Economy of organ form and function

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Organ development

Goals

- Optimize its form under constraints
- Fulfill its function in the most optimized manner

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Mathematical framework

- Cost function $\mathcal{E}$ dependent on one or several variables $x \in \mathbb{R}^n$
- One or several equality constraints: $c(x) = 0$, where $c : \mathbb{R}^n \to \mathbb{R}^m$
- Find an optimal value x^* that minimizes the function $\mathcal{E}(x)$ while $c(x^*) = 0$

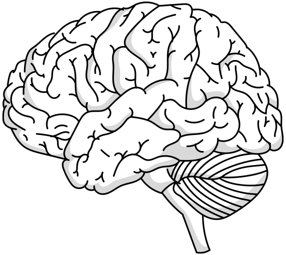
Organ form

Built with reproducible size and shape in each species.

Brain

Improved neural processing power

- Large cortical surface
- Small cranium



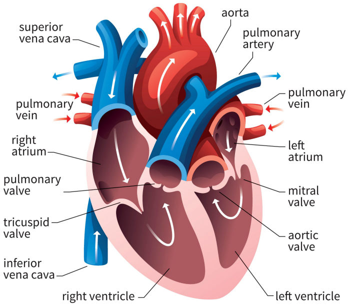
Organ function

Fulfilled as best as possible while minimizing cost variables (energy)

Heart

Different blood pressure in both ventricules

- Low pressure to irrigate the lung
- High pressure to irrigate the body



Cardiology Associates of Michigan

Focus on the lung

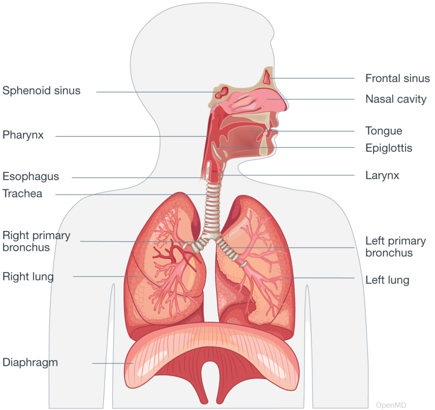
Geometry

- Complex system: exchange surface between ambient air and blood
- Divided into two parts: bronchial tree and the acini

Principal function

- Brings oxygen from the ambient air to the blood
- Removes carbon dioxide from the blood

Made possible thanks to the ventilation



Open MD

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Lung morphometry

Problematics

- Role: connects O_2 and CO_2 in atmosphere with inner body
- Medium: gas transfer by diffusion through alveolar membrane
- Major constraints:
  - Diffusion : a surface process
  - Limited thoracic volume

Lung morphometry

Problematics

- Role: connects O_2 and CO_2 in atmosphere with inner body
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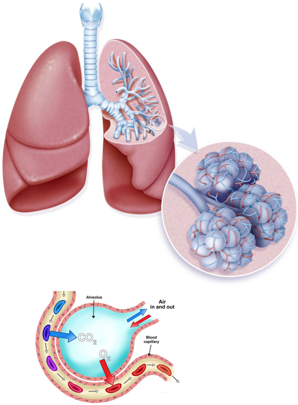
Solution

Optimize (maximize) the surface/volume ratio

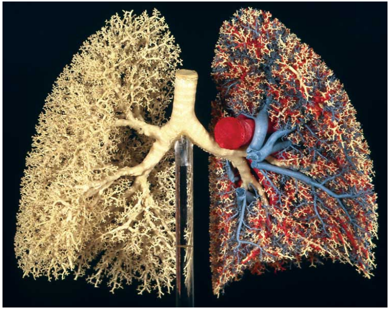


Getty Images & Mammoth Memory

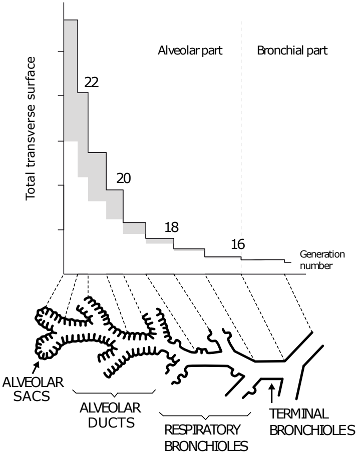
Lung morphometry

Characteristics for a proper functionning of the lung

- Space-filling
- Self-avoiding



Lung's cast made by E.R. Weibel



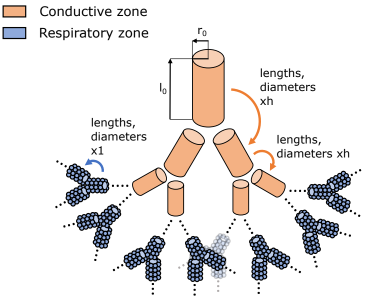
Lung morphology

Bronchial tree

- Cascade of bifurcating airways with cylindrical shapes
- Around 17 generations
- Size of the airways decreases at each bifurcation

Acini

- Exchange surface with blood $(70 - 100\,\mathrm{m}^2)$
- Alveoli: bubble-like structure
- Around 6 generations



Human's lung function

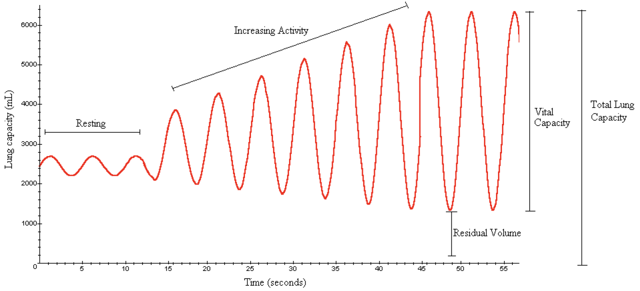
Lung's function

Objectives

- Brings O_2 to the blood
- Removes CO_2 from the blood

Ventilation parameters

- Rate of breathing (f_b)
- Depth of breathing (V_T)

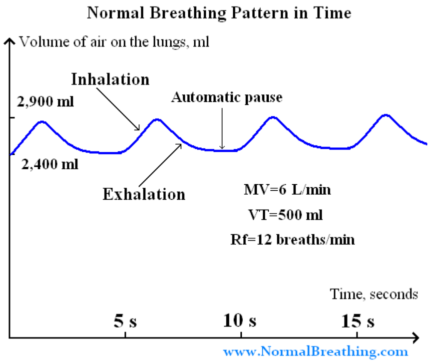


Beals et al., 2000

Natural selection of ventilation

Stereotyped ventilation

- f_b : 12 breaths per minute
- V_T : 500 mL



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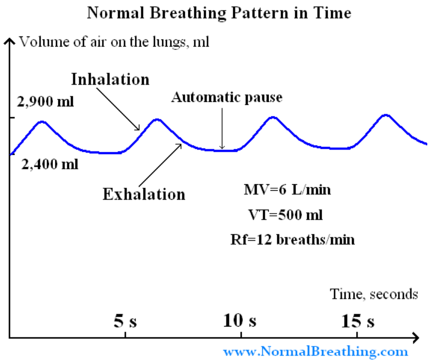


Hypothesis

Minimizing the cost of breathing while satisfying the body needs in oxygen

Oxygen transport in the lung

Diffusion

- Passive process
- Balance the concentration
- Too long for air to pass through the lung

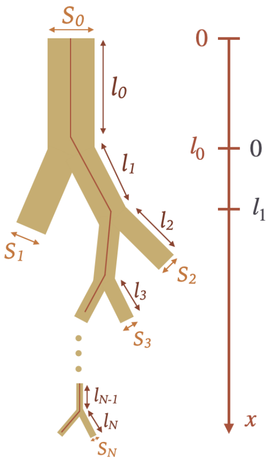
Convection

- Dynamic process
- Performed thanks to a set of muscles (ex. diaphragm)
- Two phases: inspiration and expiration

Modeling oxygen transport

Convection-diffusion-reaction equation in each airway

$$\frac{\partial P}{\partial t} - D\frac{\partial^2 P}{\partial x^2} + u(t)\frac{\partial P}{\partial x} = \beta\left(P_{\text{blood}} - P\right)$$



Link all generations by assuming:

- Continuity between generations
- Conservation of the quantity of oxygen:

$$u_i S_i = 2u_{i+1}S_{i+1}$$

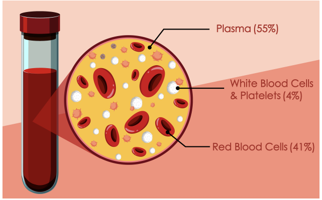
Boundary conditions:

- Partial pressure in the ambient air at the entrance of the tree
- Diffusive flow with the blood at the tree terminals

Modeling oxygen in the blood

Oxygen in the blood

- Linked to hemoglobin
- Dissolved in plasma



FreePik

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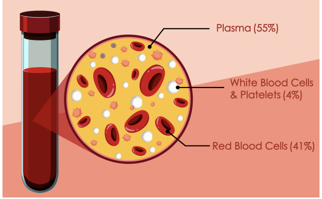


FreePik

Modeling the exchanges with the blood

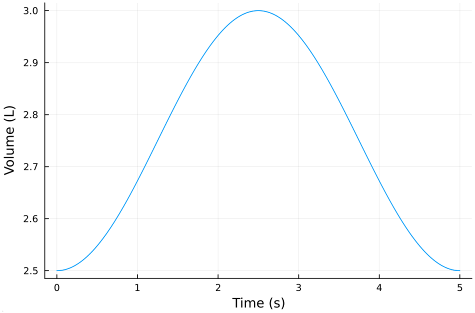
$$\underbrace{\alpha(P - P_{\text{blood}})}_{\text{flow through the membrane}} = \underbrace{4Z_0\left(S_{O_2}(P_{\text{blood}}) - S_{O_2}(P_{\text{vein}})\right)v_s + \sigma v_s\left(P_{\text{blood}} - P_{\text{vein}}\right)}_{\text{flow transported by blood}}$$

Input of the model

- Periodic ventilation dependant on V_T and f_b
- Volume of the lung:

$$V(t) = V_{FRC} + \frac{V_T}{2}\left(1 - \cos(2\pi f_b t)\right)$$

- Air velocity and airflow are deduced from the volume



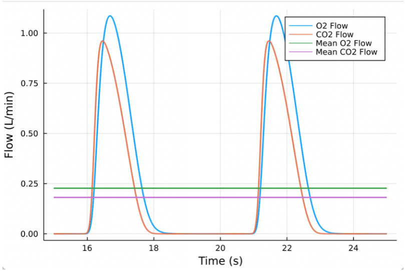
Outputs of the model

O_2 flow to blood

- Physiological value: $\dot{V}_{O_2} = 250$ mL $\cdot$ min^{-1}
- Predicted value: $\dot{V}_{O_2} = 230$ mL $\cdot$ min^{-1}

CO_2 flow to blood

- Physiological value: $\dot{V}_{CO_2} = 200$ mL $\cdot$ min^{-1}
- Predicted value: $\dot{V}_{CO_2} = 180$ mL $\cdot$ min^{-1}



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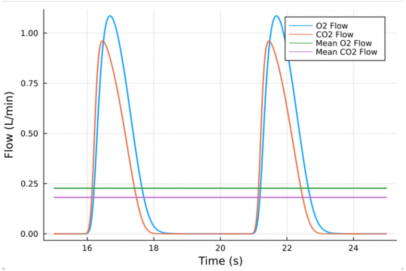


Model validated

Cost of breathing

Hypothesis

Minimizing the cost of breathing while satisfying the body needs in oxygen

Cost of breathing

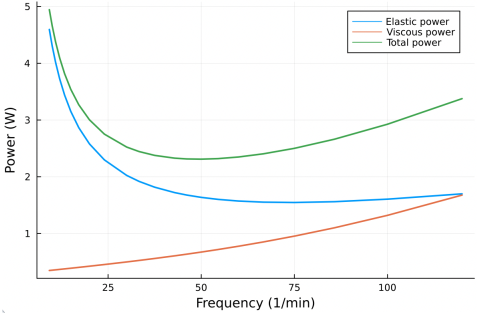
Hypothesis

Minimizing the cost of breathing while satisfying the body needs in oxygen

Action of the muscles on the lung:

- Deforms the tissues
- Displaces the air along the bronchial tree

$$\underbrace{\mathcal{P}_{\mathrm{m}}}_{\text{muscle power}} \simeq \underbrace{\mathcal{P}_{\mathrm{e}}}_{\text{elastic power}} + \underbrace{\mathcal{P}_{\mathrm{a}}}_{\text{air viscous dissipation}}$$



Power spent during ventilation

Viscous dissipation of air

- Characterized by the lung hydrodynamic resistance
  - Connects the airflow $\mathcal{F}$ to the air pressure p: $p = \mathcal{F}\mathcal{R}$
- Power dissipated

$$\mathcal{P}_{\mathrm{a}} = \mathcal{R}\mathcal{F}^2 = \frac{1}{4}\mathcal{R}(\pi f_b V_T)^2$$

Elastic power

- Characterized by the compliance of the lung
  - Relates the force per unit of surface applied by the muscles to the volume change of the lung
- Elastic power

$$\mathcal{P}_{\mathrm{e}} = \frac{V_T^2 f_b}{2\mathcal{C}}$$

Optimal ventilation for humans

$$\min_{V_T, f_b} \mathcal{P}_{\mathrm{e}}(V_T, f_b) + \mathcal{P}_{\mathrm{a}}(V_T, f_b) \quad \text{s.t. } \dot{V}_{O_2}(V_T, f_b) = \dot{V}_{O_2}^{\mathrm{obs}}$$

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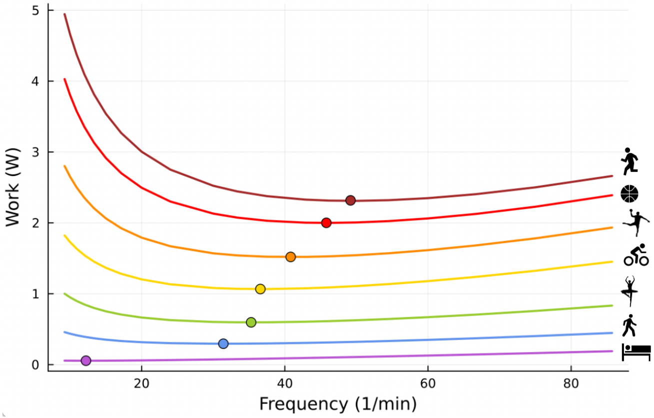

Mammals' lung function

Extension to mammals

Question

Can our model be extended to all mammals?

Extension to mammals

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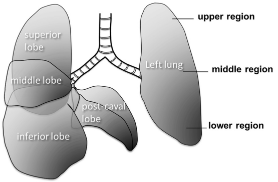
Can our model be extended to all mammals?

Why ?

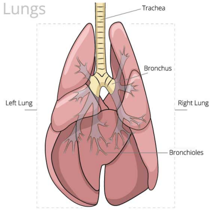
- Share morphological properties
- Share functional properties

Mouse



Sato et al., 2015

Dog

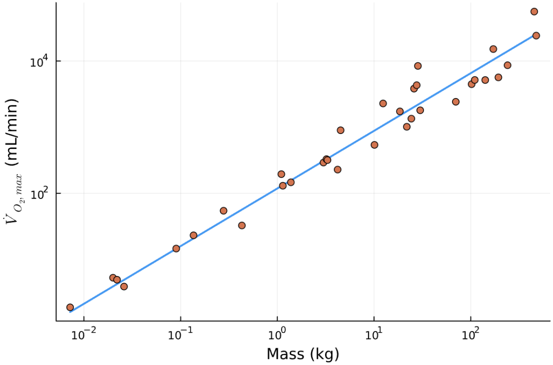


Pokusay / stock.adobe.com

Concept of allometry

Shared properties dependent on the mass M of the mammal

$$Y = aM^b$$



Adaptation of the model of the lung

Shared characteristics

- Tree-like structure with bifurcating branches
- Decomposition into two parts: bronchial tree and acini

Morphological parameters

- Tracheal radius ($\propto M^{3/8}$) and length ($\propto M^{1/4}$)
- Radius ($\propto M^{1/12}$) and length ($\propto M^{-1/24}$) of alveolar ducts
- Exchange surface ($\propto M^{3/4}$)

Adaptation of the oxygen transport model

Oxygen transport

- No modification
- Convection-diffusion-reaction equation

Constraint on the oxygen flow

- Basal Metabolic Rate (BMR): $\dot{V}_{O_2} \propto M^{0.75}$
- Field Metabolic Rate (FMR): $\dot{V}_{O_2} \propto M^{0.64}$
- Maximal Metabolic Rate (MMR): $\dot{V}_{O_2} \propto M^{0.875}$

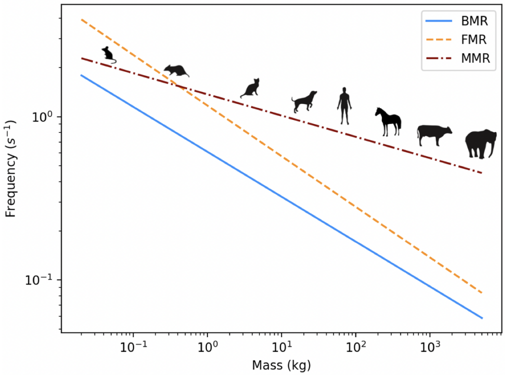
Optimal ventilation for mammals

$$\min_{V_T, f_b} \mathcal{P}_\mathrm{e}(V_T, f_b) + \mathcal{P}_\mathrm{a}(V_T, f_b) \quad \text{s.t. } \dot{V}_{O_2}(V_T, f_b) = \dot{V}_{O_2}^{\mathrm{obs}}$$

Optimal ventilation for mammals

$$\min_{V_T, f_b} \mathcal{P}_\mathrm{e}(V_T, f_b) + \mathcal{P}_\mathrm{a}(V_T, f_b) \quad \text{s.t. } \dot{V}_{O_2}(V_T, f_b) = \dot{V}_{O_2}^{\mathrm{obs}}$$

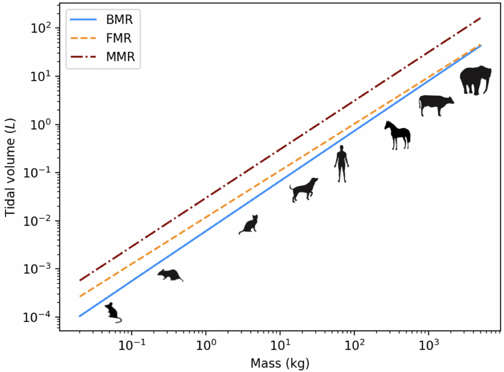
	f_b (pred)	f_b (obs)
BMR	-0.27	-0.26
FMR	-0.31	N.D
MMR	-0.17	-0.14



Optimal ventilation for mammals

$$\min_{V_T, f_b} \mathcal{P}_{\mathrm{e}}(V_T, f_b) + \mathcal{P}_{\mathrm{a}}(V_T, f_b) \quad \text{s.t. } \dot{V}_{O_2}(V_T, f_b) = \dot{V}_{O_2}^{\mathrm{obs}}$$

	V_T (pred)	V_T (obs)
BMR	1.04	1.04
FMR	0.97	N.D
MMR	1.01	N.D



Conclusion

Conclusion

- Principles of economy applied on larger living structures
- Constraints guide the development and the functioning of mammalian lung
  - form: optimize the surface/volume ratio
  - function: minimize the cost of breathing while satisfying the body needs in oxygen
- Allometric laws allow an understanding of the mechanics of breathing