# Respiratory Biophysics

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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 of its chest is opened, but survives if its lung is rythmically 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.

Pressure-volume isotherms
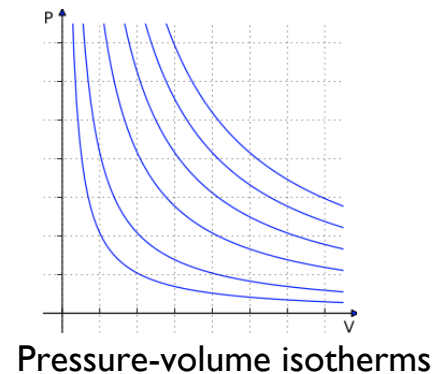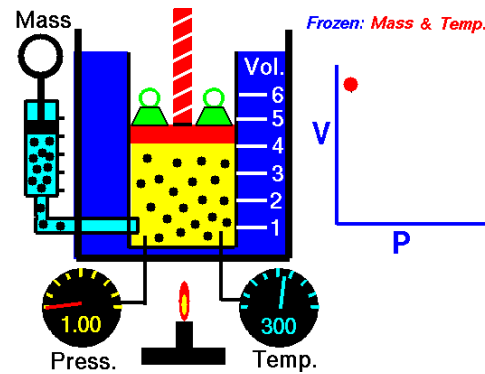
$$PV = nRT$$

P = pressure (Pa)
V = volume (m^3)
n = amount (moles)
R = gas constant (8.314 JK^{-1}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 ith gas
n = number of gases in the mixture
[$p_i = P_{total} \times r$; r = 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.
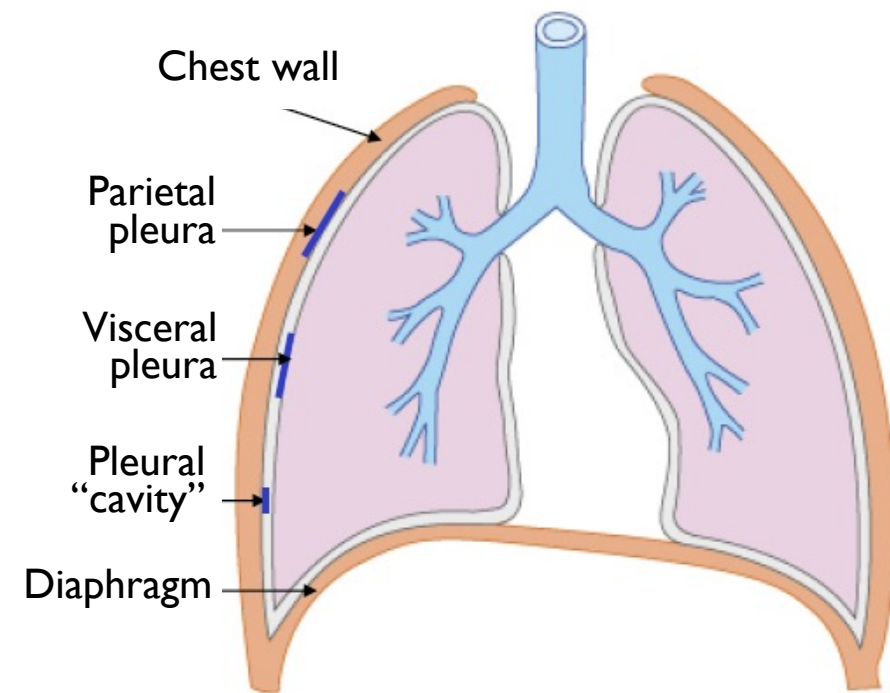
In a sufficiently narrow tube:

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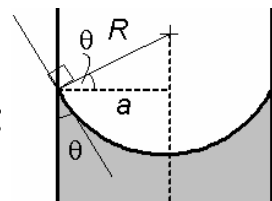
p = pressure (Nm^{-2})
γ = surface tension (Nm^{-1}; Jm^{-2})
R = radius of curvature

Simplified respiratory system

1. Box

Chest wall

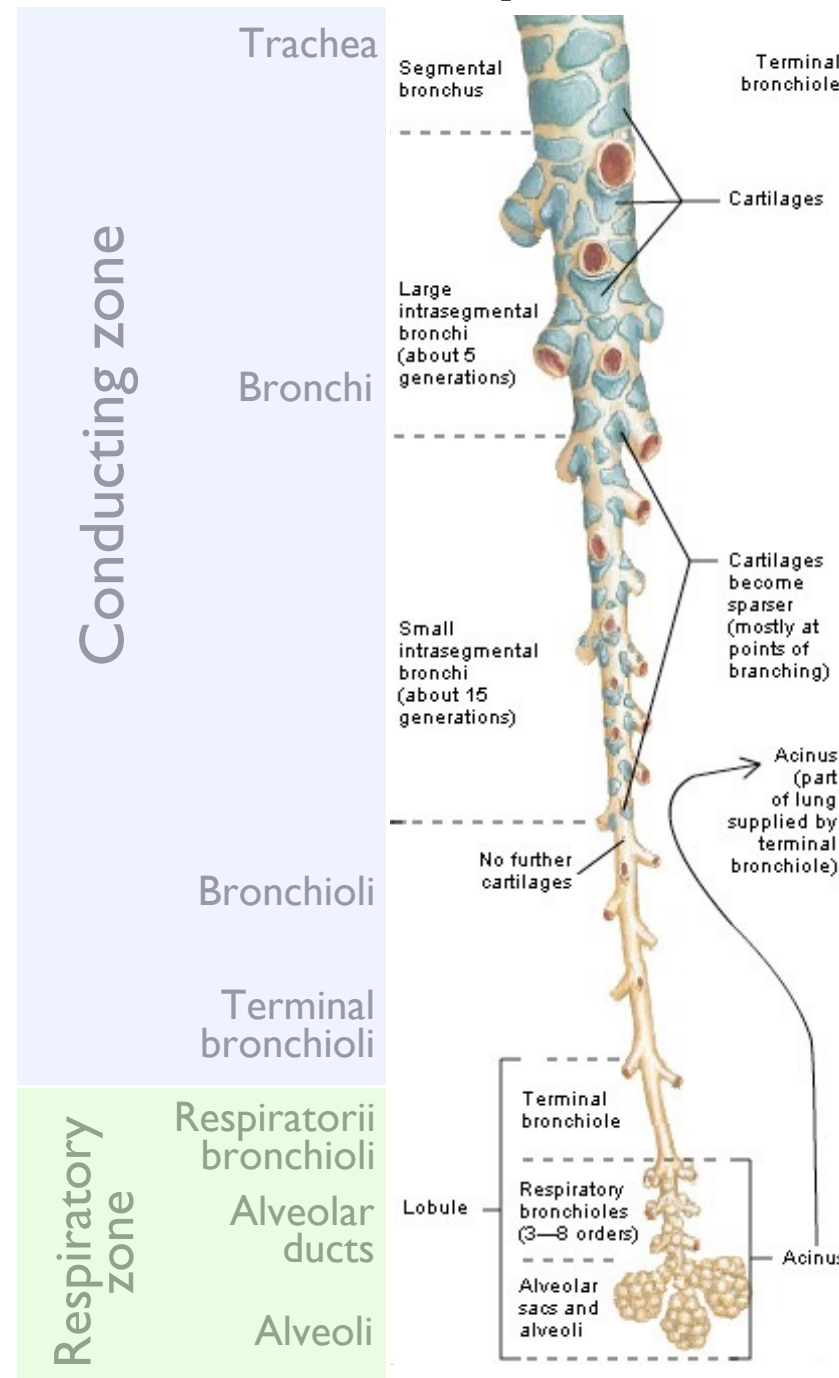Parietal pleura

Visceral pleura

Pleural "cavity"

Diaphragm

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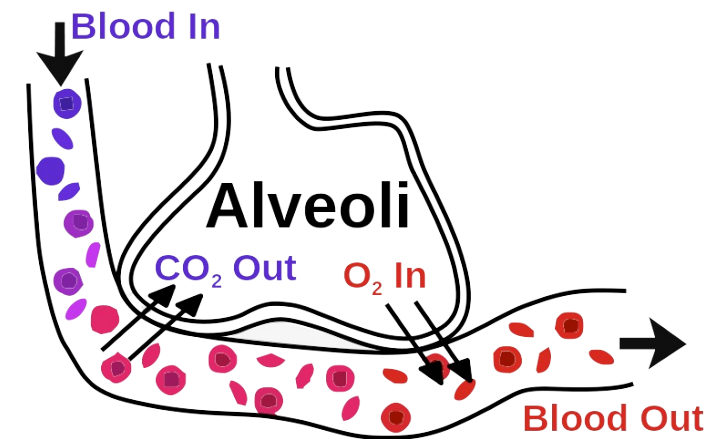- Transmural (transpulmonary) pressure (P_{tm}): pressure difference across chest wall
- *Pneumothorax!*

2. Tube system

Conducting zone

Trachea

Bronchi

Bronchioli

Terminal bronchioli

Respiratory zone

Respiratorii bronchioli

Alveolar ducts

Alveoli

Segmental bronchus

Terminal bronchiole

Cartilages

Large intrasegmental bronchi (about 5 generations)

Small intrasegmental bronchi (about 15 generations)

Cartilages become sparser (mostly at points of branching)

No further cartilages

Acinus (part of lung supplied by terminal bronchiole)

Terminal bronchiole

Respiratory bronchioles (3—8 orders)

Lobule

Acinus

Alveolar sacs and alveoli

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

3. Gas exchange surface

Blood In

Alveoli

CO_2 Out O_2 In

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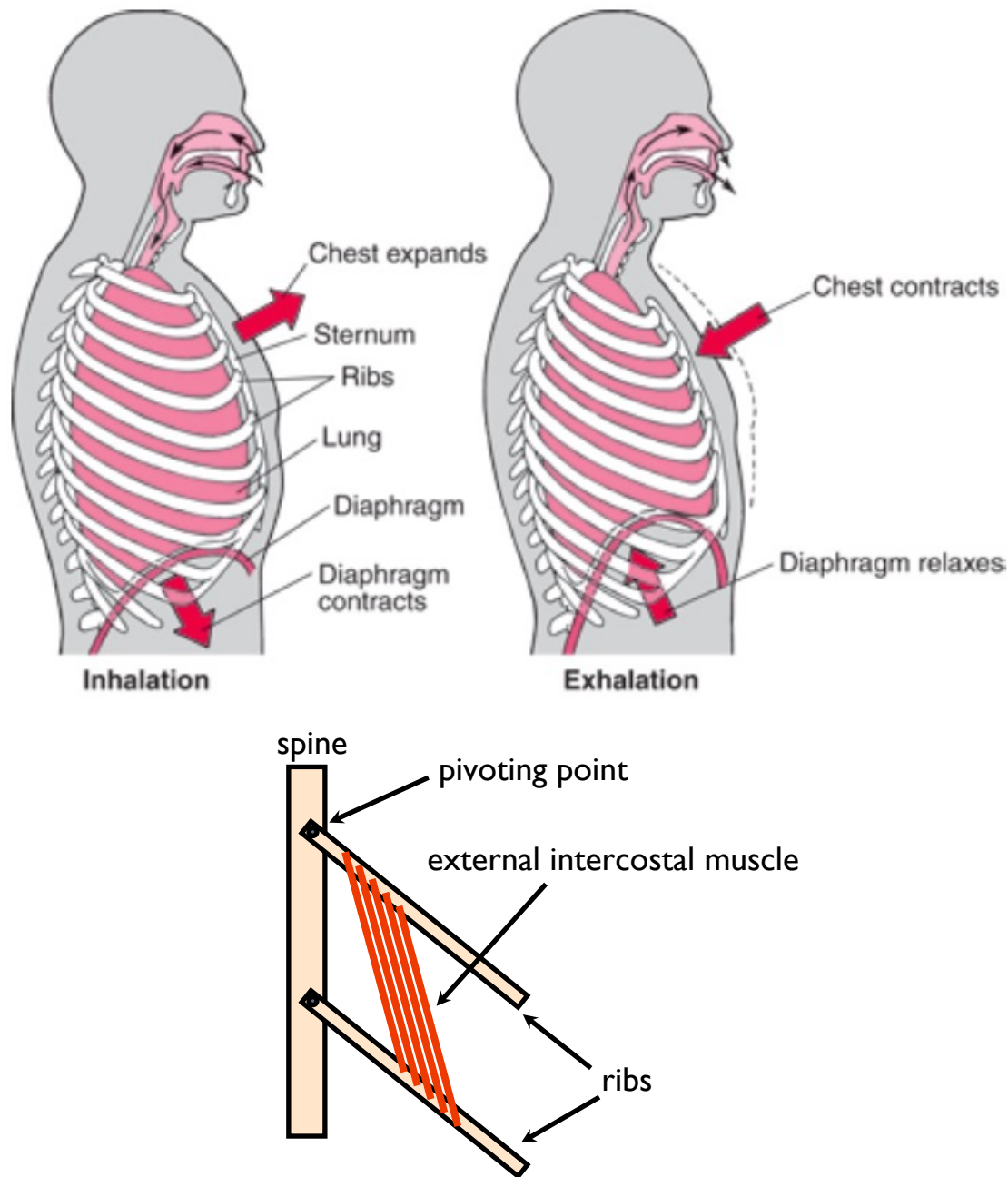
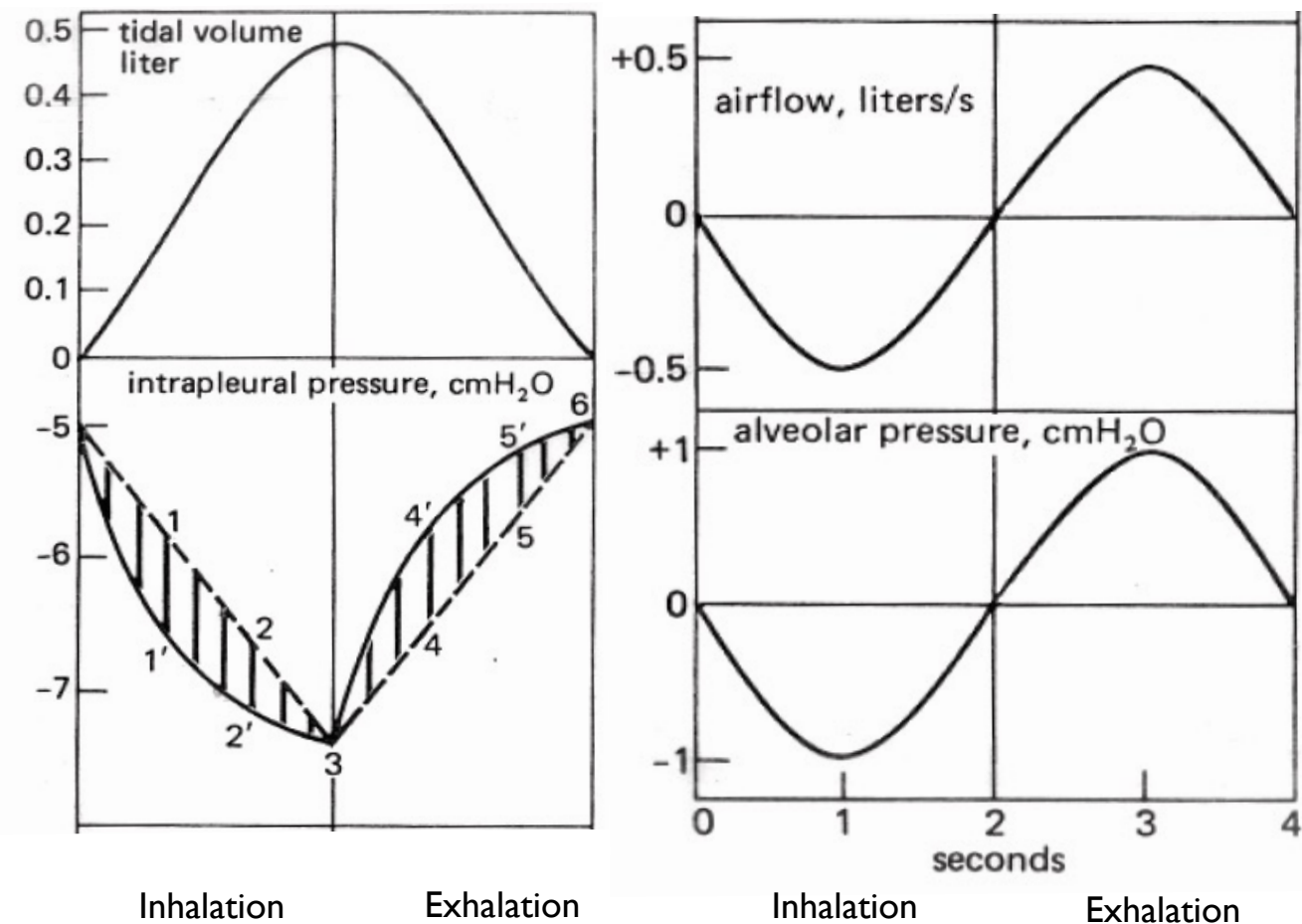- Alveole: open thermodynamic system
- Surface for gas exchange.
- Number: ~300 million (*N.B.*: $2^{25}=33,554,432$)
- Size (d~200 µm), area (5×10^{-7} m^2/alveolus)
- Total alveolar area: ~100 m^2
- Alveolar wall (~0.5 µm): alveolar epithelium (~0.2 µm) basal membrane (~0.1 µm) capillary endothelium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

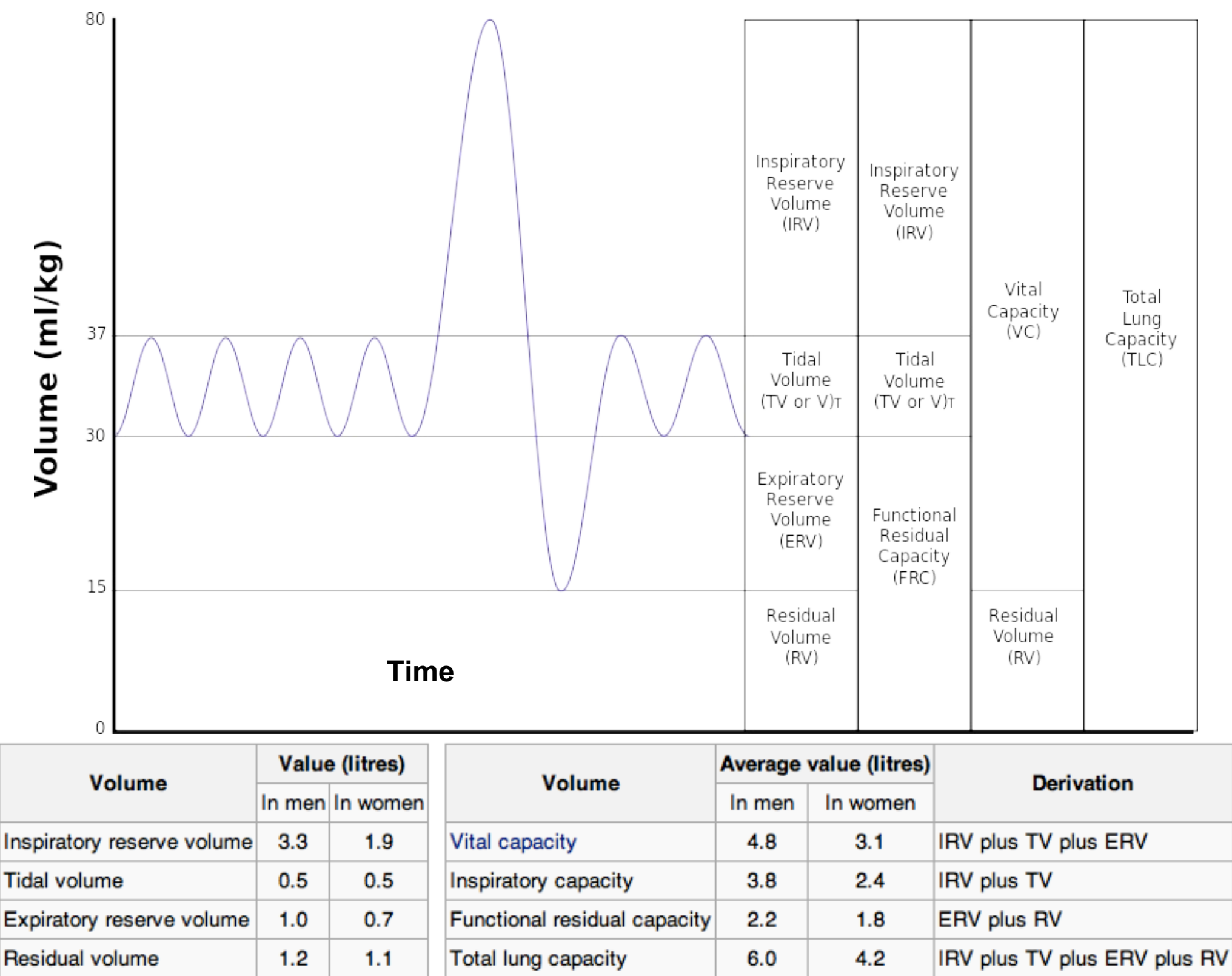# Respiratory cycle

1. Mechanical control

Chest expands
Sternum
Ribs
Lung
Diaphragm
Diaphragm contracts

Inhalation

Chest contracts
Diaphragm relaxes

Exhalation

spine
pivoting point
external intercostal muscle
ribs

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

2. Changes in physical parameters
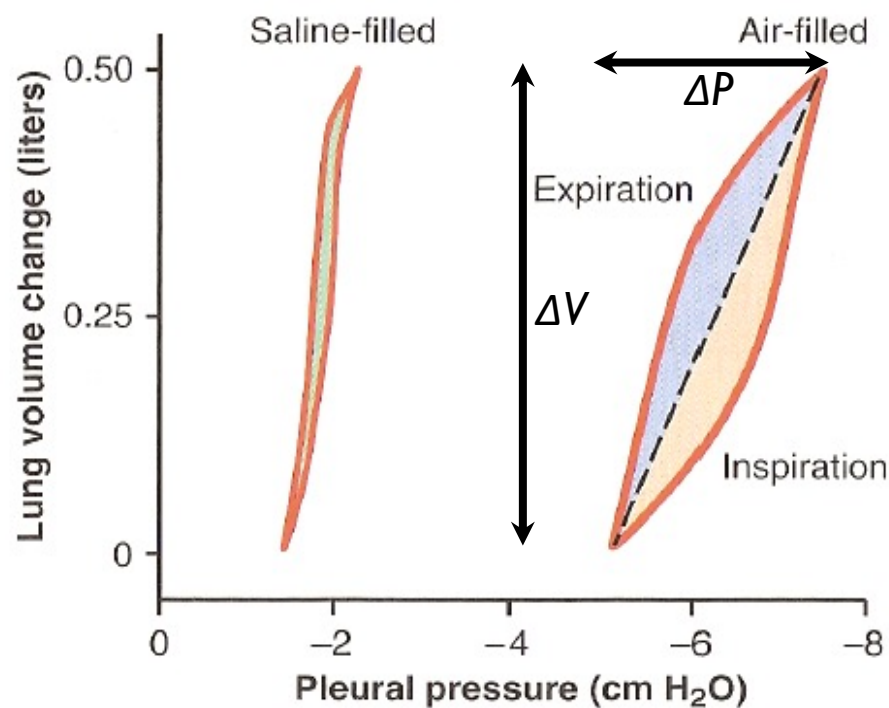

tidal volume liter

0.5
0.4
0.3
0.2
0.1
0

intrapleural pressure, cmH_2O

-5
-6
-7

Inhalation   Exhalation

airflow, liters/s

+0.5
0
-0.5

alveolar pressure, cmH_2O

+1
0
-1

0   1   2   3   4
seconds

Inhalation   Exhalation

1 cmH_2O = 0.1 kPa = 0.7 mmHg

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	Vital capacity	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^{-1}; *N.B.*: inverse of stiffness)
ΔP = change in pressure (Pa, Nm^{-2})
ΔV = change in volume (m^3)

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
η = 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").
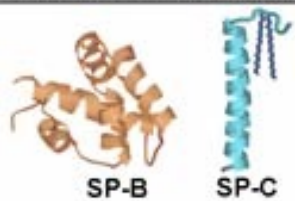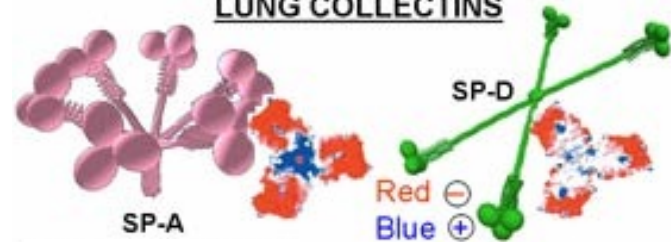
Surfactant

- 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.).

Dynamic analysis of respiration
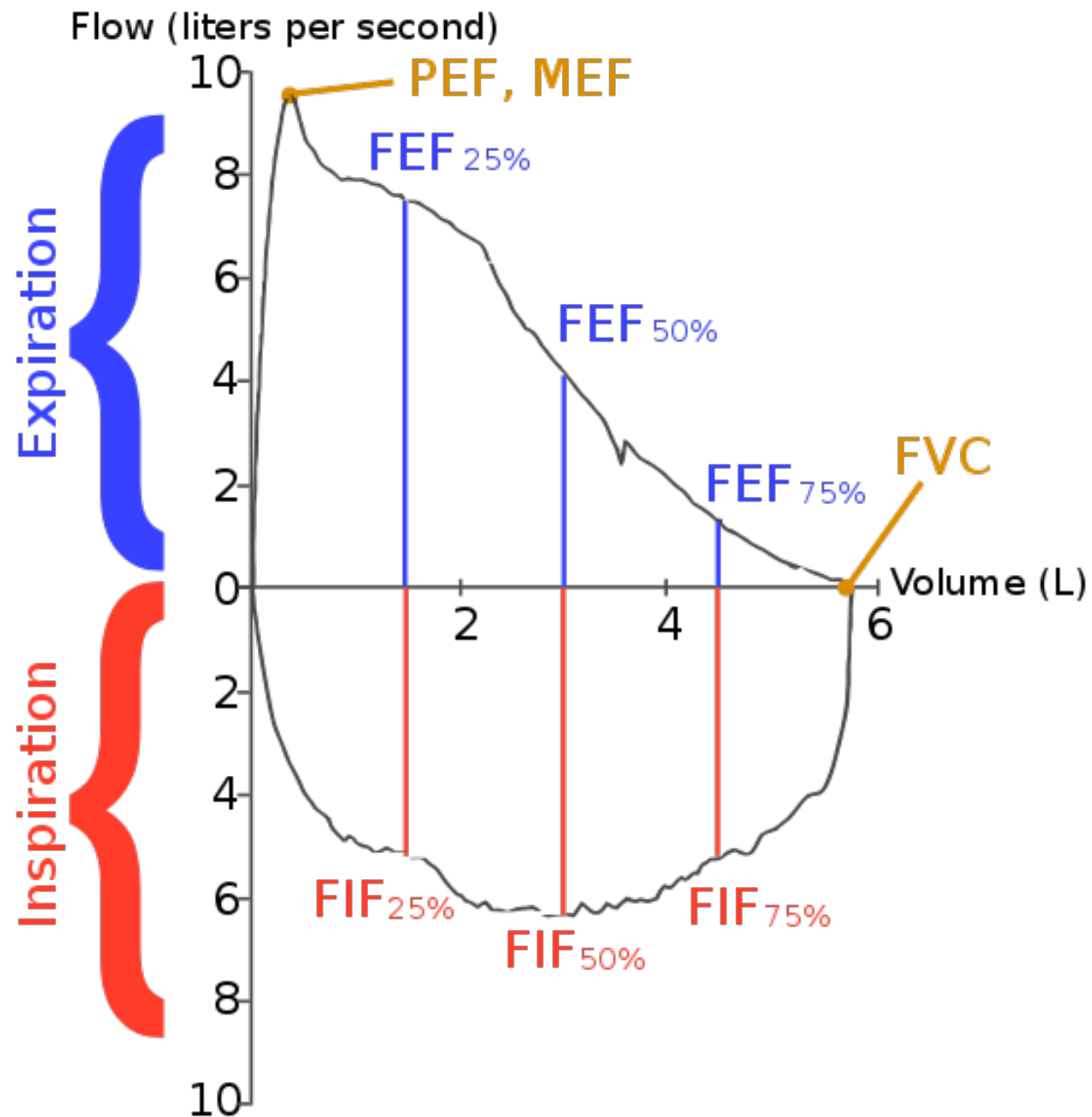
Spirometry:
- PEF, MEF: peak expiratory flow, maximal expiratory flow
- FEF: forced expiratory flow
- FIF: forced inspiratory flow
- FVC: forced vital capacity

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 (5×10^{-4} m^3)
- Work (W) = P_{tm} xV = 0.35 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

Note absorption maxima in the visible spectral range

absorbance [a. u.]

wavelength [nm]
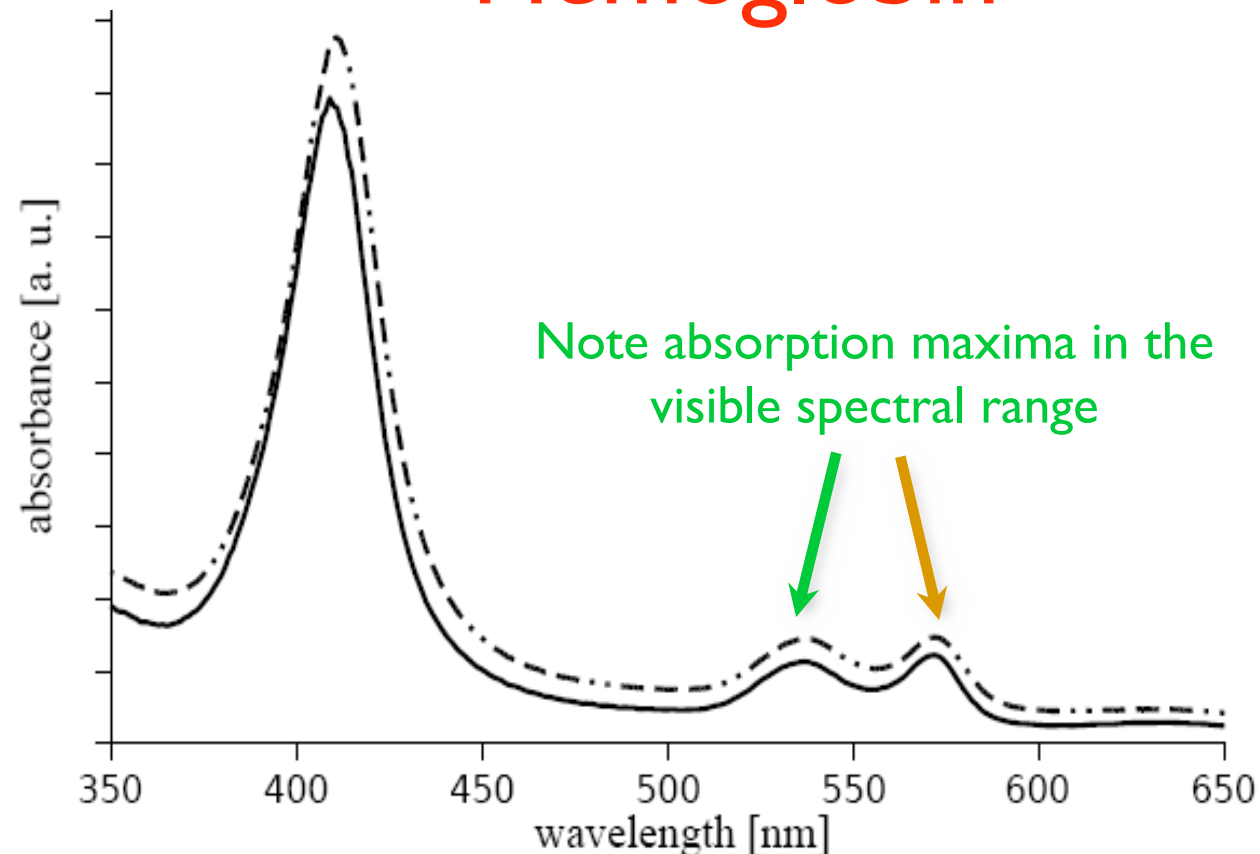
From the general law of radiation attenuation:

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

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

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

absorbance, optical density

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

Lambert-Beer's Law

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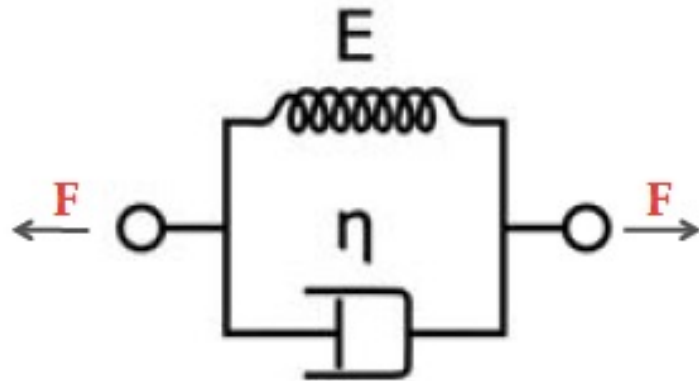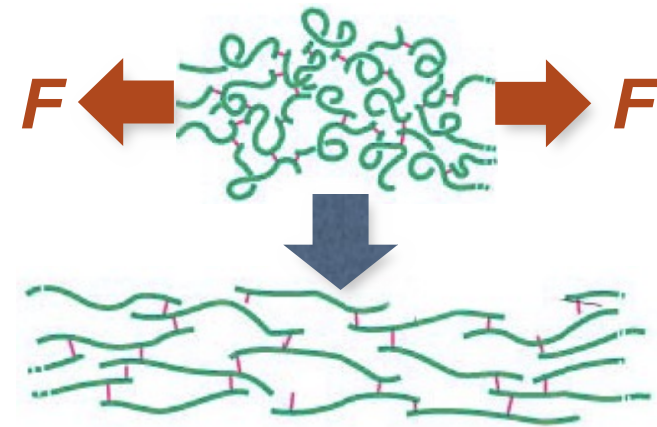
Velocity gradient versus shear stress function of newtonian and non-newtonian fluids

Schematic mechanism
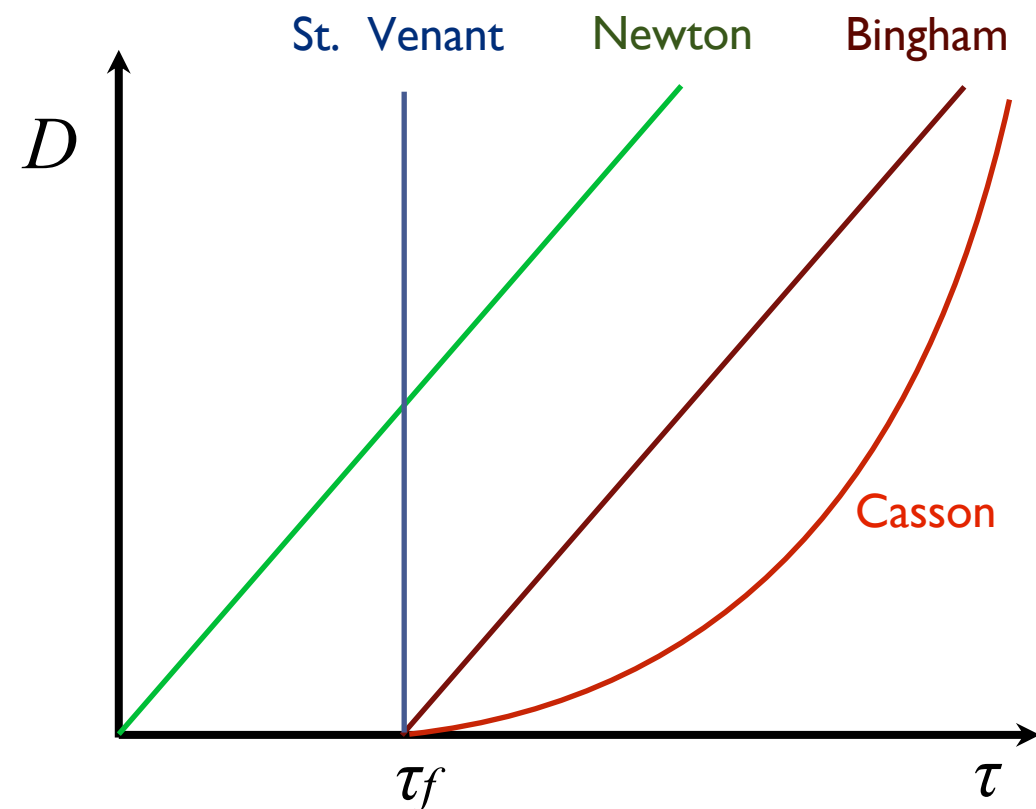
Example: edema (pitting)

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

Time domain

Fourier transformation
Inverse Fourier transormation

Frequency domain
(Fourier spectrum)

p
p_{eff}
pure sound
t

p^2
f_0
f

p
musical sound
t

p^2
fundamental frequency
harmonics
f_0 $2f_0$ $3f_0$ $4f_0$ $5f_0$ $6f_0$
f

Discrete spectra

p
white noise
t

p^2
f

Continuous spectra

p
drum beat
t

p^2
f_0
f
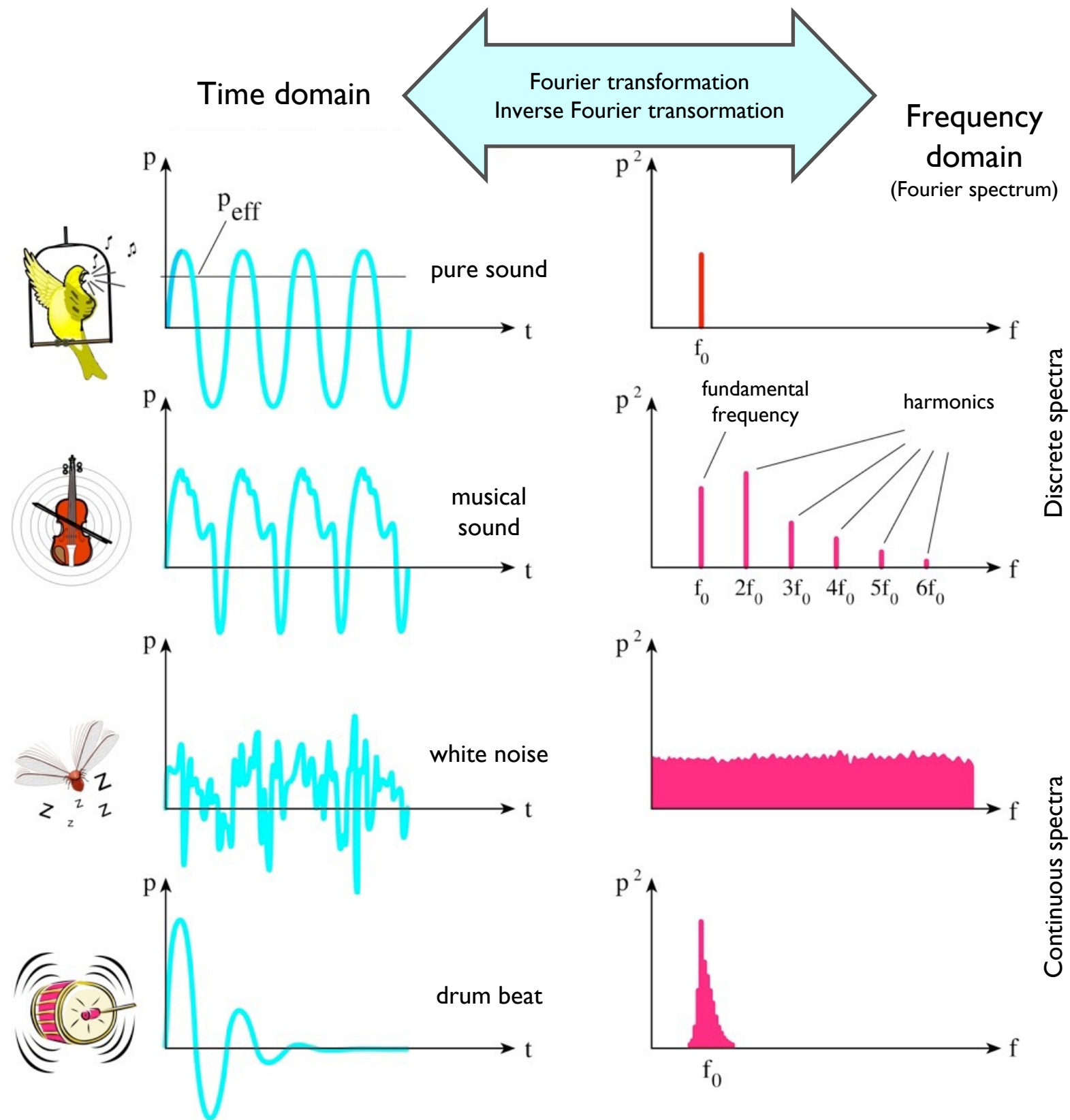
Respiratory system as a box

Chest wall

Parietal pleura

Visceral pleura

Pleural "cavity"
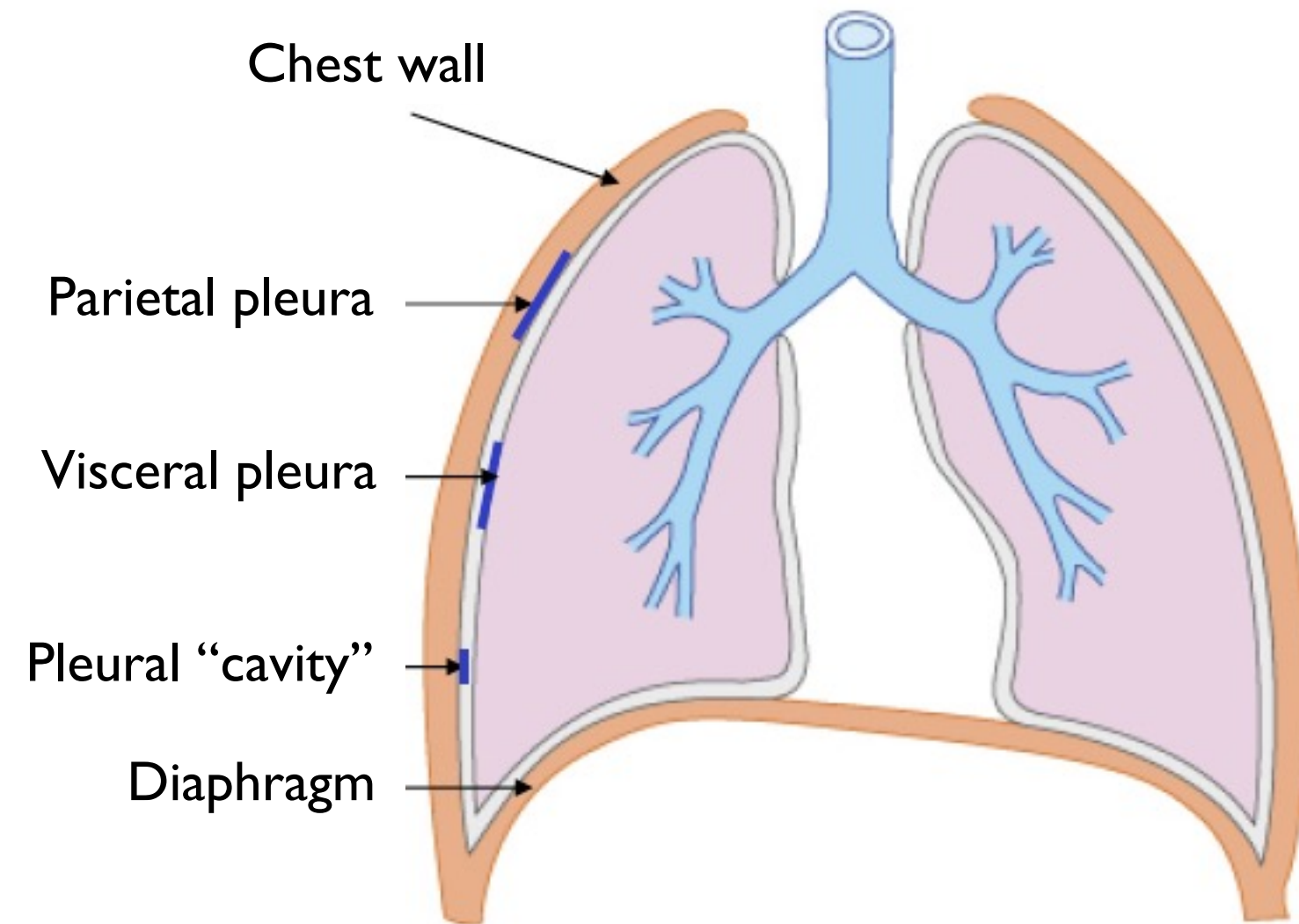
Diaphragm

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

"resonating"

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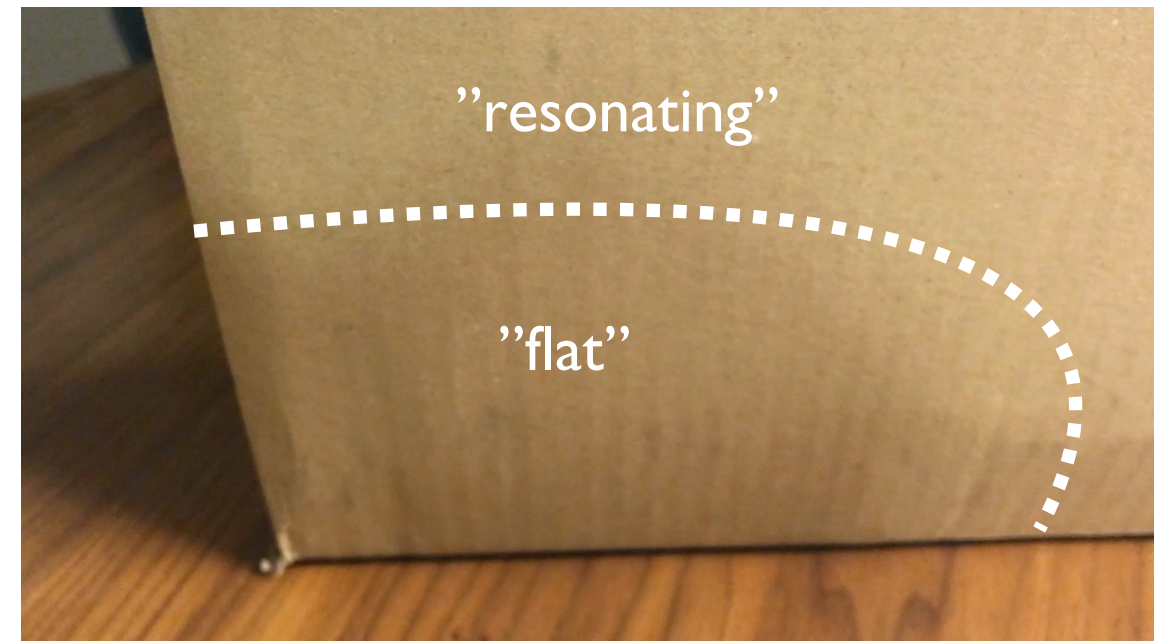
Boundaries of the diaphragm, heart, liver (and other, parenchymal organs) may be detected by percussion.

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

mm Hg
cuff pressure
systolic pressure
diastolic pressure
hand bulb
stethoscope
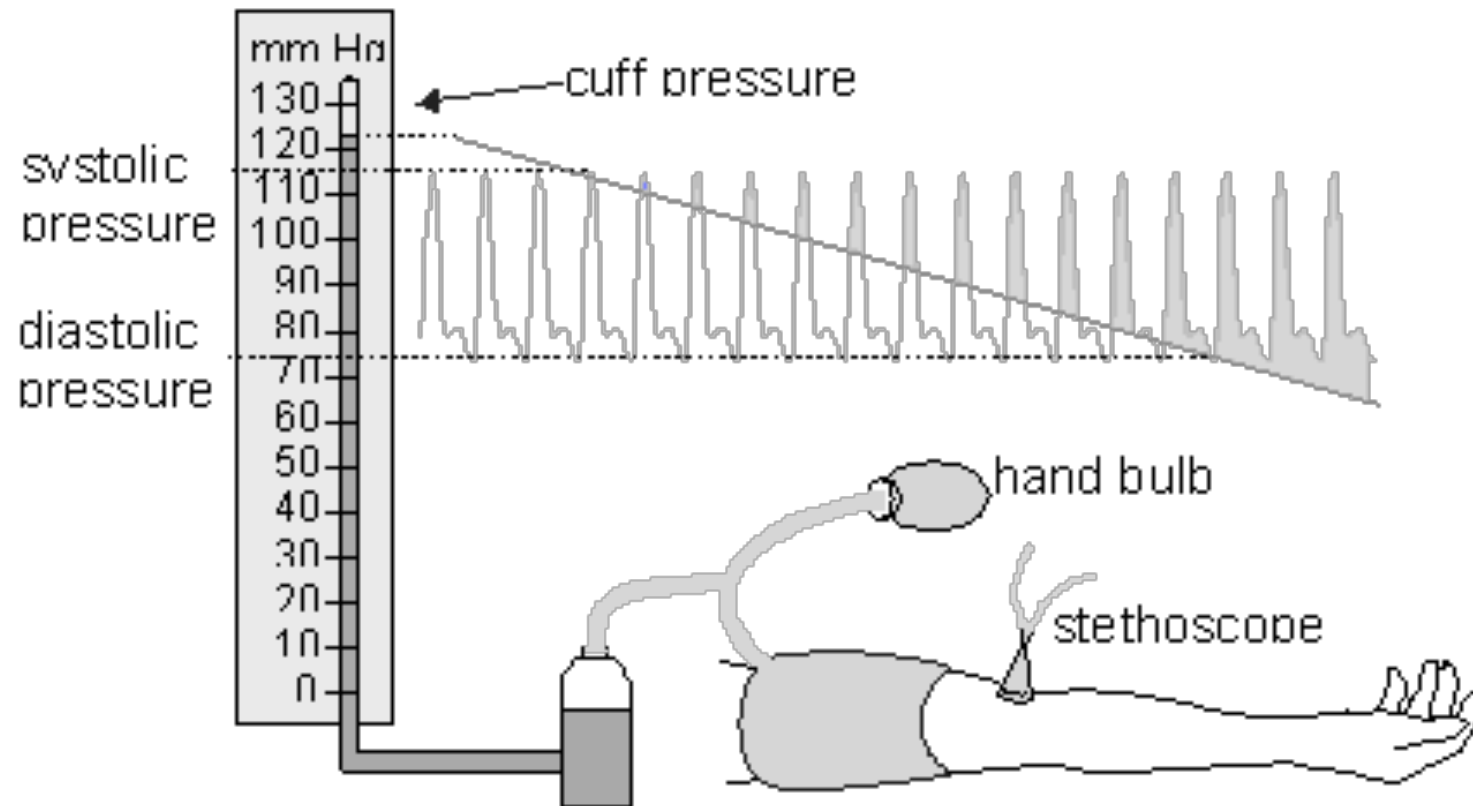
1. tapping
2. swishing
3. knocking
4. muffling

Reynolds number:

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

v=flow rate (m/s)
r=tube radius (m)
ρ=density of fluid (kg/m^3)
η=viscosity (Ns/m^2)
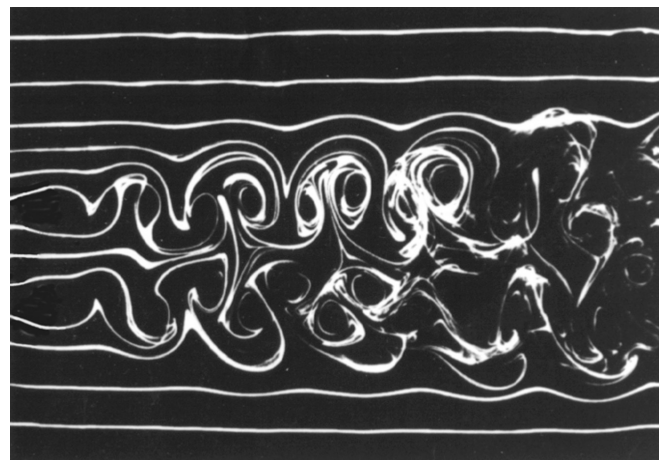
Turbulent flow ($R > \sim 1160$)
causing sound effects

- 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

Aorta

A. pulmonalis

Bulbus aortae

Left atrium

2. Aorta stenosis: systolic murmur

Aorta valve

Right atrium

Mitral (bicuspid) valve

3. Mitral stenosis: diastolic murmur

Tricuspid valve

Right ventricle

Left ventricle

1. Normal heart sound: systolic - diastolic (boo - tupp)

Septum
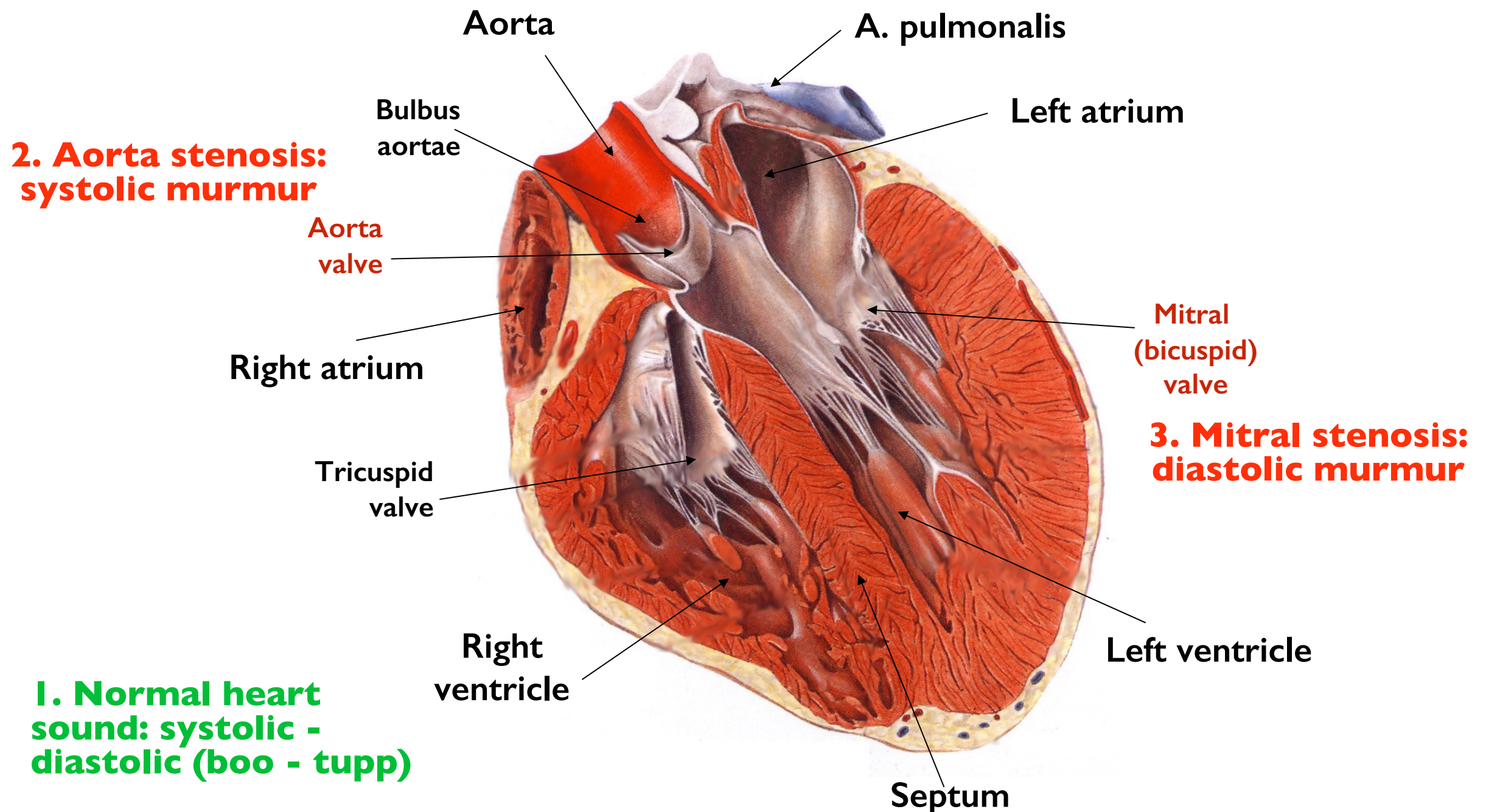
Respiratory sounds

Sources and mechanisms:
1. mechanical vibrations
   (rubbing noise)
2. mechanical resonance
   (organ-pipe action)
3. bubbling through fluid
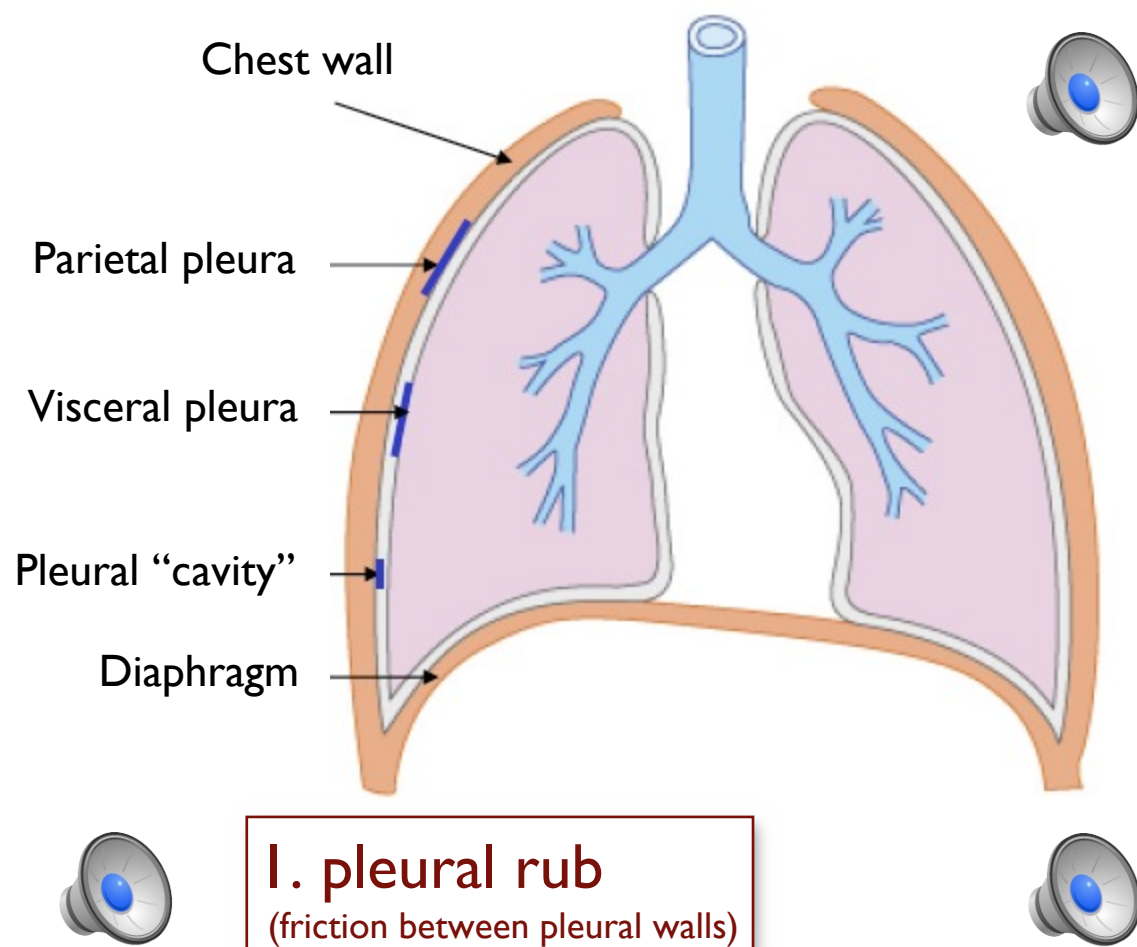
Conducting zone

Tracheobronchial sounds

- Trachea
- Bronchi
- Bronchioli
- Terminal bronchioli

Chest wall

Parietal pleura

Visceral pleura

Pleural "cavity"

Diaphragm
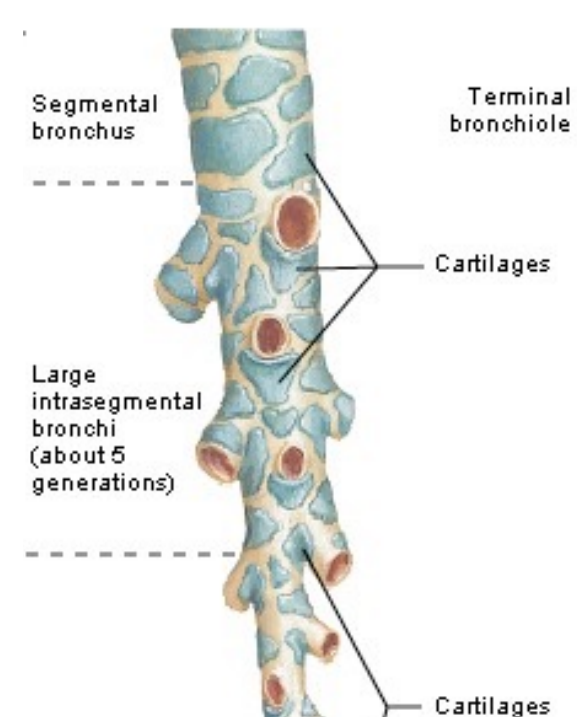
2. wheeze, stridor
(airway obstruction)

Respiratory zone

Vesicular sounds

- Respiratory bronchioli
- Alveolar ducts
- Alveoli

1. pleural rub
(friction between pleural walls)

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

Segmental bronchus

Terminal bronchiole

Cartilages

Large intrasegmental bronchi (about 5 generations)
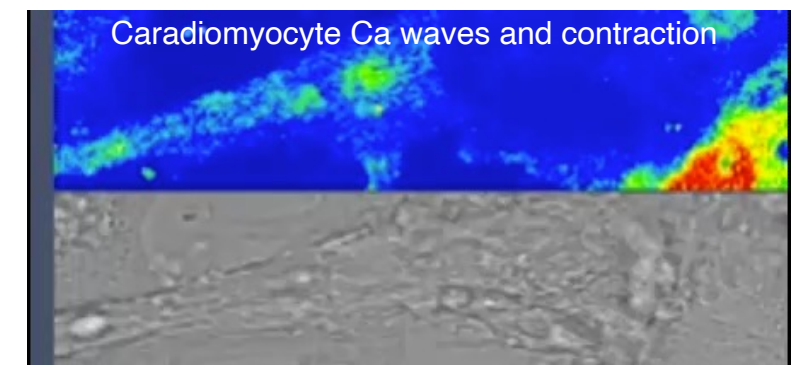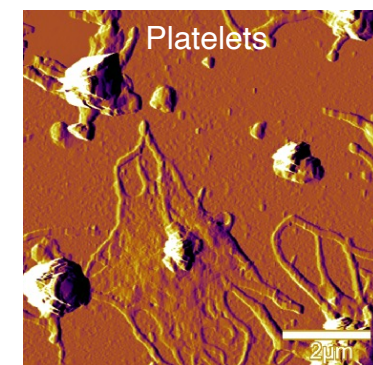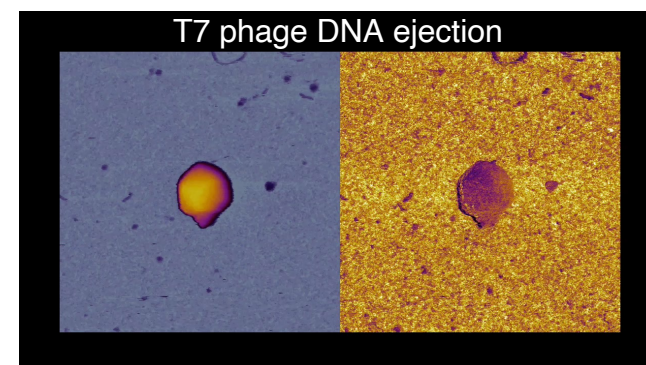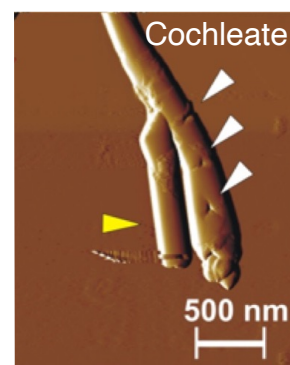
Cartilages

coarse crackles

fine crackles

Alveolar sacs and alveoli

Research in the Department of Biophysics and Radiation Biology
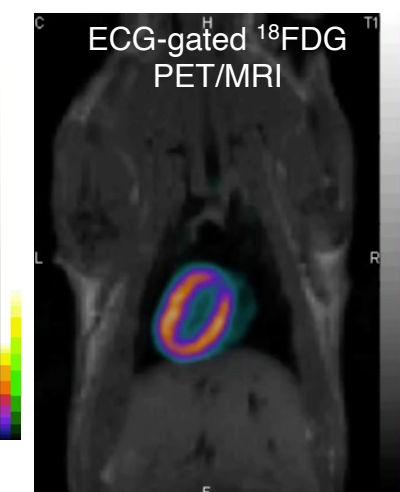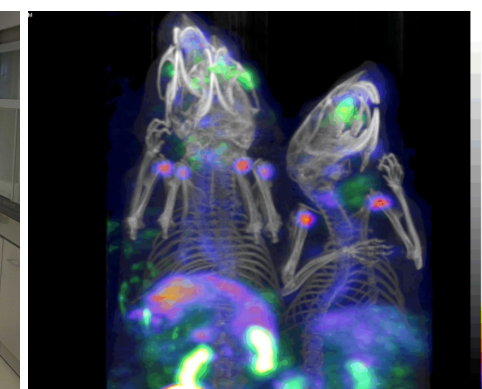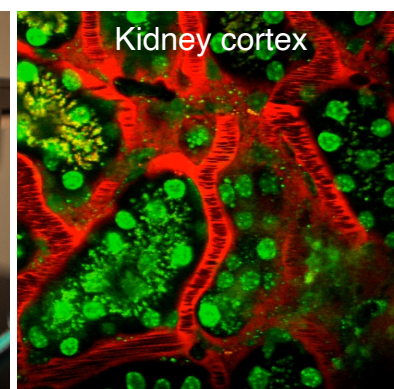

From atoms and molecules…
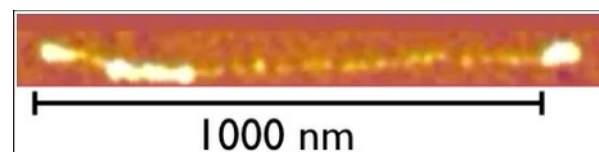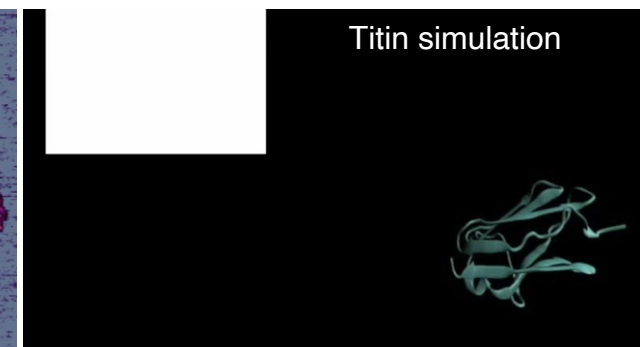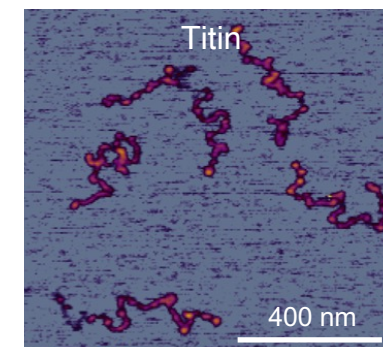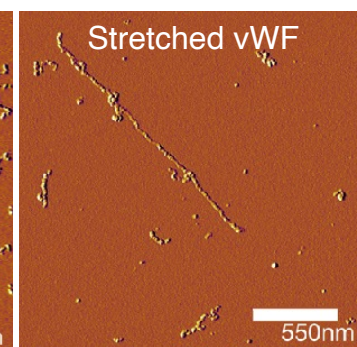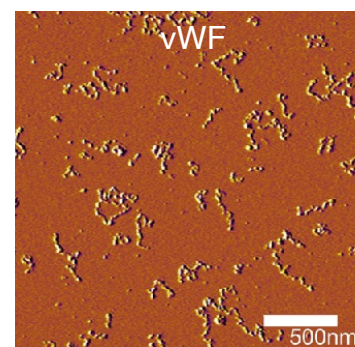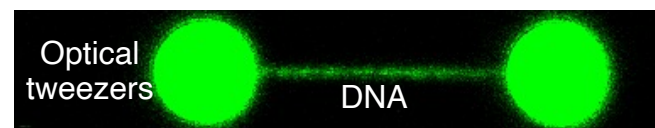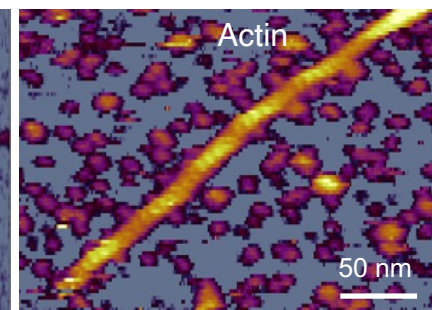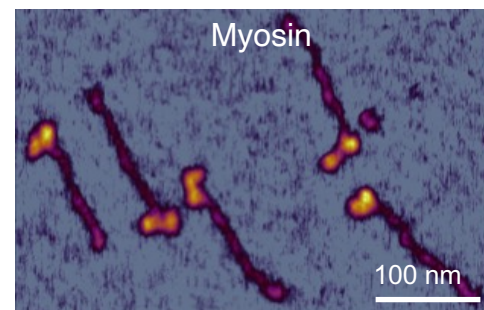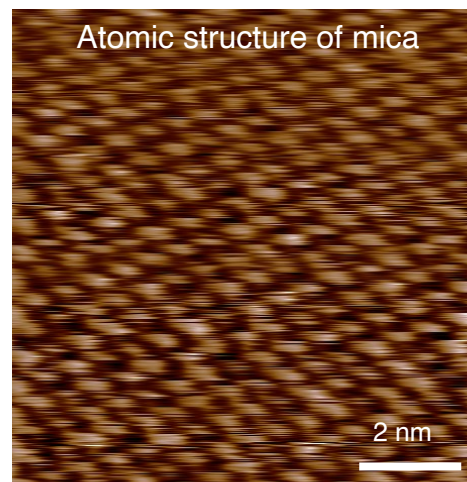
…through supra-molecular and cellular systems…

…to the living organism

Feedback

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