Chapter 4

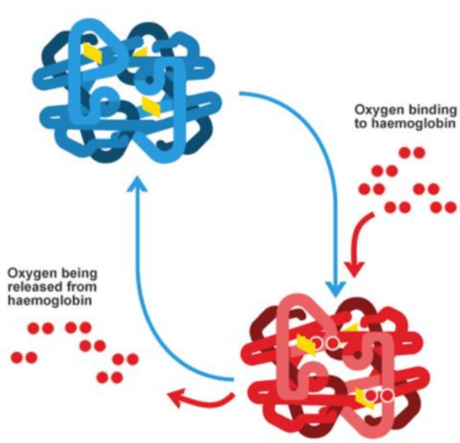
Oxygen transport in biological system

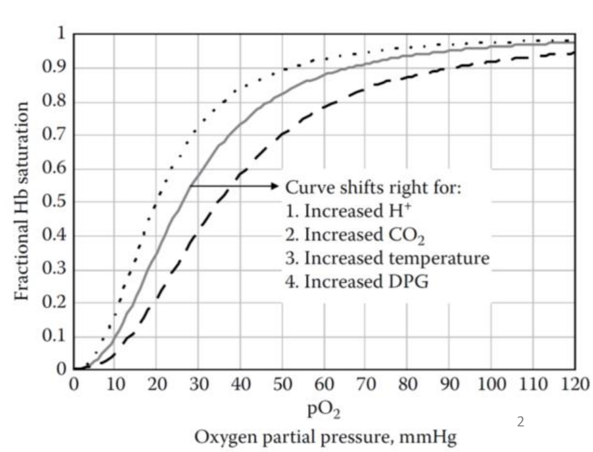
Lecture 9

1

Other factors that can affect the oxygen-hemoglobin dissociation curve

Other molecules, such as H^+, CO_2, and organic phosphates (DPG) also bind on specific sites on the hemoglobin molecule and greatly affect its oxygen binding ability.





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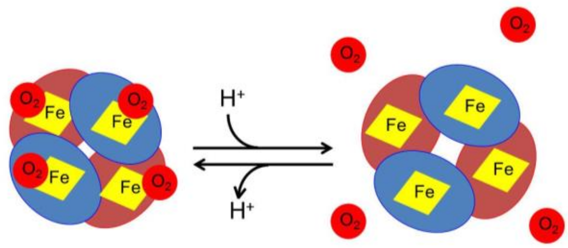
Lowering the pH shifts the oxygen dissociation curve to the right. This decreases, for a given p_{O2}, the oxygen affinity of the hemoglobin.



CO_2 at increased levels and constant pH also lowers the oxygen affinity of hemoglobin.

carbonic anhydrase

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$$

carbon dioxide + water — carbonic acid — bicarbonate + hydrogen ion

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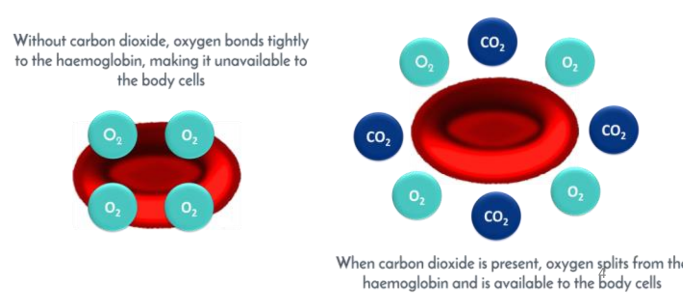
In metabolically active tissues such as the muscle, the higher levels of CO_2 and H^+ in the capillaries have a beneficial effect by promoting the release of oxygen. This is called the Bohr effect.

The oxygen hemoglobin dissociation curve shifts to the right when the partial pressure of carbon dioxide (p_{CO2}) is increased.

Under these conditions, CO_2 can reversibly bind to hemoglobin displacing oxygen to form a compound known as carbaminohemoglobin.

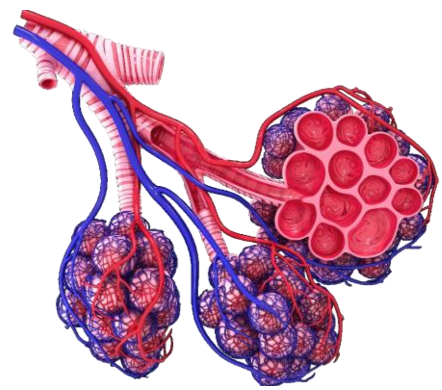
The reverse process also occurs, oxygen binding to hemoglobin has the ability to displace CO_2 that is bound to hemoglobin.



This is important in both tissues and in the lungs.

In the tissue capillaries, the higher p_{CO2} in the tissue space results in the formation of carbaminohemoglobin, which increases the release of oxygen from hemoglobin.

Within the lungs, where the p_{O2} is much higher within the gas space of the alveoli, there is a displacement of CO_2 from the hemoglobin by oxygen. This is called the Haldane effect.



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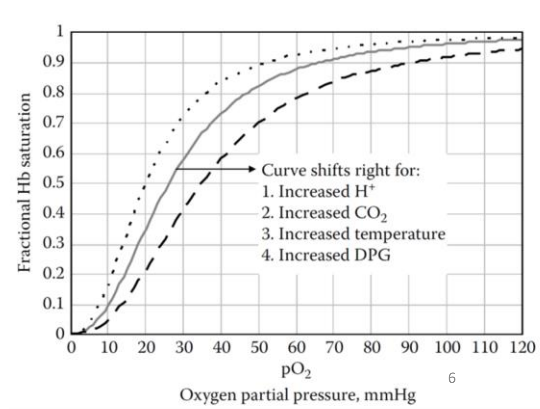
The existence of organicphosphate (DPG) reduces the oxygen binding capacity as shown in Figure since it binds to hemoglobin.

Without DPG, the value of P_{50} is reduced to about 1 mmHg.

This makes it very difficult for hemoglobin to release the bound oxygen at low values of the p_{O2}.

Without DPG, there would be essentially no release of oxygen in the physiological range of p_{O2} values from 40 to 95 mmHg. Therefore, the presence of DPG within the RBC is vital for hemoglobin to perform its oxygen carrying role.



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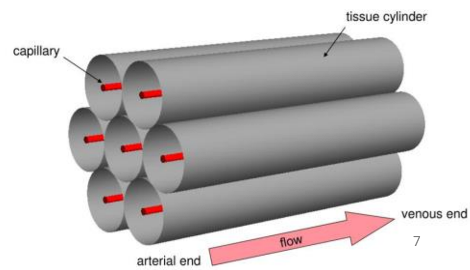
Tissue oxygenation

Hemoglobin rich with oxygen within the red blood cells (RBCs) is transported by the circulatory system to the capillaries where the oxygen is able to diffuse out of the capillary to the tissue that surrounds each capillary.

The consumption of oxygen by the tissues creates the driving force for oxygen diffusion and also causes the p_{O2} level to decrease along the length of the capillary, which causes a release of oxygen from the hemoglobin in the blood.

$$HB(O_2)_n \overset{k_{-1}}{\underset{k_1}{\longleftrightarrow}} HB + nO_2$$

Assume the capillary bed and the surrounding tissue are well mixed with respect to oxygen.



A steady-state oxygen mass balances for the blood region:

$$0 = qV_T\left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - qV_T\left(C_{O2} + C'_{HbO}\right)\Big|_{venous} - P_C S_C\left(C_{O2}\Big|_{venous} - \bar{C}_{O2}\right)$$

V_T is the volume of the tissue space (including the capillaries).

q is the tissue blood perfusion rate (Q/V_T) in ($\frac{cm^3_{blood}}{cm^3_{tissue}.min}$).

Q is the blood flow rate in ($\frac{cm^3_{blood}}{min}$).

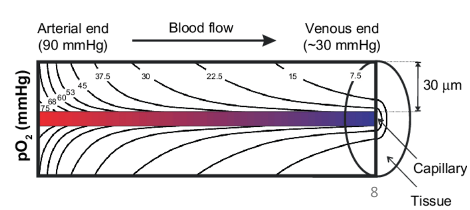
C_{O2} is the dissolved oxygen concentration in the blood (μM).

C'_{HbO} is the oxygen concentration in the blood bound to hemoglobin (μM)

$\bar{C}_{O2}$ is the concentration of oxygen in the tissue (μM).

P_C is the permeability of oxygen through the capillary wall in (cm/s).

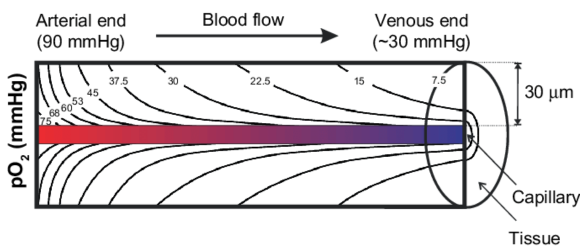
S_C is the total surface area of the capillaries (cm^2).



$$0 = qV_T\left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - qV_T\left(C_{O2} + C'_{HbO}\right)\Big|_{venous} - P_C S_C\left(C_{O2}\Big|_{venous} - \bar{C}_{O2}\right)$$

The convective terms (containing q) in the equation include oxygen transported in the dissolved states as well as that bound to hemoglobin.

However, the mass transfer of oxygen across the capillary wall is only based on the difference between the dissolved oxygen concentration in the blood and that within the tissue.



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A steady-state oxygen mass balances for the tissue region:

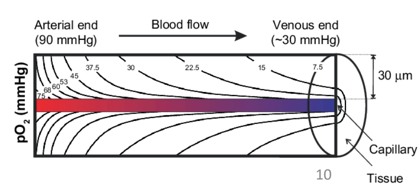
$$0 = P_C S_C\left(C_{O2}\Big|_{venous} - \bar{C}_{O2}\right) - V_T\Gamma'_{O2}$$

Γ'_{O2} is the tissue oxygen consumption rate ($\frac{\mu M}{s}$) on a tissue volume basis.

$$\Gamma'_{O2} = \varphi\Gamma_{O2}$$

Add the two equations (A steady-state oxygen mass balances for the tissue and blood) and solve to give the value of Γ'_{O2}:

$$\Gamma'_{O2} = q\left[\left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - \left(C_{O2} + C'_{HbO}\right)\Big|_{venous}\right]$$



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Nominal tissue oxygen consumption rate

To solve the last equation for the oxygen consumption rate of tissue requires a value of the tissue blood perfusion rate, q.

This table provides representative values for the blood flow to various organs and tissues in the human body.

The blood perfusion is expressed in ($\frac{mL}{g_{tissue} \cdot min}$).

A nominal tissue perfusion rate is on the order of ($\frac{0.5\ mL}{cm^3_{tissue} \cdot min}$).

(assuming the $\rho_{tissue} \approx 1\ g/cm^3$).

Organ	Percent	mL min^{-1}	mL min^{-1} (100 gm of tissue)$^{-1}$
Brain	14	700	50
Heart	4	200	70
Bronchial	2	100	25
Kidneys	22	1100	360
Liver	27	1350	95
Portal	(21)	(1050)	
Arterial	(6)	(300)	
Muscle (inactive state)	15	750	4
Bone	5	250	3
Skin (cool weather)	6	300	3
Thyroid gland	1	50	160
Adrenal glands	0.5	25	300
Other tissues	35.5	175	1.3
Total	100.0	5000	

The nominal arterial and venous p_{O2} levels are 95 and 40 mmHg.

We can use this equation to obtain an estimate of the Γ'_{O2}.

$$\Gamma'_{O2} = q\left[\left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - \left(C_{O2} + C'_{HbO}\right)\Big|_{venous}\right]$$

Oxygen Partial Pressure, pO_2, mmHg	Fractional Hemoglobin Saturation
10	0.12
20	0.28
30	0.56
40	0.72
50	0.82
60	0.88
70	0.91
80	0.93
90	0.95
100	0.96

Example

Calculate the oxygen consumption rate in $\mu M/s$ using the previous nominal values for the blood perfusion rate and the arterial and venous p_{O2} levels.

$$\Gamma'_{O2} = q\left[\left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - \left(C_{O2} + C'_{HbO}\right)\Big|_{venous}\right]$$

The nominal arterial and venous p_{O2} levels are 95 and 40 mmHg.

A nominal tissue perfusion rate is ($\frac{0.5\,mL}{cm^3_{tissue}.min}$).

$$\Gamma'_{O2} = 0.5[8630 - 6478]\frac{1\ min}{60\ s}$$

$$\Gamma'_{O2} = 17.93\ \mu M_{tissue}/s$$

Oxygen Property	Arterial	Venous
Partial pressure (tension), pO$_2$, mmHg	95	40
Dissolved O$_2$, μM	130	54
As oxyhemoglobin, μM	8500	6424
Total effective (dissolved + oxy – Hb), μM	8630	6478

Other useful data: H_{oxygen} = 0.74 mmHg μM^{-1}; saturated oxyhemoglobin = 8800 μM; P_{50} ~ 26 mmHg; n = 2.34.

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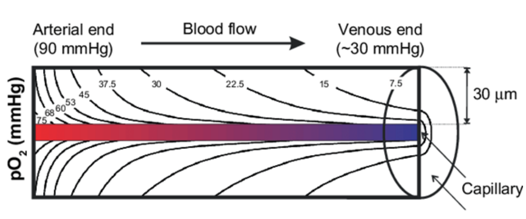
Calculating the venous p_{O2} for a given oxygen demand

If the value of Γ'_{O2} is known for a given tissue, then the last equation can be rearranged to solve for the change in blood oxygenation in order to provide the oxygen demands of the tissue:

$$\Gamma'_{O2} = q\left[\left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - \left(C_{O2} + C'_{HbO}\right)\Big|_{venous}\right]$$

$$\left(C_{O2} + C'_{HbO}\right)\Big|_{venous} = \left(C_{O2} + C'_{HbO}\right)\Big|_{arterial} - \frac{\Gamma'_{O2}}{q}$$



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The islets of Langerhans are a specialized cluster of cells located within the pancreas.

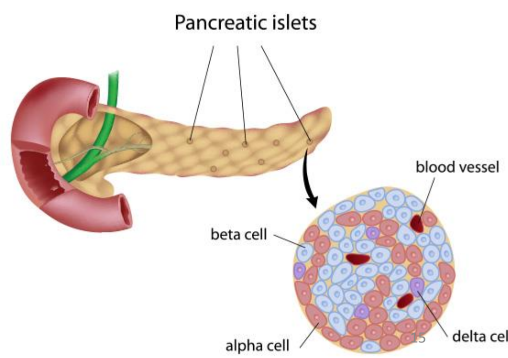
The islets is 1%–2% of the pancreatic tissue mass.

The islet is responsible for the control of glucose metabolism through the secretion of the hormones insulin (β cells) and glucagon (α cells).

The loss of the β cells results in type I or insulin-dependent diabetes.

An islet of Langerhans is only about 150 µm in diameter.

The single islet blood flow is about 7 nL/min, which gives a perfusion rate of 4 mL/cm³. min.

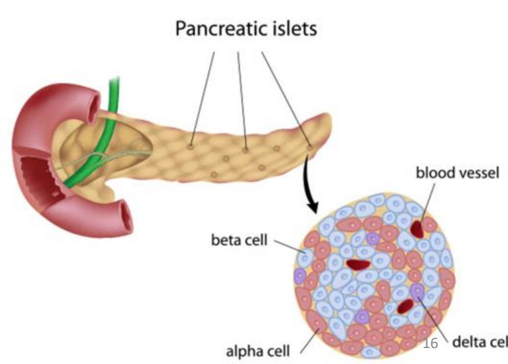


This value is about four times the blood perfusion rate of the pancreas itself and is probably related to the hormonal function of the islet.

The oxygen consumption rate for tissues like islets can be described by Michaelis-Menten type kinetics:

$$\Gamma_{O2} = \frac{V_{max} p_{O2}}{K_m + p_{O2}}$$

For islets, K_m = 0.44 mmHg and V_{max} = 26 µM/s when the islets are exposed to basal levels of glucose (100 mg/dL) and 46 µM/s under stimulated glucose levels (300 mg/dL).

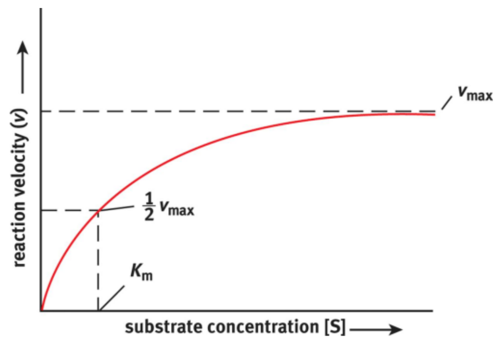


$$\Gamma_{O2} = \frac{V_{max} p_{O2}}{K_m + p_{O2}}$$

Because of the small value of K_m, the tissue oxygen consumption rate is generally independent of the tissue p_{O2} until the p_{O2} in the tissue reaches a value of just a few mmHg.

Cellular metabolic processes are therefore relatively insensitive to the local p_{O2} level until it reaches a value of about 5 mmHg.

Therefore, we can approximate the value of Γ_{O2} as simply the value of V_{max}. Only at very low p_{O2} levels would this approximation be no longer valid.



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We know the value of Γ_{O2} , and the value of $(C_{O2} + C'_{HbO})|_{arterial}$ is the nominal arterial value of 8630 μM (from Table). We can now solve for the value of $(C_{O2} + C'_{HbO})|_{venous}$ Hence,

$$C'_{HbO} = \frac{C'_{SAT}(H_{O2}C_{O2})^n}{P_{50}^n + (H_{O2}C_{O2})^n}$$

C'_{SAT} is the saturated amount of oxygen bound to hemoglobin, which is 8800 μM.

Oxygen Property	Arterial	Venous
Partial pressure (tension), pO_2, mmHg	95	40
Dissolved O_2, μM	130	54
As oxyhemoglobin, μM	8500	6424
Total effective (dissolved + oxy – Hb), μM	8630	6478

Other useful data: H_{oxygen} = 0.74 mmHg μM^{-1}; saturated oxyhemoglobin = 8800 μM; P_{50} ~ 26 mmHg; n = 2.34.

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Substituting this equation into previous equation for the venous value of C'_{HbO} , we obtain for the dissolved oxygen concentration in the venous blood:

$$\left[C_{O2} + \frac{C'_{SAT}(H_{O2}C_{O2})^n}{P_{50}^n + (H_{O2}C_{O2})^n}\right]_{Venous} = \left(C_{O2} + C'_{HbO}\right)_{arterial} - \frac{\Gamma'_{O2}}{q}$$

For the given values of q, Γ'_{O2}, and $\left(C_{O2} + C'_{HbO}\right)$ this equation can be solved for the C_{O2}in the blood leaving the tissue, which in this case is an islet of Langerhans.

Once we have obtained the value of C_{O2}, then C'_{HbO} can be found from:

$$C'_{HbO} = \frac{C'_{SAT}(H_{O2}C_{O2})^n}{P_{50}^n + (H_{O2}C_{O2})^n}$$

The P_{O2} of the exiting blood is then given by Henry's law. 19

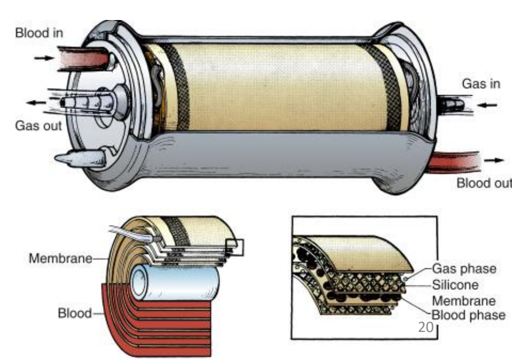
Oxygen transport in blood oxygenators

A steady-state oxygen mass balance says that the amount of oxygen transported into the blood is equal to the difference between the amount of oxygen in the blood leaving and entering the oxygenator. Hence,

$$\dot{m}_{O2} = Q_{Blood}\left[\left(C_{O2} + C'_{HbO}\right)\Big|_{out} - \left(C_{O2} + C'_{HbO}\right)\Big|_{in}\right]$$

$\dot{m}_{O2}$ is the amount of oxygen transported to the blood.

Q_{Blood} is the blood flow rate through the oxygenator.



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Example

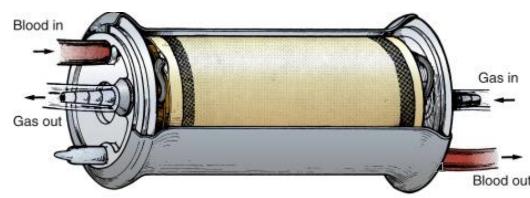
Blood travels through a membrane oxygenator at a flow rate of 5000 mL/min. The entering p_{O2} of the blood is 30 mmHg and the exiting blood p_{O2} is 100 mmHg. Calculate the amount of oxygen transported into the blood in μmol/s.

Amount of oxygen dissolved in the blood at 30 mmHg and at 100 mmHg from Henry's law:

$$p_{O2} = H_{O2}C_{O2}$$

$$C_{O2}^{in} = \left(\frac{p_{O2}}{H_{O2}}\right)_{in} = \frac{30}{0.74} = 40.54\mu M$$

$$C_{O2}^{out} = \left(\frac{p_{O2}}{H_{O2}}\right)_{out} = \frac{100}{0.74} = 135.14\mu M$$



The amount of oxygen bound to hemoglobin can be found from Figure:

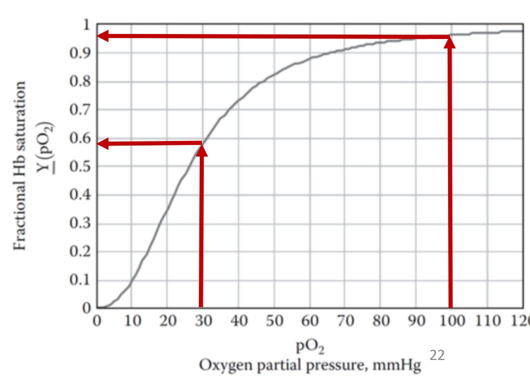
At 30 mmHg, $Y = 0.58$

At 100 mmHg, $Y = 0.97$

$$C_{Hbo}^{\prime in} = Y \times C_{SAT}^{\prime} = 0.58 \times 8800 = 5104\ \mu M.$$

$$C_{Hbo}^{\prime out} = Y \times C_{SAT}^{\prime} = 0.97 \times 8800 = 8536\ \mu M.$$

Using these values, we can calculate the amount of oxygen transported to the blood.



$$\dot{m}_{O2} = Q_{Blood}\left[\left(C_{O2} + C'_{HbO}\right)\Big|_{out} - \left(C_{O2} + C'_{HbO}\right)\Big|_{in}\right]$$

$$\dot{m}_{O2} = 5000 \times \left[(135.14 + 8536)\Big|_{out} - (40.54 + 5104)\Big|_{in}\right] \times \frac{1min}{60\ s} \times \frac{1L}{1000\ mL}$$

$$\dot{m}_{O2} = 293.9\ \mu mol/s$$

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