Pulmonary Ventilation

Pulmonary Ventilation or Breathing

- **Pulmonary ventilation** or breathing brings O\(_2\) to cells of the body and removes metabolic waste product, CO\(_2\).
- **Inspiration** or inflow of fresh air results from the contracting the muscles of the diaphragm.
- Relaxation of these muscles or contraction of the abdominals causes **expiration** of air with the waste product CO\(_2\).
- Normal **respiration** in the lungs exchanges about 500 ml of air 12 times a minute, the **tidal volume**, TV.
The **inspiratory reserve volume** (inspiration above tidal volume), $IV$, is about 3000 ml

The **expiratory reserve volume** (air forcefully expired), $EV$, is about 1100 ml

The **vital capacity**, $TV + IV + EV$, is about 4600 ml

- Well-trained athletes may have values **30-40% higher**
- Females have **20-25% less** for the quantities listed above

The **residual volume** is the amount of air that cannot be expelled and averages about 1200 ml

The lungs contain surfactants, which prevent them from totally collapsing

The body needs oxygen for the tissues

Several respiratory diseases jeopardize the vital function of the lungs

- **Respiratory muscles damage** - spinal paralysis or poliomyelitis decreases the vital capacity
- **Pulmonary compliance reduces vital capacity** in diseases like tuberculosis, emphysema, chronic asthma, lung cancer, chronic bronchitis, cystic fibrosis, or fibrotic pleurisy
- **Heart disease and others** can cause pulmonary edema, decreasing vital capacity from fluid build up

Alveoli allow $O_2$ exchange with blood

Alveoli are damaged or filled with fluid (one result of smoking), the exchange of oxygen is inhibited
Health of the Patient

- Vital capacity of the lungs is determined by a spirometer
- The experimental data are used to determine the functional reserve volume for the subjects
- Develop a model to analyze the data
- A physiologist uses this information to find the health of a subject’s lungs

Tidal volume and the functional residual capacity are found by breathing a mixture including an inert gas
- The subject breathes the mixture until the lungs are essentially filled with this mixture
- A physiologist measures the amount of the inert gas in a series of breaths after the subject is removed from the gas mixture to normal air
- The mathematical model for this experiment is a discrete dynamical system

Professor Bruce Wingerd ran dilution experiments with the inert gas argon (Ar)
- Argon is a noble gas, so is totally non-reactive
- It is the third most common gas, comprising 0.93% of Earth’s atmosphere (dry air has N$_2$ 78%, O$_2$ 21%, with CO$_2$ a distant fourth, 0.03%)
- The subjects breathe an air mixture with 10% Ar
- Then the subjects resume breathing normal air at a normal rate

<table>
<thead>
<tr>
<th>Normal Subject</th>
<th>Tidal Volume=550 ml</th>
<th>Subject with Emphysema</th>
<th>Tidal Volume=250 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breath Number</td>
<td>Percent Ar</td>
<td>Breath Number</td>
<td>Percent Ar</td>
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<td>0</td>
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<tr>
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</tr>
<tr>
<td>6</td>
<td>0.037</td>
<td>6</td>
<td>0.049</td>
</tr>
</tbody>
</table>
Breathing Experiment

- This breathing experiment is a dynamic exchange of gases, which occurs at discrete intervals of time.
- Suggests a discrete dynamical model tracking the concentration of Ar in the lungs.
- If \( c_n \) is the concentration of Ar at the end of the \( n \)th inspiration cycle, we write a dynamical model:

\[
  c_{n+1} = f(c_n)
\]

Modeling Assumptions

- The concentration at the end of the \((n + 1)\)th inspiration cycle depends on remaining air in the lungs from the previous cycle and inhaling fresh air from the atmosphere.
- Assume the gases become well-mixed during this process, which ignores the complications caused by the actual physiological structures in the lungs, such as the “anatomical dead space” in the pharynx, trachea, and larger bronchi or weak mixing from slow gas flow in the alveoli.
- 500 ml of fresh air enters by inspiration, but only 350 ml reaches the alveoli, i.e., less than 1/7 exchange of gases with a normal breath.

Physiological Parameters for Model

- \( V_i \) for the tidal volume (air normally inhaled and exhaled).
- \( V_r \) for the functional residual volume.
- \( \gamma \) for the concentration of Ar in the atmosphere.
- The fraction of atmospheric air exchanged in each breath is:

\[
  q = \frac{V_i}{V_i + V_r}
\]

- The residual air fraction is:

\[
  1 - q = \frac{V_r}{V_i + V_r}
\]
Discrete Model for Breathing

From definitions above,
\[ c_{n+1} = \frac{V_r c_n}{V_i + V_r} + \frac{V_i \gamma}{V_i + V_r} \]

Use definitions of \( q = \frac{V_i}{V_i + V_r} \) and \( 1 - q \)

Linear Discrete Dynamical Model for Breathing an Inert Gas
\[ c_{n+1} = (1 - q) c_n + q \gamma \]

Finding Functional Reserve Capacity
The diseased states are often characterized by a decreased ratio between the tidal volume and the functional reserve capacity.

Emphysema is characterized by a loss of elasticity in the lungs and a decrease in the alveolar surface/volume ratio.

The discrete dynamical model for breathing an inert gas is solved for the parameter \( q \)
\[ q = \frac{c_n - c_{n+1}}{c_n - \gamma} \]

Graph of the data above with the best fitting model for breathing

Finding Functional Reserve Capacity
Given tidal volume, \( V_i \) and \( q \), the functional reserve capacity satisfies
\[ V_r = \frac{1 - q}{q} V_i \]

Normal Patient
- From data, \( q = \frac{0.1 - 0.084}{0.1 - 0.093} = 0.18 \)
- With \( V_i = 550 \), then \( V_r = \frac{0.82}{0.18} 550 = 2500 \text{ ml} \)
- Ratio of tidal volume to functional reserve capacity is 0.22

Patient with Emphysema
- From data, \( q = \frac{0.1 - 0.088}{0.1 - 0.093} = 0.13 \)
- With \( V_i = 250 \), then \( V_r = \frac{0.85}{0.13} 250 = 1670 \text{ ml} \)
- Ratio of tidal volume to functional reserve capacity is 0.15
Example – Lung Disease

**Example:** A subject with an unknown lung ailment enters the lab for testing. She is given a supply of air that has an enriched amount of argon gas (Ar). After breathing this supply of enriched gas, two successive breaths are measured with $c_1 = 0.0736$ and $c_2 = 0.0678$ of Ar. The model for breathing is given by

$$c_{n+1} = (1 - q)c_n + q\gamma,$$

where $\gamma = 0.0093$.

- Find the fraction of air breathed, $q$
- What is the concentration of argon remaining in her lungs after 5 breaths?
- Assume that her tidal volume is measured to be $V_i = 220$. Find the functional reserve volume, $V_r$, where $q = \frac{V_i}{V_i + V_r}$

**Solution:** Since we are given $\gamma$ and the two consecutive values $c_1$ and $c_2$, we can find $q$

$$c_2 = (1 - q)c_1 + q\gamma$$

$$0.0678 = (1 - q)(0.0736) + 0.0093q$$

$$q = 0.0902$$

The concentration after 5 breaths is found by simulation

$$c_2 = 0.0678$$

$$c_3 = (1 - 0.0902)c_2 + 0.0093(0.0902) = 0.06252$$

$$c_4 = 0.9098(0.06252) + 0.000839 = 0.05772$$

$$c_5 = 0.9098(0.05772) + 0.000839 = 0.05336$$

**Solution (cont):** To find the functional reserve we recall

$$q = \frac{V_i}{V_i + V_r}$$

$$0.0092 = \frac{220}{220 + V_r}$$

This gives the functional reserve volume, $V_r = 2219$

This functional reserve is approximately normal.

The woman has a very low $q$, so the woman probably has some type of respiratory muscle disorder or neurological problem.

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**Equilibria - Breathing Model**

- The discrete dynamical model for breathing shows the concentration of Ar decreasing.
- If the simulation for the normal individual is carried out for about 3 minutes or 36 breaths, it can be seen that the concentration of Ar drops to 0.0094, which is within 1% of the atmospheric concentration.
- Since Ar is an inert gas, we expect that after breathing an enriched source of Ar, then the concentration should return to the same value as normally found in the atmosphere.
- This value is the equilibrium value of Ar for the model.
**Equilibria**

**Equilibria for Discrete Dynamical Models**

Consider a discrete dynamical system given by the equation

\[ x_{n+1} = f(x_n) \]

where \( f(x_n) \) is any function describing the dynamics of the model.

An **equilibrium**, \( x_e \), for this discrete dynamical system is achieved if \( x_{n+1} = x_n = x_e \)

The dynamic variable settles into a constant value for all \( n \) when

\[ x_e = f(x_e) \]

**Equilibrium - Breathing Model**

Consider the discrete breathing model

\[ c_{n+1} = (1 - q)c_n + q\gamma \]

An **equilibrium**, \( c_e \), for this model satisfies \( c_{n+1} = c_n = c_e \) or

\[ c_e = (1 - q)c_e + q\gamma \]

Solving this

\[ qc_e = q\gamma \]
\[ c_e = \gamma \]

Intuitively, this is the natural equilibrium, since eventually the concentration of an inert gas in the lungs will equalize to the atmospheric concentration.

**Linear Discrete Dynamical Model 1**

The equilibrium, \( y_e \), for this discrete dynamical model is

\[ y_e = \frac{b}{1 - a} \]

provided \( a \neq 1 \)

The **equilibrium** is **negative** provided

- \( a < 1 \) and \( b < 0 \) or
- \( a > 1 \) and \( b > 0 \)

**Linear Discrete Dynamical Model 2**

Since the **equilibrium** satisfies

\[ y_e = \frac{b}{1 - a} \]

The **equilibrium** is **negative** provided

- \( a < 1 \) and \( b < 0 \) or
- \( a > 1 \) and \( b > 0 \)

**Linear discrete dynamical models** have a **single unique equilibrium** if the **slope** of the linear function, \( a \neq 1 \)

If \( a = 1 \), then

- There are **no equilibria** when \( b \neq 0 \), or
- All points are **equilibria** when \( b = 0 \)
Stability of a Linear Discrete Dynamical Model

\[ y_{n+1} = ay_n + b \]

An equilibrium of a linear discrete dynamical model is **stable** if either of the following conditions hold:
- Successive iterations of the model **approach the equilibrium**
- The slope \( |a| \) is **less than 1**

An equilibrium of a linear discrete dynamical model is **unstable** if either of the following conditions hold:
- Successive iterations of the model **move away from the equilibrium**
- The slope \( |a| \) is **greater than 1**

**Example – Linear Discrete Dynamical Model 1**

Consider the linear discrete dynamical model

\[ y_{n+1} = 1.05y_n - 200, \quad y_0 = 2000 \]

- Find the first 3 iterations, \( y_1, y_2, y_3 \)
- Determine the equilibrium value
- Find the stability of the equilibrium

**Solution:** Let \( y_0 = 2000 \)

\[
\begin{align*}
y_1 &= 1.05y_0 - 200 = 1.05(2000) - 200 = 1900 \\
y_2 &= 1.05y_1 - 200 = 1.05(1900) - 200 = 1795 \\
y_3 &= 1.05y_2 - 200 = 1.05(1795) - 200 = 1684.75
\end{align*}
\]

The equilibrium satisfies

\[
\begin{align*}
y_e &= 1.05y_e - 200 \\
0.05y_e &= 200 \\
y_e &= 4000
\end{align*}
\]

The **equilibrium is unstable**, since iterations are moving away from the equilibrium and the slope \( a = 1.05 > 1 \).
Example – Linear Discrete Dynamical Model

Solution: Let $y_0 = 100$

\[
y_1 = 0.6 y_0 + 50 = 0.6(100) + 50 = 110 \\
y_2 = 0.6 y_1 + 50 = 0.6(110) + 50 = 116 \\
y_3 = 0.6 y_2 + 50 = 0.6(116) + 50 = 119.6
\]

The equilibrium satisfies

\[
y_e = 0.6 y_e + 50 \\
0.4 y_e = 50 \\
y_e = 125
\]

The equilibrium is stable, since iterations are moving towards the equilibrium and the slope $a = 0.6 < 1$.

Stability of Discrete Dynamical Model

A discrete dynamical model is given by the equation

\[x_{n+1} = f(x_n)\]

for some updating function, $f(x_n)$. Suppose that this model has an equilibrium, $x_e$, so $x_e = f(x_e)$.

The equilibrium, $x_e$, is said to be stable if one starts with some $x_0$ “near” the equilibrium, then subsequent iterations of the model have $x_n$ approaching the equilibrium.

The equilibrium, $x_e$, is said to be unstable if one starts with some $x_0$ “near” the equilibrium, then subsequent iterations of the model have $x_n$ moving away from the equilibrium.

Malthusian Growth with Immigration or Emigration

Population Growth Models

- The discrete Malthusian growth model worked for the U. S. population over only a limited time
- Malthusian model doesn’t account for time-varying effects, resource limitation, immigration, etc.
- Time-varying model substantially improved, but difficult to analyze
- Through much of the 20th century, the government has regulated legal immigration to 250,000 people per year
- Models with immigration or emigration are not closed systems

Malthusian Growth with Emigration

\[P_{n+1} = (1 + r)P_n - \mu\]

where $r$ is a rate of growth and $\mu$ is a constant population emigrating in each time interval

Given an initial population, $P_0$

\[
P_1 = (1 + r)P_0 - \mu, \\
P_2 = (1 + r)P_1 - \mu = (1 + r)((1 + r)P_0 - \mu) - \mu, \\
= (1 + r)^2P_0 - ((1 + r) + 1)\mu
\]

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Continuing the iterations

\[ P_3 = (1 + r)^3 P_0 - ((1 + r)^2 + (1 + r) + 1) \mu, \]
\[ : \]
\[ P_n = (1 + r)^n P_0 - ((1 + r)^{n-1} + ... + (1 + r) + 1) \mu, \]

which simplifies to

\[ P_n = (1 + r)^n P_0 - \frac{(1 + r)^n - 1}{r} \mu. \]

Though complicated, this is a closed form solution depending only upon \( P_0, r, n, \) and \( \mu \)

Example of Malthusian Growth with Immigration:
Assume that a population of animals in a lake satisfies

\[ P_{n+1} = (1 + r) P_n + \mu \]

where \( r \) is a rate of growth and \( \mu \) is a constant population immigrating to the lake in each time interval

Assume a census for 3 successive weeks gives populations, \( P_0 = 500, P_1 = 670, \) and \( P_2 = 874 \)

Find the rate of growth \( r \) and immigration rate \( \mu \), then determine the populations expected in the next two weeks

Solution: From the data with the model

\[ P_1 = (1 + r) P_0 + \mu \quad \text{and} \quad P_2 = (1 + r) P_1 + \mu \]
\[ 670 = (1 + r) 500 + \mu \quad \text{and} \quad 874 = (1 + r) 670 + \mu \]

Subtract the first equation from the second equation

\[ 204 = (1 + r)(670 - 500) \]
\[ 1 + r = \frac{204}{170} = 1.2 \]
\[ r = 0.2 \]

From the model

\[ 670 = 1.2(500) + \mu \]
\[ \mu = 670 - 600 = 70 \]

Solution (cont): The model is given by

\[ P_{n+1} = 1.2 P_n + 70 \]

Since \( P_2 = 874, \)

\[ P_3 = 1.2 P_2 + 70 = 1.2(874) + 70 = 1118.8 \]
\[ P_4 = 1.2(1118.8) + 70 = 1412.56 \]

This model has no positive equilibrium, and it grows unbounded (almost exponentially)
Consider the **linear discrete model**

\[ y_{n+1} = ay_n + b \]

The general solution is given by

\[ y_n = a^n y_0 + \frac{(a^n - 1)}{(a - 1)} b \]

\((a \neq 1)\)

Solution depends on parameters \(a\) and \(b\), initial condition \(y_0\), and time, \(n\)

Cobwebbing

Graphically, any intersection of the **updating function** and the **identity map**

\[ x_{n+1} = f(x_n) \quad \text{and} \quad x_{n+1} = x_n \]

produces an equilibrium

- The process of **cobwebbing** shows the dynamics of this discrete dynamical model
- Start at some point \(x_0\) on the horizontal axis, then go vertically to \(f(x_0)\) to find \(x_1\)
- Next go horizontally to the line \(x_{n+1} = x_n\)
- Go vertically to \(f(x_1)\) to find \(x_2\)
- The process is repeated to give a geometric interpretation of the dynamics of the discrete model

Cobwebbing – Breathing Model Example

The model for a normal subject breathing an air mixture enriched with Ar satisfies the model

\[ c_{n+1} = (1 - q)c_n + q\gamma = 0.82c_n + 0.0017 \]

This model has a **stable** equilibrium \((c_e = \gamma = 0.0093)\)

Initially, there was 10% Ar in the mixture, so \(c_0 = 0.1\), and subsequent breaths had the concentration of Ar tending to \(\gamma\)
Cobwebbing – Population Model with Emigration

The model for a population with Emigration satisfies the model

\[ P_{n+1} = (1+r)P_n - \mu = 1.2P_n - 500 \]

This model has an **unstable** equilibrium \( P_e = \frac{\mu}{r} = 2500 \)

- If the population begins below 2500, then the population goes to extinction
- If the population begins above 2500, then the population grows almost exponentially

\[ P_{n+1} = 1.2P_n - 500 \]