Protein Structure

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9/21/11

What do proteins do?

- Chemistry
  - Metabolism
  - Factories of cellular components (Fatty acid synthase)
- Transport
  - Oxygen in blood (hemoglobin)
  - Signals from outside cells (nervous system)
- Structure
  - Internal scaffolding in cells (actin)
  - Hair and nails (collagen)
- Movement
  - Myosin (animal muscles)
  - Flagella and Cilia (cellular propulsion)

How do proteins work?

- Biological Nano Machines
- Highly complex
- But… based on fundamentals of chemistry

Understanding Protein Structure

1. Primary structure

2. Secondary structure

3. Tertiary Structure

Sequence leads to structure

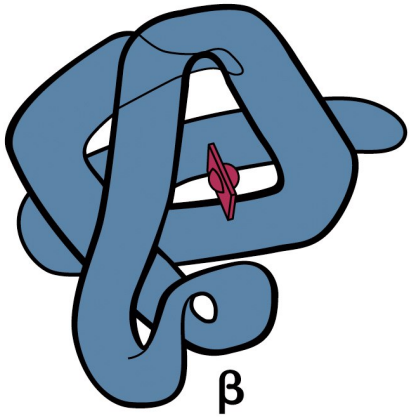
– Lys – Ala – His – Gly – Lys – Lys – Val – Leu – Gly - Ala –

Figure 6-1a Fundamentals of Biochemistry, 2/e

Primary structure
(amino acid sequence in a polypeptide chain)

Secondary structure
(helix)

Figure 6-1b Fundamentals of Biochemistry, 2/e



Tertiary structure:
one complete protein chain
(β chain of hemoglobin)

Figure 6-1c Fundamentals of Biochemistry, 2/e

Primary Structure - Sequence

- Amino-acid side chains along the Peptide Backbone
- Covalent bonds making a string
- Proteins have many “residues”
  - Proteins can be 100-1000s of residues
  - 20 regular amino acids

Side chains come in 4 “flavors”

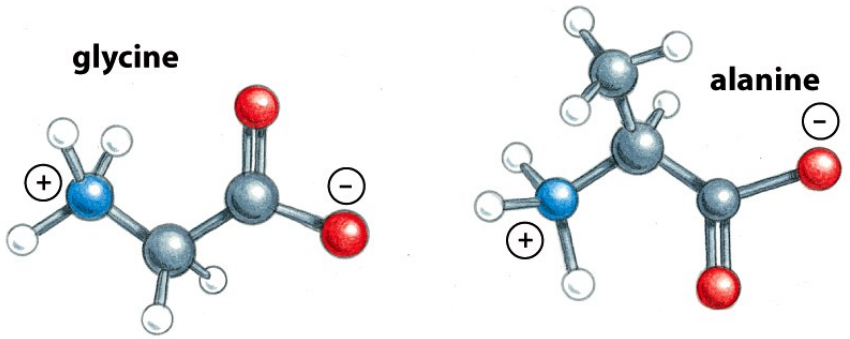
AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged polar

POLAR AMINO ACIDS
(hydrophilic)

AMINO ACID			SIDE CHAIN
Alanine	Ala	A	nonpolar
Glycine	Gly	G	nonpolar
Valine	Val	V	nonpolar
Leucine	Leu	L	nonpolar
Isoleucine	Ile	I	nonpolar
Proline	Pro	P	nonpolar
Phenylalanine	Phe	F	nonpolar
Methionine	Met	M	nonpolar
Tryptophan	Trp	W	nonpolar
Cysteine	Cys	C	nonpolar

NONPOLAR AMINO ACIDS
(hydrophobic)

The Backbone



Proteins are long stretches of amino acids

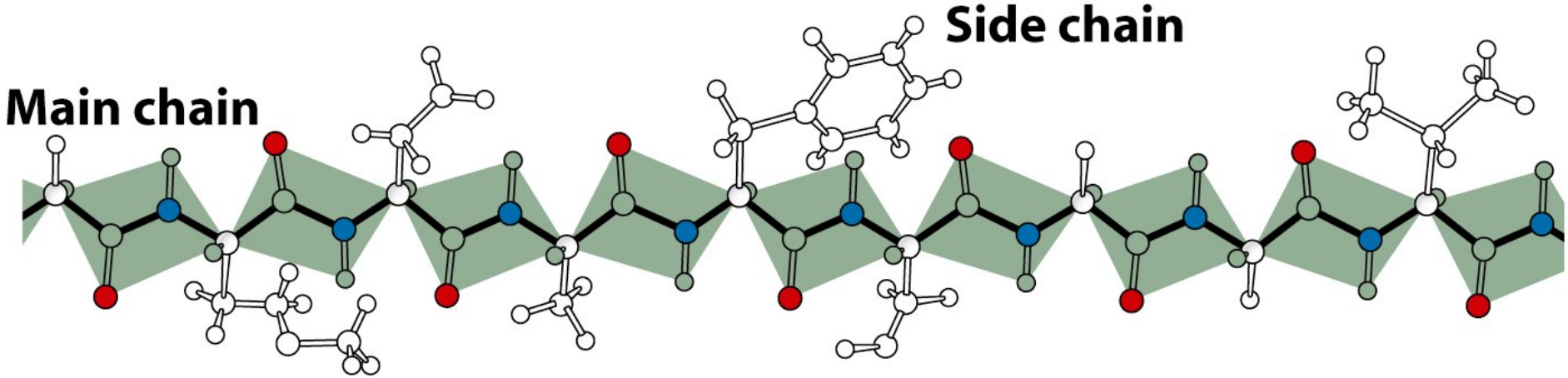


Figure 6-3 Fundamentals of Biochemistry, 2/e

9 amino acids, 20 possible
=
How many unique sequences?

Understanding Protein Structure

1. Primary structure

2. Secondary structure

3. Tertiary Structure

Secondary Structure

- Proteins have unique structures
  - i.e. not like random mess of string
- Final structure is an assembly of secondary structure elements
- Backbone carbonyl and amide-proton hydrogen bonding are key!

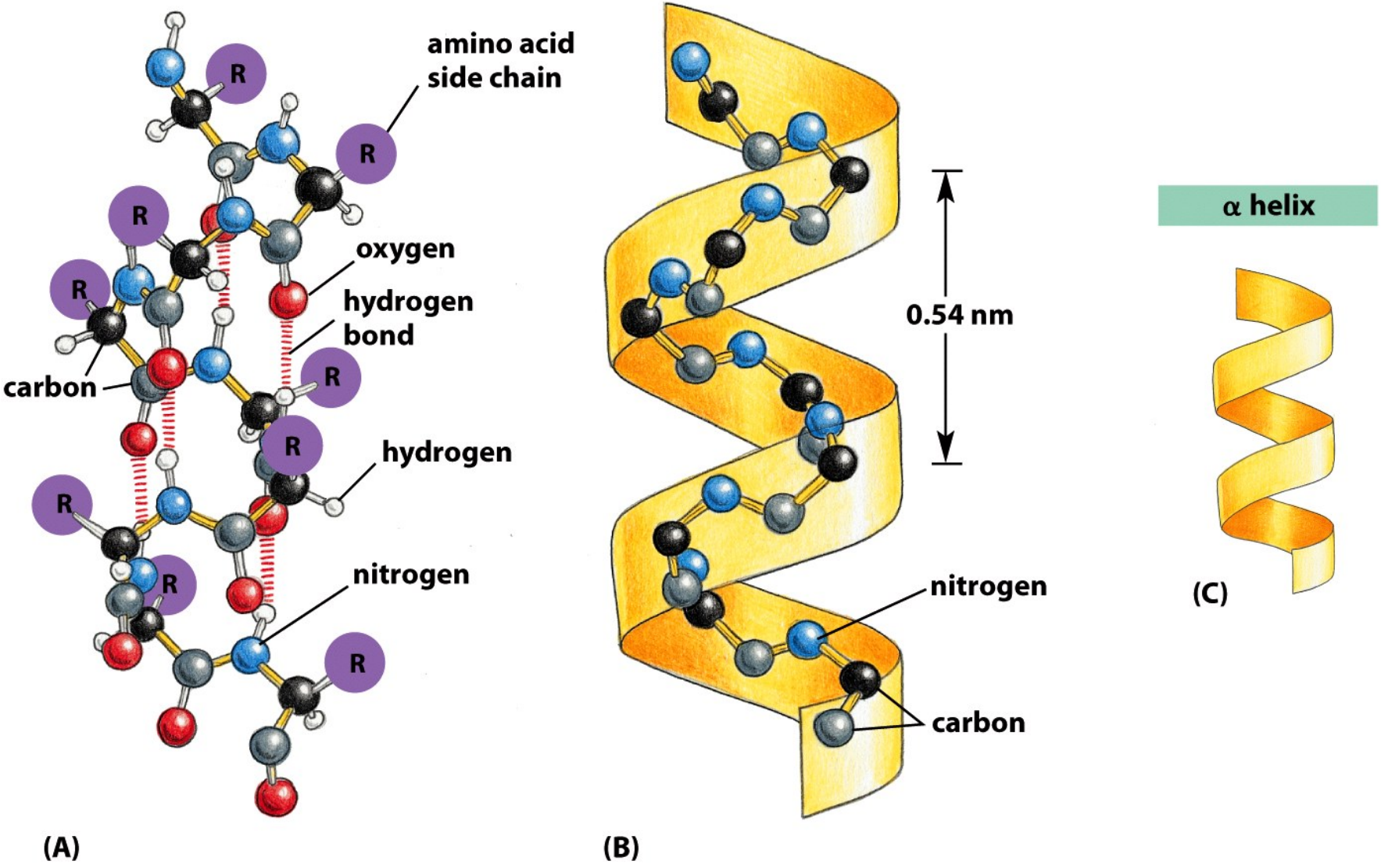
Basic forms of Secondary Structure

- Random Coil
- Alpha-Helix
  - α-helix
- Beta-sheet
  - β-sheet
- Loops

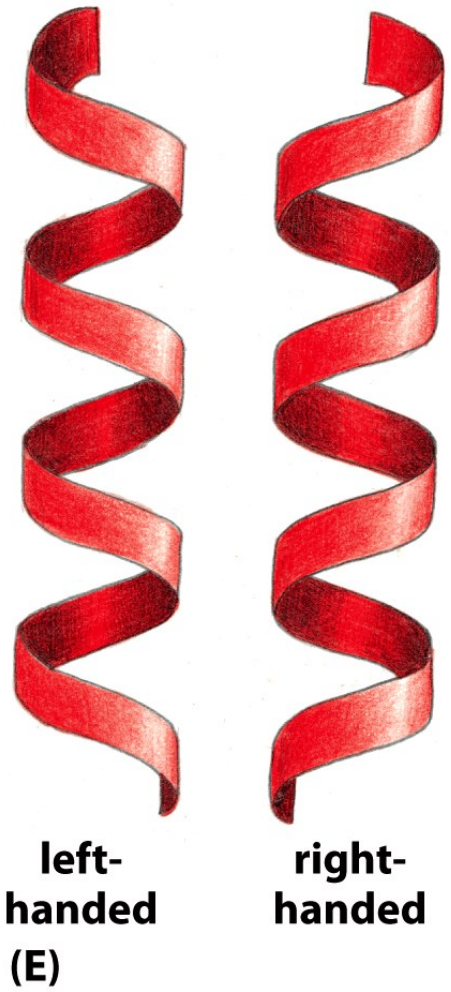
Basic forms of Secondary Structure

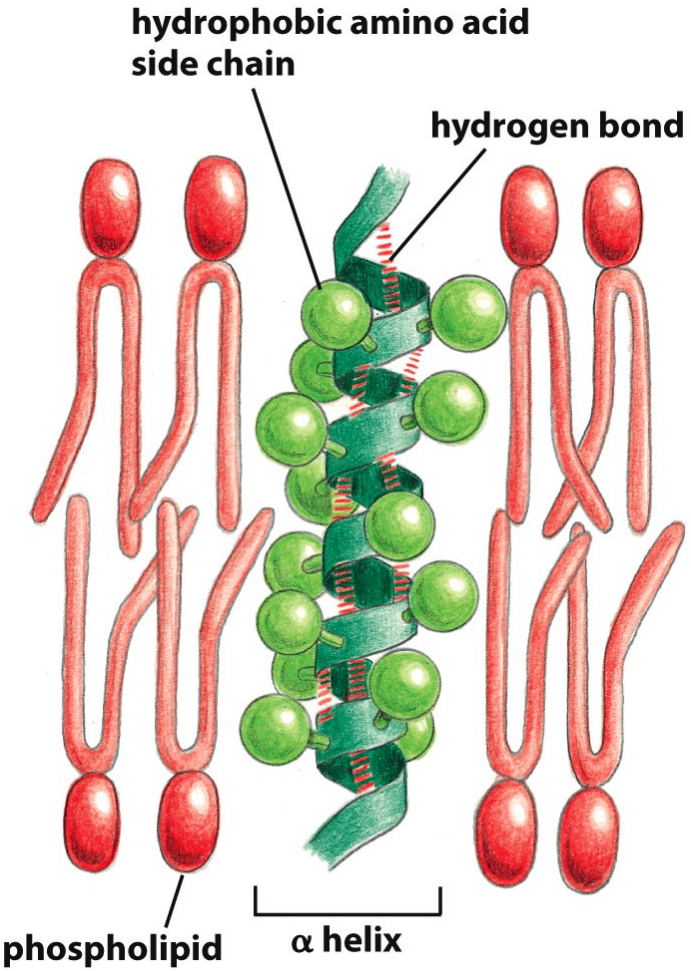
- **Random Coil**
- Alpha-Helix
  - α-helix
- Beta-sheet
  - β-sheet
- Loops

Alpha Helices

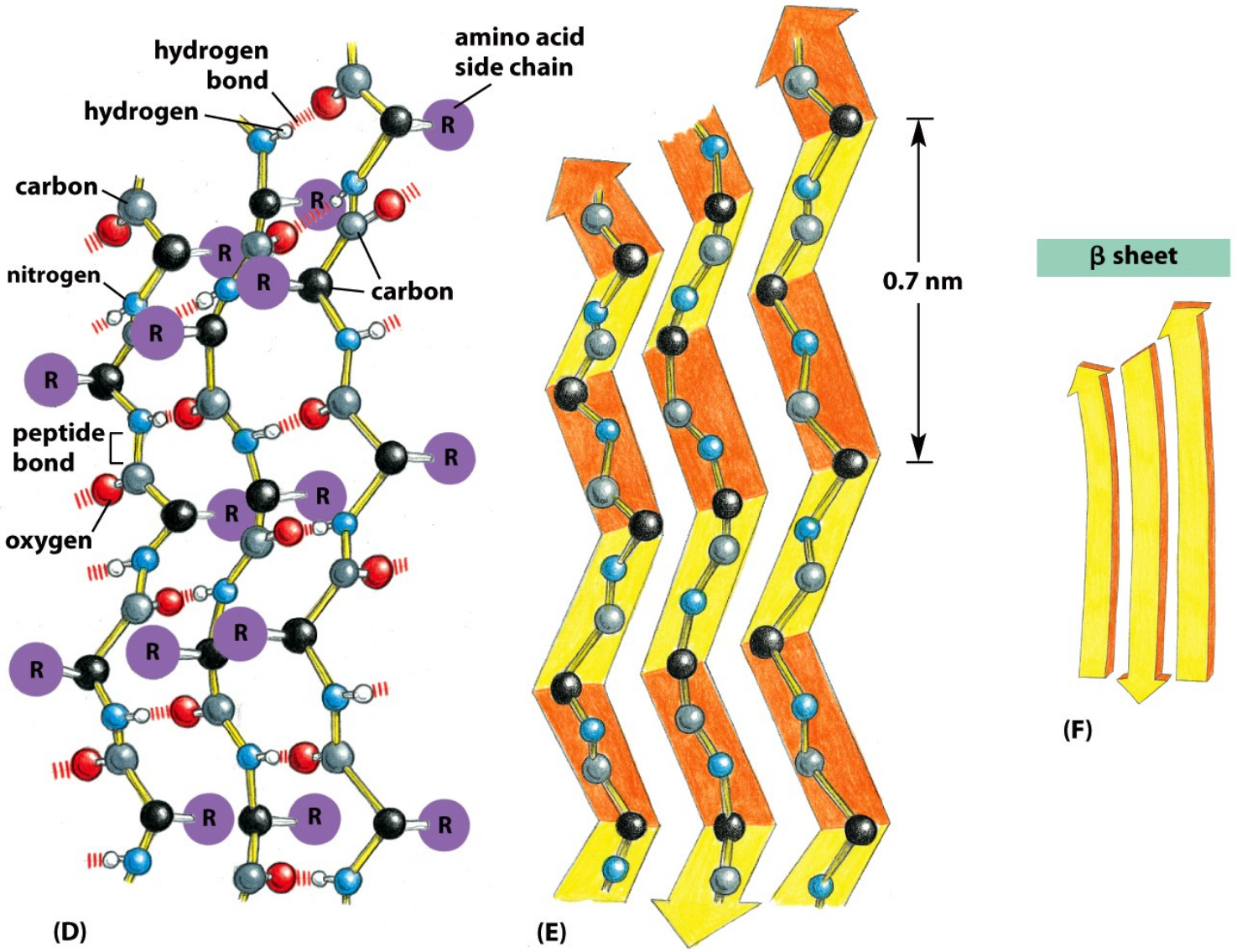


Two important helical notes

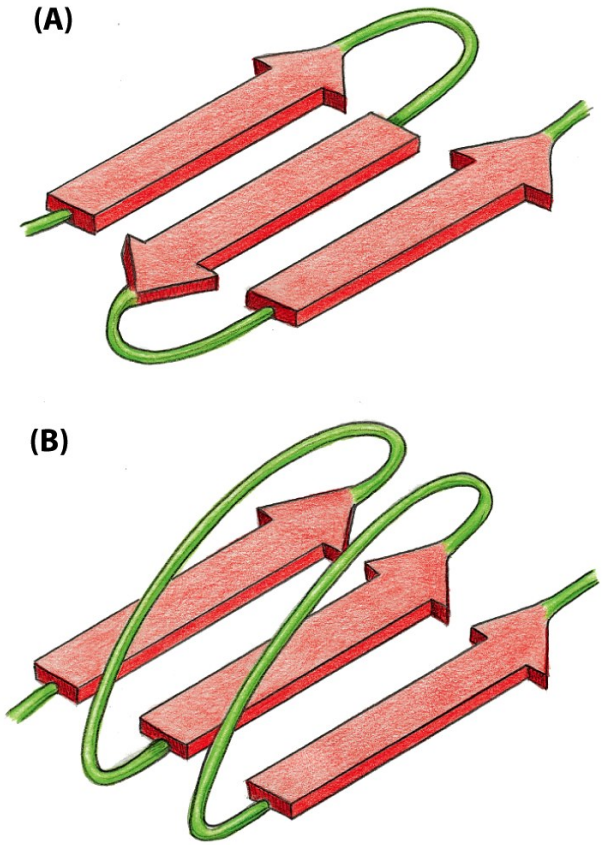




Beta Sheets


hydrogen bond
amino acid side chain
hydrogen
carbon
nitrogen
carbon
peptide bond
oxygen
R
(D)
0.7 nm
(E)
β sheet
(F)

Beta sheets can assemble different ways



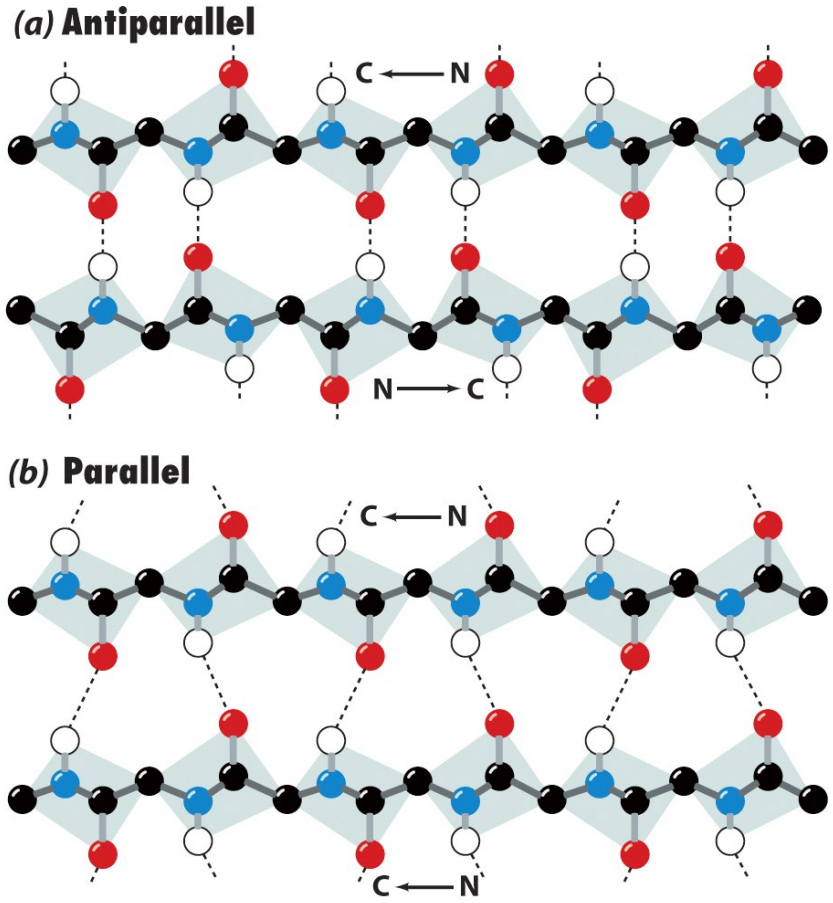


Figure 6-9 Fundamentals of Biochemistry, 2/e

Loops

- Connect helices and sheets
- Are often structured, but can be very flexible.
- Glycine often present in loops
- Mathematica Again

Tertiary Structure

- The assembly of secondary structure
- Side chains and backbone interactions determine how the secondary structure elements align
- Non-covalent bonding primary stabilization
- Only mildly stable, can be broken up by heating or using chemical denaturants

Side Chain Residues Come in 4 "flavors"

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NONPOLAR AMINO ACIDS
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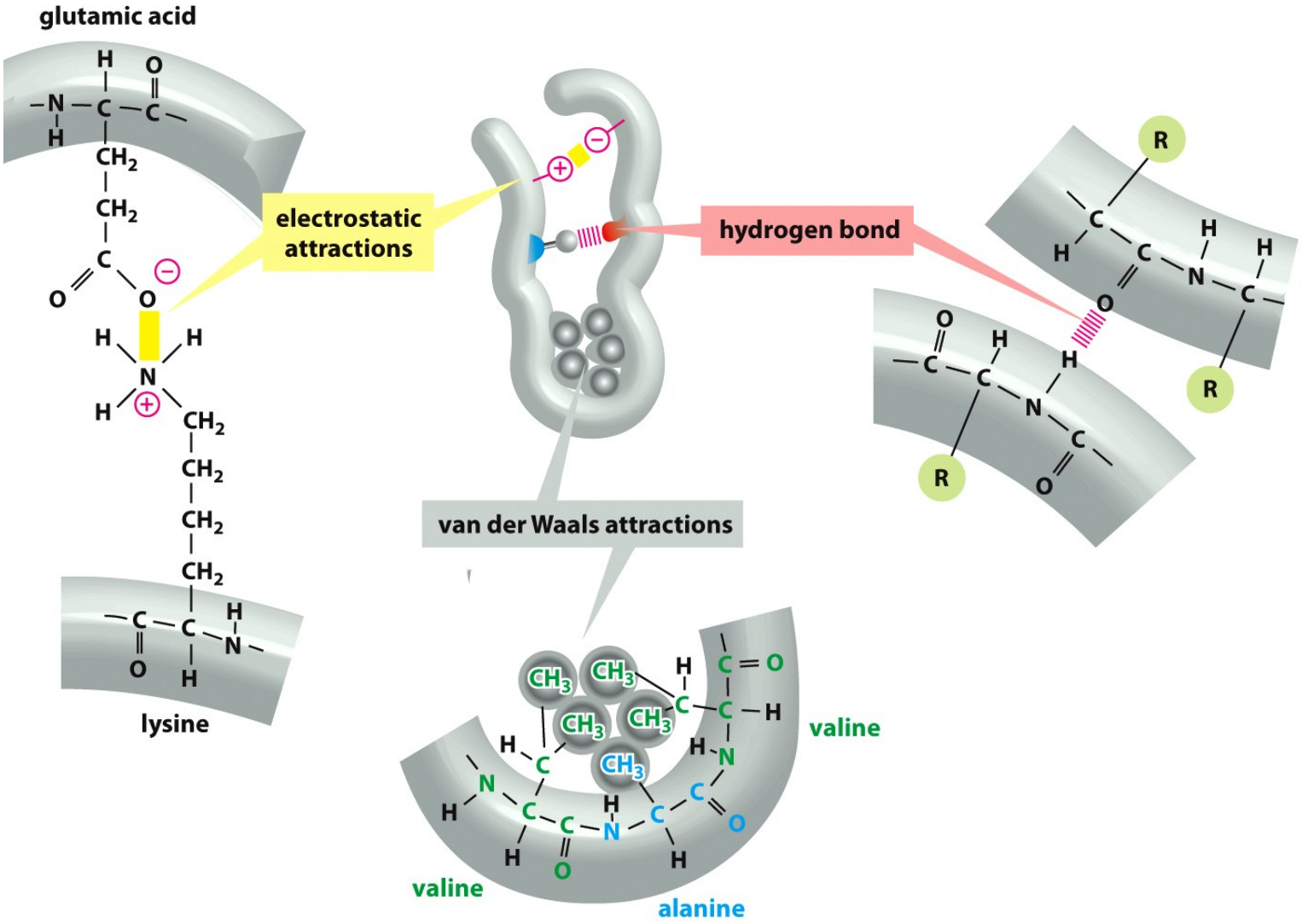
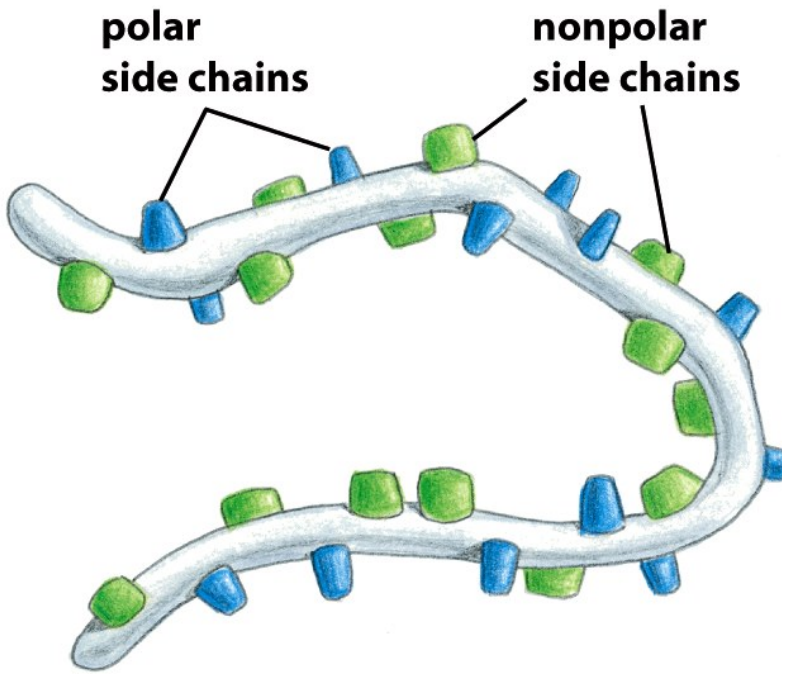
Non-covalent interactions hold it together

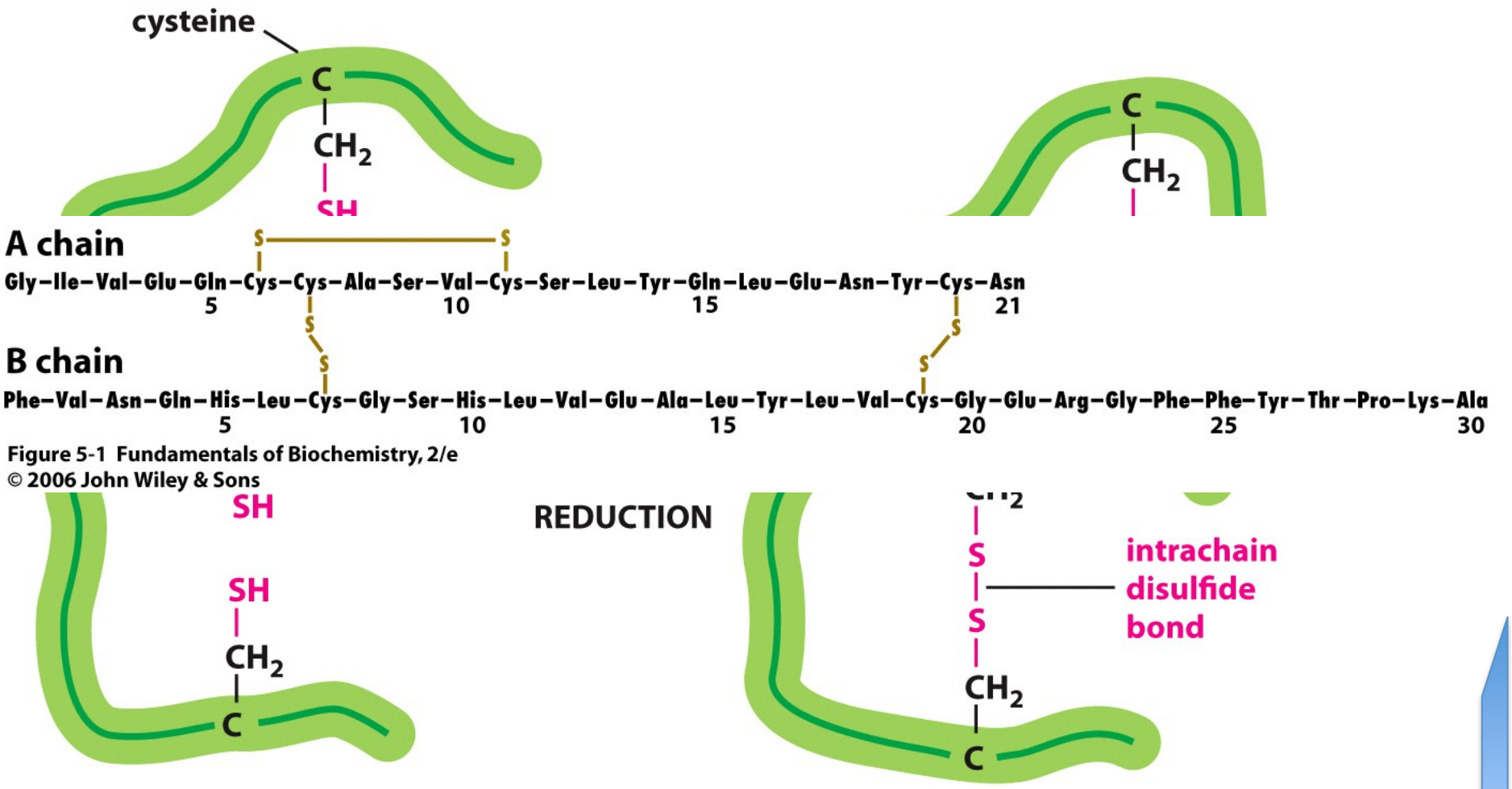


Protein's "hide" their hydrophobic core



unfolded polypeptide

Disulphide Bonds



Relative strength of Bonds

		STRENGTH IN kcal/mole	
BOND TYPE	**LENGTH (nm)**	**IN VACUUM**	**IN WATER**
Covalent	0.15	90 (377)**	90 (377)
Noncovalent: ionic bond*	0.25	80 (335)	3 (12.6)
hydrogen bond	0.30	4 (16.7)	1 (4.2)
van der Waals attraction (per atom)	0.35	0.1 (0.4)	0.1 (0.4)

*An ionic bond is an electrostatic attraction between two fully charged atoms.
**Values in parentheses are kJ/mole. 1 calorie = 4.184 joules.

The folded state is the "lowest energy" state

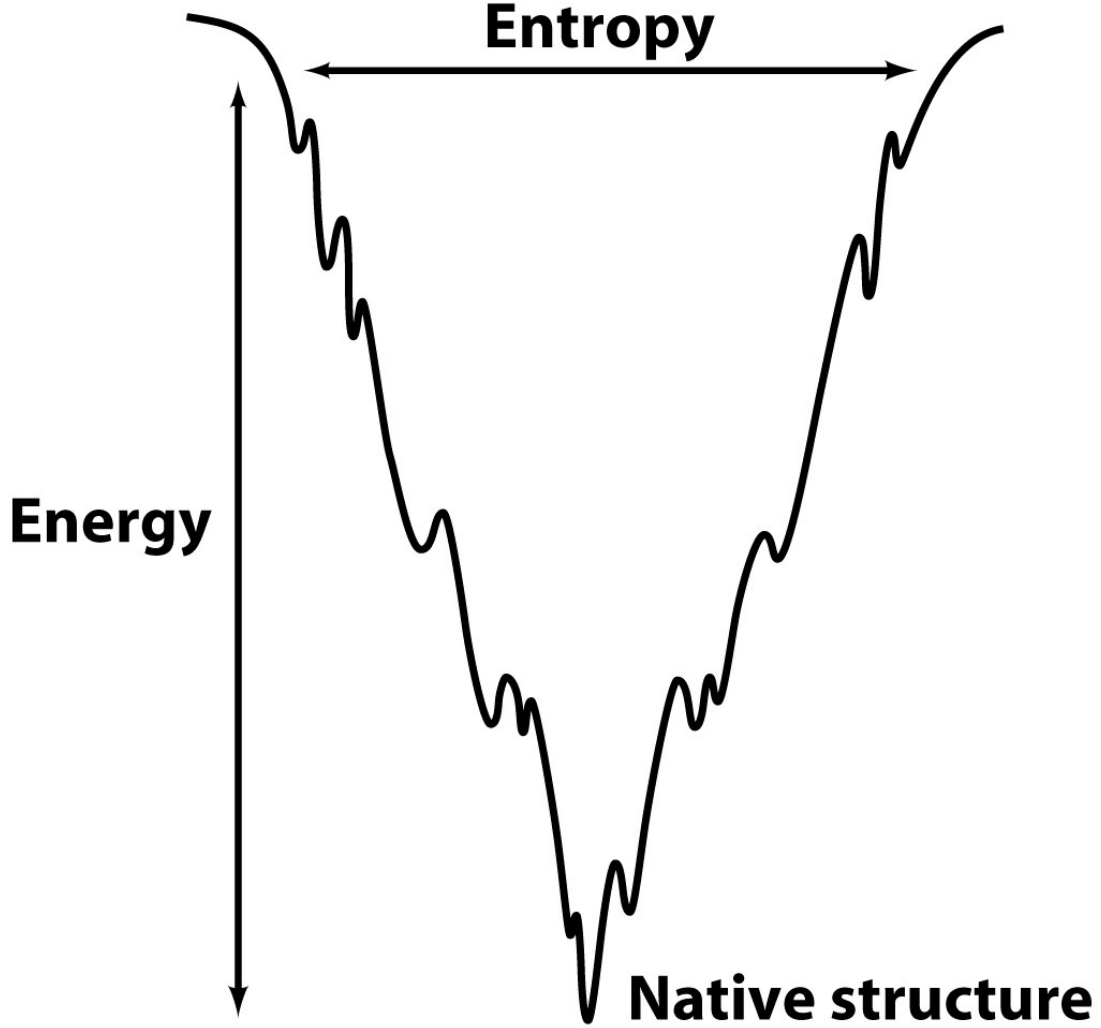


Figure 6-41 Fundamentals of Biochemistry, 2/e

Tertiary Structure

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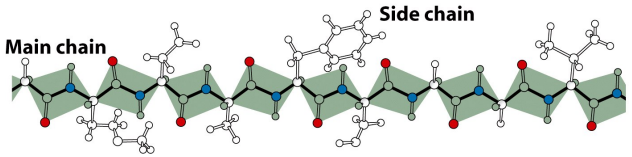

Figure 6-3 Fundamentals of Biochemistry, 2/e
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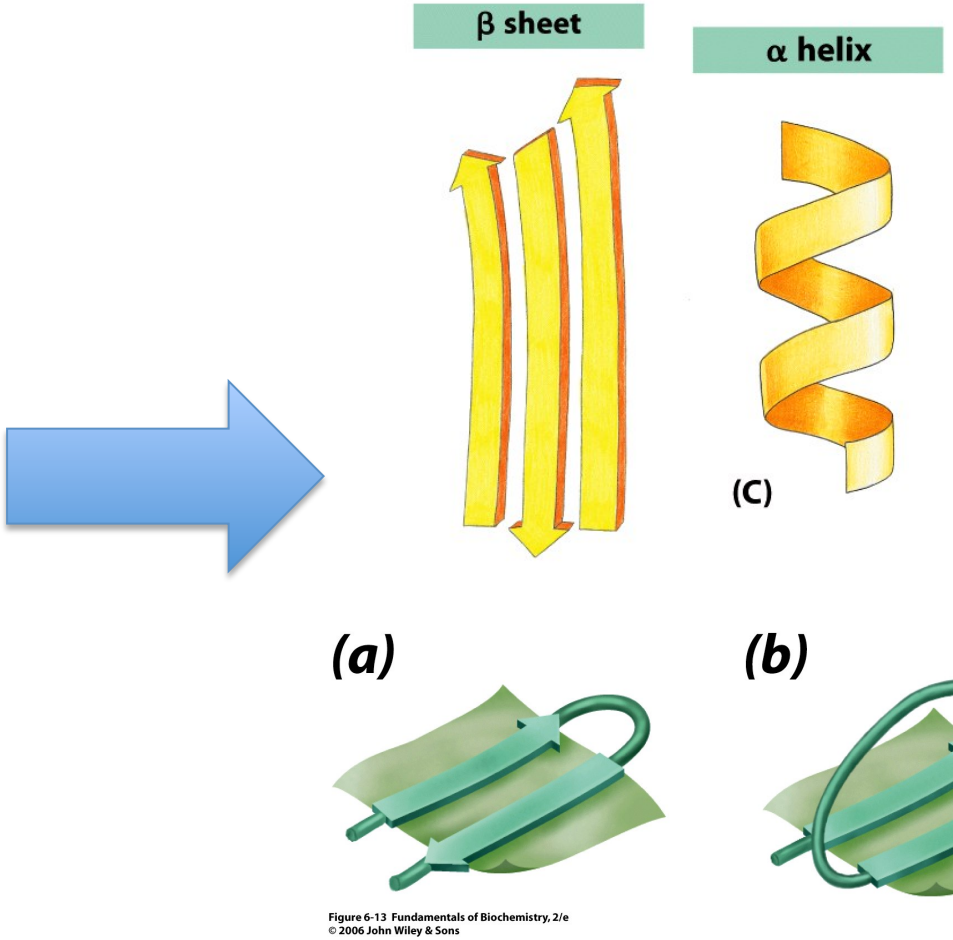

Figure 6-13 Fundamentals of Biochemistry, 2/e
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From Noodles to Nanomachines