Breathing

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And the Lord God formed man of the dust of the ground, and breathed into his nostrils the breath of life; and man became a living soul. (Genesis 2, 7)

And the rib, which the Lord God had taken from man, made he a woman, and brought her unto the man. (Genesis 2, 22)

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Oxygen

Joseph Priestley 1774

Antoine Laurent Lavoisier

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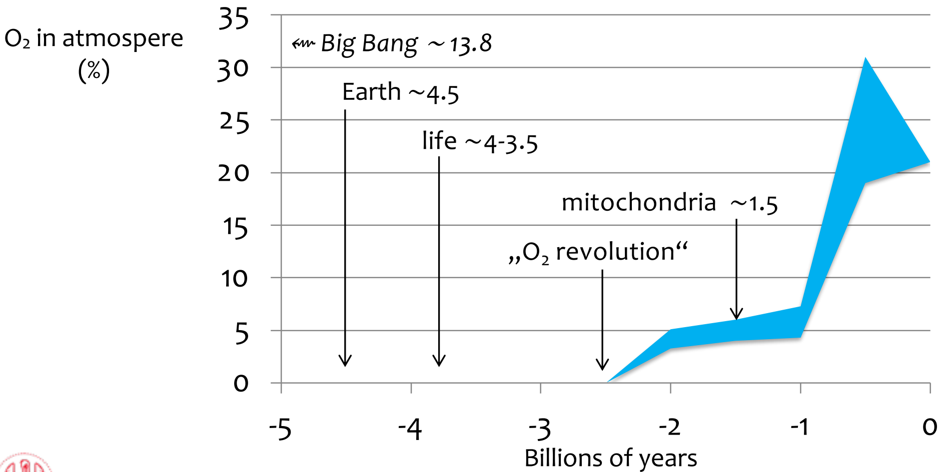
O_2 in atmosphere only recently



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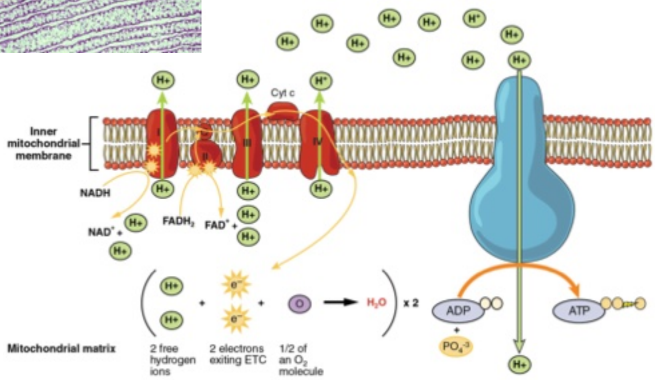
Mitochondria

endosymbiosis -1.5 bil years



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O_2 (& CO_2) transport

- small organisms – **diffusion**
  - short diffusion distance
  - large surface area relative to volume
- larger organisms – diffusion + conduction
- conduction in aquatic organisms – bringing water to diffusion surface (O_2 in water << in air)
- conduction in terrestrial vertebrates:
  - breathing
  - circulation

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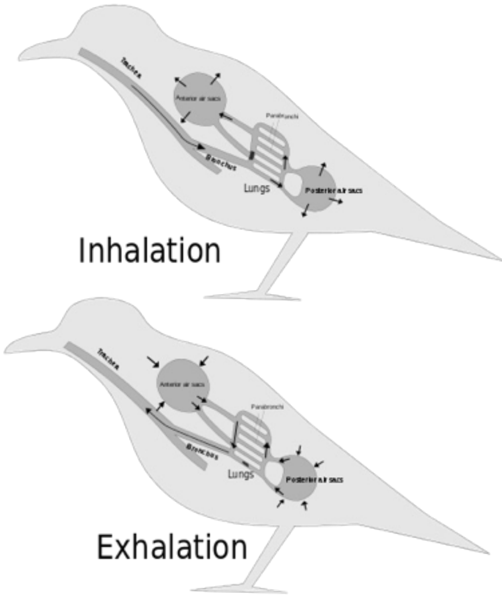
Breathing in vertebrates

- amphibians – „swallowing“ air + skin
- reptiles
  - dinosaurs – similar to birds
  - others – similar to mammals
- birds – parabronchi + air sacs (7-9)
- mammals - alveoli



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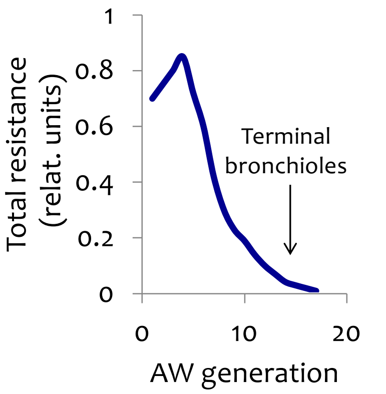
Breathing in mammals

- branching airways (dead space; total resistance↓)
- alveoli (large surface area)
- diffusion (short diffusion distance)
- perfusion
- <u>ventilation</u>:
  - active inspiration (negative pressure)
    - **<u>diaphragm</u>**, external intercostal muscles
  - passive resting exhalation
    - chest weight, lung elasticity



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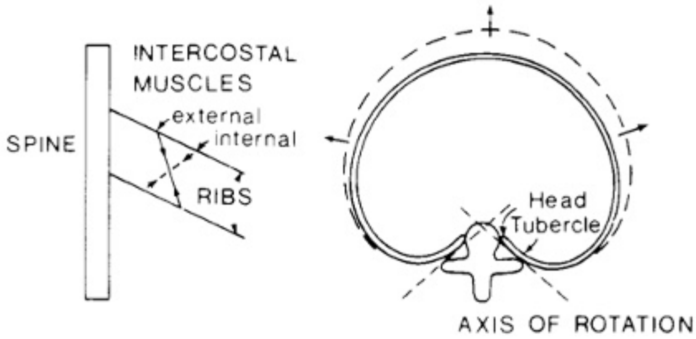
Intercostal muscles in breathing



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Determinants of lung gas transport

- Lung ventilation ($\dot{V}$)
  - how O_2 and CO_2 reach the alveolocapillary membrane
  - what determines the amount of gas that is exchanged between the atmosphere and the alveoli
    - **dead space (V_D)**
    - **functional residual capacity (FRC)**
- Diffusion in the lungs (D)
  - determines the passage of O_2 and CO_2 across the alveolocapillary membrane
- Pulmonary perfusion (Q)
  - how venous blood is led into lungs form periphery
  - how O_2 - rich blood with little CO_2 is led from lungs to periphery
- Pulmonary ventilation/perfusion ratio ($\dot{V}$/Q)

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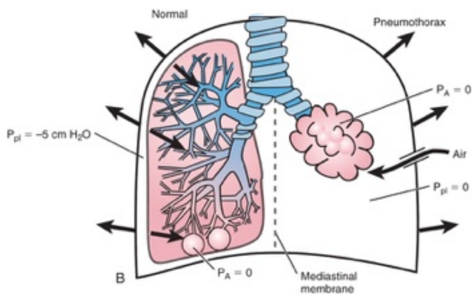
Resting lung position (end-expiration)

- lung „elastic recoil“

  x
- chest tendency to expand

  ⇓
- slight negative pressure in intrapleural space ($P_{IP}<P_B$) ($P_{IP} \sim -5\ cmH_2O$)



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Interpleural space

- very thin
- filled with fluid (~8-10 ml)
  - non-compressible – transduction of pressures
- pressure measured in esophagus
- in mammals absent only in elephants (pleurae connected by loose ligament)

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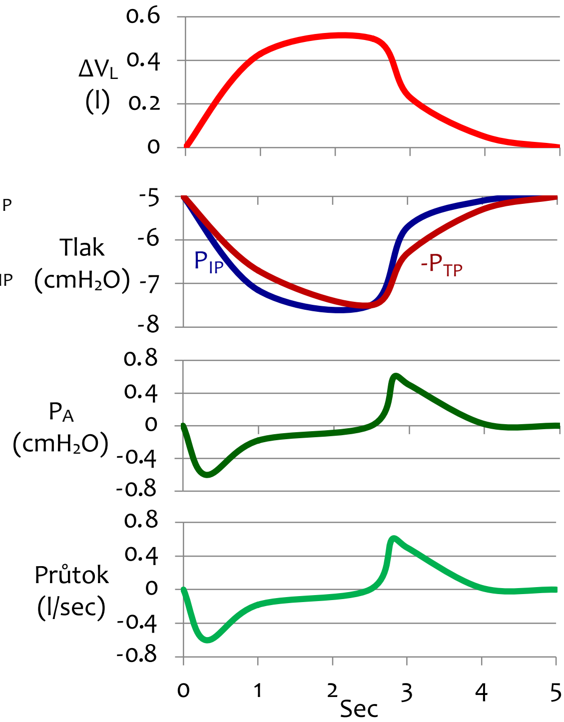
Breath cycle

- interpleural pressure (P_{IP}) controlled by the brain (via respiratory muscles)
- transpulmonary pressure (P_{TP}) = P_A - P_{IP}
  - follows P_{IP} with a short delay
  - end of inspiration & expiration: P_{TP} = -P_{IP}
  - determines volume (V_L)
    - together with compliance
- alveolar pressure (P_A) = P_{IP} - P_{TP}
  - P_A - P_B determines flow
    - together with resistance

At the beginning of inspiration & expiration more energy of ΔP_{IP} for the dynamic component of work (flow), for the rest of the cycle more for the static component (V_L)

(1 cmH_2O ~ 0.75 mmHg ~ 0.1 kPa)



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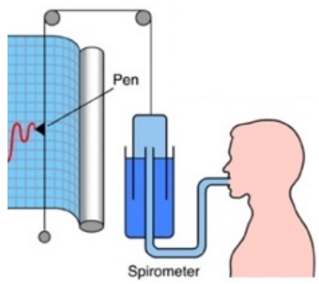
Spirometry

- Ventilatory volumes & capacities (“static”)
- Breath flow velocity (pneumotachograph) („dynamic“)



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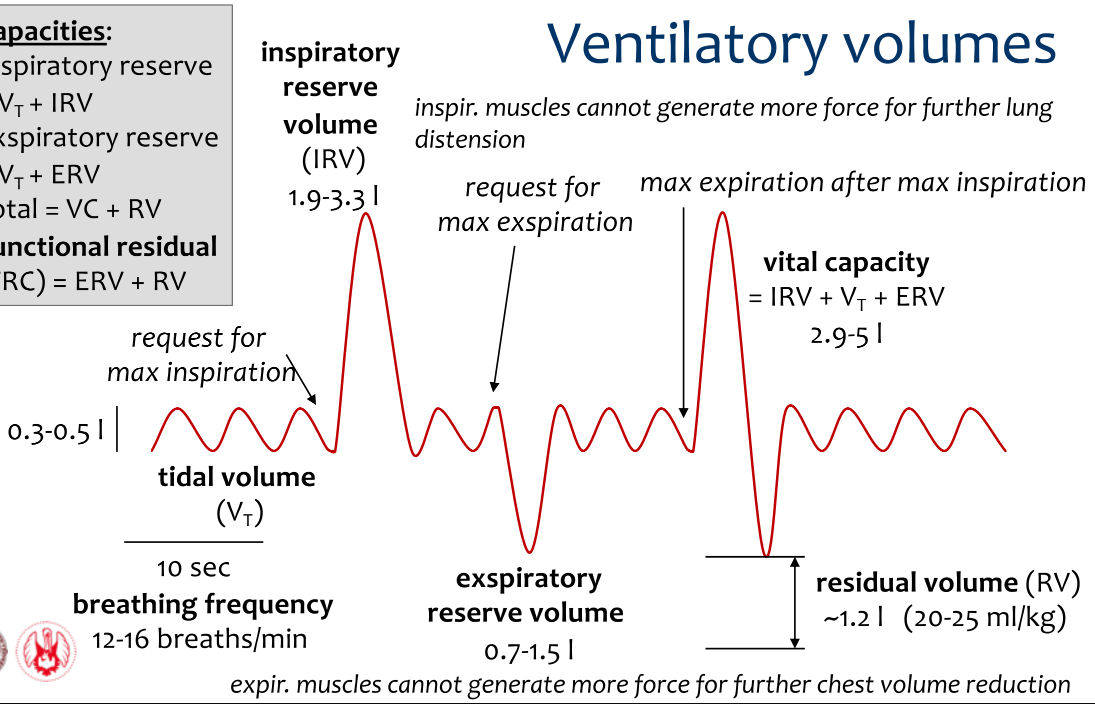
Ventilatory volumes

Capacities:
Inspiratory reserve = V_T + IRV
Exspiratory reserve = V_T + ERV
Total = VC + RV
Functional residual (FRC) = ERV + RV



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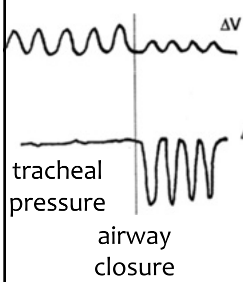
Measuring FRC - plethysmograph

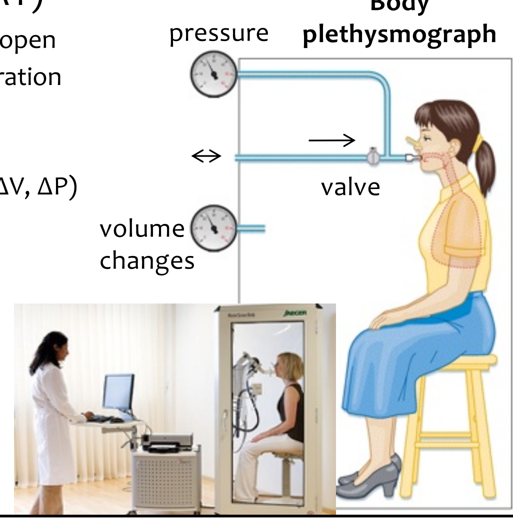
$P_1 \times V_1 = P_2 \times V_2$ (Boyle's law)
(resp. ideal gas law: PxV=nRT)

- breathing from outside w/ valve open
- P_1 & V_1 at the end of resting expiration (V_1 = FRC)
- valve closed
- small attempt at inspiration (→ ΔV, ΔP)
- P_2 & V_2 (P_1 - ΔP; V_1 + ΔV)
- P_1 x FRC = (P_1 - ΔP) x (V_1 + ΔV)
- FRC = ΔV x [(P_1 - ΔP)/ΔP]



- after max exspiration: RV

Includes air trapping



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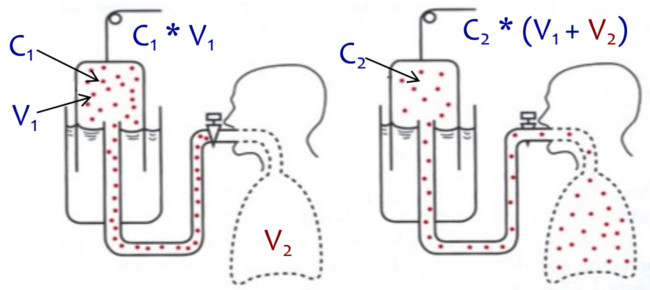
Measuring FRC – dilution methods

$c_1 \times V_1 = c_2 \times V_2$ (= amount)

- He dilution (closed method)
  - breathing from & into a bag w/ known initial [He] (usually 10% in O_2)
  - $C_1 \times V_1 = C_2 \times (V_1 + V_2)$



- N_2 washout (open method)
  - inhaling from an O_2 storage, exhaling into empty bag
  - N_2: amount: $C_P \times FRC = C_S \times V_S$ (C_P = initial, C_S a V_S = in spirometer)

Dose not include air trapping (that can be quantified from the difference against pletysmography)

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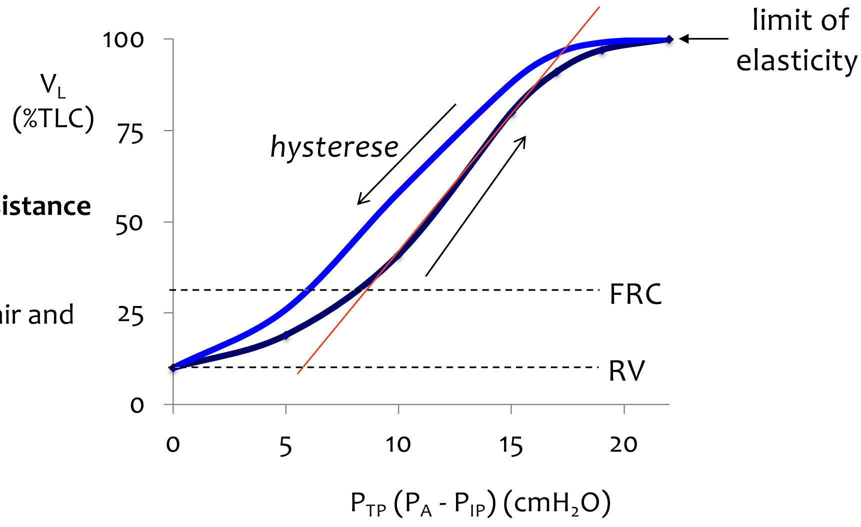
Static compliance

<u>not included</u>:
- **airway resistance**
- lung-chest friction
- inertia of air and tissues



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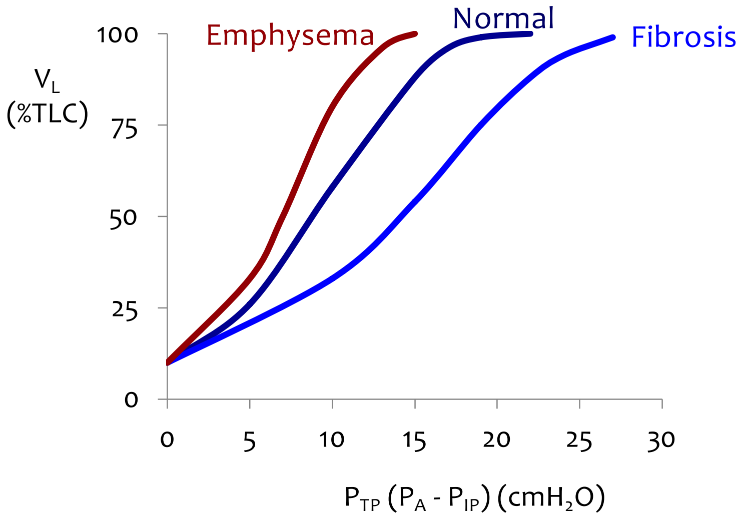
Static compliance



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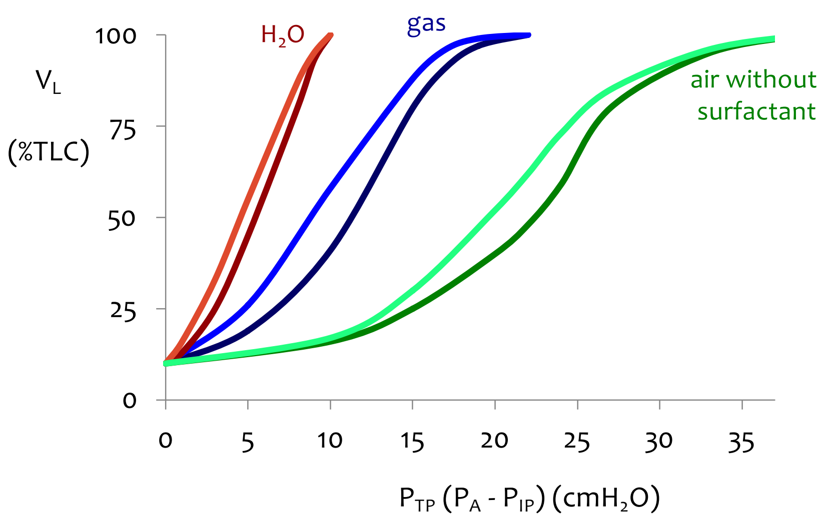
Static compliance & surface tension



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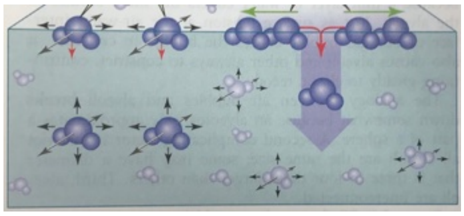
Pierre-Simon, marquis de Laplace (1806)

Surface tension

- inside water volume: molecules act on each other equally in all directions – cancels out
- on surface: only from below & laterally – pulling in → lateral pull
- on bubble surface like a strait-jacket – increases pressure inside, preventing further ↓r



- LaPlace law: $P = 2T/r$
- → smaller bubble empties into larger ($T_1/r_1 = T_2/r_2$)

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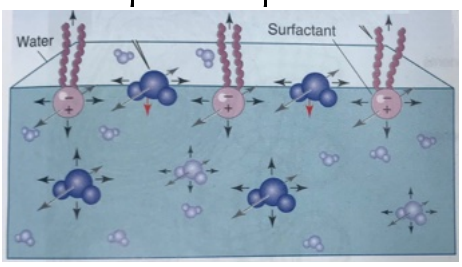
Surfactant: Type II. alveolar cells

- amphiphilic - hydrophobic & hydrophilic groups
- hydrophobic group extends out of water phase – pulls molecule out
- proteins ~10%
  - plasmatic proteins (1/2)
  - apolipoproteins (surfactant proteins SP-A, SP-B, SP-C, SP-D)



- 85% of lipids are phosphatidylcholins
  - mostly dipalmitoylphosphatidylcholin (DPPC)
  - phosphatidylglycerol - 11% of lipids

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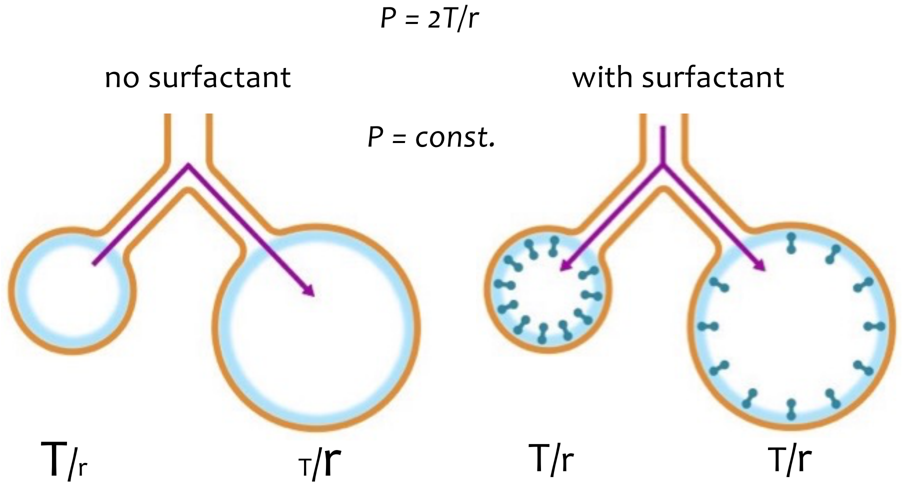
Surfactant prevents alveolar collapse



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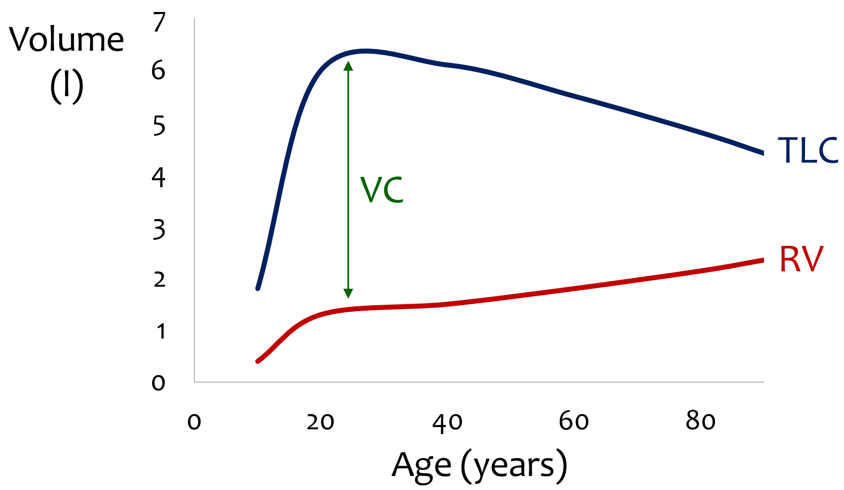
Aging: ↓elasticity



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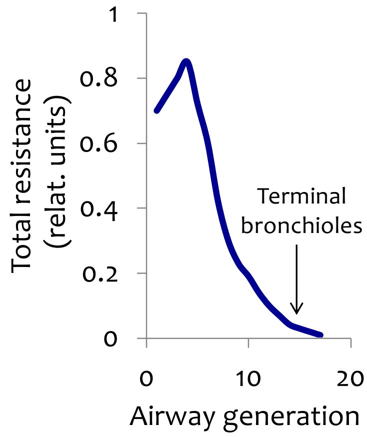
Airway resistance

- 1/3 = upper respiratory tract (nose, pharynx, larynx)
  - mouth less resistance than nose (exertion)
- middle airways relatively high resistance (flow high, total cross sectional area still quite low)
- peripheral airways low resistance



pararell: $1/R_{tot} = 1/R_1 + 1/R_2 + 1/R_3 + ...$
(*vs. serial:* $R_{tot} = R_1 + R_2 + R_3 + ...$)

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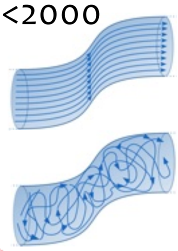
Turbulent flow

- movement of molecules in all directions → extra energy needed
- Reynolds number: Re = 2rvd/η (>2000 → turbulence)
- large airways: Re>2000
- small airways: Re<2000



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Airway resistance

- $\dot{V} = (P_A\text{-}P_B)/R$
- $R = (8/\pi) \times (\nu \times l)/r^4$ (Hagen-Poiseuille)
- $R = (P_A\text{-}P_B)/\dot{V}$
  = airway resistance
  (+20% is tissue resistance
  - friction of lungs & thoracic tissue at their movement against each other)

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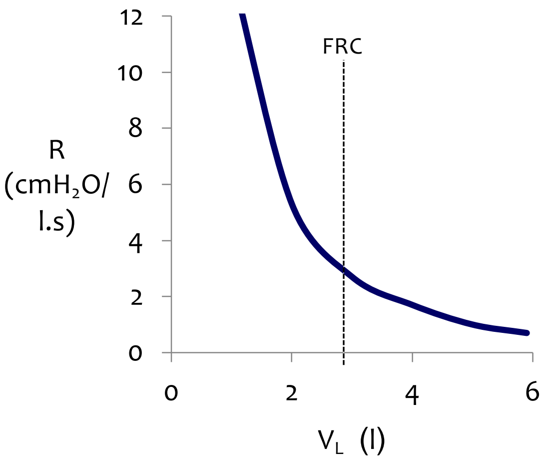
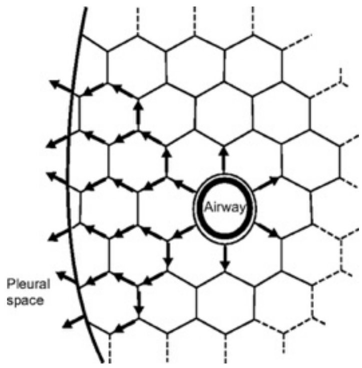
Airway resistance depends on lung volume





↑ airway r at ↑ V_L
(tissue tethering)

↑ R at expiration
(bronchiolar collapse)

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Regulation of airway resistance

- n. vagus – bronchoconstriction
- sympathicus – β_2 dilatation
  (NA weak agonist, adrenaline strong agonist)
- histamine,... - bronchoconstriction

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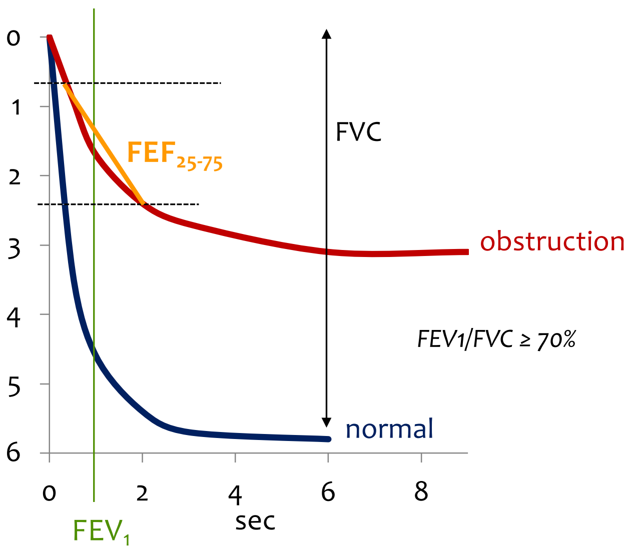
Spirogram

forced max exhalation after max inspiration (l)



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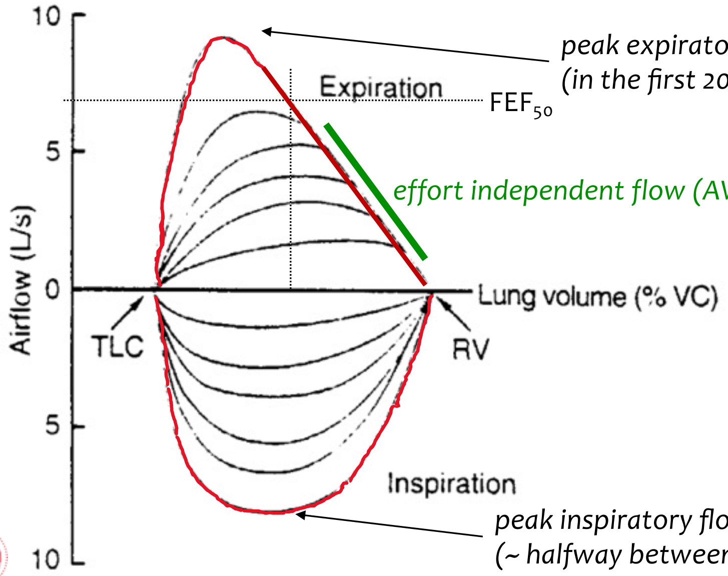
Flow-volume loops



peak expiratory flow rate (PEFR) (in the first 20% of the maneuver)

effort independent flow (AW compression)

peak inspiratory flow rate ≥ PEFR (~ halfway between RV and TLC)

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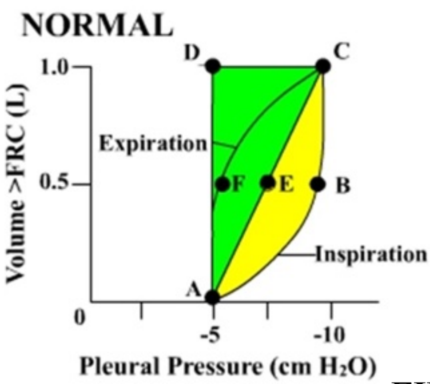
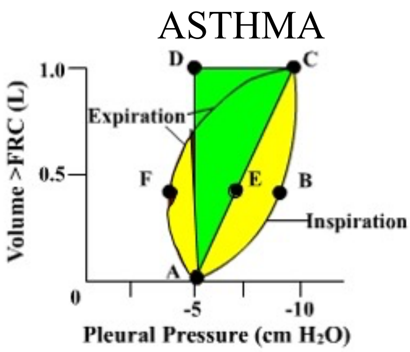
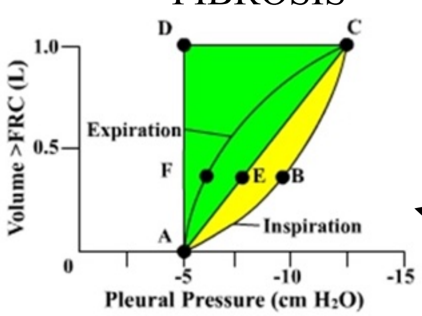
Work of breathing







W = F/d
→ P/ΔV

f	V_T

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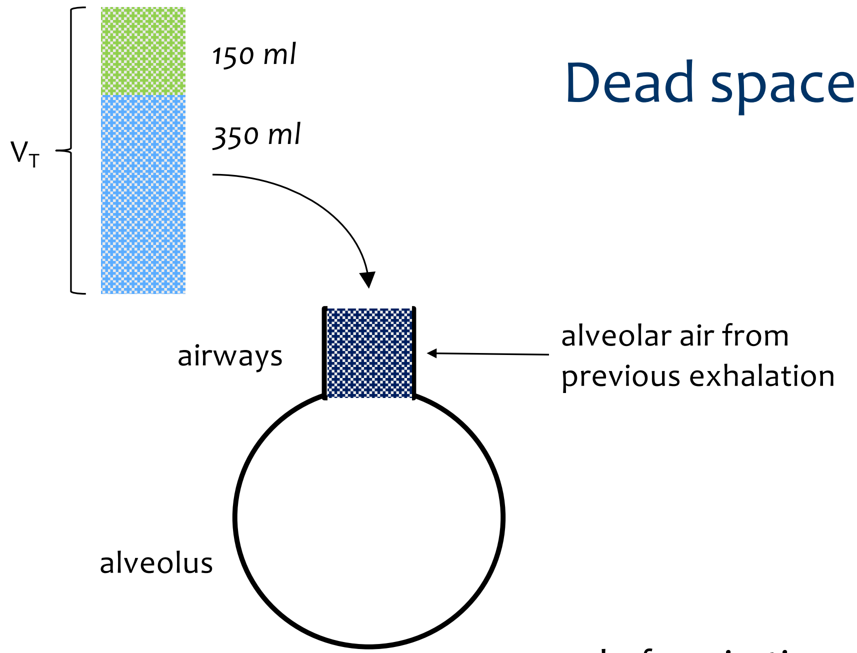
Dead space



end of expiration

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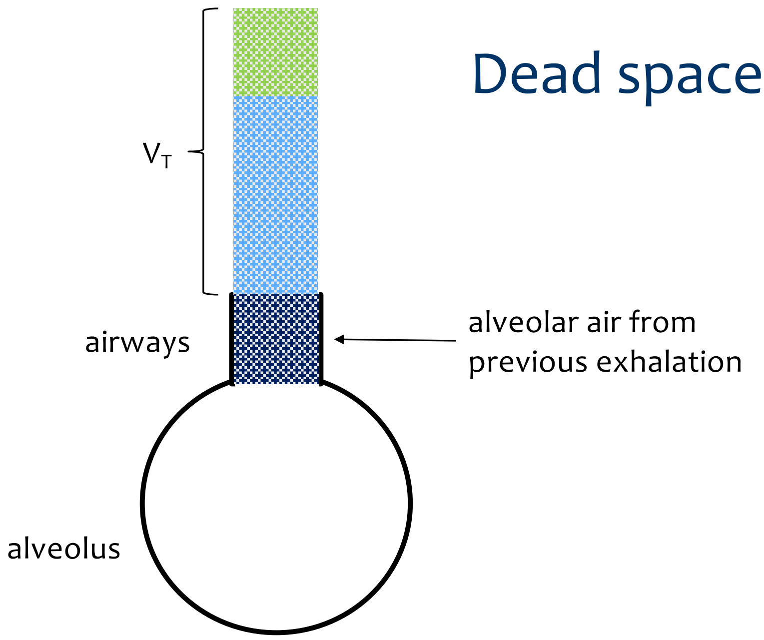
Dead space



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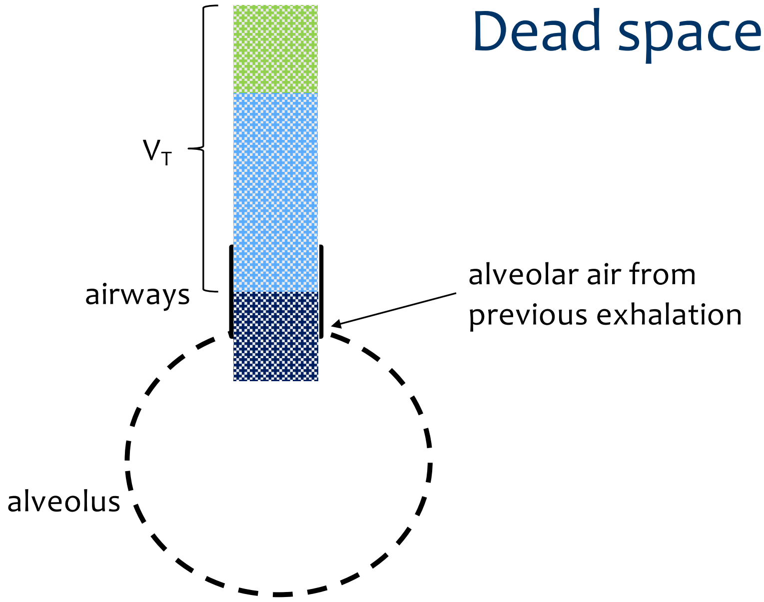
Dead space



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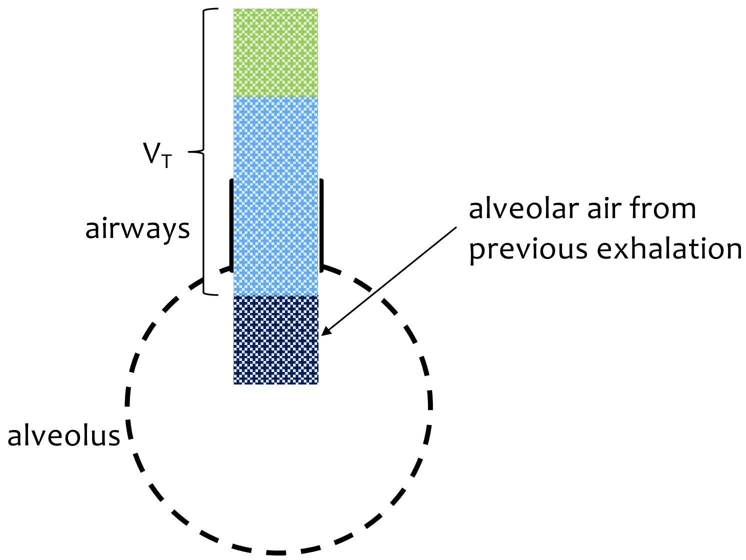
Dead space



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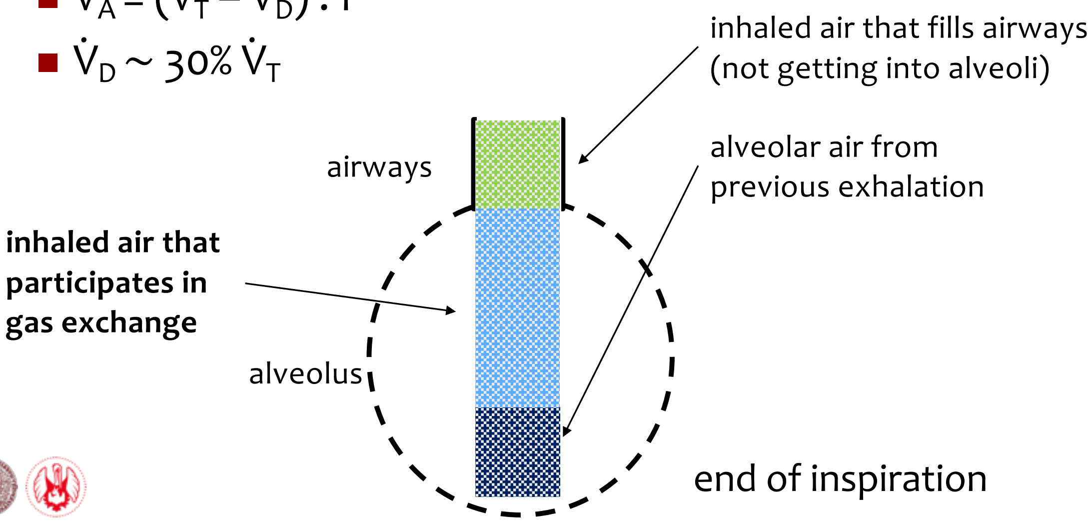
Dead space

- $\dot{V}_A = (V_T - V_D) \cdot f$
- $\dot{V}_D \sim 30\% \, \dot{V}_T$



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Dead space (V_D)

- **volume, which is**
  - **ventilated,**
  - **but does not participate in gas exchange**

- anatomical
- functional (alveolar)

} physiological

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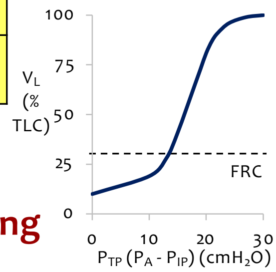
Relationship between tidal volume, frequency & effective ventilation

Minute ventilation ml/min	Tidal volume ml	**Frequency c/min**	Alveolar ventilation ml/min	Dead space ventilation ml/min	Effective ventil. %
8000	500	**16**			



Why not to breathe with minimal frequency?

Work of breathing

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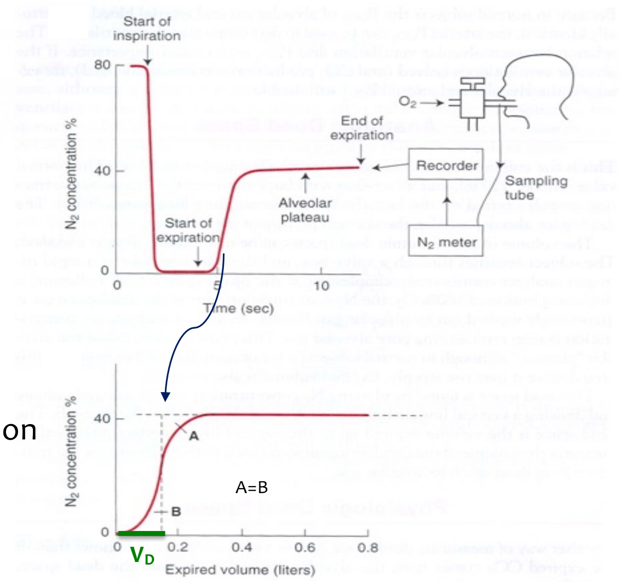
Measuring V_D: Fowler

- single-breath N_2 washout
  - 100% O_2 (0% N_2) inhaled
  - on exhalation, first 0% N_2 from V_D, then mixture
- or exhaled [CO_2]
  - virtually 0% CO_2 at inspiration



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Christian Bohr (1855–1911)

Measuring V_D: Bohr

mixed exhaled CO_2 (P_{ECO2})
= CO_2 from V_D + CO_2 from V_A

→ the higher V_D the more CO_2 from V_D (~0) "dilutes" CO_2 from V_A

$V_D/V_T = (P_{ACO2}-P_{ECO2}) / P_{ACO2}$ (Bohr equation)

P_{ACO2} – end-expiratory (or P_{aCO2})

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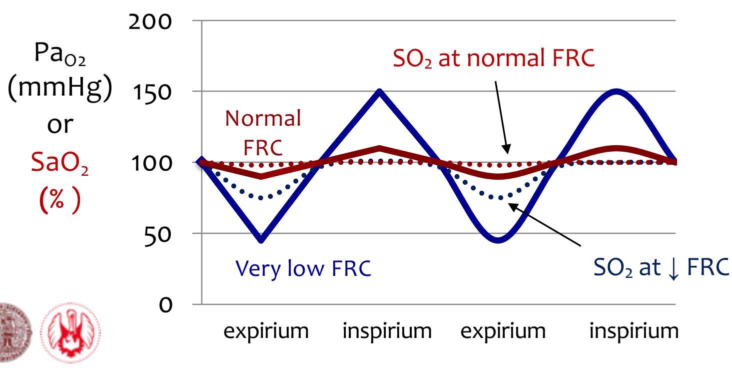
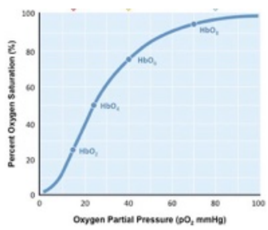
Why FRC/RV?

- prevents collapse of airways & alveoli (→ compliance)
- buffers Pa_{O2} extremes during breathing cycle (perfusion is steady → relatively stable P_{aO2})





That is (also) why we prefer to hyperventilate by ↑ inspiration

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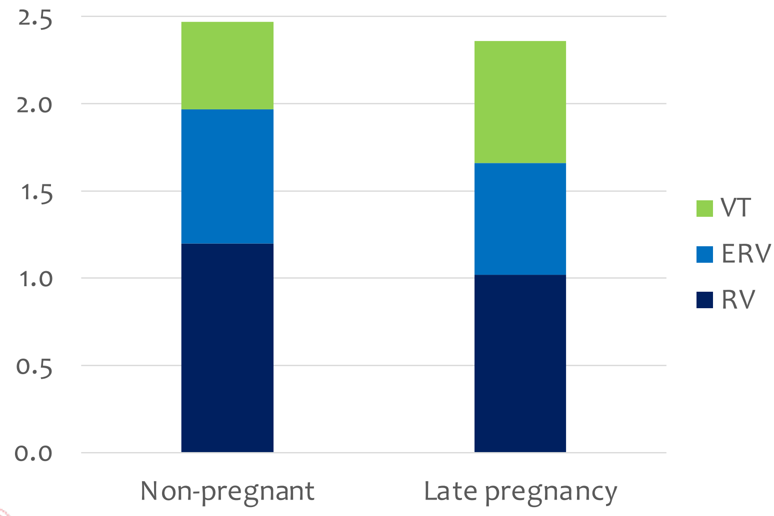
FRC ↓ in pregnancy



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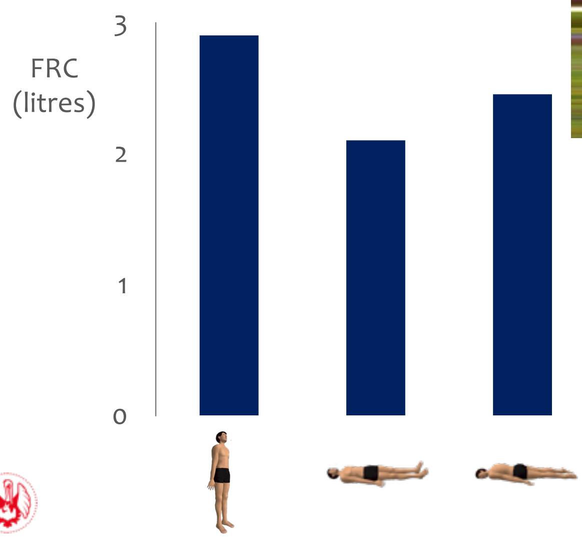
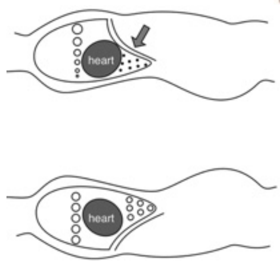
FRC depends on body posture





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Alveolar ventilation must get rid of all CO_2 produced in the body

- at rest $\dot{V}_{CO2} \sim 200$ ml/min
- $\dot{V}_A \sim 5250$ ml/min (350 x 15)
  ⇓
- 200 ml CO_2 in 5250 ml of alveolar air → $F_{ACO2} \sim 3.8\%$
- $\dot{V}_{CO2} = \dot{V}_A \times F_{ACO2}$ →
- $\mathbf{\dot{V}_A = (K * \dot{V}_{CO_2}) / P_{ACO_2}}$ ($K = 0.863$)
  (alveolar ventilation equation)
  - can be used to measure $\dot{V}_A$ ($P_{ACO2} \sim P_{aCO2}$)

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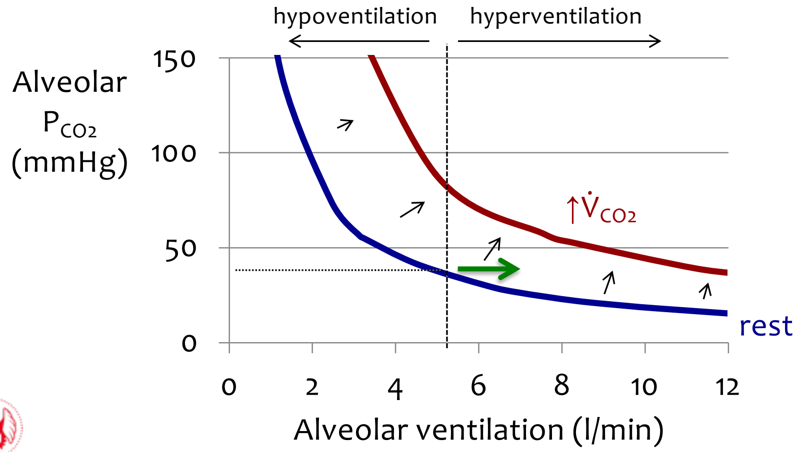
Respiratory hyperbole:
to maintain P_{ACO_2} with $\uparrow\dot{V}_{CO_2} \rightarrow \dot{V}_A$ must $\uparrow$



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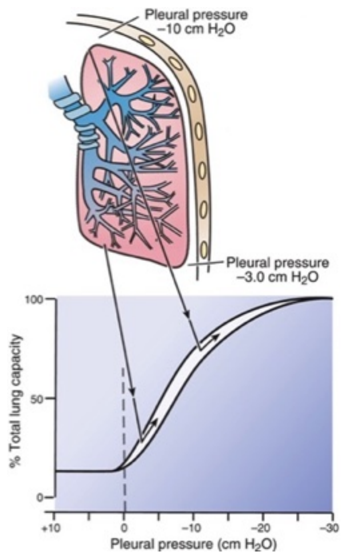
Uneven ventilation: gravity

- apex relatively overinflated at FRC (higher P_{TP})
- on a flatter part of P/V curve
- ΔP_{IP} on inspiration even in the whole chest (~2.5 cmH_2O)
- $\rightarrow \uparrow \Delta V$ near base than in apex



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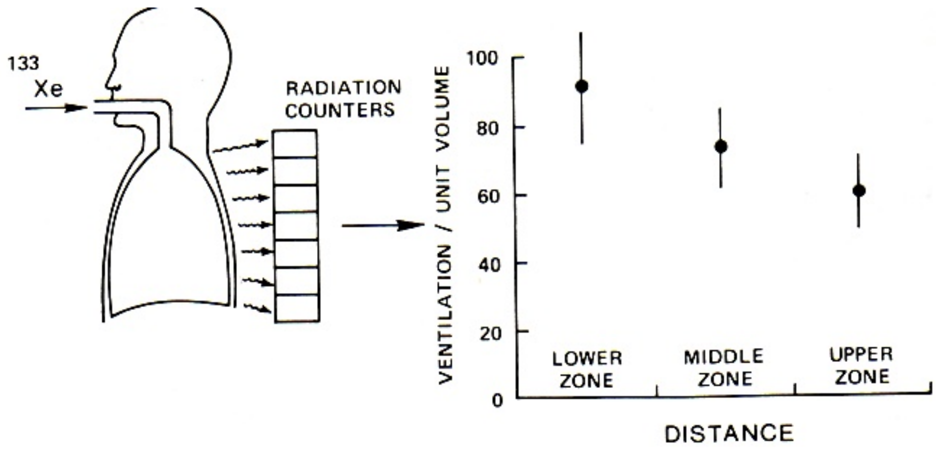
Uneven ventilation: gravity



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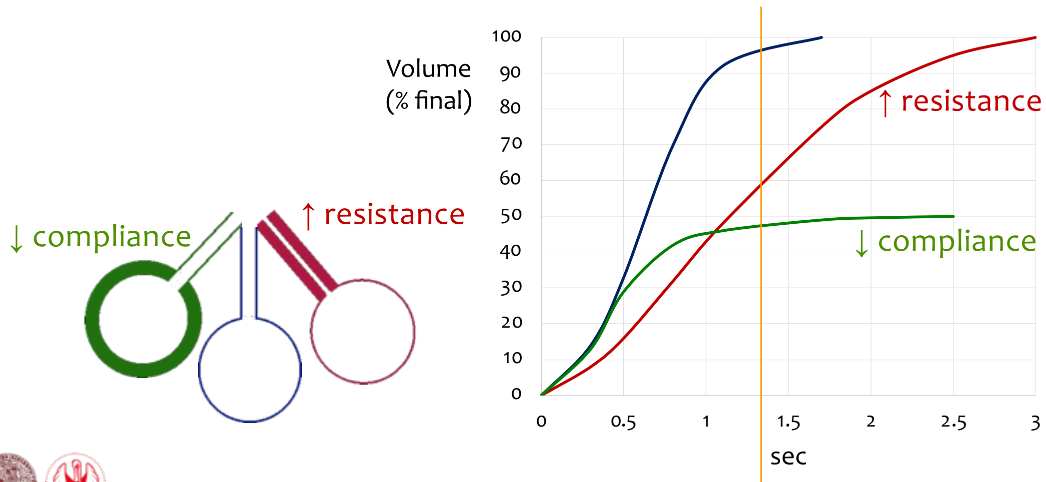
↑ resistance & ↓ compliance → ↓ ventilation at normal f



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Lung diffusion capacity

- solubility of CO_2 > O_2 → diffusion capacity for CO_2 is not limiting → diffusion capacity for O_2 (D_LO_2) used to characterize diffusion in the lungs
- $D_LO_2 = \dot{V}_{O2}/(P_{AO2}-P_{cO2})$
- $\dot{V}_{O2}$ (O_2 consumption) measured by spirometry
- P_{AO2} = end-expiratory P_{O2}
- problem:
  how to detect P_{cO2} (in pulmonary capillaries)?!

solution: use CO !

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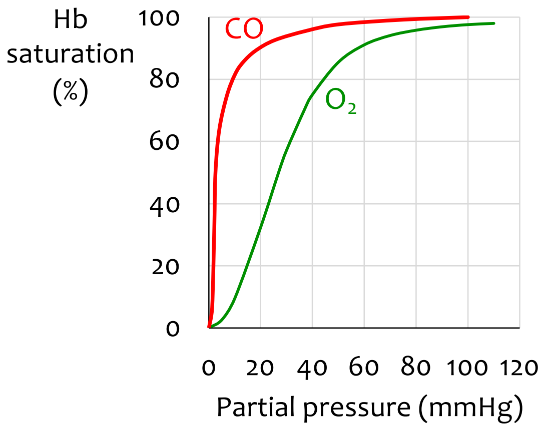
Diffusion capacity for CO (D_LCO)

- intensely & rapidly binds to Hb
- $P_{cCO} \sim 0$
- $D_LCO = \dot{V}_{CO}/(P_{ACO}-P_{vCO}\ [=0])$
  → CO disappearance from alveolar gas during breath holding
- conversion factor:
  $D_{LO2} = 1.23 \times D_{LCO}$



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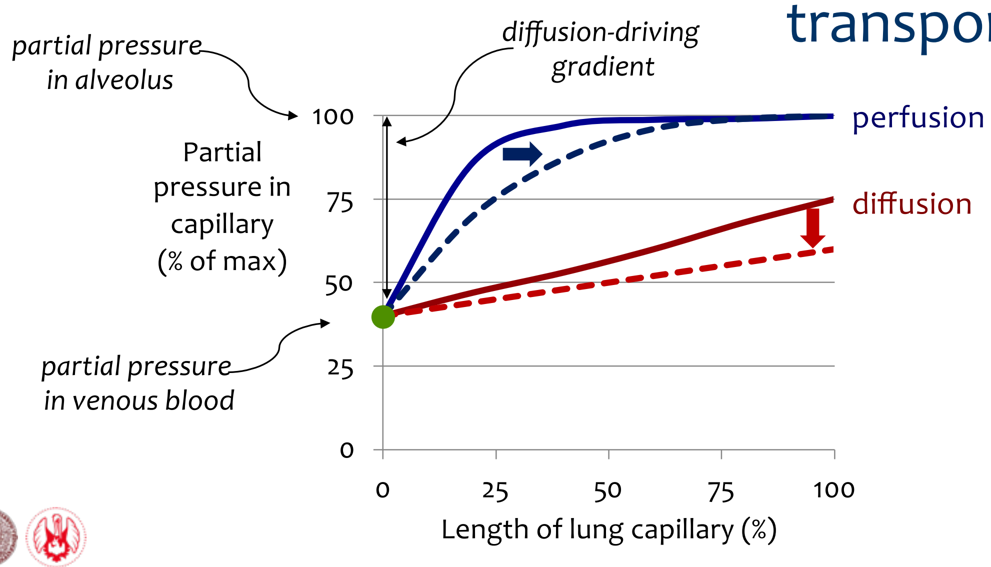
Perfusion & diffusion limitation of gas transport



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