Lecture 5

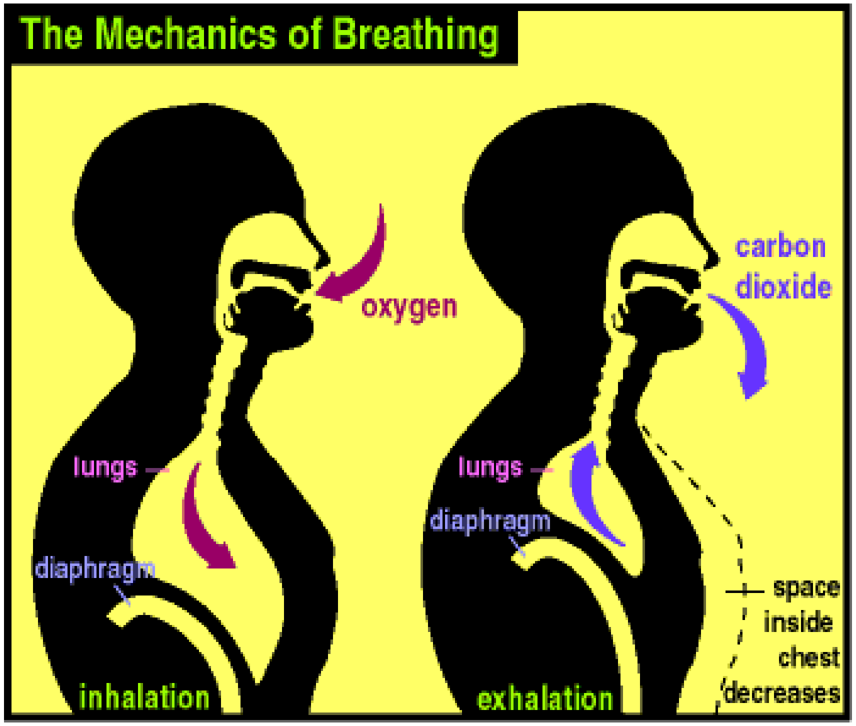
Biophysics and Gas Transport:

Transport of Gases
Physiology of Respiration

Convective Transport of Gases

- The flow of gases in the air canals of the respiratory system is similar to the flow of fluids through pipes.

- Air is ventilated in respiratory system due to the pressure difference between outside atmosphere and respiratory surface
- Respiratory muscles expand and contract the lungs
- Pressure in the alveoli (air sacks) falls and rises.



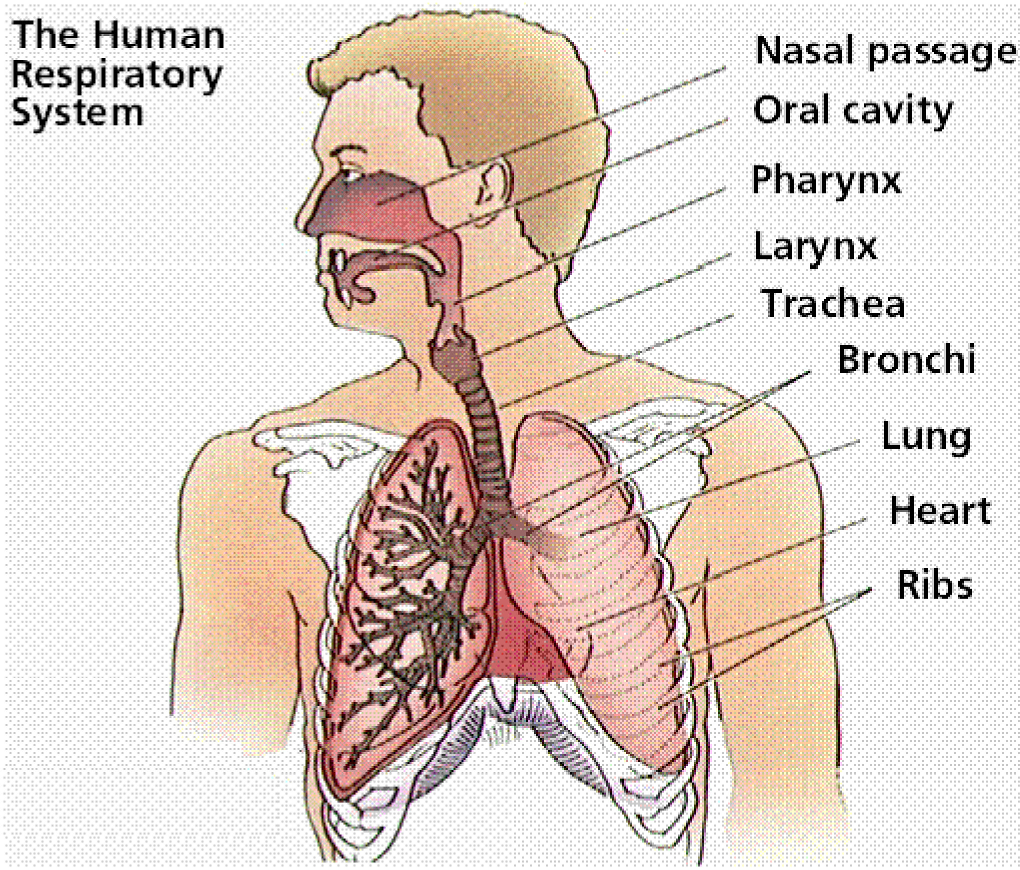
During tidal breathing:

Respiration - pressure in alveoli 3 mmHg below – air flows in

Expiration - 3 mmHg above the atmosphere – air flows out

Transport of gases - airways

- Air enters the body through the nose, is warmed, filtered, and passed through the nasal cavity.
- Air passes the pharynx
- The upper part of the trachea contains the larynx. The vocal cords are two bands of tissue that extend across the opening of the larynx.
- After passing the larynx, the air moves into the bronchi that carry air in and out of the lungs.



Airways resistance

- Air exchanged between environment and alveoli flows through a series of tubes – nasal, trachea, bronchi, etc. The airway resistance is net resistance of the entire network of air passages

- Air flows in air canals under the pressure difference ΔP, the volume of air ΔV, in time Δt,
- The airways resistance R_g is given by Poiseuille's relation:

$$\frac{\Delta V}{\Delta t} = \frac{\Delta P}{R_g}$$

- For normal adult R_g is about 3.3 cm H_2O/(L/sec)

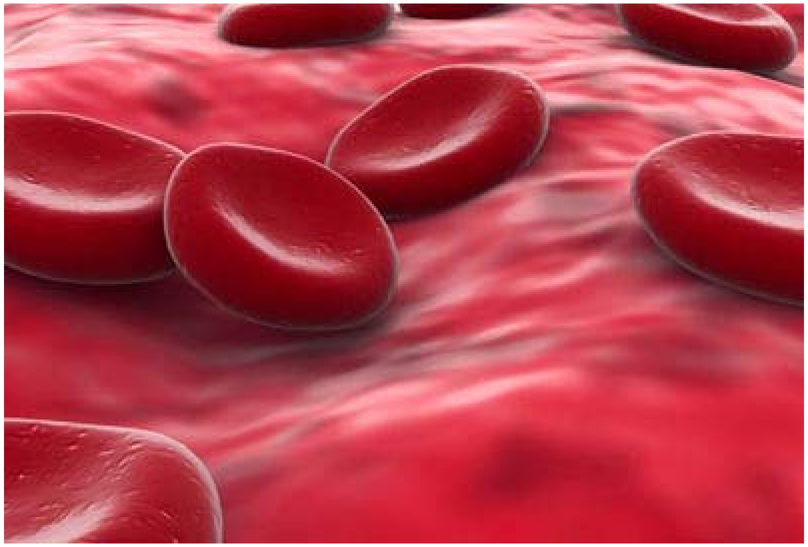
Transport of gases in blood

- The respiratory gases, like O_2 and CO_2 are transported from lungs to tissues through blood

- **Functions of Blood:**
- 1 - Transport:
  - oxygen & carbon dioxide
  - nutrients
  - waste products (metabolic wastes, excessive water, & ions)
- 2 - Regulation - hormones & heat (to regulate body temperature)
- 3 - Protection - clotting mechanism protects against blood loss & leucocytes provide immunity against many disease-causing agents
-

- **Components of Blood** - average adult has about 5 liters of blood

- 1 – Cells:
  - Red blood cells (or erythrocytes)
  - White blood cells (or leucocytes)
  - Platelets (or thrombocytes)
- 2 – Plasma = water + dissolved solutes



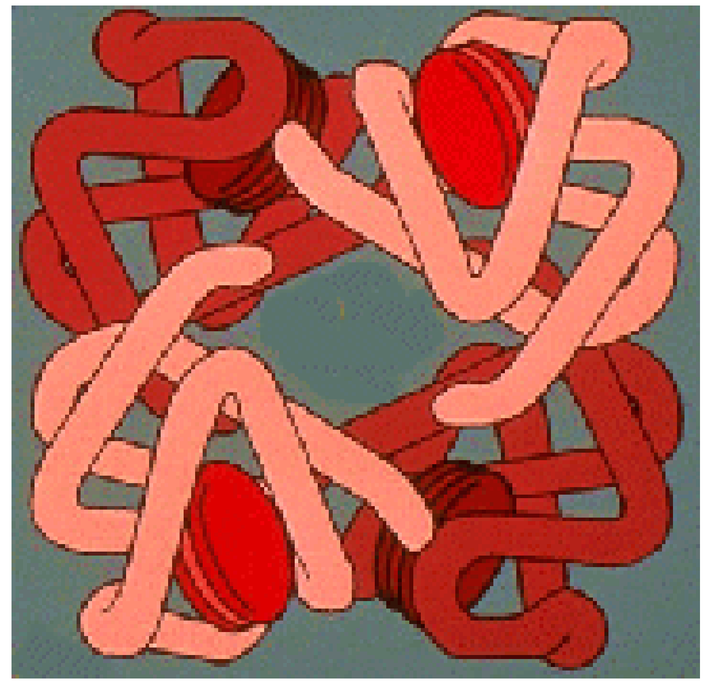
Blood is red because of Red Blood Cells, which contain pigment hemoglobin – red in color

Transport of oxygen in blood

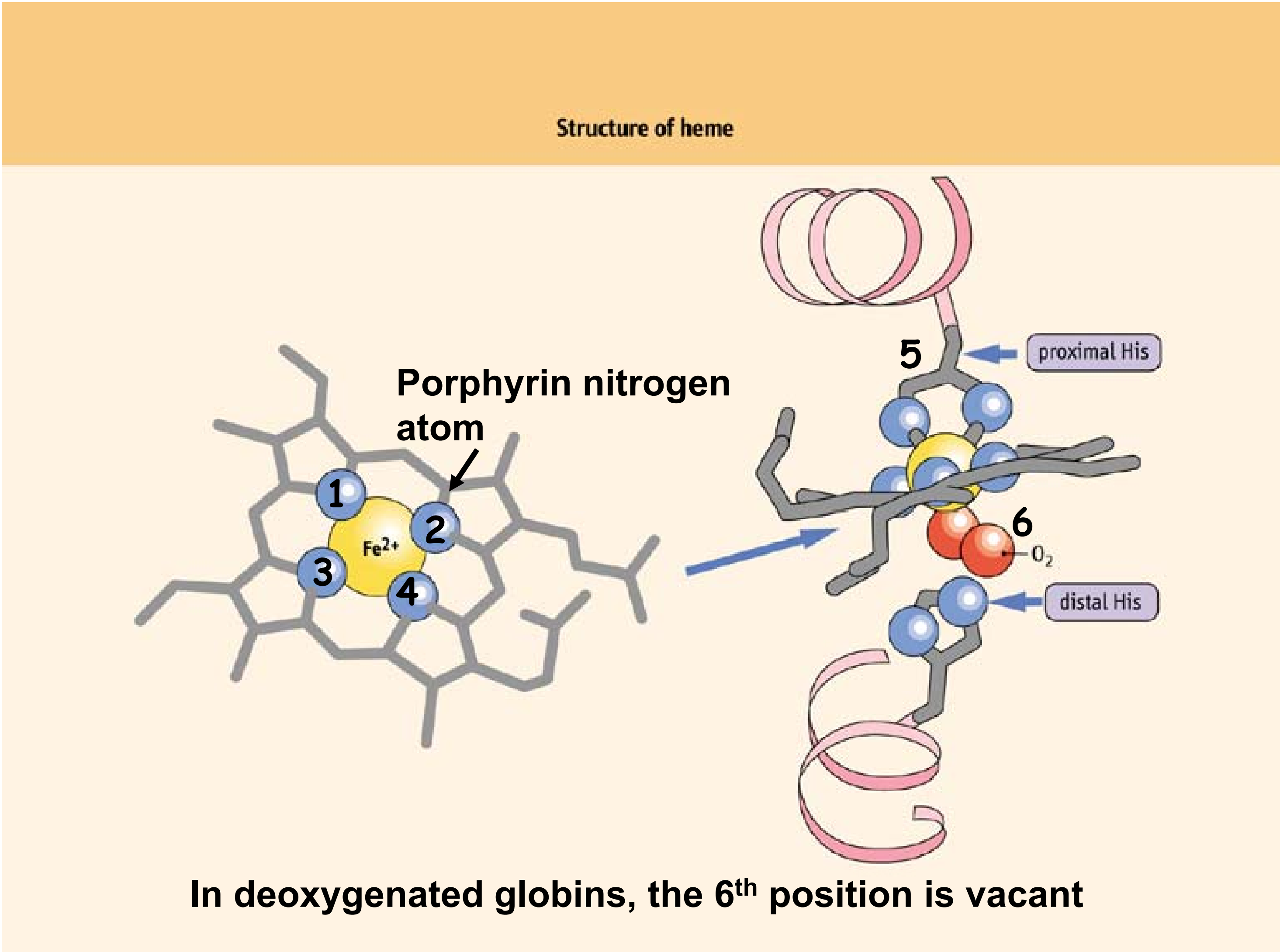
- Oxygen is carried in blood in two forms:
- 1 - bound to hemoglobin (98.5% of all oxygen in the blood)
- 2 - dissolved in the plasma (1.5%)
- almost all oxygen in the blood is transported by hemoglobin,
- the concentration (partial pressure) of oxygen and hemoglobin saturation (the % of hemoglobin molecules carrying oxygen) are related.

Hemoglobin (Hb)

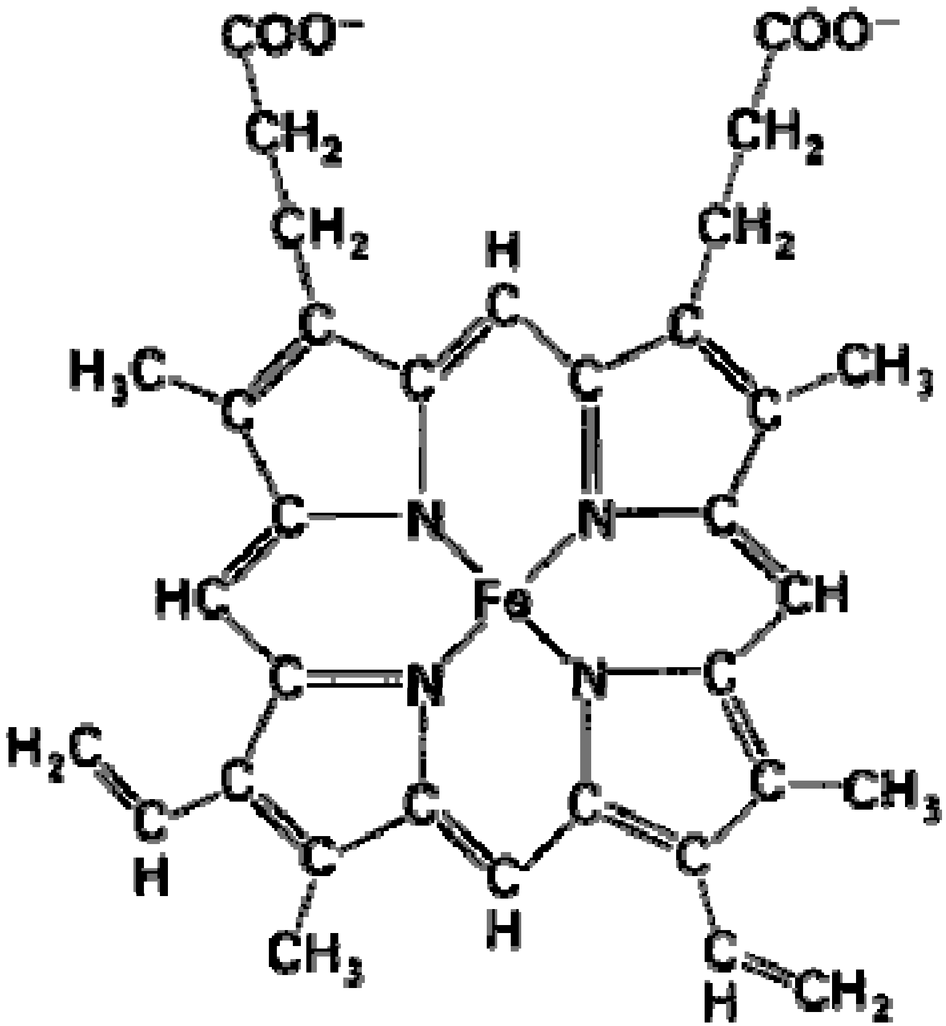
- Blood contains respiratory pigment which can bind O_2 molecules.
- In vertebrates this pigment called Hemoglobin (Hb) is found in red blood cells
- Hemoglobin contains the protein – globin (with 4 polypeptide chains)
- Each chain has a pigment – Heme, which binds one O_2 molecule



Heme



Structure of heme
Porphyrin nitrogen atom
1
2
3
4
Fe^{2+}
5
proximal His
6
O_2
distal His
In deoxygenated globins, the 6th position is vacant



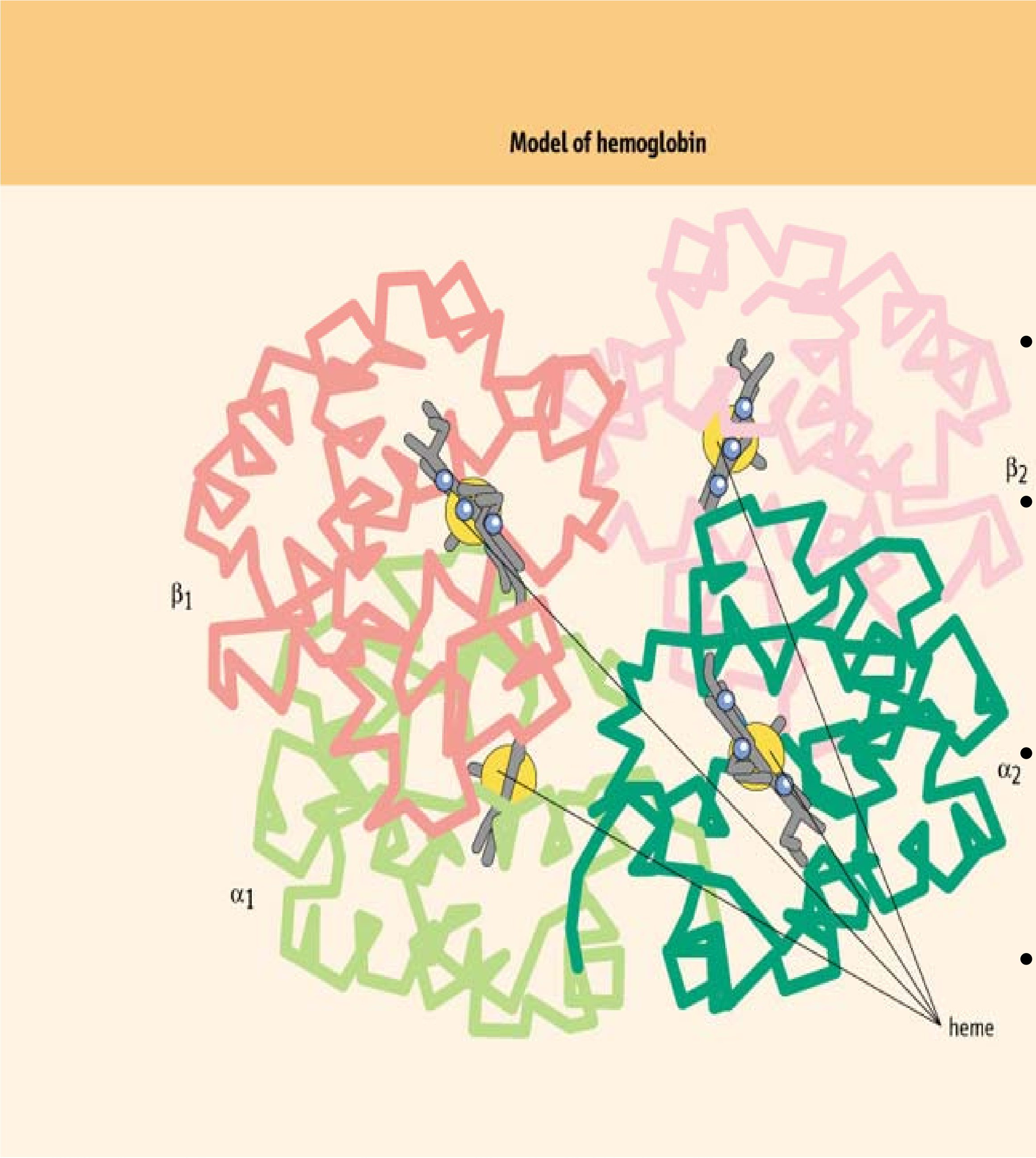
Heme
(Fe-protoporphyrin IX)

Fe2+

binds Oxygen

Fe3+

releases Oxygen



- 1 Hemoglobine can attach max 4 O_2 molecules
- If all 4 sites of Hb are occupied by O_2 molecules – the blood is 100% saturated with oxygen.
- The amount of oxygen in this case - oxygen capacity of the blood
- Oxy – and deoxy-hemoglobin

- Binding of O_2 to Hb depends on the P_{O_2} in blood.
- For human arterial blood, P_{O_2} = 95 mmHg (blood is saturated)
- For venous blood P_{O_2} = 40 mmHg (70% saturated)
- Hemoglobin binds oxygen reversibly –
- high affinity at large P_{O_2}
- low affinity at small P_{O_2}
- In the lungs - P_{O_2} is high - Hb captures oxygen from air to blood
- In the tissues - P_{O_2} is low - Hb releases oxygen

- Hill and Brown empirical relation:
-
- Fractional saturation of O_2 = $\nu = \dfrac{KP^n}{1+KP^n}$

- P – partial pressure,
- n – number of O_2 molecules in Hb
- K – equilibrium constant

- Other factors affect
- Hb- O_2 affinity: pH and partial pressure of CO_2 (Bohr's effect)

Transport of carbon dioxide in blood

- Carbon dioxide: tissues $\longrightarrow$ blood $\longrightarrow$ respiratory organs.
- Enters and leaves blood as molecular CO_2
- Transported in the blood in several forms:
- 5% dissolved molecular form
- 5% reacts with amino group of Hemoglobin:
- $$\mathrm{Hb-N(H)(H)} + CO_2 \rightleftharpoons \mathrm{Hb-N(H)(COO^-)} + H^+$$

forms
carbamino compound

- This depends on number of amino groups available and P_{O_2}
- Deoxyhemoglobin has higher affinity to CO_2 than hemoglobin (Haldane effect), venous blood has more Deoxy-Hb and loads CO_2 at tissues.

90 % of the CO2 transported as bi-carbonate ions in plasma:

- Molecular CO_2 enters the blood and diffuses into the red blood cells,
- Where they are hydrated:
- $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
- HCO_3^- diffuses out of RBC and flows in plasma
- HCO_3^- comes out Cl^- comes into RBC from plasma – this is Hamburger shift
- Diffusion coefficient of CO_2 is 6 times larger than O_2

Diffusion of Gases Fick's Law

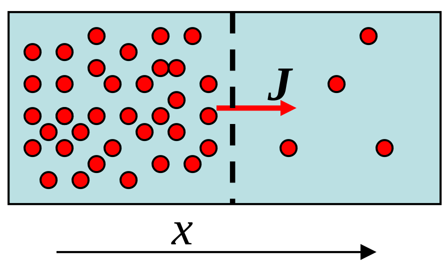
- Gases diffuse through membrane: Blood - alveoli in the lung – external respiration
- Blood - cells in the tissues – cellular respiration

- Diffusion is a kinetic process of movement of molecules from high concentration to lower concentration

J is proportional to concentration gradient $\Delta C/\Delta x$,

D – diffusion coefficient

Diffusion flux J is amount of substance diffusing per unit time per unit area normal to diffusion,



$$J = -D\frac{\Delta C}{\Delta x}$$

Fick's Law of diffusion

Fick's law is valid in the area where D is constant

- According to Henry's Law :
- concentration of a gas solute in solution is proportional to its partial pressure in a gas-phase above the liquid in equilibrium

- **Diffusion flux is related to partial pressure:**

$$J = -D\alpha \frac{\Delta P}{\Delta x} = -K \frac{\Delta P}{\Delta x}$$

solubility coefficient

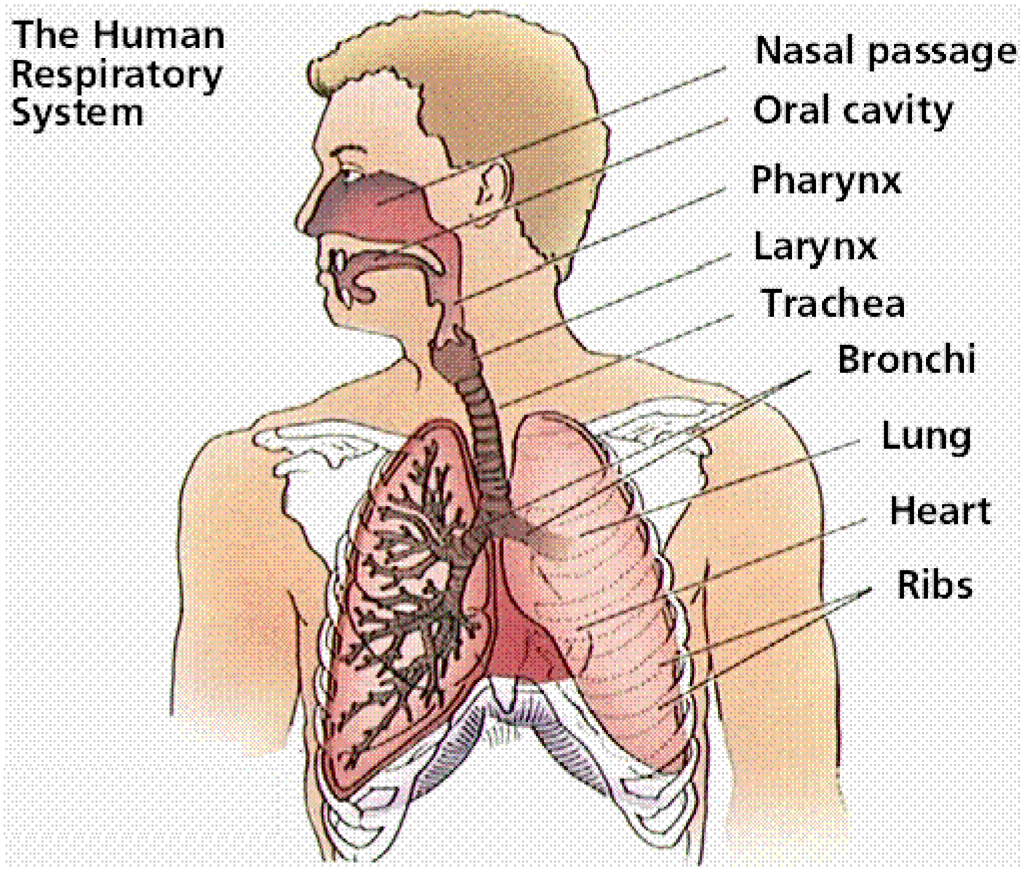
- K – diffusion conductivity
- Depends on molecular weight

- **Diffusion constants for Oxygen at 37C**

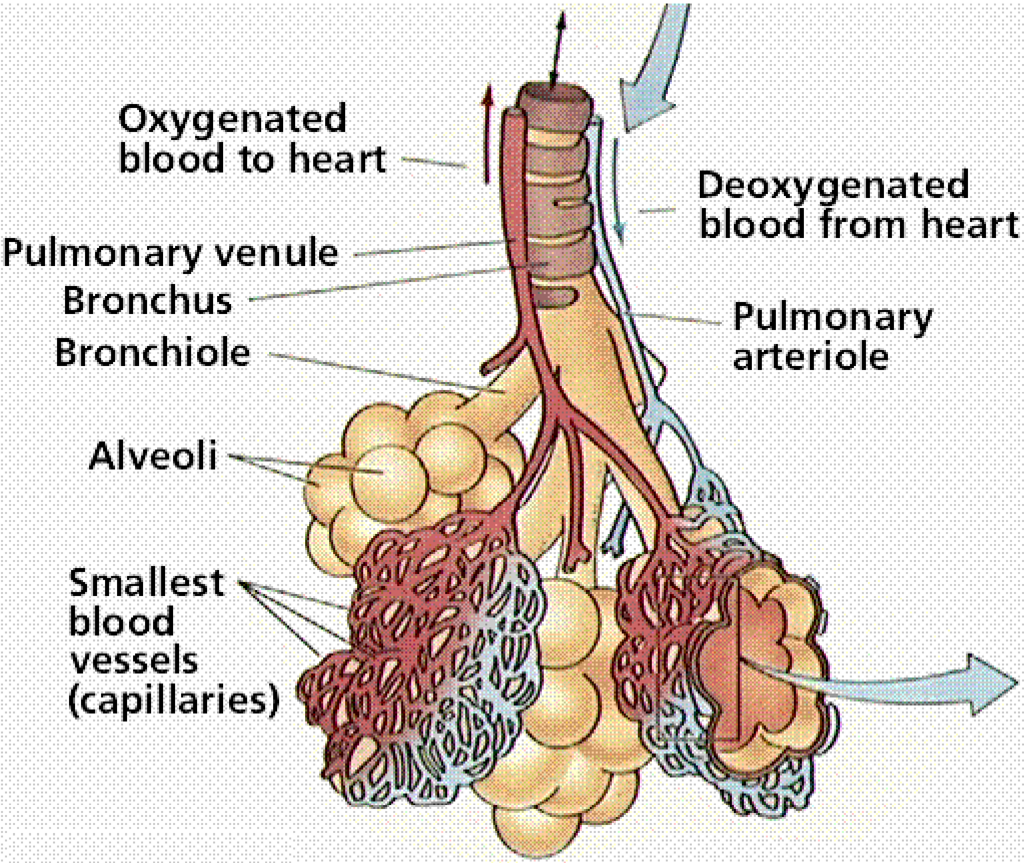
solvent	$K(m^2s^{-1}Pa^{-1})$	$D(m^2s^{-1})$
Water	0.77×10^{-15}	3.2×10^{-9}
Blood plasma	0.44×10^{-15}	2.2×10^{-9}
RBC (human)	0.22×10^{-15}	0.8×10^{-9}

Gas exchange in Lungs

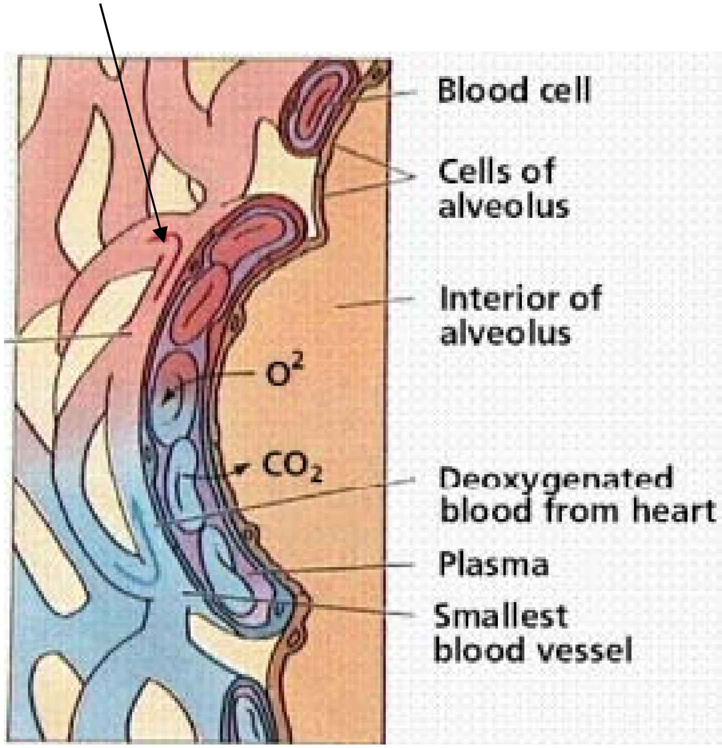
- Air enters the body through the nose, is warmed, filtered, and passed through the nasal cavity.
- Air passes the pharynx
- The upper part of the trachea contains the larynx. The vocal cords are two bands of tissue that extend across the opening of the larynx.
- After passing the larynx, the air moves into the bronchi that carry air in and out of the lungs.



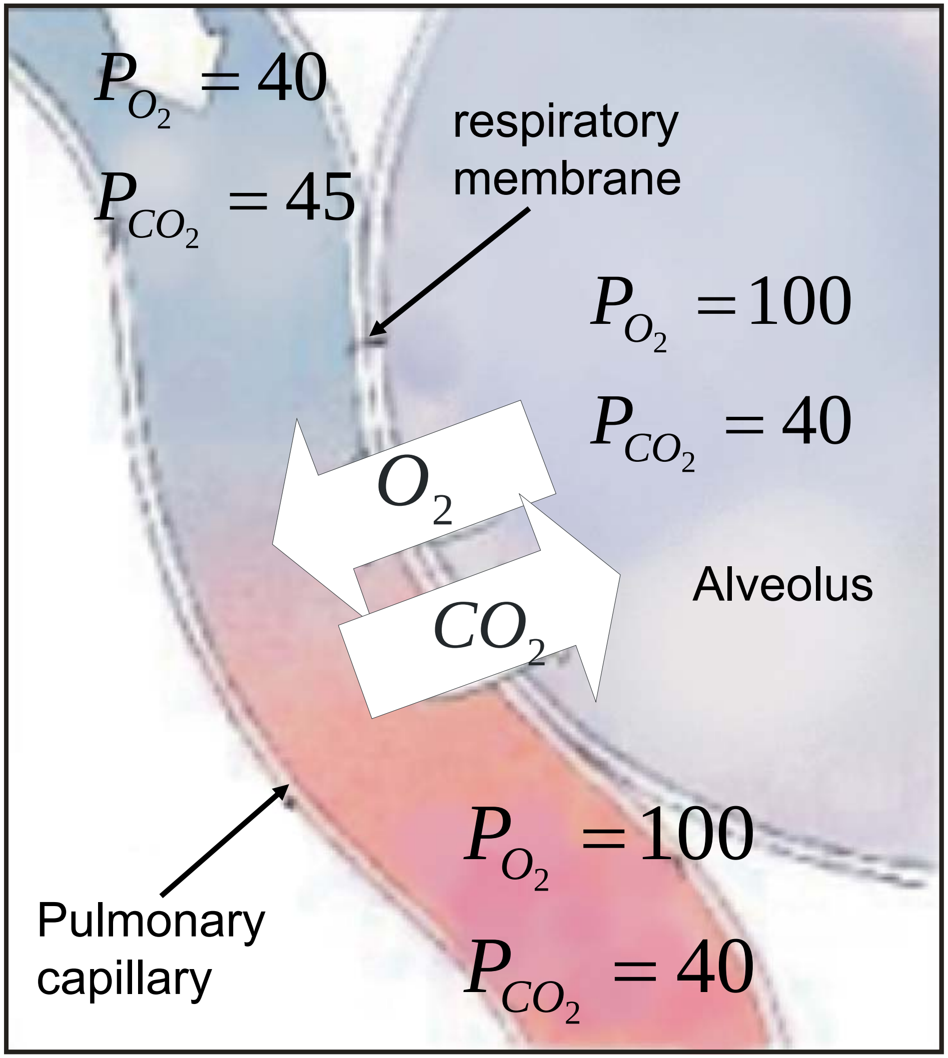
- Inhaled air fills alveoli
- Thin membrane separates alveoli and capillaries – blood exchange gases with alveoli
- diffusion occurs due to the differences in partial pressures
- The greater the difference in partial pressure the greater the rate of diffusion.



Oxygenated blood to heart



Gas exchange in alveoli – external respiration



gases exchange between alveolus and capillary through membrane

diffusion occurs due to the differences in partial pressures

Diffusion flux is proportional to the surface area of respiration and inversely proportional to the thickness of membrane

Diffusion coefficient of a gas depends on gas solubility and molecular weight

CO_2 more soluble – diffuses faster than O2

- Diffusing capacity of respiratory membrane = volume of gas that diffuses through membrane per minute under pressure difference 1 mmHg

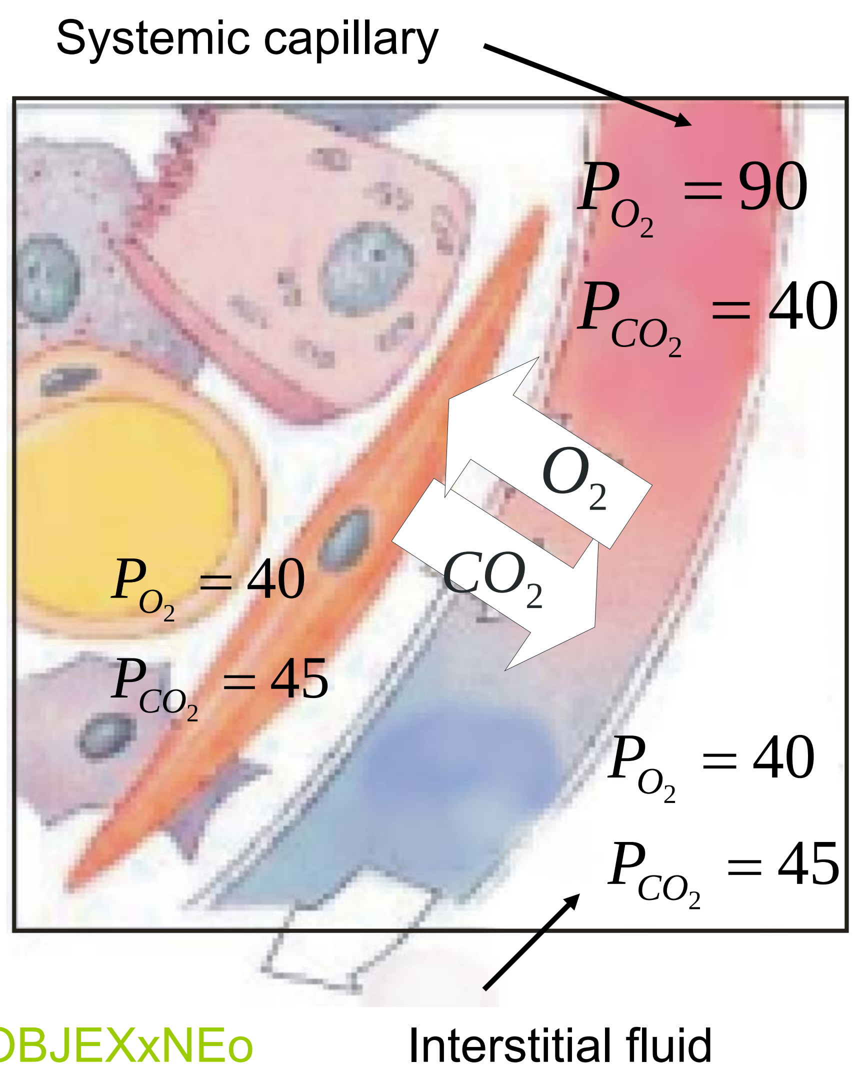
- Human : 14 breaths per minute, inhale - 0.5L each breath
- How much Oxygen is transported?

- Respiratory volume is 14 X 0.5 = 7 L per minute
- 70 % of this volume reaches lungs (5 L)
- Inspired air - 20% of oxygen, expired air – 15-16% of oxygen
- 4-5% of oxygen diffuses through the membrane
- 5% of 5 L - 250 mL of oxygen transports through the membrane each minute

Gas exchange in tissues - cellular respiration

- Gases are transported through the membrane by diffusion

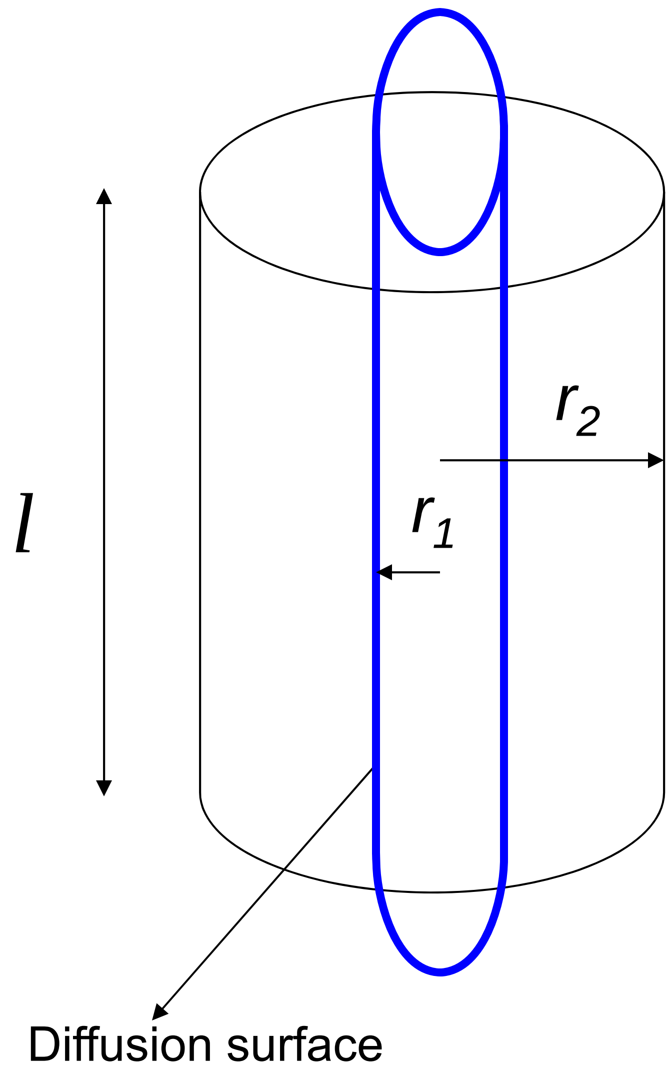
- Because of the differences in partial pressures of oxygen and carbon dioxide in the systemic capillaries and the body cells, oxygen diffuses from the blood into the cells, while carbon dioxide diffuses from the cells into the blood.
- Blood leaving the systemic capillaries returns to the heart (right atrium) via venules and veins (and no gas exchange occurs while blood is in venules and veins). This blood is then pumped to the lungs (and the alveolar capillaries) by the right ventricle.



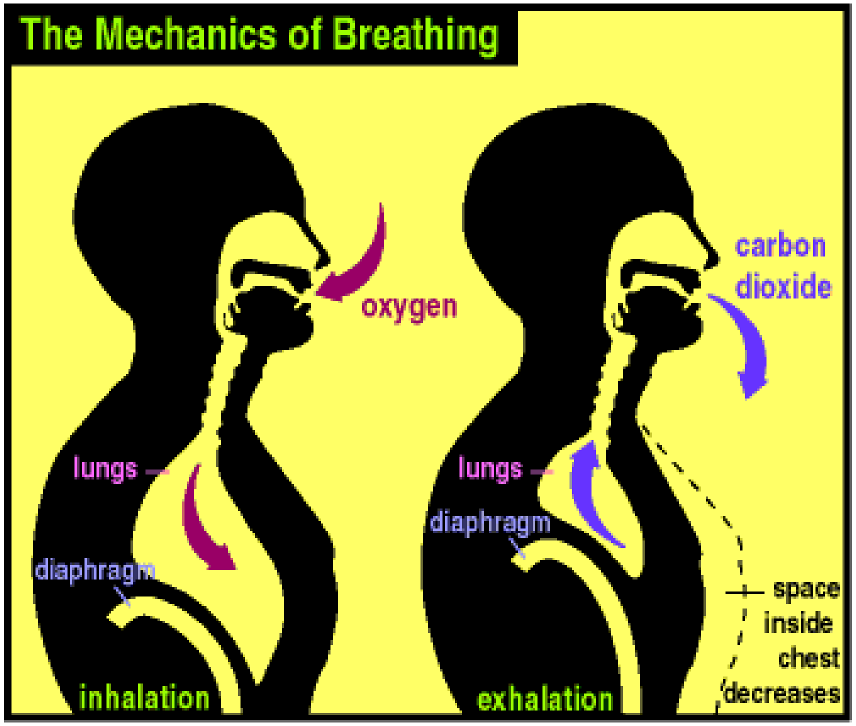
http://www.youtube.com/watch?v=WXOBJEXxNEo

- Krogh’s model:

- assumes the tissue as a cylinder of length l and radius r_2,
- blood vessel – of radius r_1, passes along the axis of the tissue – cylinder
- Diffusion of gases takes place at the interface of vessel and tissue



Terminology



In humans:
compliance of lungs:
C=0.22 L/cm H2O
Compliance of lungs
and thorax combined:
C=0.13 L/cm H2O

$$C = \frac{\Delta V}{\Delta P}$$

- **Total lung capacity** (TLC) - maximum volume of expanded lung, TLC= 5-6 L
- **Vital capacity** (VC) – max volume of air the person can expel
- VC= 4.5 L
- **Residual volume** – the air that cannot be removed from the lung =1L, RV=TLC-VC
- **Tidal volume** (TV) – volume inspired and expired during normal or tidal breathing , TV=0.5 L
- **Functional residual capacity** – the volume lungs retain after expiration during tidal breathing = 1/3 of TLC = 2L
- **Dead space volume** (DSV)- volume of respiratory passage – called dead space – nasal passage, trachea, bronchi, etc. Normal DSV=150 mL
- Volume of air in alveoli = TV-DSP
- **Compliance (C) =** expansibility of the lungs and thorax = volume increase in lungs for unit increase in intra-alveolar pressure

Physics of alveoli

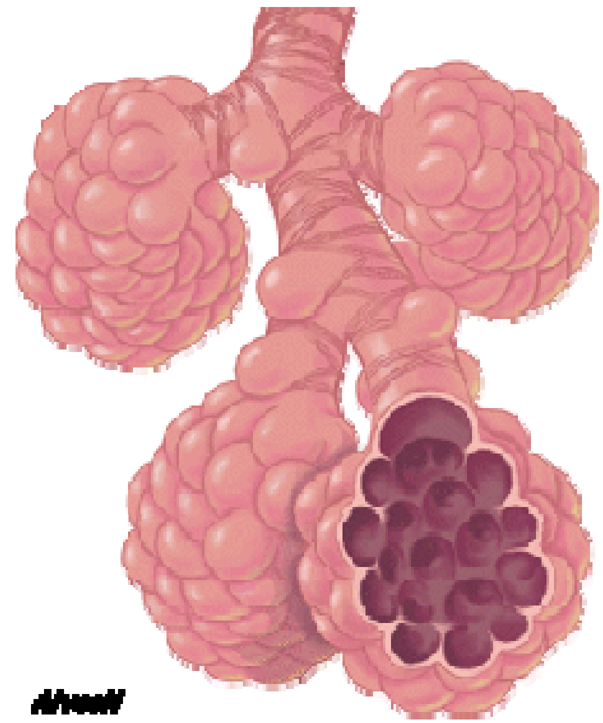
- To exchange gases – surface 1 m^2 per kg of body weight is required
- The most extensive surface in the body - in the lung -
- Total surface = 70 m^2

- 300 millions of alveoli – tiny air spaces (sacs)
- Single alveolus – 75 – 700 μm in diameter

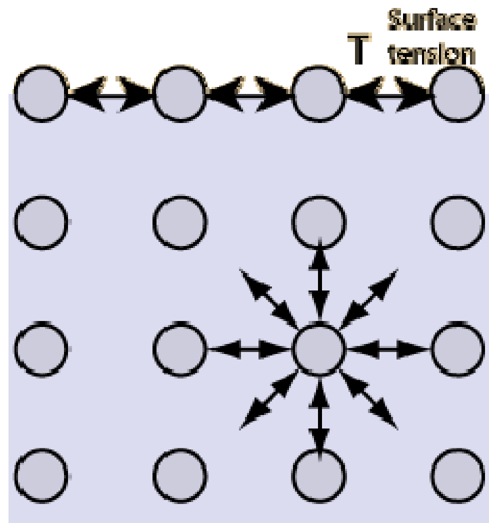
- Alveolar membrane is 1 μm thick

- Normal expansion and compression of lungs
- - stretching of alveoli membrane,

- Surface tension of the alveolar membrane is
- responsible for the most part of its elasticity



Surface Tension



- The cohesive forces between liquid molecules are responsible for the phenomenon known as surface tension.
- The molecules at the surfaces do not have other like molecules on all sides of them and consequently they cohere more strongly to those directly associated with them on the surface. This forms a surface "film" which makes it more difficult to move an object through the surface than to move it when it is completely submersed.
- Surface tension is typically measured in dynes/cm, the force in dynes required to break a film of length 1 cm. Equivalently, it can be stated as surface energy in ergs per square centimeter. Water at 20°C has a surface tension of 72.8 dynes/cm compared to 22.3 for ethyl alcohol and 465 for mercury.

Surface tension. Pulmonary surfactant

- The surface of alveoli separates air and water in the lungs

- Water molecules are more attracted to each other than to air, and this attraction creates surface tension.
- This surface tension increases as water molecules come closer together, which is what happens when we exhale & our alveoli become smaller (like air leaving a balloon).
- Potentially, surface tension could cause alveoli to collapse and, in addition, would make it more difficult to 're-expand' the alveoli (when you inhaled).

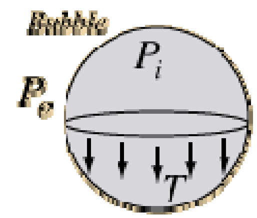
- Fortunately, our alveoli do not collapse and inhalation is relatively easy because the lungs produce a substance called surfactant that reduces surface tension.

Surfactant covers the surface of alveoli and decreases surface tension which:
reduces the effort needed to expand the lungs
reduces tendency for alveoli to collapse
balances pressure in large and small alveoli

- **Excess pressure inside the alveolus is given by Laplace's Law:**
- where T - surface tension
- r - radius of alveolus

$$\Delta P = \frac{4T}{r}$$

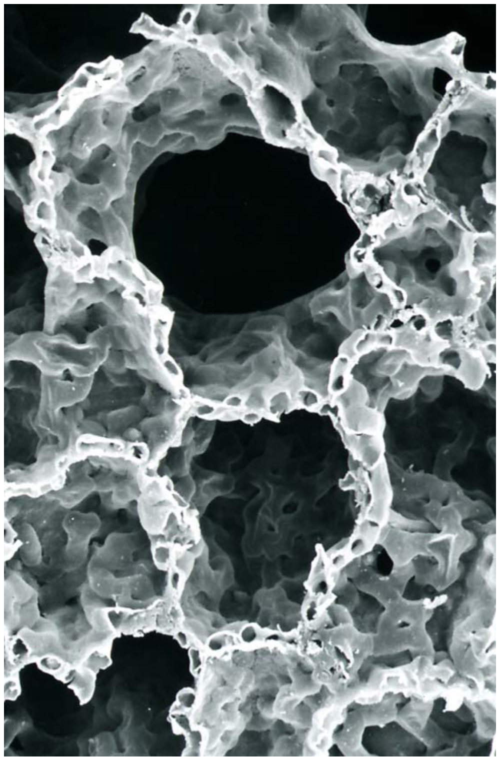
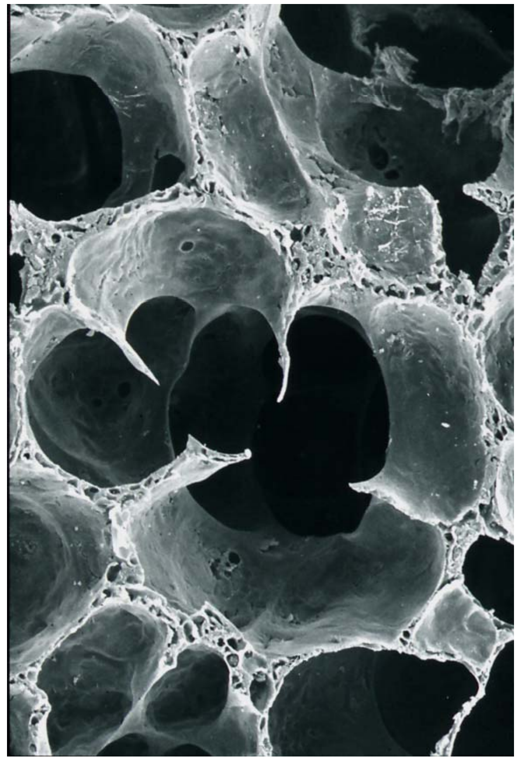
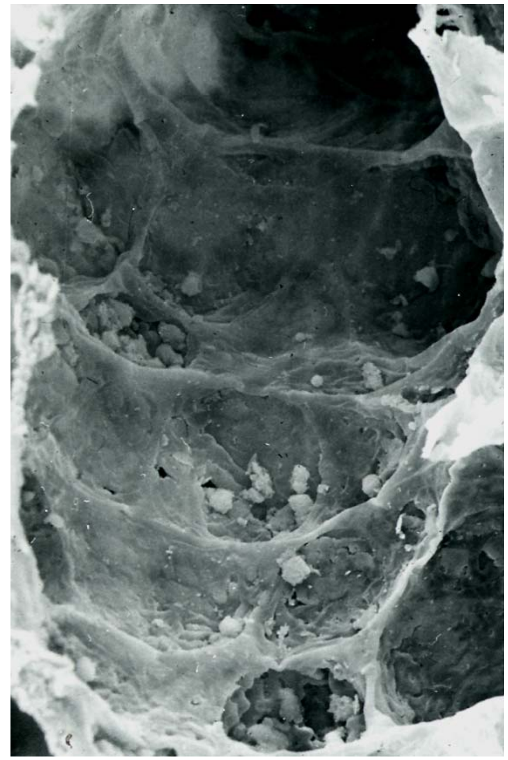
$$P_i - P_o = \frac{4T}{r}$$



- The function of alveoli of various sizes is coordinated:
- The pressure inside alveoli is averaged:
- When r is small – T is small
- When r is large – T is large

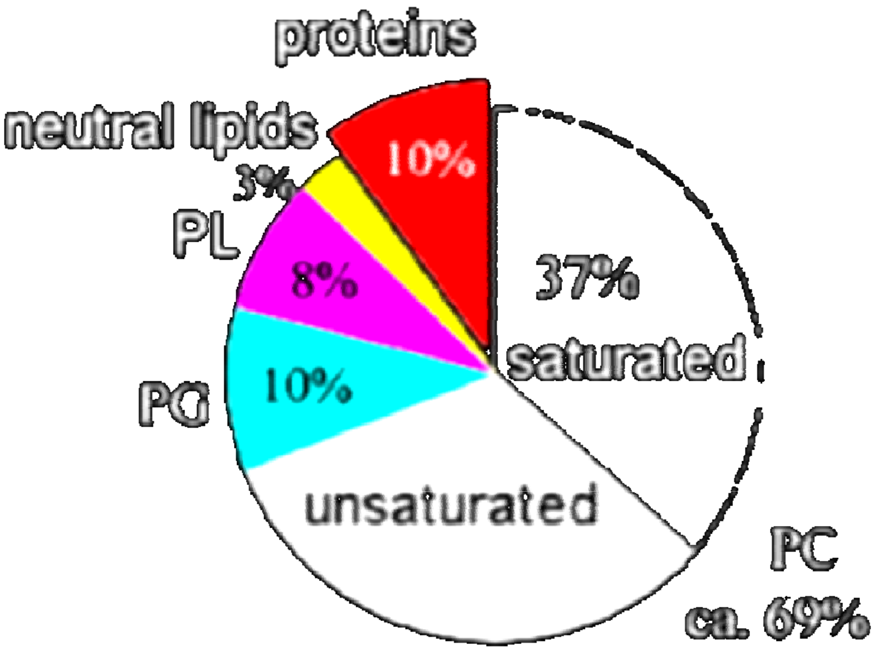
- Surfactant prevents alveoli from collapse,
- Alveoli not covered with surfactant collapse when contract

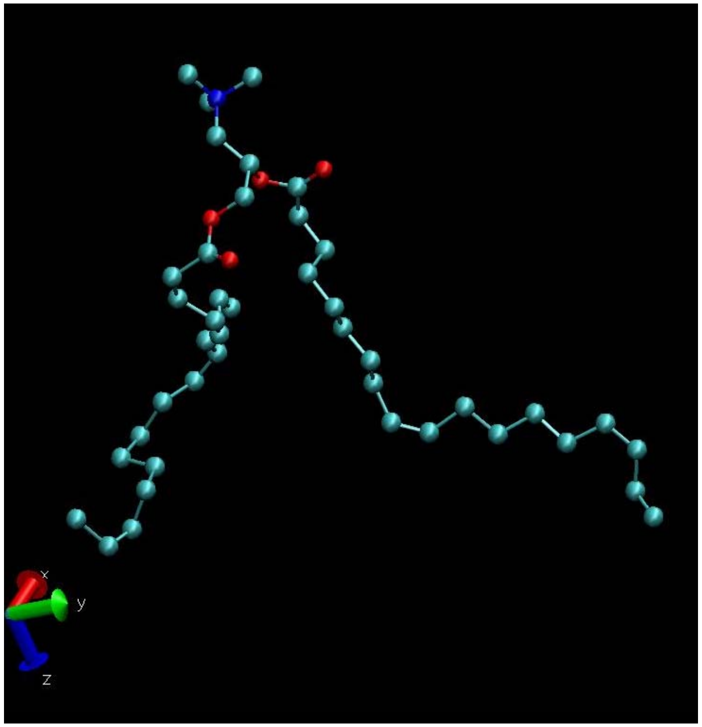
Function of Pulmonary Surfactant

Schürch, Weibel, Bachofen

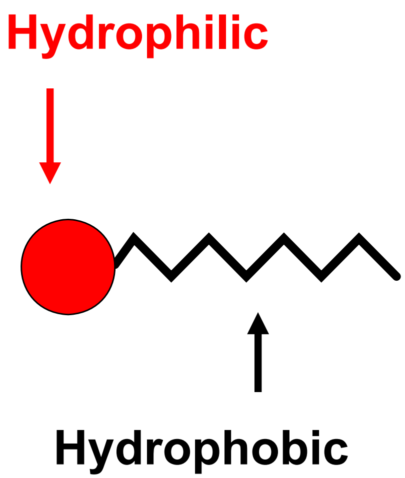
Surfactant composition

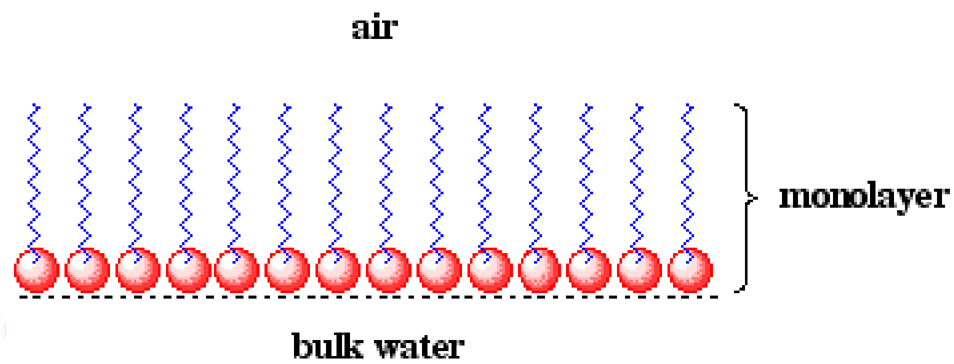


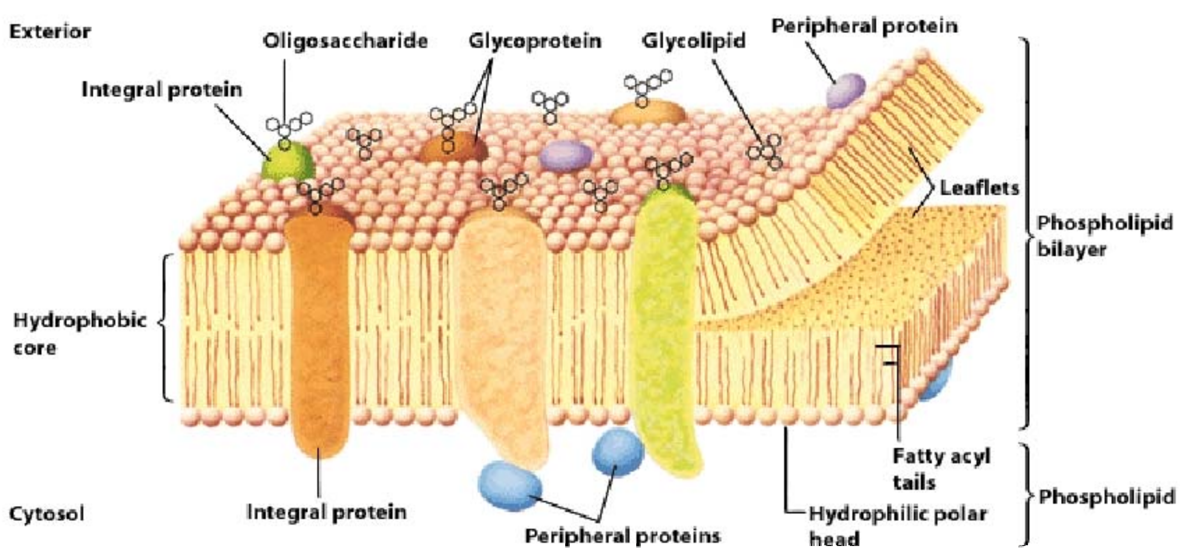


- Phospholipids, high proportion of saturated (DPPC)
- Cholesterol
- Surfactant protein C (SP-C): palmitoyl-anchor, transmembrane helix
- Surfactant proteins A, B, D

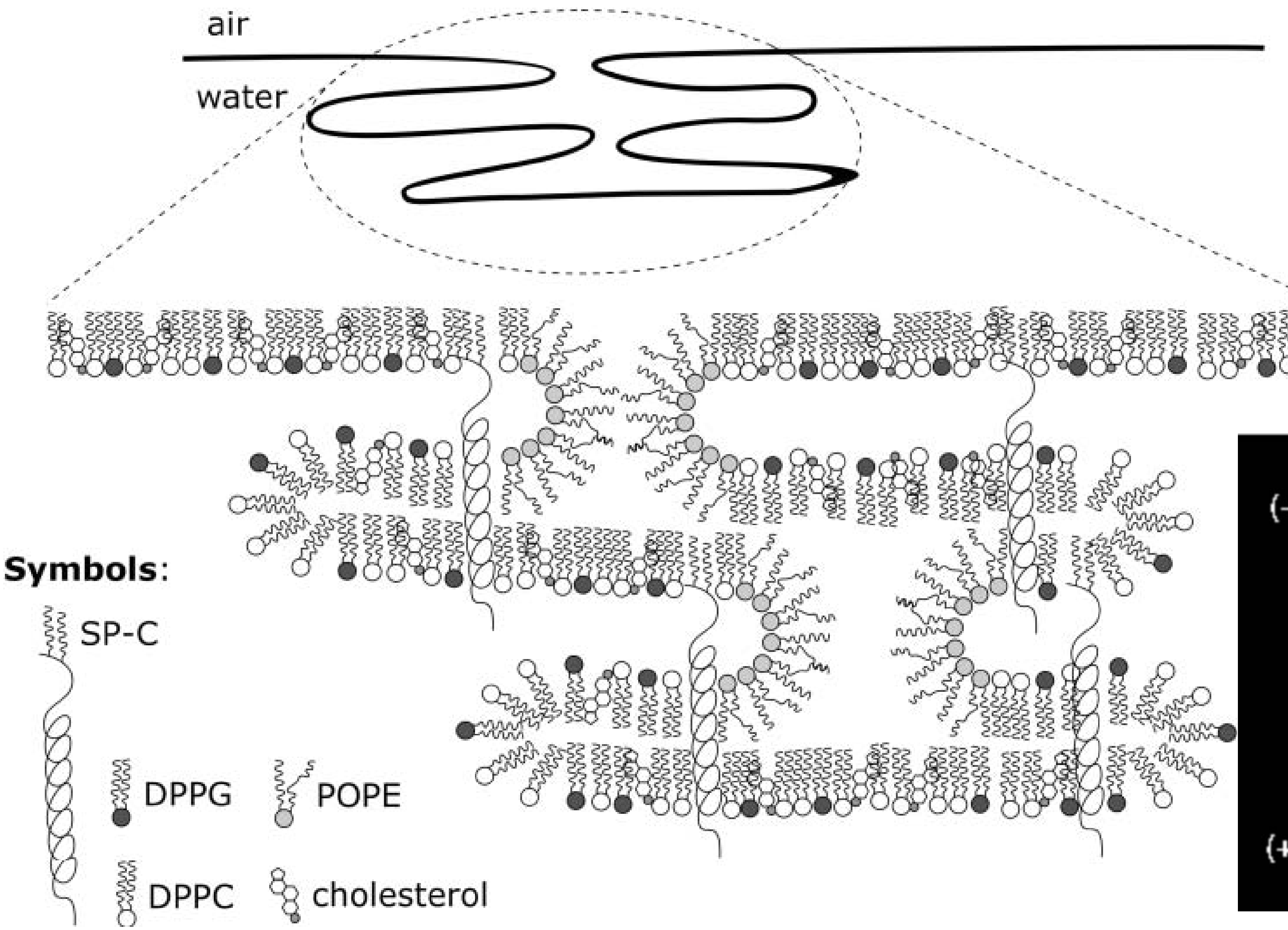
Lipid membranes and monolayers

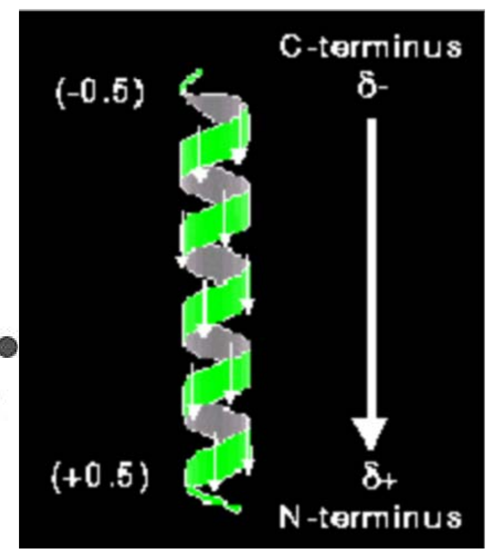






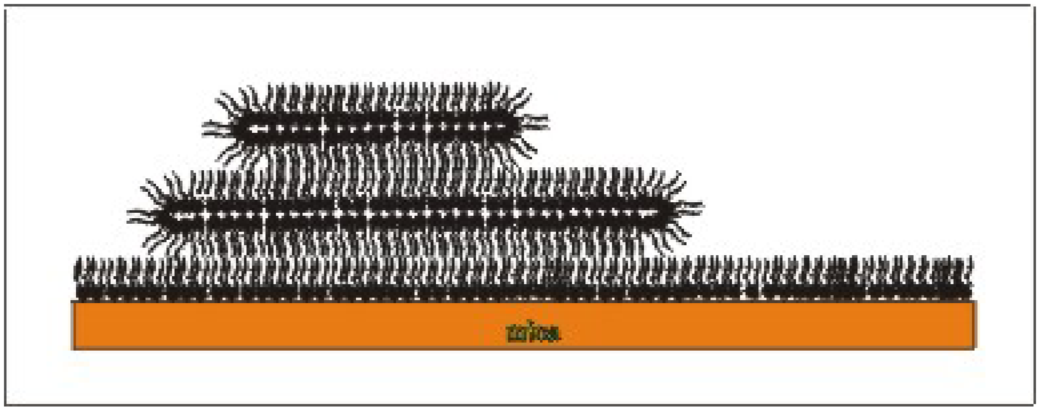
surfactant protein C

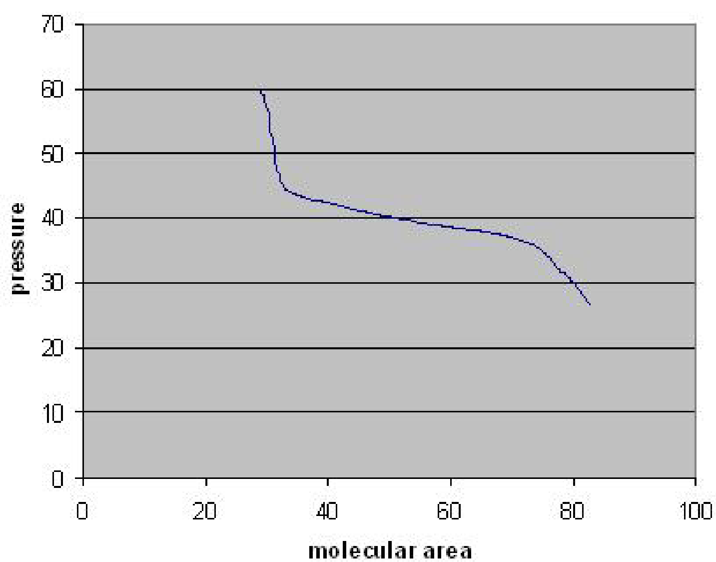


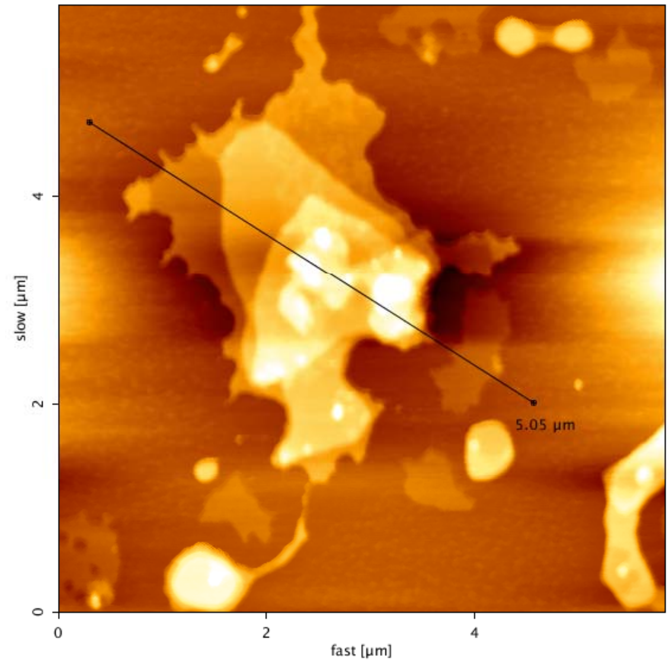


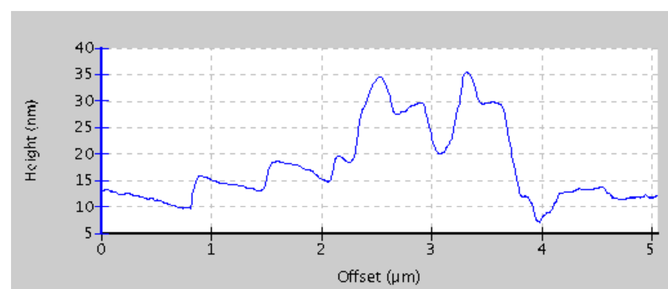
Surfactant film structure

Atomic force microscopy image of compressed surfactant film



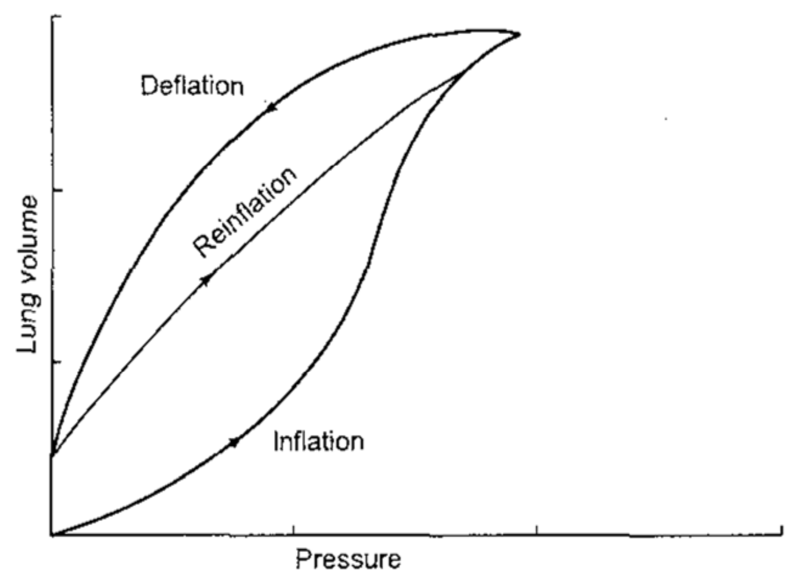






Work of breathing

- Work of breathing – amount of work done in the breathing process
- Respiratory muscles work to stretch the lungs:
- 64% - elastic stretch of lung membrane,
- 28% - non-elastic stretch – rearrange molecules in the tissues of lung and thorax as they expand – energy lost as heat
- Work of breathing depends on breathing rate
- The mechanical efficiency of breathing is ratio of work done to total chemical energy -
- normally 5% - 34 cal per day
- The work - area between inflation and deflation curve
- The energy lost as heat
- Tidal breathing – hysteresis small



Example:

- Calculate
- a) diffusion rate of oxygen and
- b) average time for a molecule to diffuse in insect

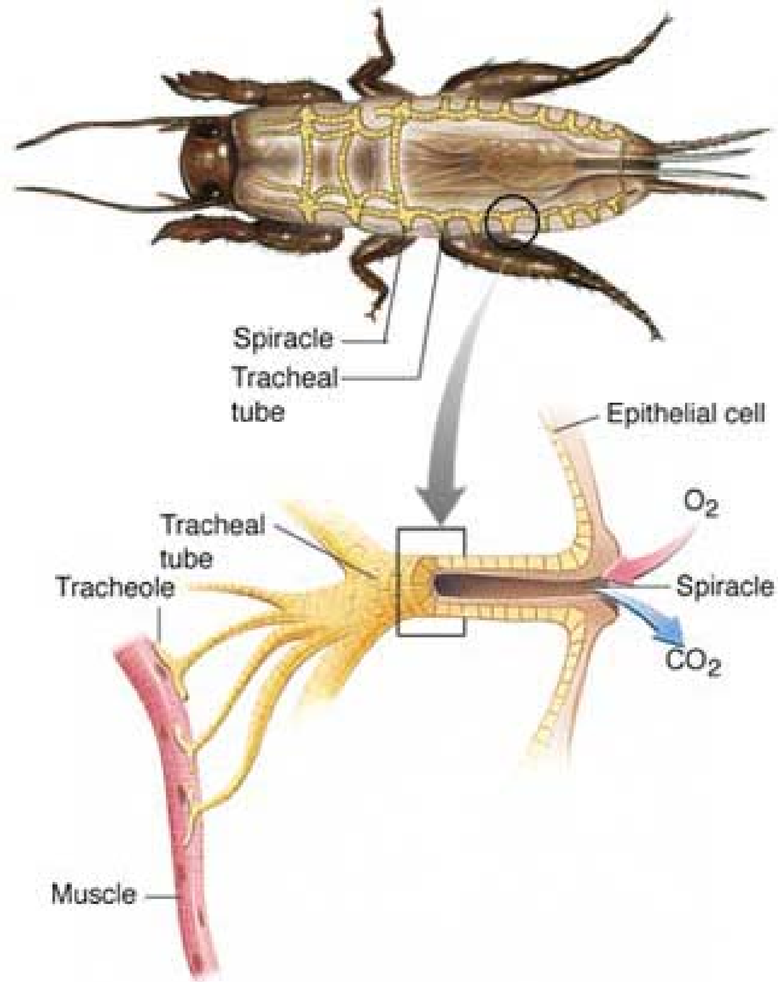
- In insect – diffusion through trachea, 2 mm long and
- cross-section 2 X 10 $^{-9}$ m^2
- Assume C inside = 1/2 C, C -outside

Diffusion coefficient :

$$D = 1 \cdot 10^{-5} m^2 / s$$

Concentration of oxygen in air:

$$\mathrm{C} = 8 \cdot 10^{-3} \mathrm{mol/ltr}$$



Solution:

a) **diffusion rate**

Concentration gradient: $$\frac{\Delta C}{\Delta x} = \frac{C}{4} \cdot 10^{3}$$

where $\Delta C = \frac{C}{2}$ concentration change over the distance Δx

$$\Delta x = 2mm = 2 \cdot 10^{-3} m$$

Diffusion rate=amount diffusing per unit time:

$$JA = DA\frac{\Delta C}{\Delta x} = (1 \cdot 10^{-5}) \cdot (2 \cdot 10^{-9}) \cdot \frac{C}{4} \cdot 10^{3} = \frac{C}{2} \times 10^{-11} = 4 \times 10^{-14} mol / \sec$$

b) average time for a molecule to diffuse

N - number of molecules in trachea,
they diffuse in time t,

J – number of molecules diffusing per unit area per unit time, A - area

$$N = JAt \qquad J = D\frac{\Delta C}{\Delta x}$$

$$\downarrow$$

$$t = \frac{N}{JA} = \frac{N\Delta x}{DA\Delta C}$$

$N=C_{av}V$, where C_{av} – average number of molecules per unit time, per unit volume,

V – volume of trachea, $V=A\cdot\Delta x$

$$t = \frac{C_{av}(\Delta x)^2}{\Delta C \cdot D} \qquad C_{av} = \frac{C + C/2}{2} = \frac{3C}{4} \qquad \Delta C = \frac{C}{2}$$

$$t = \frac{3\cancel{C}\cdot 2\cdot(\Delta x)^2}{4\cdot\cancel{C}\cdot D} = \frac{3\cdot(2\cdot 10^{-3})^2}{2\cdot 1\cdot 10^{-5}}\sec = 0.6\sec.$$