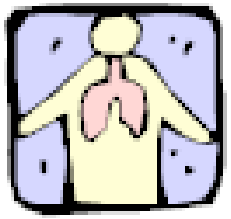
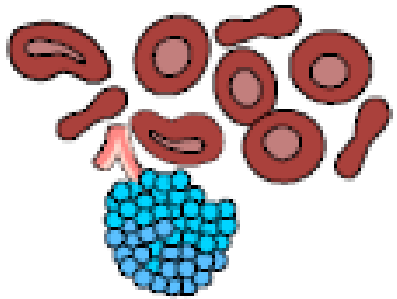
The Bohr Effect and Oxygen Transport

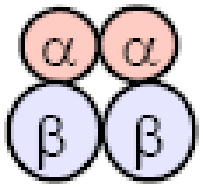


Bohr Effect



Hemoglobin (Hb) is a tetrameric protein (2 α and 2 β subunits)

- binds O_2 cooperatively
- each Hb can bind 4 O_2



H+ ions modulate O_2 binding to hemoglobin

$$Hb + O_2 \rightleftharpoons Hb(O_2) + H^+$$

Hb — H^+

high H^+ / low O_2 (capillaries), O_2 is released

low H^+ / high O_2 (lungs), O_2 is bound

Called Bohr Effect (when O_2 binds to Hb, H^+ is released)

$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^-$$

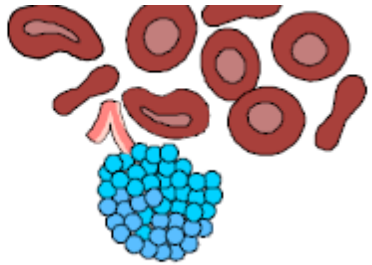
Relatively slow, need an enzyme to speed it up!

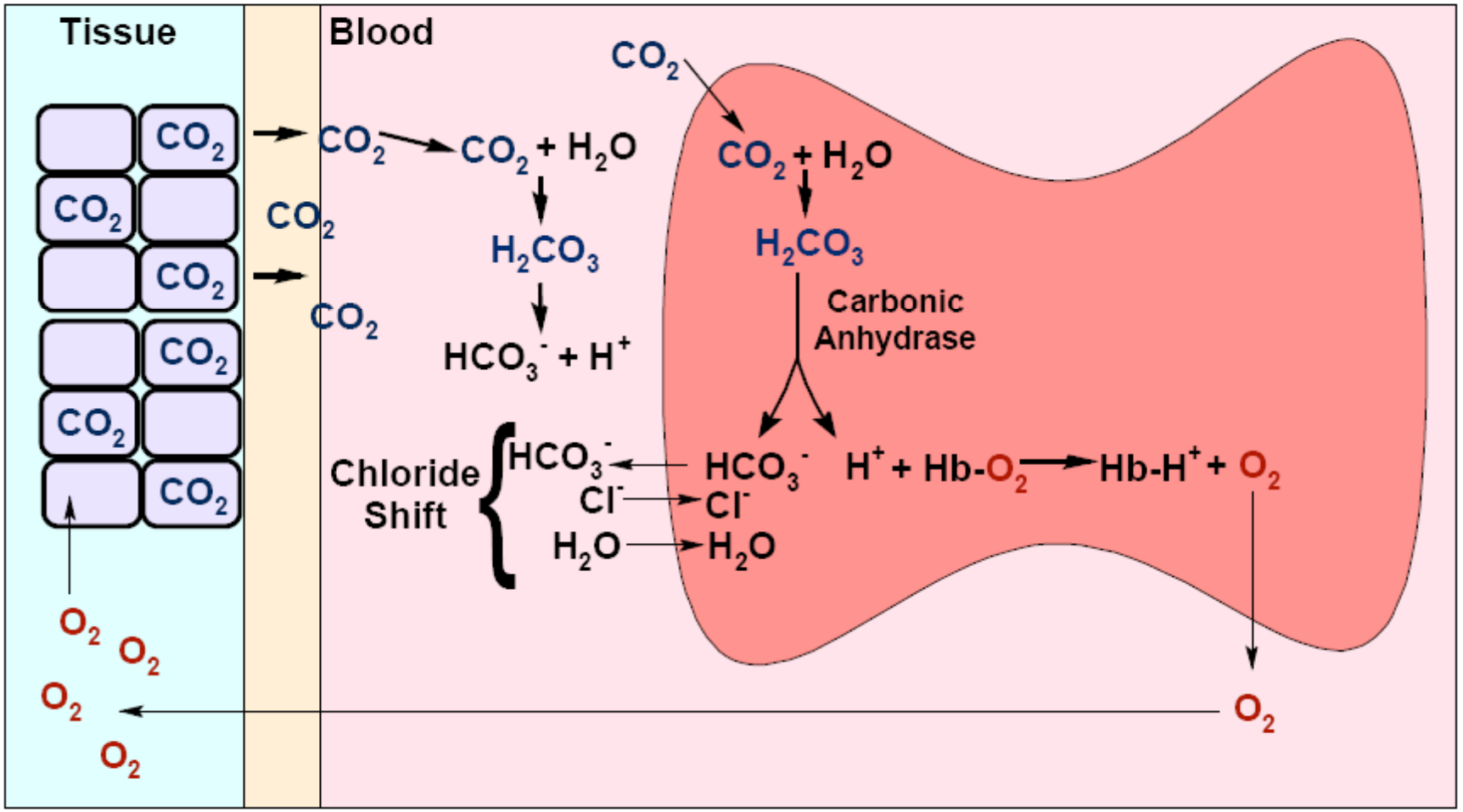
- Carbonic Anhydrase in RBC speeds up 100X

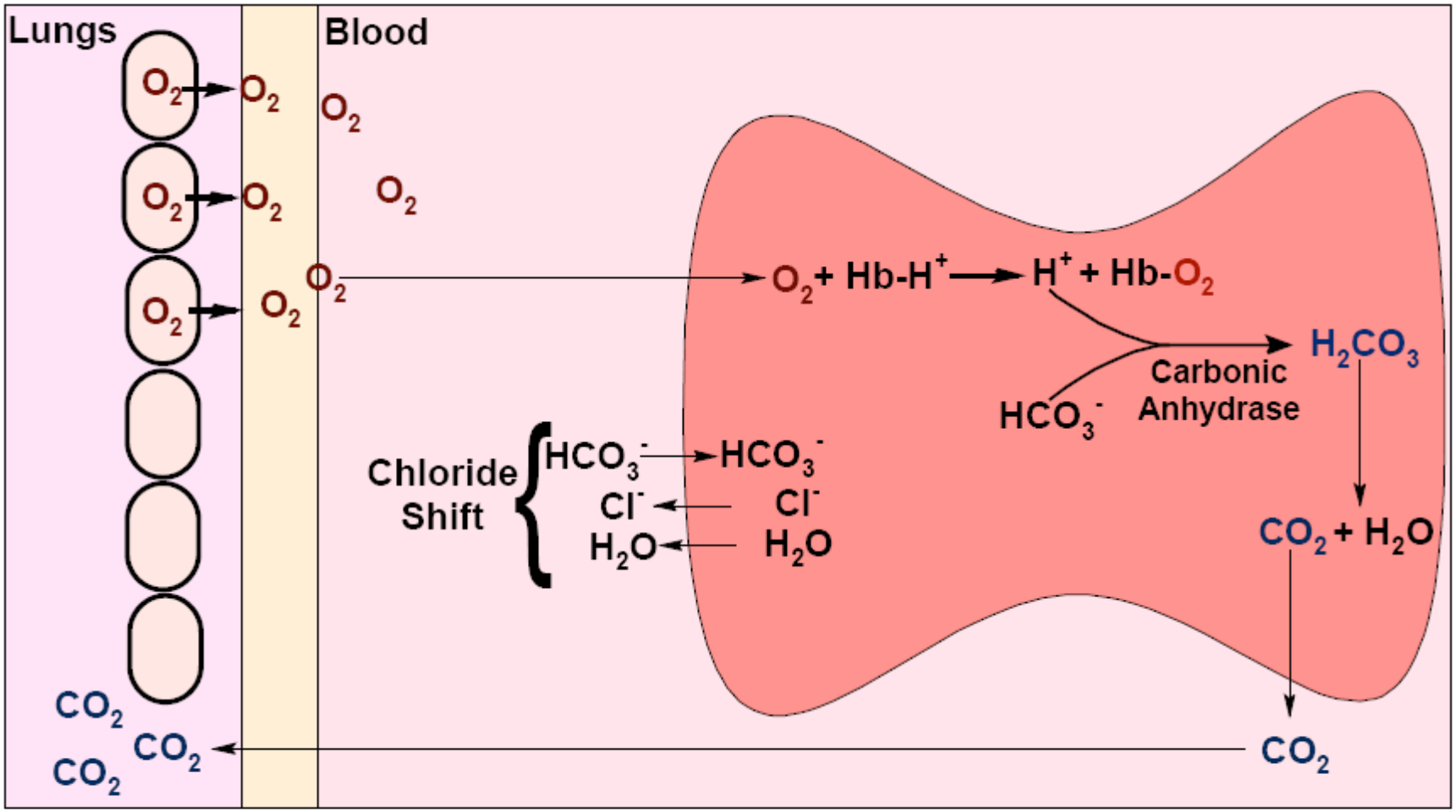
CO_2 waste is produced from metabolic processes in cells

- diffuses out of cell into blood stream

CO_2 Transport and the Bohr Effect






Lungs
Blood
O_2
O_2
O_2
O_2
O_2
O_2
O_2
O_2
O_2
O_2 + Hb-H^+
H^+ + Hb-O_2
H_2CO_3
Carbonic Anhydrase
HCO_3^-
Chloride Shift
HCO_3^-
HCO_3^-
Cl^-
Cl^-
H_2O
H_2O
CO_2 + H_2O
CO_2
CO_2
CO_2
CO_2

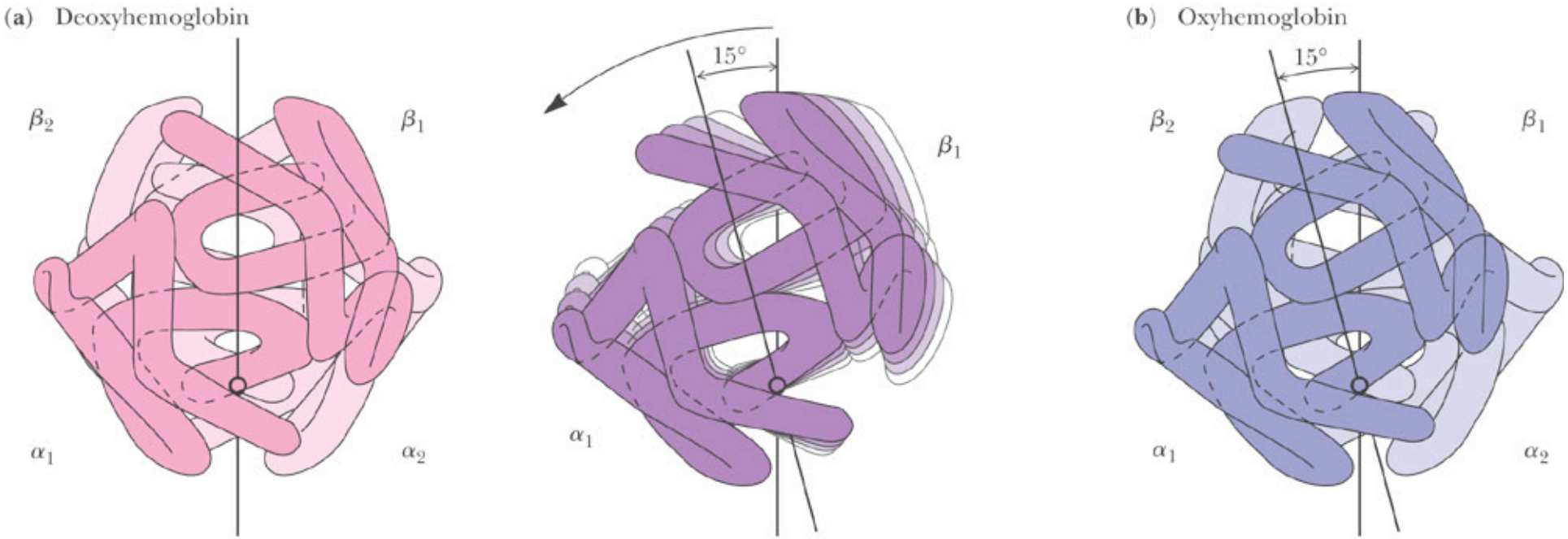


Fig. 15-30, p.497

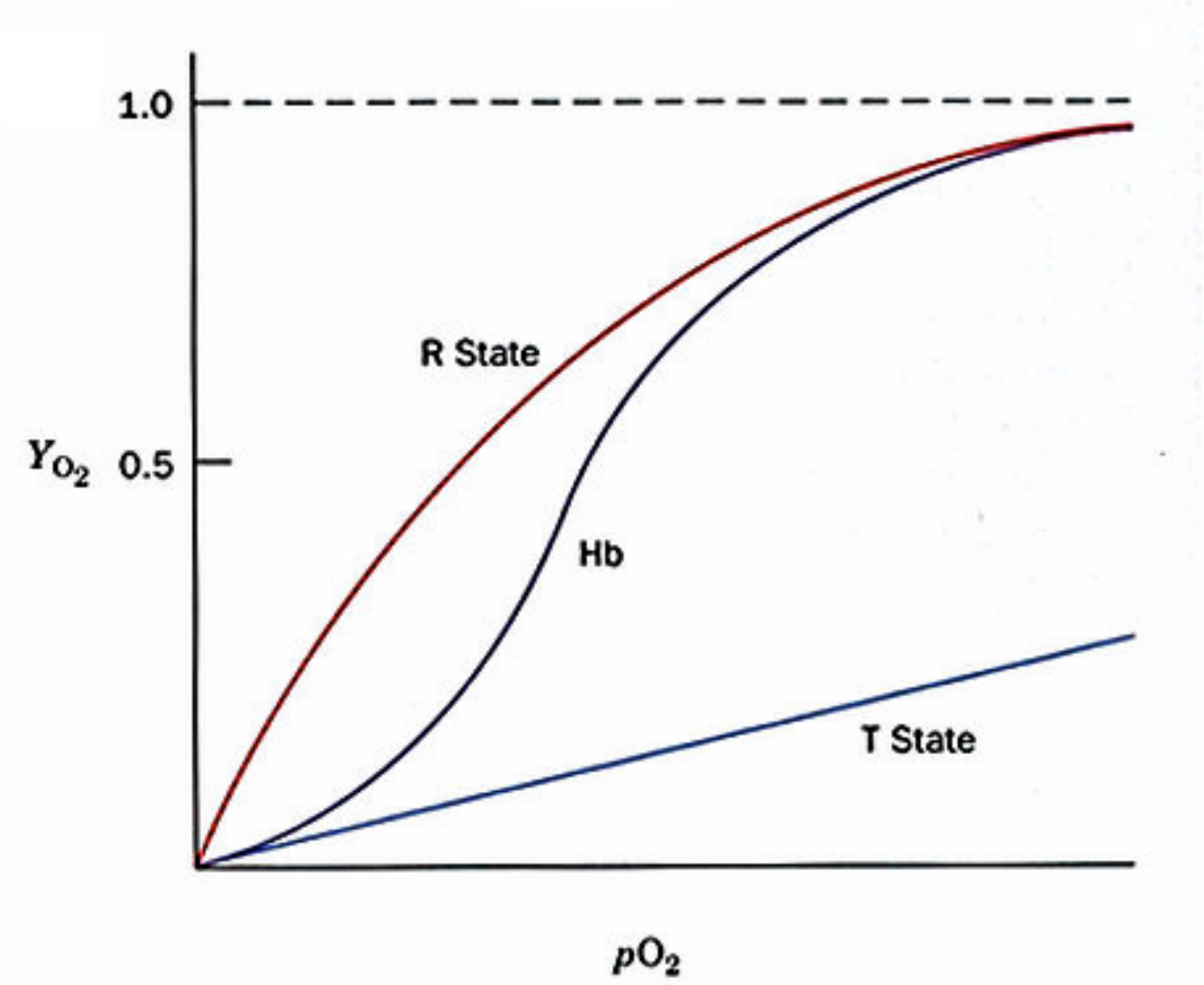


Fig 9.20 b

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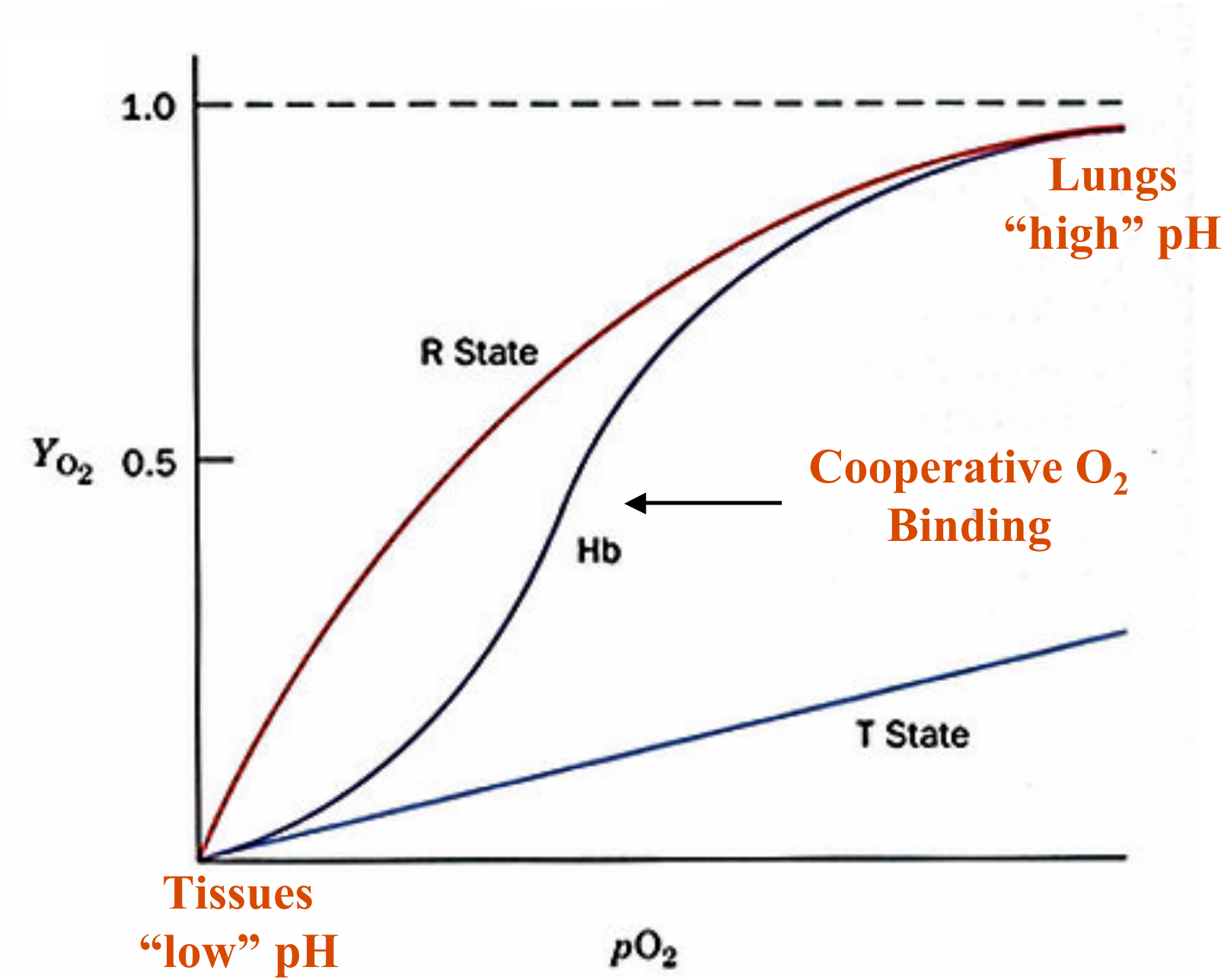


Fig 9.20 b

Biochemistry 2nd ed, Voet/Voet

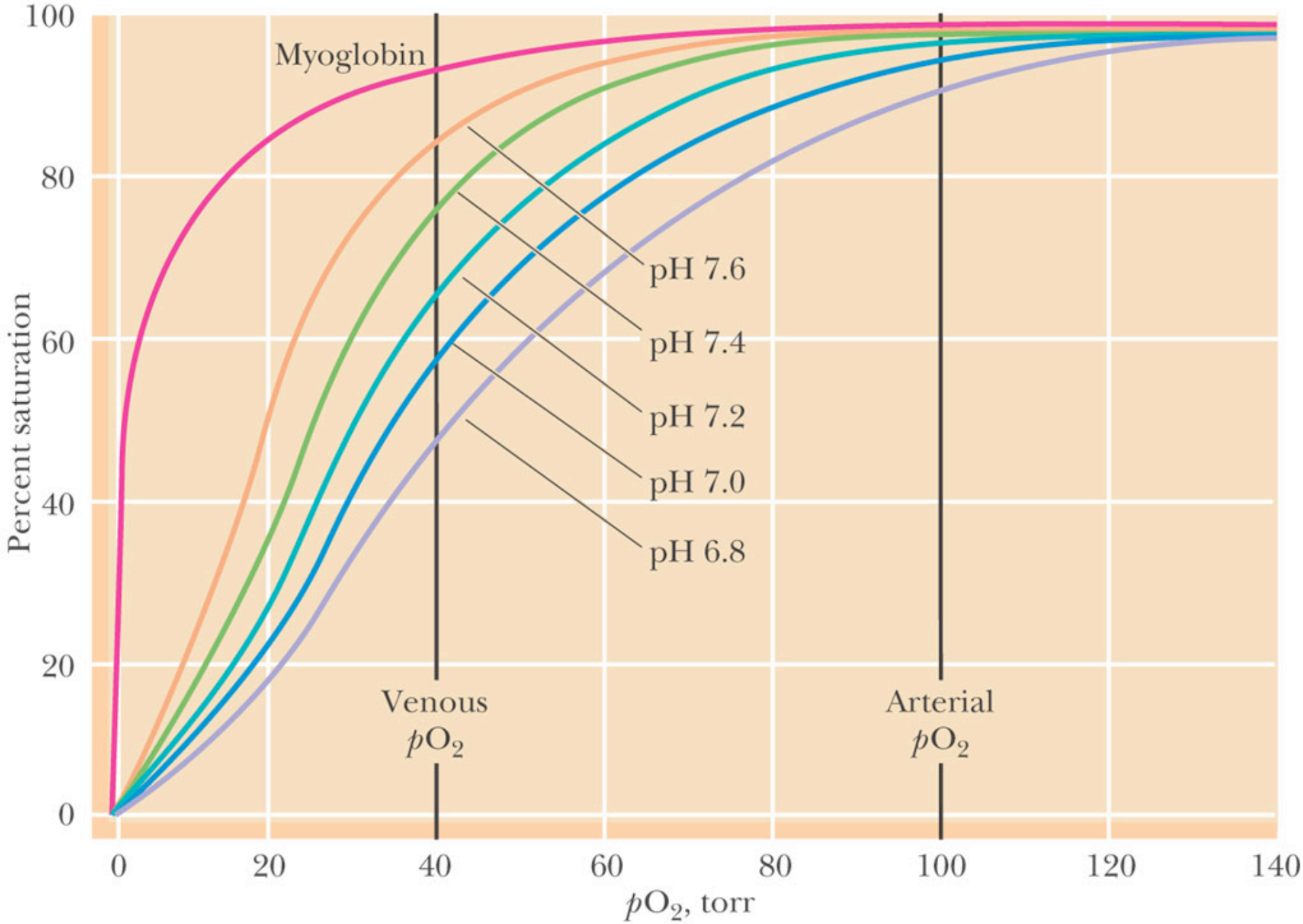
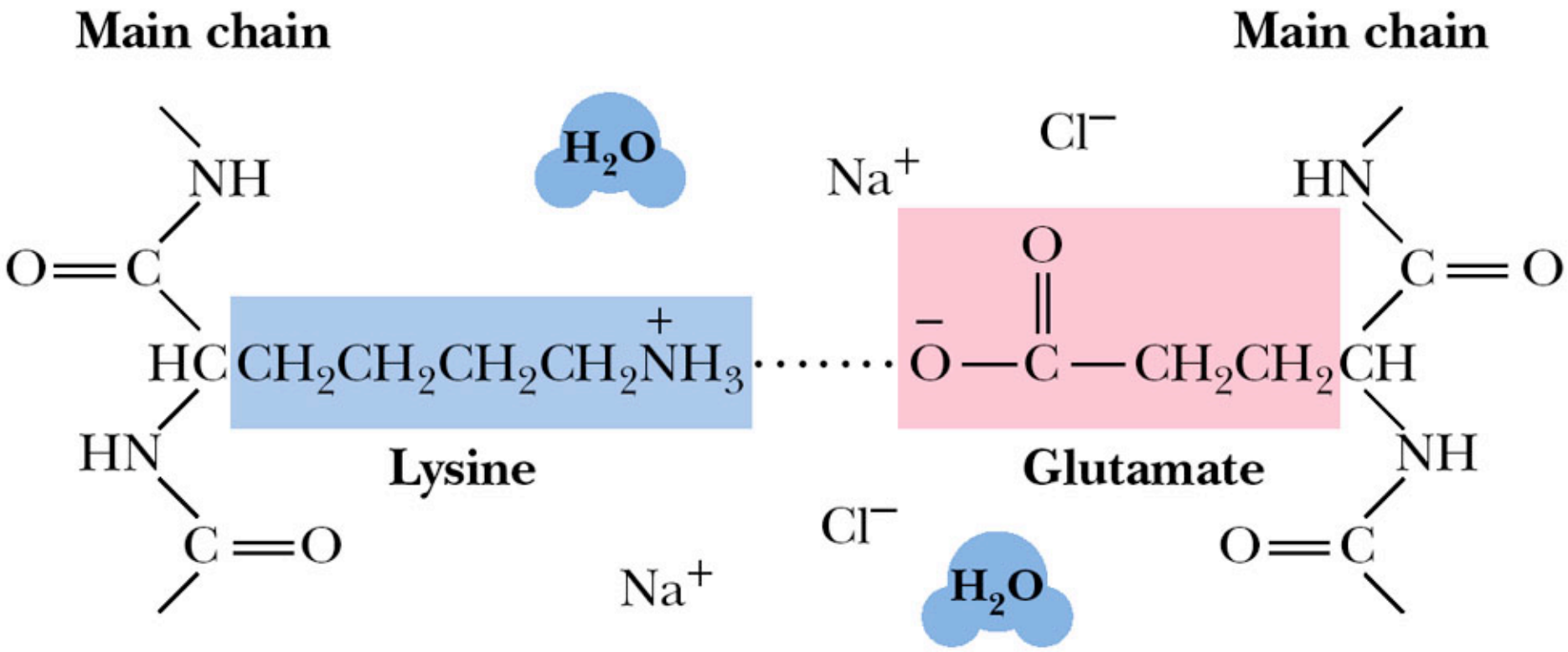
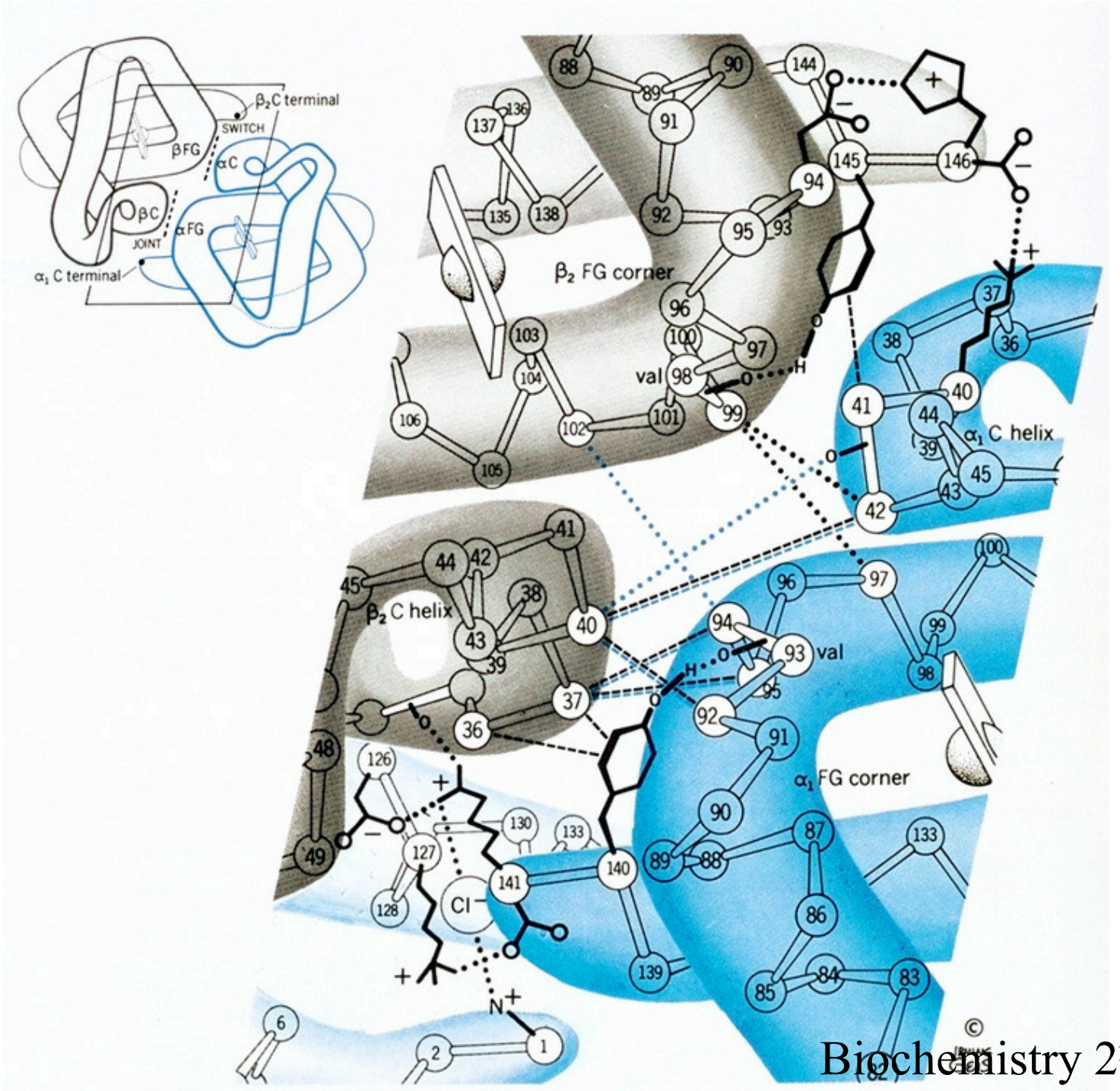


Fig. 15-33, p.499



Salt Bridge between Lys and Glu

Fig. 6-01, p.154



Deoxy HB

T-form

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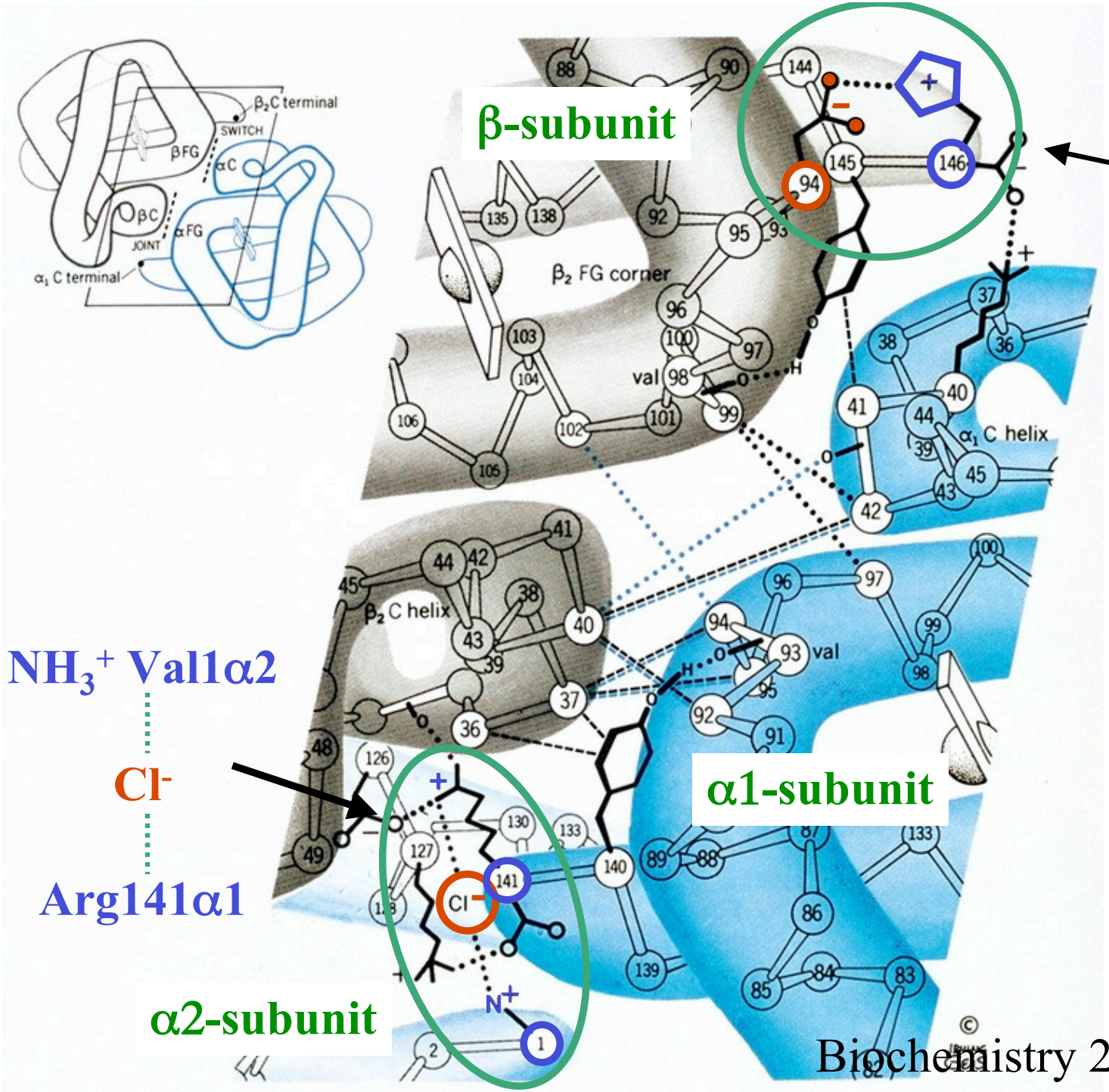

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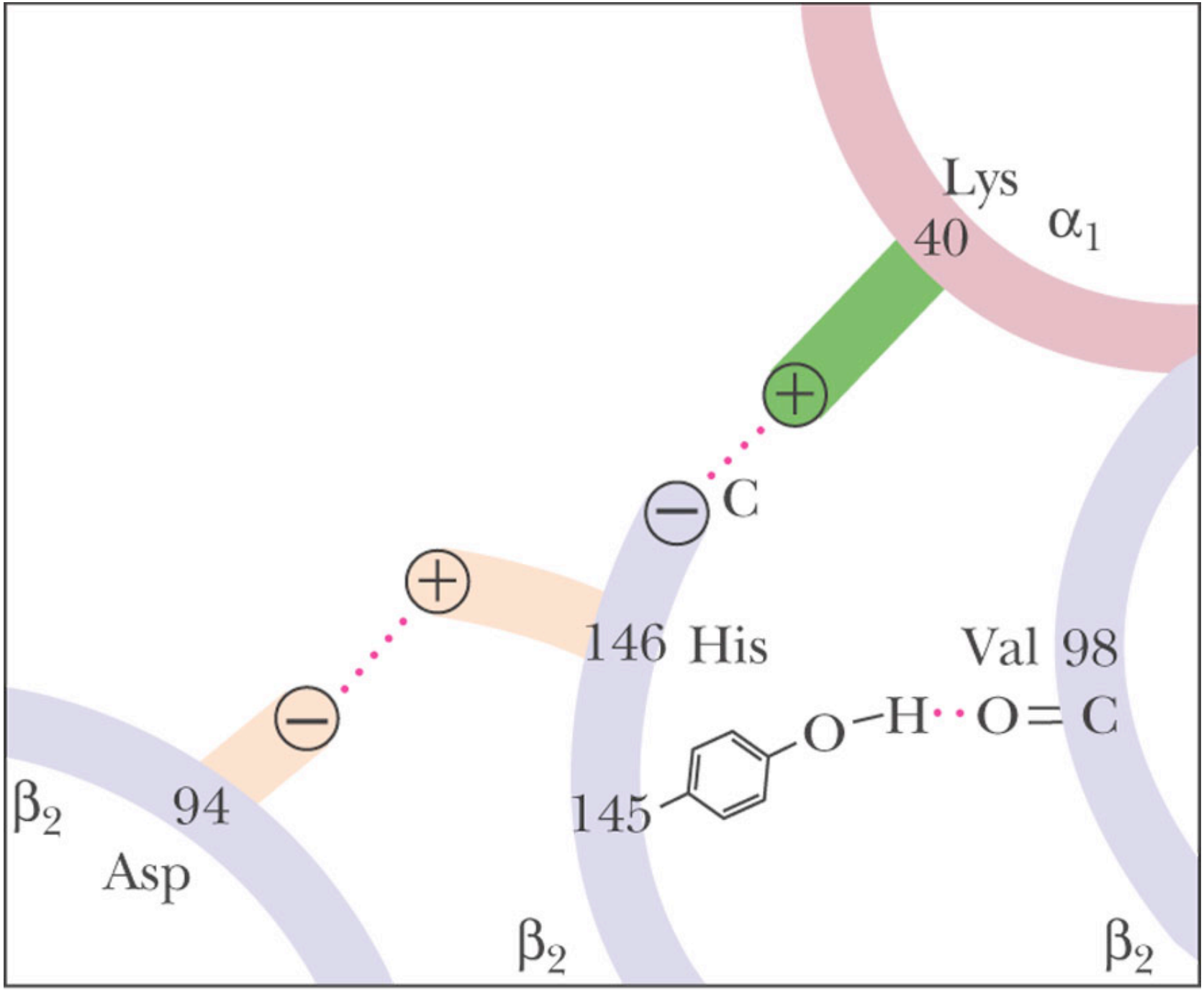
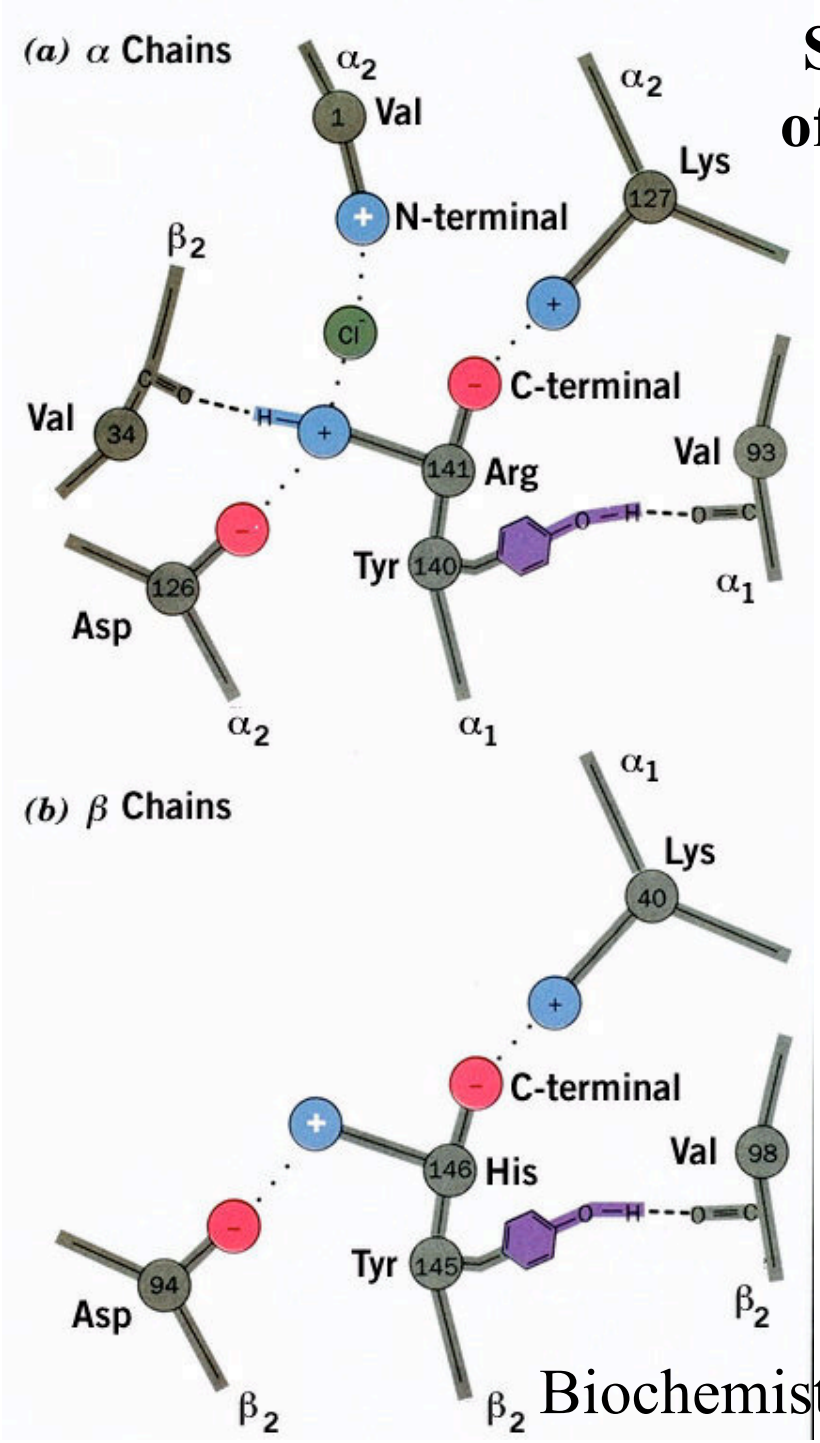


Fig. 15-32c, p.499

Structural Basis of the Bohr Effect



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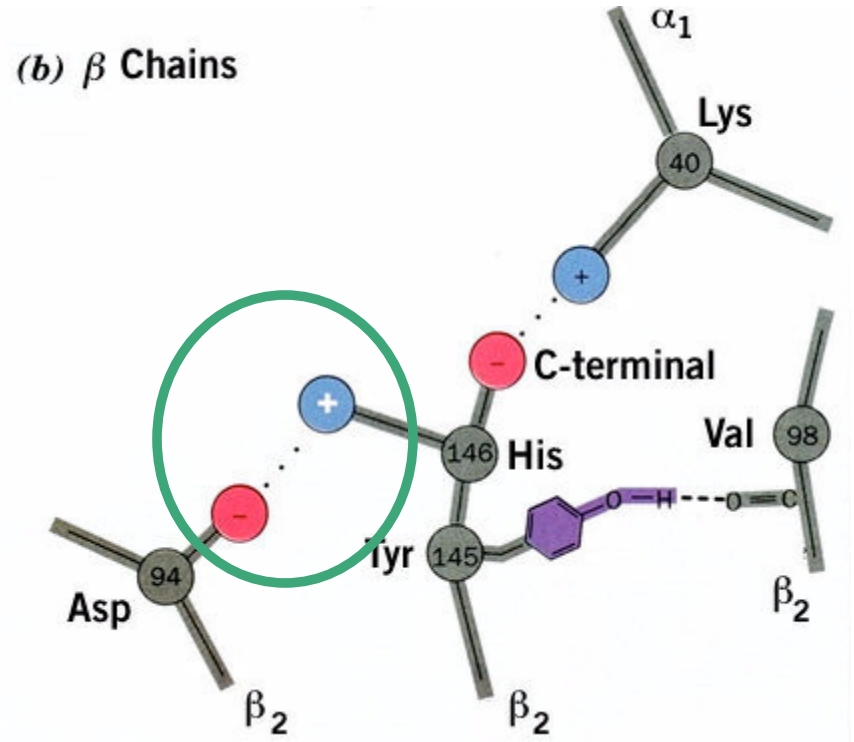

T-Form is stabilized by this salt bridge between **His146β** and **Asp94β** on the same β subunit.

This interaction causes **His146β** to retain its proton and thus its positive charge when the subunit is in the T-form.

Another way of saying this is that the pKa of **His146β** is raised from 7.1 (which favors proton loss) to 8.0 (which favors proton retention) because of the interaction with **Asp94β**.

Upon O_2 binding and conversion to the R-form, **His146b** is moved away from **Asp 94β**, thus lowering the pKa back to 7.1 and **His146 β** loses its proton. So, the binding of O_2 causes a release of H^+. The Bohr effect!

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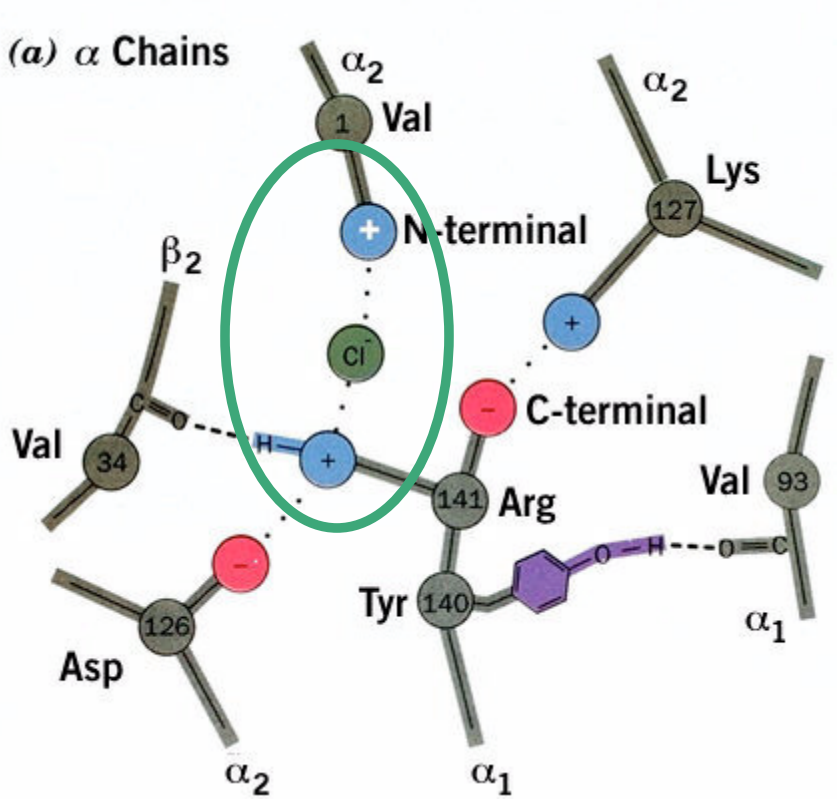


The T-form is also stabilized by the binding of a **chloride** ion at the interface between the two α subunits. In the T-form, the terminal amino group (**Val1α**) of one α subunit is close to **Arg141α** of the other α subunit.

The normally unstable association of positively charged groups is stabilized by the binding of a **chloride** ion between the two groups.

When O_2 binds and the α subunits switch to the R-form, the **NH_3^+** group of **Val1α** is moved away from **Arg141α** and the **chloride** ion is released. The pKa of the **NH_3^+** group is raised by association with the **chloride** ion. Once the ion is released, the **NH_3^+** group can lose its proton to some degree. (pKa ~8.0)

Biochemistry 2nd ed, Voet/Voet

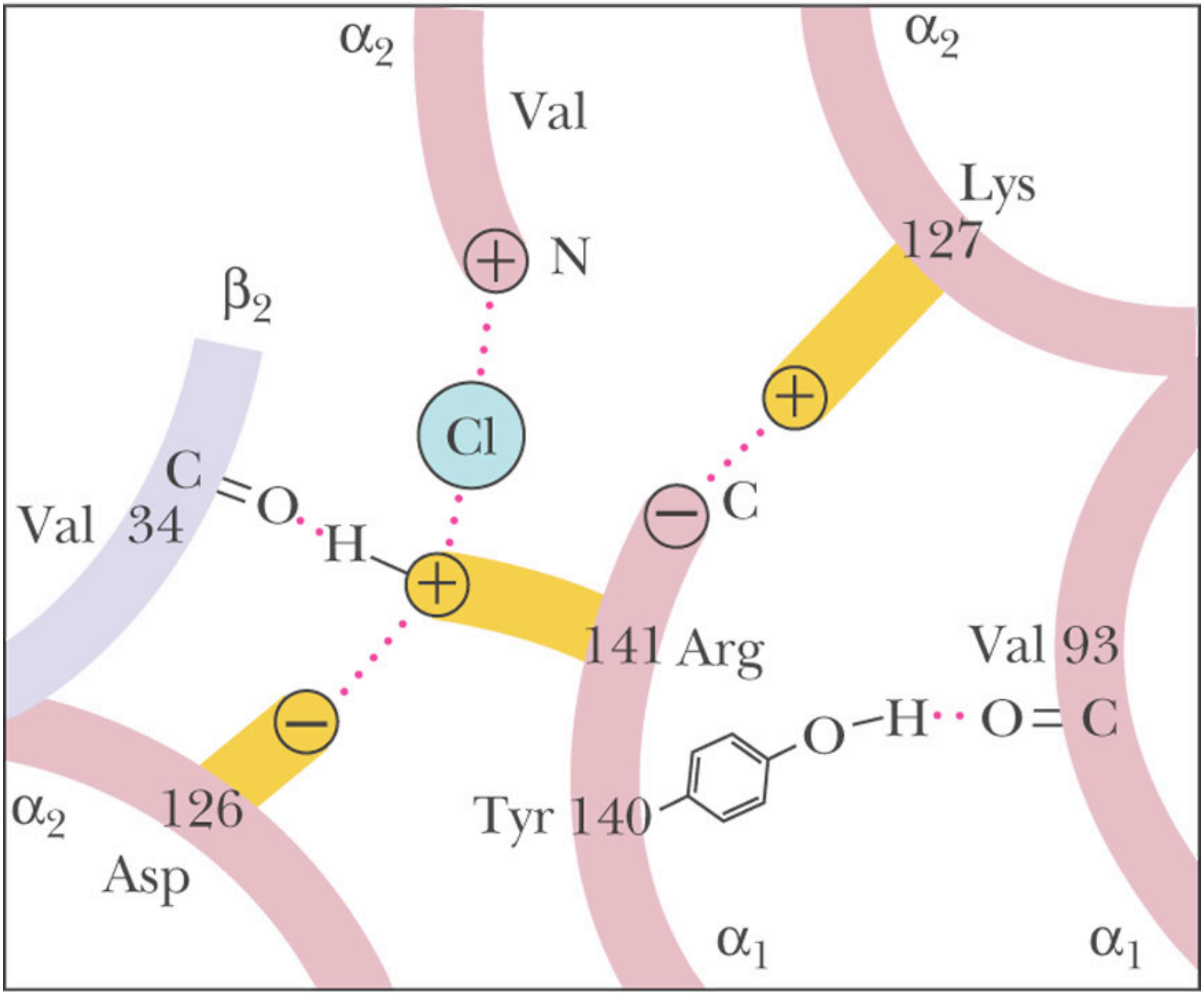
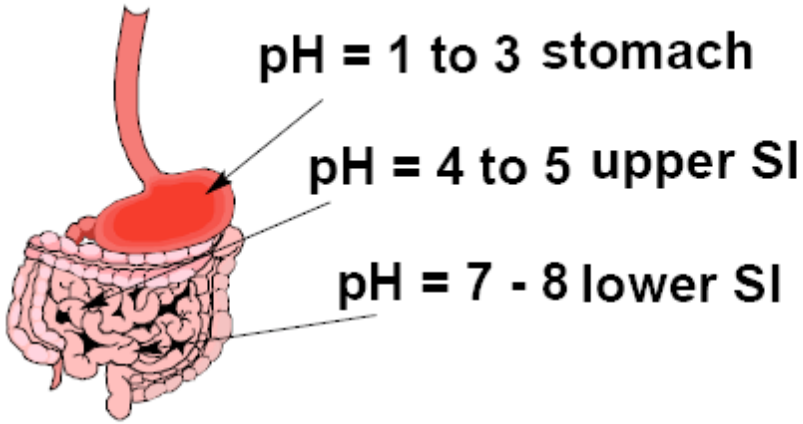


Fig. 15-32b, p.499

Factors Affecting Drug Absorption

Most drugs are given orally so must be absorbed through the digestive tract.

Drastic pH changes in different regions of digestive tract



Steps of drug absorption:

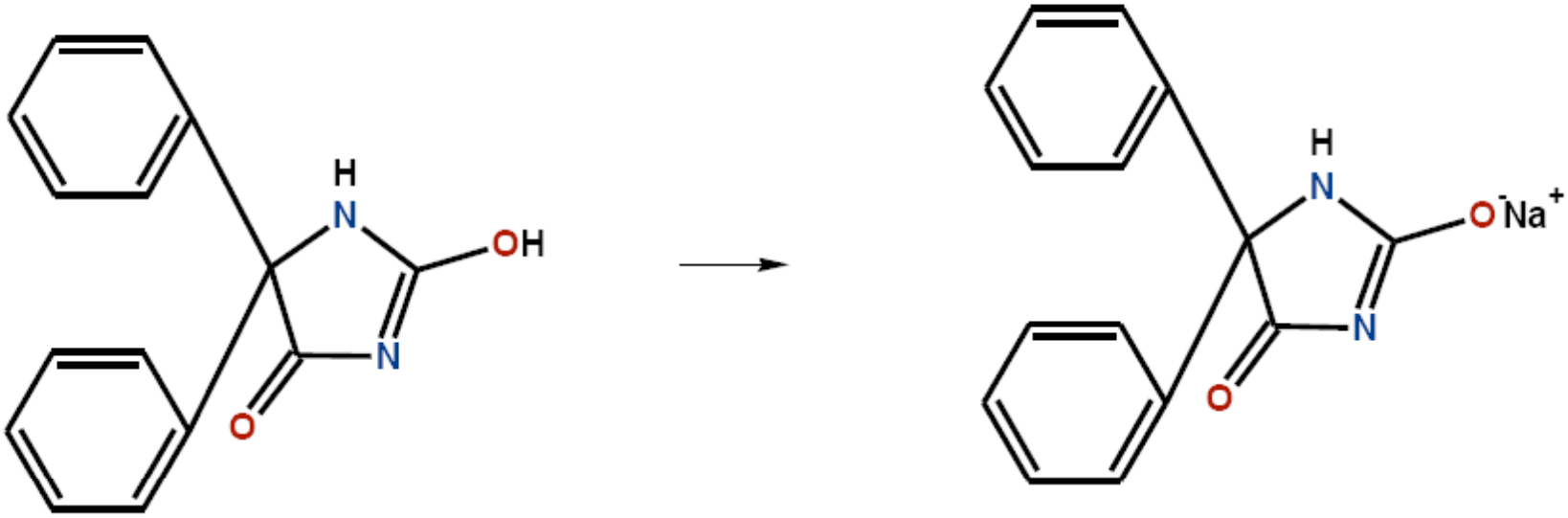
drug $\xrightarrow{\text{dissolution}}$ drug in solution $\xrightarrow{\text{absorption}}$ drug in blood

drug dissolution is often the rate limiting step in delivery

- Diffusion is the most common mechanism of absorption

- Drug must move through lipid bilayers to move from intestine to blood stream

Dilantin (Phenytoin): very weak acid (pKa ~ 8.2)



anti-convulsant, reduces neuronal activity that leads to neuronal hyperactivity in grand-mal seizures.

Activity: promotes Na+ efflux from neurons thereby reducing their excitability.