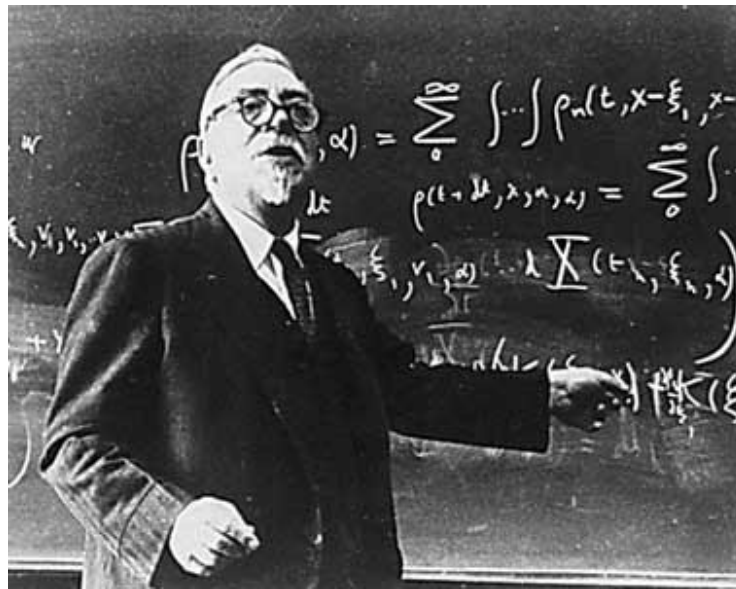


Lectures on Medical Biophysics

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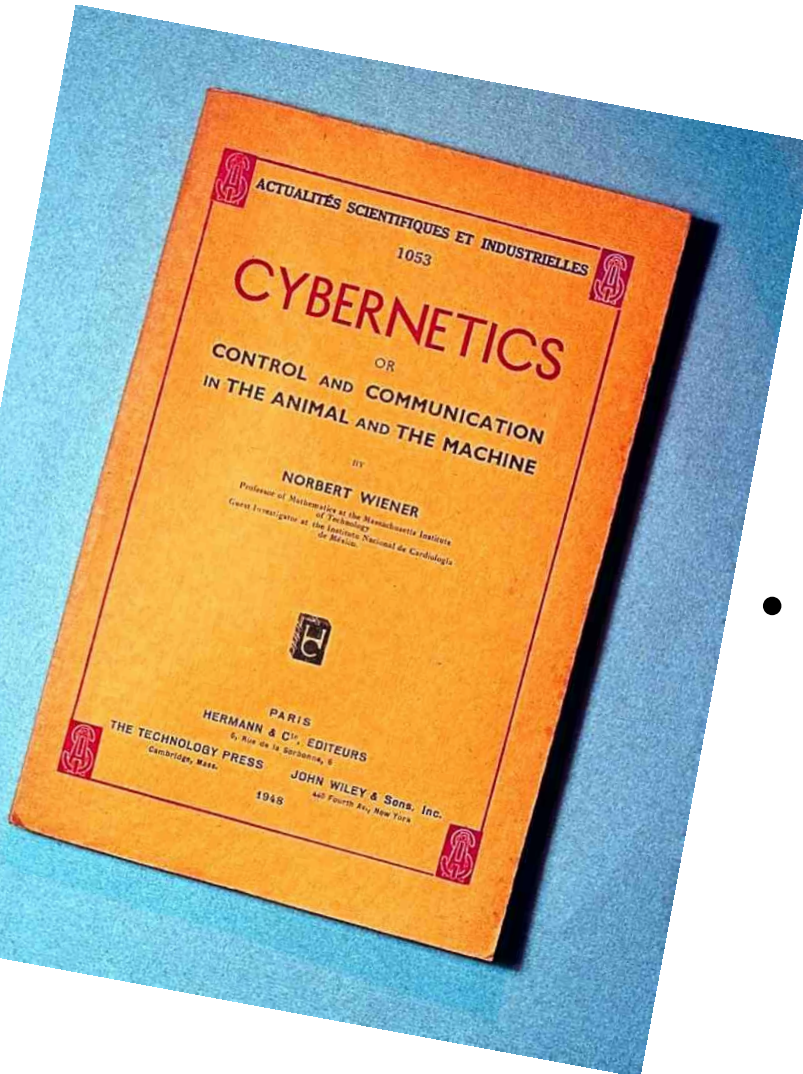
Norbert Wiener 26.11.1894 - 18.03.1964

Biocybernetics

Lecture outline

- Cybernetics
- Cybernetic systems
- Feedback
- Principles of information theory
- Information system
- Information processes in living organism
- Control and regulation
- Principles of modelling

Norbert Wiener



- ***N. Wiener: (1948)***

Definitions

- Cybernetics is the science dealing with general features and laws regulating information flow, information processing and control processes in organised systems (technical, biological or social character).
- System - a set of elements, between which certain relations exist
- Modelling – the main method in cybernetics:
 - Simplified expression of objective reality.
 - It should be understood as a set of relations between elements
 - Choice of model must reflect the specific goal
 - For an accurate modelling of a system, it is necessary to know its structure and function
- **Applied cybernetics** involves the modelling of systems in specific regions of human activity, e.g. technical cybernetics, biocybernetics and social cybernetics. These models can be:
 - **Mathematical** - mathematical modelling of systems
 - **Experimental** - building actual miniature models or computer based models (simulation)

Cybernetics and informatics

The cybernetics can be assumed a broad theoretical background of informatics and some other branches of science or knowledge (economy, management, sociology etc.)

Biomedical Cybernetics

- Main goal: analysis and modelling of regulatory and control systems of living organisms under physiological and pathological conditions (pathological processes are seen as a distortion of the normal regulatory mechanisms present in the organism)
- Medical cybernetics also involves:
 - Support of medical decisions in diagnostics and therapy planning
 - Healthcare management = healthcare cybernetics

Living Systems Are Cybernetic Systems

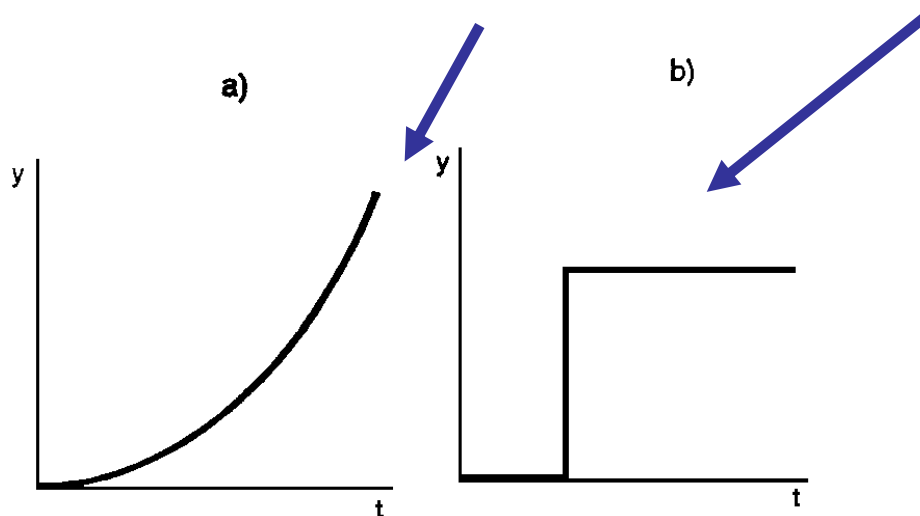
- Fundamental property of living systems: multiple interaction with surroundings
- ambient variables which act on the system = **input**
- variables by which the system acts on surroundings = **output**
- Input variables for describing the system must be chosen to be *independent*.
- The output ones depend on the input variables and the inner parameters of the given system.
- Example: the ear

Analysis and synthesis of a system

- **System analysis** - we know structure - we have to determine its behaviour
- **System synthesis** - the structure is to be determined - behaviour is known
- *Black box* - system of unknown structure and behaviour. **Identification of the system** is done on the basis of relations between input and output data.

Transfer Function

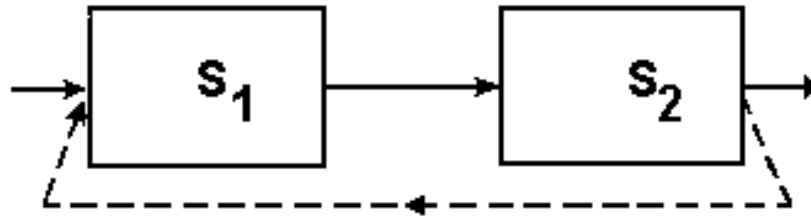
- **TRANSFER function - Dependence of the values of an output parameter on values of an input parameter**
- **We can distinguish:**
 - **linear systems (straight line, an ideal case)**
 - **non-linear**
- **linearization of a non-linear system - an approximation by a straight line**
- **Time-course of the output parameter change determines the behaviour of the system - continuous or discontinuous**



Transfer Function

- Basic forms of transfer:
 - Amplification or attenuation of the input parameters
 - Their time-delay
 - Performing simple logic operations
 - Selective permeability
 - Generation of specific time-courses etc. (also deformation of input parameters)
- All these forms are encountered in biological systems
- The transfer function need not to be constant. Dynamic systems are capable of adaptation and learning.

Feedback



- **Feedback:** changes in a system output parameter leads to changes an input parameter of the same system
- In **positive feedback** an increase / decrease of the output parameter from its normal value leads to an increase / decrease in the input parameter - the change of the input parameter in this way increases in an uncontrolled manner - positive feedback is therefore unsuitable for controlling dynamic systems.
- In **negative feedback** an increase / decrease of the output parameter from its normal value leads to a decrease / increase (i.e., vice-versa) in the input parameter - the change of the input parameter is in this way minimised hence allowing regulation. Homeostasis in the body is based on negative feedback.

Principles of information theory

Stochastic (accidental) event

- Information: any statement about events and processes inside the system and in its surrounding. Information expresses a relation between systems and/or elements of a system.
- Stochastic (accidental) event: an event which can or need not occur under given conditions
- Frequency (rate) of the event occurrence F_A :

$$F_A = n/N$$

- n - number of the events occurred
- N - total number of „experiments“

Probability and information entropy

- **Probability** $P(A)$ - mean value of the event frequency
- Probability values can vary from 1 to 0 ($1 > P(A) > 0$)
- Impossible and regular (unavoidable) event
- *Let's have an experiment which outcomes can reach values $A_1...A_n$ of equal probability $P(A)$:*
- The degree of uncertainty (given by the number of individual uncertainties) grows with increasing n . It is denoted as **information entropy**.
- Let's have n mutually excluding events with $P(A_1), P(A_2)...P(A_n)$. **Uncertainty degree** N_i of one possible outcome is:

$$N_i = -P(A_i)\log_2 P(A_i)$$

- Information entropy of the whole experiment: (the sum of individual uncertainties)

$$H = \sum -P(A_i)\log_2 P(A_i)$$

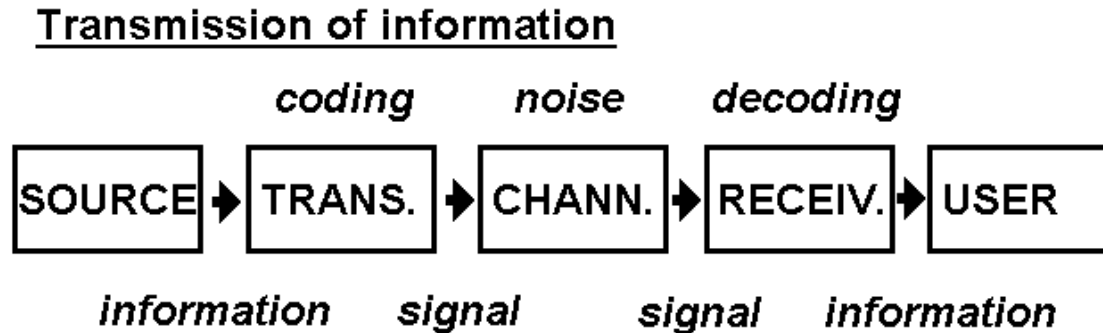
Probability and information entropy

- Intuition: the uncertainty can be removed by the delivery of respective amount of information
- Therefore, the last term is also a quantitative expression of the amount (capacity) of information.
- Information increases the system ordering.
- $P(A)$ large = small amount of information
- *An experiment gives two alternative outcomes of the same $P(A) = 0.5 \Rightarrow$*
- $H = - (0.5\log_2 0.5 + 0.5\log_2 0.5) = 1$
- 1 bit (*binary digit*)

Information system

- Five parts:
 - information source
 - transmitter (coding)
 - information channel (noise)
 - receiver (decoding)
 - user
- **Signal** = the substance or energy carrier of the information
- **Information channel** = medium in which the signal propagates
- **Symbols** = dimensionless parameters qualitatively representing the given event
- **Position** - spatial and temporal arrangement of symbols due to coding process
- The elementary signal carries 1 bit-information
- Max. amount of information which can be delivered by the information channel in unit time = **capacity of the information channel**

Redundancy



- **Noise** = influences reducing original amount of information transmitted
- Excess information (redundant information) can be used to reduce the effects of noise
- **Redundancy** R is given by the formula: $R = 1 - H/H_{MAX}$, where H is the really transmitted amount of information and H_{MAX} is capacity of the information channel.
- Language redundancy is relatively high (about 70 %), in scientific writings - relatively low

Information processes in living organism

- The human organism is able to process an information flow of about 35 bit/s under optimal conditions in average.
- Transmission and processing of information in living organism: **hormonal** and **nervous**
- Three levels:
 - basic biochemical reactions (control of protein synthesis - hormonal)
 - autonomous systems (e.g., regulation of the heart activity - hormonal and nervous)
 - central nervous system

Examples of information processes in a living organism: eye

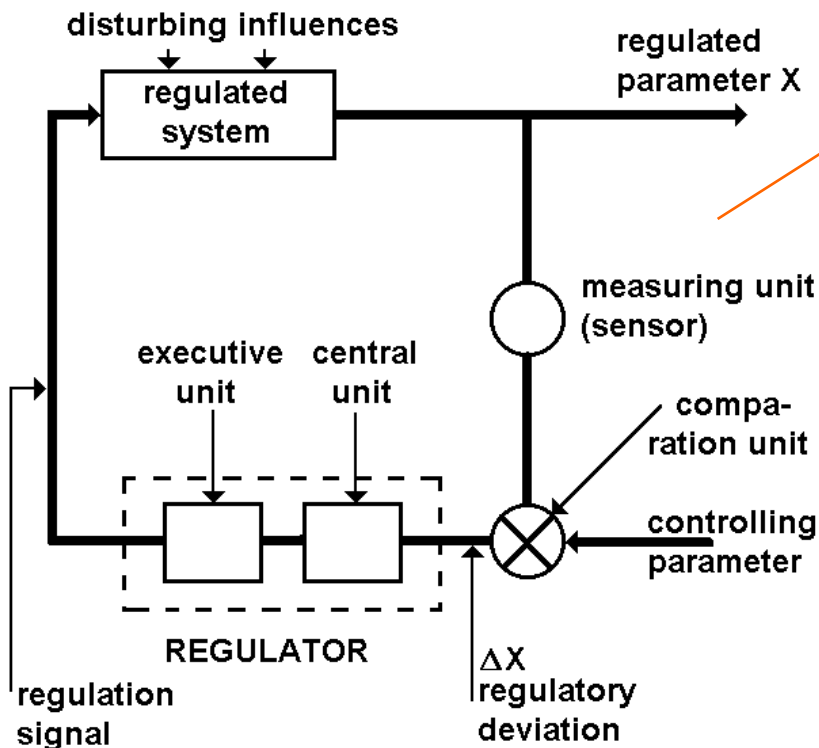
- Information processing in the vision analyser.
- In the yellow spot there are about 10^7 receptors, each can resolve 120 levels of light intensity, i.e. 7 bits of information. The eye can distinguish 10 images/s so that the capacity of the vision analyser is about $7 \cdot 10^8$ bit/s at the level of the yellow spot.
- The optical nerve consists of about 10^6 fibres. Each can pass about 300 action potentials/s, so that the nerve capacity is about $3 \cdot 10^8$ bit/s (compare with a standard TV-channel capacity 10^7 bit/s)

Examples of information processes in living organism: DNA

- **DNA:** DNA contains 4 bases (A, G, C, T). Any nucleotide contains only one base. Therefore, the information carried by one nucleotide is 2 bits. The DNA of one human sperm contains 10^9 nucleotides, i.e. information of $2 \cdot 10^9$ bits.
- **Protein:** 20 different AA - information carried by one of them is about 4 bits. Let the protein molecule contain $\approx 10^3$ AA-units, so that its inf. capacity is $\approx 4 \cdot 10^3$ bits. The quotient of the total information content of DNA molecule, and the information carried by one protein molecule determines the number of protein molecules able of synthesis: $5 \cdot 10^5$.
- Condition: 1 protein = 1 enzyme, 1 enzyme is coded by 1 gene $\Rightarrow$ the chromosomal DNA of human sperm contains about $5 \cdot 10^5$ genes*.

*The real numer is much smaller, of course. See biology.

CONTROL AND REGULATION



- Control: changes of the system behaviour are evoked by the information transmitted from the controlling part of the system.
- According to the complexity of the control process:
- systems controlled - without feedback
- systems regulated - with feedback
- Regulation - process minimising the differences between real values of regulated parameters, and the values required
- Features of the automatic regulation:
 1. Direct communication (inf. channel) between the controlling and controlled unit
 2. Feedback (negative, short or long) between the controlling and controlled unit
 3. Automatic transformation of the information received via the feedback channel into the control commands

Forms of control in living organisms:

- 1) Direct control - control commands are transmitted directly from the controlling to the controlled unit.
- 2) Control with autonomous response. The control commands are only a triggering mechanism for switching over the system states (humoral control - e.g. by hormones).
- 3) Differentiated control - it involves both the previous forms. It is performed by the controlling system with a complex feedback net (CNS)

Automata

- Technical devices utilising the control principles able to work independently in certain extent - **automatic machines:**
 - I. Without feedback - they perform only a program controlled action, they cannot modify or adapt their activity.
 - II. With feedback - they are able of autoregulation, they maintain their function in certain limits.
 - III. Able of certain logical operations, automatic adaptation and learning. When communicating with surroundings and being able of manipulation, they are called **robots**.
- In medicine, the automatic machines are used in laboratory analysis of biochemical and haematological parameters or in monitoring and analysis basic vital functions.

Principles of modelling

- Theoretical cognitional process which goal is to recognise properties of certain original on the basis of its representation. The way of re-presentation is given by the purpose of the model.
- **Each model is a simplification of reality.**
- Main principle of modelling is the **abstraction of identification**. We take into account only identical properties of the objects. A model sufficiently representing the properties of the original object can be a source of information about that object and its interactions.
- **Analogy** - structural or functional similarity of objects, processes and phenomena (events). **Structural analogy** is based on partial or total structural identity of two systems.
- **Functional analogy** (more important) - identity in functional properties of two systems - the character of both systems can be quite different (e.g. functional analogy of natural and artificial kidney).
- **Isomorphism** is a special case of analogy - the systems in question are of the same mathematical description

Types of models

- Formal: **real** (physical, chemical) and **abstract** (mathematical).
- According to the presence of accidental features, these can be divided into **stochastic** and **deterministic**.
- According to the way of origin: **induction** models (from empirically obtained information) and **deductive** ones (on the basis of supposed relations)
- According to the purpose: **descriptive** (serving for description of properties of the original) and **explanatory** (serving for verification of hypotheses)
- The choice of modelled hypotheses must be **representative** - the non-modelled properties must not disable to draw general conclusions.

Process of model construction and utilisation

- Observation of certain phenomenon
- Its experimental verification and, if possible, its quantification
- Designing the model
- Its comparison with experimental results
- **Simulation** = specific kind of modelling. Principle: The original system is re-placed by the simulation model. Regressive verification of knowledge obtained by means of the simulation model in the original system is done. The simulation is often performed using computers.
- Mathematical modelling of biological and physiological processes (stimulated, e.g., by development of radionuclide methods - substance distribution and kinetics in organism is studied).

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