Medical Physiology

Introduction and Control Theory

Prof. Gyula Sáry

Exam results, final, 2019/20 spring semester

<table>
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<th>signed up</th>
<th>(%)</th>
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<th>(%)</th>
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<th>(%)</th>
<th>passed</th>
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Lecturers

- dr. Antal Barényi
- dr. Ferenc Domoki
- dr. Mária Dux
- dr. Szabolcs Kéri
- dr. Attila Nagy
- dr. Péter Sántha
- dr. Gyula Sáry
- head of the department

Medical Physiology

- The subject
- What to expect
- Feed back
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Teaching Medical Physiology

The key: harmonisation

Learning outcomes: what we want our students to learn?

The „Learning Objectives“

Teaching and learning activities: what types of activities will help your students to learn:

- lectures (class),
- seminars (study groups),
- practicals (study groups),
- evening seminars (class)

Assessment methods: how will you know your students have learned?

- weekly seminars
- practicals
- MTOs
- end semester exam
- final exam

Lectures
Seminars (obligatory)
Practical sessions (obligatory)
Evening seminars (suggested)
Requirements on home page
What to learn and where from?
(Learning Objectives)

The Department of Physiology welcomes you

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Information to medical students
2015/2016

Schedule of the lectures
Lecture notes
Exams
Requirements in Physiology
Laboratory practical manuals 1st-4th semesters
Laboratory practical schedule 1st-4th semesters
Topics for the laboratory exams
Topics for the final exam
Useful links for students

Phenols related to the physiology course may be addressed to:
The Topic List

1. Principles of control theory.
2. Passive transport mechanisms of the cell membrane.
3. Active transport mechanisms of the cell membrane.
4. The resting membrane potential.
5. The electric properties of neuronal membranes.
7. Receptors, signal transduction mechanisms.
9. The peripheral nervous system: primary sensory neurons.
10. The parasympathetic division of the autonomic nervous system.
11. The sympathetic division of the autonomic nervous system. The adrenal medulla.
12. The peripheral nervous system: motor neurons, neuromuscular junction.
13. Skeletal muscle: structure, electromechanical coupling, the biochemistry of contraction.
15. Smooth muscle physiology.
16. ……………………………
17. ……………………………

The Learning Objectives

1. Principles of control theory
   Define the term of internal environment (milieu intérieur) and explain the importance of its control. Define the terms homeostasis and homeostatic parameters. List at least 5 controlled functions and/or parameters in human.
   Distinguish between guidance and control.
   Describe the major forms of physiological controlling circuits (humoral, neuronal).
   Describe the parts of the neuronal reflex arch and explain their respective functions in control (receptor, afferent branch/pathway, center, set point, efferent branch/pathway, effector).
   Define negative and positive feedback control. Give examples for processes controlled by negative feedback, positive feedback. Explain feed-forward control.
   Characterize endocrine, paracrine and autocrine humoral control based on the release site of the mediators and their path to the target cells.
   Define “behavioural control” and explain its importance/necessity. Give examples!
   How can the efficiency of control systems be expressed quantitatively?
   Define the term servo-control mechanism.

2. Passive transport mechanisms of the cell membrane
   Describe and make a schematic drawing of the molecular structure of the plasma membrane (fluid mosaic model). Explain how the distribution of phospholipids and proteins influences the membrane permeability of ions, hydrophylic and hydrophobic compounds. Describe lateral diffusion in the membrane.
   Contrast the following units used to describe concentration: mH, mEq/l, mmol/kgH2O.
   Define simple diffusion and explain how changes in the driving forces (chemical and electrical gradient, in steady state situation) and membrane properties will influence the transport rate. State Fick’s law of diffusion.
   Describe the role of water channels (aquaporins) in the water permeability of the cell membrane.
   Define: osmosis, osmotic, osmolality, osmolarity and tonicity, and reflection coefficient. Explain how the different permeability of the cell membrane to water and solutes will generate an osmotic pressure.
   Characterize facilitated diffusion. Define the types of the carriers: (uniporter, symporter,antiporter). Define the terms: transport maximum, saturation, competitive and non-competitive inhibition.

3. Active transport mechanisms of the cell membrane
   Define the terms primary and secondary active transport. Define the terms: transport maximum, saturation, competitive and non-competitive inhibition.
   Describe how energy from ATP hydrolysis is used to transport ions such as Na+, K+, Ca2+ and H+ against their electrochemical differences via examples.
   Explain how energy from the Na+ and K+ electrochemical gradients across the plasma membrane can be used to drive the net uphill (against gradient) movement of other solutes (e.g., Na+/H+ exchange transport; Na+/Ca2+ exchange).
**Topics and Learning Objectives**

### 1. Principles of control theory

- Define the term of internal environment (milieu interieur) and explain the importance of its control.
- Define the terms homeostasis and homeostatic parameters. List at least 5 controlled functions and/or parameters in human.
- Distinguish between guidance and control.
- Describe the major forms of physiological controlling circuits (humoral, neuronal).
- Describe the parts of the neuronal reflex arch and explain their respective functions in control (receptor, afferent branch/pathway, center, set point, efferent branch/pathway, effector).
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- Define "behavioural control" and explain its importance/necessity. Give examples!
- How can the efficiency of control systems be expressed quantitatively?
- Define the term: servo-control mechanism.

**Normal values (if relevant)**

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**Principles of Control Theory**

**Learning objectives # 1.**
Living cells and the environment: “an open system”

- stimulus
  - heat
  - chemical
  - mechanical
  - etc.

- response
  - movement
  - change in shape
  - metabolic change
  - etc.

Survival depends on the extracellular parameters!

One cell vs. multicellular organism

- Please tell us:
  - what is happening
  - ...and what shall we do?

Total body water:
- 60% of the body mass
- intracellular: 40% of body mass
- extracellular: 20% of body mass

nervous system
- circulation (hormones)

Laboratory values refer to the extracellular fluid!
Extracellular fluid: the internal environment

Laboratory values refer to the extracellular fluid!
Extracellular fluid: the internal environment

- metabolism
- waste products
- gases $O_2$, $CO_2$
- heat exchange

Laboratory values refer to the extracellular fluid!

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The internal environment - *milieu intérieur*

"The fixity of the *milieu* supposes a perfection of the organism such that the external variations are at each instant compensated for and equilibrated. All of the vital mechanisms, however varied they may be, have always one goal, to maintain the uniformity of the conditions of life in the internal environment. The stability of the internal environment is the condition for the free and independent life."

*Claude Bernard*
<table>
<thead>
<tr>
<th>Constituent</th>
<th>Normal Value</th>
<th>Normal Range</th>
<th>Approximate Short-Term Nonlethal Limit</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen (venous)</td>
<td>40</td>
<td>25–40</td>
<td>10–1000</td>
<td>mm Hg</td>
</tr>
<tr>
<td>Carbon dioxide (venous)</td>
<td>45</td>
<td>41–51</td>
<td>5–80</td>
<td>mm Hg</td>
</tr>
<tr>
<td>Sodium ion</td>
<td>142</td>
<td>135–145</td>
<td>115–175</td>
<td>mmol/L</td>
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<tr>
<td>Potassium ion</td>
<td>4.2</td>
<td>3.5–5.3</td>
<td>1.5–9.0</td>
<td>mmol/L</td>
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<tr>
<td>Calcium ion</td>
<td>1.2</td>
<td>1.0–1.4</td>
<td>0.5–2.0</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Chloride ion</td>
<td>106</td>
<td>98–108</td>
<td>70–130</td>
<td>mmol/L</td>
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<tr>
<td>Bicarbonate ion</td>
<td>24</td>
<td>22–29</td>
<td>8–45</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>90</td>
<td>70–115</td>
<td>20–1500</td>
<td>mg/dl</td>
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<tr>
<td>Body temperature</td>
<td>98.6 (37.0)</td>
<td>98–98.8 (37.0)</td>
<td>65–110 (18.3–43.3)</td>
<td>°F (°C)</td>
</tr>
<tr>
<td>Acid–base (venous)</td>
<td>7.4</td>
<td>7.3–7.9</td>
<td>6.9–8.0</td>
<td>pH</td>
</tr>
</tbody>
</table>

**Homeostasis, homeostatic parameters**

From Greek: homoios + stasis

Is the **property of a system** that regulates its internal environment and tends to maintain a stable, relatively constant condition of parameters.

It is a **process in a system** to maintain nearly constant conditions of the internal environment.

- body temperature
- body weight
- pH
- blood sugar level
- Na⁺, K⁺, Ca²⁺, Cl⁻ concentrations
- blood pressure
- etc.

Origin of nutrients
- respiratory system
- gastrointestinal tract
- liver & others with metabolic functions
- skeletonmotor system

Removal of vaste
- respiratory system
- kidneys

Laboratory values refer to the **extracellular fluid!**
Some of the Controlled Body Functions

sexuality, reproduction
feelings, experiences, behaviour
motor functions
perception
somatosensory system, thermoregulation
respiration
renal functions
excretion
feeding
digestion
excretion

(a) open
(b) feedforward
(c) feedback
**Open-Loop Control Systems**
use a mechanism (effector) to get the desired response.

**Closed-Loop Control Systems**
uses measured parameters as a feedback to compare the actual output to the desired output response.

**Multivariable Control System**

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**Guidance and control**

- **regulation**
  - guidance
    - center
      - command
        - system
    - control
      - compares
        - center set point
          - feedback
        - modifies to balance error
      - system
        - external (disturbing) stimulus
Guidance vs. control

- Open system
- No feedback
- No acting back
- Only predicted errors can be controlled
- Stable
- Have to know all factors to operate properly

- Closed system
- Feedback
- Acting back
- (Most) unforeseen errors can be controlled
- Can be a bit unstable
- No need for knowing all the factors to operate properly

A control circuit

- Setting value
- Disturbing signal
- Actual value
- Controlled parameter
- Sensor
- Controlling center
- Effector system
- Controlling value
- "Set point"
Two main types of control circuits

Nervous: very fast, short latency, well localized

Humoral: slower, longer latency time, more diffuse

...and their combination
The Neuronal Controlling Circuit (reflex)

- Center
- Afferent branch
- Efferent branch
- Receptor
- Effector (glands, vessels, muscle)
- Controlled parameter

Humoral Controlling Circuit I.
Humoral Controlling Circuit II.

hypothalamus
+ → anterior pituitary
+ → target gland
+ → hormone

inhibits

Humoral Communication

endocrine
macrophag
Interleukin 1

paracrine
T-helper
Interleukin 4
B-cell

neurotransmitter
T-helper
Interleukin 3

endocrine system
Hormone

immune system
Cytokine

nervous system
Neurotransmitter
A Mixed Control Circuit

Oxytocin reflex (Ferguson reflex)

- Works before or during feed to make milk flow

Feed Forward, Positive and Negative Feedback

Feed forward: acts only forward, not controlled by errors (heart, saliva secretion, some muscle movements)

Negative feedback: most abundant, keeps the variable around “set point” or in the reference range

Positive feedback: rare, may run into circulus vitiosus if not interrupted eg.:
- blood clotting
- voltage dependent Na+ channels
- activating of trypsin in the duodenum
- child birth
Example For Negative Feedback

- In response to the lower concentration of glucose, the pancreas stops secreting insulin.
- Food is consumed and digested, causing blood level glucose to rise.
- In response to higher glucose levels, the pancreas secretes insulin into the blood.
- In response to higher insulin levels, glucose is transported into cells and liver cells store glucose as glycogen. As a result, glucose levels drop.

Example For Positive Feedback I.

- The baby pushes against the cervix, causing it to stretch.
- Stretching of the cervix causes nerve impulses to be sent to the brain.
- The brain stimulates the pituitary to release oxytocin.
- Oxytocin causes the uterus to contract.
Example For Positive Feedback II.

Example For Negative Feedback: when it works

gastrin

- somatostatin

+ gastric acid (pH lower)
Example For Negative Feedback: when it does not work

The Zollinger-Ellison syndrome

- uncontrolled gastrin secretion (tumor) \( \ldots \) \( HCl \)
- large volume of pancreatic juice...fluid loss into the gut
- \( pH \) in the duodenum \( \ldots \) pancreatic enzymes fail to work
- malabsorption, malabsorption
- osmotic activity \( \ldots \) diarrhoea
- lipids (too) are not digested (fat soluble vitamins !!!)
- bacterial breakdown of carbohydrates in the colon...gases
- due to low \( pH \), \( B_{12} \) and intrinsic factor do not bind
- multiple ulcers
- hypertrophy of the gastric mucosa

Behavioural Control

Definition of the control range

Making the range wider: effector mechanisms + behaviour

but! fat and salt consumption
Temporal Dynamics of a Control Circuit

The Effectivity of Control Systems (Gain)

\[ \text{gain} = \frac{\text{correction}}{\text{residual error}} \]
Calculating \textit{gain}

intravenous fluid: 100 Hgmm $\rightarrow$ 175 Hgmm
correction: 50 Hgmm (125 Hgmm), error: 25 Hgmm
\textit{gain}: $\frac{50\,\text{Hgmm}}{25\,\text{Hgmm}} = 2$

by temperature control \textit{gain} $\sim 33!$

Servo Mechanisms

Normal case:
\textit{the disturbing signal pushes the system out of balance} $\rightarrow$
$\rightarrow$ the control system gets activated

Servo mechanisms:
\textit{the set point value changes} $\rightarrow$
$\rightarrow$ the control system gets activated

e.g.: hyperthermia vs. fever
Negative and Positive Feedback

- "set point" (reference range)
- "actual" value

stable

strong disturbing signal

servo mechanism

positive feedback
Example For Negative Feedback

The blood glucose and insulin levels for a healthy person.