The Bohr Effect

Or how to get Heme to pick up and drop off oxygen

Marguerite Butler

Zool 430


RIGH

The Bohr effect

Explains how high [CO_2] helps hemoglobin release O_2 in tissues that need it

O_2 Concentration

O_2 Affinity

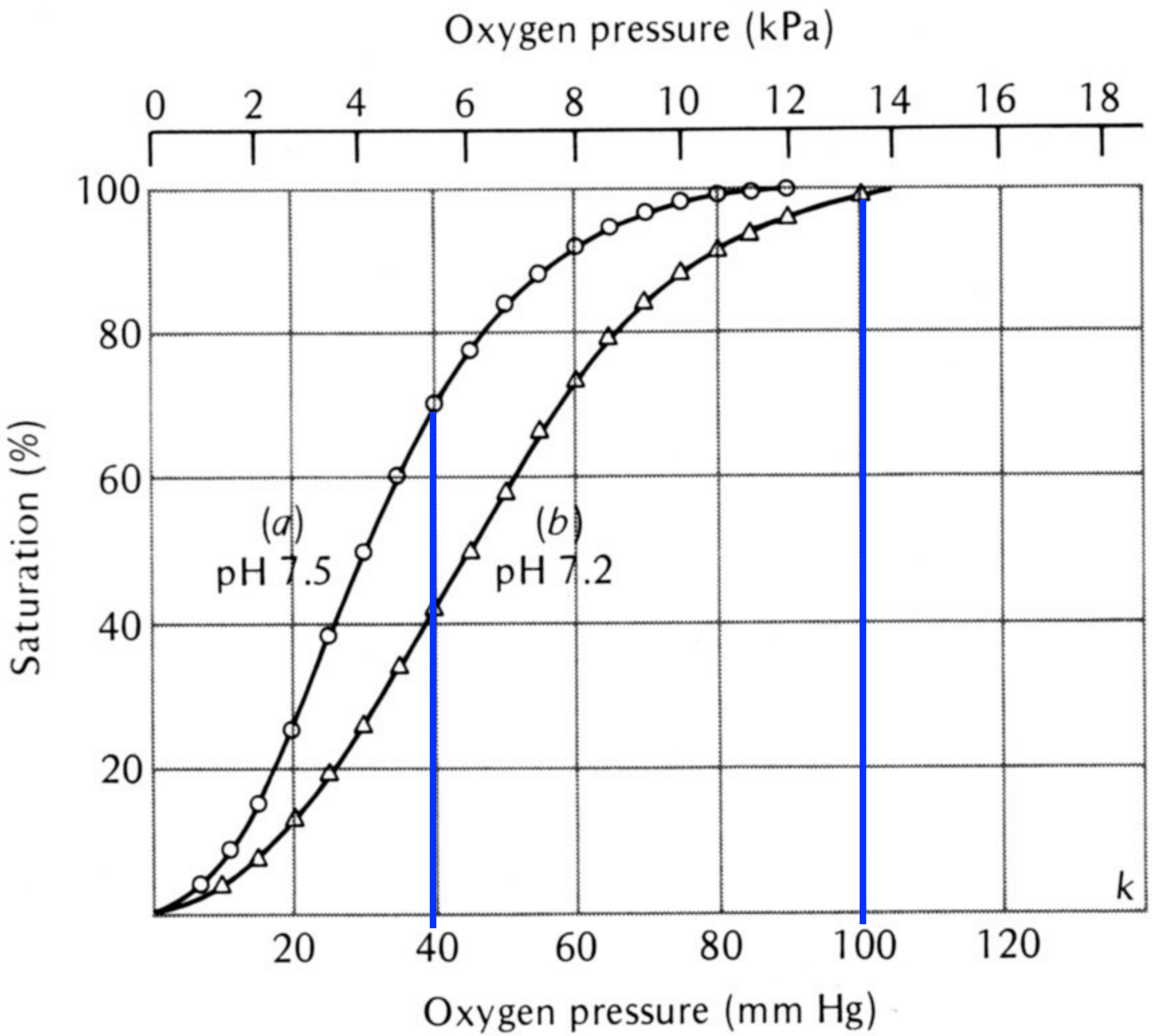
O_2-loving

O_2-meh

pH

Hb-Oxygen Dissociation Curve

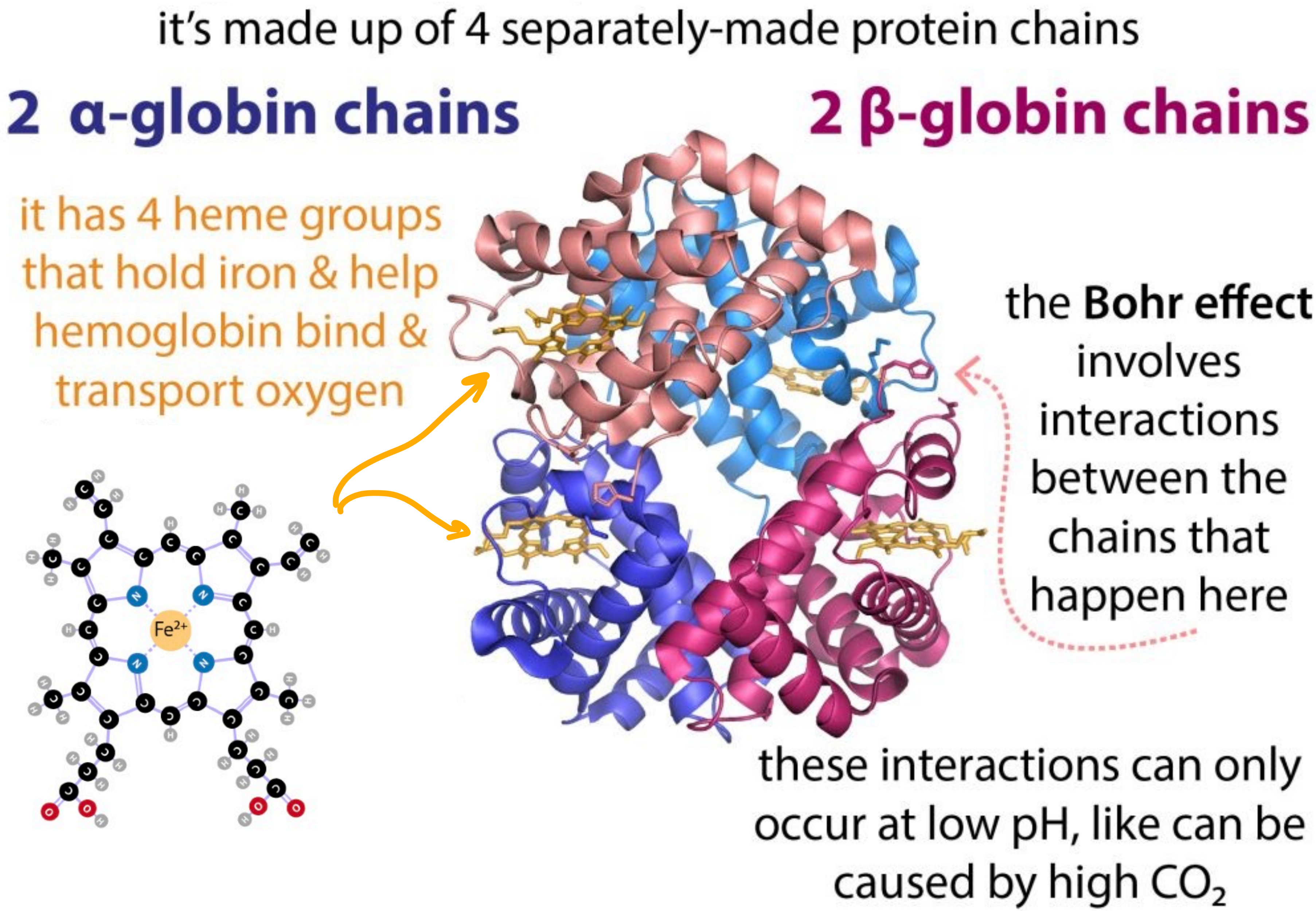
Hemoglobin binds O_2 reversibly



Hemoglobin

The oxygen shuttle.
Picks up O_2 at the lungs and dumps O_2 at the tissues.

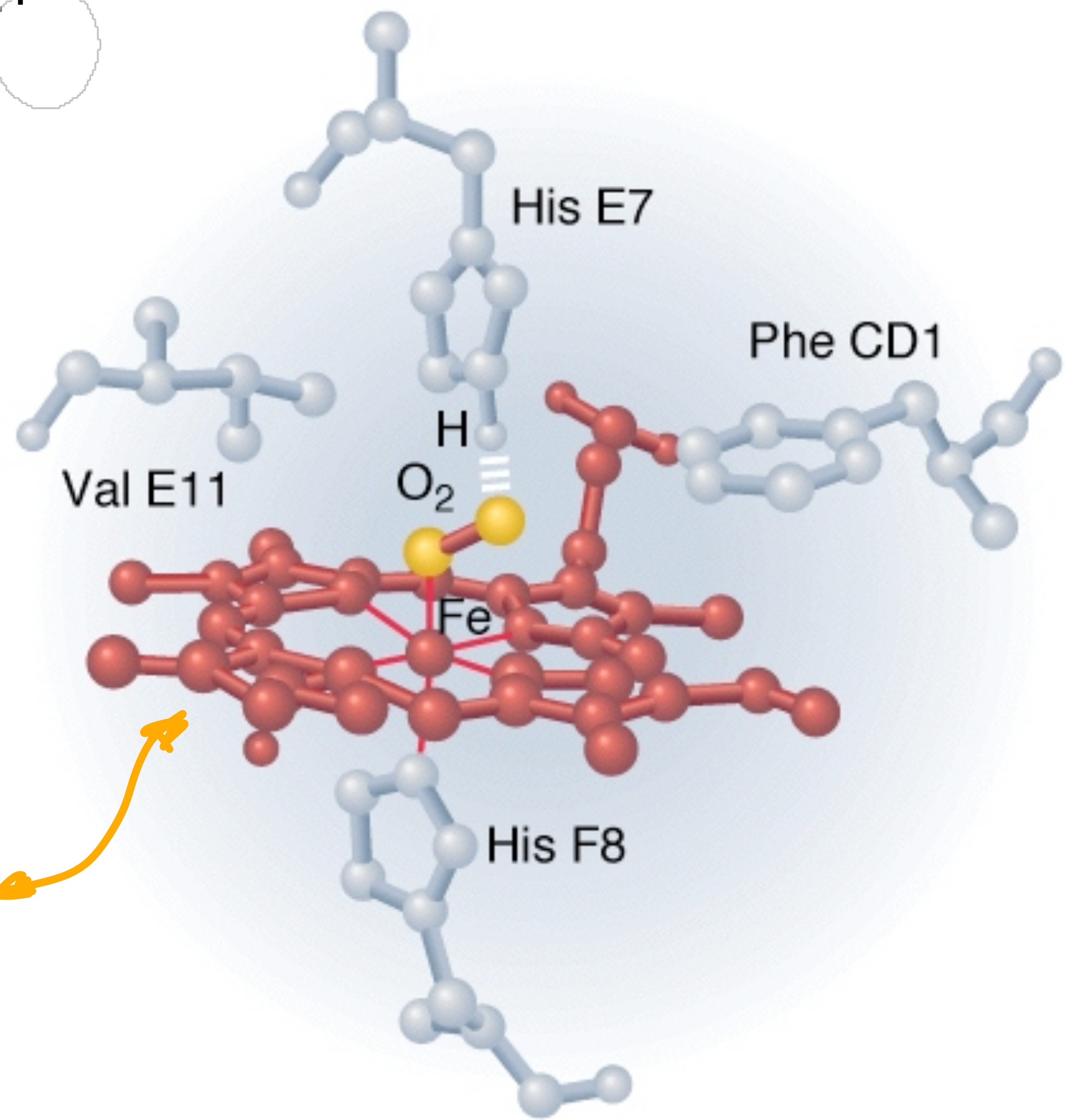
Hemoglobin

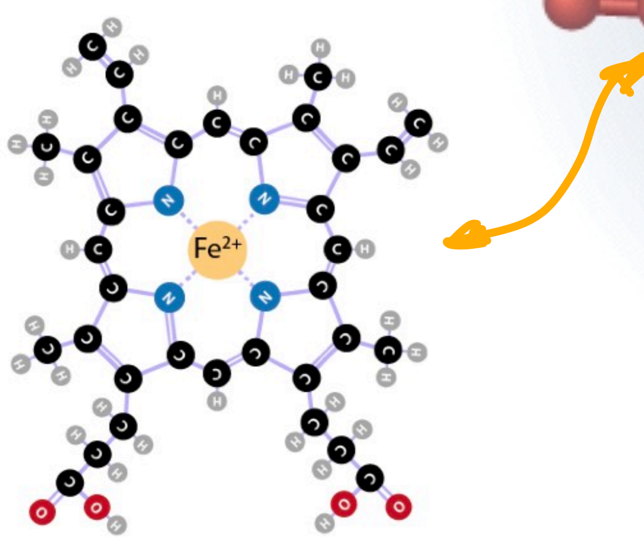


https://thebumblingbiochemist.com/365-days-of-science/the-bohr-effect-hemoglobin-oxygen-carrying-molecular-magic/

Heme Binds Oxygen Reversibly

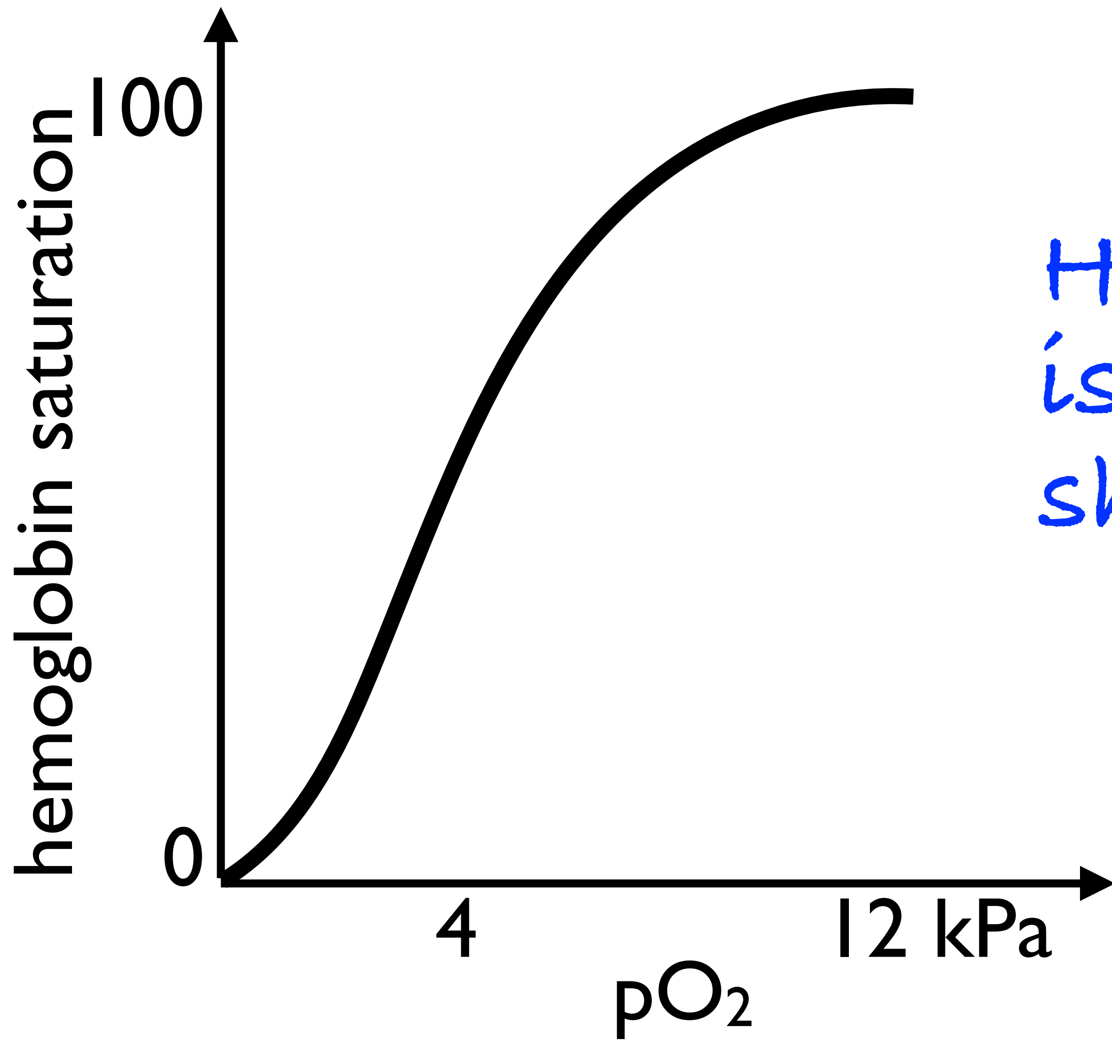
- Heme binds O_2 via Fe^{2+}
- 4 hemes => 4 O_2 per hemoglobin
- O_2 stabilized by H-bonds with Histidine residues in globin





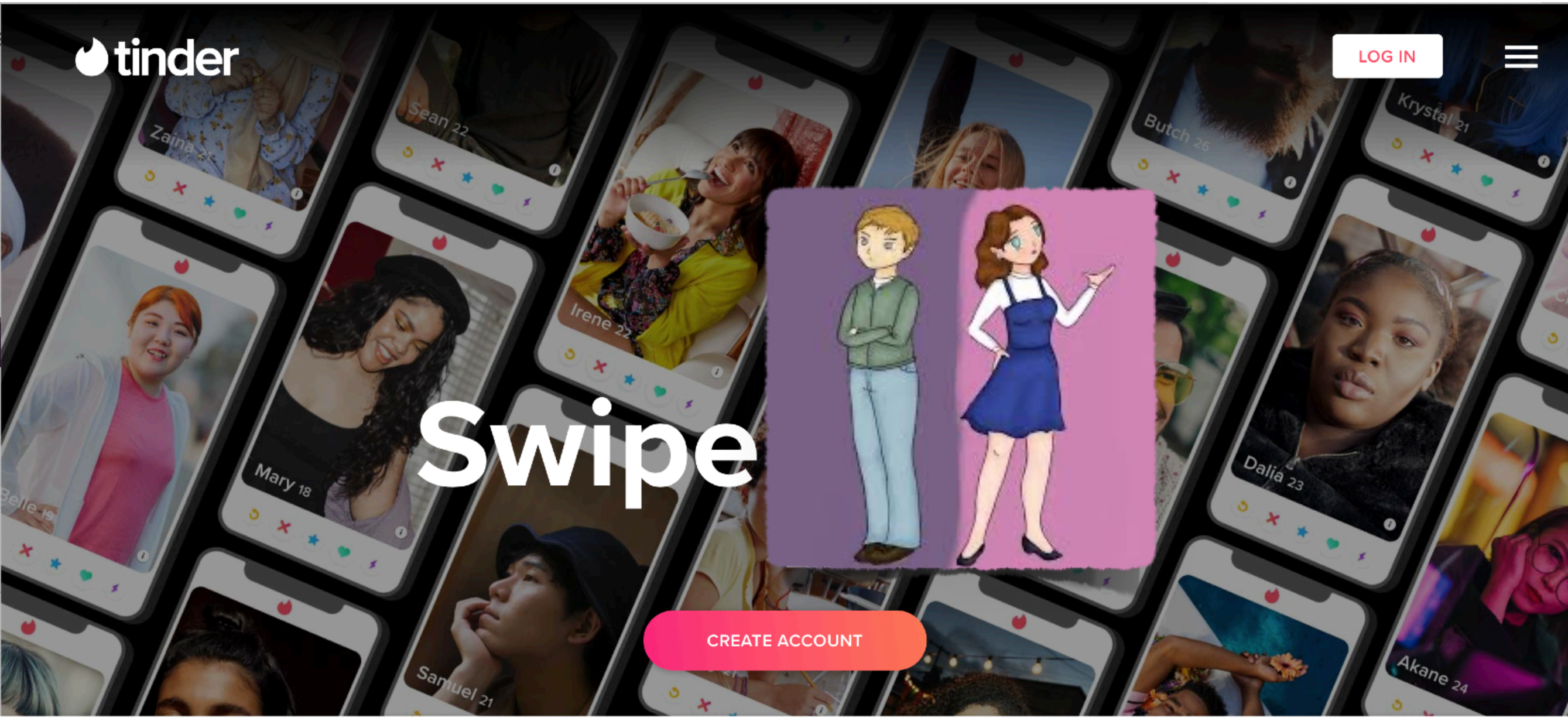
Subunits Bind O_2 Cooperatively

Hemoglobin has 4 subunits



Hemoglobin is an O_2 shuttle

Reversible, All-or-None

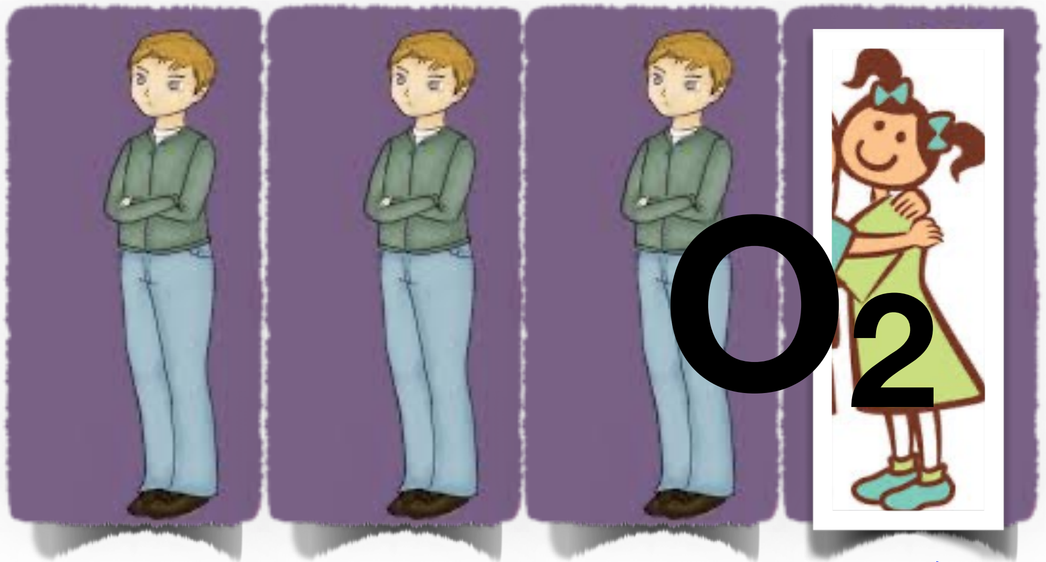


Low Affinity
"O_2 Grumpy"

High Affinity
"O_2 Sticky"

Doesn't need to meet a lot of O_2

Subunits Bind O_2 Cooperatively

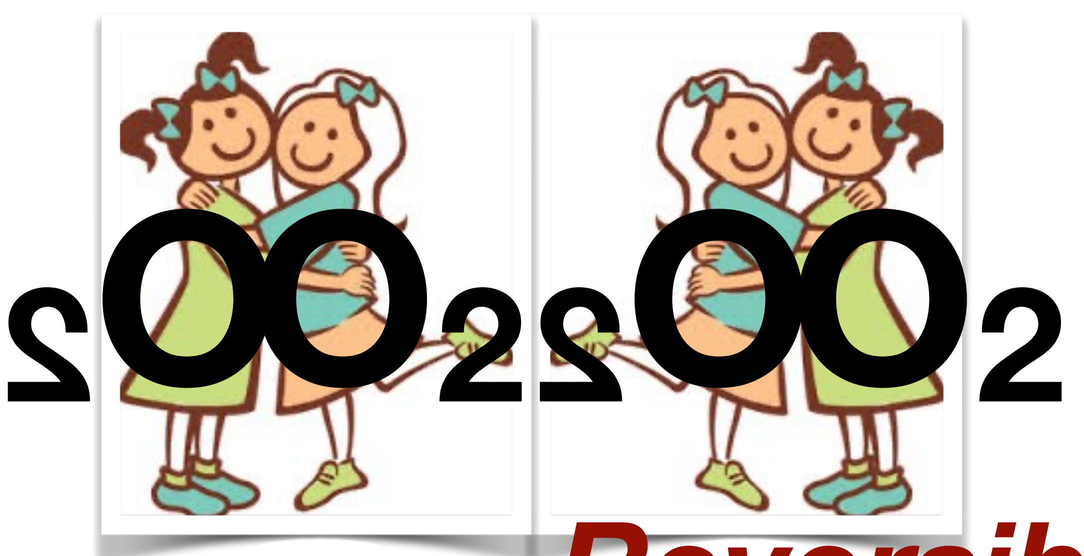


"O_2-grumpy" "O_2-sticky"

4 Subunits

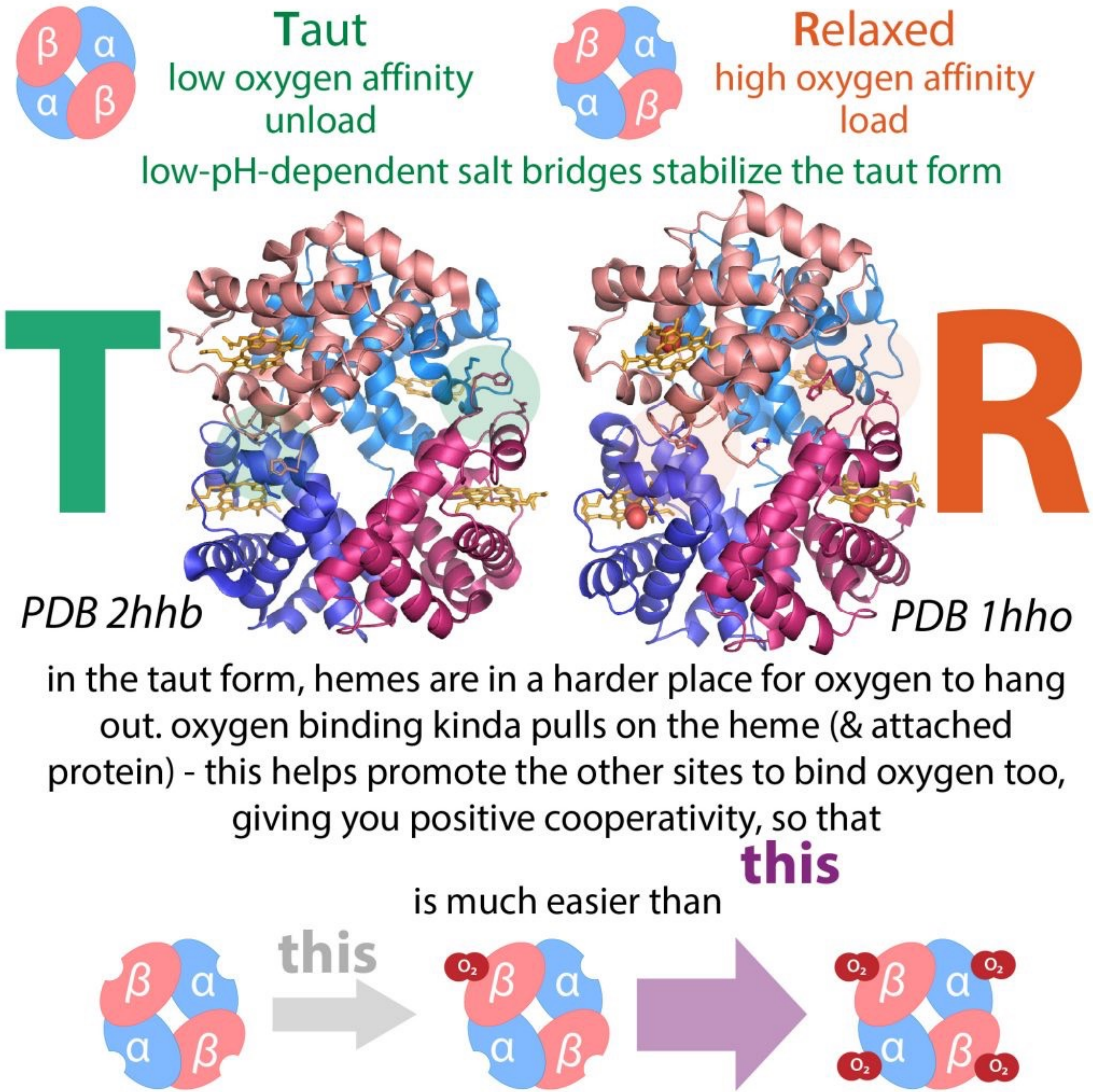
If one subunit binds O_2

All 4 change affinity "O_2-sticky"



Reversible, All-or-None

What changes hemoglobin's mood?



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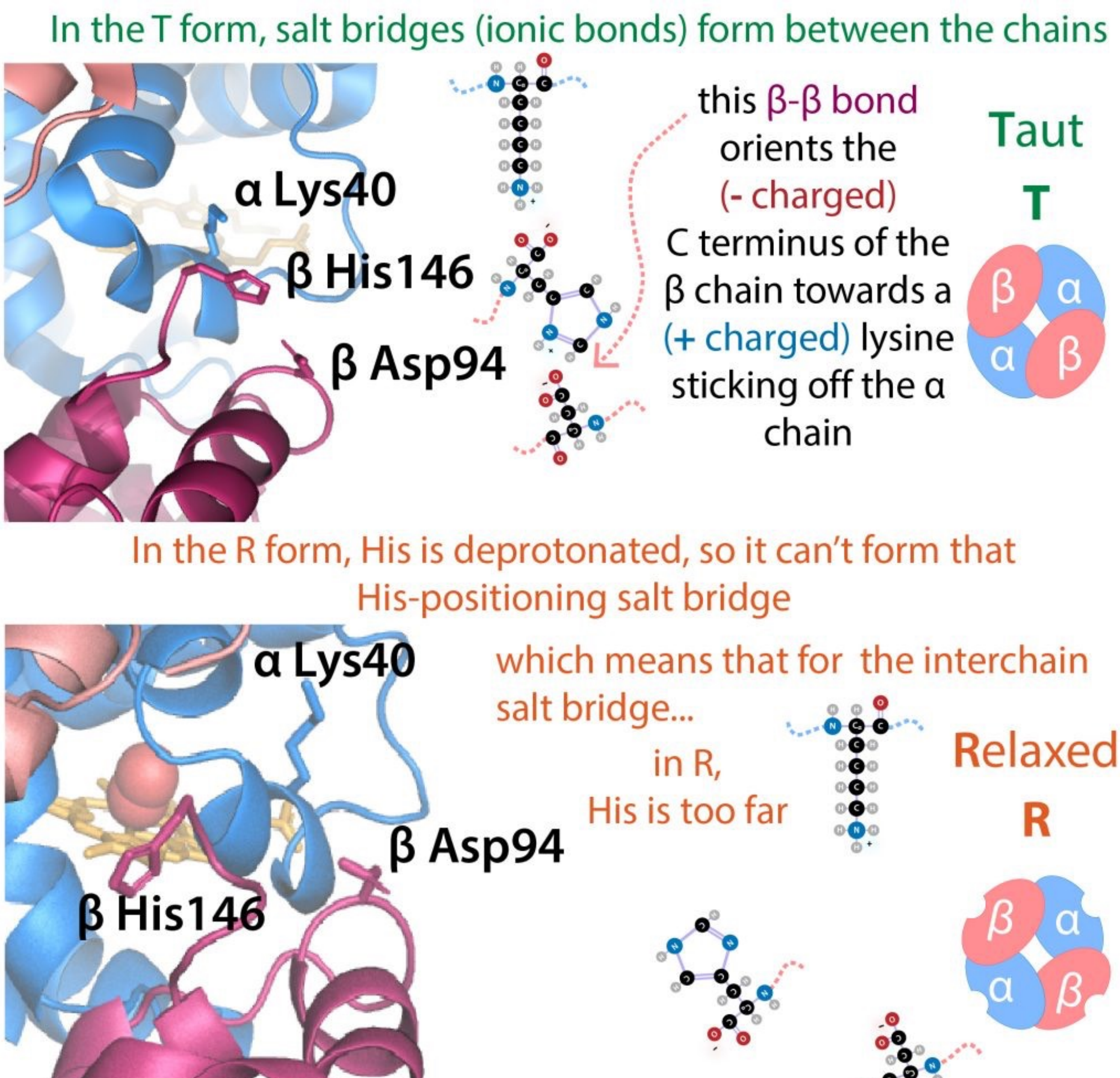

At low pH
=>lots H^+

His- residue can form salt bridge

Blocking O_2 binding

His- deprotonated, blocking salt bridge

O_2 can bind

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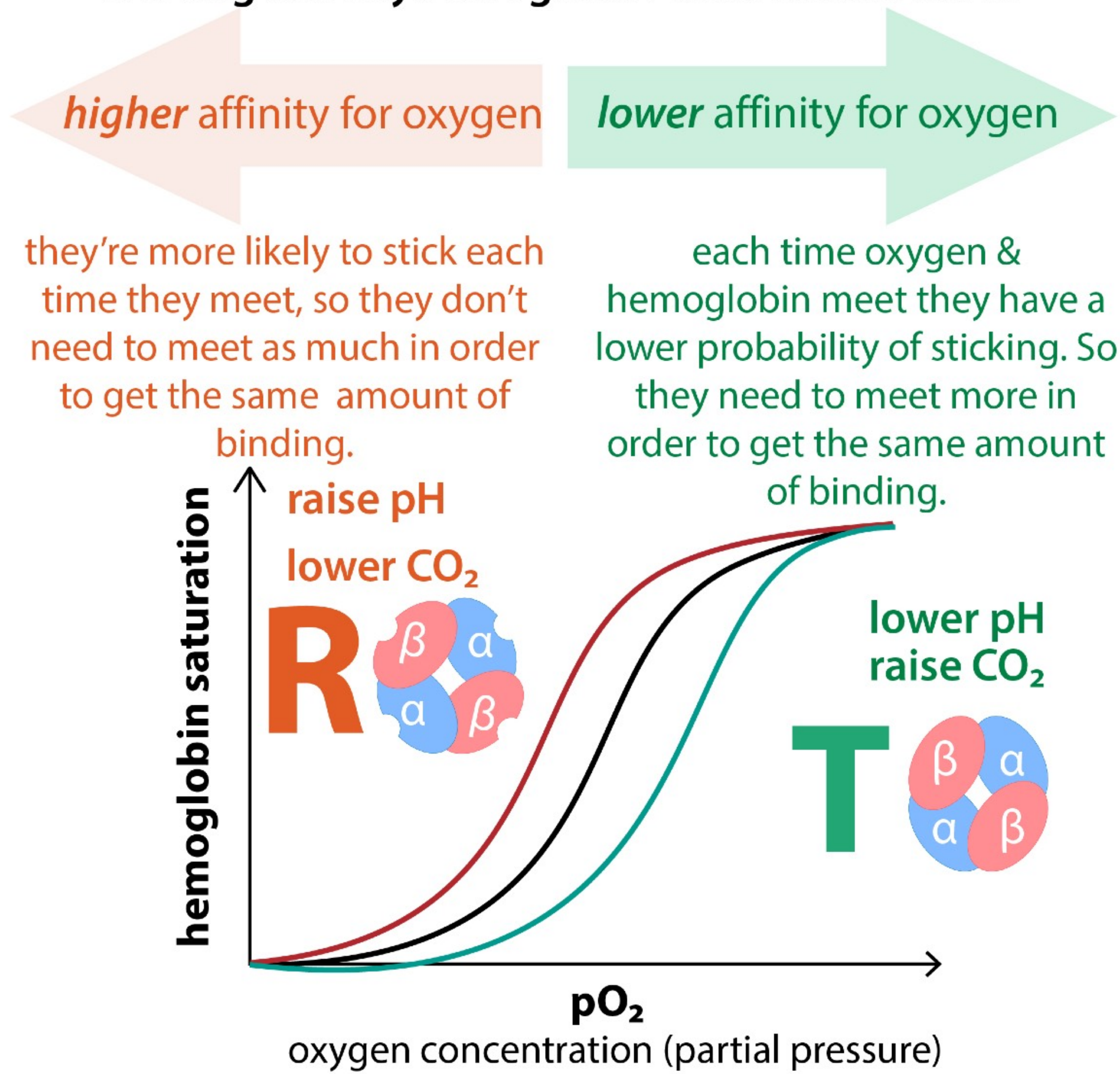
shifting the oxyhemoglobin dissociation curve



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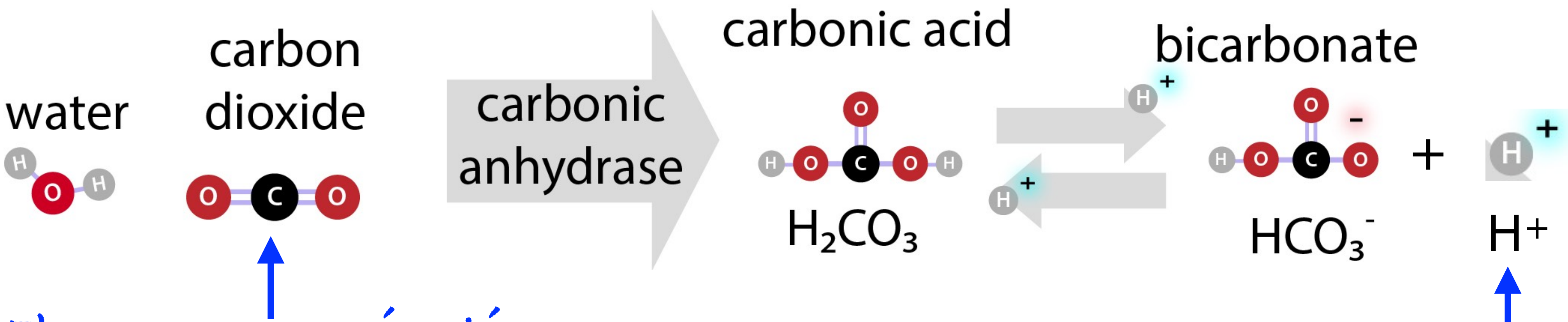
The Bohr effect

Why CO_2 and pH?



The more respiration
The more CO_2

The more
carbonic acid

The more H^+

$$pH = \log_{10}\left(\frac{1}{[H^+]}\right)$$

CO_2 Acidifies blood
Lowers pH!

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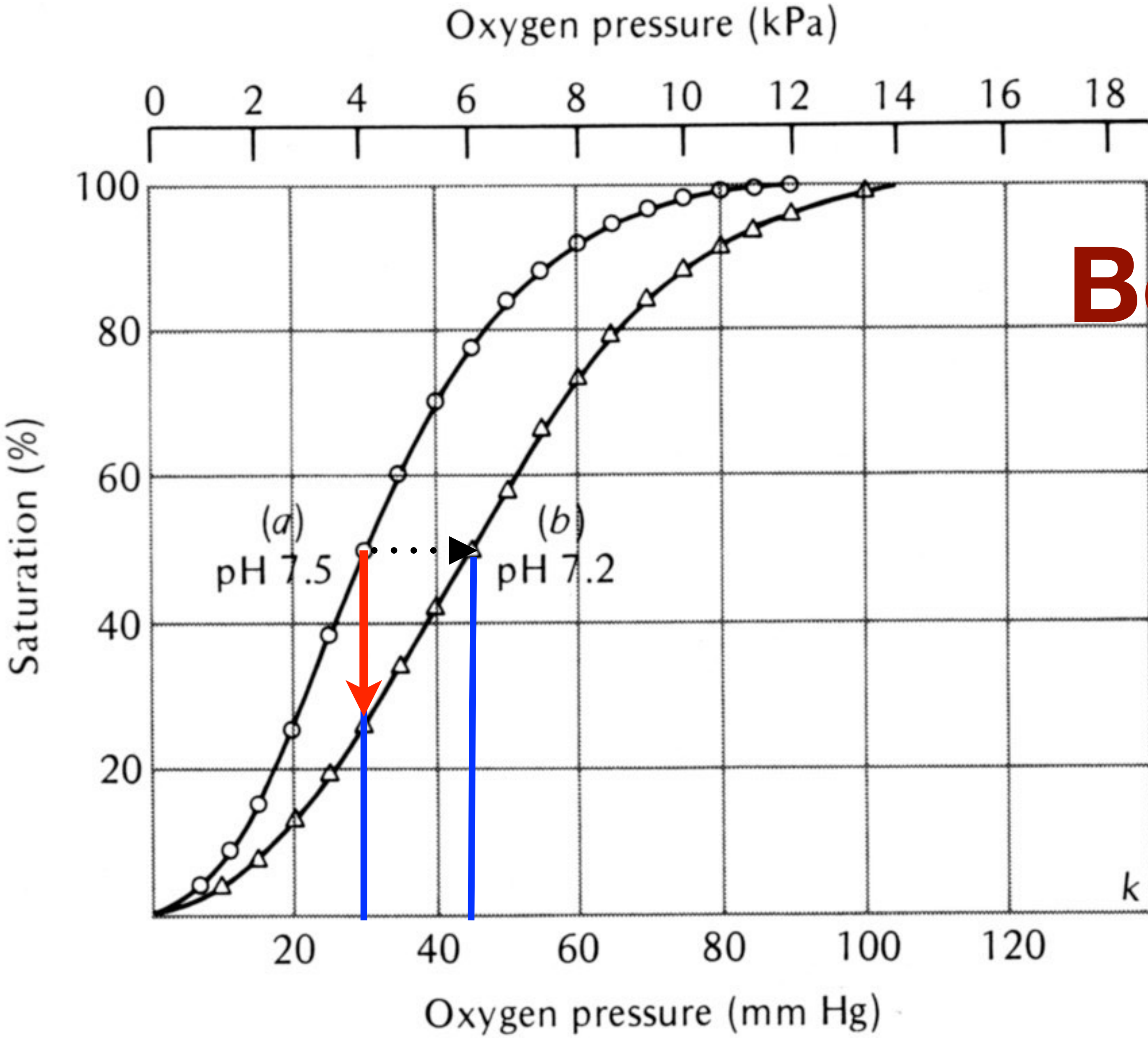
Subunits Bind O_2 Cooperatively



Bohr-Shift

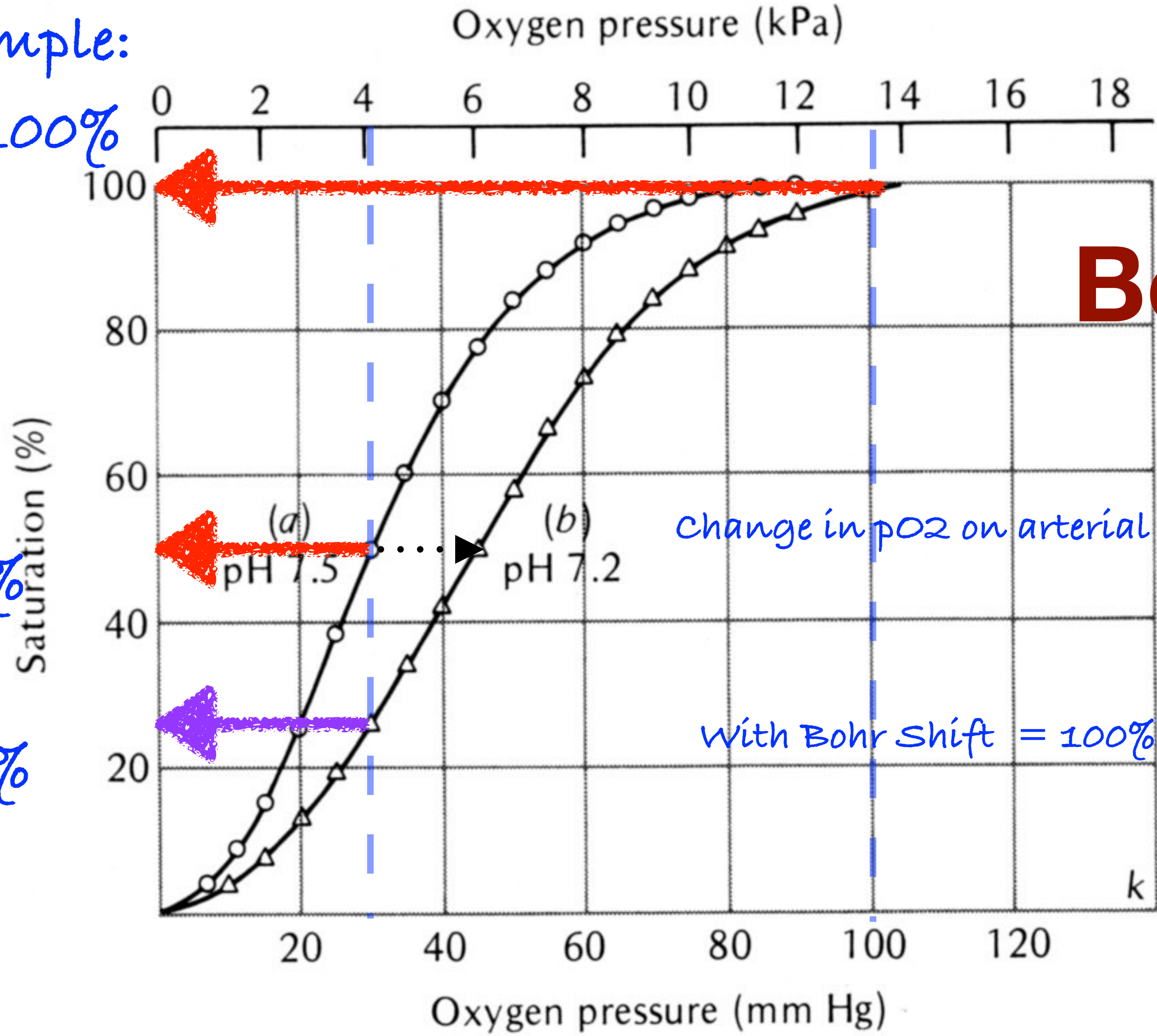
CO_2 and **pH** ***enhances*** dumping of oxygen at the tissues

Reversible, All-or-None

Subunits Bind O_2 Cooperatively

Example:

Hb 100%



Hb 50%

Hb 25%

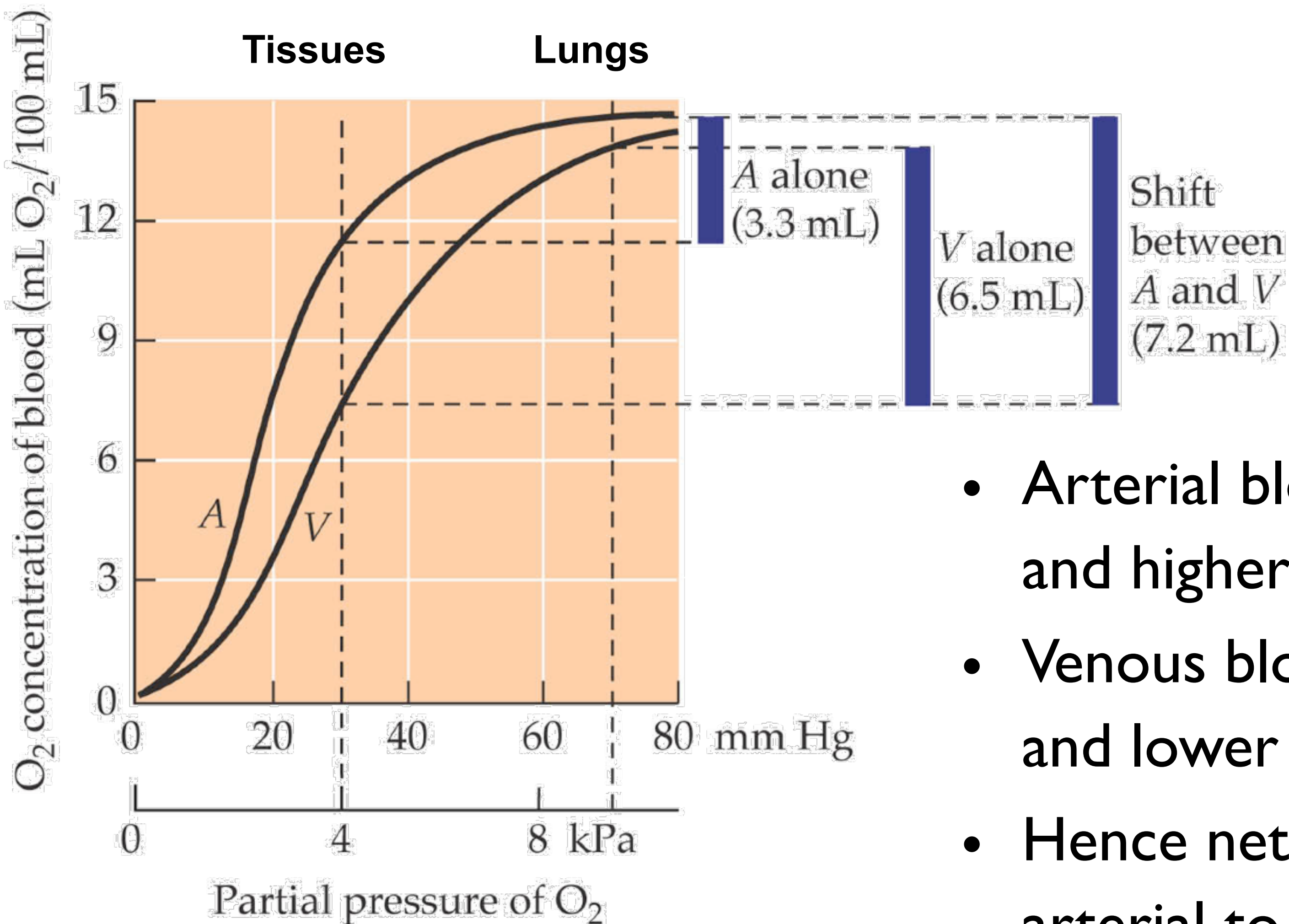
Bohr-Shift

Change in pO2 on arterial system = 100% - 50%
= 50% delivery

With Bohr Shift = 100% - 25% = 75% delivery

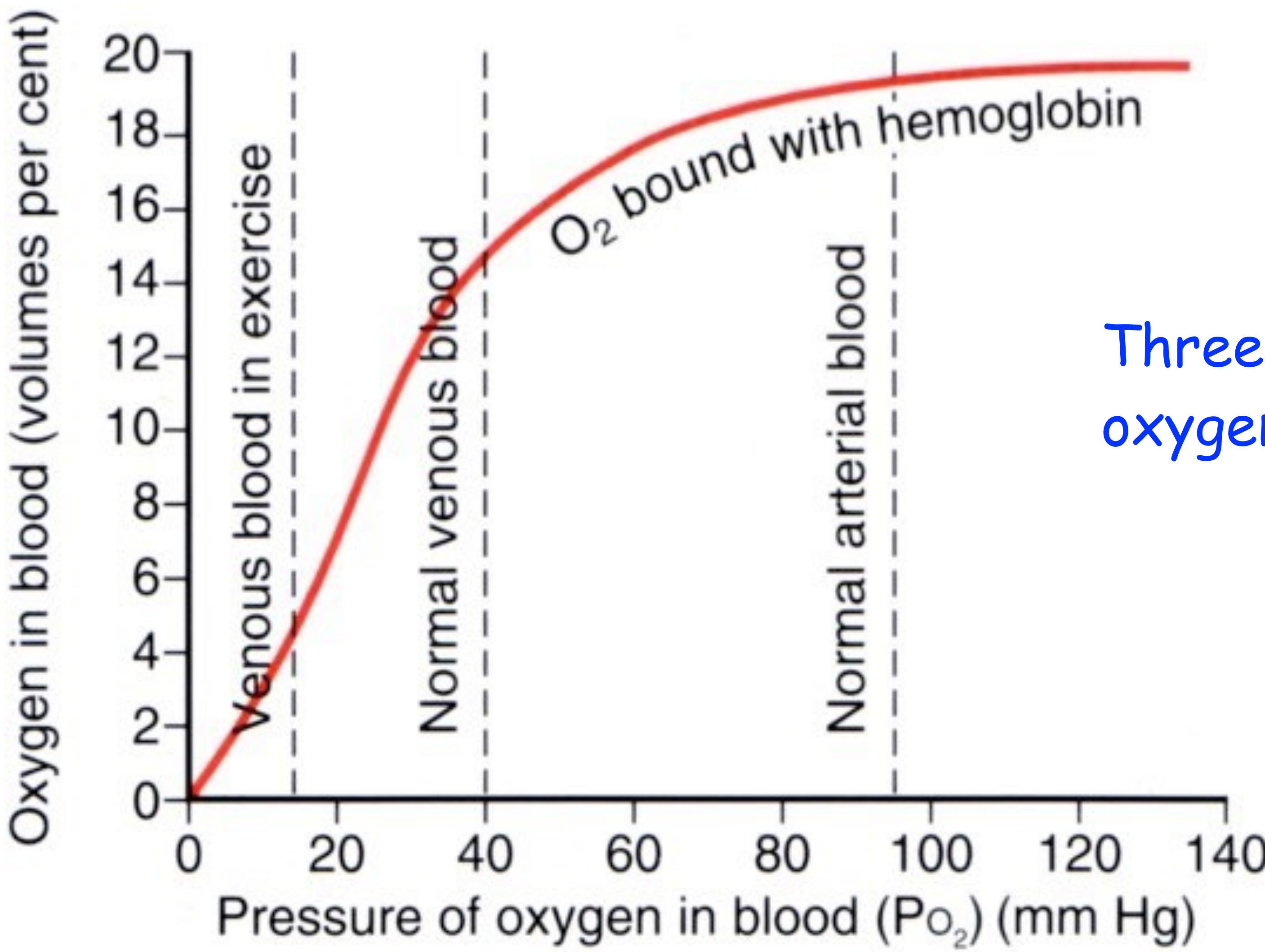
Reversible, All-or-None

Bohr Effect enhances O_2 delivery to tissues



- Arterial blood has lower CO_2 and higher pH than tissues
- Venous blood has higher CO_2 and lower pH than tissues
- Hence net O_2 delivery from arterial to venous blood enhanced by Bohr effect beyond expectations due to PO_2 alone.

Effect of Exercise on Oxygen Delivery

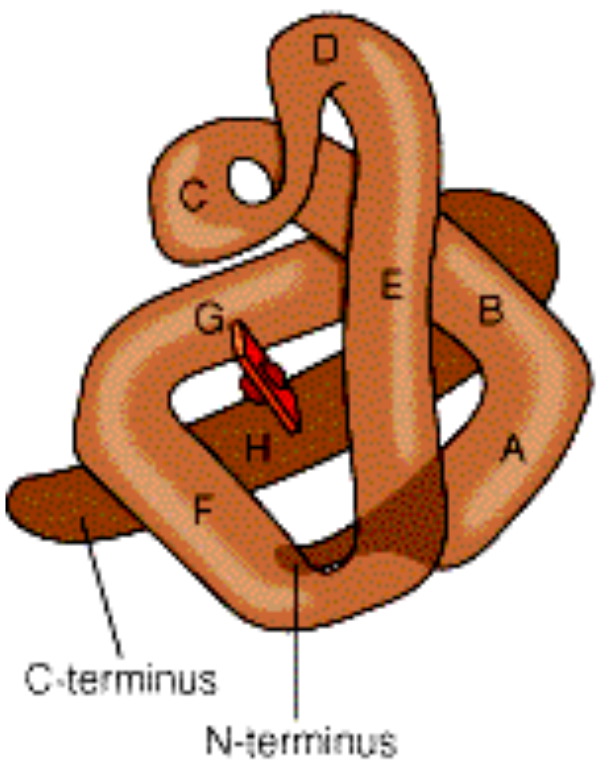


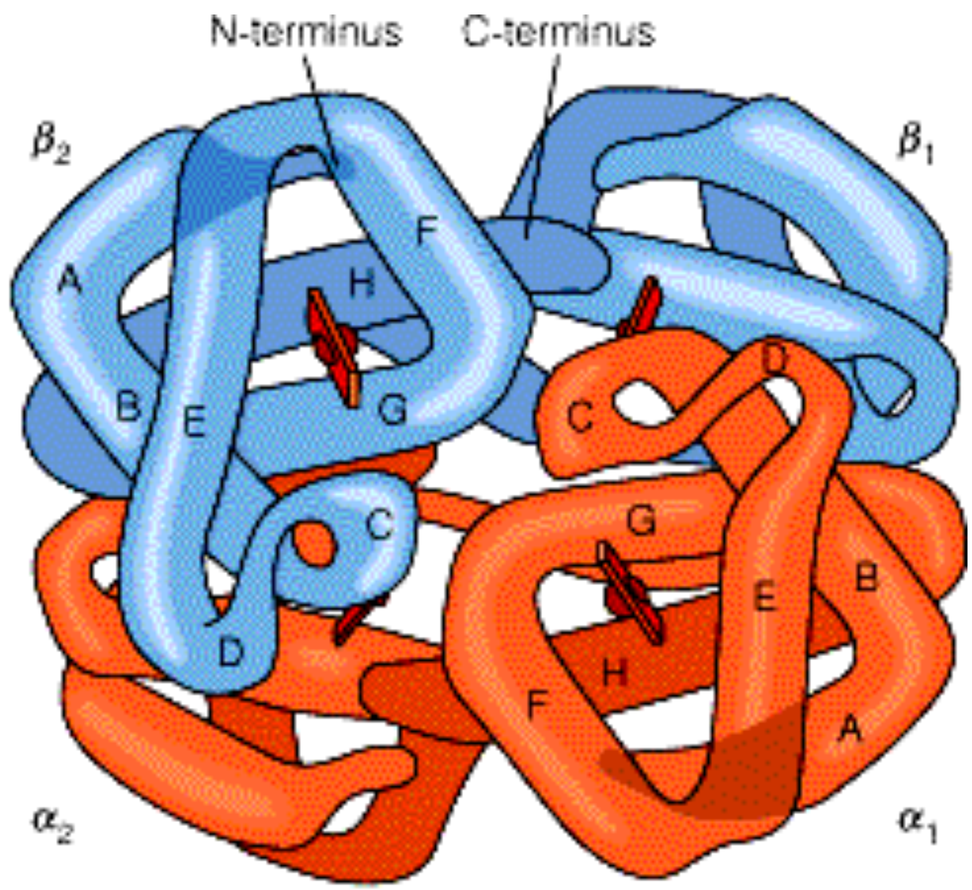
Three-fold increase in oxygen delivery.

Respiratory Pigments

Myoglobin: Monomer

within muscle cells



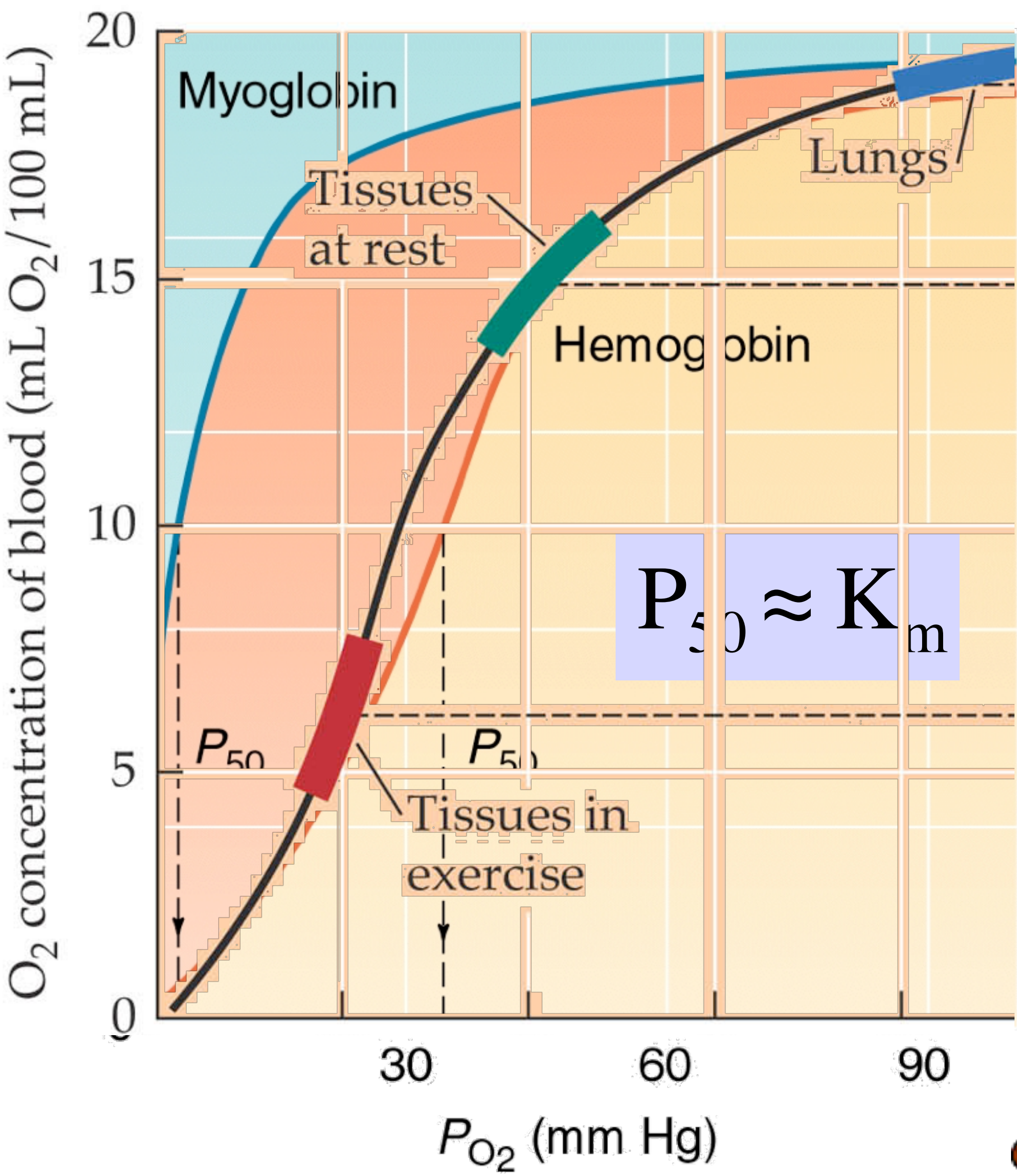


Hemoglobin: Tetramer

Heterodimer: (α1β1 & α2β2)

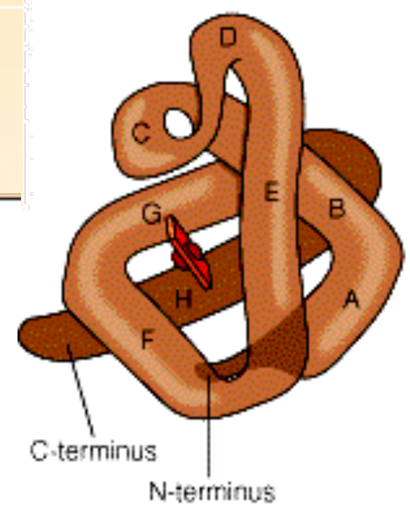
within red blood cells

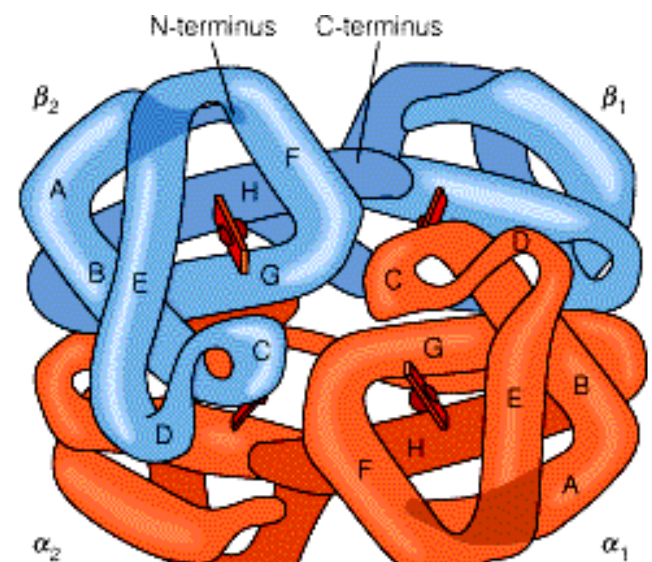
Oxygen binding of Myoglobin (Mb) and Hemoglobin (Hb)



$P_{50} \approx K_m$

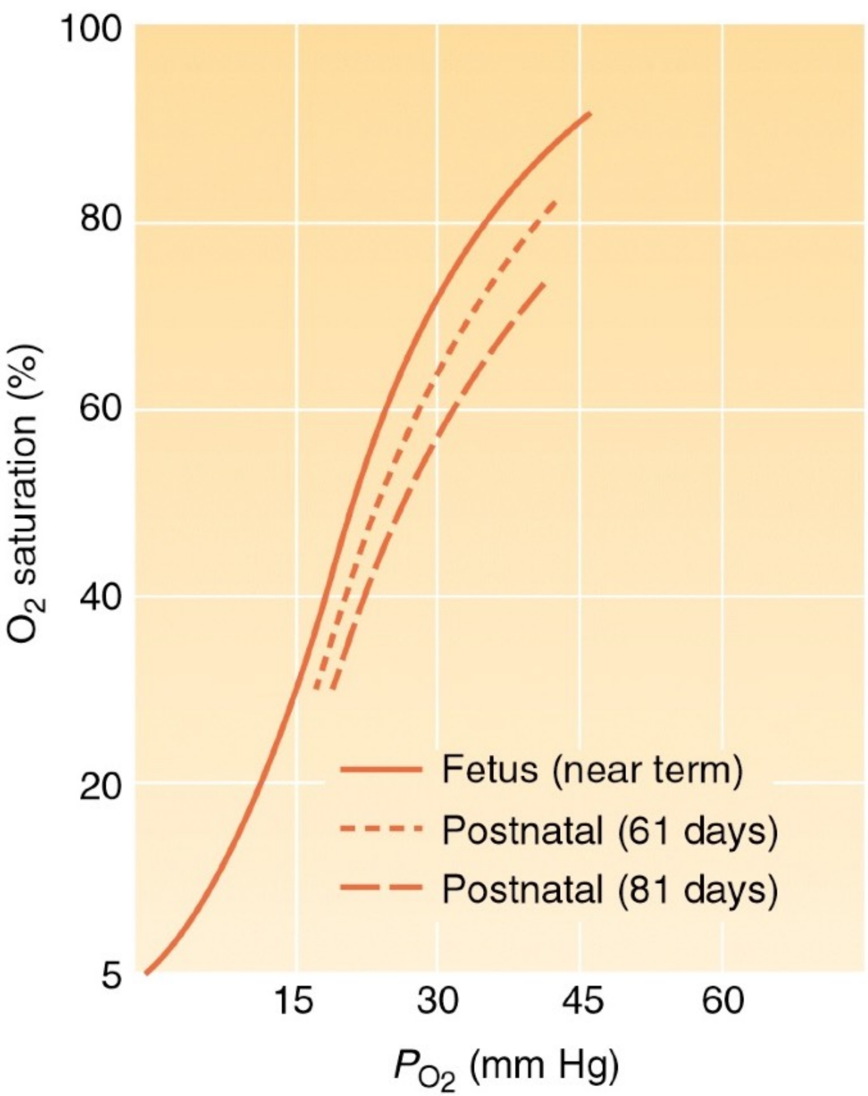
- Mb has higher affinity (lower P_{50}) than Hb
- Hb binds O_2 cooperatively
- Functional Result:
  O_2 always transferred from Hb to Mb at tissues

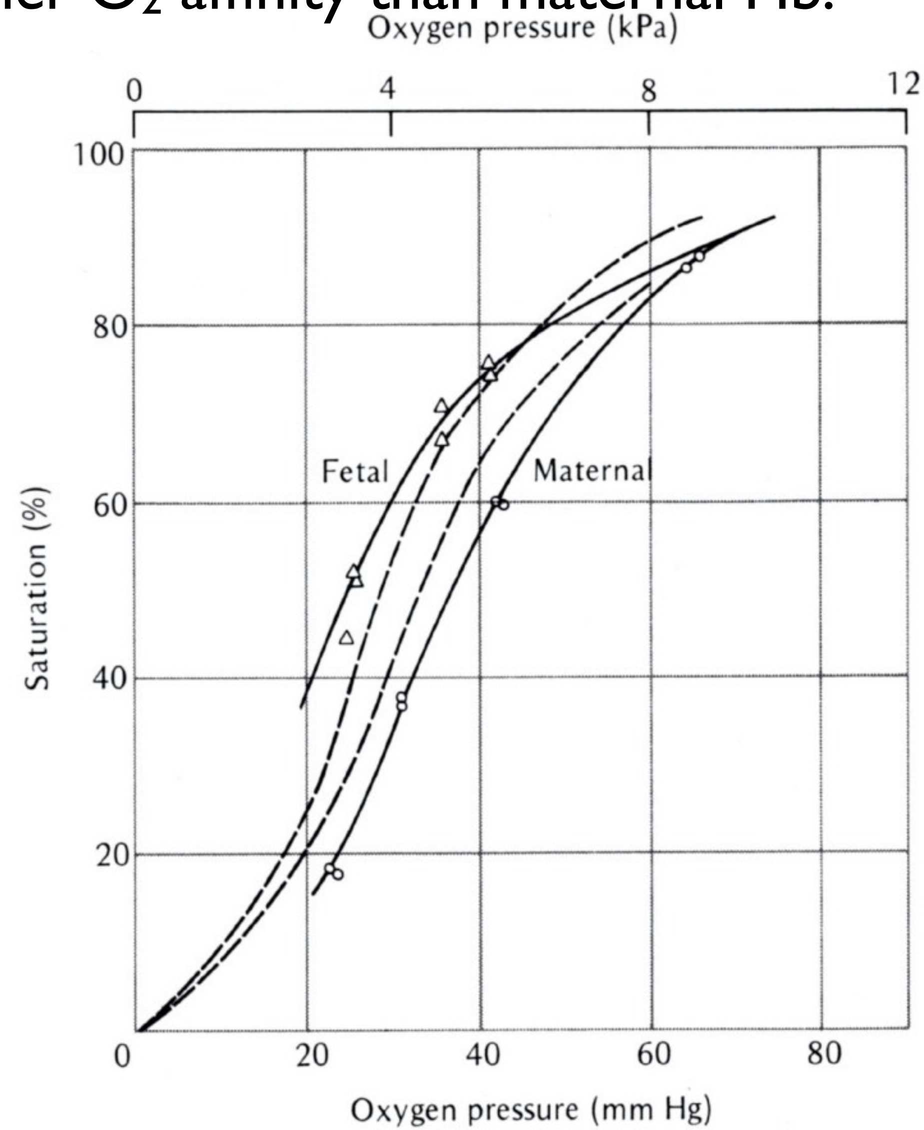




Fetal vs. Maternal Blood

- Hb subunits change with development in mammals
  - Fetal Hbs have lower P_{50} which is essential in O_2 transfer from mother to fetus
  - In other words, fetal Hb has higher O_2 affinity than maternal Hb.

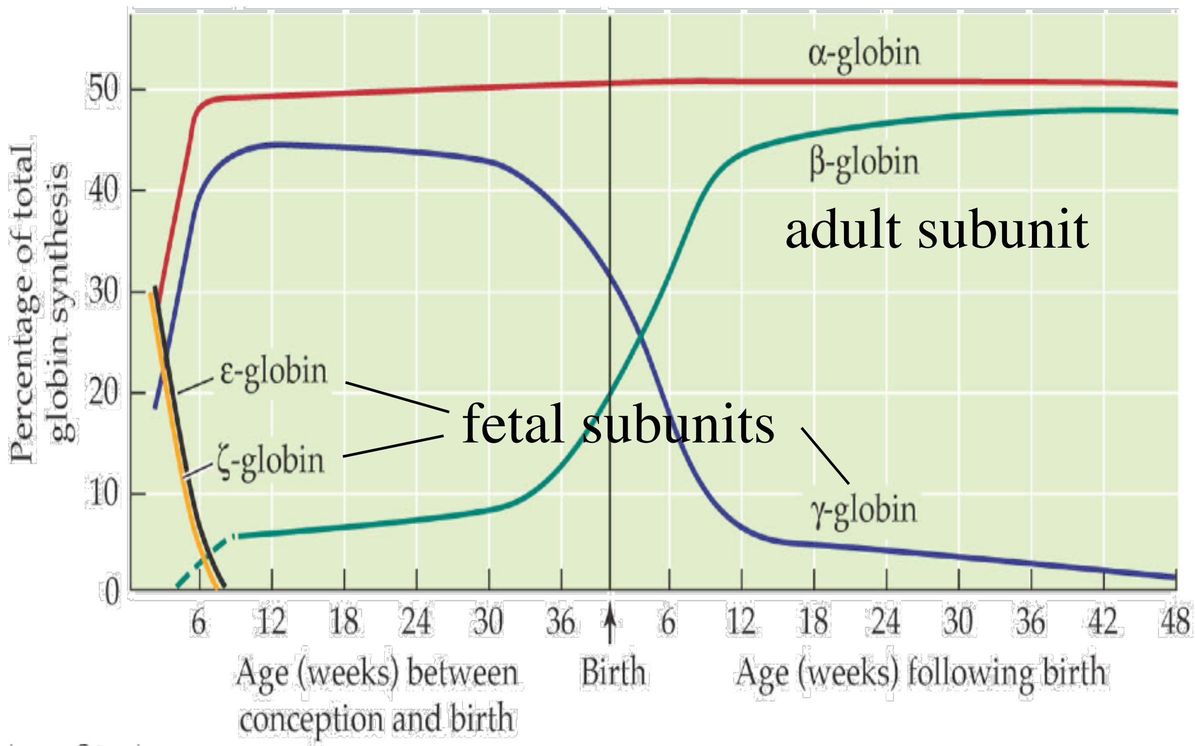


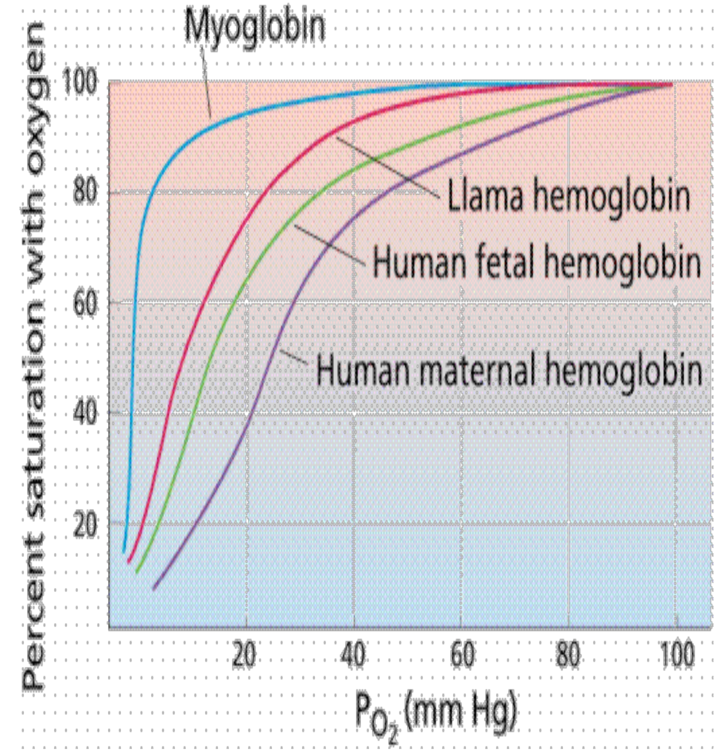


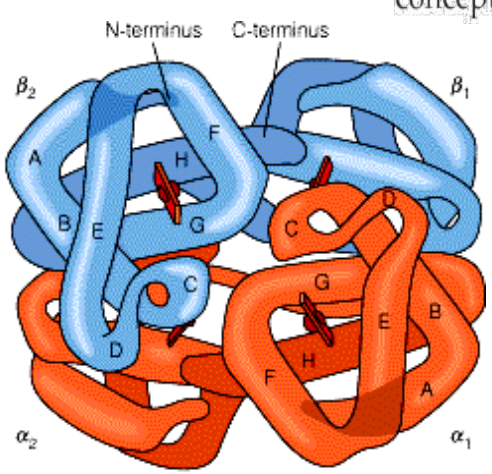
Zo

Developmental changes in Hb subunits and P_{50}

- Fetal O_2 affinity determined by globin subunit type

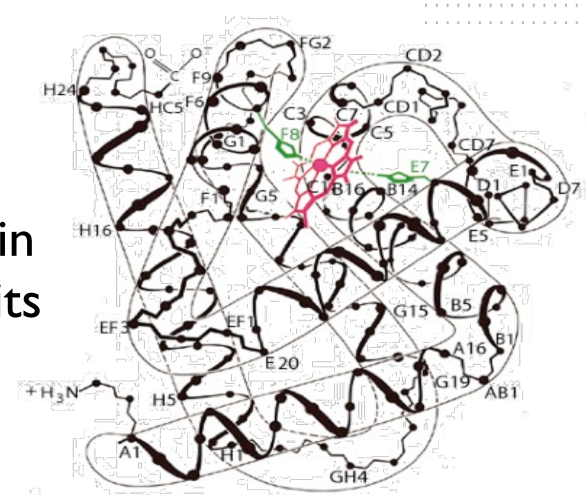






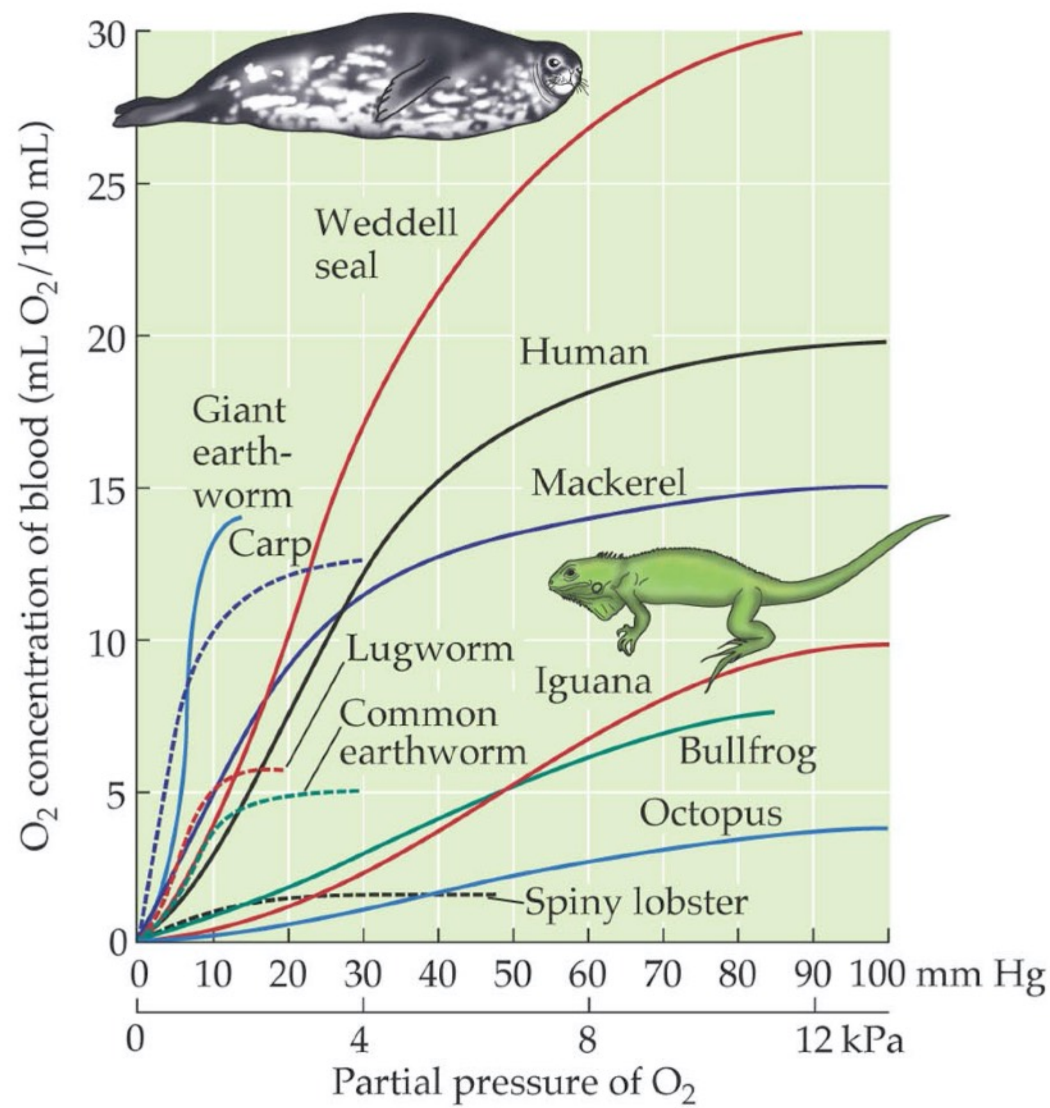
4 globin subunits

1 globin subunits



Huge interspecific variation in oxygen affinity of blood

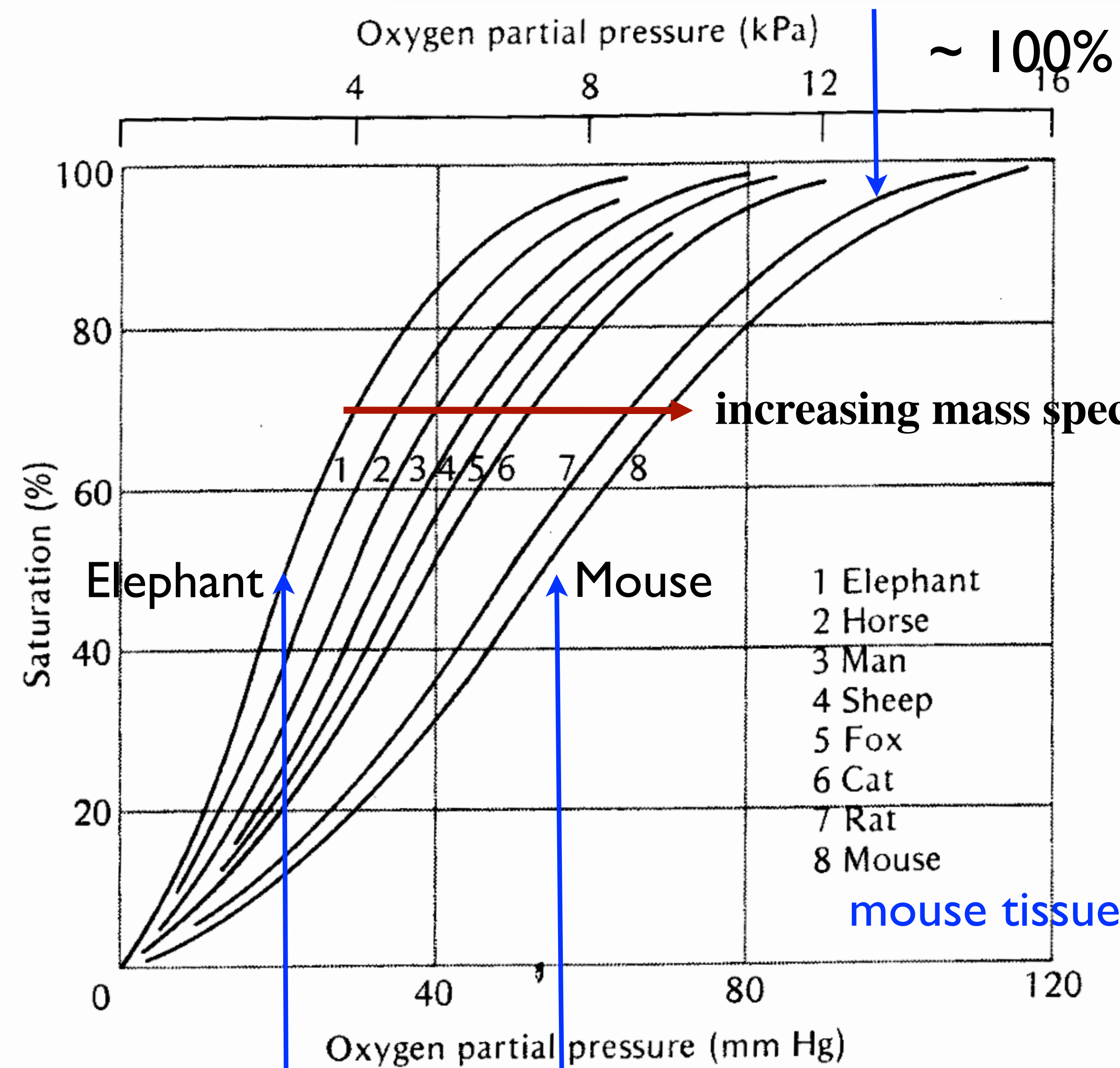
- Adaptation to
  - Temperature
  - Hypoxia
  - Activity
- Evolutionary factors
  - Respiratory protein class



Interspecific variation of Hb function

pO$_2$ of Mammalian Lung = 100 mm Hg (13kPa)

~ 100% saturated in lung

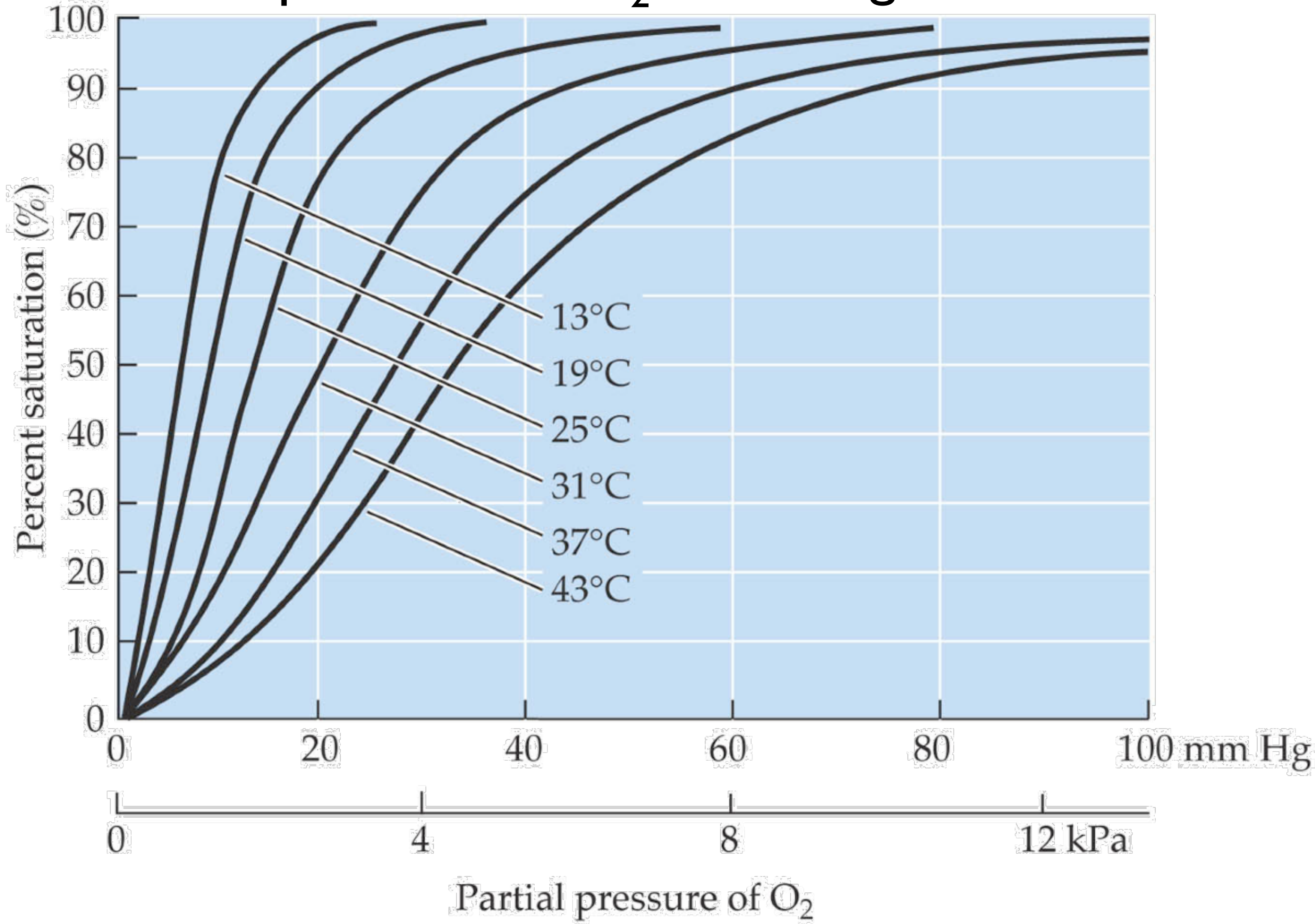


mouse tissues get more O$_2$ delivery

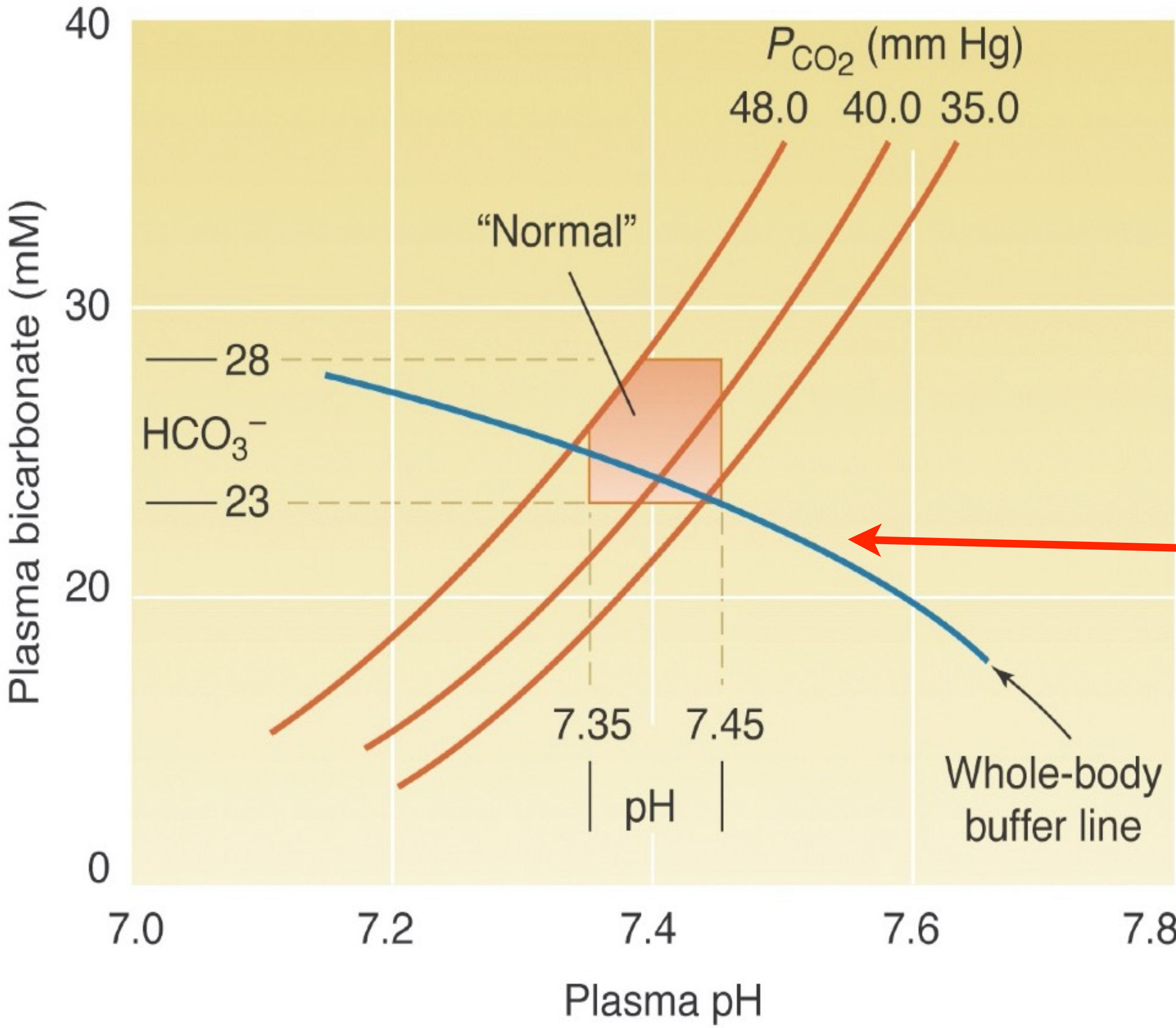
say O$_2$ is unloaded to tissues at 50% saturation

Increasing temperature increases Hb P_{50}

- Metabolic activity produces heat as a by-product
- Active muscles have higher temperatures than incoming blood
  - Thus, warmer temps will favor O_2 unloading



Ventilation can alter blood chemistry!



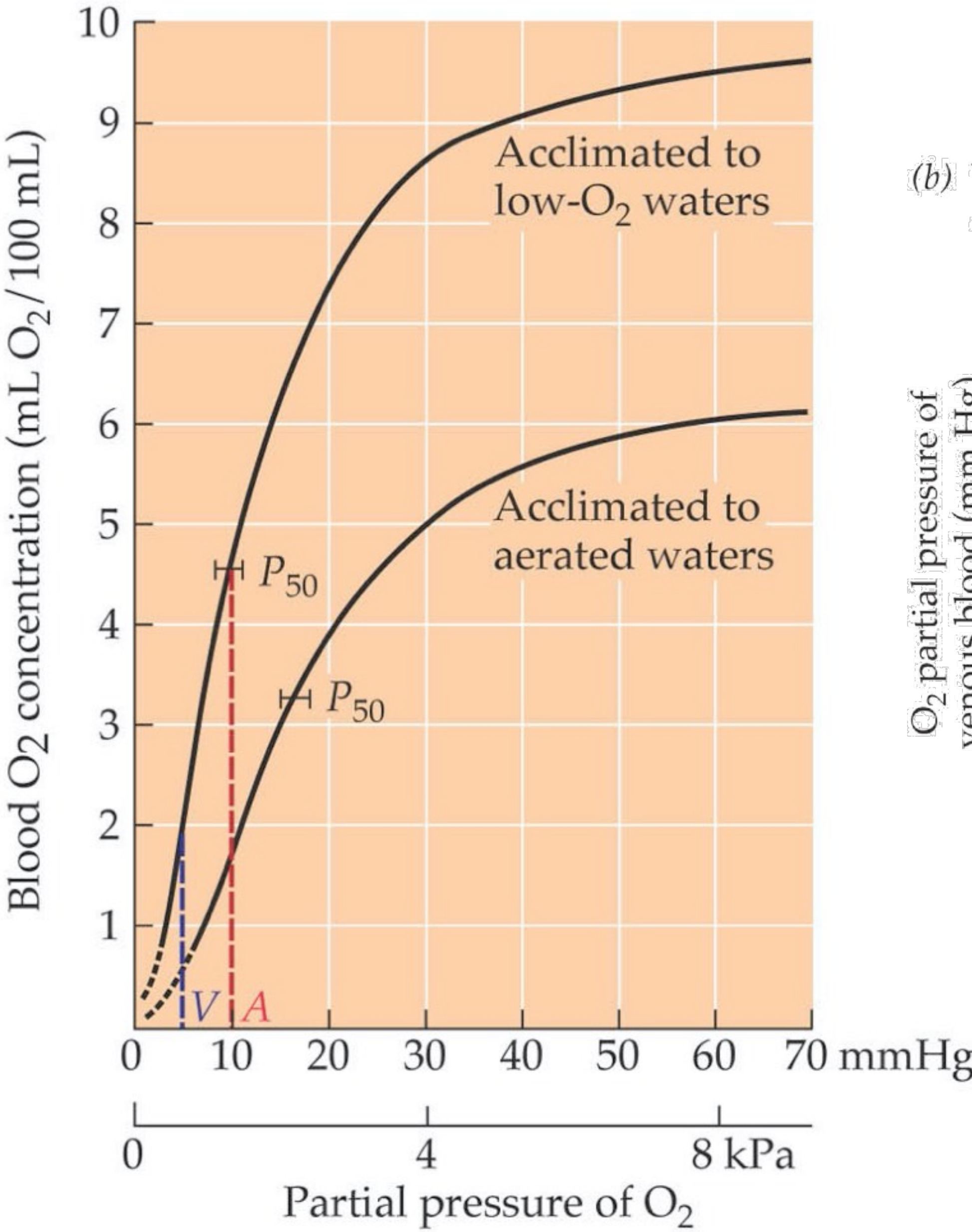
pH, Bicarb and PCO2 in human plasma usually w/ in narrow limits

hyper- and hypo-ventilation alters blood CO2 levels. THEN plasma pH and bicarb are altered beyond the normal range

CO2 levels are also affected by diet (Rq)

Acclimation of Hb function

Eels acclimated to hypoxic conditions



Trout acclimated to different temperatures

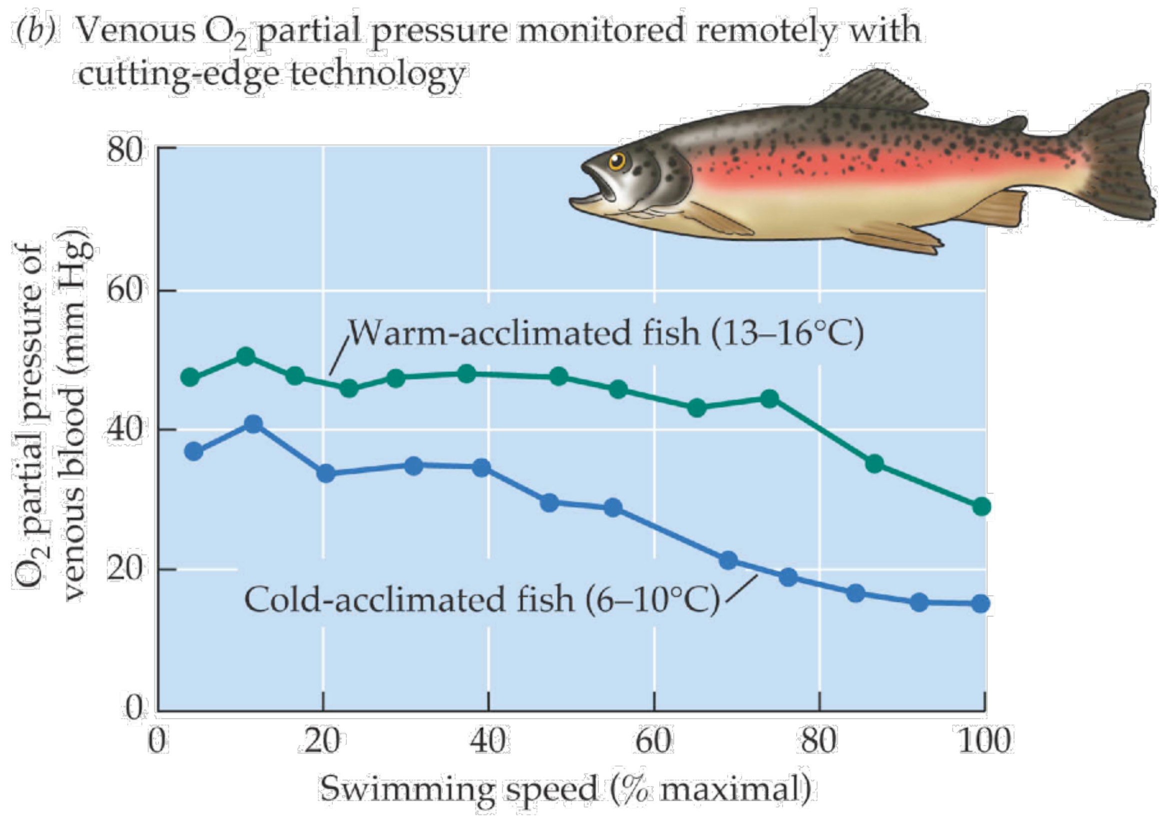


TABLE 2.2 Common respiratory pigments and examples of their occurrence in animals.

Pigment	Description	Molecular weight	Occurrence in animals
Hemocyanin	Copper-containing protein, carried in solution	300 000–9 000 000	Molluscs: chitons, cephalopods, prosobranch and pulmonate gastropods, not lamellibranchs Arthropods, crabs, lobsters Arachnomorphs: *Limulus, Euscorpius*
Hemerythrin	Iron-containing protein, always in cells, nonporphyrin structure	108 000	Sipunculids: all species examined Polychaetes: *Magelona* Priapulids: *Halicryptus, Priapulus* Brachiopods: *Lingula*
Chlorocruorin	Iron-porphyrin protein, carried in solution	2 750 000	Restricted to four families of Polychaetes: Sabellidae, Serpulidae, Chlorhaemidae, Ampharetidae; prosthetic group alone found in starfish (*Luidia, Astropecten*)
Hemoglobin	Iron-porphyrin protein, carried in solution or in cells; most extensively distributed pigment	17 000–3 000 000	Vertebrates: almost all, except leptocephalus larvae and some Antarctic fish (*Chaenichthys*) Echinoderms: sea cucumbers Molluscs: *Planorbis*, Pismo clam (*Tivela*) Arthropods: insects (*Chironomus, Gastrophilus*); crustacea (*Daphnia, Artemia*) Annelids: *Lumbricus, Tubifex, Arenicola, Spirorbis* (some species have hemoglobin, some chlorocruorin, others no blood pigment), *Serpula* (both hemoglobin and chlorocruorin) Nematodes: *Ascaris* Flatworms: parasitic trematodes Protozoa: *Paramecium, Tetrahymena* Plants: yeasts, *Neurospora*, root nodules of leguminous plants (clover, alfalfa)

Schmidt-Neilsen (1997)

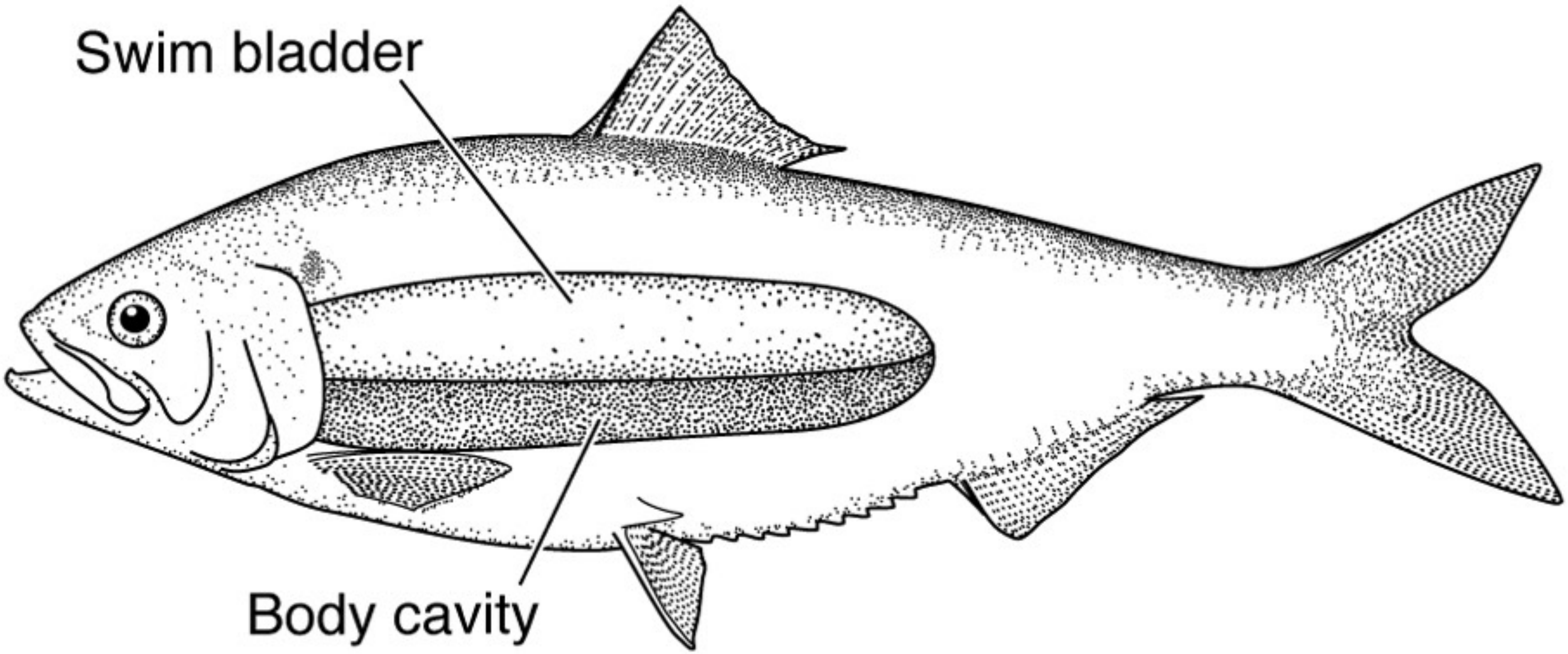
Evolutionary loss of respiratory proteins

- All fishes have respiratory pigments, except one: The Antarctic Icefish, *Chaenocephalus aceratus*

- Functional consequences - much less O_2 in blood
  - Although cold temp does incr. solubility
- Icefish adaptations:
  - Increased blood volume
  - Increased cardiac output
  - Low metabolic rate

Root Effect

Regulation of Buoyancy in Fishes with Swim Bladders/Lungs

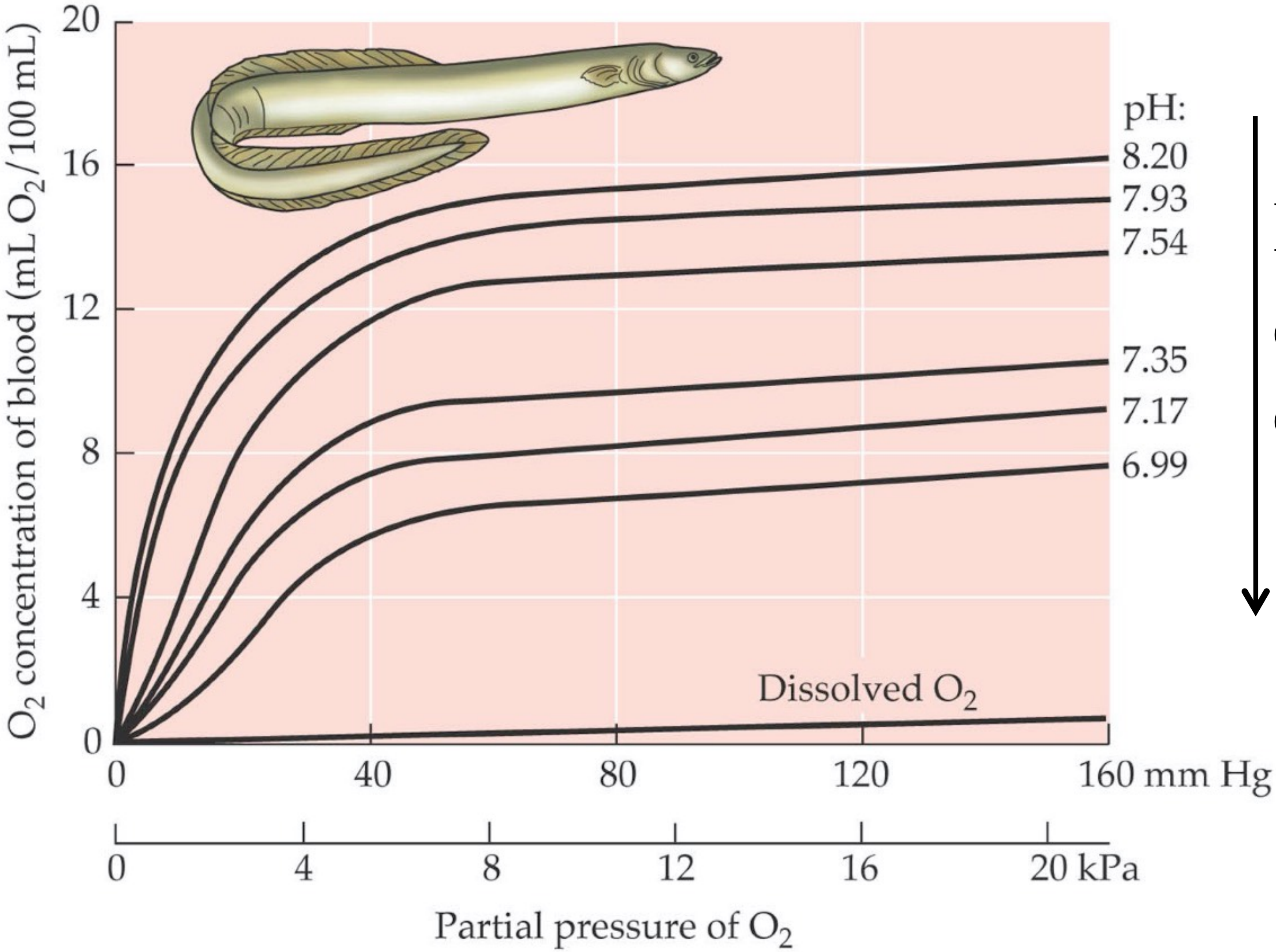


“Flesh” is slightly denser than water, so without generating any lift, a fish will sink. Most living fishes (except chondricthyans) have swim bladders or lungs to regulate buoyancy (by controlling the amount of gas inside).

Neutral buoyancy = having the same average density as water so that animal does not sink or float in the water column.

Root Effect

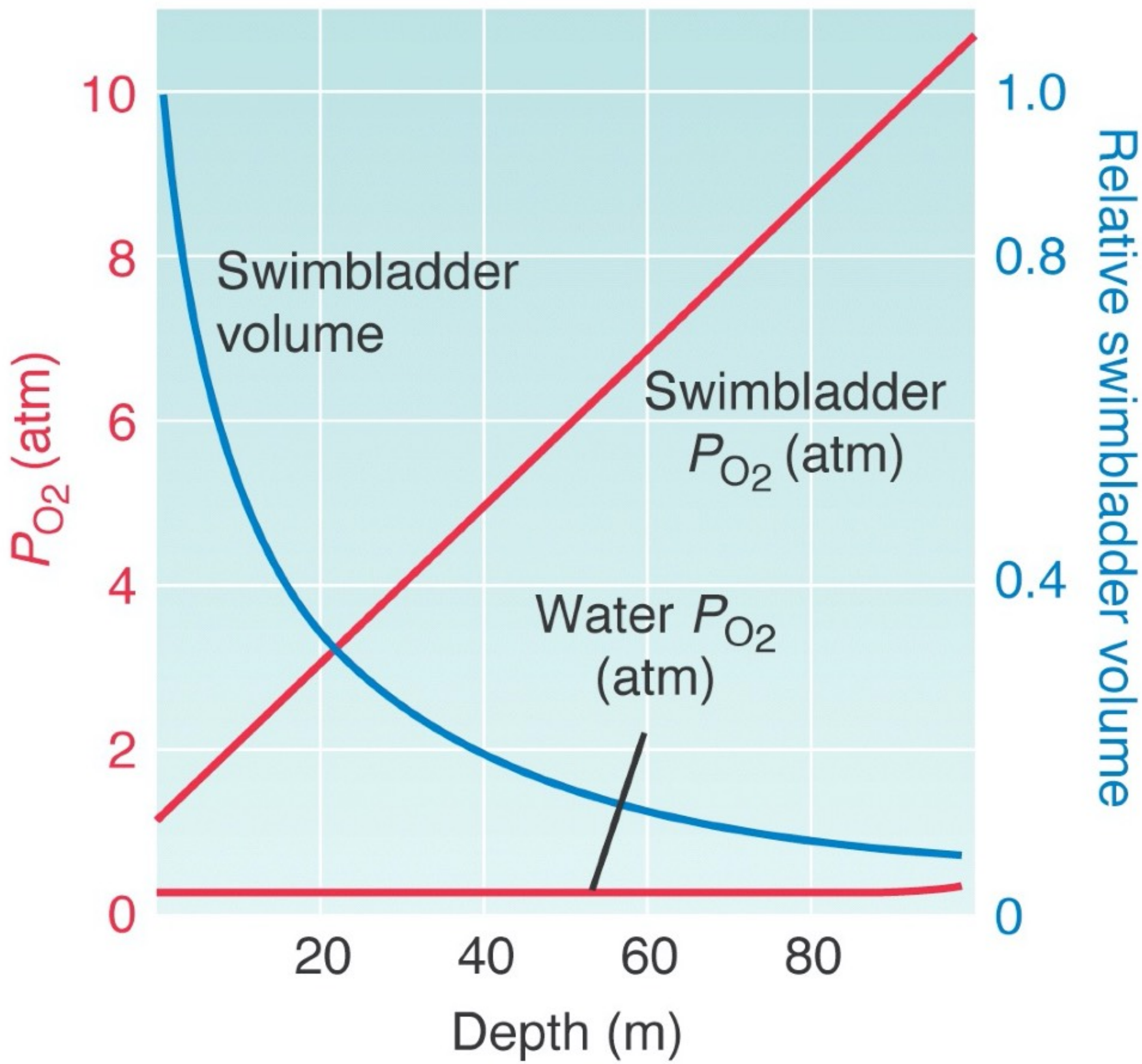
Under the root effect, Hb unloads O2



Hb O_2 carrying capacity

Root Effect

The swim bladder challenge: working against huge O_2 gradients



- Plot assumes no change in swimbladder gas content with depth
- Result: must move O_2 into swim bladder against a pressure gradient of many atmospheres at depth

Root Effect

How to get O2 into swim bladder against a high pressure?

say swimbladder contains O_2 at high pressure (100atm for 1000m depth), but arterial O2 tension is no more than 0.2 atm.

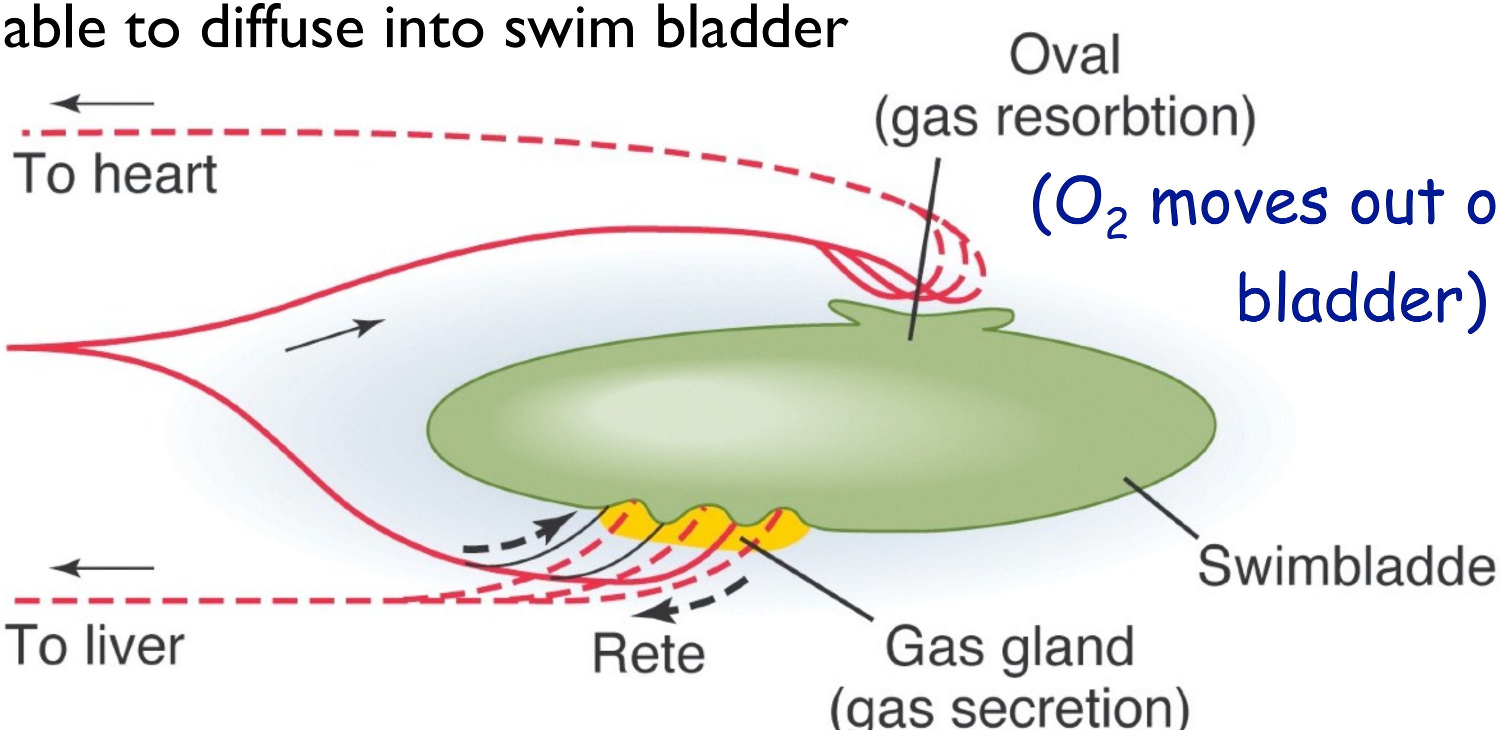
Gas secretion produces lactic acid

Lactic acid enters blood and reduces affinity for O2 (Root effect)

Drives O2 off the hemoglobin

Countercurrent flow tends to concentrate lactic acid and O2 concentration effects at the rete capillaries/gas gland interface

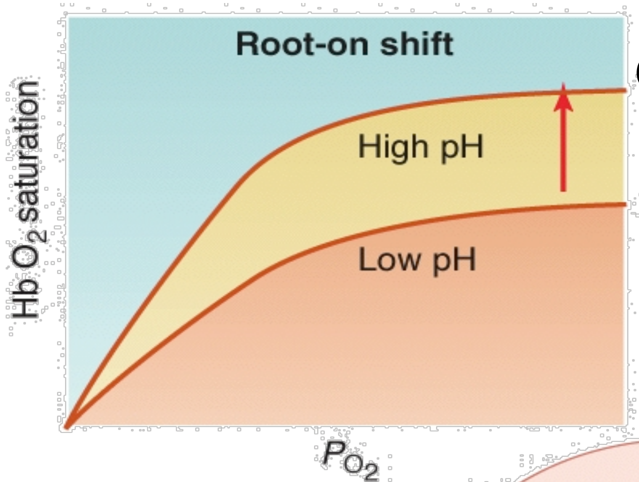
Eventually, O_2 able to diffuse into swim bladder



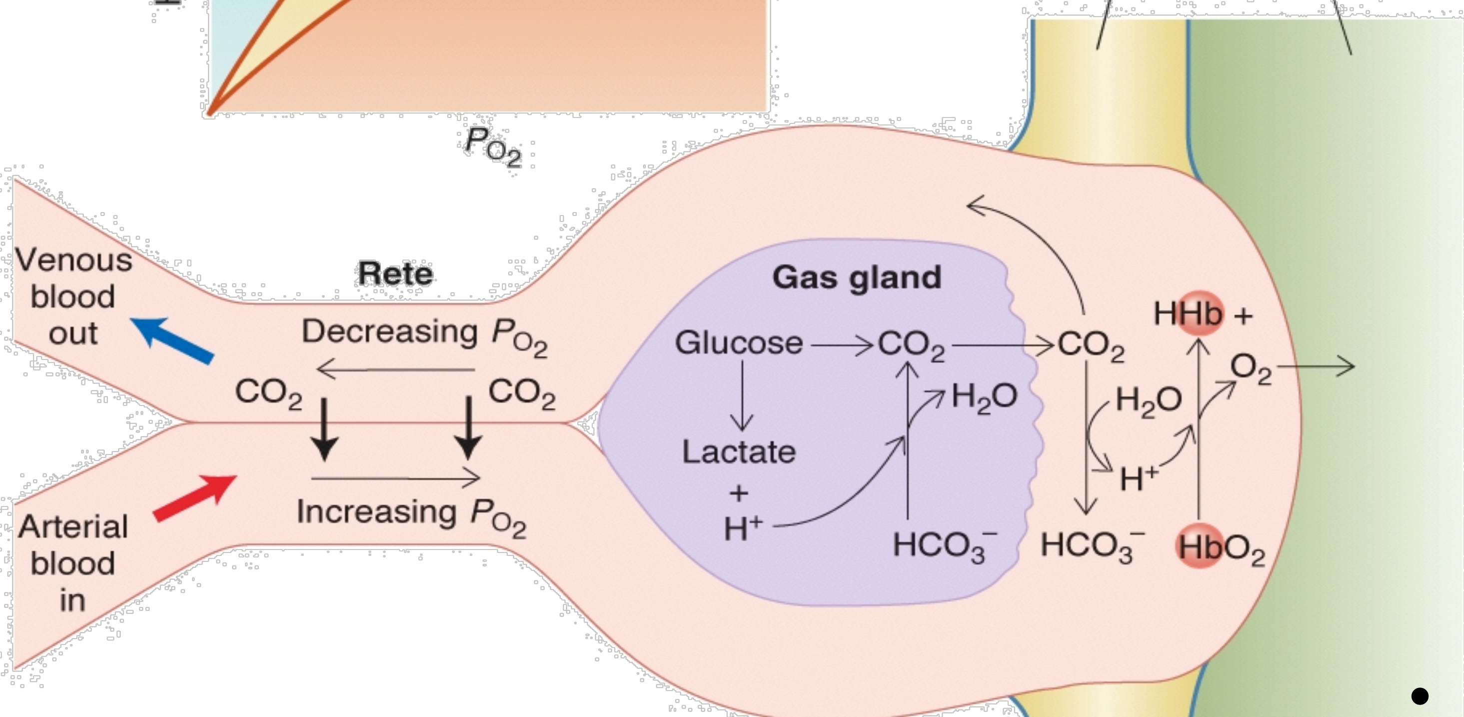
(O_2 moves out of swim bladder)

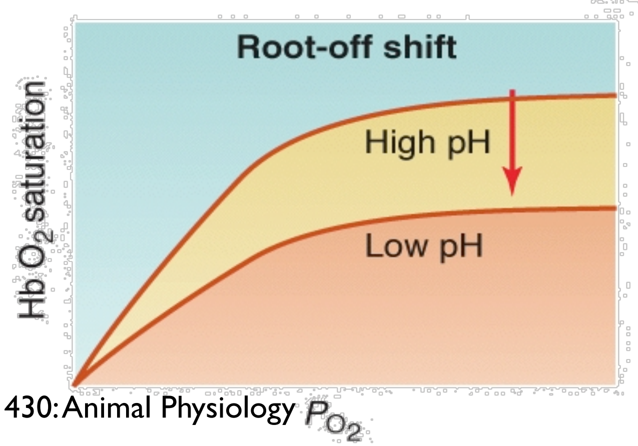
(O_2 moves into swim bladder)

Root Effect



Oxygen bound to Hb: Decreases P_{O_2}





Oxygen released from Hb: Increases P_{O_2}

Root shifts are key

- Gas Gland:
  - Glycolysis H^+ production
  - Pentose phosphate CO_2 production
  - Activity decreases pH and increases ionic concentration
    - Root-off shift lower O_2 solubility
- Rete:
  - counter current gas exchanger for CO_2
    - Drives CO_2 into arterial blood causing Root-off

The Bohr Effect