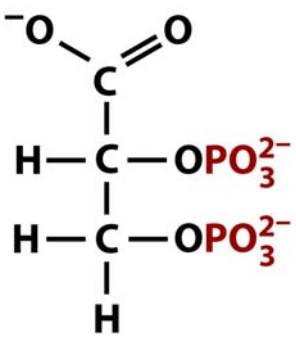
The effects of BPG and CO2 on hemoglobin's O2 dissociation curve

Carbamates: CO2 reversibly binds with the N-terminal amino group of Hb

R-NH2 (T-form) + CO2 ↔ R-NH-COO$^-$ + H$^+$

BPG has an indispensible physiological function

binds tightly to deoxy Hb but only weakly to oxy Hb



D-2,3-Bisphosphoglycerate (BPG)

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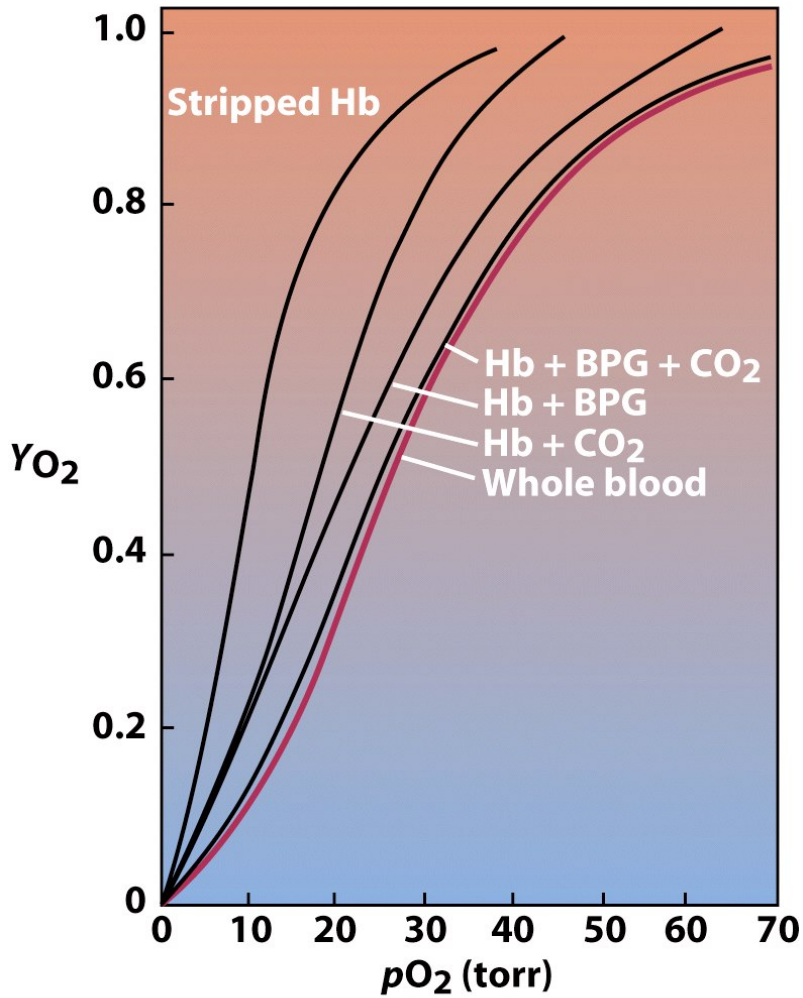

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Binding of BPG to deoxyhemoglobin

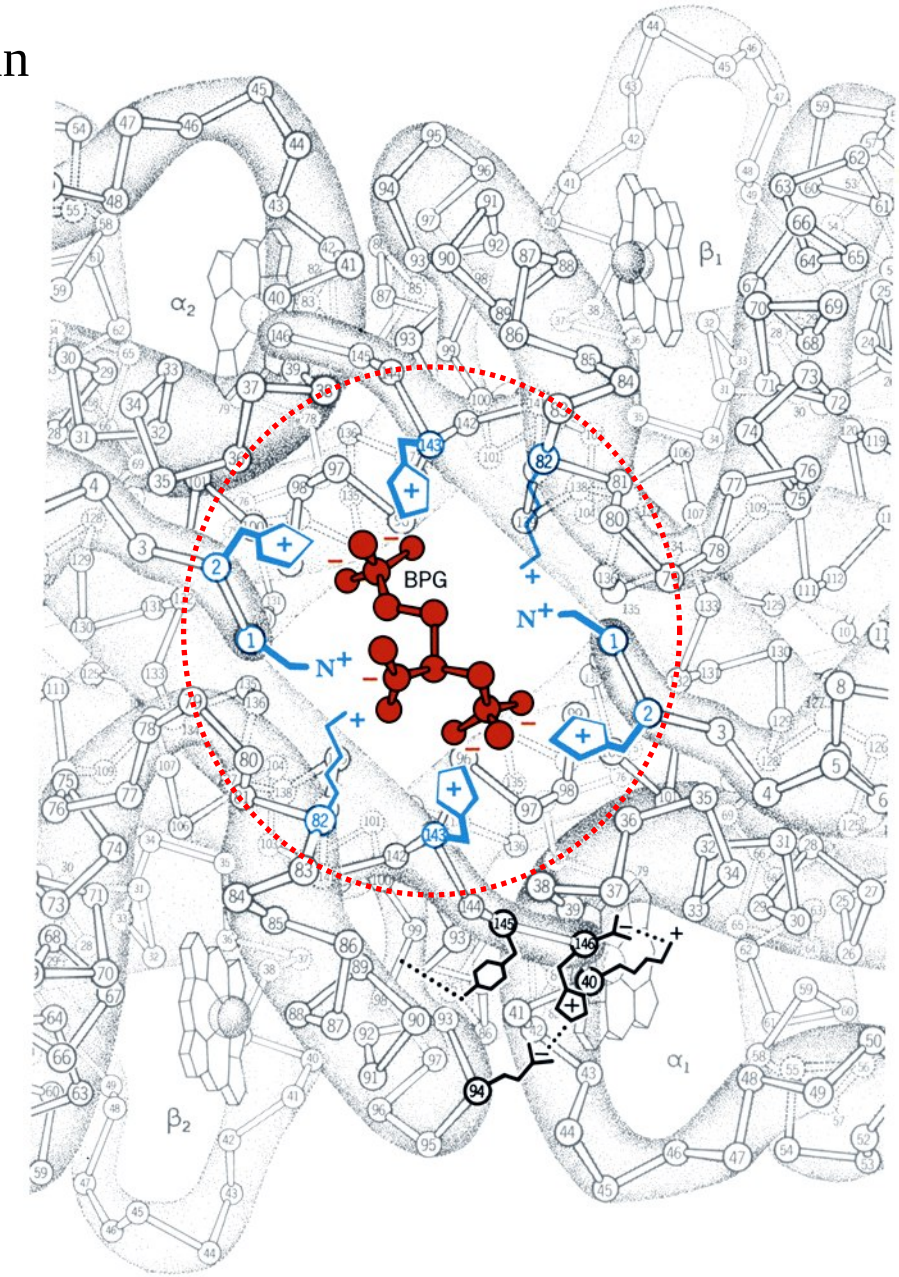


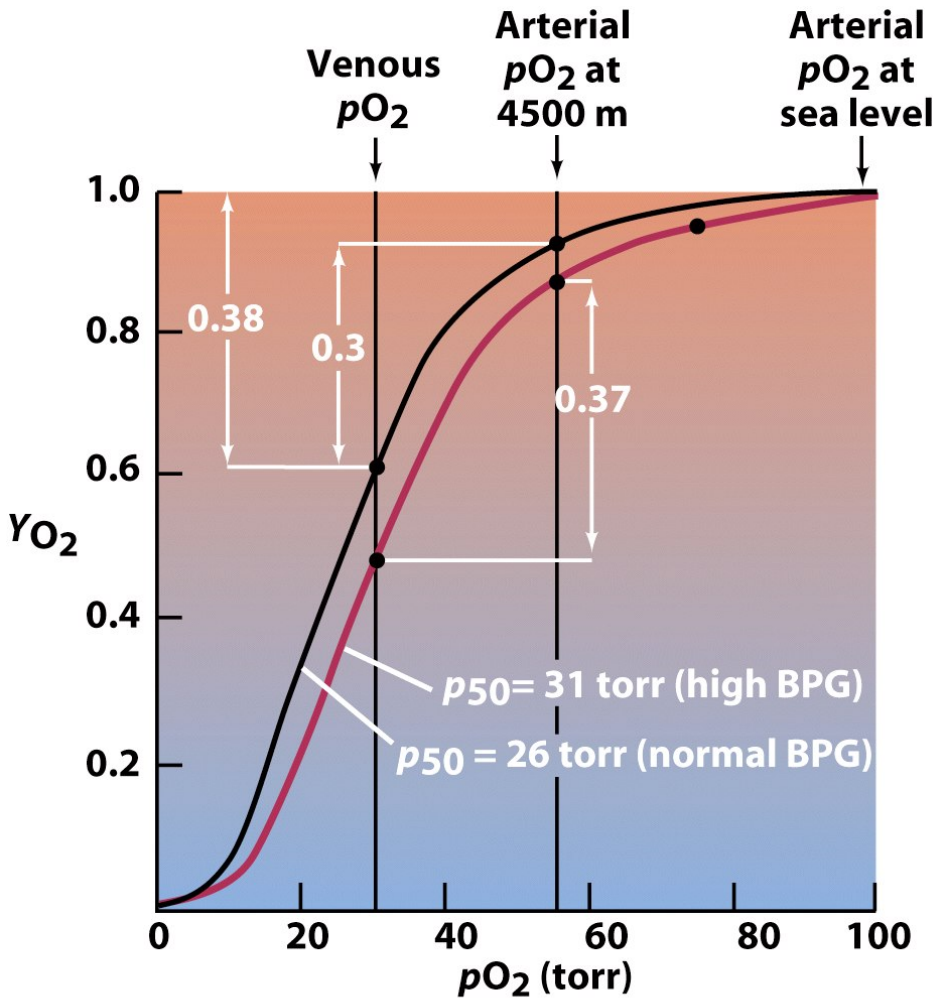
Figure 7-15 Fundamentals of Biochemistry, 2/e

High altitude adaptation

Long term change
Increase in the amount of Hb per erythrocyte
Increase in the number of erythrocyte

Short term change
Increase in erythrocyte BPG
Hyperventilation: respiratory alkalosis

Fetal Hb has low BPG affinity
α2ɣ2
β has His at 143 a.a. residue
ɣ has Ser



Box 7-3 Fundamentals of Biochemistry, 2/e

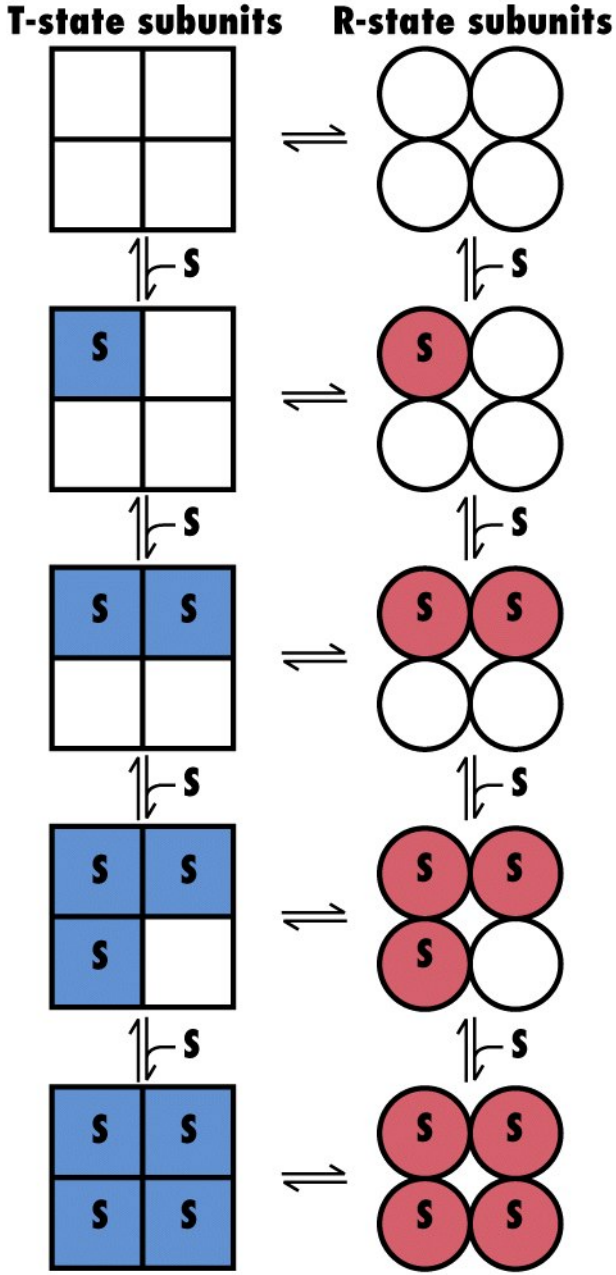
Allosteric proteins

Allos: other
Stereos: space

Allosteric interaction: interaction among subunits

Two models accounting for cooperative ligand binding
Symmetry model: concerted manner
Sequential model: progressive induction

The symmetry model of allosterism



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The sequential model of allosterism

Positively and negatively cooperative
If mechanical coupling between subunits is strong the conformational changes occur simultaneously
Symmetry model may be an extreme case of the more general sequential model

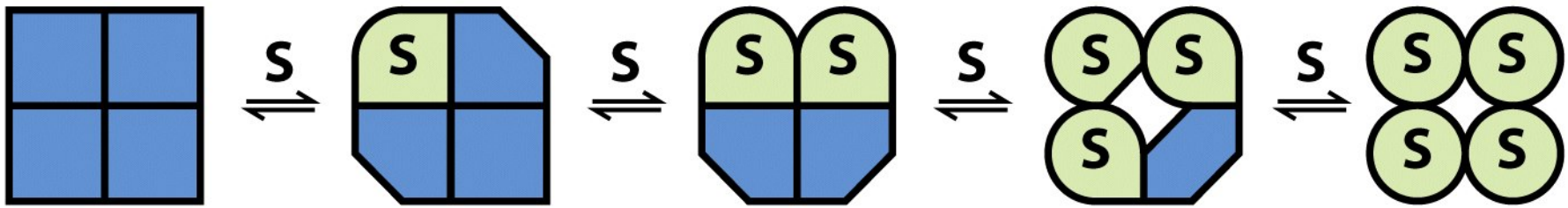

Figure 7-17 Fundamentals of Biochemistry, 2/e

Abnormal hemoglobins

Nearly 900 variant Hb

>90% result from single amino acid substitution

Reduced cooperativity

Hemolytic anemia: Unstable Hb: degradation and erythrocyte lysis

Cyanosis: methemoglobin-Fe(III)

Increased oxygen affinity

Table 7-1 Some Hemoglobin Variants

Name[a]	Mutation	Effect
Hammersmith	Phe CD1(42)β → Ser	Weakens heme binding
Bristol	Val E11(67)β → Asp	Weakens heme binding
Bibba	Leu H19(136)α → Pro	Disrupts the H helix
Savannah	Gly B6(24)β → Val	Disrupts the B–E helix interface
Philly	Tyr C1(35)α → Phe	Disrupts hydrogen bonding at the α_1–β_1 interface
Boston	His E7(58)α → Tyr	Promotes methemoglobin formation
Milwaukee	Val E11(67)β → Glu	Promotes methemoglobin formation
Iwate	His F8(87)α → Tyr	Promotes methemoglobin formation
Yakima	Asp G1(99)β → His	Disrupts a hydrogen bond that stabilizes the T conformation
Kansas	Asn G4(102)β → Thr	Distrupts a hydrogen bond that stabilizes the R conformation

[a]Hemoglobin variants are usually named after the place where they were discovered (e.g., hemoglobin Boston).

Table 7-1 Fundamentals of Biochemistry, 2/e

Sickle cell anemia: β chain Glu to Val

Scanning electron micrographs of human erythrocytes

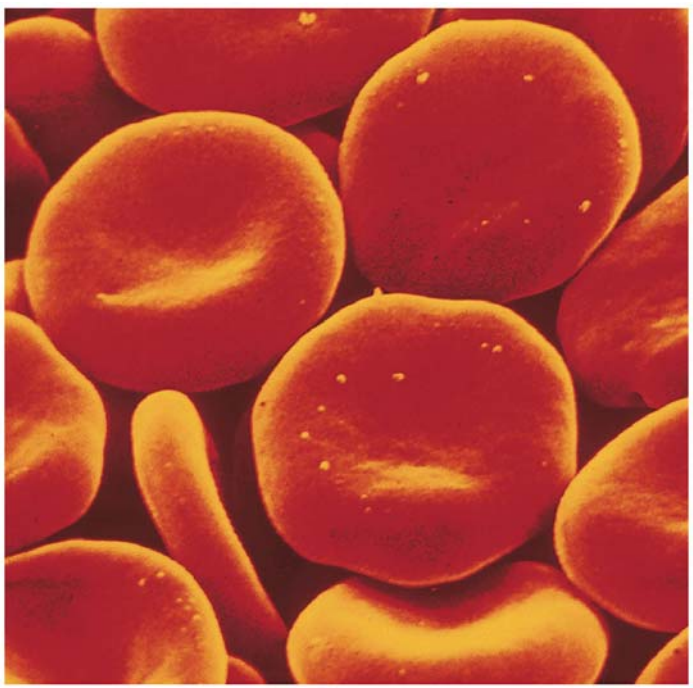

Figure 7-18a Fundamentals of Biochemistry, 2/e

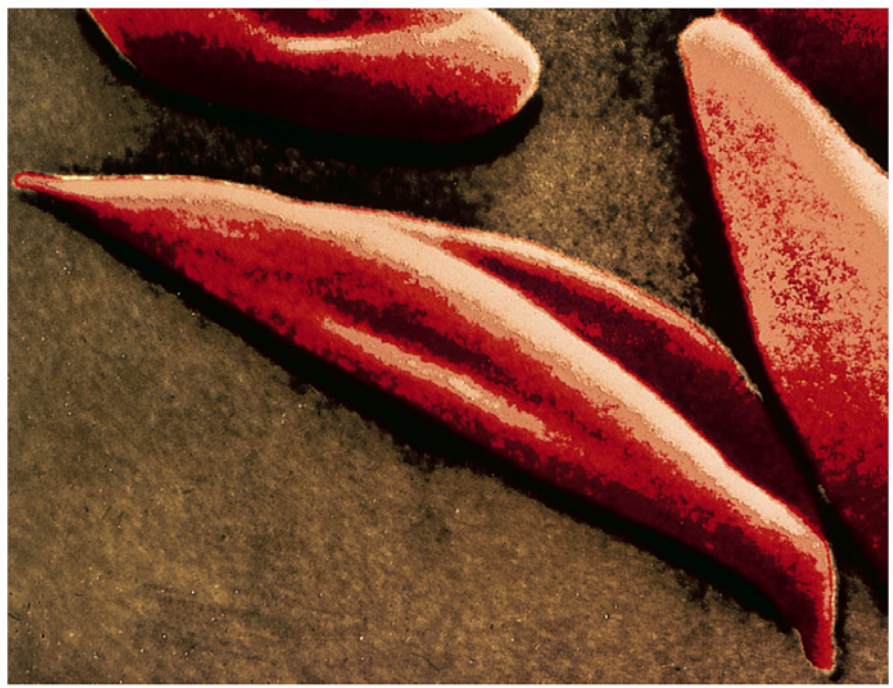

Figure 7-18b Fundamentals of Biochemistry, 2/e

Structure of a deoxyhemoglobin S fiber

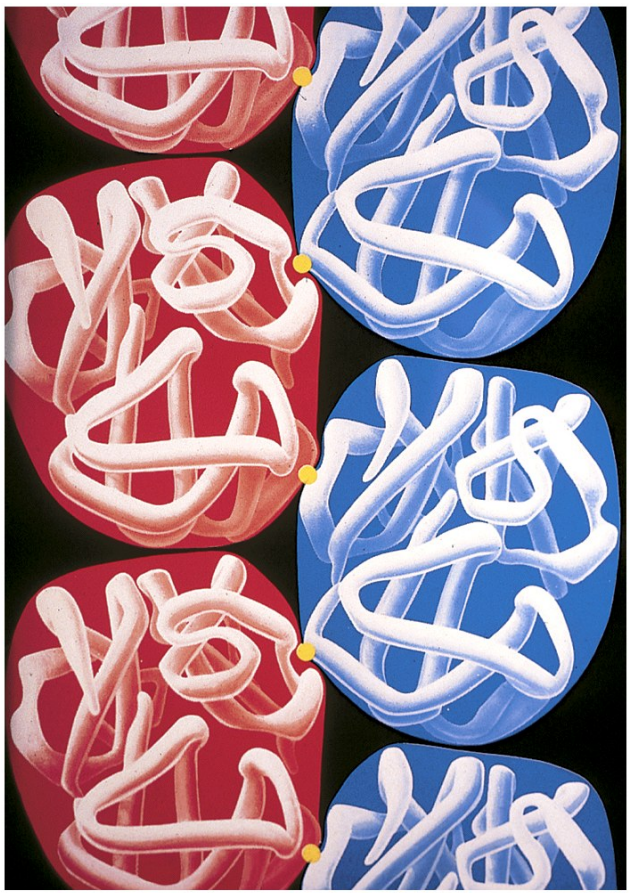

Figure 7-19a Fundamentals of Biochemistry, 2/e

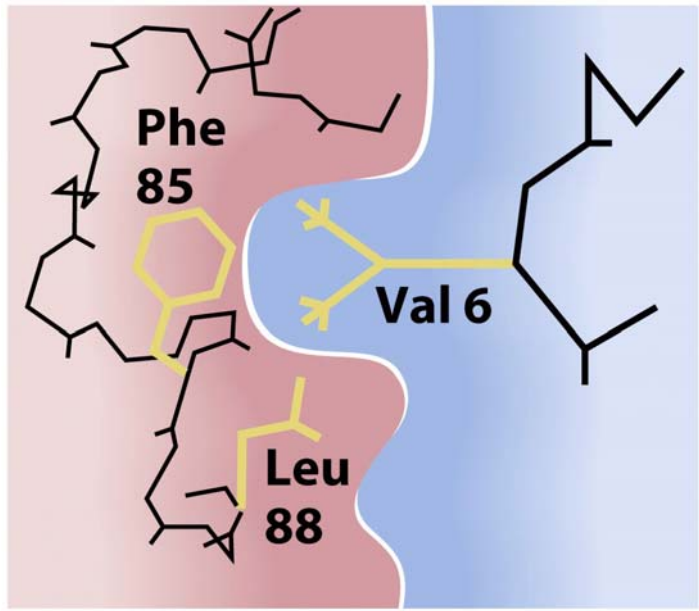

Figure 7-19b Fundamentals of Biochemistry, 2/e

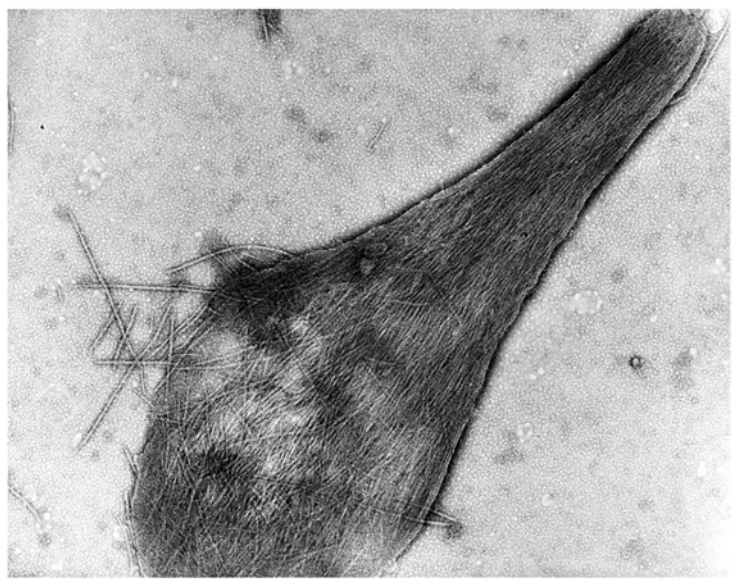

Figure 7-20 Fundamentals of Biochemistry, 2/e

Malaria and hemoglobin

Correspondence between malaria and the sickle-cell gene

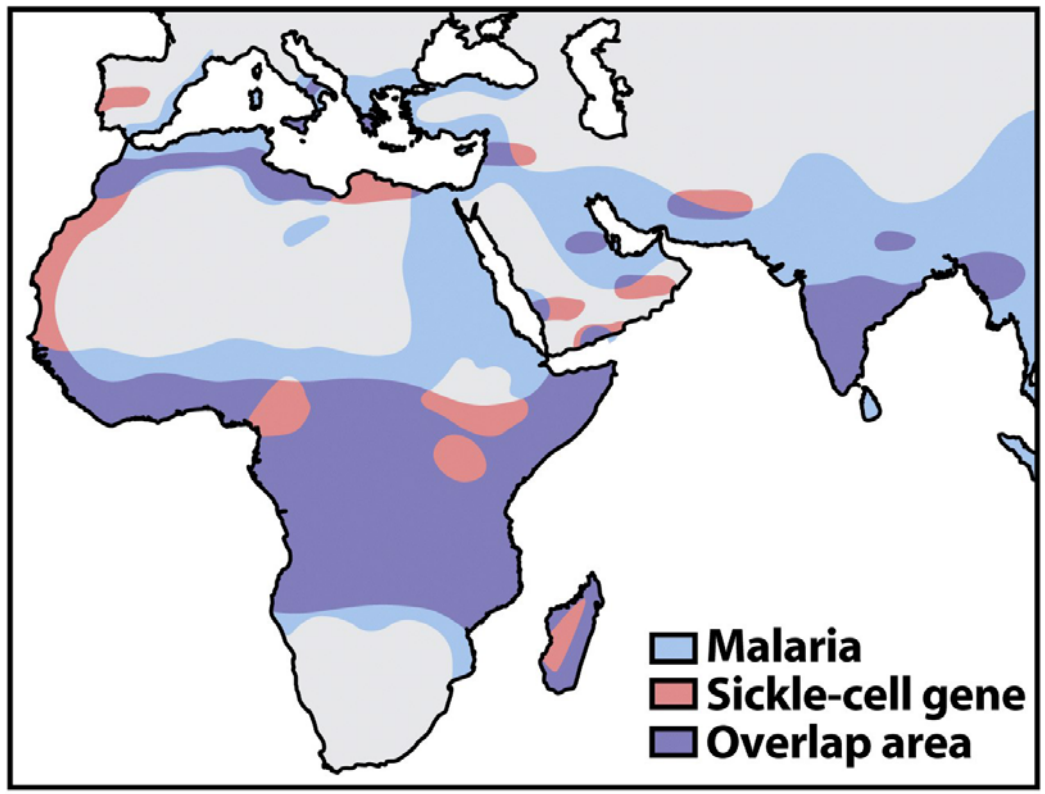

Figure 7-21 Fundamentals of Biochemistry, 2/e