

# RESPIRATORY BIOPHYSICS

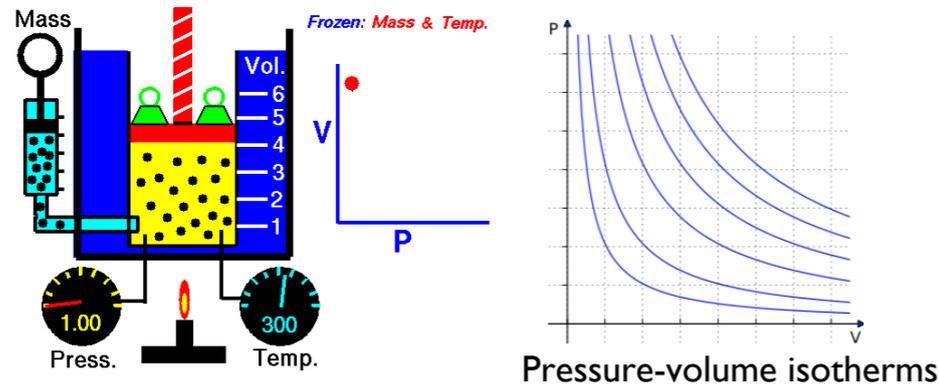
MIKLÓS KELLERMAYER

# History of respiratory biophysics

- Aristotle (300 BC): respiration cools the heart and blood
- Galenus (170 BC): breathing adds something to the blood (“*spiritus vitalis*”)
- Leonardo da Vinci (1452-1519): animals die in a closed room where air refreshment is blocked.
- Vesalius (1543): the animal dies if its chest is opened, but survives if its lung is rhythmically ventilated.
- Gas laws (17-18. century, Clausius, Clapeyron, Boyle, Mariotte, Gay-Lussac, Charles)
- Black (1754): discovery of carbon dioxide. Priestley (1771): discovery of oxygen.
- “Blood gases”: Magnus (1837), Haldane (1900)
- Surfactant: Neergaard (1920s), Pattle and Clements (1950s)

# Relevant physical and physico-chemical laws

**1. Ideal gas law** (derives from Clausius-Clapeyron's, Boyle-Mariotte's, Charles's laws): Relationship between the pressure, volume, temperature and amount of gas.



$$PV = nRT$$

$P$  = pressure (Pa)  
 $V$  = volume ( $\text{m}^3$ )  
 $n$  = amount (moles)  
 $R$  = gas constant ( $8.314 \text{ J K}^{-1} \text{ mol}^{-1}$ )  
 $T$  = absolute temperature (K)

**2. Dalton's law** (John Dalton, 1801): The total pressure exerted by the mixture of non-reactive gases is equal to the sum of the partial pressures of individual gases.

$$P_{total} = \sum_{i=1}^n p_i$$

$p_i$  = partial pressure of the  $i$ th gas  
 $n$  = number of gases in the mixture  
 $[p_i = P_{total} \times r; r = \text{ratio of the gas in the mixture}]$

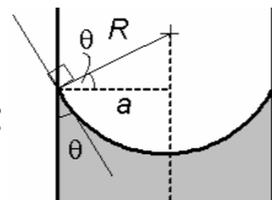
**3. Henry's law** (William Henry, 1803): At a constant temperature, the amount of a given gas that dissolves in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid.

$$p = k_H c$$

$p$  = partial pressure (Pa; atm)  
 $k_H$  = Henry's constant (l.atm/mol)  
 $c$  = concentration of dissolved gas (mol/l)

**4. Young-Laplace equation:** Describes the capillary pressure difference sustained across the interface between two static fluids (e.g., water, air) due to surface tension.

In a sufficiently narrow tube:

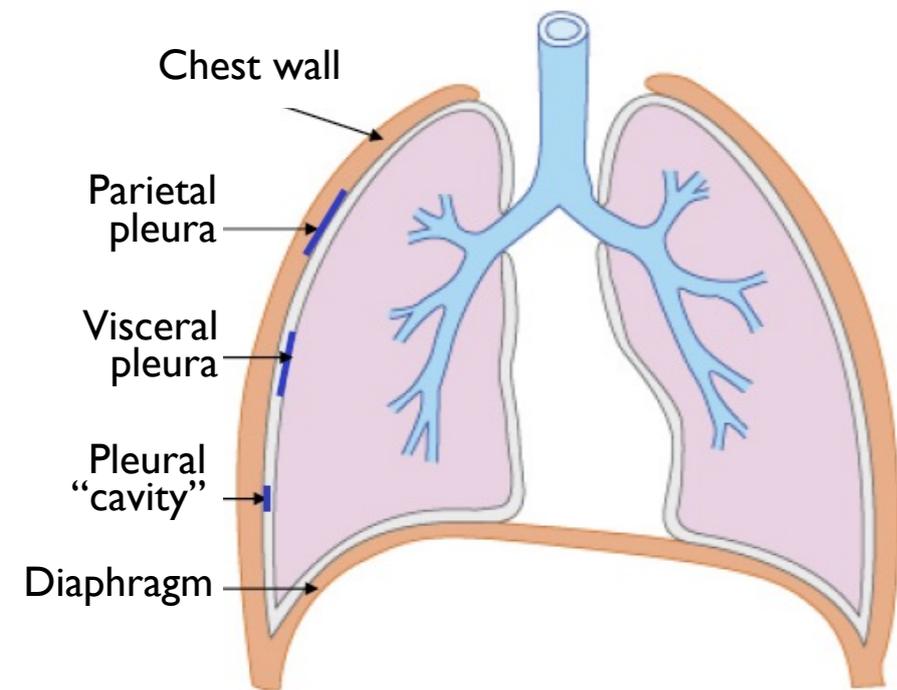


$$\Delta p = \frac{2\gamma}{R}$$

$p$  = pressure ( $\text{Nm}^{-2}$ )  
 $\gamma$  = surface tension ( $\text{Nm}^{-1}; \text{Jm}^{-2}$ )  
 $R$  = radius of curvature

# Simplified respiratory system

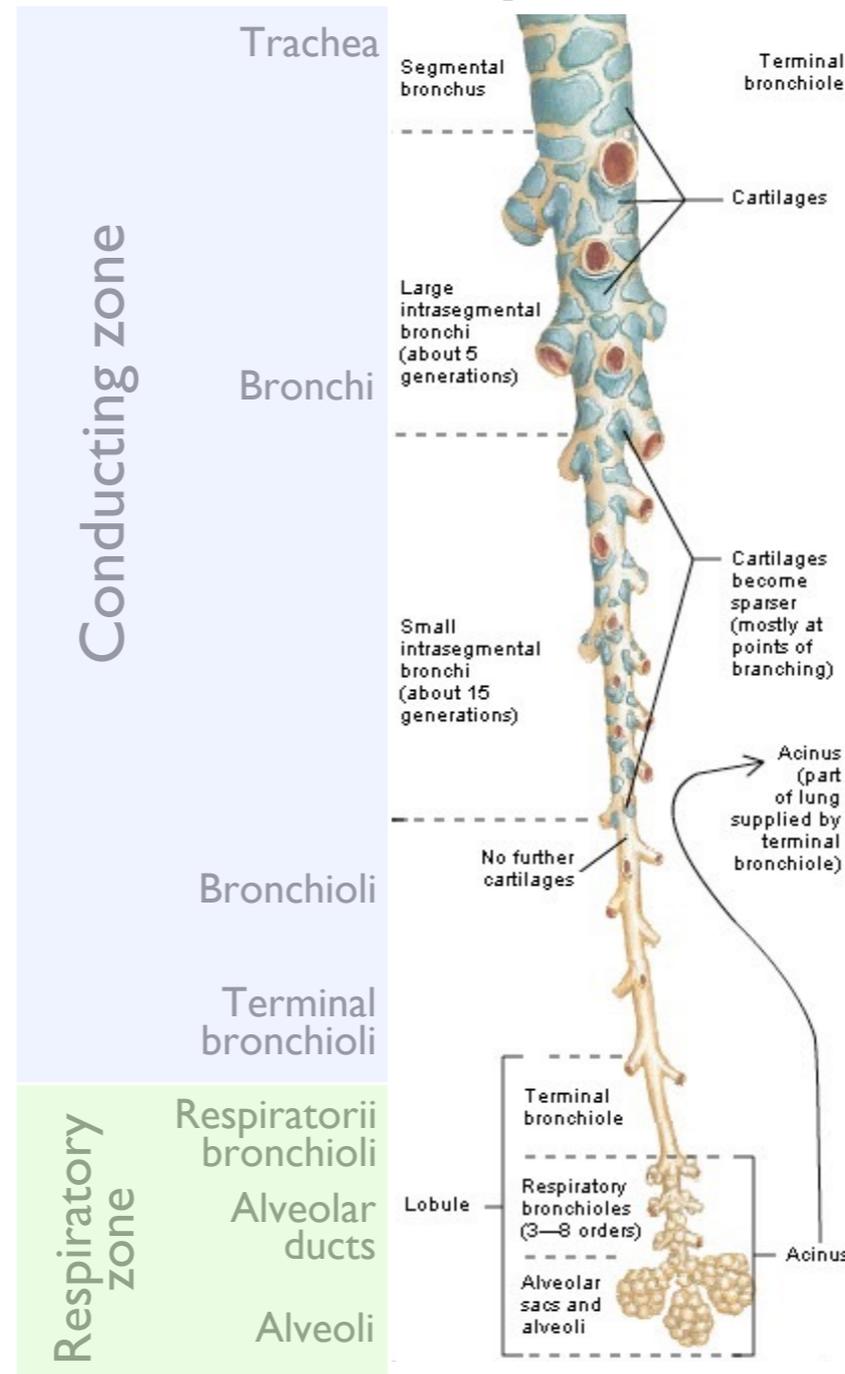
## I. Box



- Intrapulmonary pressure ( $P_{pulm}$ ): fluctuates around external (atmospheric) pressure
- Intrathoracic or intrapleural pressure ( $P_{pl}$ ): "negative" (balance between atmospheric pressure, adhesional and contractile forces)
- Transmural (transpulmonary) pressure ( $P_{tm}$ ): pressure difference across chest wall

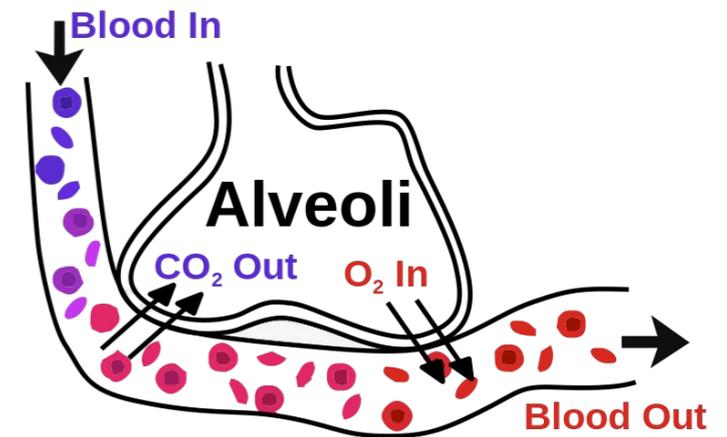
• *Pneumothorax!*

## 2. Tube system



- 23-25 dichotomic divisions
- Laws of fluid flow (Hagen-Poiseuille!)

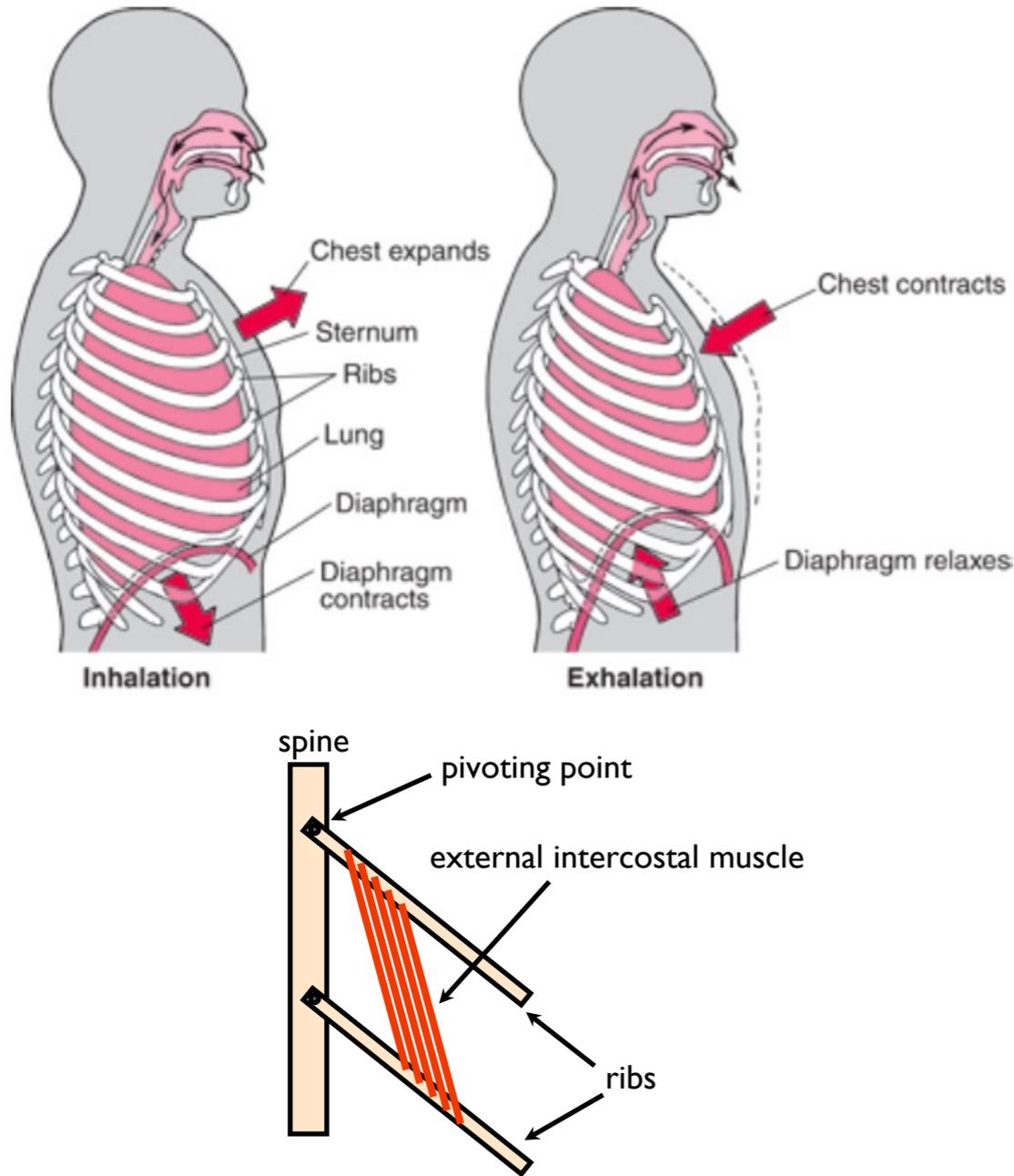
## 3. Gas exchange surface



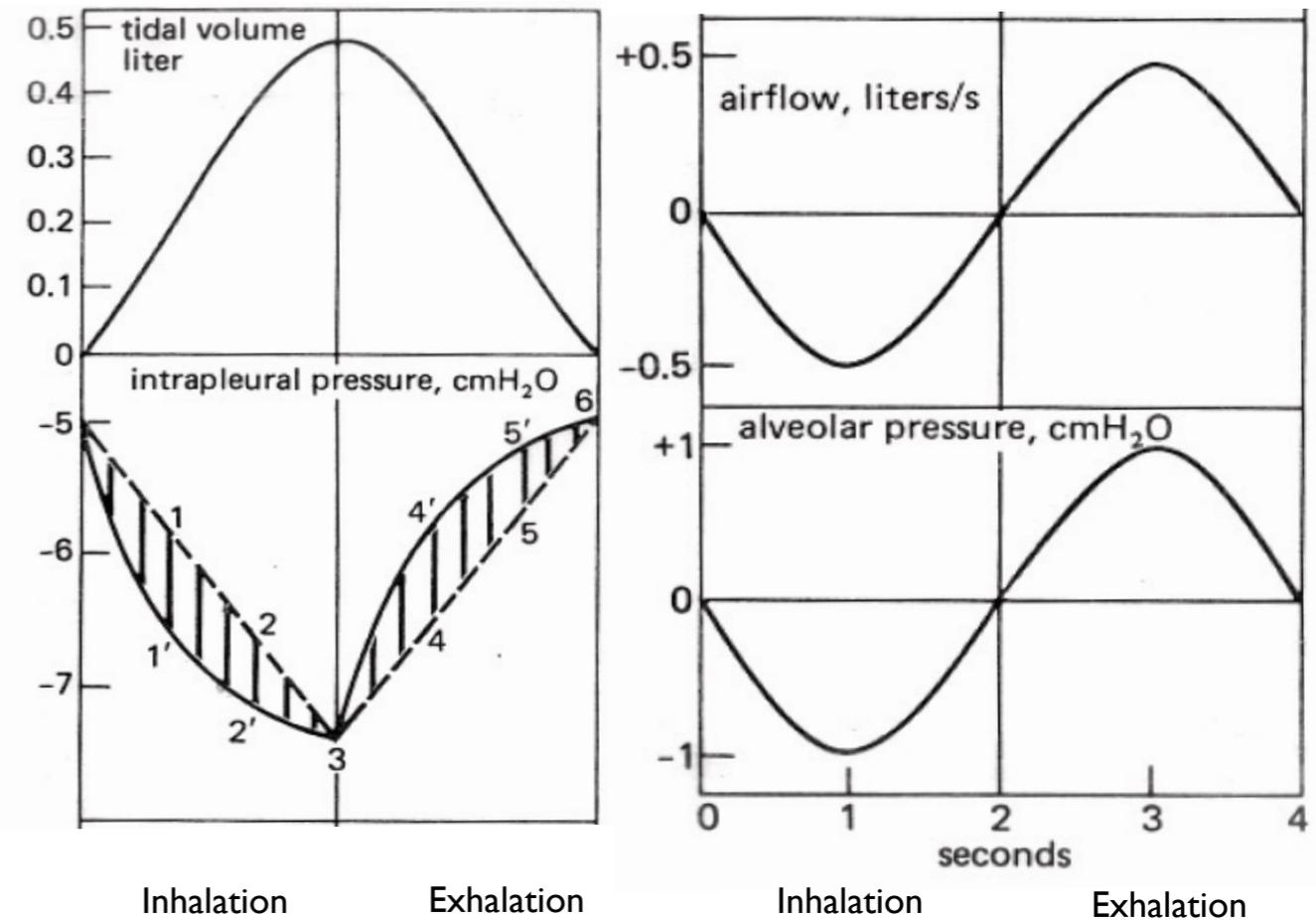
- Alveole: open thermodynamic system
- Surface for gas exchange.
- Number: ~300 million (N.B.:  $2^{25}=33,554,432$ )
- Size ( $d \sim 200 \mu\text{m}$ ), area ( $5 \times 10^{-7} \text{ m}^2/\text{alveolus}$ )
- Total alveolar area:  $\sim 100 \text{ m}^2$
- Alveolar wall ( $\sim 0.5 \mu\text{m}$ ): alveolar epithelium ( $\sim 0.2 \mu\text{m}$ ) basal membrane ( $\sim 0.1 \mu\text{m}$ ) capillary endothelium ( $\sim 0.2 \mu\text{m}$ )
- Driving force of gas exchange: diffusion (Fick's laws!)
- The partial pressures of gas phases tend to equilibrate with blood plasma gas tensions.

# Respiratory cycle

## I. Mechanical control



## 2. Changes in physical parameters

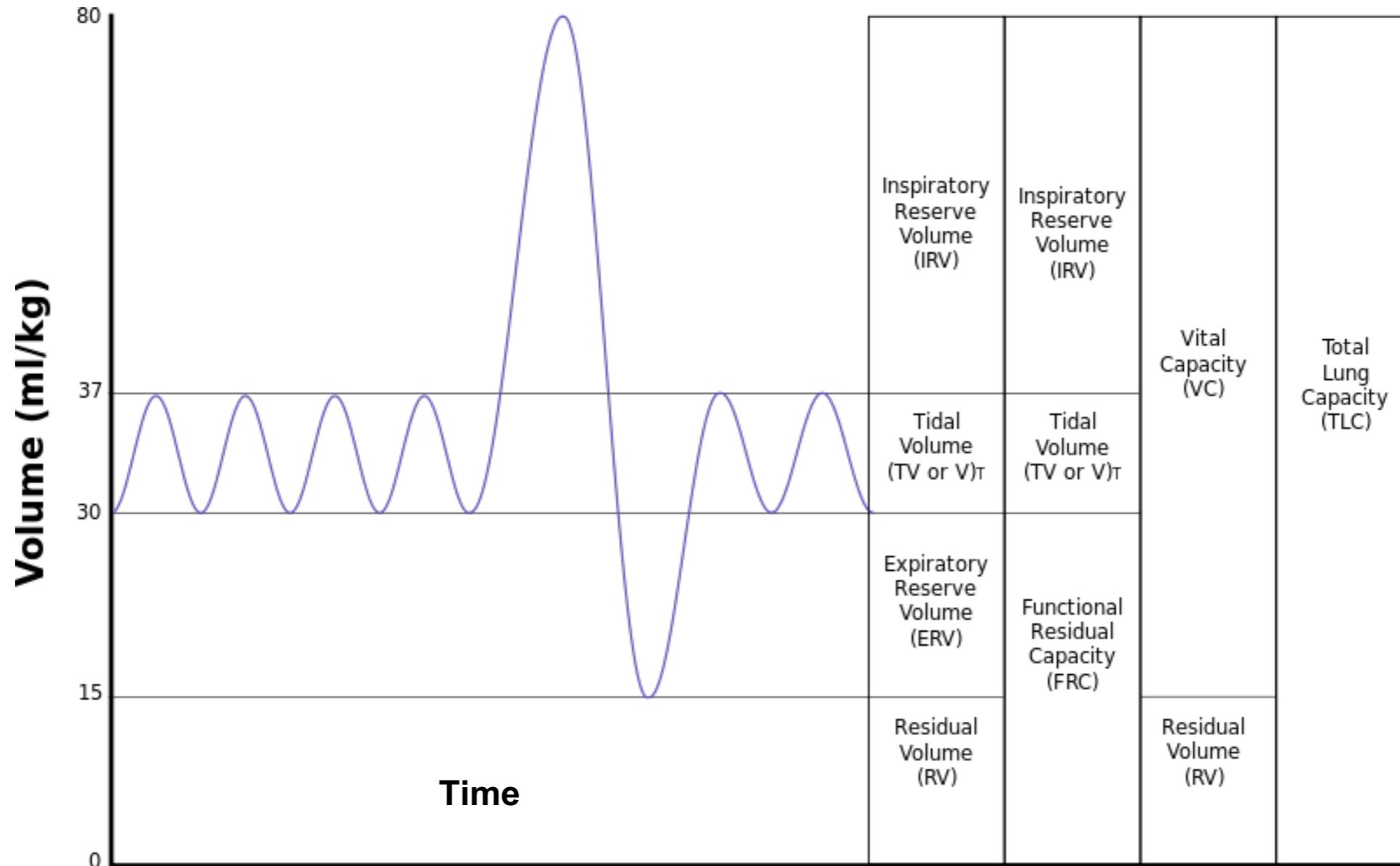


$$1 \text{ cmH}_2\text{O} = 0.1 \text{ kPa} = 0.7 \text{ mmHg}$$

- Eupnoe: normal breathing (14-16/min)
- Polypnoe, tachypnoe: number of breaths >16/min
- Dyspnoe: shortness of breath

# Pulmonary volumes and capacities

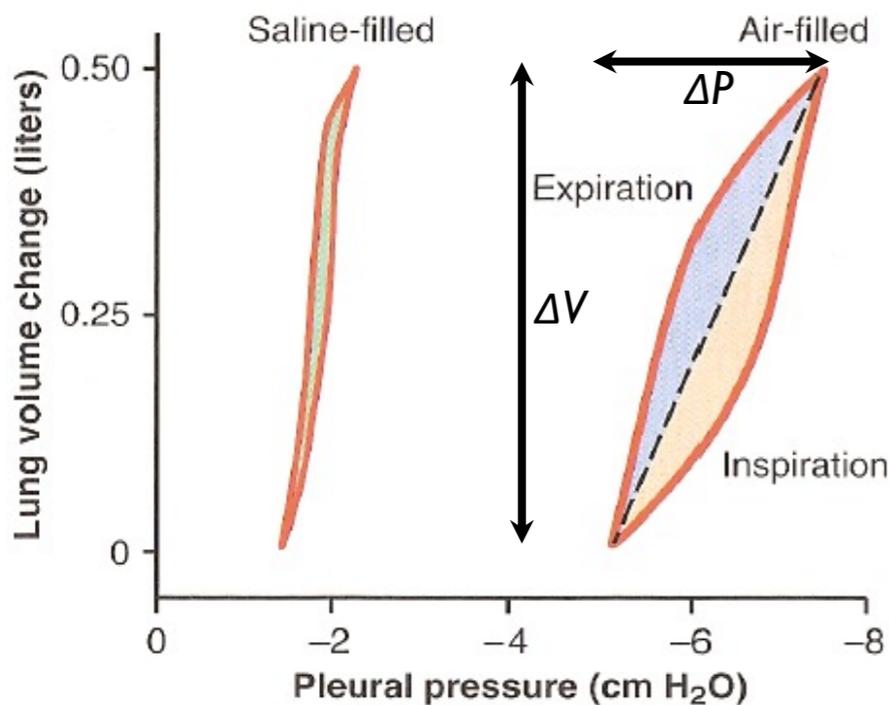
**Capacity:** sum of volumes



Volume	Value (litres)		Volume	Average value (litres)		Derivation
	In men	In women		In men	In women	
Inspiratory reserve volume	3.3	1.9	<b>Vital capacity</b>	4.8	3.1	IRV plus TV plus ERV
Tidal volume	0.5	0.5	Inspiratory capacity	3.8	2.4	IRV plus TV
Expiratory reserve volume	1.0	0.7	Functional residual capacity	2.2	1.8	ERV plus RV
Residual volume	1.2	1.1	Total lung capacity	6.0	4.2	IRV plus TV plus ERV plus RV

# Processes of the respiratory cycle

## 1. Lung cyclically expands and contracts



Compliance  
("deformability",  
"stretchability",  
"distensibility"):

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

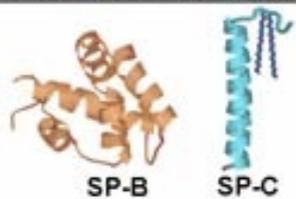
$C$  = compliance (mN<sup>-1</sup>; N.B.: inverse of stiffness)

$\Delta P$  = change in pressure (Pa, Nm<sup>-2</sup>)

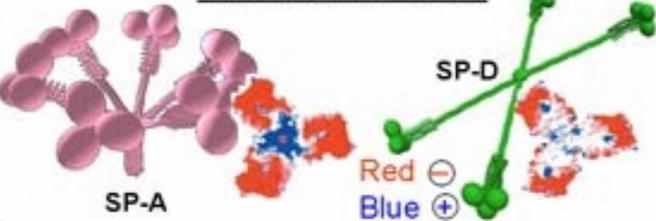
$\Delta V$  = change in volume (m<sup>3</sup>)

## Surfactant

### SMALL HYDROPHOBIC PROTEINS

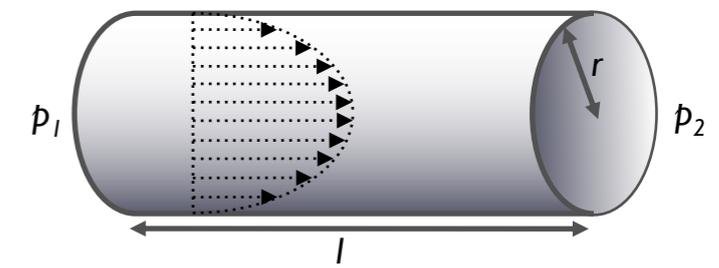


### LUNG COLLECTINS



- Pulmonary surfactant: surface-active lipoprotein complex (phospholipoprotein) formed by (type II) alveolar cells (starting from the 20th gestational week).
- Composition: 90 % phospholipids, 10 % proteins ("surfactant protein" SP-A, SP-B, SP-C, SP-D)
- Function: reduces surface tension
- Effect: the smaller the surface tension, the smaller pressure needed to keep alveoli open (for a given pressure, smaller alveoli can be opened) (Young-Laplace equation!).
- **Restrictive diseases:** pulmonary compliance is reduced (fibrosis, lack of surfactant, etc.).

## 2. Gas flows in airways



Hagen-Poiseuille's law

$$\frac{V}{t} = \frac{\pi r^4}{8\eta} \frac{dp}{dl}$$

$V$  = volume

$t$  = time

( $V/t = Q$  = flow intensity)

$r$  = tube radius

$\eta$  = viscosity

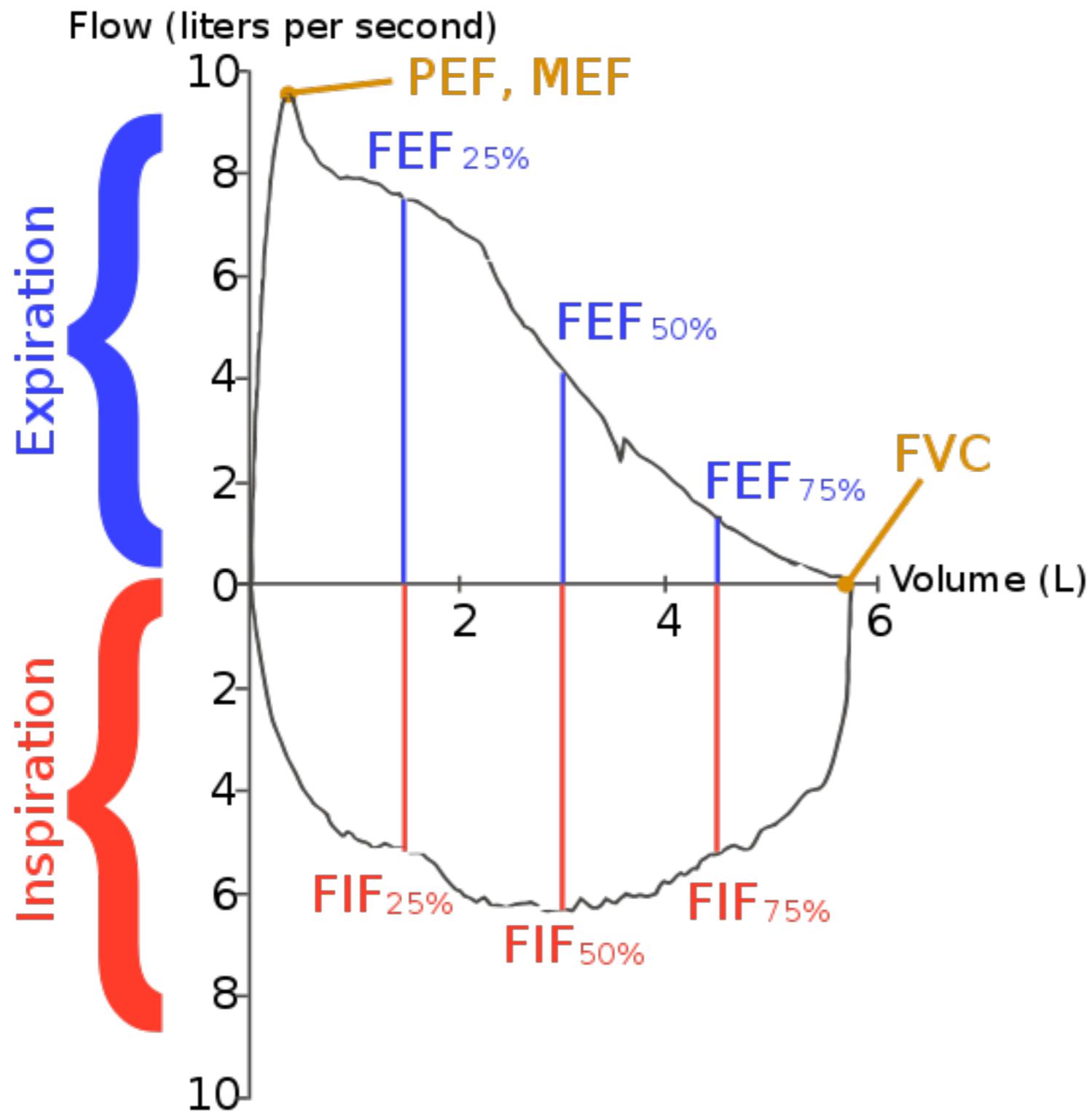
$p$  = pressure

$l$  = length of tube

( $dp/dl$  = pressure gradient, maintained by  $p_1 - p_2$ )

- Normally (eupnoe): flow is laminar.
- Tachypnoe or disease: turbulent airflow
- **Obstructive diseases:** pulmonary airflow is compromised (COPD - "chronic obstructive pulmonary disease").

# Dynamic analysis of respiration



## Spirometry:

- PEF, MEF: peak expiratory flow, maximal expiratory flow
- FEF: forced expiratory flow
- FIF: forced inspiratory flow
- FVC: forced vital capacity

# Respiratory work

- Volume change against average transmural pressure
- Minute volume ( $MV$ ) = 7 l
- Breathing rate ( $BR$ ) = 14/min
- Pressure ( $P_{tm}$ ) = 0.7 kPa
- Respiratory volume ( $V$ ) = 0.5 l ( $5 \times 10^{-4} \text{ m}^3$ )
- Work ( $W$ ) =  $P_{tm} \times V = 0.35 \text{ J/inspiration}$  (294 J/h)
  
- At large loads it may reach 8400 J/h

# BIOPHYSICAL BASIS OF PHYSICAL EXAMINATION

# Physical examination

- Inspection
- Palpation
- Percussion
- Auscultation

# Inspection

## **What is this?**

Visual examination of the patient

## **What do we visualize?**

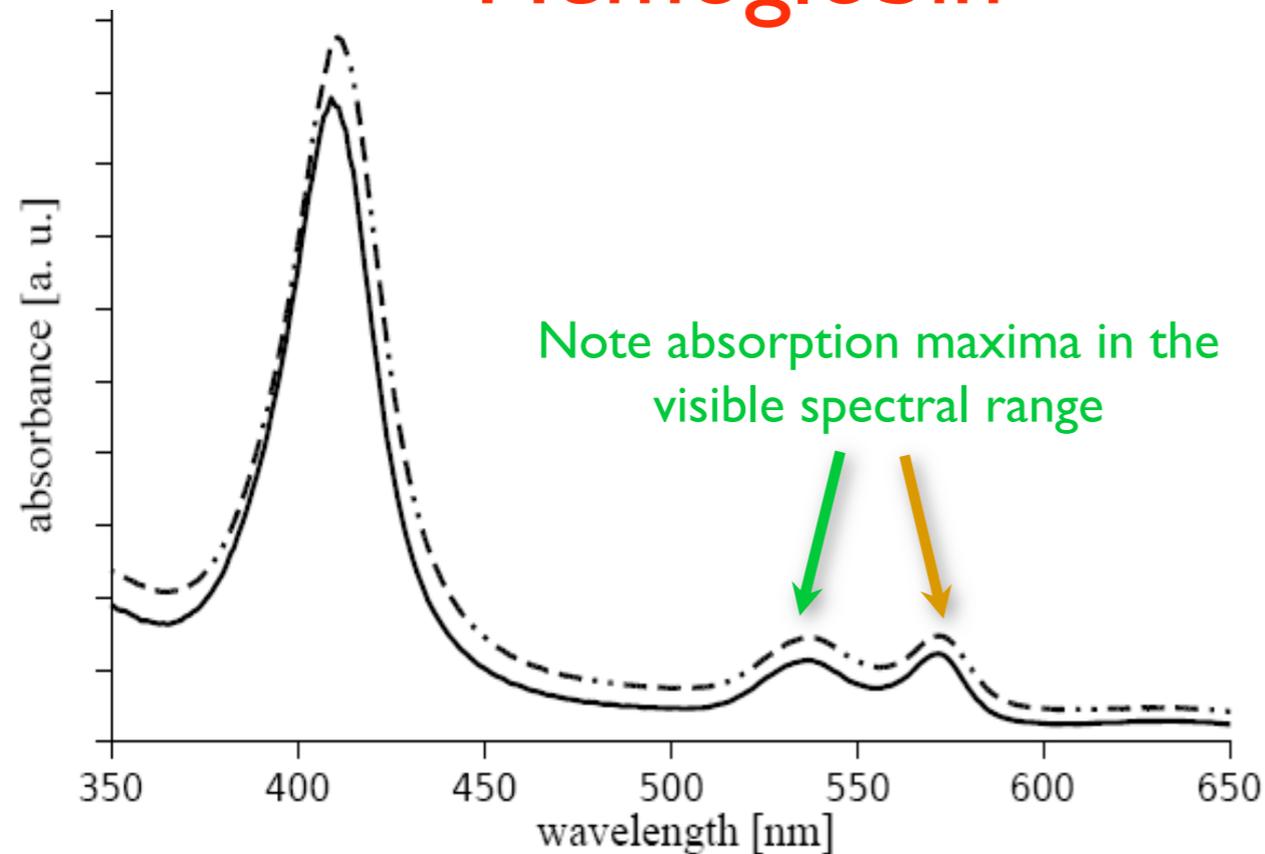
Behavior, morphology, structure, **color**

## **Relationship to biophysics:**

Absorption spectroscopy

# Light absorption

## Hemoglobin



From the general law of radiation attenuation:

$$J = J_0 e^{-\mu x}$$

$$\lg \frac{J_0}{J} = \mu x \lg e$$

$$\lg \frac{J_0}{J} \approx \mu$$

absorbance, optical density

$$\lg \frac{J_0}{J} = \epsilon_{\lambda} c x$$

Lambert-Beer's Law

$\epsilon_{\lambda}$  = molar extinction coefficient

c = concentration

# Examples



**Cyanosis**  
(rise in deoxygenated hemoglobin)



**Icterus**  
(jaundice, hyperbilirubinaemia)



**Erythema**  
(redness of the skin)

# Palpation

## **What is this?**

Examining the patient by touching

## **What do we palpate?**

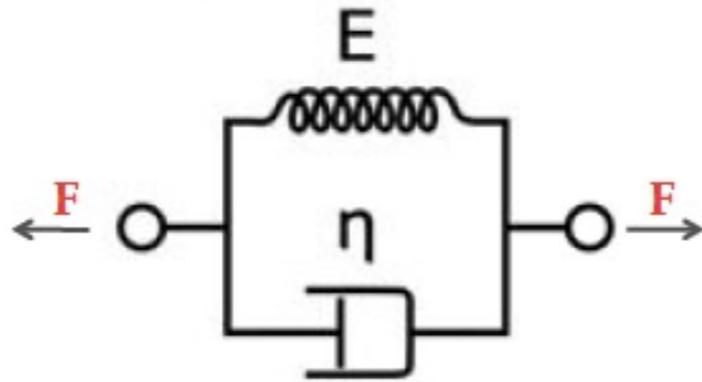
Size, shape, location, ***firmness***  
***(elasticity, viscosity)***

## **Relationship to biophysics:**

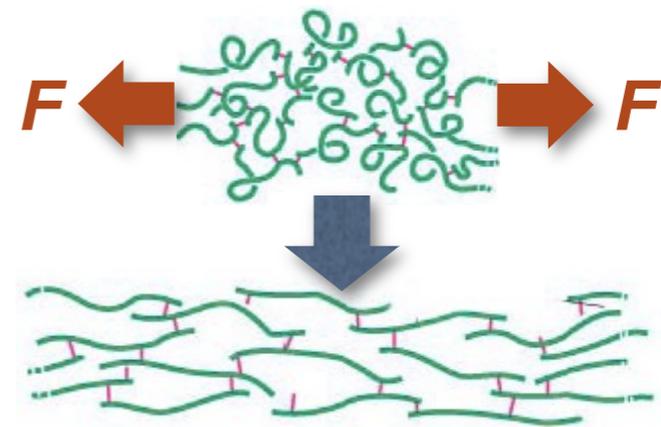
Biomechanics

# Viscoelasticity

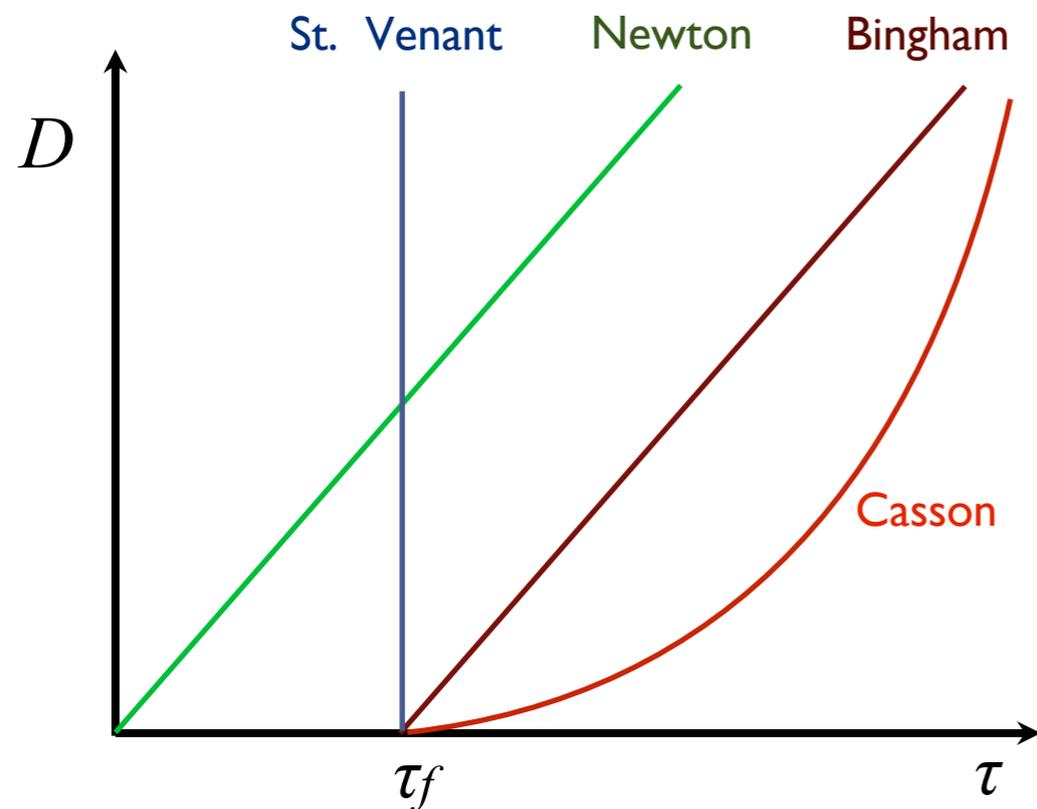
Spring-dashpot model



Schematic mechanism



Velocity gradient versus shear stress function of newtonian and non-newtonian fluids



Example: edema (pitting)

# Percussion

## **What is this?**

Examining the patient by locally striking (tapping) with short, sharp blows

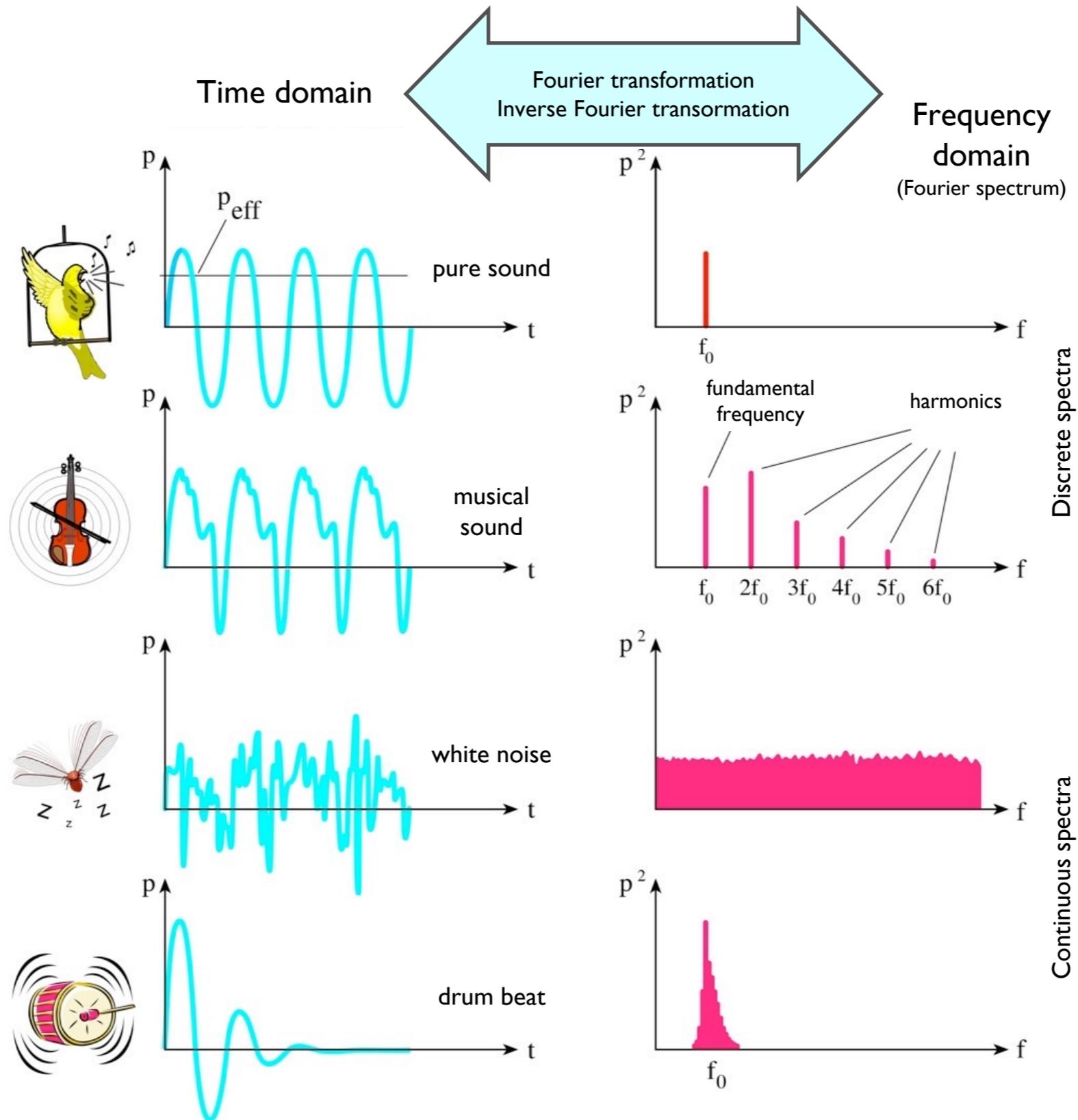
## **What do we examine by percussion?**

Material content, shape, boundaries

## **Relationship to biophysics:**

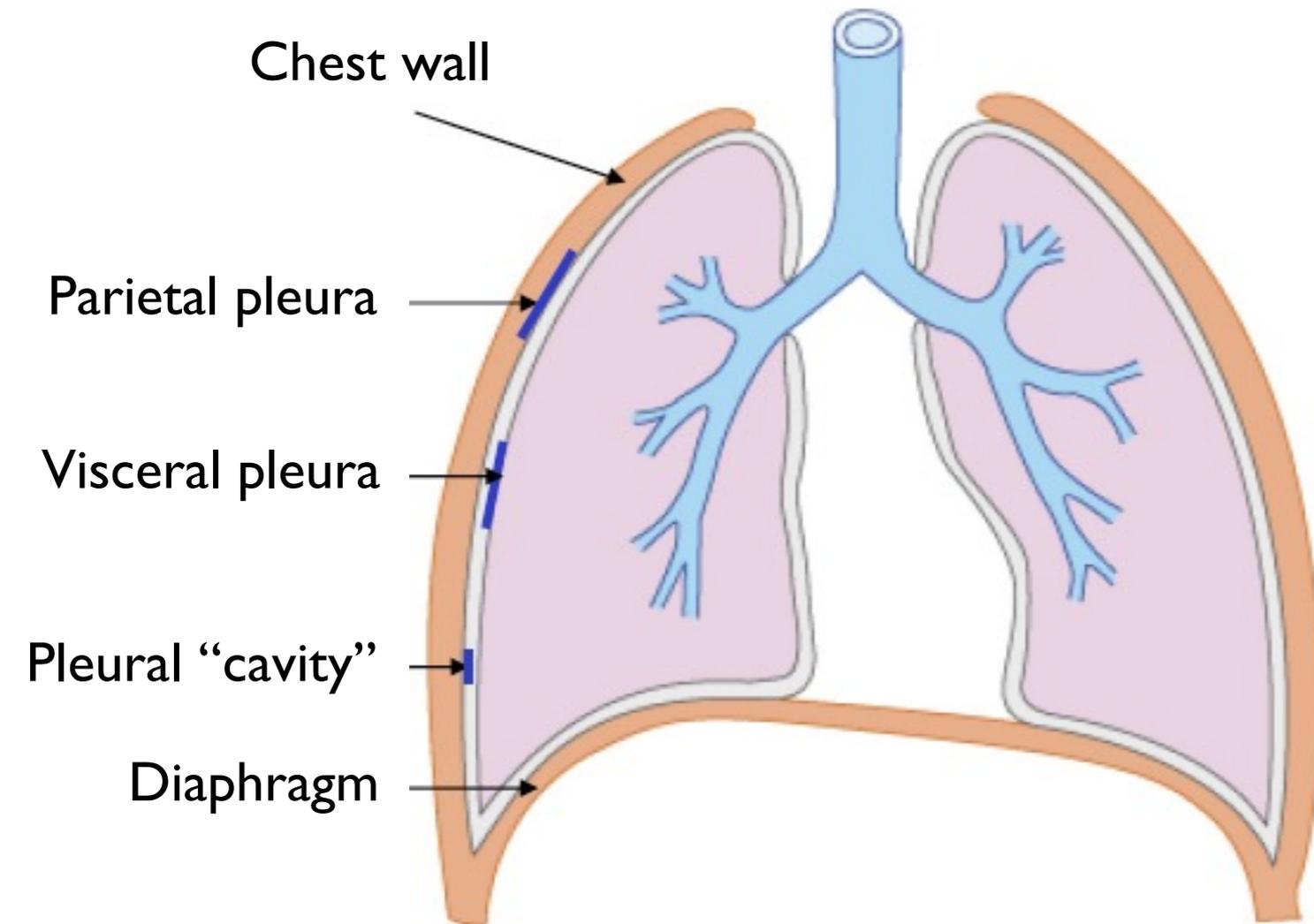
Sound generation, propagation and detection

# Sounds and their spectra



# Respiratory system as a box

Percussion sounds may be flat (muscle), dull (liver), or resonating (normal lung)



Boundaries of the diaphragm, heart, liver (and other, parenchymal organs) may be detected by percussion.

# Auscultation

## **What is this?**

Examining the patient by listening (with a stethoscope) for sounds (murmurs) within the body

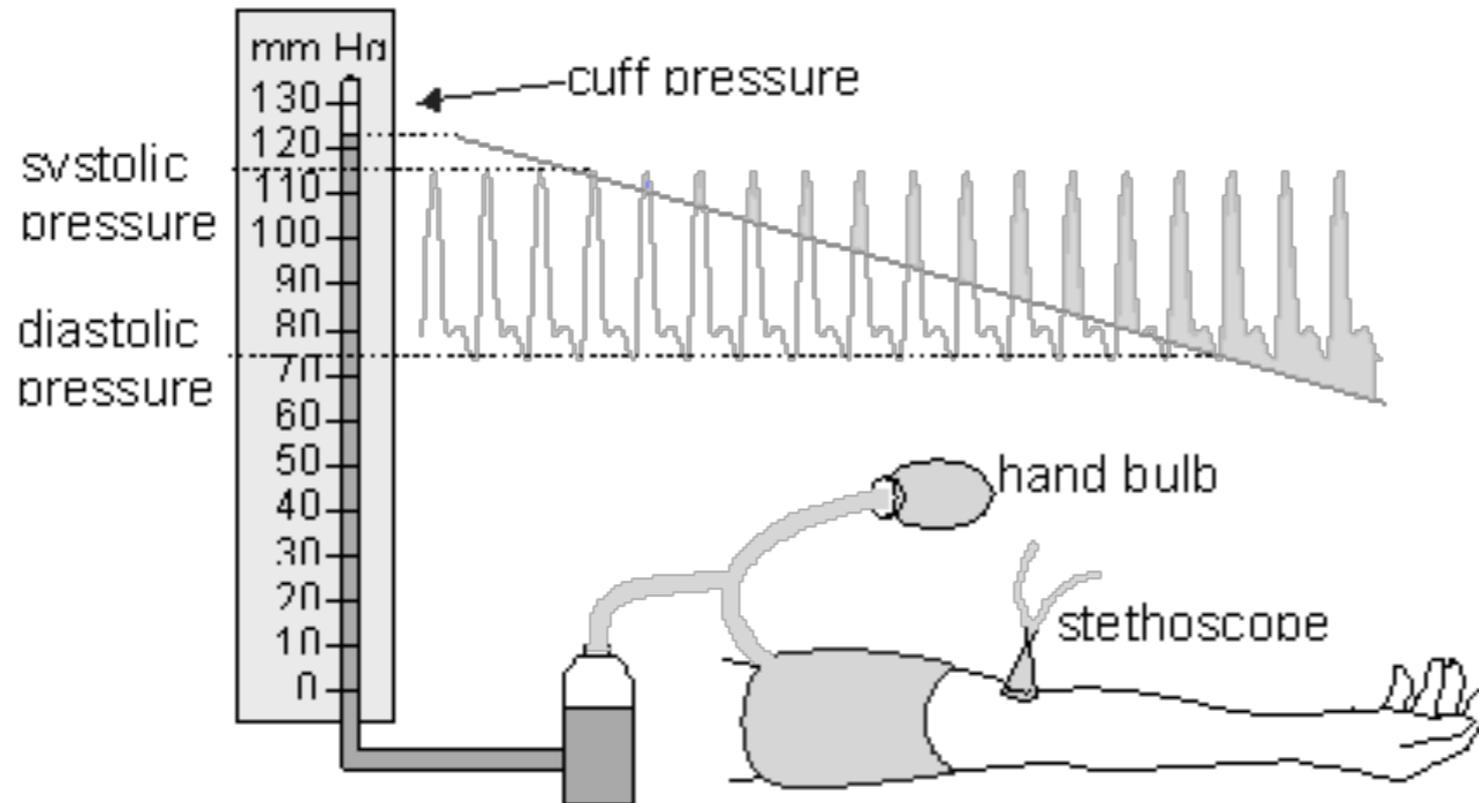
## **What do we examine by auscultation?**

Loudness, pitch, tone, duration, temporal variation (rythm)

## **Relationship to biophysics:**

Sound generation, propagation, fluid flow, turbulence

# Korotkow's sound



1. tapping
2. swishing
3. knocking
4. muffling

## Reynolds number:

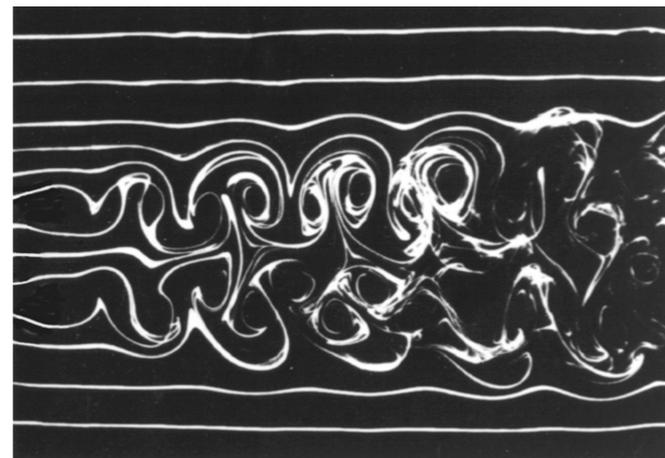
$$R = \frac{vr\rho}{\eta}$$

$v$ =flow rate (m/s)

$r$ =tube radius (m)

$\rho$ =density of fluid (kg/m<sup>3</sup>)

$\eta$ =viscosity (Ns/m<sup>2</sup>)



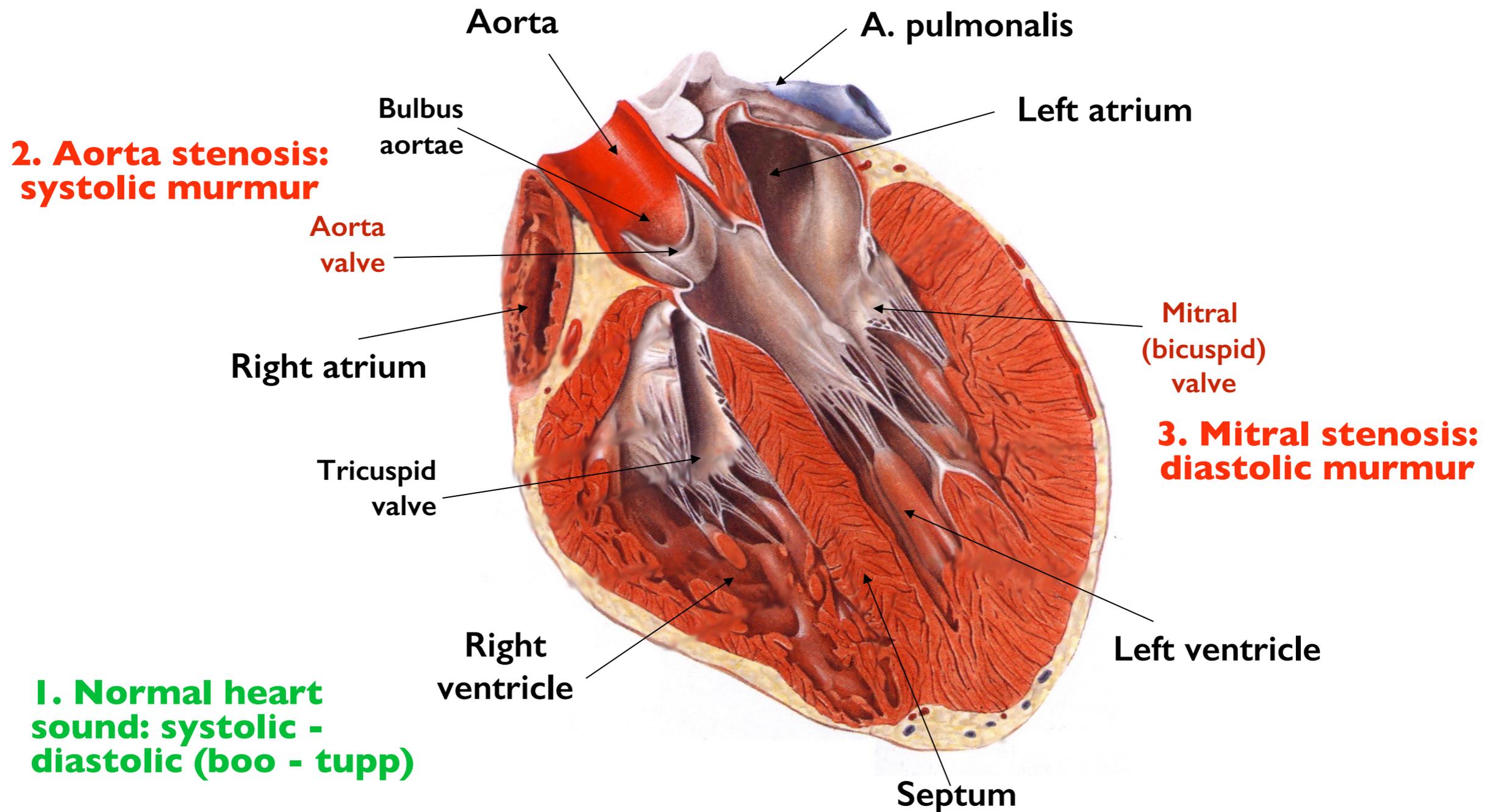
Turbulent flow ( $R > \sim 1160$ )  
causing sound effects

- Constriction of artery with cuff - flow rate increases according to continuity equation
- If flow rate exceeds the critical velocity, then turbulence, hence sound effect occurs.

# Heart sounds and murmurs

**Sources:** mechanical vibrations (e.g., valve closing), turbulent flow

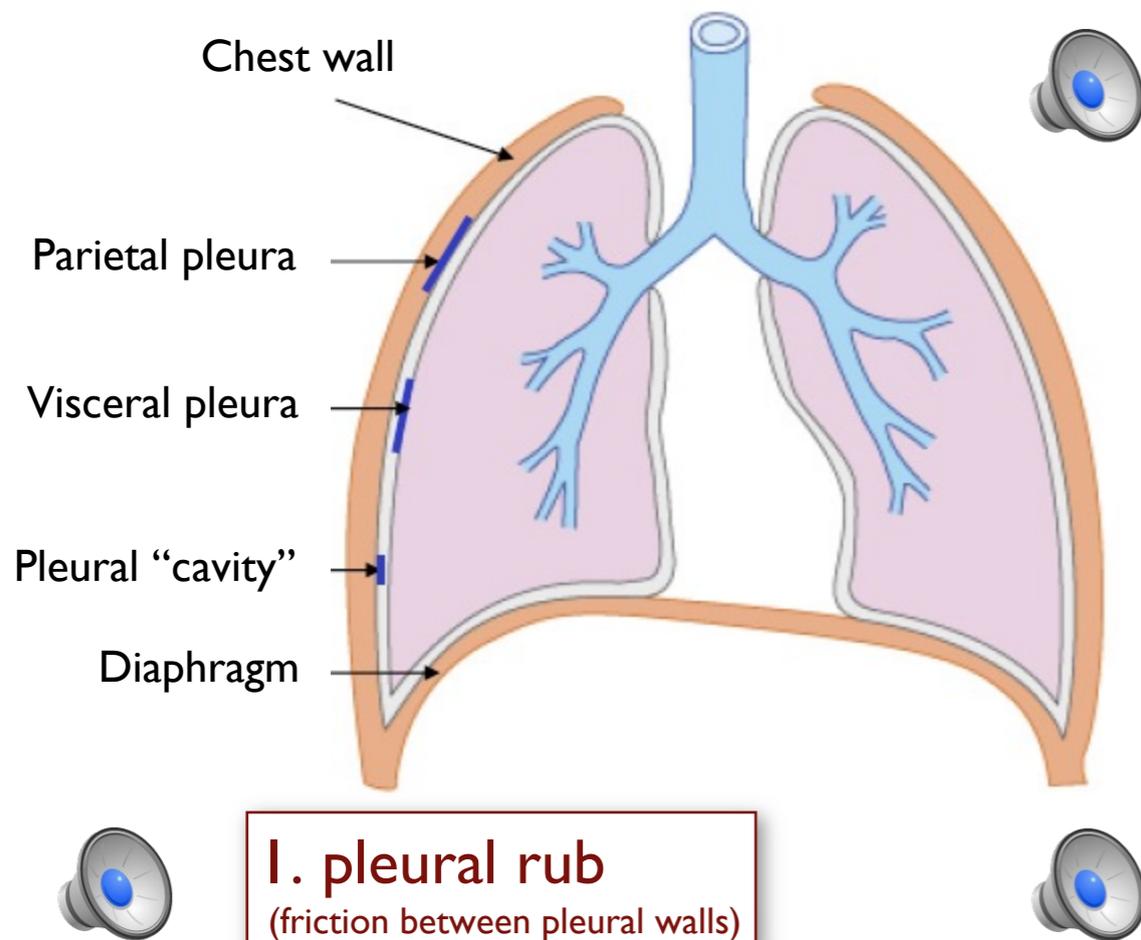
**Conductance:** towards blood-filled compartments



# Respiratory sounds

## Sources and mechanisms:

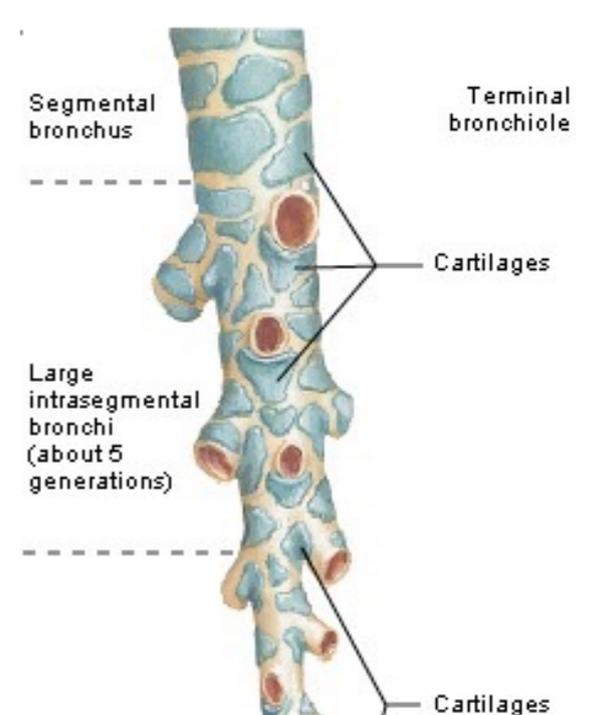
1. mechanical vibrations (rubbing noise)
2. mechanical resonance (organ-pipe action)
3. bubbling through fluid



## Tracheobronchial sounds

### Conducting zone

- Trachea
- Bronchi
- Bronchioli
- Terminal bronchioli



**2. wheeze, stridor**  
(airway obstruction)

### Respiratory zone

## Vesicular sounds

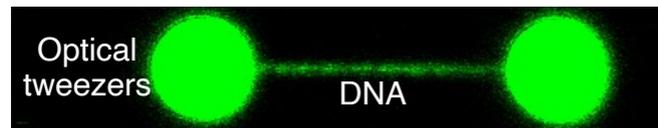
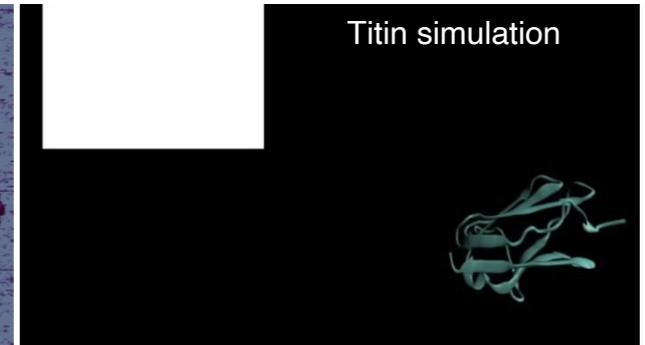
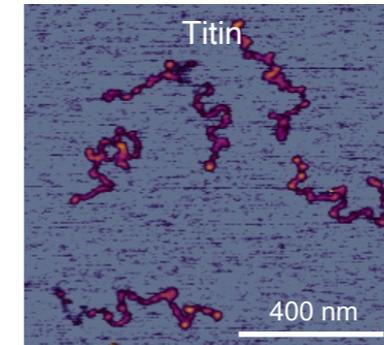
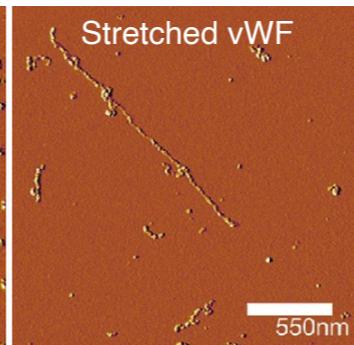
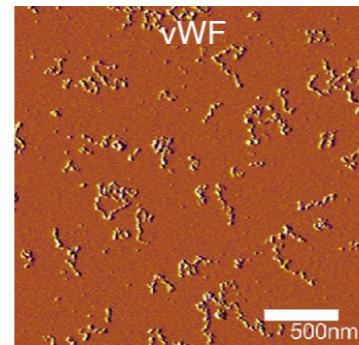
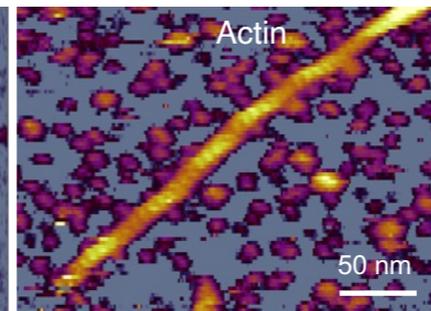
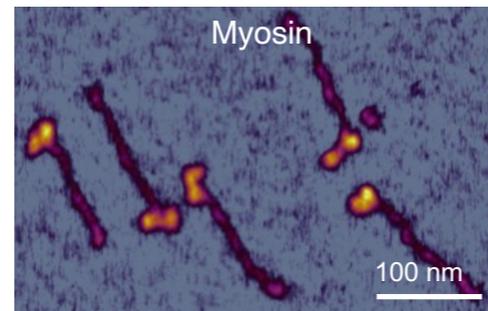
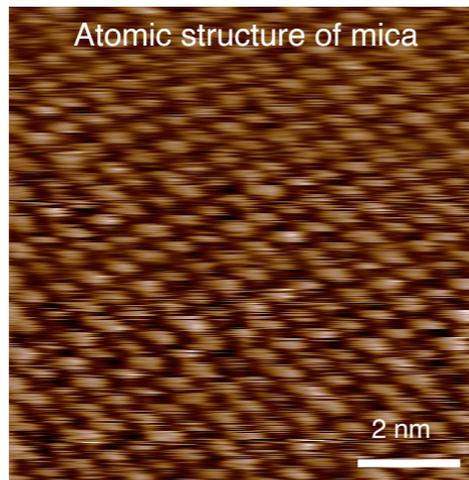
- Respiratory bronchioli
- Alveolar ducts
- Alveoli

**3. crackles**  
(fine, medium, coarse; bubbling through ducts)  
**-crepitation**  
(alveolar opening-closing)

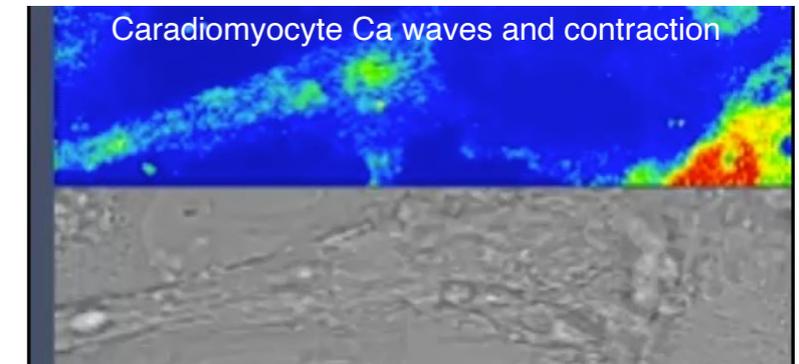
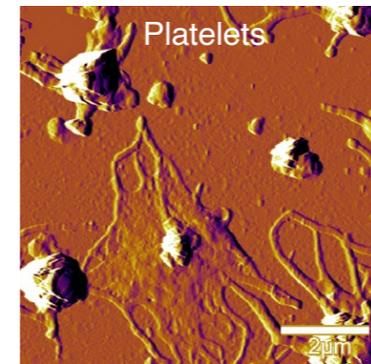
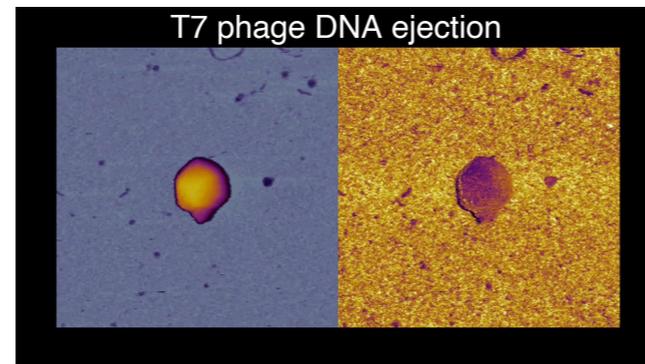
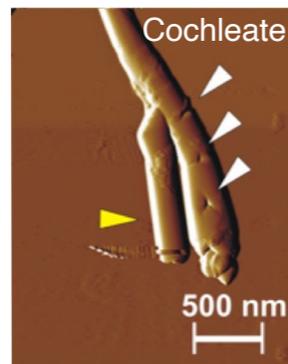


# Research in the Department of Biophysics and Radiation Biology

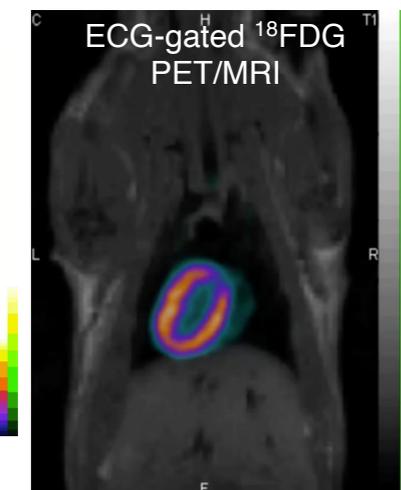
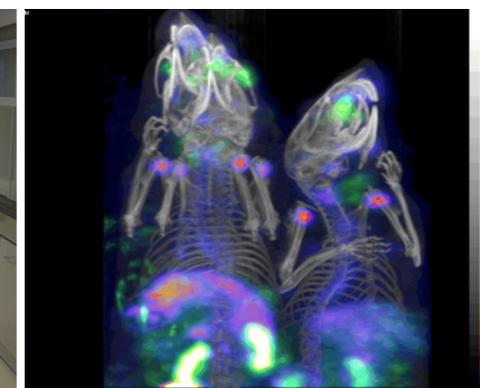
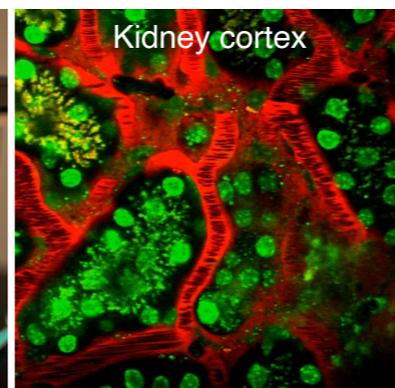
From atoms and molecules...



...through supra-molecular and cellular systems...



...to the living organism



# Feedback



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