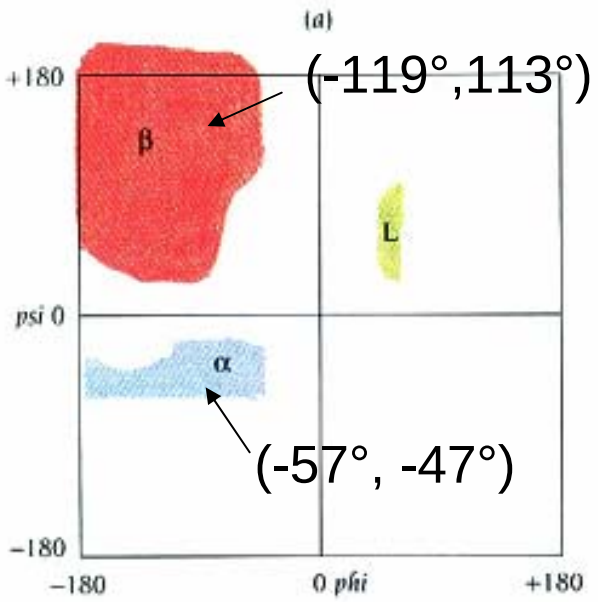
They are each compatible with their characteristic sets of main chain dihedral angles

The part of a protein without regular secondary structure is often called a random coil and includes **turns**, **loops**, and **coils**, but these don't necessarily have to be random

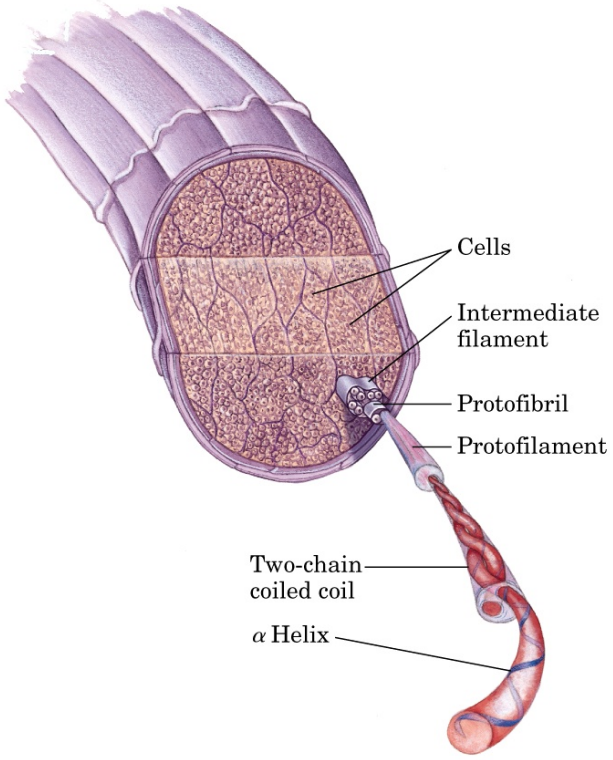
DSSP – 2nd structure determination



Alpha helix Beta sheet



Prediction of alpha helix



Cross section of a hair (b)

Pauling and Corey twisted the peptide backbone to create a regular structure consistent with the fiber diffraction pattern of alpha keratin

They assumed that

i) peptide bond is exactly flat

ii) main chain conformation is independent of sequence

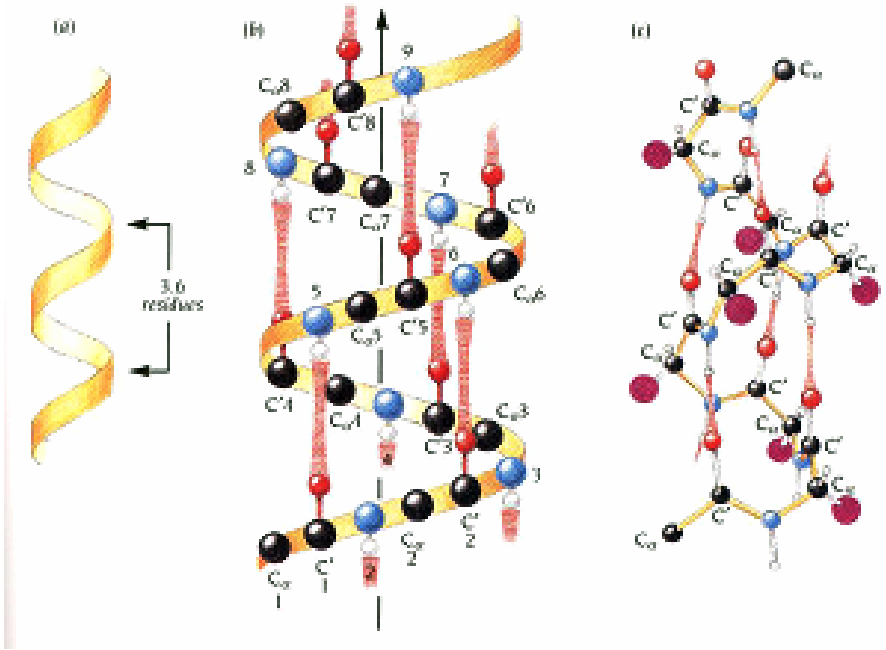
The hydrogen bonding pattern gives rise to a structure that is highly repetitive and stable

Pauling et al, PNAS 37, 205 (1951)

Gross anatomy of alpha helix

Alpha helix consists of a series of main chain hydrogen bonds involving the main chain oxygen of *i*th residue (written as O(i)) and the amide nitrogen of (*i+4*)th residue (written as N(i+4)) : O(i) --- N(i+4)

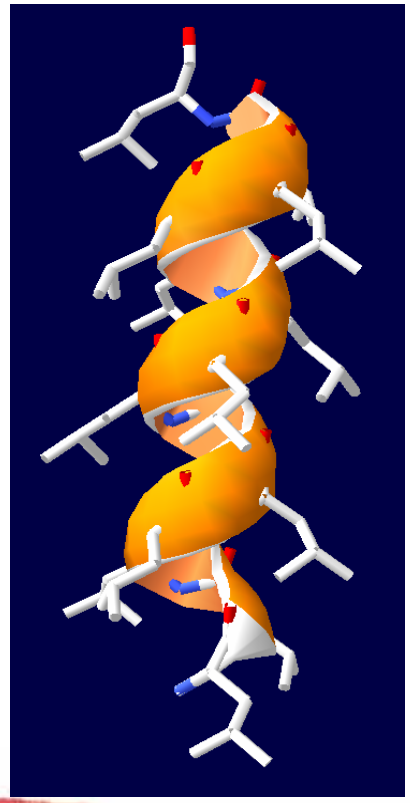
e.g. 1➔5, 2➔6, 3➔7, …



Branden & Tooze

•Helices make up ~ 30% of all globular proteins

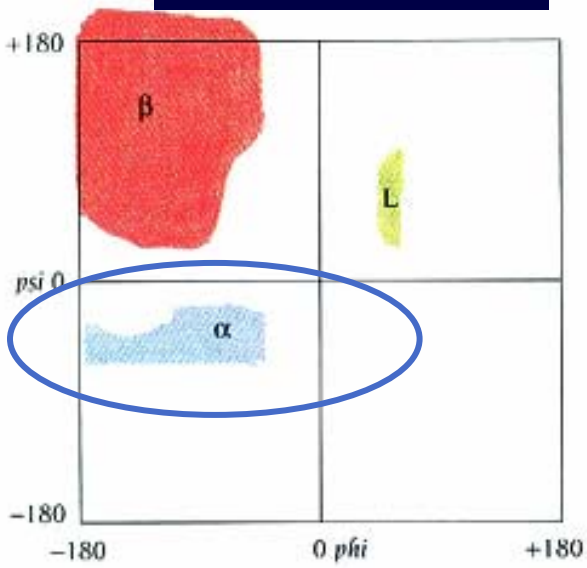
•Are often found on the surface, and many are bent toward the center



•Helix has a pitch of 5.4 Å (i.e. each turn advances the chain by this amount), 3.6 amino acids per turn (i.e. 100° between adjacent Calpha), giving a rise of 5.4 / 3.6 = 1.5 Å per amino acid

•The residues of a helix occupy a narrow region of the Ramachandran plot

– typical values of phi = -60 °, psi = -50 °



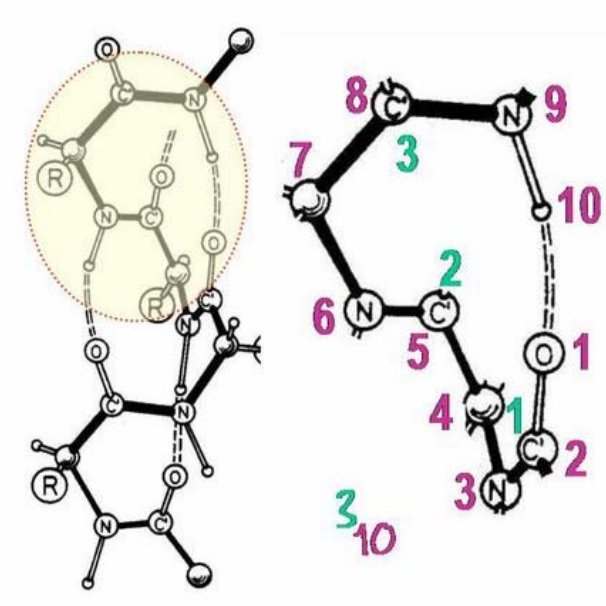
•The first residue of a helix is called the N-cap

•The last residue of a helix is called the C-cap

•Side chains point toward N-terminus

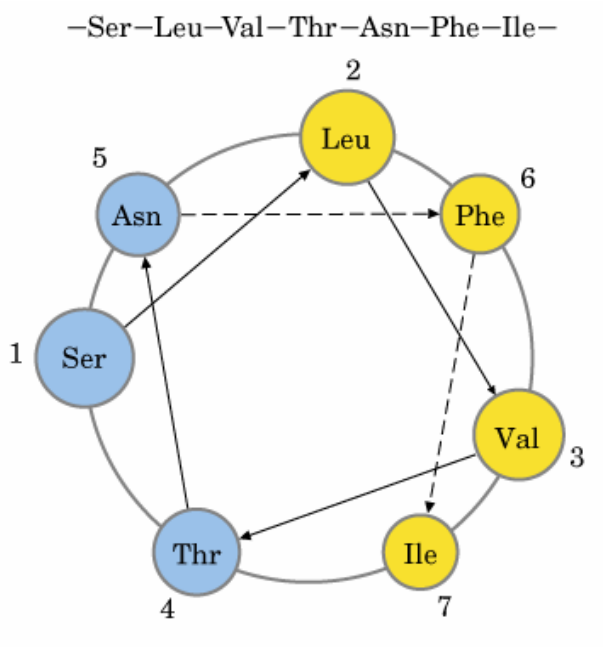
Two other less common forms of helix

- 3_{10} helix : O(i) --- N(i+3) (occurs at the ends of alpha-helices)
  - » Dipoles do not line up, side chain packing unfavorable
  - » The name refers to the number of residues and atoms between hydrogen bonding atoms
- Pi (π) helix : O(i) --- N(i+5) (not observed in protein)



Heptad repeat

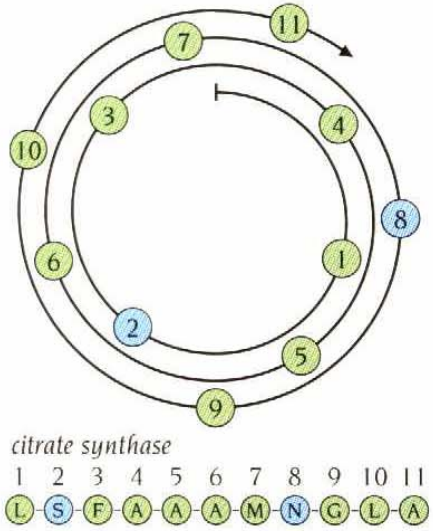
- 3.6 residues per turn give rise to **sided-ness** in a helix—the residues on one side of the helix may be different from the residues on the other side
- Sequences are often displayed on a “helical wheel” down the axis
- The characteristic pattern in a helix may repeat itself every seven residues, resulting in a heptad repeat



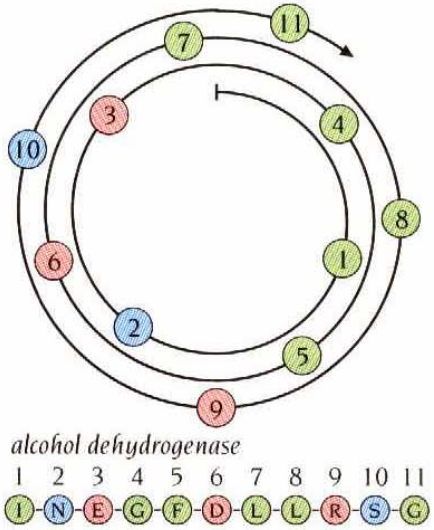
Glucose transporter

Helical wheels

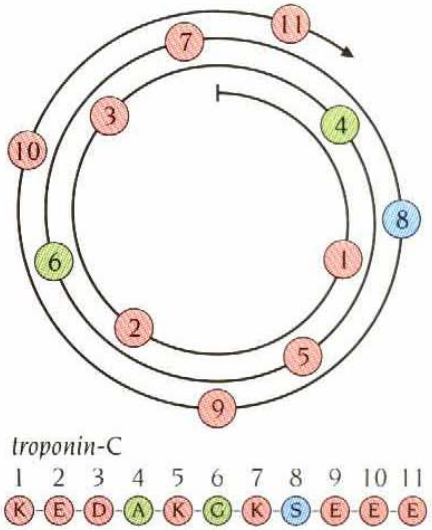
Green - hydrophobic
Blue - polar
Red - charged



Buried



Partially buried
“amphipathic” or
“amphiphilic”



Exposed

Distribution of residues along a helix

<----loop----| |--loop---->
....N″-N′-Ncap-N1-N2-N3.....C3-C2-C1-Ccap-C′-C″
|----------helix----------|

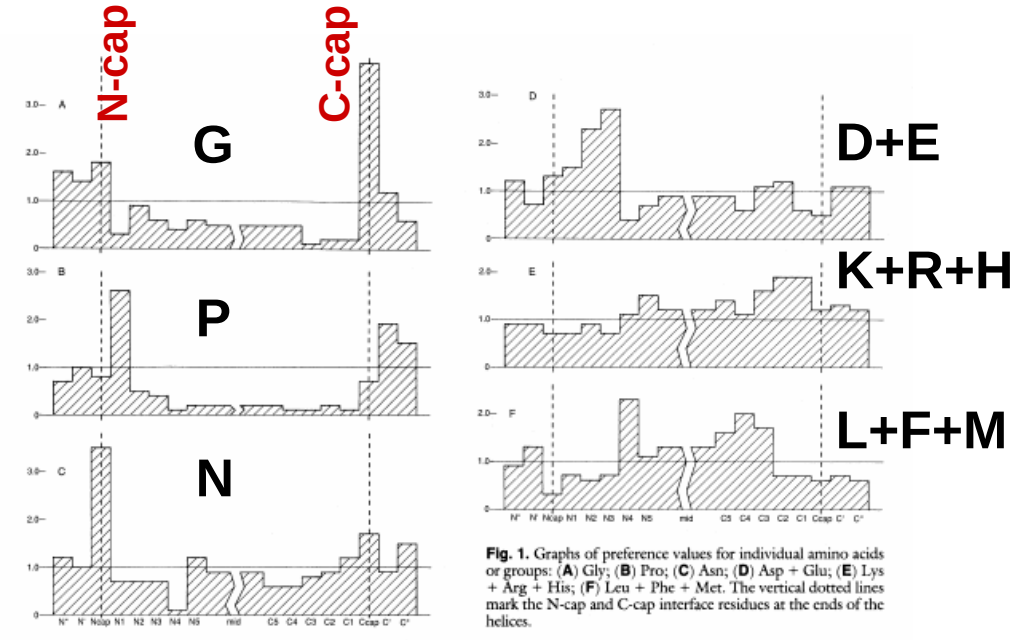


Fig. 1. Graphs of preference values for individual amino acids or groups: (A) Gly; (B) Pro; (C) Asn; (D) Asp + Glu; (E) Lys + Arg + His; (F) Leu + Phe + Met. The vertical dotted lines mark the N-cap and C-cap interface residues at the ends of the helices.

N-, C-caps: “first and last residues whose alpha carbon lies approximately in the cylinder formed by the helix backbone and approximately along the helical spiral path”

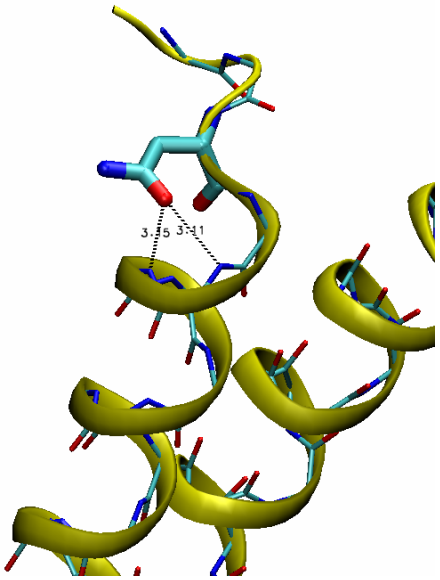
Richardson & Richardson, Science 240, 1648 (1988)

The distribution of different amino acids along the helix is position-dependent

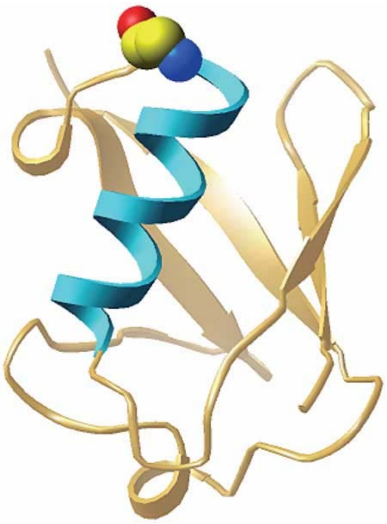
- Asn has a strong preference for the N-cap position
- Pro has an above average frequency at the beginning of a helix and serves as a helix initiator
- Gln cannot replace Asn (incorrect side chain geometry)
- C-terminal capping residues terminate a helix
- Gly is the most common C-cap residue (34% of the time)
- Ala has a smooth and favorable distribution throughout the helix
- Positively charged residues (K+R+H) occur more often near the C-terminus
- Negatively charged residues (D+E) occur more often near the N-terminus

Ala, Leu, Met are preferred within helix

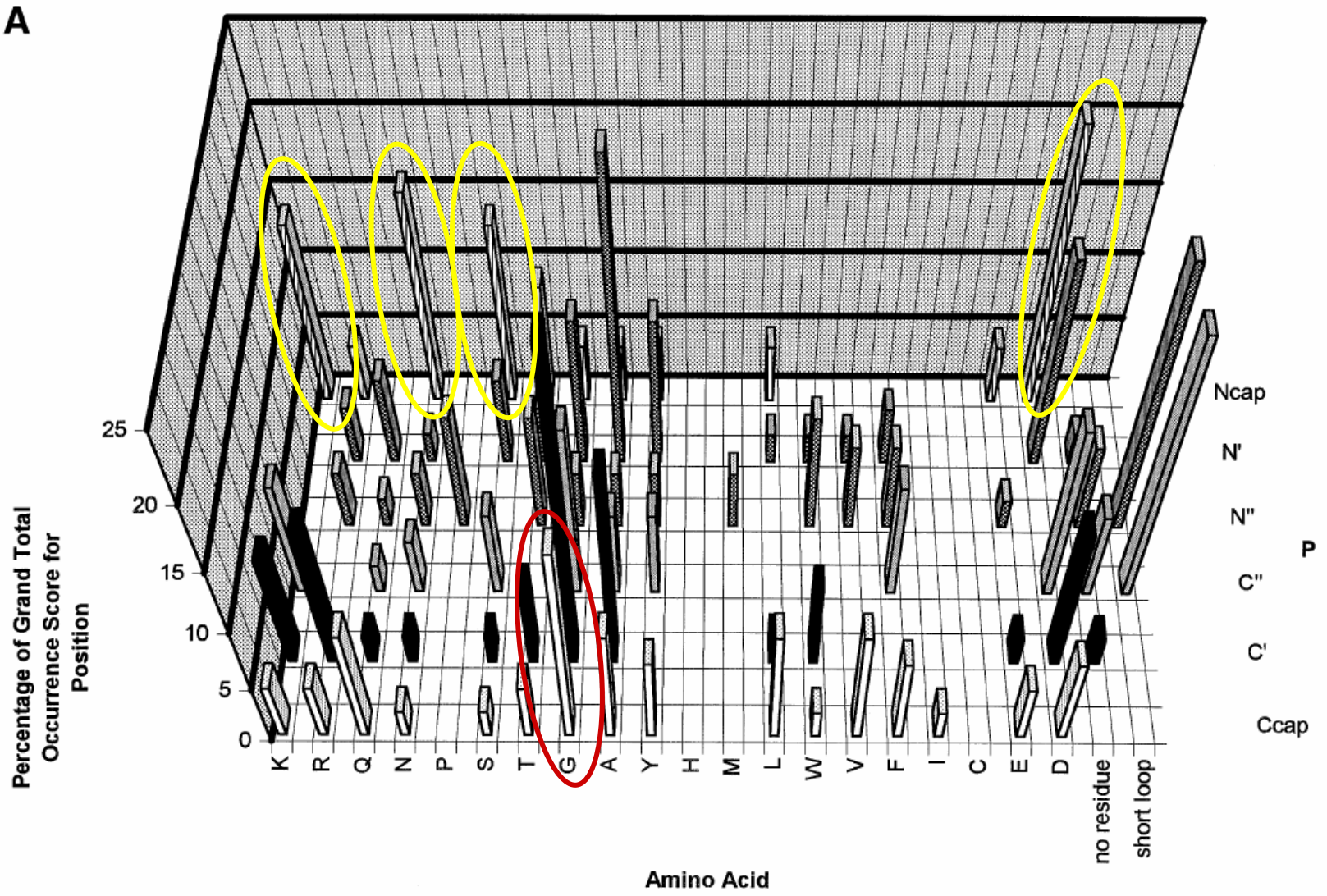
Branched residues (Val, Ile, Thr) are poor helix formers



Asn N-cap

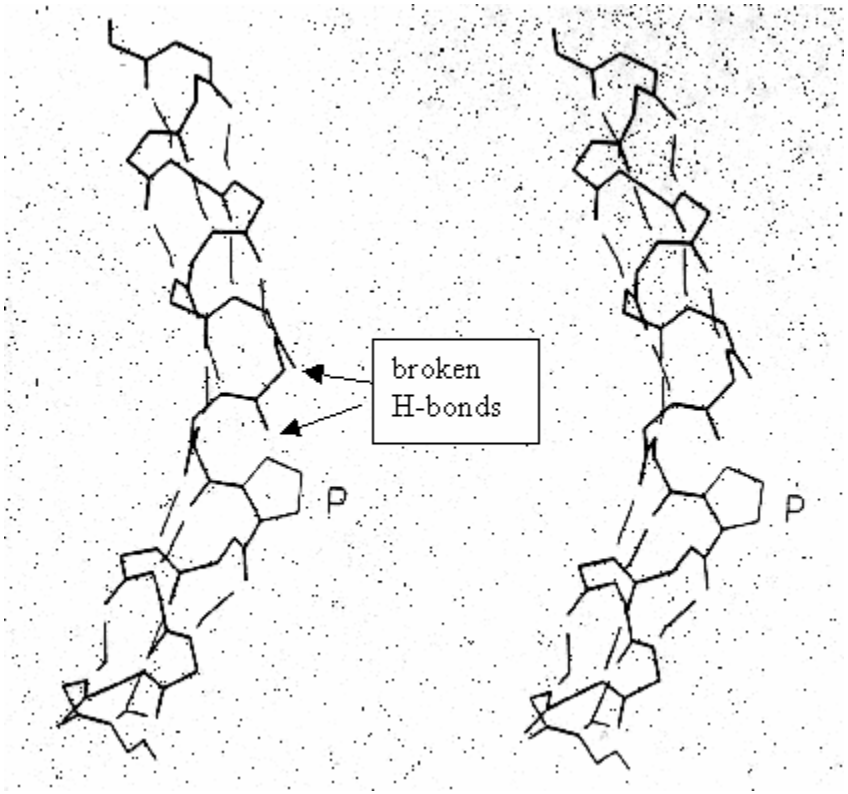


Gly C-cap
(ubiquitin)



Parker and Hefford, Protein Engineering 10, 487, (1997)

Pro disrupt helix



Inclusion of a proline severely disrupts the progression of a helix and destabilizes the structure

The main chain dihedral angles of Pro (phi=-60°, psi=-55° or 145°) are compatible with an alpha helix

However, Pro has no amide hydrogen for use as a donor in hydrogen bond

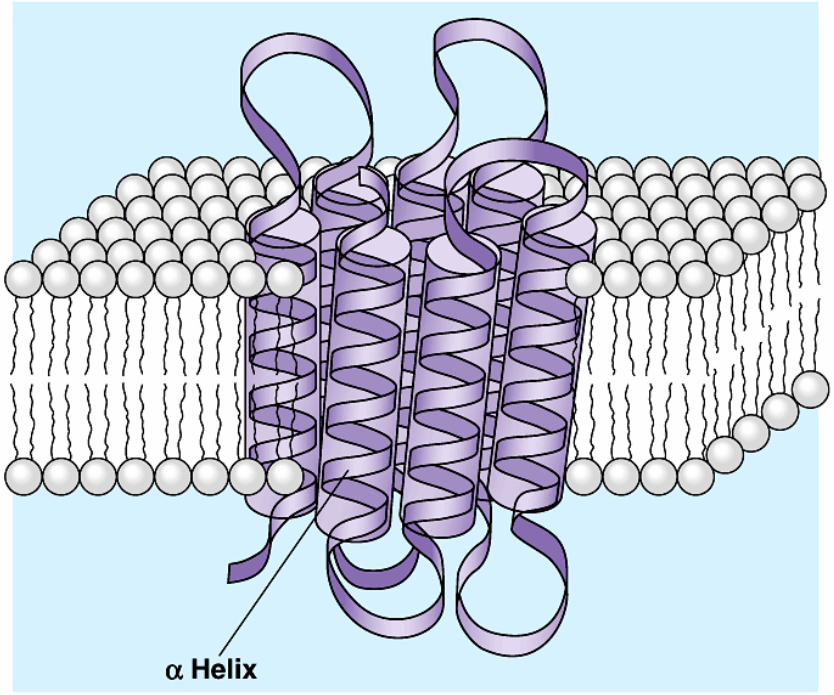
In the helix center, the cyclic ring of Pro (pyrrolidine) pushes away the preceding (N-terminal) turn of the helix by ~1Å producing a 30° bend and breaking the next H-bond as well.

Gly is common in membrane proteins

Gly is disruptive as a helix residue in globular proteins but common in integral membrane proteins embedded in the lipid bilayer of the cell

GXXXG motif – Russ & Engelman, JMB 296, 911 (2000)

Transmembrane (TM) domain of membrane proteins often comprises helices TM helices often contain Gly and Pro, which play important functional roles



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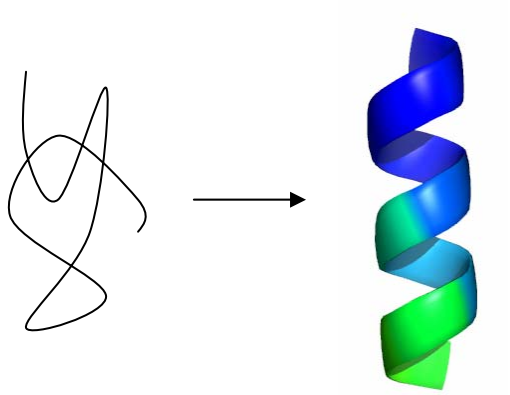
Helix propensity

- Helix propensity refers to how much an amino acid stabilizes a helix
- Statistically, this information may be inferred by measuring the frequency with which a given amino acid occurs within a helix in known proteins
  - Some amino acids (e.g. Ala) occur in a helix more often than others (e.g. Ser)
  - Thus, we conclude Ala stabilizes the helix more than Ser

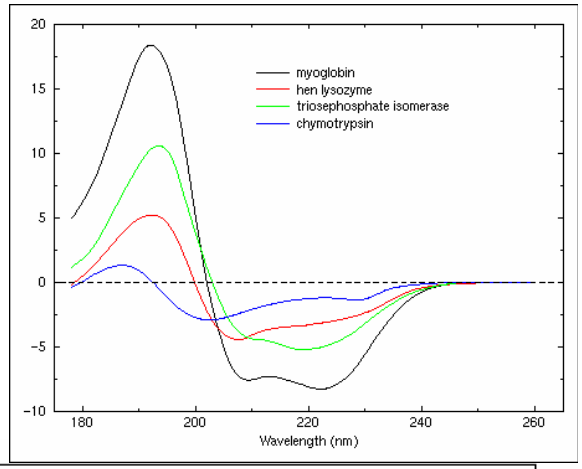
- Experimentally, helix propensity can be measured by comparing the stability of helices that are identical in sequence except at one location
  1. constructing short peptides (e.g. Ac-LLLLLXLLLLL) where L is Leu, X is random residue
  2. measure the helix content of the peptide by CD

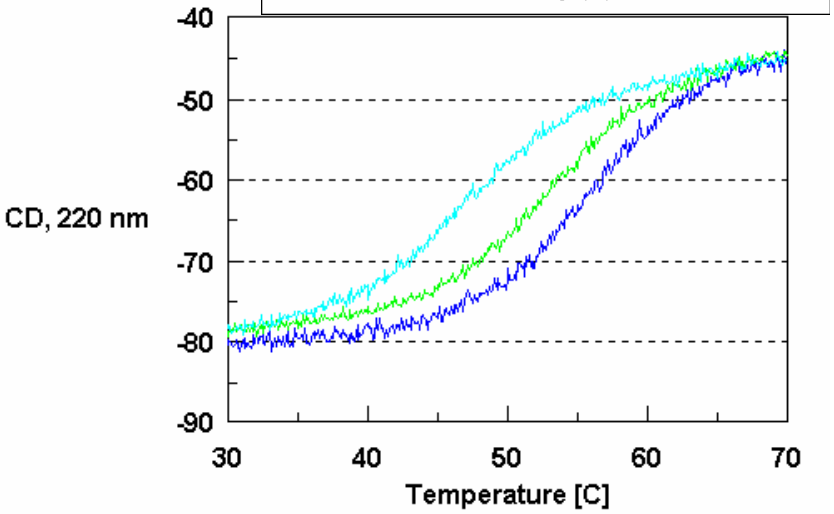


Denatured Structured

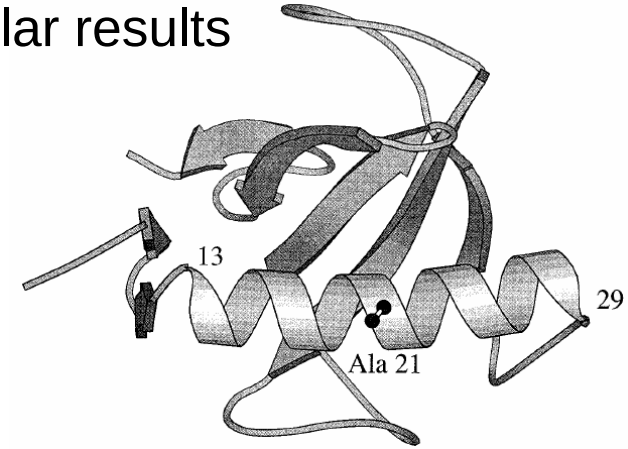
Measuring the helix content of a peptide

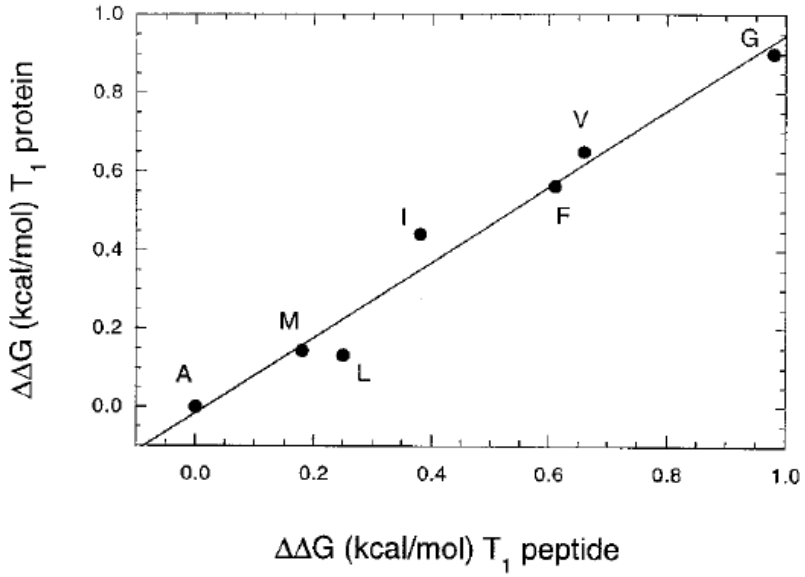
- When a protein/peptide unfolds, it also loses its secondary structure
- Circular dichroism (CD) spectroscopy can estimate the secondary structure by measuring dichroism in far UV wavelengths (< 250 nm)
- Repeated measurements at progressively elevated temperature can be used to measure the melting temperature (Tm)





- Isolated helices of short peptides are often unstable
- Measurements were made both using peptides and proteins and yield the similar results





Myers, et al. PNAS 94, 2833 (1997)

Amino acid	$\Delta\Delta G_\alpha$ (kcal/mol)
Ala	−0.77
Aib	−0.69
Arg	−0.68*
Lys	−0.65*
Leu	−0.62
Met	−0.50
Trp	−0.45
Phe	−0.41
Ser	−0.35
Gln	−0.33
Glu	−0.27*
Cys	−0.23
Ile	−0.23
Tyr	−0.17
Asp	−0.15*
Val	−0.14
Thr	−0.11
Asn	−0.07
His	−0.06*
Gly	0.00
Pro	~3

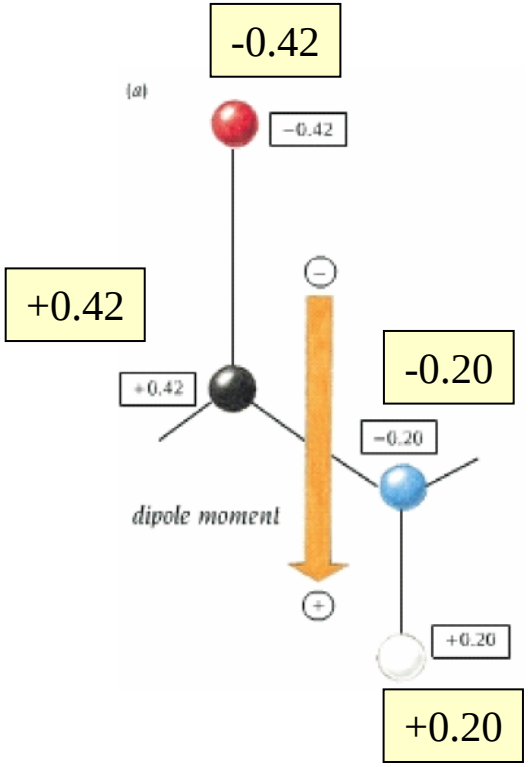
O'Neil and DeGrado, Science 250, 646 (1990)

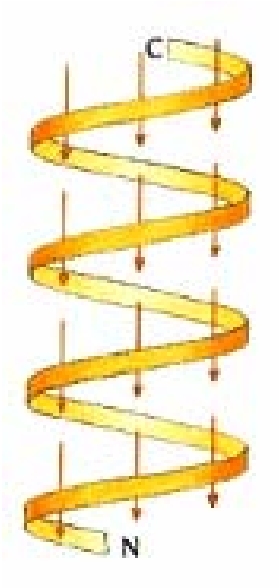
Origin of helix propensity

- The differing alpha helix propensity derives from the entropic difference between folded and unfolded states
  - Creamer & Rose, PNAS 89, 5937 (1992)

- Two competing effects go into folding an alpha helix
  - enthalpy of hydrogen bonds in a helix wins (~ -1 kcal/mol per residue) when helix contains Ala
  - entropy of unfolded peptide backbone (~ 1.5 – 2 kcal/mol per residue compared to Ala) wins when the peptide contains Gly
  - for all residues other than Gly, the initial main chain entropy is less, and side chain degrees of freedom is also lost upon folding

Additive dipole moment





Branden & Tooze

Helix has a net positive charge near the N-terminus and a net negative charge near C-terminus

Salt bridge stabilizes helix

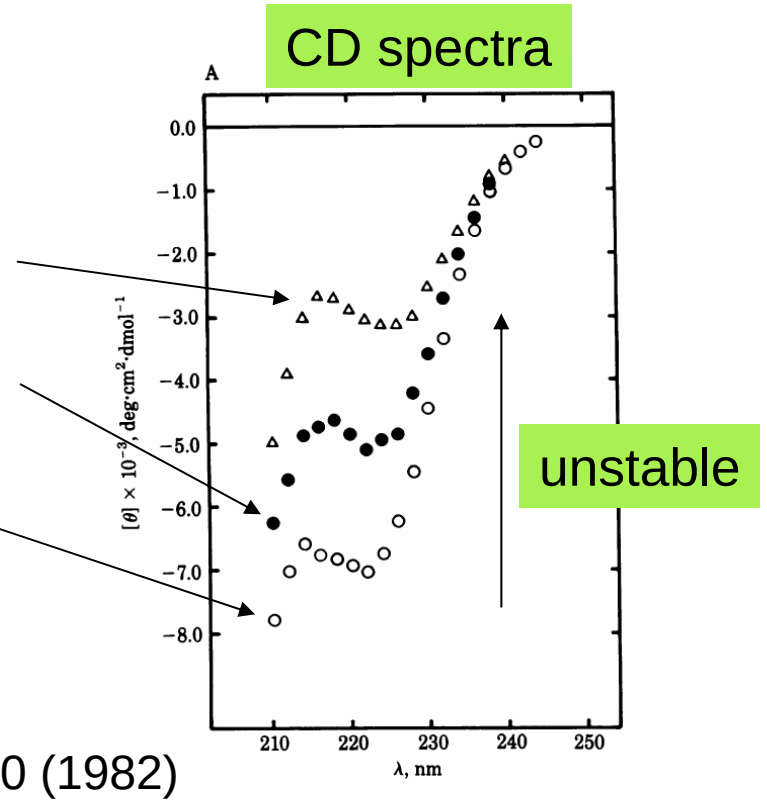
C-peptide of ribonuclease A forms a weakly stable helix at 1 ° C

Helix stability depends strongly on pH

Deprotonated E9, E2 and protonated H12 are required for stability

Salt bridge E9-H12 stabilizes the helix

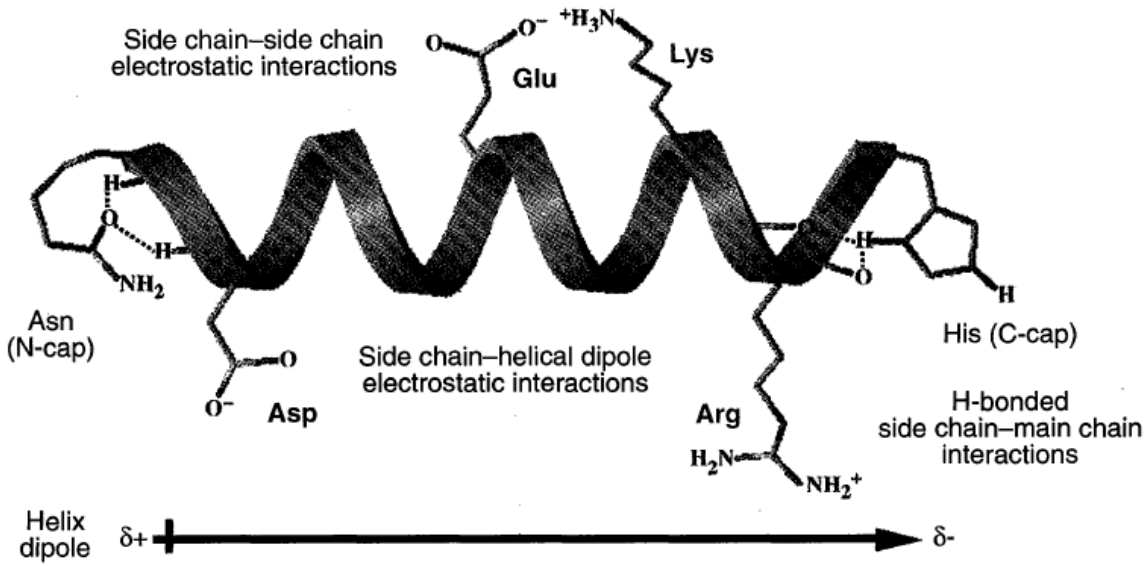
The salt bridge stabilizes one turn of the alpha-helix, helping to nucleate it



Bierzynski et al, PNAS79, 2470 (1982)

Idealized Helix

A net +0.5 charge at the N-terminus and a net -0.5 charge at the C-terminus

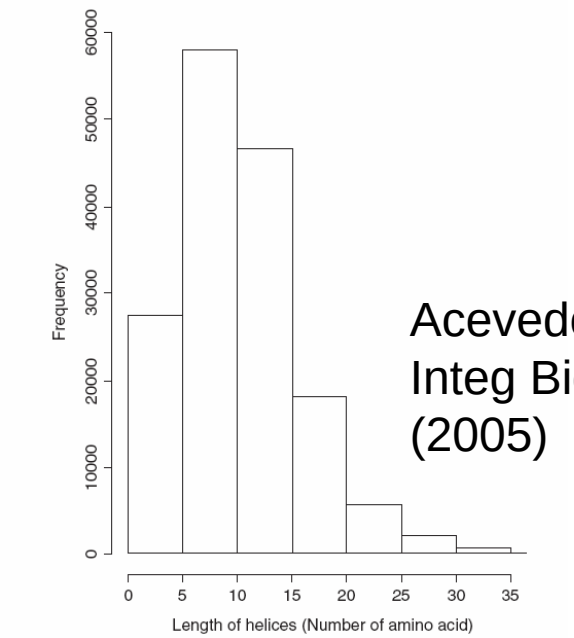


Groupwise free energies of interactions (in 0.15 M NaCl):

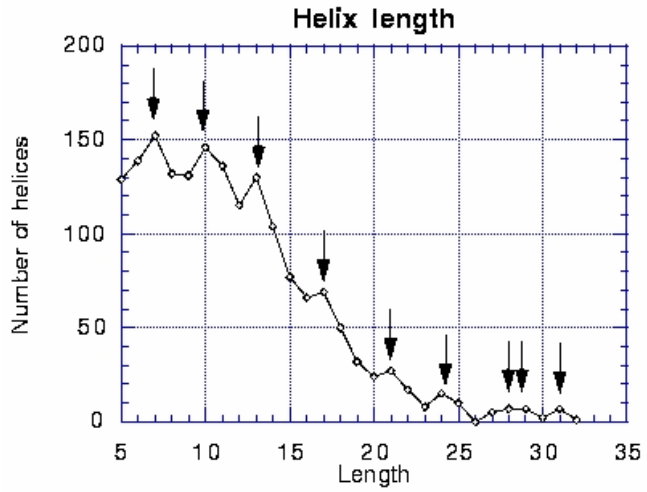
N-cap	1 to 2 kcal/mol
C-cap	~0.5 kcal/mol
Charge-macrodipole electrostatic	~0.5 kcal/mol
Side chain–side chain electrostatic	~0.5 kcal/mol
Range of helix propensities	~1 kcal/mol
Dehydration of an isobutyl group (Leu)	2 to 5 kcal/mol

Bryson, et al Science 270, 935 (1995)

Length distribution



Acevedo & Lareo, J Integ Biol 9, 391 (2005)

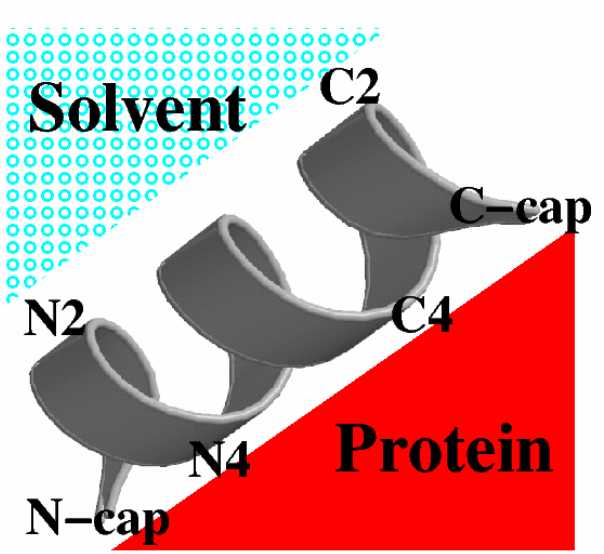


Penel, et al. JMB 293, 1211 (1999)

- The distribution of helix lengths is periodical.
- The maxima appear with a periodicity of 3-4 amino acids.

•Length periodicity is caused by the amphipathic nature of many helices.

- Helices are often found on the surface of the proteins and are therefore amphipathic (i.e. amphiphilic).
- The N-cap usually faces the protein.
- If there are integer number of turns in the helix, the C-cap will also face the protein, i.e. the same side as the N-cap, which is favorable



Penel, et al. JMB 293, 1211 (1999)

Beta Sheet

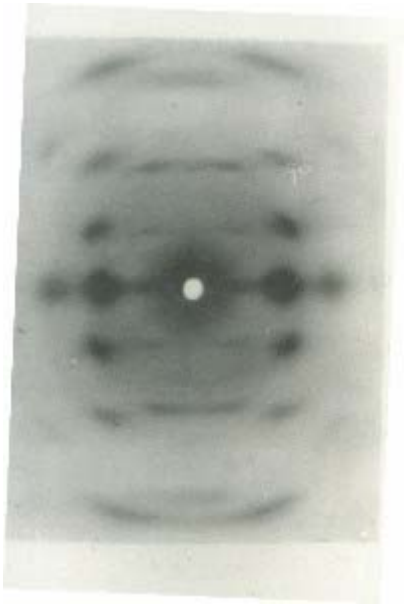
Pauling and Corey predicted the beta sheet structure in order to explain the fiber diffraction pattern of beta keratin (e.g. spider silk)

CONFIGURATIONS OF POLYPEPTIDE CHAINS WITH FAVORED ORIENTATIONS AROUND SINGLE BONDS: TWO NEW PLEATED SHEETS

By Linus Pauling and Robert B. Corey

Gates and Crellin Laboratories of Chemistry,* California Institute of Technology, Pasadena, California

Communicated September 4, 1951

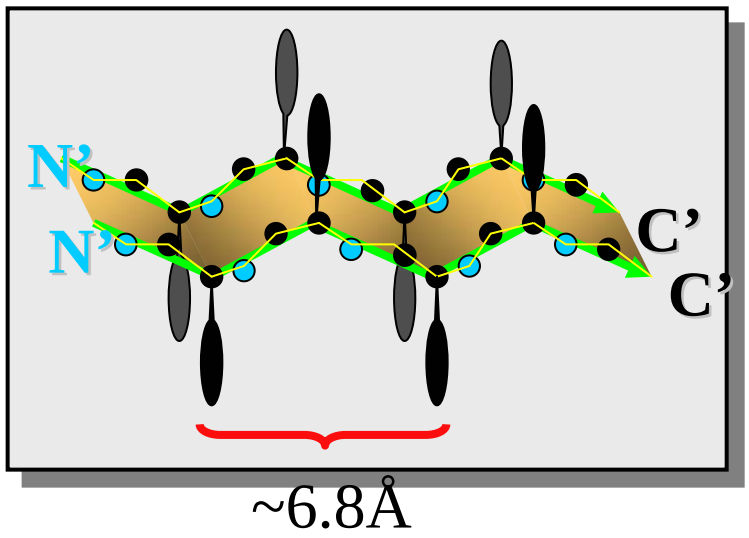


A. Trans-trans Configurations:

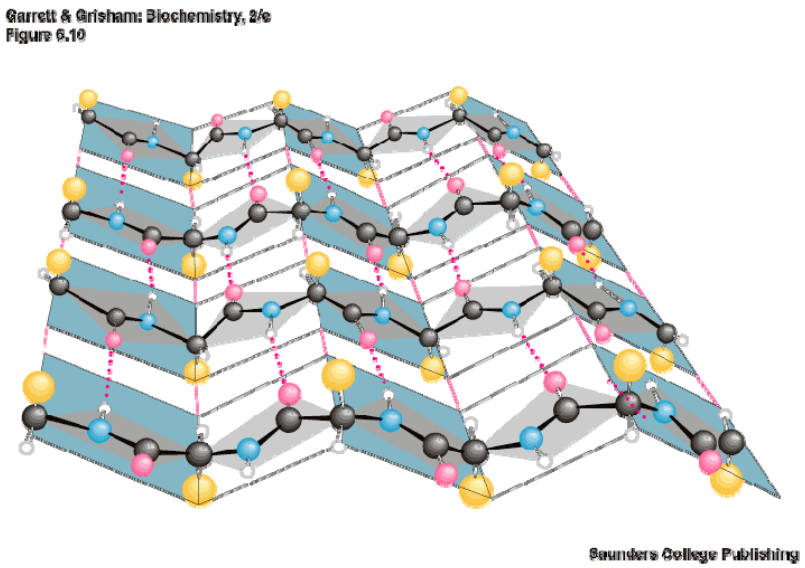
1. CH trans to NH, CH trans to CO. Pitch 6.68 A, 2 residues per turn. Lateral CO and NH suited to forming the two pleated sheets described below.

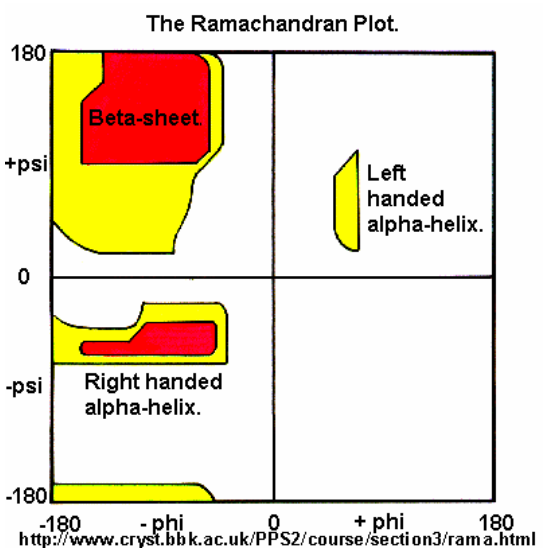
Not stabilized by hydrogen bond between nearby residues. Rather the hydrogen bonds come from distant parts of a protein. These parts are each called "**beta strand**".

The axial distance between adjacent residues is ~3.4 Å; or equivalently, the beta sheet has a pitch of ~6.8 Å. This is "extended" compared to helical conformation, where the rise was 1.5 Å per residue.



Structural features





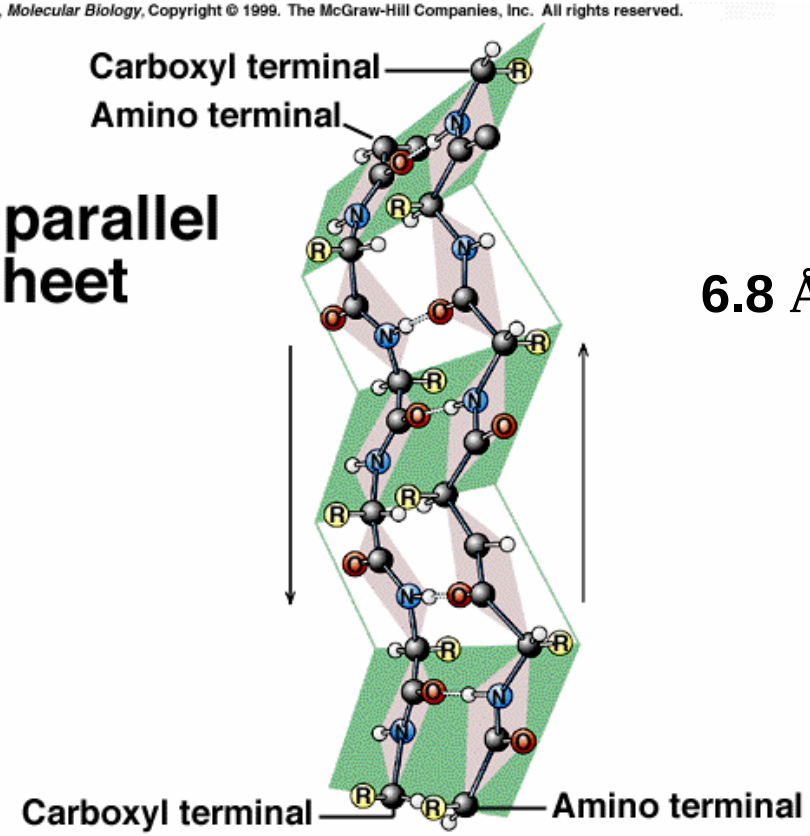
•Successive Ca atoms are just above and just below the plane of the sheet, resulting in a “pleated” look.

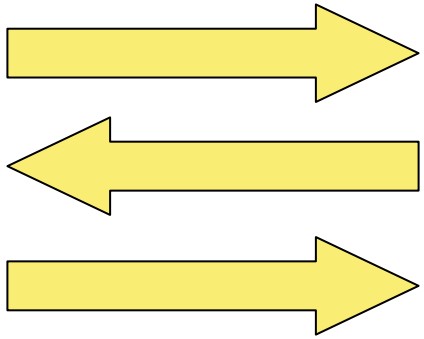
•Every other side chain is found on the same side of the chain

•The residues in beta sheet have negative phi values (-140 °) and positive psi values (130 °)

Robert Weaver, *Molecular Biology*, Copyright © 1999. The McGraw-Hill Companies, Inc. All rights reserved.

An antiparallel β-sheet





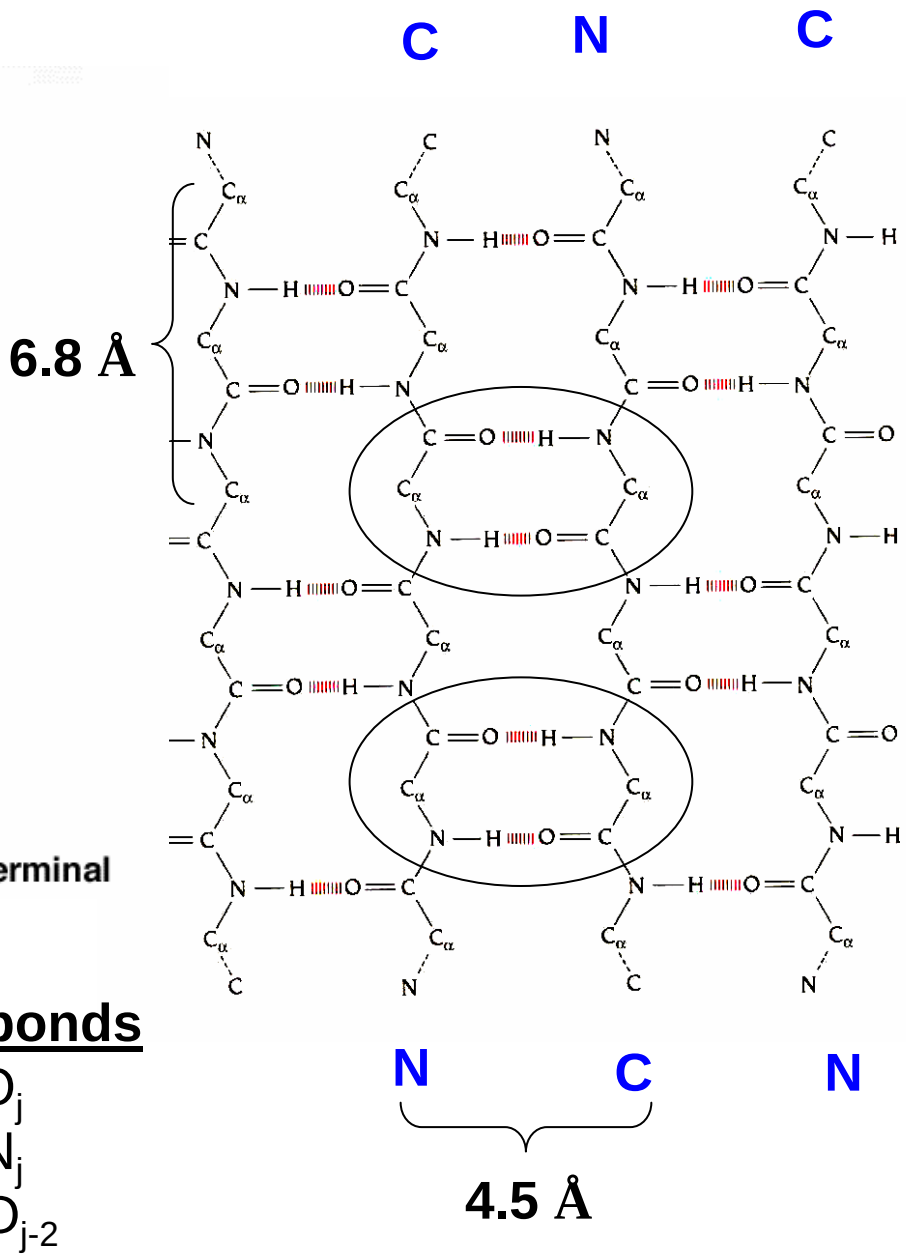
Hydrogen bonds

N_i *** O_j

O_i *** N_j

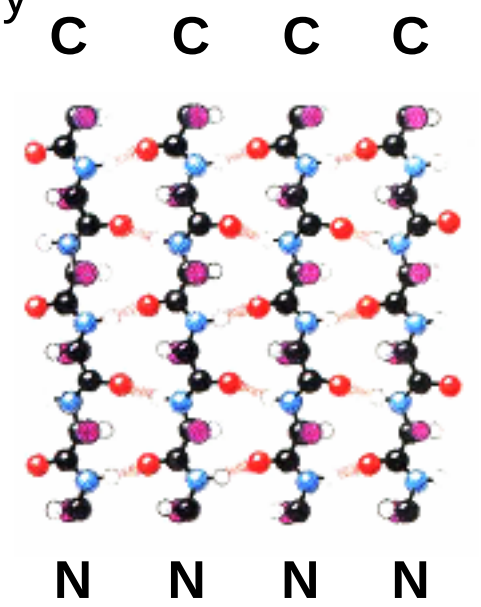
N_{i+2} *** O_{j-2}

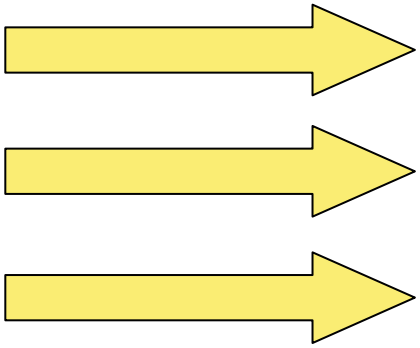
O_{i+2} *** N_{j-2}

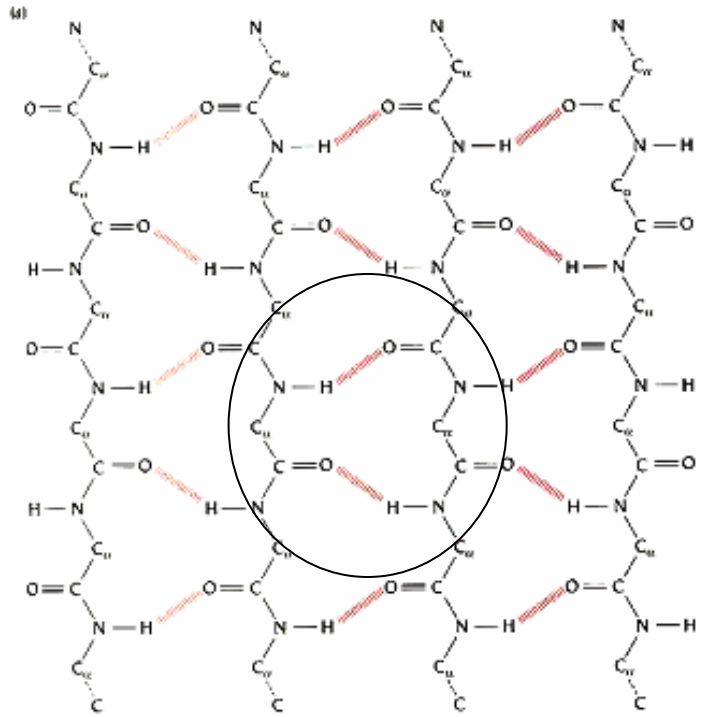


Parallel beta sheet

The hydrogen bonds are more evenly spread out but deviate from ideal geometry





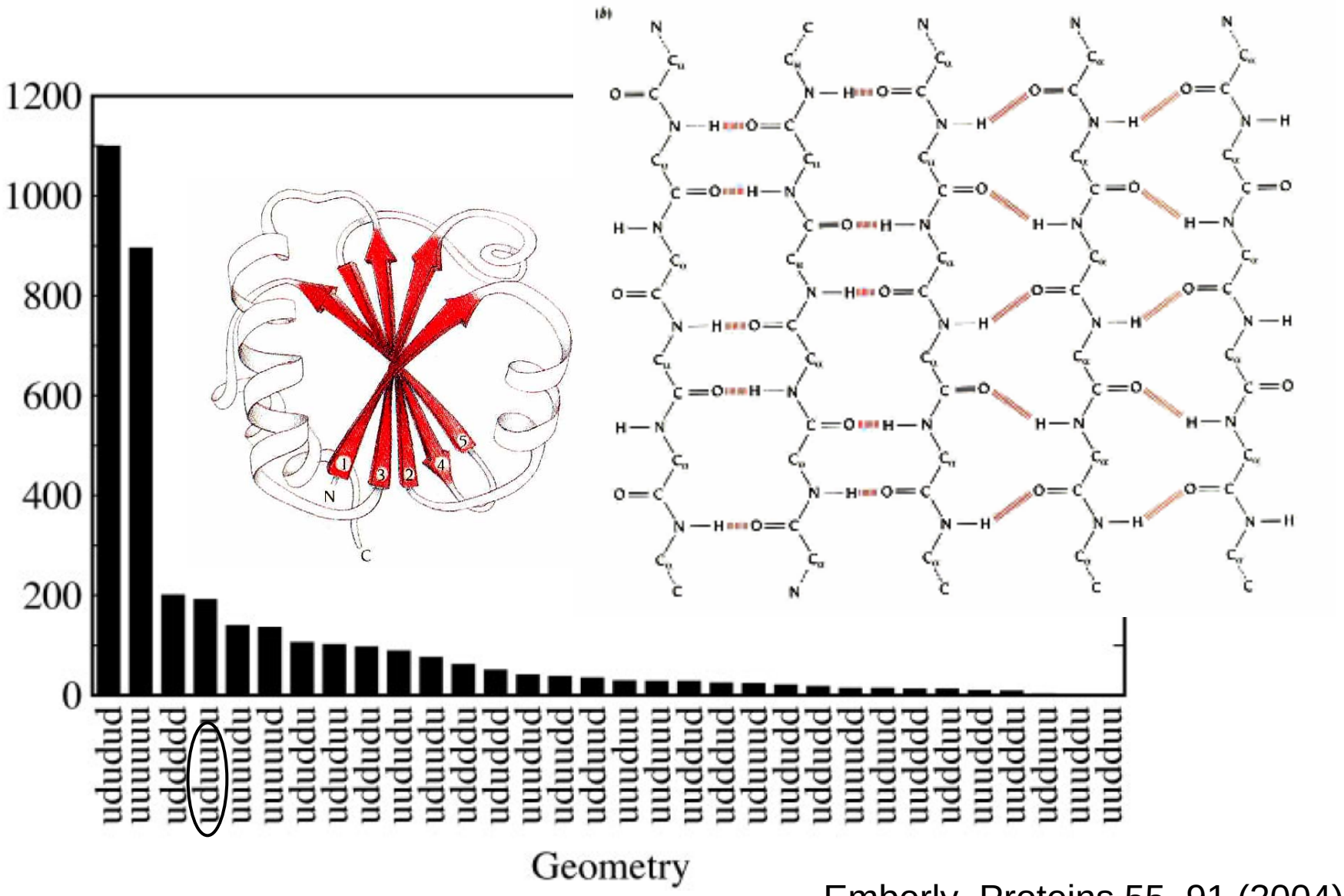


Hydrogen bonds

N_i *** O_j

O_i *** N_{j+2}

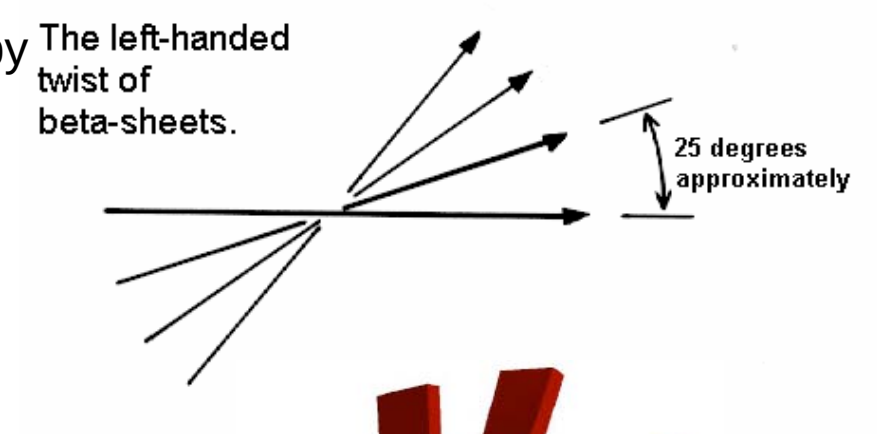
Mixed beta sheets are rare (relatively speaking)



Emberly, Proteins 55, 91 (2004)

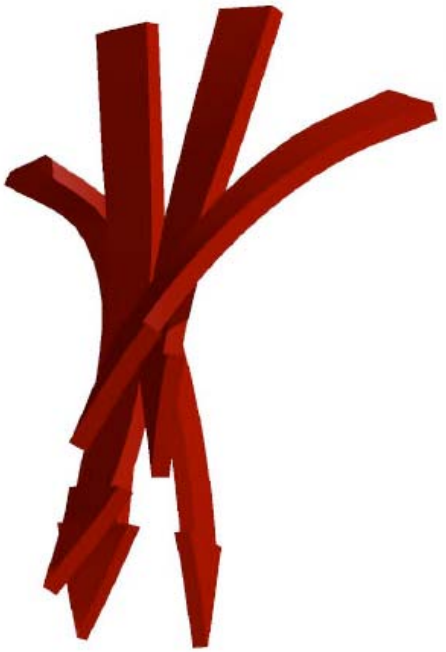
Twist in the sheet

When seen from the side, the beta sheet is twisted counter-clockwise (i.e. left-handed) by about 30° per strand (However, if seen from the ends, the twist is twisted clockwise i.e. right-handed)



No satisfactory explanation for this twist has been found

Parallel sheets are usually buried and less twisted than antiparallel sheets, suggesting that it is energetically less stable



Beta sheet propensity

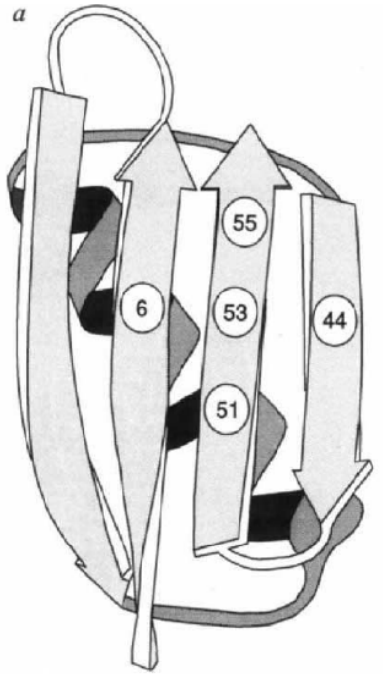
Different amino acids have different beta-sheet propensity

Minor and Kim, Nature 367, 660 (1994)

Beta sheet propensity can be measured by substituting a residue on a strand and comparing the stability of the mutant to that of wild type by CD

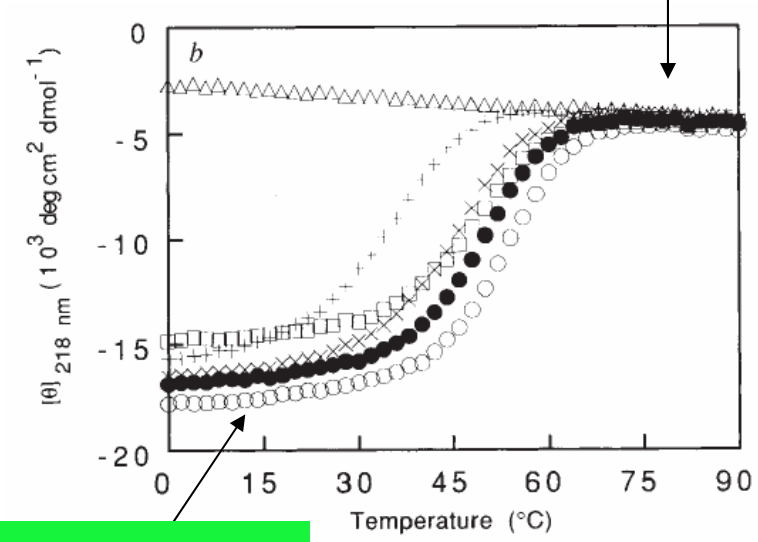
single of minimum at 218 nm

cf. alpha helix has two minima at 208 nm and 222 nm



B1 domain of protein G

no secondary structure



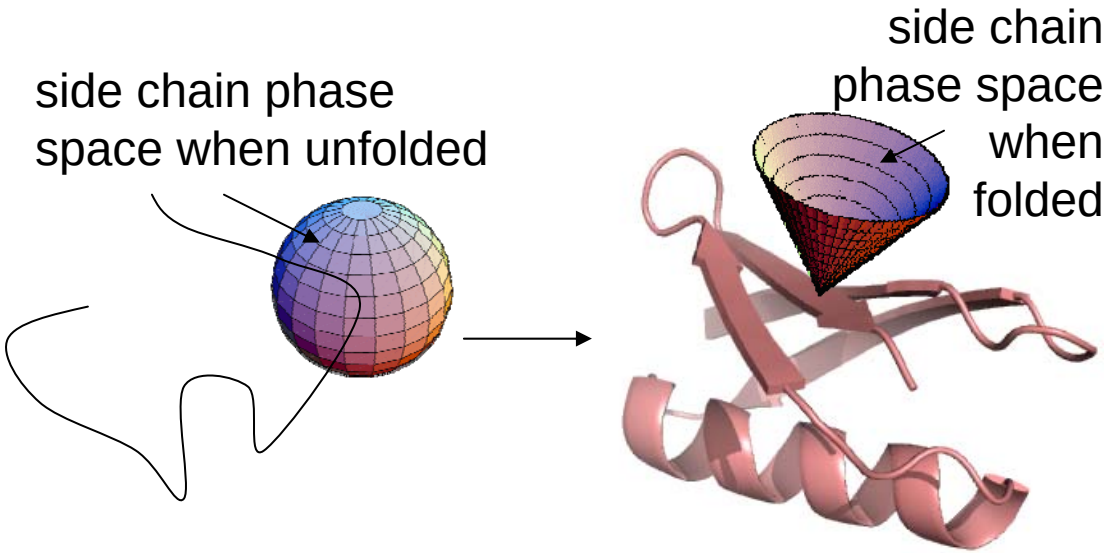
secondary structure

Beta branched side chains
favor beta-sheet formation

TABLE 1 ΔΔG values for β-sheet formati
melting temperatures (T_m), and relative b
for the AASS-53Xaa proteins normalized

Amino acid	ΔΔG (kcal mol^{-1})
Thr	1.1
Ile	1.0
Tyr	0.96
Phe	0.86
Val	0.82
Met	0.72
Ser	0.70
Trp	0.54
Cys	0.52
Leu	0.51
Arg	0.45
Lys	0.27
Gln	0.23
Glu	0.01
Ala	0.00
His	−0.02
Asn	−0.08
Asp	−0.94
Gly	−1.2
Pro	< −3

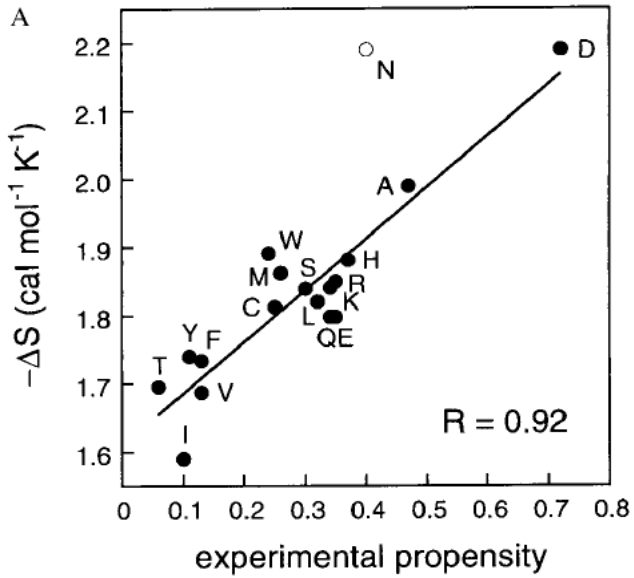
Origin of beta sheet propensity



$$\Delta S = k_B \log \frac{W_B}{W}$$

where W is the amount of conformation space available to an amino acid when the protein is denatured, and W_B is the corresponding available conformation space when the protein is folded to a beta sheet

Street and Mayo, PNAS 96, 9074 (1999)



The dominant factor for intrinsic beta sheet propensity is the avoidance of steric clashes between the side chain of an amino acid and its local backbone (i.e. entropic)

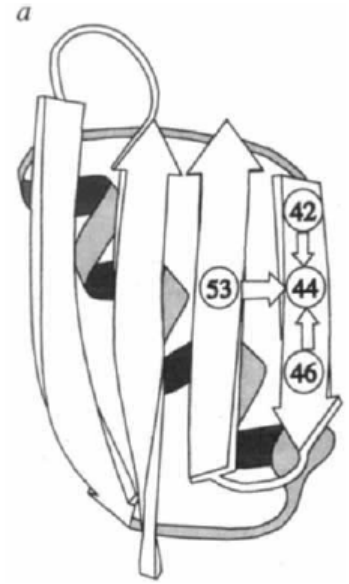
Coulombic and solvation effects are less important.

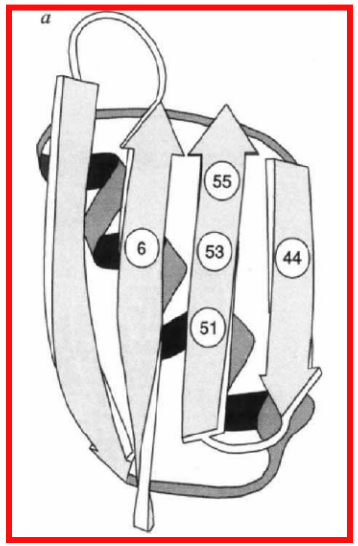
- Street and Mayo, PNAS 96, 9074 (1999)

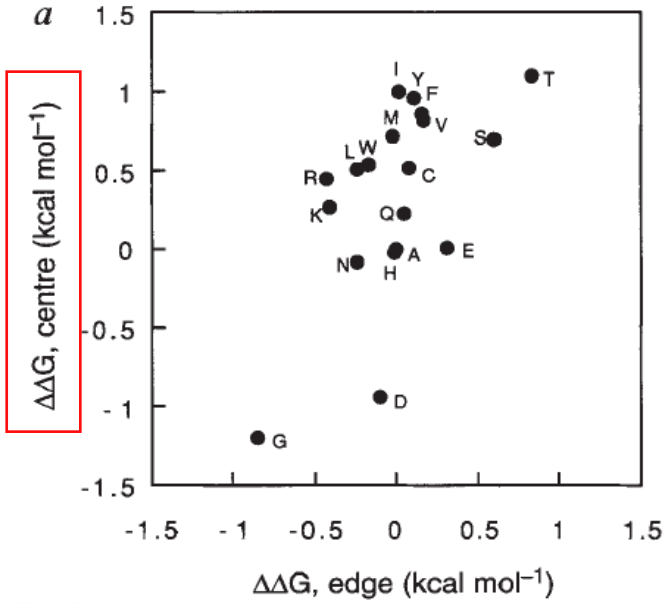
Context dependent beta sheet propensity

The beta sheet propensity also differs depending on the location of a beta strand within a sheet

–Minor & Kim, Nature 371, 264 (1994)

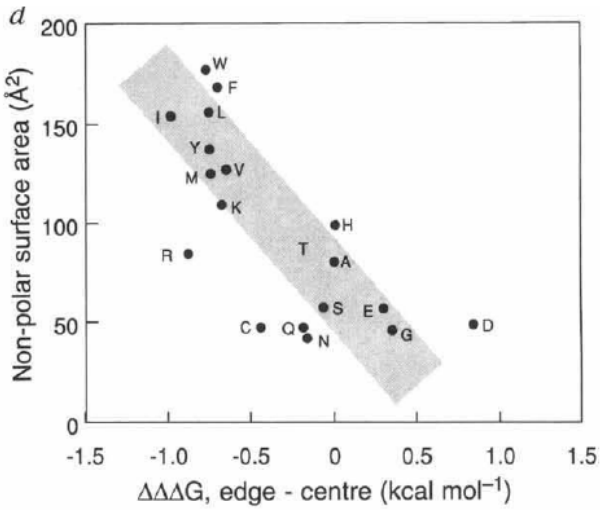






Not a good correlation!

Non-polar surface area



Propensity difference between edge and center

There is a correlation with the non-polar solvent accessible surface area

The interaction with the surrounding beta structure is a dominant force for determining beta sheet propensity—i.e. the tertiary structure is an important determinant of beta sheet propensity

Turns, loops and bends

- **Nonrepetitive** structural elements include tight turns, bulges, bends and random coils. These are all referred to as residues without secondary structure

- Turns give proteins their compact appearance
- Tight turns nearly completely reverse the direction of the peptide chain

- Loops often play important functional roles—the active sites of many enzymes and receptors are made of loop residues

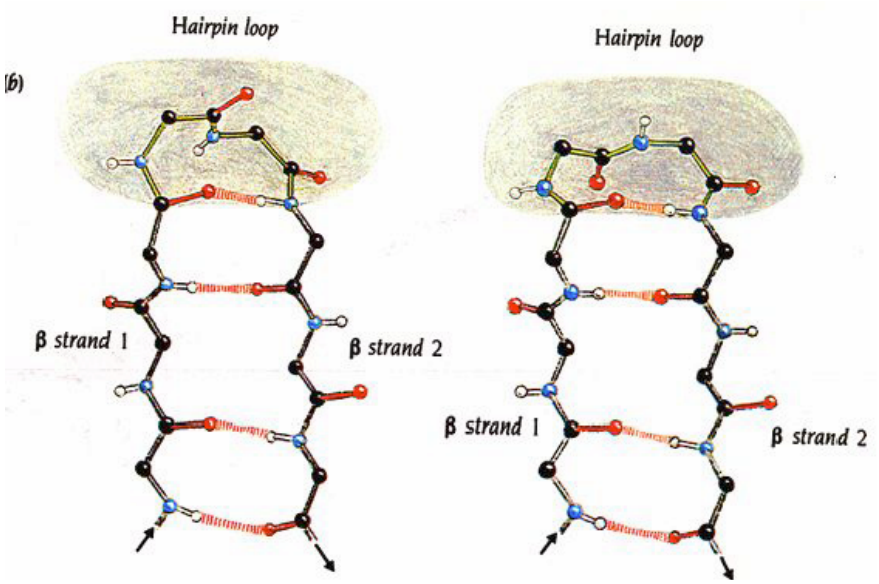
- Bends in alpha helix allows the helix to “hug” the protein
- Bulges in edge beta strands are important negative design elements

Tight turns

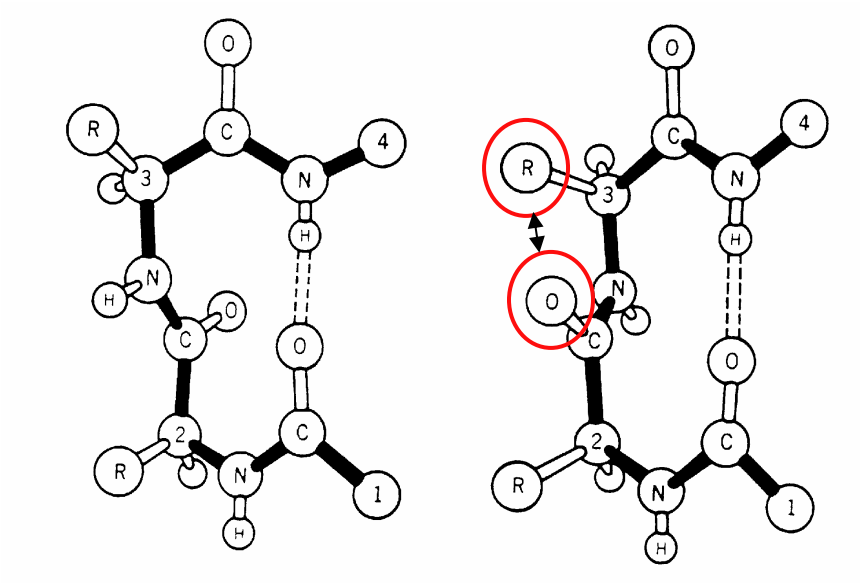
- Tight turns include δ, γ, β, α, and π turns comprising 2 – 6 amino acids

- Beta turns are most common
  - Four consecutive residues (i – i+3) **not present in alpha-helix**
  - i) in which the distance between Ca(i) and Ca(i+3) is less than 7Å
  - ii) in which O(i) hydrogen bonds with N(i+3)

  Richardson, Adv Protein Chem 34, 167 (1981)

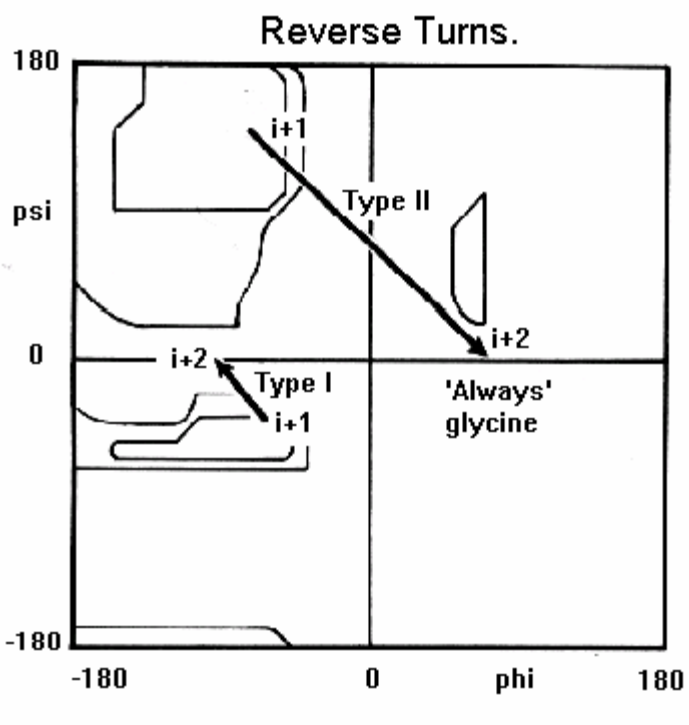


Beta turn



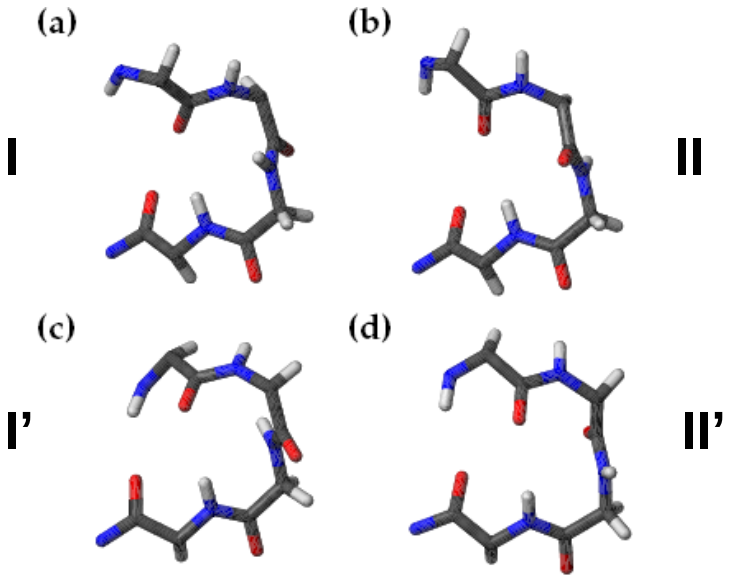
Type I

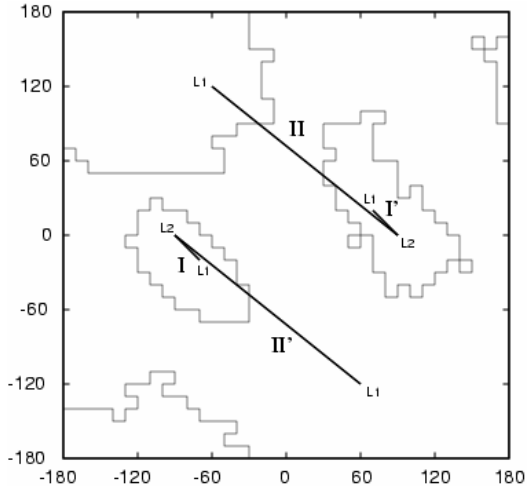
Type II



- Beta turns usually appear on the surface and are often involved in molecular interaction, catalysis and antigenicity, **protein folding and stability**
- There are six types of beta turns (I,I',II,II',VIa and VIb)
- Due to potential steric clash with the carbonyl oxygen of the preceding residue, the position i+2 in type II turn is always Gly

- Type I’ and II’ turns are mirror images of I and II, i.e. the signs of phi and psi have been reversed
- I and II are most common, but I’ and II’ are energetically more favorable in beta hairpins (to be discussed later)
- I’ and II’ more compatible with the twist of the beta-sheet





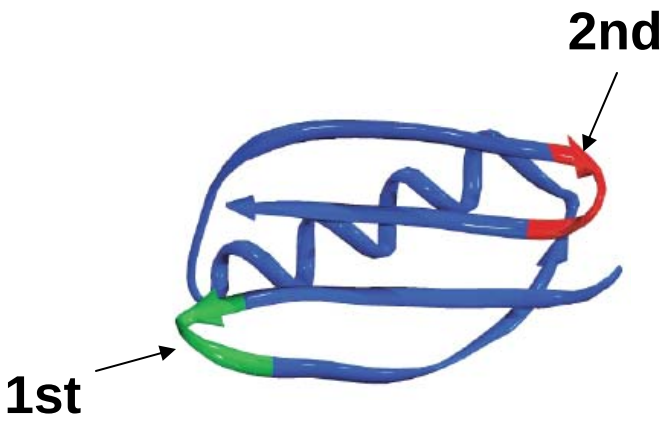
Sequence preference in Type I’ turn

	–XG–	XNG–	–NGX
A	14	4	3
C	4	1	0
D	57	6	2
E	16	5	5
F	6	4	1
G	56	0	3
H	15	1	3
I	0	5	3
K	24	4	10
L	9	5	2
M	1	0	0
N	66	5	1
P	0	0	0
Q	10	2	6
R	9	0	5
S	11	3	2
T	1	2	8
V	1	14	6
W	0	0	1
Y	8	5	5

Griffiths-Jones, JMB 292, 1051 (1999)

Beta turn in protein folding

In protein G, the second beta hairpin forms first and the formation of the first hairpin is the rate limiting step in folding



Protein G

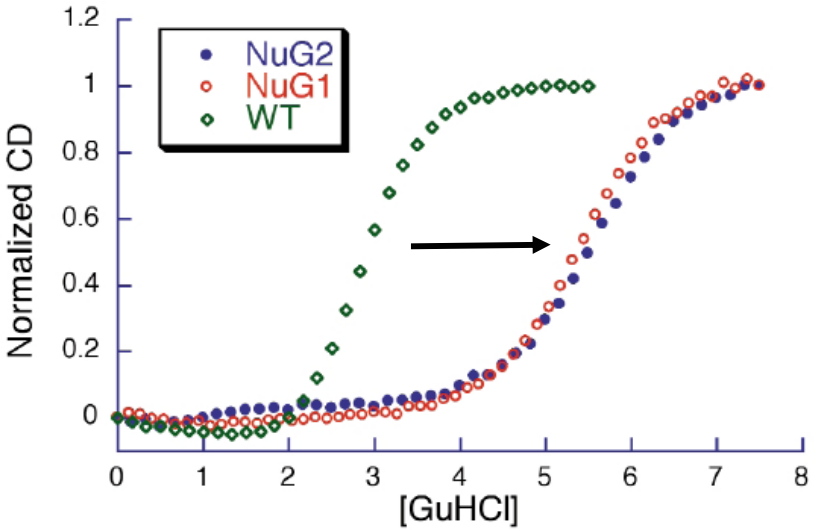


Table 1 Sequences of designed proteins[1]

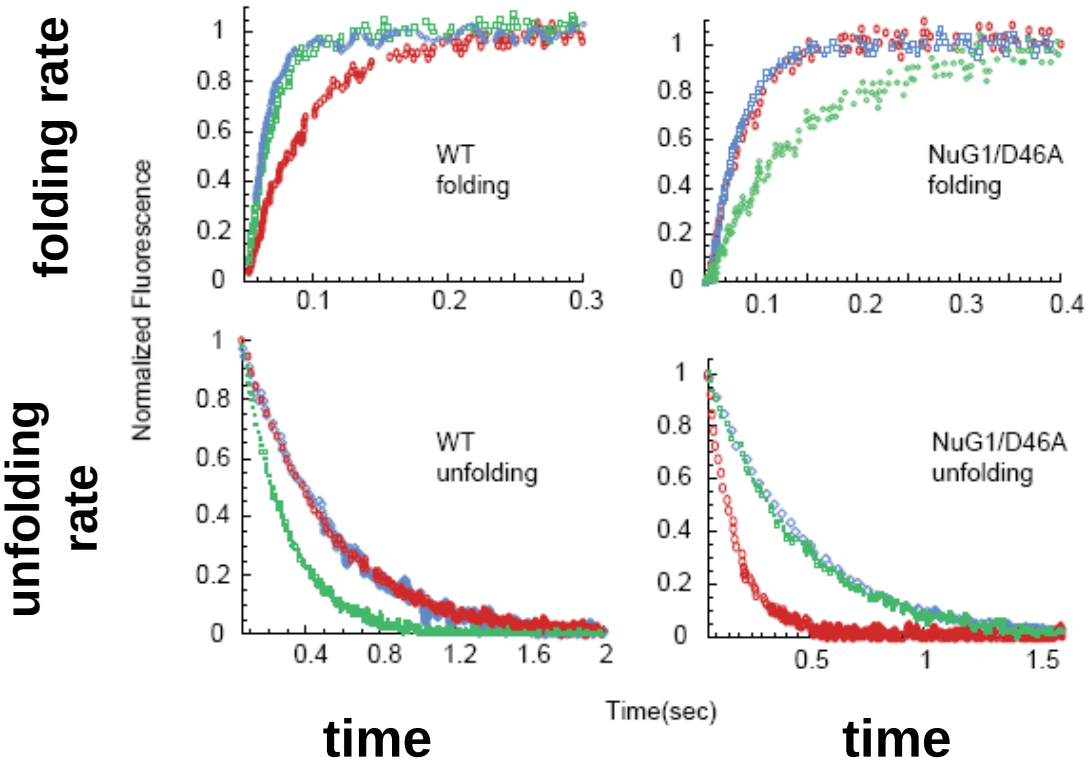
WT	6-ILNG**KT**LKGET-16
NuG1	6-FIVIG**D**RVVVV-16
NuG2	6-VIVL**N**GTTFTY-16

[1]Residues 1–5 and 17–57 are identical to wild type protein G. Turn residues are shown in bold. All variants of protein G were made and purified using published methods[9]. The identity of the proteins were verified by mass spectrometry.

Increase in stability by ~ 3.5 – 4 kcal/mol

Nauli et al, NSB 8, 602 (2001)

- NuG1/NuG2 fold ~100 times faster than wild type
- Destabilize turn #2 by mutating Asp 46 to Ala (D46A with loss of stability by ~ 1.5 kcal/mol)
- Further mutations in turn #1 and #2 result in different folding kinetics



blue: wt or NuG1/D46A
red: #2 hairpin mutation
green: #1 hairpin mutation

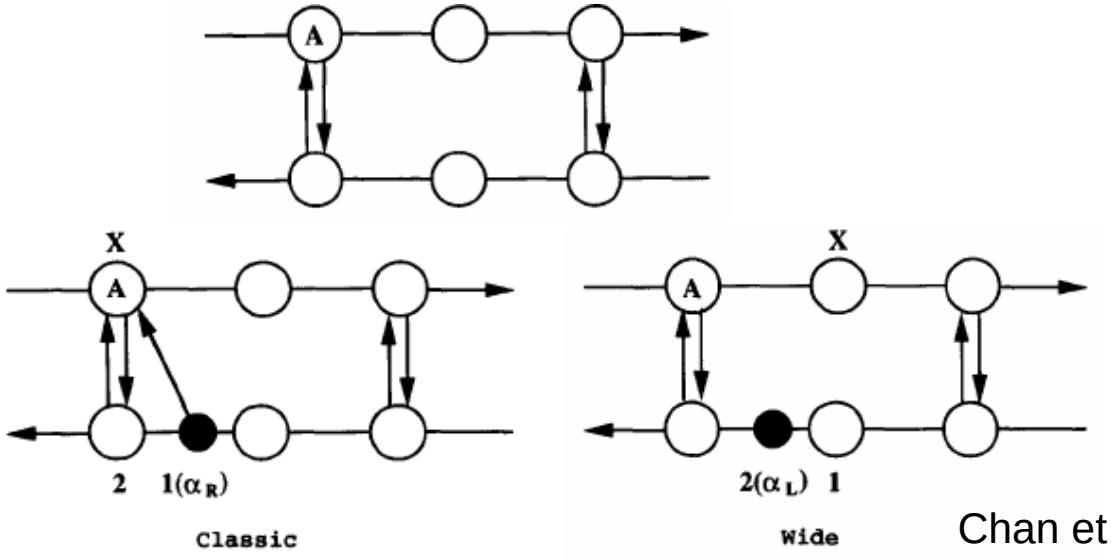
Nauli et al, NSB 8, 602 (2001)

Beta bulge

The region between two consecutive beta strands joined by hydrogen bonds which include two residues on one strand opposite a single residue on the other strand

may affect the direction of the strand

extra length in the backbone, causes the strand bend out of the plane and the curvature in the sheet is accentuated



Chan et al, Protein Sci 2, 1574 (1993)

Classic bulge

bulges are more common in antiparallel beta sheet with more than 50% of them occurring in the “classic +” conformation

NH(1) *** CO(X) (average strength)

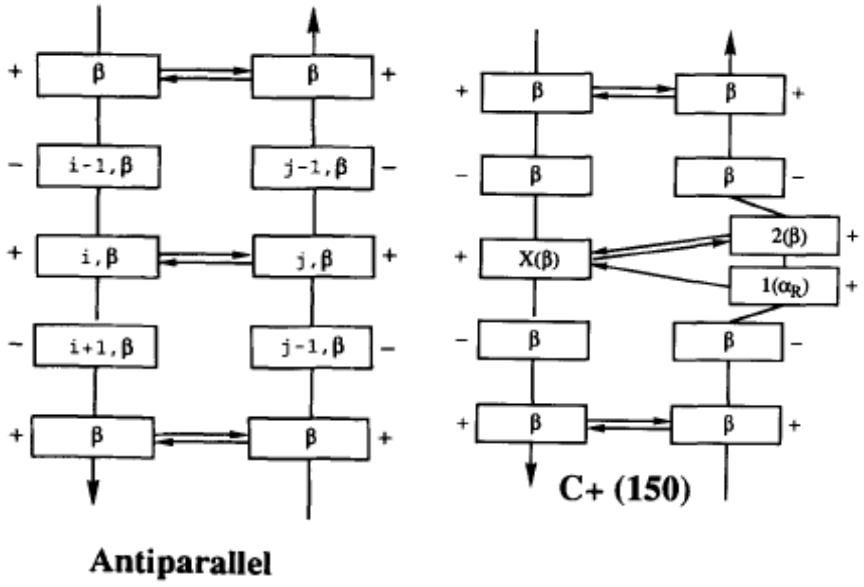
NH(2) *** CO(X) (weaker than average)

NH(X) *** CO(2) (average strength)

Res #1 in alpha-R conformation, Res #2 & X in beta conformation

Res #1 & X: large hydrophobic

Res #2: small amino acid gly, ala, ser



G1 bulge (second most common)

Occurs only in antiparallel beta sheets

Res #1 adopts alpha-L conformation and is usually Gly but can be Asn

Res #2 is often charged and its side chain hydrogen bonds with Res X (D, N)

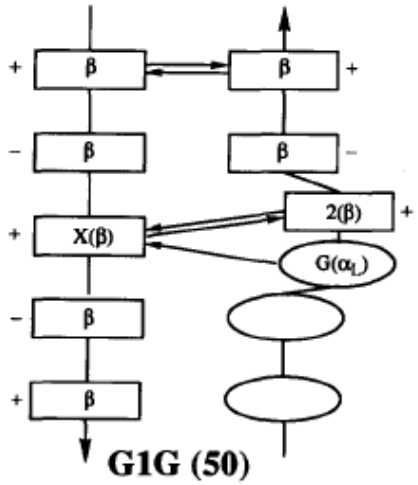


Table 6. *Amino acid preferences for β-bulges*

Class	1	2	X
C+	Ile, Val, Leu	Gly, Ala, Ser	Trp, Val, Arg, Ile
G1	Gly, Asn	Arg, Lys, Asp, Glu, Gln	Asn, Asp, His, Cys, Ser
Wide (anti)	Pro, Asp, Glu	Gln, Asn, Asp	Thr

Wide bulge

Res #1 and #2 do not participate in hydrogen bond

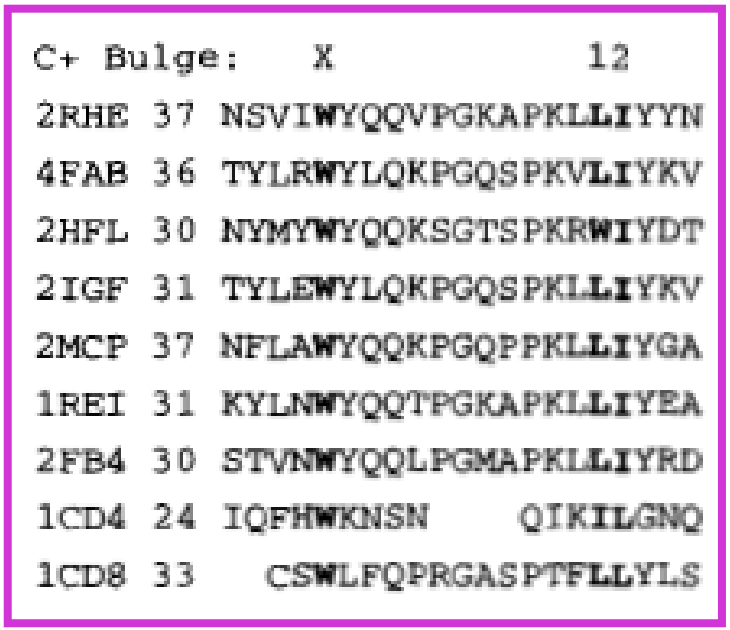
#1 adopts beta conformation, #2 alpha-L conformation

#2 is often Gly, Asn, Asp, and rarely hydrophobic

In general, prolines are not very common in the bulge, although they appear at the position just before Res #1

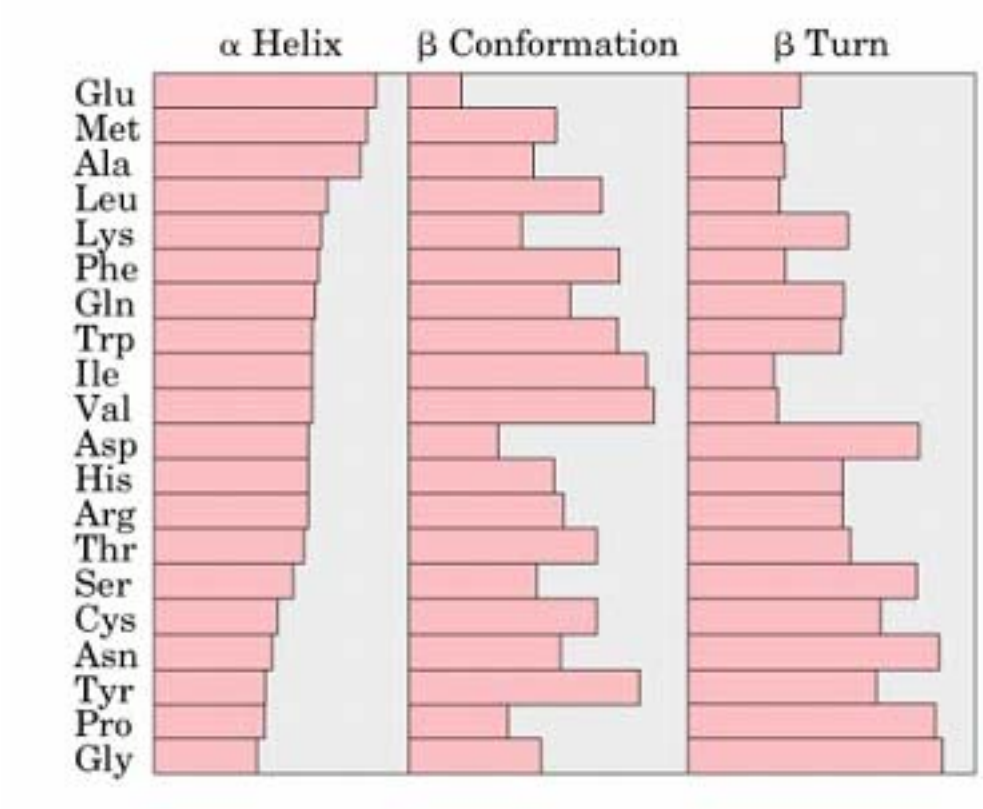
Creating a bulge is not energetically unfavorable

Bulges may be functionally important since some bulges are conserved in homologous proteins



immunoglobulin domain

Summary of secondary structure propensity



Conformational Preferences of the Amino Acids

Amino acid	Preference α-helix	β-strand	Reverse turn
Glu	**1.59**	0.52	1.01
Ala	**1.41**	0.72	0.82
Leu	**1.34**	1.22	0.57
Met	**1.30**	1.14	0.52
Gln	**1.27**	0.98	0.84
Lys	**1.23**	0.69	1.07
Arg	**1.21**	0.84	0.90
His	**1.05**	0.80	0.81
Val	0.90	**1.87**	0.41
Ile	1.09	**1.67**	0.47
Tyr	0.74	**1.45**	0.76
Cys	0.66	**1.40**	0.54
Trp	1.02	**1.35**	0.65
Phe	1.16	**1.33**	0.59
Thr	0.76	**1.17**	0.90
Gly	0.43	0.58	**1.77**
Asn	0.76	0.48	**1.34**
Pro	0.34	0.31	**1.32**
Ser	0.57	0.96	**1.22**
Asp	0.99	0.39	**1.24**

Figure 1-20 Table of conformational preferences of the amino acids The normalized frequencies for each conformation were calculated from the fraction of residues of each amino acid that occurred in that conformation, divided by this fraction for all residues. Random occurrence of a particular amino acid in a conformation would give a value of unity. A value greater than unity indicates a preference for a particular type of secondary structure. Adapted, with permission, from Table II of Williams, R.W. *et al.*: *Biochim. Biophys. Acta* 1987, **916**:200–204.

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