COMPUTATIONAL STRUCTURAL BIOLOGY

STRUCTURE, SIMULATION, FUNCTION & PREDICTION

Lecture 2

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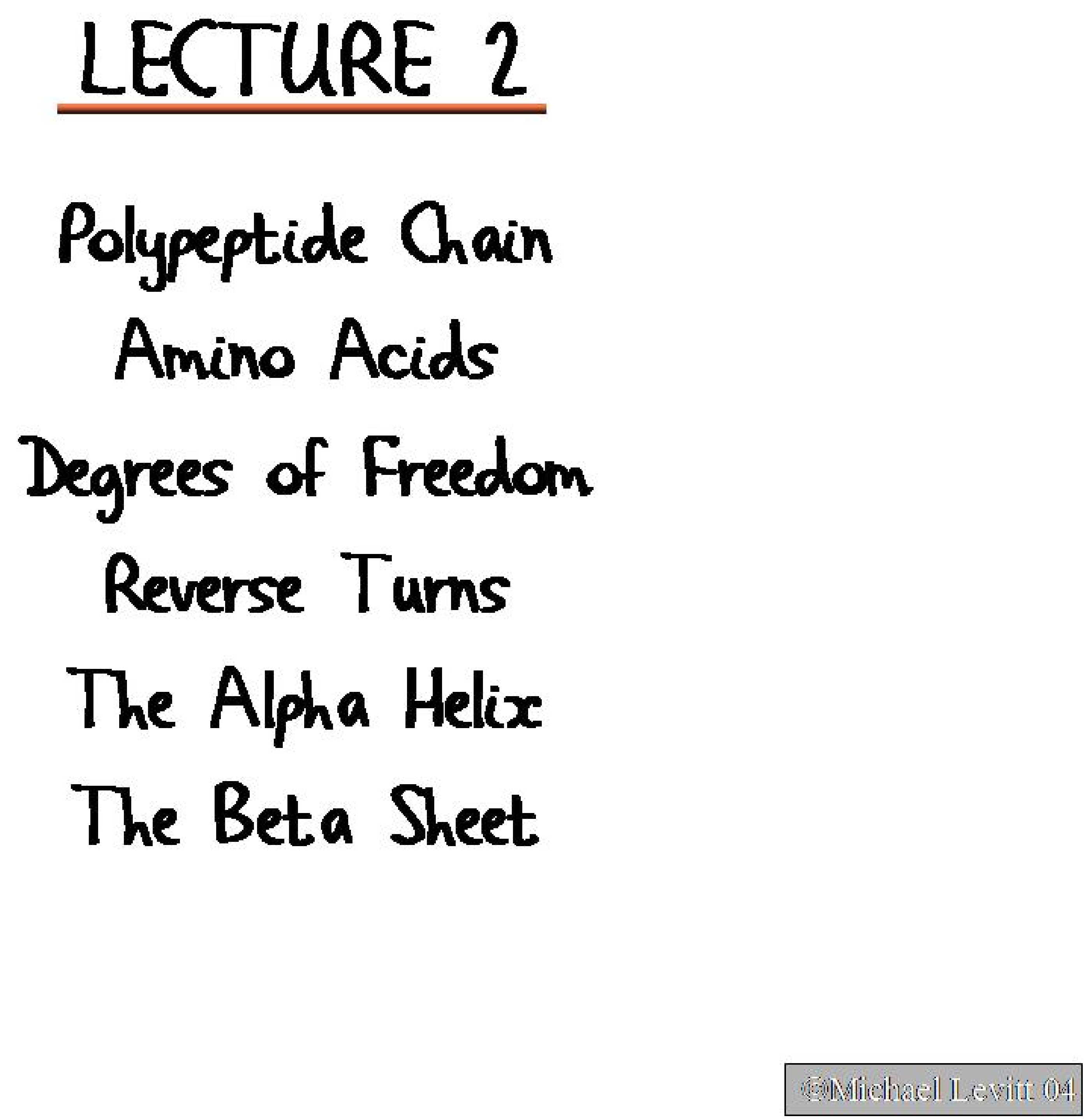
http:/csb.stanford.edu/class



LECTURE 2

Polypeptide Chain

Amino Acids

Degrees of Freedom

Reverse Turns

The Alpha Helix

The Beta Sheet

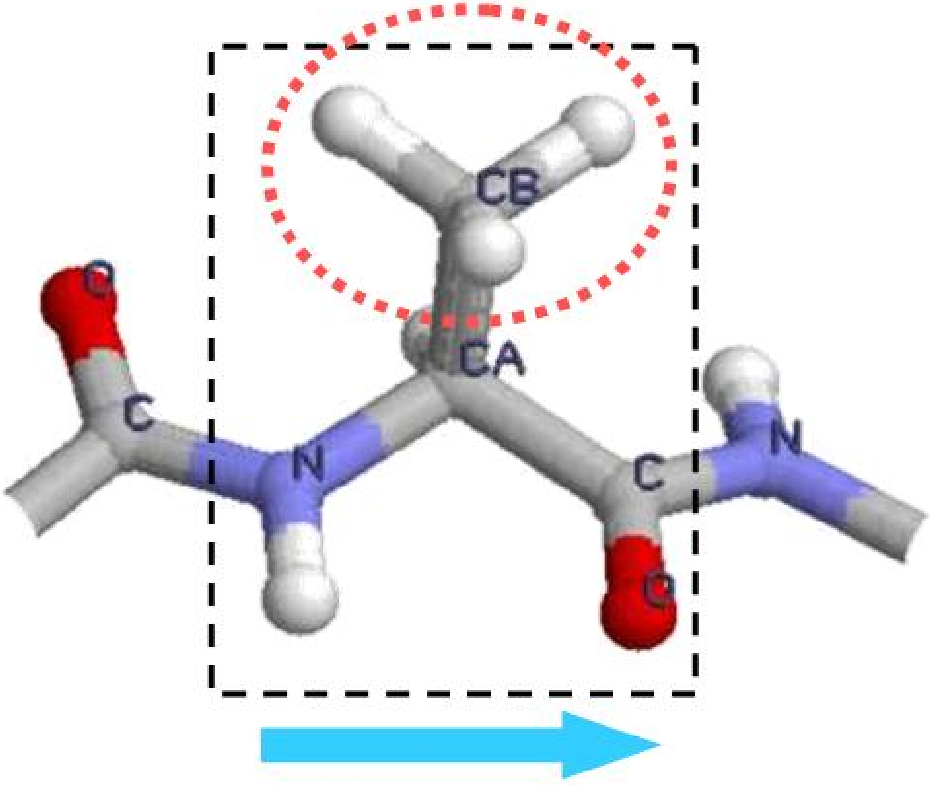
Polypeptide Chain Concept 2.1

THE POLYPEPTIDE CHAIN

Chemical Structure

The Peptide Group

CHEMICAL STRUCTURE

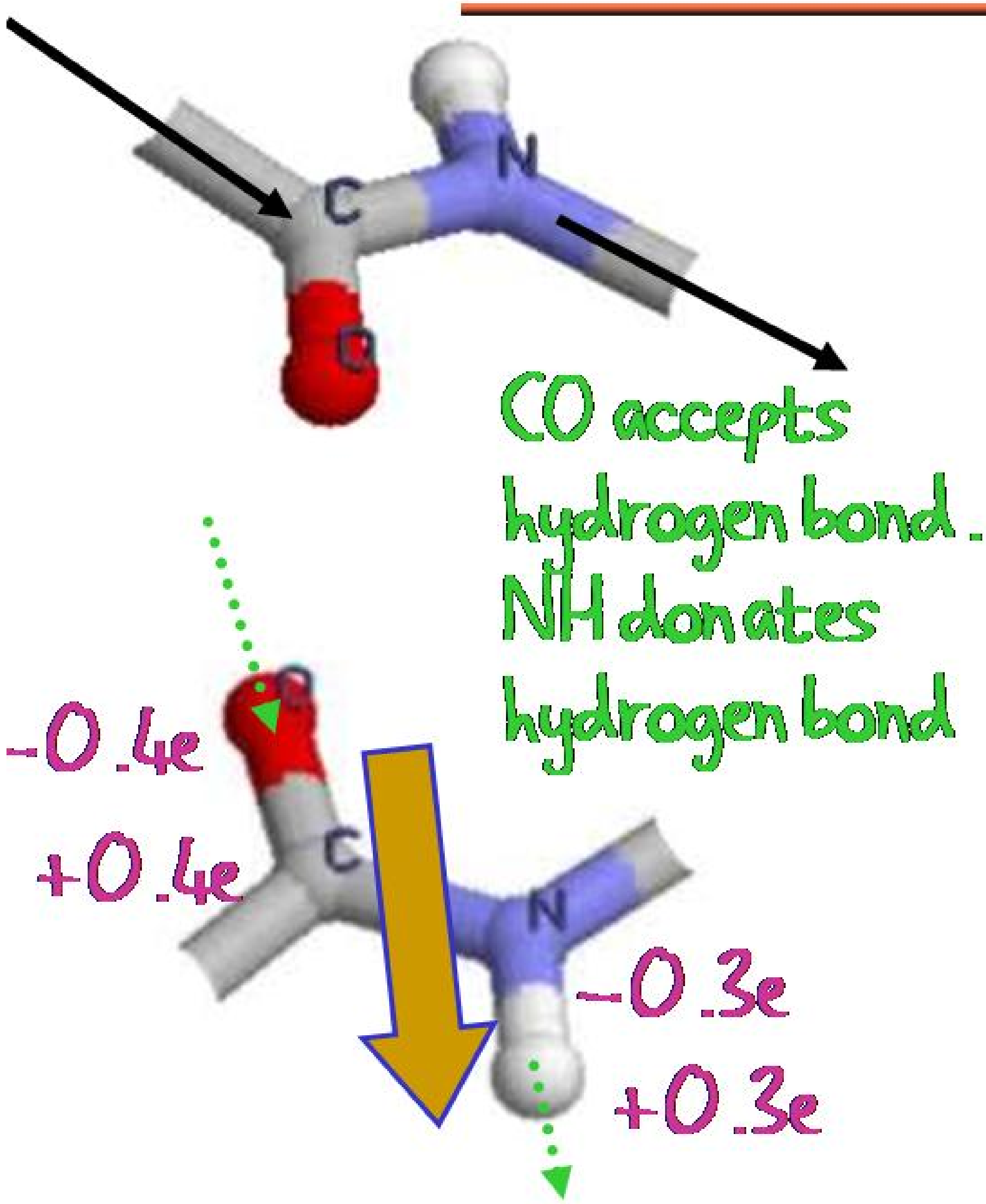


- An amino acid runs from the NH group to the CO group.

- The amino acid side chain is attached to the CA atom.

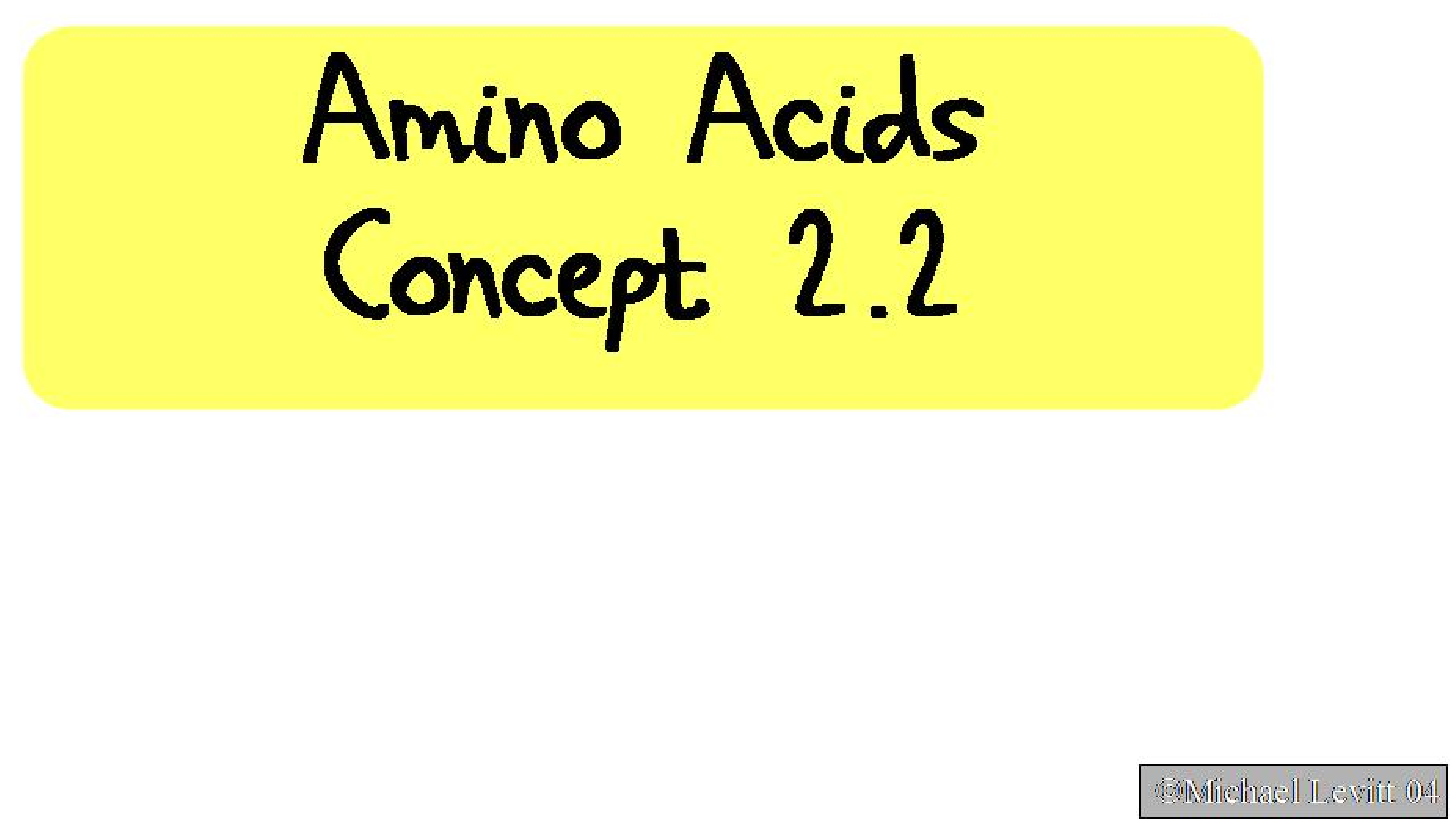
- It has L chirality always pointing up in the orientation shown.

THE PEPTIDE GROUP



CO accepts hydrogen bond.
NH donates hydrogen bond

- The peptide group between amino acids is rigid and planar (resonance).
- It has co-linear bonds entering and leaving.
- The peptide group has a strong dipole moment due to partial charges on NH and CO groups.

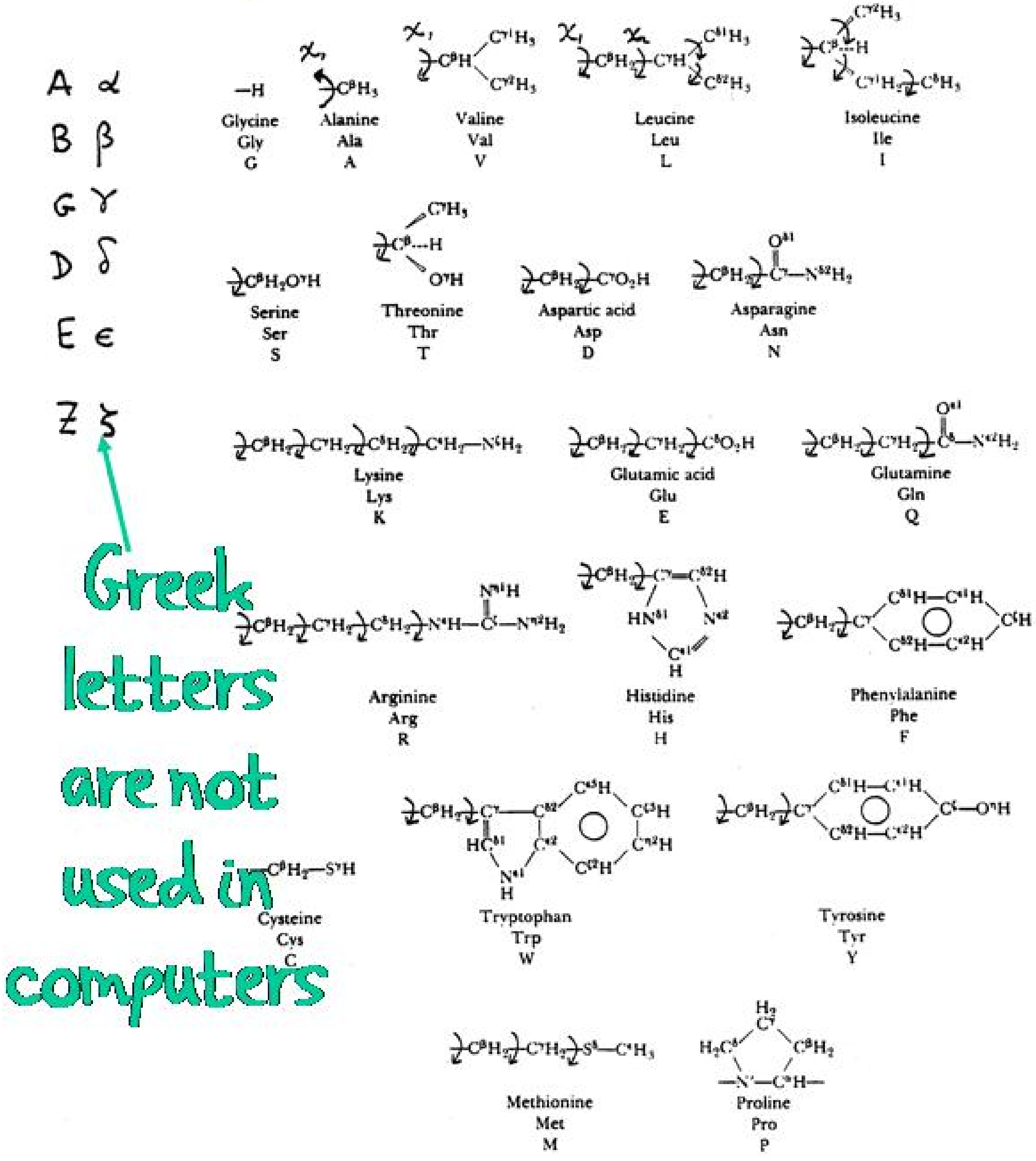


Amino Acids
Concept 2.2

AMINO ACIDS

Amino Acid Side Chains
Amino Acid Names
Amino Acid Classification 1
Amino Acids: Gly & Pro
Amino Acids: Cys
Amino Acids: Leu & Phe
Amino Acids: Glu & Arg
Amino Acids: Val & Ile
Amino Acid Classification 2

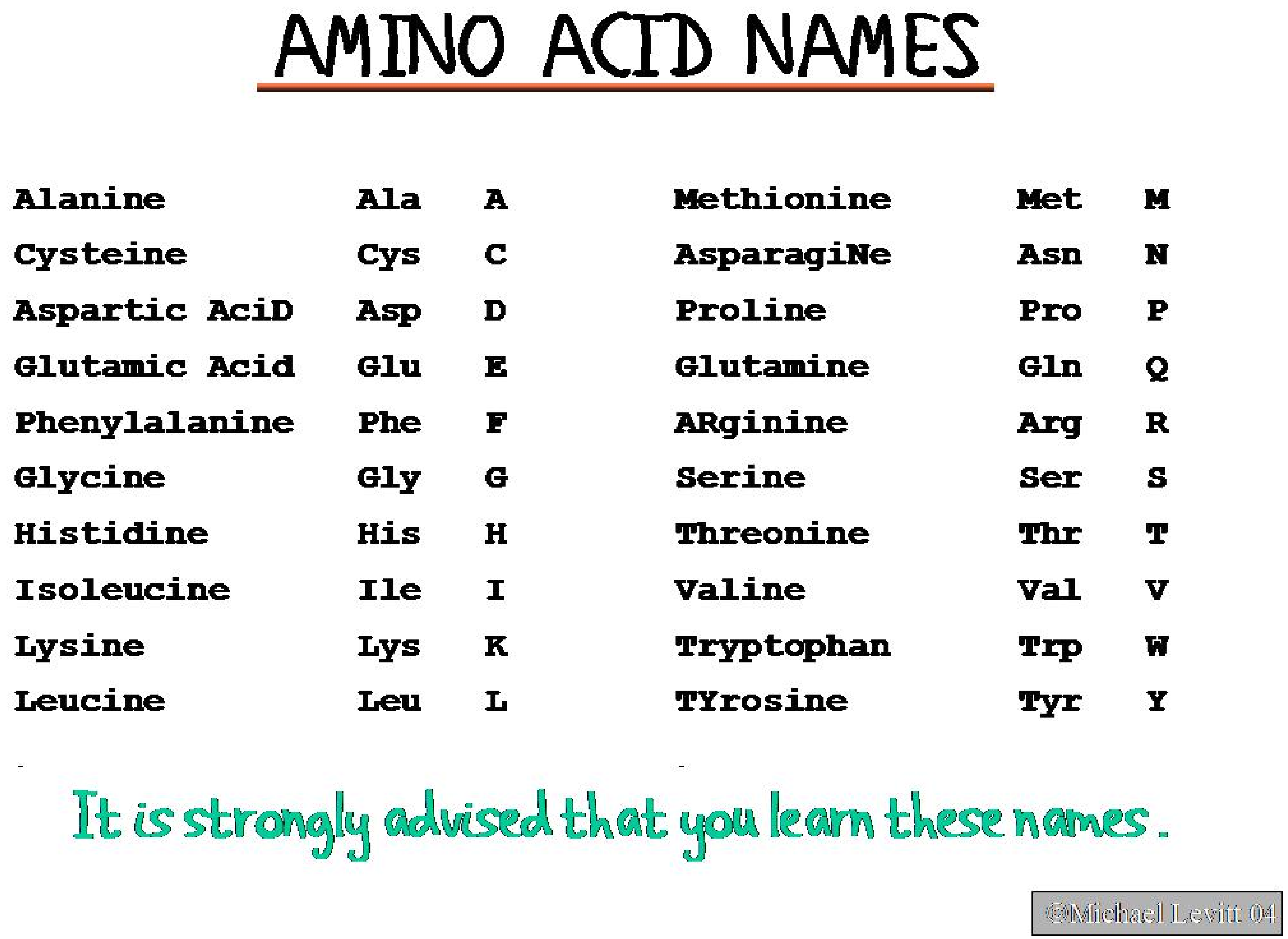
AMINO ACID SIDE CHAINS



A α
B β
G γ
D δ
E ε
Z ζ

Greek letters are not used in computers

- There are 20 naturally occurring amino acids.
- It is worth learning the amino acid names.
- There are many text books that say much more about amino acids.

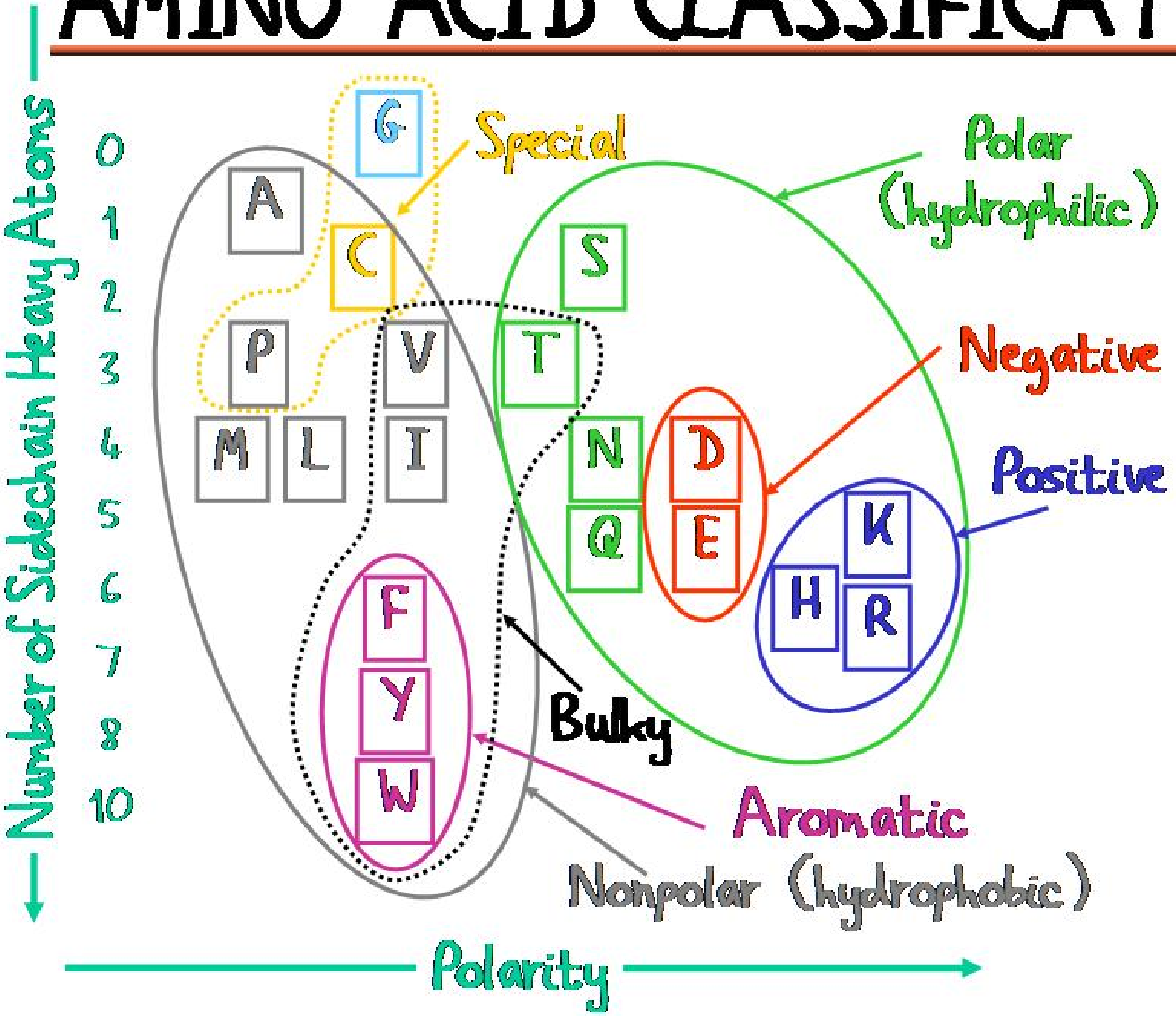


AMINO ACID NAMES

Alanine	Ala	A	Methionine	Met	M
Cysteine	Cys	C	AsparagiNe	Asn	N
Aspartic AciD	Asp	D	Proline	Pro	P
Glutamic Acid	Glu	E	Glutamine	Gln	Q
Phenylalanine	Phe	F	ARginine	Arg	R
Glycine	Gly	G	Serine	Ser	S
Histidine	His	H	Threonine	Thr	T
Isoleucine	Ile	I	Valine	Val	V
Lysine	Lys	K	Tryptophan	Trp	W
Leucine	Leu	L	TYrosine	Tyr	Y

It is strongly advised that you learn these names.

AMINO ACID CLASSIFICATION 1



There are many properties.

They cluster logically.

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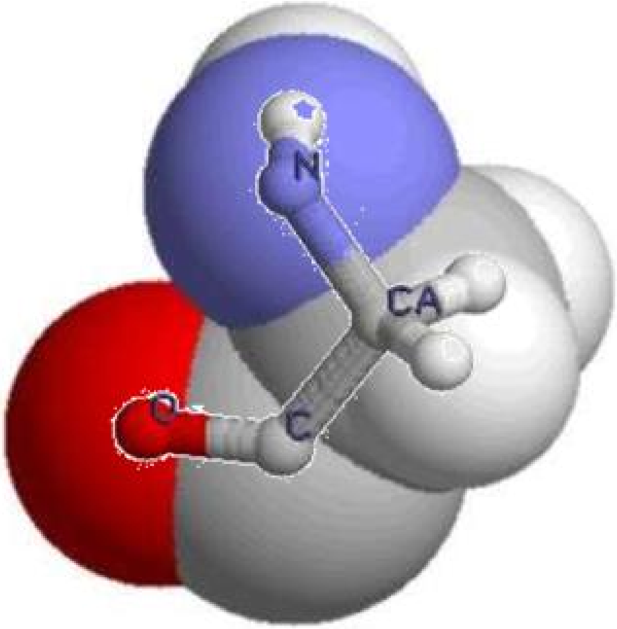
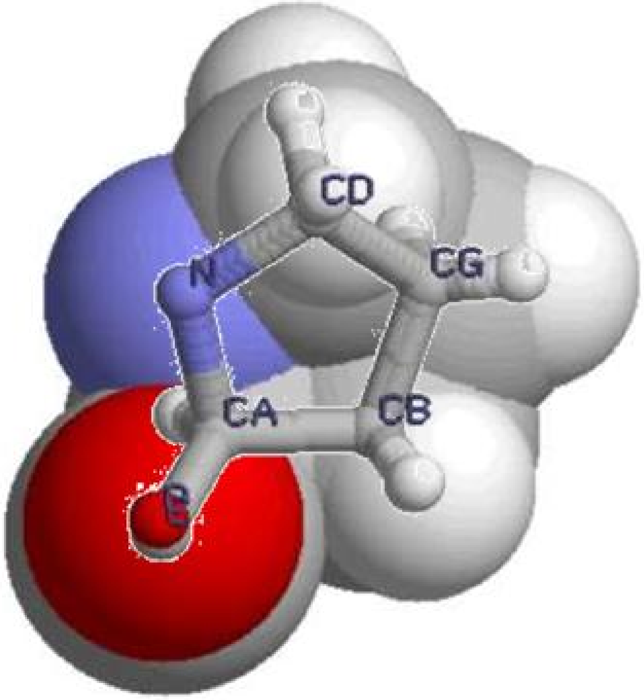
AMINO ACIDS GLY AND PRO

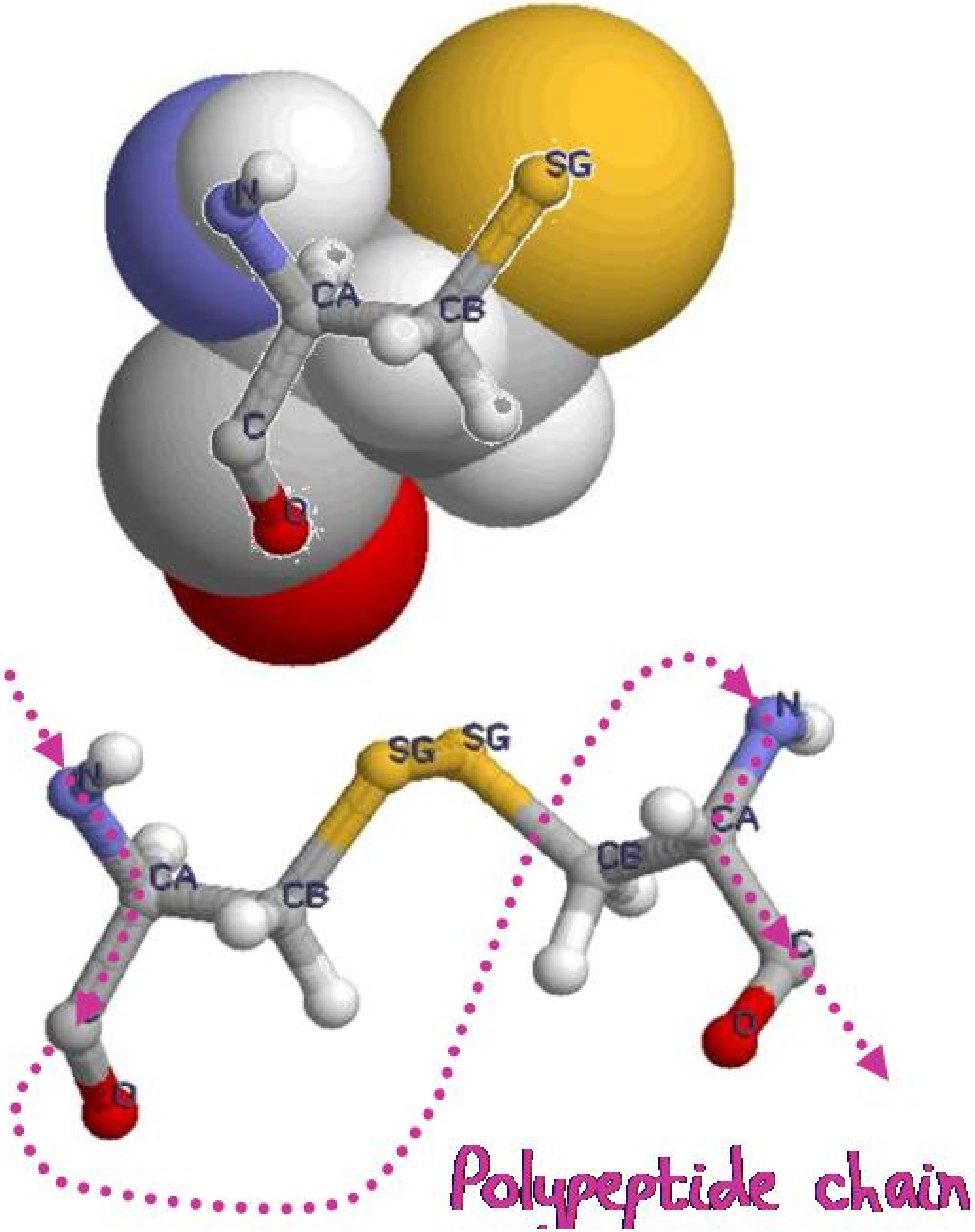


- Glycine is simplest, without a sidechain. It is very flexible.

- Proline is the only cyclic amino acid used in proteins. It is very rigid.

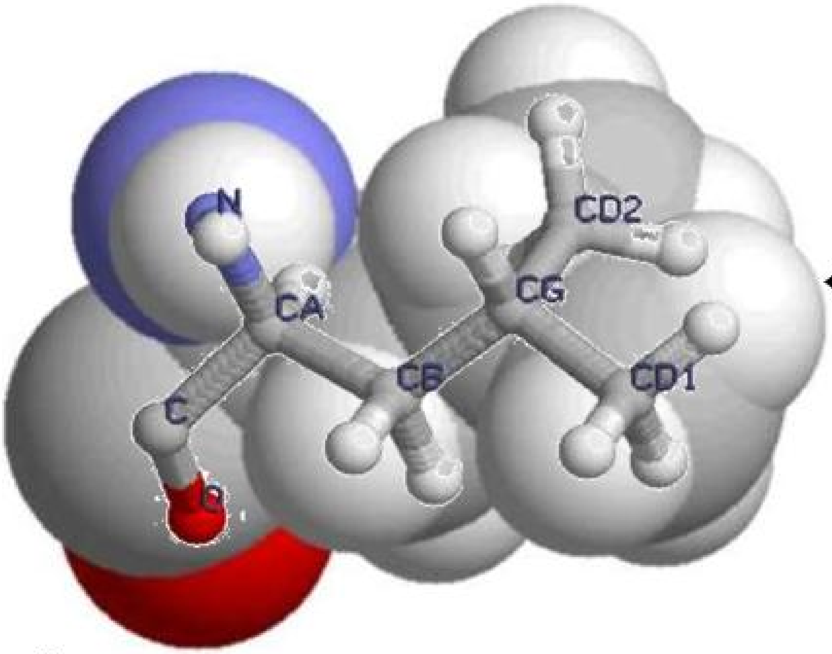


AMINO ACIDS CYS



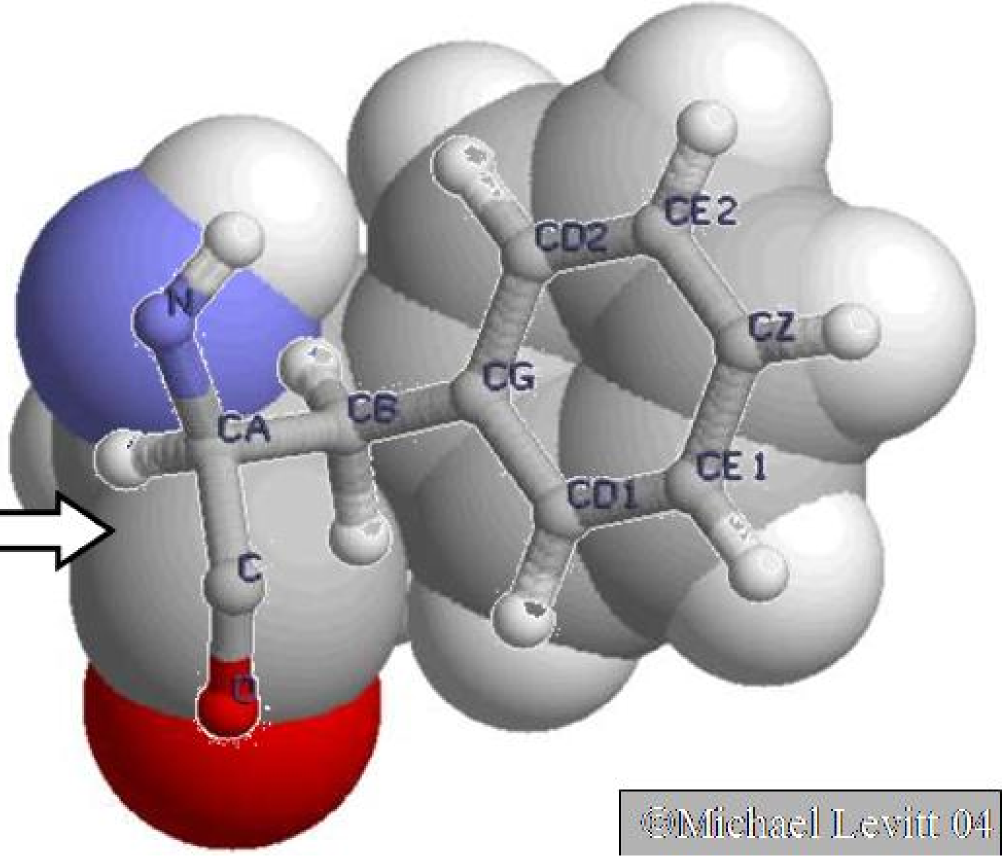
- Cystine is special in that it forms covalent bonds.
- These are called SS bonds or disulfide bridges.
- They make closed loops in the polypeptide chain.

AMINO ACIDS LEU AND PHE

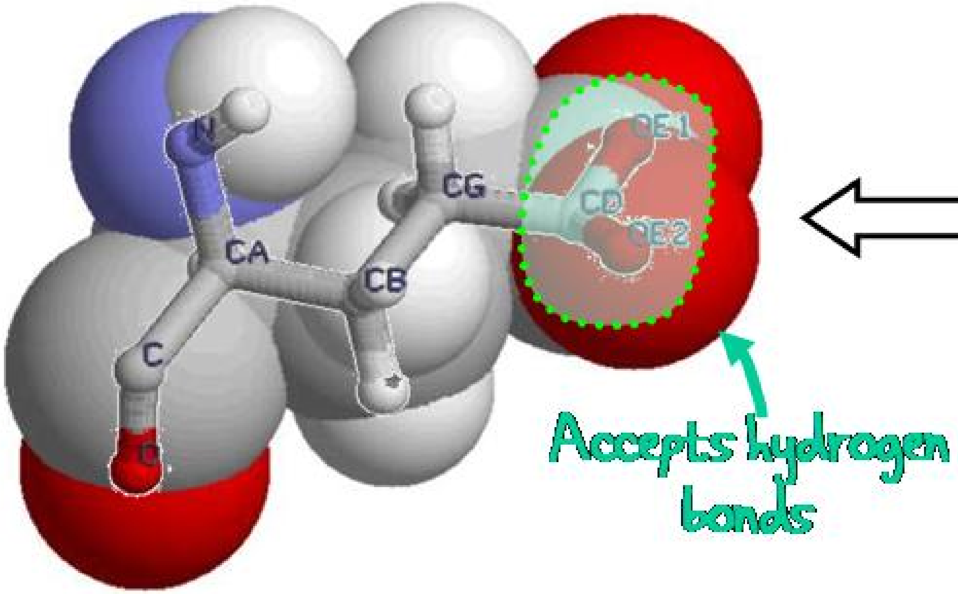


- Leucine is a branched aliphatic hydrophobic amino acid.

- Phenylalanine is an aromatic hydrophobic amino acid. It is one the largest amino acids.



AMINO ACIDS GLU AND ARG



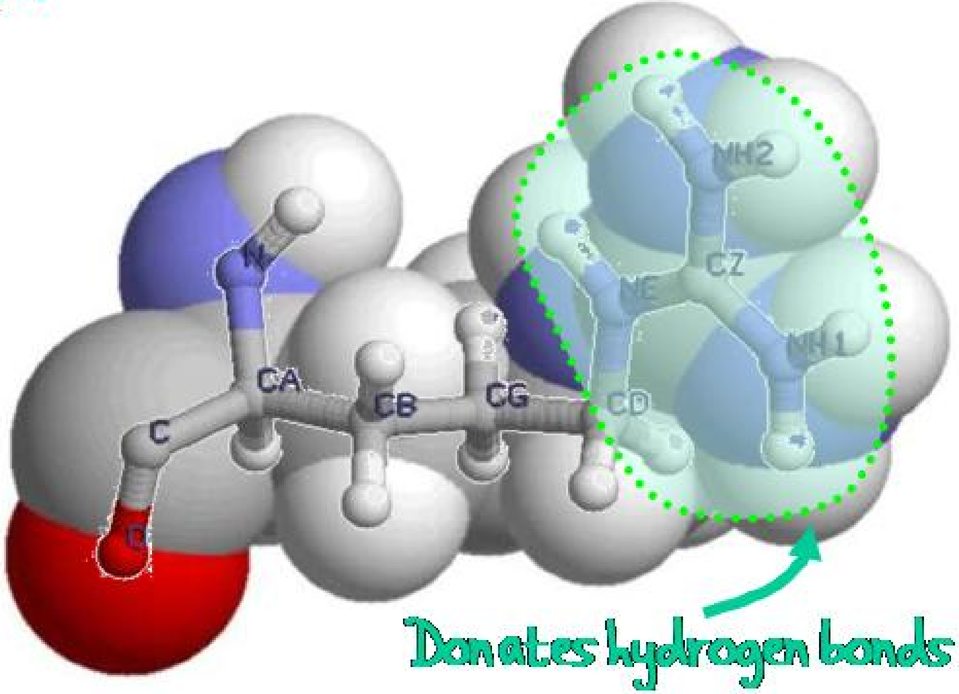
Accepts hydrogen bonds

- Glutamic Acid is a large polar amino acid.

  It accepts hydrogen bonds and is normally ionized (−1e).

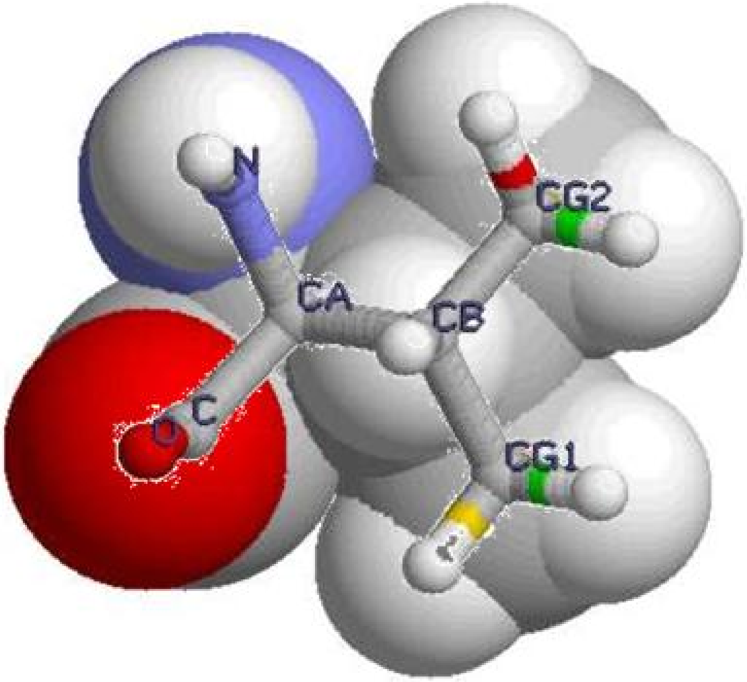
- Arginine is a large polar amino acid.

  It donates hydrogen bonds and is normally ionized (+1e).



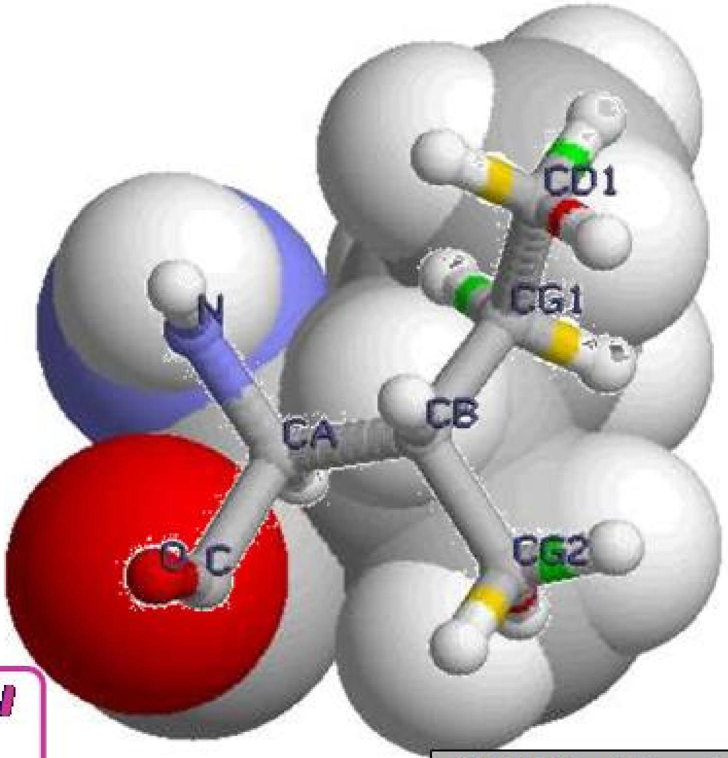
Donates hydrogen bonds

AMINO ACIDS VAL AND ILE

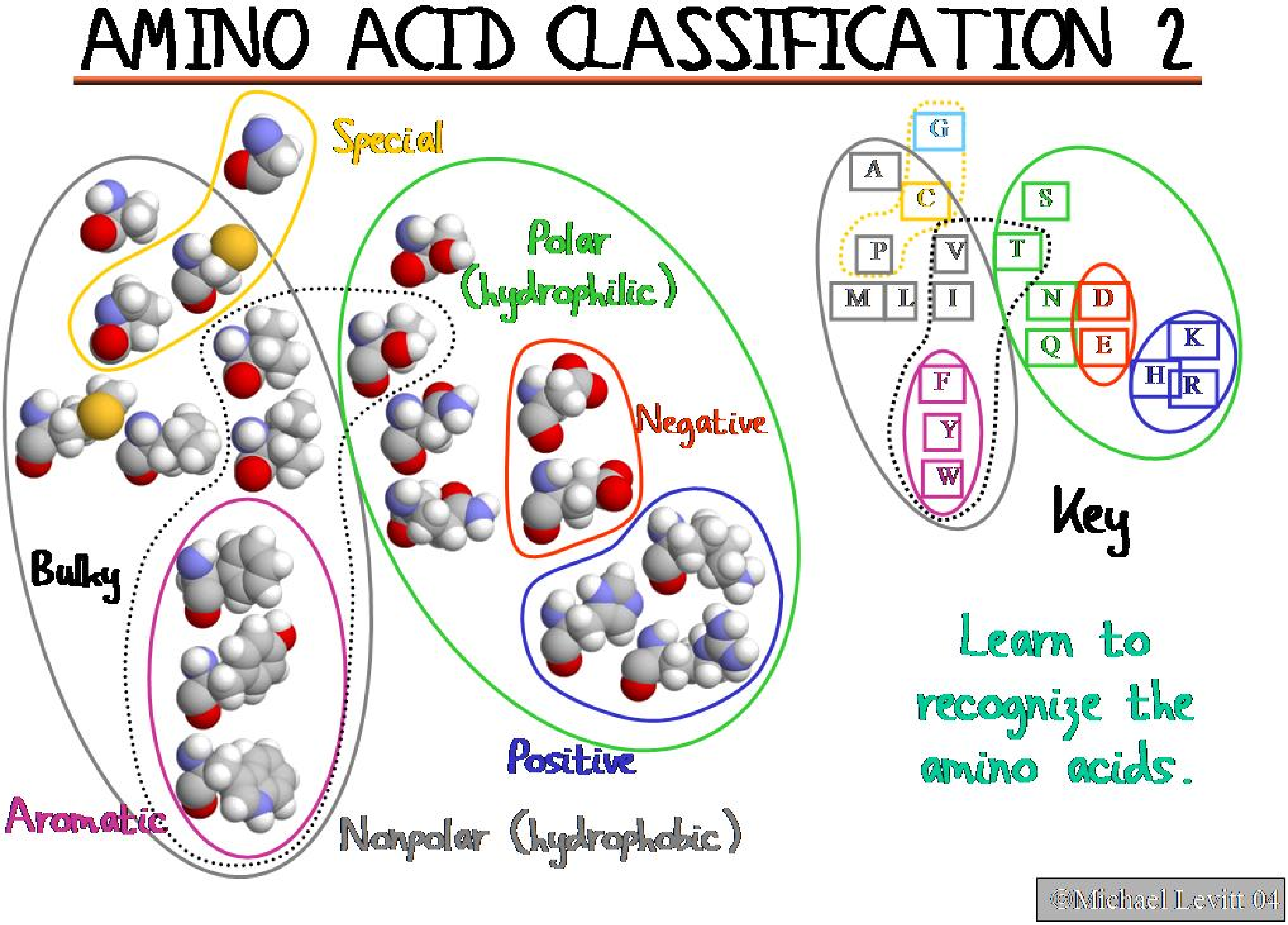


- Valine is a branched aliphatic hydrophobic amino acid. It branches at the CB atom.

- Isoleucine is also a branched aliphatic hydrophobic amino acid.



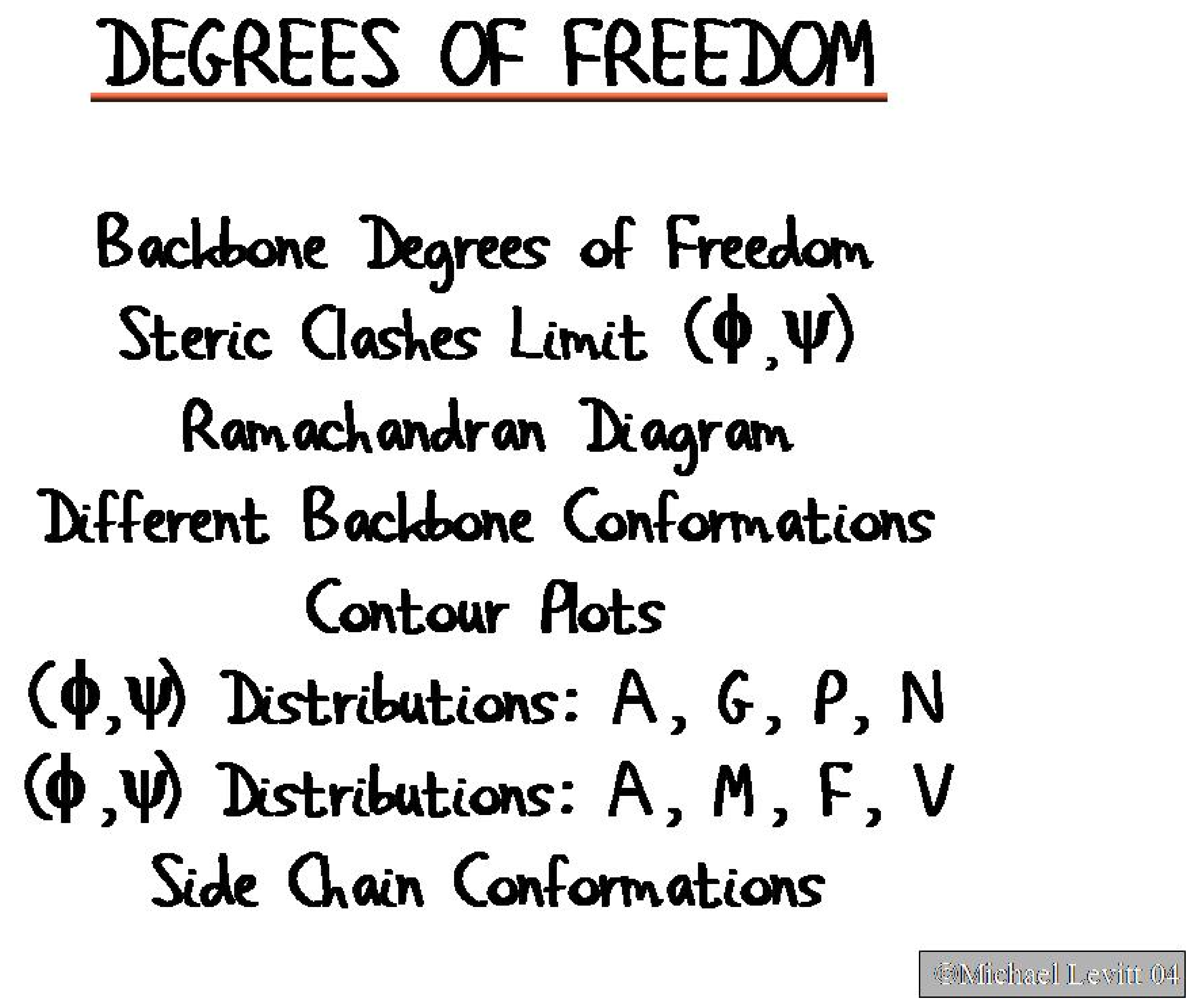
These amino acids are "Bulky"



AMINO ACID CLASSIFICATION 2

Learn to recognize the amino acids.

Degrees of Freedom
Concept 2.3



DEGREES OF FREEDOM

Backbone Degrees of Freedom

Steric Clashes Limit (ϕ, ψ)

Ramachandran Diagram

Different Backbone Conformations

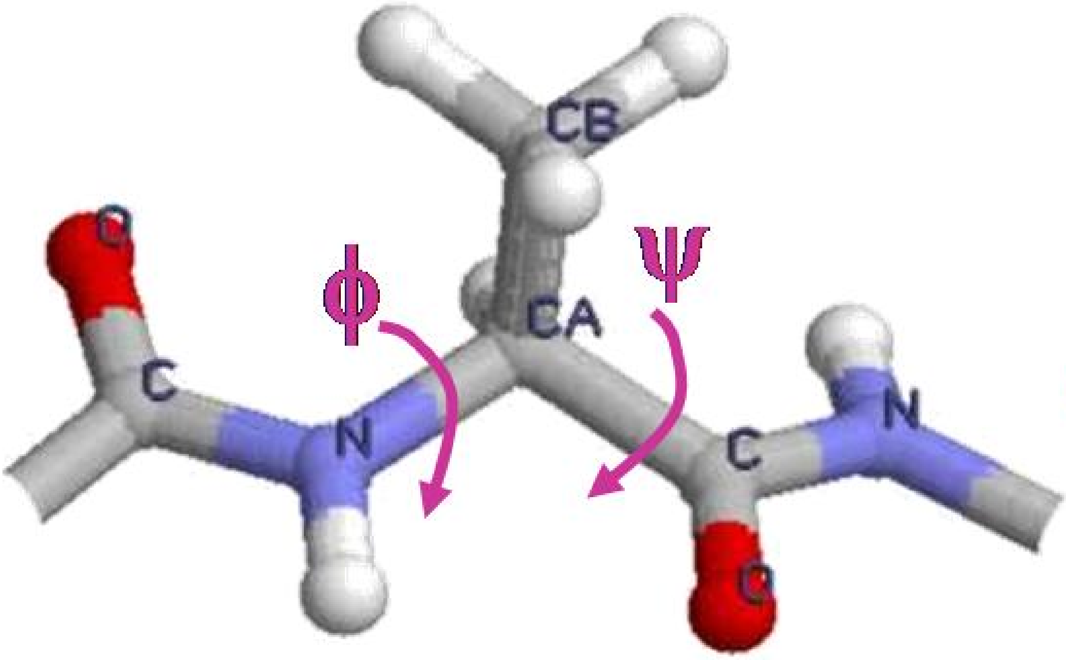
Contour Plots

(ϕ, ψ) Distributions: A, G, P, N

(ϕ, ψ) Distributions: A, M, F, V

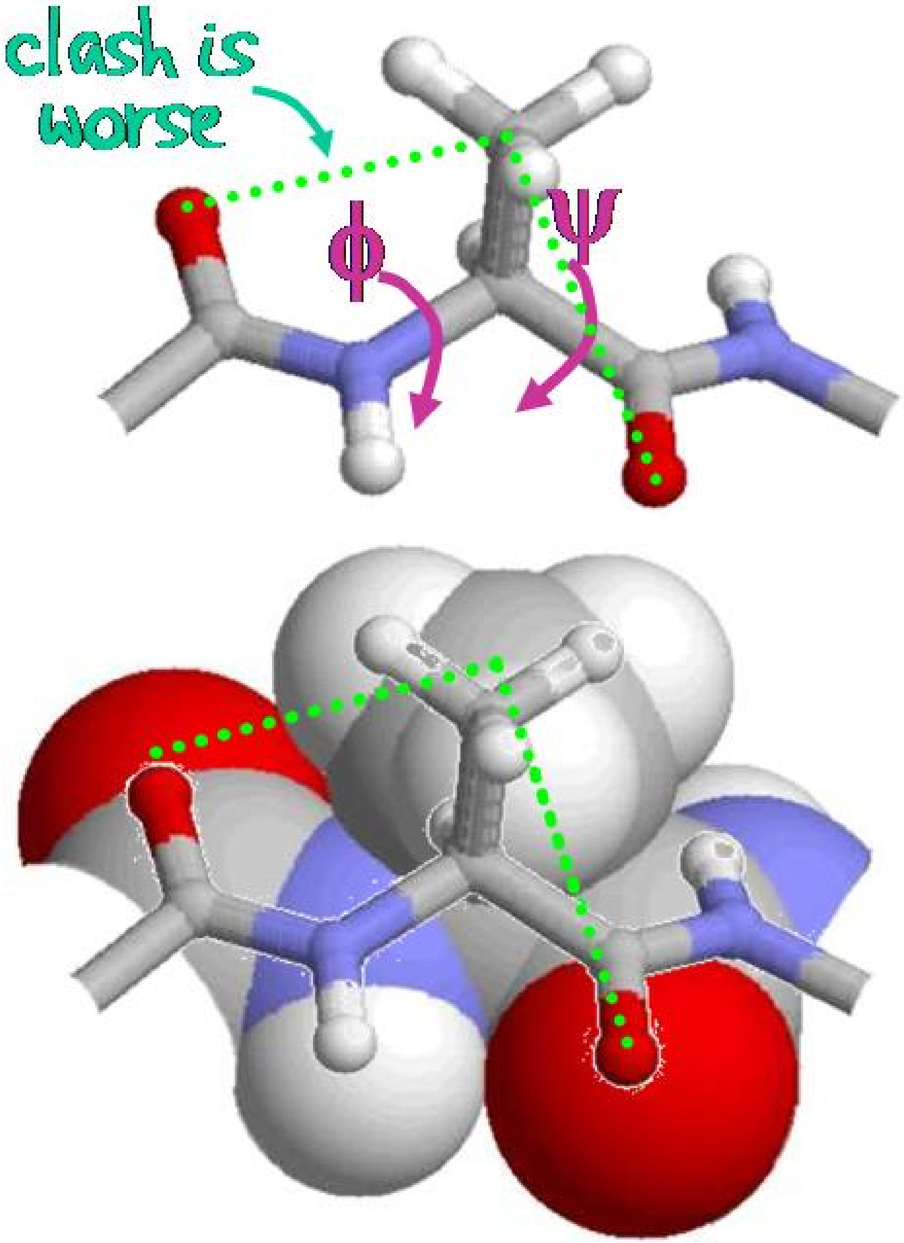
Side Chain Conformations

BACKBONE DEGREES OF FREEDOM



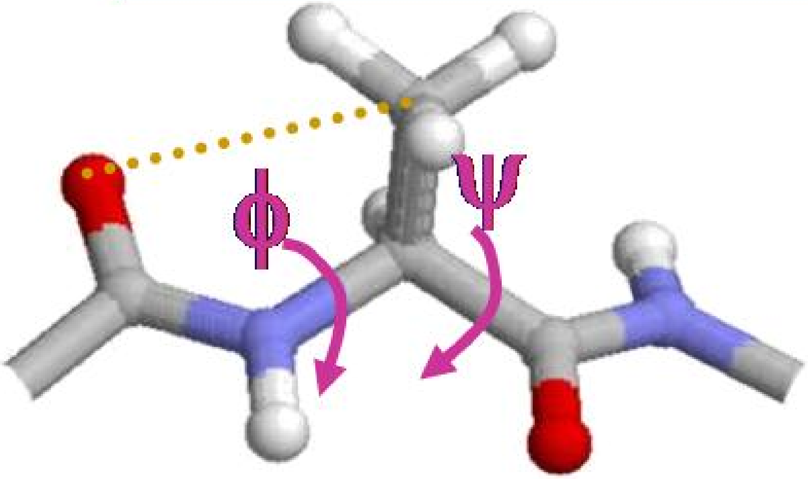
- The torsion angle rotating about the N–CA bond is called φ
- The torsion angle rotating about the CA–C bond is called ψ
- Together they are the (φ,ψ) angles

STERIC CLASHES LIMIT PHI, PSI

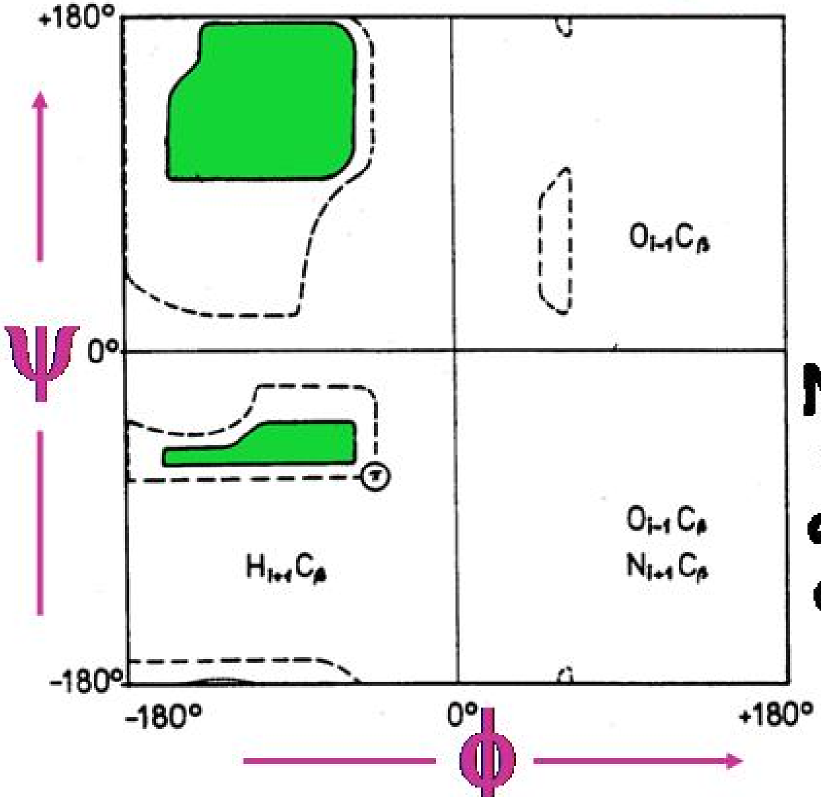


- The peptide O atom is much bigger than the peptide H atom. It can clash with the side chain.
- As the CO group is closer for rotation about φ than for ψ, the clash is worse.

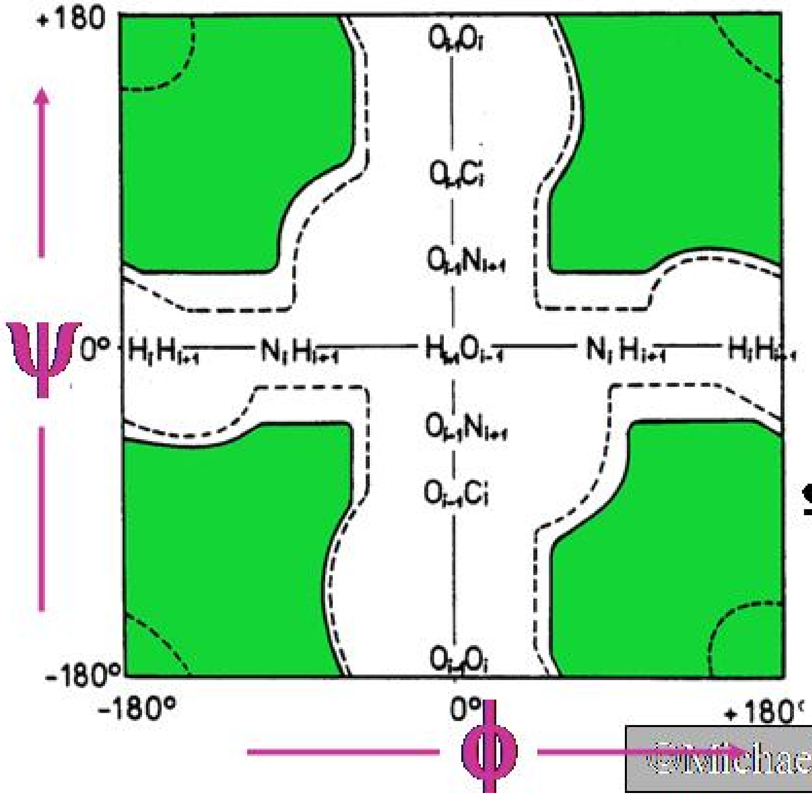
RAMACHANDRAN DIAGRAM



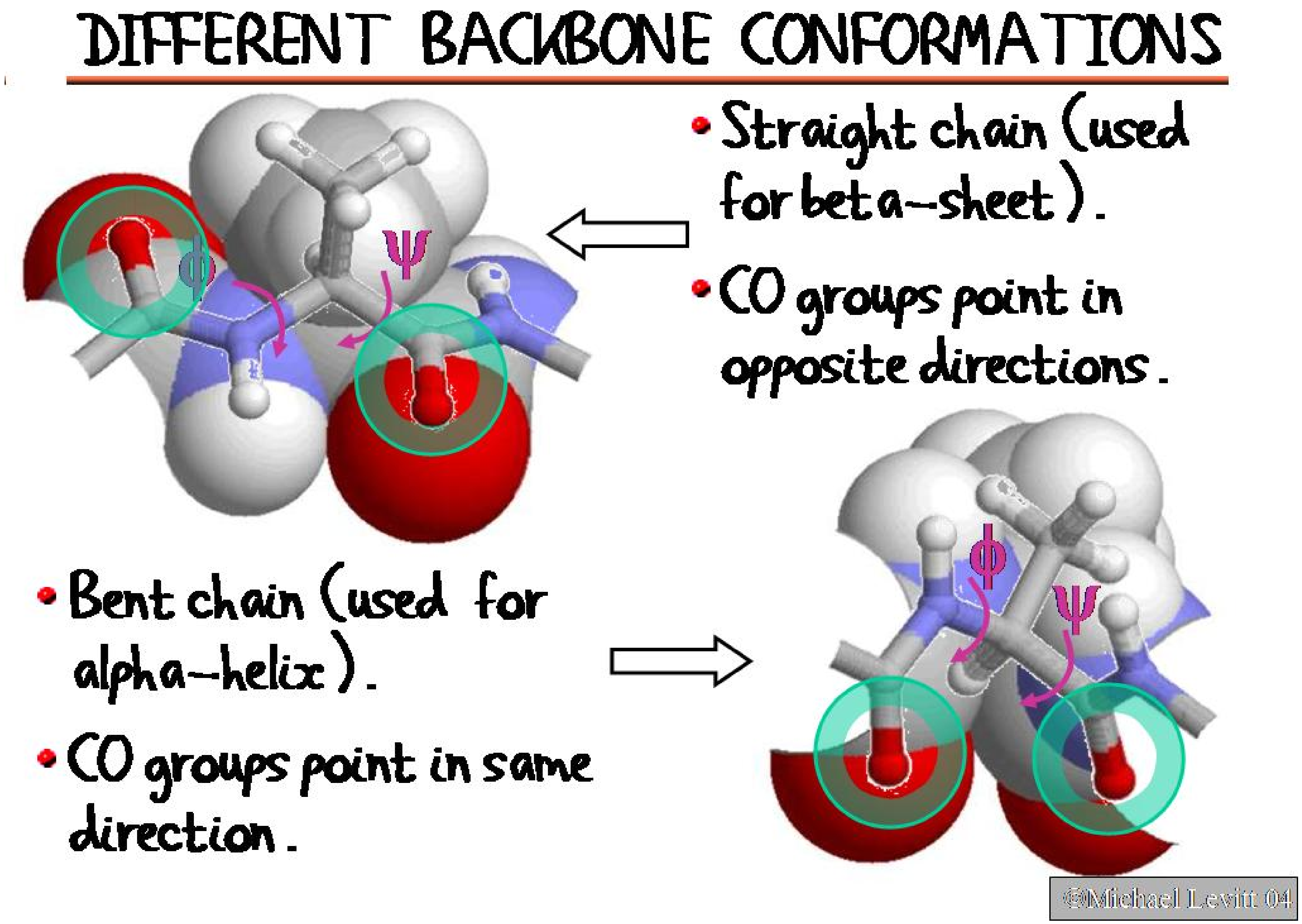
- Map the clashes. (Done in 1963).
- Green is allowed.



Non-GLY amino acids



GLY special No CB



DIFFERENT BACKBONE CONFORMATIONS

- Straight chain (used for beta-sheet).
- CO groups point in opposite directions.

- Bent chain (used for alpha-helix).
- CO groups point in same direction.

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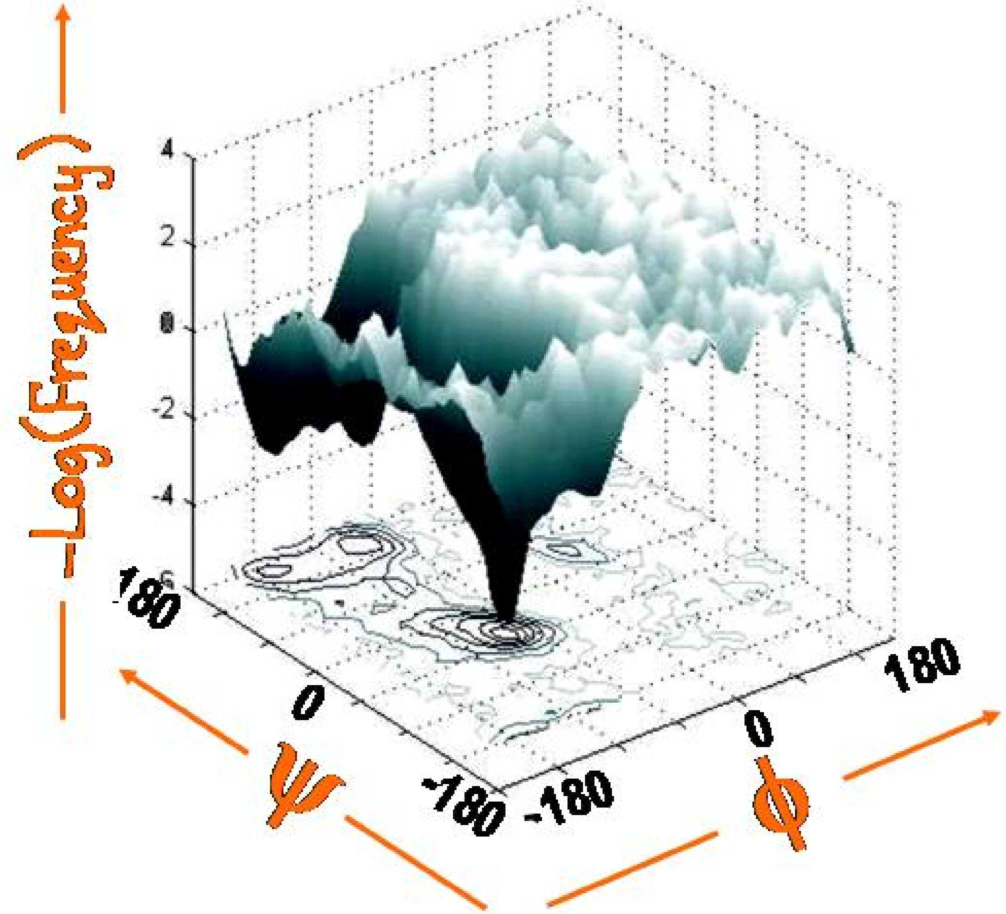
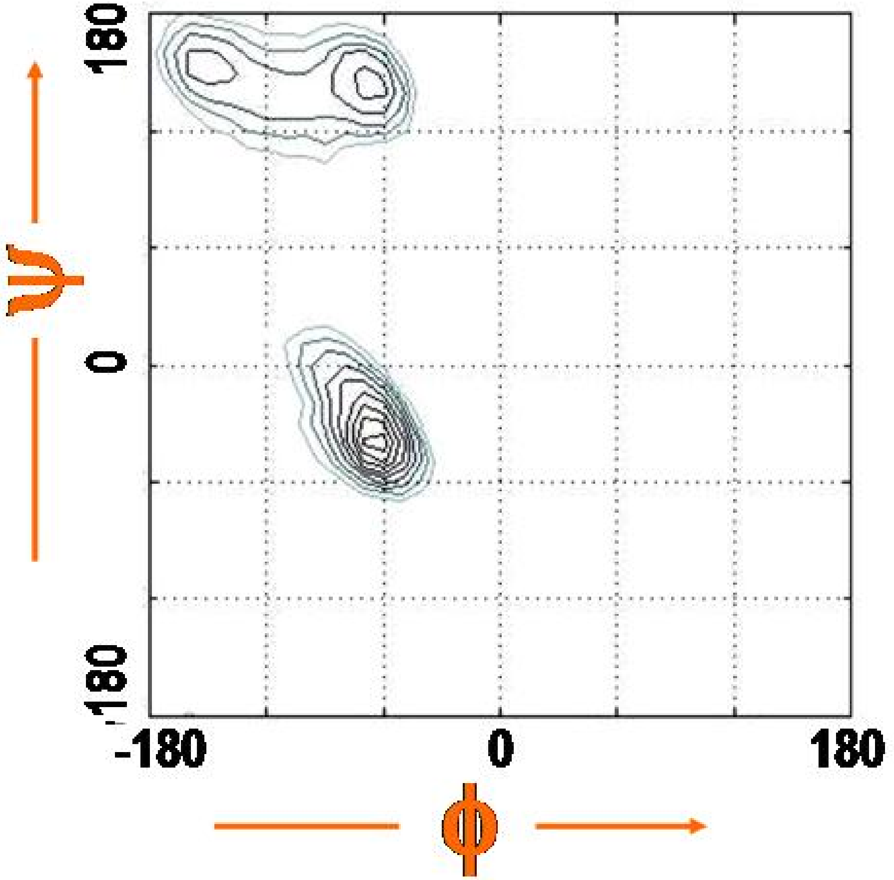
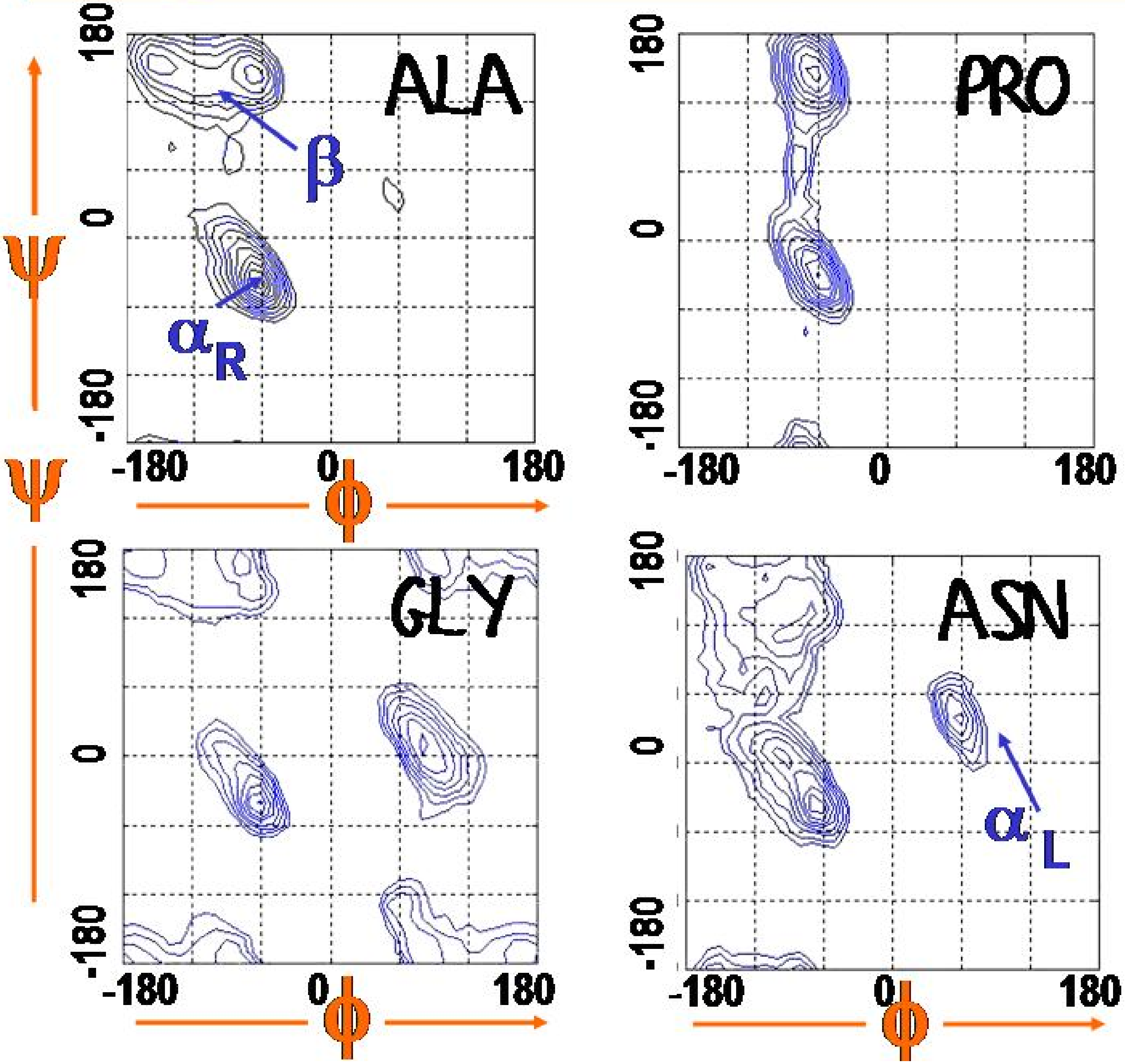
CONTOUR PLOTS





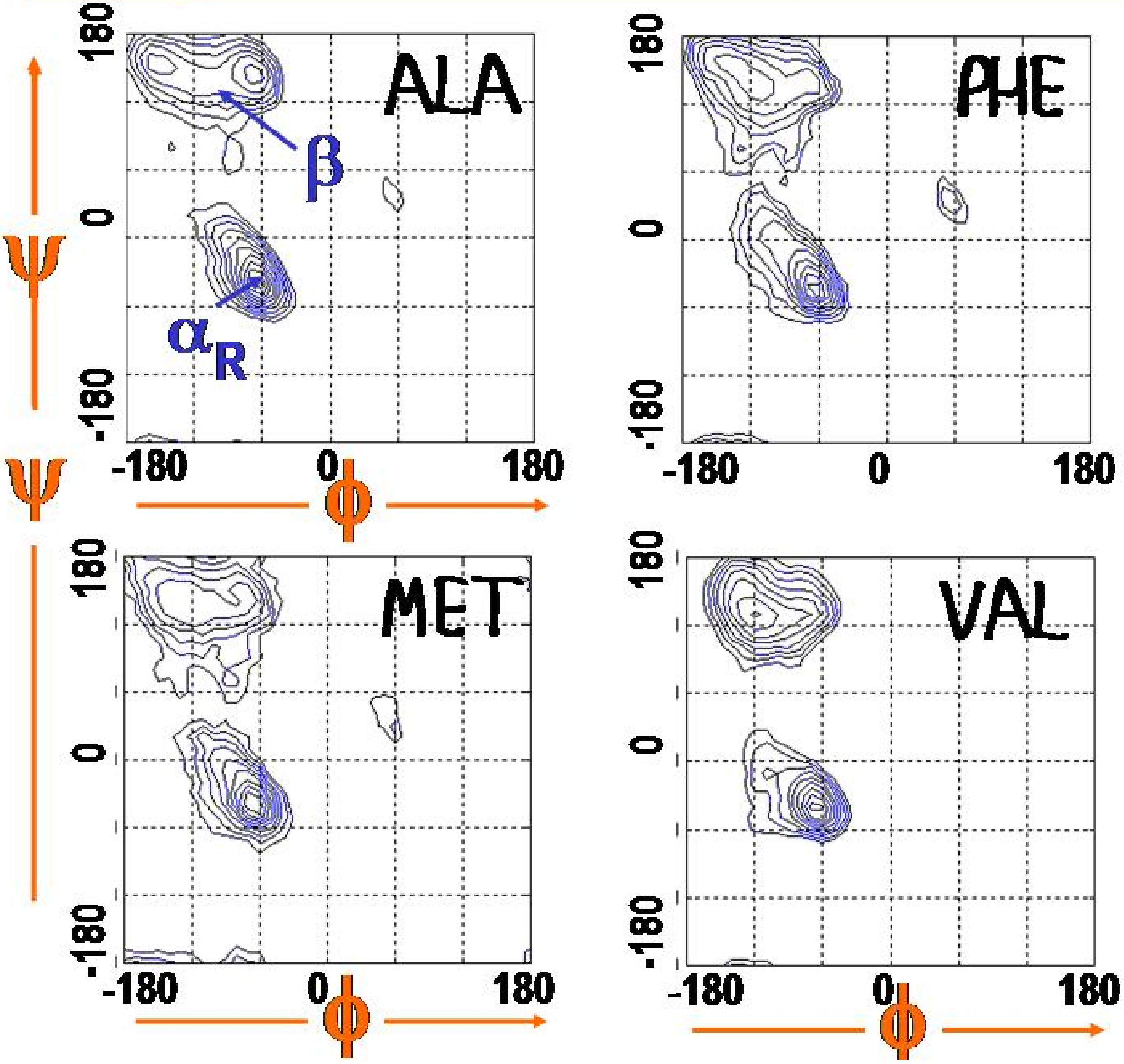
- Count number of N(φ, ψ) found in known proteins and then convert to a pseudo energy using –log(N(φ, ψ))

PHI, PSI DISTRIBUTIONS A, G, P, N



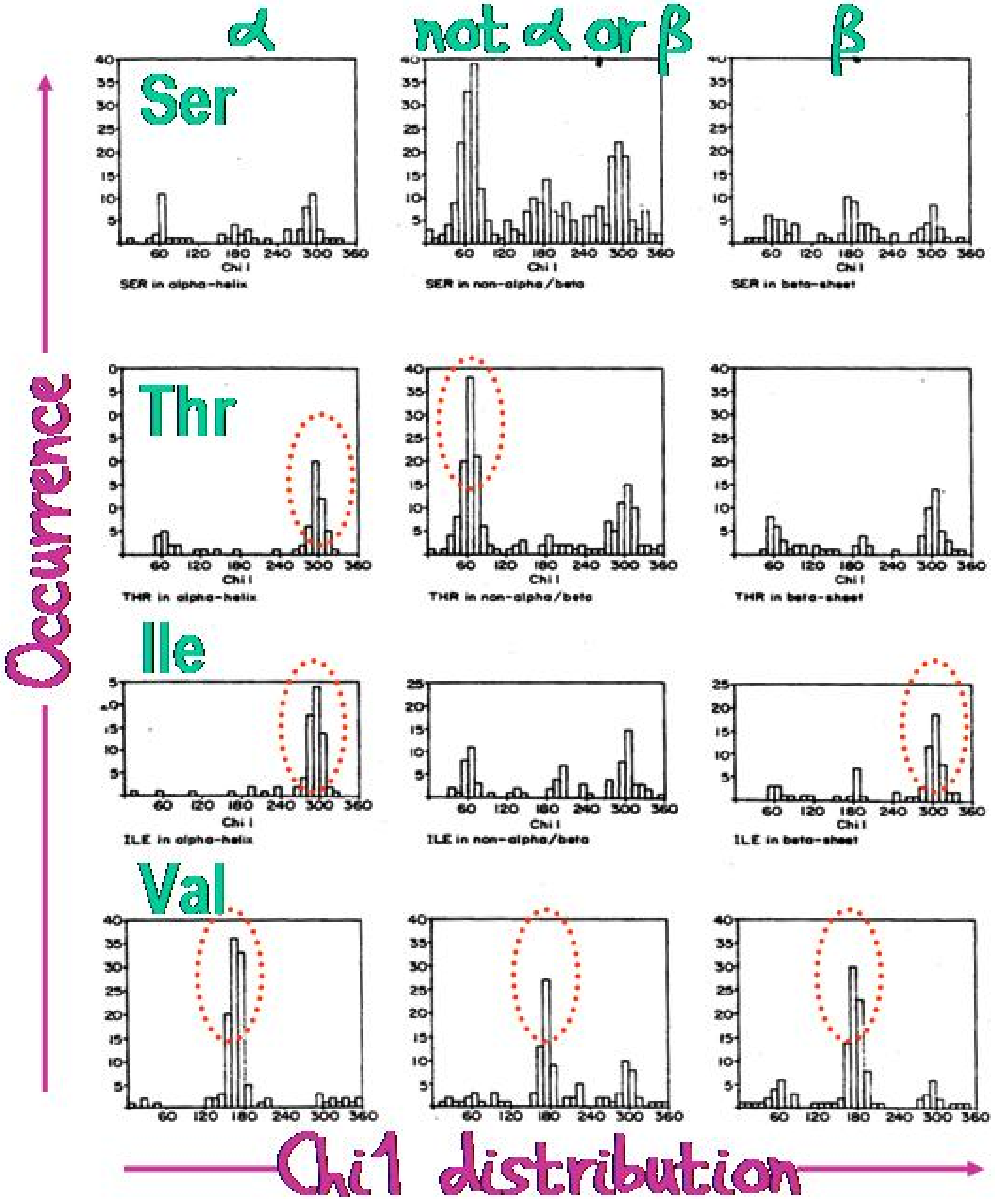
- GLY and PRO are special.
- ASN is a bit like GLY.
- Most are like ALA due to CB atom.

PHI, PSI DISTRIBUTIONS A, M, F, V

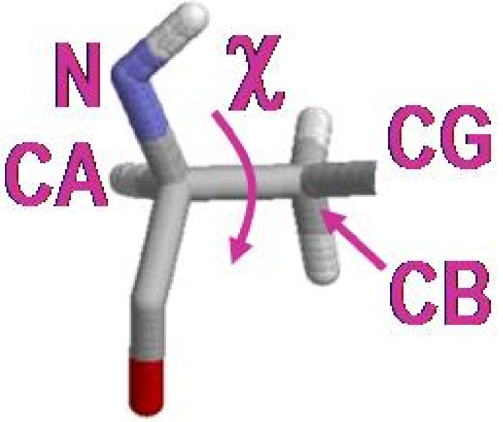


- Four amino acids with very different side chains have similar (ϕ,ψ) preferences.
- They all have a CB atom.

SIDE CHAIN CONFORMATIONS



- Chi1 distributions are very non-uniform.
- The preferred chi1 values depend on the amino acid side chain and the backbone conformation.



χ is defined by N-CA-CB-CG.

Reverse Turns
Concept 2.4

REVERSE TURNS

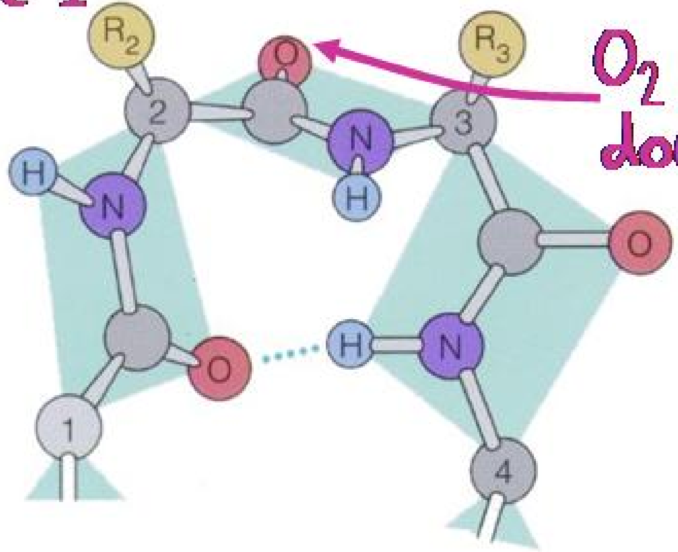
Beta Turns

Virtual Bonds

Beta Turns Types

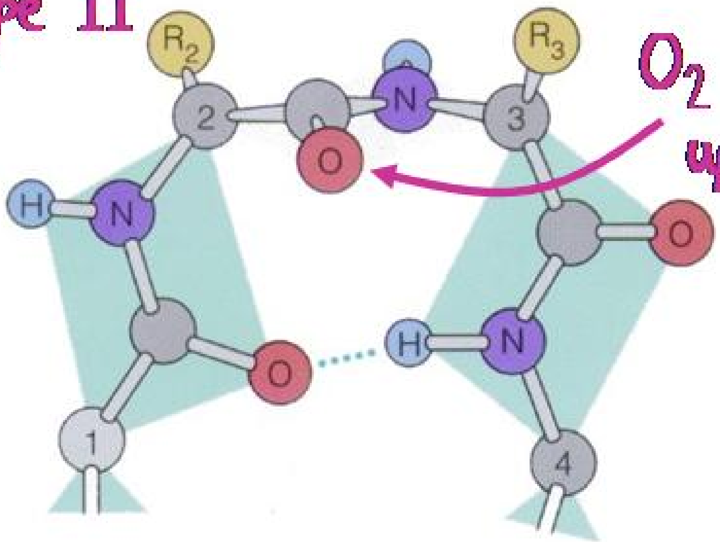
BETA TURNS

Type I



O_2 is down

Type II

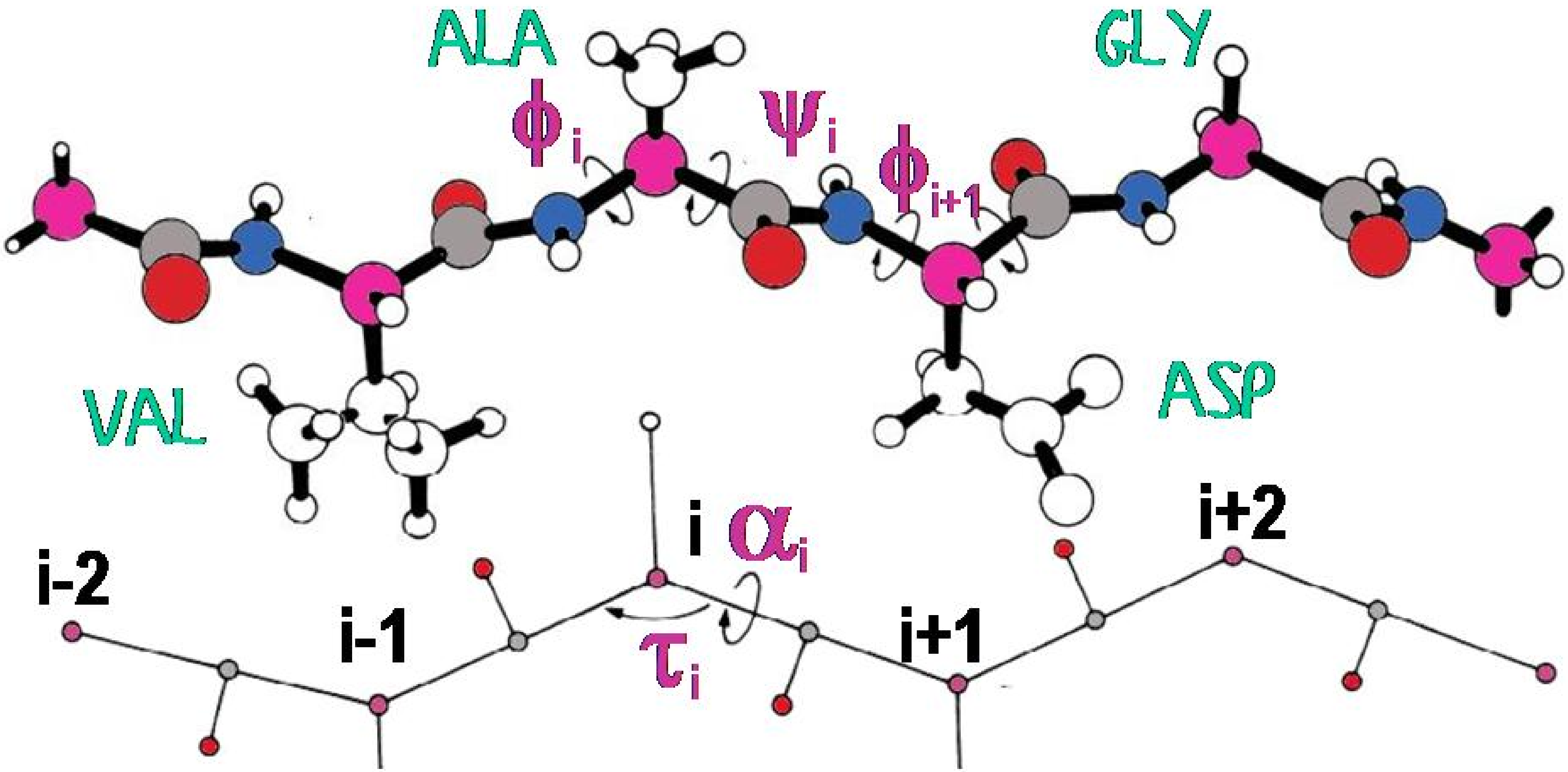


O_2 is up

- The chain directions changes 180 degrees.
- This can be done in many ways giving types: I, I', II, II', IV & VIII.
- There are sequence restrictions. For example, in Type II', position 2 must be GLY.

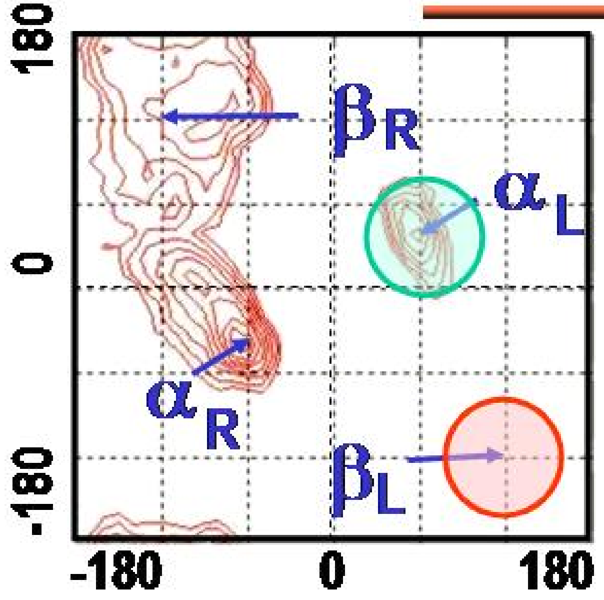
From Mathews and van Holde: *Biochemistry 2/e.* © The Benjamin/Cummings Publishing Co., Inc.

VIRTUAL BONDS



- α_i is defined by CA_{i-1} - CA_i - CA_{i+1} - CA_{i+2}
- α_i is approximately $\psi_i + \phi_{i+1} + 180$

BETA TURN TYPES



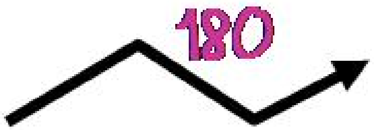
Ser
Asn
Asp
Gly

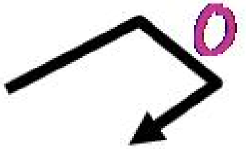
Only
Gly

There are four allowed (ϕ,ψ) values:

αR (−60,−40) βR (−120,+120)

αL (+60,+40) βL (+120,−120)





For turn need small alpha angle: $\alpha_i = \psi_i + \phi_{i+1} + 180 = 0$

Try allowed conformations at i and i+1

αR	αR	I	$\alpha = -40-60+180$	=	80
αL	αL	I’	$\alpha = +40+60+180$	=	−80
βR	αL	II	$\alpha = +120+60+180$	=	0
βL	αR	II’	$\alpha = -120-60+180$	=	0
αR	βL	VIII	$\alpha = -40-120+180$	=	20
αL	βR	VIII’	$\alpha = +40+120+180$	=	−20

The Alpha Helix
Concept 2.5

THE ALPHA-HELIX

Proteins have Alpha-Helices

The Alpha-Helix

The Helix Surface

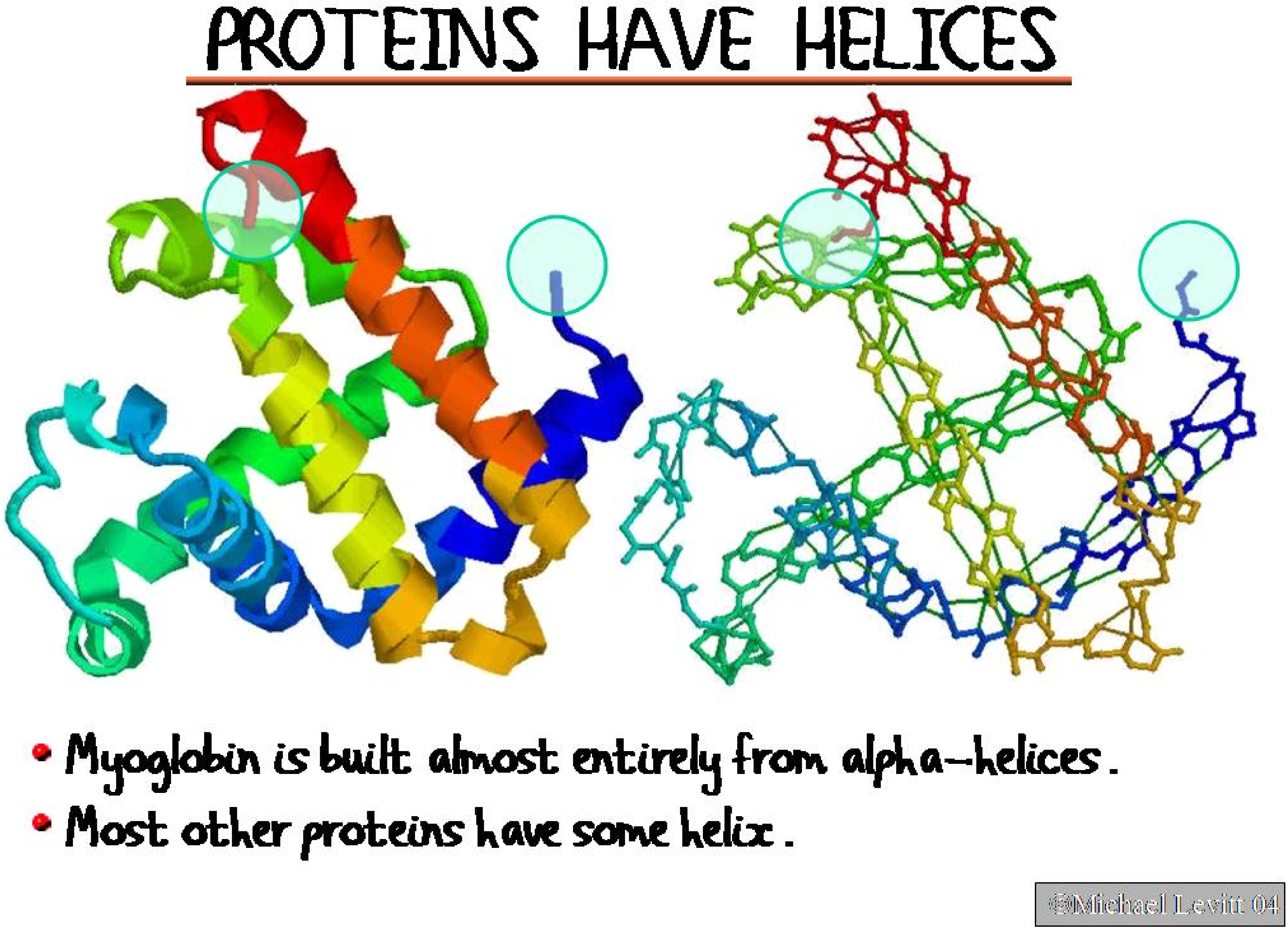
Helix Surface Ridges

Helix Ridge Lines

Different Possible Helices

3_{10} Explained

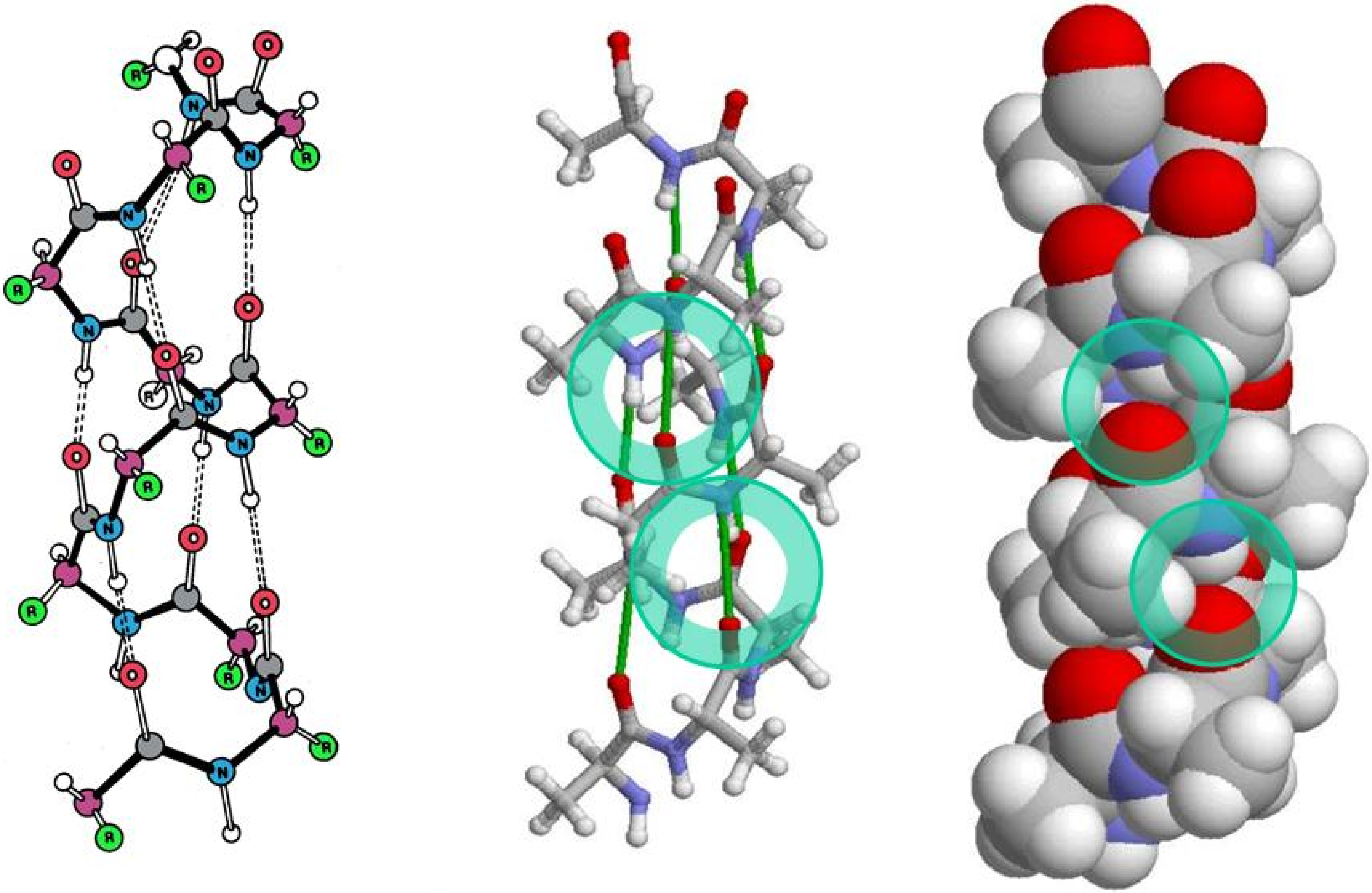
Alpha-helix Dipole



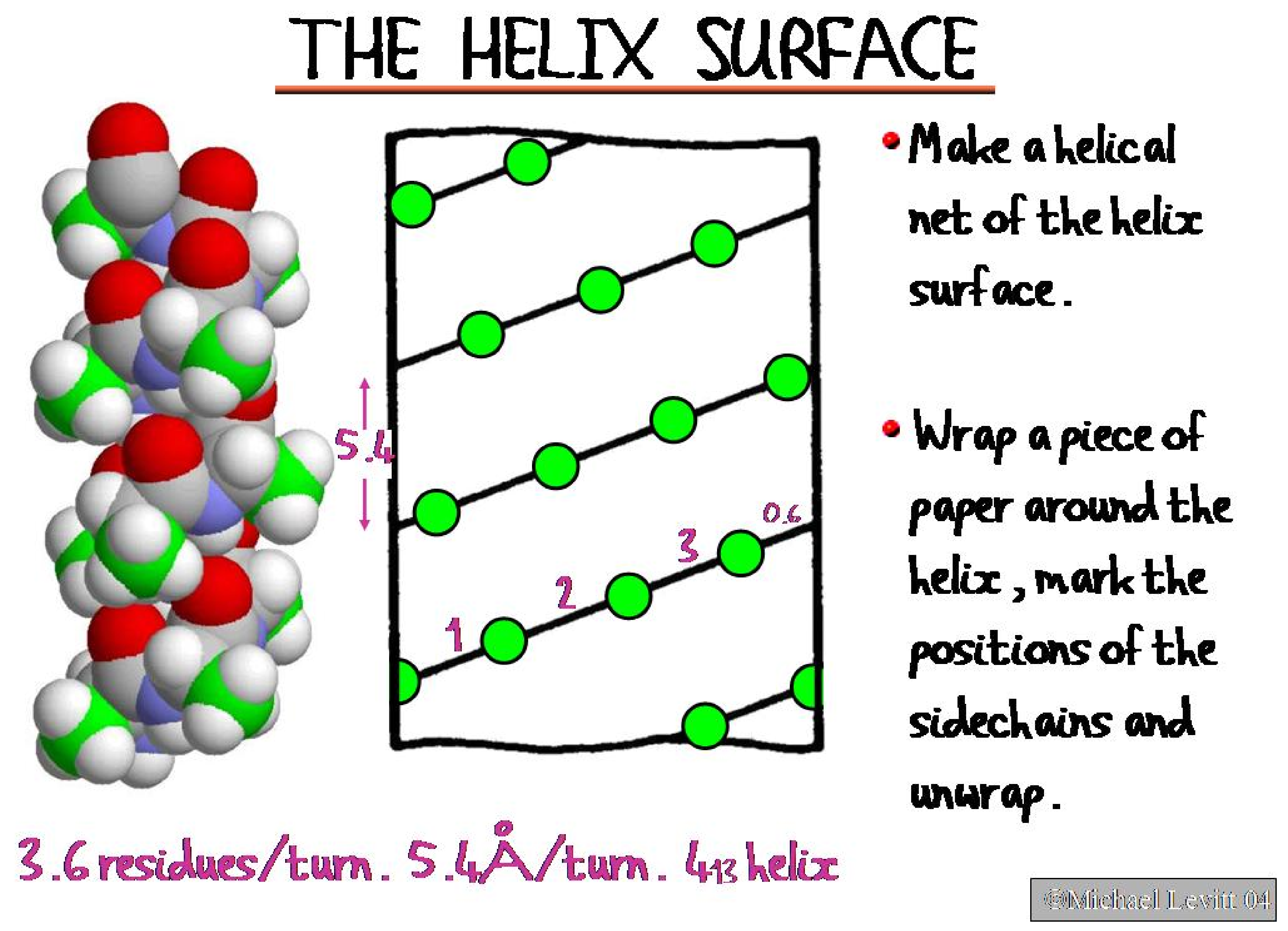
PROTEINS HAVE HELICES

- Myoglobin is built almost entirely from alpha-helices.
- Most other proteins have some helix.

THE ALPHA HELIX



- Pauling et al. 1951 original.
- The alpha helix is formed by NH..O=C hydrogen bonds.



THE HELIX SURFACE

- Make a helical net of the helix surface.
- Wrap a piece of paper around the helix, mark the positions of the sidechains and unwrap.

3.6 residues/turn. 5.4Å/turn. 4_{13} helix

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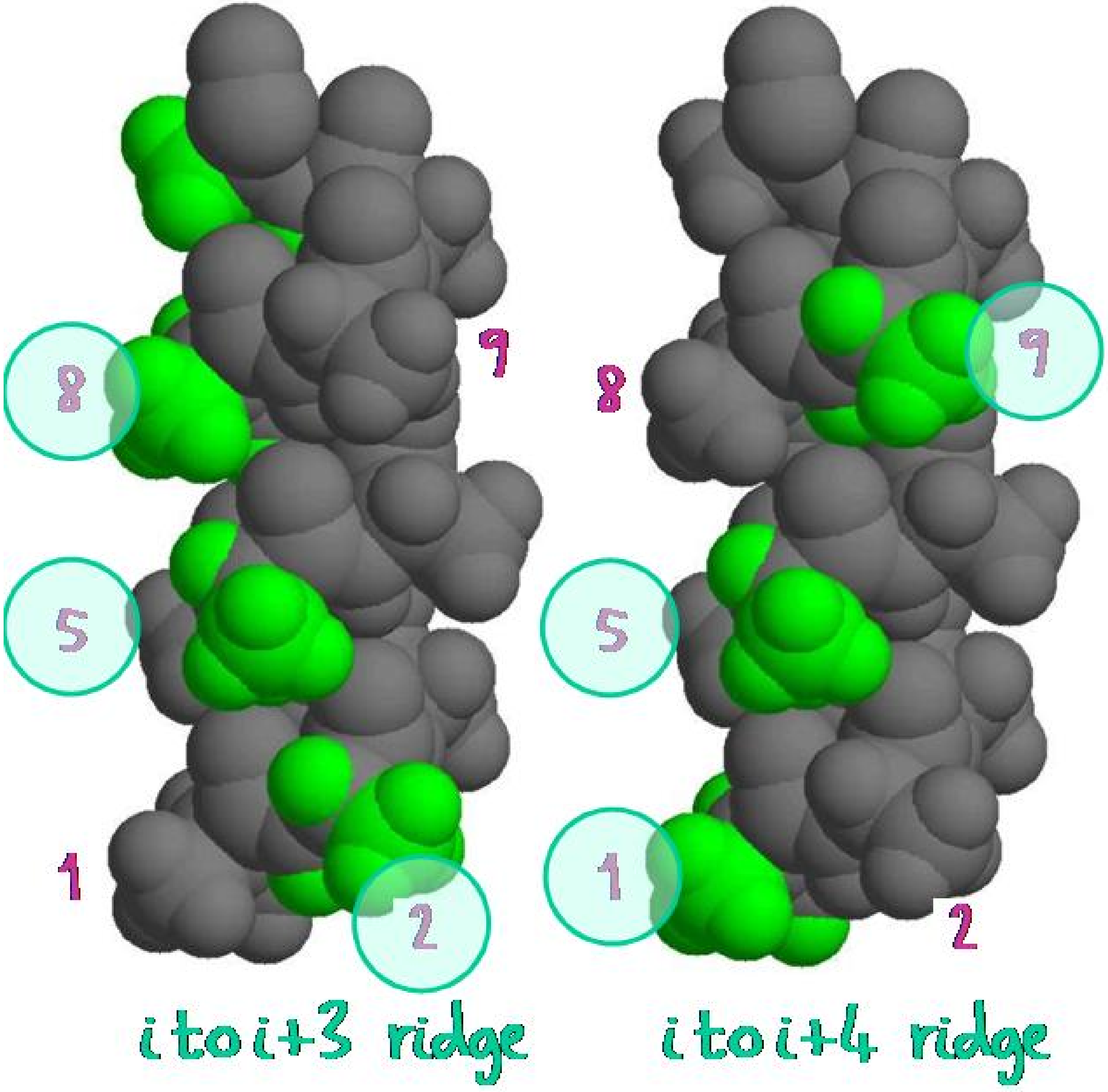
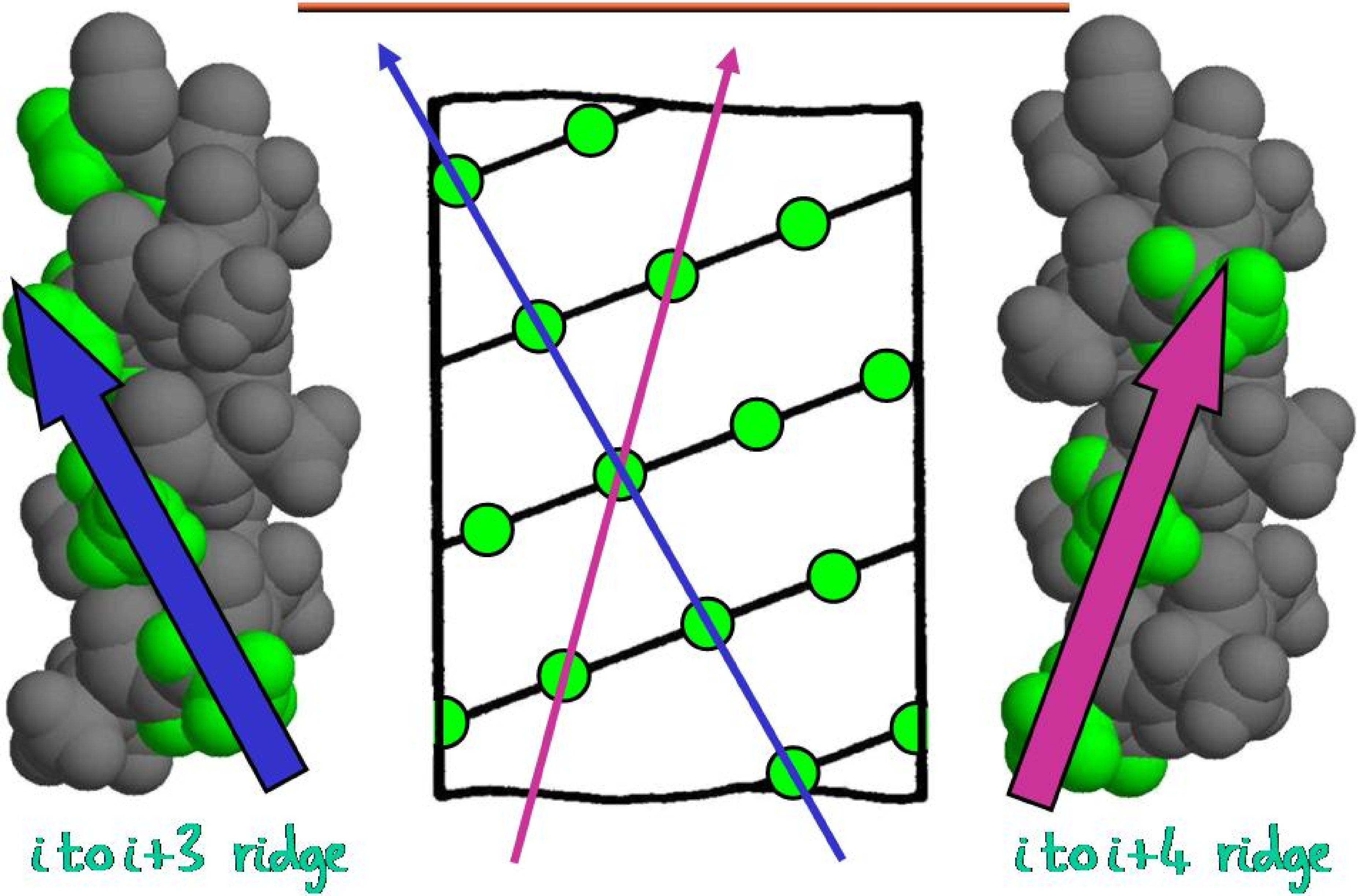
HELIX SURFACE RIDGES

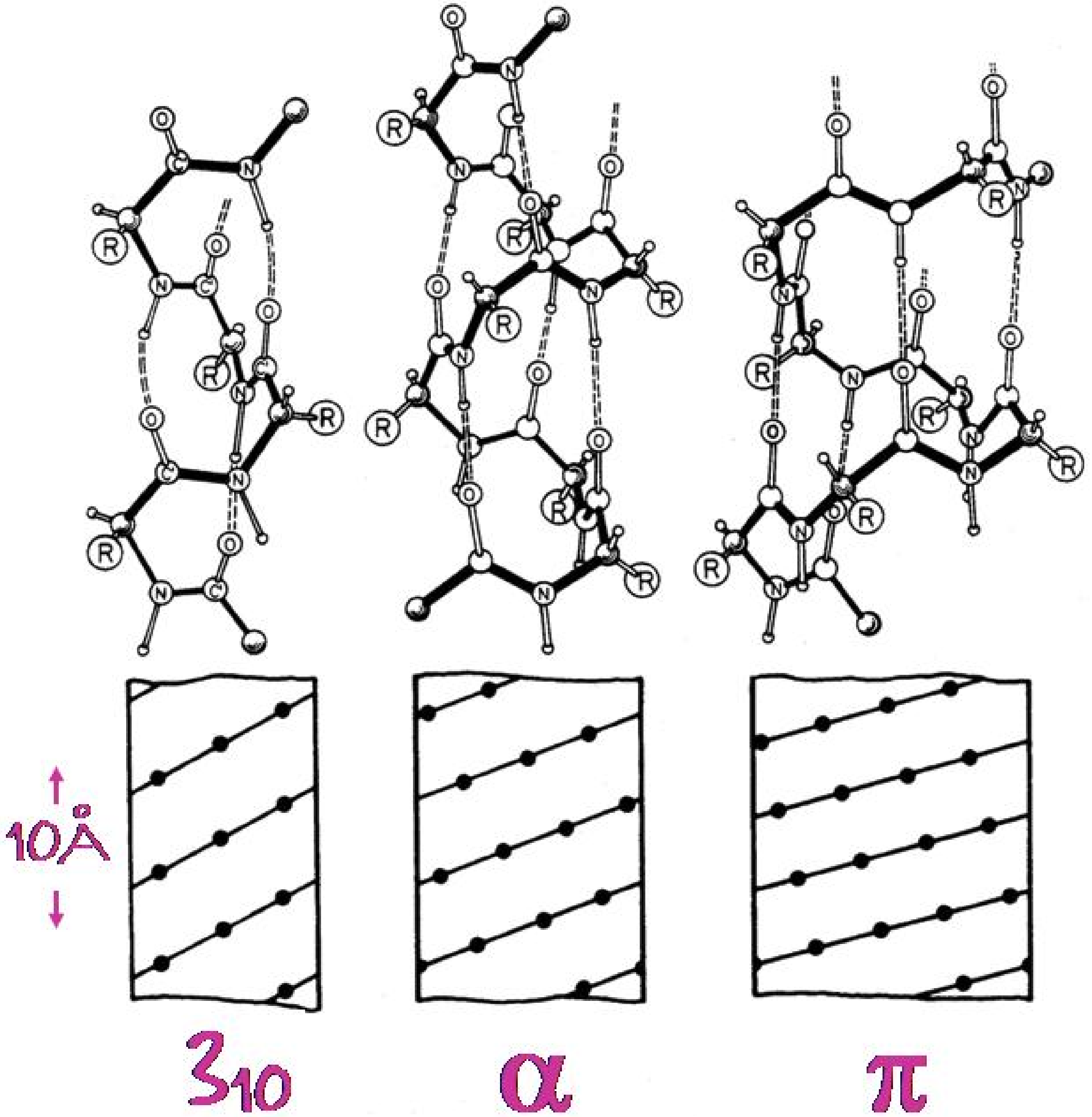


- Sidechains that are in positions i and i+3 form a ridge that is a left-handed helix.
- Sidechains in positions i and i+4 form a ridge that is a right-handed helix.

HELIX RIDGE LINES

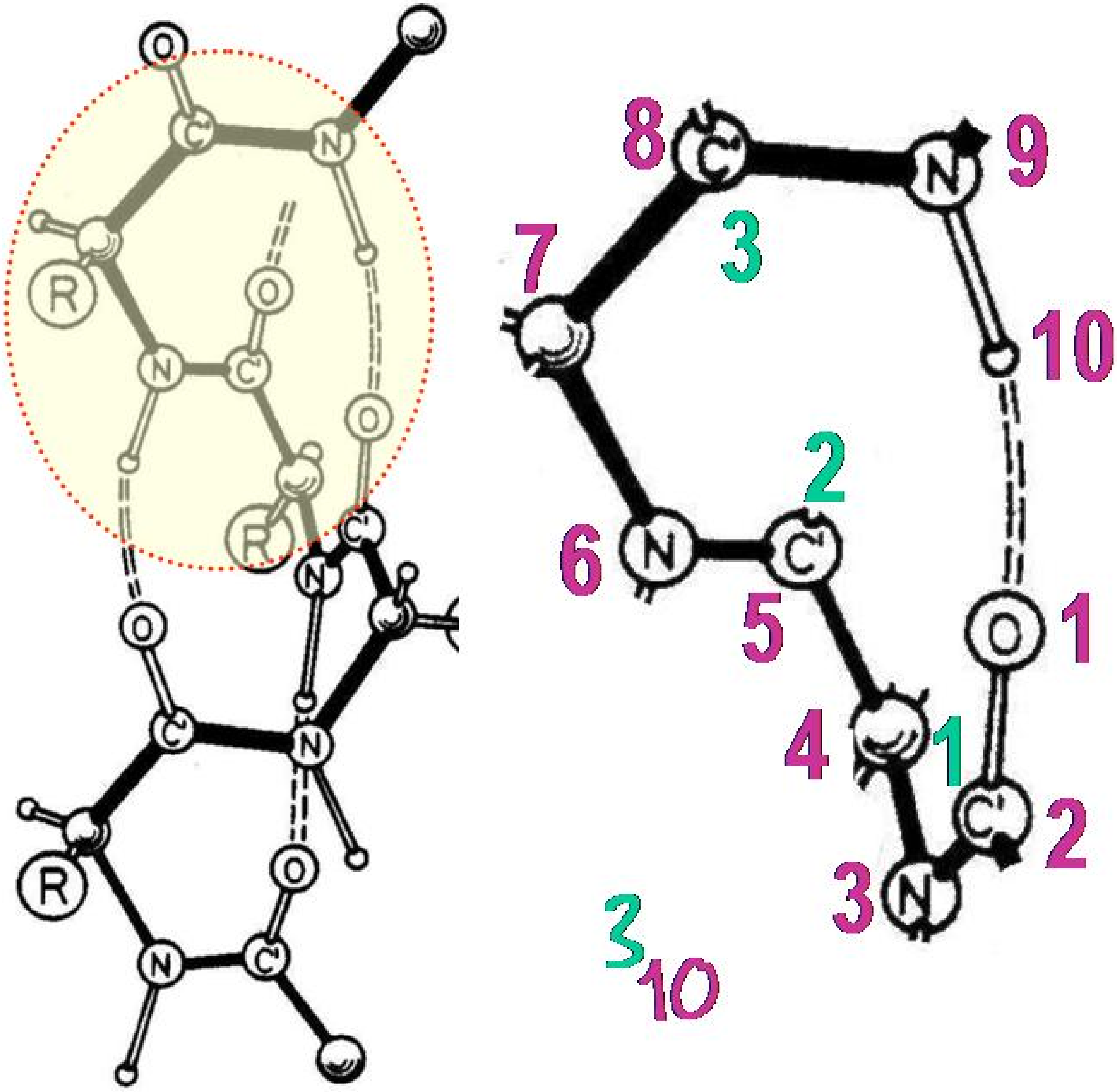


DIFFERENT POSSIBLE HELICES



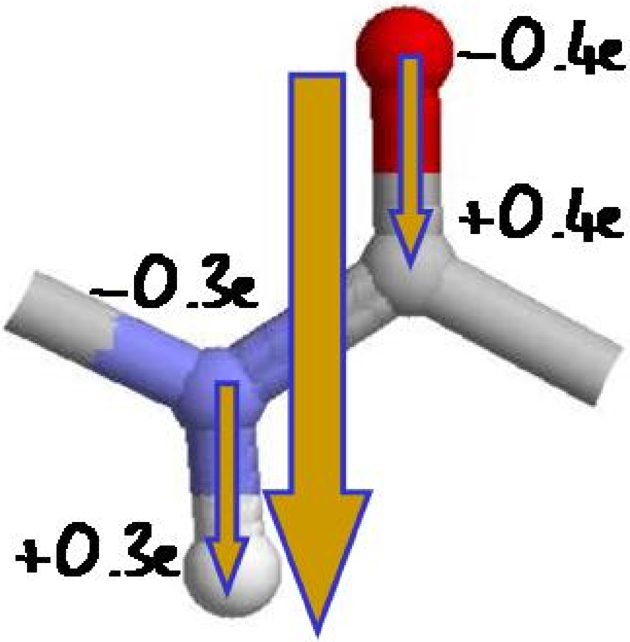
- The 3_{10} helix is thin and has 3.0 residues/turn.
- The π or 5_{16} helix is fat and has 4.2 residues /turn.
- The α helix is just right. It is a 4_{13} helix with 3.6 residues/turn.

3_{10} EXPLAINED



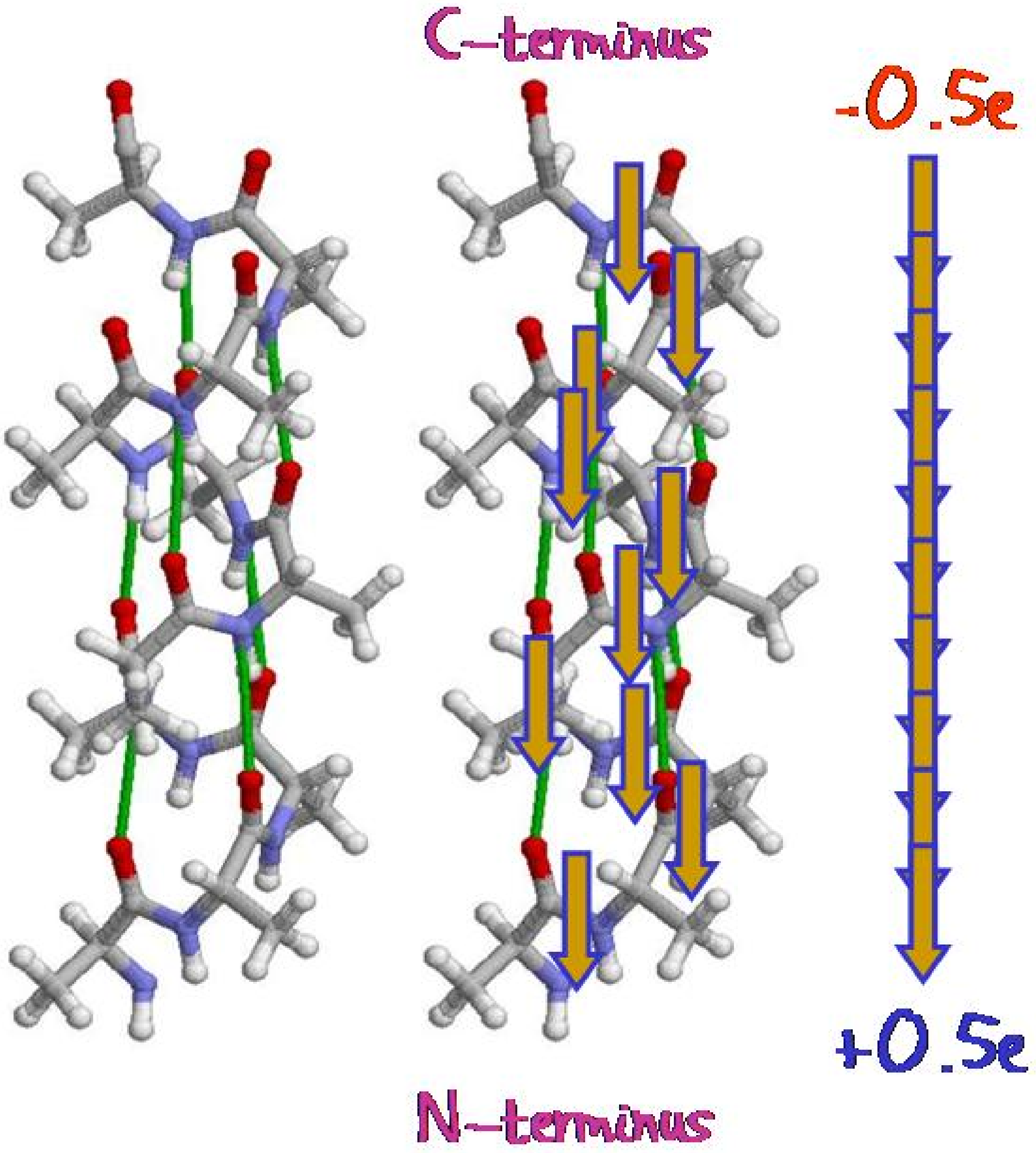
- Find a hydrogen bonded loop.
- Count residues by number of CA atoms in the loop. Here 3.
- Count atoms in loop including O and H. Here 10.

ALPHA-HELIX DIPOLE 1



- The peptide group has a strong dipole moment due to partial charges on NH and CO groups.

ALPHA-HELIX DIPOLE 2



- In the α-helix, peptide dipoles line up to give the helix a large dipole.
- This dipole is equivalent to having a charge of +0.5e at the N-terminus and -0.5e at the C-terminus.
- The N-terminal +0.5e charge is important in many enzymes. It acts like a short positively charged side chain.

The Beta Sheet Concept 2.6

BETA SHEETS

Proteins have Beta-Strands

The Beta-Strand

Beta Sheets

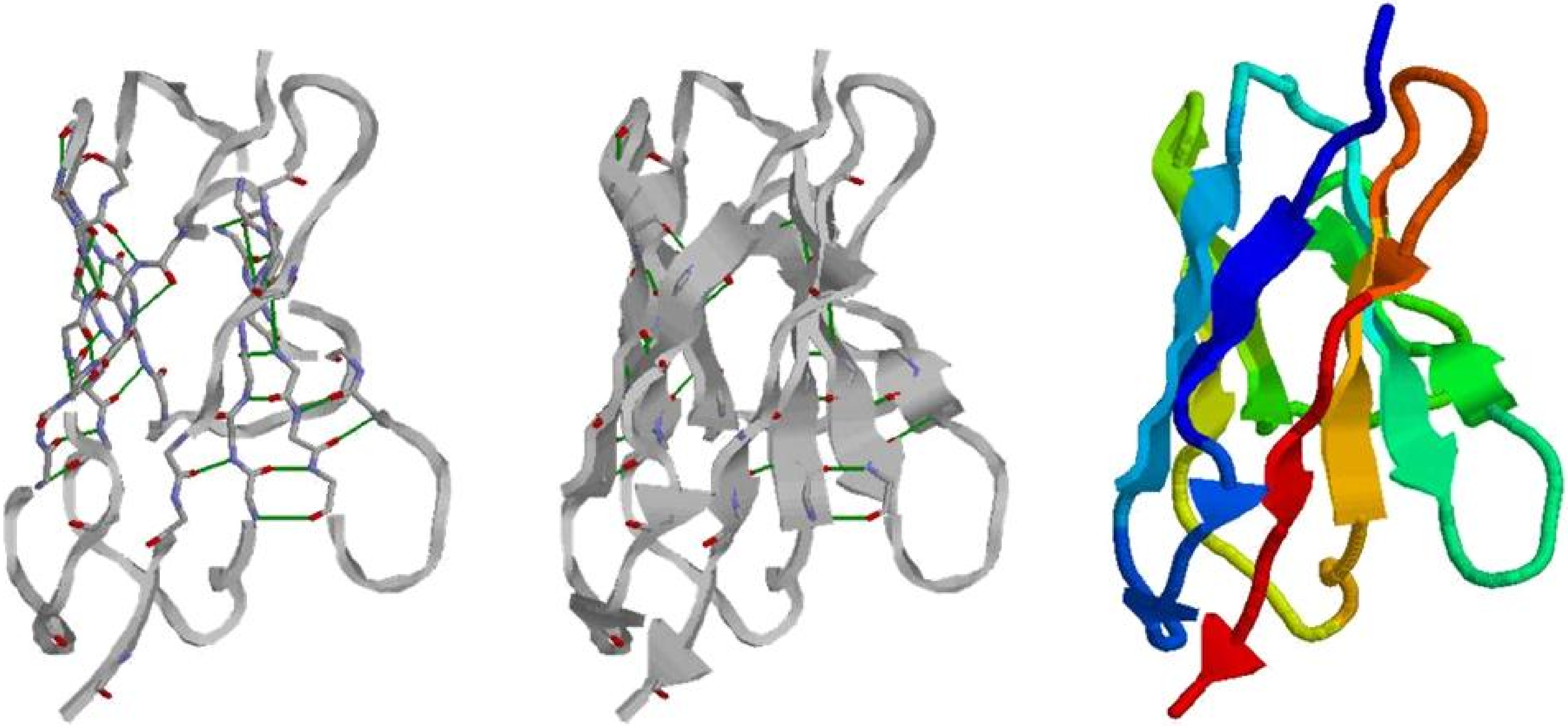
Beta Sheet Sidedness

Beta Sheets are Solid

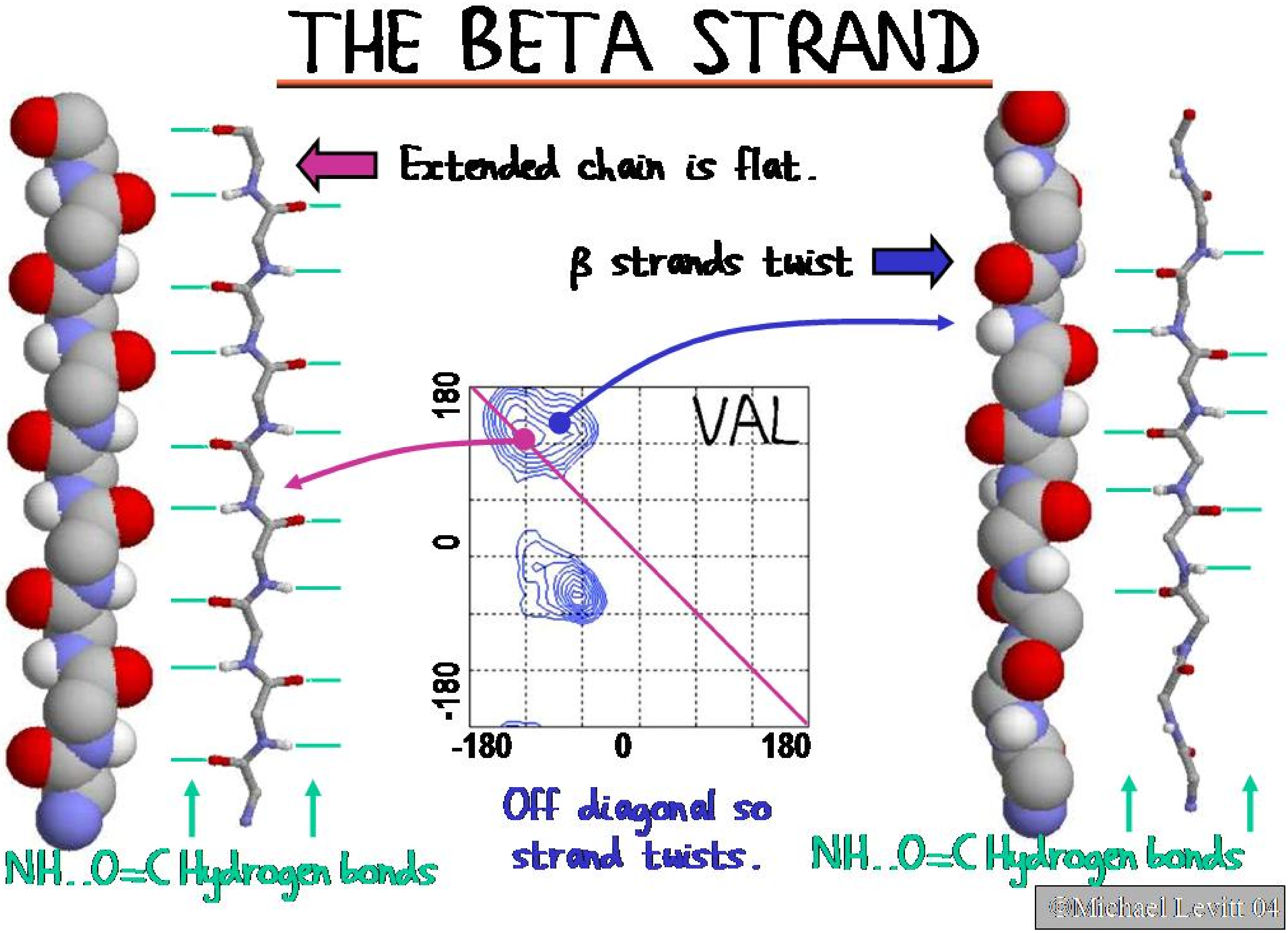
Beta Sheets are Twisted

The Beta-Hairpin

PROTEINS HAVE STRANDS



- Immunogobulin domains are built entirely from β-strands.
- Most other proteins have some beta structure.



THE BETA STRAND

Extended chain is flat.

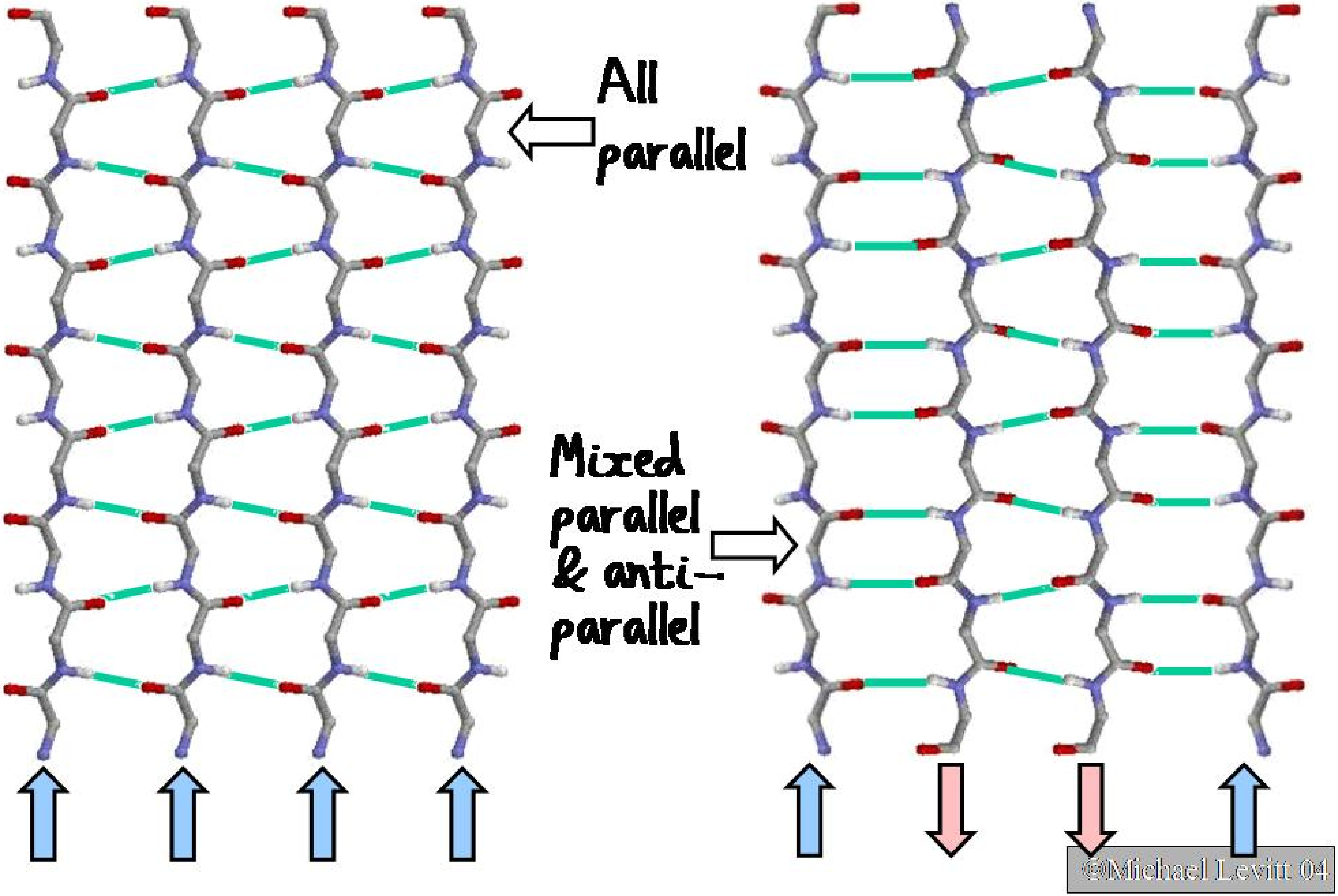
β strands twist

Off diagonal so strand twists.

NH..O=C Hydrogen bonds

NH..O=C Hydrogen bonds

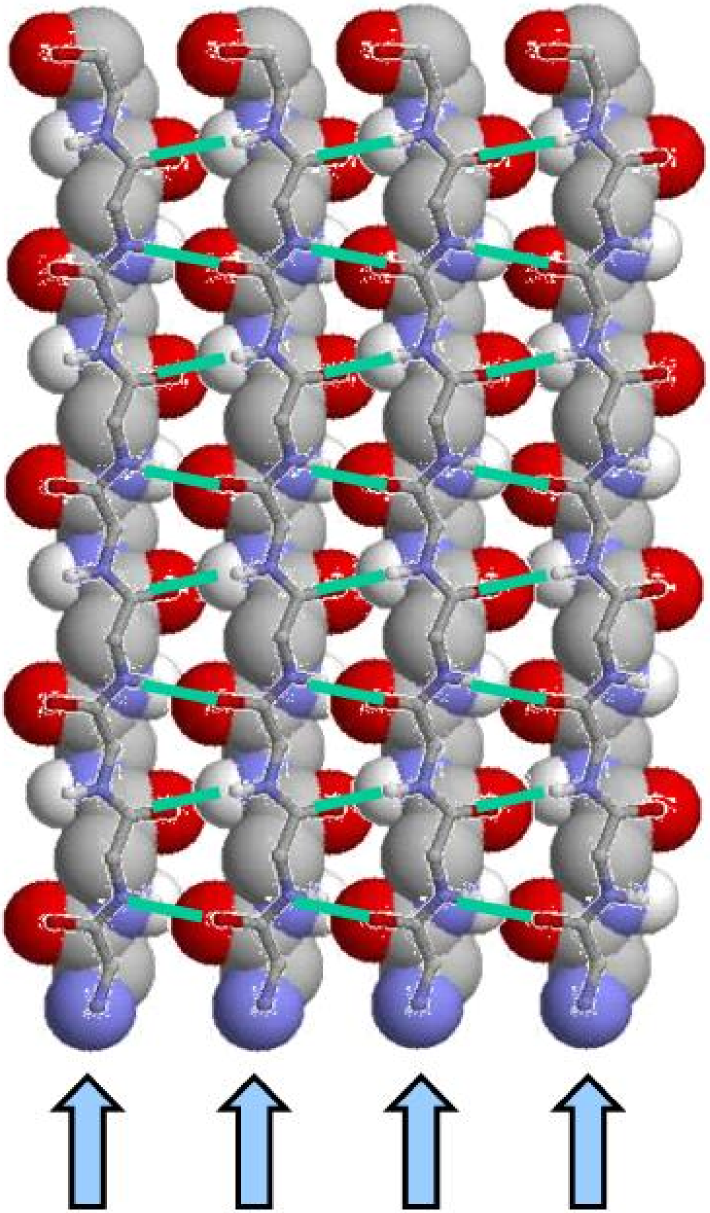
BETA SHEETS



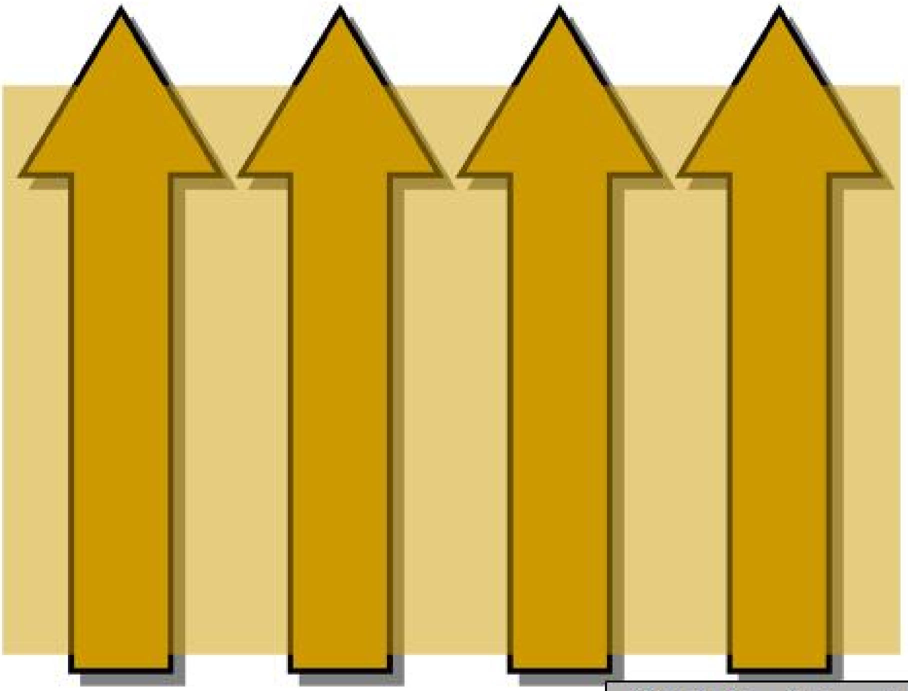
All parallel

Mixed parallel & anti-parallel

BETA SHEETS ARE SOLID



The hydrogen bonds bring the atoms of the strands in close contact forming a solid surface, which is flexible.



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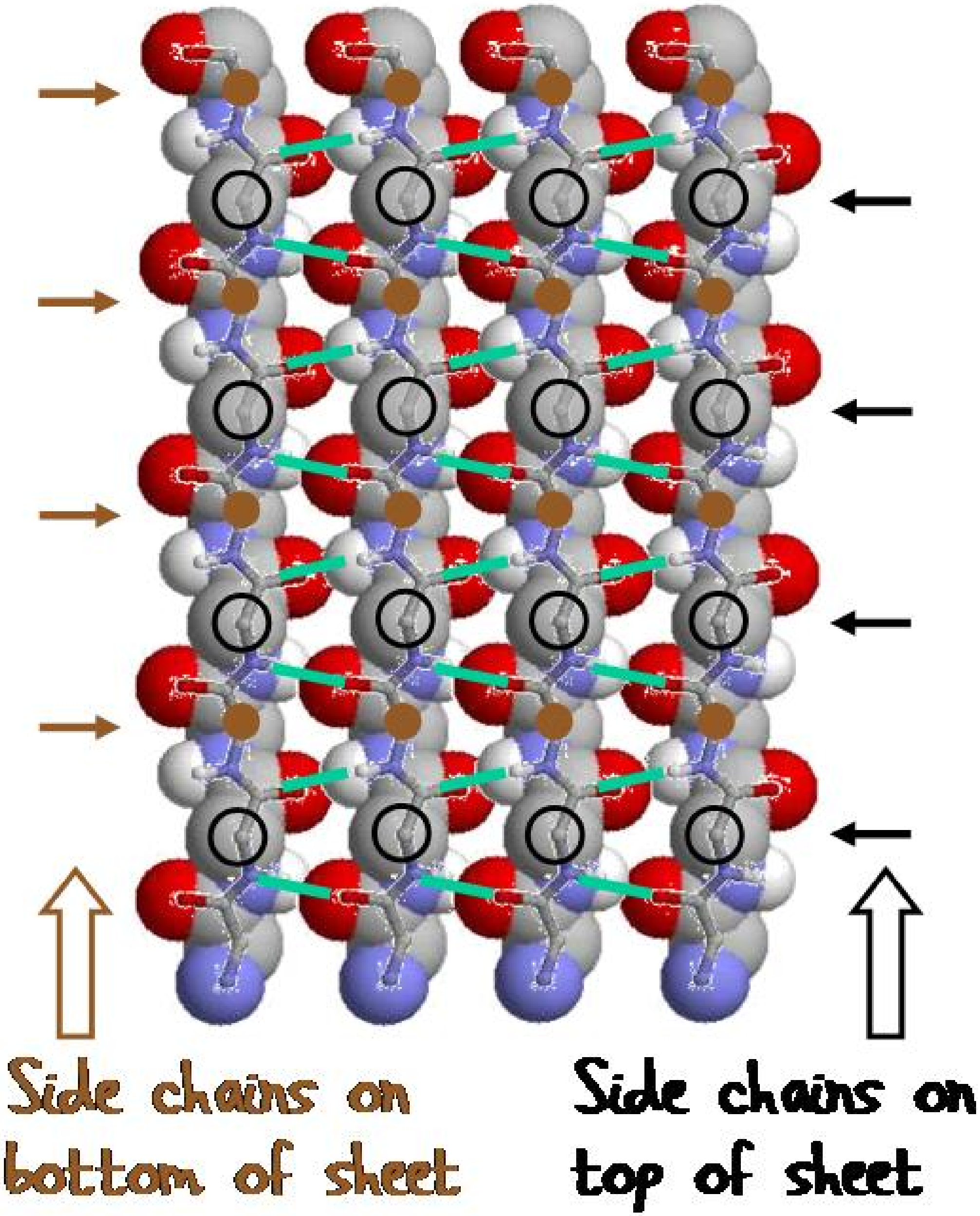
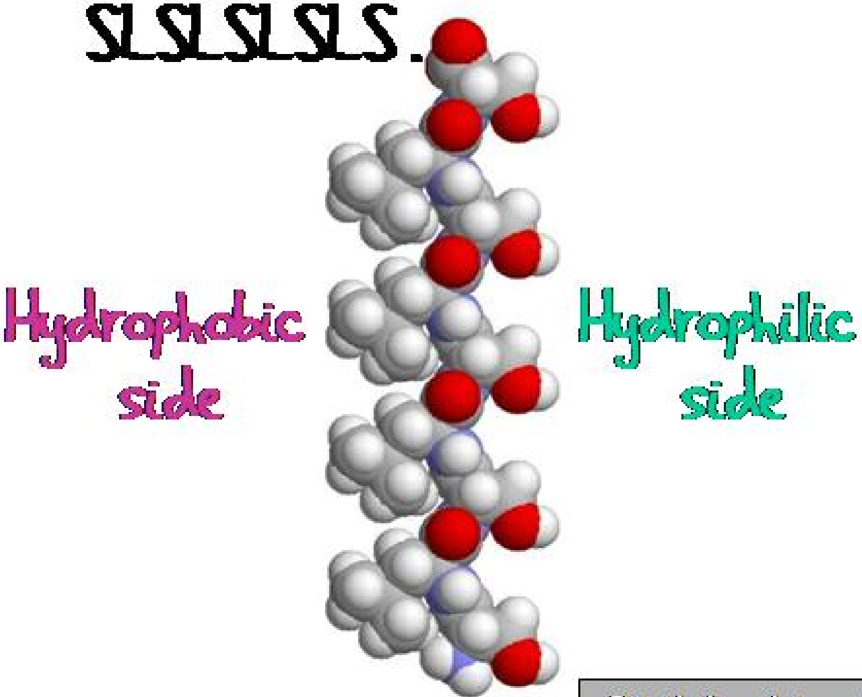
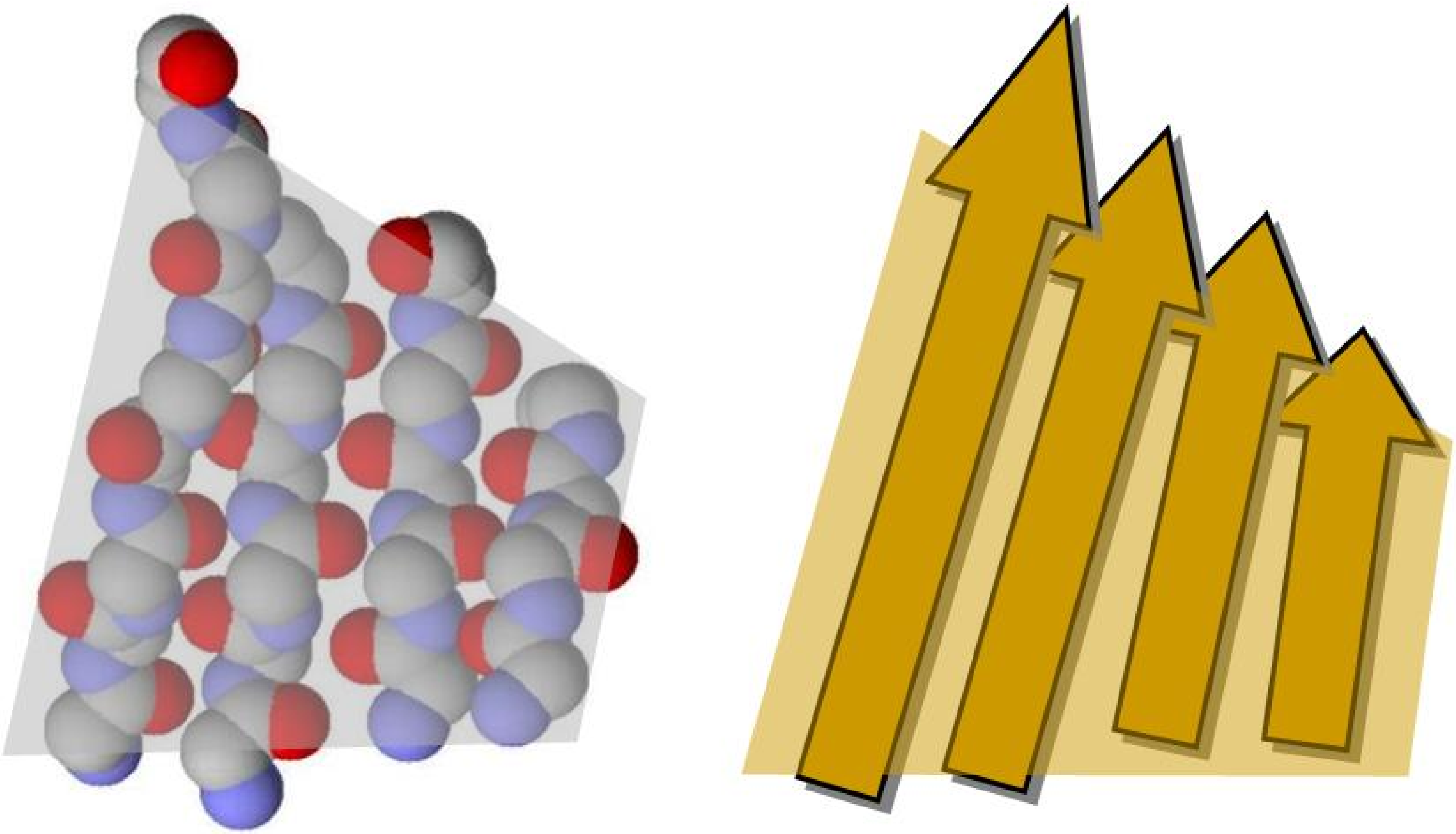
BETA-SHEET SIDEDNESS



- Every second residue in a β-strand in on the same side of the β-sheet.
- β-sheet can be totally amphipathic. Sequence is SLSLSLSLS.

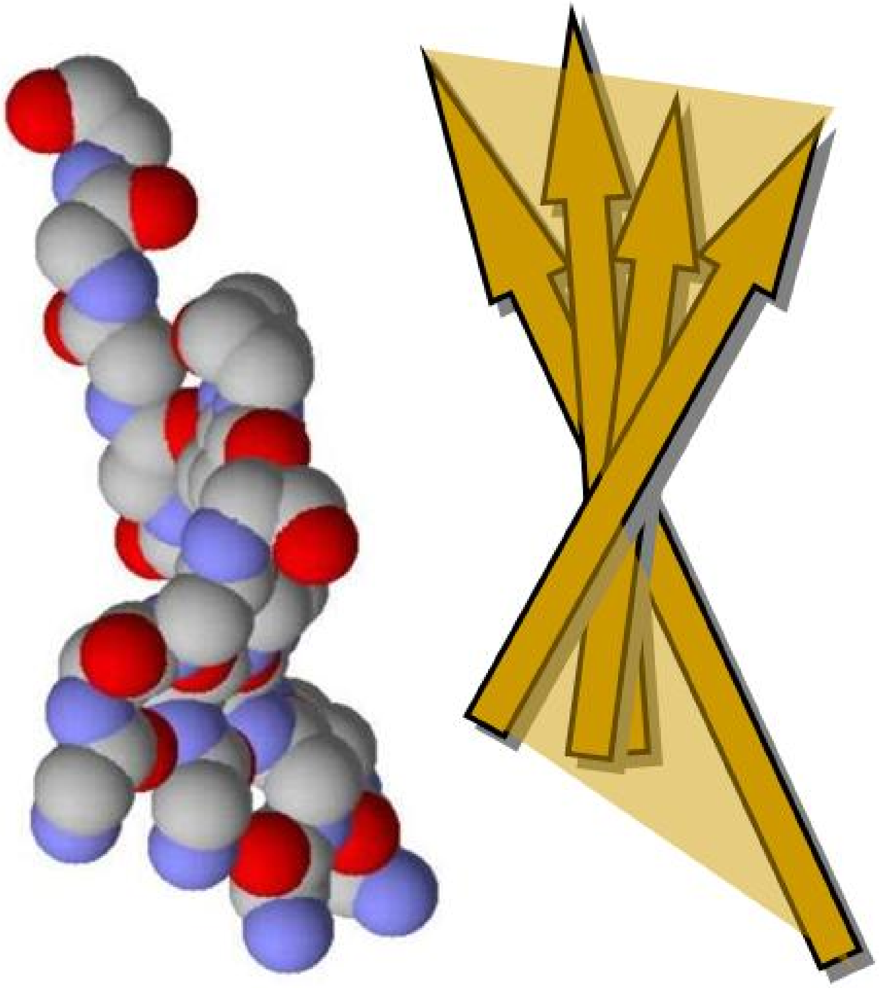


REAL SHEETS ARE TWISTED 1

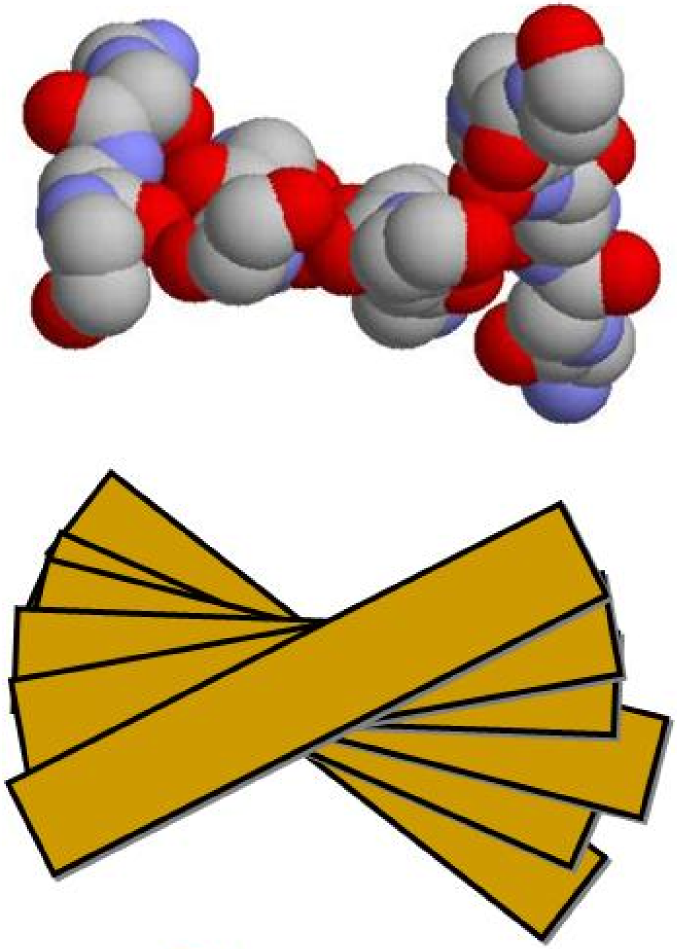


Top view of parallel sheet in flavodoxin

REAL SHEETS ARE TWISTED 2

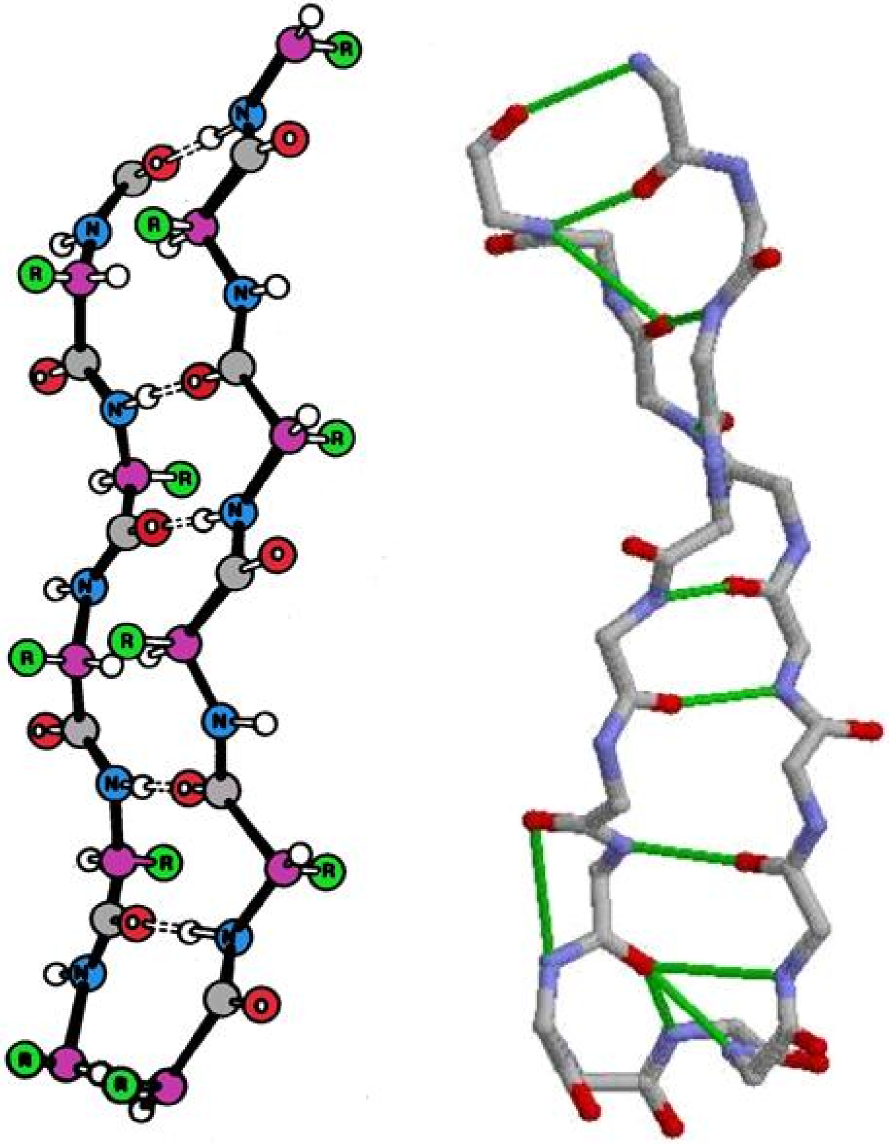


Side view



Edge on view

THE BETA HAIRPIN



- The beta-hairpin can be very twisted.
- This is because the beta-strand is twisted.
- It is possible to have long twisted hairpins as they do not involve increasing distortion.