Department of Mathematical Sciences

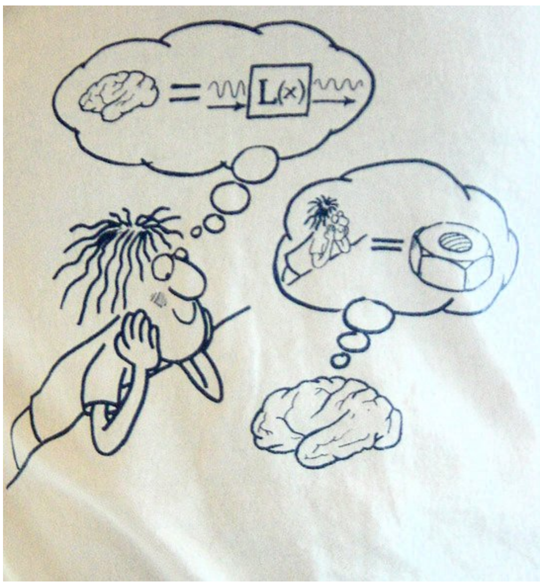
B12412: Computational Neuroscience and Neuroinformatics

What are Computational Neuroscience and Neuroinformatics?

Computational Neuroscience

Computational Neuroscience[1] is an interdisciplinary science that links the diverse fields of neuroscience, computer science, physics and applied mathematics together. It serves as the primary theoretical method for investigating the function and mechanism of the nervous system. Computational neuroscience traces its historical roots to the the work of people such as Andrew Huxley, Alan Hodgkin, and David Marr. Hodgkin and Huxley's developed the voltage clamp and created the first mathematical model of the action potential. David Marr's work focused on the interactions between neurons, suggesting computational approaches to the study of how functional groups of neurons within the hippocampus and neocortex interact, store, process, and transmit information. Computational modeling of biophysically realistic neurons and dendrites began with the work of Wilfrid Rall, with the first multicompartmental model using cable theory. Computational neuroscience is distinct from psychological connectionism and theories of learning from disciplines such as machine learning,neural networks and statistical learning theory in that it emphasizes descriptions of functional and biologically realistic neurons and their physiology and dynamics. These models capture the essential features of the biological system at multiple spatial-temporal scales, from membrane currents, protein and chemical coupling to network oscillations and learning and memory. These computational models are used to test hypotheses that can be directly verified by current or future biological experiments. Currently, the field is undergoing a rapid expansion. There are many software packages, such as NEURON, that allow rapid and systematic in silico modeling of realistic neurons.

Most computational neuroscientists collaborate closely with experimentalists in analysing novel data and synthesizing new models of biological phenomena.



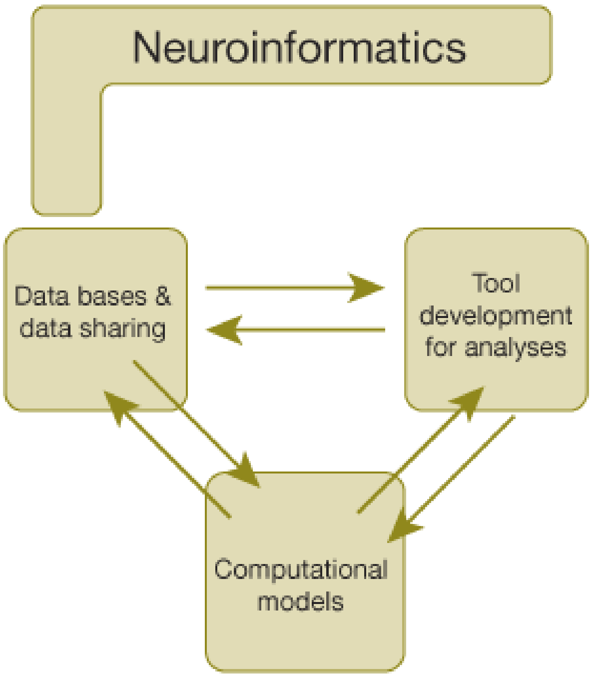
Cold Spring Harbor Summer School in Computational Neuroscience, 1992: the official T-shirt.

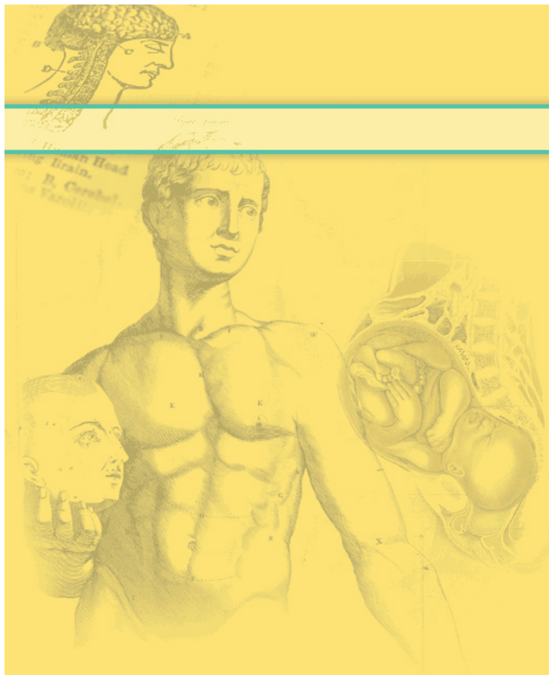
[1]from Wikipedia: http://en.wikipedia.org/wiki/Computational_neuroscience

Neuroinformatics

Neuroinformatics[2] combines neuroscience and informatics research to develop and apply advanced tools and approaches essential for a major advancement in understanding the structure and function of the brain. The field covers three primary areas:

- Neuroscience data and knowledge bases, increasingly capable of handling the full complexity and organization of the nervous system, from molecular to behavioral levels. e.g. see activities of the Nottingham Brain & Body Center[3] – "...an interdisciplinary setting for studies of environmental and genetic factors that are shaping structure and function of the human brain and body."
- Tools for data-acquisition, analysis, visualization and distribution of nervous system data.
- Theoretical, computational and simulation environments for modeling and understanding the brain (Computational Neuroscience!)





Informatics

Informatics[4] includes the science of information and the practice of information processing. Bioinformatics is a specialised example, targetted at sequence alignment, gene finding, genome assembly, protein structure alignment, protein structure prediction, prediction of gene expression and protein-protein interactions.

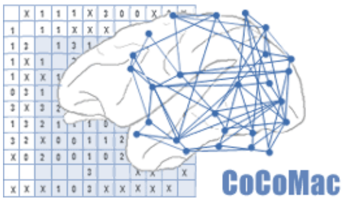
A common thread in informatics specialisations (neuro-, bio-, ...) is the use of mathematical tools to extract useful information from high dimensional data sets (e.g. the genome, spike-trains, fMRI, ...).

[2] as defined by the International Neuroinformatics Coordinating Facility: http://www.incf.org/
[3] http://brainbody.nottingham.ac.uk/
[4] from Wikipedia: http://en.wikipedia.org/wiki/Informatics

Some resources

CoCoMac (Collations of Connectivity data on the Macaque brain)

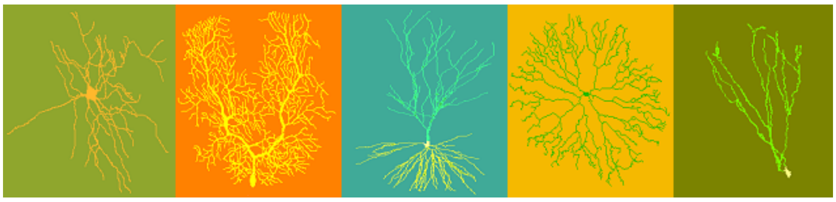
This is a systematic record of the known wiring of the primate brain. The main database contains details of hundreds of tracing studies in their original descriptions. Further data are continuously added.



http://www.cocomac.org/

NeuroMorpho

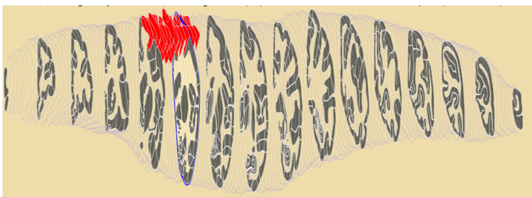
NeuroMorpho.Org is a centrally curated inventory of digitally reconstructed neurons. It contains contributions from over two-dozen labs and is continuously updated as new morphological reconstructions are collected, published, and shared, with the goal of densely covering all available data. Morphological data are essential for understanding the cellular complexity of the nervous system, and are used for analysis, visualization, and modeling. It allows for neuronal morphologies to be saved in NEURON format.



http://neuromorpho.org/

The Scaleable Brain Atlas

Visualization of neuroscientific data is important for a number of reasons. For purposes of presentation, a well-designed visualization has the capability to provide an intuitive illustration of modelled phenomena where words can fall short. It is also quite useful to the researcher to have a visual means of interpreting his or her model and the data obtained from it. The Scaleable Brain Atlas is a visualization tool for portraying a brain atlas in 3D space.



http://scalablebrainatlas.incf.org/

See also the website of the International Neuroinformatics Coordinating Facility

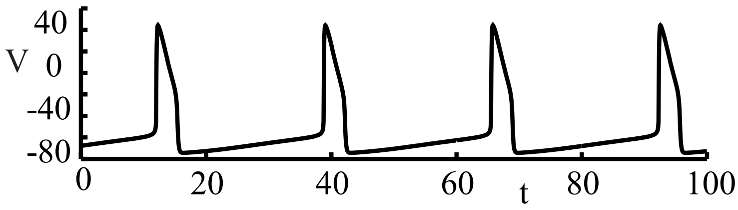
http://www.incf.org/

Major Topics

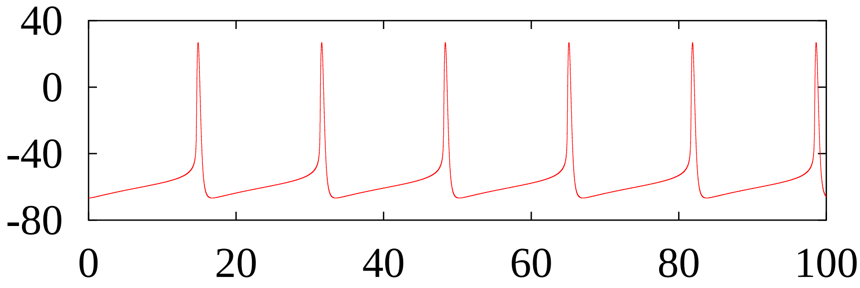
Single Neuron Modeling

Even single neurons have complex biophysical characteristics. In Hodgkin and Huxley's original model only employed two voltage-sensitive currents, the fast-acting sodium and the inward-rectifying potassium. Though successful in predicting the timing and qualitative features of the action potential, it nevertheless failed to predict such things important as adaptation. We now know that there is a zoo of voltage-sensitive currents, and the implications of the differing dynamics, modulations and sensitivity of these currents is an important topic of computational neuroscience.

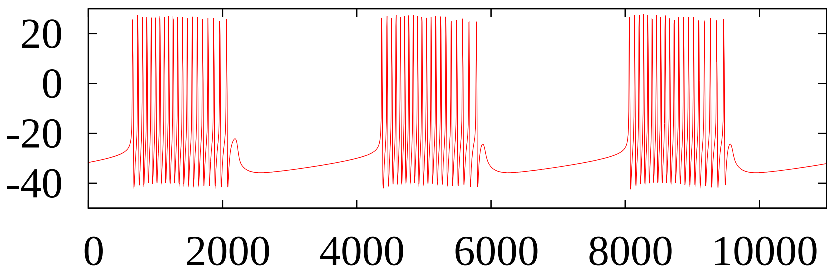
- Hodgkin-Huxley model output (train of action potentials)



- Wang-Buzsáki model (of hippocampal and neocortical fast-spiking interneurons)



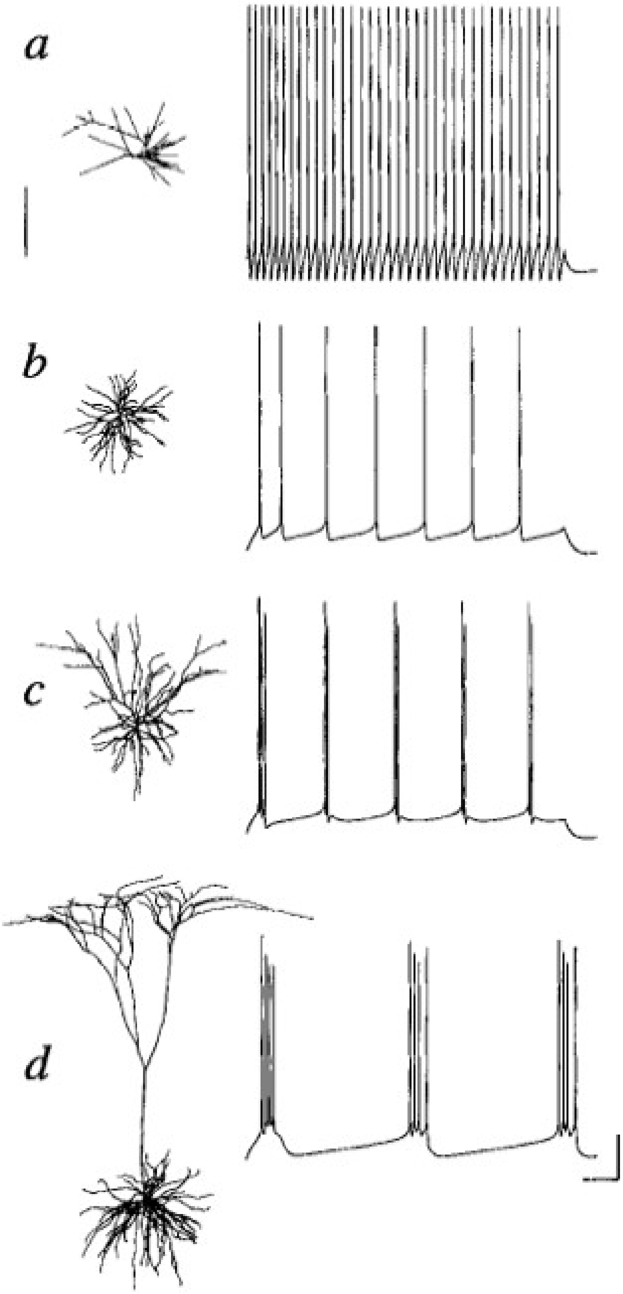
- Aplysia R-15 neuron model, showing calcium mediated (parabolic) bursting



The above plots were obtained using XPP - software that can evolve *ordinary differential equation* (ODE) models forward in time. Most single neuron modelling is based around the notion of *current balance*:

Current through capacitor = Current through resistive pathways + Injected Current

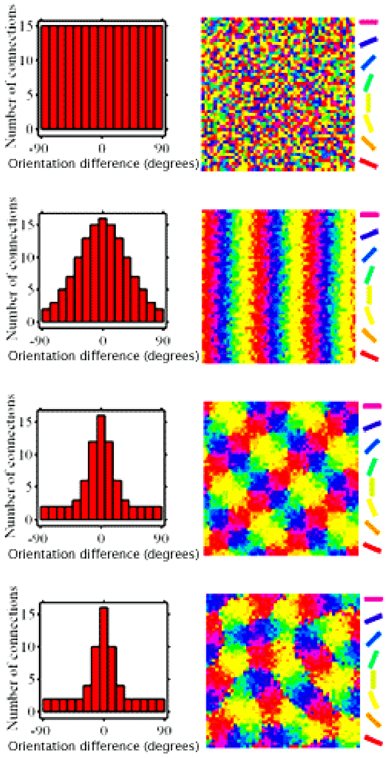
The computational functions of complex dendrite are also under intense investigation. There is a large body of literature regarding how different currents interact with geometric properties of neurons.



From Mainen, Z. F.; Sejnowski, T. J.; Influence of Dendritic Structure on Firing Pattern in Model Neocortical Neurons, Nature, 382, 363-366, 1996.
NEURON code available at http://www.cnl.salk.edu/~zach/patdemo.html.

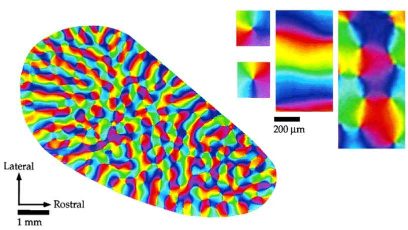
Development, Axonal Patterning and Guidance

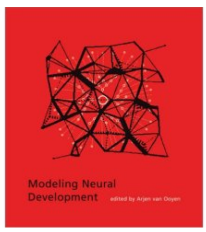
How do axons and dendrites form during development? How do axons know where to target and how to reach these targets? How do neurons migrate to the proper position in the central and peripheral systems? How to synapses form? We know from molecular biology that distinct parts of the nervous system release distinct chemical cues, from growth factors to hormones that modulate and influence the growth and development of functional connections between neurons. Theoretical investigations into the formation and patterning of synaptic connection and morphology is still nascent. One hypothesis that has recently garnered some attention is the **minimal wiring hypothesis**, which postulates that the formation of axons and dendrites effectively minimizes resource allocation while maintains maximal information storage.



Statistics of inter-neuronal connections in the visual cortex (left column) and corresponding maps of orientation preference (right column) obtained by minimizing the length of these connections. The minimal wiring hypothesis explains the observed inter species variability in map appearance as a result of the variability in inter-neuronal connectivity. Several features of the orientation maps, such as pinwheels and fractures (two bottom rows), could be evolutionary adaptations that minimize the length of inter-neuronal connections. From the Chklovskii lab – http://www.cshl.edu/labs/mitya/chklovskiilabhome.html.

See also the nice book *Modeling Neural Development* by Arjen van Ooyen, Bradford Books, 2003.

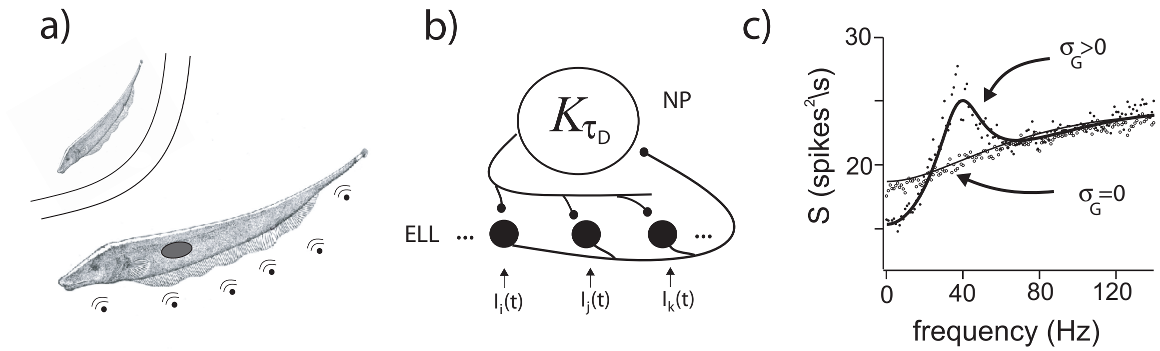




Orientation Preference in Tree Shrew: Complete map of orientation preference (left) and detail of singularities, linear zone and saddlepoints (right)

Sensory processing

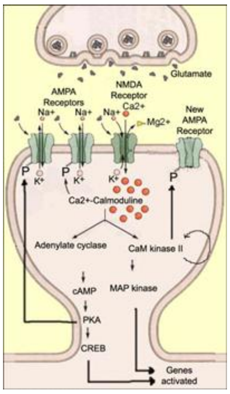
Models of sensory processing understood within a theoretical framework is credited to Horace Barlow. Barlow understood the processing of the early sensory systems to be a form of efficient coding, where the neurons encoded information which minimized the number of spikes. Experimental and computational work have since supported this hypothesis in one form or another. Current research in sensory processing is divided among biophysical modelling of different subsystems and more theoretical modelling function of perception. Current models of perception have suggested that the brain performs some form of Bayesian inference and integration of different sensory information in generating our perception of the physical world (and borrows from the field of *machine learning*).

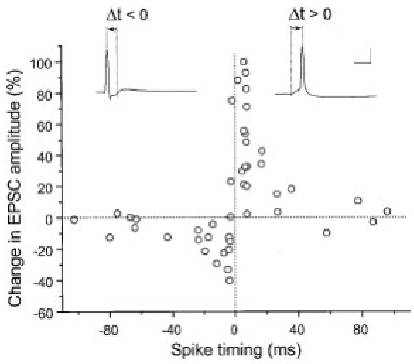


a: An electric fish experiences *global* electrosensory inputs from a communicating fish (upper left), and *local* inputs from swarm of prey Daphnia (bottom right). The filled circle on the body is the approximate size of the receptive field of an electrosensory lateral line lobe (ELL) pyramidal neuron. b: Schematic of the ELL pyramidal cell population and global inhibitory feedback from populations of bipolar cells in the NP nucleus. c: The spike train power spectrum S of a representative neuron in an integrate-and-fire model network. Simulations of the system are circles and solid lines are from a linear response calculation.

Memory and synaptic plasticity

Earlier models of memory are primarily based on the postulates of Hebbian learning (neurons that fire together wire together). Biologically relevant models such as the Hopfield net have been developed to address the properties of associative, rather than content-addressable style of memory that occur in biological systems. These attempts are primarily focusing on the formation of medium-term and long-term memory, localising in the hippocampus. Models of working memory, relying on theories of network oscillations and persistent activity, have been built to capture some features of the prefrontal cortex in context-related memory. One of the major problems in biological memory is how it is maintained and changed through multiple time scales. Unstable synapses are easy to train but also prone to stochastic disruption. Stable synapses forget less easily, but they are also harder to consolidate. It is likely that computational tools will contribute greatly to our understanding of how synapses function and change in relation to external stimulus in the coming decades.



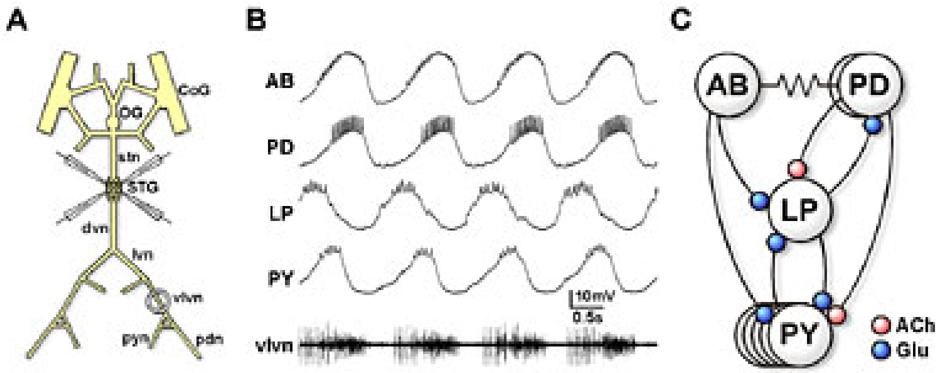


Timing requirements between pre- and postsynaptic spikes. Synaptic changes occur only if presynaptic firing and postsynaptic activity occur sufficiently close to each other. Experimentally measured weight changes (circles) as a function of relative pre- and post-synaptic firing times (showing a two-phase learning window). A positive change (LTP) occurs if the presynaptic spike precedes the postsynaptic one; for a reversed timing, synaptic weights are decreased. From Bi, G. and Poo, M. (1998). Synaptic modifications in cultured hippocampal neurons: dependence on spike timing, synaptic strength, and postsynaptic cell type. J. Neurosci., 18:10464-10472.

Behaviors of Networks

Biological neurons are connected to each other in a complex, recurrent fashion. These connections are, unlike most artificial neural networks, sparse and most likely, specific. It is not known how information is transmitted through such sparsely connected networks. It is also unknown what the computational functions, if any, of these specific connectivity pattern are. The interactions of neurons in a small network can be often reduced to simple models such as the Ising model (of a magnet). The statisical mechanics of such simple systems are well-characterized theoretically.

Central Pattern Generators



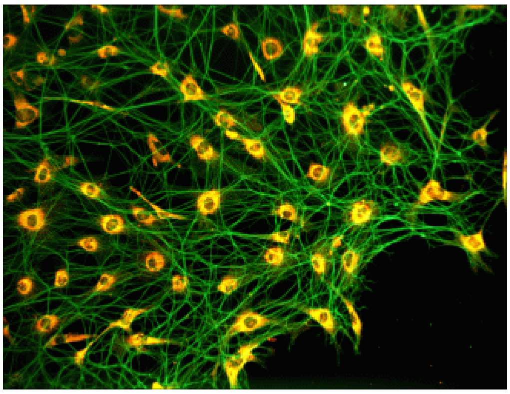
One of the fundamental problems in neuroscience is understanding how circuit function arises from the intrinsic properties of individual neurons and their synaptic connections. Of particular interest is the extent to which similar circuit outputs can be generated by multiple mechanisms, both in different individual animals, or in the same animal over its life-time. The Marder lab[5] is actively pursuing this for central pattern generating circuits in the crusctacean stomatogastric nervous system. Central pattern generators are groups of neurons found in vertebrate and invertebrate nervous systems responsible for the generation of specific rhythmic behaviors such as walking,

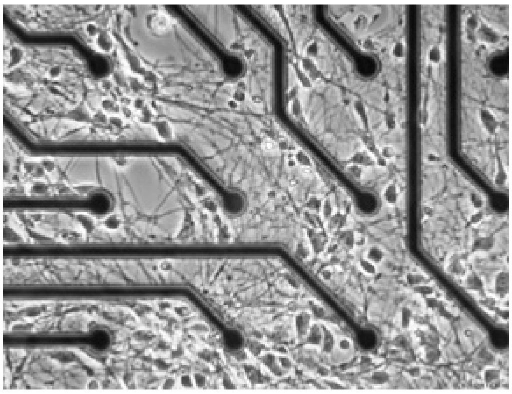
[5] http://www.bio.brandeis.edu/faculty01/marder.html

swimming, and breathing. The central pattern generators in the stomatogastric ganglion (STG) of lobsters and crabs are ideal for many analyses because the STG has only about 30 large neurons, the connectivity is established, the neurons are easy to record from, and when the stomatogastric ganglion is removed from the animal, it continues to produce rhythmic motor patterns.

Cultures

With the emergence of two-photon microscopy and calcium imaging, there are now powerful experimental methods with which to test new theories regarding neuronal networks, particularly for neuronal cultures. Cultures of dissociated neurons from rat embryos can rapidly form synapses in culture and develop complex patterns of spontaneous activity. Moreover, more traditional electrophysiology can be used to both record and stimulate cells. Interestingly cells may be cultured on multi-electrode arrays (MEAs), to form a long-term, two-way interface between the cultured networks and a computer. The cultured nets can serve as the 'brain' of simulated animats or robotic creatures[6].

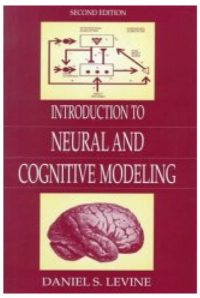




Cognition, Discrimination and Learning

Computational modeling of higher cognitive functions has only begun recently. Experimental data comes primarily from single unit recording in primates. The frontal lobe and parietal lobe function as intergrators of information from multiple sensory modalities. There are some tentative ideas regarding how simple mutually inhibitory functional circuits in these areas may carry out biologically relevant computation. The brain seems to be able to discriminate and adapt particularly well in certain contexts. For instance, human beings seem to have an enormous capacity for memorizing and recognizing faces. One of the key goals of computational neuroscience is to dissect how biological systems carry out these complex computations efficiently and potentially replicate these processes in building intelligent machines.

See Introduction to Neural and Cognitive Modeling, Lawrence Erlbaum Associates, 2000.



[6]See work of the Potter Lab - - http://www.neuro.gatech.edu/groups/potter/index.html

Some web-sites

- Computational Neuroscience on the World Wide Web. An index for computational neurobiology, focusing on compartmental modeling and realistic simulations of biological neural systems.
  http://home.earthlink.net/
- Encyclopedia of Computational Neuroscience. A peer-reviewed Wiki.
  http://www.scholarpedia.org/article/Encyclopedia_of_Computational_Neuroscience
- Nature Neuroscience Blog.
  http://blogs.nature.com/nn/actionpotential/
- Society for Neuroscience.
  http://apu.sfn.org/