THE MATHEMATICS OF BRAIN

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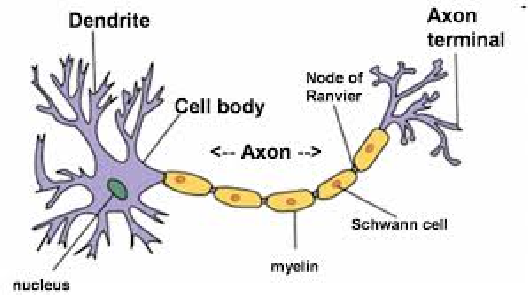
OUTLINE OF THE TALK

1. Introduction
2. Evolution of Mathematical Models
3. Mathematical Tools
4. Applications
5. Conclusion

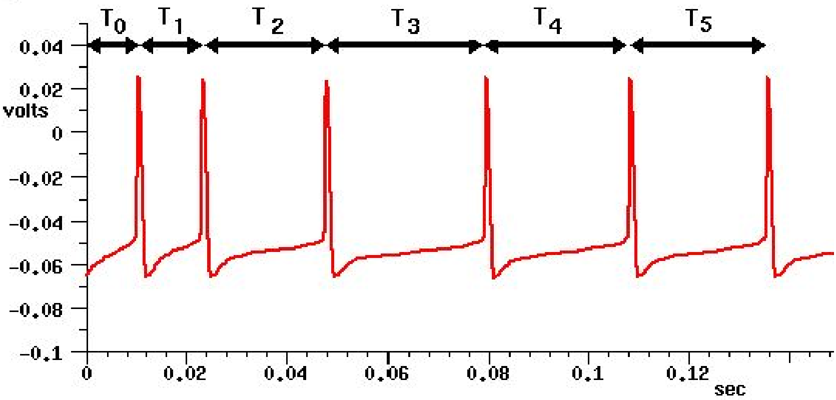
1.a. INTRODUCTION -THE HUMAN BRAIN

According to a lower estimate from 2009, the human nervous system contains 0.89×10^{11} neurons, which are connected by about 10^{15} synapses.



1.b.COMMUNICATION BETWEEN NEURONS

The change of voltage in the cell membrane of a neuron results in a voltage spike called an action potential, which triggers the release of other neurotransmitters. That is, neurons communicate with each other by firing.

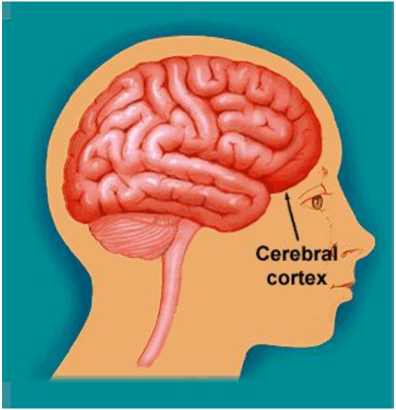


1.c THE CEREBRAL CORTEX

The cerebral cortex is the brain's outer layer of neural tissue in humans and other mammals.

It plays a key role in controlling memory, attention, perception, awareness, thought, language and other important processes.

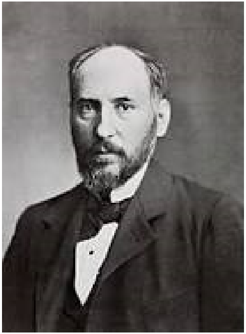
The cortex of a human is about 2-4 mm thick and contains about one fifth of all the neurons.



2.a. DISCOVERY OF NEURON

In the middle of XIX century there were two theories about the structure of nervous cells:

- Reticularism: The nervous system consists of a large network of tissue (reticulum);
- Neuronism: The nervous systems consists of distinct cells (neurons).

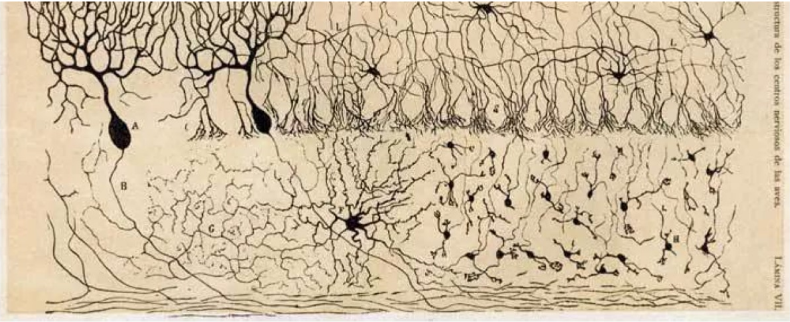


The second theory was defended by Ramon y Cajal (1852-1938) who was awarded the Nobel Prize in Physiology in 1906 (together with Colgi).

2.a. DISCOVERY OF NEURON

The term neuron was introduced in 1891. Ramon y Cajal developped the so-called Neuron Doctrine:

- The neuron is the structural and functional unit of the nervous system;
- Each neuron is a distinct cell which is not fused with others;
- The neuron is composed by three parts: dendrites, axon and cell body;
- Information flow : dendrites $\rightarrow$ cell body $\rightarrow$ axon.

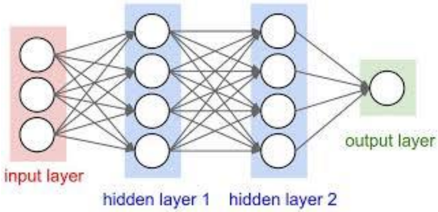


Drawing of the chicken cerebellum by S. Ramon y Cajal

2.b. NEURAL NETWORKS

The investigation of biological neuron networks in animal brains has inspired the mathematicians to create artifical neural networks (ANN).
In 1943 Warren McCulloch and Walter Pitts created a computational model for neural networks based on mathematics and algorithms. The original goal of the neural network approach was to solve problems in the same way that a human brain would. The ANN learns to do tasks by considering examples, generally without task-specific programming.
An ANN is based on a set of connected units called artificial neurons.Each connection(synapse) between neurons can transmit a signal to another neuron. The receiving neuron can process the signal and then send a new signal to neurons connected to it.

2.b. NEURAL NETWORKS



Neurons are organized in layers. Different layers may perform different kinds of transformations on their inputs. Signals travel from the first (input), to the last (output) layer.

Neural networks have been used on a variety of tasks, including computer vision, speech recognition, machine translation, social network filtering.

2.c. HODGKIN-HUXLEY EQUATIONS

In 1952 A.H. Hodgkin and A.F.Huxley introduced a mathematical model that describes the ionic mechanism underlying the iniciation and propagation of action potentials (nervous stimulus) in an axon.
The Hodgkin-Huxley model describes de ionic exchanges between the extracellular and intracellular medium, using the language of electrical circuits (conductance, capacitance, current sources).
In 1963 A.H. Hodgkin and A.F.Huxley were awarded the Nobel Prize in Physiology or Medicine for this work.

2.c. HODGKIN-HUXLEY EQUATIONS

The mathematical model consists of a system of 4 nonlinear ordinary differential equations:

$$I = C_m \frac{dV_m}{dt} + g_k n^4 (V_m - V_k) + g_{Na} m^3 h (V_m - V_{Na}) + g_l (V_m - V_l)$$

$$\frac{dn}{dt} = \alpha_n(V_m)(1-n) - \beta_n(V_m) n$$

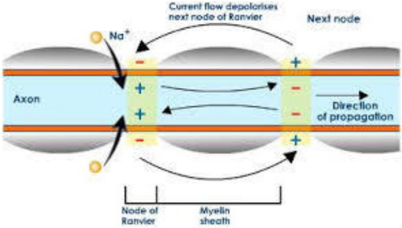
$$\frac{dm}{dt} = \alpha_m(V_m)(1-m) - \beta_m(V_m) m$$

$$\frac{dh}{dt} = \alpha_h(V_m)(1-m) - \beta_h(V_m) h$$

where I- current; V_m - membrane potential, n, m, h -quantities describing activation of sodium ion channel, activation of potassium ion channel and inactivation of sodium ion channel;α_i, β_i - constant rates; g_i- conductances.

2.d. FITZHUGH-NAGUMO EQUATIONS

Further investigation of the propagation of nervous stimulus has lead to the FitzHugh-Nagumo equations (1962), which describe the propagation of signals in myelinated axons.

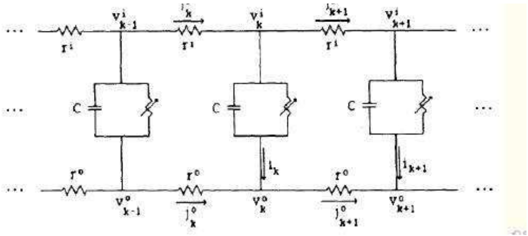


The myelin completely insulates the membrane, so that all the electric processes occur at the Ranvier nodes.

2.d. FITZHUGH-NAGUMO EQUATIONS

Circuit Model

Impulse conduction in a myelinated axon can be simulated using a circuit model: the nodes of Ranvier correspond to condensators and the space between them, to resistances.



2.d FITZHUGH-NAGUMO EQUATIONS

Assumptions of the Nerve Conduction Model

- the nodes are uniformly spaced and electrically identical,
- the axon is infinite in extent,
- the cross-sectional variations in potential are negligible,
- a supra-threshold stimulus begins a signal which travels down the axon from node to node.

2.d FITZHUGH-NAGUMO EQUATIONS

The propagation of nervous stimulus can be modeled by the following system of difference equations:

$$\left\{ \begin{array}{c} \frac{1}{R}(v_{k+1} - 2v_k + v_{k-1}) = C\frac{dv_k}{dt} - f(v_k) + w_k \\ \sigma v_k - \gamma w_k = \frac{dw_k}{dt} \end{array} \right. , \; k \in Z, \qquad (1)$$

where v_k represents the membrane potential at the k-th node , w_k is the so-called recovery variable, σ and γ are non-negative rate constants, R and C are the axoplasmical resistance and the nodal membrane capacitance. Equations (1) are known as the discrete FitzHugh-Nagumo equations.

2.d FITZHUGH-NAGUMO EQUATIONS

The nonlinear function f in discrete FitzHugh-Nagumo equations represents a current-voltage relation (activation function) and is supposed to satisfy the following conditions:

$$\begin{gathered} f \in C^1([0,b]),\ f(0) = f(a) = f(1) = 0, \\ f(v) < 0,\ \textit{if}\ 0 < v < a; \\ f(v) > 0,\ \textit{if}\ a < v < 1. \end{gathered} \tag{2}$$

In many applications this function is taken as

$$f(v) = bv(v-a)(1-v), \tag{3}$$

where $b > 0$.

2.d FITZHUGH-NAGUMO EQUATIONS

The discrete FitzHugh-Nagumo equations can be simplified by neglecting the recovery process (that is, it is assumed that the constants σ and γ are so small that the recovery process has no influence in propagation). Let us assume that

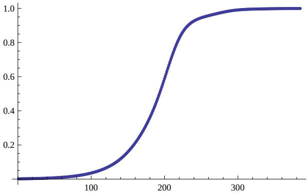
$$v_{k+1}(t) = v_k(t-\tau),$$

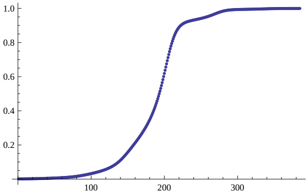
where τ is is a certain delay, which is proportional to the space between nodes and to the reciprocal of propagation speed. Then we obtain a mixed-type functional differential equation:

$$\frac{1}{R}(v(t-\tau) - 2v(t) + v(t+\tau)) + f(v(t)) = C\frac{dv(t)}{dt}, \qquad (4)$$

2.d FITZHUGH-NAGUMO EQUATIONS

Conditions for the existence of solution: $0 < a < 1/2$.
The solution cannot be solved by analytical methods.
Numerical solutions a)with $a = 0.1$; b) with $a = 0.3$.





2.e LEAKY INTEGRATE AND FIRE MODELS

In the LIF (Leaky Integrate and Fire) model, each neuron i can be fully described in terms of a single internal variable, namely the depolarization potential $V_i(t)$ of the neural membrane.

$$\tau \frac{dV_i}{dt} = -\left(V_i(t) - V_L\right) + RI_i(t),$$

where V_L -leaky (resting) potential;RI_i- total synaptic current (the sum of the action of all the synapses):

$$RI_i(t) = J \sum_{j=1}^{N} K_{ij} \sum_{k} \delta(t - t_j^{(k)}),$$

N - number of neurons connected with i; K_{ij} -efficacy of the connection between i and j; $t_j^{(k)}$ -time of the k_{th} spike of the j_{th} neuron;J -constant. When V_i reaches a certain threshold θ, the i-th neuron firesand the system is reset: V_i is set to the resting value V_L.

2.f. NEURAL FIELDS

A new approach was introduced in the years 70:
Wilson and Cowan, 1972 and Amari, 77
Consider a region Ω of the n-dimensional space and a function $V(\bar{x}, t)$, with $\bar{x} \in \Omega$;
$V(\bar{x}, t)$ represents the spatiotemporal structure of the neuronal population:
- spatial distribution of potential;
- time evolution;

2.f. NEURAL FIELDS

Neural Field Equation (NFE):

$$c\frac{\partial}{\partial t}V(\bar{x},t) = I(\bar{x},t) - V(\bar{x},t) + \int_{\Omega} K(\|\bar{x}-\bar{y}\|_2)S(V(\bar{y},t))d\bar{y}, \quad (5)$$

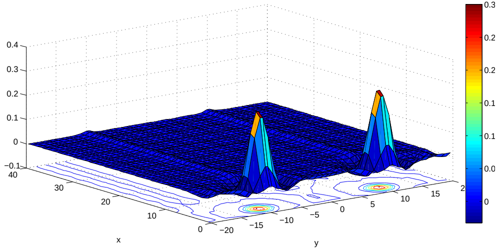
$$t \in [0,T], \bar{x} \in \Omega \subset \mathbb{R}^2;$$

Initial Condition: $V(\bar{x},0) = V_0(\bar{x}), \qquad \bar{x} \in \Omega.$

- $V(\bar{x},t)$ - the membrane potential in point $\bar{x}$ at time t;
- $I(\bar{x},t)$ - external sources of excitation;
- $S(V)$ - dependence between the firing rate of the neurons and their membrane potentials (sigmoidal or Heaviside function);
- $K(\|\bar{x}-\bar{y}\|_2)$ - connectivity between neurons at $\bar{x}$ and $\bar{y}$.

2.f. NEURAL FIELDS

Activation Domain : subset of Ω where the potential is higher than the threshold. In this domain there is a strong connection between neurons. The stationary solutions of NFE often have one or several activation domains (multibump solutions).



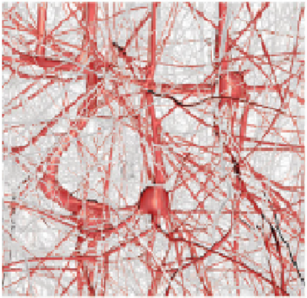
2.g .ALGEBRAIC TOPOLOGY METHODS

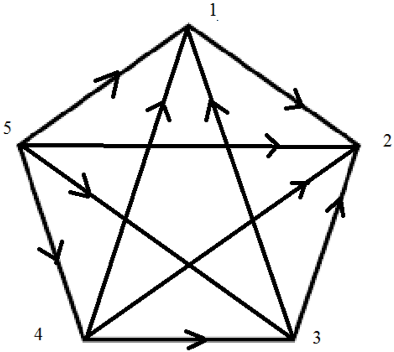
Blue Brain Project

M. Reimann et al., Cliques of Neurons Bound into Cavities Provide a Missing Link between Structure and Function, Frontiers of Mathematical Neuroscience, June 2017.

Construct graphs of a network that reflect the direction of information flow and analyse these directed graphs using algebraic topology.

2.g ALGEBRAIC TOPOLOGY METHODS





clique of neurons	directed graph
neuron	node
synapsis	directed edge
number of connected neurons	dimension

source: node that is source of all edges (5);

sink: node that is target of all edges (2)

2.g ALGEBRAIC TOPOLOGY METHODS

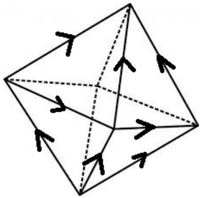
directed simplex of dimension $n-1$ - clique of n all-to-all connected neurons.
Each neuron belongs to many directed simplices of various dimensions.
A collection of simplices 'glued' together along common faces forms a simplicial complex.
The space enclosed by directed graphs forming a simplicial complex is called a cavity. The dimension of a cavity is the dimension of the simplices that enclose it.

Measures of Topological Complexity of a Simplicial Complex S

Betti number -β_n- number of cavities of dimension n enclosed in S.
Euler characteristic - $\chi(S) = \sum_{n \geq 0} (-1)^n |S_n|$, where S_n is the number of n-dimensional simplices contained in S.

2.g ALGEBRAIC TOPOLOGY METHODS

EXAMPLE



Betti number - $\beta_2 = 1$ (one 2-dimensional cavity);
$S_0 = 6$ - number of 0-dimensional simplices (vertices);
$S_1 = 12$ - number of 1-dimensional simplices (edges);
$S_2 = 8$ - number of 2-dimensional simplices (faces);
Euler characteristic: $\chi(S) = 6 - 12 + 8 = 2.$

2.g ALGEBRAIC TOPOLOGY METHODS

How do the topologic measures of geometrical objects reflect the properties of neural networks?

- Local flow of information is well described by directed graphs;
- Global measures of information are given by Betti numbers and Euler characteristic.

2.g ALGEBRAIC TOPOLOGY METHODS

"The variation in Betti numbers and Euler characteristic over time (in response to stimulus) indicates that neurons become bound into cliques and cavities by correlated activity."

"A stimulus may be processed by binding neurons into cliques of increasingly higher dimension, as a specific class of cell assemblies, possibly to represent features of the stimulus."

"'The presence of high-dimensional topological structures is a general phenomenon across nervous systems".

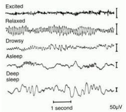
Michael Reinmann et al., 2017

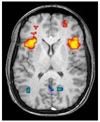
3. MATHEMATICAL TOOLS

- Differential equations
- Dynamical systems
- Bifurcation theory
- Algebraic topology
- Stochastic processes (essential to take into account the influence of random factors)
- Computational methods (most of the considered equations cannot be solved analytically)

4. APPLICATIONS

INTERPRETATION OF MEDICAL DATA





Output from EEG Output from fMRI

Neural field models provide a framework for unifying data from different imaging modalities , for example, EEG (good temporal resolution) and fMRI (good spatial resolution).

S. Coombes, 2010

4. APPLICATIONS

NEURAL FIELDS IN ROBOTICS

"To efficiently interact with another agent in solving a mutual task, a robot should be endowed with cognitive skills such as memory, decision making, action understanding and prediction. The proposed architecture is strongly inspired by our current understanding of the processing principles and the neuronal circuitry underlying these functionalities in the primate brain."
W. Erlhagen and E. Bicho, The dynamic neural field approach to cognitive robotics, J. Neural Eng. 3 (2006) R36 R54

Neural fields are a good tool to simulate working memory.
They simulate how a population of neurons can encode in its firing pattern the features of an external stimulus.

5. CONCLUSION

"We have the Mathematics to make neurons come alive. We also have the Mathematics to describe how neurons collect information, and how they create a lightning bolt to communicate with each other."

Henry Markram, Professor of Ecole Polytechnique Federale de Lausanne, director of Blue Brain and Human Brain Projects

The Blue Brain Project, created in May 2005, in Switzerland, aims to create a digital reconstruction of the brain.

Even after this goal is achieved, the secrets of the brain will keep the researchers busy for many years!

CREDITS

- Michael W. Reimann, Max Nolte, Martina Scolamiero, Katharine Turner, Rodrigo Perin, Giuseppe Chindemi, Pawel Dlotko, Ran Levi , Kathryn Hess and Henry Markram, Cliques of Neurons Bound into Cavities Provide a Missing Link between Structure and Function, Frontiers in Computational Neuroscience, 2017, doi: 10.3389/fncom.2017.00048.
- Mo Constandi, The Discovery of Neuron, posted on 29/8/2006, https://neurophilosophy.wordpress.com/2006/08/29the-discovery-of-the-neuron

BIBLIOGRAPHY

- S.L. Amari, Dynamics of pattern formation in lateral-inhibition type neural fields, Biol. Cybernet. 27 (2) (1977) 77–87.
- J. Bell, Behaviour of some models of myelinated axons, IMA Journal of Mathematics Applied in Medicine and Biology, 1 (1984), 149–167.
- J. Bell and C. Cosner, Threshold conditions for a diffusive model of a myelinated axon,J. Math. Biology , 18 (1983), 39-52.
- I. Bojak, D.T.J. Lily, Axonal Velocity Distributions in Neural Field Equations, Comput. Biol. 6(1), (2010), e1000653.
- H. Chi, J. Bell and B. Hassard, Numerical solution of a nonlinear advance-delay-differential equation from nerve conduction theory,J. Math. Biol., 24 (1986), 583-601.
- Mo Constandi, The Discovery of Neuron, posted on 29/8/2006, https://neurophilosophy.wordpress.com/2006/08/29the-discovery-of-the-neuron
- S.Coombes, Large-scale neural dynamics: Simple and complex, NeuroImage 52, (2010), 731–739.

BIBLIOGRAPHY

- S.Coombes, N.A.Venkov, L.Shiau, I.Bojak, D.T.J.Liley, C.R.Laing, Modeling electrocortical activity through improved local approximations of integral neural field equations, Phys. Rev. E , 76, (2007), 051901.
- Gustavo Deco, Viktor K. Jirsa, Peter A. Robinson, Michael Breakspear, and Karl Friston, The Dynamic Brain: From Spiking Neurons to Neural Masses and Cortical Fields, Comput Biol. 2008 Aug; 4(8): e1000092
- W.Erlhagen, E.Bicho, The dynamic neural field approach to cognitive robotics, J. Neural Eng. 3, (2006), R36-R54.
- G. Faye and O. Faugeras, Some theoretical and numerical results for delayed neural field equations, Physica D 239 (2010) 561–578.
- R. FitzHugh, Impulses and physiological states in theoretical models of nerve membrane, Biophysical J., 1(1961), 445-466.
- R. FitzHugh, Computation of impulse initiation and saltatory condition in a myelinated nerve fiber, Biophysical J. , 2 (1962), 11-21.

BIBLIOGRAPHY

- N.J. Ford, P. M. Lima and P. M. Lumb, Commputational methods for a mathematical model of propagation of nervous signals in myelinated axons, Applied Numerical Mathematics 85(2014), 38-53.
- A. Hodgkin and A. Huxley, A qualitative description of nerve current and its application to conduction and excitation in nerve, J. Physiology, 117 (1952), 500-544 .
- A. Hutt and N. Rougier, Activity spread and breathers induced by finite transmission speeds in two-dimensional neuronal fields, Physical Review,E 82 (2010) 055701.
- A. Hutt and N. Rougier, Numerical Simulations of One- and Two-dimensional Neural Fields Involving Space-Dependent Delays, in S. Coombes et al., Eds., Neural Fields Theory and Applications, Springer, 2014.
- J.P. Keener, Propagation and its failure in coupled systems of discrete excitable cells, SIAM J. Appl. Math. , 47 (1987), 556-572.

BIBLIOGRAPHY

- P.M . Lima , E. Buckwar, Numerical solution of the neural field equation in the two-dimensional case, SIAM Journal of Scientific Computing, 37 (2015) B962- B979.
- J. Nagumo, S.Arimoto and S. Yoshizawa, An active pulse transmission line simulating nerve axon, Proceedings of the IRE, 50 (1962), 2061–2070.
- R. Potthast and P. beim Graben, Existence and properties of solutions for neural field equations, Math. Meth. Appl. Sci., 33 (2010) 935-949.
- Michael W. Reimann, Max Nolte, Martina Scolamiero, Katharine Turner, Rodrigo Perin, Giuseppe Chindemi, Pawel Dlotko, Ran Levi , Kathryn Hess and Henry Markram, Cliques of Neurons Bound into Cavities Provide a Missing Link between Structure and Function, Frontiers in Computational Neuroscience, 2017, doi: 10.3389/fncom.2017.00048.
- H.R. Wilson and J.D. Cowan, Excitatory and inhibitory interactions in localized populations of model neurons, Bipophys. J., 12 (1972) 1-24.