More invasive procedures, such as spinal cord stimulation and intraspinal delivery of drugs, are used if pain relief cannot be obtained by any other means. These treatment modalities require a well-trained and experienced team.

As stated earlier, a comprehensive treatment program also includes rehabilitation. Physical and occupational therapists can best assess patients' abilities and disabilities, and it is their input that is used to develop a rehabilitation treatment program. Psychologists with experience in pain management can best assess patients' coping skills and psychiatric comorbidities, and their input is also crucial in treatment planning.

Neither the pathophysiology nor the natural course of CRPS, which can range from complete recovery to spread and unrelenting progression, is well-known. Despite the fact that pain and many other symptoms persist for a long time, clinical experience has shown that most patients can obtain partial but satisfactory pain and symptom control and improve their function.

—Misha-Miroslav Backonja

***See also*–Complex Regional Pain Syndrome, Diagnosis and Pathophysiology of**

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Computational Neuroscience

Encyclopedia of the Neurological Sciences

COMPUTATIONAL NEUROSCIENCE uses computer models to bridge the gap between the objects of neuroscience study, neurons and their connections, and the subjects of clinical or psychological study, patients and their brain function or dysfunction. The ultimate goal of computational modeling is to use basic data about neurons to help explain how organisms move, perceive, and behave. Although this goal remains remote, progress has been made.

Computational neuroscience remains somewhat split along the lines of its dual parentage. The computer science side of the field, artificial neural networks, remains committed to maintaining a highly simplified, perhaps simplistic, view of neurons and their function. Artificial neural networks illustrate that even such simple neurons can do complicated information-processing tasks in networks. The more neuroscience-based part of the field, realistic neural networks, tries to accommodate as much as possible the many details of neurons and neurochemicals into models. Although artificial neural networks can directly examine high-level questions such as the origins of memory, realistic neural networks are more useful for clinical and therapeutic questions.

The standard digital computer is often cited as a model for brain function, but the brain is no more a digital computer than it is a post office or a telephone switchboard or any of a dozen other metaphors. The computer has a general-purpose architecture, whereas the brain uses dedicated, special-purpose circuits. Digital computers use transistors as binary devices, whereas brain elements are continuous and are probably used for analog processing. Most important, the computer processes information serially, whereas the brain processes information in parallel. Neural network research arose as an effort to provide explicit brain models to use instead of metaphors.

Neuroscience techniques generate data that can be difficult to correlate. For example, an anatomical tracing of a single neuron cannot be used to predict the neurophysiology of that neuron, even though both measurements are made at the neuron level. This problem is compounded when we try to correlate molecular and cellular data with clinical findings to produce a coherent pathophysiology of a clinical syndrome. Pathophysiological theories and hypotheses always imply some underlying model for how the brain functions, although this model is not always explicitly discussed.

The best understood part of the nervous system from an information standpoint is the peripheral coding of motor information in action potential trains. Increased action potential frequency will increase muscle contraction in the motor system. It has been shown that this coding is present centrally as well: Cortical sensory cells can be driven to high frequency by specific stimuli. Newsome and collaborators have shown that stimulation of sensory cells can alter perception. Rate coding is used implicitly or explicitly in most network models.

ARTIFICIAL NEURAL NETWORKS

The basic processing unit of artificial neural networks is the sigmoid unit. In the artificial neural networks paradigm, each unit simply adds up the synaptically weighted outputs from presynaptic neurons (Fig. 1). Depending on the network, these outputs may be either binary or analog, but their values are always kept within a certain range, usually −1 to 1 or 0 to 1. The squashing or sigmoid function serves to take the broad range of summed input values and squash them into the desired range to produce an output. This simple neuron model is based on rate coding. The input–output relation of the squashing function is meant to correspond to the current–frequency (I–f) curve, the increase in firing frequency with increasing current injection in a neuron.

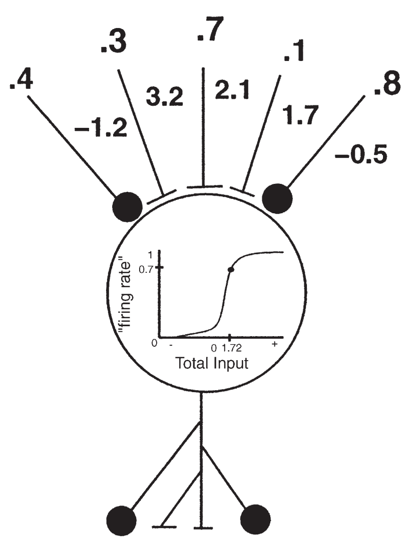

Figure 1
The simplified neural model used in artificial neural networks modeling. Multiply each presynaptic state by the corresponding weight and add the numbers to obtain the total input. Use the squashing (sigmoid) function to determine an output. This will be the state that will then be multiplied by follower synaptic weights. Another simplification allows the neuron to have both excitatory (line segments) and inhibitory (•) outputs.

Because the neurons are so simple, the power of artificial neural networks lies in the organization of the network and in the learning rules that determine how synaptic weights are changed. Network organization or architecture is described as being either feedforward or recurrent. Learning algorithms are usually variations on Hebbian learning, whereby synaptic strength increases with simultaneous pre- and postsynaptic activity. Common learning algorithms for feedforward networks include delta learning and backwards propagation. These techniques are used to produce pattern-matching networks, which can gradually learn to produce particular outputs when presented with particular inputs. A well-known example of such a network is Rosenberg and Sejnowski's NetTalk, a network trained to read English, producing correct grapheme-to-phoneme correspondences despite the irregular orthography that makes such learning difficult. Feedforward networks can be viewed as statistical tools that describe one data set in terms of another. At best, however, these networks can uncover rules and relations that are not otherwise obvious. Such artificial neural networks have also been used as processors in commercial products such as the explosives sniffer used at airports.

The best known recurrent artificial neural network is the Hopfield network, which is a model of neural memory. Computer memory is pointer based. In order to recover something, one must know its address. Computer memory organization is similar to that of a file cabinet: A location must be identified before information can be accessed. Human memory, by contrast, is content addressable. A fragment of a memory or a related memory is enough to bring up related information. Similarly, Hopfield was able to show that a heavily interconnected system of sigmoid units with Hebbian learning could store information so that a small piece of that information could bring up the whole. The Hopfield network also showed resistance to noise. The network could clean up and restore a corrupted memory.

Both feedforward and recurrent artificial neural networks show features that concord with brain function. Artificial neural networks show graceful degradation with damage. A computer will cease to function if a transistor is pulled out. Artificial neural networks carry on despite the removal of multiple units. As a corollary, these networks deal well with the noisy or incomplete information provided in real-world problems.

REALISTIC NEURAL NETWORKS

The network is the focus for modeling artificial neural networks. The single neuron is the modeling focus for realistic neural networks. The two basic modeling techniques for realistic neural networks are Hodgkin–Huxley ion channel modeling and dendritic compartment modeling. Hodgkin and Huxley demonstrated half a century ago that the squid axon action potential could be explained by voltage-sensitive elements that they identified correctly as ion channels. They showed that a set of linked differential equations could accurately model the action potential. Since then, many more voltage- and ligand-sensitive ion channels have been described. Although more sophisticated channel modeling techniques have been developed, variations on the Hodgkin–Huxley formulation are still generally used.

In addition to modeling the many ion channels, realistic models use compartment models to capture the electrodynamics of complex dendritic trees. In order to do this, anatomists trace out the trees under the microscope using systems that enter the coordinates directly into the computer. These coordinates can in turn be automatically translated into computer code for neuron models. In these models, small segments of dendrites are defined to be electrically homogeneous compartments that are connected to each other by resistors that represent the cytoplasmic resistance to current flowing down the membrane. Each individual compartment is a variation on the Hodgkin–Huxley parallel conductance model, with a leak resistor, capacitor, and one or more active conductances connecting the cytoplasm to extracellular space (Fig. 2). Synapses are similarly handled as additional conductances in the parallel conductance model. These single-neuron models can be enormous, with hundreds of compartments each modeled with 10 or more differential equations.

Compartment models are used for examining various input–output functions for the neuron. How does a distal excitatory input differ from a proximal input in producing neuron spiking? What is the time course and effect of spikes back-propagating from the soma up the dendrite? How do different forms of inhibition affect signal propagation in the dendrite? Many of these questions have been answered for particular neuron types in particular brain structures, but the major functional question remains elusive: How do the complexities of neuron structure contribute to information processing?

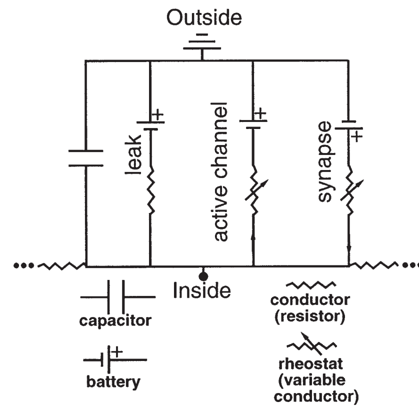

Figure 2
The Hodgkin–Huxley parallel conductance model is extended to produce compartments that include a variety of synaptic and intrinsic channels. Synapses and active channels can be handled similarly, with the rheostats controlled by ligands and voltage, respectively. The flanking cytoplasmic resistors below connect this compartment with neighboring compartments.

In addition to being used for single-neuron modeling, these complex single-neuron models are put together into realistic neural networks. Although artificial neural networks are used to examine functional issues, such as learning and memory and pattern matching, realistic neural networks are typically used to model phenomenology, such as oscillations and epileptic spike generation.

CLINICAL USE OF NEURAL NETWORKS

Clinically, these models of learning and memory have started to provide insights by marrying the network sophistication of artificial neural networks with the receptor details available in realistic neural networks. The brain is a dynamical system and several classes of neurological disease, including Parkinson's disease and epilepsy, can be regarded as dynamical diseases. (The word dynamics and the term dynamical system, applied originally to systems in motion such as the planets, have been generalized to refer to any system in which quantities change with time.) Even in diseases such as stroke that produce a relatively static condition, the disruption of ongoing dynamics and dynamics of recovery can be studied.

Epilepsy is certainly the best studied neural network disease. Pioneering research by Traub revealed that the abnormal activity characteristic of seizures is largely an emergent property of the network. Complex systems such as the brain are said to show emergent properties when their behavior cannot be explained by solely considering the properties of the underlying units. For example, the laws of thermodynamics emerge from the approximately Newtonian behavior of gas particles. Further work has studied the therapeutic implications of various forms of excitatory–inhibitory imbalance. In Alzheimer's disease, Hasselmo and collaborators considered the hippocampus as a modified Hopfield network. They utilized a realistic neural network to demonstrate how the synaptic effects of cholinergic deficit would interfere with learning. In stroke, Lytton and collaborators demonstrated that immediate alterations in receptive field sizes can be explained by alterations in activity propagation in a simple cortical model. They suggested that these immediate changes could contribute to beneficial long-term plasticity. Early work in basal ganglia has begun to explore the direct and indirect pathways and their implications for the cardinal manifestations of Parkinson's disease. As molecular investigation obtains more clues regarding the molecular and cellular bases of neurological disease, there will be increased need for models that explain how these result in the clinical manifestations observed.

In the long term, computational neuroscience holds promise for the emerging area of rational pharmacotherapeutics. Currently, the traditional trial-and-error approach to new drug development is giving way to rational design at the molecular level. In the brain, the interaction of ligand and receptor is only the first step in a complex series of feedback loops that progressively involve synaptic, dendritic, cellular, and network interactions. Therefore, a truly rational pharmacological approach to brain disease will have to involve an understanding of emergent properties at these various levels that can only be studied in the context of a complex explicit model.

CONCLUSION

What do neurons do and how do they do it? The artificial neural networks sigmoid paradigm holds that neurons sum and squash: Add up excitation, subtract inhibition, and constrain the result to the range of neural firing rate. This hypothesis appears inadequate compared to the complexities of real cells. Realistic modeling and basic neurophysiology will need to readdress this question. Despite this hole in our knowledge, neural network research has made progress in understanding what networks do and how they do it, providing preliminary models of brain function and dysfunction.

—William Lytton

***See also*–Action Potential, Generation of; Brain Anatomy; Central Nervous System, Overview; Neurons, Overview; Sensory System, Overview**

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Computerized Axial Tomography (CAT)

Encyclopedia of the Neurological Sciences

COMPUTERIZED AXIAL TOMOGRAPHY, also known as CT or CAT scanning, uses x-rays and digital computer analysis of x-ray data to create cross-sectional images of the human brain, spine, and their coverings. Developed in the late 1970s, CT launched a new era in central nervous system (CNS) imaging. Unlike conventional plain film radiography, CT displays anatomical data in a slice format, which avoids confusing superimposition of adjacent or overlying anatomical structures. Prior to the introduction of CT, detailed evaluation of the CNS required the invasive and potentially dangerous techniques of arteriography or pneumoencephalography. Noninvasive CT scanning has become a primary tool for exploring the normal and diseased CNS.

PRODUCTION OF CT IMAGES

The creation of CT images requires ionizing radiation in the form of x-rays. As part of the