

## A model for experience-dependent changes in the responses of inferotemporal neurons

Vikaas S Sohal†‡ and Michael E Hasselmo†§||

† Department of Psychology, Harvard University, 33 Kirkland Street, Cambridge, MA 02138, USA

‡ Department of Neurology and Neurological Sciences, Room M016, Stanford University School of Medicine, Stanford, CA 94305, USA

§ Department of Psychology, Boston University, 64 Cummington Street, Boston, MA 02215, USA¶

E-mail: hasselmo@bu.edu

Received 1 November 1999

**Abstract.** Neurons in inferior temporal (IT) cortex exhibit selectivity for complex visual stimuli and can maintain activity during the delay following the presentation of a stimulus in delayed match to sample tasks. Experimental work in awake monkeys has shown that the responses of IT neurons decline during presentation of stimuli which have been seen recently (within the past few seconds). In addition, experiments have found that the responses of IT neurons to visual stimuli also decline as the stimuli become familiar, independent of recency. Here a biologically based neural network simulation is used to model these effects primarily through two processes. The recency effects are caused by adaptation due to a calcium-dependent potassium current, and the familiarity effects are caused by competitive self-organization of modifiable feedforward synapses terminating on IT cortex neurons.

### 1. Introduction

Inferior temporal (IT) cortex has been implicated in both working memory (Mishkin and Delacour 1975, Delacour 1977) and object recognition (Gaffan and Weiskrantz 1980, Mishkin 1982). IT neurons respond selectively to classes of complex stimuli (Gross *et al* 1969, Hasselmo *et al* 1989a, b, Miller *et al* 1991a). Several researchers have recorded from IT neurons during a variant of the delayed matching-to-sample (DMS) task. In this task, an individual trial consists of the presentation of a sample stimulus, followed by presentation of a variable number of nonmatching stimuli which differ from the sample, and concludes with the presentation of a match stimulus which is identical to the sample.

An IT neuron may respond differently to successive presentations of a single stimulus. For example, the responses of macaque IT neurons habituate during repeated presentations of visual stimuli (Miller *et al* 1991a). In monkeys performing a DMS task with visual stimuli, the responses of some IT neurons to matching stimuli are suppressed relative to both nonmatch and sample responses (Miller *et al* 1991b, 1993, Brown *et al* 1987, Riches *et al* 1991). This change in response, termed ‘match suppression’, was maintained if up to six nonmatching stimuli intervened between the sample and match, but the amount of suppression generally

|| Corresponding author.

¶ Address for correspondence.

decreased as the number of intervening stimuli increased (Miller *et al* 1991b, 1993, Riches *et al* 1991). These changes in the response of an IT neuron to a single stimulus are collectively described as ‘recency effects’, because the period of time between successive presentations of the stimulus is short, e.g. one or a few seconds. These recency effects appeared whenever the repeated stimuli were not relevant to performance of the task, but when the same stimulus was relevant—e.g. when it was repeated as the sample on consecutive trials of the DMS task—then the stimulus repetition did not always produce recency effects. When the same stimulus was repeated as the sample on consecutive DMS trials, responses to each sample were not significantly different (Miller *et al* 1991b, 1993). Neither these recency effects (habituation and match suppression) nor this ‘active reset’ of response suppression between trials has a known physiological basis.

In addition to these recency effects, the responses of approximately one-third of studied IT neurons (‘negative cells’) to an initially novel stimulus declined by an average of 40% over the course of many DMS trials (Miller *et al* 1991b, Li *et al* 1993). The responses of other neurons exhibited no change or infrequently increased. The response to initially novel stimuli reached a stable level after about six to eight trials and responses to already familiar stimuli did not change significantly. Unlike what would be predicted if nonspecific neuronal fatigue were the cause of the response decrement, the response decrement was stimulus-specific and was greater when fewer trials intervened between successive presentations of a stimulus. Unlike the recency effects (habituation and match suppression) described earlier, this decrement in response lasted through presentations of > 150 other stimuli. Other researchers have also found that the responses of IT neurons decline during repeated presentations of initially novel stimuli (Hasselmo 1988, Rolls *et al* 1989, Riches *et al* 1991). Because this response decrement is long lasting and occurs during successive presentations of initially novel stimuli, it is called a ‘familiarity effect’.

Recency and familiarity effects appear to summate in IT cortex (Li *et al* 1993). Nevertheless, no model has been presented which shows how both effects could progress simultaneously in the same subset of IT neurons. Here a biologically based neural network simulation will be used to model the short-term recency through adaptation caused by a calcium-dependent potassium current and the long-lasting familiarity effects through competitive self-organization of modifiable feedforward synapses terminating on IT cortex neurons.

## **2. Methods (computational modelling)**

### *2.1. Overall organization*

Model units represent neurons that are organized into three regions: (1) input areas for IT cortex, (2) IT cortex and (3) basal forebrain. Stimuli consisted of patterns of external input applied to units in the input region. Activity spread from these units via feedforward connections to units in the IT cortex region. This IT region contained recurrent excitatory connections and an interneuron which provided feedback inhibition. Activity in IT cortex influenced activity in the basal forebrain region, causing changes in the level of neuromodulation.

### *2.2. Model neurons*

The representation used here is similar to that used in previous papers (Wilson and Cowan 1972, Hasselmo *et al* 1995). The units in the network are highly simplified and intended to model the average dynamics of a neuron or the summed activity of a pool of neurons. Hence the model

units do not exhibit spiking behaviour. Parameters have been chosen so that each timestep of the simulation represents approximately one millisecond. The variable  $a_i$  represents the membrane potential relative to rest of excitatory unit  $i$  (a model neuron in either the input region or IT cortex).  $a_i$  evolves according to

$$\frac{da_i}{dt} = A_i - \eta a_i + (E_{\text{Na}} - a_i) \sum_j W_{i,j} [a_j - \theta]_+ + (E_{\text{Cl}} - a_i) H_i [h - \theta]_+ + (E_{\text{K}} - a_i) \mu c_i. \quad (1)$$

The first term on the right-hand side,  $A_i$ , represents afferent input and is zero for units in IT cortex and may be nonzero for units in the input region. The second term represents passive decay of the membrane potential towards rest with a time constant of  $1/\eta = 10$  timesteps. The third term represents total excitatory synaptic input. The excitatory input to unit  $i$  from unit  $j$  is the product of three factors: the difference between the post-synaptic membrane potential and the sodium reversal potential;  $W_{i,j}$ , the synaptic strength; and the pre-synaptic output.  $[x]_+$  denotes the threshold-linear output function, i.e.  $[x]_+ = 0$  for  $x < 0$  and  $[x]_+ = x$  for  $x \geq 0$ . This is more biologically realistic than sigmoid functions because neurons show linear gain over the range of firing frequencies of cortical neurons observed *in vivo* (Hasselmo *et al* 1989a, b). The output threshold for all units in the model,  $\theta$ , was set to 8.0. The fourth term represents feedback inhibition, which was the product of three analogous factors.  $E_{\text{Cl}}$  is the reversal potential of chloride,  $H_i$  represents the strength of the inhibitory synapse from the interneuron to unit  $i$ , and the interneuron has membrane potential  $h$ . Only units in IT cortex receive feedback inhibition, so  $H_i = 0$  for all units in the input region. The fifth term represents adaptation resulting from a calcium-dependent potassium current (Lancaster and Adams 1986, Schwindt *et al* 1988, 1992, Barkai and Hasselmo 1994). The magnitude of this current is proportional to  $c_i$ , the concentration of calcium inside unit  $i$ , multiplied by the difference between the membrane potential and the potassium resting potential. The proportionality constant,  $\mu$ , was set to 0.05.

The variable  $c_i$  evolves according to

$$\frac{dc_i}{dt} = \gamma [a_i - \theta]_+ - \Omega c_i. \quad (2)$$

The first term on the right-hand side represents calcium influx, which is proportional to the output of the corresponding model neuron. The proportionality constant,  $\gamma$ , was 0.001. Calcium is removed from the model neuron via passive diffusion. The slow afterhyperpolarization (AHP) in neocortical pyramidal cells lasts approximately 1–5 s (McCormick and Prince 1987) and the first few seconds of slow AHP can be described as an exponentially decaying hyperpolarization with a time constant of approximately 1 s (Schwindt *et al* 1988). Our model neglects a small residual amount of slow AHP that occasionally lasts up to 30 s (Schwindt *et al* 1988). Thus we set the time constant for the outward diffusion of calcium,  $1/\Omega$ , to 1000 timesteps (which represents approximately 1 s).

The variable  $h$ , the membrane potential of the interneuron, is governed by

$$\frac{dh}{dt} = A' - \eta h + (E_{\text{Na}} - h) \sum_i W'_i [a_i - \theta]_+ + (E_{\text{Cl}} - h) H' [h - \theta]_+. \quad (3)$$

The first term on the right-hand side,  $A'$ , represents external input. The second term represents passive decay of the membrane potential to rest with a time constant of  $1/\eta = 10$  timesteps. The third term represents excitatory synaptic input to the interneuron. Each unit in the IT region makes an excitatory synapse, with strength  $W'_i$ , onto the interneuron. The fourth term represents an inhibitory synapse, with strength  $H'$ , from the interneuron to itself.

### 2.3. Network connectivity

Neurons in IT cortex selectively respond to complex visual stimuli (Gross *et al* 1969, Hasselmo *et al* 1989a, b, Miller *et al* 1991b, 1993, Li *et al* 1993, Miller and Desimone 1994). Recordings from IT neurons have revealed that they alter their patterns of responsiveness both to (1) sets of novel stimuli as they become familiar and to (2) sets of familiar stimuli after addition of a novel stimulus (Hasselmo 1988, Rolls *et al* 1989). These findings suggest that IT neurons learn distributed representations for large sets of stimuli and that these representations change to accommodate new stimuli.

Competitive self-organization of feedforward connections can produce distributed representations that behave this way (Rumelhart and Zipser 1986, Hasselmo and Cekić 1996). Therefore, the network contained modifiable feedforward connections from the input region to excitatory IT neurons which could undergo self-organization. We use the term *self-organizing* to describe connections which are the primary source of excitatory input to a region (here IT cortex) and for which modification is driven entirely by intrinsic network variables (e.g. post-synaptic activity). The initial strengths of these feedforward connections were drawn from a Gaussian distribution (mean =  $2.5 \times 10^{-4}$ , standard deviation =  $2 \times 10^{-5}$ ).

Neurons in IT cortex have been shown to maintain activity in the absence of a stimulus (Fuster and Jervey 1981, 1982, Fuster 1990, Miller *et al* 1993). Such activity can be sustained by recurrent excitation, but maintaining bounded levels of activity above the baseline firing rate normally requires the presence of feedback inhibition (Zipser *et al* 1993, Hasselmo *et al* 1995). In the model, recurrent connections between IT neurons were initialized with the uniform strength of  $8 \times 10^{-4}$ . In addition, each excitatory neuron in IT cortex had an excitatory connection with strength  $W' = 2.1 \times 10^{-4}$  to the interneuron, and this interneuron had an inhibitory connection to each IT neuron with strength  $H = 6 \times 10^{-2}$  and inhibited itself via an inhibitory connection with strength  $H' = 3 \times 10^{-2}$ .

Most of our simulations used a network with 20 input and 20 IT Neurons, but to model the decline in IT activity with increasing stimulus familiarity we needed to store representations for 25 distinct stimuli. In that case, we used a network with 50 neurons in both the input and IT regions. All synaptic strengths were rescaled appropriately and the connections from input neurons to the IT region were initialized with strengths drawn from the positive portion of a Gaussian distribution (mean =  $4 \times 10^{-5}$ , standard deviation =  $1.2 \times 10^{-4}$ ). Figure 1 diagrams the connectivity between units in the input region and IT cortex. Connections to and from the basal forebrain neuron region will be discussed later.

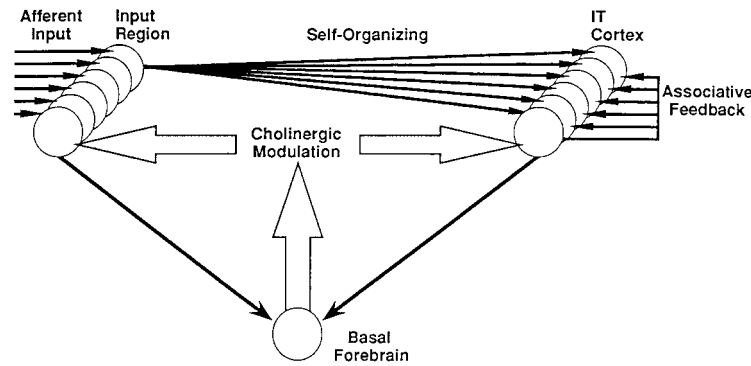
### 2.4. Modification of synapses

In this model, excitatory feedforward connections from the input layer to model IT neurons were modifiable so that they could undergo competitive self-organization. IT neurons may be involved in formation of long-term associations between complex stimuli (Miyashita 1988, Desimone *et al* 1994). Hence, the recurrent excitatory connections between IT neurons were also modifiable.

Synaptic modification proceeded in two steps. First, after each timestep, the strength of each synapse was modified according to a local Hebbian-type learning rule supported by evidence of long-term potentiation (LTP) (Gustafsson and Wigstrom 1988), which has been found in neocortical structures (Bear *et al* 1992). This Hebbian learning rule for each set of modifiable connections took the form

$$\Delta W_{i,j} = \varepsilon(a_j - \theta_{\text{pre}})_+(a_i - \theta_{\text{post}})_+ \quad (4)$$

The rate constant of learning,  $\varepsilon$ , was  $1 \times 10^{-5}$  for the feedforward connections from input



**Figure 1.** Connectivity between regions in the neural network model of IT cortex. Afferent input enters the network in the input region, and spreads into the IT cortex region via self-organizing feedforward connections. IT cortex contains feedback connections representing recurrent excitation and some units mediating feedback inhibition. The cholinergic neuron in the basal forebrain region is driven by the presence of a stimulus in the input region. However, strongly active neurons in IT cortex can excite other basal forebrain neurons, which inhibit the cholinergic neuron. As a result, the cholinergic neuron is most active when activity in the input region elicits diffuse, nonspecific responses in IT cortex (e.g. as occurs in response to novel stimuli). In contrast, focused activity in IT cortex (e.g. as occurs in response to a familiar stimulus) suppresses activity of the cholinergic neuron. Activity of the cholinergic neuron determines the level of cholinergic modulation in IT cortex and the input regions.

neurons to IT neurons and  $1 \times 10^{-4}$  for recurrent synapses between IT neurons. The modification thresholds  $\theta_{pre}$  and  $\theta_{post}$  were both 8.0 in the input region and 10.0 in IT cortex. We found that setting the modification thresholds higher than the output thresholds in IT cortex facilitated a ‘winner-take-all’ mode of self-organization.

Second, after application of the Hebbian learning rule (4), the sum of the squares of all synaptic weights was normalized for each pre-synaptic neuron  $j$ . The sum of the squares of all synaptic weights were then normalized for each post-synaptic neuron  $i$ .

Consider a simplified network in which only the self-organizing, feedforward connections are modifiable. Let  $W_{i,j}$  be the strength of the connection from input neuron  $i$  to IT neuron  $j$ , and  $\Delta W_{i,j}$  be the unnormalized change in  $W_{i,j}$  given by the Hebbian learning rule, equation (4). We computed the net change in  $W_{i,j}$  after pre- and post-synaptic normalization. When we expand this expression and drop terms higher than first order, this net change becomes

$$W_{i,j} = \Delta W_{i,j} - W_{i,j} \frac{\sum_k W_{i,k} \Delta W_{i,k}}{\sum_k (W_{i,k})^2} - W_{i,j} \frac{\sum_k W_{k,j} \Delta W_{k,j}}{\sum_k (W_{k,j})^2} + W_{i,j} \frac{\sum_{k,l} W_{k,l} \Delta W_{k,l}}{\sum_{k,l} (W_{k,l})^2}. \quad (5)$$

By considering each of the terms on the right-hand side of (5), we can interpret the physiological meaning of our two-step procedure for synaptic modification. The first term represents Hebbian-type synaptic strengthening, e.g., LTP. The second term is analogous to synaptic decay due to strengthening of synapses from other input neurons to IT neuron  $i$ , and could represent heterosynaptic depression (Levy 1989). The third term is analogous to synaptic decay due to strengthening of synapses from input neuron  $j$  to other IT neurons, and could represent homosynaptic depression (Stanton and Sejnowski 1989). The fourth term is synaptic strengthening due to decay of synapses from input neuron  $j$  to other IT neurons or from other input neurons to IT neuron  $i$ , and represents long-term redistribution of cellular resources for synaptic maintenance. Thus, synaptic modification consisting of Hebbian synaptic modification followed by normalization is approximately equivalent to these four biologically plausible processes.

Networks combining modifiable feedforward connections and recurrent excitation can

show complex behaviour, e.g., both self-organization of input and maintained activity as observed in IT cortex. However, such networks must also prevent feedback or recurrent excitation from interfering with self-organization (Hasselmo and Cekić 1996). For this reason, we included cholinergic modulation, described below.

### 2.5. Role of cholinergic modulation

IT cortex receives cholinergic innervation from the nucleus basalis of the substantia innominata region (also known as the magnocellular nucleus basalis of Meynert) in the basal forebrain (Mesulam *et al* 1983). Cholinergic antagonists have been shown to increase the average visual response of all recorded IT neurons during a DMS task with delay (Miller and Desimone 1993, Dudkin *et al* 1994). Finally, cholinergic neurons of the basal forebrain project to IT cortex (Mesulam *et al* 1983). This suggests that acetylcholine can modulate the responses of IT neurons.

Cholinergic agonists cause depolarization and suppress adaptation in piriform cortex (Hasselmo and Bower 1992, Barkai and Hasselmo 1994), somatosensory neocortex (Schwindt *et al* 1988) and motor cortex (Woody and Gruen 1987). Acetylcholine also suppresses feedback but not feedforward excitatory synapses in neocortex (Cauller and Connors 1994, Hasselmo and Cekić 1996). Other effects of acetylcholine include suppression of inhibitory transmission and direct depolarization of inhibitory interneurons (Pitler and Alger 1992) and enhancement of LTP (Burgard and Sarvey 1990, Blitzer *et al* 1990, Hasselmo and Barkai 1995). The selective suppression of recurrent excitatory transmission by acetylcholine could prevent recurrent connections from interfering with self-organization, as shown in the results section.

We assume that the effects of acetylcholine in IT cortex are similar to those described in other cortical regions. The model contained a representation of the level of acetylcholine,  $\psi$ , which varied between zero and one. Intrinsic synapses, those excitatory connections originating in IT cortex and terminating on either other IT neurons or else on the inhibitory unit, were suppressed by a factor of  $0.8\psi$ . Connections from the inhibitory unit were suppressed by a factor of  $0.8\psi$ . The magnitude of the adaptation current in IT neurons was reduced by a factor of  $1.0\psi$ . To model the cholinergic enhancement of synaptic modification, the rate synaptic modification was multiplied by the factor  $(0.02 + 0.98\psi)$ . Finally, the excitation of both excitatory and inhibitory units in both the input region and IT cortex was represented by a direct depolarization of the cells sufficient to bring their resting potentials to 4.0.

### 2.6. Feedback regulation of cholinergic modulation

Since cholinergic modulation serves to suppress recurrent excitation during self-organization (Hasselmo and Cekić 1996), we hypothesize that cholinergic modulation is strongest during presentation of a novel stimulus and decreases as that stimulus becomes more familiar and self-organization becomes nearly complete. In fact, experimental data shows that cholinergic neurons of the substantia innominata respond more strongly to novel stimuli than to familiar stimuli (Wilson and Rolls 1990). Note that self-organization should cause initially diffuse neural representations of novel stimuli to converge to sparser representations (von der Malsburg 1973, Grossberg 1976, Rummelhart and Zipser 1986, Hasselmo and Cekić 1996). This is consistent with the focusing of inferotemporal activity with increasing stimulus familiarity (Miyashita 1988, Miller *et al* 1991b, Li *et al* 1993). Cholinergic modulation used to suppress recurrent connections during learning, when neural representations are diffuse, is similar to the '2/3 rule' used by adaptive resonance networks to suppress feedback activity that does not coincide with feedforward activity (Carpenter and Grossberg 1993).

In order to produce the levels of cholinergic modulation described above the model includes feedback from IT neurons to the basal forebrain neurons, as diagrammed in figure 1. The equation governing the evolution of  $a$ , the activity of a basal forebrain neuron, was similar to equation (1).  $\Psi$ , the level of cholinergic modulation in the network, was determined by the activity of one cholinergic neuron. This neuron received afferent input to produce the tonic firing observed during wakefulness (Richardson and DeLong 1991), excitation from the input region and inhibition from other basal forebrain neurons, as diagrammed in figure 1.

This sort of circuit, in which feedback from IT neurons regulates the output of a cholinergic neuron, is supported by several anatomical studies that have found feedback connections from IT cortex to the substantia innominata (Whitlock and Nauta 1956, Mesulam and Mufson 1984, Russchen *et al* 1985, Wilson and Rolls 1990). Furthermore, whereas the substantia innominata projects to much of the neocortex (Mesulam *et al* 1983), IT cortex is one of the few regions of neocortex with feedback connections to the substantia innominata (Mesulam and Mufson 1984, Russchen *et al* 1985). Mesulam and Mufson (1984) found that the feedback connections from IT cortex to the substantia innominata are concentrated in the particular sector (Ch4i) from which most of the connections to IT cortex originate. Finally, the responses of IT neurons differentiate between novel and familiar stimuli approximately 100 ms after stimulus presentation (Li *et al* 1993) whereas neurons in substantia innominata do so approximately 200 ms after stimulus presentation (Wilson and Rolls 1990), so there is enough time for feedback from IT cortex to reach neurons in the substantia innominata before they exhibit familiarity effects. Thus it seems reasonable to assume that IT cortex could control the amount of cholinergic modulation it receives in such a way that the observed decrease in substantia innominata activity as stimuli become familiar is due to feedback from IT cortex.

### 2.7. Active reset mechanism and cholinergic modulation

Cholinergic modulation might provide a mechanism for the ‘active reset’ of match suppression between trials. As described in the introduction, during DMS tasks in which the same sample stimulus appeared on two consecutive trials, IT neurons’ responses to the second presentation did not differ significantly from their responses to the first presentation (Miller *et al* 1991b, 1993). In our model, the level of cholinergic modulation was initially high, but fell during presentation of the sample stimulus. However, by focusing their attention on the sample stimulus at the beginning of each DMS trial, monkeys may have maintained a high level of cholinergic modulation for the duration of the sample presentation. Because high levels of acetylcholine suppress the currents which cause adaptation (Hasselmo and Bower 1992, Barkai and Hasselmo 1994), they could prevent the response to the sample stimulus from being suppressed even when that stimulus had been seen on the previous trial. To test whether higher levels of cholinergic modulation due to increased attention could produce an ‘active reset’ between trials, we performed simulations in which a single sample stimulus was repeated on consecutive trials, but the tonic input to the cholinergic neuron was doubled.

## 3. Results

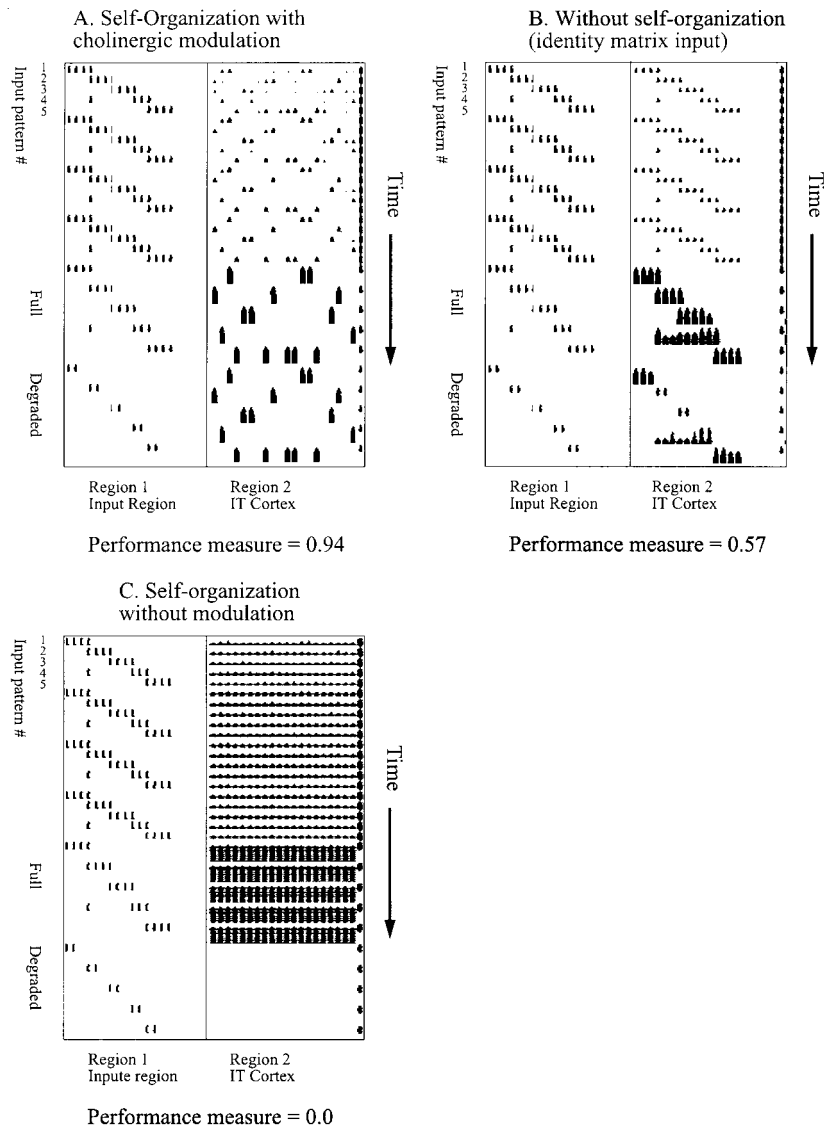
We present the results in three parts. First, we store several input patterns in the network by repeatedly presenting them to the input region, and we show that the network can subsequently recall these patterns. Second, to study short-term recency effects, we use these stored patterns to simulate either repeated presentations of a single stimulus, or DMS trials (which have been described in the introduction). Third, to study long-term familiarity effects, we simulate DMS trials in a new network, using initially novel input patterns.

### 3.1. Cholinergic modulation prevents recurrent connections from interfering with self-organization

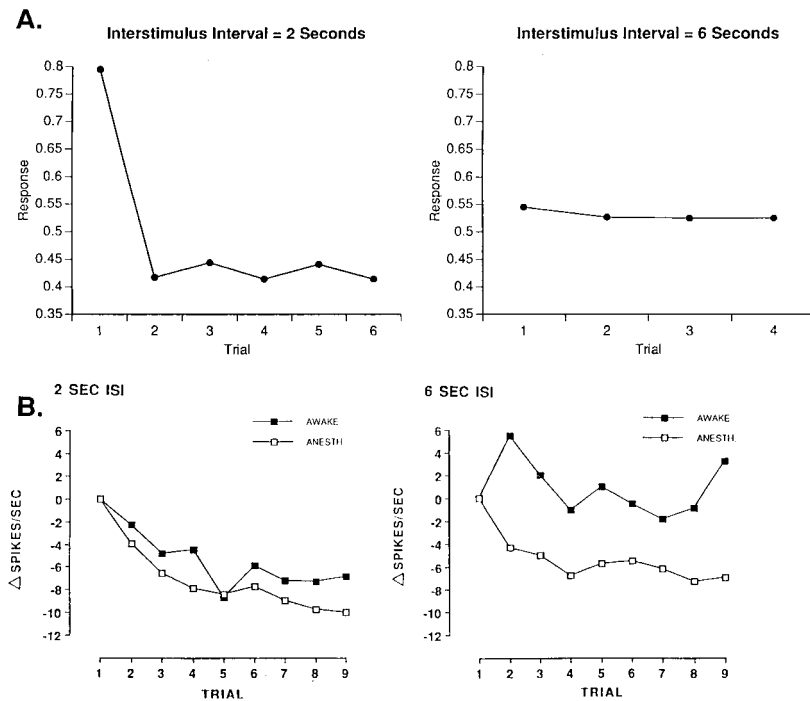
Self-organization normally proceeds via competition between patterns. Consider two input stimuli, pattern A and pattern B. Presentation of one of these patterns to the input region activates a set of IT neurons, called the 'IT representation' for that input pattern. Now suppose that the representations for patterns A and B initially overlap in a single neuron. In the absence of recurrent excitation, presentation of pattern A in the input region will strengthen connections from pre-synaptic neurons in pattern A to all of the neurons in the IT representation of pattern A, including the overlapping neuron which is in the IT representations of both patterns. At the same time, as a consequence of normalization, connections from pre-synaptic neurons in input pattern B to the overlapping neuron are weakened. Similarly, presentation of pattern B in the input region will strengthen connections from the pre-synaptic neurons in pattern B to all of the neurons in its IT representation, and weaken connections from pre-synaptic neurons in pattern A to the overlapping neuron. The net result is that connections between both patterns and the nonoverlapping elements of their respective IT representations are strengthened, while they compete for the overlapping elements.

However, when recurrent excitatory connections are present, the spread of activity along these connections can interfere with self-organization. Suppose that the IT representations for two input patterns, A and B, overlap in one or more elements. Then, when input pattern A is presented, excitation spreads along recurrent excitatory connections in IT cortex to activate elements of the IT representation for pattern B. As a result, connections between the neurons in input pattern A and the IT representations for pattern A *and* pattern B are strengthened. After normalization, connections between the input neurons for pattern B and all of the neurons in its IT representation will be weakened. When pattern B is presented, the converse occurs. As a result, the representations for two patterns which initially overlapped only in one element may become completely overlapping. Figure 2(c) shows how this can occur in a network without cholinergic modulation. At time zero, the network was initialized with random synaptic weights, as described in the methods. Then, we repeatedly presented a set of five random patterns of activity to the input region. As described above, because of the spread of activity along recurrent connections between IT neurons, the IT representations for these input patterns become totally overlapping. As a result, every IT neuron responds in the same way to each of these five stimuli, so these responses are noninformative. Furthermore, as shown in the figure, when the network was tested with degraded versions of the original input patterns, it failed to recall the corresponding IT representations.

However, cholinergic modulation suppresses recurrent connections during learning. As a result, self-organization is able to proceed in a network with cholinergic modulation, as shown in figure 2(a). Recent experimental evidence supports this role for cholinergic modulation (Gil *et al* 1997, Hsieh *et al* 1998). With cholinergic modulation in the model, repeated presentation of the five random input patterns produces a unique, nonoverlapping IT representation for each one. When the network was tested with degraded versions of the input stimuli, it correctly recalled the corresponding IT representation. The recurrent connections allow IT neurons to maintain self-sustained activity. Figure 2(b) shows a similar network in which the feedforward connections from the input areas to the IT region do not undergo self-organization but are instead initialized with an identity mapping. The performance of each network in figure 2 is measured using a normalized dot product to compare activity in the IT region during presentation of the degraded and complete patterns. The network with self-organization and cholinergic modulation attains optimal performance.



**Figure 2.** Self-organization in the presence and absence of cholinergic modulation. After the set of input patterns is presented for learning, each network is tested using degraded versions of those patterns and performance is measured using a normalized dot product to compare activity in the IT cortex region during presentation of the degraded and complete patterns. (a) When cholinergic modulation is present, self-organization proceeds normally and nonoverlapping representations of input patterns form in the IT cortex region. Degraded versions of input patterns recall the complete IT cortex representation, indicating that stable attractor states have formed to represent input patterns. (b) Performance when cholinergic modulation is present, but there is an identity mapping rather than self-organizing synapses from input areas to IT cortex. In the absence of self-organization, representations for the input patterns form in IT cortex, but are not nonoverlapping. This causes interference between patterns. (c) In the absence of cholinergic modulation, recurrent excitation interferes with self-organization and stable, nonoverlapping attractor states do not form.



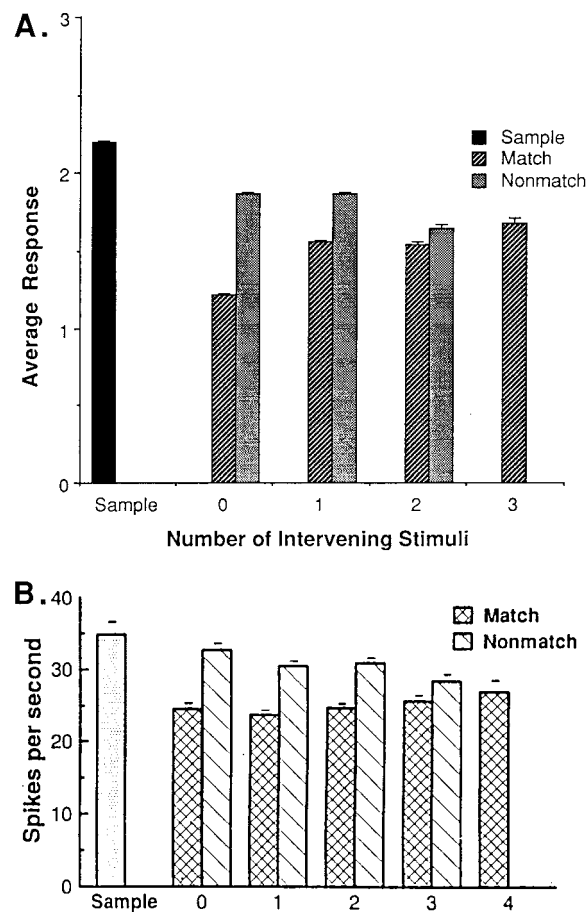
**Figure 3.** (a) The average response of model IT neurons to successive presentations of a familiar stimulus for 1 s, when 2 s intervene between each presentation and when 6 s intervene between each presentation. (b) The average responses recorded intracellularly from IT neurons in awake macaque monkeys to successive presentations of visual stimuli with interstimulus intervals of 2 and 6 s (Miller *et al* 1991a). As in (a) there is habituation with an interstimulus interval of 2 s, but not for one of 6 s.

### 3.2. Recency effects

**3.2.1. Habituation of individual neurons.** In the model, activation of an IT neuron causes a calcium influx. Subsequent responses are suppressed due to activation of a calcium-dependent potassium current. Figure 3(a) shows the average response of simulated IT neurons to repeated stimulation by presentation of a familiar visual stimulus for interstimulus intervals of 2 and 6 s. For comparison, figure 3(b) shows analogous responses obtained by extracellular recording from IT neurons in awake macaque monkeys (Miller *et al* 1991a).

As the interstimulus interval increased in the simulation, increasing amounts of calcium diffused out of neurons between stimulus presentations so that the amount of habituation decreased until the habituation due to adaptation disappeared altogether. As can be seen from figures 3(a) and (b), both the simulation and extracellular recordings found significant habituation at an interstimulus interval of 2 s but not at an interstimulus interval of 6 s.

**3.2.2. Match suppression.** Presentation of a sample stimulus activates a subset of IT neurons, leading to a buildup of calcium in these neurons. Presentation of the match stimulus activates the same subset of neurons and their responses are therefore suppressed due to adaptation of the individual neurons. To study the suppression of responses to match stimuli during DMS tasks, we simulated DMS trials using a network which had stored several random input patterns (as described above). Each input pattern corresponded to one stimulus in a DMS trial.



**Figure 4.** (a) The average response of model IT neurons during a DMS task to sample, match and nonmatch stimuli as a function of the number of intervening stimuli. The responses were averaged over all of the IT neurons in the network and five different random input patterns. (b) The average response of IT neurons recorded extracellularly from awake monkeys during performance of a similar DMS task (Miller *et al* 1991b). In both cases match and nonmatch responses are both suppressed relative to sample responses. In addition, match responses are suppressed relative to nonmatch responses and the amount of match–nonmatch difference decreases as the number of intervening stimuli increases. The responses were averaged over all cells and those trials on which there was a significant difference between responses to matching and nonmatching stimuli.

Figure 4(a) shows the average response of all IT neurons in the model to sample, match and nonmatching stimuli in a DMS task as a function of the number of intervening stimuli. Results from corresponding experiments are shown in figure 4(b) (Miller *et al* 1993). In both simulations (figure 4(a)) and experiments (figure 4(b)), suppression of match responses, relative to responses to either sample or nonmatching stimuli, decreases as the number of intervening stimuli increases. This decrease in response may contribute to differences in activation of visual association cortex measured by functional magnetic resonance imaging (Stern *et al* 1996).

3.2.3. *Suppression of responses to repeated nonmatching stimuli.* In both simulations and experiments (Miller and Desimone 1994), responses to nonmatch stimuli presented twice during one trial ('repeated nonmatches') were lower on the second than on the first presentation, and the amount of suppression was slightly greater than the difference between responses to sample and match stimuli. This suggests that the mechanism of match suppression affects both repeated nonmatch and match stimuli (Miller and Desimone 1994). Indeed, in the simulations, residual adaptation currents in recently activated neurons produced this suppression of responses to the second presentation of a repeated nonmatch.

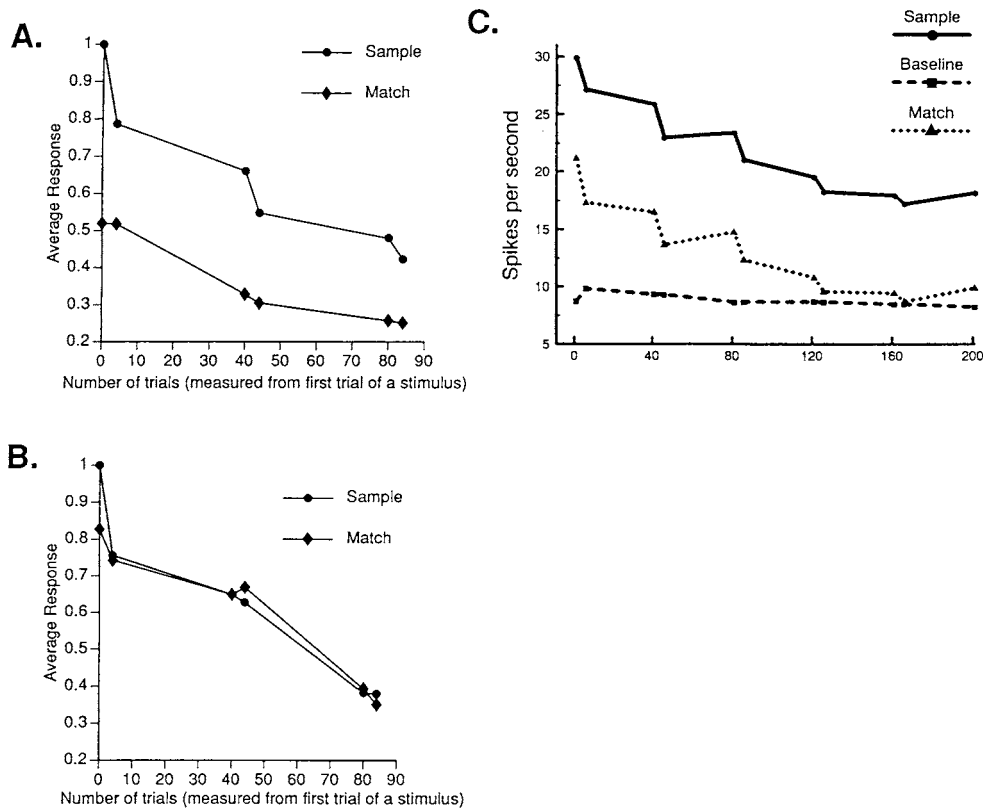
3.2.4. *Nonmatch suppression.* Self-organization in this network led to the formation of distributed representations for input patterns in IT cortex. In such distributed representations, the amount of overlap between the representations for two input patterns reflected their similarity. Nonmatch responses are suppressed relative to sample responses in proportion to the number of IT neurons that the representations of the two stimuli have in common. Thus, the amount of nonmatch suppression reflects the degree of similarity between the sample and nonmatch stimuli, consistent with experimental evidence (Miller *et al* 1993).

### 3.3. Familiarity effects

3.3.1. *Decline of response with increasing stimulus familiarity.* The recency effects described above (habituation, match suppression, suppression of repeated nonmatches and nonmatch suppression) occurred for responses to familiar stimuli, i.e. stimuli that had already been learned by the network. As described earlier, we also simulated DMS trials using initially novel input patterns for the sample/match stimuli and familiar input patterns for nonmatching stimuli. This modelled previous experiments (Miller *et al* 1991b, Li *et al* 1993). In order to study how responses of IT neurons to initially novel sample and match stimuli changed as those stimuli became familiar to the network, simulations and experiments (Miller *et al* 1991b, Li *et al* 1993) both used the following protocol. After each initially novel stimulus appeared as the sample and match stimulus in a DMS trial, it would be absent from a certain number of subsequent DMS trials before appearing as the sample and match stimuli in another DMS trial. The number of intervening trials alternated between three and 35, so that the effects of different numbers of intervening trials could be compared.

Figure 5(a) shows the response of neurons in the network model (averaged over four runs of the simulation, each with 20 initially novel random stimuli) to sample and match stimuli as they became familiar. To demonstrate that match suppression results from calcium-dependent adaptation currents, figure 5(b) shows the average responses to sample and match stimuli from an identical network in which the amount of calcium in IT neurons was reset to zero after each stimulus presentation. This reset should eliminate recency effects due to adaptation. Figure 5(c) shows the experimentally observed decline in the responses of these neurons to sample and match stimuli as they become familiar.

In accordance with previous experimental studies (Miller *et al* 1991b, Li *et al* 1993), we used linear regression to find the best fit line for the average response of each neuron as a function of the number of presentations, and used the slope of this line to determine whether the average response of an IT neuron declined over the course of the simulation. On average, 45% of model IT neurons (referred to as 'negative cells') satisfied this criterion, and their responses to sample stimuli declined by an average of 58% after 12 presentations of the stimuli (six as samples and six as matches). Experimental studies have classified approximately one-third of IT neurons *in vivo* as 'negative cells' using the same criteria (Miller *et al* 1991b, Li *et al* 1993).

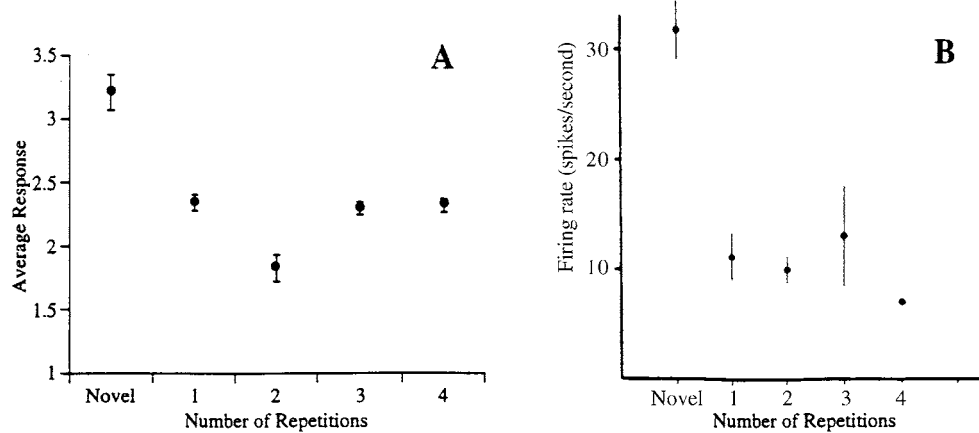


**Figure 5.** (a) The response of model IT neurons to sample and match stimuli as they became familiar during repeated DMS trials. The number of trials intervening between successive presentations of a particular sample/match stimulus alternated between three and 35. The average response was computed for those IT neurons whose responses declined over the course of each simulation (an average of 13 out of 20 neurons). (b) The average responses to sample and match stimuli from an identical network in which calcium levels were reset after each stimulus presentation, eliminating any recency effects caused by adaptation currents. (c) The experimentally observed decline in the responses of IT neurons to sample and match stimuli as they become familiar (Miller *et al* 1991b, Li *et al* 1993). Here the number of trials intervening between successive presentations of a particular stimulus alternated between three and 35. Again, the average included only those neurons whose responses declined significantly over the course of the recording session (approximately one-third of the total number of IT neurons studied).

Other studies have found that as many as 66% of IT neurons satisfy similar criteria (Riches *et al* 1991).

### 3.4. Recency and familiarity effects summate and result from different mechanisms

In this paradigm, which uses initially novel sample and match stimuli, response to match stimuli are still suppressed relative to sample responses. Responses to match stimuli also decline with increasing stimulus familiarity. This is consistent with experimental evidence which suggests that recency effects (match suppression) and familiarity effects summate in IT cortex (Li *et al* 1993). This suggests that match suppression and the decline in responses to increasingly familiar stimuli are caused by independent mechanisms. Indeed, in the network



**Figure 6.** (a) The average response of the cholinergic neuron in the model to initially novel stimuli as they are repeated. (b) The average response of a cholinergic neuron in primate basal forebrain to initially novel visual stimuli, as a function of the number of repetitions (Wilson and Rolls 1990). In both cases the response is higher for novel than for familiar stimuli.

with normal calcium dynamics and adaptation currents (figure 5(a)) sample responses are greater than match responses by an average of 44%, whereas in the network in which calcium levels are reset after each stimulus presentation (figure 5(b)) average match responses are only 4% weaker than average sample responses. This confirms that most of the match suppression observed under this paradigm in the model results from adaptation, not from the synaptic changes that produce the decline in response with increasing stimulus familiarity.

### 3.5. Familiarity effects result from competitive self-organization

Whereas match suppression results from adaptation currents that decay in seconds, the decline in response with increasing stimulus familiarity results from long-term changes in synaptic weights and persists through presentations of at least 105 other stimuli. In the model, these synaptic changes result from the competitive self-organization described earlier. Presentation of a novel stimulus activates a fixed subset of input neurons. IT neurons ‘compete’ for connections from these input neurons. The dominant processes during this competition are described by the first and third terms on the right-hand side of equation (5), namely, Hebbian-type synaptic strengthening and homosynaptic depression. IT neurons whose connections from input neurons undergo depression ‘lose’ the competition and their responses to the stimulus decline as it becomes familiar.

Both input patterns and the IT representations of those patterns are relatively sparse. As a result, during the interval between successive presentations of an initially novel stimulus, those connections from input neurons to IT neurons which had been weakened, are strengthened because of the last term on the right-hand side of equation (5), synaptic strengthening due to nonlocal processes. Thus, as intervening stimuli are presented, there is some recovery in the synaptic connections of those neurons which had been ‘losing’ the competition for connections to input neurons, and the response decrements are gradually ‘forgotten’.

As a result of these learning processes, the responses of many IT neurons to a stimulus fall after each presentation of that stimulus, but recover during the presentation of different intervening stimuli. In the model, responses of ‘negative cells’ to a stimulus fell by an average

of 16% when there were only three intervening trials between successive presentations of that stimulus, but fell by an average of only 10% when 35 trials intervened. Experimental studies of ‘negative cells’ in IT cortex have also found larger response decrements when there were fewer intervening trials (Miller *et al* 1991b, Li *et al* 1993). This explains the staircase-like appearance of figures 5(a) and (c), where response decrements are large when there are few intervening stimuli but small when there are many intervening stimuli.

### 3.6. Decline in levels of cholinergic modulation with increasing stimulus familiarity

In the model, as in experimental recordings from the substantia innominata (Wilson and Rolls 1990), responses of the cholinergic neuron fell as stimuli became familiar. Figure 6(a) shows the average response of the cholinergic neuron in the model to initially novel stimuli as a function of the number of repetitions. For comparison, figure 6(b) shows an analogous decline in the responses of cholinergic neurons *in vivo* (Wilson and Rolls 1990).

**3.6.1. Acetylcholine masks recency effects.** To simulate focusing of attention on the sample stimulus, tonic input to the cholinergic neuron was doubled during presentation of the sample stimulus. Under this condition, responses to a single sample stimulus presented on two consecutive trials increased slightly on the second presentation even though the same stimulus had just been seen on the preceding trial as the match stimulus. Thus, cholinergic modulation could provide the active reset mechanism described in the introduction.

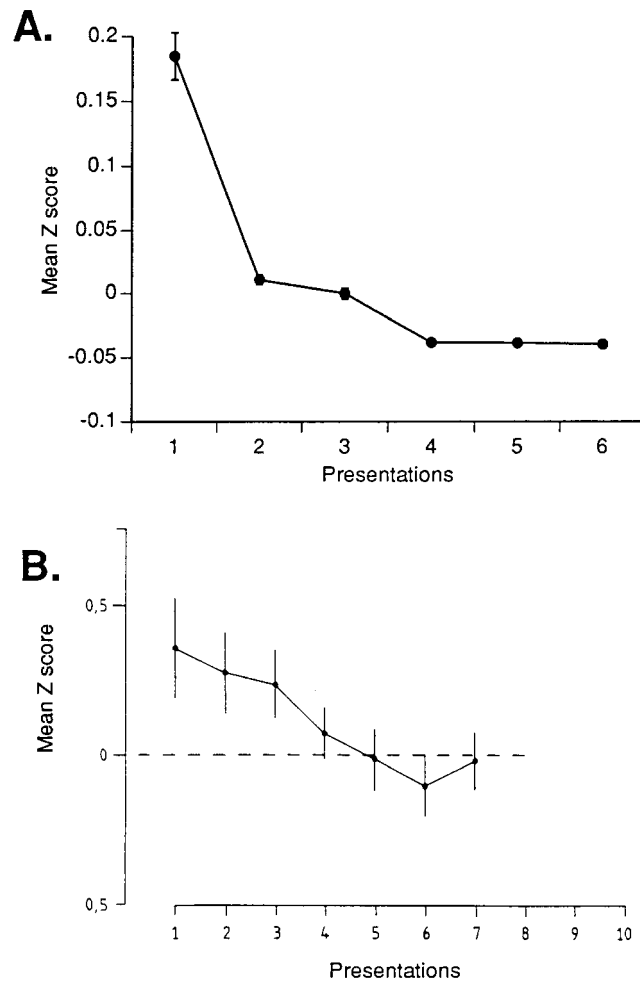
### 3.7. Combination of recency and familiarity effects

Familiarity and recency effects can summate in IT cortex, when initially novel stimuli are presented repeatedly with short (500 ms) interstimulus intervals. Figure 7(a) shows the average Z score, computed from responses of model IT neurons to initially novel stimuli, as a function of presentation number. Figure 7(b) shows analogous data computed from the responses of IT neurons in awake macaque monkeys to initially novel faces (Hasselmo 1988). The rapid decline of the Z scores suggests that in both cases the responses to the first presentations are much higher than responses to subsequent presentations. As in previous experimental studies (Hasselmo 1988, Rolls *et al* 1989), the distribution of responses across neurons changes as initially novel stimuli become familiar.

## 4. Discussion

This network model of IT cortex reproduces the following experimental observations:

- (1) The responses of IT neurons decline during repeated presentations of a single stimulus (habituation).
- (2) During DMS trials, IT neurons’ responses to nonmatch stimuli are suppressed relative to responses to sample stimuli (nonmatch suppression). Responses to match stimuli are suppressed relative to responses to both sample and nonmatch stimuli (match suppression).
- (3) When a single nonmatch stimulus is presented twice during a single trial, the response to the second presentation is suppressed relative to that to the first (suppression of repeated nonmatch).
- (4) Elevated levels of cholinergic modulation during presentation of the sample stimulus prevent suppression of the response to a sample stimulus that is repeated on two consecutive trials (active reset mechanism).



**Figure 7.** (a) The average Z score, computed from responses of model IT neurons to a set of four initially novel stimuli, as a function of presentation number. Stimuli were presented for 500 ms and 500 ms intervened between consecutive stimuli. (b) The average Z score as a function of the number of presentations for responses recorded extracellularly from IT neurons in awake macaque monkeys during presentation of an initially novel set of faces (Hasselmo 1988).

- (5) The decline in response to an initially novel stimulus as it becomes familiar is greater when fewer other stimuli intervene between successive presentations of the initially novel stimulus.
- (6) This decrease in response with increasing familiarity summates with match suppression in IT cortex.
- (7) The responses of cholinergic neurons in the basal forebrain decline with increasing stimulus familiarity.

Observations (1)–(3) describe recency effects that are produced by adaptation currents in our model. Observation (4) suggests that cholinergic modulation may underlie the active reset mechanism. Observation (5) describes a familiarity effect that results from competitive self-organization of feedforward connections terminating on IT neurons. Observation (7) shows

that feedback from IT neurons to the basal forebrain can regulate the level of cholinergic modulation, such that it prevents recurrent connections from disrupting self-organization.

#### 4.1. Cholinergic modulation and arousal

Several researchers have suggested that feedback from adaptive memory filters in IT cortex could control attention and orienting systems (Li *et al* 1993, Desimone *et al* 1994). In this scheme novel stimuli elicit high levels of activity in IT cortex, indicating that they are worthy of attention whereas familiar stimuli elicit lower levels of activity, freeing the organism to focus its attention on other stimuli. In our model, widespread activity in IT cortex results in high levels of cholinergic modulation and focused activity in IT cortex is associated with low levels of cholinergic modulation. Thus, the level of cholinergic modulation in our model reflects the amount of attention focused on IT cortex by attention or orienting systems.

In fact, levels of acetylcholine release do seem to be correlated with levels of cortical activation and arousal (Richardson and DeLong 1991). This relationship and the ability of acetylcholine to facilitate long-lasting changes in the efficacy of synaptic transmission have led other authors to suggest that phasic increases in levels of cholinergic modulation may accompany learning (Richardson and DeLong 1991), as this model assumes.

#### 4.2. Relation to cholinergic modulation in other cortical structures

Our results suggest that acetylcholine may facilitate the encoding of novel stimuli by IT cortex. The observed effects of cholinergic modulation on neuronal responses in other cortical structures are consistent with this hypothesis. For example, in the cat somatosensory cortex, pairing of acetylcholine infusion with somatosensory stimuli causes long-term enhancement of the neuronal response to this same somatosensory stimuli (Tremblay *et al* 1990), suggesting that cholinergic modulation could provide a strong 'encode' signal which activates neurons in a manner which makes them more selectively responsive during a subsequent match episode (Dykes 1997). Muscarinic activation also enhances the response of auditory cortex neurons to auditory stimuli (Metherate *et al* 1990) and pairing application of acetylcholine with auditory stimuli of specific frequencies can selectively enhance the response of a recorded neuron to those specific frequencies (Metherate and Weinberger 1989). Iontophoretic injection of acetylcholine into the primary visual cortex (Sillito and Kemp 1983) greatly enhances the stimulus-specific response of many visually responsive neurons (and causes depression of other responses).

#### 4.3. Comparison to adaptive resonance theory

The role of cholinergic modulation may also be understood by comparing this model to the adaptive resonance theory (ART) model of Carpenter and Grossberg (1993). Both our model and the ART model contain two sets of units. One set receives input and has self-organizing feedforward connections to the other set of units, which could represent IT neurons. The units representing IT neurons compete for connections from the units receiving input. The effects of cholinergic modulation in our model resemble the function of the orienting subsystem in the ART model. Cholinergic modulation and the orienting subsystem of ART both nonspecifically activate units until the IT units become active.

While these overall dynamics are similar, we have tried to relate the parameters of our model to specific neural processes. For example, unlike the ART model our model includes adaptation currents with dynamics determined by *in vitro* studies of slow AHP. Also, the

neural network described here uses a learning rule representing LTP, LTD and long-term redistribution of resources for synaptic maintenance. In the presence of cholinergic modulation, this biologically plausible learning rule causes self-organization in which the responses of many IT neurons decline as stimuli become familiar. In contrast, the ART model learns by searching for a recognition code among the units representing IT neurons until the dot product between the output of these units and the input pattern exceeds a vigilance parameter.

#### 4.4. Comparison to other models

Recently, several new models of learning in IT cortex have appeared (Brunel 1996, Wallis 1998, Riesenhuber and Poggio 1999). These models focus on describing data from experiments (Miyashita 1988) showing increases in responses to visual stimuli after they have been consistently paired with stimuli evoking a stronger neuronal response. Thus, they focus on different experimental phenomena than the ones addressed here. Furthermore, none of these models have combined learning at feedforward and recurrent synapses. Learning at both sites is critical in our model—at the former learning changes the distribution of IT neurons activated by a stimulus, and at the latter learning enables IT neurons to sustain stimulus-specific activity following removal of that stimulus. The model of Brunel (1996) and related work by Amit (see Amit (1999) for an overview) study how recurrent connections between IT neurons develop during repeated presentations of stimuli, but the set of IT neurons activated by feedforward input to IT cortex does not change. In contrast, other models have focused on how learning affects feedforward connections onto IT neurons, without specific mechanisms for maintaining activity in the absence of stimuli (Wallis 1998, Riesenhuber and Poggio 1999). None of these models specifically addresses the subject of this work: short- and long-term decreases in the responses of IT neurons. Wallis (1998) has proposed that activity in IT cortex is maintained via connections with prefrontal cortex, and while we tried to build a model which shows how mechanisms within IT cortex could explain many experimental observations, we cannot rule out a role for prefrontal cortex.

#### 4.5. Predictions

- (1) The adaptation current of neurons which had been ‘match suppressed’ should continue to exert a hyperpolarizing effect on these neurons after any stimulus presentation, reducing their baseline firing rate for a few seconds.
- (2) Another consequence of the adaptation of individual neurons is that for a short time after the presentation of one stimulus, responses to subsequent stimuli that activate the same IT neurons should also be suppressed. Although they have not explicitly tested this claim, past studies have found suggestive evidence that the amount of suppression of a neural response to a nonmatch stimulus may be greatest when the sample and nonmatch activate the neuron to a similar degree (Miller *et al* 1993).
- (3) In our simulations, IT neurons show response decrements after their connections from input neurons become weaker. These are neurons which either do not respond strongly enough for Hebbian synaptic modification to strengthen their connections from input neurons, or which respond to too many stimuli, and therefore do not develop stable connections from a single set of input neurons. Therefore, the population of ‘negative cells’ should generally consist of those neurons which do not respond strongly to a particular stimulus or particular class of stimuli. Conversely, those neurons which continue to respond to stimuli even after they become familiar should respond strongly to a small subset of stimuli.

- (4) We hypothesize that high levels of cholinergic modulation are sustained during presentation of a sample stimulus so that sample responses are not suppressed even when the sample stimulus is repeated. However, this should not affect adaptation currents during the response to the match stimulus. Therefore presenting the same sample/match stimulus on consecutive DMS trials should result in a higher than normal amount of match suppression on the second trial.
- (5) Another prediction of our hypothesis for the active-reset mechanism is that if cholinergic antagonists are applied to IT neurons, this active reset should be blocked.
- (6) Blocking cholinergic innervation should also interfere with effective self-organization, as described earlier.
- (7) One final prediction of our model is that cholinergic agonists or acetylcholinesterase blockers should reduce the amount of match suppression by blocking adaptation currents.

#### *4.6. Limitations of the model*

We have found some limitations of our model for IT cortex which result from the small size of this network. Because there were only a limited number of IT neurons available to participate in representations of input stimuli, some neurons were removed from the representations of previously learned familiar stimuli as representations of novel stimuli were learned. As a result, whenever novel stimuli were learned, the pattern of IT neurons' responses to familiar stimuli changed, so that some neurons' response decrements to familiar stimuli were gradually 'forgotten'. This characteristic of the network could be alleviated by increasing the number of IT neurons.

Larger networks may enjoy other desirable properties. For example, there is evidence that IT neurons have different stimulus selectivity properties during the stimulus presentation than during the subsequent delay interval of a DMS task. In our model, connectivity between IT neurons is all-to-all. During presentation of a stimulus, synapses between all active IT neurons are strengthened. These neurons form an attractor state which maintains activity during the delay. As a result, the same neurons are active during the stimulus presentation and subsequent delay. However, in a larger network, in which IT cortex was only partially connected, the neurons which are active during presentation of a stimulus could excite cells from which they do not receive reciprocal excitatory connections. As the cholinergic suppression of excitatory connections between IT neurons falls, neurons active during the stimulus presentation could activate a distinct subset of neurons, which contained recurrent connections and would remain active during the delay. Thus, different sets of neurons could be active during presentation of the stimulus and during the delay.

Another limitation of this model is that unlike the decline in sample responses, the decline in match responses is not significantly greater when fewer trials intervene between successive presentations of a stimulus. This is because in the model learning occurs instantaneously, so that familiarity effects accrued during a sample presentation manifest themselves in the match response. These instantaneous familiarity effects also explain why in figure 5(b), even when calcium levels are reset to zero after every stimulus presentation, match responses are still suppressed slightly relative to sample responses. In real neurons, changes in synaptic efficacy might occur gradually so that the familiarity effects accrued during the sample presentation would not manifest themselves during the match response. This could explain why in the experimental data, unlike the model, the decline in match response has the same staircase-like appearance as the decline in the sample response.

## 5. Conclusions

The results demonstrate that in a biologically based neural network model of IT cortex, adaptation with a time constant determined by *in vitro* studies of slow AHP causes responses to a stimulus to decrease depending on its recency. They also show how self-organization using a learning rule that represents the physiological processes of LTP, LTD and long-term redistribution of resources for synaptic maintenance causes responses to a stimulus to decrease depending on its familiarity. These results provide mechanisms for similar response decrements observed experimentally (Brown *et al* 1987, Hasselmo 1988, Rolls *et al* 1989, Miller *et al* 1991b, 1993, Riches *et al* 1991, Li *et al* 1993).

This model also shows how a sustained, high level of cholinergic modulation during sample presentations provides a possible mechanism for the observed active reset between DMS trials (Miller *et al* 1991b, 1993). Finally, a feedback circuit from IT cortex to basal forebrain, like that used in this model, could explain why some neurons in substantia innominata respond more strongly to novel than to familiar stimuli (Wilson and Rolls 1990). These results provide a possible relationship between IT cortex, the level of cholinergic modulation and the monkey's behaviour during a DMS task.

## Acknowledgments

This work was supported by grant NSF IBN9996177, NIMH MH52732, NIMH 60013 and the Human Frontier Science Program.

## References

- Amit D J 1999 What is and what is not a theory of context correlations *Network: Comput. Neural Syst.* **10** 273
- Barkai E and Hasselmo M E 1994 Modulation of the input/output function of rat piriform cortex pyramidal cells *J. Neurophysiol.* **72** 644–58
- Bear M B, Press W A and Connors B W 1992 Long-term potentiation in slices of kitten visual cortex and the effects of NMDA receptor blockade *J. Neurophysiol.* **67** 841–51
- Blitzer R D, Gil O and Landau E M 1990 Cholinergic stimulation enhances long-term potentiation in the CA1 region of rat hippocampus *Neurosci. Lett.* **119** 207–10
- Brown M W, Wilson F A and Riches I P 1987 Neuronal evidence that inferomedial temporal cortex is more important than hippocampus in certain processes underlying recognition memory *Brain Res.* **409** 158–62
- Brunel N 1996 Hebbian learning of context in recurrent neural networks *Neural Comput.* **8** 1677–710
- Burgard E C and Sarvey J M 1990 Muscarinic receptor activation facilitates the induction of long-term potentiation (LTP) in the rat dentate gyrus *Neurosci. Lett.* **116** 34–9
- Carpenter G A and Grossberg S 1993 Normal and amnesic learning, recognition and memory by a neural model of cortico-hippocampal interactions *Trends Neurosci.* **16** 131–7
- Cauler L J and Connors B W 1994 Synaptic physiology of horizontal afferents to layer I in slices of rat SI neocortex *J. Neurosci.* **14** 751–62
- Delacour J 1977 Cortex inférotémporal et mémoire visuelle à court terme chez le singe: Nouvelles données *Exp. Brain Res.* **28** 301–10
- Desimone R, Miller E K and Chelazzi L 1994 The interaction of neural systems for attention and memory *Large Scale Neuronal Theories of the Brain* ed C Koch and J Davis (Cambridge, MA: MIT Press)
- Dudkin K N, Kruchinin V K and Chueva I V 1994 Participation of cholinergic structures of the prefrontal and inferotémporal cortex in the processes of visual recognition in monkeys *Neurosci. Behav. Physiol.* **24** 341–50
- Dykes R W 1997 Mechanisms controlling neuronal plasticity in somatosensory cortex *Can J. Physiol. Pharmacol.* **75** 535–45
- Fuster J M 1990 Inferotémporal units in selective visual attention and short-term memory *J. Neurophysiol.* **64** 681–97
- Fuster J M and Jervey J P 1981 Inferotémporal neurons distinguish and retain behaviourally relevant features of visual stimuli *Science* **212** 952–5
- 1982 Neuronal firing in the inferotémporal cortex of the monkey in a visual memory task *J. Neurosci.* **2** 361–75

- Gaffan D and Weiskrantz L 1980 Recency effects and lesion effects in delayed nonmatching to randomly baited samples by monkeys *Macaca mulatta Brain Res.* **196** 373–86
- Gil Z, Connors B W and Amitay Y 1997 Differential regulation of neocortical synapses by neuromodulators and activity *Neuron* **19** 679–86
- Gross C G, Bender D G and Rocha-Miranda C E 1969 Visual receptive fields of neurons in inferotemporal cortex of the monkey *Science* **166** 1303–6
- Grossberg S 1976 On the development of feature detectors in the visual cortex with applications to learning and reaction-diffusion systems *Biol. Cybernet.* **21** 145–59
- Gustafsson B and Wigstrom H 1988 Physiological mechanisms underlying long-term potentiation *Trends Neurosci.* **11** 156–62
- Hasselmo M E 1988 The representation and storage of visual information in the temporal lobe *PhD Thesis* Oxford University
- Hasselmo M E and Barkai E 1995 Cholinergic modulation of activity-dependent synaptic plasticity in the piriform cortex and associative memory function in a network biophysical simulation *J. Neurosci.* **15** 6592–604
- Hasselmo M E and Bower J M 1992 Cholinergic suppression specific to intrinsic not afferent fibre synapses in rat piriform (olfactory) cortex *J. Neurophysiol.* **67** 1222–9
- Hasselmo M E and Cekic M 1996 Cholinergic suppression of synaptic transmission may allow combination of associative feedback and self-organizing feedforward connections in the neocortex *Behav. Brain Res.* **79** 153–61
- Hasselmo M E, Rolls E T and Baylis G C 1989a The role of expression and identity in the face-selective responses of neurons in the temporal visual cortex of the monkey *Behav. Brain Res.* **32** 203–18
- Hasselmo M E, Rolls E T, Baylis G C and Nalwa V 1989b Object-centered encoding by face-selective neurons in the cortex in the superior temporal sulcus of the monkey *Exp. Brain Res.* **75** 417–29
- Hasselmo M E, Schnell E and Barkai E 1995 Dynamics of learning and recall at excitatory recurrent synapses and cholinergic modulation in rat hippocampal region CA3 *J. Neurosci.* **15** 5249–62
- Hsieh C Y, Cruikshank S J and Metherate R 1998 Cholinergic agonist differentially suppresses auditory thalamocortical and intracortical transmission *Soc. Neurosci. Abstr.* **24** 1879
- Lancaster B and Adams P R 1986 Calcium dependent current generating the afterhyperpolarization of hippocampal neurons *J. Physiol.* **387** 519–48
- Levy W B 1989 A computational approach to the hippocampal formation *Computational Models of Learning in Simple Neural Systems* ed R D Hawkins and G H Bower (Orlando, FL: Academic)
- Li L, Miller E K and Desimone R 1993 The representation of stimulus familiarity in anterior inferior temporal cortex *J. Neurophysiol.* **69** 1918–29
- McCormick D A and Prince D A 1987 Post-natal development of electrophysiological properties of rat cerebral cortical pyramidal neurons *J. Physiol.* **393** 743–62
- Mesulam M M and Mufson E J 1984 Neural inputs into the nucleus basalis of the substantia innominata (Ch4) in the rhesus monkey *Brain* **104** 253–74
- Mesulam M M, Mufson E J, Wainer B H and Levey A I 1983 Central cholinergic pathways in the rat: an overview based on an alternative nomenclature *Neuroscience* **10** 1185–201
- Metherate R, Ashe J H and Weinberger N M 1990 Acetylcholine modifies neuronal acoustic rate-level functions in guinea pig auditory cortex by an action at muscarinic receptors *Synapse* **6** 364–8
- Metherate R and Weinberger N M 1989 Acetylcholine produces stimulus-specific receptive field alterations in cat auditory cortex *Brain Res.* **480** 372–7
- Miller E K and Desimone R 1993 Scopolamine affects short-term memory but not inferior temporal neurons *Neuro Rep.* **4** 81–4
- 1994 Parallel neuronal mechanisms for short-term memory *Science* **263** 520–2
- Miller E K, Gochin P M and Gross C G 1991a Habituation-like decrease in the responses of neurons in inferior temporal cortex of the macaque *Visual Neurosci.* **7** 357–62
- Miller E K, Li L and Desimone R 1991b A neural mechanism for working and recognition memory in inferior temporal cortex *Science* **254** 1377–9
- 1993 Activity of neurons in anterior inferior temporal cortex during a short-term memory task *J. Neurosci.* **13** 1460–78
- Mishkin M 1982 A memory system in the monkey *Phil. Trans. R. Soc. B* **298** 83–95
- Mishkin M and Delacour J 1975 An analysis of short-term visual memory in the monkey *J. Exp. Psychol.* **1** 326–34
- Miyashita Y 1988 Neuronal correlate of visual associative long-term memory in the primate temporal cortex *Nature* **335** 817–20
- Pitler T A and Alger B E 1992 Cholinergic excitation of GABAergic interneurons in the rat hippocampal slice *J. Physiol.* **450** 127–42
- Richardson R T and DeLong M R 1991 Functional implications of tonic and phasic activity changes in nucleus

- basalis neurons *Activation to Acquisition: Functional Aspects of the Basal Forebrain Cholinergic System* ed R T Richardson (Boston, MA: Birkhäuser)
- Riches I P, Wilson F A and Brown M W 1991 The effects of visual stimulation and memory on neurons of the hippocampal formation and the neighbouring parahippocampal gyrus and inferior temporal cortex of the primate *J. Neurosci.* **11** 1763–79
- Riesenhuber M and Poggio T 1999 Hierarchical models of object recognition in cortex *Nature Neurosci.* **2** 1019–25
- Rolls E T, Baylis G C, Hasselmo M E and Nalwa V 1989 The effect of learning on the face selective responses of neurons in the cortex in the superior temporal sulcus of the monkey *Exp. Brain Res.* **76** 153–64
- Rumelhart D E and Zipser D 1986 Feature discovery by competitive learning *Foundations (Parallel Distributed Processing: Explorations in the Microstructure of Cognition vol 1)* (Cambridge: MIT Press)
- Russchen F T, Amaral D J and Price J L 1985 The afferent connections of the substantia innominata in the monkey *Macaca fascicularis J. Comput. Neurol.* **242** 1–27
- Schwandt P C, Spain W J and Crill W E 1992 Calcium-dependent potassium currents in neurons from cat sensorimotor cortex *J. Neurophysiol.* **67** 216–26
- Schwandt P C, Spain W J, Foehring R C, Stafstrom C E, Chubb M C and Crill W E 1988 Slow conductances in neurons from cat sensorimotor cortex and their role in slow excitability changes *J. Neurophysiol.* **59** 450–67
- Sillito A M and Kemp J A 1983 Cholinergic modulation of the functional organization of the cat visual cortex *Brain Res.* **289** 143–55
- Stanton P K and Sejnowski T J 1989 Associative long-term depression in the hippocampus induced by Hebbian covariance *Nature* **339** 215–8
- Stern C E, Corkin S, Gonzalez R G, Guimaraes A R, Baker J R, Jennings P J, Carr C A, Sugiura R M, Vedantham V and Rosen B R 1996 The hippocampal formation participates in novel picture encoding: evidence from functional magnetic resonance imaging *Proc. Natl Acad. Sci. USA* **93** 8660–5
- Tremblay N, Warren R A and Dykes R W 1990 Electrophysiological studies of acetylcholine and the role of the basal forebrain in the somatosensory cortex of the cat II. Cortical neurons excited by somatic stimuli *J. Neurophysiol.* **64** 1212–22
- von der Malsburg C 1973 Self-organization of orientation sensitive cells in the striate cortex *Kybernetik* **14** 85–100
- Wallis G 1998 Spatio-temporal influences at the neural level of object recognition *Network: Comput. Neural Syst.* **9** 265
- Whitlock D G and Nauta W J H 1956 Subcortical projections from the temporal neocortex *Macaca mulatta J. Comput. Neurol.* **106** 184–207
- Wilson F A W and Rolls E T 1990 Neuronal responses related to the novelty and familiarity of visual stimuli in the substantia innominata, diagonal band of Broca and periventricular region of the primate basal forebrain *Exp. Brain Res.* **80** 104–20
- Wilson H R and Cowan J D 1972 Excitatory and inhibitory interactions in localized populations of model neurons *Biophys. J.* **12** 1–24
- Woody C D and Gruen E 1987 Acetylcholine reduces net outward currents measured *in vivo* with single electrode voltage clamp techniques in neurons of the motor cortex of cats *Brain Res.* **424** 193–8
- Zipser D, Kehoe B, Littlewort G and Fuster J 1993 A spiking network model of short-term active memory *J. Neurosci.* **13** 3406–20