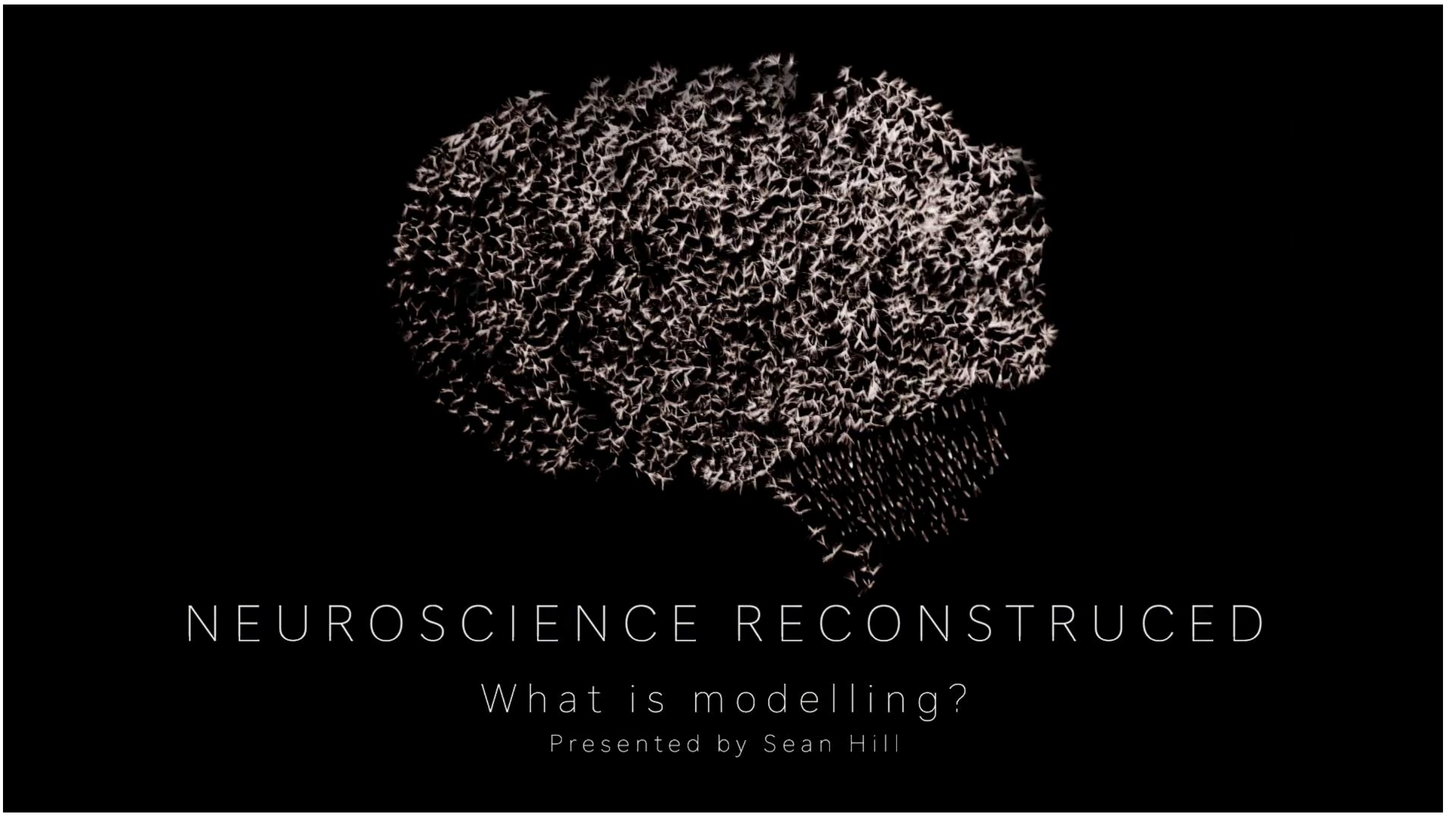
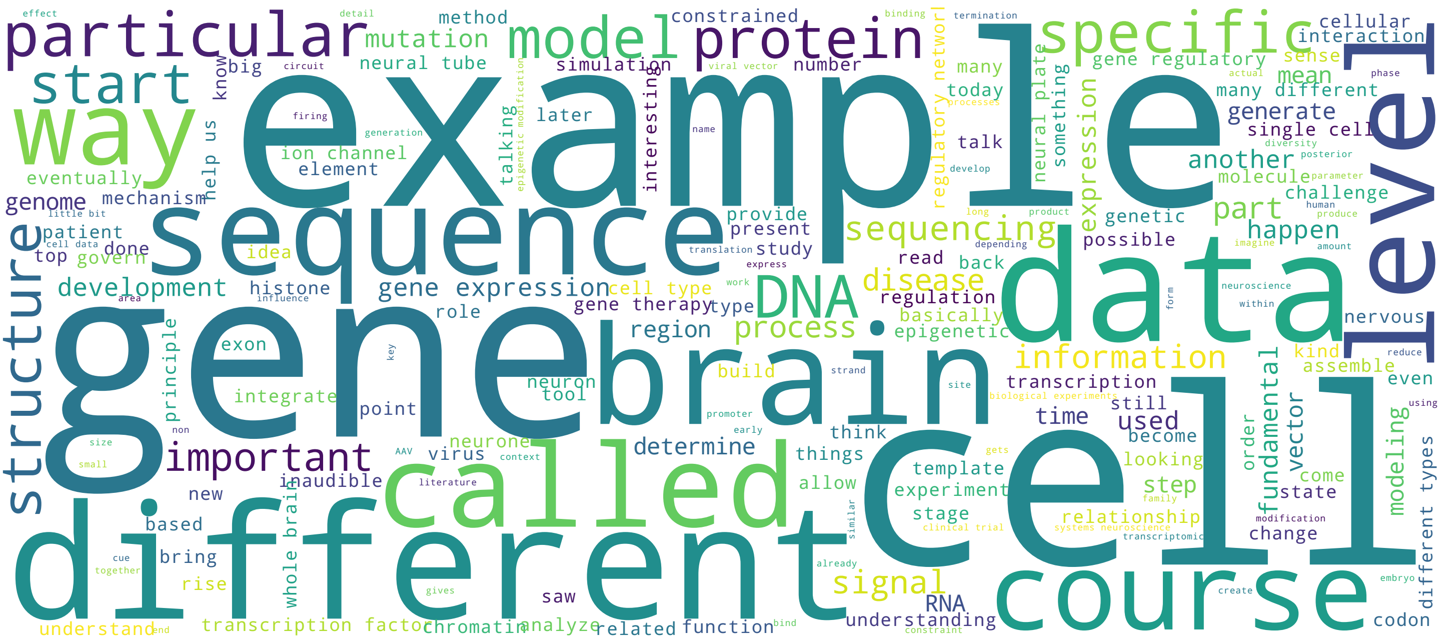




Search MOOC

Video

Coming up

Previous lectures

- Basics of genetics
- Genome, transcriptome and epigenome
- Gene therapy
- Experimental tools in genomics, transcriptomics & epigenomics
- Big Data in neuroscience

Today

- What is systems neuroscience?
- Goals and scales of modeling and simulation
- Basic principles of modeling
- Types of models
- Reconstruction and simulation

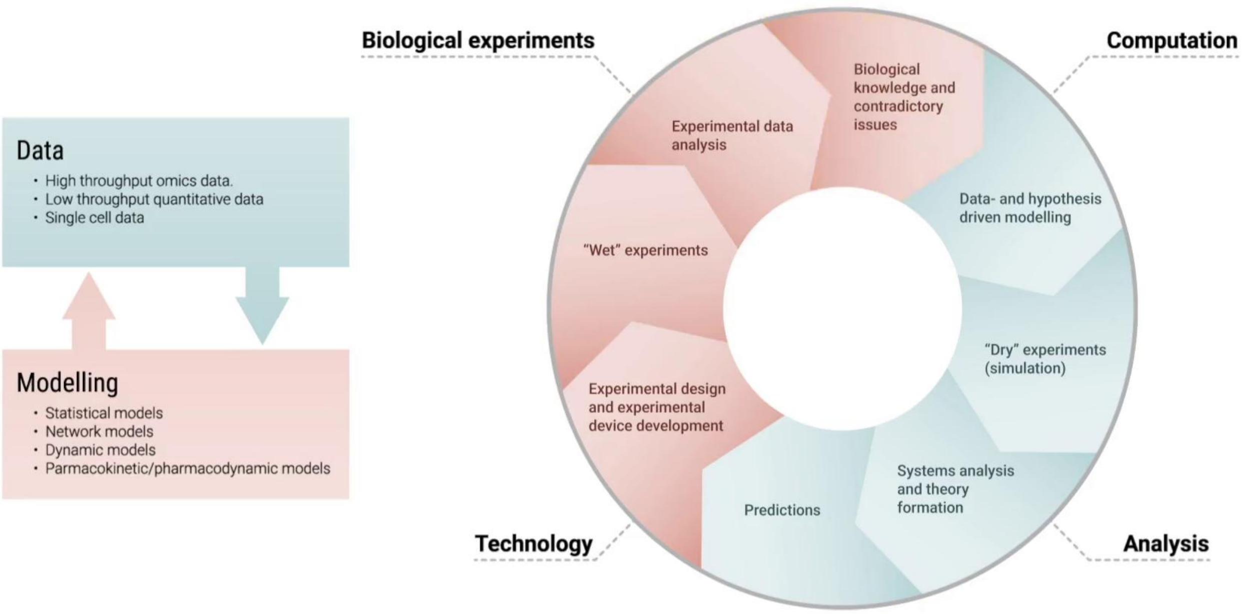
Hello, I'm Sean Hill, and today I'll be talking to you about an introduction to modeling and simulation in neuroscience. First of all, what is systems neuroscience? What are some of the goals and scales of modeling and simulation? What are the basic principles of modeling? What are the types of models? What does it mean to create reconstruction and simulation? I'll take you through all of that today.

Notes

Summary

0m 10s

What is modeling?



In systems neuroscience, we start with data looking at, for example, high throughput OMICS data or low throughput quantitative data. It could be single cell data. Actually, there are many large scale single cell data projects today measuring from throughout the brain. Then the challenge is developing models that help us understand that data. So there are many different types of models, statistical models, network models, dynamic models. Of course, you can do pharmacokinetic or pharmacodynamic models looking at biological systems level interactions. Of course, starting from biological experiments, you can analyze the data. Of course, looking at the literature for the biological knowledge and contradictory issues. Then from that, assemble a hypothesis and what model can be built given the data available. Then you can run what we would call dry experiments, simulations using the model that you've assembled. Of course, using systems analysis and theory formation, making predictions that you can then test in those experiments, and then bring all of that back to inform your experimental design on the biological side. This is really an iterative approach of gathering data, building models, running simulations, analyzing, and then iterating and refining to use simulation as an integral part of the biological experiments.

Notes

Summary

0m 38s

What is modeling?

Modeling is the mathematical representation of a physical process.
With modeling, one can:

- **Infer principles** governing a biological system based on the data
- **Study relationships** between elements of the system
- **Simulate and predict the behavior** of the system under specific conditiions
- **Identify experiments** that would help better understand the system
- **Visualize** the knowledge we have about the system

So what is modeling? Modeling is really about developing a mathematical representation of a physical process. With modeling, we can infer principles. For example, what are those principles that govern how a biological system operates? We can study the relationships between elements of the system. We can simulate and predict the behavior of the system under specific conditions. Then it can help us design in a more informed way experiments that would help us better understand the system. Of course, building visualizations is a very powerful way of seeing the dynamics, understanding the relationships, and interpreting complex data about systems. Of course, it's fundamental to really understanding the role of specific mechanisms that govern the system's dynamics.

Notes

Summary

2m 18s

Theory & simulation

Theoretical neuroscience:

- Reduce biological concepts to the bare minimum
- Simple model expressed by a set of mathematical equations that have analytical solutions
- Analysis of the parameter space

Simulation neuroscience:

- Biologically faithful models that incorporate many biophysical elements
- Analysis of models using numerical simulations
- Enables integrating data as measured in the laboratory

So in theoretical neuroscience, typically you want to reduce to a minimum the biological concepts, really simplify this absolutely and come up with a simple model expressed by a set of mathematical equations that you can solve analytically. That gives you a way to look at the parameter space of the system and develop an intuition and an understanding of at a high level, how does the system work and what are some of the key interactions. However, in simulation neuroscience, there's another approach which is saying, well, we actually don't yet know necessarily how to build a simplified model of the system, but let's integrate the data. Let's build a biologically faithful model that incorporates the biophysical representations, again, mathematically, and analyze those models using numerical simulations because these cannot be simply analyzed, mathematically. That helps us bring in data at the same level as it's measured in the laboratory. So biophysical level measurements that we can then integrate into the model to use that as a constraint in the model itself.

Notes

Summary

3m 18s

Theory & simulation

Theoretical neuroscience:

- Reduce biological concepts to the bare minimum
- Simple model expressed by a set of mathematical equations that have analytical solutions
- Analysis of the parameter space

Simulation neuroscience:

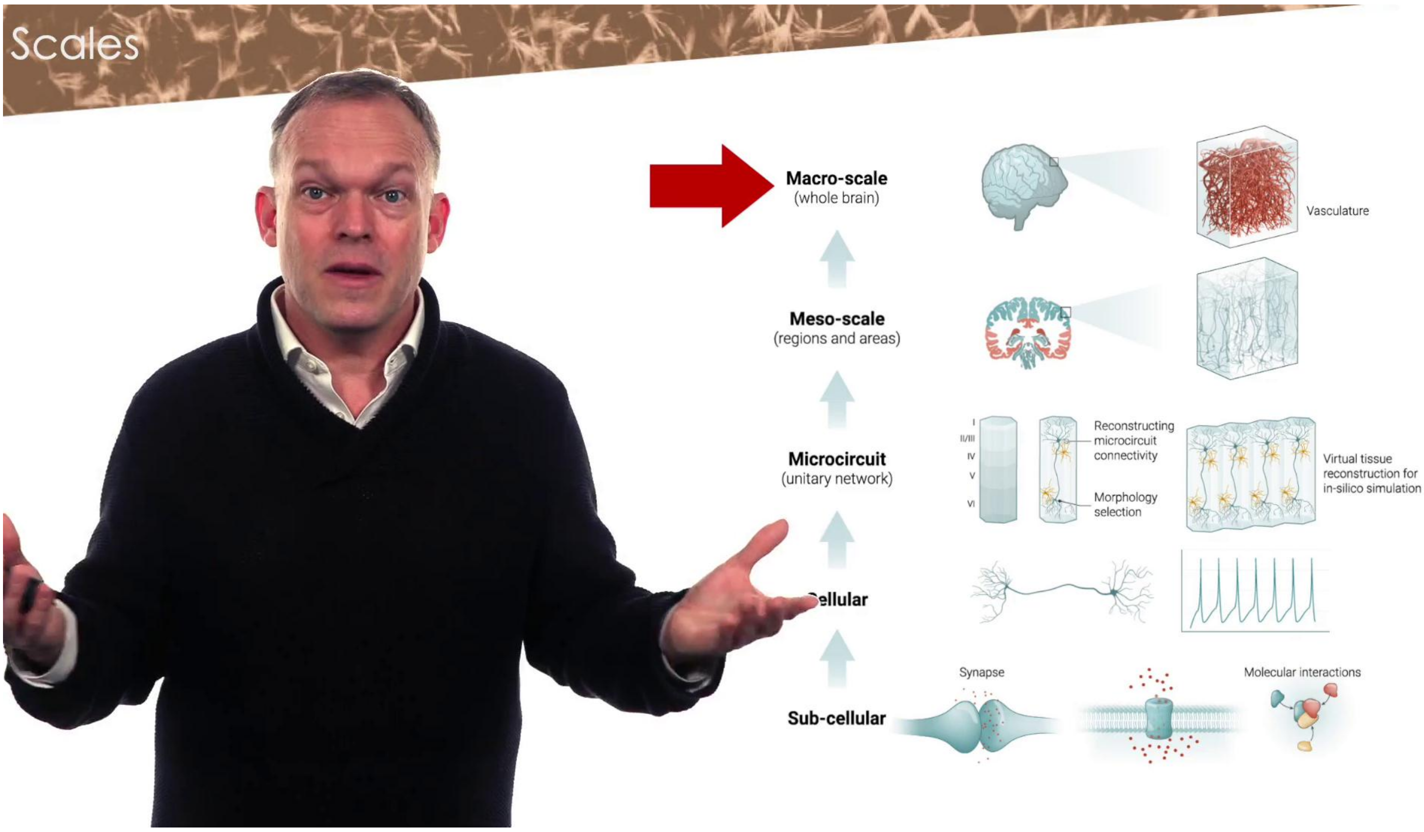
- Biologically faithful models that incorporate many biophysical elements
- Analysis of models using numerical simulations
- Enables integrating data as measured in the laboratory
- Strategy is to ensure parameters are constrained by biological data or known biophysical limits.

So for example, we want to make sure that the parameters of the model are constrained constrained by either specific biological measures, for example, the conductance of a synapse, or action potential amplitudes, things like that, resting membrane potentials, or they should be constrained. So the peak conductance could be constrained by the surface area and the size of the actual, for example, ion channel that can be placed in that membrane. So we try to keep everything in a realm where we know that it can be at least constrained by biophysical limits.

Notes

Summary

4m 39s

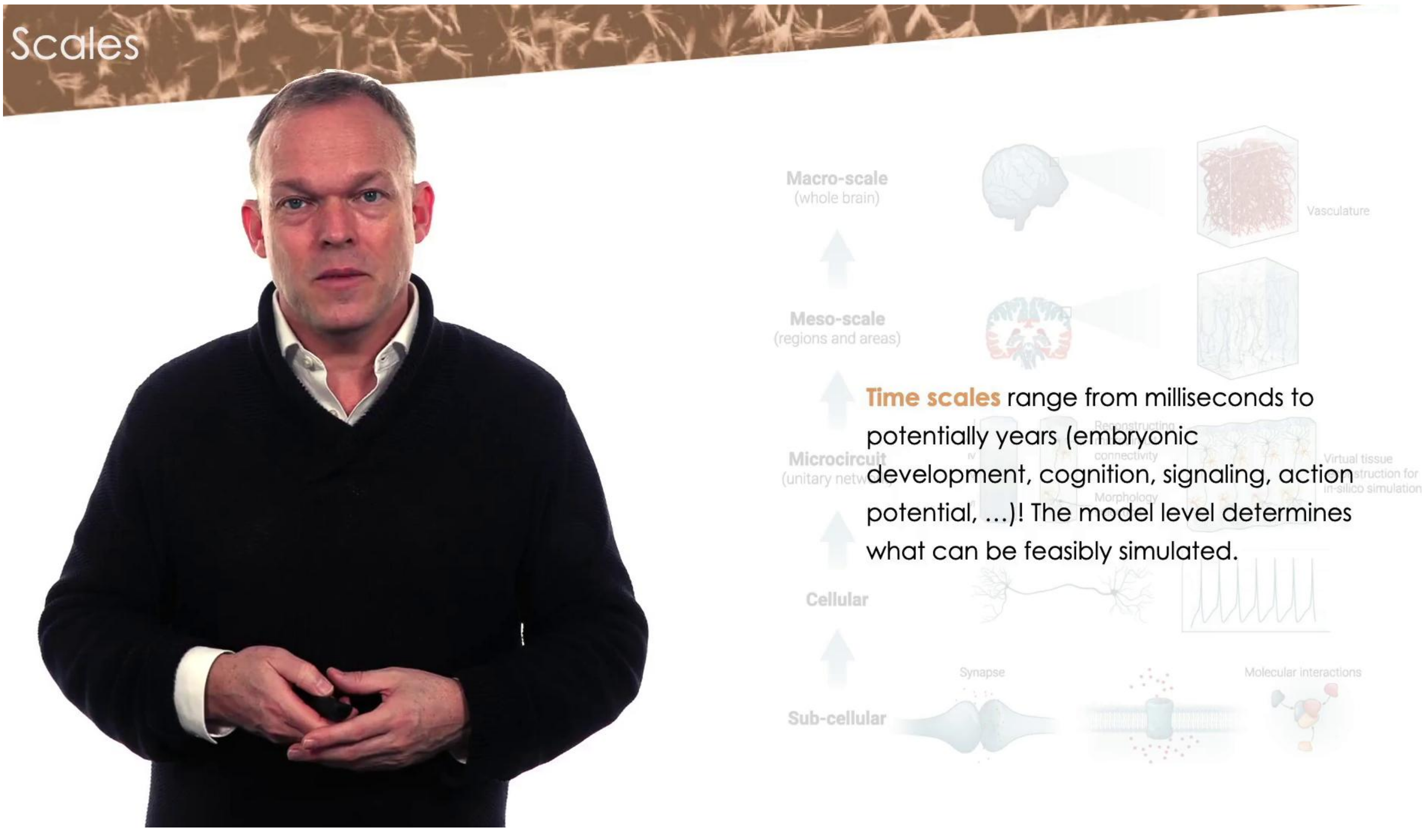


Then, of course, there are many different scales to consider, from the subcellular level, to the cellular, to the microcircuit, to the Mesa scale, to the macroscale. That really takes us from, for example, synapses and ion channels to cells, neurons, networks, regions, and to the whole brain. In doing so, we can find out, first of all, capture unique behavior at each level and also the interactions across levels. For example, how does synapses affect the firing of neurons and when you assemble those into a circuit, what's the emergent behavior of the network interactions? When you've got large areas across the brain, their interactions, coupled for example, to the whole brain level, where things like the vasculature and metabolism actually has a significant impact.

Notes

Summary

5m 21s



The timescales that we're talking about can actually range from milliseconds to potentially years if you're looking at developmental aspects and long term plasticity or neurodegeneration. But it's really the level of the model that determines what we can feasibly simulate. Of course, the way in which you formulate the model means that you could simulate maybe at a coarse grain over minutes, hours, months, years, but again, depending on the choice when you're building the model.

Notes

Summary

6m 23s