RESPIRATORY BIOPHYSICS

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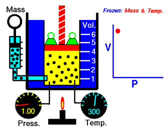
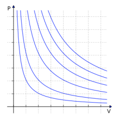
History of respiratory biophysics

- 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]

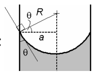
3. Henry's law (William Henry, 1803): At a constant temperature, the amount of a given gas that dissolves in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid.

$$p = k_H c$$

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:

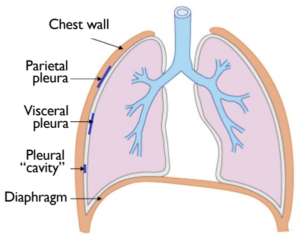


$$\Delta p = \frac{2\gamma}{R}$$

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

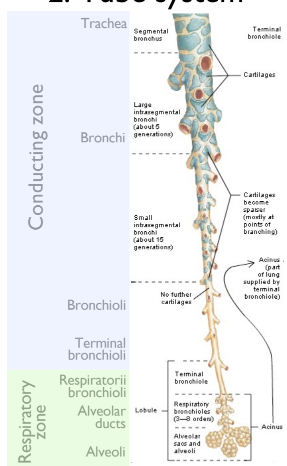
Simplified respiratory system

1. Box



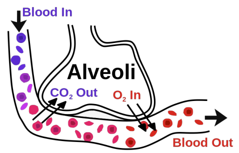
- Intrapulmonary pressure (P_{pulm}): fluctuates around external (atmospheric) pressure
- Intrathoracic or intrapleural pressure (P_{pl}): "negative" (balance between atmospheric pressure, adhesional and contractile forces)
- Transmural (transpulmonary) pressure (P_{tm}): pressure difference across chest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

2. Tube system



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

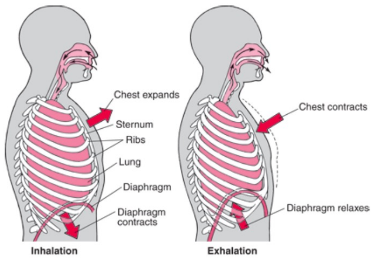
3. Gas exchange surface

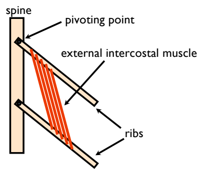


- Alveole: open thermodynamic system
- Surface for gas exchange.
- Number: ~300 million (*N.B.*: 2^{25}=33,554,432)
- Size (d~200 μm), area ($5x10^{-7}$ m^2/alveolus)
- Total alveolar area: ~100 m^2
- Alveolar wall (~0.5 μm): alveolar epithelium (~0.2 μm) basal membrane (~0.1 μm) capillary endothelium (~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

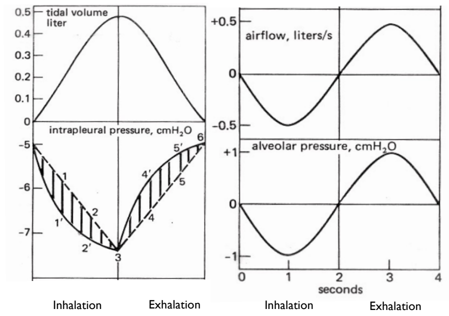
1. Mechanical control





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

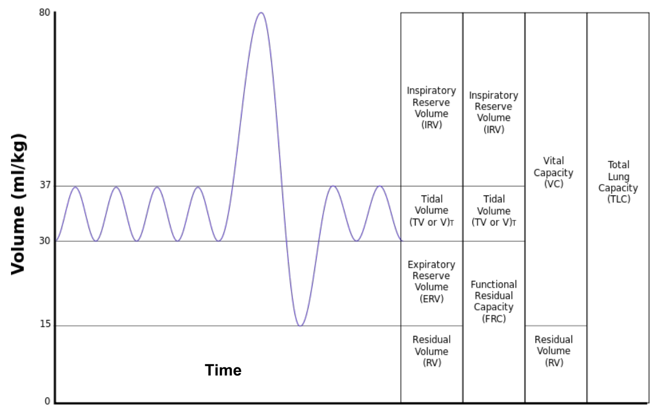
2. Changes in physical parameters



1 cmH_2O = 0.1 kPa = 0.7 mmHg

Pulmonary volumes and capacities

Capacity: sum of volumes

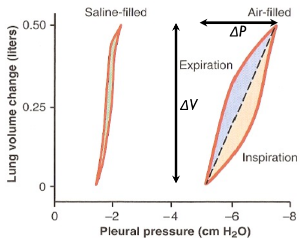


Volume	Value (litres) In men	Value (litres) In women
Inspiratory reserve volume	3.3	1.9
Tidal volume	0.5	0.5
Expiratory reserve volume	1.0	0.7
Residual volume	1.2	1.1

Volume	Average value (litres) In men	Average value (litres) In women	Derivation
Vital capacity	4.8	3.1	IRV plus TV plus ERV
Inspiratory capacity	3.8	2.4	IRV plus TV
Functional residual capacity	2.2	1.8	ERV plus RV
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

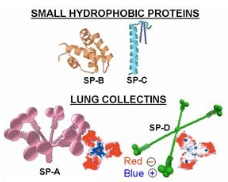


Compliance ("deformability", "stretchability", "distensibility"):

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

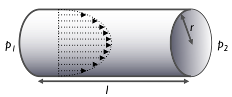
C = compliance (mN^{-1}; *N.B.*: inverse of stiffness)
ΔP = change in pressure (Pa, Nm^{-2})
ΔV = change in volume (m^3)

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.).

2. Gas flows in airways



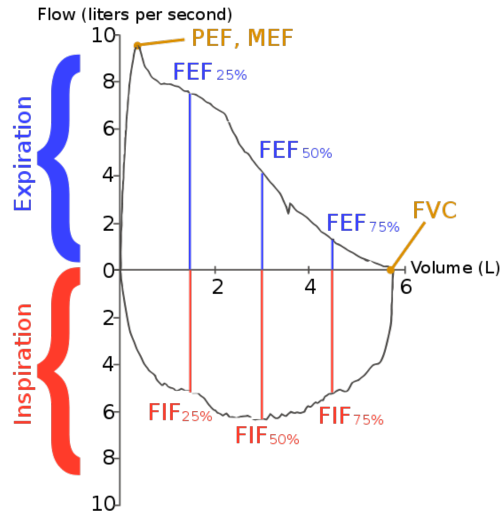
Hagen-Poiseuille's law

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

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").

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) = $P_{tm} \times V$ = 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

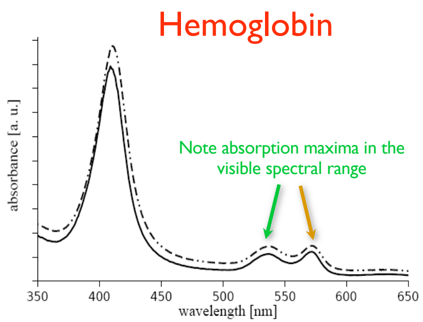
Inspection

What is this?
Visual examination of the patient

What do we visualize?
Behavior, morphology, structure, ***color***

Relationship to biophysics:
Absorption spectroscopy

Light absorption



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

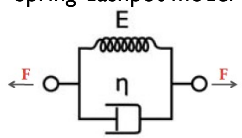
What is this?
Examining the patient by touching

What do we palpate?
Size, shape, location, ***firmness (elasticity, viscosity)***

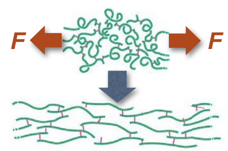
Relationship to biophysics:
Biomechanics

Viscoelasticity

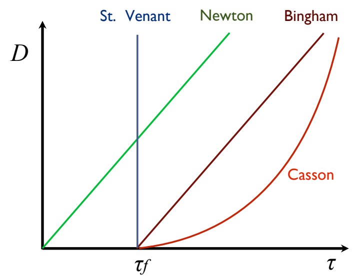
Spring-dashpot model



Schematic mechanism



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



Example: edema (pitting)

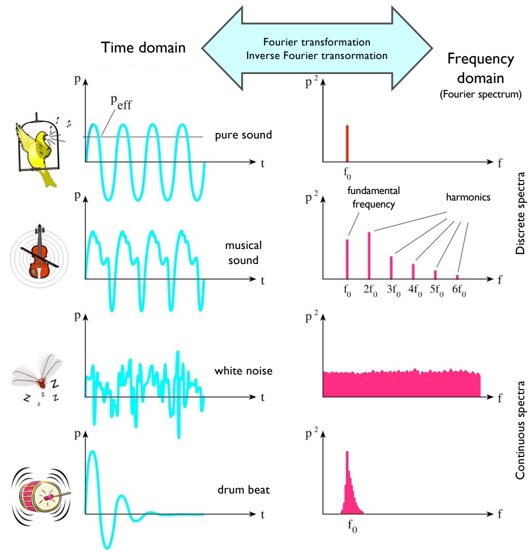
Percussion

What is this?
Examining the patient by locally striking (tapping) with short, sharp blows

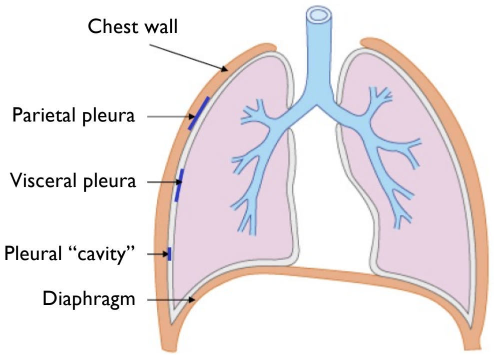
What do we examine by percussion?
Material content, shape, boundaries

Relationship to biophysics:
Sound generation, propagation and detection

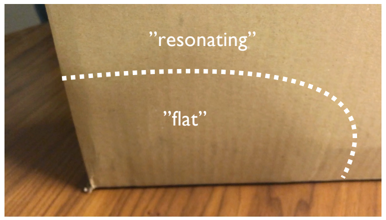
Sounds and their spectra



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.

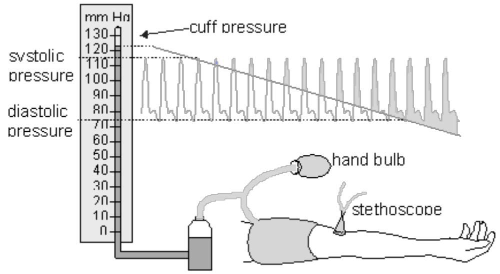
Auscultation

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

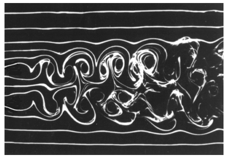


1. tapping
2. swishing
3. knocking
4. muffling

Reynolds number:

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

v=flow rate (m/s)
r=tube radius (m)
ρ=density of fluid (kg/m^3)
η=viscosity (Ns/m^2)

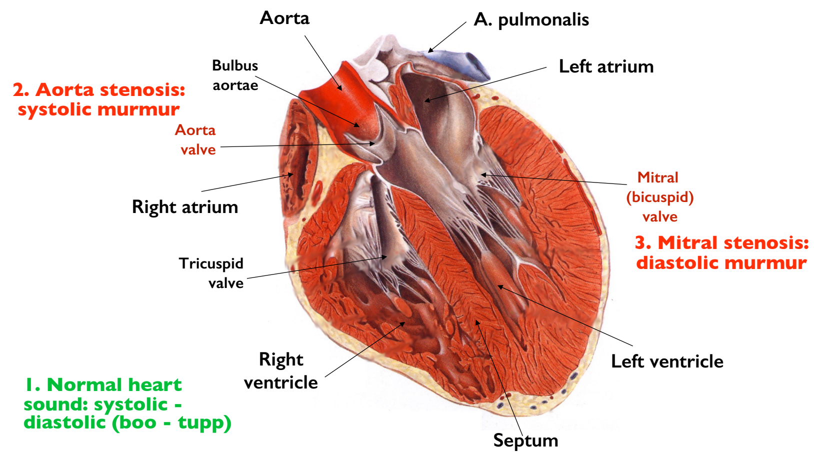


Turbulent flow ($R > \sim 1160$) causing sound effects

- 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.

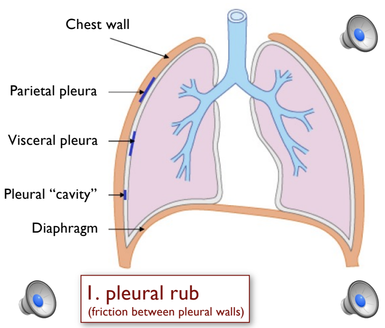
Heart sounds and murmurs

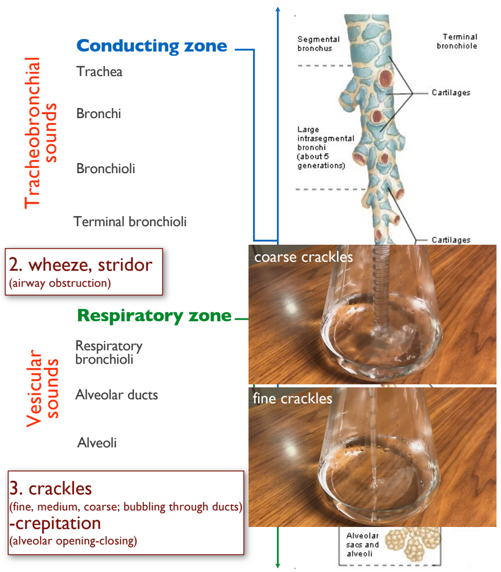
Sources: mechanical vibrations (e.g., valve closing), turbulent flow
Conductance: towards blood-filled compartments



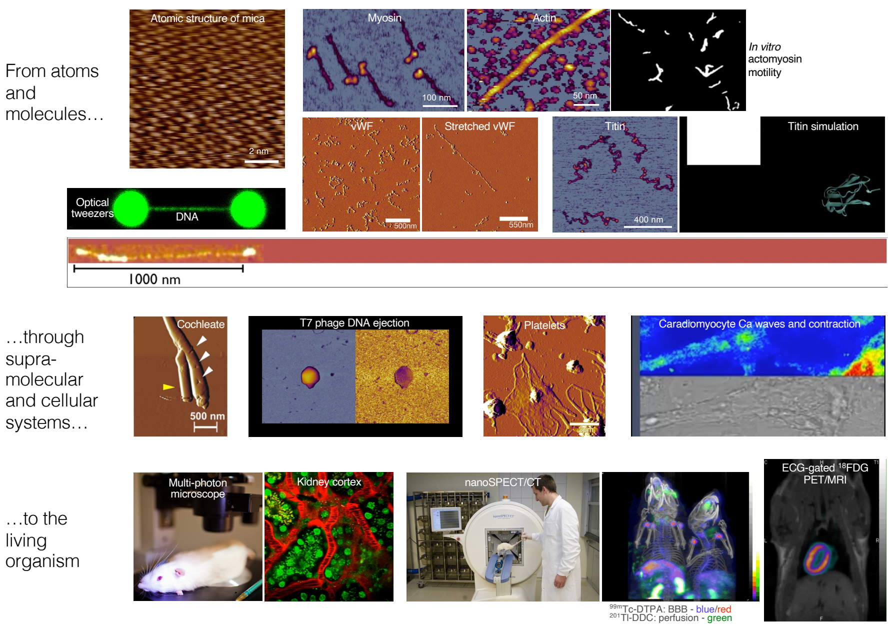
Respiratory sounds

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

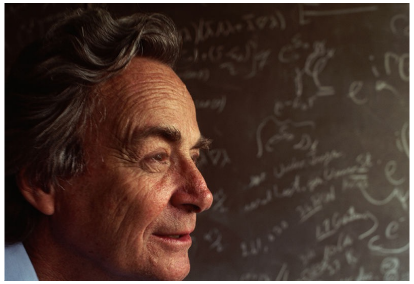




Research in the Department of Biophysics and Radiation Biology



- I am Nature's greatest miracle
- I will make a plan for the day and checkmark it at the day's end
- I will live this day as if it was the last
- There will be love in my heart
- Failure will never overtake me if my determination to succeed is strong enough



"The imagination of nature is far, far greater than the imagination of man."

Richard P. Feynman
(1918-1988, Nobel-prize 1965)

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