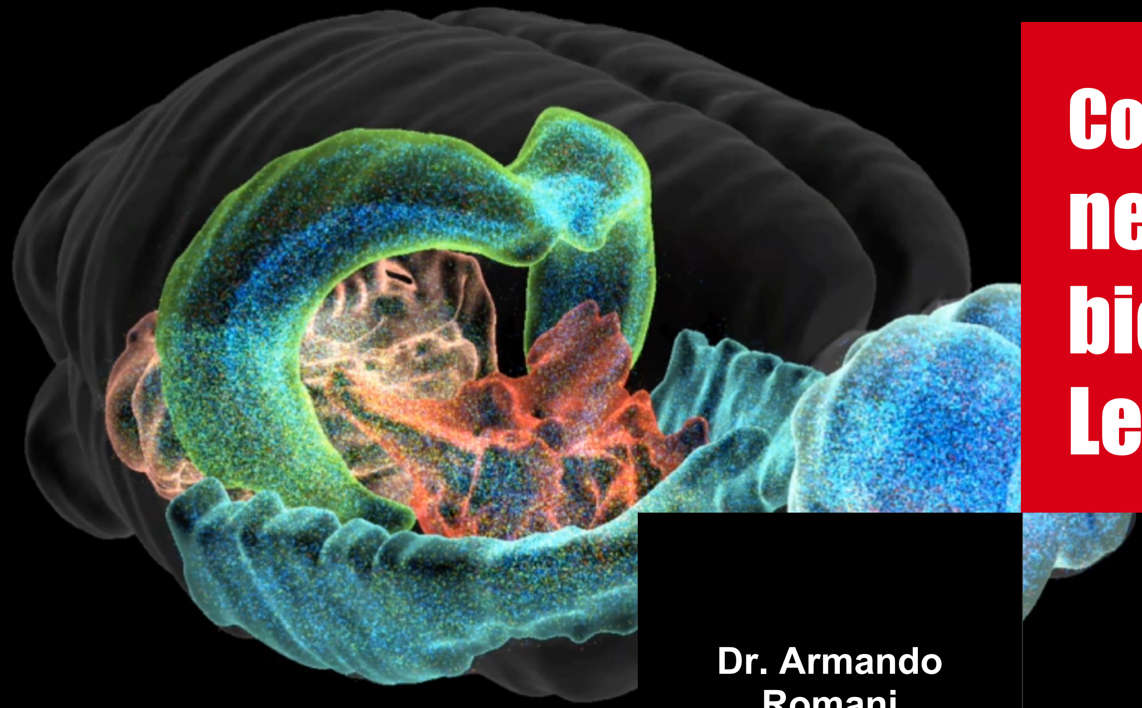


Computational neuroscience: biophysics - Lecture 1

Dr. Armando Romani

EPFL, 2024

Course Overview

Computational neuroscience: biophysics (NX-450)

Dr. Armando Romani
Lecturer
email: armando.romani@epfl.ch
EPFL/BBP, Campus Biotech, Geneva

Dr. Natali Barros Zulaica
Tutorial Oversight
natali.barroszulaica@epfl.ch

Dr. James Isbister
Teaching assistant
james.isbister@epfl.ch

Couse timeline plan

	Week 1 9-10th Sep	Week 2 16-17th Sep	Week 3 23-24th Sept	Week 4 30th Sept-1st Oct	Week 5 7-8th Oct	Week 6 14-15th Oct	Week 7 28-29th Oct
Lectures Monday 10:15 – 11:00 11:15 – 12:00	Introduction to the course + Neuroinformatics	**Holiday – Lecture on morphologies will be provided on line**	Ion Channels	Single cells I: Multicompartmental models	Single cells II: examples, simulation part 1	**Skipped**	Connections
Exercises Tuesday 13:15 – 14:00 14:15 – 15:00	Introduction to Python + Neuroinformatics	Intro to Neuron I: Morphologies	Intro to Neuron II: Ion Channels	Intro to Neuron III: Building a Multicompartmental neuron model	Simulating and Analysing single cell electrical activity	**Test 1**	Cell set connectivity. Connectivity analysis.

	Week 8 4-5th Nov	Week 9 11-12th Nov	Week 10 18-19th Nov	Week 11 25-26th Nov	Week 12 2-3th Dec	Week 13 9-10th Dec	Week 14 16-17st Dec
Lectures Monday 10:15 – 11:00 11:15 – 12:00	Synapses	Plasticity	Networks 1	Networks 2	Network 3 and sustainability	Simulation and scientific computing	Perspectives
Exercises Tuesday 13:15 – 14:00 14:15 – 15:00	Simulating synapses with Neuron. Synaptic traces analysis.	STDP and LTP	**Test 2**	Networks 1: cells in space. Centering, rotating, placing and orienting cells in space.	Network 2: Regular and Irregular stimuli. + Network 3:LFPy	**Test 3**	**Skipped**

Our Approach

We introduce biology, we treat the established theories, we make concrete examples, and finally we do exercises

In the lecture for each block, address

- Scope
- Approaches
- Applications

In the practical part

- Computational thinking
- Applied modelling, simulation and analysis

EPFL

We learn by doing: tutorials and exercises.

- In tutorials, you will find examples and exercises.
- They are part of the course and show implementations of the theory shown at lectures.
- Spend time on them and you will have a deeper understanding of the lectures
- Some of the questions in the tests are inspired by the tutorials/exercises

Material

- All the supporting material (lecture slides, python notebooks, papers, recorded lectures) will be posted on MOODLE before the lecture: https://moodle.epfl.ch/course/view.php?id=17101

- Execution of tutorial python notebooks happens online under: https://noto.epfl.ch

  (but if you really want, you can download the tutorials and necessary software locally but at your own risk)

Assessment

- Three tests during the course
- Each test covers different lectures:
  - ➢ Test 1: lectures 2-5
  - ➢ Test 2: lectures 7-9
  - ➢ Test 3: lecture 10-12
- For each week, you will have three questions:
  - ➢ Multiple-choice question
  - ➢ Open question
  - ➢ More practical question inspired by tutorials and exercises

Introduction

Overview

1. Brain as a complex system
2. A forest of approaches
    - Course approach
3. Build a computer model

Overview

1. **Brain as a complex system**
2. A forest of approaches
    - Course approach
3. Build a computer model

Brain as a complex system

Reductionism vs. complex systems

Many elements on many different scales with all of these scales affecting each others (interdependency)

We cannot fully isolate one component or reduce the whole system to one level

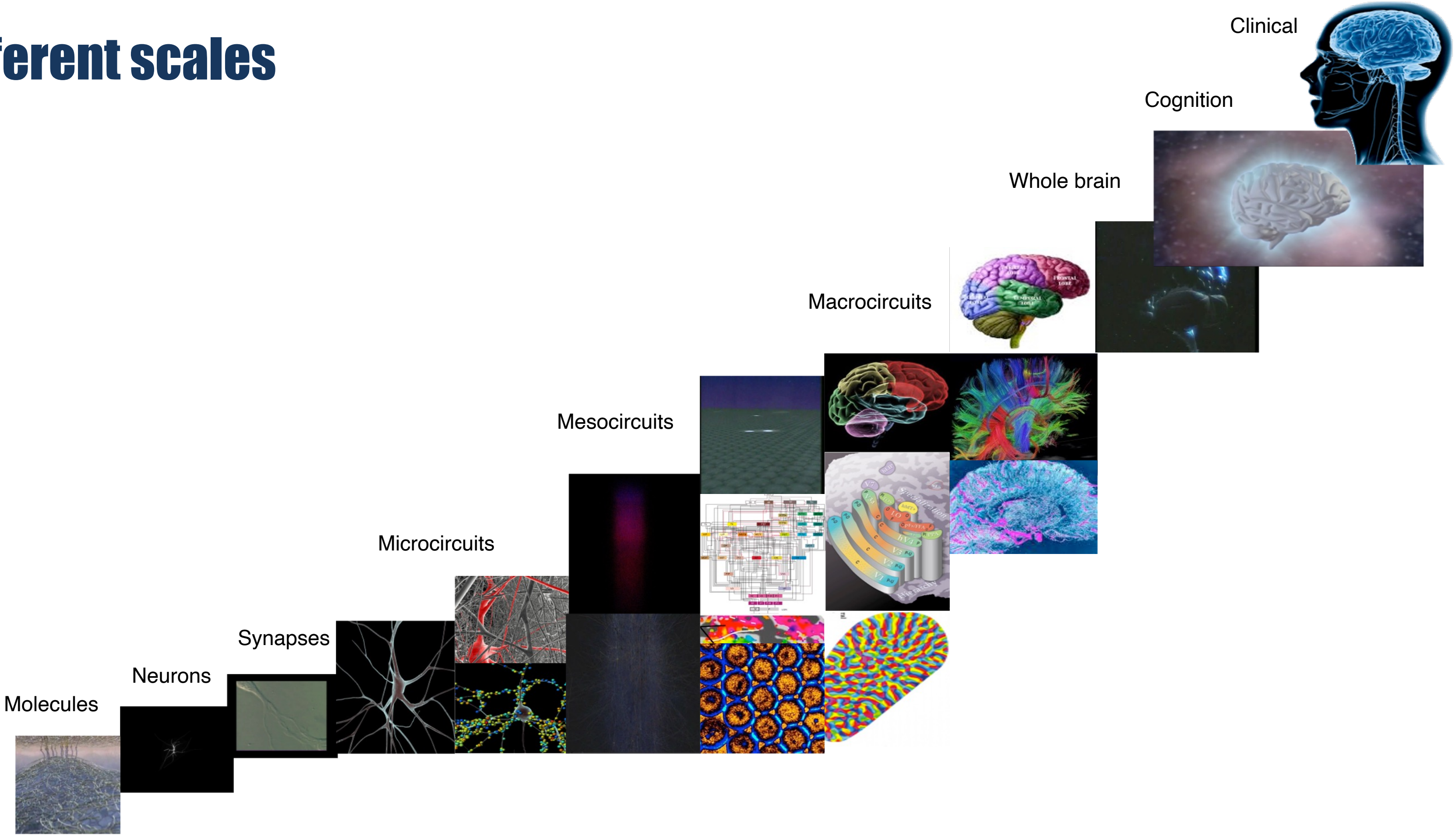
Emergent properties

Non linearity, feedback loops, phase transition, sensitivity to initial condition (butterfly effect)

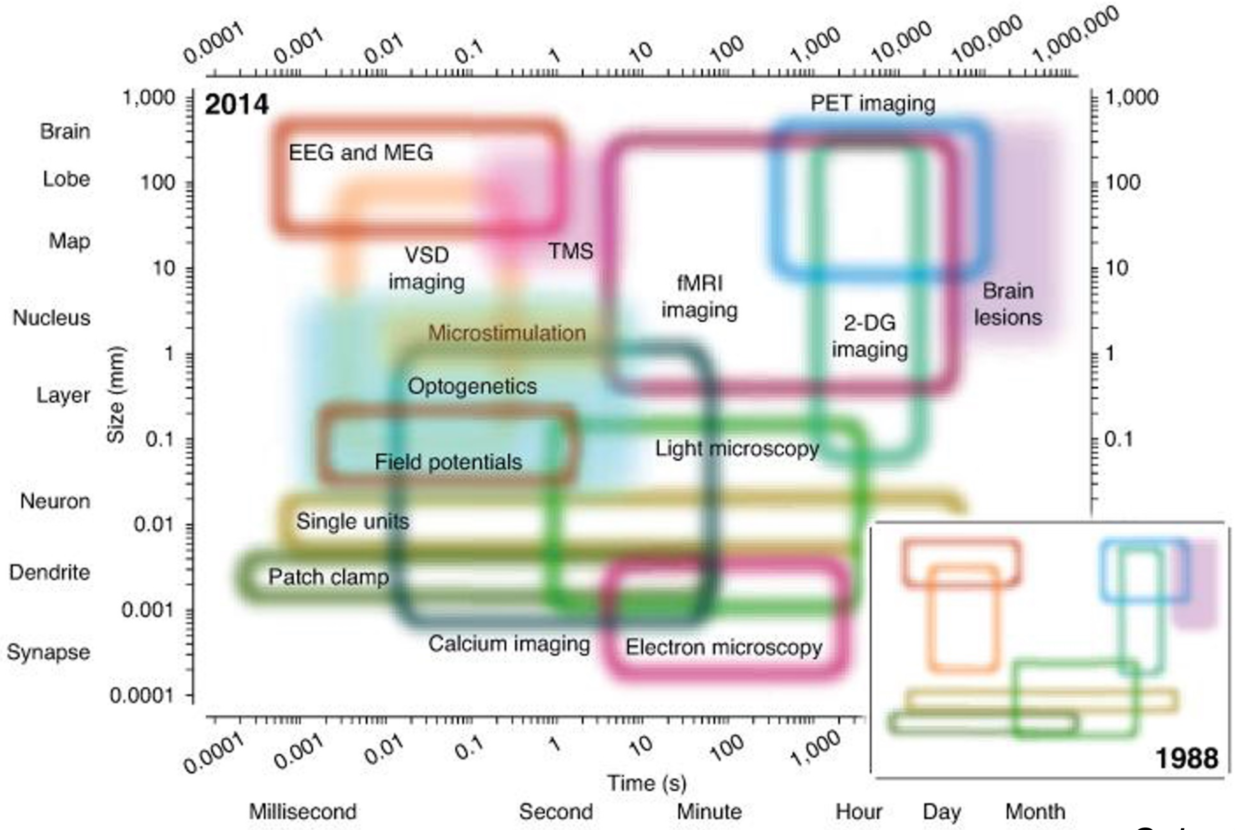
Other complex systems are society, economy, ecosystem

https://www.projectencephalon.org/post/the-brain-as-a-complex-system

Different scales



Different scales - Experimental neuroscience

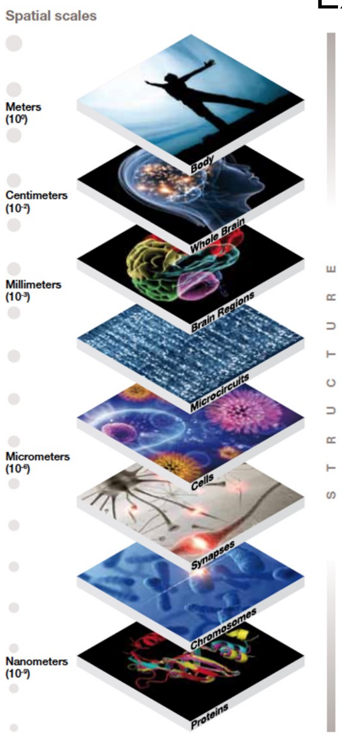


Sejnowski et al., 2014

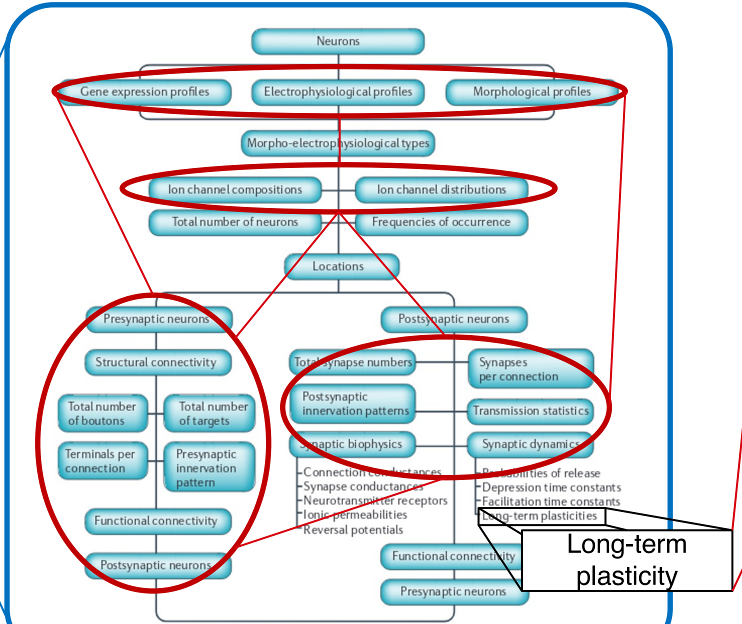
EPFL

Different scales interact

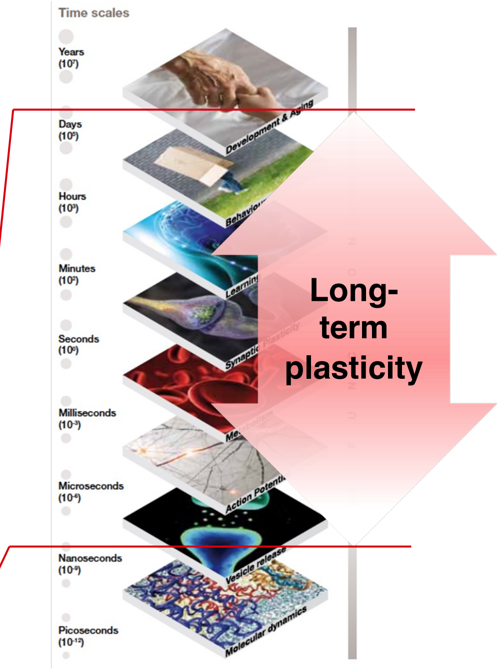
Example: Microcircuit plasticity, a synaptic correlate of learning



Interdependencies of the microcircuit



Markram et al., 2006



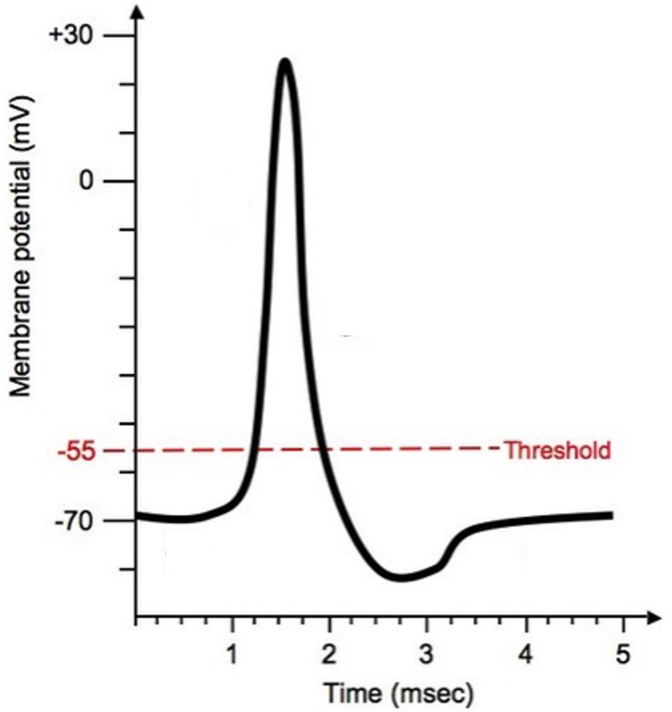
EPFL

Non-linearity

In simple IF models, subthreshold synaptic inputs can be linear

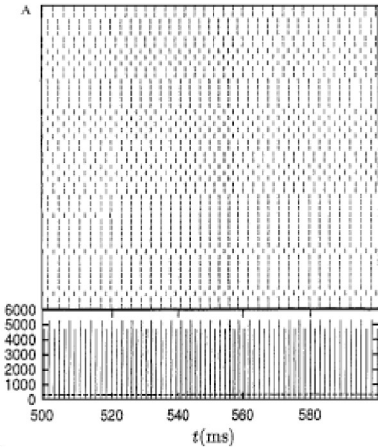
Spike generation introduces a non-linearity in the model

Other examples of non-linearity in more complex models are ion channels, synaptic integration in the dendrites…



http://www.vce.bioninja.com.au/aos-2-detecting-and-respond/coordination--regulation/nervous-system.html

Emergent properties, phase transition



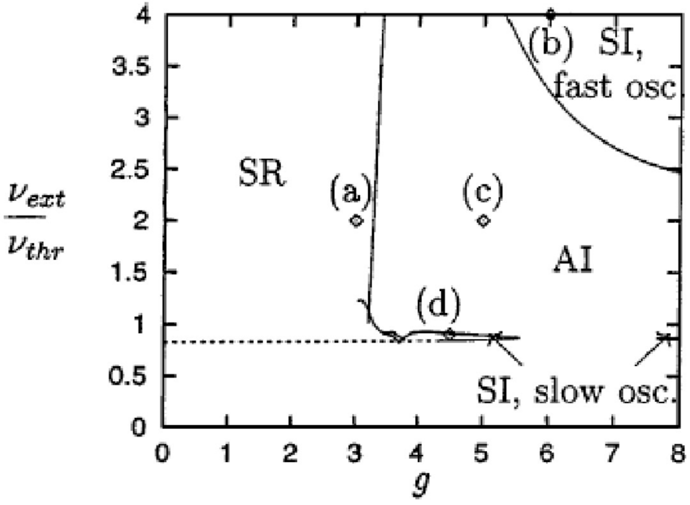
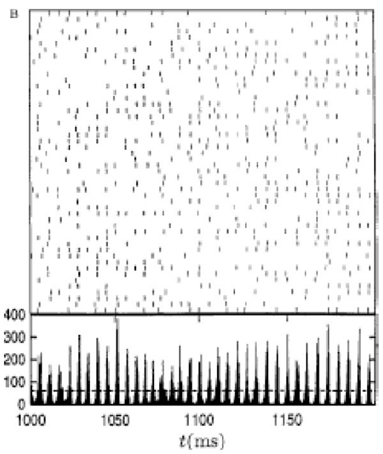
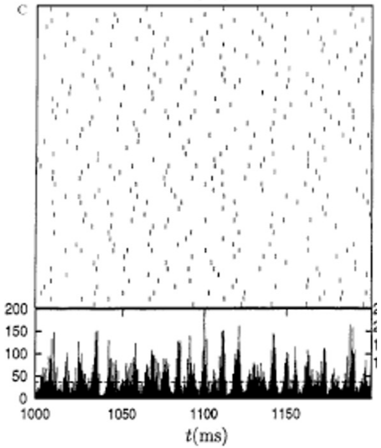
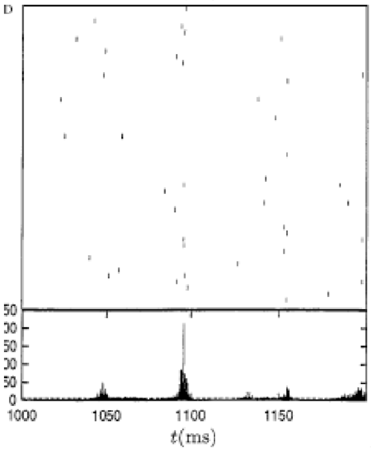


Figure 7. Phase diagram of the network characterized by the parameters of Fig. 8 ($C_E = 1000$, $C_I = 250$, $J = 0.1$ mV, $D = 1.5$ ms). Diamonds indicate the parameter sets chosen for the simulations shown in Fig. 8.





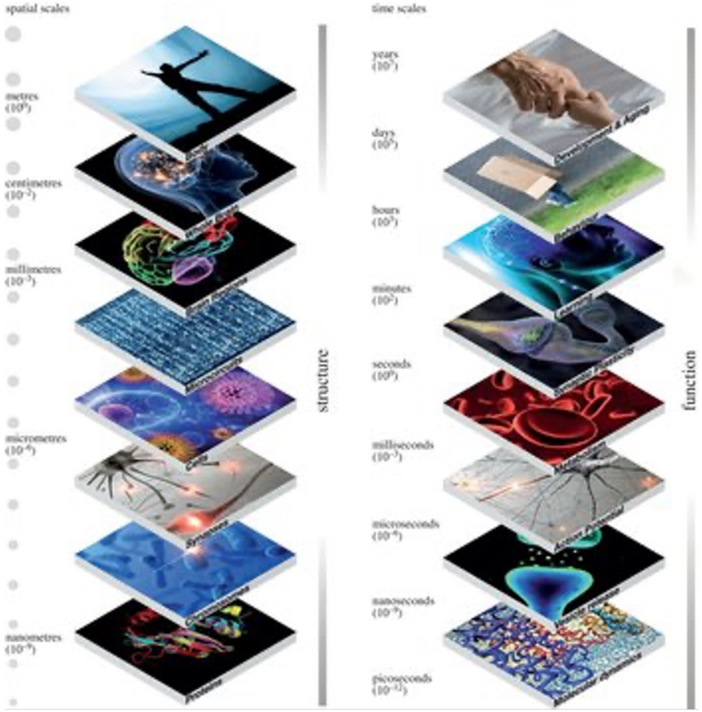


Overview

1. Brain as a complex system
2. **A forest of approaches**
    - Course approach
3. Build a computer model

EPFL

Different scales - Computational neuroscience



Mean-field models

Point-neurons

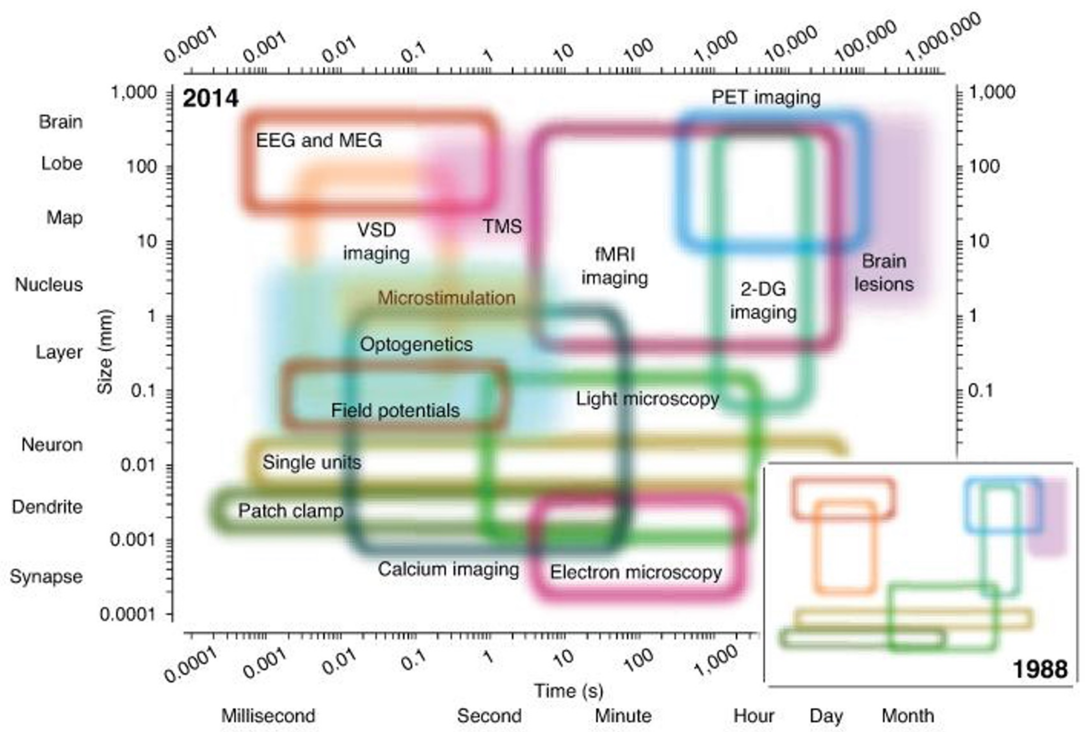
Multi-compartment models

Reaction-diffusion models

Molecular dynamics

Bottom-up vs. Top-down approaches

Top-down



Bottom-up

Sejnowski et al., 2014

EPFL

Biophysical vs. Phenomenological model

Biophysical Models

- Employ the mathematical formalizations of the physical properties of that system
- Promise of generalization

Phenomenological models

- Postulated mathematical form, not derived from first principles
- May be qualitative or quantitative description of data
- Limited predictive power, but better at higher scales
- Eventually required to avoid *turtles all the way down...*

EPFL

Data- vs. Hypothesis-driven model

Data-driven model ⟷	Hypothesis-driven model
Data	Hypothesis
↓	↓
Model	Minimum model
↓	↓
Test multiple hypotheses	Accept or reject the hypothesis
More ambitious Find new relationships	More pragmatic Exclude important elements

EPFL

Overview

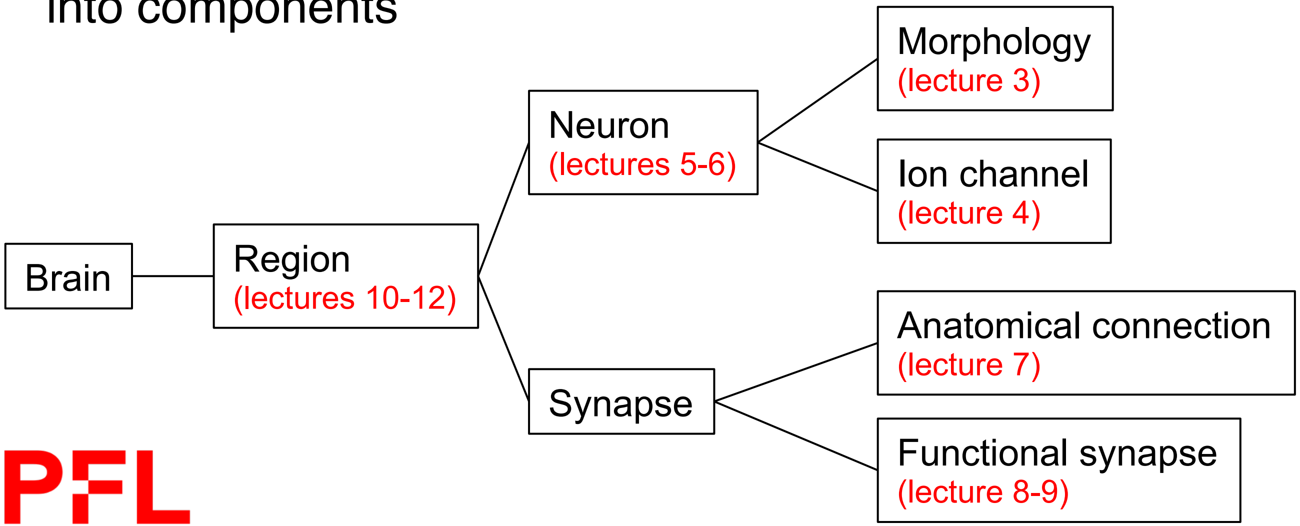
1. Brain as a complex system
2. A forest of approaches
    - **Course approach**
3. Build a computer model

The approach followed by the course

- Consider different scales, using a bottom-up approach from ion channels to large-scale network
- Biophysical models
- Data-driven approach
- Multi-compartment models of neurons
- Lower-scale phenomena are captured with phenomenological models

Divide and conquer

- A principle used in computer science and when the problem is particularly complicated
- This principle is also useful in the case of computational neuroscience
- Our ultimate objective is to reconstruct the entire brain and we can divide it into components



Transversal lectures:
1, 2, 13, 14

EPFL

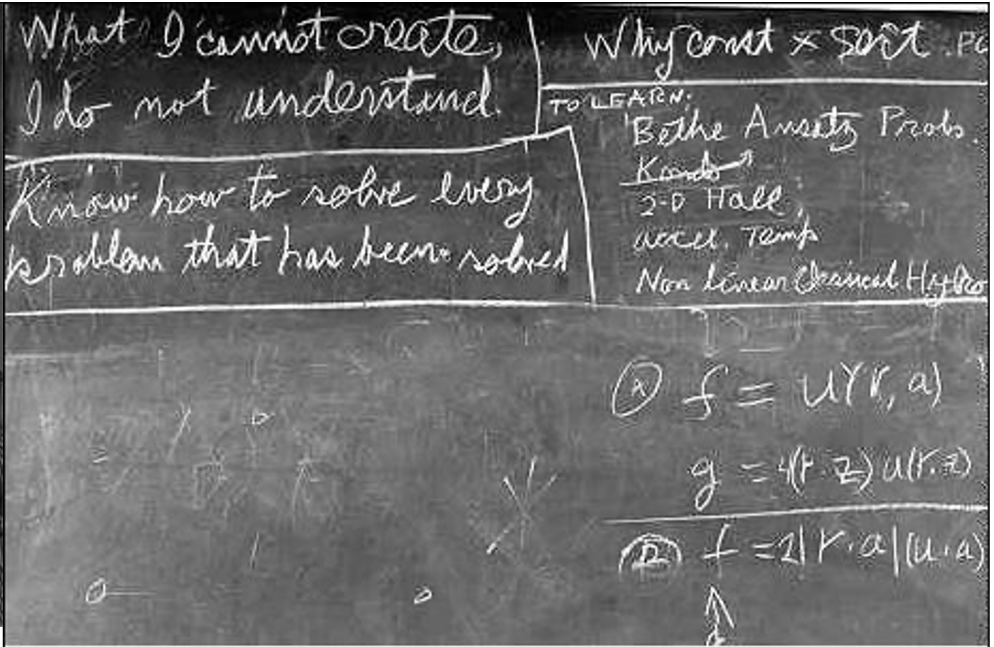
Still a young science

- Not all the topics treated in the course are well established in the community.
- Some approaches have been characterized in depth, the theory is relatively consolidated, there are books (e.g. ion channels, point neurons).
- For other topics (e.g. models of brain regions), the community is still in an exploratory phase. We have to rely on scattered papers, the skills of your colleagues… There are no rigorous definitions, procedures… There is a variety of solutions to the same problem.
- Computational neuroscience is a multidisciplinary field and evolve with the progresses of many other disciplines. For example, it depends on the power of moderns computers and computer architectures.
- Our knowledge is still quite fragmented due to a variety of reasons.
- The course tries to organize this knowledge and present it in a pedagogic way

Overview

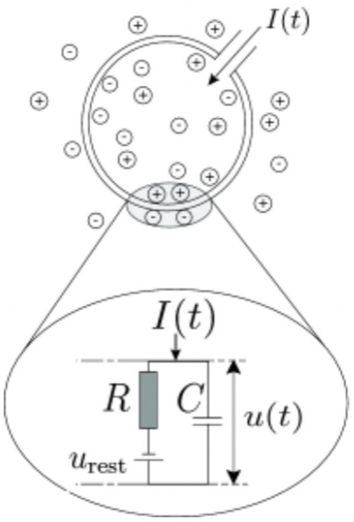
1. Brain as a complex system
2. A forest of approaches
   - Course approach
3. **Build a computer model**

"What I cannot create, I do not understand"
- Richard P. Feynman



EPFL Nobel Prize in Physics 1965

Make a computational model



System

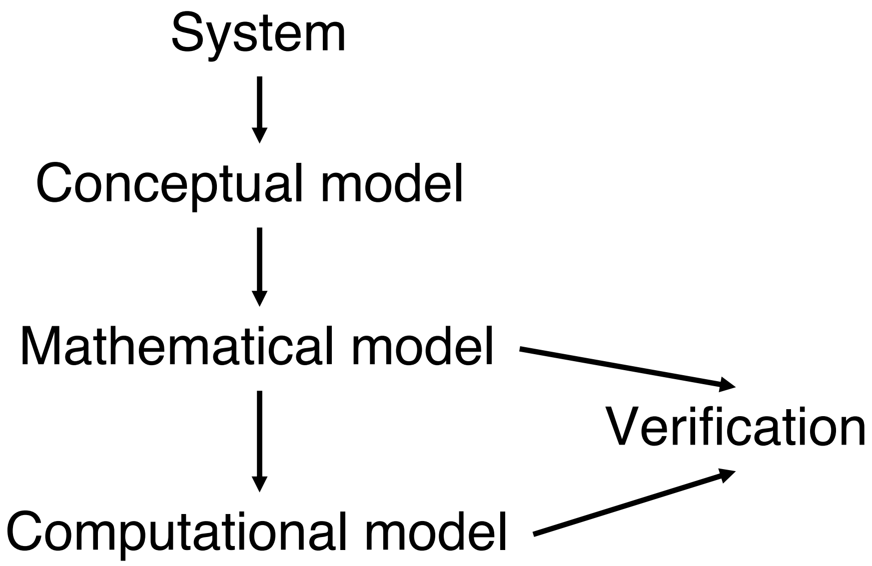
Conceptual model

Mathematical model

$$I\,(t) = I_R + I_C \;\ldots$$

Computational model

```
I_t = I_R + I_C
# ...
```

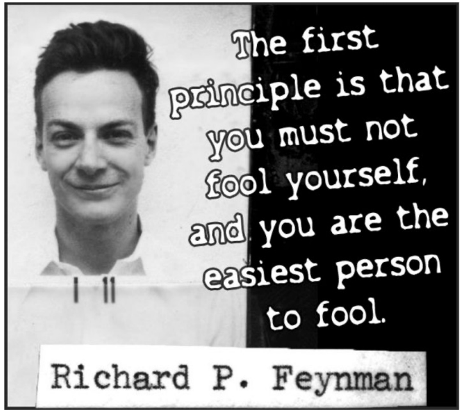

System
Conceptual model
Mathematical model
Verification
Computational model

Verification

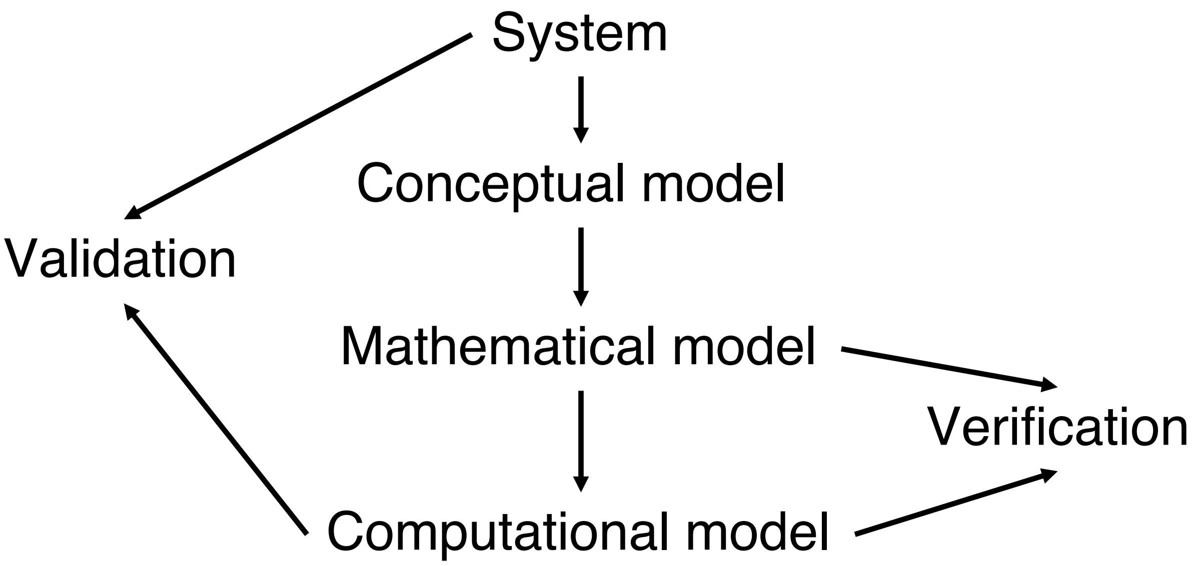
Check that the computer simulation correctly implements the mathematical model

Approaches for verification:

- Code review by your peers
- Interactive debugger
- Check simulation output for cases where output is known by other means (analytical derivation)
- Software engineering techniques for software verification, such as unit testing



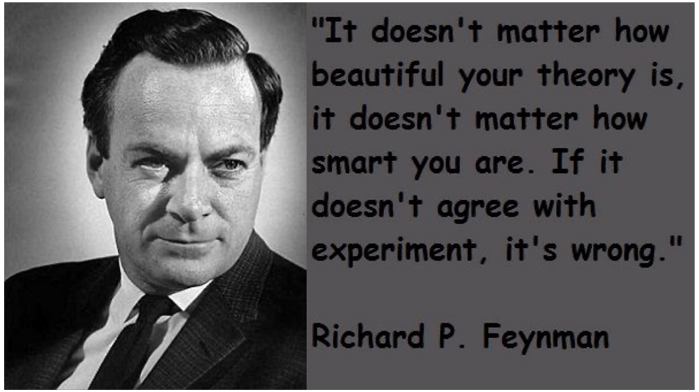
EPFL


System
Conceptual model
Validation
Mathematical model
Verification
Computational model

Validation

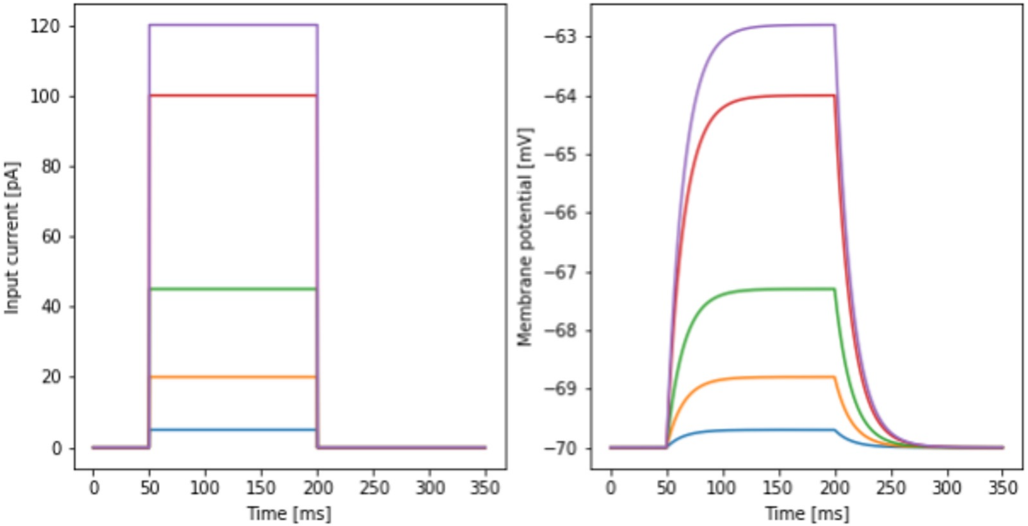
Check that the model accurately captures the system being modeled

- Validation does not prove a model right!
- Compare to experimental data not used to constrain the model
- Models have a domain of validity, or applicability
- Models may *generalize* beyond their established domain of validity
- Make a prediction, and test it experimentally



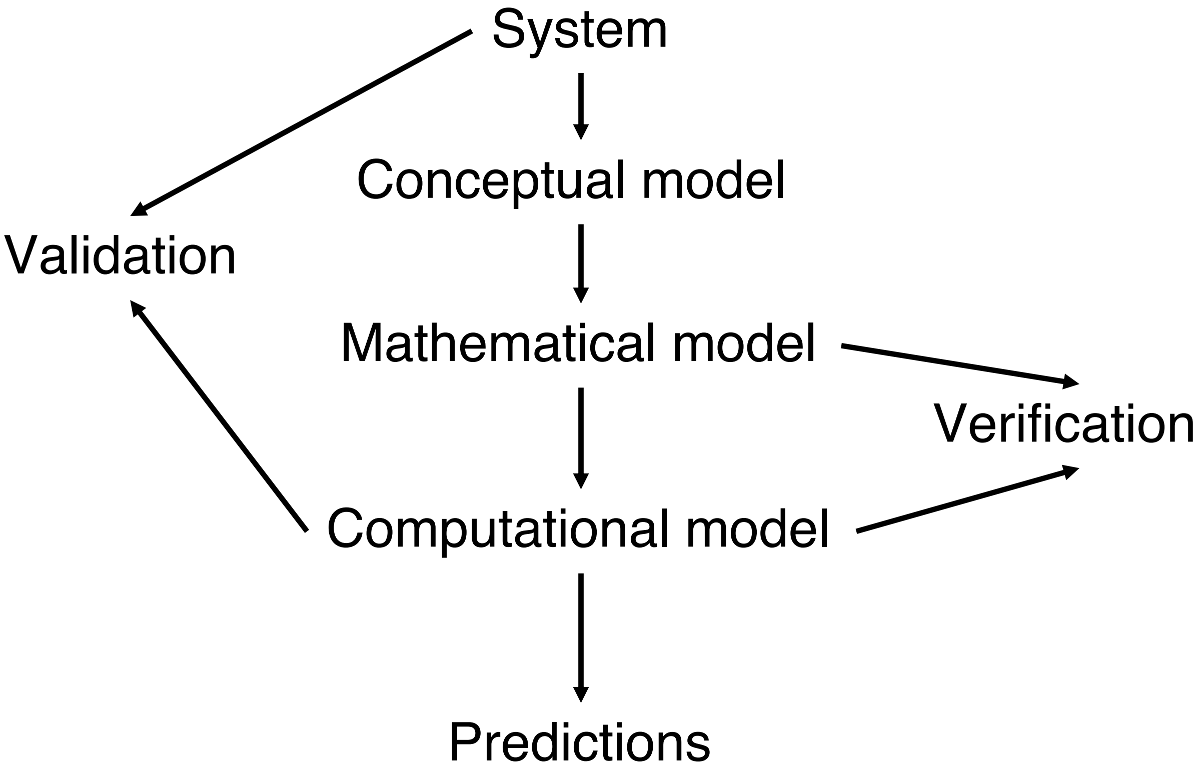
Model vs. Experiment

Sub-threshold stimulus

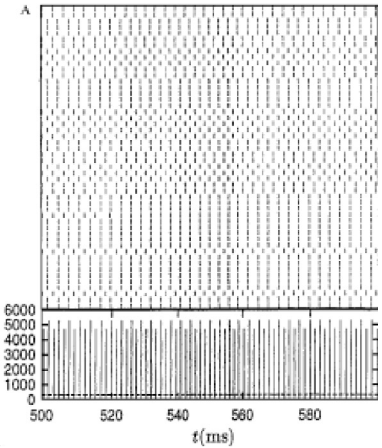


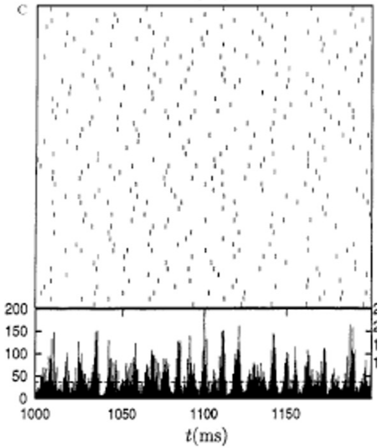
u_0

Time course of the membrane potential of a cat spinal motor neuron to a 3nA current step of duration about 25ms (Barrett and Crill, 1974)


System
Conceptual model
Validation
Mathematical model
Verification
Computational model
Predictions

Predictions





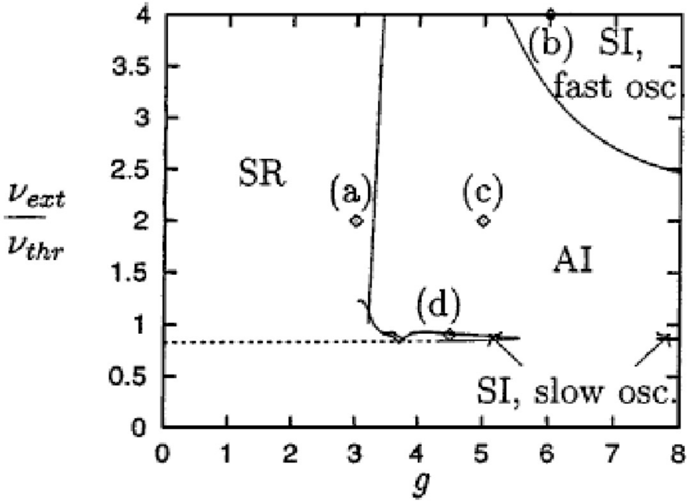
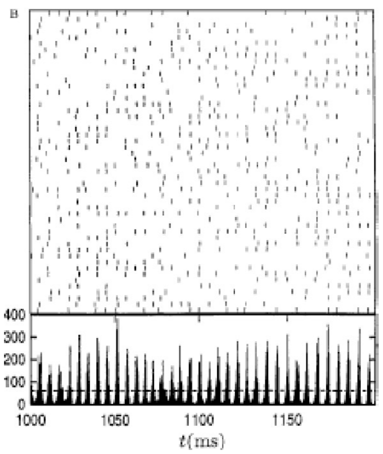
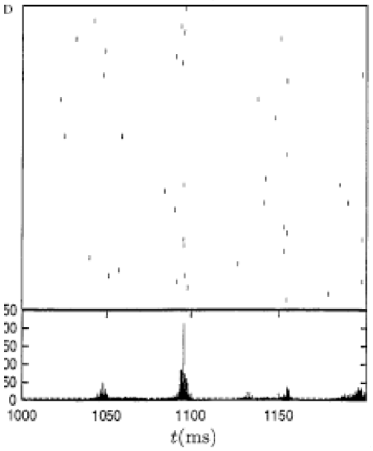


Figure 7. Phase diagram of the network characterized by the parameters of Fig. 8 ($C_E = 1000$, $C_I = 250$, $J = 0.1$ mV, $D = 1.5$ ms). Diamonds indicate the parameter sets chosen for the simulations shown in Fig. 8.





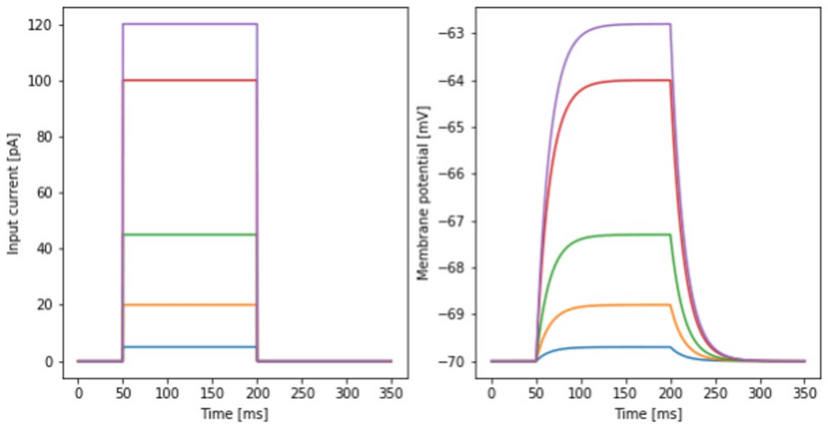
Simulation

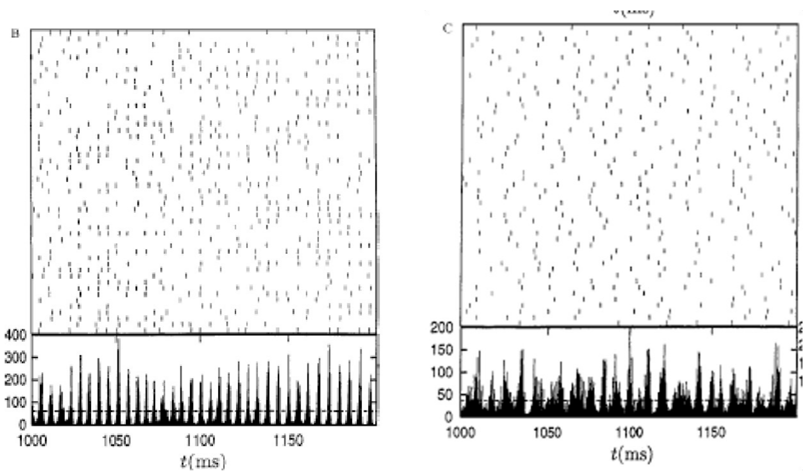
Solve the time dimension of the model

We normally solve u(t)

We can save u(t), spike times…

We can combine and present the results in different ways (e.g. raster plots)





EPFL

What you have learn

- Brain is a complex system. It spans multiple scales in time and space, it shows non-linearity, emergent properties. Interdependency of the system elements.
- There are multiple approaches to model the brain: bottom-up and top-down, biophysical and phenomenological, hypothesis- and data-drive.
- Building a model requires several steps: conceptual model, mathematical model, computer model, verification, and validation