

Universitatea Politehnica Bucuresti -
LMN

Modelarea multifizica in neurostiinta computationala

Daniel Ioan, Gabriela Ciuprina, Ruxandra Barbukescu

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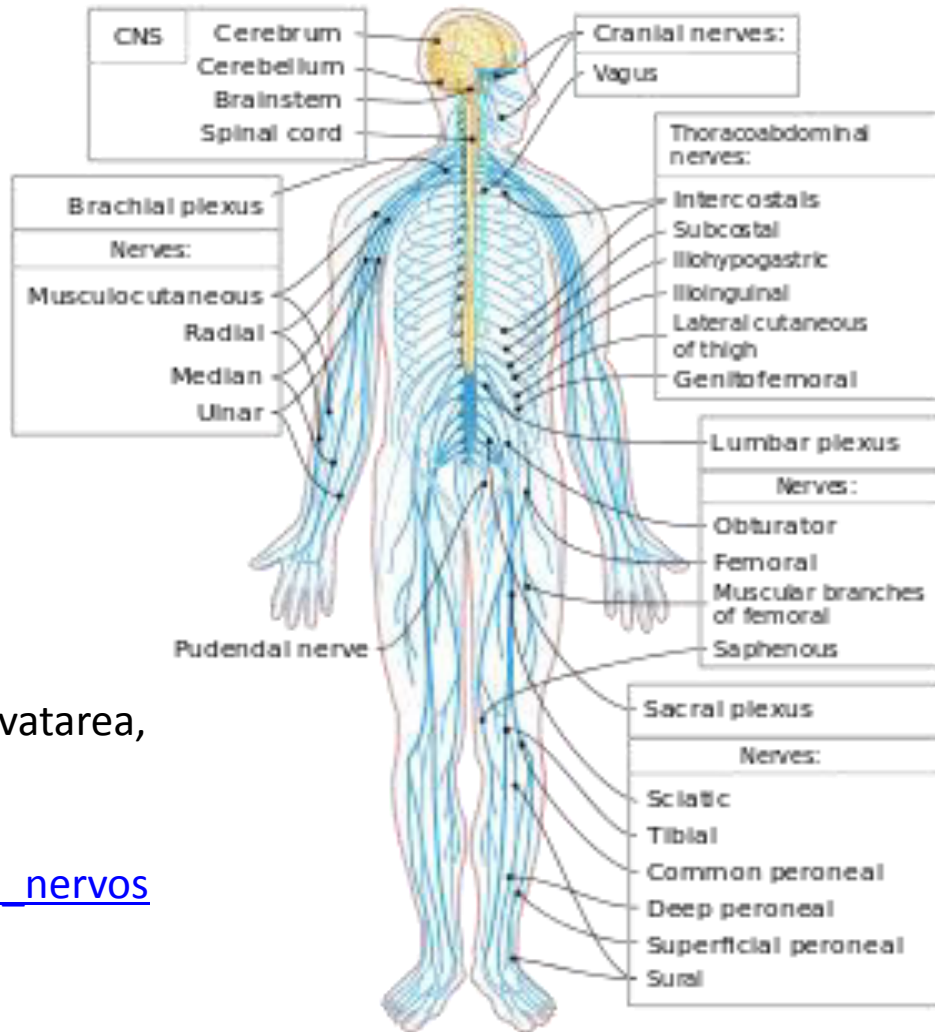
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1. Introducere. Morfologia si fiziologia neuronilor
2. Modele neuronale 0D
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4. Modele neuronale cu parametri distribuiti 1,2,3D
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1. Introducere

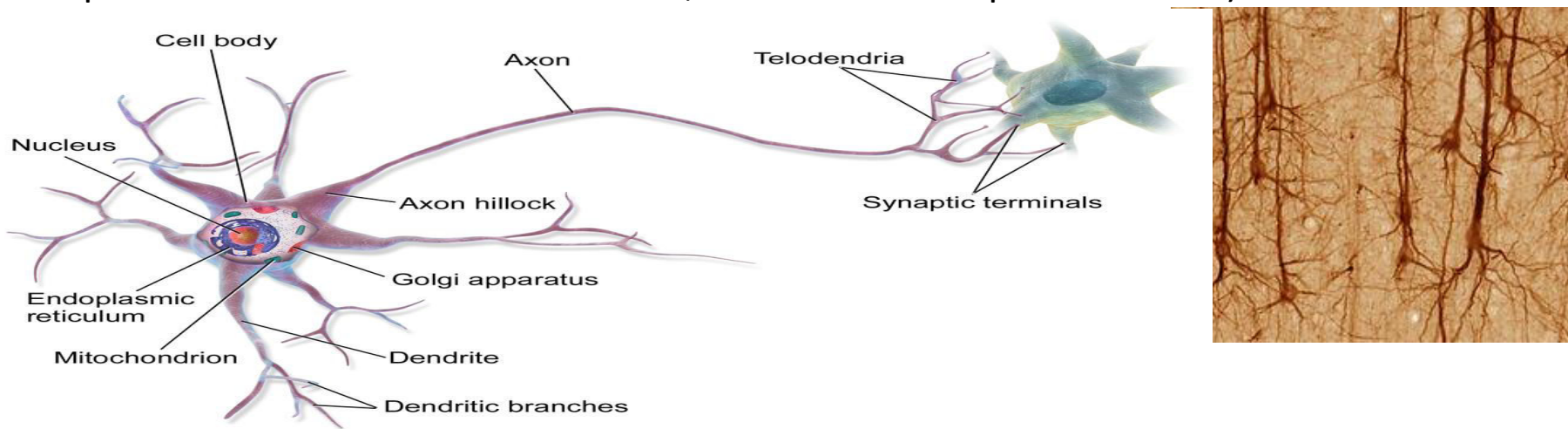
- Sistemul neural – structura:
 - Sistemul periferic:
 - Ascendent (nervi senzitivi)
 - Descendent (nervi motorii)
 - Sistemul nervos central (SNC):
 - Encefal (trunchi, prozencefal)
 - Maduva spinarii
- Sistemul neural-functii
 - Transmite semnale neurale
 - Proceseaza semnale
 - Functia reflex
 - Controlul emotiilor
 - Activitatea voluntara: gandirea, invatarea, limbajul, coordonarea miscarilor

https://ro.wikipedia.org/wiki/Sistem_nervos



Neuronul, morfologie

- Sistemul nervos este un tesut alacatuit din (<https://en.wikipedia.org/wiki/Neuron>):
 - Neuroni-celule alungitae– ramificate, excitabila electric, cu rolul de a recepta , transmite si emite semnale neurale, uneori si de a le genera. Numarul lor este de 20 miliarde in cortex si de patru ori mai mult in total
 - Celule gliale – celuele auxiliare care deservasc neuronii, mai multe decat neuronii
- Partile neuronului:
 - Corpul celulei (soma 10-200um), contine citoplasma, nucleul si organele , in membrana
 - Danditre – excrescente ale corpului cu mii de butoni superficiali (ce au receptori-proteine plasate pe membrana, sensibile la neurotransmitatori)
 - Axon - incepe cu conul axonic, cu structura fibrosa cu diametru 1-20um, lungime de 200um-1m si inconjurat de membrana, poate fi ramificat
 - Ramificatii axonice, terminate cu butoni (care contin vezicule cu neurotransmitatori ce pot fi secretati in lichidul extracelular, si canale de Ca - pe membrana)

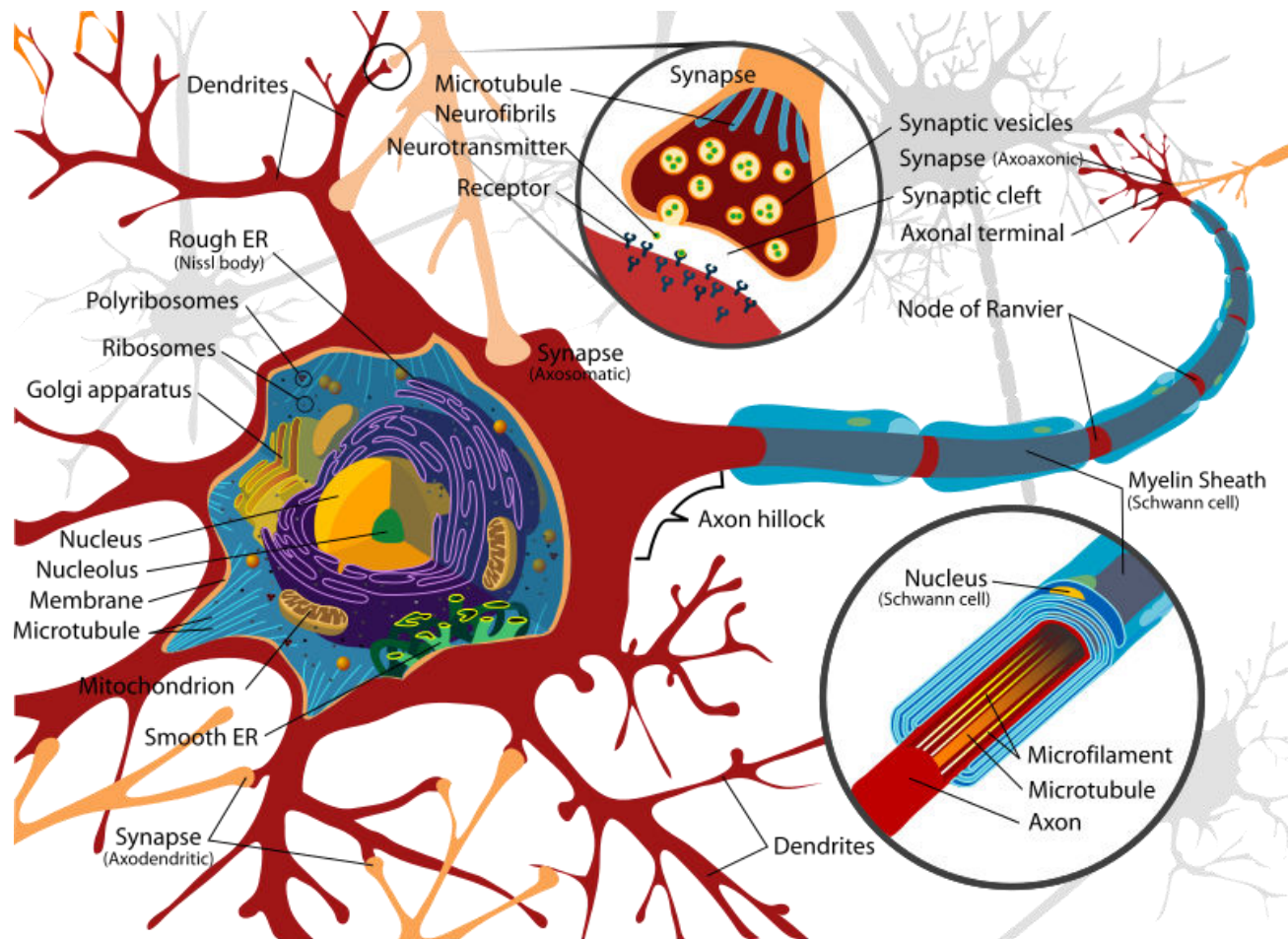


Mielinizarea, sinapsele

- O parte din neuroni sunt mielinizati - au axonul infasurat in celule gliale (Schwann), spatiul dintre ele reprezentand nodurile Ranvier, distantate la 0.1 mm
- Neuronii alcatuiesc retele neuronale, fiind interconectati prin sinapse (spatiul dintre butonii axonici terminali presinaptici si cei dendritici postsinaptici). Sunt cca 7000 sinapse in medie per neuron.

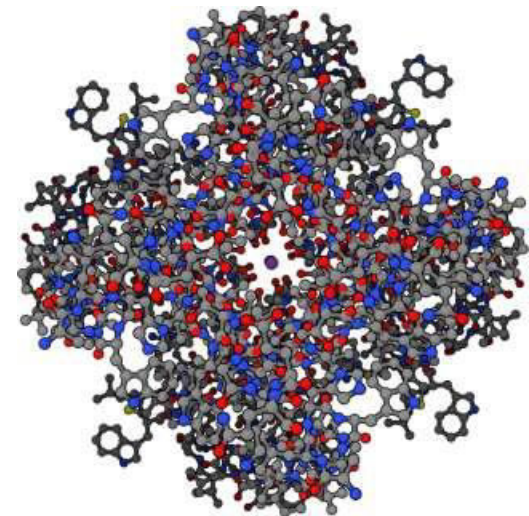
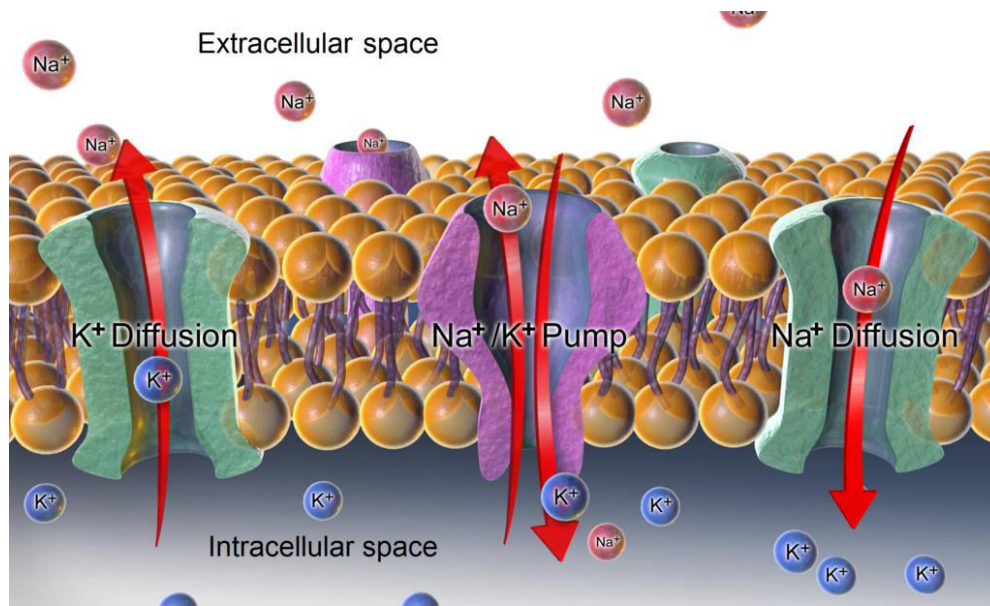
https://en.wikipedia.org/wiki/Schwann_cell

<https://en.wikipedia.org/wiki/Synapse>



Membrana, canalele si pompele ionice

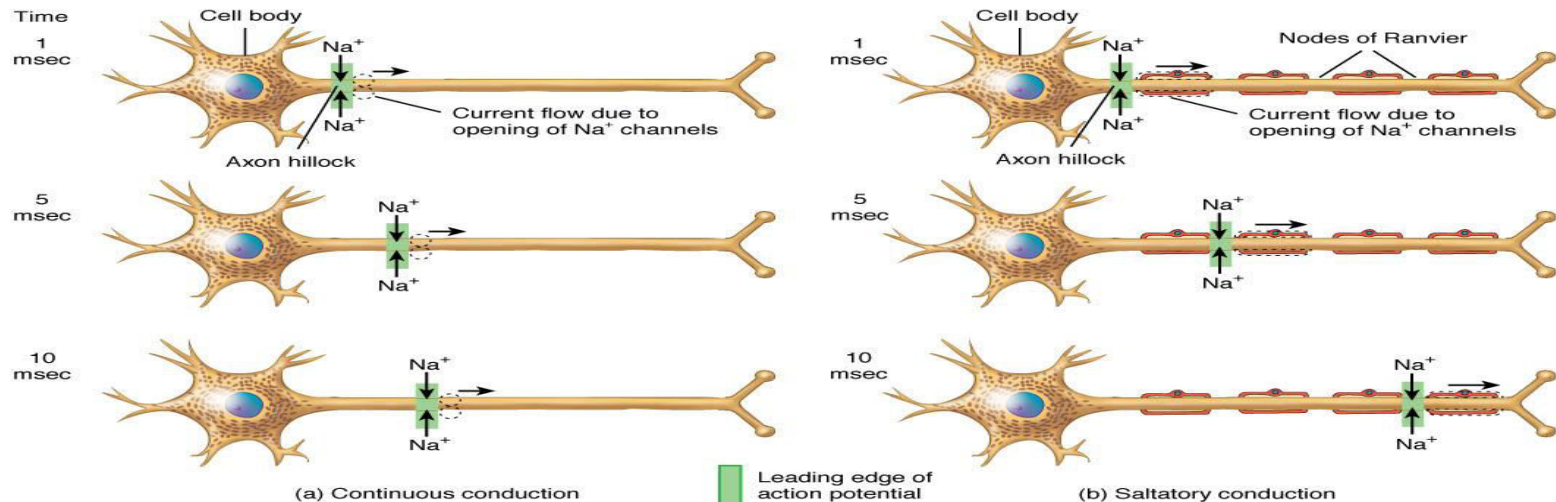
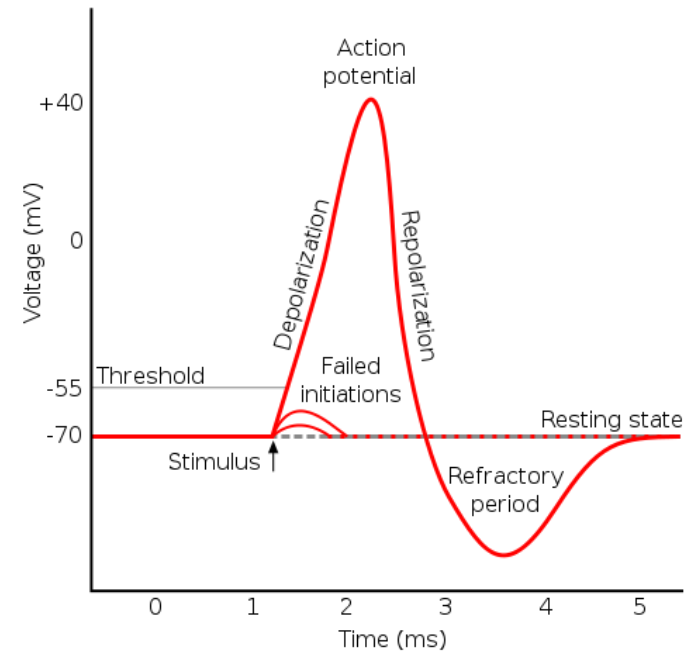
- Membrana neuronului este un bistrat lipidic cu grosime de 5nm care incorporeaza molecule proteice distribuite superficial (cca 1 milion per neuron) cu functia de:
 - Canalele ionice – (controleaza difuzia pasiva, selectiva a ionilor) sensibile la potentialul electric (devin permeabile pentru Na^+ , K^+ , Ca^+)
https://en.wikipedia.org/wiki/Ion_channel
 - Pompe de ioni – sunt active - restabilesc echilibru ionic intre citoplasma si lichidul exterior, prin consum energetic (ATP)
<https://en.wikipedia.org/wiki/Na%2B/K%2B-ATPase>



Fiziologia neuronului, potentialul de actiune

Semnalul neuronal:

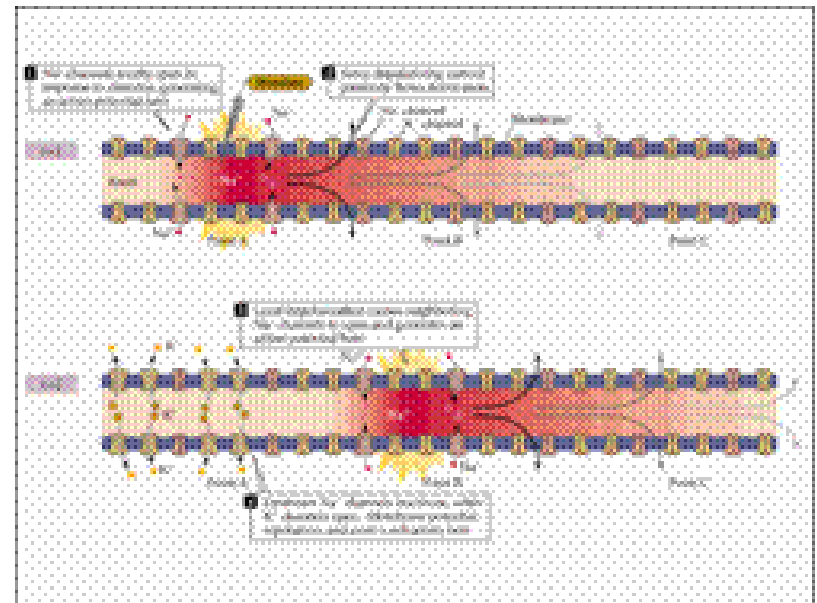
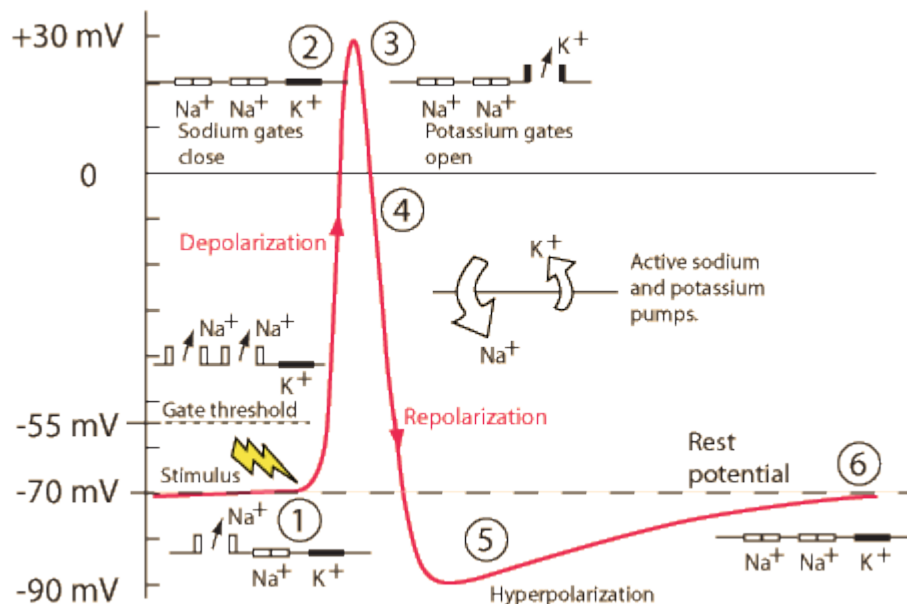
- impuls de potential (de actiune) care se propaga de-a lungul axonului catre terminatia acestuia.
https://en.wikipedia.org/wiki/Action_potential
- Fenomenul este de natura electro-chimica.
- Daca ar fi doar electric difuzia EQS din citoplasma ar deprecia (atenua) impulsul.
- Acesta este reconditionat electrochimic (prin difuzia controlata I/O a ionilor prin membrana)
- In cazul axonilor mielinizati, sub celula Schwann transmisia este prin difuzie EQS (conductie in cablu RC), iar in nodurile Ranvier are loc reconditionarea impulsului (transmisie saltatorie)



Fazele potentialului de actiune

- **Echilibru:** -70mV in interior (citoplasama cu exces de K⁺ iar in exteriorul membranei exces de Na⁺)
- **Depolarizare** (0.5-1ms)– sub actiunea excitatiei potentialul creste si cand depaseste nivelul de prag (-55mV) se deschid canalele de Na, care declanseaza depolarizarea (V ajunge la +40mV) prin invazia in interior a ionilor de Na⁺
- **Repolarizarea** (0.5-1ms)- se deschid canalele K si ionii K⁺ difuzeaza in exterior, repolarizand pana la hiperpolarizare citoplasma (V=-85mV)
- **Etapa refractara** (1-2ms, asigura unidirectionalitatea propagarii)–prin actiunea pompelor de ioni, care pompeaza 3Na⁺ spre exterior si 1K⁺ spre interior, consumand 1ATP se restabileste starea de echilibru

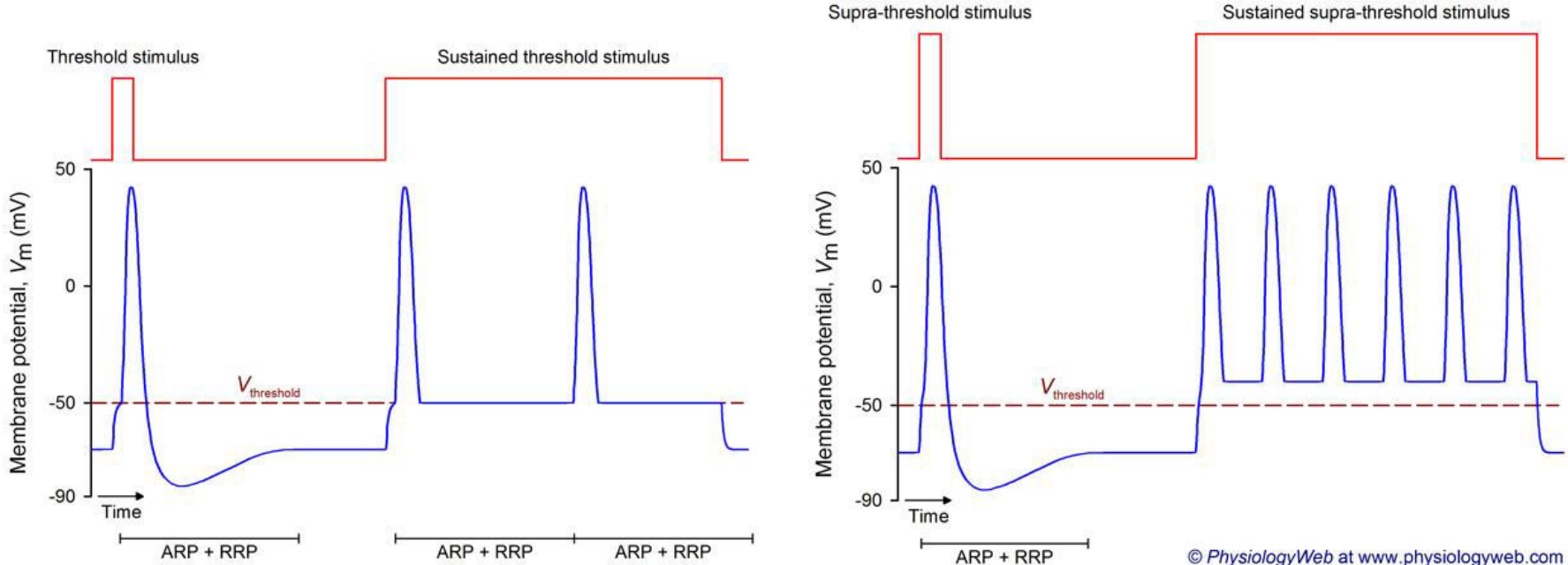
<http://www.centenary.edu/attachments/biophysics/bphy304/11a.pdf>



Codificarea prin impulsuri

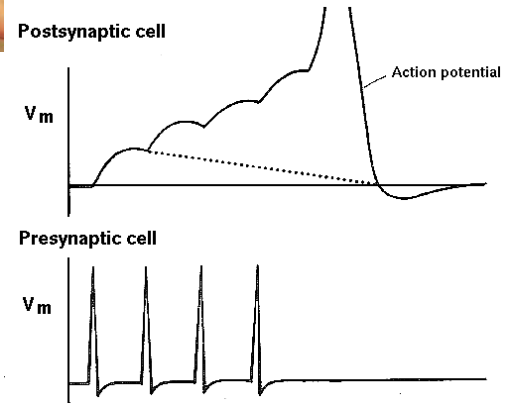
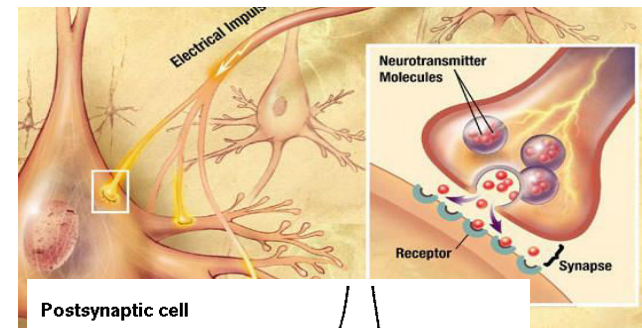
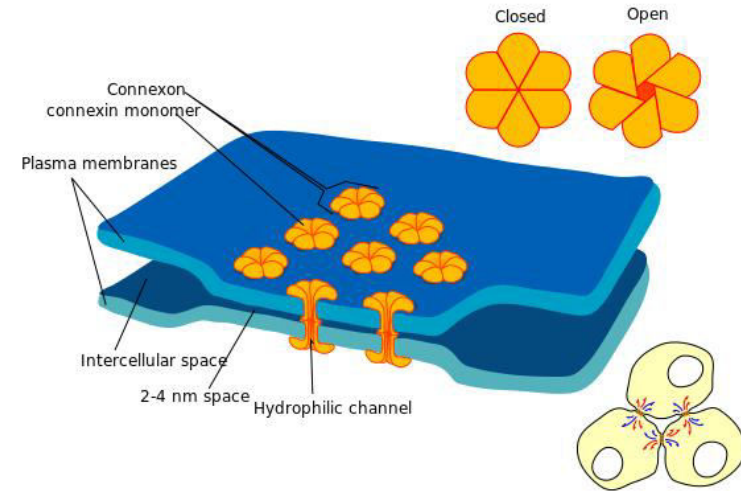
- Cat timp excitatia este continua, ciclul este reluat si rezultatul este un tren de impulsuri care dureaza cat timp excitatia este peste prag
- Daca nivelul excitatiei creste, etapa refractara se scurteaza si impulsul urmator este generat mai repede, fara sa se modifice forma si durata lui
- In consecinta, transmiterea informatiei referitoare la nivelul excitatiei se face prin modulatie in frecventa

http://www.physiologyweb.com/lecture_notes/neuronal_action_potential/neuronal_action_potential_frequency_coding_in_the_nervous_system.html



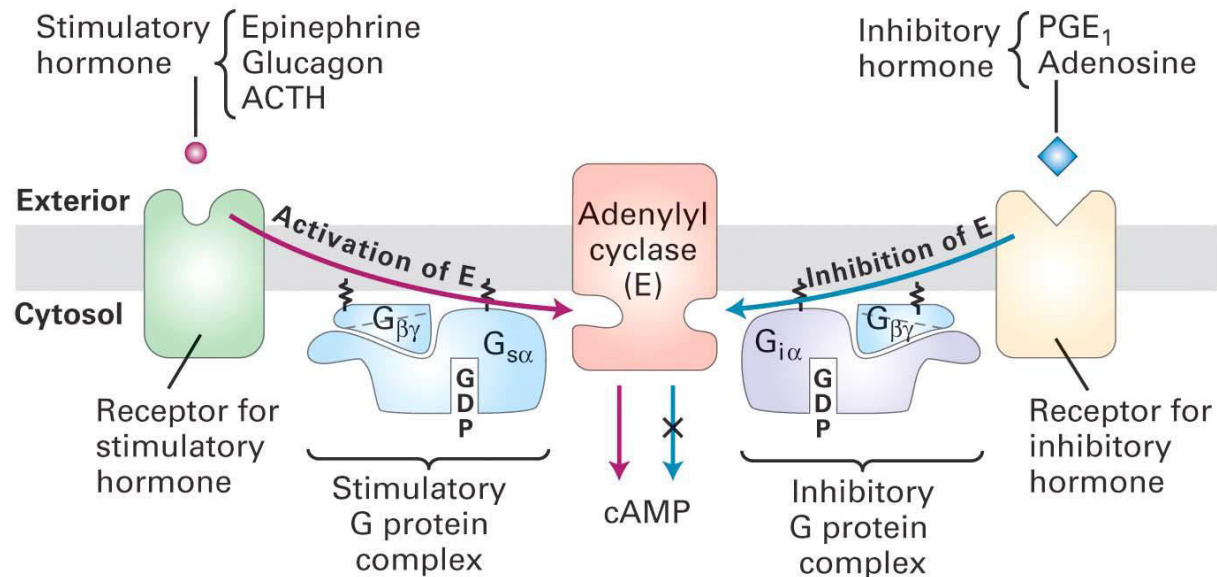
Interconectarea neuronilor

- Se realizeaza prin intermediul sinapselor, care sunt de natura electrica sau chimica
<https://en.wikipedia.org/wiki/Synapse>
- Semnalul trece de la butonul axonal la cel dendritic, si se propaga de-a lungul lor cu atenuare/inversare (inhibitie) sau amplificare/reconditionare (excitare)
- Activitatea cerebrala echilibrata rezulta in urma echilibrului inhibitei/excitatie (intr-o extrema se afla somnul si coma, iar in cealalta epilepsia)
- Plasticitatea sinapselor: utilizarea repetata a unei sinapse o face mai permeabila (postulatul lui Hebb, conform principiului "functia dezvolta organul"), fenomen esential pentru memorie, invatare si gandire
- Sarcinile transportate de semnalele neurale prin dedrite sunt acumulate in corp (in special in conul axonal care actioneaza ca o palnie), timp in care o parte este progresiv pierduta (difuzeza in lichidul extracelular)
- In consecinta potentialul creste, iar daca potentialul atinge valoarea de prag, are loc activarea neuronului si impulsul generat se propaga de-a lungul axonului
- Neuronul este deci un dispozitiv cu intrari multiple, cu ponderi diferite (excitabilitate dendritica/sinaptica)



Retelele biochimice

- Pe langa sinapse, neuronii sunt interconectati prin intermediul a zeci de retele biochimice (**signaling pathways**), care transporta hormoni, enzime sau substante simple, droguri la nivel intracelular
- Aceste semnale biochimice afecteaza profund functionarea neuronilor: metabolism, formarea scheletului celulei, reglarea genelor, raspunsul la excitatii externe, diferentierea celulelor, ciclul celular, functionarea sinapselor, long term potentiation (LTP – plasticitate sinapse)
- Retelele biochimice interactioneaza cu cele neuronale, modificandu-le caracteristicile, inclusiv pe cele electrice: conductante, reactivitate, excitabilitate.



https://mcb.berkeley.edu/courses/mcb110spring/nogales/mcb110_s2008_4signaling.pdf

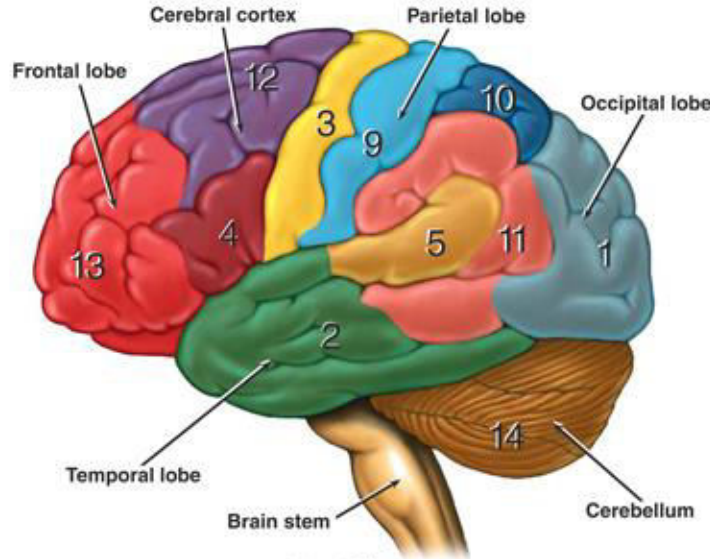
Anatomy and Functional Areas of the Brain

Functional Areas of the Cerebral Cortex

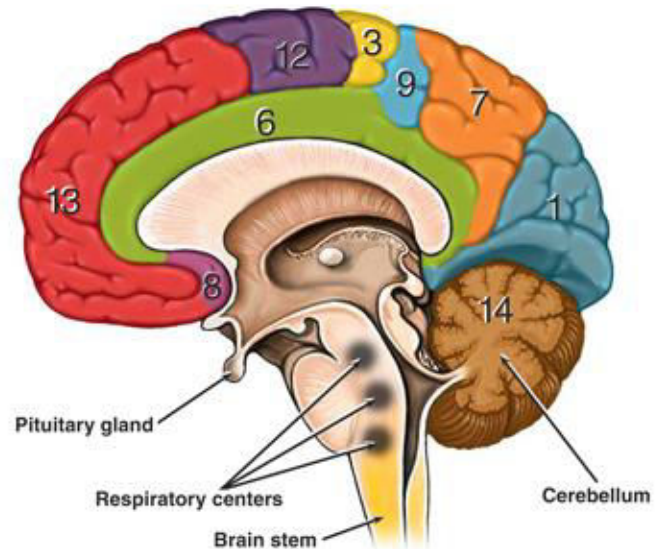
- 1 **Visual Area:**
Sight
Image recognition
Image perception
- 2 **Association Area**
Short-term memory
Equilibrium
Emotion
- 3 **Motor Function Area**
Initiation of voluntary muscles
- 4 **Broca's Area**
Muscles of speech
- 5 **Auditory Area**
Hearing
- 6 **Emotional Area**
Pain
Hunger
"Fight or flight" response
- 7 **Sensory Association Area**
- 8 **Olfactory Area**
Smelling
- 9 **Sensory Area**
Sensation from muscles and skin
- 10 **Somatosensory Association Area**
Evaluation of weight, texture, temperature, etc. for object recognition
- 11 **Wernicke's Area**
Written and spoken language comprehension
- 12 **Motor Function Area**
Eye movement and orientation
- 13 **Higher Mental Functions**
Concentration
Planning
Judgment
Emotional expression
Creativity
Inhibition

Functional Areas of the Cerebellum

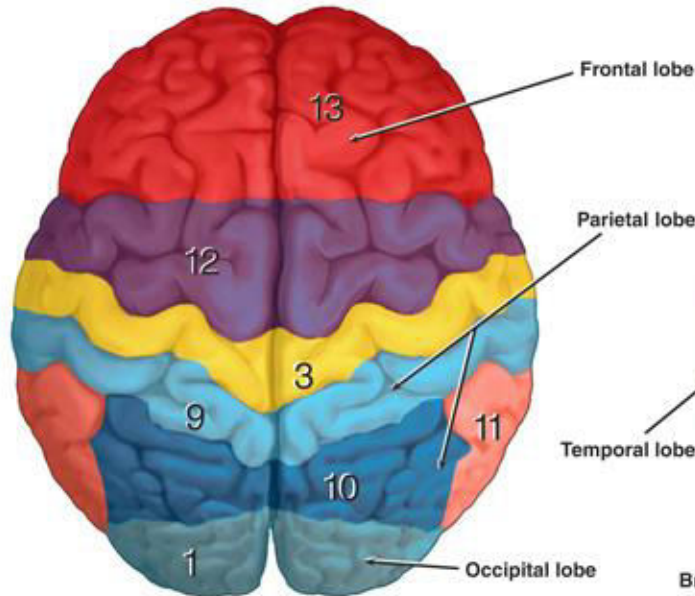
- 14 **Motor Functions**
Coordination of movement
Balance and equilibrium
Posture



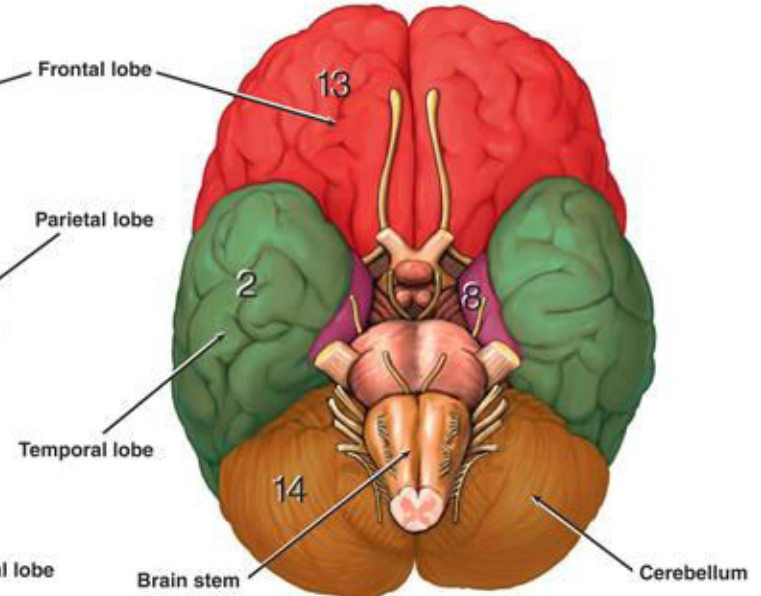
Lateral View



Sagittal View



Superior View

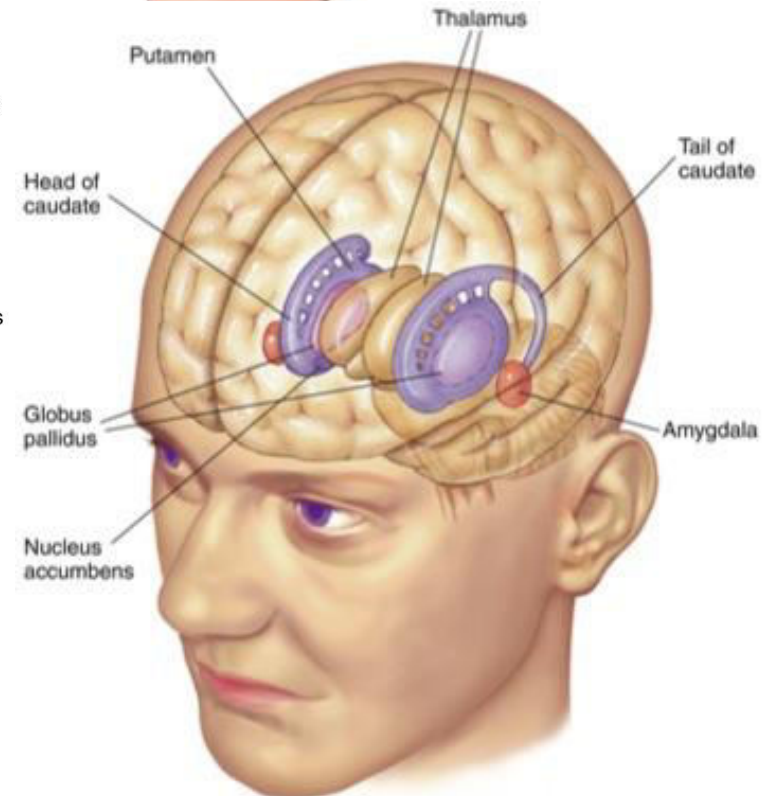
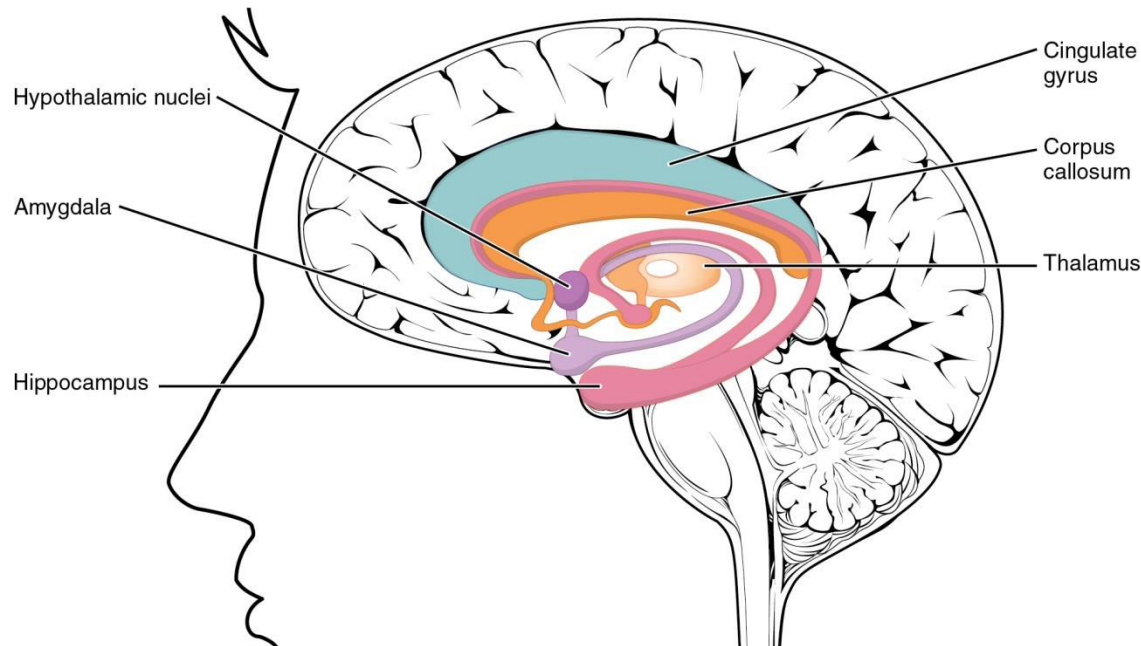
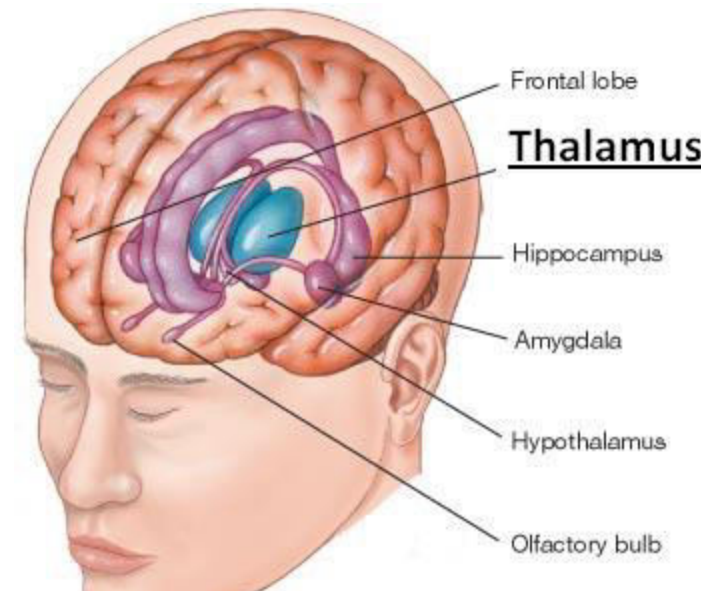


Inferior View

Sistemul subcortical

https://en.wikipedia.org/wiki/Limbic_system

Functii: esentiale vietii (bazale), emotii, memorie, navigatie, somn, talamusul este statie releu pentru informatii vizuale, auditive redistribuite apoi spre cortex. Corpus callosum: comunicare interemisfere

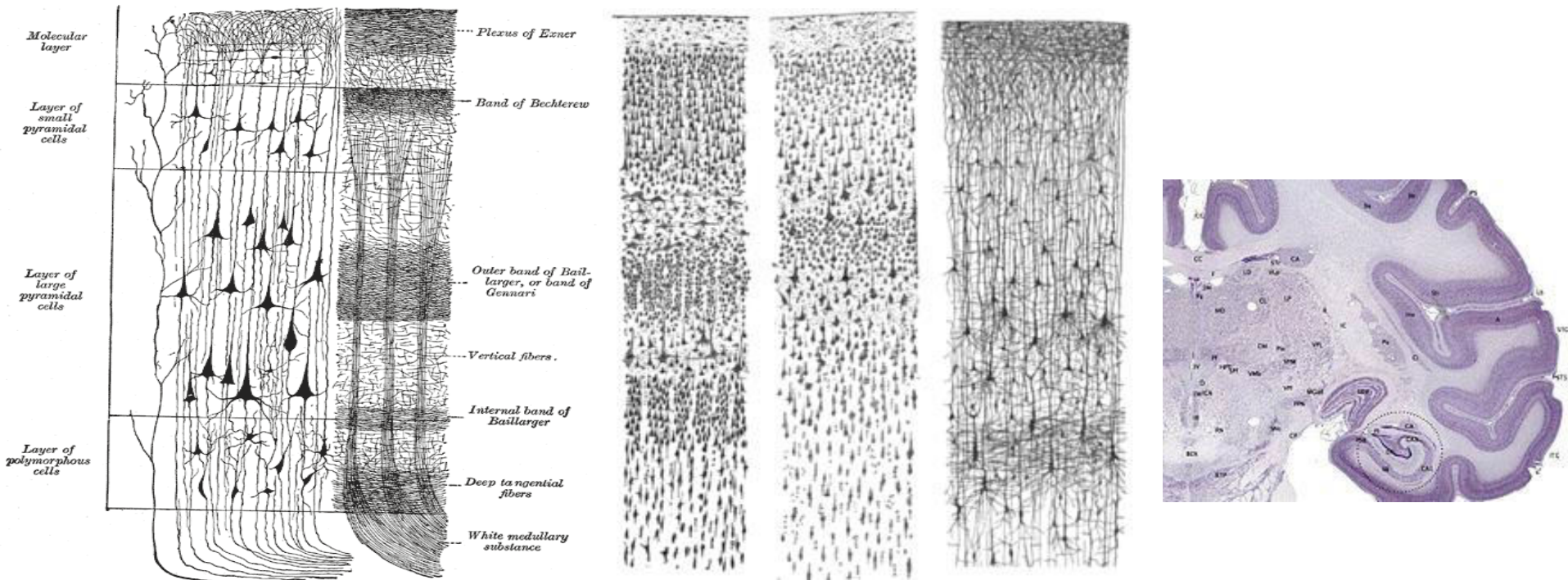


Structura scoartei cerebrale

https://en.wikipedia.org/wiki/Cerebral_cortex

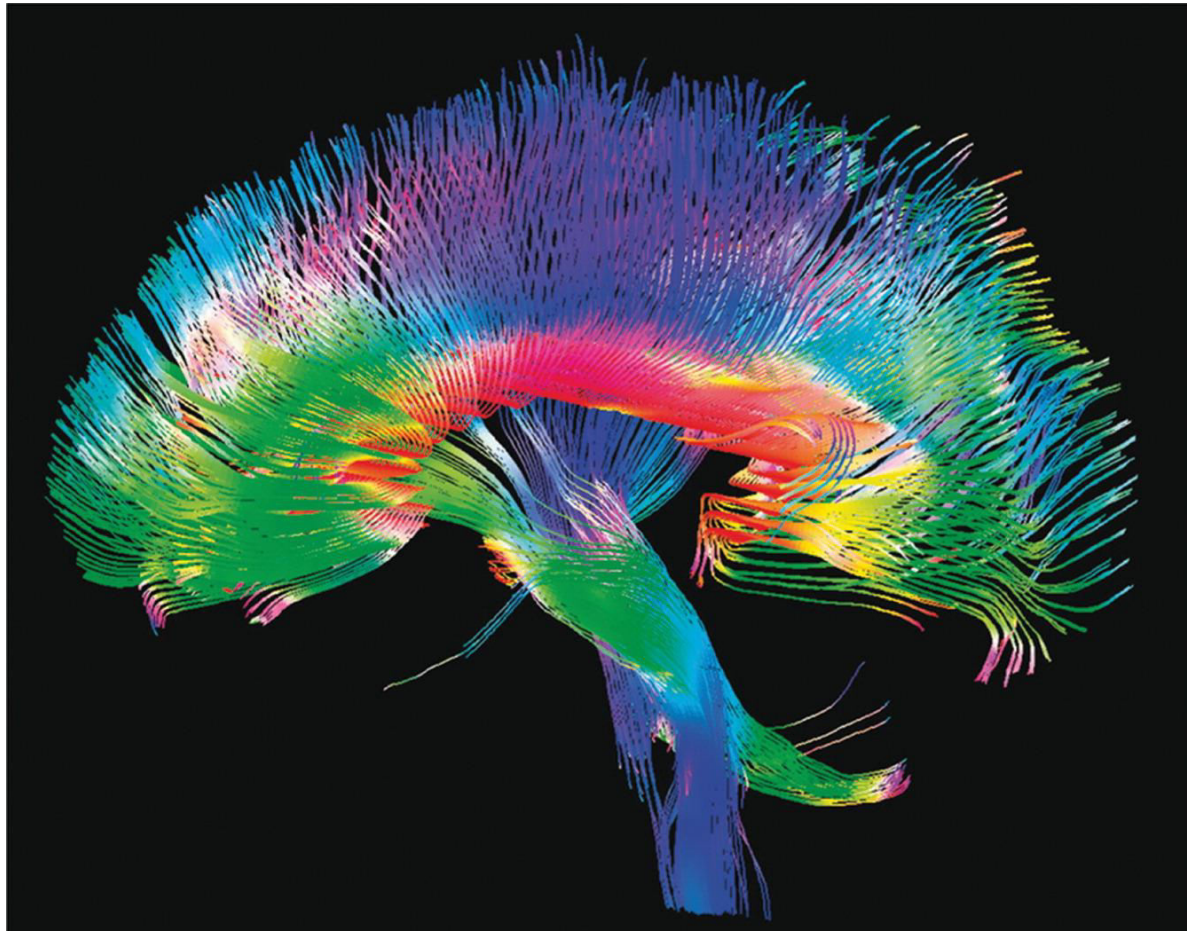
- 2.4mm grosime cu 6 straturi neuronale (materia gri), frontiera a materiei albe (mielina axonilor)
- Este structurata modular/ierarhic: 2 emisfere, 52 arii pe emisfera, 1 milion minicoloane pe arie, fiecare cu cca 100 neuroni, grupate in macro/hiper-coloane

<http://williamcalvin.com/1990s/1995Handbook.htm>



The Human Connectome Project

- <http://www.humanconnectomeproject.org/gallery/> din 2010
- S-au identificat magistralele neurale (principalele fascicule neurale) pt 1200 persoane
- In 1970-82 – conectomul viermelui c.elegans: 300 neuroni cu 7000 sinapse
- La om s-a folosit tehnica neinvaziva DW-MRI ([https://en.wikipedia.org/wiki/Diffusion MRI](https://en.wikipedia.org/wiki/Diffusion_MRI))



2. Modele neuronale 0D

- **Neuron DB:** <https://senselab.med.yale.edu/neurondb/>

Baza de date contine urmatoarele informatii despre neuroni (30, inclusiv corticali -piramidali, talamici, din uipocampus si cerebel , care sunt principalele tipuri):

- Neuron List [Alphabetically](#)
- Neuron List [By Brain Regions](#)
- [Membrane properties: Channels, Receptors, Neurotransmitters/Neuromodulators, Currents, Receptors, Neurotransmitters/Neuromodulators](#)
- Canonical [forms](#) of neurons (vezi figura)
- [Bibliographic](#) citations

- **Model DB** <https://senselab.med.yale.edu/ModelDB/>

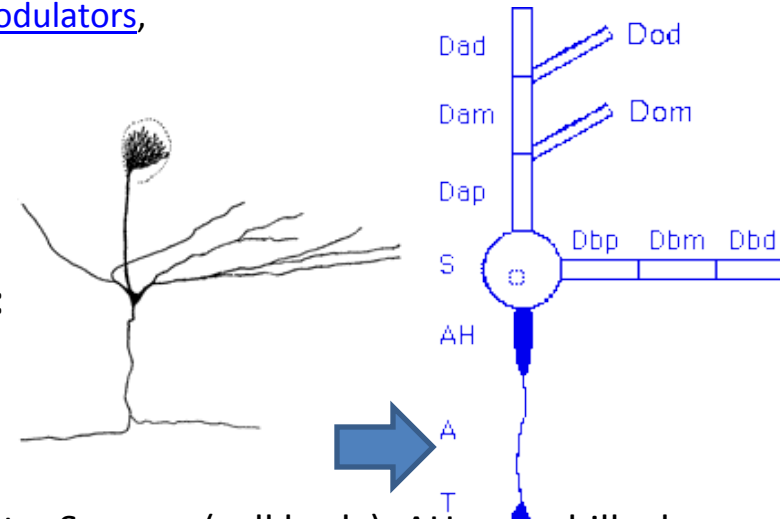
Baza de date cu modele pentru neuroni (1104 modele) cu:

- | | |
|---------------------|------------------|
| – Accession number | • Receptor(s) |
| – Short description | • Gene(s) |
| – References | • Transmitter(s) |
| – Model Type | • Simulation |
| – Cell Type(s) | • Environment |
| – Channel(s) | • Model files |
| – Gap Junctions | |

- **PyNN - limbaj independent de simulator pt scrierea modelelor neurale**

<http://neuralensemble.org/PyNN/>

1. Distal apical dendrite
2. Middle apical dendrite
3. Proximal apical dendrite
4. Distal oblique dendrite
5. Middle oblique dendrite
6. Distal basal dendrite
7. Middle basal dendrite
8. Proximal basal dendrite
9. Soma
10. Axon
11. Axon hillock
12. Axon fiber
13. Axon terminal



D, dendrite; S, soma (cell body); AH, axon hillock-initial segment of the axon; A, axon; T, axon terminal. Type of dendrite: e, equivalent cylinder (for single dendrites and multipolar trees); a, apical; b, basal; o, oblique. Level of dendrite: (p) proximal, (m) middle, and (d) distal with respect to the cell body.

Modelul Hodgkin-Huxley (HH)

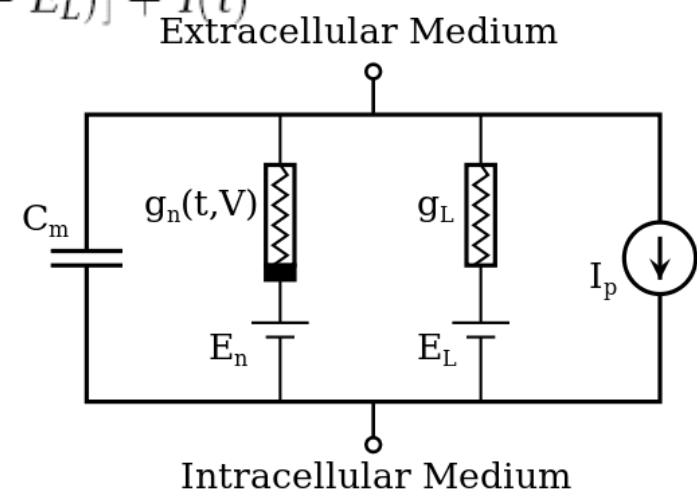
- Modelele neuronilor biologici descriu cantitativ potentialul de actiune
http://labs.seas.wustl.edu/bme/raman/Lectures/Lecture4_SimplerModels.pdf
- HH (1952- premiul Nobel in 1963) este modelul de referinta al neuronilor biologici
https://en.wikipedia.org/wiki/Hodgkin%E2%80%93Huxley_model
- 4ODEs care descriu un sistem dinamic nelinier, cu 4 variabile de stare: u-tensiunea membranei, concentratiile m, h – Na, n-K si I –curent de excitatie, conductantele gNa si gK pentru Na si K
- Este realist biologic, dar prea complicat (solicita efort computational)
http://virtualrat.org/sites/default/files/downloads/Hodgkin%20Huxley%20Action%20Potential%20Model_0.pdf

$$C \frac{du}{dt} = -[g_{Na} m^3 h (u - E_{Na}) + g_K n^4 (u - E_K) + g_L (u - E_L)] + I(t)$$

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

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

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



Modelul FitzHugh–Nagumo

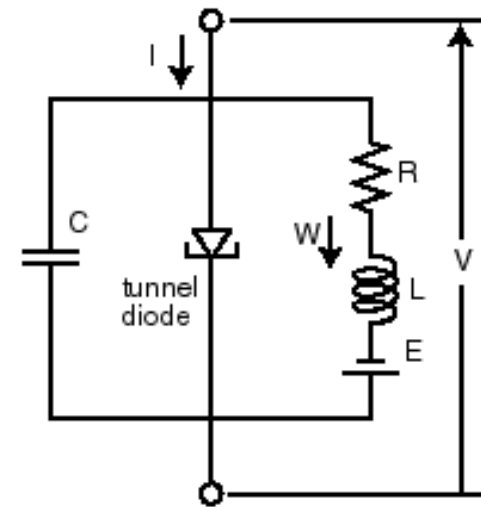
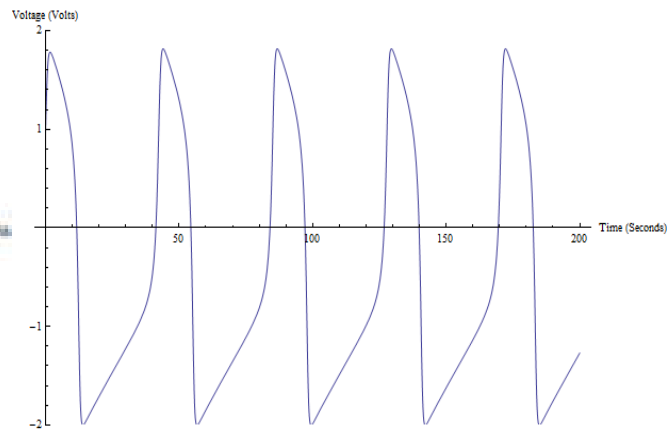
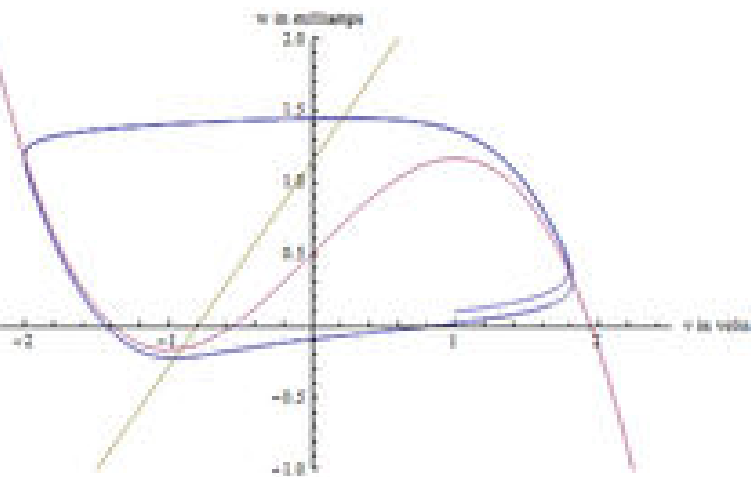
- Un model de ordin redus (doar cu 2 variabile de stare) din 1961

https://en.wikipedia.org/wiki/FitzHugh%E2%80%93Nagumo_model

$$dV/dt = f(V) + W + I \quad = \quad V - V^3/3 - W + I \text{ in particular}$$

$$dW/dt = a(b + V - cW) \quad = \quad 0.08(V + 0.7 - 0.8W)$$

- Cu toate ca nu este rezulta direct din biologie, permite descrierea simplificata a dinamicii neliniare, fara sa fie rudimentar



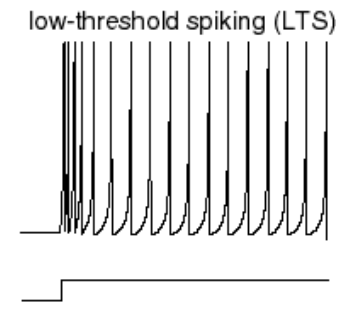
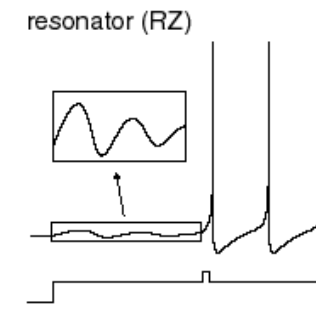
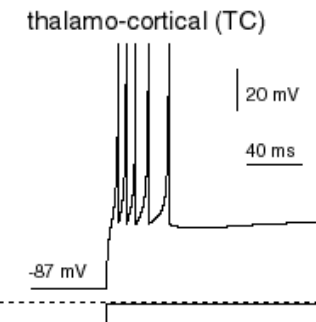
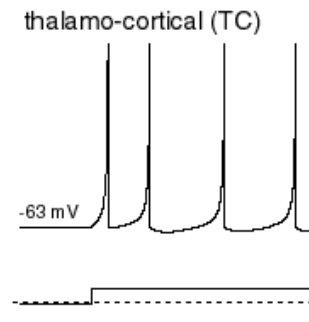
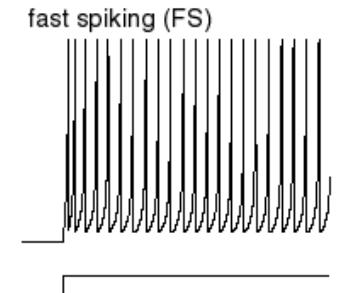
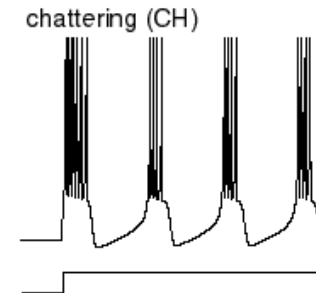
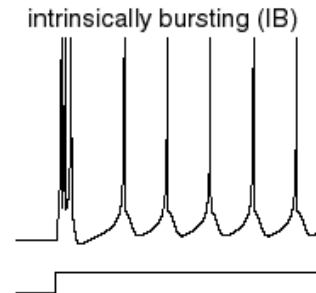
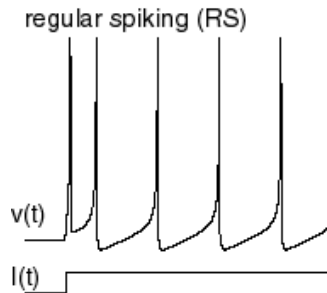
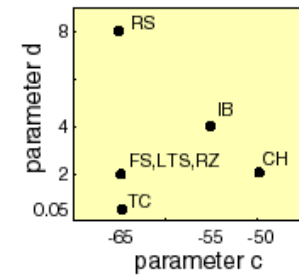
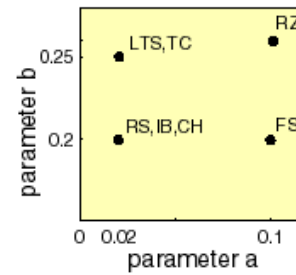
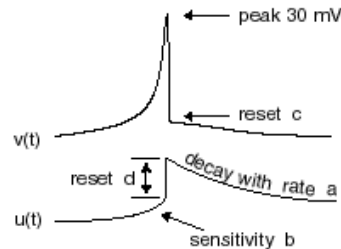
Modelul Izhikevich

- Este tot un model de ordin redus , nelinar de ordinul doi
<http://www.izhikevich.org/publications/spikes.htm>

$$v' = 0.04v^2 + 5v + 140 - u + I$$

$$u' = a(bv - u)$$

if $v = 30$ mV,
then $v \leftarrow c$, $u \leftarrow u + d$



3. Retele neuronale si simulatoare

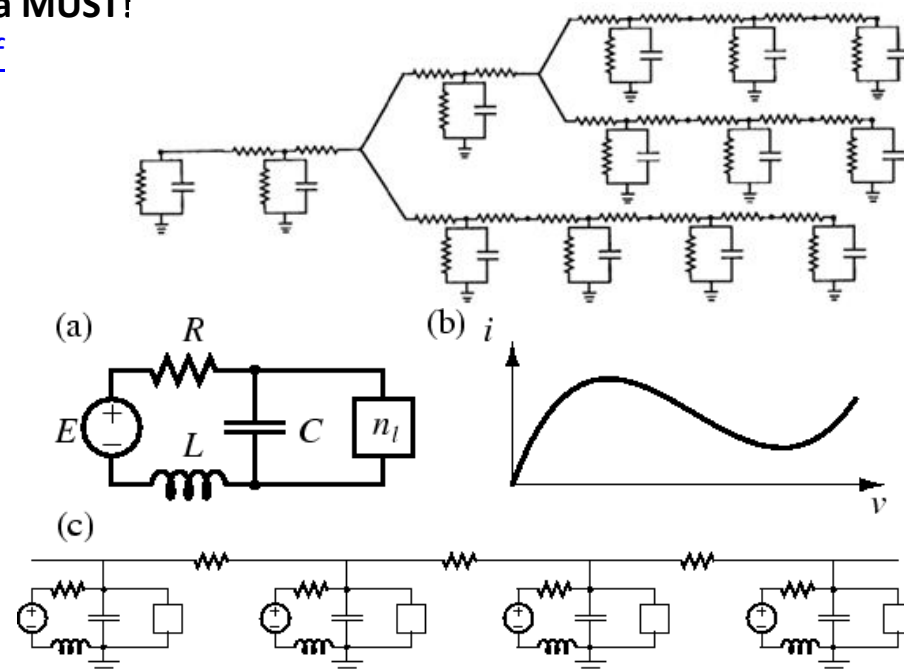
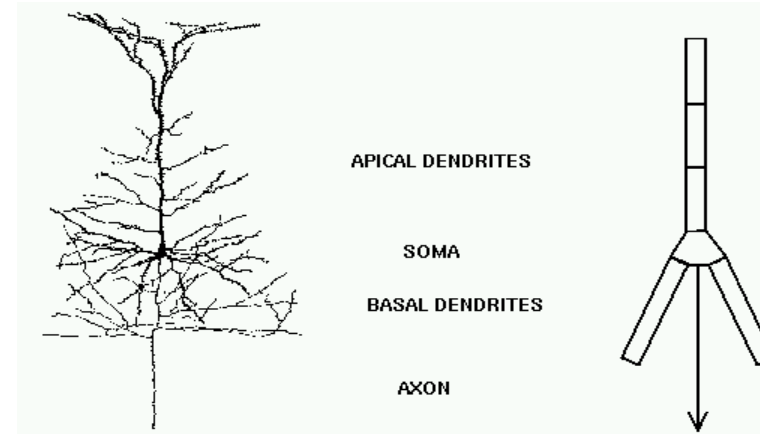
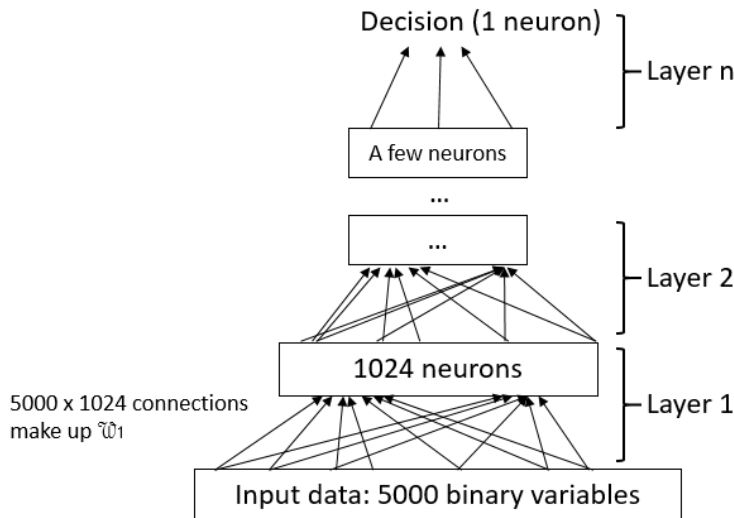
- Circuite electrice (analogice) alcatuite din subcircuite care reprezinta modele interconectate ale segmentelor de neuroni si ale sinapselor

http://www.iact.ugr-csic.es/personal/julyan_cartwright/papers/diversity/node2.html

- Pot fi liniare (imprecise, deoarece nu descriu generarea/conditionarea impusurilor) sau nliniare (mai realiste biologic)
- Simularea lor presupune rezolvarea unor sisteme ODE de mari dimensiuni, fiecare segment introduce 2-4 variabile de stare
- Alegerea segmentelor si comasarea lor este legata de MOR
- Automatic (euristic?!) extraction of **reduced model it's a MUST!**

http://www.caam.rice.edu/tech_reports/2009/TR09-05.pdf

(DEI – MOR for nonlinear systems)

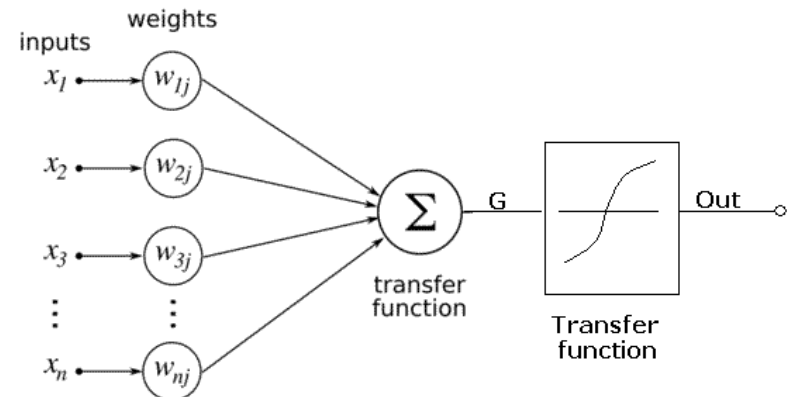
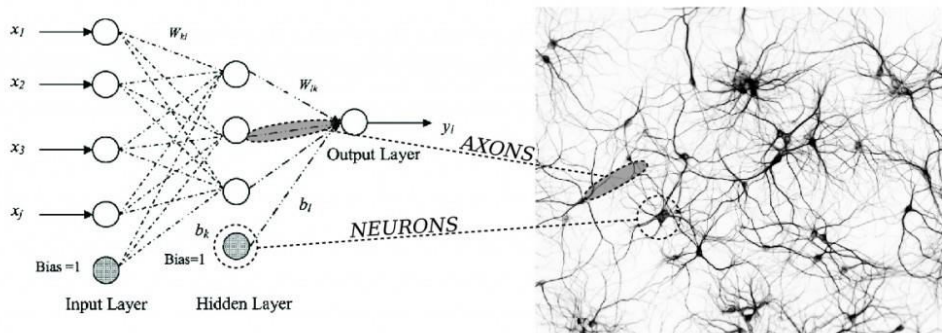


Retele neurale biologice vs artificiale

BNN-ANN

- **ANN** sunt o punte între Biofizica (computational neuroscience) și Informatica (nature inspired AI soft-algorithms, unde ANN sunt abstractizate – sumare ponderată și saturare, cu unul sau mai multe straturi ascunse - [McCulloch & Pitts](#) - 1943)
- **Caracteristici ANN abstracte (AI):**
 - Caracterul universal al ANN (http://en.wikipedia.org/wiki/Universal_approximation_theorem Cybenko theorem)
 - Capacitatea de a clasifica/recunoaște https://en.wikipedia.org/wiki/Artificial_neural_network
 - Capacitatea de a învăța (independenți și supervizat – backpropagation sau prin repetiție) <https://en.wikipedia.org/wiki/Backpropagation>
 - Permite înțelegerea riguroasă, teoretic-abstractă, în profunzime a funcționării sistemelor biologice neurale (mecanismele memorării, gândirii, învățării). S-au dezvoltat teorii matematice și algoritmi.
- **BNN** sunt mult mai complexe (au topologii arbitrare, care generează oscilații) și au fenomene mai complicate (plasticitatea sinaptică și nonsinaptică), care permit învățarea, memorarea și gândirea .

NEURAL NETWORK MAPPING



Simulare BNN/ANN

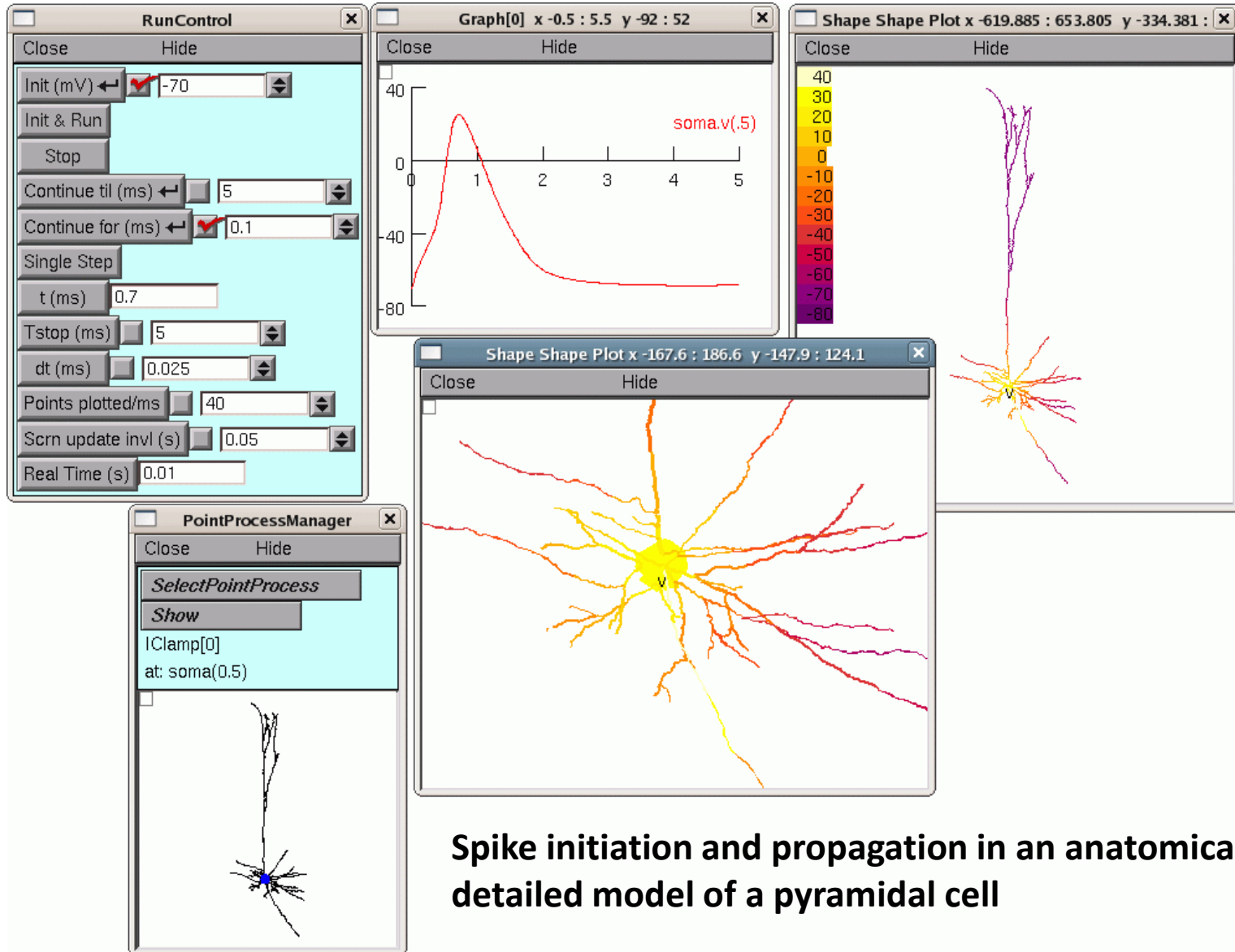
- **Comparatie intre simuiloare** disponibile (cca 50 din care 23 pentru neuroni bio):
https://grey.colorado.edu/emergent/index.php/Comparison_of_Neural_Network_Simulators
- Pentru fiecare sunt date:
 - Publications
 - Release history
 - License
 - Platforms
 - Community
 - Language
 - Focus
 - Coding Style
 - Virtual environment
 - [Backpropagation](#)
 - [Self Organizing](#)
 - [Constraint Satisfaction](#)
 - Supported Neurons
 - Parallel Computing
- **Medii software** (biblioteci de functii specializate, tools) pentru dezvoltarea de solutii si aplicatii de neurostiinte comutationale:
 - How to code a neural network simulation in MATLAB
http://www.mjrlab.org/wp-content/uploads/2014/05/CSHA_matlab_2012.pdf
 - Biological Neural Networks (BNNs) Toolbox for MATLAB: User Guide
<http://www.ymer.org/research/files/bnntoolbox/ver1.1/BNNToolbox.pdf>
 - Spiking Neurons simulator in MATLAB
<http://www.mathworks.com/matlabcentral/fileexchange/25931-spiking-neurons-simulator>

Simulatoare BNN: NEURON

<http://www.neuron.yale.edu/neuron/>

- **Un simulator puternic si felexibil de neuroni si retele neurale**
- **Separa aspectele biologice de cele computationale:** permite lucrul cu concepte familiare, utilizatorul poate gandi in termeni biofizici, cu referire la proprietatile membranei si citoplasmei, morfologia neuronului, efectul sinapsei asupra celulei;
- **Eficienta computationala si flexibilitate numerica:** permite specificarea modelului fara referire la tehnica de simulare si integrare numerica, cu discretizare eficienta, automta, atat spatial cat si temporal. Aspectele matematice/numerice sunt separate.
- **O interfata convenabila cu utilizatorul: Text iterpretat (C-like and Python),** inclusiv pentru executii in paralel (optimizari si variatia parametrilor) **si Grafica – GUI** pentru descrierea diferitelor aspecte: the Channel Builder, The CellBuilder, The Import3D tool, The Linear Circuit Builder, The Network Builder, The ModelView tool, The Impedance tools ,The Multiple Run Fitter.
- **Biblioteca extensbila de utilizator pentru mecanisme biofizice**
- **Imbunatatirea modelarii retelelor: distribuirea evenimentelor, model genralizat pentru sinapse permitand plasticitatea lor** (use-dependent and/or spike-timing-dependent plasticity), variabile locale si globale, posibilitatea de a distribui reteaua neurala pe procesare cu executie paralela.
- **Baza larga de utilizatori ([1450 scientific articles and books](#))**
- **Bine documentat si suportat**
- **In domeniul public, open sources si ruleaza pe aproape orice sistem**

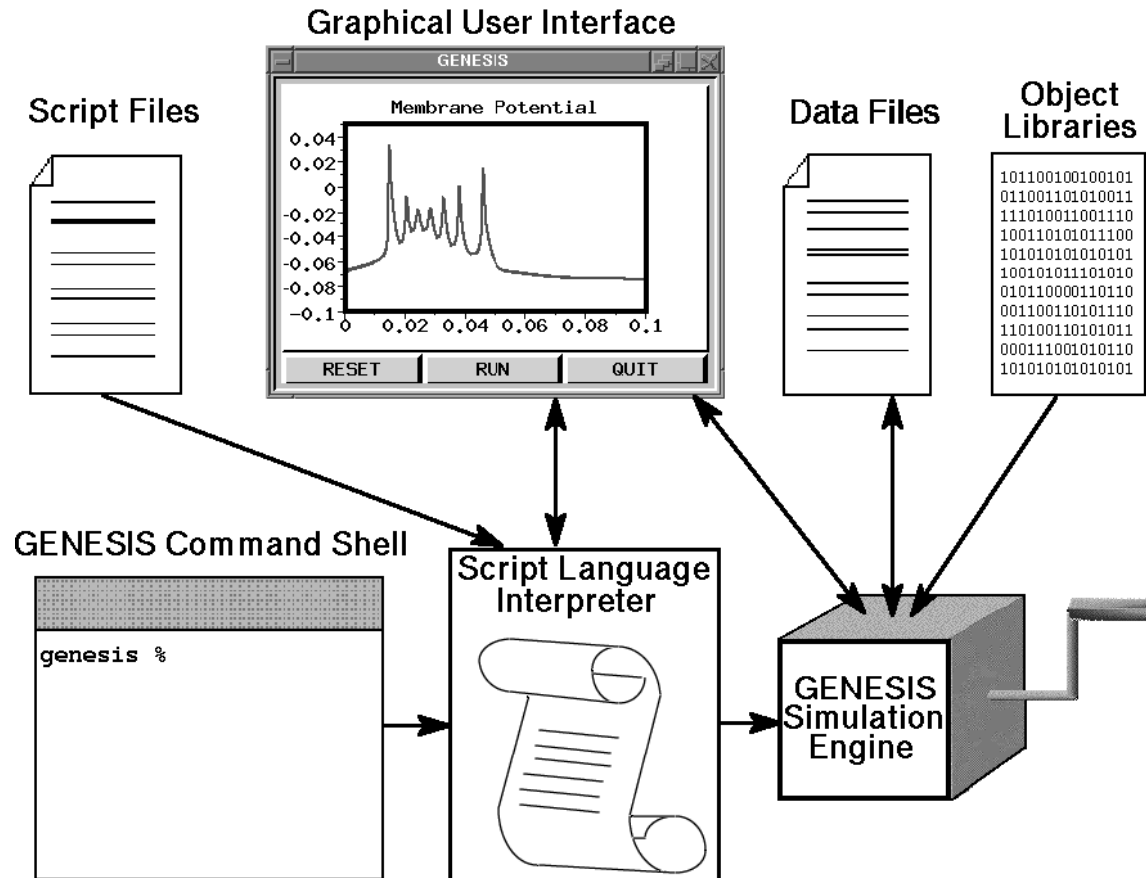
NEURON simulation Example



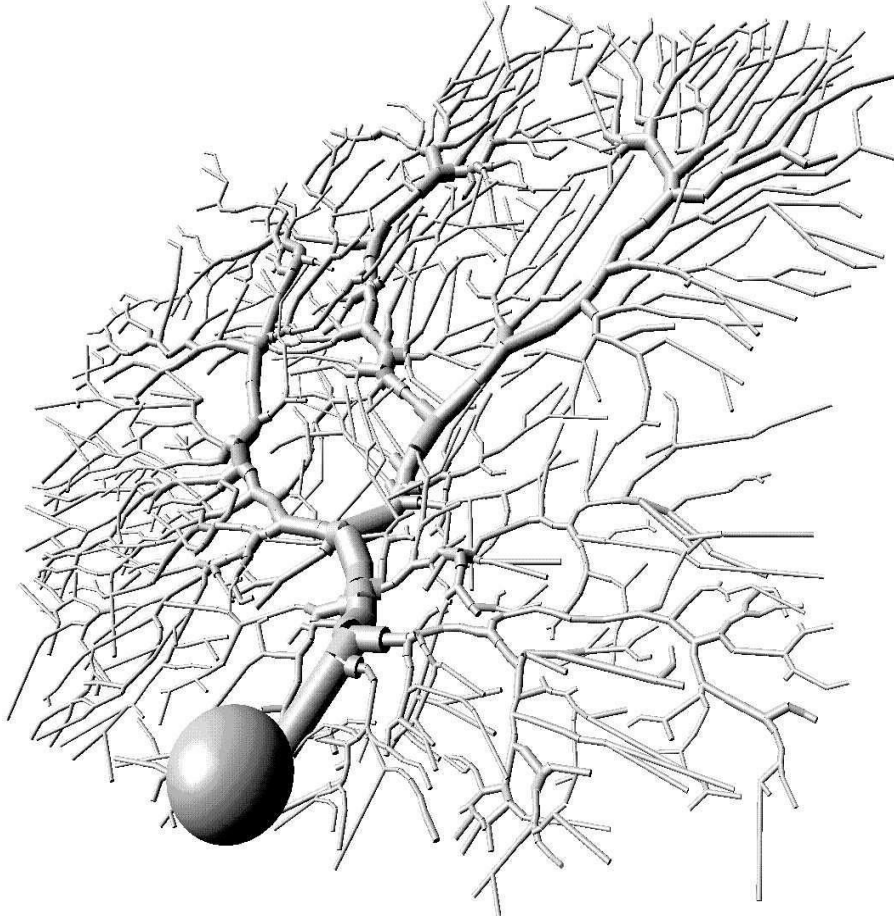
Spike initiation and propagation in an anatomically detailed model of a pyramidal cell

Simulatorul GENESIS

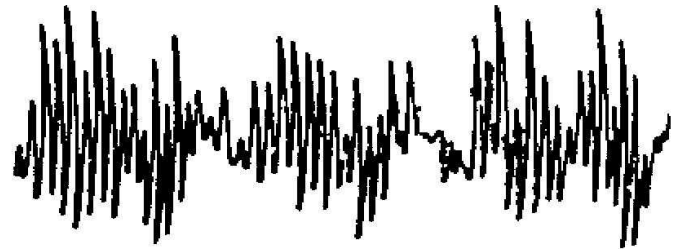
- <http://www.genesis-sim.org/GENESIS/>
- Simuleaza neuroni, retele neuronale si biochimice



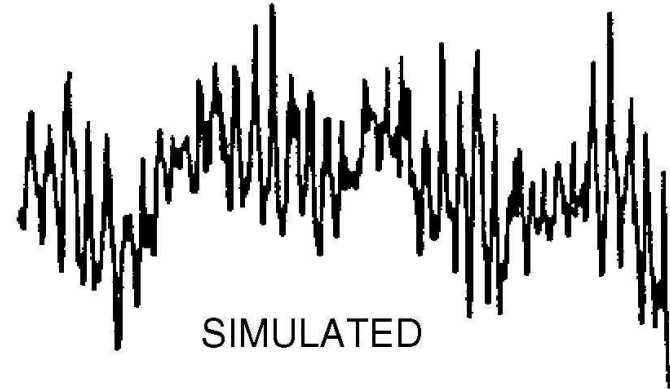
Exemple in GENESIS



Un model multi-comportamental detaliat al unei celule Purkinje (neuron din cerebel)



EXPERIMENTAL



SIMULATED

Comparatie intre EEG masurat si simulat pentru cortexul unui soarece

Merita reproduse in LMN!

<http://www.genesis-sim.org/GENESIS/iBoG/index.html>

Simulatorul NEST

<http://www.nest-initiative.org/> - pagina proiectului, pentru conceptie:

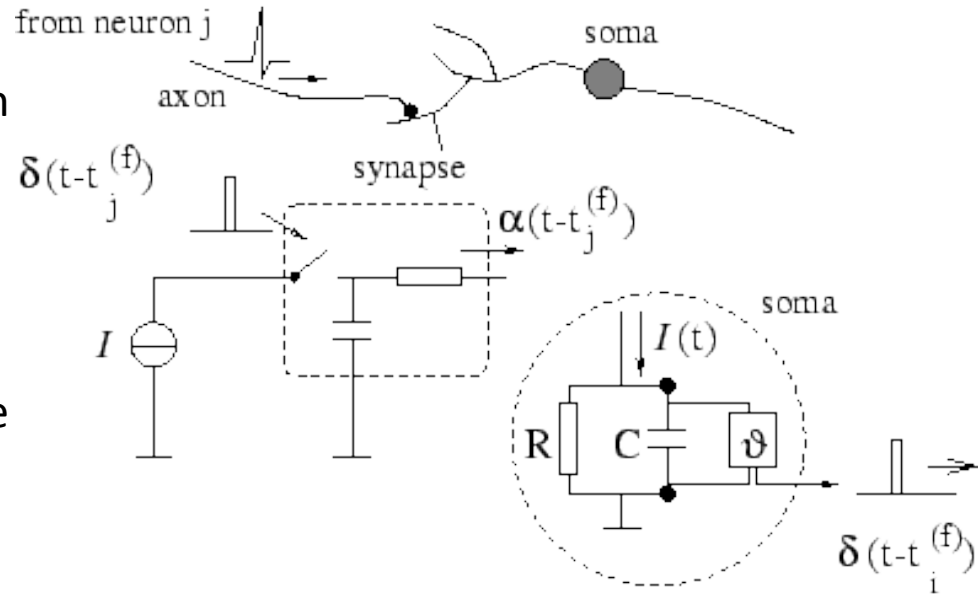
<http://www.nest-initiative.org/publications/Plotnikov2016.pdf>

[https://en.wikipedia.org/wiki/NEST_\(software\)](https://en.wikipedia.org/wiki/NEST_(software)) pentru functii.

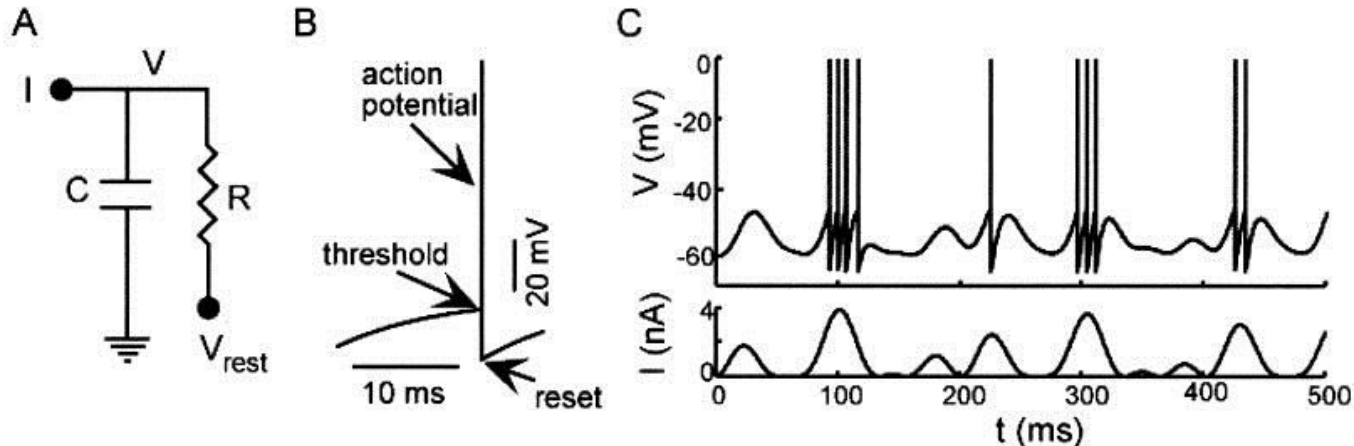
- **NEST este focalizat** pe dinamica, marimea si structura sistemului neural simulat, si mai putin pe geometria individuala a fiecarui neuron, permitand modelarea procesarii informatiei in retele mari cum sunt cortexul vizual sau cel auditor, analiza activitatii reteleor cu structura in straturi sau arbitrara, analiza sincronizarii in retelele de mari dimensiuni, si modelarea invatarii si a plasticitatii.
- Are o biblioteca de diverse **modele neuronale** si permite simularea **retelelor neurale** cu structura topologica data sau intamplatoare, retele orientate pe date
- **Modelarea sinapselor** cu permeabilitate si intarzieri omogene sau neomogene, cu plasticitate dependenta de timingul impulsurilor, cu efectul neuromodelatorilor
- **Permite modelarea diverslor dispozitive** cum sunt: detectorul de impulsuri, multimetre pentru indicarea potentialelor sau curenilor, genatoare de cureni de excitatie treapta, AC si DC, impuls si zgomot aleator.

Modelul integrate-and-fire

- Este un model foarte simplu: descrie integrarea sarcinii in corpul neuronului (in capacitatea C) si difuzia acestei prin membrana (prin rezistenta de pierderi R):
- $I(t) = u(t)/R + Cdu/dt$
- Cand tensiunea u atinge pragul theta, se emite un impuls si se reseteaza u
- Curentul injectat este suma curenților care sunt injectati prin diferite sinapse de neuronii presinaptici
- Fiecare sinapsa actioneaza ca un filtru trece jos de ordinul intai



<http://icwww.epfl.ch/~gerstner/SPNM/node26.html>



Spiking Neural Network (SNN)

Un nou nivel de abstractizare: circuite (Hopfield 95) similare cu cele digitale (functionand in impulsuri) alcatuite din:

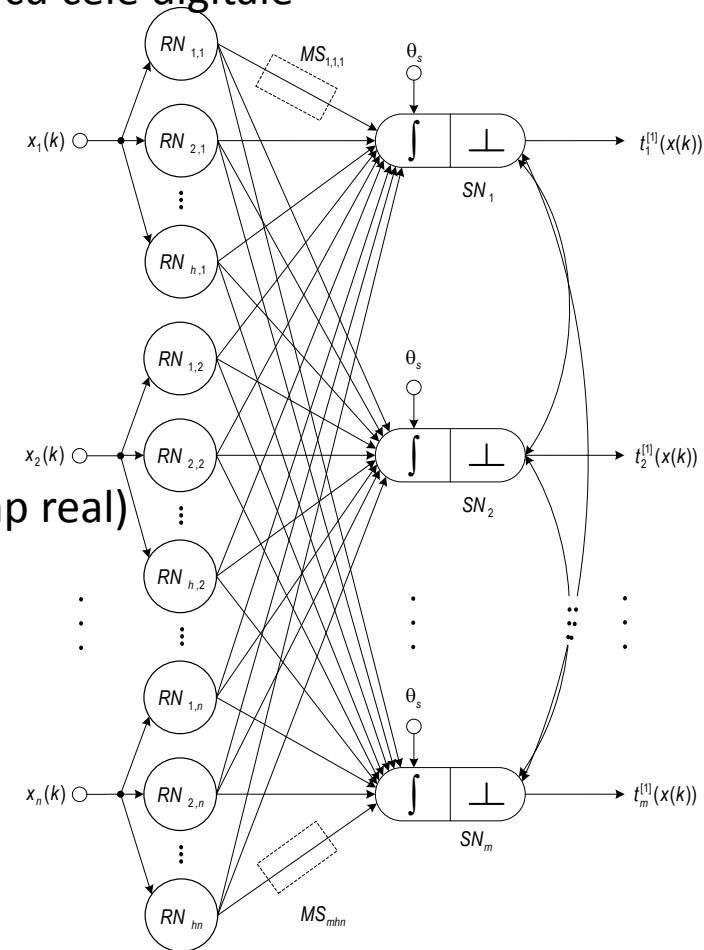
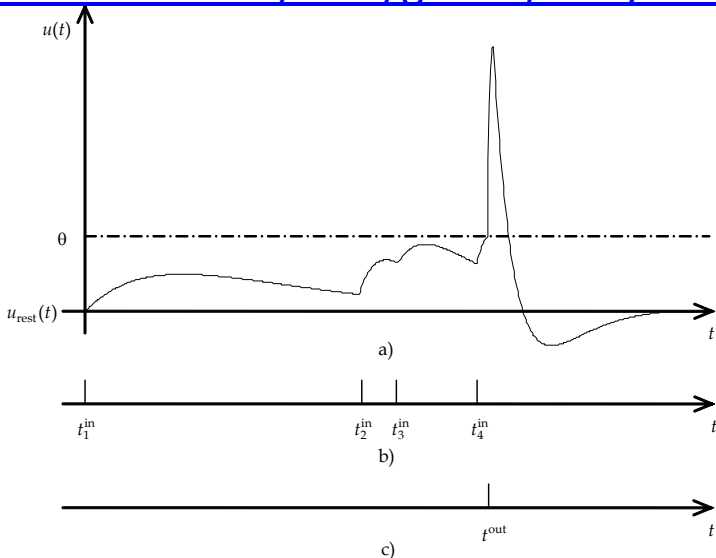
- SN - Spiking neurons
- MS - Multiple Synapses
- RN – Receptive Neurons

Functionare SN: primeste impulsuri, le integreaza cu pierderi si genereaza un puls la iesire. Ele sunt

- mult mai plauzibile biologic
- mai puternice computational (solutii AI mai bune)
- mai rapide (pot fi simulate 10 000 neuroni pe laptop in timp real)

decat ANN. **SNN alternativa superioara la ANN.**

iktdk.dcc.ttu.ee/data/guests/Bodyanskiy_2011/lecture7.ppt

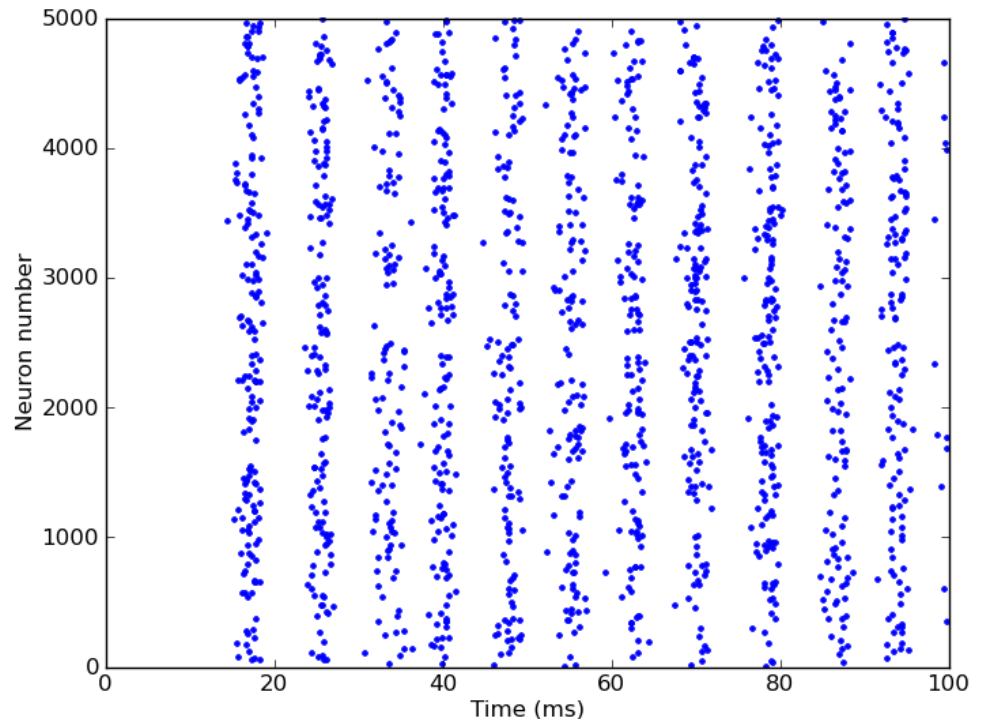


Spiking Neuron Models, Single Neurons, Populations, Plasticity [Wulfram Gerstner](http://www.wulframgerstner.com) and [Werner M. Kistler](http://www.werner-kistler.com):
<http://lcn.epfl.ch/~gerstner/SPNM/SPNM.html>

Brain: un simulator SNN

- <http://briansimulator.org/>
- Simulator pentru rețele SNN de mari dimensiuni
- **Exemplu:** rețea de 5000 neuroni (interconectați rar 1/5, aleator), care se sincronizează într-o oscilație globală. Descrisă doar de 20 de comenzi.

```
from brian import *
# Network parameters
N = 5000; ...
# Neuron model
eqs = "dV/dt=(-V+muext+sigmaext*
sqrt(tau)*xi)/tau : volt" ....
# Connections
conn = Connection(group, group, state='V',
....
# Monitors
M = SpikeMonitor(group)
# Run
run(duration)
# Plot
raster_plot(M)
show()
```



Demo simulari SNN

- Retea simpla cu patru straturi si 7 neuroni pe strat

<https://www.youtube.com/watch?v=IhIdisK7akI>

- Retea cu 200 neuroni cu structura amorfa, 80% excitati si 20% inhibati, intarzierea proportionala cu distanta parcursa

<https://www.youtube.com/watch?v=QhKsz-BWJHE>

- Retea multistrat de mari dimensiuni (coloana corticala)

<https://www.youtube.com/watch?v=T2aZAWXyw6c>

<https://www.youtube.com/watch?v=T4bXnSiANAs>

- Turnurile din Hanoi rezolvate de o SNN

<https://www.youtube.com/watch?v=sUvHCs5y0o8>

- Recunoasterea numerelor cu SNN

<https://www.youtube.com/watch?v=2j9rRHChXk>

- Invata sa conduca o masina

<https://www.youtube.com/watch?v=5lJuEW-5vr8>

- Simularea hipocampusului de soarece

<https://www.youtube.com/watch?v=rrM1aStW2lc>

- Simularea sistemului cortico-talamic uman folosind 1.4 milioane neuroni si 127 milioane de sinapse. (**Hobbyivan @dimkovic.com**)

<https://www.youtube.com/watch?v=Yq7d4ROvZ6I>

<https://www.youtube.com/watch?v=33K1zTtoow> 8 milioane neuroni din retina si cortexul vizual

4. Modele neurale cu parametri distribuiti (1D)

- Permit determinarea cu acuratete a **distributiei spatiale a potentialului** si a **timpului de de intarziere** a semnalului transmis de-a lungul axonului si dendritelor, prin descrierea propagarii longitudinale.
- Cele mai simplu model de acest tip este cel ale **liniei de transmisie liniara** (“cable model”), care nu iau in considerare fenomenele neliniare din membrana (canalele ionice si amorsarea neuronului).
- In acest model, **membrana** este modelata ca o folie dielectrica izolant imperfect, iar **citoplasma** ca un conductor slab, in timp ce **lichidul exterior** celulei ste considerat de conductivitate foarte mare.
- Deoarece variatia in timp este relativ lenta, se neglijeaza efectul inductiei electromagnetice (deci si campul magnetic si efectele sa). In consecinta regimul campului este cel **EQS**.
- Din punct de vedere **geometric** asimilam segmentul studiat cu un cilindru de diametru D si lungime L , inconjurat de membrana de grosime $t \ll D$. Problema are simetrie axiala (**2.5D**), dar daca vom considera ca fiecare plan transversal este echipotential, solutia problemei $V(x,t)$, va depinde doar de coordonata longitudinala x si de timpul t , ceea ce insemana ca din punct de vedere spatial, problema este **1D**.
https://en.wikipedia.org/wiki/Cable_theory
http://www.scholarpedia.org/article/Neuronal_cable_theory

Regimul EQS al campului el-mg

- Ipoteze:**

- Corpuri imobile
- Se neglijeaza efectul inductiei el-mg

- Ecuatii:**

$$\left\{ \begin{array}{l} \text{div} \mathbf{D} = \rho; \quad \text{rot} \mathbf{E} = 0; \quad \text{div} \mathbf{J} = -\frac{\partial \rho}{\partial t} \\ \mathbf{D} = \varepsilon \mathbf{E} + \mathbf{P}_p \quad (\mathbf{P}_p = 0); \quad \mathbf{J} = \sigma(\mathbf{E} + \mathbf{E}_i) \end{array} \right.$$

- Ecuatii de ordinul doi (pentru potential)**

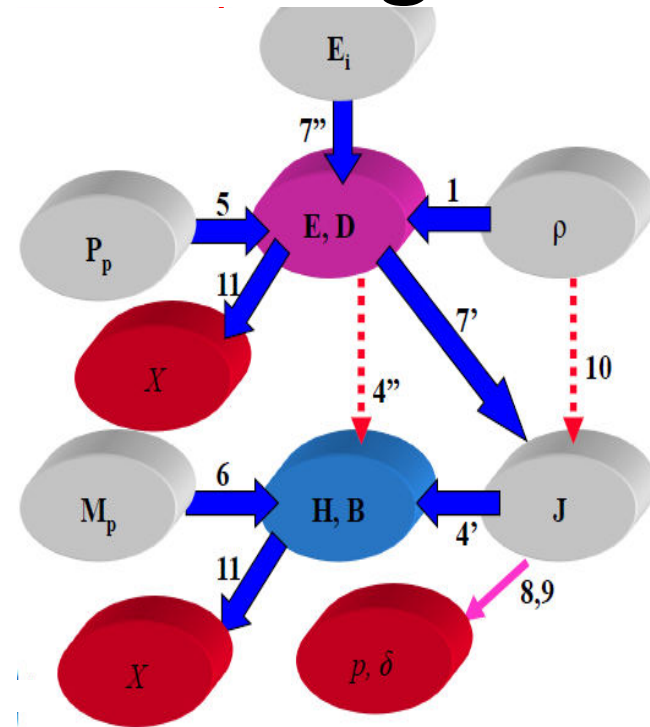
$$\text{div} \mathbf{D} = \rho; \quad \text{rot} \mathbf{E} = 0 \Rightarrow \mathbf{E} = -\text{grad} V$$

$$\text{div} \mathbf{J} = -\frac{\partial \rho}{\partial t} \Rightarrow \text{div}(\sigma \mathbf{E} + \mathbf{J}_i) + \text{div} \frac{\partial(\varepsilon \mathbf{E})}{\partial t} = 0 \Rightarrow$$

$$\mathbf{D} = \varepsilon \mathbf{E}; \quad \mathbf{J} = \sigma(\mathbf{E} + \mathbf{E}_i) \Rightarrow \mathbf{J} = \mathbf{J}_i - \sigma \text{grad} V; \quad \mathbf{J}_i = \sigma \mathbf{E}_i$$

- Formulara corecta a problemei de analiza, nec.: $V(M, t), M = M \in \Omega, t \in (0, T)$ date:**

- Domeniul de calcul Ω
- Caracteristicile de material: $\varepsilon(M), \sigma(M); M \in \Omega$
- Sursele interne : $\mathbf{E}_i(M, t); M \in \Omega, t \in (0, T)$
- Conditii de frontiera: $V(M, t) = f_D(M, t)$ sau $dV / dn = f_N(M, t); M \in \partial\Omega, t \in (0, T)$
- Conditii initiale: $V(M, 0) = V_0(M); M \in \Omega$

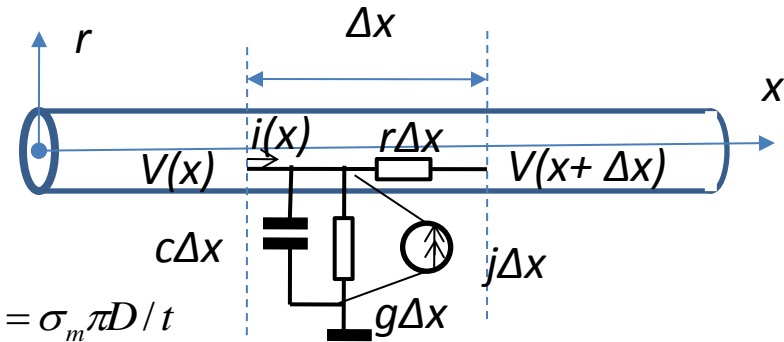


$$\text{div} \left(\sigma \text{grad} V + \varepsilon \text{grad} \frac{\partial V}{\partial t} \right) = \text{div} \mathbf{J}_i$$

Ecuatiile liniei de transmisie RC

Segmentul omogen este caracterizat de:

- Capacitatea lineica: $c = C/L = \varepsilon\pi D/t$
- Rezistenta lineica: $r = R/L = 4/(\sigma_c\pi D^2)$
- Conductanta lineica a membranei $g = G/L = \sigma_m\pi D/t$
- Curentul lineic imprimat de membrana $j = J_i\pi DL/L = \sigma_m E_i\pi D$



K1 si K2 pe segmentul Δx :

cu $r = 6 \text{ MOhm/mm}$, $c = 2 \text{ pF/mm}$, $g = 1/290 \text{ mS/mm}$, $j=0$

$$i(x) = i(x + \Delta x) + g \cdot \Delta x \cdot V(x) - j(x) \cdot \Delta x + c \cdot \Delta x \Rightarrow \frac{dV(x)}{dt} \Rightarrow \frac{\partial i}{\partial x} = g \cdot V(x, t) + c \cdot \frac{\partial V}{\partial t} - j(x)$$

$$V(x) - V(x + \Delta x) = r \cdot \Delta x \cdot i(x + \Delta x) \Rightarrow \frac{\partial V}{\partial x} = r \cdot i(x, t) \Rightarrow \frac{1}{r} \frac{\partial^2 V}{\partial x^2} = g \cdot V(x, t) + c \cdot \frac{\partial V}{\partial t} - j(x)$$

$$\Leftrightarrow \lambda^2 \frac{\partial^2 V}{\partial x^2} = \cdot V(x, t) + \tau \frac{\partial V}{\partial t} - j(x) / g \quad \tau = c / g = 0.6 \mu\text{s}, \lambda = 1 / \sqrt{r \cdot g} = 223 \mu\text{m}$$

Sunt PDE de tip parabolic, de difuzie si nu pe propagare

Conditii initiale: $V(x, 0) = V_0 = -70 \text{ mV}$, Conditii la limita: $V(0, t) = e(t)$, $dV(L, t)/dx = 0$.

Unde $e(t)$ este un impuls neural standard aproximat ca $e(t) = V_0 + V_m (e^{-t/\tau_1} - e^{-t/\tau_2})$

Timotin a folosit acest model pentru a demonstra optimalitatea mielinizarii.

http://www.acad.ro/sectii2002/proceedings/doc1_2004/09_timotin.pdf

Solutia prin transformata Laplace

$$\frac{d^2V}{dx^2} = r(g + sc) \cdot V(x, s) - rc \cdot V_0 \Rightarrow V(x, s) = \frac{c \cdot V_0}{(g + sc)} + C_1 sh(\lambda x) + C_2 sh(\lambda(x - L)); \lambda = \sqrt{r(g + sc)};$$

$$\text{verificare : } C_1 sh(\lambda x) + C_2 sh(\lambda(x - L)) = \frac{1}{r(g + sc)} (r(g + sc) \cdot V(x, s) - rc \cdot V_0) = V(x, s) - \frac{V_0}{(s + g/c)}$$

$$x = 0 \Rightarrow V(0, s) = \frac{V_0}{(g + s + g/c)} - C_2 sh(\lambda L) = E(s) = \mathcal{L}(e(t)) \Rightarrow C_2 = \left(-E(s) + \frac{V_0}{(s + g/c)} \right) / sh(\lambda L);$$

$$x = L \Rightarrow \frac{dV}{dx} = C_1 \lambda ch(\lambda x) + C_2 \lambda ch(\lambda(x - L)) = C_1 \lambda ch(\lambda L) + C_2 \lambda = 0 \Rightarrow C_1 = -C_2 / ch(\lambda L)$$

$$V(x, s) = \frac{V_0}{(g + s + g/c)} + \frac{\left(-E(s) + \frac{V_0}{(s + g/c)} \right)}{sh(\lambda L)} \left(-\frac{1}{ch(\lambda L)} sh(\lambda x) + sh(\lambda(x - L)) \right) \Rightarrow$$

$$V(L, s) = \frac{V_0}{(s + g/c)} + \frac{1}{ch(\lambda L)} \left(E(s) - \frac{V_0}{(g + s + g/c)} \right) = \frac{E(s)}{ch(\lambda L)} + \frac{V_0(1 - 1/ch(\lambda L))}{(s + g/c)}$$

$$t \rightarrow 0 \Rightarrow s \rightarrow \infty; \lambda \rightarrow \infty; V(x, t) \rightarrow V_0$$

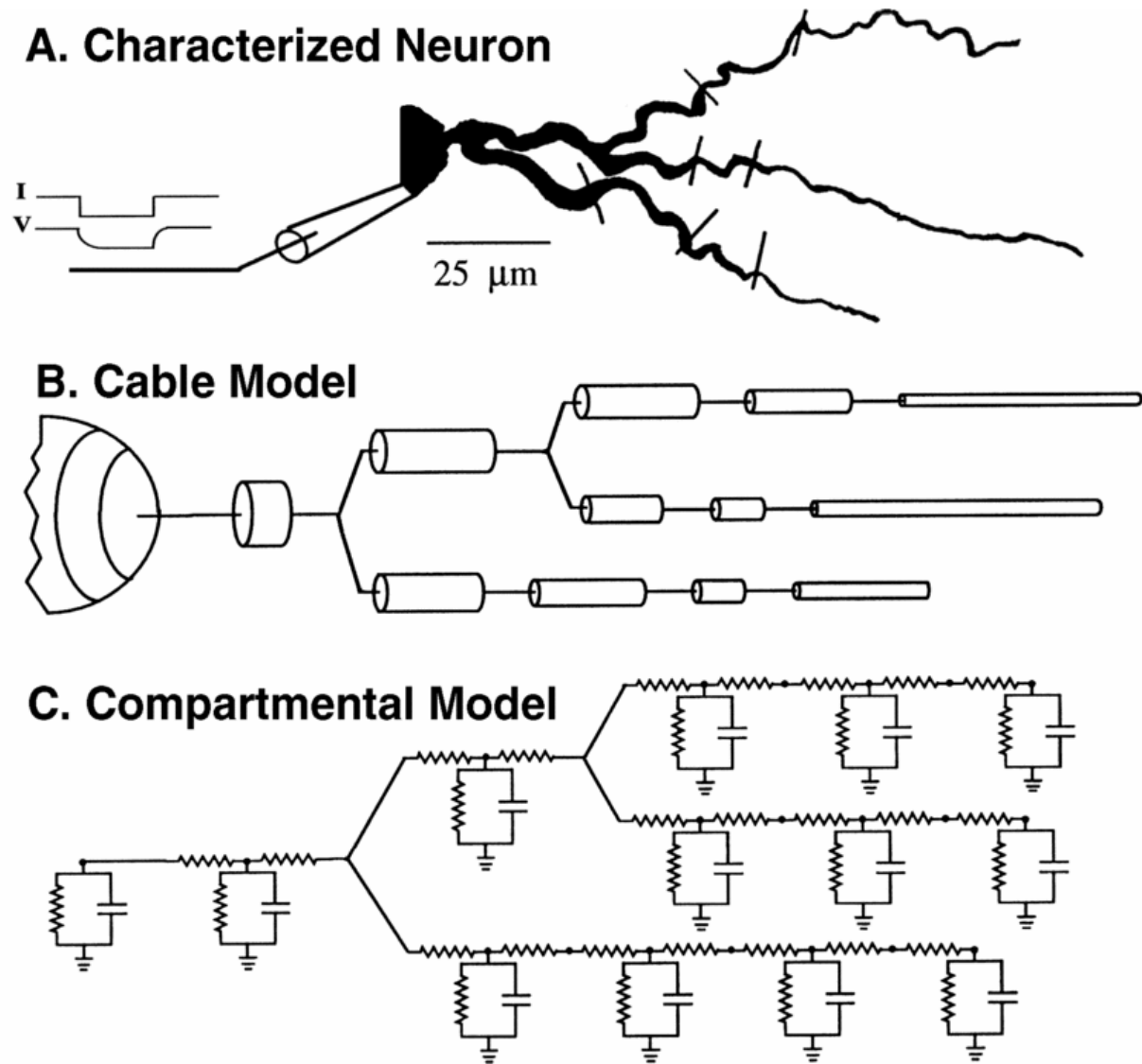
$$t \rightarrow \infty \Rightarrow s \rightarrow 0; \lambda \rightarrow \sqrt{rg}; V(x, t) \rightarrow V_0 / ch(L\sqrt{rg})$$

$$e(t) = V_0 + V_m (e^{-t/\tau_1} - e^{-t/\tau_2}) \Rightarrow E(s) = \frac{V_0}{s} + V_m \left(\frac{1}{s + 1/\tau_1} - \frac{1}{s + 1/\tau_2} \right)$$

Modele comportamentale (compacte)

De regula modelele RC distribuite se aproximeaza cu modele RC compacte, folosind segmentarea sau reducerea ordinului

Aici grafice de variatie in timp, pentru modelul de linie si cel compact. Compartie timpi de simulare



Model neliniar cu parametri distribuiti

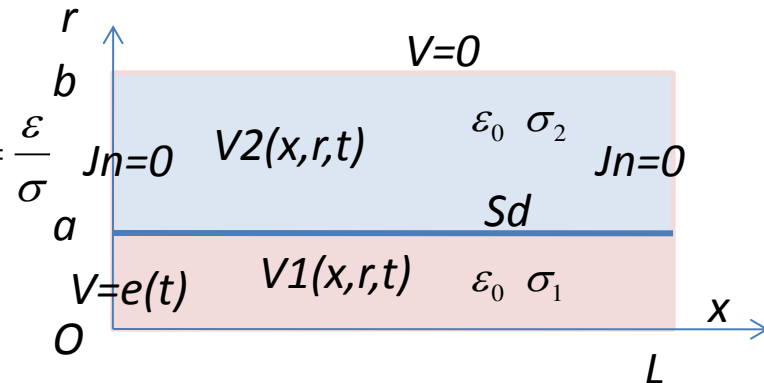
2D

- Se vor modela atat citoplasma cat si membrana si lichidul extracelular
- Modelul geometric: unul axisimetric, cu segmentul de axon/dendrita un cilindru de lungime finita, membrana o suprafata de discontinuitate S_d (de grosimea neglijabila $t \rightarrow 0$, cu conditii de trecere de tip operator de admitanta neliniara), iar exteriorul o coaja cilindrica
- Regimul campului EQS cu $\varepsilon = \varepsilon_0, \sigma = \sigma_1$ sau σ_2 constante pe subdomenii
- Conditii de frontiera: Dirichlet nule pe suprafata cilindrica laterala, Neuman nule pe cele doua capace cu exceptia urmei citoplasmei, unde conditiile sunt de tip Dirichlet nenule (impuls neural standard)
- Conditii initiale $V_1 = V_0 = -70\text{mV}$ in interior si $V_2 = 0$ in exterior
- Ecuatia EQS in medii omogene:

$$\text{div}\left(\sigma \text{grad} V + \varepsilon \text{grad} \frac{\partial V}{\partial t}\right) = \text{div} \mathbf{J}_i = 0 \Rightarrow \Delta\left(V + \tau \frac{\partial V}{\partial t}\right) = 0, \tau = \frac{\varepsilon}{\sigma}$$

$$\Delta U = 0, \text{ cu } U = V + \tau \frac{\partial V}{\partial t};$$

$$\mathbf{J}_t = \mathbf{J} + \mathbf{J}_d = \sigma \mathbf{E} + \frac{\partial \mathbf{D}}{\partial t} = -\text{grad}\left(\sigma V + \varepsilon \frac{\partial V}{\partial t}\right) = -\sigma \text{grad} U$$



Formulara matematica

$$U(x, r, t) = \begin{cases} U_1; & \text{pt } 0 < r < a; \text{ cu } \Delta U_1 = 0 \\ U_2; & \text{pt } a < r < b; \text{ cu } \Delta U_2 = 0 \end{cases}$$

- La trecerea prin membrana:

$$\mathbf{n} \cdot (\mathbf{J}_{t2} - \mathbf{J}_{t1}) = 0 \Rightarrow \sigma_1 \frac{dU_1}{dr} = \sigma_2 \frac{dU_2}{dr}$$

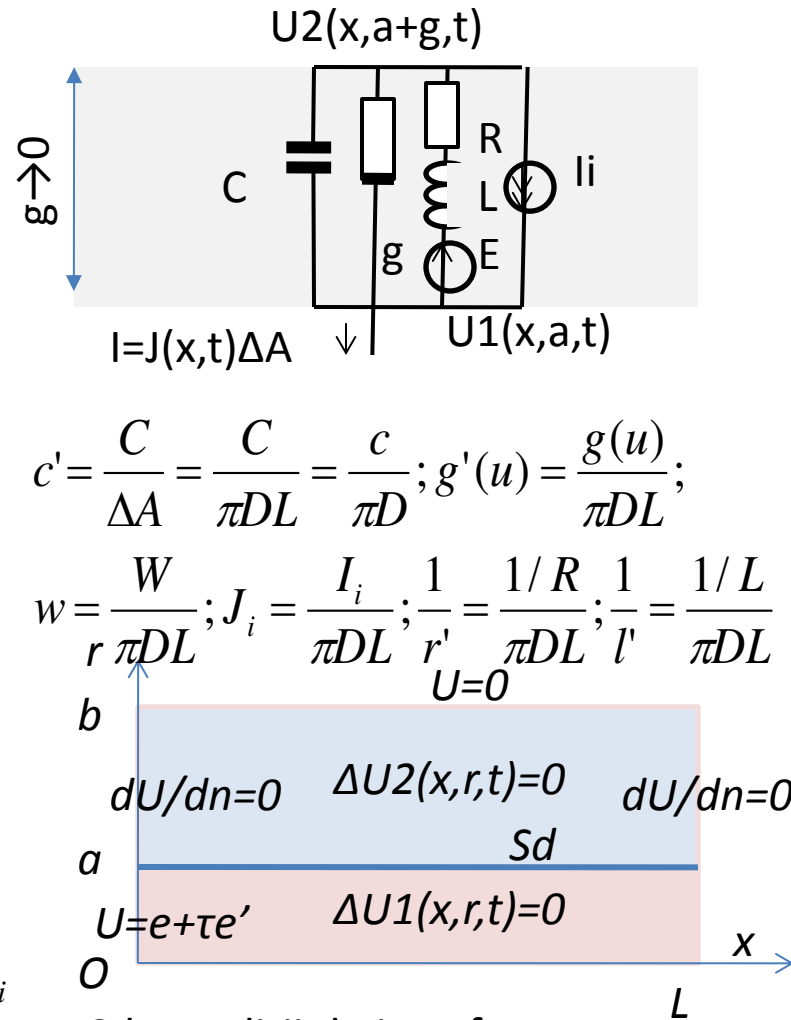
$$u = V_2(x, a, t) - V_1(x, a + g, t) \Rightarrow U_2 - U_1 \cong u + \tau \frac{\partial u}{\partial t};$$

$$i = J_{nt} \Delta A = C \frac{du}{dt} + g(u) + W + I_i \Rightarrow$$

$$J_{nt} = c' \frac{du}{dt} + g'(u) + w + J_i; \quad J_{nt} = \eta u$$

$$u = RW + LdW/dt + E = r' \frac{dw}{dt} + l'w + E \Rightarrow$$

$$\begin{cases} c' \frac{du}{dt} = -g'(u) - w + J_{nt} - J_i \\ r' \frac{dw}{dt} = u - l'w - E \end{cases} \Leftrightarrow \begin{cases} \frac{du}{dt} = f(u) + w + I_i \\ \frac{dw}{dt} = au + bw + c \end{cases}$$



Pe Sd : conditii de interfata cu operator nelinier de admitanta superficiala.

Mielinizarea: operator parametric (de x)

Rezolvare

- Ecuatii Lapalce cu conditii de frontiera:

$$\begin{cases} \Delta U_1 = 0; \text{ cu } U_1(0, r, t) = e(t) + \tau_1 de / dt; dU_1(x, r, t) / dx = 0 \text{ pt } x = L \\ \Delta U_2 = 0; \text{ cu } dU_2(x, r, t) / dx = 0 \text{ pt } x = 0 \text{ si } x = L; U_2(x, b, t) = 0 \end{cases}$$

- Conditiiile de trecere:

$$\sigma_1 \frac{dU_1}{dr} = \sigma_2 \frac{dU_2}{dr} = J_{nt}$$

$$U_2 - U_1 \cong u + \tau \frac{\partial u}{\partial t}; \text{ cu } u \text{ solutie}$$

a ecuatiilor neliniare de stare:

$$\begin{cases} c' \frac{du}{dt} = -g'(u) - w + J_{nt} - J_i \\ r' \frac{dw}{dt} = u - l'w - E \end{cases}$$

- Cu operatorul Poincaré–Steklov (D2N) se obtine o conditie de frontiera de tip Robin generalizata pentru U1:

(https://en.wikipedia.org/wiki/Poincar%C3%A9%E2%80%93Steklov_operator)

$$\frac{dU_2}{dr} = \mathcal{P}_2(U_2) \Rightarrow \frac{\sigma_2}{\sigma_1} \mathcal{P}_2(U_2) = \frac{dU_1}{dr};$$

$$U_2 - U_1 = u + \tau \frac{\partial u}{\partial t} \Rightarrow \frac{\sigma_2}{\sigma_1} \mathcal{P}_2(u + \tau \frac{\partial u}{\partial t} + U_1) = \frac{dU_1}{dr}$$

Rezolvare numerica

- Potentialul se distribuie instantaneu spatial, deoarece satisface ec. Laplace
- Suprafata de discontinuitate se discretizeaza longitudinal in n noduri echidistante iar intervalul de timp in m noduri
- Solutia este data cu Green de vectorii u_1, d_1, u_2, d_2 potentialului si a derivatei sale dupa raza in nodurile suprafetei, la diferite momente de timp:

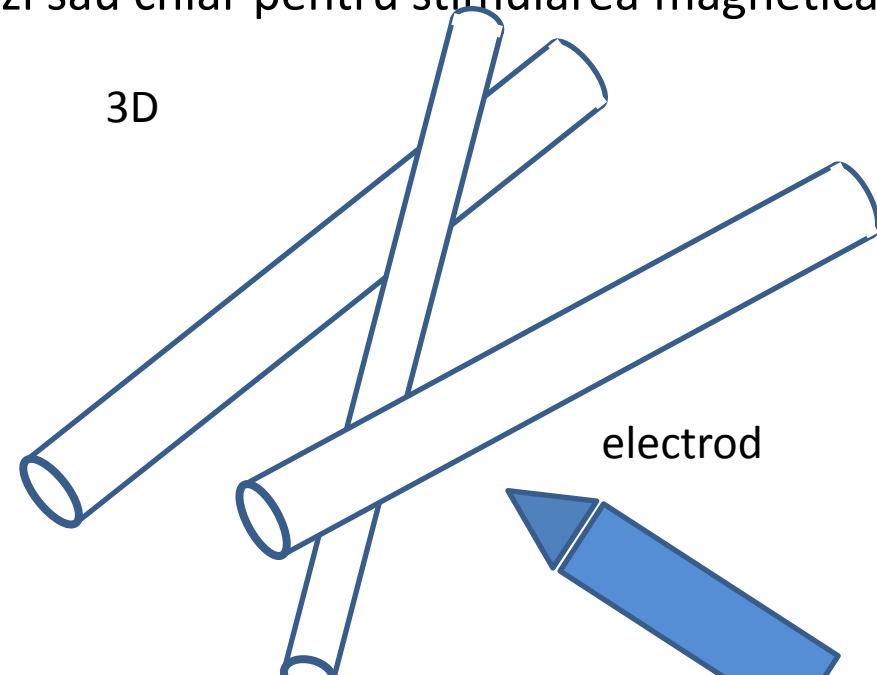
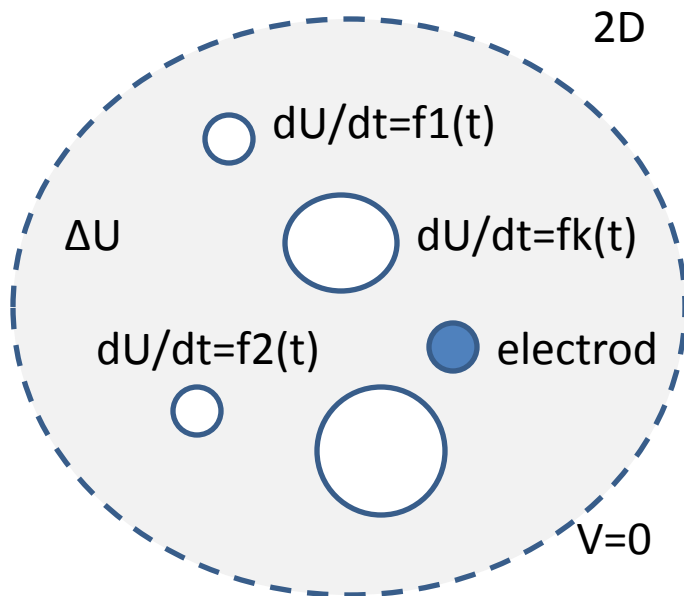
$$U_2(\mathbf{r}, t) = \int_{\partial\Omega} \left(U_2(\mathbf{r}') \frac{dG(\mathbf{r}, \mathbf{r}')}{dr'} - G(\mathbf{r}, \mathbf{r}') \frac{dU_2}{dr'} \right) ds = - \int_{S_d} G(\mathbf{r}, \mathbf{r}') \frac{dU_2}{dr'} ds \cong \mathbf{g}^t \cdot \mathbf{d}_1; V + \tau \frac{\partial V}{\partial t} = U_2 \Rightarrow V$$

- Se determina forma discreta a operatorului P-S rezolvand (analitic sau numeric) ecuatia Laplace in subdomenii: $d_2 = P_2 u_2; d_1 = P_1 u_1 + P_3 (e + \tau_1 e')$
cu $(\sigma_2 / \sigma_1) d_2 = d_1 \Rightarrow (\sigma_2 / \sigma_1) P_2 u_2 = P_1 u_1 + P_3 (e + \tau_1 e')$
- Se integreaza pas pas cele n ecuatii de stare si se obtine solutia u din care se determina u_1 la momentul curent, prin rezolvarea sistemului liniar:

$$\left((\sigma_2 / \sigma_1) P_2 - P_1 \right) u_1 = - (\sigma_2 / \sigma_1) P_2 \left(u + \tau \frac{\partial u}{\partial t} \right) + P_3 (e + \tau_1 e')$$

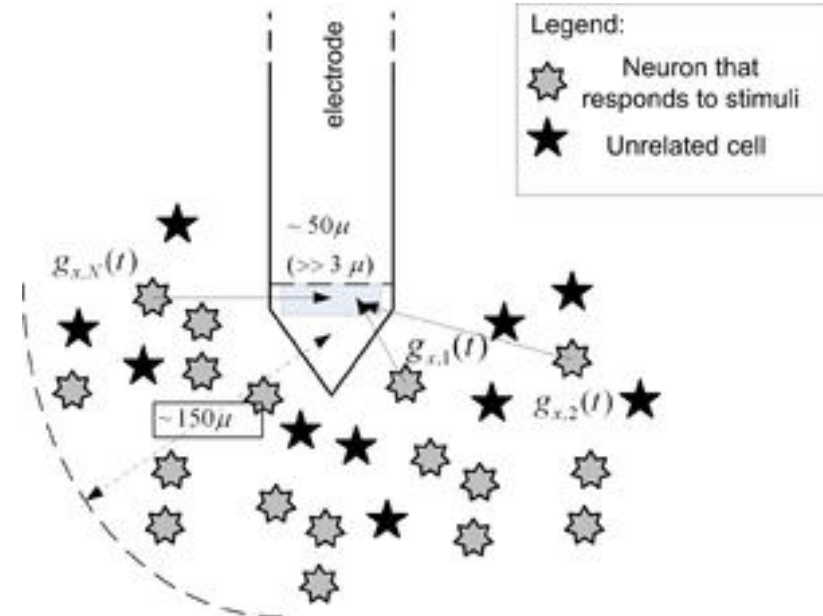
Modele 2D si 3D

- Metoda prezentata anterior se poate extinde pentru determinarea distributiei potentialului intr-o sectiune transversala a spatiului extracelular strabatut de axoni paraleli, prin rezolvarea unei probleme 2D. Potentialul satisface ecuatia Lapalce cu conditii nule pe frontiera (deschisa) fictiva si conditii Neumann nenule, rezultate in urma rezolvari ecuatiilor de stare ale membranelor fiecarui neuron.
- Rezultatul poate fi extrins si la cazul axonilor cilindrici cu orientari arbitrare, mielinizati sau nu, prin rezolvarea unei probleme 3D
- Solutiile acestor probleme sunt utile atat pentru a modela masurarii potentialului extracelular cu electrozi transcarnieni EEG, sau MEG dar si pentru modelarea stimularii neurale electrice cu microelectrozi sau chiar pentru stimularea magnetica



5. Verificarea modelelor

- Un model care nu poate fi validat nu are valoare
- Verificarea experimentală a rezultatelor simularilor neuronale se face de regula prin: clamping, EEG, MEG și fMRI și prin stimulare electrică sau magnetică.
- Dificultatea constă în faptul că paradigma clasică V&V nu poate fi aplicată deoarece sistemele neurale nu funcționează strict determinist ci stohastic
- <https://people.cs.umass.edu/~btaylor/publications/PSI000008.pdf> Verification and validation of neural networks: a sampling of research in progress
- Modelele cu parametri distribuiți, pentru potențialul extracelular sunt esențiale în validarea prin tehnici neinvazive



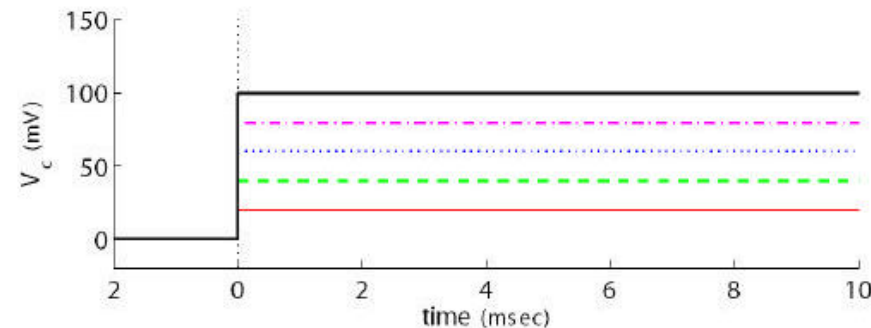
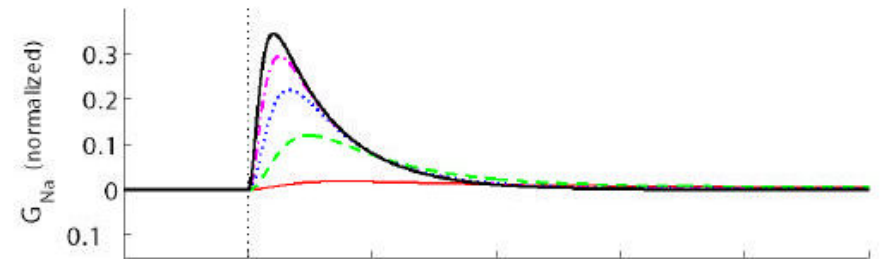
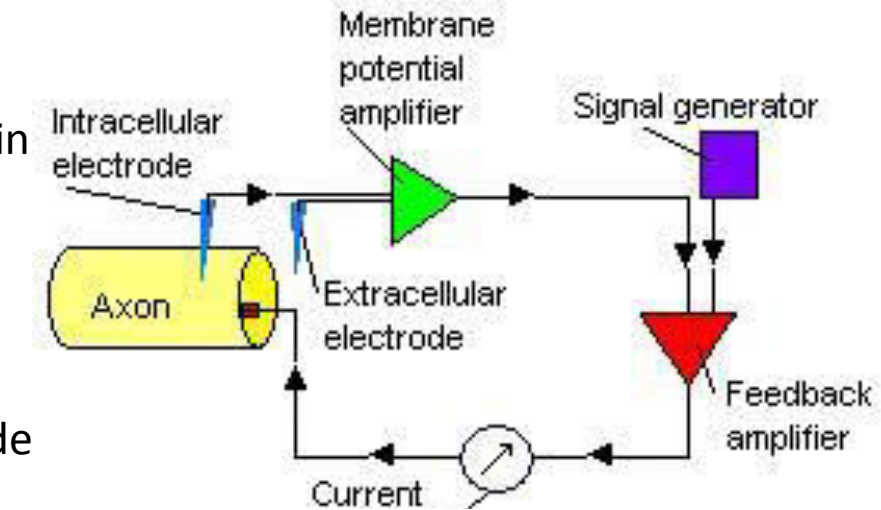
https://en.wikipedia.org/wiki/Biological_neuron_model

Pachete software dedicate procesării imaginilor și semnalelor neurologice:

<http://www.brainvoyager.com/bvqx/doc/UsersGuide/GeneralInfo/GettingStarted.html>

Tehnica agatarii (clamp)

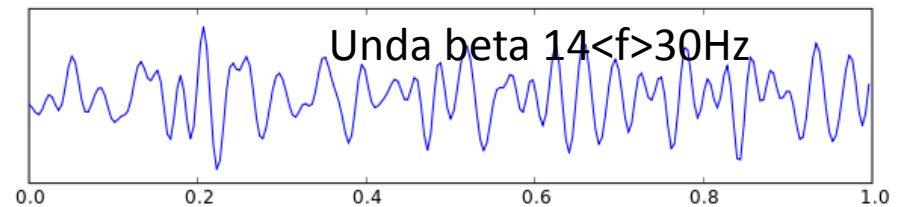
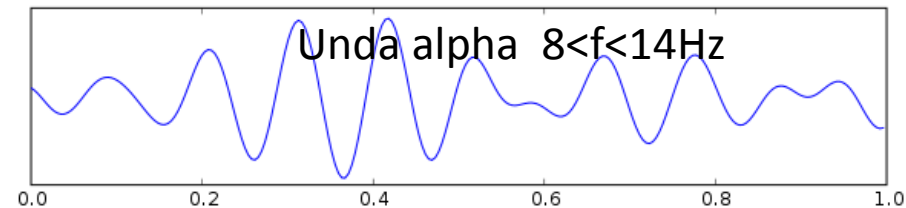
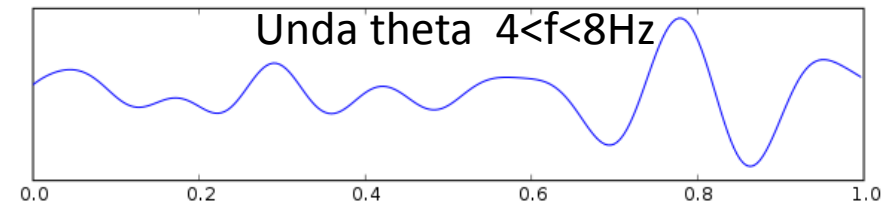
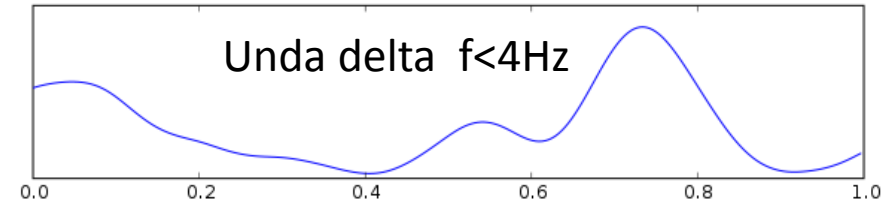
- Este o metoda experimentala utilizata de elctrofiziologi pentru a masura curentul ionic prin membrana neuronului cand aceasta are o anumita tensiune transversala.
- Se foloseste o bucla inchisa care injecteaza automat curent in celula pentru a asigura o variatie in timp a tensiunii membranei impusa de un generator
- Se studiaza cum reactioneaza celula la schimbarile potentialului membranei sale
- Sunt studiate astfel relatia curent-tensiune specifica canalelor de ioni ale membranei
- Cu aceasta tehnica aplicata pe neuronul unui calamar gigant a fost stabilit modelul Hodgkin-Huxley de referinta pentru neuron



https://en.wikipedia.org/wiki/Voltage_clamp

EEG-electroencefalografia

- Metoda de inregistrare a activitatii electrice a creierului.
- De regula este neinvaziva, bazat pe plasarea unor electrozi pe scalp, dar se foloseste si varianta in care microelectrozi sunt implantati transcranial.
- Pentru diagnosticul diferitelor stari patologice (epilepsie, somn anormal, coma, tumori cerebrale, atac cerebral) se analizeaza continutul spectral al semnalelor culese, pentru a identifica diferite tipuri de oscilatii neurale.
- Din EEG a fost derivata tehnica potentialelor evocate (EP), care urmareste modificarea EEG in urma unui stimul vizual, auditiv sau de alta natura.
- O problema deschisa este trecerea de la semnalele SNN la EEG si invers



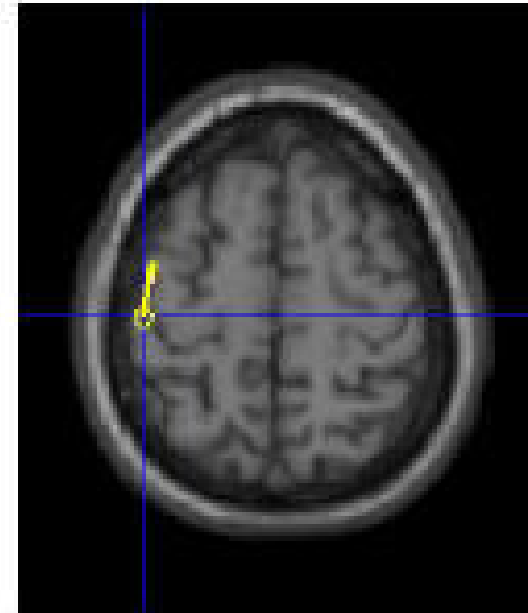
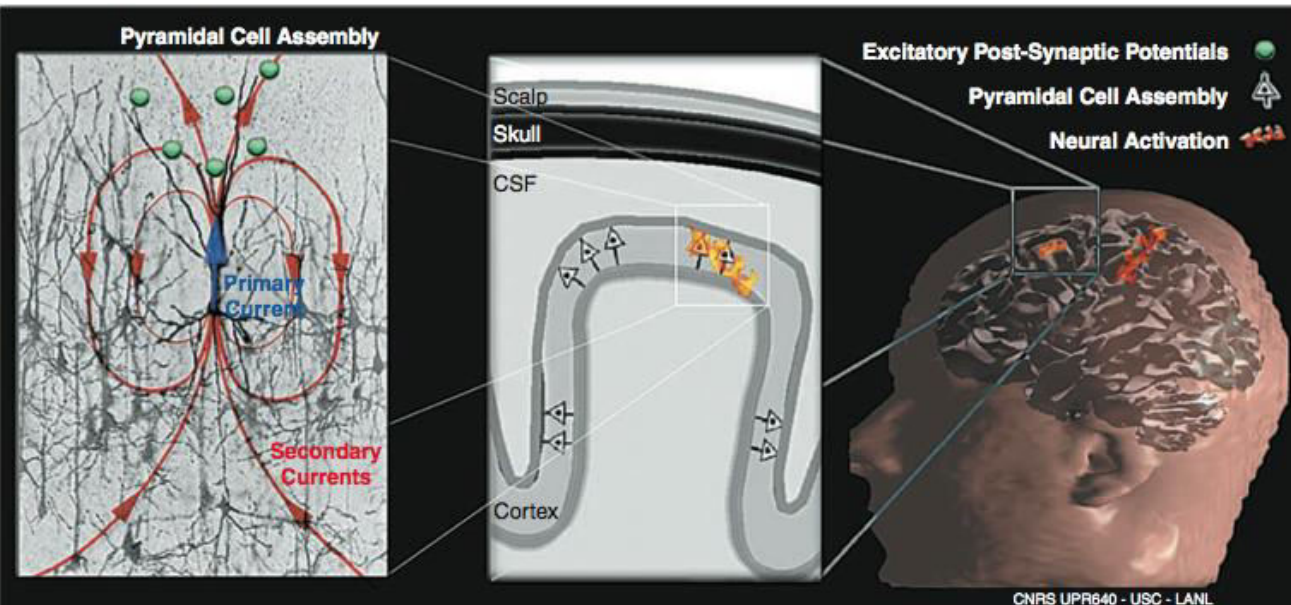
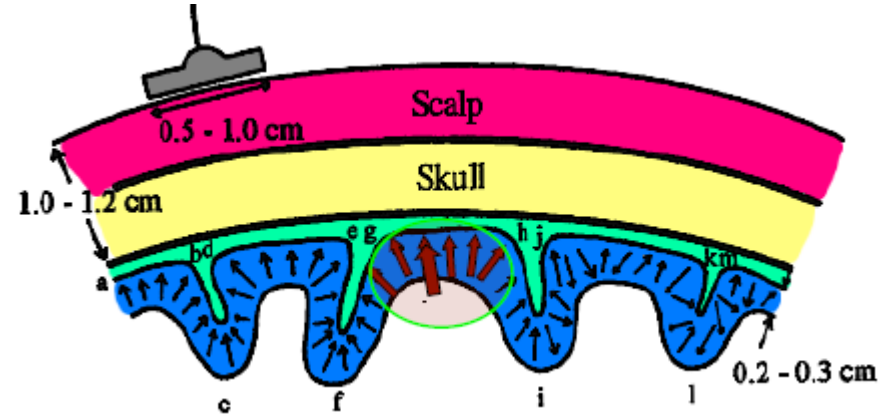
Unda gama $30 < f < 100\text{Hz}$

Modelare EEG

Generarea semnalului EEG

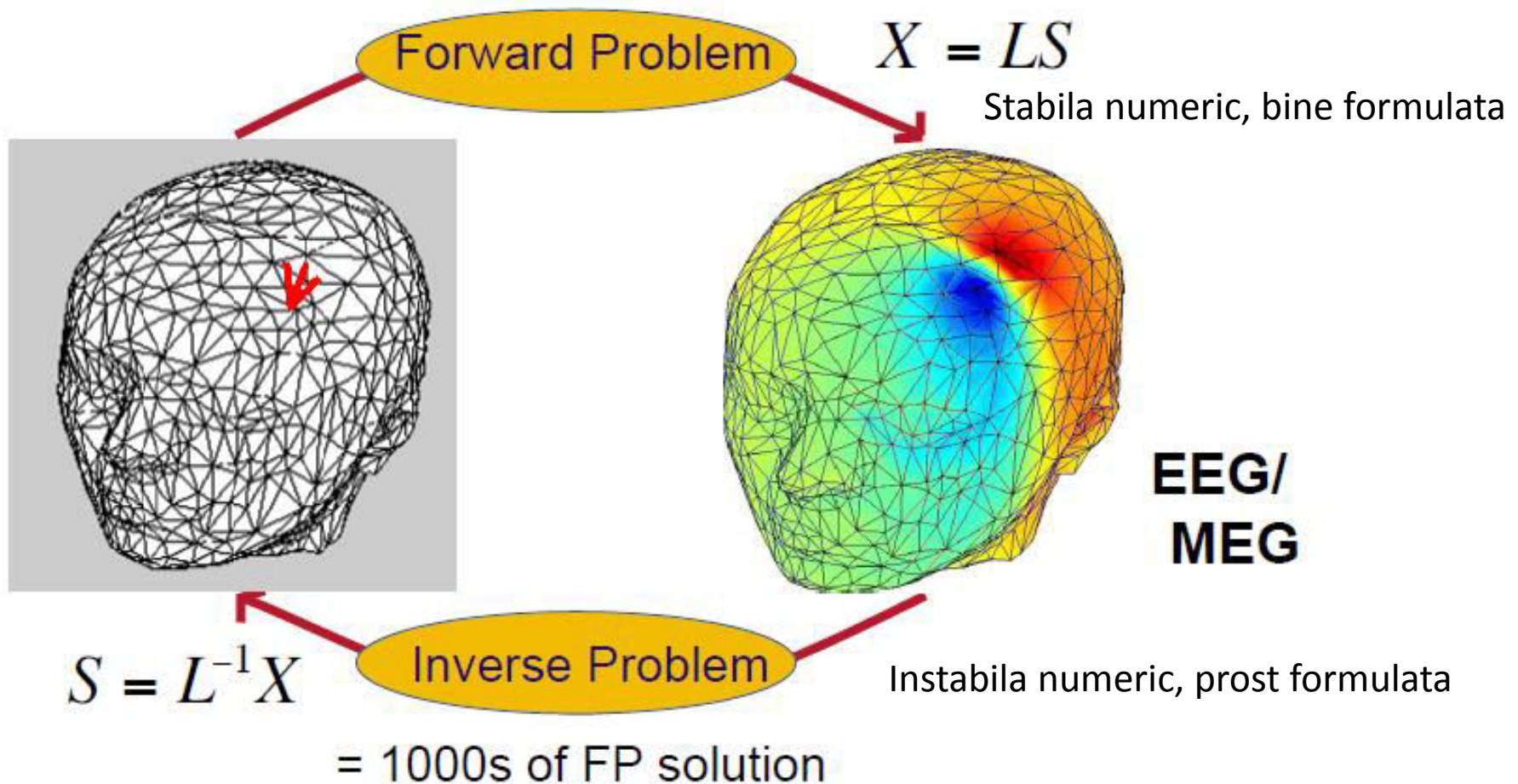
http://cfmriweb.ucsd.edu/tliu/be280a_12/B_E280A12_eeg5.pdf

<http://www.brainvoyager.com/bvqx/doc/UsersGuide/EMEGSuite/EEGAndMEGForwardModels.html>



Problema directa si inversa

S = vectorul (curentilor) sursa; X = vectorul potentialelor masurate semnale EEG,
 L = matricea de transfer (modelul capului cu conductie de volm)

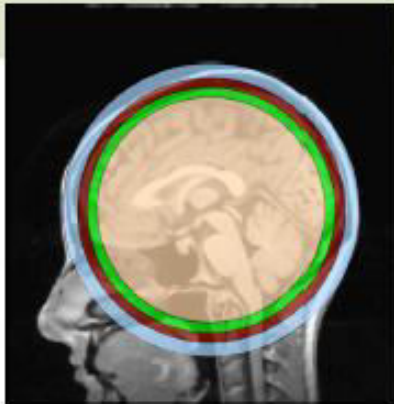


Matricea de transfer (de conductie a capului)

Simple Head Models

- ◆ Single layer sphere, spheroid
- ◆ 3-4 layer sphere

ANALYTICAL SOLVER
Simple, fast, but not accurate



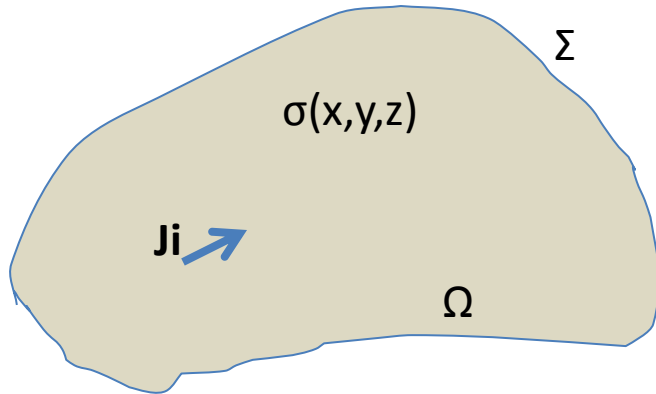
Realistic Head Models

- ◆ Boundary Element (BEM)
- ◆ Finite Element (FEM)
- ◆ Finite Difference (FDM)

NUMERICAL SOLVER
Represents head shape better, but computationally complex



Problema de camp in regim electrocinetic



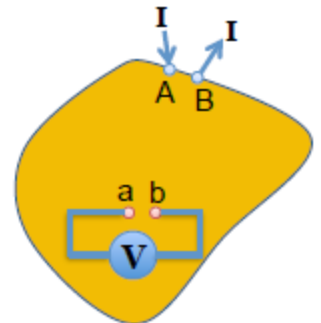
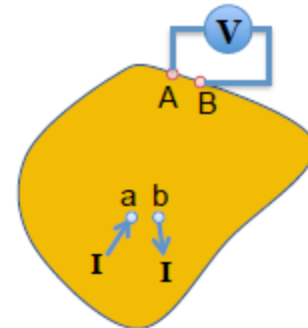
$$\operatorname{div}(\overline{\overline{\sigma}} \operatorname{grad} V) = -\operatorname{div} \mathbf{J}_i \quad \text{in } \Omega$$

$$\overline{\overline{\sigma}} \frac{dV}{dn} = 0 \quad \text{pe } \Sigma = \partial\Omega$$

Anizotropia: materia alba 9:1, scalpul 10:1

Determinarea matricei de transfer L prin FEM:

- Rezolvarea problemei de camp pentru fiecare sursa este lenta
- Deoarece avem nevoie de potentiele in electrozii d epe frontiera, care au locatii cunoscute
- Putem folosi teorema reciprocitatii, injectam curenti in elctozii si determinam sursele interne de camp
- Abordarea se poate extinde si in regim EQS (armonic)
- In mod similar (dar in regim magnetostationar) se formuleaza problema MEG



Deep Brain Stimulation (DBS)

- **Christian Schmidt, Ursula van Riener**
Influence of Uncertainties in the Material Properties of Brain Tissue or the Probabilistic Volume of Tissue Activated, anizotropie:

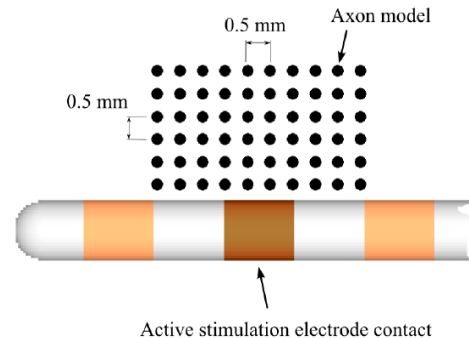
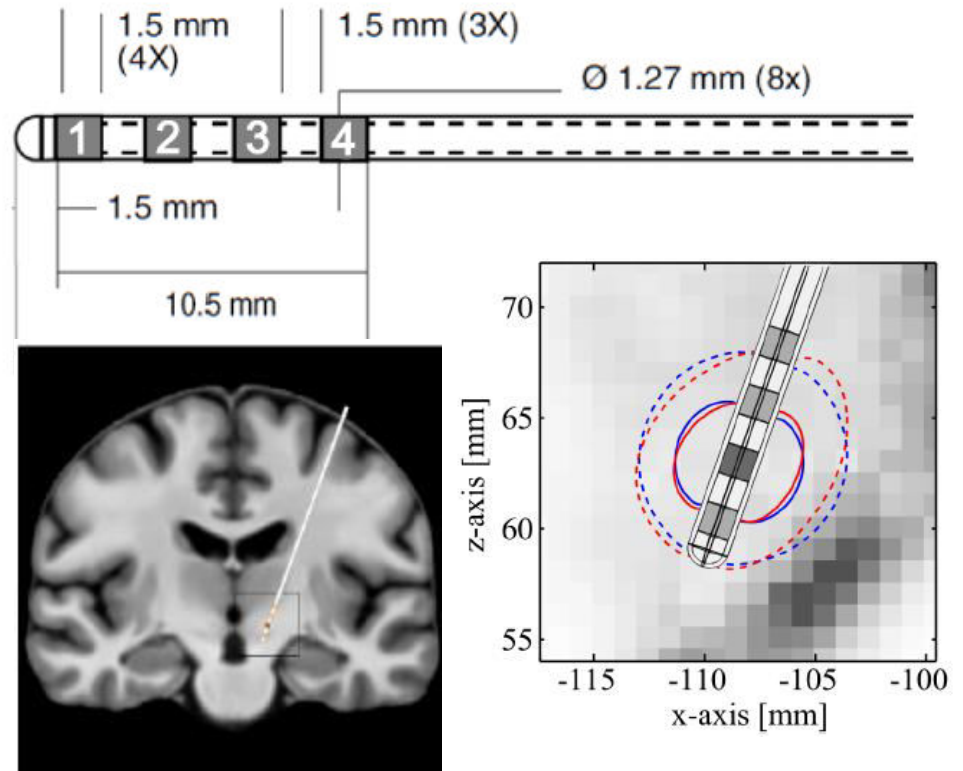
<http://ieeexplore.ieee.org/stamp/stamp.sp?arnumber=6392218>

<http://ieeexplore.ieee.org/stamp/stamp.sp?arnumber=6165340>

- Christian Schmidt PhD

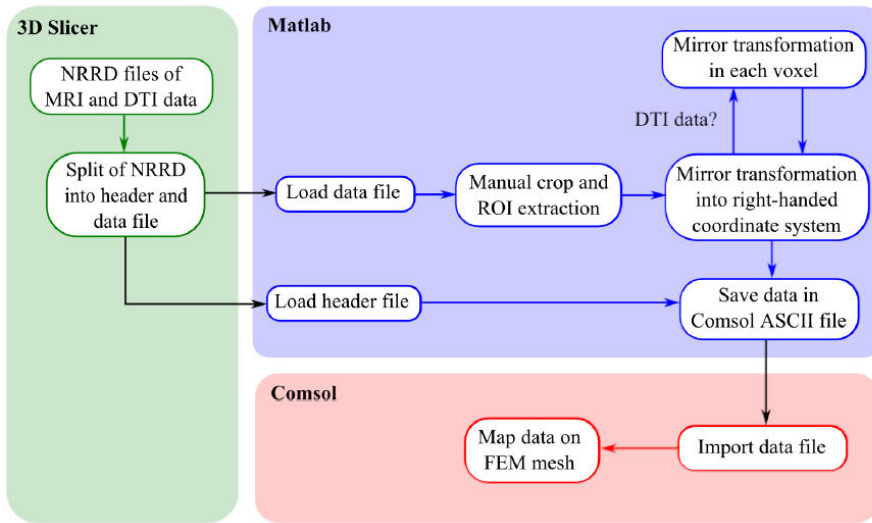
http://rosdok.uni-rostock.de/file/rosdok_disshab_000001072/rosdok_derivate_0000005204/Dissertation_Schmidt_2014.pdf

- **Critica:** chiar daca este intens folosit modelul cu conductie de volum, inclusiv cel anizotrop nu descrie traseele corecte ale semnalelor neurale. **Propunem sa fie folosite abordari cuplate camp-circuite.**

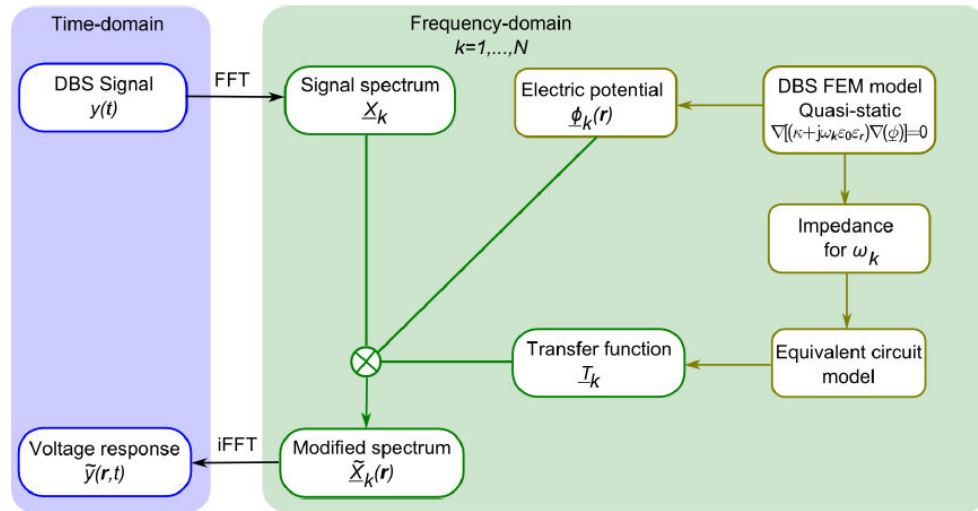


Metoda de analiza

Preprocesarea



Rezolvarea si validarea

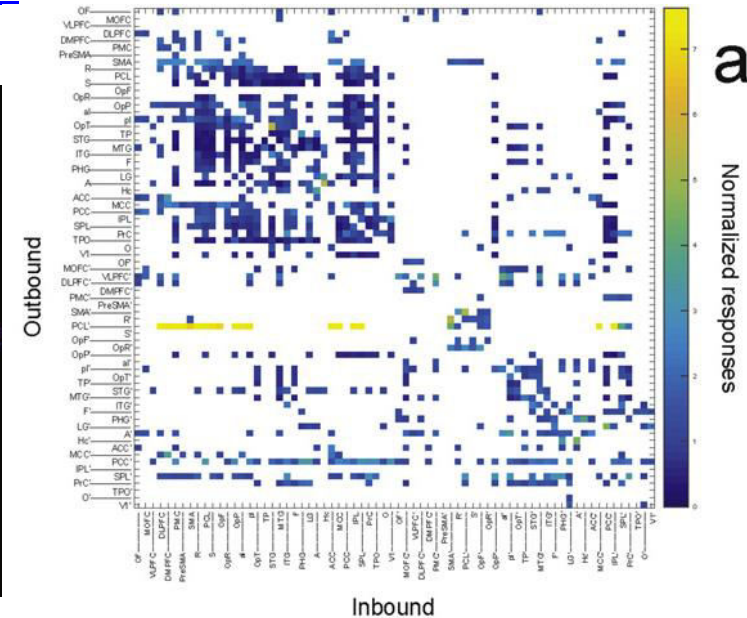
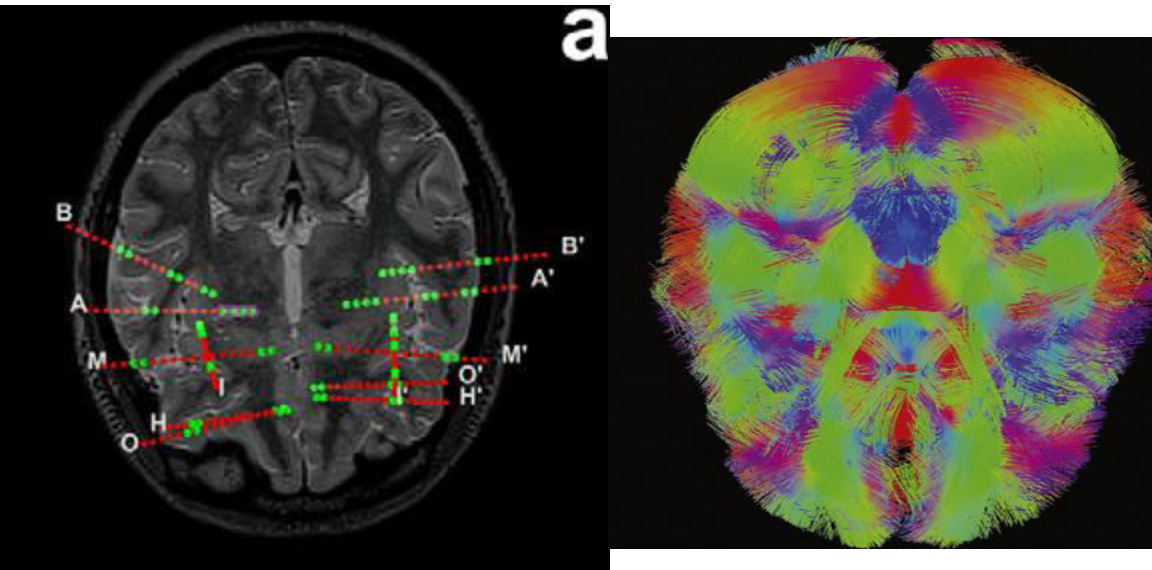


Postprocesarea: cu NEURON

DBS model with connectomics

- **Donos, C. Mandruta, Ciurea, A connectomics approach combining structural and effective connectivity assessed by intracranial electrical stimulation.**

<http://www.ncbi.nlm.nih.gov/pubmed/26921715>



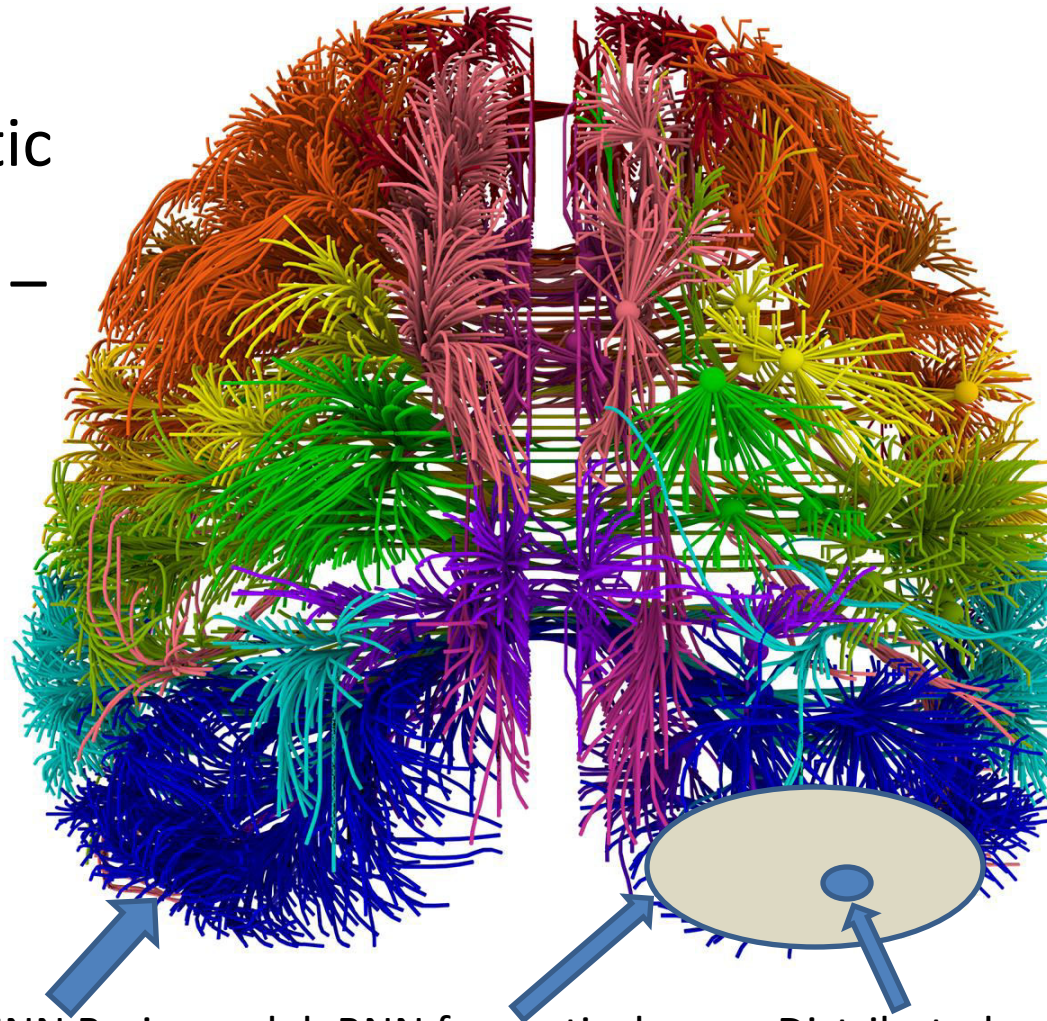
24 pacienti, cu 9-17 electrozi avand 104-211 contacte , stimuli: 20 pulsuri de de 3ms , monotoni crescatori in plaja 0.25–5mA, cu pauza de 15 sec. Au fost luate in considerare raspunsurile in fereastra de timp 10-110ms, concondante (monoton crescator) cu stimulii.

6. Concluzii

- Sistemul neural este extrem de complex, cerebelul fiind cel mai complex sistem existent in natura
- Comunitatea stiintifica dedicata studiului acestui sistem este ampla, diversa si foarte activa. Exista mari proiecte de ex. <https://www.humanbrainproject.eu/>.
- “Computational neuroscience” este o ramura recenta, in care lucreaza cercetatori din diverse specialitati aduce contributii remarcabile in acest studiu, in special in modelare si simulare.
- In acest context, competentele noastre stiintifice si tehnice pot fi utile

Concluzii-Cuvinte cheie care definesc competente utile si abordarea propusa

- Computational electromagnetics: automatic circuit model extraction, based on 7 steps modeling – ACES type.
- Multiphysics (multiscale, multidisciplines, multidomain)
- Model order reduction (nonlinear and parametric)
- HPC numerical techniques
- AI (soft computing) approaches



Multiscale+MOR: SNN Brain model > BNN for cortical area > Distributed models for neurons close to electrodes micro/mezo/macro scala

Concluzie finala

Tinand cont de amploarea echipelor de cercetare din intreaga lume dedicate acest sbiect si de consistenta resurselor financiare investite este de asteptat ca realizările noastre sa fie pe masura resurselor umane si finaciare implicate.

Dar abordarea riguroasa interdisciplinara pe care o propunem, in care vor fi implicati cercetatori competenti, matematicieni, informaticieni, biologi, biofizicieni si medici din tara si strainatate, cu un sprijin financiar pe masura ne indreptateste sa credem ca vom aduce o contributie binedefinita la avansul cunostintelor in domeniu.