SeRC Complex Diseases - Neuro:

e-Science challenges in the Neuroscience field

- and examples of SeRC related projects

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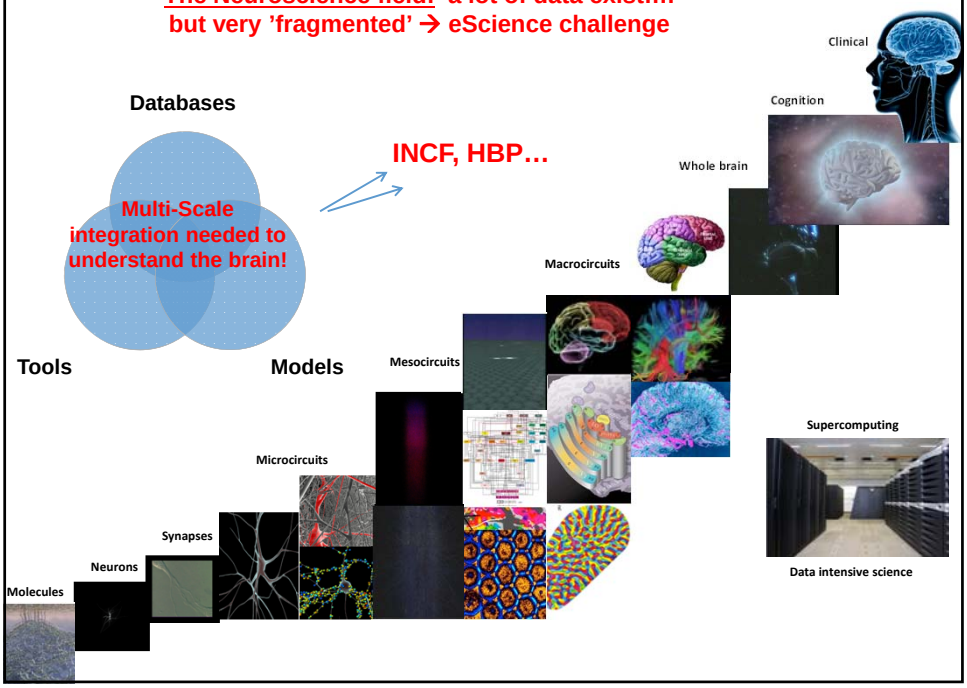
The brain a challenge for science and society

- **Amazing information processing capabilities**
- **Energy efficient**
- **'Robust' and adaptive**

→ 'Alien' technology that we need to understand better

Diseases - 800 billions Euro/year in EU → motivation to put efforts into understanding better how the brain works, from molecule to behaviour

The Neuroscience field: a lot of data exist.... but very 'fragmented' → eScience challenge



SeRC projects: Building a framework for in silico experiments in the basal ganglia, and the downstream control of motor behaviour

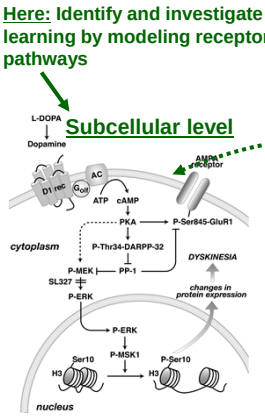
Interests of the computational neuroscience community at KTH/KI much wider: memory and learning in the cortex and hippocampus, data analysis, neuromechanical or neurorobotics systems, vision, epilepsy, decision making in the basal ganglia, generation of motor behaviour; also *tool* development for large- and multi-scale simulations.

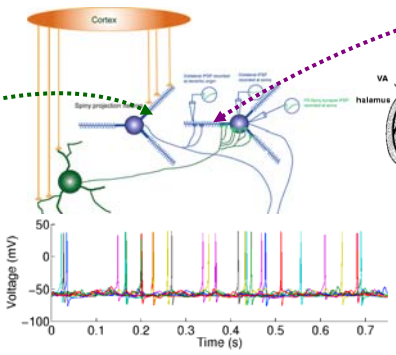
Systems level

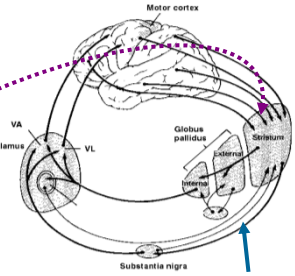
Here: Identify and investigate rules for learning by modeling receptor induced pathways

Microcircuit level

Subcellular level





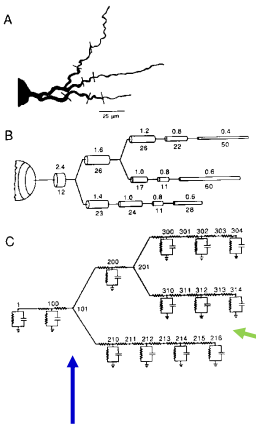


Often somewhat 'reduced', or abstract, models to study e.g.: selection of behaviour, and reward dependent learning

This level also is a bridge over to 'systems biology' and links to drug discovery…

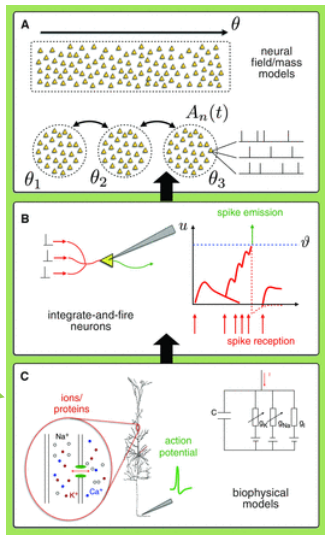
Biophysically detailed models to identify role of membrane and synaptic properties on the local network, for input integration, etc

Modeling neurons/networks – *compartmentalize* to deal with the spatial problem; use an *equivalent electrical circuit* for the membrane

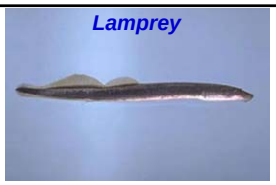


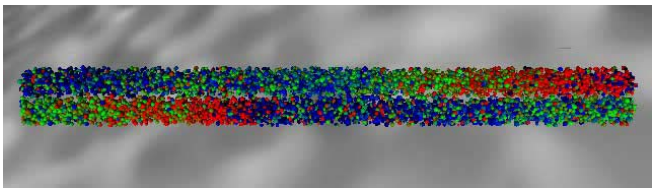
"Equivalent electrical circuits"
(can result in many thousand differential equations per model cell when many ion channels represented → computationally heavy, but scales well on parallel computers)

Model reductions used sometimes:



Example of simulations of detailed and large networks (KI/KTH collaborations) – motor pattern generation in the lamprey

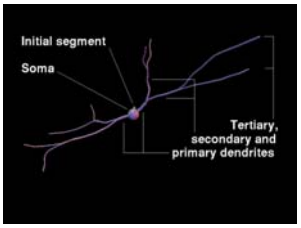




around one full wave length along the body

spiking inhibited depolarized

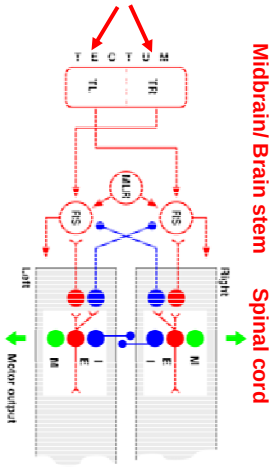
- Full scale models have been simulated (10000 neurons, almost 760000 synapses, 86 compartments per cell)
- Compare predictions from model with *in vitro* or *in vivo* experiments: control of swimming frequency/speed; role of endogenous modulators (DA, 5-HT, etc)
- Control of the coordination along cord (phase lag)
- Recently: use above as platform to study the control from brainstem and basal ganglia, etc

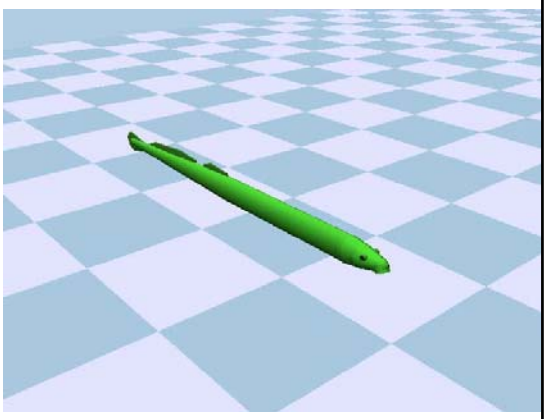


above from Kozlov et al, 2009, PNAS 106:20027-32, and Huss et al, 2007, J Neurophysiol. 97:2696-711

Study the control of such motor networks during steering – can the neural activity generated explain behaviour?*

Inputs from basal ganglia, the eyes, etc





Kozlov, et al, PNAS 111(9):3591-6 (2014) – spinal cord network linked to mechanical part, controlled by brain stem, etc

→ Future work: use a more detailed basal ganglia module to control behaviour

* (SeRC supported)

Also investigate the subcellular level….

1- Build network, e.g. X reactions; Y species; Z parameters

$$A + B \underset{k_r}{\overset{k_f}{\rightleftharpoons}} AB$$

2- Convert it to ODEs

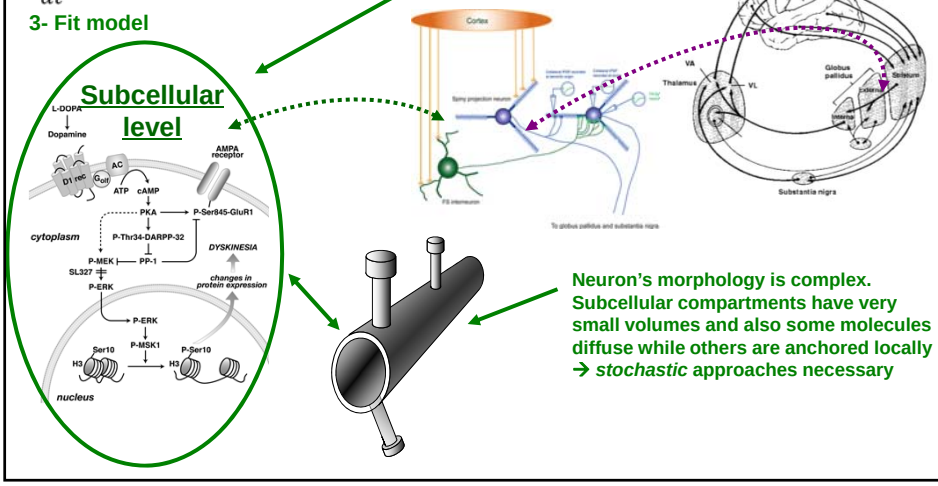
$$\frac{d[AB]}{dt} = k_f \cdot [A] \cdot [B] - k_r \cdot [AB]$$

3- Fit model

Modeling of subcellular systems to understand learning; also a bridge over to drug discovery

Systems level

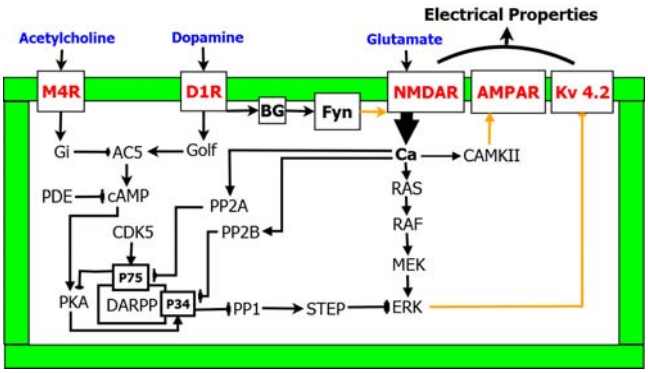
Microcircuit level



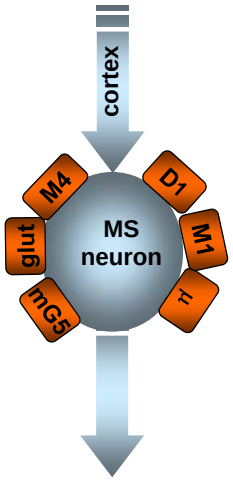
Neuron's morphology is complex. Subcellular compartments have very small volumes and also some molecules diffuse while others are anchored locally → *stochastic* approaches necessary

Ongoing or recent work on subcellular level*

Questions: What are the mechanisms underlying reward dependent learning in the basal ganglia? How is signaling changed in addiction? How can plasticity be restored in disease? How are membrane conductances affected by different neuromodulators?



Example system



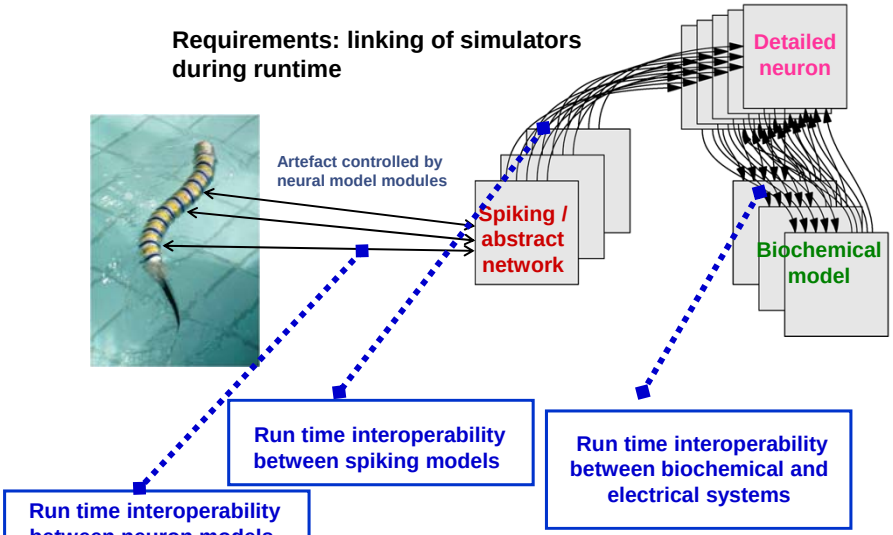
Basal ganglia output stage

Synthesizing conflicting data related to dopamine and glutamate interactions: Gutierrez-Arenas O, Eriksson O, Kotaleski JH (2014) PLoS Comput Biol. 10(1):e1003445
(SeRC supported)

Further visions….

Fields involved: HPC, visualization, numerical analysis, robotics, neuroscience

Requirements: linking of simulators during runtime



MUSIC – Multi-Simulation Coordinator (developed in collaboration with INCF), see Djurfeldt et al, 2010, Neuroinformatics 8:43-60

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Neuro Informatics 2014

Leiden, The Netherlands | August 25 - 27

Confirmed speakers: **Margarita Behrens**
Dmitri (Mitya) Chklovskii
Daniel Choquet
Ila Fiete
Michael Milham
Felix Schürmann

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INCF 2014 Short Course

Introduction to Neuroinformatics

August 22-23, 2014
Prior to the INCF Annual Congress
Leiden, the Netherlands

Application deadline:
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Travel support available

data analysis and neuronal coding
databases and ontologies
multiscale modeling
neuroengineering
simulation/computation/workflows
clinical applications
visualization

For:
neuroscience researchers
informatics researchers
advanced students
postdoctoral researchers
faculty members

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In interactions with…..

- **KTH and KI collaborators (Sten Grillner, Gilad Silberberg, Alex Kozlov, Anders Lansner, Michael Hanke, Olivia Eriksson)**
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- **Laurent Venance, Paris (experiments, synaptic plasticity)**
- **Arvind Kumar, Freiburg and Matthias Hennig, Edinburgh (modeling/theory)**
- **Upi Bhalla, Bangalore (modeling/experiments)**

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