

# Studies of Artificial Neural Systems, SANS

*Anders Lansner and Örjan Ekberg*

Our research centers around mathematical modeling and computer simulation of biological nervous systems, the brain in particular. The primary aim is to improve our understanding of the principles underlying their information processing capabilities. Our models extend from those incorporating biological details of cellular processes, neurons and neuronal networks to abstract connectionist type models. Our field of research, theoretical and computational neuroscience, is quite young but has in recent years achieved a broad acceptance.

Being a computer science group, it is natural for Sans to emphasize also the engineering and applications aspects of understanding biological information processing, namely the use of this knowledge in the design of advanced technical systems. From a computer science perspective, the brain is unique among biological entities since, like the computer, it is specifically designed for information processing. The human brain still outperforms today's supercomputers by several orders of magnitude in terms of processing and memory capacity as well as in compactness, robustness, and power dissipation. No technical design comes anywhere close to its performance in tasks like vision, speech and language understanding, or motor control. Not surprisingly, the brain is often seen as a model for future man-made autonomous learning systems. Despite considerable progress in recent decades, the working principles of the brain remain mysterious. We regard it as our major research challenge to find out how such performance is possible and to contribute in uncovering the underlying information processing principles.

It is quite likely that progress along these lines will be rapid in the next couple of decades. Increasingly advanced experimental techniques together with mathematical modeling and computer simulation are enabling methodologies for achieving this. Furthermore, provided that the historical trends in hardware development continues, man-made computing technology will approach the estimated capacity of the human brain within the next few decades. If so, the technical potential of brain-like computing will begin to materialize in the first decades of the third millennium.

The Sans research group was formed in 1987. During 1998 and 1999 it consisted of two lecturers, two research assistants, one postdoc, and six PhD students. Two members of the group completed their doctorate degrees [Wadden, 1998; Hellgren Kotaleski, 1998] and one his licentiate degree [Orre, 1998]. The Sans group benefits from a long-standing and close

*Our research centers around mathematical modeling and computer simulation of biological nervous systems, the brain in particular.*

[www.kth.se/sans/](http://www.kth.se/sans/)

*The human brain still outperforms today's supercomputers by several orders of magnitude...*

*The SANS research group was formed in 1987.*

*The main sources of external funding are presently TFR, MFR and Nutek.*

collaboration with neurophysiologists at the Dept. of Neuroscience, Karolinska Institutet (Prof. Grillner and co-workers). In recent years, collaboration has been further extended to other experimental groups in neuroscience and neuropsychology. Sans is also engaged in technical applications of artificial learning systems in collaboration with Sics (the NNRC group, G. Sjödin). The main sources of external funding are presently TFR, MFR and Nutek. Sans has also served as the Swedish managing node for an EU funded network of excellence, NEuroNet, in the area of neural networks.

### **Sans research themes**

The major components of the brain are the sensory-perceptual systems, the behavior-motor systems, and the sub-cortical motivational and emotional systems. Throughout, plasticity, self-organization, and learning are fundamental properties. Over the years, the Sans group has investigated several of these fundamental components and their functions, including associative memory and stimulus-response learning, generation and control of locomotion, behavior selection and reinforcement learning.

A man-made autonomous system, be it a robot searching for mines or an electronic agent negotiating for bandwidth on the Internet, faces much the same challenges as a living animal. For both, it is crucial to get a quick grasp on the situation at hand, to identify alternative actions, to decide which action to execute, and, finally, to do so before it is too late. The execution itself must be accurate and effective. The structure of the cerebral cortex is surprisingly homogenous with small differences between the different systems and areas, whether these are mainly engaged in sensory-perceptual or motor-action tasks. This indicates that a few general principles are widely used, allowing for efficient global coherence and integration. The subcortical motivational and emotional systems are crucial in regulating the cortical systems and providing goal-directedness to their operation. The research goal of Sans is to uncover and characterize these general principles and demonstrate how they can be efficiently implemented in future autonomous learning systems.

In our study of adaptivity and plasticity we are focusing on biologically plausible forms like self-organization of structure and unsupervised and trial-and-error kinds of learning. We further emphasize the network level of information processing rather than cellular level computation. Below follow descriptions of the different sub-projects conducted over the last two years.

### **Cortical associative memory and BCPNN**

One theme studied for a long time within Sans concerns cortical associative memory function. Previously we have shown that a recurrent attractor network model with cortical minicolumns as its computational units is a biologically plausible model of a patch of cortex. We have demonstrated that such a network is compatible with cortical dynamics, network organization, and microarchitecture. A Bayesian-Hebbian learning rule developed at Sans provides a functional model of synaptic plasticity. The biologically inspired network architecture and learning rule has further been formalized as an abstract learning paradigm, BCPNN (Bayesian Confidence Propagation Neural Network).

More recently we have introduced continuous time into all aspects of the network model. This includes looking at architectures for temporal and sequential association as well as modification of the learning rule to allow for adaptation of learning and forgetting rates.

### **Memory Consolidation**

Long term memory is normally attributed to the neocortex. It is, however, not obvious how to reconcile slow forgetting with fast learning in this structure; a memory with fast learning also forgets quickly. One hypothesis [McClelland et al., 1995] is the existence of a fast intermediate memory in the medial temporal lobe which learns quickly, and a consolidation process during sleep whereby the information is transferred into long term storage in the neocortex.

We have been investigating the dynamics of this process in connected attractor neural networks with different learning time constants. An incremental learning rule extending previous work on Bayesian confidence propagation neural networks has been developed. The dynamics of attractors during learning has been studied, showing that as new information is learned old attractors shrink and convergence to older memories becomes slower [Sandberg et al., 1999].

### **Working memory in the entorhinal cortex**

In this project biophysical modeling of nerve cells is done in order to study the function of the entorhinal cortex (EC). The EC is strategically positioned as a gateway between neocortex – the region of the brain responsible for higher cognitive functions, and the hippocampal system – one of the key components of the brain's memory system. It is also important from a clinical perspective. One of the major forms of epilepsy involves the EC. Further, in Alzheimers disease, the first region to show signs of change is the EC.

*One theme studied for a long time within SANS concerns cortical associative memory function.*

*We are currently studying working memory function in EC in terms of cellular properties and network connectivity.*

We are currently studying working memory function in the EC in terms of cellular properties and network connectivity. The results so far include models of stellate, pyramidal and inhibitory cells [Fransén et al., 1999a; Fransén et al., 1999b]. For the stellate cell an ion-channel, named the H-channel, has been studied thoroughly. For the pyramidal cell the effects of internal calcium on some potassium and cationic ion-channels have been studied.

### **Sequential and temporal association**

Generating sequences of actions and thoughts is a basic feature of the human being. Connectionist models of the cerebral cortex should therefore include the time dimension in order to be realistic, but so far they have put little emphasis on this aspect.

In this recently initiated project, we investigate self-organization of feature detectors sensitive to temporal structure as well as suitable network architectures for temporal association and sequence processing [Gillblad, 1999]. The network model learns temporal sequences of data and reproduces them by temporal association. The reproduction of a learned sequence is triggered by presenting the initial elements from that sequence to the model. BCPNN is used as the key component of this extended model.

### **Hierarchical clustering**

Clustering and categorization are fundamental operations of intelligent systems. The attractor network paradigm performs such operations naturally, since an input pattern belonging to the basin of attraction of a stored memory will recall this memory. The real world is however not structured as a set of random patterns, which is what these networks are usually trained on. On the contrary, there are structures and hierarchies and it is important that these are appropriately represented in memory. A recent project demonstrated that a recurrent BCPNN network is capable of doing this. Further it was demonstrated that by varying some of the network parameters it is possible to control at what level in the hierarchy the network operates [Gars and Tamsen, 1999].

### **BCPNN applications**

The application of BCPNN networks to data mining of drug adverse reactions was initiated several years ago. This has been done by Sans in collaboration with the WHO Collaborating Centre for International Drug Monitoring in Uppsala. It has been demonstrated that it is quite feasible to process the entire database of some 1.5 million entries thus extracting interesting correlations to be subjected to further examination by experts. It was shown that in several cases use of this technique would have resulted in

*Clustering and categorization are fundamental operations of intelligent systems.*

earlier detections of some adverse reactions, by a matter of years [Bate et al., 1998; Orre et al., 1999].

### **Neural generation and control of locomotion**

One of the most important tasks of the nervous system is to generate and control movements of the body. The neural mechanisms behind vertebrate locomotion has been the subject of extensive modeling by Sans for more than ten years in close collaboration with experimentalists at the Dept. of Neuroscience, Karolinska Institutet (Prof. Grillner and co-workers), who have identified many cellular mechanisms that may contribute. The spinal cord network underlying locomotor activity in the lamprey, an evolutionarily old vertebrate, has been used as a model system. The simulations have been on different levels of abstraction ranging from detailed models building on Hodgkin-Huxley equations for the membrane currents to simplified cell models reminiscent of those used in artificial neural networks. The general goal is to synthesize experimental data, pinpoint critical mechanisms and generate experimental predictions. In addition, the biological insights form the basis to look at legged animal locomotion from more of an engineering perspective.

*One of the most important tasks of the nervous system is to generate and control movements of the body.*

### **Rhythm generation, Intersegmental co-ordination**

In this project, mechanisms for local rhythm generation and phase delays are studied using computational modeling. Two alternative models for the production of left-right alternating swimming activity have been explored. In one, the reciprocal inhibition between the sides is critical for burst generation, whereas in the other each side is self-oscillatory due to the adaptation properties of participating neurons, and inhibition serves mainly to impose left-right alternation. In both these networks different experimentally observed characteristics can be reproduced, including an appropriate intersegmental phase delay [Hellgren-Kotaleski et al., 1999a; Hellgren-Kotaleski et al., 1999b].

### **Synaptic plasticity in the spinal locomotor network**

The aim of this project is to explore consequences of synaptic plasticity in the lamprey locomotor network. This means that the connectivity strength between neurons may change dynamically. This work is motivated by the experimentally found effects which two neuromodulators, substance P and 5-HT, have on the inhibitory and excitatory synaptic transmission.

*The aim of this project is to explore consequences of synaptic plasticity in the lamprey locomotor network.*

Preliminary simulations show that network level effects (i.e. swimming frequency) of substance P and 5-HT can to a substantial extent be explained based on their effects on the plasticity of the synaptic connectivity [Kozlov et al., 1999a]. Future plans involve a more thorough investiga-

tion of synaptic plasticity in the different models for rhythm generation of the lamprey locomotor network, as well as consequences for the intersegmental coordination.

*This project is aimed at understanding two functions of the reticulospinal (RS) nuclei in the brain stem of the lamprey:*

### **Vestibular control and turning**

This project is aimed at understanding two functions of the reticulospinal (RS) nuclei in the brain stem of the lamprey: (i) posture control via vestibulospinal reflexes and (ii) production of turning commands during swimming. Phenomenological modeling is used to isolate key features of the control system from experimental data; a form of reverse engineering.

A model of posture control mechanisms in the roll plane using recent experimental data has been presented [Kozlov et al., 1999b]. Existence of a stable equilibrium state corresponding to dorsal-side-up body orientation is shown analytically in the model. Stability of this equilibrium is studied for a wide range of parameter values of sensitivity and inertia of the control scheme, as well as the effective viscosity of the water. Our models of turning commands are at a preliminary stage of discussion with the experimental team from KI.

### **Walking and neuromechanics**

Understanding animal movement control from an engineering point-of-view suggests novel ways of constructing more flexible and efficient mechanical control systems. This project is a cross-disciplinary effort in order to increase our understanding of how animals manage to control their bodies with such precision and gracefulness without the use of excessive power.

A simulated mechanical model of a generic four-legged mammal has been developed and is currently the target for a simulated neural control system with rhythm generating and learning capabilities. By manually setting up a neural circuit based on current neurophysiological knowledge, a controller capable of coordinated leg control has been derived [Wadden and Ekeberg, 1998; Wadden, 1998]. We are now studying how adaptable pattern recognition techniques can improve this by generating predictive commands.

*The aim of this project is to simulate the learning and control of the human precision grip.*

### **Hand Motor Control**

The aim of this project is to simulate the learning and control of the human precision grip. The precision grip is defined as the grip between the tip of the index finger and the tip of the thumb and displays a number of non-trivial coordination phenomena. The project, which is a collaboration with Prof. Hans Forssberg at Karolinska Institutet, is divided into four parts:

- 1) Develop a biomechanical model of the hand and arm.
- 2) Control the model using artificial neural networks (ANN).

- 3) Study the ANN control mechanisms.
  - 4) Identify biological counterparts in the central nervous system.
- The first part of the project has been finished and resulted in a quantitative biomechanical model based on physiological grip force data [Fagergren et al., 1999].

### **Goal directedness, behavior selection and reinforcement learning**

Animals are highly goal-oriented both in their perception and behavior. Attention is directed towards aspects in the environment relevant to the animal's current motivational state. Behavior is selected in such a way as to achieve maximum reward and avoid negative consequences, and learning is most effective in situations with a high emotional content. Clearly, such mechanisms are also essential for a man-made autonomous agent. The neural mechanisms underlying such goal direction are now being studied experimentally in many places, thus generating information useful for modeling.

*Animals are highly goal-oriented both in their perception and in behavior.*

Reinforcement learning [Sutton and Barto, 1998] is a goal-oriented learning paradigm of particular interest from a biological perspective. It utilizes a kind of reward-punishment feedback readily available in the natural environment. Therefore, reinforcement learning also has considerable technical interest. Contrary to when using supervised learning, this kind of learning needs no teacher. If there is one, reinforcement learning allows the student to surpass the capability of the teacher. We have initiated a study of robot navigation using reinforcement learning as a MSc project. In parallel we are also studying a model of animal navigation in collaboration with Chalmers, Dept. of Computer Engineering (Prof. Bertil Svensson and MSc Guang Li).

### **Basal ganglia model**

This project addresses how the brain learns to behave. The nervous system contains a vast amount of motor programs on different levels. The basal ganglia are believed to be a key component in the selection of which programs to activate in a given context, and their integration to form an adaptive behavior. Many major neurological diseases, such as Parkinson's disease, are due to malfunction of the basal ganglia.

*This project addresses how the brain learns to behave.*

Drawing on recent results in neurobiology and in the subfield of machine learning theory called reinforcement learning, a functional model of information processing in the basal ganglia has been constructed. The model aims to explain in detail how these neural structures interact to form a learning system capable of behavioral selection.

*A robot that learned to navigate and deliver messages and objects in an office environment was simulated.*

*...a joint project between Sans and Chalmers...*

### **Biologically inspired autonomous robot navigation**

In a recent MSc thesis project reinforcement learning (RL) was evaluated in a multiple-goal situation [Åhländer, 1999]. A robot that learned to navigate and deliver messages and objects in an office environment was simulated. An RL based experts/gating architecture was developed to achieve task decomposition. It was shown that such an approach gives appropriate generalization and reduces learning times considerably compared to a monolithic solution.

The problem of autonomous navigation was also studied in a joint project between Sans and Chalmers, Dept. of Computer Engineering (Prof. Bertil Svensson and MSc Guang Li). Methods were developed based on biological knowledge about the heading and place systems in the rat brain [Li et al., 1997]. This project will be finished with a PhD in November 1999.

### **Modeling of cellular processes and biochemical networks**

Neural modeling has so far mostly concerned the level of neurons and neuronal networks. It is, however, obvious that neuronal function and communication can be described at a finer level of detail, that of cellular biochemistry and molecular biology.

Today's increasingly detailed knowledge of the cell's molecular mechanisms is beginning to make it possible to mathematically model parts of or even the whole metabolism of the cell, that is, to move from a purely qualitative description to a more quantitative one. This is achieved for example by formulating coupled differential equations representing metabolic pathways and ion fluxes across the cell's membranes. A recent example of such a model concerns synaptic plasticity in the hippocampus [Bhalla and Iyengar, 1999].

This is the next logical step in biology and medicine, where previously quantitative models have been very difficult to establish due to scarce or noisy data [Hellgren Kotaleski and Lansner, 1999]. Accurate models will help for example in describing and explaining synaptic plasticity and learning, metabolic diseases, or in the development of new drugs for example through prediction of the effect of drug candidates blocking a metabolic pathway and in developing catalytic antibodies.

### **Modeling of insulin secretion in pancreatic $\beta$ -cells**

In cooperation with Pharmacia-Upjohn and Psci (Parallel Scientific Computing Institute) at Nada, Sans has recently initiated a modeling and simulation study focused on insulin secretion from pancreatic  $\beta$ -cells. The underlying processes bear a close resemblance to those involved in synaptic transmitter release at nerve terminals.

*In cooperation with Pharmacia-Upjohn and Psci (Parallel Scientific Computing Institute) at Nada,...*



During the last 15 years a couple of quantitative models of varying complexity have successfully described the fast oscillatory pattern of  $\text{Ca}^{2+}$  concentration which accompanies insulin secretion, yet it remains to describe and explain the presence of slow oscillations, the involvement of earlier stages of insulin metabolism and ATP synthesis, the effects of many cells interacting through gap-junctional couplings and the role of intra-cellular  $\text{Ca}^{2+}$  stores. Large-scale simulations of several coupled cells will also require parallel processing and the development of suitable software.

### **Tools for modeling and simulation**

Being a computer science group it is natural that Sans is also engaging in simulator development. In recent years we have also been using standard simulators but we have found that they sometimes do not meet up to our demands, e.g. with regard to simulations of very large networks. The SPLIT program developed some years ago [Hammarlund, 1996; Hammarlund and Ekeberg, 1998] is a parallelizing simulator that allows such simulations. Our largest network model simulated so far had more than 50.000 neurons and 4 million synapses. Efficient neural networks simulators are important for another reason as well: They tell us how to implement neural network operations efficiently, e.g. in an on-board embedded system.

*Being a computer science group it is natural that Sans is also engaging in simulator development.*

### **See**

“See” is a modular software framework for simulation of biologically detailed and artificial neural networks and systems [Djurfeldt et al., 1999]. It includes a general purpose scripting language (Scheme) which can also be used interactively, but the basic framework is written in C++. Models can be built on the Scheme level from “simulation objects”, each representing a population of neurons, a projection, etc. The simulator provides a flexible and efficient protocol for data transfer between such objects. See contains a user interface to the parallelized, platform independent library SPLIT intended for biologically detailed modeling of large-scale networks and is easy to extend with new user code, both on the C++ and Scheme levels.

## References-Sans

### *Refereed journals and books*

- [Bate *et al.*, 1998] Bate A., Lindquist M., Edwards I. R., Olsson S., Orre R., Lansner A., and Melhado de Freitas R. (1998). “A Bayesian neural network method for adverse reaction signal generation”, *European J. Clin. Pharmacol.*, **54**, 315–321.
- [Bhalla and Iyengar, 1999] Bhalla U. S., and Iyengar R. (1999). “Emergent Properties of Networks of Biological Signaling Pathways”, *Science*, **283**, 381–387.
- [Djurfeldt *et al.*, 1999] Djurfeldt M., Sandberg A., Ekeberg Ö., and Lansner A. (1999). “See - a framework for simulation of biologically detailed and artificial neural networks and systems”, *Neurocomputing*, **26-27**, 999–1003.
- [Fagergren *et al.*, 1999] Fagergren A., Ekeberg Ö., and Forsberg H. (1999). “Precision Grip Force Dynamics, a System Identification Approach”, Submitted.
- [Fransén *et al.*, 1999a] Fransén E., Alonso A. A., Dickson C. T., Magistretti J., and Hasselmo M. E. (1999a). “Properties and Role of  $I_h$  in the Pacing of Subthreshold Oscillations in Entorhinal Cortex Layer II Neurons: I Voltage-clamp Analysis”, *J. Neurophys.*, Submitted.
- [Fransén *et al.*, 1999b] Fransén E., Alonso A., Dickson C., Magistretti J., and Hasselmo M. (1999b). “Properties and Role of  $I_h$  in the Pacing of Subthreshold Oscillations in Entorhinal Cortex Layer II Neurons: II Modeling and Simulation”, Submitted.
- [Gars and Tamsen, 1999] Gars J., and Tamsen F. (1999). “Clustering in Bayesian Neural Networks” *TRITA-NA-P9910*, Nada, KTH.
- [Gillblad, 1999] Gillblad D. (1999). “Sequence analysis using a Bayesian artificial neural network” *TRITA-NA-E9942*, Nada, KTH.
- [Hammarlund, 1996] Hammarlund P. (1996). “Techniques for Efficient Parallel Scientific Computing” PhD thesis, Royal Institute of Technology, Stockholm, Sweden, Dept. of Numerical Analysis and Computing Science, TRITA-NA-P9611.
- [Hammarlund and Ekeberg, 1998] Hammarlund P., and Ekeberg Ö. (1998). “Large Neural Network Simulations on Multiple Hardware Platforms”, *J. Comp. Neurosci.*, **5**, 443–459.
- [Hellgren -Kotaleski and Lansner, 1999] Hellgren Kotaleski J., and Lansner A. (1999). “Modeling Cellular Processes – Bioinformatics beyond Sequences” *TRITA-NA-P9906*, PSCI at Nada, KTH.

- [Hellgren-Kotaleski *et al.*, 1999a] Hellgren-Kotaleski J., Grillner S., and Lansner A. (1999a). “Neural Mechanisms potentially contributing to the intersegmental Phase Lag in Lamprey. I: Segmental oscillations dependent on reciprocal inhibition”, *Biol. Cybernetics*, **81**(4), 317–330.
- [Hellgren-Kotaleski *et al.*, 1999b] Hellgren-Kotaleski J., Lansner A., and Grillner S. (1999b). “Neural Mechanisms potentially contributing to the intersegmental Phase Lag in Lamprey. II: Hemisegmental oscillations produced by mutually coupled excitatory neurons”, *Biol. Cybernetics*, **81**(4), 299–315.
- [Hellgren-Kotaleski, 1998] Hellgren-Kotaleski J. (1998). “Modeling of Bursting Mechanisms and Coordination in a Spinal Central Pattern Generator” PhD thesis, Kungl. Tekniska Högskolan, ISBN 91-7170-225-5, ISSN 0348-2952, ISRN KTH/NA/R-98/10-SE, TRITA-NA-P9810.
- [Kozlov *et al.*, 1999a] Kozlov A., Hellgren Kotaleski J., Aurell E., Grillner S., and Lansner A. (1999). “Modeling of plasticity of synaptic connections in the lamprey spinal CPG - consequences for network behavior”, *Neurocomputing*, In press.
- [Kozlov *et al.*, 1999b] Kozlov A., Aurell E., Orlovsky G. N., Deliagina T. G., Zelenin P. V., Hellgren Kotaleski J., and Grillner S. (1999). “Modeling control of body orientation in lamprey”, *Neurocomputing*, In press.
- [Li *et al.*, 1997] Li G., Svensson B., and Lansner A. (1997). “Self-orienting with on-line learning of environmental features”, *Adaptive Behavior*, **6**(3-4), 534–566.
- [McClelland *et al.*, 1995] McClelland J. L., McNaughton B. L., and O’Reilly R. C. (1995). “Why there are complementary learning systems in the hippocampus and the neocortex: Insights from the success and failures of connectionist models of learning and memory”, *Psychol. Rev.*, **102**, 419–457.
- [Orre, 1998] Orre R. (1998). “Data Mining and Process Modelling using a Bayesian Confidence Propagation Neural Network” Licenciate thesis, Kungl. Tekniska Högskolan, TRITA-NA-P9810, ISSN 1101-2250, ISRN KTH/NA/P-98/10-SE, ISBN 91-7170-273-3.
- [Orre *et al.*, 1999] Orre R., Lansner A., Bate A., and Lindquist M. (1999). “Bayesian neural networks with confidence estimations applied to data mining”, *Computational Statistics and Data Analysis*, Accepted for publication.
- [Sandberg *et al.*, 1999] Sandberg A., Lansner A., Petersson K.-M., and Ekeberg Ö. (1999). “A Palimpsest Memory based on an Incremental Bayesian Learning Rule”, *Neurocomputing*, In press.

- [Sutton and Barto, 1998] Sutton R., and Barto A. (1998). *Reinforcement learning*, MIT Press, London.
- [Wadden and Ekeberg, 1998] Wadden T., and Ekeberg Ö. (1998). “A neuro-mechanical model of legged locomotion: single leg control”, *Biol. Cybernetics*, **79**(2), 161–173.
- [Wadden, 1998] Wadden T. (1998). “Neural Control of Locomotion in Biological and Robotic Systems” PhD thesis, Kungl. Tekniska Högskolan, ISBN 91-7153-775-9, ISSN 1101-2250, ISRN KTH/NA/R-P98/09-SE, TRITA-NA-P9809.
- [Åhlander, 1999] Åhlander M. (1999). “Reinforcement Learning for a Mobile Service Robot” *TRITA-NA-E9934*, Nada, KTH.

***Other references***

- [McClelland *et al.*, 1995] McClelland J. L., McNaughton B. L., and O’Reilly R. C. (1995). “Why there are complementary learning systems in the hippocampus and the neocortex: Insights from the success and failures of connectionist models of learning and memory”, *Psychol. Rev.*, **102**, 419–457.
- [Bhalla and Iyengar, 1999] Bhalla U. S., and Iyengar R. (1999). “Emergent Properties of Networks of Biological Signaling Pathways”, *Science*, **283**, 381–387.