Biased Random-Walk Learning: 
A Neurobiological Correlate to Trial-and-Error

Russell W. Anderson
Theoretical Biology and Biophysics 
and The Center for Nonlinear Studies
Los Alamos National Laboratory
Los Alamos, NM 87545
email: rwa@temin.lanl.gov
(505) 667-9455

For copies of the figures,
please write or FAX R. Anderson
IN PRESS: Progress in Neural Networks

ABSTRACT

Neural network models offer a theoretical testbed for the study of learning at 
the cellular level. The only experimentally verified learning rule, Hebb’s rule, is 
extremely limited in its ability to train networks to perform complex tasks. An 
identified cellular mechanism responsible for Hebbian-type long-term potentiation, 
the NMDA receptor, is highly versatile. Its function and efficacy are modulated by a 
wide variety of compounds and conditions and are likely to be directed by non-local 
phenomena. Furthermore, it has been demonstrated that NMDA receptors are not 
essential for some types of learning. We have shown that another neural network 
learning rule, the chemotaxis algorithm, is theoretically much more powerful than 
Hebb’s rule and is consistent with experimental data. A biased random-walk in 
synaptic weight space is a learning rule immanent in nervous activity and may 
account for some types of learning – notably the acquisition of skilled movement.

KEY WORDS: biological neural networks, random walk, chemotaxis, stochastic 
optimization, biological plausibility.

INTRODUCTION

In their landmark paper, “A Logical Calculus of the Ideas Immanent in Nervous 
Activity”, McCulloch and Pitts [1943] demonstrated how a network of extremely
simplified ("all-or-nothing") neurons could compute any Boolean function. Mathematical analyses of modern neural network models have since revealed them to be potentially universal computing devices [Seigelman and Sontag 1991].

Neural network modeling has not only been helpful in understanding the collective behavior of existing networks, but also provides a theoretical framework with which one can experiment with models of learning. Rosenblatt [1958] demonstrated that these networks, when endowed with modifiable connections ("perceptrons"), could be "trained" to classify patterns (see also Arbib [1964; 1987]). Thus, Rosenblatt had developed a theoretical testbed for the study of learning (formerly the near-exclusive domain of psychology) at the cellular level.

Theoretical neural network studies (mathematical analyses and empirical computer simulations) are useful for exploring the capabilities and limitations of a proposed learning rule. The only experimentally verified learning rule, Hebb’s rule, has profound limitations in this respect. Engineering optimization algorithms (such as back-propagation or genetic algorithms) are capable of training neural networks to perform much more sophisticated tasks, but are biologically implausible [Crick 1989a,b; Mel 1990; Anderson 1991].

Long underestimated by both the experimental and theoretical neural network communities is perhaps the most intuitive mode of learning – trial-and-error. We have shown [Bremermann and Anderson 1989,1991] that the mathematical analog to trial-and-error, a Gaussian biased random-walk in synaptic weight space, is capable of training neural networks to perform the same complex, nonlinear mappings as backpropagation.

In this paper, we review theoretical and empirical neural network studies of random-walk learning which demonstrate the effectiveness of this learning rule. We argue the biological plausibility of a trial-and-error learning rule, though a discussion of existing neurobiological data and identified molecular mechanisms. Finally, we identify the directions of experimental research most likely to identify its necessary elements.

2. HEBB’S RULE
In 1949, Hebb proposed a neuronal learning rule which could integrate associative memories into neural networks [Hebb 1949]. Hebb postulated that when one neuron repeatedly excites another, the synaptic knobs are strengthened. Undoubtedly, the emerging dominance of behaviorism in many fields lent Hebb’s rule a certain amount of intellectual support. Hebb’s rule is also appealing from a genetic point of view, since it requires very little genetic “overhead” to implement in actual nervous systems. All that is required is a mechanism for distinguishing simultaneous stimuli at the cellular level.

Verification has taken time, but there is now evidence that Hebbian-type long term potentiation (LTP) (with some modifications of the original hypothesis) does indeed occur [Lynch 1986; Kennedy 1988; Stevens 1989]. Long-term depression (LTD) has been observed in the same system supporting an ancillary “Hebbian covariance learning rule” [Stanton and Sejnowski 1989].

2.1 Experimental Evidence: The NMDA Receptor

Long-term potentiation is mediated by the N-methyl-D-aspartate (NMDA) receptor. It is useful to review the mechanisms current model of LTP for two reasons. First, it illustrates how the proposed (Hebbian) learning rule influenced experimental efforts. Secondly, the actual mechanisms discovered are subtly different from the Hebbian ideal of strengthening correlated inputs.

According to the current model of LTP [Zalutsky and Nicoll 1990; Buonomano and Bryne 1990; Kandel and O’Dell 1992], for the NMDA receptor channel to open, two conditions must be met simultaneously: (i) the receptor must bind glutamate, and (ii) the postsynaptic cell must be depolarized through activation of non-NMDA receptors. At resting potential, the NMDA receptor channel is blocked by Mg\(^{2+}\). Depolarization removes the voltage-dependent Mg\(^{2+}\) block, allowing Ca\(^{2+}\) to flow into the cell. Ca\(^{2+}\) appears to trigger LTP, through the activation of at least three different protein kinases (see Fig. 1).

There is also evidence for chemical and/or structural presynaptic changes [Zalutsky and Nicoll 1990; Edwards 1991]. Presynaptic modification is thought to be effected via retrograde messengers released across the synaptosomal junction. The retrograde messenger is presumed to be a labile, diffusible substance synthesized
and released by the postsynaptic cell. The synthesis and/or release of such messengers is likely to be a calcium-dependent process as well. Several substances have been postulated to function as retrograde messengers. Among them are nitric oxide [Gally et al. 1990], hydrogen peroxide [Colton et al. 1989; Zoccarato et al. 1989] and archidoinic acid [Williams et al. 1989]. (For a review, see Montague et al. [1991].)

Many other substances have been shown to have modulatory effects on LTP. A partial list of proteins, hormones, neurotransmitters and other compounds includes glycine and D-serine [Salt 1989], serotonin [Ropert and Guy 1991], acetylcholine and noradrenaline [Bear and Singer 1986; Brocher et al. 1992], human epidermal growth factor [Abe and Saito 1992], antidepressant drugs [Birnstiel and Haas 1991], milacemide [Quartermain et al. 1991], opioids [Xie and Lewis 1991] and ethanol [Iorio et al. 1992]. Thus, it is not surprising that mental states and other factors such as “attention”, blood flow, “excitement”, etc. can influence learning. That so many compounds can modulate LTP indicates that the NMDA receptor may be a much more universal tool for synaptic modification, and not only employed in local, Hebbian-type learning.

Finally, NMDA clearly mediates some, but not all, forms of learning. For instance, Malenfant et al. [1991] showed that application of an NMDA receptor antagonist (MK801) could block the acquisition of a spatial maze task in a dose-dependent manner. However, MK801 did not block the acquisition of experience-based maternal behavior. The same maternal experience effects can be blocked by chemical inhibition of protein synthesis.

In summary, the NMDA receptor requires coincident events and makes possible a type of associative learning. Its discovery required intricate experiments at synaptic junctions. It is currently unclear whether synaptic change occurs at the postsynaptic dendritic spine, the presynaptic glutamate axon terminal, the presynaptic depolarizing axon, the axonal processes themselves, or a combination of all of these structures. Several chemical compounds have been identified which can facilitate or inhibit LTP. Many compounds which modulate LTP are common physiological chemical compounds, proteins or neurotransmitters and, as such, do not necessarily originate from either the pre- or postsynaptic neuron(s). Thus, it is
conceivable that several forms of learning are operating in neural tissues, and these other forms of learning can be mediated via the NMDA receptor as well as by other, independent neural processes.

2.2 Limitations of Hebbian Learning

Theoretically, Hebbian learning can account for some types of biological learning. Hebbian mechanisms have been shown to be sufficient to account for topographic mappings [Kohonen 1984; Grajski and Merzenich 1990], plasticity in cortical representation [Merzenich et al. 1987; Montague et al. 1991] and, when applied to “sigma-pi” neurons, some nonlinear pattern recognition tasks [Mel 1992]. But there is more to the brain than conditioned reflexes and associative memories. For anything but special cases, Hebb’s rule is insufficient as a learning rule [Rosenblatt 1962; Rumelhart and McClelland 1986].

Since Hebbian learning requires near simultaneous or synchronous stimuli, it is limited temporally. In many biological situations, instantaneous performance results are not available. Motor control tasks, for example, are inherently sequential. Temporal delays are also involved in many phenomena observed in psychophysical and electrophysiological studies of classical conditioning, such as anticipation of an unconditioned stimulus [Chester 1990; Deno 1991]. Hebbian learning would have to be combined with additional memory mechanisms or neuronal structures to account for such phenomena. Recent attempts to expand Hebbian learning rules to include short-term memory [Sutton and Barto 1983, Klopf 1989, Grossberg and Schmajuk 1989] have met with limited success [Chester 1990].

To account for more complex phenomenon, such as skilled movement, many have postulated the brain utilizes “model-reference control”, that is, the brain develops an internal model of the musculature and environment to predict performance of a control signal. A Hebbian mechanism can then be used to control such a system, since presumably, the temporal delay has been removed from correlated events. Such a system may in fact be used, especially for rapid, open-loop eye and hand movements [Crossman 1983; Anderson and Vemuri 1992]. But the “model” must still be updated by a global supervisory signal which takes its cues from the external environment.
Since the Hebbian rule applies only to correlations at the synaptic level, it is also limited \textit{locally}. Strengthening a local correlation in the context of a nonlinear mapping of several variables (such as the N-bit parity problem) often reduces overall performance. Consequently, Hebbian learning is unable to reliably train a multilayer perceptron network to learn arbitrary, nonlinear decision boundaries [Rumelhart and McClelland 1986].

3. THEORETICAL LEARNING RULES

We have seen how influential a simple theoretical concept, Hebb’s rule, has been in neurobiology. Current artificial neural network (ANN) research has provided valuable insights into the collective behavior of small networks of neurons [Hopfield 1984; Lehky and Sejnowski 1988, 1990; Lockery et al. 1989]. However, most of these results were obtained using more sophisticated algorithms than Hebb’s rule. Do any of the multitude of ANN learning rules have any implications for experimental neurobiology?

Learning rules employed to train ANN’s are more appropriately referred to as optimization procedures. These algorithms, most of which are based on minimization of a defined error function, are capable of overcoming the limitations of Hebb’s rule. Among the most popular today are genetic algorithms [Montana and Davis 1989; Austin 1990] and gradient-descent learning [Rumelhart et al. 1986]. (For an overview of “connectionist” learning rules, see Hinton [1989].) Most of these algorithms have little biological basis and are used primarily for engineering problems in pattern recognition, classification, signal reconstruction, and so on.

Criticisms of the biological plausibility of ANN training algorithms are abundant in the literature. In his article “The recent excitement about neural networks”, Francis Crick [1989a] writes:

“It is hardly surprising that such achievements [referring to the successes using back-propagation] have produced a heady sense of euphoria. But is this what the brain actually does? Alas, the back-prop nets are unrealistic in almost every respect….Obviously what is really required is a brain-like algorithm which produces results of the same general character as back propagation” [emphasis added].

Bartlett Mel [1990] poses the problem this way:
“Is it...a fundamental law that neural associative learning algorithms must be either representationally impoverished or mechanistically overcomplex?”

What are the necessary features of a biologically plausible learning rule? First, it must have a mechanism for synaptic modification that is consistent with experimental data. Secondly, a learning rule must not involve so much specific neural structure that an excessive number of genes are required for its coding. Lastly, to be of any use to biologists, it must be observable. Clearly, Hebb’s rule satisfies these criteria, while back-propagation violates all three. As the title of this paper suggests, there is at least one other ANN learning rule that satisfies these criteria—a biased random-walk [Bremermann and Anderson 1989, 1991].

3.1 Learning via Random-Walks

In its most basic form, a random-walk can be generated by spontaneous, random variation in synaptic strength. This way, the mechanism for synaptic change is local and independent of any higher-level teaching signals. Successful changes in architecture or synaptic strength are rewarded or punished after the fact. Such a biased random-walk in synaptic weight space can be considered a cellular analog of trial-and-error.

The first attempt to apply such an algorithm to neural networks was by Lewey Gilstrap, Jr., Cook and Armstrong at Adaptronics, Inc. (McLean, VA) around 1970. They called their algorithm “accelerated, guided random search” (GARS):

“[T]he accelerated random search begins by exploring the vicinity of its initial estimate. The random trials are governed by a normal distribution of probabilities which is centered on the initial point. ... the accelerated random search follows an unsuccessful random step, with a step of equal magnitude in the opposite direction. By this means, a successful step is usually achieved on the second trial if not on the first random trial. ... A successful step is always followed by another step in the same direction ... each successive step is given double the magnitude of the prior step.”[Barron 1968]

Barron [1968; 1970] used GARS to optimize control parameters in flight control systems. Mucciardi [1972] applied GARS to neural net-like classification structures
called “neuromine nets”. Mucciardi’s paper presented an analysis of neuromine nets and the algorithm, but provided only simple examples of its application. Interest in neural networks was waning at that time, especially because of well-known limitations of simple perceptrons acknowledged by Rosenblatt [1962] and highlighted in *Perceptrons* [Minsky and Papert 1969]. Unfortunately, Mucciardi and his colleagues never applied their algorithm to the complex classification problems emphasized in *Perceptrons* - the exclusive OR and “connectedness” problems. Another aspect of random search, overlooked by the group at Adaptronics, was its potential relevance to biology.

In 1988, we began experimenting with a similar algorithm, which we dubbed the “chemotaxis algorithm” [Bremermann and Anderson 1989, 1991; see also Appendix], by analogy to the strategy employed by bacteria to find chemottractants in a spatial concentration gradient [Alt 1980; Koshland 1980; Berg 1983]. We showed that a biased Gaussian random-walk could, in fact, train neural networks to solve the same difficult Boolean mappings that had eluded single layer perceptrons and Hebbian networks (exclusive OR, N-bit parity, etc.).

Random-walk learning has not received much attention for several reasons:

Criticism #1: *Random walks were known to get trapped in local minima in conventional optimization problems.*

In the case of neural networks, local minima is not as much of a problem as one might expect. What is a local minimum in a small network with a lower dimensional weight space, often becomes a multi-dimensional saddle point in higher dimensions [Baldi and Hornik 1989; Conrad and Ebeling 1992; Yu 1992]. This is because of the degeneracy inherent in neural network architectures: there are usually a much larger number of free parameters (weights) than are theoretically required to solve the task at hand.

Evolutionary optimization is also easier in high-dimensional, redundant systems [Conrad 1983]. A biased random-walk can be considered a rudimentary genetic algorithm – where the environment selects one of two possible mutant structures at each step. Conrad and Ebeling [1992] have shown that saddle points, not isolated peaks, dominate high dimensional fitness landscapes: “Increasing the dimensionality
of a system...increases the chances of finding an uphill [favorable] pathway to still higher peaks.” Conrad refers to this phenomenon as “extradimensional bypass”.

Criticism #2: *A random walk was thought to be inefficient.*

A biased random walk is also a form of gradient descent (random descent), and is quite efficient. In the case of a 3-dimensional spherical gradient (a condition that is ideal for gradient descent), the path taken to reach the optimum by the chemotaxis algorithm is, on average, only 39% longer than the optimal, direct gradient path [Bremermann 1974]. Empirical studies show that the chemotaxis algorithm, while usually slower to converge, compares favorably in final network performance with back-propagation on a variety of benchmark tasks [Bremermann and Anderson 1989; Wilson 1991]. Furthermore, in cases where local minima do exist, there is no reason to expect it is more prone to local minima than back-propagation [Anderson 1991; Baldi 1992]. An extensive analytical comparison of random descent and gradient descent learning is given by Baldi [1992].

Criticism #3: *Neural network researchers generally did not believe a random walk could train neural networks to solve complex, nonlinear mappings such as the exclusive OR.*

The perceived problem of local minima reinforced this belief. This belief, however, turned out simply to be unfounded [Bremermann and Anderson 1989] (Table I). In addition to the benchmark problems, the chemotaxis algorithm has been applied successfully to training neural networks to solve a variety of problems: discrimination of seismic signals [Dowla et al. 1990; Anderson 1991], training “recurrent” neural networks [Anderson 1991], process control [Willis et al. 1991a,b], and motor control [Anderson and Vemuri 1992; Styer and Vemuri 1992a,b]. Experiments with other stochastic training algorithms have had similar successes [Harth and Tzanakou 1974; Tzanakou et al. 1979; Harth et al. 1988; Smalz and Conrad 1991; Jabri and Flower 1992].

Criticism #4: *“Reinforcement” learning models had not been presented in a distilled, biologically plausible way.*

Reinforcement signals are generally thought to carry only general information about the overall performance (“good”, “better”, “target was missed by x amount”, etc.). Specific information to individual synapses as to their relative responsibility
in the task would be very difficult to determine. Biological mechanisms for assigning responsibility to each individual synapse is highly unlikely [Crick 1989a].

Most proposed reinforcement learning rules are “mechanistically overcomplex”. In Barto and Sutton’s reinforcement learning schemes, for example, synaptic change is generated by the reinforcement signal itself, as interpreted by an adaptive critic element [Barto et al. 1981; Barto and Sutton 1983]. Although this work has generated many interesting and non-trivial applications, the complexity of its synaptic adjustment rules makes it an unlikely candidate for a biological learning rule. Other reinforcement algorithms have similar drawbacks [Williams 1992]. Surprisingly, in a comparison between adaptive critic and chemotaxis in controlling a cart-pole system, chemotaxis performed as well or better than the more complicated (and less biological) adaptive critic networks [Styer and Vemuri 1991a,b].

Criticism #5: Experimentalists are limited by what is observable.

The final, and most important obstacle to finding biological evidence for reinforcement learning has been, and continues to be experimental observability. This is because random walks are a non-local phenomenon. Experimental protocols involving single neurons, synapses, or even a small collection of interacting neurons cannot directly verify a non-local learning rule. Local measurements of a global phenomenon can only verify two of the necessary elements, local synaptic variation and neuromodulation (facilitation or inhibition of synaptic change). We devote the majority of the remainder of this article to addressing this problem.

4. BIOLOGICAL EVIDENCE

Reinforcement learning requires three components: (i) a mechanism for the generation of synaptic change, (ii) a structure for evaluating performance, or “trainer”, and (iii) a reinforcement signal. To build a case for biological plausibility, we must show that all of the necessary elements are consistent with biological observations.

Two components required for random-walk learning are clearly consistent with biological observations - random synaptic variation and neural structures for evaluating performance. Indeed, it is generally believed that local random explorations account for some types of neural development [Montague et al. 1991]. In developmental models, however, the reinforcement signal is provided by the target cell. The
random walk ends when a process finds its target. This type of locally reinforced random-walk has the same limitations as Hebbian learning. The difference with what is being proposed here is that the reinforcement signals are not generated locally, through retrograde messengers or cell-adhesion molecules. Instead, reinforcement is generated and broadcast from “supervisory” neural structures (Figure 2).

4.1 Random Structural Variation

Cellular events are dominated by stochastic processes. It is highly probable that the organism makes use of this fact in the process of learning. It has been shown that structural variation can be guided or influenced by chemical or neural signals. What remains to be found is if this modulation is a local phenomenon or mediated by higher centers. Here, we cite just two examples of experimental systems which are consistent with this view.

Growth of neurites in cerebellar granule cell cultures progresses stochastically [Rashid and Cambray-Deakin 1992]. Stimulation with NMDA results in a marked increase in growth rate, while the addition of an NMDA receptor antagonist, aminophosphonovalerate (APV), causes a marked retraction of pre-existing processes. Either of these effects could be directed from more distant neural structures.

In another experiment, Glanzman et al. [1990] studied an in vitro coculture of Aplysia sensory neurons and their target (L7 motor) cells. The sensorimotor cocultures were grown for 5 days and observed by fluorescence video micrographs. One group of preparations was repeatedly treated with the facilitating transmitter serotonin (5-HT) for 24 hours. At the end of the experiment, the coculture was imaged again to look for structural changes. Morphological changes (changes in the size of varicosities or new processes) at the junctions between the sensory and motor cells were rated on a subjective scale. This study was significant in that they were able to directly image structural changes - rather than relying on comparisons between two different populations of neurons. In the control group, morphological changes were found to be normally distributed with a mean change of zero on their rating scale. In the cocultures treated with serotonin, however, structural change was shown to be highly biased toward increases in varicosities or processes.
Furthermore, they showed that these structural changes corresponded to measurable changes in monosynaptic excitatory post-synaptic potential (EPSP) produced in L7 motor cells by firing the sensory neuron. Thus, they were able to show both physical and electrophysiological facilitation can be induced in vitro by a single chemical signal - serotonin.

We suggest that these random variations serve a vital role in learning, that is, generating new trial connections and efficacies. Serotonin release in a cluster of neurons may serve as a local “print” (or fixing) signal to retain effective changes. However, the experiment described by Glanzman et al. cannot differentiate between serotonin’s putative role as a simple growth factor or a reinforcement signal.

Serotonin has been shown to serve a role as a neuromodulator as well as a facilitation signal. There is evidence for a brainstem serotonergic projection to the ventrobasal thalamus, thus linking facilitory signal to higher brain centers [Eaton and Salt 1989]. Does facilitation reinforce existing changes, or does the change occur as a result of the presence of serotonin?

4.2 Reinforcement Signals

A biased random-walk requires that the performance of a net be evaluated. This evaluation could be accomplished by other brain circuits. We do not consider this requirement problematic, since evaluation of performance tends to be computationally easier than improvement. For example, throwing a ball requires precise coordination and timing of numerous muscles. Good performance is hard to achieve and may require extensive training. But, how close a ball comes to hitting the target is relatively easy to determine. Evaluation of accuracy can be processed separately by the visual cortex - independent of networks involved in generating the movement. One portion of the brain thus could act for another system as “supervisor”.

The reinforcement signal is likely to carry only general, non-specific, information. Thus, it could be neural or chemical (hormonal) in origin. Many of the substances which have been shown to modulate LTP (including the candidate retrograde messengers) are candidate reinforcement signals as well. To complete a model of random-walk learning, one must demonstrate that other brain centers
have projections to the sites of synaptic variation which release (directly or indirectly) substances which can act to facilitate or inhibit the process of structural change.

One known reverse pathway is a projection from the locus coeruleus to the olfactory bulb. Locus coeruleus neurons are known to have norepinephrine (NE) as a neurotransmitter. Gray et al. [1986] demonstrated that intrabulbar infusion of NE into the rabbit olfactory bulb can prevent or delay the habituation to unreinforced odors. Locus coeruleus neurons are known to be activated by unconditioned stimuli [Aghajanian and Vandermaelen 1982], and several forms of use-dependent synaptic plasticity in cortical tissues require the presence of NE [Bliss et al. 1983; Bear and Singer 1986]. These signals from the locus coeruleus are diffuse but may still serve a neuromodulatory role [Crick 1989a]. Taken together, these data suggest that norepinephrine could be functioning as a reinforcement signal.

5. CONCLUSIONS

It is self-evident that some form of trial-and-error learning is involved in the acquisition of skilled movement [Crossman 1959; Anderson 1981]. But training a tabula rasa of randomly connected masses of neurons to perform complex control tasks is evidently a hopeless endeavour [Anderson 1991]. High level control of movement is thought to involve the coordination or modulation of existing Central Pattern Generators (CPG’s) [Selverston 1980]. A biased random-walk can be used to optimize crudely organized network of CPG’s during the acquisition of skilled movement [Anderson 1991; Anderson and Vemuri 1992; Styer and Vemuri 1992a,b]. This is somewhat analogous to Edelman’s selectionist hypothesis in that learning entails the “selection”, or education of an existing repertoire of dynamical “groups” [Edelman 1987; Crick 1989b]. Furthermore, we point out that the chemotaxis algorithm is the most primitive form of trial-and-error; undoubtedly, more sophisticated, higher level neural mechanisms will have evolved to coordinate and compliment this process [Smalz and Conrad 1991].

Experimental verification of this type of learning will require protocols involving collections or assemblies of neurons, rather than individual synaptic junctions, to observe the stochastic variation and the effects of putative reinforcement signals.
Furthermore, a more ambitious effort must be made to link reinforcement signals backwards to their projective sources.

McCulloch and Pitts offered a solution to the embodiment problem by demonstrating the computational properties of neural networks. Hebb proposed an neurobiological correlate to associative learning or classical conditioning. Biased random-walks in synaptic weight space can be seen as the neurobiological “embodiment” of trial-and-error learning. A biased random walk may some day be shown to be “a learning rule immanent in nervous activity”.

Acknowledgements

I thank Daniel Chester for calling to my attention the work done at Adaptronics, Inc.. I also thank Hans J. Bremermann, Lee Segel Michael Conrad and V. (Rao) Vemuri for their encouragement and editorial comments. This work was performed under the auspices of the U.S. Department of Energy and supported by the Center for Nonlinear Studies at Los Alamos.
APPENDIX

The Chemotaxis Algorithm

The “chemotaxis training algorithm” consists of a biased random-walk in weight space. One advantage to this training method is that it does not require gradient calculations or detailed error signals. It also allows for automatic adjustment of the single learning parameter, which otherwise has to be found empirically.

The network is initialized with an arbitrary set of weights, \( w^o \), and performance \( E(w^o) \) is evaluated. A random vector \( \Delta w \) is chosen from a multivariate Gaussian distribution with a zero mean and a unit standard deviation. This random vector is added to the current weights to create a “tentative” set of weights \( (w^t) \):

\[
w^t = w^o + h\Delta w
\]

where \( h \) is a stepsize parameter. Performance \( E(w^t) \) is then calculated for the tentative weights. If the error of the new configuration is lower than the original configuration, the tentative changes in the weight vector are retained; otherwise, the system reverts to its original configuration. If a successful direction in weight space is found, weight modifications continue along the same random vector until progress ceases. A new random vector is then chosen, and the process is repeated. More details are available in the cited literature.
TABLE AND FIGURE CAPTIONS

Table I: Training Time for the N-bit Parity Problem.

N-bit parity can be considered a generalization of the 2-bit “exclusive OR” (XOR) problem since class membership of a given pattern is dependent on all N inputs. Network architecture was N-(2N+1)-1, where N represents the number of hidden units. The networks were trained on all $2^N$ possible binary input patterns. Training was continued until the network responses were within 10% of the ideal Boolean values. Chemotaxis averages are taken from Bremermann and Anderson [1989]. No attempt was made to optimize algorithm parameters. Backpropagation averages are taken from Tesauro and Janssens [1988], who used optimal values for the learning and momentum parameters. Note that the computational effort is double these values in the case of backpropagation.

Figure 1: NMDA Implementation of Hebbian Learning.

Simultaneous membrane depolarization and activation of the NMDA receptor allows calcium ions to flow into the cell. Calcium dependent proteins trigger a cascade of intracellular events leading to structural and/or chemical changes post-synaptically as well as potential presynaptic changes via retrograde messengers. (Adapted from [Montague et al. 1991; Kandel and O’Dell 1992].)

Figure 2: Neural Implementation of a Biased Random-Walk

Random variation in synaptic connectivity and efficacy is rewarded after the fact if performance has improved. Performance is evaluated by sensory systems (somatosensory, visual, auditory, etc.) and a non-specific, reinforcement signal is broadcast to the participating neural circuitry. The reinforcement signal could be chemical (hormonal) or neural in origin.
### Table I

Chemotaxis Algorithm Performance

| Dimension (N) | Chemotaxis (epochs) | Backpropagation (epochs) |
|---------------|---------------------|--------------------------|
| 2(XOR)        | 113                 | 25                       |
| 3             | 251                 | 33                       |
| 4             | 962                 | 75                       |
| 5             | 1259                | 130                      |
| 6             | 4169                | 310                      |
| 7             | 5789                | 800                      |
K. Abe and H. Saito (1992). Epidermal growth factor selectively enhances NMDA receptor-mediated increase of intracellular Ca2+ concentration in rat hippocampal neurons. *Brain Research*, **587**:102-8.

G. K. Aghajanian and C. P. Vandermaelen (1982). Intracellular identification of central noradrenergic and serotonergic neurons by a new double labeling procedure. *J. of Neuroscience*, **2**:1786-1792.

W. Alt (1980). Biased random walk models for chemotaxis and related diffusion approximations. *J. Mathem. Biology*, **9**:147-177.

J. R. Anderson, Ed. (1981). Cognitive Skills and Their Acquisition. Lawrence Erlbaum Associates, Hillsdale, N.J.

R. W. Anderson and V. Vemuri (1992). Neural Networks can be used for Open-Loop, Dynamic Control. *Int. J. Neural Networks*, **2**(3) (Abstract in: Proc. Int. AMSE Conf. Neural Networks, San Diego, CA, **2** pp. 227-237 (May 29-31, 1991).

R. W. Anderson (1991). *Stochastic Optimization of Neural Networks and Implications for Biological Learning* Ph.D. Dissertation, University of California, San Francisco.

M. A. Arbib (1987). *Brains, Machines, and Mathematics, Second Edition* (First Edition: McGraw 1964), Springer-Verlag, New York.

S. Austin (1990). Genetic Solutions To XOR Problems. *AI Expert*, pp. 52–57

P. Baldi and K. Hornik (1989). Neural Networks and Principle Component Analysis: Learning from Examples Without Local Minima. *Neural Networks*, **2**:53-58.

P. Baldi (1991). Gradient Descent Learning Algorithms: A General Overview. JPL Technical Document.

R. L. Barron (1968). Self-Organizing and Learning Control Systems. In: Cybernetic Problems in Bionics (Bionics Symposium, May 2-5, 1966, Dayton, Ohio), New York, Gordon and Breach, pp. 147-203.

R. L. Barron (1970). Adaptive Flight Control Systems. In: Principles and Practice of Bionics (NATO AGARD Bionics Symposium, Brussels, Belgium, Sept. 18-20, 1968), pp. 119-167.

A. G Barto, R. S Sutton and P. S Brouwer (1981). Associative Search Network: A Reinforcement Learning Associative Memory. *Biological Cybernetics*, **40**:201-211.
A. G. Barto and R. S. Sutton (1983). Neuronlike Adaptive Elements That Can Solve Difficult Learning Control Problems. *IEEE Transactions on Systems, Man, and Cybernetics, SMC-13* (5):835-846.

M. F. Bear and W. Singer (1986). Modulation of visual cortical plasticity by acetylcholine and noradrenaline. *Nature, 320*:172-17.

H. Berg (1983). *Random Walks in Biology* Princeton University Press, Princeton.

S. Birnstiel and H. L. Haas (1991). Acute effects of antidepressant drugs on long-term potentiation (LTP) in rat hippocampal slices. *Naunyn-Schmiedebergs Archives of Pharmacology, 344*:79-83.

W. W. Bledsoe (1961a). —tiThe Use of Biological Concepts in the Analytical Study of Systems, Technical Report, Panoramic Research Inc., Palo Alto, CA

T. V. Bliss, G. V. Goddard and M. Riives (1983). Reduction of long-term potentiation in the dentate gyrus of the rat following selective depletion of monoamines. *J. of Physiol., 334*:475-491.

H. J. Bremermann (1974). Chemotaxis and Optimization. *J. of the Franklin Institute, (Special Issue: Mathematical Models of Biological Systems)* 297:397-404.

H. J. Bremermann and R. W. Anderson (1989). An Alternative to Back-propagation: A Simple Rule of Synaptic Modification For Neural Net Training and Memory. Technical Report: U. C. Berkeley Center for Pure and Applied Mathematics PAM-483.

H. J. Bremermann and R. W. Anderson (1991). How the Brain Adjusts Synapses - Maybe. In: Automated Reasoning: Essays in Honor of Woody Bledsoe, R. S. Boyer (ed.), Chapter 6, pp. 119-147, Kluwer Academic Pub., Boston.

S. Brocher, A. Artola and W. Singer (1992). Agonists of cholinergic and noradrenergic receptors facilitate synergistically the induction of long-term potentiation in slices of rat visual cortex. *Brain Research, 573*:27-36.

D. V. Buonomano, and J. H. Bryne (1990). Long-Term Synaptic Changes Produced by a Cellular Analog of Classical Conditioning in Aplysia. *Science, 249*:420-3.

D. L. Chester (1990) A Comparison of some Neural Network Models of Classical Conditioning. *Proc. 5th IEEE Int. Symposium on Intelligent Control*, Philadelphia, PA, 2:1163-1168.

C. A. Colton, L. Fagni and D. Gilbert (1989). The action of hydrogen peroxide on paired pulse and long-term potentiation in the hippocampus. *Free Radical Biol. Med., 7*:3-8.

M. Conrad (1983). *Adaptability* (Chapter 10), Plenum Press, N.Y.
M. Conrad and W. Ebeling (1983). M.V. Volkenstein, evolutionary thinking and the structure of fitness landscapes. *Biosystems, 27*:125-128.

F. Crick (1989a). *The Recent Excitement about Neural Networks*, *Nature, 337*:129-132.

F. Crick (1989b). Neural Edelmanism. *Trends in Neurosciences, 12* (7):240-248.

E. R. F. W. Crossman (1959). A Theory of the Acquisition of Speed-Skill. *Ergonomics, 2*(2):153-166.

E. R. F. W. Crossman and P. J. Goodeye (1983). Feedback Control of Hand-Movement and Fitt’s Law. *Quarterly Journal of Experimental Psychology, 35A*:251-278.

Y. Dan and M. Poo (1992). Hebbian Depression of Isolated Neuromuscular Synapses in Vitro. *Science, 256*:1570-1573.

K. Deno (1991). Ph.D. Thesis, Dept. EECS, U.C. Berkeley.

F. U. Dowla, S. R. Taylor and R. W. Anderson (1990). Seismic Discrimination with Artificial Neural Networks: Preliminary Results with Regional Spectral Data. *Bull. Seismological Society of America, 80*(5):1346-1373.

S. A. Eaton and T. E. Salt (1989). Modulatory Effects of Serotonin on Excitatory Amino Acid Responses and Sensory Synaptic Transmission in the Ventrobasal Thalamus. *Neuroscience, 33*(2):285-292.

G. M. Edelman (1987). *Neural Darwinism* Basic Books, New York.

F. Edwards (1991). LTP is a long term problem. *Nature, 350*:271-272.

J. A. Gally, P. R. Montague, G. N. Recke and G. M. Edelman (1990). The NO hypothesis: possible effects of a rapidly diffusible substance in neural development and function. *Proc. Natl. Acad. Sci. USA, 87*:3547-3551.

D. L. Glanzman, E. R. Kandel and S. Schacher (1990). Target-Dependent Structural Changes Accompanying Long-Term Synaptic Facilitation in Aplysia Neurons. *Science, 249*:799-802.

K. A. Grajski and M. M. Merzenich (1990). Hebb-Type Dynamics is Sufficient to Account for the Inverse Magnification Rule in Cortical Somatotopy. *Neural Computation,*.

C. M. Gray, W. J. Freeman and J. E. Skinner (1986). Chemical Dependencies of Learning in the Rabbit Olfactory Bulb: Acquisition of the Transient Spatial Pattern Change Depends on Norepinephrine. *Behavioral Neuroscience, 100*(4):585-596.

S. Grossberg and N. A. Schmajuk (1989) Neural dynamics of adaptive timing and temporal discrimination during associative learning. *Neural Networks, 2*(2):79-102.
E. Harth, T. Kalogeropoulos, A. S. Pandya and K. P. Unnikrishnan (1988). A Universal Optimization Network. AT&T Technical Memorandum #11118-881026-23TM.

E. Harth and E. Tzanakou (1974). A Stochastic Method for Determining Visual Receptive Fields. *Vision Res.*, 14: 1475-1482.

G. E. Hinton (1989). Connectionist Learning Procedures. *Artificial Intelligence*, 40(1):143-150.

D. O. Hebb (1949). *The Organization of Behavior* Wiley, New York.

J. J. Hopfield (1984). Neurons with graded response have collective computational properties like those of two-state neurons. *PNAS (USA)*, 81: 3088-92.

K. R. Iorio, L. Reinlib, B. Tabakoff and P. L. Hoffman (1992). Chronic exposure of cerebellar granule cells to ethanol results in increased N-methyl-D-aspartate receptor function. *Molecular Pharmacology*, 41:1142-8.

Y. Izumi, D. B. Clifford and C. F. Zorumski (1992). Inhibition of Long-Term Potentiation by NMDA-Mediated Nitric Oxide Release. *Science*, 257:1273-1276.

M. Jabri and B. Flower (1992). Weight Perturbation: An Optimal Architecture and Learning Technique for Analog VLSI Feedforward and Recurrent Multilayer Networks. *IEEE Trans. Neural Networks*, 3(1):154-157.

E. R. Kandel and T. J. O’Dell (1992). Are Adult Learning Mechanisms Also Used for Development?. *Science*, 258:243-245.

J. A. Kauer, R. C. Malenka and R. A. Nicoll (1988). NMDA application potentiates synaptic transmission in the hippocampus. *Nature*, 334: 249-252

M. B. Kennedy (1988). Synaptic Memory Molecules. *Nature*, 335:770-772.

A. H. Klopf (1989). Classical conditioning phenomena predicted by a drive-reinforcement model of neuronal function. In: Neural Models of Plasticity: Experimental and Theoretical Approaches, J. H. Byrne and W. O. Berry (eds.), Chapter 7, pp. 104-132, Academic Press

T. Kohonen (1984). *Self-Organization and Associative Memories* Springer-Verlag, Berlin.

D. Koshland (1980). *Bacterial chemotaxis as a model behavioral system* Raven Press, New York.

S. R. Lehky and T. J. Sejnowski (1988). Computing 3-D Curvatures from Images of Surfaces Using a Neural Model. *Nature*, 333:452.
S. R. Lehky and T. J. Sejnowski (1990). Neuronal Model of Stereoaucuity and Depth Interpolation Based on a Distributed Representation of Stereo Disparity. *J. of Neuroscience, 10*(7):2281-2299.

S. R. Lockery, G. Wittenberg, W. B. Kristan and G. W. Cottrell (1989). Function of Identified Interneurons in the Leech Elucidated Using Neural Networks Trained by Back-Propagation. *Nature, 340*:468-71.

G. Lynch (1986). *Synapses, Circuits, and the Beginnings of Memory* Bradford/MIT Press, Cambridge, MA.

S. A. Malenfant, S. O’Hearn and A. S. Fleming, (1991). MK801, an NMDA antagonist, blocks acquisition of a spatial task but does not block maternal experience effects. *Physiology and Behavior, 49*:1129-37.

W. S. McCulloch and W. Pitts (1949). A Logical Calculus of the Ideas Immanent in Nervous Activity. *Bulletin of Mathematical Biophysics, 5*:115-133.

B. W. Mel (1990). *Connectionist Robot Motion Planning* Academic Press, Boston, San Diego.

B. W. Mel (1992). NMDA-Based Pattern Discrimination in a Modeled Cortical Neuron. *Neural Computation, 4*:502-517.

M. M. Merzenich, R. J. Nelson, J. H. Kaas, M. P. Stryker, W. M. Jenkins, J. M. Zook, M. S. Cynader and A. Schoppman (1987). Variability in Hand Surface Representations in Areas 3b and 1 in Adult Owl and Squirrel Monkeys. *J. of Comparative Neurology, 258*(2):281-96.

M. Minsky and S. Papert (1969). *Perceptrons: An Introduction to Computational Geometry* MIT Press, Cambridge, Mass.

P. R. Montague, J. A. Gally and G. M. Edelman (1991). Spatial Signaling in the Development and Function of Neural Connections. *Cerebral Cortex, 1*(1):1047-3211.

D. Montana and L. Davis (1989). Training Feedforward Neural Networks Using Genetic Algorithms. *Proc. 11th IJCAI,*

P. G. Montarolo, E. R. Kandel and S. Schacher (1988). Long-Term Heterosynaptic Inhibition in Aplysia. *Nature, 333*:171-4.

A. N. Mucciardi (1972). Neuromine Nets as the Basis for the Predictive Component of Robot Brains. in: Cybernetics, Artificial Intelligence, and Ecology, H. W. Robinson and D. E. Knight (eds.), (Fourth Annual Symposium Amer. Soc. of Cybernetics), Spartan Books, pp. 159-193.
J. C. Pearson, L. H. Finkel and G. M. Edelman (1987). Plasticity in the Organization of Adult Cerebral Cortical Maps: A Computer Simulation Based on Neuronal Group Selection. *J. of Neuroscience*, 7(12):4209-4223.

N. A. Rashid and M. A. Cambray-Deakin (1992). N-methyl-D-aspartate effects on the growth, morphology and cytoskeleton of individual neurons in vitro. *Brain Research*, 67:301-308.

D. Quartermain, T. Nuygen, J. Sheu and R. L. Herting (1991). Milacemide enhances memory storage and alleviates spontaneous forgetting in mice. *Pharmacology, Biochemistry and Behavior*, 39:31-5.

N. Ropert and N. Guy (1991). Serotonin facilitates GABAergic transmission in the CA1 region of rat hippocampus in vitro. *Journal of Physiology*, 441:121-36.

F. Rosenblatt (1958). The Perceptron, a probabilistic model for information storage and organization in the brain. *Psych. Rev.*, 62:386-408.

F. Rosenblatt (1962). Principles of Neurodynamics Spartan Books, Washington, D. C..

D. E. Rumelhart, G. E. Hinton and R.J. Williams (1986). Learning Internal Representations by Error Propagation. In: Parallel Distributed Processing Vol.1, D. E. Rumelhart and J. L. McClelland, eds., MIT Press, Cambridge, MA pp. 318-362.

T. E. Salt (1989). Modulation of NMDA receptor-mediated responses by glycine and D-serine in the rat thalamus in vivo. *Brain Research*, 481:403-6.

A. I. Selverston (1980). Are Central Pattern Generators Understandable?. *Behavioral and Brain Sciences*, 3: pp. 535-571.

H. Seigelman and E. Sontag (1991). Neural Nets are Universal Computing Devices., Technical Report SYCON-91-08, Rutgers University, Center for Systems and Control.

R. Smalz and M. Conrad (1991). A Credit Apportionment Algorithm for Evolutionary Learning with Neural Networks. In: Neurocomputers and Attention Vol.II: Connectionism and Neurocomputers, A. V. Holden and V. I. Kryukov, eds., Manchester University Press: New York, pp. 663-673.

P. K. Stanton and T. J. Sejnowski (1989). Associative long-term depression in the hippocampus induced by hebbian covariance. *Nature*, 339:215-218 (1989).

C. F. Stevens (1989) Strengthening the synapses. *Nature*, 338:460-461.

D. L. Styer and V. Vemuri (1992a). Adaptive Critic and Chemotaxis in Adaptive Control. Conf. Artificial Neural Networks in Engineering (ANNIE), St. Louis, MO. (Nov.).
D. L. Styer and V. Vemuri (1992b). Control by Artificial Neural Networks Using Model-Less Reinforcement Learning. Preprint: Biomedical Engineering Graduate Group, University of California, Davis, CA, USA 95616.

R. S. Sutton and A. G. Barto (1981). Toward a Modern Theory of Adaptive Networks: Expectation and Prediction. *Psychological Review*, 88(2):135-170.

G. Tesauro and B. Janssens (1988). Scaling Relationships in Backpropagation Learning. *Complex Systems*, 2:39-44.

E. Tzanakou, R. Michalak and E. Harth (1979). The Alopex Process: Visual Receptive Fields by Response Feedback. *Biol. Cybern.*, 35:161-174.

J. H. Williams, M. L. Errington, M. A. Lynch and T. V. P. Bliss (1989). Arachidonic Acid Induces a Long-Term Activity-Dependent Enhancement of Synaptic Transmission in the Hippocampus. *Nature*, 341:739-42.

R. J. Williams (1992). Simple Statistical Gradient-Following Algorithms for Connectionist Reinforcement Learning. *Machine Learning*, 8:229-256.

M. J. Willis, C. Di Massimo, G. A. Montague, M. T. Tham and A. J. Morris (1991a) Artificial Neural Networks in Process engineering. *IEE Proceedings-D*, 138 pp. 256-266.

M. J. Willis, G. A. Montague, C. Di Massimo, M. T. Tham and A. J. Morris (1991b). Non-Linear Predictive Control Using Optimization Techniques. Proc. ACC, Boston, pp. 2788-2793.

J. M. Wilson (1991). Back-Propagation Neural Networks: A Comparison of Selected Algorithms and Methods of Improving Performance. Proc. 2nd Annual Workshop Neural Networks WNN-AIND, Auburn, Alabama (Feb. 11-13, 1991).

C. W. Xie and D. V. Lewis (1991). Opioid-mediated facilitation of long-term potentiation at the lateral perforant path-dentate granule cell synapse. *Journal of Pharmacology and Experimental Therapeutics*, 256:289-96.

X. H. Yu (1992). Can Backpropagation Error Surface Not Have Local Minima. *IEEE Trans. Neural Networks*, 3:1019-1021.

R. A. Zalutsky and R. A. Nicoll (1990). Comparison of Two Forms of Long-Term Potentiation in Single Hippocampal Neurons. *Science*, 248:1619-1624.

F. Zoccarato, R. Deana, L. Cavallini and A. Alexandre (1989). Generation of hydrogen peroxide by cerebral cortex synaptosomes. *Eur. J. Biochem*, 180:473-478.