課程名稱： 醫學工程概論

（Introduction to biomedical engineering）

生物系統與生醫訊號分析

Biomedical Systems and Biological Signal Analysis

授課教師： 潘力誠副教授

開課單位 ： 通識教育中心

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學 習 目 標：

- 生物系統簡介
- 週期性訊號簡介
- 線性訊號及非線性訊號簡介
- 生醫訊號分析
- 生醫訊號臨床應用簡介

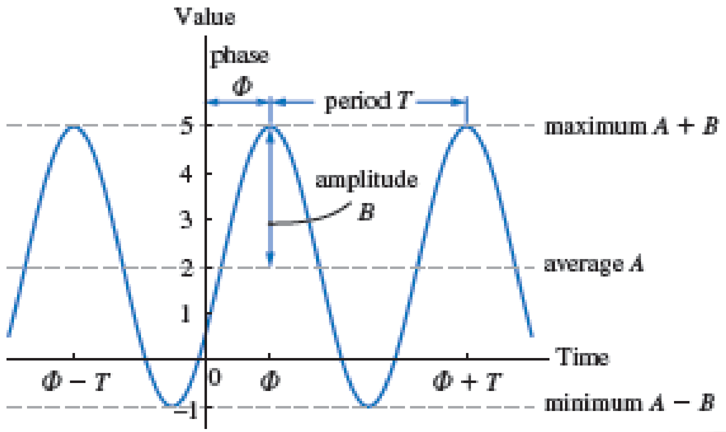
週期性訊號簡介

Sine and Cosine: A Review

In applied mathematics, angles are measured in **radians**, defined as the distance along the perimeter of the circle of radius 1.
The **basic identity** between radians and degrees is given by 2π rad = 360◦

Describing Oscillations with the Cosine

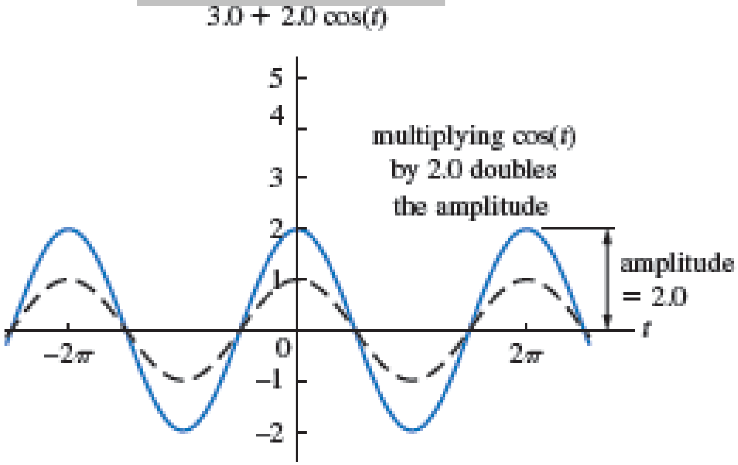
Oscillations that are shaped like the graph of the sine or cosine function are called **sinusoidal.** There are four numbers needed to describe an oscillation with the cosine function: the **average**, the **amplitude,** the **period**, and the **phase**.



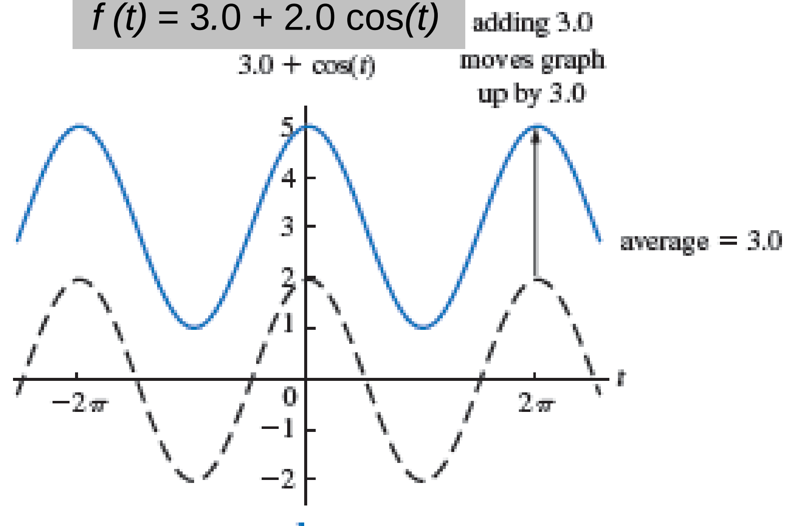
- The **amplitude** is the difference between the maximum and the average.
- The **period** is the time between successive peaks.
- The **phase** is the time of the first peak.

Building an Oscillation by Shifting and Scaling the Cosine Function

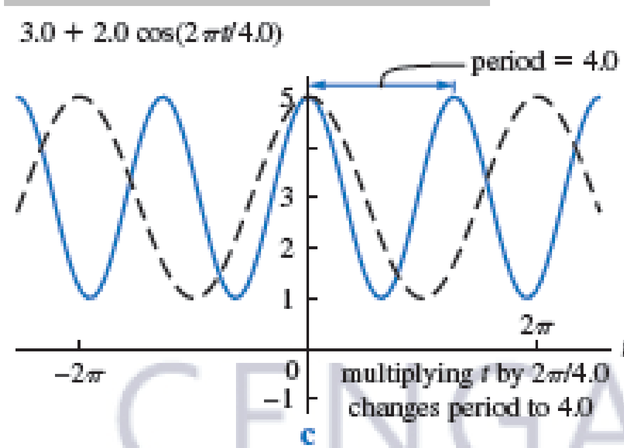
f (t) = 2.0 cos(*t*).



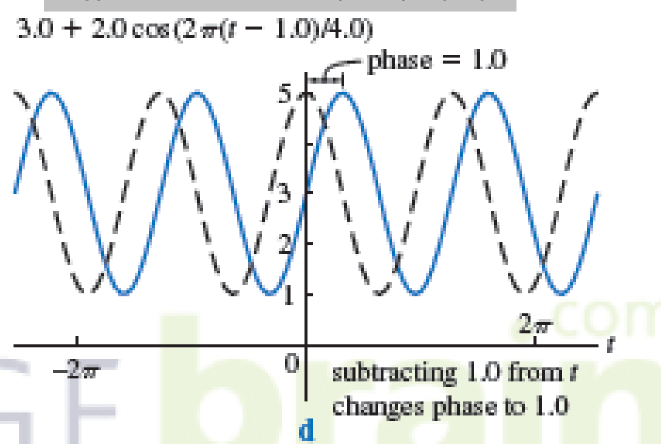
f (t) = 3.0 + 2.0 cos(*t*)



f (t) = 3.0 + 2.0 cos(2π*t/4)



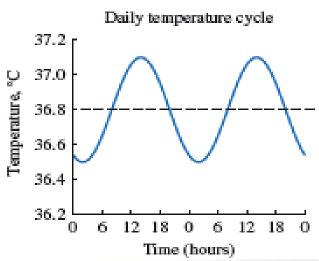
f (t) = 3.0 + 2.0 cos(2π*(t-1)/4)

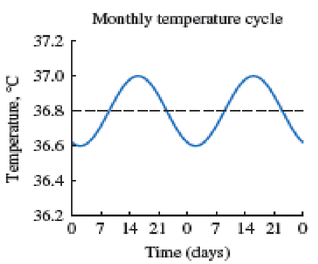


The Daily and Monthly Temperature Cycles

Women have two cycles affecting body temperature: a daily and a monthly rhythm. The key facts about these two cycles are given in the following table:

	Minimum	Maximum	Average	Time of Maximum	Period
Daily cycle	36.5	37.1	36.8	2:00 p.m.	24 hours
Monthly cycle	36.6	37.0	36.8	Day 16	28 days





The amplitude of a cycle is : amplitude = maximum − average.

For the daily cycle, the amplitude is

daily cycle amplitude = 37.1 − 36.8 = 0.3.

For the monthly cycle, the amplitude is

monthly cycle amplitude = 37.0 − 36.8 = 0.2.

$$P_d(t) = 36.8 + 0.3\cos\left(\frac{2\pi}{24}(t-14)\right). \quad P_m(t) = 36.8 + 0.2\cos\left(\frac{2\pi}{28}(t-16)\right).$$

線性及非線性訊號簡介

We now derive a model of two competing bacterial populations that leads naturally to a discrete-time dynamical system that is not linear. Nonlinear dynamical systems may have more than one equilibrium. By comparing the two equilibria, we will catch a glimpse of an important theme, the **stability** of equilibria.

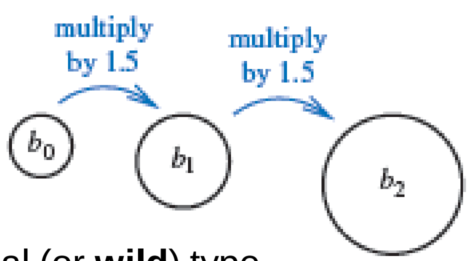
Model of Selection: An invasion by mutant bacteria

If the original (or **wild**) type has a per capita reproduction of 1.5 and the mutant type has a per capita reproduction of 2.0, the two populations will follow the discrete-time dynamical systems

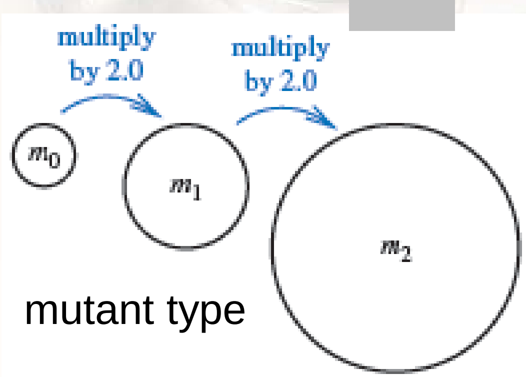
$b_{t+1} = 1.5b_t$ discrete-time dynamical system for wild type

$m_{t+1} = 2.0m_t$ discrete-time dynamical system for mutants.

Selection occurs when the frequency of a gene (the mutation) changes over time.



original (or **wild**) type



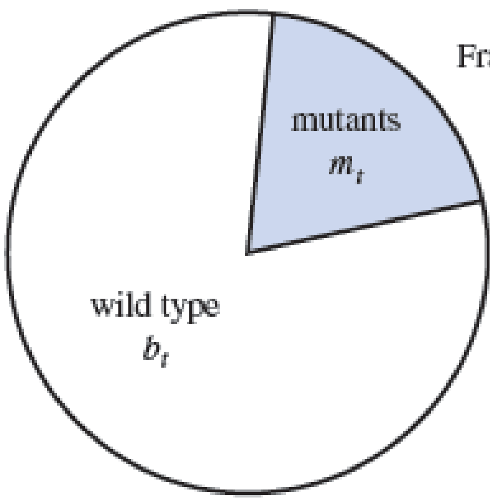
mutant type

$$m_{t+1} = sm_t$$
$$b_{t+1} = rb_t.$$

線性及非線性訊號簡介

A new variable called *pt* was defined to be the fraction of mutants at time *t*. Then

$$p_t = \frac{\text{number of mutants}}{\text{total number}} = \frac{\text{number of mutants}}{\text{number of mutants} + \text{number of wild type}} = \frac{m_t}{m_t + b_t}.$$



$$\text{Fraction of mutants} = p_t = \frac{m_t}{m_t + b_t}$$

$$\text{Fraction of wild type} = 1 - p_t = \frac{b_t}{m_t + b_t}$$

$$p_{t+1} = \frac{m_{t+1}}{m_{t+1} + b_{t+1}} = \frac{sm_t}{sm_t + rb_t} = \frac{s\frac{m_t}{m_t+b_t}}{s\frac{m_t}{m_t+b_t} + r\frac{b_t}{m_t+b_t}} = \frac{sp_t}{sp_t + r(1-p_t)}.$$

線性及非線性訊號簡介

Example Finding the Updated Fraction

If $m_t = 2.0 \times 10^5$ and $b_t = 3.0 \times 10^6$ (Example 1.10.1), the updated populations are

$$m_{t+1} = 2.0m_t = 4.0 \times 10^5$$
$$b_{t+1} = 1.5b_t = 4.5 \times 10^6.$$

The updated fraction of the mutant type, p_{t+1}, is

$$p_{t+1} = \frac{4.0 \times 10^5}{4.0 \times 10^5 + 4.5 \times 10^6} = 0.0816.$$

We can follow these same steps to find the discrete-time dynamical system for p_t. By definition

$$p_{t+1} = \frac{m_{t+1}}{m_{t+1} + b_{t+1}}.$$

Using the discrete-time dynamical systems for the two types (Equation 1.10.1), we find

$$p_{t+1} = \frac{2.0m_t}{2.0m_t + 1.5b_t}.$$

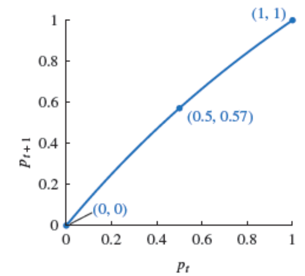
$$p_{t+1} = \frac{2.0\frac{m_t}{m_t+b_t}}{2.0\frac{m_t}{m_t+b_t} + 1.5\frac{b_t}{m_t+b_t}}.$$

$$p_{t+1} = \frac{2.0p_t}{2.0p_t + 1.5(1 - p_t)}.$$

線性及非線性訊號簡介

If p_t = 0.0625, the discrete-time dynamical system tells us that

$$p_{t+1} = \frac{2.0 \cdot 0.0625}{2.0 \cdot 0.0625 + 1.5(1 - 0.0625)} = 0.0816.$$



The discrete-time dynamical system for the fraction is not linear because it involves division. The graph of the function is curved. We plotted it by substituting in representative values for a fraction, which must lie between 0 and 1.

The equilibria of this discrete-time dynamical system are found by solving

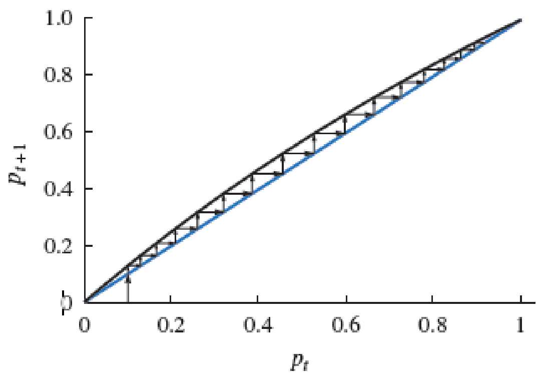
$p^* = \dfrac{2.0p^*}{2.0p^* + 1.5(1 - p^*)}$	the equation for the equilibrium
$p^*(2.0p^* + 1.5(1 - p^*)) = 2.0p^*$	multiply through by denominator
$p^*(2.0p^* + 1.5(1 - p^*)) - 2.0p^* = 0$	move everything to one side
$p^*(2.0p^* + 1.5(1 - p^*) - 2.0) = 0$	factor out p^*
$p^*(2.0p^* + 1.5 - 1.5p^* - 2.0) = 0$	multiply out terms in parentheses
$p^*(0.5p^* - 0.5) = 0$	simplify

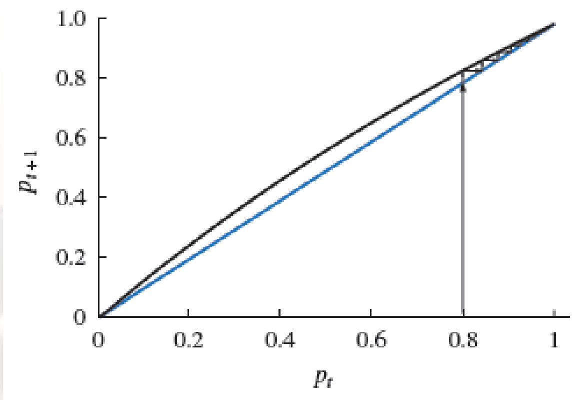
Extinction of the mutant (at $p*$ =0), extinction of the wild type (at $p*$ =1)

Stable and Unstable Equilibria

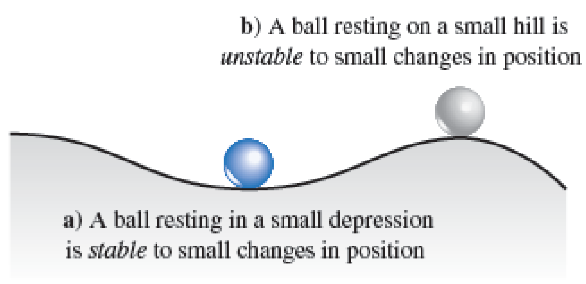
If we started **exactly** at $p_0 = 0$, the solution would remain at *pt* = 0 for all times *t*. Similarly, if we started **exactly** at $p_t = 1$, the solution would remain at *pt* = 1 for all times *t*. The two equilibria behave quite differently, however, if our starting point is nearby. A solution starting **near** $p_0 = 0$ moves steadily **away** from the equilibrium.

A solution starting **near** $p_0 = 1$ moves **toward** the equilibrium.



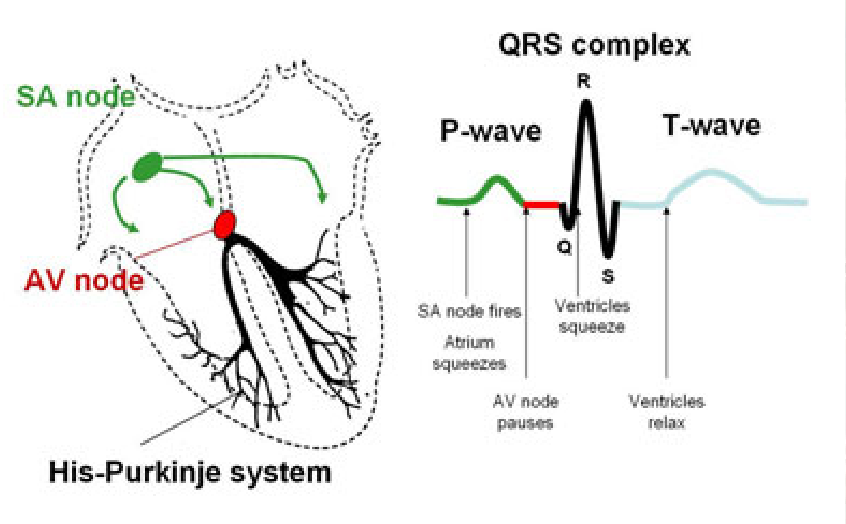


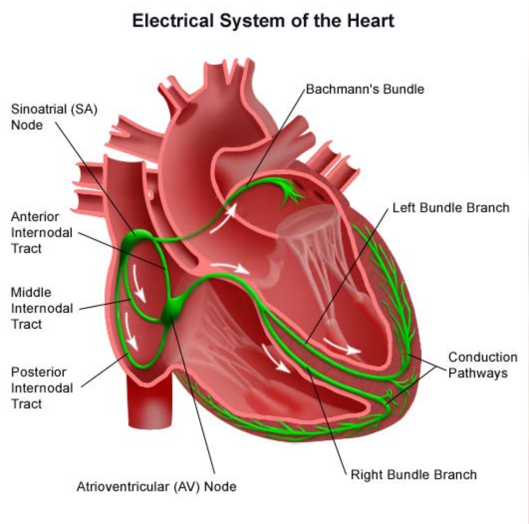
Stable and unstable resting points for a ball



An Excitable Systems: The Heart

- The sinoatrial node (SA node) is the pacemaker, sending regular signals to the atrioventrical node (AV node). The AV node then tells the heart to beat if conditions are suitable.
- Our goal is to understand how simple changes in the parameters of a heart can produce heartbeat patterns called **second-degree block**. With these syndromes, people's hearts either beat half as often as they should or beat normally for a while, skip a beat, and return to beating.





Membrane Potential

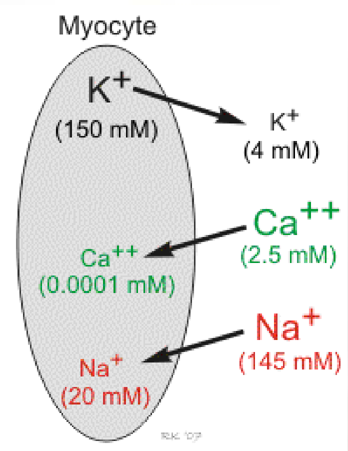
Membrane potentials in cells are determined primarily by three factors:

1) the concentration of ions on the inside and outside of the cell;
2) the permeability of the cell membrane to those ions through specific ion channels;
3) by the activity of electrogenic pumps (e.g. $Na^{\pm}$ /$K^{\pm}$ –ATPase and $Ca^{\pm\pm}$ transport pumps) that maintain the ion concentrations across the membrane.

Equilibrium potential for K^+ (E_K; **Nernst potential**)

$$E_K = \frac{-61}{z} \log \frac{[K^+]_i}{[K^+]_o} = -96 \text{ mV}$$

(where $[K^+]_i$ = 150 mM and $[K^+]_o$ = 4 mM; and z=1 because K^+ is monovalent)



Equilibrium potential for Na^+(E_{Na})

$$E_{Na} = \frac{-61}{z} \log \frac{[Na^+]_i}{[Na^+]_o} = +52 \text{ mV}$$

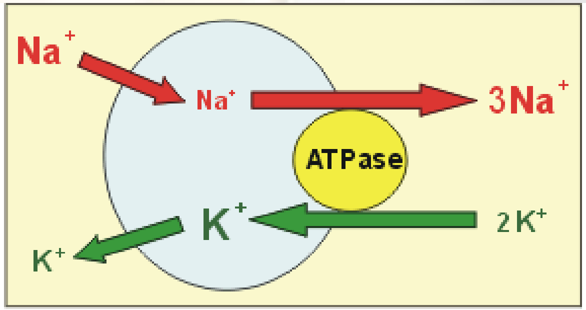
(where $[Na^+]_i$ = 20 mM and $[Na^+]_o$ = 145 mM; and z=1 because Na^+ is monvalent)

Equilibrium potential for Ca^{++} (E_{Ca})

$$E_{Ca} = \frac{-61}{z} \log \frac{[Ca^{++}]_i}{[Ca^{++}]_o} = +134 \text{ mV}$$

Membrane Potential

- To maintain the concentration gradients for Na^+ and K^+, it is necessary to transport Na^+ out of the cell and K^+ back into the cell. There is located on the sarcolemma an energy dependent (ATP-dependent) pump system **Na^+/K^+-ATPase**) that that performs this function.
- Pump is electrogenic in nature because it extrudes 3 Na^+ for every 2 K^+ entering the cell.
- Inhibition of this pump, therefore, causes depolarization resulting not only from changes in Na^+ and K^+ concentration gradients, but also from the loss of an electrogenic component of the membrane potential.
- By pumping more positive changes out of the cell than into the cell, the pump activity creates a negative potential within the cell.
- Small increases in external K^+ can stimulate the pump activity and thereby cause hyperpolarization.



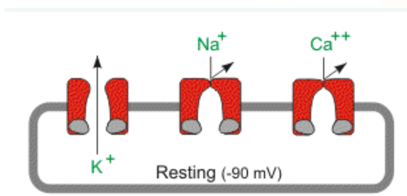
生醫訊號臨床應用簡介

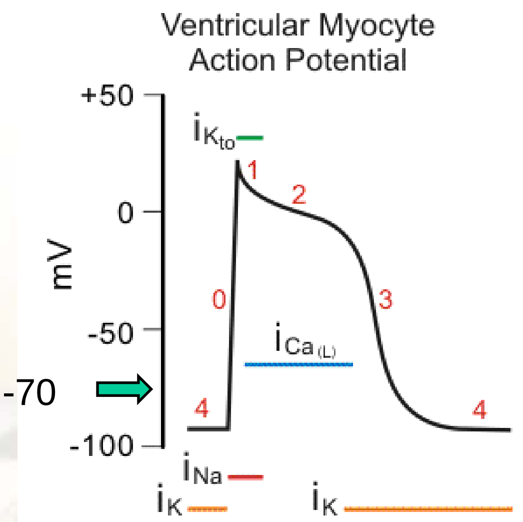
Action Potentials

Many cells in the body have the ability to undergo a transient repolarization and depolarization that is either triggered by external mechanisms.

Resting membrane potential (phase 4, about -90 mV)

Positive potassium ions are leaving the cell and making the membrane potential more negative inside. At the same time, fast sodium channel and slow calcium channels are closed.



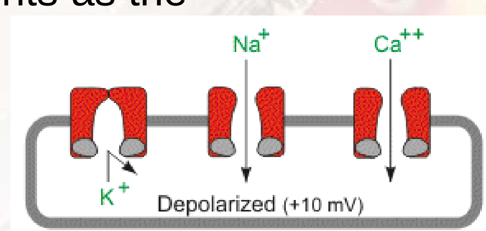


threshold voltage -70

http://www.cvphysiology.com/Arrhythmias/A010.htm

When depolarized to a **threshold voltage** (phase 0,+10mV)

Caused by a transient increase in fast Na^+ currents (I_{Na}), due to the opening of sodium channels, and concomitant outward directed K^+ currents as the potassium channel closed.



Action Potentials

Repolarization (phase 1)

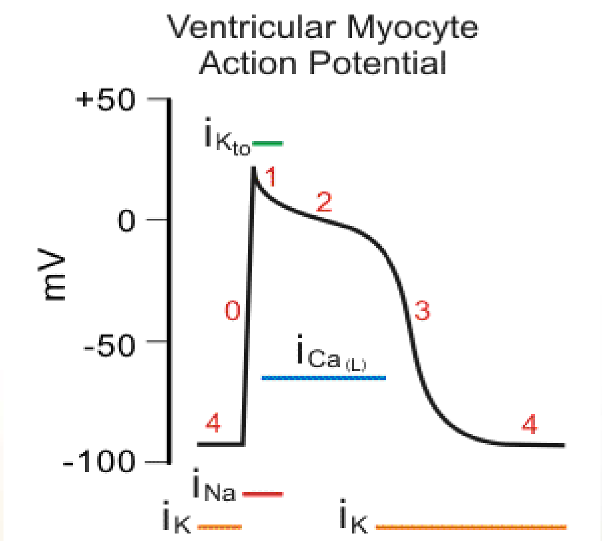
represents an initial repolarization that is caused by the opening of a special type of transient outward K^+ channel (K_{to}), which causes a short-lived, hyperpolarizing outward K^+ current (I_{Kto}).

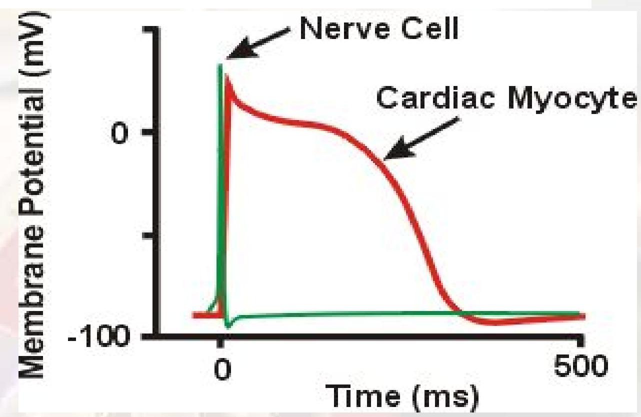
Repolarization (phase 2)

Large increase in slow inward gCa^{++} occurring at the same time and the transient nature of I_{Kto}, the repolarization is delayed and there is a plateau phase in the action potential.

Repolarization (phase 3)

Occurs when gK^+ (and therefore I_K) increases, along with the inactivation of Ca^{++} channels (decreased gCa^{++}).

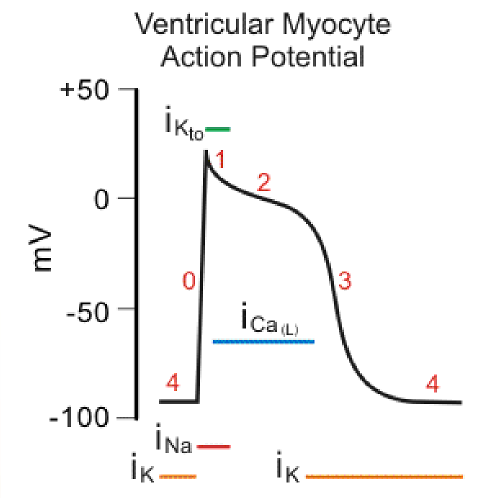


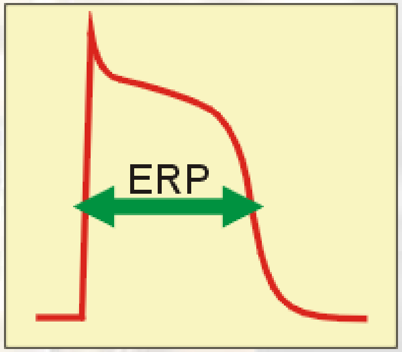


Effective Refractory Period

- Once an action potential is initiated, there is a period of time comprising **phases 0, 1, 2, and part of phase 3** that a new action potential cannot be initiated. This is termed the **effective refractory period** (ERP) or the **absolute refractory period** (ARP) of the cell.

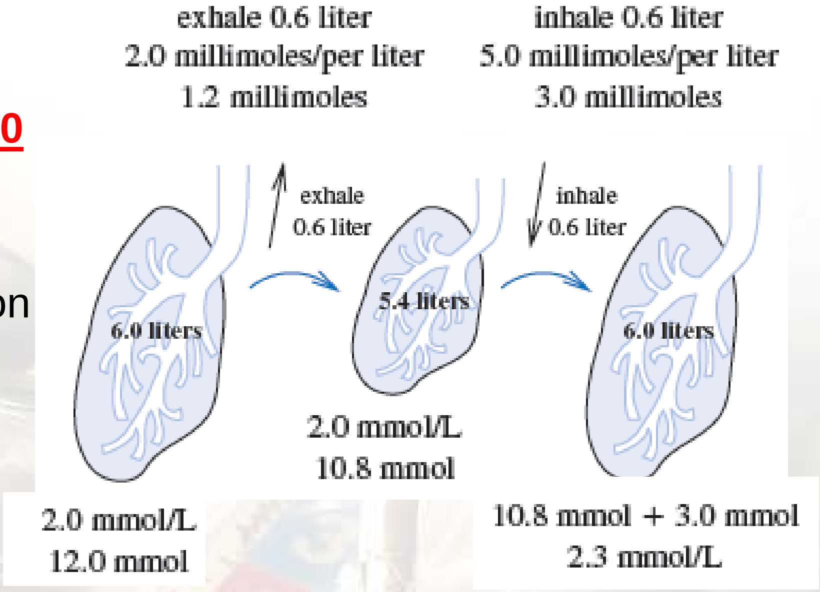
- During the ERP, stimulation of the cell by an adjacent cell undergoing depolarization does not produce new, propagated action potentials. The ERP acts as a **protective mechanism** in the heart by preventing multiple, compounded action potentials from occurring (i.e., it limits the frequency of depolarization and therefore heart rate).





A Model of Gas Exchange in the Lung

- An adult male lung has a volume of about **6.0 L** when full. With each breath, **0.6 L** of the air in the lungs are exhaled, and replaced by 0.6 L of outside (or **ambient**) air.
- Suppose further that the lung contains a particular chemical with a concentrationof **2.0 mmol/L** before exhaling that the lungs contain.
- The ambient air has a chemical concentration of **5.0 mmol/L**. What is the chemical concentration after one breath?



$$\text{concentration} = \frac{\text{total amount}}{\text{volume}}.$$

(A millimole is 6.02×10^{20} molecules)

total amount = concentration X volume.

Assumption: Neither air nor chemical is produced or used while breathing.

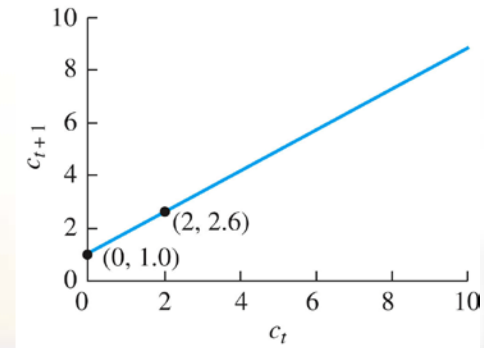
生醫訊號臨床應用簡介

Breathing creates a discrete-time dynamical system. The original concentration of 2.0 mmol/L is updated to 2.3 mmol/L after a breath.

Step	Volume (L)	Total Chemical (mmol)	Concentration (mmol/L)	What We Did
Air in lungs before breath	6.0	$6.0c_t$	c_t	Multiplied volume of lungs (6.0) by concentration (c_t) to get $6.0c_t$.
Air exhaled	0.6	$0.6c_t$	c_t	Multiplied volume exhaled (0.6) by concentration (c_t) to get $0.6c_t$.
Air in lungs after exhalation	5.4	$5.4c_t$	c_t	Multiplied volume remaining (5.4) by concentration (c_t) to get $5.4c_t$.
Air inhaled	0.6	3.0	5.0	Multiplied volume inhaled (0.6) by ambient concentration (5.0) to get 7.5.
Air in lungs after breath	6.0	$3.0 + 5.4c_t$	$0.5 + 0.9c_t$	Added inhaled chemical (3.0) to remaining chemical ($+5.4c_t$) and divided by volume (6.0) to get $0.5 + 0.9c_t$.

Discrete-time dynamical system

$$c_{t+1} = 0.5 + 0.9c_t \, .$$



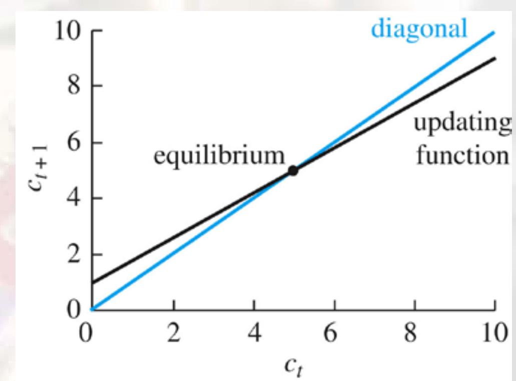
The solutions of the updating equation are equilibria.

$$c^* = 0.5 + 0.9c^* \quad \text{the original equation}$$

$$c^* - 0.9c^* = 0.5 \quad \text{subtract } 0.9c^* \text{ to get unknowns on one side}$$

$$0.1c^* = 0.5 \quad \text{do the subtraction}$$

$$c^* = \frac{0.5}{0.1} = 5.0. \quad \text{divide by 0.1}$$



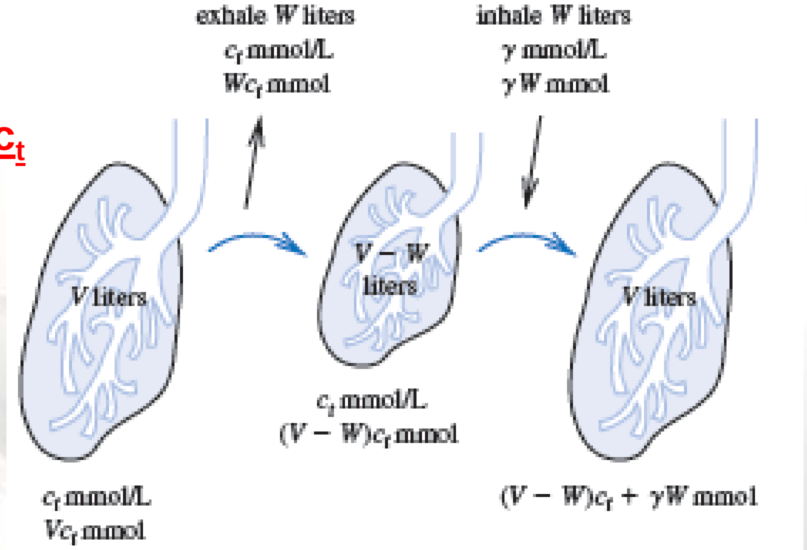
The equilibrium value is 5.0 mmol/L.

$$c_{t+1} = 0.5 + 0.9 \text{ x} 5.0 = 5.0 = c_t$$

生醫訊號臨床應用簡介

A "General" Model of Gas Exchange in the Lung

- An adult male lung has a volume of about **V** liter when full. With each breath, **W** liter of the air in the lungs are exhaled, and replaced by , **W** liter of outside (or **ambient**) air.
- Suppose further that the lung contains a particular chemical with a concentration of **c_t mmol/L** before exhaling that the lungs contain.
- The ambient concentration of chemical is γ **mmol/L** ("gamma").



Discrete-time dynamical system

$$c_{t+1} = \frac{c_t(V-W)+\gamma W}{V} = \frac{c_t V - c_t W + \gamma W}{V} = c_t - c_t\frac{W}{V} + \gamma\frac{W}{V}.$$

$$q = \frac{W}{V} = \text{fraction of air exchanged}$$

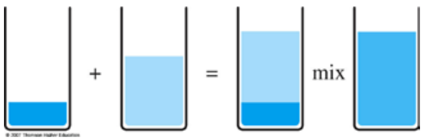
General lung discrete-time dynamical system

$$c_{t+1} = (1-q)c_t + q\gamma.$$

The term c_{t+1} is a **weighted average** of the old concentration c_t and the ambient concentration γ .

生醫訊號臨床應用簡介

Definition A weighted average of two values *x* and *y* is a sum of the form $qx + (1 - q)\,y$ for some value of *q* between 0 and 1.



Suppose 1.0 L of liquid with a concentration of 10.0 mmol/L of salt are mixed with 3.0 L of liquid with a concentration of 5.0 mmol/L of salt. What is the concentration of the resulting mixture?

$$0.25 \times 10.0 \text{ mmol/L} + 0.75 \times 5.0 \text{ mmol/L} = 6.25 \text{ mmol/L}.$$

Suppose 1.0 L of liquid with a concentration of 10.0 mmol/L of salt are mixed with 3.0 L of liquid with a concentration of 5.0 mmol/L of salt and 1.0 L of liquid with a concentration of 2.0 mmol/L of salt. What is the concentration of the resulting mixture?

$$0.20 \times 10.0 \text{ mmol/L} + 0.60 \times 5.0 \text{ mmol/L} + 0.20 \times 2.0 \text{ mmol/L} = 5.4 \text{ mmol/L}.$$

(1L/5L) (3L/5L) (1L/5L)

A "Absorption" Model of Gas Exchange in the Lung

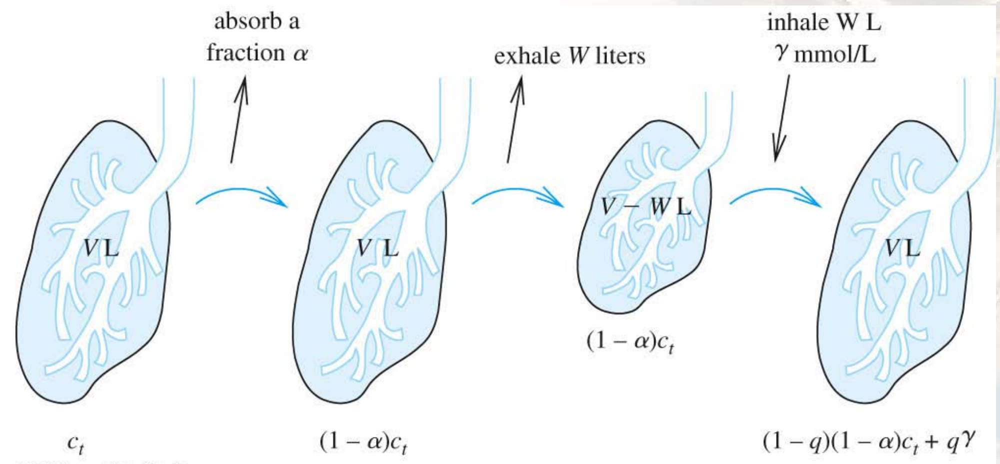
- An adult male lung has a volume of about **V** liter when full. With each breath, **W** liter of the air in the lungs are exhaled, and replaced by , **W** liter of outside (or **ambient**) air.

- Suppose further that the lung contains a particular chemical with a concentration of c_t **mmol/L** before exhaling that the lungs contain.
- The ambient concentration of chemical is γ **mmol/L** ("gamma").

- Suppose that a fraction q of air is exchanged each breath, and that a fraction α of chemical is absorbed

Lung discrete-time dynamical system

$$c_{t+1} = (1 - q)(1 - \alpha)c_t + q\gamma.$$



$$q = \frac{W}{V} = \text{fraction of air exchanged}$$

Example: Absorption of Oxygen by the Lung

Consider again a lungs that has a volume of 6.0 L(V) and that replaces 0.6 L(W) each breath with ambient air (q = 0.6/6). Suppose that we are tracking oxygen, with an ambient concentration of 21% (γ), and assume that 30% (α) of the oxygen in the lungs is absorbed each breath.

The discrete-time dynamical system is then

$$c_{t+1} = 0.9 \times 0.7c_t + 0.1 \times 0.21 = 0.63c_t + 0.021.$$

The equilibrium concentration in the lungs then becomes

$$\begin{aligned} c^* &= 0.63c^* + 0.021 \\ 0.37c^* &= 0.021 \\ c^* &= 0.057. \end{aligned}$$

The equilibrium concentration of oxygen in the lungs, which is equal to the concentration of oxygen in the air breathed out, would be about 5.7%, or roughly one fourth of the ambient concentration.

$$\begin{aligned} c^* &= (1-q)(1-\alpha)c^* + q\gamma \\ c^* - (1-q)(1-\alpha)c^* &= q\gamma \\ c^*(1-(1-q)(1-\alpha)) &= q\gamma \\ c^* &= \frac{q\gamma}{1-(1-q)(1-\alpha)}. \end{aligned}$$

Total absorbed per breath = $\alpha c{*}V$