Dopaminergic Regulation of Neuronal Circuits
in Prefrontal Cortex

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Abstract. Neuromodulators, like dopamine, have considerable influence on the processing capabilities of neural networks. This has for instance been shown in the working memory functions of prefrontal cortex, which may be regulated by altering the dopamine level. Experimental work provides evidence on the biochemical and electrophysiological actions of dopamine receptors, but there are few theories concerning their significance for computational properties ((Servan-Schreiber et al., 1990), (Hasselmo, 1994b)). We point to experimental data on neuromodulatory regulation of temporal properties of excitatory neurons and depolarization of inhibitory neurons, and suggest computational models employing these effects. Changes in membrane potential may be modelled by the firing threshold, and temporal properties by a parameterization of neuronal responsiveness according to the preceding spike interval. We apply these concepts to two examples using spiking neural networks. In the first case, there is a change in the input synchronization of neuronal groups, which leads to changes in the formation of synchronized neuronal ensembles. In the second case, the threshold of interneurons influences lateral inhibition, and the switch from a winner-take-all network to a parallel feedforward mode of processing. Both concepts are interesting for the modeling of cognitive functions and may have explanatory power for behavioral changes associated with dopamine regulation.

Keywords: synchronization, spiking neural networks, neuromodulation, dopamine, cortical networks, spike frequency adaptation, ensemble formation

1. Introduction

1.1. Dopaminergic action at single neurons

There is ample evidence that the availability of neuromodulators at neuronal synapses influences cognition and behavior in systematic ways. In this paper we will concentrate on the action of a specific neuromodulator, dopamine (DA), on single neurons and neuronal circuits.

DA acts on receptors on pyramidal or inhibitory neurons in cortical networks, which are “slow”, and change properties of the single neuron or its synapses, in contrast to glutamatergic, excitatory and GABAergic, inhibitory synapses, which allow fast transmission of signals by activating ion channels directly.

The action of a neuromodulator is determined by the type of receptor - the same neuromodulator has different, even reverse effects according to the receptor type.

The main receptor types for dopamine are the $D_1$- and $D_5$-receptor, and the $D_2$, $D_3$ and $D_4$ receptors (Starke, 1997). They all act through ‘second messengers’ of different G-proteins within the cell. Shortly stated, $D_2/D_3/D_4$-receptors act on $G_\text{i}$-proteins which break up in at least two parts, one ($\alpha$) which inhibits adenylyl cyclase (AC) and another ($\beta$) which opens $K^+$-channels, i.e. induces a hyperpolarization of the membrane with a delay of about 1-2 s. $D_1/D_5$-receptors act on $G_\text{s}$-proteins, which stimulate AC. Dopamine acts most strongly on $D_1/D_5$ receptors, i.e. the same amount of extracellular dopamine will have a stronger effect on $D_1$ than $D_2$ receptors.

There are pharmacological selective agonists/antagonists for most of the receptor types or combinations (such as $D_2/D_3/D_4$). A specific class of dopamine receptor antagonists (mostly $D_2$ and $D_4$) is noted for its anti-psychotic potential in the treatment of schizophrenia. Exposure to receptor-specific $D_1/D_5$ or $D_2/D_3/D_4$ agonist and antagonists in humans or trained animals provides important experimental tools for the analysis of behavior on various cognitive tasks (see below).

AC is the catalyst for the transformation of ATP to cAMP, which is an important ‘second messenger’ that spreads out throughout the cell. It plays an important role in the phosphorylation of proteins by protein kinase A. Since receptors are themselves proteins, it may also be the case that a number of receptors are inactivated in response to heightened cAMP-levels. It has been noted that the activation of second-messengers means a significant amplification of a signal received at a receptor. With each transmission step the signal is multiplied in a snowball fashion such that a single receptor may act on very many molecules within the cell.

The complexity of intracellular signaling may contribute to the difficulties of reliably exerting computational properties of receptor activation in in vitro slices.

However, recent studies (Seamans et al., 2000) have established that $D_1$ receptor activation in deep layer neurons of rat prefrontal cortex influences synaptic properties, essentially strengthening synaptic connections on a short-term basis (“dynamic synapses”, cf. Wiskott and v.d. Malsburg, 1995)).

The activation of $D_1$ receptors also influences a calcium-gated $K^+$-channel in hippocampal neurons, and reduces the effect of an after-hyperpolarization of the membrane after the occurrence of a spike (Pedarzani and Storm, 1995)). This means that temporal properties of the cell such as interspike intervals, i.e. periods between spikes, are
changed, and that activation of $D_1$ receptors results in a capacity for faster responses of the neuron.

$D_2$ receptors occur as presynaptic autoreceptors, which reduces volume transmission, and increases spatial and temporal focusing of the effect of released DA.

It has also been shown that large concentrations of $D_1$ agonists abolish the calcium currents that convey signals along dendrites, disrupting information transfer from dendrite to soma. With high dopamine or $D_1$-receptor agonist levels, it could be shown that the balance of synaptic inputs on different parts of the dendritic tree is changed, favoring basal (local) inputs over apical (distal) inputs ((Zahrt et al., 1997), (Yang and Seamans, 1996)).

Finally, there are a number of indications for DA raising the activity of inhibitory neurons by enhancing the firing rate through membrane depolarization. This effect may be primarily $D_2$ or $D_1$ modulated ((Retaux et al., 1991), (Grobin and Deutch, 1998)).

In this work we will only look at the effects of varying thresholds and the role of altering temporal properties in collections of neurons. We want to show that the short-term regulation of single-neuron properties leads to alterations in the functionality of neural networks. A few indications concerning cognitive implications of altered network function are given in the discussion (section 5).

1.2. Models of DA function in cortical networks

In cortical networks, the action of dopamine has been studied mostly with respect to working memory function. Working memory functions are mediated by the prefrontal cortex ((Desimone, 1995)) and prefrontal cortex function relies on the mesocortical dopamine system ((Sawaguchi and Goldman-Rakic, 1991), (Goldman-Rakic, 1987)). DA availability is regulated by the activity of DA-producing neurons (DA-neurons) in the ventral tegmental area (VTA) ((Kitai et al., 1999)) and by glutamatergic innervation of axon terminals of DA-neurons ("terminal release") ((Gobert et al., 1998)). Fluctuation of the dopamine level, however, stays within narrowly defined limits, as evidenced by the action of re-uptake mechanisms, the rate-control of tyrosine hydroxylase, which is necessary for dopamine production, and the regulation of activity in VTA itself ((Scheler, 1998)).

Models of neuromodulatory action have been developed within connectionist models, using 'rate-coding neurons', i.e. formal neurons that have a continuous value as output corresponding to the firing rate of biological neurons ((Levine, 1991), (Servan-Schreiber et al., 1990), (Ludik and Stein, 1996), (Usher et al., 1999)). For dopamine,
a change in the activation function of the neuron has been proposed, leading to a difference in the signal/noise ratio. It is assumed that the sigmoidal activation function may be steeper or less steep according to the level of dopamine input ("gain" parameter) ((Cohen and Servan-Schreiber, 1993), (Cohen et al., 1992), (Servan-Schreiber et al., 1996), (Cohen and Usher, 1996)). This allows a simple way of addressing issues of neuromodulation within cognitive modeling, however the temporal structure of the neural code and influences on synchronization cannot be addressed ((Shadlen and Newsome, 1994), (von der Malsburg, 1994), (von der Malsburg, 1995), (Maass, 1997)).

It has been hypothesized that synchronous firing of neurons indicates functional groups of neurons ((Singer and Gray, 1995), (Fetz, 1997), (Usher and Donnelly, 1998)) as in the perceptual binding of various objectual features to a single perceived object. There have been experiments which indicate that the presence or absence of synchronicity in the population response may correspond to the perception of an object ((Fries et al., 1997)) or an auditory event ((deCharms and Merzenich, 1996)). These synchronizations occur dynamically, they form groups of neurons (ensembles) which are processing units for later stages. The process of ensemble formation and switching of ensembles has been modeled by ((Hansel and Sompolinsky, 1998)), on the basis of changes in neuronal adaptation by a local negative feedback mechanism, but without reference to neuromodulation.

There is another group of models ((Hasselmo, 1994b), (Hasselmo, 1994a), cf. (Fellous and Linster, 1998)) which makes critical use of compartmental modeling, i.e. regards the anatomical complexity of the dendrite. In this way we may model greater or smaller electrotonic distance between apical and basal section of the dendrite, which is a property of the neuron under neuromodulatory control ((Yang and Seamans, 1996)).

2. Principles of network modeling for neuromodulatory effects

2.1. Temporal dependence of excitability

The temporal properties of single neurons ((Maass, 1997)), and the influences that determine spike timing, may be influenced by several factors:

- recovery function
  The variability of spike frequency adaptation may be modeled by a
threshold function that has a high value immediately after a spike and a descent until the next spike is generated.

- temporal integration
  We may assume that the decay factor that determines how long sub-threshold activations are being kept is altered, which would result in prolonged or shortened periods for the integration of different signals.

- reliability
  Given a certain amount of excitation, a spike may be generated with a certain probability. Under the influence of neuromodulation this probability may be altered, i.e. spike generation may become more reliable.

All of these effects have been found in biological neurons, under dopaminergic (D₁-receptor) modulation: spike frequency adaptation (Pedrazzani and Storm, 1995), increase of the influence of NMDA-receptors (Seamans et al., 2000), and increase of reliability (J.-M. Fellous, unpublished observations).

If we take $D_{in}$ as a factor linked to the degree of stimulation of a neuron by its dopamine receptors, we have in each case a functional modification of a single value:

(a) $\theta(t + 1) = \theta(t) \times D_{in}(t)$ (threshold or threshold function)

(b) $\epsilon(t + 1) = \epsilon(t) \times D_{in}(t)$ (decay factor)

(c) $p(t + 1) = p(t) \times D_{in}(t)$ (reliability)

We assume that the degree of dopamine modulation of a neuron $i$ is dependent both on the dopamine availability and the dopamine receptor density of $i$. Receptor density of neurons is regulated on a long-term basis (Hess et al., 1988)) and may be different for individual neurons. It has been shown that differences in receptor density have functional significance (Goldman-Rakic et al., 2000).

Dopamine availability is due to both the actions of dopaminergic neurons in midbrain (Scheler, 2000)) and glutamatergic effects at axon terminals (terminal release) (Gobert et al., 1998), where the latter effect is probably region-specific. In our system, however, dopamine availability is modeled as a global parameter. Formally:

$$D_{in}^i = \text{rec}_\text{den}(i) \times D_{level}$$

In the following, we have only used parameters for a variability of threshold and for the adaptation period, i.e. the length of decay for the threshold to return to normal threshold, assuming a linear function.
The simulation model

The simulations presented in the next sections are based on an event-paced implementation of spiking neural networks, i.e. collections of neurons that emit individual action potentials (spikes) upon activation. Single neurons are modeled as compact entities, to facilitate the construction of functional cognitive models in the connectionist tradition, but extensions to compartmental modeling are possible. The simulation is parametrized for several properties, either to allow different formal neuron models to be realized within the system, or to allow a setting of parameters by internal activity, i.e. a regulation of system parameters by crucial neuronal activity such as neuromodulatory influences. The activity of neuromodulators is simulated by the setting of neuronal parameters following stimulation of DA receptors, by using different receptor densities per neuron and setting a general level of dopamine availability which is determined by the activity of dopamine-producing neurons.

Each neuron is formally a summation device (‘integrate-and-fire’) (Gerstner, 1998) with a short time window for concurrent signals (cf. (Tam, 1998)).

\[ V(t) = \frac{I_{in}}{g}(1 - e^{-t/\tau}) - V_{rest} \]

\( I_{in} \) is the total synaptic input, \( g \) is the membrane conductance, and \( \tau \) is a time constant. If \( V(t) \) reaches a threshold value \( \theta \), then the neuron fires and the membrane voltage is reset to \( -V_{rest} \).

The neuron has a number of “fast” synapses with inhibitory or excitatory activity corresponding to AMPA/NMDA and GABAergic synapses and weights as measures for synaptic efficacy. Incoming signals are multiplied by the weight factor. In our simulations, the synaptic efficacy is always kept fixed, i.e. there is no learning or adaptivity by long-term potentiation or depression. This is done to ensure that the models can be kept simple and that other forms of adaptivity become more apparent. Also, short-term adaptivity of synaptic strength is not employed, although it is under dopaminergic control.

The neuron’s activation depends on the size of the EPSP’s (excitatory postsynaptic potential) and IPSP’s (inhibitory PSP), and the membrane conductance. The membrane conductance is influenced by the number of cationic and anionic ion channels and the time course of ion flow. In the simulation, membrane conductance is summarily modeled by a threshold that determines the size of the total activation that induces firing. Activation value and output value of the neuron are linked either by identity or subtraction of the threshold (transfer func-
Since thresholds are subject to neuromodulation, a parameter for the firing threshold can be influenced by DA receptor activation, i.e. the combined effects of receptor density per neuron and dopamine availability in the network. Upon activation, a neuron generates a sequence of action potentials, a spike train. In general, the size of the activation determines the frequency of the spikes rather than their amplitude. For fluctuating input, i.e. synaptic input with an oscillatory or irregular structure, the occurrence of a spike depends on the amplitude of the input, the temporal integration time, and the excitability state of the neuron.

We have used two different ways of altering the excitability of the neuron, both of which are under dopaminergic control.

- Depolarization, or influences on firing rate alone, can be modeled as a lowering of the firing threshold.

\[ \theta(t+1) = \theta(t) \times D_{\text{in}}(t) \]

- Temporal dependence of firing on previous spikes has been modeled as an extended adaptation period, consisting of a short absolute refractory period (synaptic input has no effect), and a relative adaptation period, with a dependence of spiking probability on amplitude of input and distance to a previous spike. As a first approximation this can be modeled by a variable threshold, which is heightened after a spike and gradually drops to its normal level.

\[ \theta = \Delta \theta \times (1 - (t - t_{\text{fire}})/\epsilon \times \Delta t) + \theta_0 \]

for \( t_{\text{fire}} \leq t \leq t_{\text{fire}} + \Delta t; \theta = \theta_0 \) otherwise

\( \Delta \theta \) is the maximal raise of the threshold after a firing event, \( \Delta t \) is the length of the adaptation period, \( \epsilon \) a scaling factor, \( \theta_0 \) is the normal threshold and \( t_{\text{fire}} \) the time of the last firing event.

The time between the last spike and the generation of a new spike may be regarded as the temporal integration period. Obviously, the state of the neuron depends upon the distance to the last spike. However, previous spikes also influence the probability of generating a new spike, with a certain decay time. The mean temporal integration period is therefore dependent on a decay factor of sub-threshold activations.
2.3. **Dopaminergic effects on synchronization**

It has been noted before that there may be specific effects of spike frequency adaptation on synchronization (Crook *et al.*, 1998). Similarly, ensemble formation, as the synchronization of firing of a subset of neurons, may be influenced by temporal properties of neurons, and the ability of individual neurons to switch groups and become entrained with a different ensemble (Hansel and Sompolinsky, 1998). Models of working memory capacity, which take account of the limited amount of units that can be held available at any time (Callicott *et al.*, 1999), have assumed tight synchronization of groups of neurons as representation for single units (chunks) and a sequence of firing of different groups to account for the number of units maintained (Jensen and Lisman, 1996), (Dehaene *et al.*, 1998), (Luck and Vogel, 1997). Ensemble formation and switches of ensembles may therefore be a mechanism under dopaminergic control, and DA receptor activity may influence synchronization properties of excitatory neurons.

3. **Synchronization and ensemble formation**

The main effect of a variable adaptation period are on the frequency of successive spikes in a spike train - where a short adaptation period allows higher frequency spike trains - and on synchronization and ensemble formation. We may regard a situation where a number of neurons receive identical input of high frequency. This would be the case if the neurons are activated by an ensemble of neurons firing in synchrony, e.g. in response to a perceptual input. Spikes that arrive during the period of a heightened threshold (adaptation period) will be lost and will not be processed.

In Fig. 2, we can see the spiking behavior of six neurons (with connections as shown in Fig. 1). In Fig. 2 A we have a common adaptation period of 4 time units, in Fig. 2 B, after raising the DA-level, neurons A, B and C have different adaptation periods. We can see how the regular pattern of synchronized firing breaks up and neurons fire at different times, although they still receive the same input. Accordingly, the postsynaptic neurons X, Y and Z receive less coincident input - depending on their excitability and temporal integration period, they may fire fewer spikes at shorter time periods, or fire less in general.

Depending on the spacing of input spikes, small differences in the adaptation period will not change the neuron’s firing pattern, while larger differences lead to a difference of processed input.

If we want to control the adaptation period by dopamine levels, we must consider how $D_i^{in}$ and $\Delta^i_t$ are related in the model. Due to
Figure 1. Connection pattern of six neurons in a feedforward structure

variations in receptor density and scaling effects on the adaptation period, we get different values for $\Delta^i_t$.

Let us first assume that the scaling factor $\epsilon$ does not vary with different DA levels $D_{\text{level}}$. In that case, $\Delta^i_t$ decreases linearly with the level and only depends on the receptor density. We obtain functions for adaptation periods $\Delta^i_t$ as shown in Fig. 3. Neurons fire in synchrony at a low DA level (indicated by a small variation of their adaptation periods), but with increasing DA levels, their adaptation periods become increasingly dissimilar (due to the fact that neurons with higher receptor densities react more strongly to increased DA stimulation).

The synchrony between the neurons can be observed by looking at the spiking behavior on different DA levels. On a lower level, adaptation periods are relatively similar to each other, leading to a synchronous firing of the neurons (see again Fig 2,A). When DA is increased (here to about 1.5), adaptation periods for the neurons are different enough to cause asynchronous spiking, as shown in Fig 2,B.

This change in adaptation period may have effectively two meanings in a network of neurons: (a) individual neurons fall out of synchrony, and (b) neurons switch between ensembles (groups of temporal concordance).

In Fig. 3, dashed lines indicate a bandwidth of variation in adaptation period which may be tolerable in the sense that it will lead to essentially the same behavior with respect to input spikes. (The size of the variation is linked to the temporal integration period. It is clear however that this is only an approximate boundary, and that neurons have a reduced probability to fire simultaneously which is proportional to the difference in their adaptation periods.)
With low DA levels, neuron A, B and C belong to the same group 2. A raise in DA level causes individual neurons to fall out of that group (e.g., neuron B leaves group 2 at the dotted line 1 in Fig. 3). With increased dopamine levels, the adaptation periods of neurons with different receptor densities become increasingly dissimilar causing neurons to change between temporal concordance groups. In Figure 3, with dopamine levels higher than marked by the dotted line 2, neurons B and C have changed from group 2 to group 1.

Vice versa, if a decrease in dopamine level causes adaptation periods to become more similar, fewer groups of distinct synchronized firing will remain.

*Figure 2.* Alteration of spiking behavior by DA-level. A: response to synchronous input with uniform adaptation periods B: desynchronisation due to different adaptation periods for A (ap=4), B (ap=3) and C (ap=2).
In the linear case (Fig. 3) as discussed above, changes in a neuron’s adaptation period require correspondingly large changes in the dopamine level. Accordingly, a quick change in the formation of ensembles requires a rapid change in the dopamine level. With a non-linear dependence of $\epsilon$ on the dopamine level, we may have a critical interval where the dopamine level has a strong influence on the adaptation period and rapid changes of synchronized firing are possible. For instance, with the formula,

$$ l_\theta = l_\theta + \epsilon_0 \times D_{in}^i \times \left(1 + \frac{2}{\sqrt{\pi}} \int_0^{D_{level}} \exp\left(-\frac{(l - D_0)^2}{\epsilon_{rec}\epsilon_{len}(i)}\right) dl\right) $$

as an example for a non-linear function with a critical period, we get a situation as shown in Fig. 4. The two dotted lines mark the levels of dopamine where neuron B leaves group 2 and joins group 1. It can be observed that this interval is much smaller than in the linear case and the ranges for stable groups are larger.

If we assume that $\epsilon$ depends on $D_{level}$, we can obtain these desynchronisation and group-changing effects with small variations of the DA level. Typically, with low dopamine levels, $\epsilon$ should be small. Then, in the “interesting” interval of $D_{level}$, $\epsilon$ should rise quickly, corresponding
to an increased activity of the receptors. Finally, with high DA levels, the receptors get saturated, limiting the effect of DA on $\Delta_t$.

Figure 4. Influence of $D_1$ receptor stimulation on synchronization (non-linear case). Changing of an ensemble requires less variations of the dopamine level (marked by the dotted lines) than in the linear case (Fig. 3).

In general, heightened DA-levels reduce adaptation periods in $D_1$-modulated neurons. Beyond the question of individual neuronal variability this means that a neuron can fire at a greater frequency, and therefore that the firing rate of a $D_1$-modulated neuron can be higher. With a set of neurons with different adaptation periods, we get different synchronized groups, each oscillating with its own frequency.

A reduction of groups of neurons firing in synchrony may be associated with a reduction in the number of units held in working memory and may be directly related to attentional capacity. Increased changes in ensemble formation, where features are bound to different neuronal groups, may imply increased attentional shifting of perceptual grouping.

4. Reduced contrast by low DA activation levels

Another mechanism of action of changed dopamine concentrations is the effect on inhibition. It seems that DA receptor activation raises the
firing rate of inhibitory neurons by depolarization of the membrane, which we may model by lowering the firing threshold of the neuron.

We may look at a small network of three pyramidal cells A, B and C and two interneurons, which link A and B (cf. Fig. 5).

![Diagram of neuronal network](image)

**Figure 5.** Blocking of activation with different DA levels: raising the threshold (t) on interneurons

Both A and B receive positive input from C. The connection C-B is stronger than C-A, i.e. B would be the stronger associated feature.

With a low dopamine level, the threshold on both i1 and i2 is high and B, which receives the stronger input will inhibit A.

With a higher dopamine level, thresholds on i1 and i2 may become lowered, in a differential way, i.e. i1 may receive a lower threshold than i2, and now A may inhibit B.

In general, lateral inhibition will be influenced by dopamine modulation of interneurons. When the dopamine level is high, the threshold on interneurons will be low, and thus there will be increased lateral inhibition, and reduced concurrent firing of different features. When the dopamine level is low, there will be less lateral inhibition and thus more concurrent activation of different features.

I.e., depending on the level of inhibition within the network, either the main feature will ”win” and suppress other features, or a number of features may become activated in parallel. Thus, a winner-take-all network, which may play a role in selective attention, may arise out of a parallel feature processing structure with high dopamine levels.

There are two points that can be illustrated here:

(a) As before, an individual reactivity of neurons to dopamine levels allows a form of plasticity, in this case, of differentially activating firing thresholds, that is complementary to synaptic plasticity and undergoes regulation by dopamine levels, i.e. it is state-dependent.
(b) Changing properties of interneurons may also change the properties of a network as such, i.e. it may convert a feedforward network into a winner-take-all network by increasing lateral inhibition between features.

5. Discussion

In section 4, we have shown that with heightened dopamine levels acting at the DA receptors of interneurons, there is more lateral inhibition (and possibly a shift from the activation of a strongly connected feature to a more weakly connected feature by individual differences in inhibitory activation).

In (Grunze et al., 1996) aberrant activity of local circuit inhibition in the CA1 region of hippocampus has been conjectured to be the source of increased lateral excitation and an inability to distinguish patterns, which might be a substrate for the loosened associations in schizophrenia (Nestor and O'Donnell, 1998), (Miller, 1989)). In that case, the mechanism involved NMDA-dependent long-term potentiation. In contrast to that, we propose a mechanism for increased/decreased lateral inhibition in prefrontal cortex that is state-dependent and regulated by dopamine availability. This might also explain the action of D2-antagonists in restoring focussed association: blocking D2 receptors may increase DA availability at D1 receptors in prefrontal cortex.

The action of D1 receptors at excitatory neurons has been explored in a separate model (section 2.3) and we have looked at the influence of changed temporal properties, i.e. different adaptation periods, on synchronization and ensemble formation. The action of catecholamines, noradrenaline and dopamine, on width of attentional capacity, or working memory span has been documented e.g. by (Mehta et al., 2000)). This involves both digit memory span and spatial memory, i.e. it is independent of material.

We have related attentional capacity to the capacity of individual neurons to form ensembles of synchronized activity. We have conjectured two basic mechanisms to coexist: (a) increased D1 receptor stimulation shortens adaptation periods and (b) increased DA availability will increase the individual differences between neurons according to their sensitivity or receptor density. However, we have only looked at input synchrony, i.e. synchronous firing of neurons due to common input, and have disregarded the effects of the local inhibitory network and the excitatory connections between neurons. With respect to input synchrony, there will be a regimen of more asynchronous firing with higher DA levels together with a higher frequency of firing. The stability
of neurons firing in groups will be less - a change in DA availability may split ensembles into more groups of neurons with similar adaptation periods, however, that number may be restricted by the shortening of adaptation periods throughout.

Working memory span is increased by heightened DA availability especially for individuals with low baseline capacity (Mehta et al., 2000)). This may indicate that the capacity for forming separate ensembles, which fire synchronously, but which do not overlap, is heightened with increased DA levels, if receptor occupancy is low before drug administration.

Physiological fluctuations of dopamine release occur in response to emotional evaluation of perceptual states. There must be an adaptive advantage in being able to modulate certain neuronal circuits by dopamine availability and this advantage must rely on a change in the functional characteristics of these neuronal circuits.

We have suggested two cases where changing some of the basic parameters of single neurons by dopamine modulation influences the functional properties of neural circuits. One case involves the degree of lateral inhibition with applications to the processing of patterns and associations, the other case involves ensemble formation with applications to working memory span and attentional capacity. We have also applied these ideas to a model of word sense disambiguation (Scheler and Fellous, 2000)), which shows the combined effects of inhibitory and excitatory modulation for a specific cognitive task.

References


