

공학석사 학위논문

뉴런의 내부 특성 변화를 통한 학습
Learning via intrinsic property changes of
neurons

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Abstract

Learning is one of the most important properties of human cognition. In order for learning to occur, plasticity in neural systems is an important issue. Synapses had been considered as the main site for plasticity in human brain. Hebbian rules, LTP, LTD, STDP (spike timing dependent plasticity) are examples of such plasticity. Also, in the field of artificial neural networks, where biological insight had been successfully applied to enhance how the information is processed in artificial systems, only synaptic weights were modified to account for learning.

It has been shown in recent experiments that the cell's intrinsic conductances change in varying environments and this might be a different kind of learning. Also information processing in dendrites has been shown to be not passive and there are some active elements in it. These two results suggest that single cell does not process inputs passively, but intrinsic property changes of cell could endow a single cell with more computational ability.

Simulations were made on two different levels. One on a highly specific model cell in cell level and the other on an abstract cell in network level to address the issue of learning via intrinsic property change.

Realistic neuron model simulator 'neuron' was used for low level simulation. Hodgkin-Huxley type ion channels were used and maximum intrinsic conductances of ions were modified to account for cell's intrinsic property change.

On the abstract level, Infomax (Information maximization) rule was used for single cell learning and backpropagation learning algorithm was used for synaptic learning. Backpropagation algorithm which had been criticized for not having its biological counterpart was used by the model based on Koerding and Koenig (Koerding & Koenig 1999, 2000, 2001). This model uses the results of the recent experimental findings and applied it to the artificial neural network. The model used the fact

that dendrites were also an active site of summation and the Ca^{2+} spike generated in apical dendrites contributed to learning in synapses. Ca^{2+} signal which seems to convey the error signal was seen to be the correlate of the backpropagation error signal.

Information maximization was used for the learning rule of a single cell, Stemmler and Koch (Stemmler&Koch 1999), showed theoretically that a single cell could change its input-output function so as to maximize mutual information between input and output .

The classification of cancer data, and the orientation detection were used to see the validity of the algorithm. The performance was not as good as using only gradient descent backpropagation algorithm.

Applying the idea of intrinsic learning to problem solving in neural networks is an interesting question in both artificial neural networks and real neural system. The network is comprised of single cells and unless we know how the individual cell processes information it gets and changes adaptively to the environment it encounters, we will not be able to know how the neural system or network actually works and this will give a new insight to artificial neural networks as well as natural neural networks.

Key words: Intrinsic property, neural network, learning, Ca^{2+} , two sites of change, backpropagation

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1. Introduction

1.1 Background and motivations

Learning is one of the most important properties of human cognition. In order for learning to occur, plasticity in the system is an important issue.

Most works on how brain does learning were mostly confined to the synapses of the neuron. Ramon y Cajal, a neuroanatomist who first found out the structure of the nerve cell had also postulated about the functions of its static structure. He formulated a hypothesis that the strength of synaptic connection is not fixed but is plastic and modifiable and this is the location for learning. It is what is now called synaptic plasticity hypothesis, and the synaptic strength can be modulated by neural activity.

Synapse is a site at which a neuron makes functional contact with other neurons. The synapse is composed of presynaptic terminal in presynaptic neuron and postsynaptic terminal in postsynaptic neuron. Synapse also is a part of a neuron, so synaptic change happens in a neuron. But the idea of taking synapse as the only site for change does not change how information is processed in a single neuron. If we take a

neuron as a function that deals with the input it gets, in case of synaptic changes it is only the inputs that change and not the function itself. In contrast to that, intrinsic property change would be regarded as changing the function itself that deals with the input it receives.

Eric Kandel's pivotal finding about the change in connection strength in Aplysia (Kandel and Tauc 1964, Kandel and Spencer 1968, Kandel 1976) when it learned to do gill withdrawal reflex which is now termed as LTP is also a way of synaptic strength learning.

Marr describes in his book Vision, the three different levels of description involved in understanding complex information processing systems. First level is the computational level, the most abstract level that maps input information to output information. Second level is the algorithmic level that describes how the computation is executed in terms of information processing operation, just as the choice of a program in computer science. Third level is the implementational level and it specifies how an algorithm is actually implemented within a physical system.

In this paper I will talk about the neural networks in two levels - algorithmic and implementational. The experimental results showing the proof of intrinsic property change would be on the implementational level,

whereas artificial neural network that is later used is on the algorithmic level.

Computational neuroscience is a new field that deals with how the brain deals with the information it gets in perspective of information processing, and the field of artificial neural networks deals with how the neural network could be used to enhance the processing of information in various fields. For both neuroscience and artificial intelligence communities, the synapses were considered as a main sight for change.

Current results in experiments suggest that a single neuron does change its input-output function according to its history and environment.

Computation inside a single cell which had been considered as a mere summation and sigmoid function is also a problem. Nonlinearity of the computation inside a single cell is now generally accepted in neuroscience community.

Ca^{2+} spikes which mainly hinders cell's linear processing of its inputs is used in Koerding and Koenig's model (Koerding and Koenig 1999, 2000, 2001) to improve how the information processing in realistic neurons can be used to enhance information processing in artificial neural networks. Ca^{2+} could be thought of as a correlate for backpropagation error signal.

1.2 Issues of the Research

This research based on the experimental result that synapse is not the only site for change and the input output function of a single neuron might change according to the input history. This was added to general multilayer perceptron.

Many papers had been produced each year, regarding synaptic plasticity, over >7000 by pubmed search. Whereas, intrinsic plasticity results in less than 500 (115 references by Zhang 2003).

There has not been many works on that intrinsic property change of a neuron could be used for information processing. So here based on biological results on intrinsic change, had used intrinsic plasticity in information processing of artificial neural networks.

1.3 Organization of the Dissertation

Past models of learning in neural networks will be discussed, and experimental results showing learning through change in intrinsic property will be introduced and two sites of change model by Koerding and Koenig will be reviewed.

A model that deals with both intrinsic change and synaptic change will be used to test a data. UCI repository cancer data classification and orientation classification data were used to verify the algorithm.

Finally, the limitations of the algorithm and the future works will be discussed.

2. Classical ways of explaining learning

2.1 Learning in biological systems

2.1.1 Hebbian rule

From his book *The Organization of Behavior*, Hebb proposes below.

When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic changes take place in one or both cells such that A's efficiency as one of the cells firing B, is increased.

This mechanism, and what is now called hebbian synapse has proven to be true in neurobiological context and proved to be useful in artificial neural network context.

The hebb rule can be described as follows.

$$\Delta w_{kj}(n) = \eta y_k(n)x_j(n)$$

The adjustment applied to the synaptic weight w_{kj} between j th presynaptic and k th postsynaptic neuron, at each time step n is proportional to the presynaptic and postsynaptic signals denoted by x_j and y_k .

General forms of the Hebb rule state that synaptic change is proportional to the correlation (above case) or covariance of the activities of the pre- and postsynaptic neurons.

Hebbian rules are found to be true in many systems and LTP, LTD and STDP are examples of such.

2.1.2 LTP (Long Term Potentiation)

Repetitive activity in some areas of the central nervous system were known to produce changes in synaptic efficacy that persist for tens of minutes or longer which are called LTP (Long Term Potentiation) .

LTP seems a biological mechanism for Hebbian learning for it exhibits a characteristic postulated by Hebb to be required for associative learning -the increases in synaptic strength should occur when the presynaptic and postsynaptic elements are coactive.

A number of correlations between learning in animals and LTP in hippocampal slices have been found.

The experimental work on the Aplysia gill withdrawal reflex (Fig. 1) and hippocampal slices, in which long-lasting change in synaptic strengths could be produced and the mechanisms underlying these changes had been studied (Hawkins et al 1993, Bliss et al 1993) provides a strong impetus to look primarily at a synaptic plasticity as the mechanism underlying memory in intact animals. (Marder & Abbott 1996)

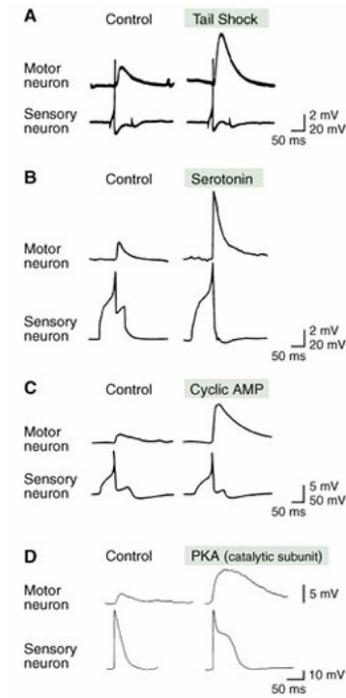


Fig. 1 The strength of the synaptic connections between the sensory and the motor neurons is increased in response to a single tail shock that produces short-term sensitization, in response to a single pulse of serotonin, and in response to direct injection of either cAMP or PKA into the presynaptic sensory neurons. (Nobel Lecture, Eric Kandel)

2.1.3 STDP

Synapses undergo long-term depression (LTD) or long-term potentiation (LTP) depending on the order of activity in the pre- and postsynaptic cells. This process has been referred to as spike-timing dependent plasticity (STDP).

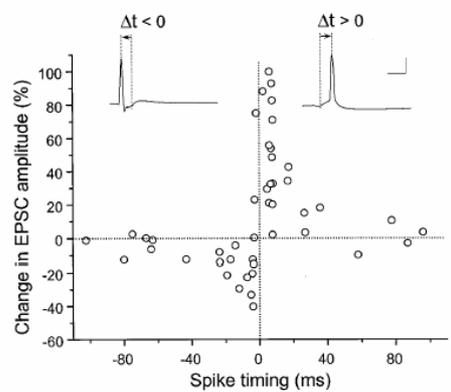


Fig. 2 STDP Whether potentiation or depression occurred depending on the time order of pre and postsynaptic spike (Bi & Poo 1998)

Bi and Poo (Bi & Poo 1998) varied the time interval between presynaptic and postsynaptic spiking to induce synaptic modifications, and observed highly asymmetric dependence on spike timing. Potentiation was induced when the postsynaptic spikes peaked within a time window of 20 ms after the onset EPSP (excitatory post synaptic potential)s, whereas depression was induced when the spikes peaked within a window of 20 ms before the onset of EPSP. (Fig. 2)

2.2 Learning in artificial neural networks

2.2.1 Multilayer perceptron

Artificial neural networks are generally referred to as Neural Networks. It has been used in a lot of applications such as pattern recognition, function approximation, optimization, prediction and automatic control tasks. The fields that this neural network has been

applied to are mostly the fields which classic algorithms didn't do so well.

The neural network basically has the same structure. A neuron that is a basic processing unit, and the weights which are connection links, or connection between the neurons. The function that is computed inside a single neuron is an adder, that adds all the input a neuron gets, and the activation function which limits the amplitude of a neuron. The activation function is usually a sigmoid function. The structure of a neural network varies from a single layer network, multilayer network to recurrent network. Multilayer neural network has one or a few hidden layers. A recurrent neural network has more than one feedback loop.

The way a neural network learns is through a learning algorithm. Most often used learning algorithm is the backpropagation algorithm, it propagates back the error between the desired output and the actual output and updates weights accordingly. This is performed in a way that gradient descents in weight space.

Gradient descent search determines a weight vector that minimizes the error E by starting with an arbitrary initial weight vector, then repeatedly modifying it in small steps. At each step, the weight vector is altered in the direction that produces the steepest descent along the error surface depicted in Figure 3. This process continues until

the global minimum error is reached. (Machine Learning , 1998)

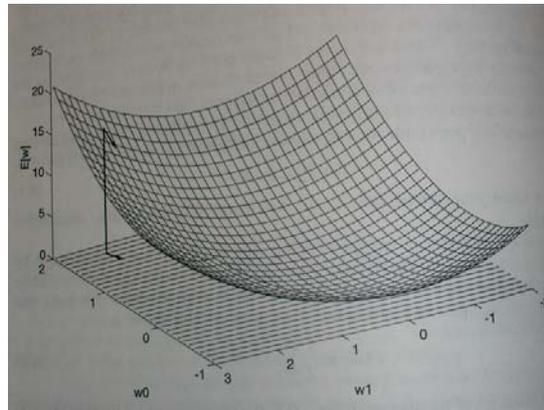


Fig. 3 Gradient descent in the error space (*Machine Learning*, 1997)

The activation function of a neuron in most cases has been set. It is usually a sigmoidal activation function.

$$\sigma(x) = \frac{1}{1 + e^{-x}}$$

A sigmoid activation function is first used for biological reason, since a biological neuron does not fire before it reaches a threshold, and when it reaches it, it fires an action potential. It is also good for mathematical reason in that it is nonlinear and differentiable. The backpropagation algorithm requires a neuron's activation function to be a differentiable function and also nonlinear algorithm is needed to approximate a nonlinear function.

Numerous alternatives for activation functions do exist but they are no different in the sense that they are set in the process of learning.

3. Emerging complex mechanisms

3.1 Computation inside a single cell

3.1.1 Defining input-output function inside a single cell

One of the fundamental problems in neuroscience is how a neuron turns into action potential, the synaptic inputs it gets. Dendrite is the first structure that receives input in a neuron. This input from the dendrite is passed on to the soma and to the axon hillock and there the all-or-none regenerative action potential is generated. (Segev & Rall 1998)

It is very complex and the summation is both time and voltage dependent because of time and voltage dependency of dendritic conductances. There had not been many attempts to simplify the computation inside a single cell into a schematic form. Recently Poirazzi et al. (Poirazzi et al 2003) in their modeling study defined the computation inside a cell into a very simple two layer neural network.

Poirazzi et al. had defined the computation inside a single cell as a two layer neural network. This is not so much different from the accepted and usual formulation that single cell does summation and sigmoid. In Poirazzi's model what it did was however, sigmoid, summation and sigmoid. Using realistic model neuron, they could deduce the relationship between many inputs and the output.

A simple model with passive dendrites attached to an active soma showed the cell's firing output was determined by the average synaptic current that reaches the soma. And early experiments demonstrated that synaptic inputs and current injection at the soma have equivalent effects on the firing rate. (Granit et al 1966, Kernell et al 1969, Schwindt & Calvin 1973). So in those cases, the slope of the $F(\text{firing rate})-I(\text{current})$ relation recorded intracellularly with current injection, could be used to deterministically predict the firing rate caused by the synaptic input. (Powers et al. 1992, Powers & Binder 1995)

Traditional view on dendrite was that it was only passive structure and it only funneled inputs into the soma. Recent findings suggest that dendrite is a complex information processing unit and a lot of nonlinear computations are made in the dendrites. Defining input output function is not easy inside a single cell because of this nonlinearity.

Because of this nonlinearity at the dendrites, tonic stimuli delivered to the dendrites can evoke at least 3 different firing patterns at the soma. Repetitive action potential, repetitive bursts, plateau-mediated repetitive firing are such. The evoked firing depends substantially on the location of the synapses in neocortical and pyramidal neurons. Stimuli delivered at the dendrite are more likely to evoke bursts of action

potentials whereas stimuli delivered at the soma are more likely to evoke repetitive action potentials. (Wong & Stewart 1992, Kim & Connors 1993, Andreasen & Lambert 1995, Schwindt & Crill 1999, Golding et al 1999, Williams & Stuart 1999, Oviedo & Reyes 2000, Zhu 2000).

Burst firing involves interaction between back-propagating action potentials and dendritic Ca^{2+} -mediated regenerative potentials. (Schwindt & Crill 1999, Williams & Stuart 1999, Larkum et al 1999 a, b)

Active properties of dendrites could be summarized as Na^+ mediated action potentials in the dendrites, Ca^{2+} -mediated regenerative potentials, and Ca^{2+} mediated-plateau potentials (Reyes 2001). Na^+ spike is initiated at the axon hillock and propagated through axon and dendrites through backpropagation, because the threshold is lowest in the axon hillock or axon, depolarization of the dendrites usually triggers an action potential first at the axon hillock and then at the soma and dendrites (Stuart & Sakmann 1994, Colbert & Johnston 1996, Larkum et al 1996, Schiller et al 1997, Stuart et al 1997). Na^+ spike is mostly generated in the basal dendrites.

Ca^{2+} mediated regenerative potentials are also generated in dendrites. Mostly in the apical dendrites.

3.1.2 Ca^{2+} spikes

Ca^{2+} is known to play many different roles.

In LeMasson et al 1993, the intracellular Ca^{2+} concentration correlates closely with the pattern of electrical activity exhibited by the model neuron. Figure 4 illustrates activity as a function of the maximal conductances of I_{Ca} .

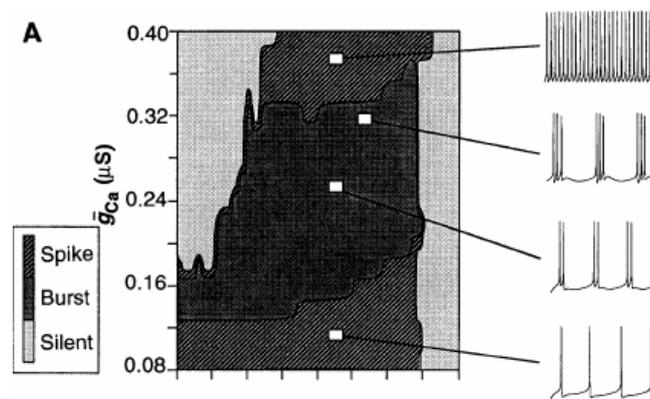


Fig. 4 The pattern of activity for a model neuron as a function of the g of I_{Ca} (Lemasson et al 1993)

Ca^{2+} also plays the role of modulating intrinsic conductances. Marder, Abbott and the colleagues, in their series of papers (Abbott et al 1993, Le Masson et al 1993, Siegel et al 1994, Turrigiano et al 1994, Marder et al 1996, Abbott et al 1996), modeled the crab stomatogastric ganglion neurons. Ca^{2+} current, that changed according to the activity pattern, was used to modulate the intrinsic firing pattern. When the neuronal activity increased, which was conveyed by the increase in

intracellular Ca^{2+} , there was increase in maximal conductances of the outward currents (which tend to make neurons less excitable), and decrease in maximal conductances of the inward currents (which tend to make neurons more excitable). In here the modulation of the activity seems mostly for homeostatic reasons.

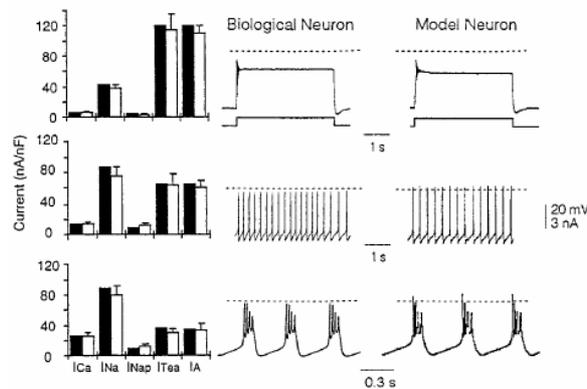


Fig. 5 Changes in activity patterns and current densities of cultured stomatogastric ganglion neurons with time in culture (Turrigiano et al 1995)

From Turrigiano et al 1994 (Fig. 6), changes in activity patterns and current densities of cultured stomatogastric ganglion neurons with current densities measured in voltage clamp in day 1(top), day 2(middle), day 3(bottom), in the figure below. Activity alters the intrinsic properties of cultured stomatogastric ganglion neurons. After 1 hr stimulation of hyperpolarizing current pulses as in the inset, the neuronal activity pattern changed (stimulation), but it later returned to the original pattern.

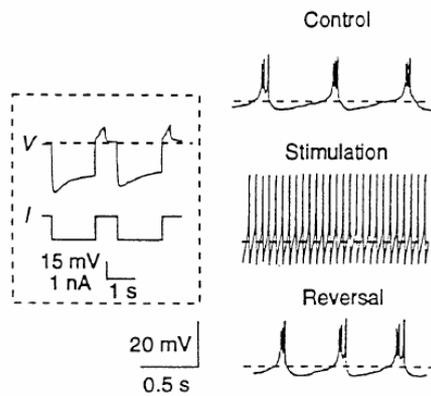


Fig. 6 Activity alters the intrinsic properties of cultured stomatogastric ganglion neurons : top – activity before stimulation, middle – after one hour stimulation, bottom – 1hr after the stimulation stopped (Turrigiano et al 1994)

These above results suggest that intracellular Ca^{2+} and activity can regulate membrane currents and this was also used to model the Long-term control of intrinsic conductances by the activity (Marder & Abbott 1996).

Calcium spikes cause a strong and prolonged depolarization, typically leading to bursts of action potentials. It was recently shown that a bAP can lower the threshold for initiation of a Ca^{2+} -AP, thus enabling L5 pyramidal neurons to couple synaptic inputs from different cortical layers if they coincide within a short time window. (Larkrum et al, 1999, Fig. 7) (Schaffer et al, 2003) Experiments on hippocampal slices by Pike et al. support the idea that postsynaptic bursting is essential for the induction of long-term potentiation. (Koerding and Koenig 2001)

Experimental studies support the view that excitation to the apical dendrite is strongly attenuated on its way to the soma unless calcium spikes are induced. Pyramidal cells, the most abundant cell type in the cerebral cortex, in the layer 5 has prominent apical dendrite and another regenerative event happens here. Sodium based APs(Na^+ -APs) are initiated close to the soma and propagate back into the dendritic arbor(backpropagating AP(bAP)), (Stuart and Sakmann 1994), whereas long-lasting, mainly Ca^{2+} -mediated depolarizations (Ca^{2+} -APs) are initiated predominantly in the distal regions of the apical dendrite (Helmchen et al. 1999, Schiller et al. 1995, 1997) and can be evoked by strong distal synaptic input.

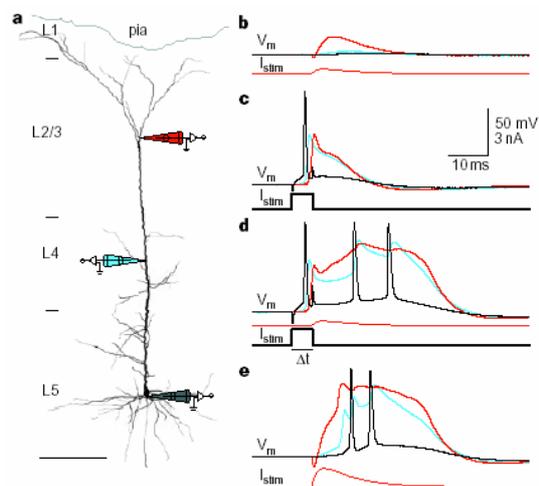


Fig. 6 Coupling of a back-propagating action potential (AP) with distal subthreshold current injection (Larkum et al 1999)

It can be said that Ca^{2+} spikes, which is also influenced by the Na^+ -

spike or activity of the cell, plays an important role in LTP and also for the intrinsic learning.

3.1.3 2 sites of change model by Koerding and Koenig

Koerding and Koenig's model of 2 sites of change (Koerding & Koenig 1999, 2000a, b, 2001a, b) had made use of the experimental evidence that Ca^{2+} spike in the apical dendrites has the effect of learning for synapses.

So in contrast to taking a neuron as having only one site as one site of integration, they had divided the neuron as two sites of integration, one at the soma, the activation site, and the other at the apical dendrite, the learning site. They made use of the Ca^{2+} as learning signal that is assumed to act as a signal for the synaptic change.

With neural network model they could find some interesting properties such as transmitting only relevant information and development of feature selectivity.

The meaning of the model would be giving more biological meaning to classical artificial neural network model, where supervisory signal had little biological meaning. But the 2 sites model is not different from classic artificial neural network model in the sense that the classical model had also used 2 sites in the sense that, modifying synaptic strength

with backpropagating artificial learning signal, aside from its activation could be considered as having 2 sites of integration, too.

3.2 Changes in intrinsic property

3.2.1 Experimental result showing the changes in intrinsic property

There have been some homeostatic mechanisms. Manipulation to decrease the network activity (by TTX blockade of action potentials, or the use of antagonists of excitatory neurotransmitters), tends to produce changes that increase the probability and duration of spike firing (such as attenuation of voltage-sensitive K⁺ channels and enhancement of voltage-sensitive Na⁺ or Ca²⁺ channels), whereas treatments that enhance network activation mostly decrease the probability and duration of spike firing. It has been suggested that homeostatic processes function to maximize information storage by keeping the dynamic range of signaling within useful limits (Turrigiano & Nelson 2000, Stemmler & Koch 1999) (Zhang & Linden 2003).

One example of such homeostatic activity is the stomatogastric ganglion neuron of a crab. Ordinarily, stomatogastric ganglion makes rhythmical activity on the presence of modulatory inputs. When these modulatory inputs are removed(at t=0), the activity in the stomatogastric

ganglion decreases dramatically and loses the rhythmic activity pattern. However, after almost 2 days ($t = 44$ hr), rhythmic activity returns. Since the modulatory inputs are no longer present, the interpretation of this event, is the intrinsic property change. (Marder & Abbott 1996)

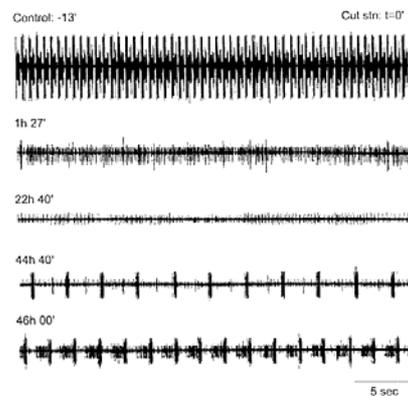


Fig. 8 Resumption of rhythmic pyloric activity after 2 days in organ culture (marder & abbot 1996)

On rat visual cortical pyramidal cells, chronic activity blockade by the sodium channel blocker TTX increased firing probability, and lowered the spike threshold. Also showed increased slope of $f-I$ curve when the activity was blocked (Desai et al. 1999). Similar change of $f-I$ curve was also seen in *Xenopus* tadpoles when there was visual stimulation (Aizeman et al 2003). The change of $f-I$ curves in both cases were the result of intrinsic change, since the $f-I$ curve was measured by direct somatic current injection, by which no synaptic conductance change could be expressed.

On striatal output neurons of rats, decrease in spike threshold and firing latency was observed after spontaneous action potential, whereas no such effect was observed when there was no action potential (EPSP). (Mahon et al. 2003) Spike threshold and firing latency could also be considered intrinsic property. So it could be said that the postsynaptic action potential which are known to affect the synaptic conductance in STDP, also has influence on the plasticity of intrinsic properties.

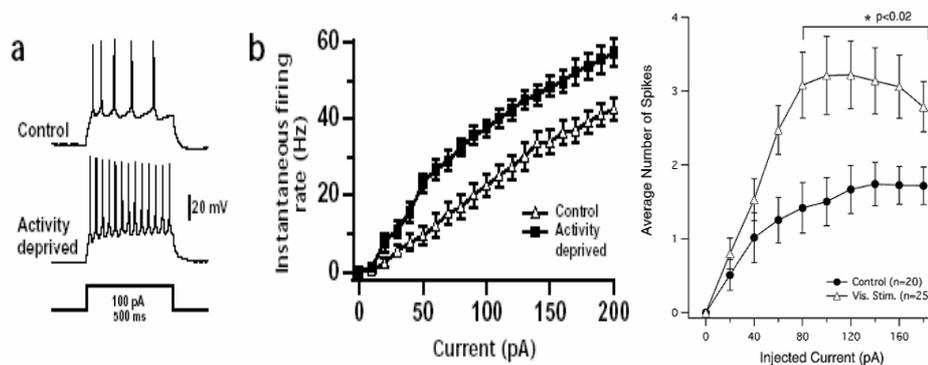


Fig. 9 (Left) Chronic activity blockade increased the firing frequency and lowered the spike threshold of pyramidal neurons (Desai et al. 1999), (Right) Stimulation increases intrinsic excitability (Aizeman et al 2003)

One of the possible mechanisms of such intrinsic change seems the modulation of intrinsic conductances of ions. (Fig. 5, Marder & Abbott 1996). Also the associative mechanisms have been shown in Aplysia (Cleary et al, 1998).

It seems that there should be more stern distinction between the synaptic change and intrinsic change, because synapse also is a part of

the cell. From recent review by Zhang & Linden 2003, they have separated intrinsic plasticity from synaptic learning in following way. Synaptic plasticity mostly refers to the change in single synapse and is input specific. In contrast to that, intrinsic learning occurs pretty global like in the whole cell or rather local change in the branch of a dendritic tree. (see Fig. 10)

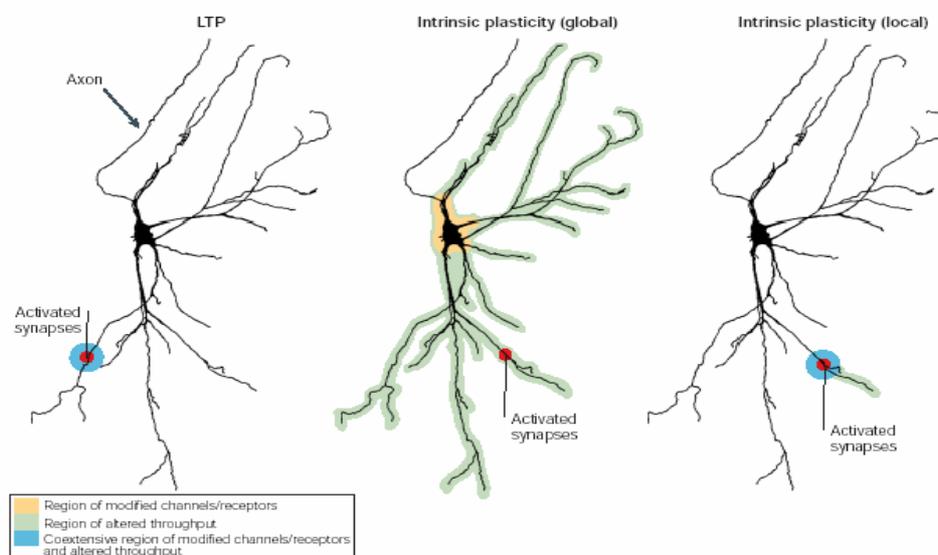


Fig. 10 Intrinsic property change vs. synaptic change (Zhang & Linden 2003)

If the neurons were endowed with such intrinsic learning properties, the information capacity of the system would be much bigger than modulating just the synapses.

3.2.2 Possible biological mechanism

Electrical signals in the nervous system are generated by the

movement of ions across the nerve cell membrane. These ionic currents flow through the pores of membrane proteins known as ion channels. A neuron has many different ion channels and this affects how information is processed in a single cell. The opening of these ion channels are determined by the voltage of the cell and the opening of the channel affects the voltage of the cell in reciprocal way.

Hodgkin-Huxley developed the mathematical framework that is still used to describe neuronal conductances. Below is the Hodgkin-Huxley equation (1952). (j denotes different ions, such as Na^+ , K^+ , m is for membrane, p , q is determined separate for different ions)

C_m is the total capacitance of the neuron, $\frac{dV}{dt}$ is the rate of change of the membrane potential, m is the activation variable, h is inactivation variable, and E_j is the equilibrium potential for each ion.

$$C_m \frac{dV}{dt} = \sum_j \bar{g}_j m_j^p h_j^q (E_j - V)$$

The maximal conductance \bar{g}_j had been considered to be a fixed parameter since in conductance based models. (for the Hodgkin-Huxley model , following values were used, $\bar{g}_L = - 0.003\text{mS/mm}^2$, $\bar{g}_{\text{Na}} = 1.2 \text{mS/mm}^2$, $\bar{g}_K = 0.36\text{mS/mm}^2$)

Currently there have been results showing that maximum

conductance of each ions changes according to the history or activity of the cell. (Fig. 5) The results by Abbott et al. suggest that change of ionic current densities is one possible mechanism for regulating cell's intrinsic property.

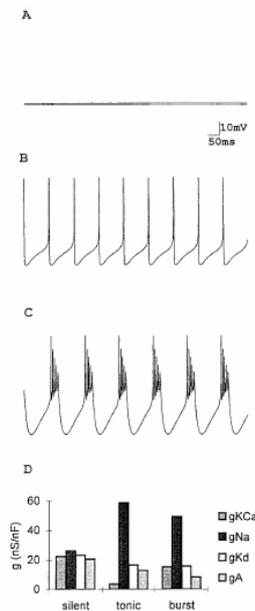


Fig. 11 Different patterns of activity in a model neuron (Marder & Abbott 1996)

These results show that different combinations of ionic conductances could lead to different activity patterns.

Excitability is also known to be modulated through regulating the amount of excitatory and inhibitory inputs (Turrigiano et al. 1998), but since this is not the issue here, this will not be considered.

Here the effect of changing maximum ionic conductances had been considered in the realistic model neuron simulator Neuron (Hines &

Carnevale 1998) environment. The model was based on Zach Mainen's 1996 multi-compartmental model (Mainen & Sejnowski 1996). Based on it, showed how different combinations of ionic channel densities could lead to different outputs in case of same input -the change in input output function.

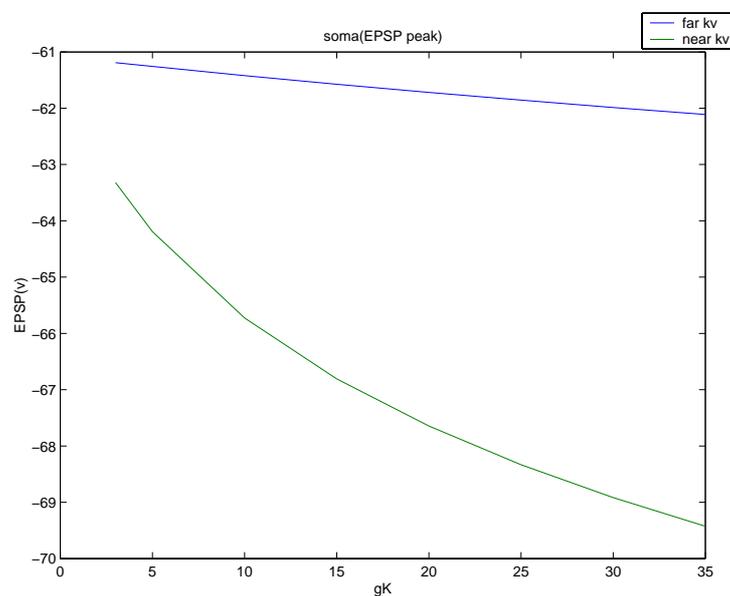


Fig. 12 EPSP peak at the soma depending on the maximum K⁺ conductance change (near vs. far)

Simulation was performed using realistic simulator Neuron(Hines and Carnevale 1997) version 5.0 running on a i586 pc. Here changing the maximum ionic conductance of the different ions of the cell could lead to different results in resulting EPSP at the soma. Axon was cut in this model to remove the nonlinear effect of spike initiation. Increasing

maximum Na conductance led to bigger EPSP at the soma, whereas increasing maximum K conductance led to smaller EPSP at the soma. The result differed also by changing the site of maximum ionic conductance change. Changing the site of maximum conductance near soma led to bigger EPSP change than changing the site far from the soma.

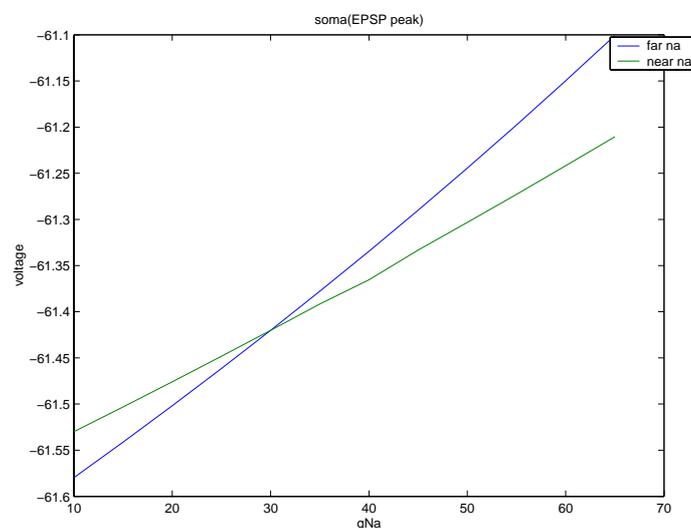


Fig. 13 EPSP peak at the soma depending on maximum Na+ conductance change

Stemmler and Koch in their 1999 paper had suggested a plausible learning rule that could change the intrinsic property of a single cell.

Intrinsic excitability (LTP-IE) along with synaptic LTP in layer 5 pyramidal neurons was observed (Sourdet et al. 2003) by synaptic or pharmacological activation of metabotropic glutamate receptor subtype5 (mGluR5), associated with a persistent reduction of the afterhyperpolarization (AHP) outward current, resulting in the

potentiation of EPSP–spike coupling. The role is facilitation of excitation, also the reliability of timing was enhanced. Reliability of spike timing is important in reducing noise and for reliable data transmission (Mainen & Sejnowski 1995).

3.2.3 Artificial neural network implementation

3.2.3.1 RBF (Radial Basis function)

Radial basis function (RBF) is one alternative to multilayer perceptron. In its basic form, RBF involves 3 layers with different roles. The first layer is the input layer, whose member is equal to the input dimension m . The second layer which is the only hidden layer, is composed of units each of which has nonlinear Gaussian activation function (Kernel function $K(d(x_u, x))$). The third layer is a linear output layer.

Learning in RBF can be explained as follows in a two-stage process. First, the number k of hidden units is determined and each hidden unit u is defined by choosing the values of x_u and σ_u^2 that define its Kernel function $K(d(x_u, x))$. Second, the weights w_u are trained to minimize the fit of the network to the training data, using the global error criterion, given by squared error form.

RBF outperformed Multilayer perceptron, when the centers of the

Gaussians changed with the weights, whereas Multilayer perceptron outperformed RBF when the center didn't change. The performance of the RBF and multilayer perceptron had been compared for the example of NETtalk, a neural network that learns to map English spelling into its phonetic pronunciation. (Wettschereck and Dietterich 1992)

3.2.3.2 Neuron-adaptive neural network model

There had been a few models that had dealt with intrinsic property change in artificial neural network.

In (Chen and Chang 1996), real variables a (gain) and b (slope) in the generalized sigmoid activation function were adjusted during learning process. The result showed that an adaptive sigmoid(ie, a sigmoid with free parameters) leads to an improved data modeling. In (Campolucci et al 1996), an adaptive activation function built as a piecewise approximation with suitable cubic splines had arbitrary shape and allowed to reduce the overall size of the neural networks, trading connection complexity with activation function complexity. Other authors such as Hu et al.(Hu&Shao 1992), and Yamada et al.(Yamada & Yabuta 1992) had also studied the properties of neural networks with adaptive activation function. (Xu & Zhang 2002)

Zhang's NAF(Neuron-adaptive activation function) would be

counted as the most general adaptive activation function neural network of all those.

$$\Psi(x) = A1 \cdot \sin(B1 \cdot x) + A2 \cdot e^{-B2 \cdot x^2} + \frac{A3}{1 + e^{-B3 \cdot x}}$$

A1, B1, A2, B2, A3, B3 are the parameters that will be adjusted during training along with the weights. Steepest descent rule (Rumelhart et al. 1994) has been used to adjust free parameters in above free parameters as well as connection weights between neurons. The authors chose above three functions with some historic reasons. Sigmoid function as the very first function used for artificial neural networks, the exponential function as being used for RBF neural networks, and the sine function as an example of squashing functions.(not published personal communication) And Above equation is a combination of the three functions.

This function is more generalized forms of usual activation functions, for example, by setting the values of the above parameters actually above function can approximate many functions that are used as activation function in general neural networks. Such as, with $A1 = B1 = A2 = B2 = 0$, $A3 = B3 = 1$, the activation function becomes sigmoid function.

Their models of NAF (Neuron-adaptive activation function)

demonstrated the advantages over traditional fixed sigmoid function with regard to network size, training speed and simulation error.

4. The model and the simulation

Here the activation function was modified to maximize the information between input and output of a neuron (Infomax).

Stemmler & Koch in their 1999 paper, 'How voltage-dependent conductances can adapt to maximize information encoded by neuronal firing rate' (Stemmler & Koch 1999), showed theoretically that a single neuron can change its input-output function by adaptively changing its ionic conductances.

The firing rate of a neuron is the simplest way of encoding information. If a neuron's available firing range was unbounded, it could transmit an unlimited amount of information. However, the firing rate cannot fall below zero, and also cannot exceed some maximal frequency, which is set by the duration of action potential, and the refractory period. As a result, the sensory information must be compressed into a finite range of firing rates. (Stemmler & Koch, 1999)

They assumed that a neuron changes its input-output function as to the information between input and output, that is 'mutual information', should be maximized. The definition of mutual information is connected

with the definition of entropy which follows below.

Entropy is a quantity that measures how “surprising” a set of response is. The most widely used measure of entropy, due to Shannon, expresses the “surprise” associated with seeing a response rate r as a function of the probability of getting that response, $h(P[r])$, and quantifies the entropy as the average of $h(P[r])$ over all possible responses. The function $h(P[r])$ should satisfy a set of conditions, first, it should be a decreasing function of $P[r]$, and the surprise measure for two independent spike counts should be the sum of measures for each spike count separately.

$$h(P[r]) = -\log_2 P[r]$$

Shannon’s entropy is just this measure averaged over all responses.

$$H = -\sum_r P[r] \log_2 P[r]$$

Responses that are informative about the identity of the stimulus should exhibit larger variability for trials involving different stimuli than for trials that use the same stimulus repetitively. The mutual information is the difference between the total response entropy and the average response entropy on trials that involve repetitive presentation of the same stimulus.

$$I_m = H - H_{\text{noise}} = - \sum_r P[r] \log_2 P[r] + \sum_{s,r} P[s] P[r|s] \log_2 P[r|s]$$

We could ask whether neural responses to natural stimuli are optimized to convey as much information as possible. This hypothesis can be tested by computing the response characteristics that maximize the mutual information conveyed about naturally occurring stimuli and comparing the results with responses observed experimentally.

Laughlin(1981) has provided evidence that responses of the large monopolar cell(LMC) in the visual system of the fly satisfy the entropy maximizing condition.

Mutual information, first used in the information theoretic context, is a graded measure of the dependence between random variables. If we take our nervous system to be optimal, maximizing the mutual information will give the best decoding algorithm, and give possible neural code. Also important implicit assumption in using Mutual information in the neural systems is that the system is used for communication. So the optimality and the communication would be two important assumptions when we use mutual information in neural systems.

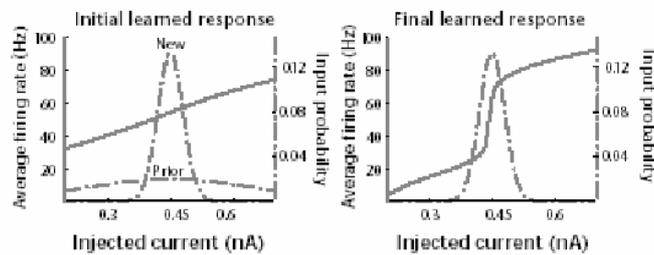


Fig. 14 The neuron's response curve changes so as to maximize the Mutual Information as the input probability distribution changes (Stemmler & Koch 1999)

Here they had taken synaptic conductance changes (or synaptic input) as input x , and the firing frequency f as the output. The mutual information $I(x,f)$ between the synaptic conductance changes x and the firing rates f , specifies how much one can learn about one variable's value by knowing the other. Synaptic input is considered stable, for a certain amount of time (200ms here), – which is not so in real neurons, in real neurons, synaptic conductance changes very fast according to the order of pre and postsynaptic spike (Bi & Poo, 1998) –. Every 200ms intervals, a neuron according to its input history(input probability distribution), changes the intrinsic properties, so that it can maximize the mutual information, and can achieve the optimal firing rate distribution.

Learning the proper representation of stimulus information goes beyond simply correlating input and output, and must invoke the voltage-dependent properties of membrane conductances. (1999, Stemmler &

Koch) There has also been studies that showed intrinsic conductance change as a form of learning. (LeMasson et al. 1993, Bell 1992) This change of intrinsic conductances differs from the original postulate of Hebb, which had been most common, and well known learning rule in neural systems, which states the synaptic learning in networks is a consequence of correlated activity between pre and postsynaptic neurons.

Below is a learning rule they had used.

$$\Delta \bar{g}_j = \frac{\eta}{\bar{g}_j} \left\langle \frac{\delta I_j}{\delta V_d(t)} + c(\langle V_d \rangle) I_j \right\rangle$$

η is a learning rate, angular brackets indicate averaging over the stimulus duration, $V_d(t)$, voltage in the dendritic compartment, I_j , inward current through the j th conductance, $dI_j/dV_d(t)$, the variational derivative of this current with respect to the instantaneous voltage, $V_d(t)$, and $c(\langle V_d \rangle)$ is a simple function that implements the constraints on the firing rate.

Biophysically, $\overline{\Delta g_j}$ can be thought of as a change in the maximal conductance of the underlying ion channels or as a change in the membrane density of these channels. (Stemmler & Koch 1999)

The importance of this learning rule is that, showing how information maximization in a single cell could be achieved through the modulation of

maximum ionic conductances, which could be considered as a postulate for intrinsic changes inside a single cell.

4.1 The 2 sites model and information maximization in single cell

Here starting with the assumption that if learning occurs inside a single cell, wanted to show how much change in the information processing of the whole network could be changed. Also wanted to show how much biological insight could benefit the information processing in artificial neural networks.

4.1.1 The backpropagation and the Ca²⁺ signal

Ca²⁺ signals are known to carry the information that acts as learning.

Koerding and Koenig based on this fact constructed a 2 sites model, that separates learning site(dendrite) from the activation site(soma).

In their model, basal dendrite was the site for Na⁺ spike, and the apical dendrite was the site for Ca²⁺ spike. Ca²⁺ generated in the apical dendrite, and was related with learning. This Ca²⁺ signal, which could also act as a kind of error signal, like δw in backpropagating artificial neural network. Based on this model, here used backpropagation error signal which had been criticized for not having its biological correlate, but now seems to have an appropriate counterpart.

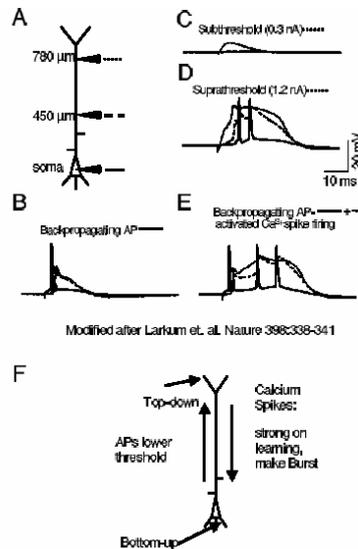


Fig. 15 (A-E) The interaction between the signal from the soma and the apical dendrite (Larkrum et al 1999), F the model (Koerding & Koenig 2000)

4.1.2 Information maximization in single neuron

Information maximization has been used to explain the development of receptive fields in sensory systems. LMC (large monopolar cell) in the fly's visual system were known to satisfy the Infomax constraint. (Laughlin 1981). Also artificial sensory systems that made use of information maximization principle have also been made. Still all this changes had been attributed to synaptic changes, or the study of the learning rule is still going on.

Here based on increasing experimental results of cell's intrinsic change, and also with the theoretical work of how this could be achieved by Stemmler & Koch, used information maximization learning rule for

single neuron, and compared the result with the synaptic learning of multilayer perceptron.

For the learning rule, the activation function changed according to its input probability distribution, as in Fig. 14 (Stemmler & Koch, 1999).

Because calculating the mutual information takes a lot of time and space, here constructed alternative infomax algorithm and later found that it was also made by Laughlin in 1991. The derivative of the transfer function is constructed as equal to the probability distribution function (p.d.f) of the input, and so the every possible output occurs with equal probability. (Table 1)

BACKPROPAGATION with INFOMAX (training_examples, n , n_{in} , n_{out} , n_{hidden} , DIVMAX)

Each training example is a pair of the form $\langle x, t \rangle$, where x is the vector of the network input values, and t is the vector of target network output values.

H is the learning rate (e.g., 0.5). n_{in} is the number of network inputs, n_{hidden} the number of units in the hidden layer, and n_{out} the number of output units.

The input from unit i into unit j is denoted by x_{ji} , and the weight from unit i to unit j is denoted w_{ji} .

For every DIVMAX number of epochs, input-output function of hidden layer neuron is updated based on infomax rule.

- Create a feed-forward network with n_{in} inputs, n_{hidden} hidden units, and n_{out} output units.
- Initialize all network weights to small random numbers(e.g., between $-.05$ and $.05$).
- Until the termination condition is met, Do

If epochs == DIVMAX

Calculate new input-output function for each hidden layer neurons,

Based on input probability distribution of single unit.

$_xVectors[i] = (((real_inputMax-(real_inputMin))/(real)DIVMAX * i) + _inputMin;$

$_yVectors[i] = _yVectors[i-1] + ((double)_inputCounts[i]/_totalInput);$

- For each $\langle x, t \rangle$ in training_examples, Do

Propagate the input forward through the network:

1. Input the instance x to the network and compute the output o_u of every unit u in the network.

Propagate the errors backward through the network:

2. For each network output unit k , calculate its error term δ_k

$$\delta_k \leftarrow o_k(1 - o_k)(t_k - o_k)$$

3. For each hidden unit h , calculate its error term δ_h

$$\delta_h \leftarrow o_h(1 - o_h) \sum_{k \in \text{outputs}} \omega_{kh} \delta_k$$

Table 1. Backpropagation with INFOMAX

4.2 Methods

Simulation was first done only with synaptic learning, and later intrinsic learning rule along with the synaptic learning rule was applied and compared with the previous results.

The selection of learning rule is very important in what kind of learning to occur. Synaptic learning was based on Backpropagation learning algorithm, which would correlate with the Ca²⁺ based learning and the intrinsic learning rule was based on infomax learning rule based on experimental result on Large Monopolar Cells and the theoretical study by Stemmler & Koch.

From Table 1, the gray part explains the Infomax rule. Infomax rule was applied for every 100 epochs, whereas backpropagation rule was applied every epoch, this reflects the experimental result that cell's intrinsic change happens in longer time scale than the synaptic change.

Other than that, the algorithm is just the same as the usual backpropagation algorithm. Input is propagated and the modification on the weights are made in the direction that decreases the error term in the output layer and the hidden layer.

4.3 Simulations

The connections between the neurons were updated using the

backpropagation learning rule, and the input-output function of the neuron was also modified according to infomax learning principle.

Simulations were done on two different data sets.

Breast Cancer data which had often been used in machine learning tasks, and the classification of orientation used by Koerding & Koenig (Koerding & Koenig 1999, 2000) was used.

4.3.1 Cancer data classification

Wisconsin Breast Cancer Database 1991 from UCI repository was used.

Classification of cancer data was made as to whether it was benign or malign, based on 9 attributes (clump thickness, uniformity of cell size, uniformity of cell shape, marginal adhesion, single epithelial cell size, bare nuclei, bland chromatin, normal nucleoli, mitoses). The data had total 699 instances.

90% of the data were used to train the network, and then later 10% of the data was used to test the network (10 fold cross validation).

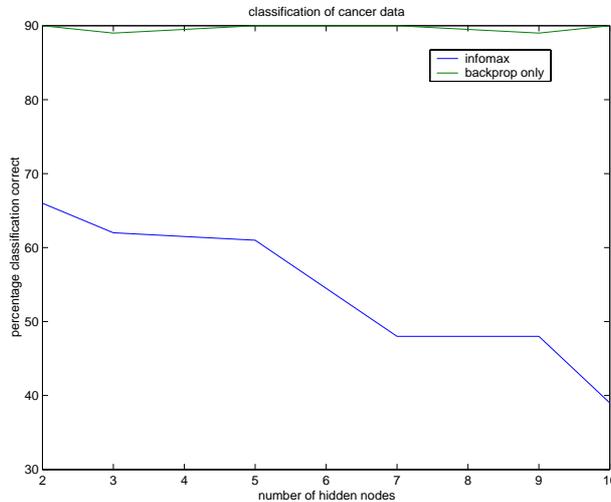


Fig 16. The error rate on the classification of cancer data

It can be seen from above that when there was only backpropagation, the algorithm does better. Also the performance of Infomax algorithm degrades as the number of hidden nodes increases. It can be said that Infomax algorithm only perturbs the activity of the backpropagation algorithm. Only the application of backpropagation algorithm does better.

4.3.2 Orientation data classification

Classification of orientation

Generating orientation data was done in the same way as by Koerding & Koenig's.

Input was 9 nodes based on 9 input locations, 4 hidden nodes, and 4 output nodes were used to classify the orientation. The selection of orientation was different from Koerding & Koenig's way of doing it. Here

more simplified version was used. In their model, the input was 9 by 9 matrix, and so the orientation could have more diverse values(below), whereas here, to simplify the problem, only 3 by 3 input matrix was used, and it could be classified to only 0, 45, 90, 135 degrees.

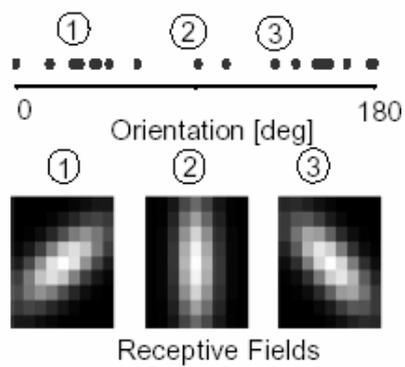


Fig. 17 Input data for Koerding & Koenig (Koerding & Koenig 1999, 2000)

Classification was done to 4 different categories. In counter-clockwise order, 0 degrees, 45 degrees, 90 degrees, 135 degrees. The task was either to classify clear input or noisy input into the category of four different orientations.

0	1	0
0	1	0
0	1	0

In case of 90 degrees – clear input

0.18	0.46	0.41
0.45	0.41	0.14
0.42	0.14	0.02

In case of 45 degrees – noisy input

Fig 18. Input data for the orientation classification

Infomax backpropagation neural network as in the previous task, did worse than only gradient descent backpropagation neural network.

	Classification right	Specificity index
Sigmoid	86%	60%
Infomax	45%	15%

Table 2. Orientation data classification results

The development of specificity in hidden neurons were compared and in this task too the multilayer perceptron was doing better.

It can be concluded from above that the multilayer perceptron is doing very well on its own, and infomax rule only seems to perturb the well-behaving gradient descent algorithm.

4.3.3 Discussion

Infomax rule would be more apt to data which reflects the history of past events.

The data used here are data the order (whether one instance is provided prior to the other) of which is not important, it is only the examples, and even if the order changes it doesn't affect much to how the system processes the data. . Moreover, the number of epochs which had been selected for modifying internal function is not correlated with time.

In classical neural networks, training and testing sessions were separated, but in order for the environment to be conveyed, the system changes adaptively according to the history. So the separation of training and testing sessions is not separated in real neurons and in order for infomax to work properly the separation between the training and testing sessions is meaningless.

Also the minimum and maximum values that had been set by the predefined value is not so meaningful here, whereas in biological system, the minimum and maximum possible firing frequency had been set by physical limitation.

5. Conclusions and discussions

5.1 Summary

The known benefits for Infomax rule are reducing reduction, and the development of sensory specificity index.

Here both backpropagation learning rule and infomax learning rule were applied and the result was compared with the result when only backpropagation algorithm was applied. The result here shows that the backpropagation learning alone does much better in classical classification problem. It seems that infomax learning rule for single neuron only perturbs the well-performing backpropagation algorithm and the result got worse.

One explanation for this is that backpropagation is so optimized in itself for processing artificial information and there is not much room for amelioration.

Another explanation is that some learning rules work better for one task than for other tasks, and for this classification task, gradient descent method works best. Infomax might work better for other tasks.

Also nobody yet knows how different learning rules are working in parallel.

It is true that Infomax might not be the only learning method that

the brain adopts for single cell learning, but the increasing experimental results showing intrinsic property change opens us new era to learning. Neural networks, if it were endowed with intrinsically changing neurons, would have more capacity to store information inside.

There exist 10^{14} synapses and 10^{11} neurons in a brain. Modifying intrinsic neuron provides bigger mathematical possibility for human cognition. The variables that the neural system plays with gets bigger from 10^{14} to 10^{25} at least or much bigger.

Biological insight provided by the study of neural systems will open more possibility of the possible computations in artificial systems. Simulations using computers will also guide us in studying the computation brain does.

Realistic neuronal modeling using computer simulations opens us new way to understanding neuroscience, and to human cognition. It would also be a nice work to study this intrinsic learning that combines recent results on STDP and intrinsic conductance change rule by Stemmler and Koch.

Inputs to distal synapses are more attenuated on its way to the soma, compared to more proximal synapses. But it is known that in several cell types, synaptic conductance was constant (Willams & Stuart

2002) or even increased with distance from the soma (Magee & Cook 2000, Haeusser 2001). This phenomenon is known as ‘synaptic democracy’, since distal and proximal synapses could exert almost equal power to the soma. In order for the synapse to have different value according to the distance from the soma, the synapse should know where it is located from the soma. Recent (Dec.17.2003) article by Rumsey & Abbott (Rumsey&Abbott 2003) explains this by anti-STDP rule.

As can be seen from above example, in the biological reality, many intrinsic, synaptic and homeostatic learning rules are operating in parallel. Anti-STDP and STDP are working in parallel, and until now, this has been shown to be very different for different cell type and different location.

5.2 Future works

Nervous system is a very complex system, and the most important function of it is that it learns through experience.

Neural correlate of learning had generally been considered to be located in synapse, but current experimental result shows that synapse is not the only possible site.

This work has its meaning in that biological learning could also happen in the cell, and this could be applied to processing of data in

artificial neural networks.

Selection of learning rule is important depending on the task in artificial neural networks, but in reality many learning rules are working in parallel. And understanding of the learning rules in brain will give us more possibility to produce an artificial cognition that is more manlike.

Future works should be on how different learning rules contribute on learning, how they work harmoniously, and how these learning rules could benefit the information processing in artificial neural networks or artificial systems in general.

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초 록

학습은 인간의 인지 기능 가운데 가장 중요한 특성 가운데 하나이다. 학습이 일어나기 위해서는 신경계에서의 가소성이 중요하고, 시냅스는 인간의 뇌에서 가소성이 있고 따라서 학습이 일어나는 곳으로 간주되어 왔다. 헤브 규칙(Hebb rule), LTP, LTD, STDP(spike timing dependent plasticity)는 그러한 시냅스 가소성의 예이다. 또한 생물학적인 뉴럴넷이 인공 시스템에서의 정보 처리에 이용되는 인공 뉴럴넷 분야에서도 학습이 일어날 때, 단지 시냅스의 강도만 변화하였다.

최근의 실험적 결과는, 세포 내부의 컨덕턴스(conductance)가 세포 외부 환경이 변화할 때 변하고, 이것이 다른 종류의 학습의 가능성이 있음을 시사하고 있다. 또한 수상돌기에서의 정보 처리도, 수동적이지만은 않고 능동적인 속성이 있다. 이러한 두 결과를 종합해 보면 단위 세포는 입력을 수동적으로 처리하는 것이 아니고, 단위 뉴런의 내부 특성이 변화할 때 이것은 단일 세포에 더 많은 계산 능력을 부여할 수도 있다는 것이다.

시뮬레이션은 서로 다른 두 레벨에서 이루어졌다. 매우 세부적인 모델 세포에서의 세포 레벨과 추상적인 세포의 네트워크 레벨에서, 내부 특성 변화를 통한 학습에 대해 설명하였다.

사실적인 뉴런 모델 시뮬레이터 ‘뉴런’이 낮은 레벨 시뮬레이션을 위해 사용되었다 Hodgkin-Huxley 타입의 이온 채널이 사용되었고, 이온들의 최대 내부 conductance가 변화하여 내부 특성 변화를 살펴 보았다.

높은 레벨에서는, 정보 최대화(Infomax: information maximization) 기법이 세포 단위에서의 학습에 사용되었고, backpropagation 학습 알고리즘이 사용되었다. Backpropagation 알고리즘은 생물학적인 대응이 없다고 알려져 왔었으나, Koerding과 Koenig의 연구(Koerding & Koenig 1999, 2000, 2001) 에 의해서 생물학적인 대응물이 보였고 따라서 여기에서 사용되었다. 그들의 모델은 최근의 실험적인 결과들을 이용하여서 인공 뉴럴넷에 적용하였다. 또한 수상 돌기가 능동적인 덧셈의 장소이고, 꼭대기의(apical) 수상돌기에서 만들어지는 Ca^{2+} 스파이크는 시냅스에서의 학습과 관계가 있음을 이용하였다. 오류 신호를 전달하는 것으로 보이는 Ca^{2+} 신호는 backpropagation 오류 신호의 대응으로 여겨졌다.

정보 최대화가 세포에서의 학습 규칙으로 사용되었다. Stemmler와 Koch (Stemmler & Koch 1999)는 이론적인 방법으로 한 세포는 입력과 출력 사이의 정보

를 최대화할 수 있도록 그것의 입출력 함수를 조절할 수 있음을 증명하였다.

암 데이터의 분류와 방향 데이터의 방향성 발견이 알고리즘의 유효성을 증명하기 위해서 사용되었다. 결과는 gradient descent backpropagation 알고리즘만 사용하는 것 만큼은 좋지 못했다.

단위 뉴런의 내부 학습을 뉴럴넷에서의 문제 풀이에 사용하는 것은 인공 뉴럴넷과 실제 신경계에서 모두 흥미로운 질문이다. 망은 단위 뉴런들로 구성되어 있고 우리가 단위 뉴런들이 입력을 어떻게 처리하고, 입력에 따라 어떻게 변하는지에 대해 제대로 알지 못하고서는, 전체 신경계가 어떻게 작용하는 지 알 수 없을 것이기 때문이다. 따라서 내부 학습에 대한 연구는 실제 뉴럴넷 뿐만 아니라 인공 뉴럴넷에 있어서도 새로운 통찰을 제공해 줄 것이다.

주요어: 내부 학습, 신경망, 학습, 칼슘, 두 곳에서의 변화, backpropagation

감사의 글

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