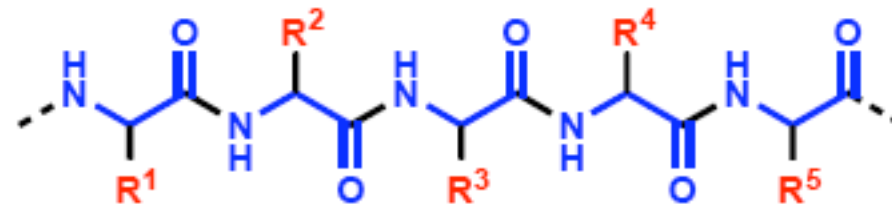


# Topic 2 Proteins as Drug Targets

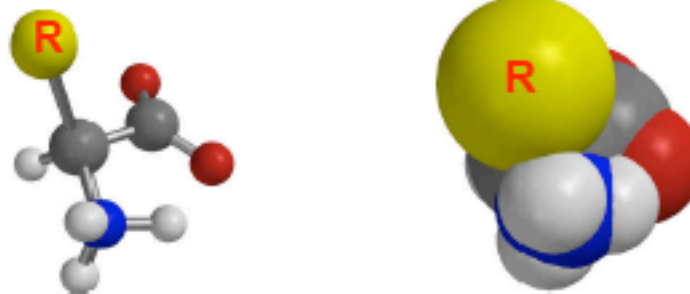
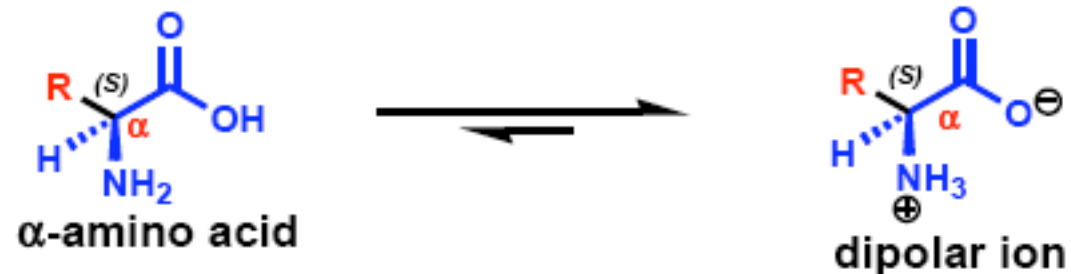
Protein Structure-Chapter 3  
Patrick and Part I Corey

# Proteins and Three-Dimensional Protein Structures

## Proteinogenic Amino Acids I.



Portion of a protein/polypeptide chain

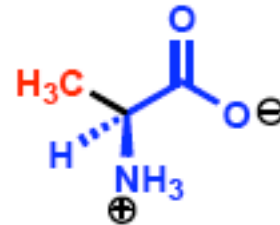


# Proteins and Three-Dimensional Protein Structures

## $\alpha$ -Amino Acids with Hydrophobic Side Chains



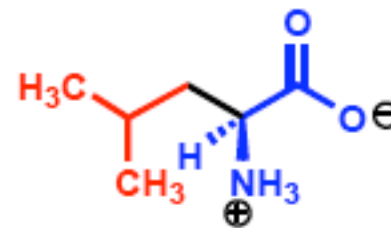
glycine (Gly)



alanine (Ala)



valine (Val)



leucine (Leu)



isoleucine (Ile)



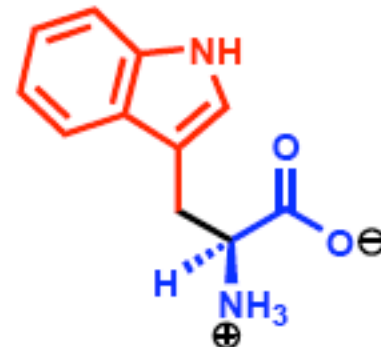
proline (Pro)

## Proteins and Three-Dimensional Protein Structures

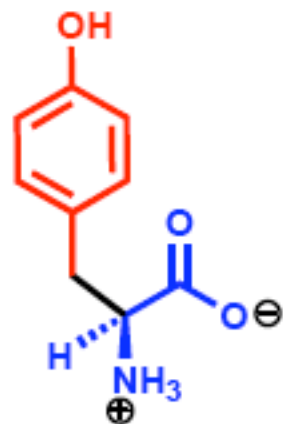
### $\alpha$ -Amino Acids with Aromatic Side Chains



phenyl-  
alanine (Phe)



tryptophan (Trp)

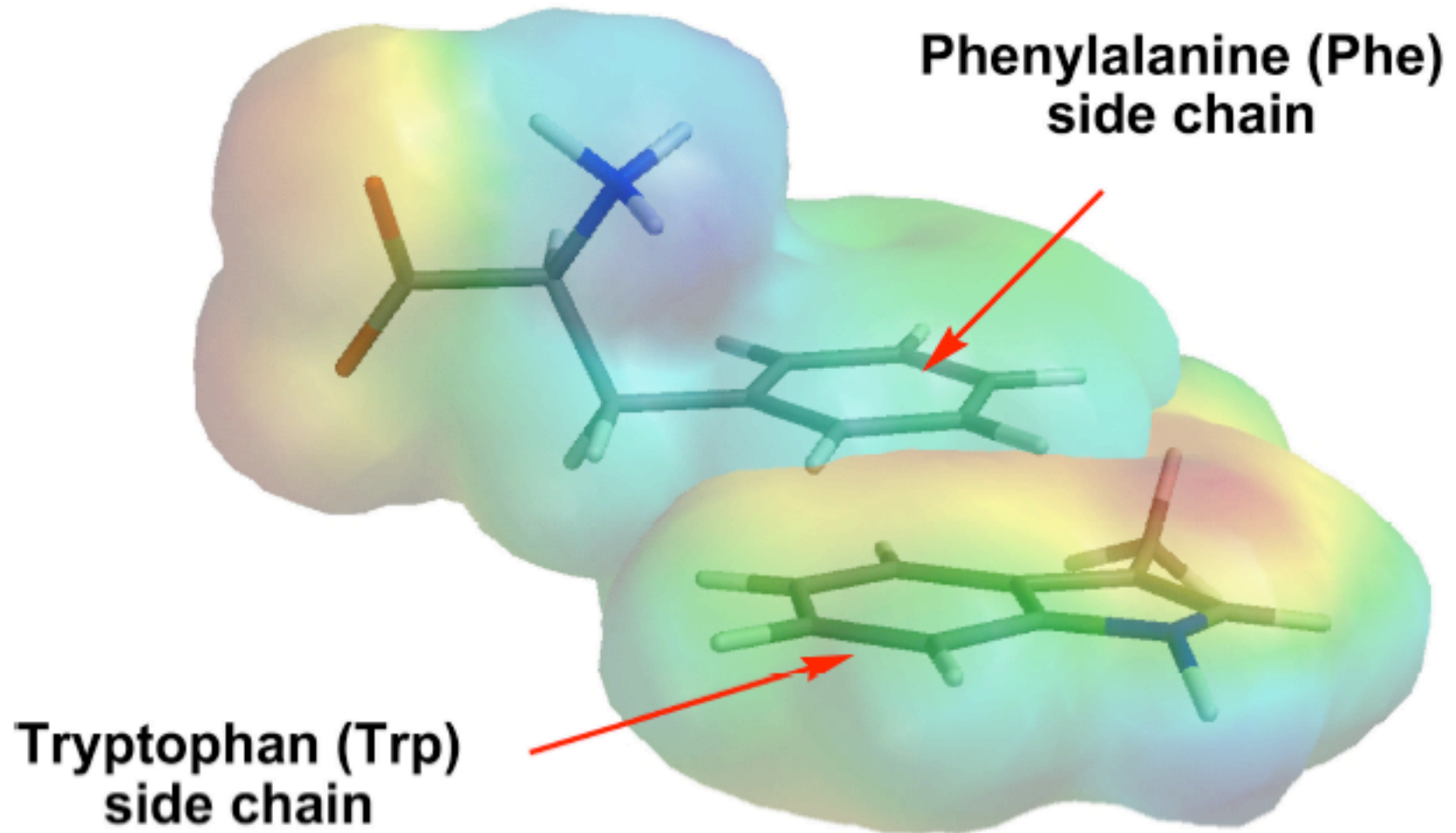


tyrosine (Tyr)



histidine (His)

Proteins and Three-Dimensional Protein Structures  
 $\alpha$ -Amino Acids with Aromatic Side Chains



# Proteins and Three-Dimensional Protein Structures

## $\alpha$ -Amino Acids with Hydroxyl or Dicoordinate Sulfur Functional Groups



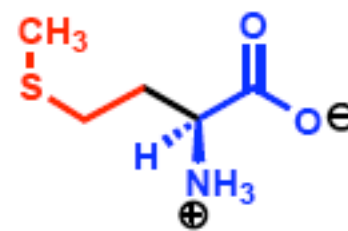
serine (Ser)



threonine (Thr)



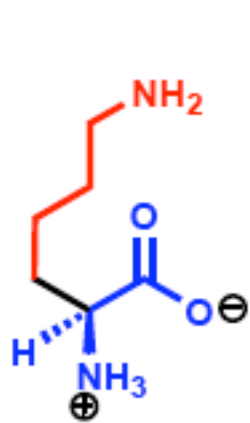
cysteine (Cys)



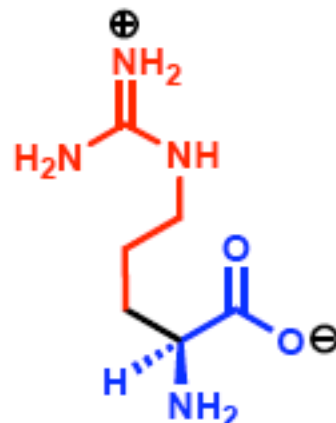
methionine (Met)

# Proteins and Three-Dimensional Protein Structures

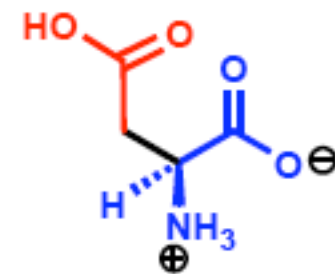
## Hydrophilic Amino Acids with Polar Side Chains



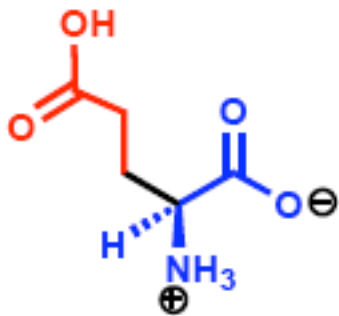
lysine (Lys)



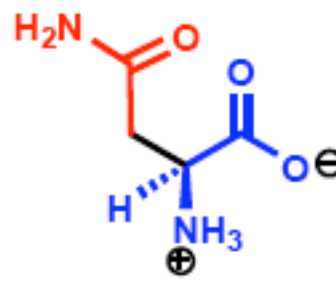
arginine (Arg)



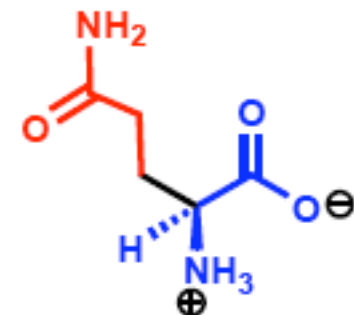
aspartic acid (Asp)



glutamic acid (Glu)



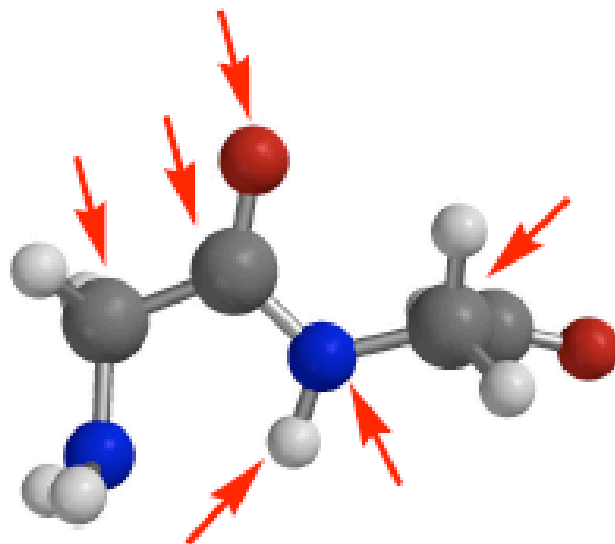
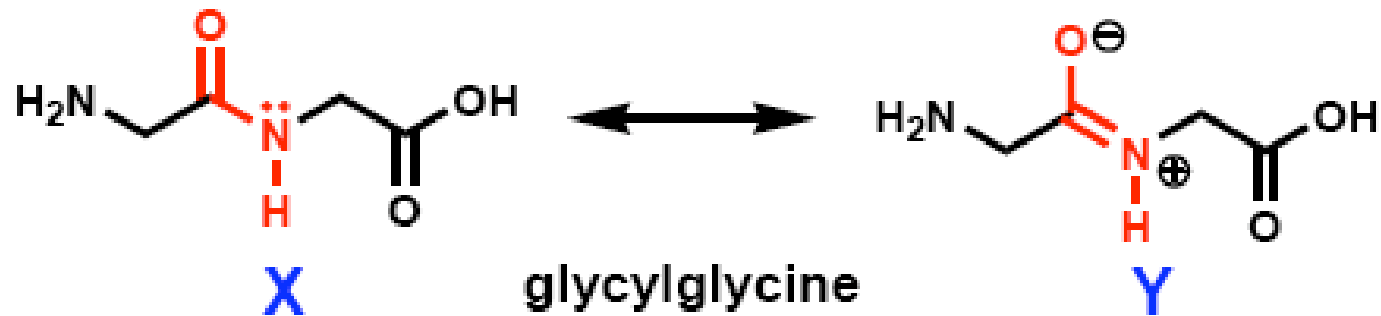
asparagine (Asn)



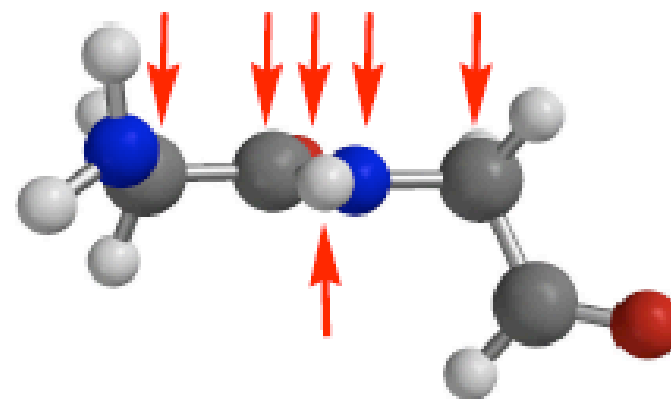
glutamine (Gln)

# Proteins and Three-Dimensional Protein Structures

## The Simplest Peptide



Top view

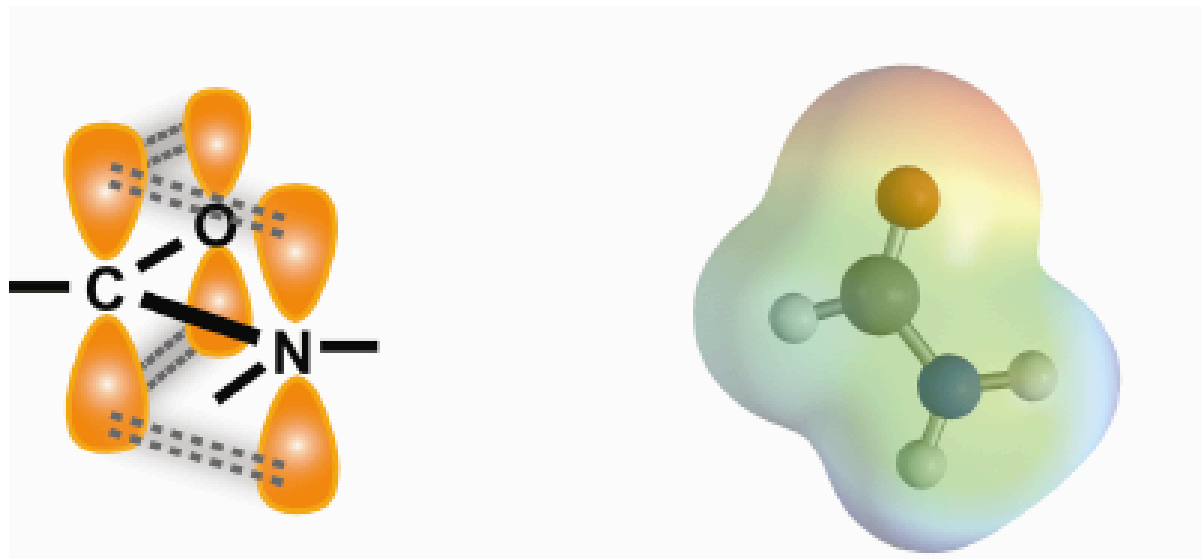
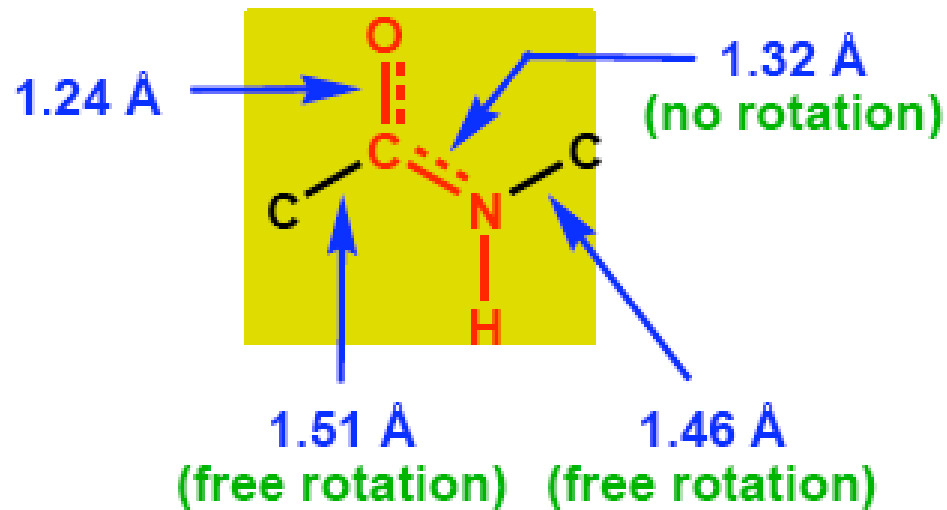


Side view



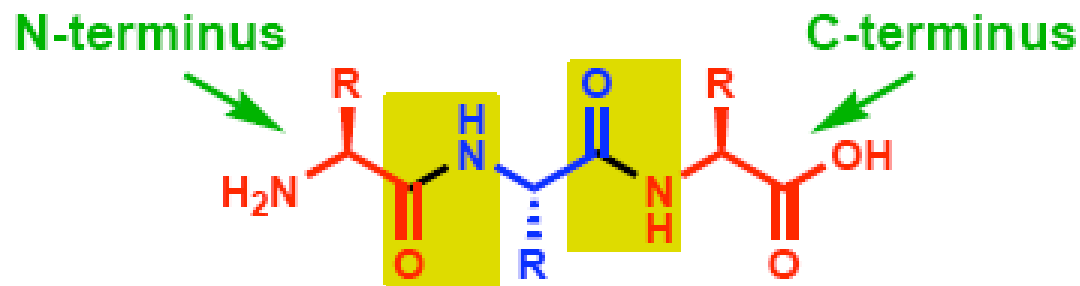
# Proteins and Three-Dimensional Protein Structures

## Structure of the Peptide Bond I.

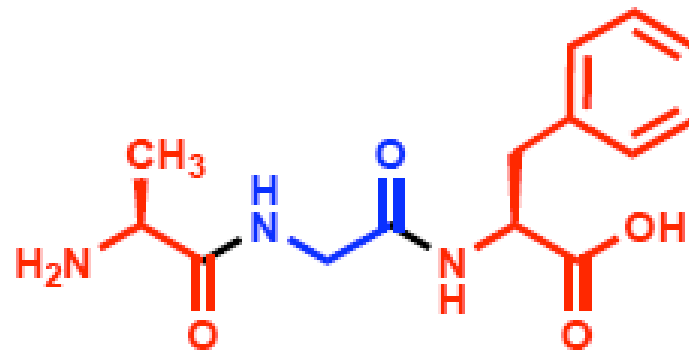


# Proteins and Three-Dimensional Protein Structures

## Structure of the Peptide Bond II.



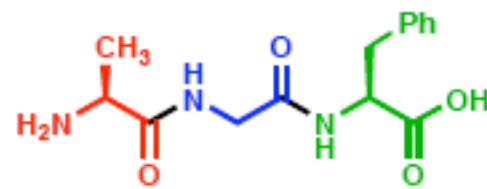
generic tripeptide



Ala-Gly-Phe  
(alanyl-glyciny-phenylalanine)

# Proteins and Three-Dimensional Protein Structures

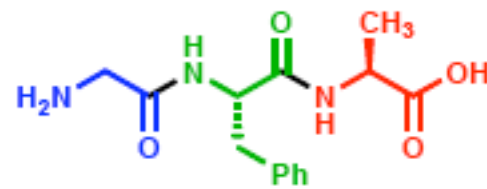
## Primary Structure of Proteins



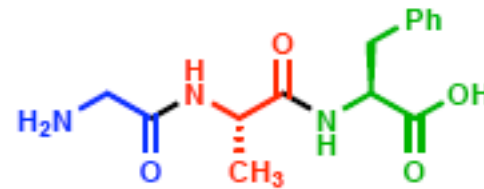
Ala-Gly-Phe



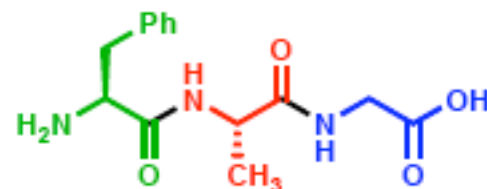
Ala-Phe-Gly



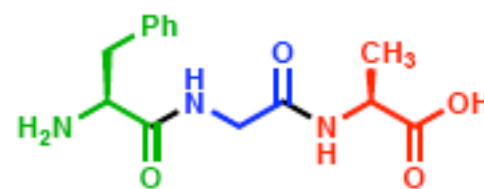
Gly-Phe-Ala



Gly-Ala-Phe



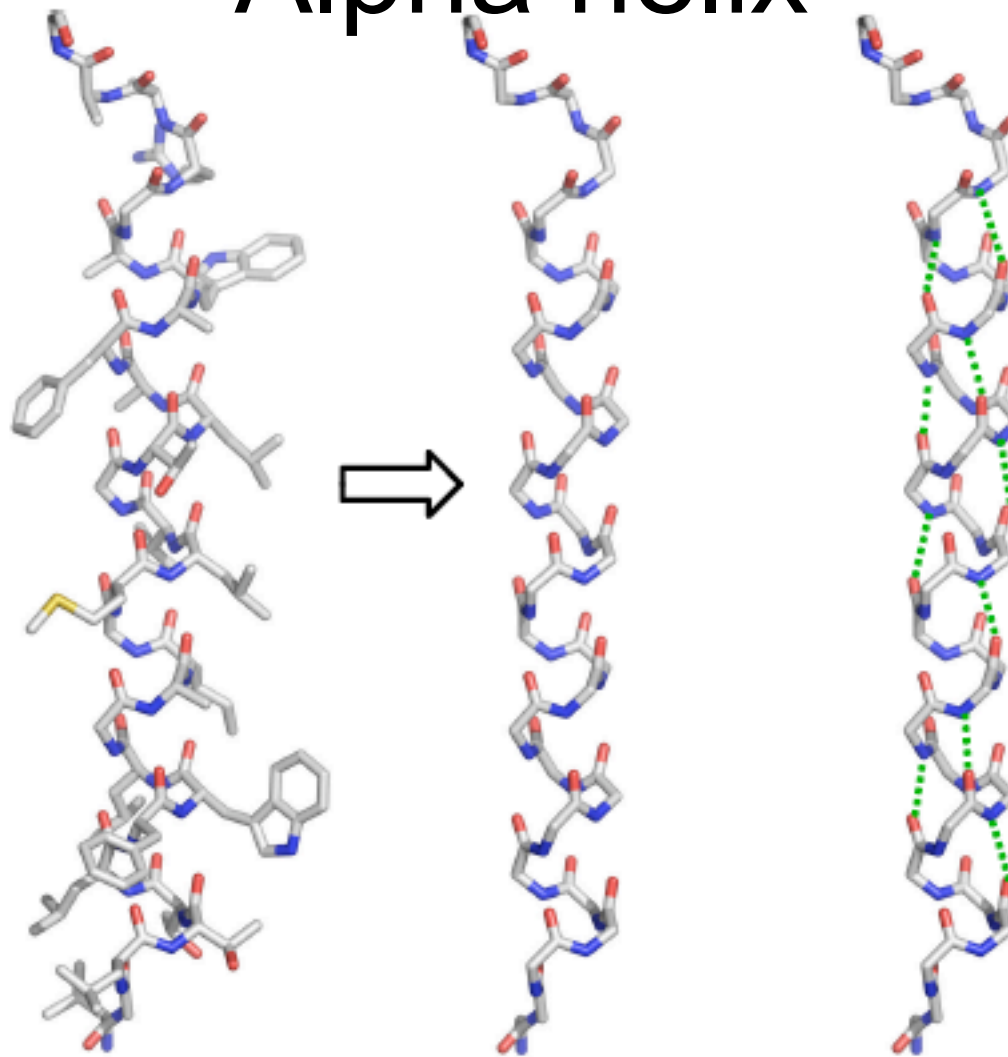
Phe-Ala-Gly



Phe-Gly-Ala

Proteins and Three-Dimensional Protein Structures  
Secondary Structure of Proteins I.

# Alpha helix



A

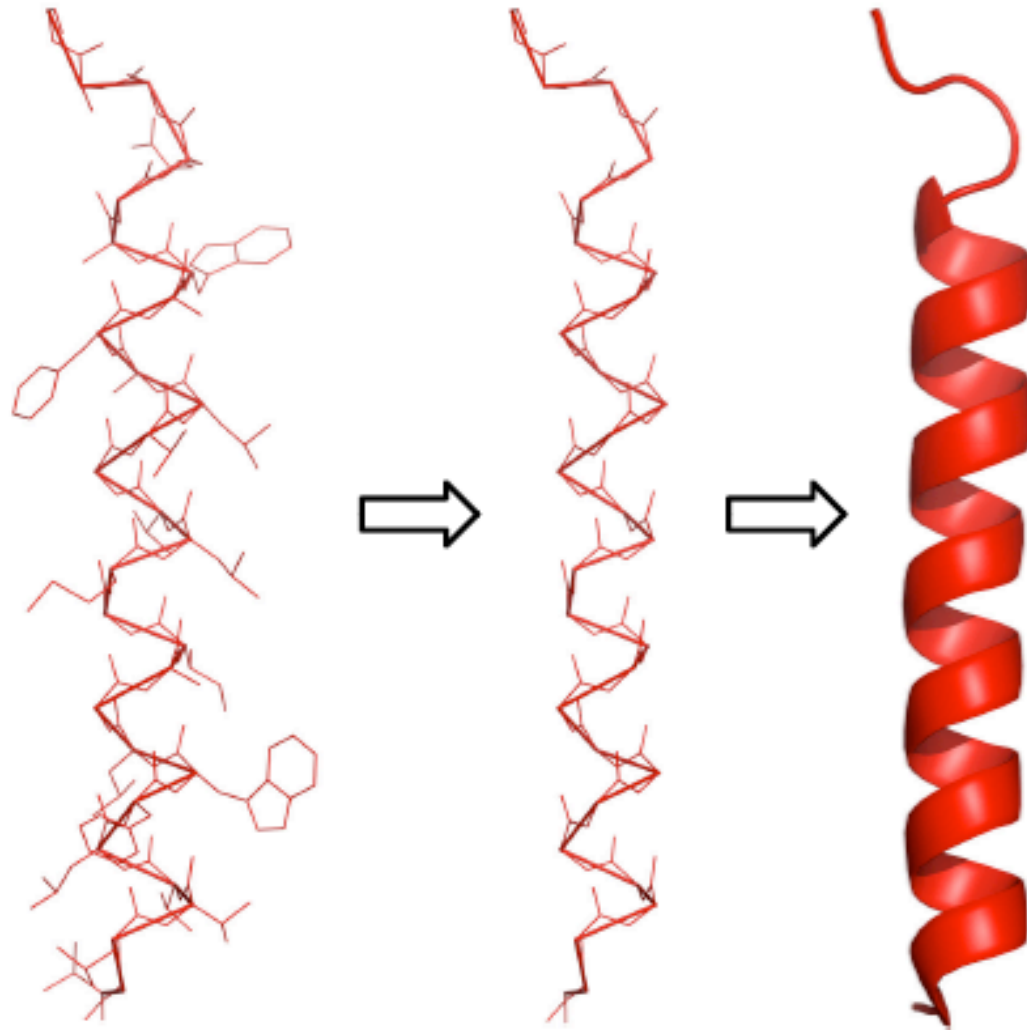
B

C

# Proteins and Three-Dimensional Protein Structures

## Secondary Structure of Proteins II.

Making a cartoon



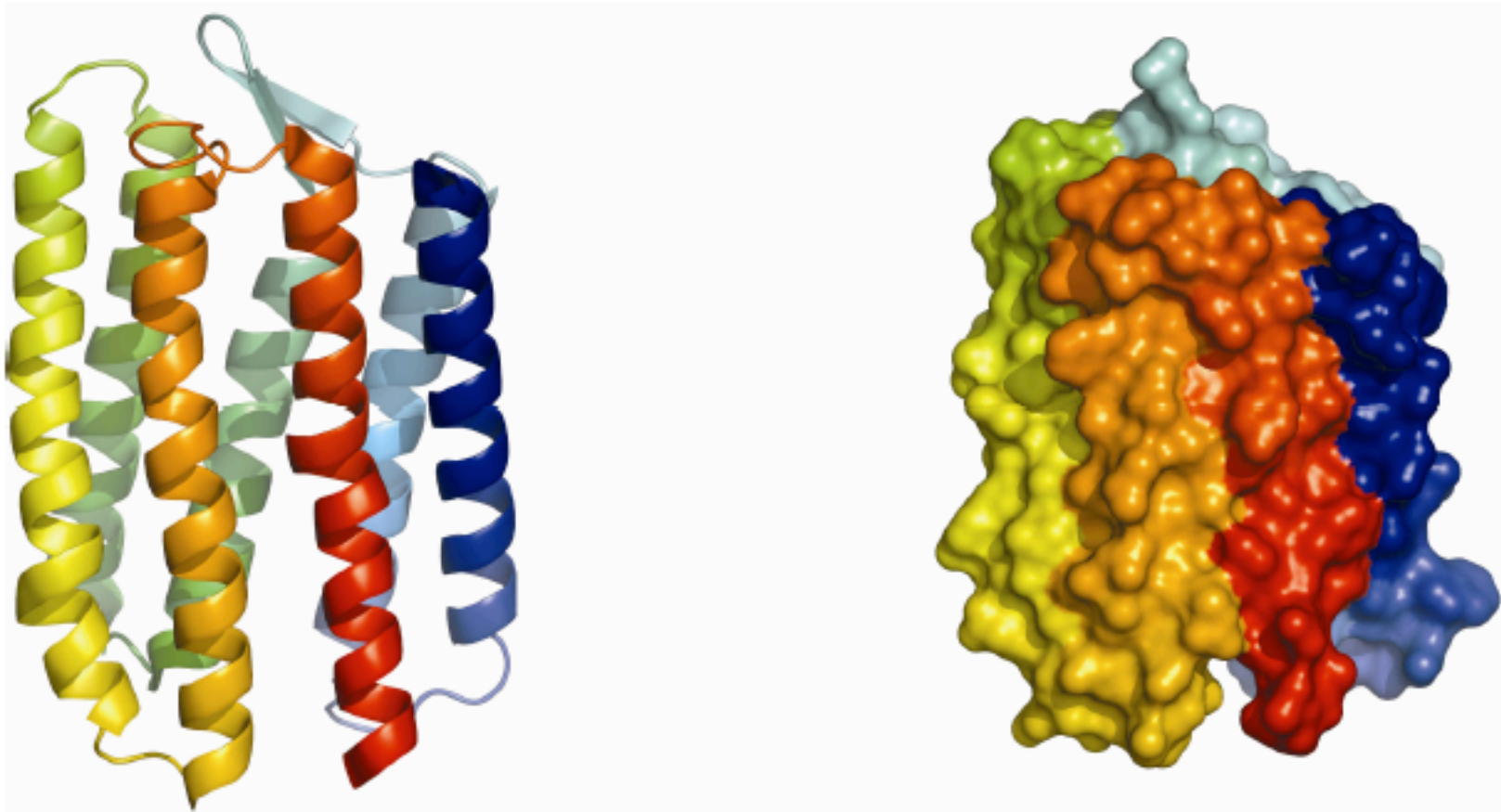
D

E

F

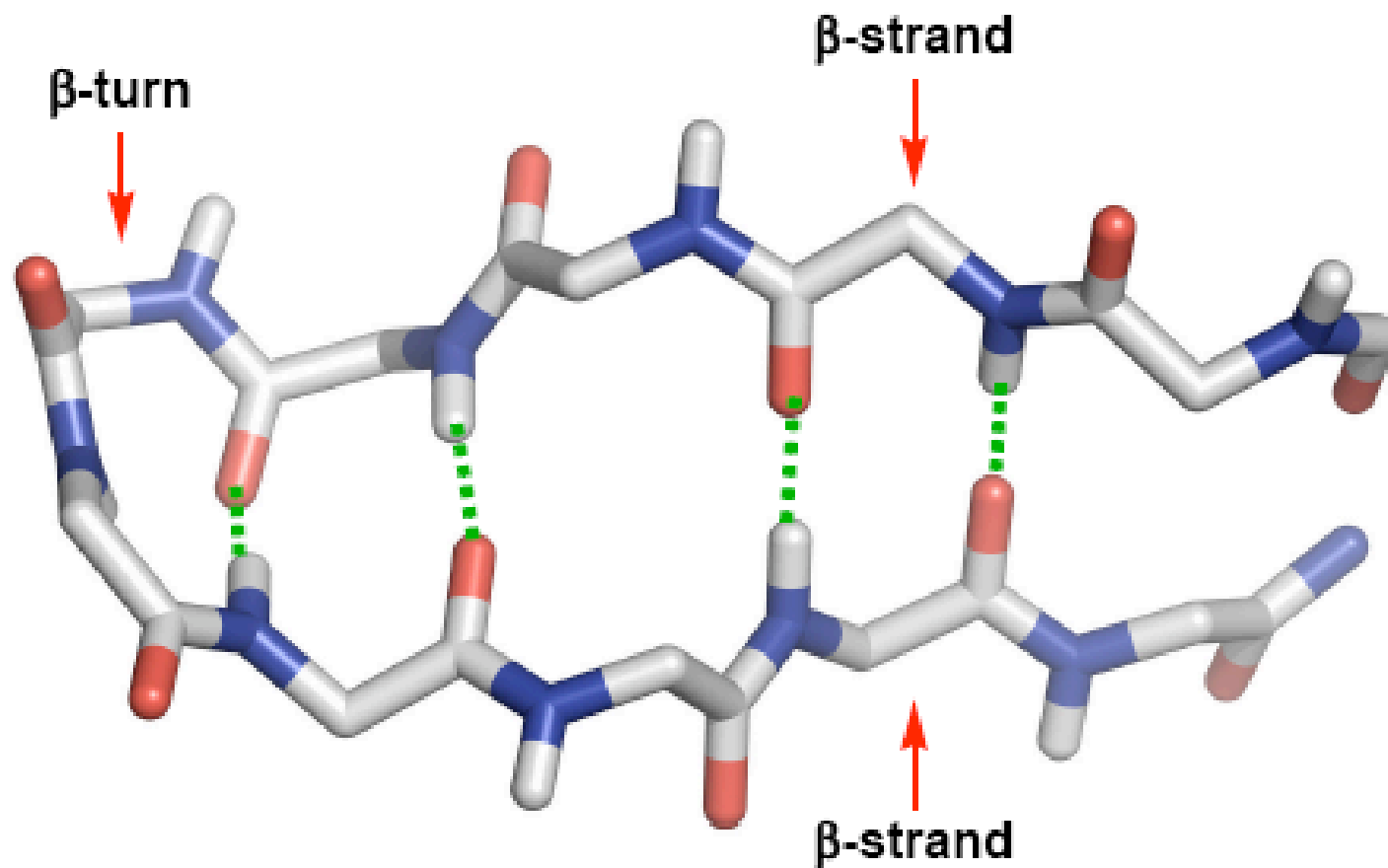


Proteins and Three-Dimensional Protein Structures  
Secondary Structure of Proteins IV.



# Proteins and Three-Dimensional Protein Structures

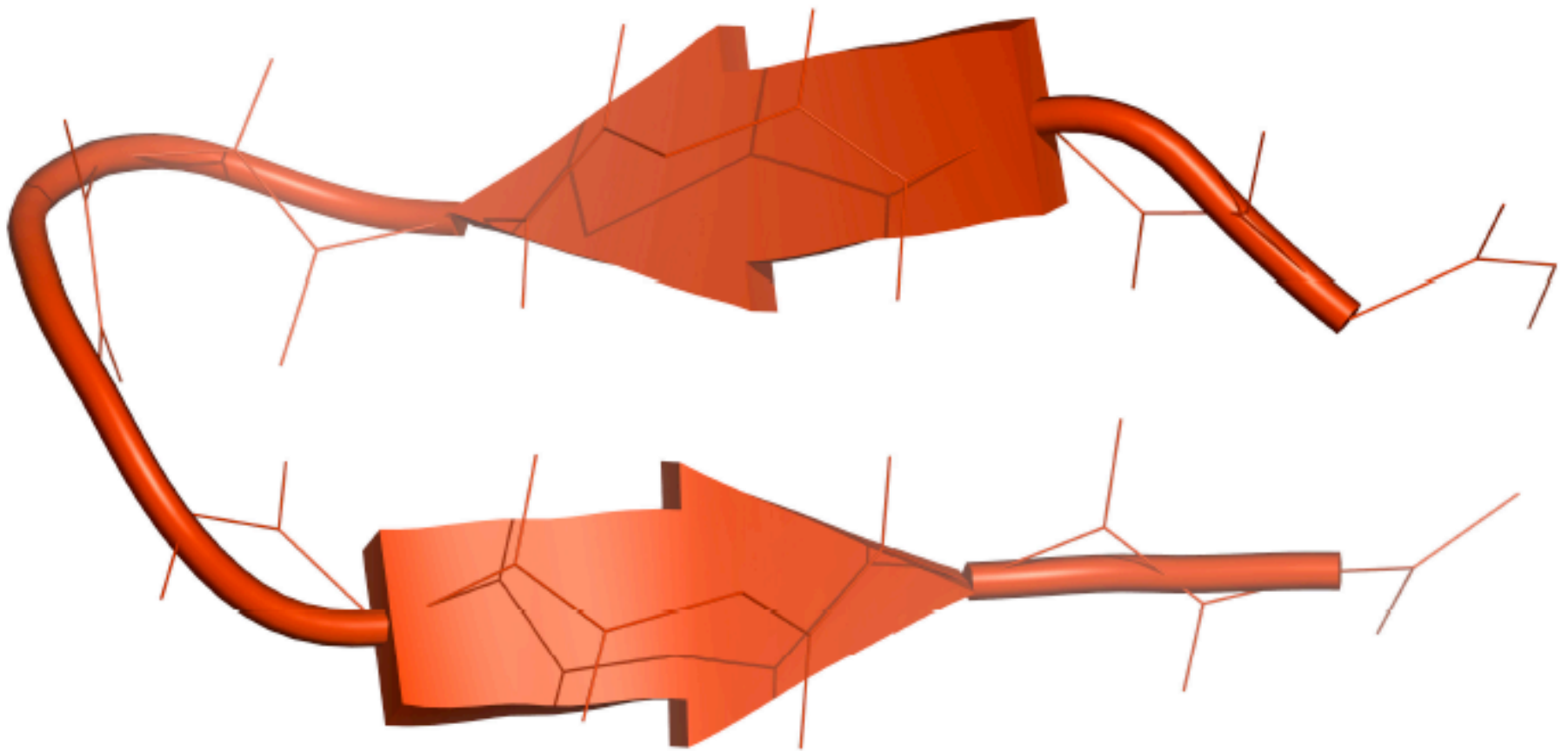
## Secondary Structure of Proteins V.



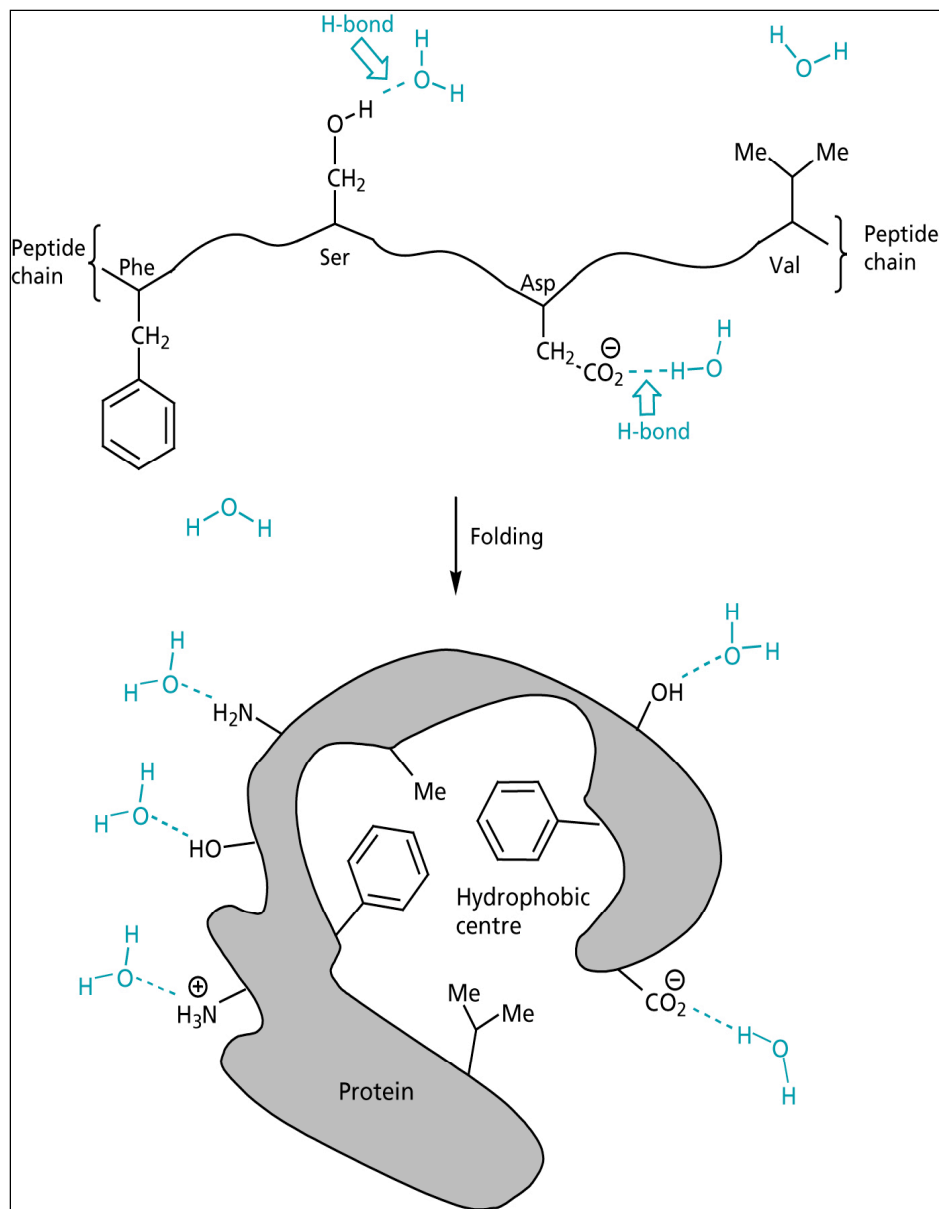
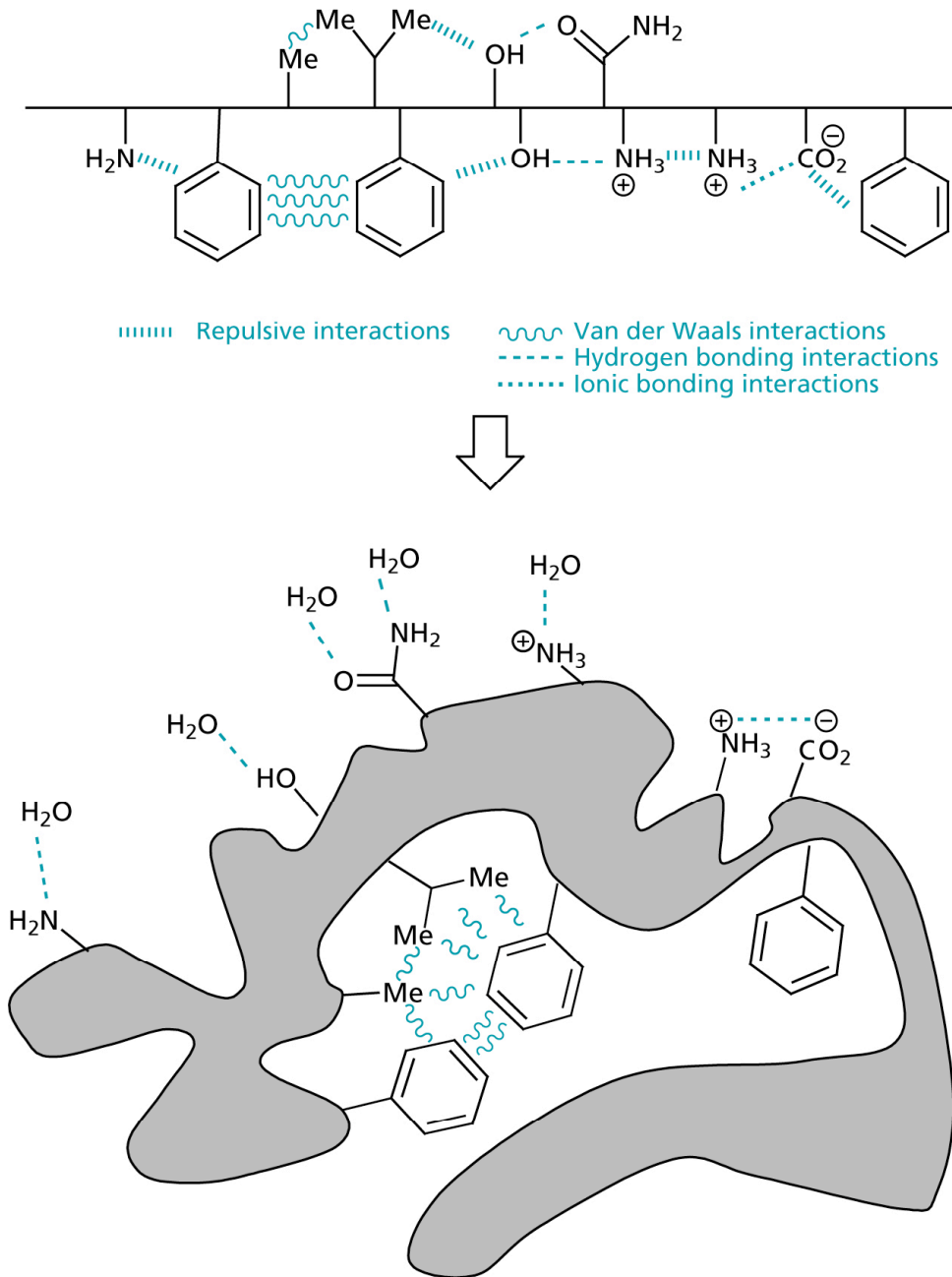


# Proteins and Three-Dimensional Protein Structures

## Secondary Structure of Proteins VI.

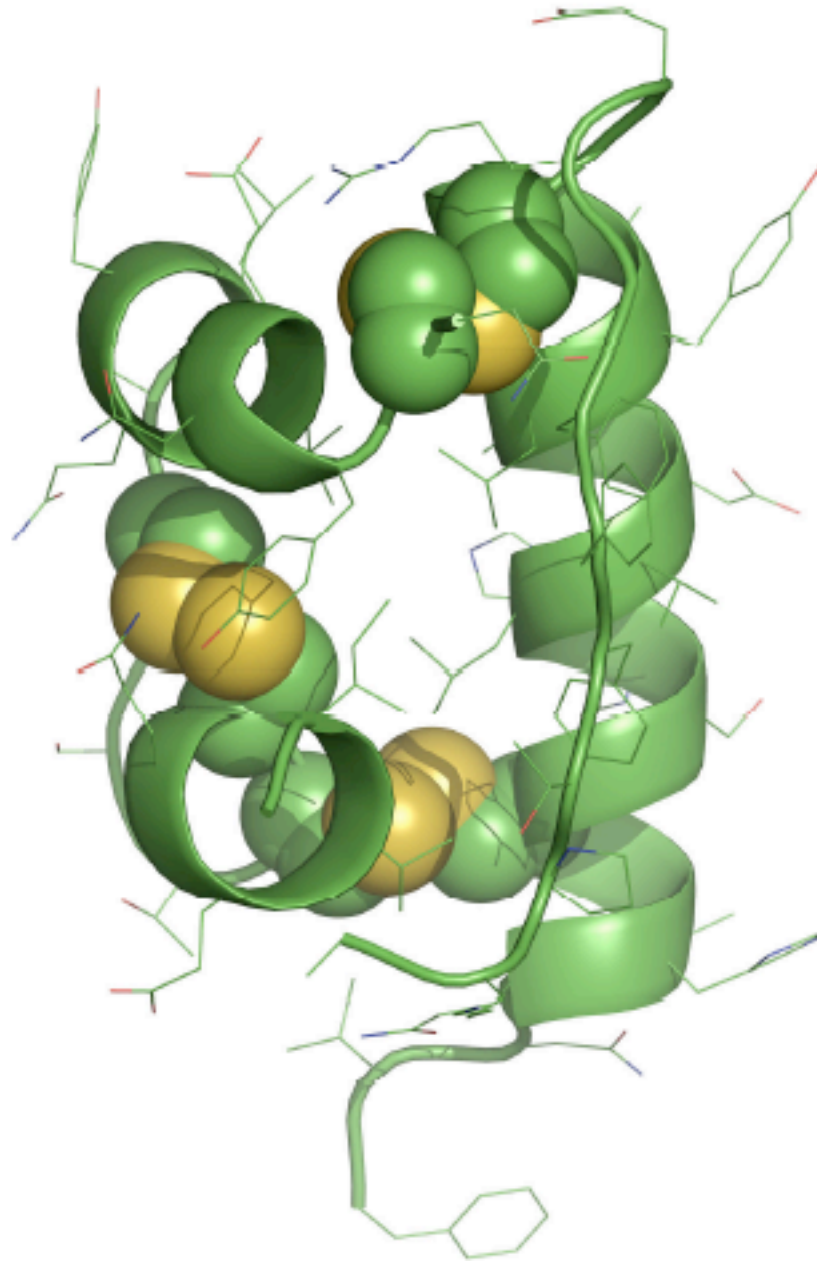


# 3D FOLDING



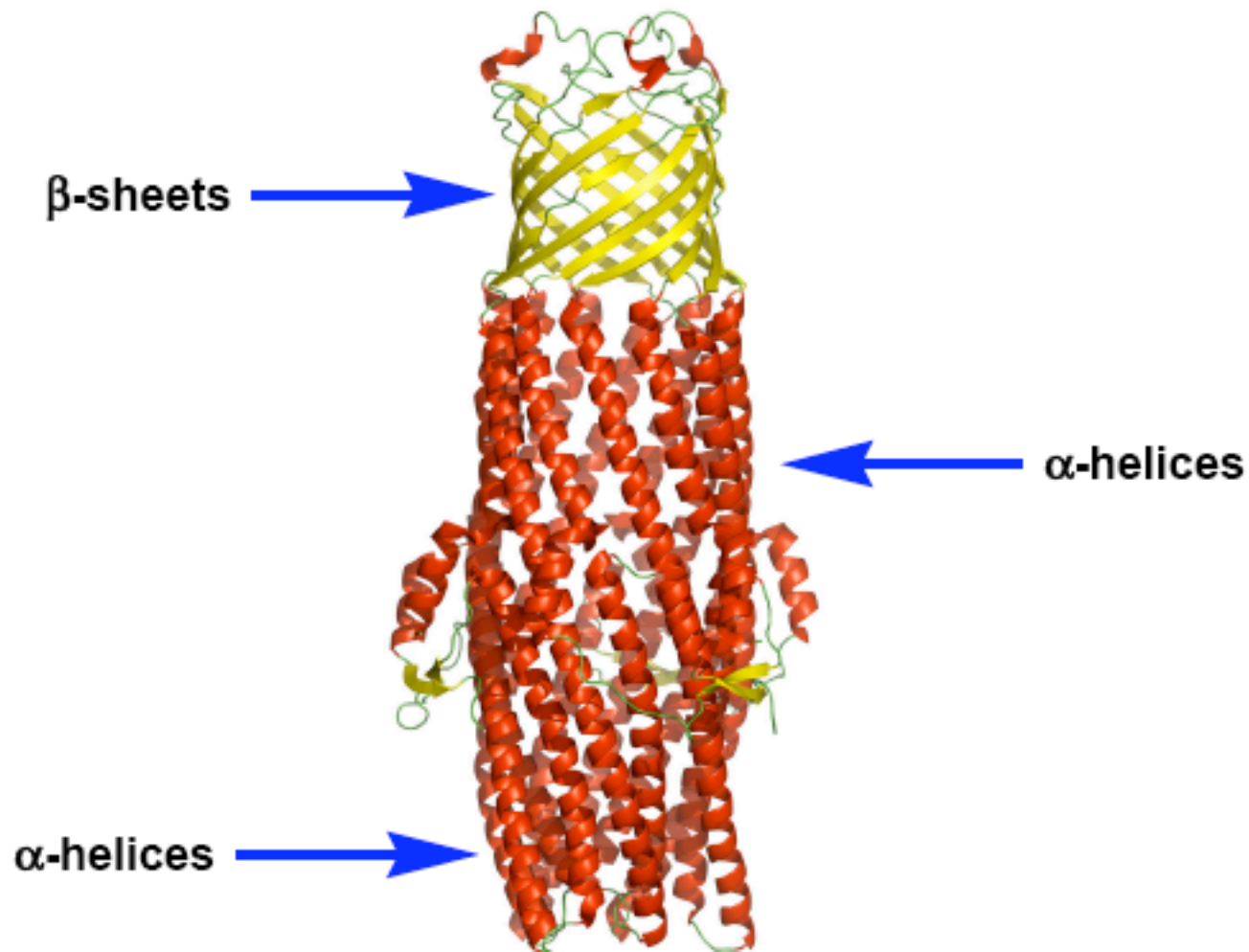
# Proteins and Three-Dimensional Protein Structures

## The Structure of Insulin



# Proteins and Three-Dimensional Protein Structures

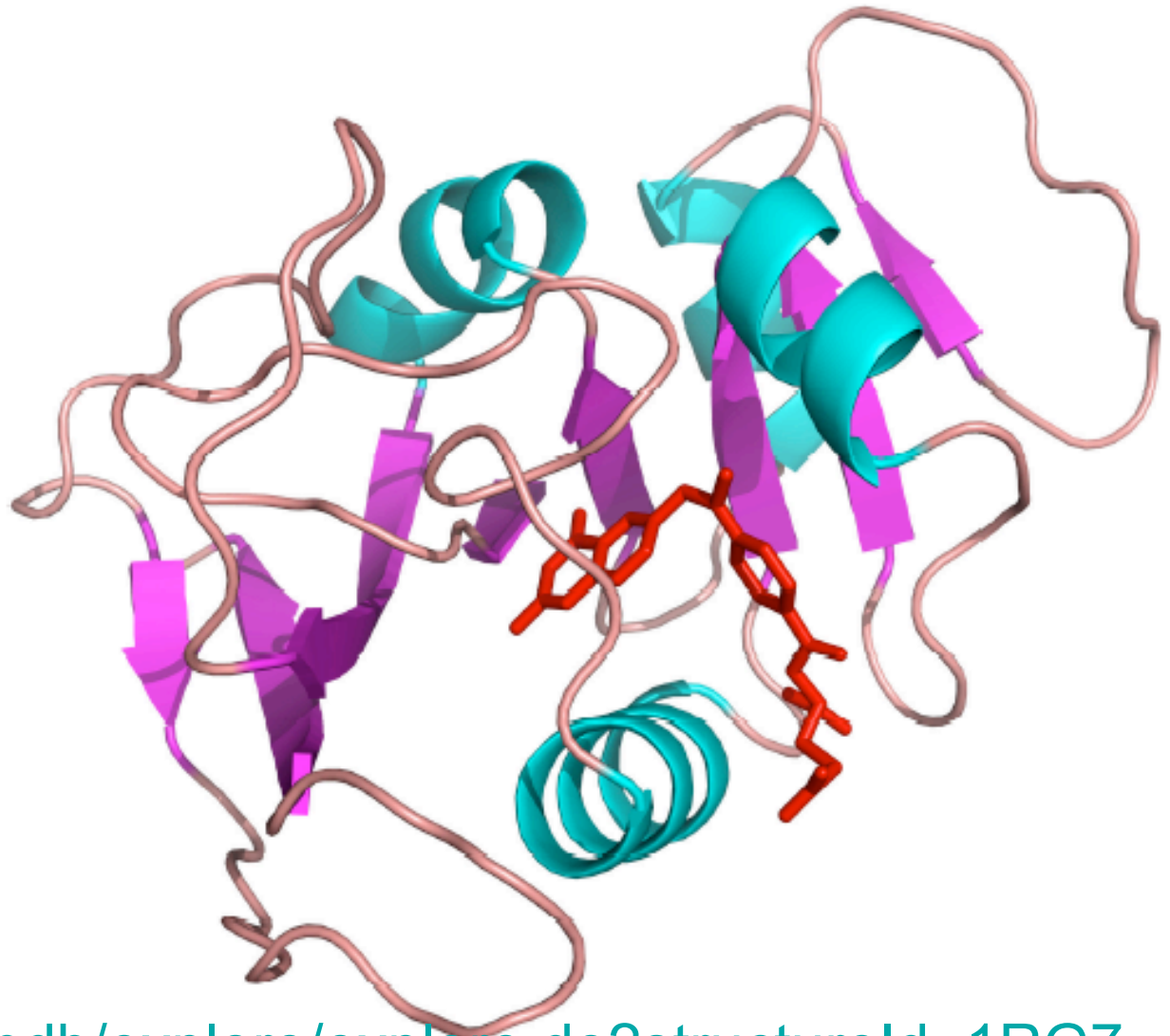
## The Structure of TolC



## Proteins and Three-Dimensional Protein Structures

### Some Protein Structures that Appear in this Book I.

**Methotrexate** (Trexall™), used to treat rheumatoid arthritis, is shown in red bound in the active site of its target, the enzyme dihydrofolate reductase (see page 46; PDB ID: **1RG7**). The image shows the full protein. The  $\alpha$ -helical domains are colored cyan, the  $\beta$ -sheets are magenta and the loops are orange.



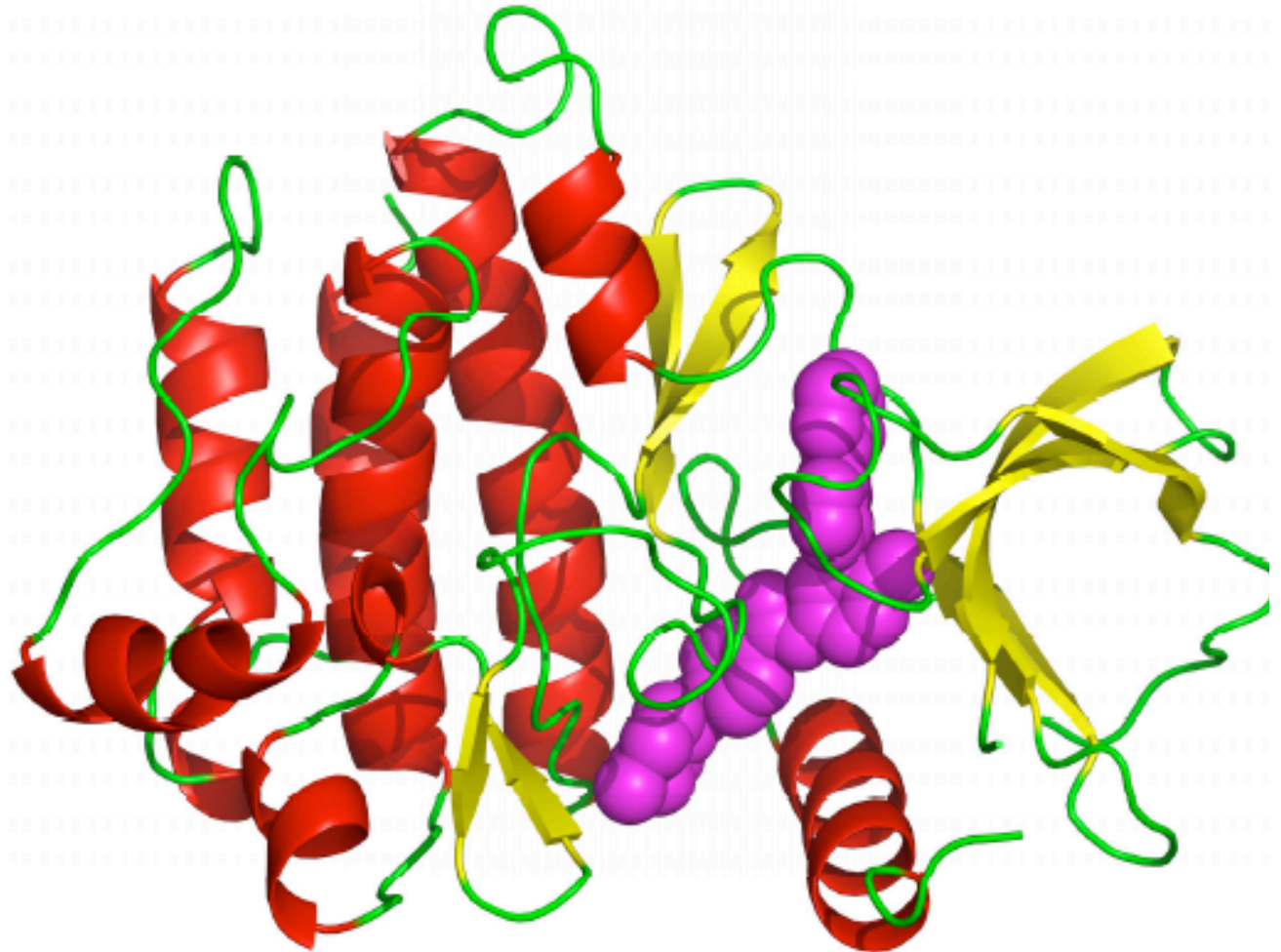
<http://www.rcsb.org/pdb/explore/explore.do?structureId=1RG7>



## Proteins and Three-Dimensional Protein Structures

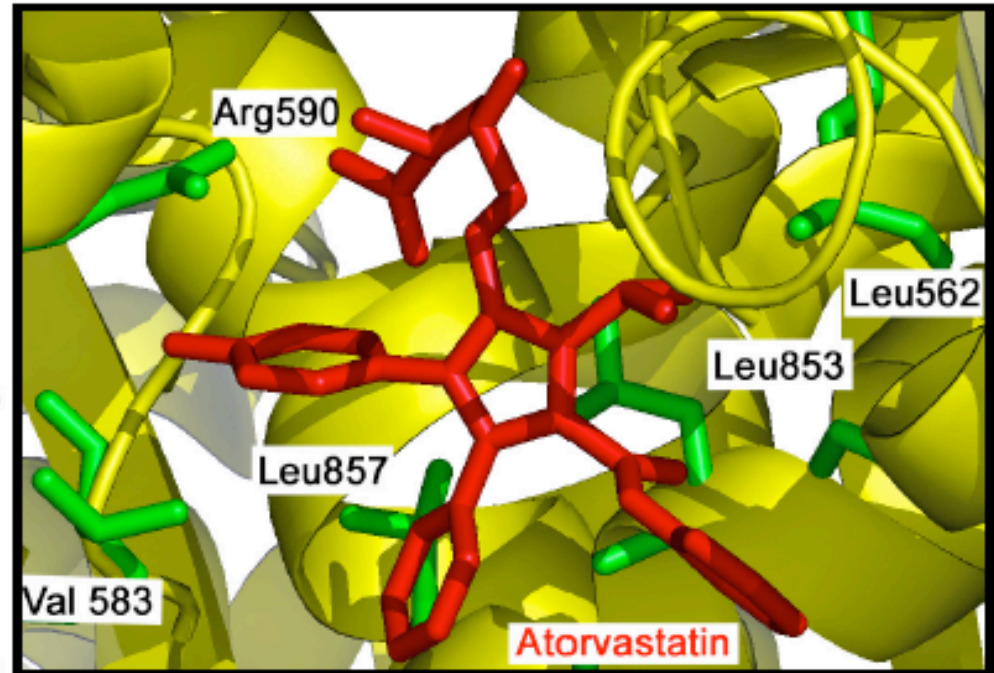
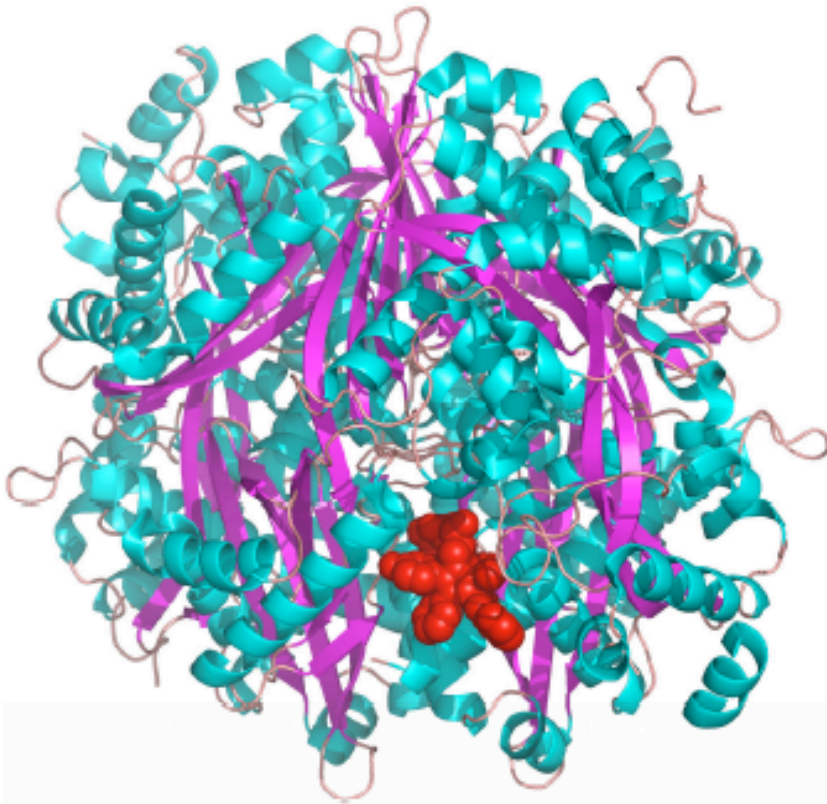
### Some Protein Structures that Appear in this Book II.

**Imatinib** (Gleevec™) used to treat leukemia, is shown in magenta bound in the active site of its target, the enzyme tyrosine kinase (see page 195; PDB ID: **1IEP**). The image shows the full protein. The  $\alpha$ -helical domains are colored red, the  $\beta$ -sheets are yellow and the loops are green.



## Proteins and Three-Dimensional Protein Structures

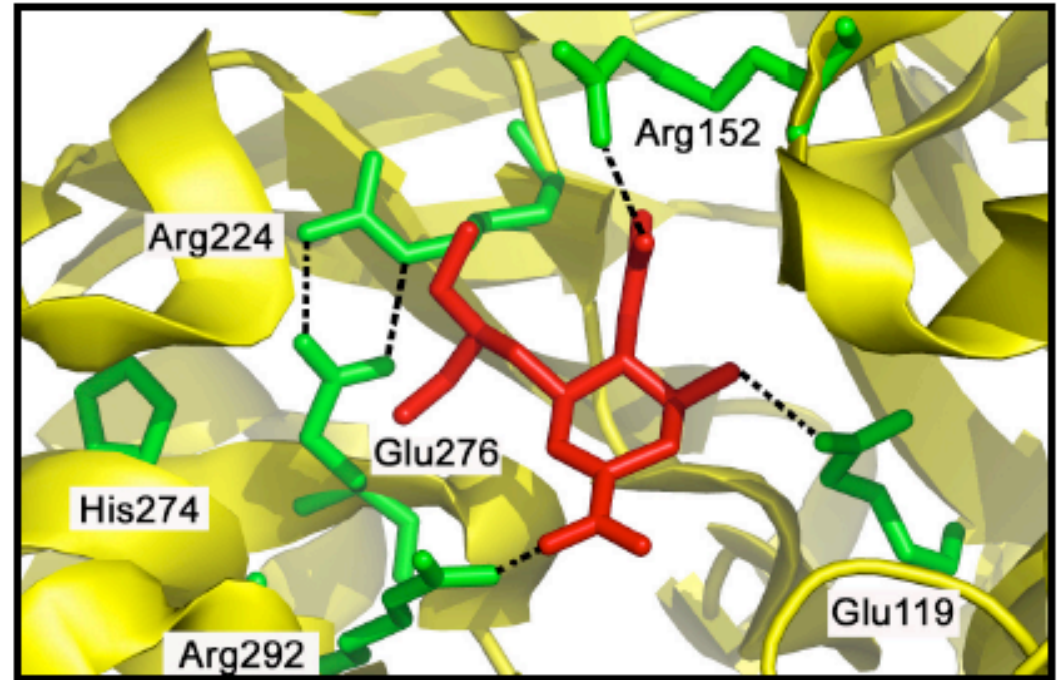
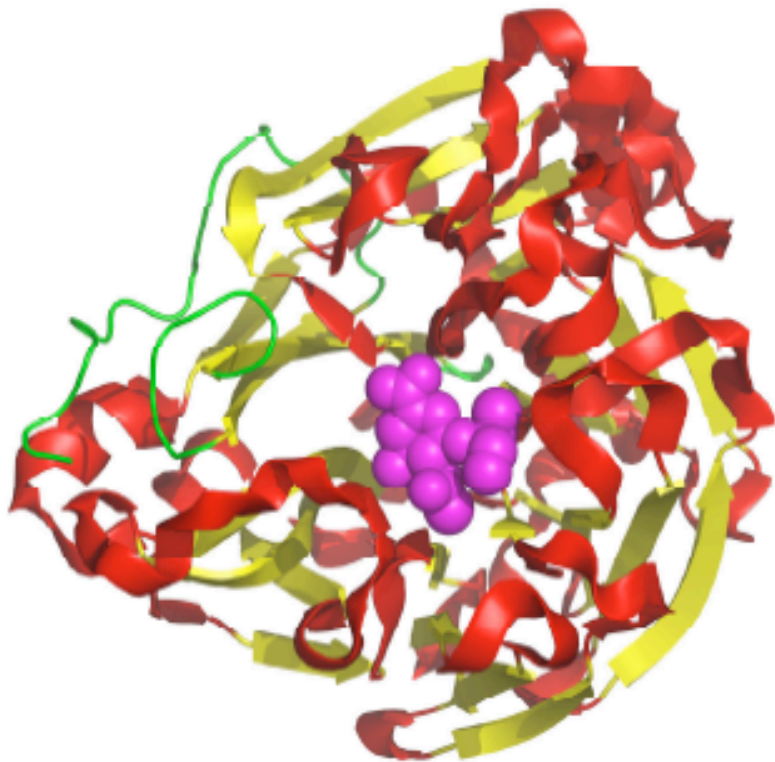
### Some Protein Structures that Appear in this Book III.



**Atorvastatin** (Lipitor™), used for the reduction of LDL cholesterol levels, is shown in red bound in the active site of its target, the enzyme HMG-CoA reductase (see page 64; PDB ID: 1HWK). The top image shows the whole enzyme, whereas the bottom image is a close-up view.

## Proteins and Three-Dimensional Protein Structures

### Some Protein Structures that Appear in this Book IV.



**Oseltamivir** (Tamiflu™), used to prevent influenza A and B viral infections, is shown in magenta bound in the active site of its target, the viral enzyme neuraminidase (see page 150; PDB ID: **2HT8**). The top image shows the whole enzyme whereas the bottom image is a close-up view in which oseltamivir is colored red.