

ME 411 / ME 511

Biological Frameworks for Engineers

Class Organization

- HW1 due today
- HW2 online
- Lab 1 – Protein Structure
 - Bring to laptops to class
 - Handouts provided

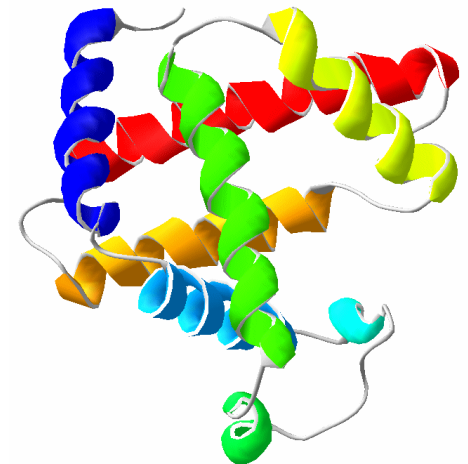


ME 411 / ME 511

Proteins

Protein

- Greek 'protas' (of primary importance)
- Proteins are essential to the structure and function of all living cells
- Human genome contains 25,000 genes that encode proteins*



**Alternative splicings and post-translational modifications can lead to 100,000 'distinct' proteins*

Form is Function

- Folding and assembly define function
- 3-D shape has enzymatic nooks and structural parts
- Form determined by non-covalent bonds between AAs.
- Interactions between local and proximal regions in linear sequence of AAs

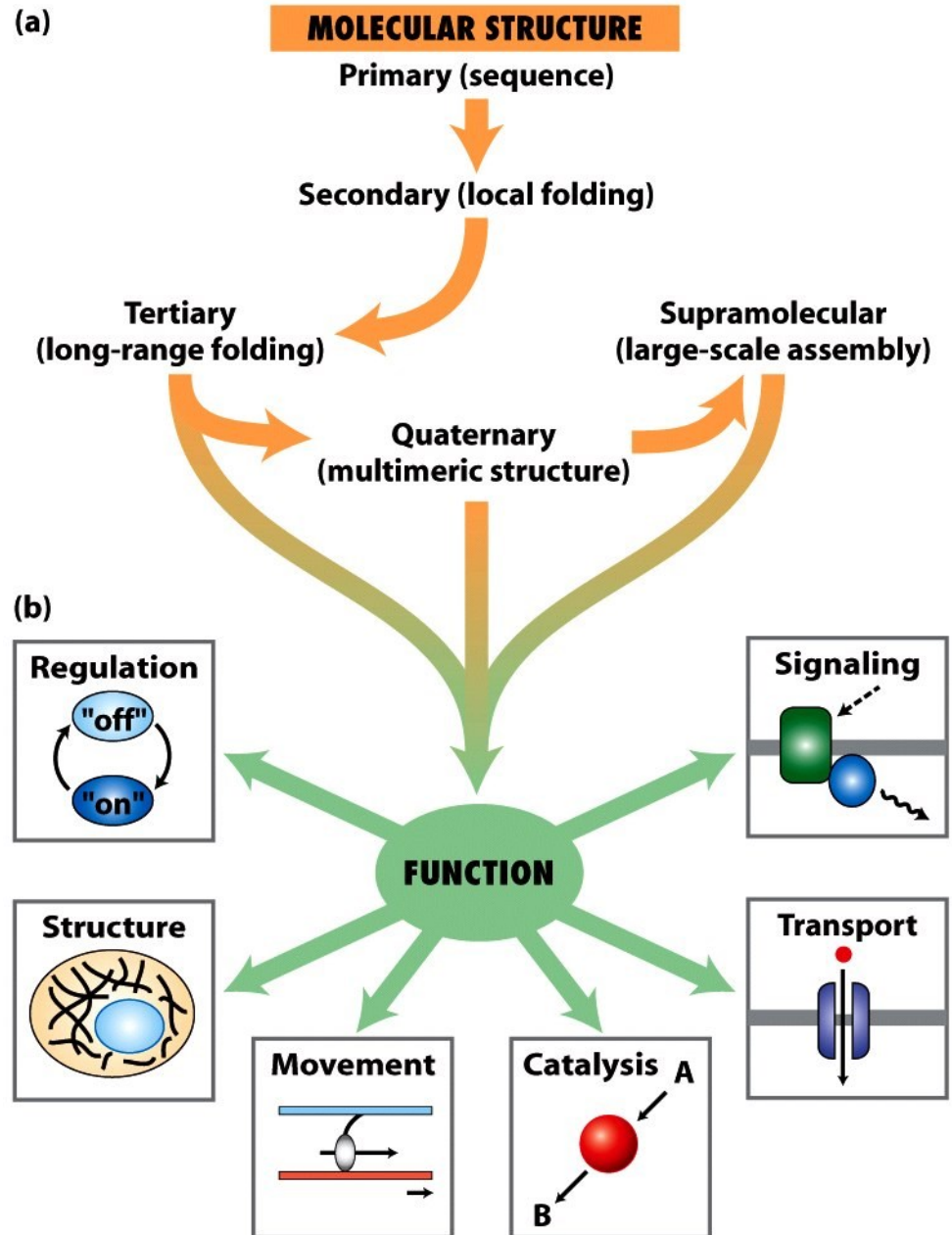


Figure 3-1
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Noncovalent interactions

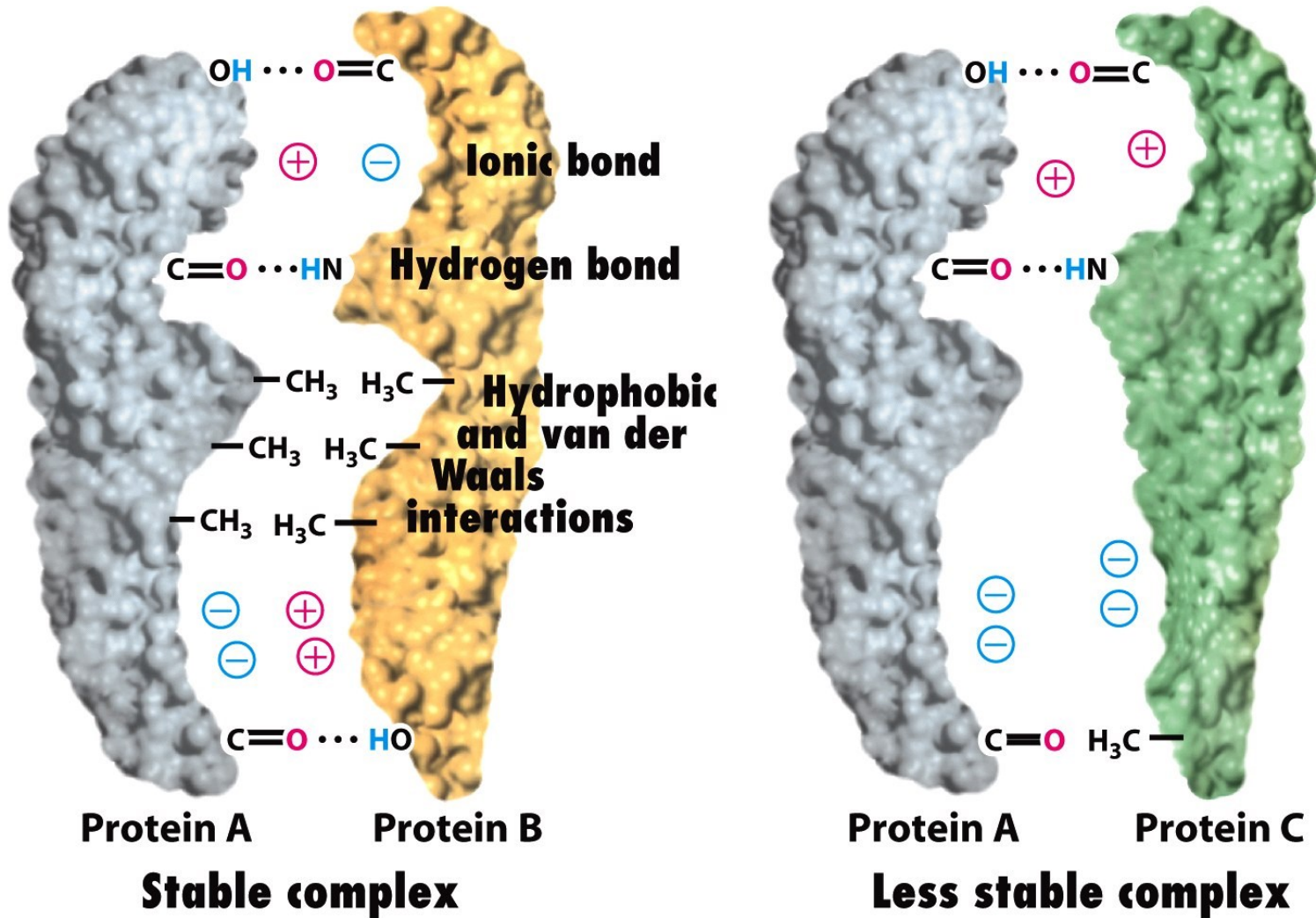


Figure 2-12
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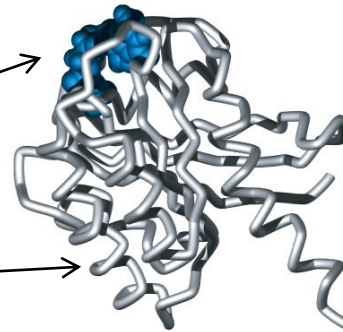
Form-Function Example

Ras GTPase

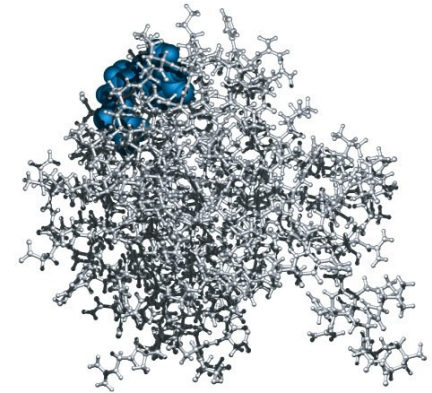


GAP binding site

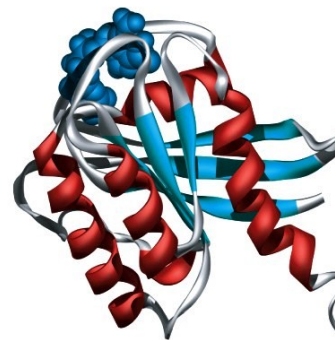
(a) C_α backbone trace



(b) Ball and stick



(c) Ribbons



(d) Solvent-accessible surface

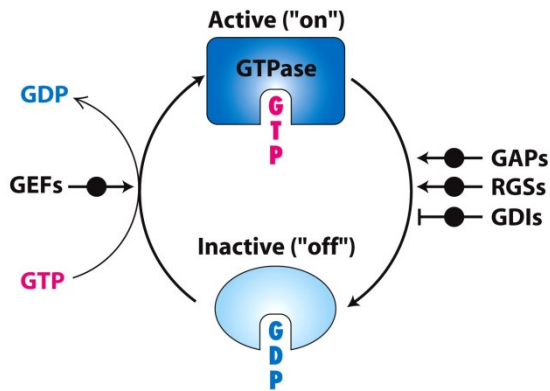
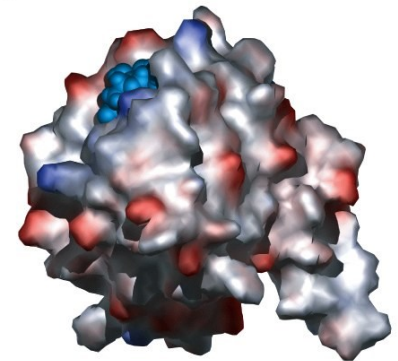
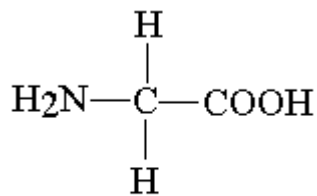


Figure 3-32
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Figure 3-8
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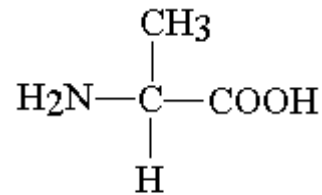
Amino Acids

- Central alpha carbon atom ($C\alpha$)
 - Amino group ($-NH_2$)
 - Carboxyl group ($-COOH$)
 - Hydrogen atom ($-H$)
 - Unique side chain/residue (20 in total)



glycine

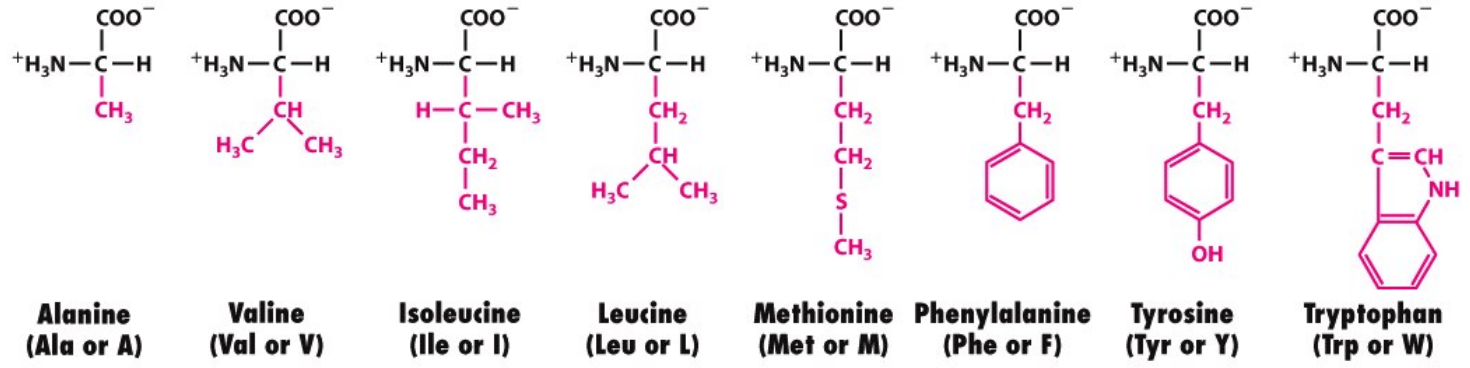
Gly, G



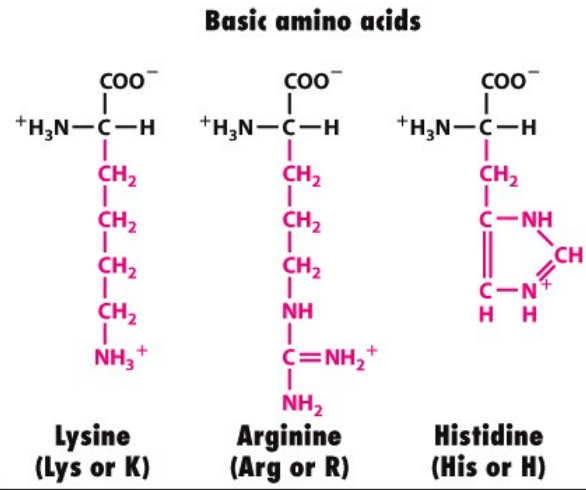
alanine

Ala, A

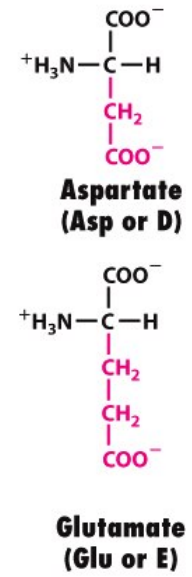
HYDROPHOBIC AMINO ACIDS



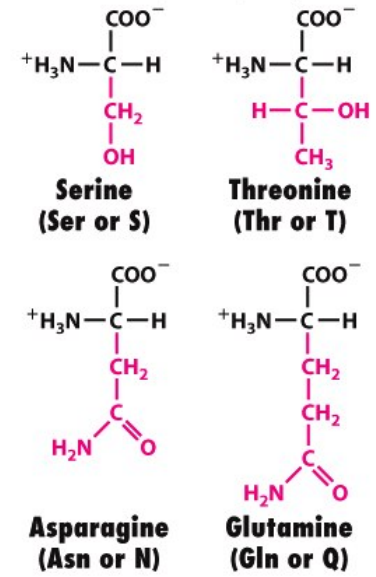
HYDROPHILIC AMINO ACIDS



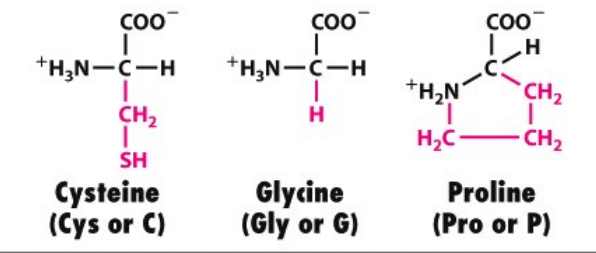
Acidic amino acids



Polar amino acids with uncharged R groups



SPECIAL AMINO ACIDS



carbon
 hydrogen
 oxygen
 nitrogen
 sulfur

HYDROPHOBIC

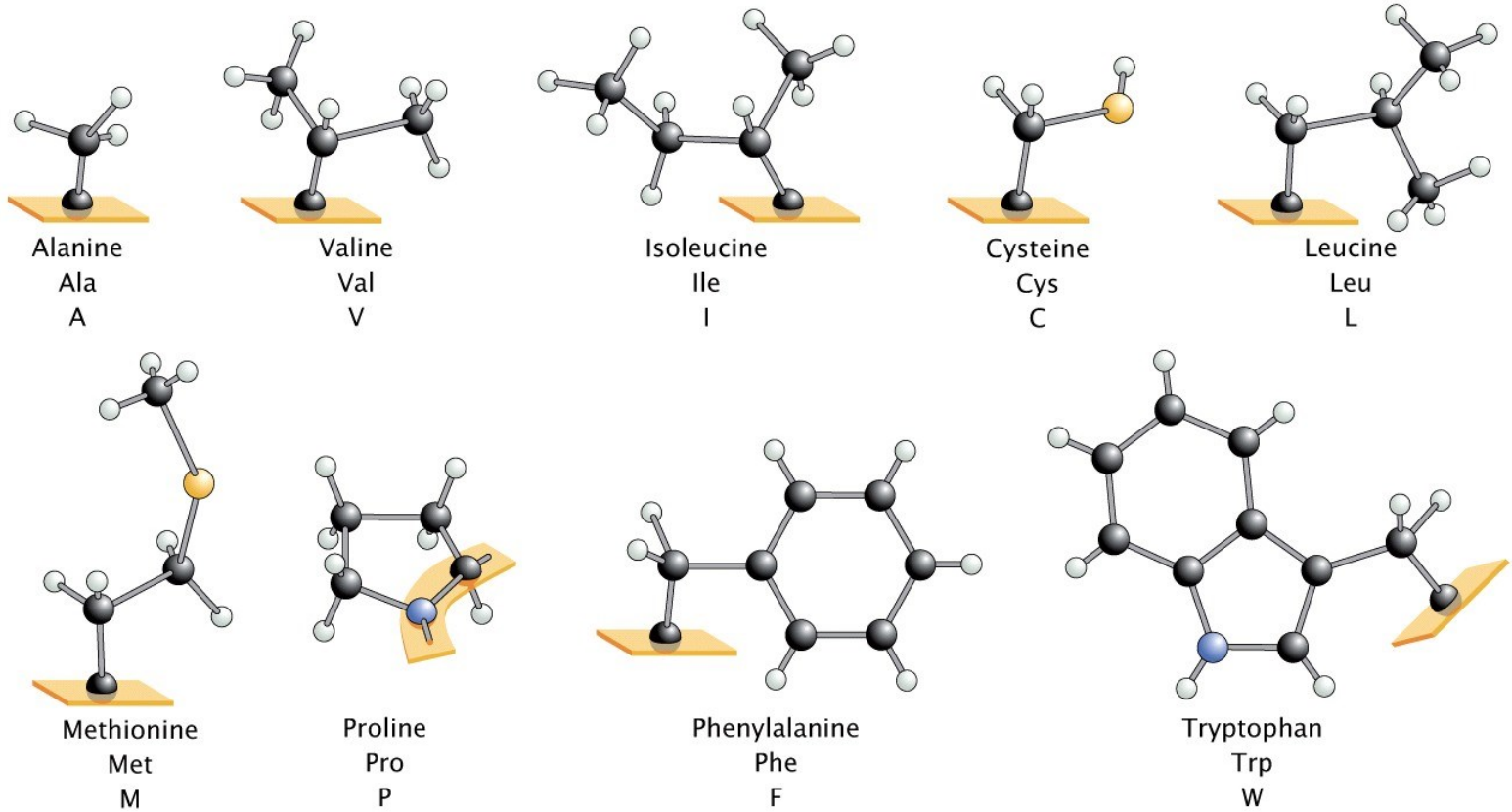


Figure 2.33 (part 1 of 3) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

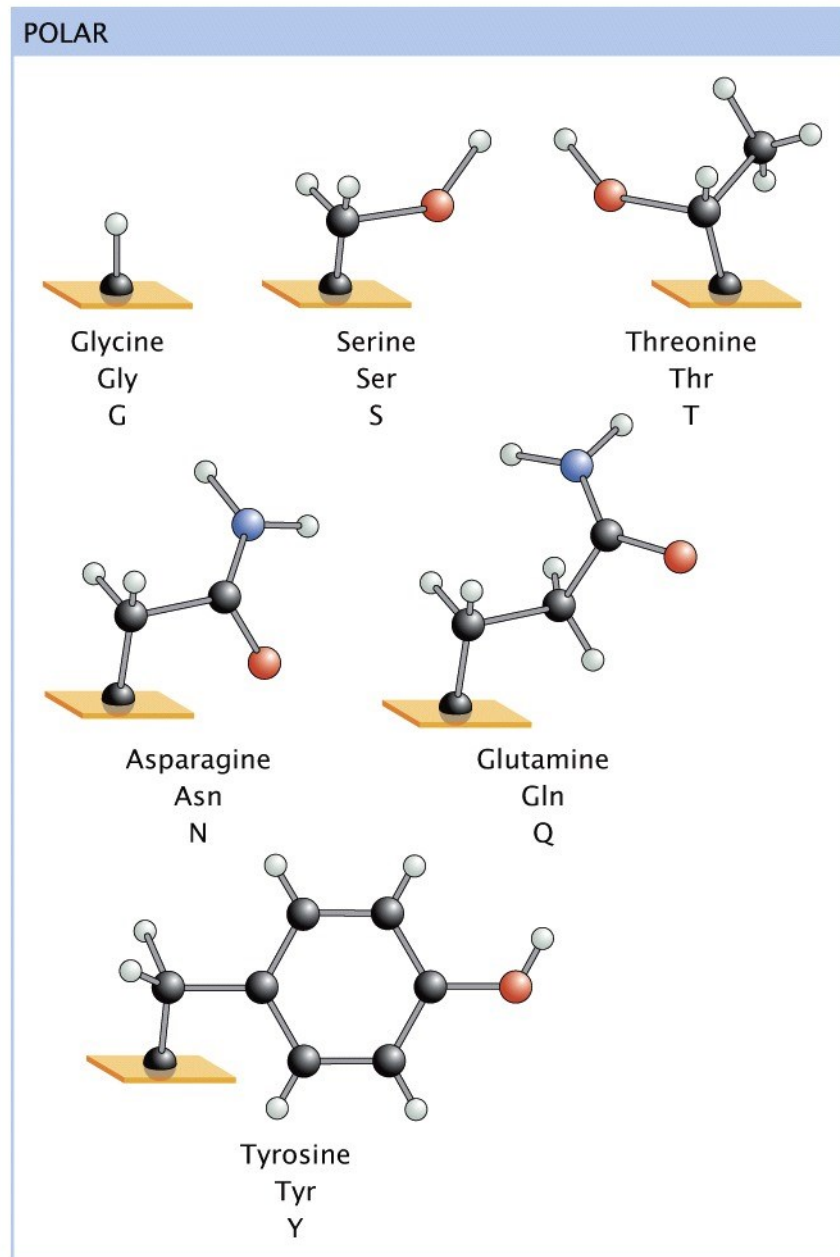


Figure 2.33 (part 2 of 3) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

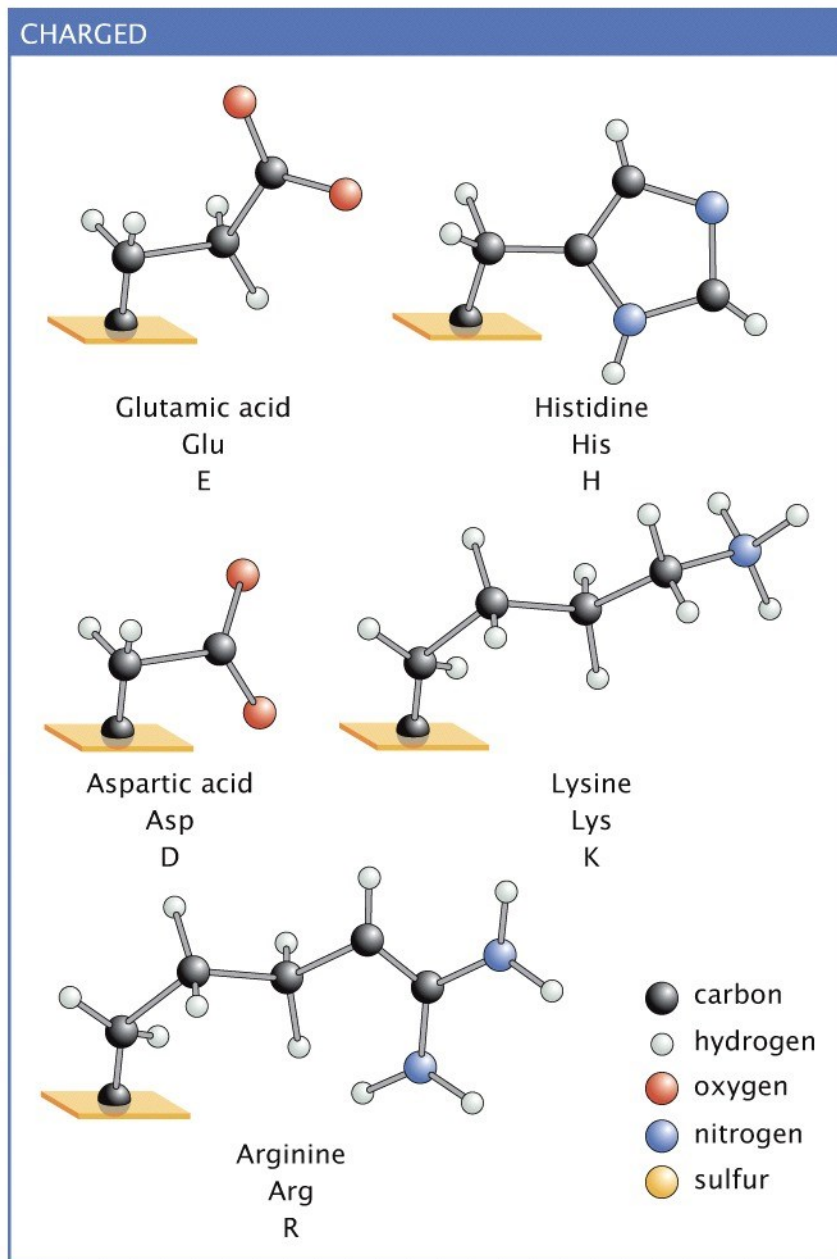
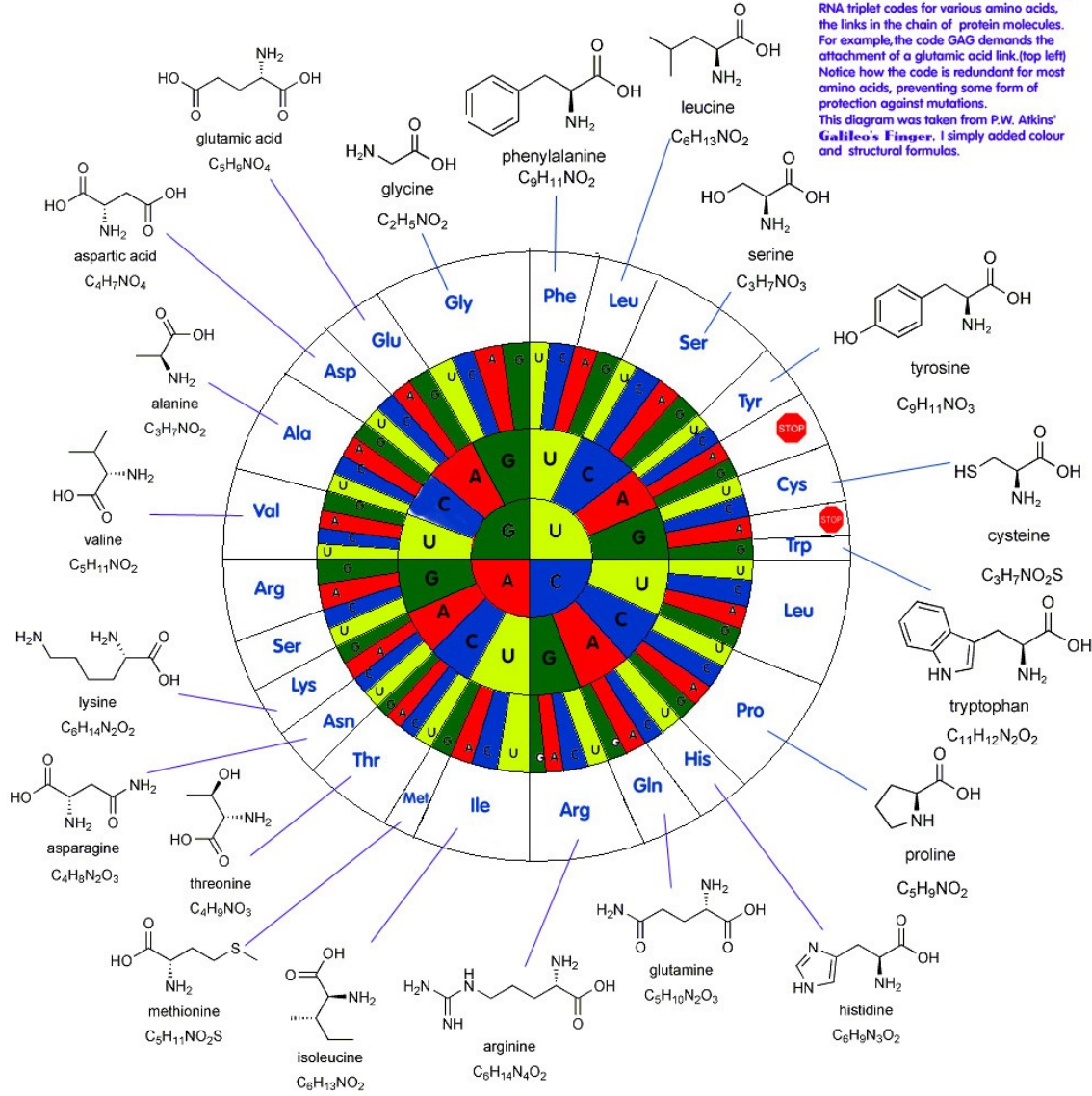


Figure 2.33 (part 3 of 3) Physical Biology of the Cell, 2ed. (© Garland Science 2013)

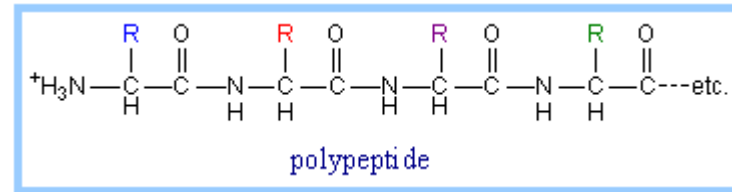
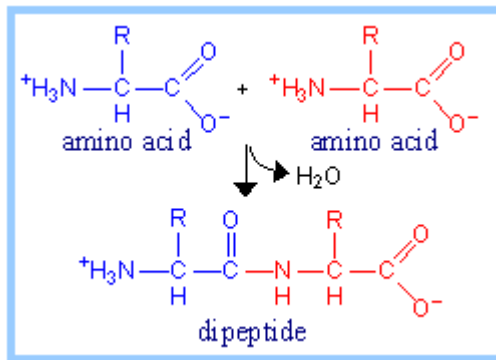
Recall: DNA → RNA → AA

The Genetic Code: The colour wheel reveals RNA triplet codes for various amino acids, the links in the chain of protein molecules. For example, the code GAG demands the attachment of a glutamic acid link. (top left)
 Notice how the code is redundant for most amino acids, preventing some form of protection against mutations.
 This diagram was taken from P.W. Atkins' **Galileo's Finger**. I simply added colour and structural formulas.



Amino Acids to Polypeptides

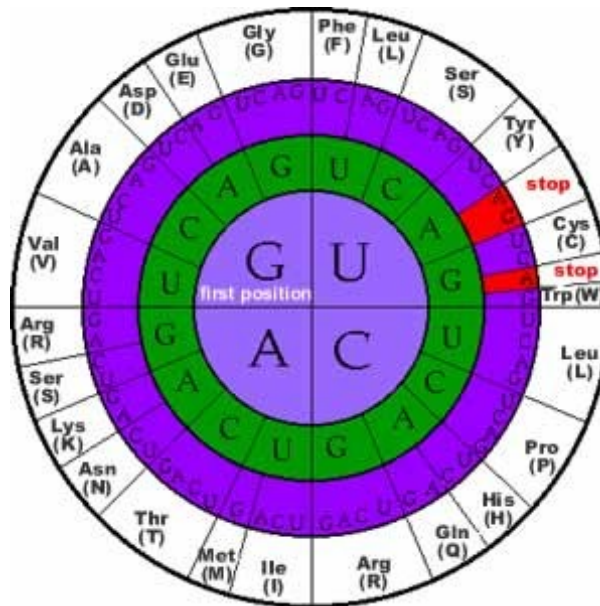
- Peptide bond – carboxyl reacting with an amino group: $C - NO + H_2O$



- Amino end is called N-terminus (starting end for translation)
- Carboxyl end is C-terminus

Residue Sequence for Actin

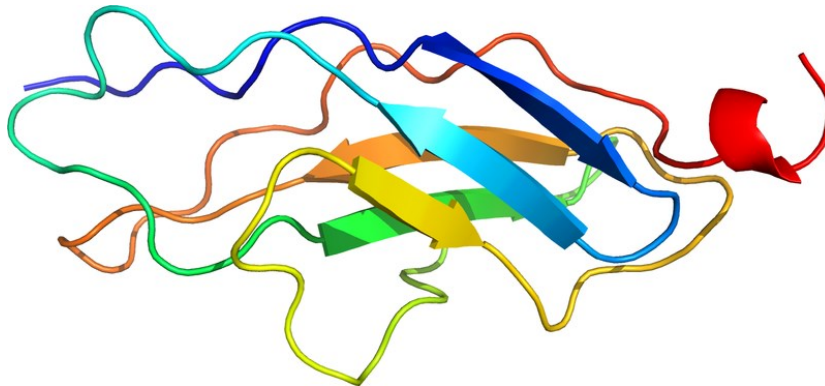
MCEEETALV CDNGSGLCKA GFAGDDAPRA VFPSIVGRPR
 HQGVMVGMGQ KDSYVGDEAQ SKRGILTLKY PIEHGIITNW
 DDMEKIWHHS FYNELRVAPE EHPTLLTEAP INPKANREKM
 TQIMFETFNV PAMYVAIQAV LSLYASGRTT GIVLDSGDGV
 THNVPIYEGY ALPHAIMRLD LAGRDLTDYL MKILTERGYS
 FVTTAEREIV RDIKEKLCYV ALDFENEMAT AASSSSLEKS
 YELPDGQVIT IGNERFRCPE TLFQPSFIGM ESAGIHETTY
 NSIMKCDIDI RKDLYANNVL SGGTTMYPGI ADRMQKEITA
 LAPSTMKIKI IAPPERKYSV
 WIGGSILASL STFQQMWISK
 PEYDEAGPSI VHRKCF



Peptide Mass

- Protein weight is reported in Daltons
 - 1.66×10^{-24} Da = 1 gram
- Average amino acid is ~113 Da

Titin



Largest protein
3816 kDa
34,350 residues
(111 Da/AA)

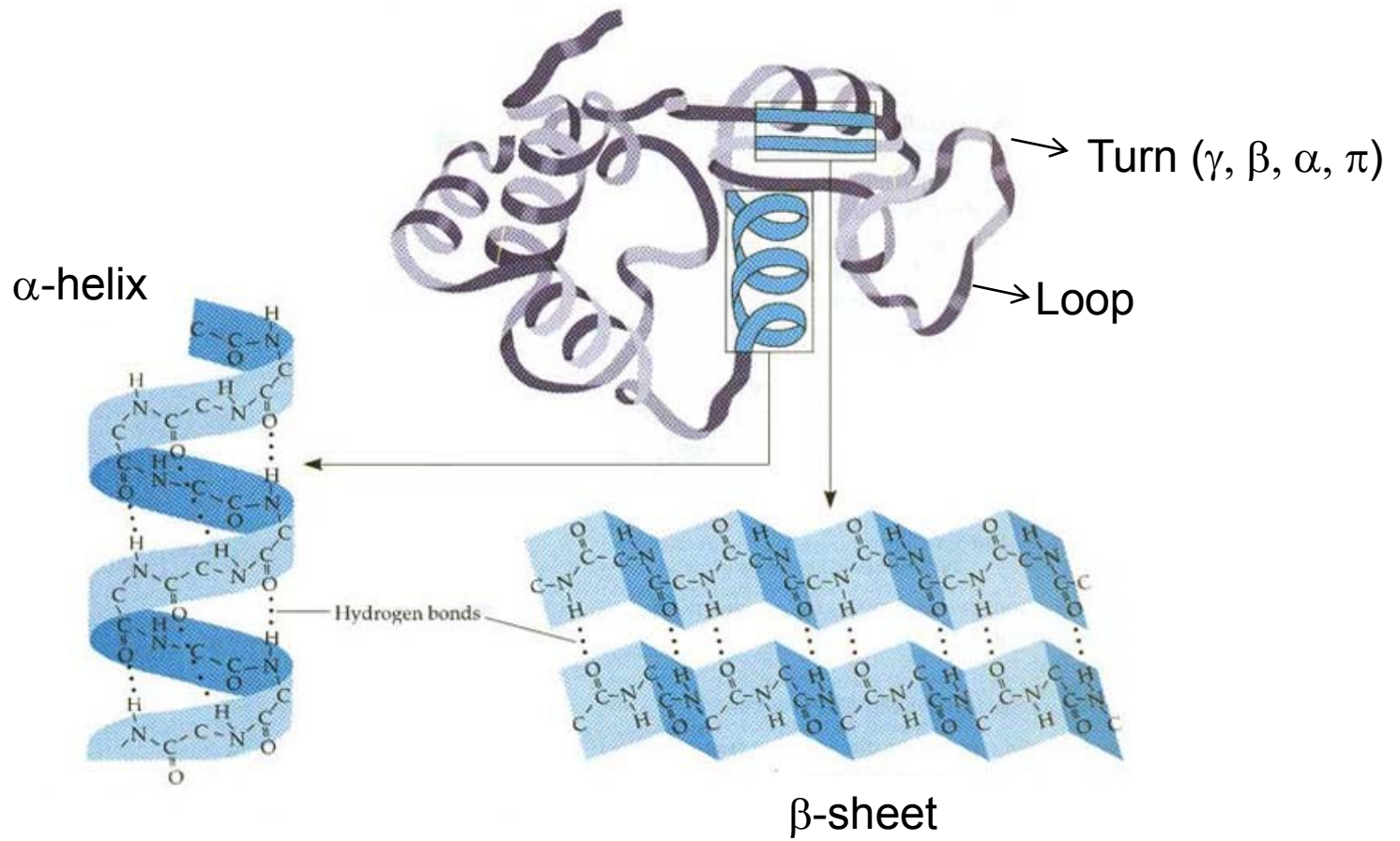
Protein Structure

- Primary – amino acid sequence
- Secondary – patterned sub-structures
- Tertiary – overall shape of a single protein molecule or unit
- Quaternary – union of more than one protein units

Primary Structure

MCEEETALV CDNGSGLCKA GFAGDDAPRA VFPSIVGRPR
HQQVMVGMGQ KDSYVGDEAQ SKRGILTLKY PIEHGIITNW
DDMEKIWHHS FYNELRVAPE EHPTLLTEAP INPKANREKM
TQIMFETFNV PAMYVAIQAV LSLYASGRTT GIVLDSGDGV
THNVPIYEGY ALPHAIMRLD LAGRDLTDYL MKILTERGYS
FVTTAEREIV RDIKEKLCYV ALDFENEMAT AASSSSLEKS
YELPDGQVIT IGNERFRCPE TLFQPSFIGM ESAGIHETTY
NSIMKCDIDI RKDLYANNVL SGGTTMYPGI ADRMQKEITA
LAPSTMKIKI IAPPERKYSV WIGGSILASL STFQQMWISK
PEYDEAGPSI VHRKCF

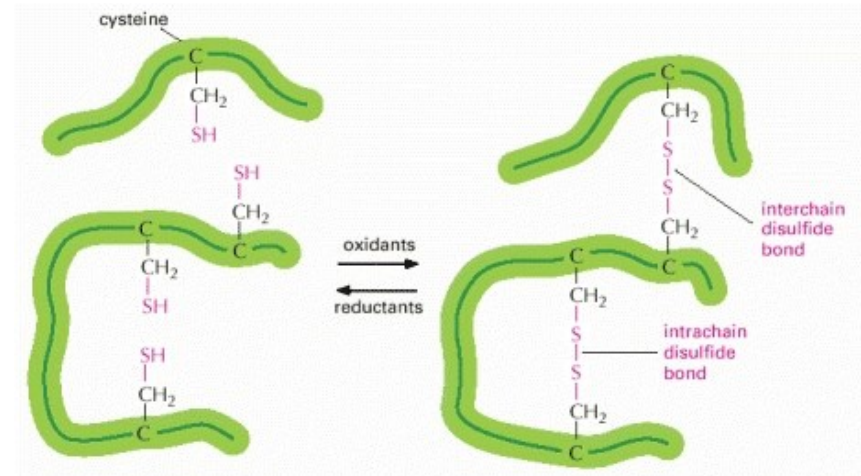
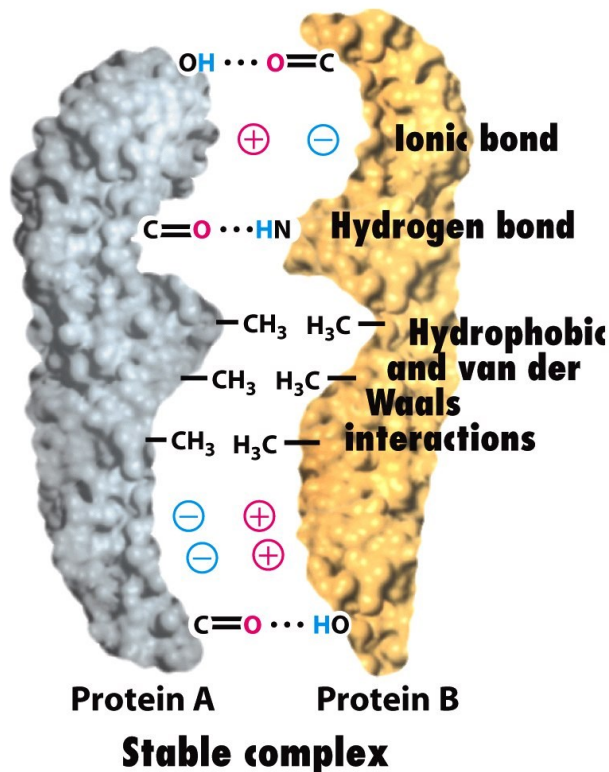
Secondary Structure



Tertiary Structure

- Hydrogen Bonds,
- Ionic Interactions

- Hydrophobic Bonds
- van der Waals
- Disulfide Bonds



Quaternary Structure

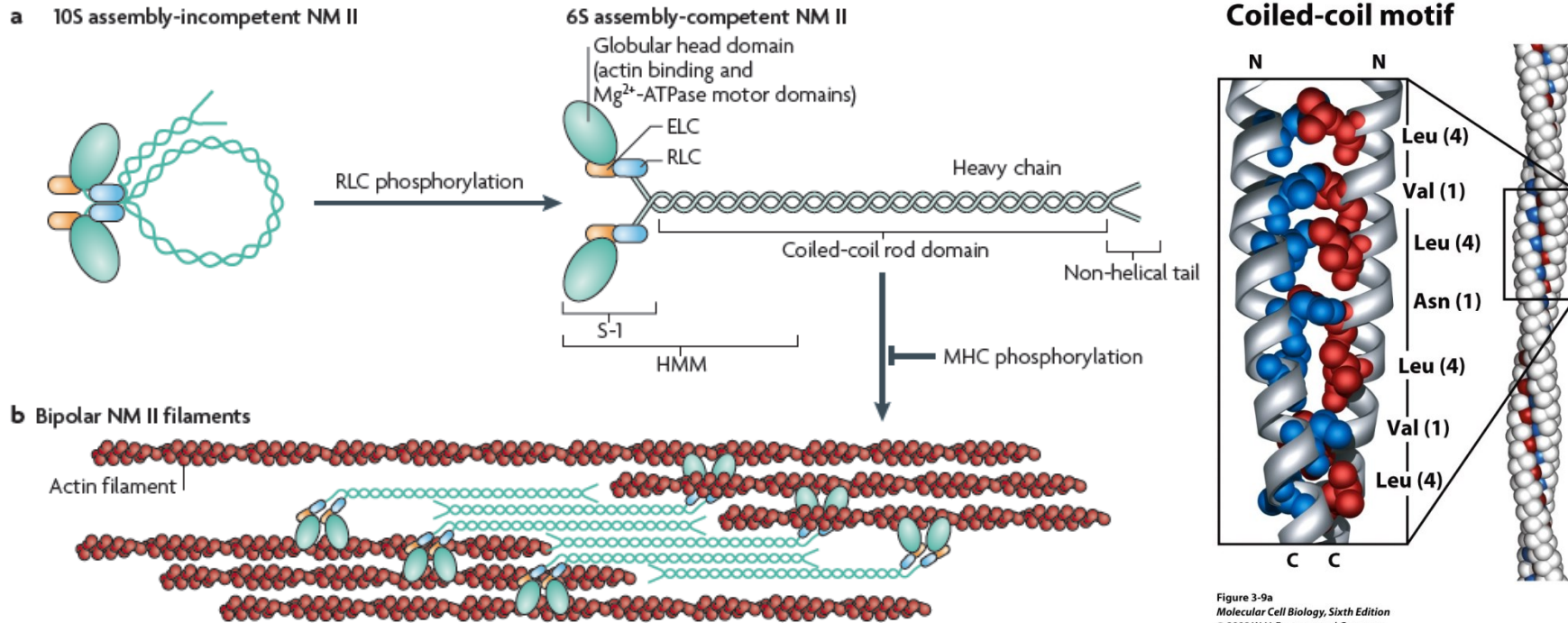
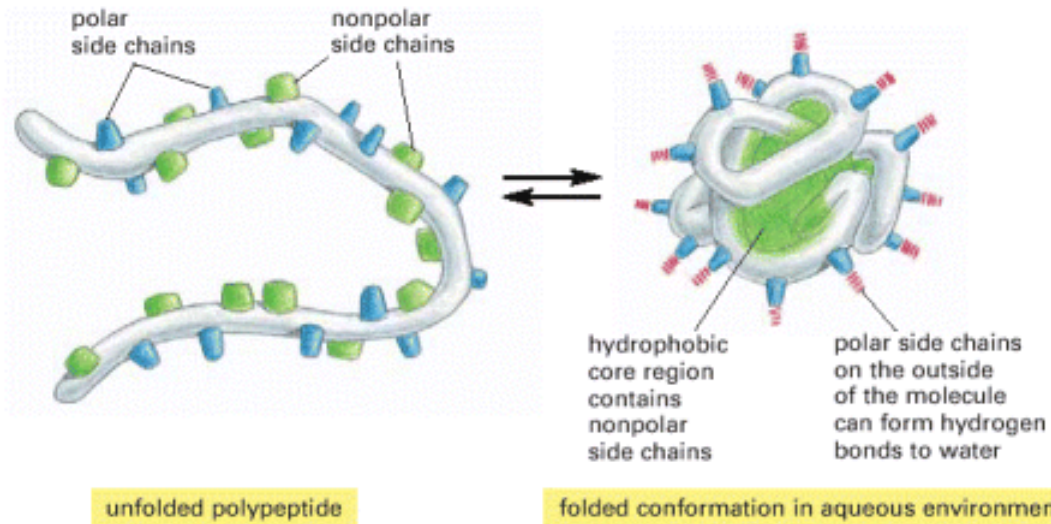
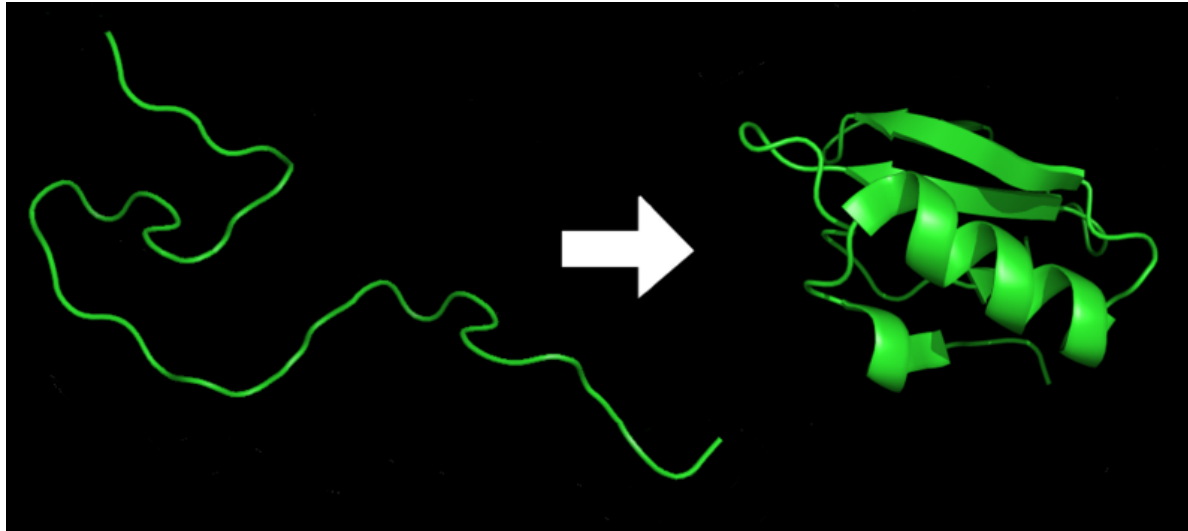


Figure 3-9a
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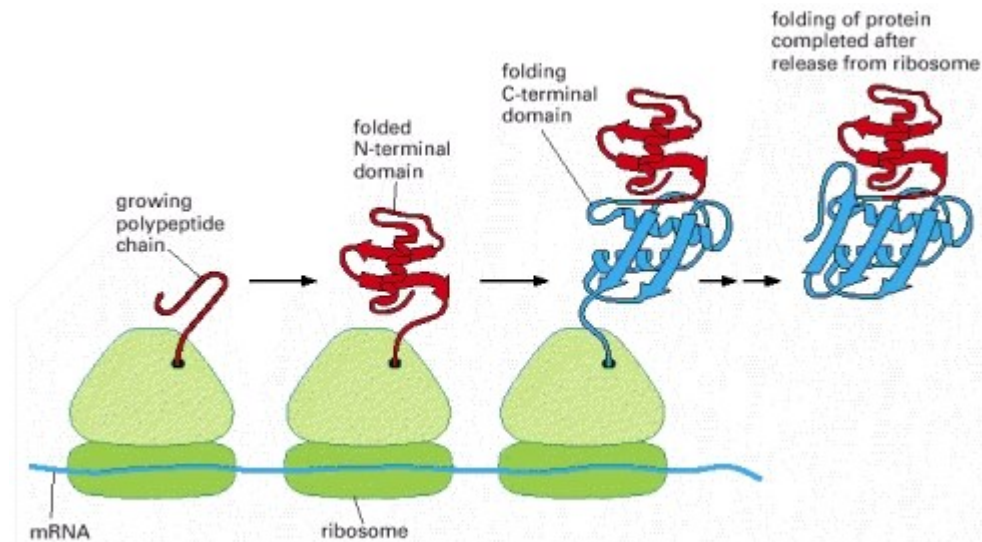
Figure 1 | Domain structure of NM II. a | The subunit and domain structure of non-muscle myosin II (NM II), which forms a dimer through interactions between the α -helical coiled-coil rod domains. The globular head domain contains the actin-binding regions and the enzymatic Mg^{2+} -ATPase motor domains. The essential light chains (ELCs) and the regulatory light chains (RLCs) bind to the heavy chains at the lever arms that link the head and rod domains. In the absence of RLC phosphorylation, NM II forms a compact molecule through a head to tail interaction. This results in an assembly-incompetent form (10S; left) that is unable to associate with other NM II dimers. On RLC phosphorylation, the 10S structure unfolds and becomes an assembly-competent form (6S). S-1 is a fragment of NM II that contains the motor domain and neck but lacks the rod domain and is unable to dimerize. Heavy meromyosin (HMM) is a fragment that contains the motor domain, neck and enough of the rod to effect dimerization. **b** | NM II molecules assemble into bipolar filaments through interactions between their rod domains. These filaments bind to actin through their head domains and the ATPase activity of the head enables a conformational change that moves actin filaments in an anti-parallel manner. Bipolar myosin filaments link actin filaments together in thick bundles that form cellular structures such as stress fibres.

Protein Folding



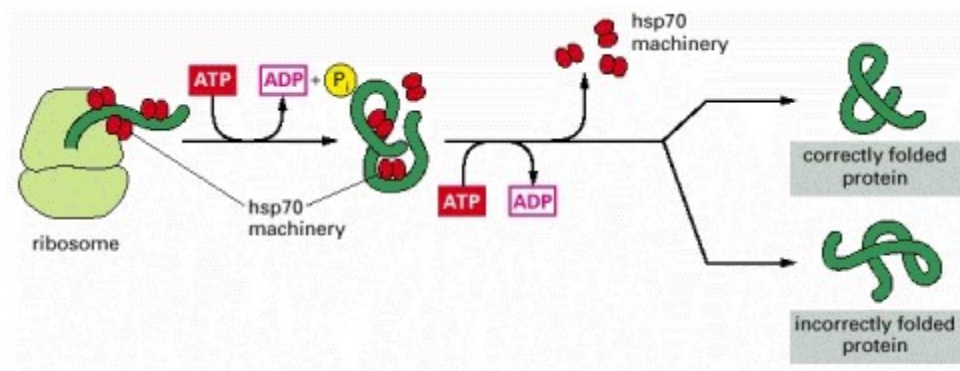
Co-translational Folding

- Polypeptide chain can acquire its secondary and tertiary structure as it emerges from a ribosome
- N-terminus folds first

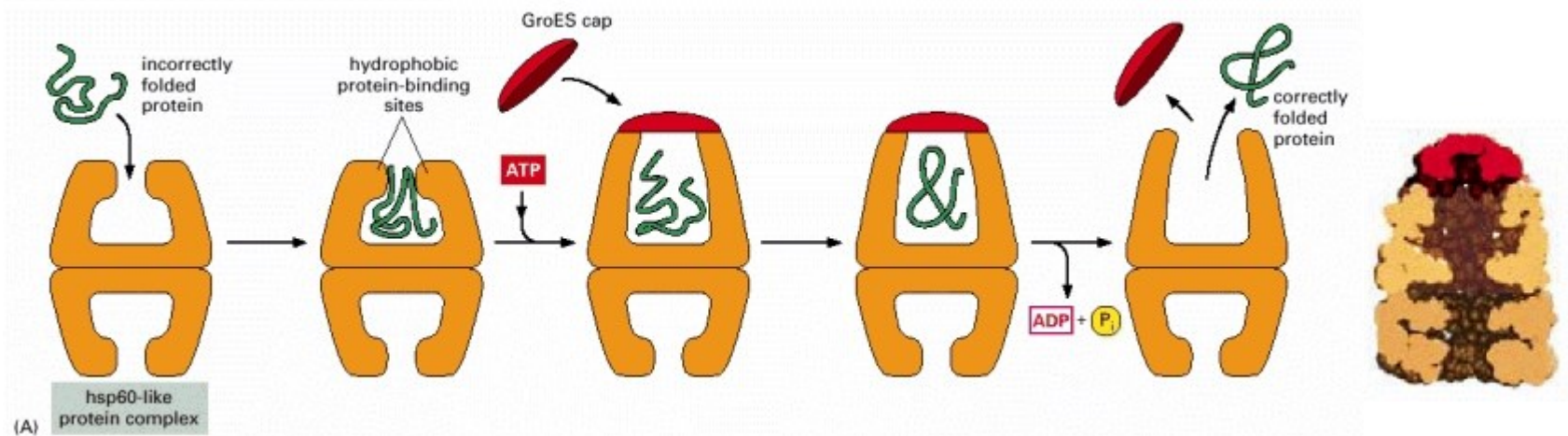


Molecular Chaperones

- Heat shock protein (hsp70)



- Chaperonin



Functional Folding Domains

- e.g., EF hand is a helix-loop-helix domain in Ca^{2+} binding proteins
- Domains are similar amongst proteins

Calmodulin without calcium

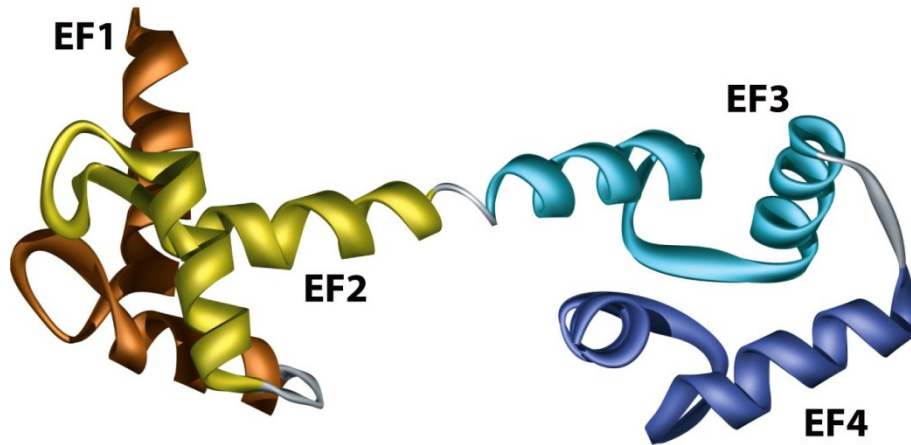


Figure 3-31a
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Ca^{2+} / calmodulin bound to target peptide

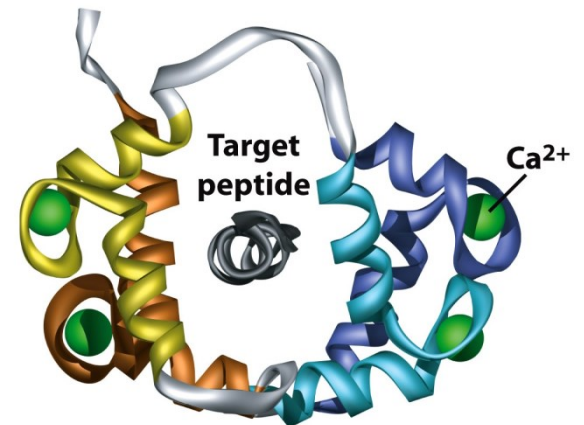
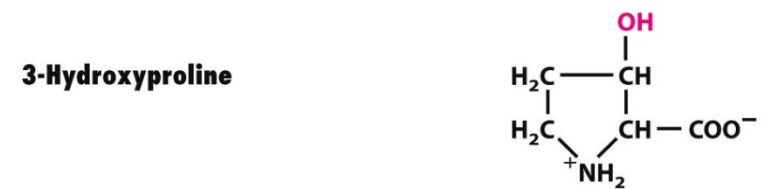
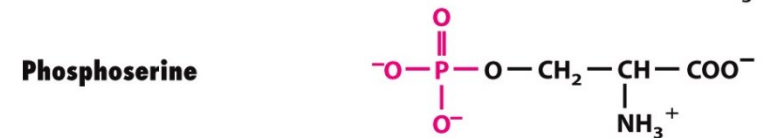
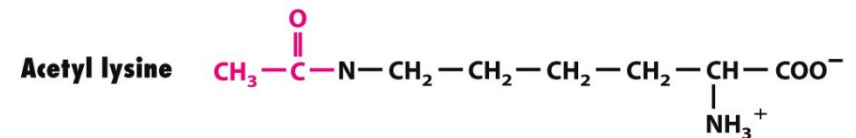


Figure 3-31b
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Posttranslational Modifications

- Functional Groups
 - Phosphorylation
 - Acetylation
 - Hydroxylation
- Proteins
 - Ubiquitination
 - Sumoylation

- Glycans
- Lipids
- Disulfide bonds



Worksheet



- Identify the Dictator
 - a. DNA sequence in a gene and amino acid sequence?
 - b. amino acid sequence and structure?
 - c. protein structure and protein function?
 - d. DNA sequence in a gene and protein function?

Worksheet



- Identify the Dictator
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 - d. DNA sequence in a gene and protein function?

Worksheet



- Identify the Dictator
 - a. DNA sequence in a gene and amino acid sequence?
 - b. amino acid sequence and structure?
 - c. protein structure and protein function?
 - d. DNA sequence in a gene and protein function?

Questions ?