Persistent activity and the single-cell frequency–current curve in a cortical network model

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Abstract. Neurophysiological experiments indicate that working memory of an object is maintained by the persistent activity of cells in the prefrontal cortex and infero-temporal cortex of the monkey. This paper considers a cortical network model in which this persistent activity appears due to recurrent synaptic interactions. The conditions under which the magnitude of spontaneous and persistent activity are close to one another (as is found empirically) are investigated using a simplified mean-field description in which firing rates in these states are given by the intersections of a straight line with the f–I curve of a single pyramidal cell. The present analysis relates a network phenomenon—persistent activity in a ‘working memory’ state—to single-cell data which are accessible to experiment. It predicts that, in networks of the cerebral cortex in which persistent activity phenomena are observed, average synaptic inputs in both spontaneous and persistent activity should bring the cells close to firing threshold. Cells should be slightly sub-threshold in spontaneous activity, and slightly supra-threshold in persistent activity. The results are shown to be robust to the inclusion of inhomogeneities that produce wide distributions of firing rates, in both spontaneous and working memory states.

Neurophysiological studies of neuronal correlates of working (short-term) memory show that the maintenance of a visual stimulus in working memory is accompanied, in inferotemporal (IT) cortex as well as in prefrontal (PF) cortex, by persistent (enhanced relative to spontaneous activity) activity in a selective subset of neurons (see e.g. Miyashita 1993, Goldman-Rakic 1995, Fuster 1995). The persistent, or ‘memory activity’, of such cells is often not much higher than the spontaneous activity. The ratio between the two rates is typically between 2.5 and 5 (Nakamura and Kubota 1995), though there is a lot of variability in the absolute values of both spontaneous and persistent activity between areas and between neurons in the same area (Nakamura and Kubota 1995).

A long-standing hypothesis has been that persistent activity is a collective property of a network, and that it is maintained by recurrent excitatory feedback (e.g. Hopfield 1982). This idea has been supported by earlier studies of models of networks of spiking neurons (see e.g. Amit et al 1990, Gerstner and van Hemmen 1992a, Zipser et al 1993). However, these studies ignored both the issue of spontaneous activity and the problem of low persistent rates. The issue of the coexistence between spontaneous and memory activity has been considered recently analytically in a network of integrate-and-fire neurons (Amit and Brunel 1997b). This model introduced a framework in which the spontaneous and memory activities could be related to the anatomical and physiological properties of a module of interconnected

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neurons, but left some questions unanswered: (i) which parameters control the magnitude of memory activity? In particular, how close can memory and spontaneous activity be in such models? (ii) Are the network parameters which produce physiological persistent and spontaneous rates plausible themselves, given the present knowledge about cortical physiology and anatomy? (iii) Are working memory states with physiological rates stable with respect to synchronized oscillations that can easily occur in such systems? Furthermore, since, in these models, persistent activity appears due to a network phenomenon, it has been difficult to put forward predictions that could be tested in experiments. One of the main goals of this paper is to understand how spontaneous and persistent activity are related to single-cell properties, and in particular how single-cell data, which are more easily accessible, can allow one to predict the magnitude of persistent activity. These issues are considered in a cortical network model.

The cortical network model

The cortical module

The model is as described by Amit and Brunel (1997a, b), except when stated otherwise. The network is composed of a large number of cells, \( N_E \) pyramidal cells (80%) and \( N_I \) interneurons (20%) (Braitenberg and Schütz 1991, Abeles 1991). It is assumed to represent a ‘cortical module’ of an area receiving information about the identity of objects, i.e. IT cortex or ventral PF cortex. In the absence of detailed information about synaptic connectivity in these areas, two connectivity scenarios have been studied. In the first scenario (fixed random connectivity), the synaptic structure is random but fixed. Each neuron receives \( C_E = c N_E \) randomly chosen excitatory synaptic contacts from pyramidal cells and \( C_I = c N_I \) randomly chosen inhibitory contacts from interneurons, where the connection probability \( c \) is low (typically 10%). In the second scenario (fluctuating random connectivity), the synaptic structure fluctuates in time. The network is potentially fully connected, but each emitted spike reaches a postsynaptic neuron with probability \( c \). Again, the transmission probability \( c \) is chosen to be low. In both cases, neurons also receive \( C_E \) excitatory connections from outside the network. These connections send to the network all the information (stimuli) received from the outside world, as well as background noise due to spontaneous activity outside the module, that arrive at a rate \( \nu_{\text{ext}} \) at each external synapse.

Neurons

Pyramidal cells and interneurons are described by leaky integrate-and-fire neurons (see e.g. Tuckwell 1988), and are characterized by the following: a firing threshold \( \theta = 20 \) mV above resting potential; a reset potential \( V_r = 10 \) mV above resting potential; a membrane capacitance \( C_{\text{mE}} = 0.5 \) nF for pyramidal cells, \( C_{\text{mI}} = 0.2 \) nF for interneurons; a membrane leak conductance \( g_{\text{mE}} = 25 \) nS for pyramidal cells, \( g_{\text{mI}} = 20 \) nS for interneurons; the corresponding membrane integration time constant is \( \tau_E = C_{\text{mE}}/g_{\text{mE}} = 20 \) ms for excitatory cells, and \( \tau_I = C_{\text{mI}}/g_{\text{mI}} = 10 \) ms for interneurons; a refractory period \( \tau_{\text{rp}} = 4 \) ms (McCormick et al 1985). Below threshold, the membrane potential \( V \) of a cell relative to its resting potential obeys the equation \( C_{\text{mE,ml}} \dot{V}(t) = -g_{\text{mE,ml}} V(t) + I(t) \) where \( I(t) \) represents the total synaptic current flowing into the cell, and subscripts E and I are used for excitatory and inhibitory cells, respectively.
Persistent activity

Synapses

There are four families of synapses: excitatory (glutamatergic) on pyramidal cells; inhibitory (GABAergic) on pyramidal cells; excitatory on interneurons and inhibitory on interneurons. When a spike is emitted by a neuron at time \( t \), the effect on the postsynaptic side is a jump at time \( t + \delta \), where \( \delta \) is a transmission delay, of the postsynaptic current \( I(t) \) by an amount \( C_{ma} J_{ab} / \tau_a' \), where \( J_{ab} \) corresponds to the postsynaptic potential (PSP) amplitude for a synapse connecting a \( b \) neuron to an \( a \) neuron \((a, b = E, I)\), and \( \tau_a' \) is the decay time constant of synaptic currents on excitatory \((a = E)\) or inhibitory \((a = I)\) neurons. The postsynaptic current then decays exponentially with a time constant \( \tau_a' \). The corresponding PSP is a difference of exponentials, with a rise time equal to the synaptic decay time constant \( \tau_a' \), and decay time equal to the membrane time constant \( \tau_a \). Typically, the transmission delay \( \delta \) is uniformly distributed between 0 and 4 ms, \( \tau_E' = 4 \) and \( \tau_I' = 2 \) ms. Note that for simplicity, and to allow a detailed analytical study, time constants of excitatory and inhibitory synapses on the same neuron are chosen to be equal. On the other hand, synapses on interneurons are taken to have a smaller time constant (see Destexhe et al 1998 and references therein).

The values of the PSP amplitudes \( J_{ab} \) are determined by the mean-field analysis, using the requirement of a stable asynchronous spontaneous activity state at desired firing rates, \( \nu_E \) and \( \nu_I \). The obtained EPSP amplitudes are in the range of experimentally reported values, i.e. between 0.05 and 0.5 mV (see e.g. Mason et al 1991). IPSPs are chosen stronger than EPSPs to maintain the network at low activity levels.

External stimuli

There are \( p \) external stimuli, representing \( p \) distinct pictures shown to a monkey on a video monitor in a delayed response task. Each of them activates a distinct sub-population composed of \( f N_E \) excitatory cells, with \( fp < 1 \). Thus external stimuli define \( p \) functional excitatory populations of \( fN \) neurons, each labelled by the external stimulus that activates it, and one population of \((1 - fp)N \) neurons, which do not respond to any of the stimuli. This classification of cells according to their selectivity properties corresponds to the phenomenology of neurophysiological data during delayed response tasks in IT or PF cortex of the monkey. In these experiments, cells that are visually responsive at least one of the shown pictures can be classified according to their ‘best stimulus’. Cells that do not show any significant activation for any of the shown pictures can be classified in the ‘non-selective’ group. In the following we use \( p = 5, f = 0.1 \).

Structure of recurrent pyramidal to pyramidal cell connections

Excitatory to excitatory synapses are assumed to have been subject to Hebbian modifications during a training period. During the training period, when a stimulus is shown, two neurons which are visually responsive see their connections increase, by a long-term potentiation mechanism. Connections from non-responsive to visually responsive cells decrease, by a long-term depression mechanism. After stimuli are shown repetitively, the efficacy of synapses connecting two cells belonging to the same selective population becomes \( g_+ J_{EE} \) where \( g_+ > 1 \) is an adimensional parameter equal to the relative strength of potentiated synapses with respect to the baseline. \( g_+ \) measures the strength of synaptic potentiation. The efficacy of synapses connecting two cells belonging to two different selective populations, and of synapses connecting a non-selective cell to a selective one, becomes \( g_- J_{EE} \), where \( g_- < 1 \) measures the strength of synaptic depression. The
Figure 1. The cortical network model. The model is composed of excitatory (E cell) and inhibitory (I cell) neurons, both receiving synaptic inputs from other areas. The excitatory neurons are divided into \( p \) selective populations, labelled by the stimulus that activates them (e.g. population 1 is activated when object 1 is shown to the network), and one non-selective population (neurons activated by none of the stimuli). The relative strength of the connections between populations is represented by the relative thickness of the corresponding arrows. Strong inhibitory synapses stabilize a stable low spontaneous activity. Strong excitatory connections inside selective populations stabilize ‘working memory states’, in which only one of the selective populations (the one activated previously by a stimulus) remain active at rates higher than spontaneous activity. For clarity, some connections between selective populations and some connections between selective and non-selective populations have been omitted. Populations 2,...,\( p \) have the same pattern of connectivity as population 1. See the text for more details.

‘depression factor’ \( g_− \) is chosen such that \( g_− = 1 - f g_+/(1 - f) \), which ensures that the average synaptic efficacy is not changed by the learning process. Other connections remain unchanged at \( J_{EE} \). The resulting structure of the cortical network is illustrated in figure 1.

Analysis

The model is studied using both numerical simulations and analytical techniques. The analysis allows us to calculate the firing frequencies of each of the populations in stationary (asynchronous) states of the network, as a function of the system parameters (Amit and Brunel 1997b). The situation of interest here corresponds to the ‘delay period’ following the presentation of a stimulus that has been previously shown repetitively to the network during the training period. In this situation there are four functionally different populations of cells: cells belonging to the population that is activated by the shown stimulus (this population is denoted by act); cells belonging to populations which are activated by other stimuli (population +); excitatory cells which are activated by none of the stimuli (population 0) and interneurons (population I). Again, this classification into four populations corresponds to the phenomenology of delayed response tasks in monkeys. Indeed, in such tasks, a recorded pyramidal cell can fall in one of three categories: either its ‘best stimulus’ is the shown stimulus (population act); its ‘best stimulus’ is a different stimulus (population +) or the cell has no ‘best stimulus’ (population 0).
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Figure 2. Mean-field parameters $\mu$ and $\sigma$. The curve represents the fluctuations of the membrane potential of a cell receiving a random bombardment of EPSPs and IPSPs. $\mu$ is the average depolarization, while $\sigma$ represent the magnitude of the fluctuations around the average due to the random arrival of spikes.

Mean-field techniques

The mean firing rates in each of the four populations are given by the following ‘mean-field’ equations:

\[
\begin{align*}
\nu_{\text{act}} &= \phi_E(\mu_{\text{act}}, \sigma_{\text{act}}), \\
\nu_+ &= \phi_E(\mu_+, \sigma_+), \\
\nu_0 &= \phi_E(\mu_0, \sigma_0), \\
\nu_I &= \phi_I(\mu_I, \sigma_I)
\end{align*}
\]

in which $\phi_{E,I}$ is the response function, or f–I curve, of excitatory (inhibitory) cells, which gives the firing rates as a function of two parameters, both expressed in mV.

- $\mu_{\text{act},+0,I}$ represents the average depolarization of the cell of the corresponding population in the absence of firing threshold, i.e. it would be the average depolarization of a cell whose spiking mechanism is blocked. It is linearly related to the average synaptic currents arriving at a cell of the corresponding population $\langle I(t) \rangle$ by $\langle I(t) \rangle = g_m \mu$ where $g_m$ is the membrane leak conductance of the cell.

- $\sigma_{\text{act},+0,I}$ represents the standard deviation of the fluctuations of the membrane potential of the cell, again in the absence of a firing threshold. It is related to the variance of the fluctuations of the synaptic current $\langle (\Delta I(t))^2 \rangle$ by the equation $\langle (\Delta I(t))^2 \rangle = g_m^2 \sigma^2 \tau / \tau'$, where $g_m$ is the membrane leak conductance, $\tau$ is the membrane time constant and $\tau'$ is the synaptic time constant of the cell.

We show in figure 2 an ‘intracellular’ trace of a simulated neuron. The figure illustrates the meaning of the parameters $\mu$ and $\sigma$. The parameters $\mu$ and $\sigma^2$ are in turn related linearly to
the firing rates $v_{\text{act}}$, $v_s$, $v_0$ and $v_1$ by the equations

$$
\begin{align*}
\mu_{\text{act}} &= C_E J_{EE} \tau_{EE} f g_+ v_{\text{act}} + (p - 1) f g_- v_+ + (1 - pf) g_- v_0 + v_{\text{ext}} \right) - C_I J_{EI} \tau_{EI} v_1 \\
\sigma_{\text{act}}^2 &= C_E J_{EE}^2 \tau_{EE}^2 f g_+^2 v_{\text{act}} + (p - 1) f g_-^2 v_+ + (1 - pf) g_-^2 v_0 + v_{\text{ext}} + C_I J_{EI}^2 \tau_{EI} v_1 \\
\mu_s &= C_E J_{EE} \tau_{EE} f g_+ v_{\text{act}} + f [g_+ + (p - 2) g_-] v_+ + (1 - pf) g_- v_0 + v_{\text{ext}} - C_I J_{EI} \tau_{EI} v_1 \\
\sigma_s^2 &= C_E J_{EE}^2 \tau_{EE}^2 f g_+^2 v_{\text{act}} + f [g_+ + (p - 2) g_-^2] v_+ + (1 - pf) g_-^2 v_0 + v_{\text{ext}} + C_I J_{EI}^2 \tau_{EI} v_1 \\
\mu_0 &= C_E J_{EE} \tau_{EE} f v_{\text{act}} + f (p - 1) v_+ + (1 - pf) v_0 + v_{\text{ext}} - C_I J_{EI} \tau_{EI} v_1 \\
\sigma_0^2 &= C_E J_{EE}^2 \tau_{EE}^2 f v_{\text{act}} + f (p - 1) v_+ + (1 - pf) v_0 + v_{\text{ext}} + C_I J_{EI}^2 \tau_{EI} v_1 \\
\mu_1 &= C_E J_{EE} \tau_{EE} f v_{\text{act}} + (p - 1) f v_+ + (1 - pf) v_0 + v_{\text{ext}} - C_I J_{EI} \tau_{EI} v_1 \\
\sigma_1^2 &= C_E J_{EE}^2 \tau_{EE}^2 f v_{\text{act}} + (p - 1) f v_+ + (1 - pf) v_0 + v_{\text{ext}} + C_I J_{EI}^2 \tau_{EI} v_1.
\end{align*}
$$

(2)

The f–I curve (response function) of the leaky integrate-and-fire neuron is, when $\tau_{EE} \ll \tau_{EI}$ (Ricciardi 1977, Brunel and Sergi 1998),

$$
\phi_{E;I}(\mu, \sigma) = \left( \frac{\tau_{EE} + \tau_{EI}}{\tau_{EI}} \int_0^{\hat{\theta}} \frac{\exp(\mu^2)\left[1 + \text{erf}(\mu)\right]}{\sqrt{\pi} \mu} \ d\mu \right)^{-1},
$$

$$
\hat{\theta} = \frac{\theta - \mu}{\sigma} \left(1 + 0.5 \frac{\tau_{EI}}{\tau_{EE}}\right) + 1.03 \left[ \frac{\tau_{EI}}{\tau_{EE}} - 0.5 \frac{\tau_{EI}}{\tau_{EE}} \right], \quad \hat{V}_r = \frac{V_r - \mu}{\sigma}
$$

(3)

where erf is the standard error function (see e.g. Abramowitz and Stegun 1970). It is important to note that the firing frequency does not depend only on the average inputs $\mu$, but also on their temporal fluctuations, measured by $\sigma$. The solutions to equations (1)–(3) for which $v_{\text{act}} = v_s$ correspond to a pure spontaneous activity state. In such a state, the network keeps no memory of the shown stimulus. Solutions for which $v_{\text{act}} > v_s$ correspond to ‘working memory’ activity, since the network activity remains correlated in the delay period with the shown stimulus.

**Simplified mean field**

The system of equations (1)–(3) is a system of four coupled nonlinear equations for the firing rates of the four populations. Though easily solvable with a computer, it is still fairly complex and it is difficult to identify clearly which parameters control the various properties of the network behaviour. To identify more easily such parameters, and to gain a more intuitive insight into the operation of the network, the mean-field equations (1)–(3) have been further analysed using several simplifications. The full mean-field equations are then solved numerically to check that relaxing these simplifications does not modify the conclusions of the simplified analysis. The simplifications are (i) the variance in the synaptic input to all cells of the network in a ‘working memory’ state are assumed to be equal to the corresponding variances in the spontaneous activity state, i.e. these variances are assumed not to vary with respect to changes of the firing rates from their spontaneous level (ii) the relative size, $f$, of the excitatory population that is visually responsive to a given stimulus is assumed to be very small, (iii) the number of stimuli $p$ is taken such that $pf \ll 1$ and (iv) the potentiation factor $g_+$ is assumed to be large and to scale as $1/f$. For matters of convenience we define $L = f C_E J_{EE} g_+$, $L$ represents the total synaptic efficacy impinging on a neuron from potentiated synapses. It corresponds to the amplitude of a population EPSP resulting from a synchronous spike of the whole selective population to which the neuron belongs. Note that $g_+$ is an adimensional parameter, being the ratio of a potentiated EPSP and a baseline EPSP, while $L$ is measured in mV.

The analysis is performed starting from $g_+ = g_- = 1$, corresponding to no structure in the excitatory to excitatory connectivity. Synaptic parameters are set such that the network has a stable asynchronous spontaneous activity state with low firing rates. This is done by
adjusting the connections to and from interneurons (Amit and Brunel 1997b), and checking that the resulting state is stable with respect to synchronized oscillations (Brunel and Hakim 1999, Brunel 2000). In such a state, all cells fire randomly at low rates, typically a few spikes per seconds. The firing rates in the spontaneous state are \( \nu_{E,sp} \) for pyramidal cells and \( \nu_{I,sp} \) for interneurons. The noisy synaptic currents giving rise to such a low and irregular firing have the following characteristics: they bring the membrane potential of the cells on average typically a few millivolts below threshold, while fluctuations of the membrane potential, that allow cells to fire, are typically of order a few millivolts. The parameters describing the synaptic inputs in the spontaneous state are \( \mu_{E,sp} \) and \( \sigma_{E,sp} \) for pyramidal cells and \( \mu_{I,sp} \) and \( \sigma_{I,sp} \) for interneurons. These parameters obey the equations

\[
\nu_{E,sp} = \phi_{E}[\mu_{E,sp}, \sigma_{E,sp}] \quad \text{and} \quad \nu_{I,sp} = \phi_{I}[\mu_{I,sp}, \sigma_{I,sp}].
\]

The aim of the analysis is then to study how the state reached by the network, in the delay period following the presentation of a learned stimulus, varies with \( g_+ \), which measures the structure of the feedback excitatory connections induced by learning. This is equivalent to studying how the solutions of equations (1)–(3) change when the parameter \( g_+ \) (or \( L \)) is varied. With the simplifications made above, the mean-field equations (1)–(3) have solutions for which all populations except the one activated by the stimulus remain at their spontaneous rates,

\[
\nu_+ = \nu_{E,sp}, \quad \nu_0 = \nu_{E,sp}, \quad \nu_I = \nu_{I,sp},
\]

while the population that was activated by the stimulus just before the delay period has its firing rate given by

\[
\nu_{\text{act}} = \phi_{E}[(\mu_{E,sp} + L\tau_{E}(\nu_{\text{act}} - \nu_{E,sp}), \sigma_{E,sp}].
\]

Equation (4) forms the basis of the simplified analysis which reveals the main properties of the network in a delay period, and its solutions will be discussed in detail in the results section.

**Simulation procedures**

The network has been simulated using the following protocol. (i) Network parameters are initialized using the mean-field equations. (ii) The simulation starts by a pre-stimulus interval of 1 s, during which the network receives no selective external stimulation. This pre-stimulus interval is used to estimate the spontaneous activity of the cells of the network. (iii) Stimulus presentation lasts 500 ms. It consists of increasing the frequency of spikes arriving at external synapses of cells selective to the shown stimulus, from \( \nu_{\text{ext}} \) to \( \nu_{\text{ext}}(1 + \lambda) \), where \( \lambda \) represents the ‘contrast’ of the stimulus, and is typically a few per cent. Other cells are unaffected. (iv) Last, during the delay period (varying from 1 to 4 s), the selective external inputs are removed. Delay period activity is estimated excluding the first 100 ms following stimulus presentation.

All parameters used in this study are summarized in table 1.

**Results**

*Spontaneous and working memory activity are given by the intersection of a straight line with the f–I curve of a pyramidal neuron*

The starting point of the analysis is a qualitative description of the f–I curve (sometimes called transfer or response function in modelling studies) of the integrate-and-fire neuron. The features of the f–I curve are crucial for understanding the solutions of the mean-field equations, and thus the collective properties of the network. The firing frequency is represented as a function of the mean synaptic input \( \mu \), for several values of the standard deviation of the synaptic input \( \sigma \), in figure 3. It shows two regimes: (1) for mean synaptic inputs \( \mu \) well
Table 1. Parameters of the network. (∗) \( J_{EE} \) and \( J_{IE} \) are chosen using mean-field equations (1)–(3), such that the spontaneous activity of excitatory cells and interneurons is at the desired level, between 2.5 and 5 spikes per second for pyramidal cells, and between 5 and 10 spikes per second for interneurons. The resulting EPSP amplitudes are in the indicated range, which is consistent with available experimental data (see e.g. Mason et al 1991).

<table>
<thead>
<tr>
<th>Network parameters</th>
<th>Typical value in simulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N_E ): number of pyramidal cells</td>
<td>16 000</td>
</tr>
<tr>
<td>( N_I ): number of interneurons</td>
<td>4000</td>
</tr>
<tr>
<td>( c ): connection probability between cells</td>
<td>0.1</td>
</tr>
<tr>
<td>( C_E ): number of recurrent e connections per cell</td>
<td>1600</td>
</tr>
<tr>
<td>( C_I ): number of recurrent i connections per cell</td>
<td>400</td>
</tr>
<tr>
<td>( C_E ): number of e connections from outside</td>
<td>1600</td>
</tr>
<tr>
<td>( \nu_{ext} ): spike rate at external synapse</td>
<td>5–10 s(^{-1})</td>
</tr>
<tr>
<td>Single cell parameters</td>
<td>Pyramidal cells</td>
</tr>
<tr>
<td>( \theta ): firing threshold</td>
<td>20 mV</td>
</tr>
<tr>
<td>( V_r ): post-spike reset potential</td>
<td>10 mV</td>
</tr>
<tr>
<td>( C_m ): membrane capacitance</td>
<td>0.5 nF</td>
</tr>
<tr>
<td>( g_m ): leak conductance</td>
<td>0.025 ( \mu )S</td>
</tr>
<tr>
<td>( \tau : ) membrane time constant</td>
<td>20 ms</td>
</tr>
<tr>
<td>( \tau_{rp}: ) absolute refractory period</td>
<td>4 ms</td>
</tr>
<tr>
<td>Synaptic parameters</td>
<td>Typical value</td>
</tr>
<tr>
<td>( \delta ): transmission delay</td>
<td>0–4 ms</td>
</tr>
<tr>
<td>( \tau_{EE}: ) decay time of synaptic currents on e cells</td>
<td>4 ms</td>
</tr>
<tr>
<td>( \tau_{EI}: ) decay time of synaptic currents on i cells</td>
<td>2 ms</td>
</tr>
<tr>
<td>( J_{EE} ): EPSP amplitude on pyramidal cells</td>
<td>0.05–0.25 mV (∗)</td>
</tr>
<tr>
<td>( J_{II} ): IPSP amplitude on pyramidal cells</td>
<td>3( J_{EE} )</td>
</tr>
<tr>
<td></td>
<td>1.8–2( J_{EE} )(*)</td>
</tr>
<tr>
<td>( J_{IE} ): EPSP amplitude on interneurons</td>
<td>3( J_{EE} )</td>
</tr>
<tr>
<td>( J_{II} ): IPSP amplitude on interneurons</td>
<td>3( J_{EE} )</td>
</tr>
<tr>
<td>Stimuli and structure of e to e synapses</td>
<td>Typical value</td>
</tr>
<tr>
<td>( p ): number of external stimuli (pictures)</td>
<td>5</td>
</tr>
<tr>
<td>( f ): fraction of pyr cells responding to a given stimulus</td>
<td>0.1</td>
</tr>
<tr>
<td>( g_e: ) relative strength of single potentiated synapses</td>
<td>1.5–2</td>
</tr>
<tr>
<td>( L: ) total synaptic strength from potentiated synapses</td>
<td>( f C_E J_{EE} g_s )</td>
</tr>
<tr>
<td>( g_{-}: ) relative strength of single depressed synapses</td>
<td>( 1 – f (g_{e} – 1)/(1 – f) )</td>
</tr>
<tr>
<td>( \lambda: ) 'contrast' of visual stimuli</td>
<td>0.0025–0.1</td>
</tr>
<tr>
<td>Mean-field parameters</td>
<td>Given by equation</td>
</tr>
<tr>
<td>( \nu_{act}: ) mean firing rates in given population</td>
<td>(1)</td>
</tr>
<tr>
<td>( \phi_{I, 1}: ) response function (f–I curve)</td>
<td>(3)</td>
</tr>
<tr>
<td>( \mu_{act}: ) mean synaptic inputs in given population</td>
<td>(2)</td>
</tr>
<tr>
<td>( \sigma_{act}: ) standard deviation of synaptic inputs</td>
<td>(2)</td>
</tr>
<tr>
<td>( \nu_{EE, sp}: \nu_{II, sp}: ) spontaneity of e, i cells</td>
<td>(2)</td>
</tr>
<tr>
<td>( \mu_{EE, sp}: \mu_{II, sp}: ) mean synaptic inputs in sp. activity</td>
<td>(2)</td>
</tr>
<tr>
<td>( \sigma_{EE, sp}: \sigma_{II, sp}: ) SD of synaptic inputs in sp. activity</td>
<td>(2)</td>
</tr>
<tr>
<td>( \nu_{onset}: ) delay activity of stimulus-selective cells</td>
<td>(4)</td>
</tr>
<tr>
<td>( \nu_{mem}: ) boundary of the basin of attraction of memory state</td>
<td>(4)</td>
</tr>
<tr>
<td>( \nu_{min}: ) minimal 'working memory' firing rate</td>
<td>(4)</td>
</tr>
</tbody>
</table>

below threshold, firing is driven by the fluctuations around the mean input. In this region \( \phi \) is convex. (2) For mean synaptic inputs well above threshold, the neuron is in a supra-threshold firing mode. Firing is essentially driven by the mean synaptic input \( \mu \), the firing frequency is relatively independent from the fluctuations and \( \phi \) is concave. These two firing behaviours are
The bonus of the simplification will be emphasized in the following. The firing rate of the activated population is given by equation (4) (see methods), i.e.

$$v_{act} = \phi_{E}(\mu_{act}, \sigma_{E,sp})$$

(5)

while other populations remain at spontaneous activity levels. The mean synaptic input to the activated population, $$\mu_{E,sp} + L \tau_{E} (v_{act} - v_{E,sp})$$, is the sum of a contribution due to spontaneous firing from both outside the network and other cells of the network $$\mu_{E,sp}$$, and of an excitatory selective feedback from other activated cells, given by the term $$L \tau_{E} (v_{act} - v_{E,sp})$$. This excitatory selective feedback is proportional to $$L$$, the total EPSP amplitudes of synapses from other activated cells, and to the selective signal $$v_{act} - v_{E,sp}$$, i.e. the difference between the activity of the activated population and spontaneous activity. Such a selective excitatory feedback does not influence other cells because activated cells represent only a small minority of all pyramidal cells, and synaptic long-term depression has been chosen to balance long-term potentiation.

The bonus of the simplified analysis (see ‘Methods’) is that we now have a single equation to solve, rather than a system of four coupled nonlinear equations. Furthermore, the solution(s) of equation (4) can be found by a graphical analysis. They are the intersections of the curve $$v_{act} = \phi_{E}(\mu_{act}, \sigma_{E,sp})$$, i.e. the f-I curve, and a straight line $$v_{act} = v_{E,sp} + (\mu_{act} - \mu_{E,sp})/(\tau_{E} L)$$ in the plane $$(v_{act}, \mu_{act})$$. This can be seen readily by defining $$\mu_{act} = \mu_{E,sp} + L \tau_{E} (v_{act} - v_{E,sp})$$ and rewriting the equation as $$v_{act} = v_{E,sp} + (\mu_{act} - \mu_{E,sp})/(\tau_{E} L)$$.

The left panel of figure 4 shows the intersections of the f-I curve with several straight lines $$v_{act} = v_{E,sp} + (\mu_{act} - \mu_{E,sp})/(\tau_{E} L)$$ corresponding to different values of $$L$$, the total synaptic

![Figure 3](image-url)
They all share the same point $v_{\text{act}} = v_{\text{E,sp}} + (\mu_{\text{act}} - \mu_{\text{E,sp}})/(\tau_f L)$, corresponding to $L = 8$ mV (high slope, short-dashed curve), 11 mV (intermediate slope, long-dashed curve) and 16 mV (low slope, dotted curve). Parameters: $\theta = 20$ mV, $V_i = 10$ mV, $v_{\text{E,sp}} = 2.6$ Hz, $\sigma_{\text{E,sp}} = 2$ mV, $\tau_f = 20$ ms, $\tau_\ell = 0$ ms. Intersections between the f-I curve and a straight line correspond to solutions of equation (5). When $L$ is low (high slope of the straight line), there is a single solution: the stable spontaneous activity $v_{\text{act}} = v_{\text{E,sp}}$. Increasing $L$ leads to a qualitative change: two additional solutions with activity higher than the spontaneous activity $v_{\text{E,sp}}$ appear. The solution with largest activity is stable. It corresponds to persistent, working memory, activity, denoted by $v_{\text{act}}$. The intermediate solution is unstable and corresponds to the boundary of the basin of attraction of working memory $v_*$. A further increase of $L$ increases working memory activity, and decreases the unstable fixed point, that merges with the spontaneous activity state. The evolution of the solutions with $L$ is shown in the bifurcation diagram on the right, which shows spontaneous activity (full horizontal curve, lowest branch), working memory activity (full curve, highest branch), and the unstable intermediate solution (dashed curve). Arrows illustrate the dynamics of the network after a stimulus was shown to the network: if, after stimulus presentation, $v_{\text{act}}$ is above $v_*$, the network goes to the ‘working memory’ state. If it is below, it returns to the ‘spontaneous activity’ state.

For low $L$, the slope is high, and the only solution to equation (4) is the ‘spontaneous’ solution $v_{\text{act}} = v_{\text{E,sp}}$. This means that, following any external stimulus, the network falls back to pure spontaneous activity during the delay period, with no cells showing persistent activity. The network is unable to perform as a working memory device.

Increasing synaptic potentiation, and thus $g_\text{e}$ and $L$, has the effect of decreasing the slope of the straight line to a value at which the line meets the transfer function at a new location. At this value the line is actually the tangent of the transfer function. In figure 4 this occurs when $L \approx 10.4$ mV. At this point the f–I curve is necessarily concave. This intersection, at $v_{\text{act}} = v_{\text{onset}}$, represents the onset of working memory. As $g_\text{e}$, and hence $L$, increases further, the solution of equations (4) splits, into two intersections. The higher one, denoted $v_{\text{act}}$, in the following, represents the memory activity and is stable. The intermediate one, denoted $v_\ell$, is unstable. It represents the boundary of the basins of attraction of memory and spontaneous activity. Thus, beyond the ‘critical’ or onset value of the strength of potentiated synapses, the network has two types of collective behaviour. After a stimulus is shown, it can either fall back...
Persistent activity

to the ‘spontaneous state’, corresponding to a failure of maintaining the stimulus in working memory, or go to a ‘working memory state’, in which the subset of activated cells sustain a persistent activity by virtue of their potentiated recurrent collaterals.

As the strength of the recurrent collaterals increases, working memory activity increases. This is due to the fact that the feedback inside the population which is selective for the shown stimulus becomes stronger, as the EPSP amplitude at single synapses between cells in that population grows. Figure 4 also shows that the intermediate, unstable, fixed point decreases as $L$ increases, until it meets the spontaneous solution. At this point the solution $v_{\text{act}} = v_{\text{E,sp}}$ becomes unstable. Beyond this point, a new solution with $v_{\text{act}} < v_{\text{E,sp}}$ appears. There is therefore a finite range of the synaptic potentiation parameter for which spontaneous activity at rate $v_{\text{E,sp}}$ and persistent activity coexist. For the parameters of figure 4 this range corresponds to $10.4 < L < 15.7 \text{ mV}$. In the right-hand panel of figure 4, the evolutions of both spontaneous and memory rates are plotted as functions of the ‘potentiation strength’ $L$. It shows the two bifurcations that occur as $L$ is varied: first, the memory state appears (through a saddle-node bifurcation); second, the state $v_{\text{act}} = v_{\text{E,sp}}$ becomes unstable (through a transcritical bifurcation).

Parameters controlling the magnitude of working memory activity

The next question is, which parameters control working memory activity, and the ratio between memory and spontaneous rates, besides the ‘potentiation strength’ $L$? The graphical analysis developed above helps to answer to this question, since it relates spontaneous and memory activity to the single-cell parameters that determine the $f$–$I$ curve. Four independent parameters might control the value of memory rates near the onset of working memory: the value of the post-spike reset potential $V_r$ relative to the firing threshold $\theta$; the membrane time constant $\tau_E$; the magnitude of the fluctuations of the synaptic inputs $\sigma_{\text{E,sp}}$ and the spontaneous rate $v_{\text{E,sp}}$. In figure 4, $V_r = 10 \text{ mV}$, $\tau_E = 20 \text{ ms}$, $\sigma_{\text{E,sp}} = 2 \text{ mV}$, $v_{\text{E,sp}} = 2.6 \text{ Hz}$ and the memory rate is $v_{\text{onset}} = 22 \text{ Hz}$. This value is in the range of experimentally reported values but the ratio $v_{\text{onset}}/v_{\text{E,sp}}$ is around ten, larger than experimentally reported ones.

The easiest way of manipulating the ratio $v_{\text{onset}}/v_{\text{E,sp}}$ turns out to be a variation of the spontaneous activity $v_{\text{E,sp}}$, by tuning accordingly the synaptic efficacies involving the population of interneurons. Increasing the spontaneous activity decreases the minimal memory activity, and these two effects concur to decrease the ratio $v_{\text{onset}}/v_{\text{E,sp}}$. The reason is that, as spontaneous activity increases, the corresponding intersection moves to the right, in the direction of the point where the curvature of the $f$–$I$ curve vanishes (the diamond in figure 3). On the other hand, the ‘working memory’ intersection at the bifurcation point (the point for which the straight line is tangent to the $f$–$I$ curve) moves to the left, again towards the point where the second derivative of the $f$–$I$ curve vanishes. Thus, the onset of working memory occurs at lower rates, $15 \text{ Hz}$ in the case illustrated in figure 5. Consequently, the ratio $v_{\text{onset}}/v_{\text{E,sp}}$ has decreased to two.

There is however a trade-off to the decrease in the ratio $v_{\text{onset}}/v_{\text{E,sp}}$: the width of the region in which spontaneous and memory activity coexist decreases. In the example of figure 5, memory activity appears at $L \sim 9.7 \text{ mV}$, but the spontaneous activity becomes unstable at $L \sim 10.2 \text{ mV}$. This is a price paid for bringing memory rates close to the spontaneous rates. Note that in the example in figure 5 the ratio between memory and spontaneous rates is between 2 and 3.5 in the entire range in which stable spontaneous and memory activity coexist.

The value of $v_{\text{E,sp}}$ can be increased up to the point at which the second derivative of the $f$–$I$ curve vanishes. At this point, the bifurcation leading to the appearance of memory activity and the one leading to the destabilization of spontaneous activity merge together. The onset
memory activity is equal to spontaneous activity, but the range of coexistence between the two states vanishes, since the spontaneous activity becomes unstable immediately after the appearance of working memory activity. Figure 5 shows that \( \nu_{\text{onset}} \) continuously decreases as \( \nu_{E,sp} \) increases, until they merge, but at this point the spontaneous activity becomes unstable. The constraint that working memory is necessarily in the concave region of the \( f-I \) curve leads to an absolute lower bound on its magnitude. This lower bound is the value of the firing rate at the point where the curvature of the \( f-I \) curve vanishes (represented by a \( \diamond \) in figure 3). The value of the minimal working memory rate also depends on the magnitude of the fluctuations in the synaptic input \( \sigma_{E,sp} \) and on the post-spike reset potential \( V_r \). The dependence on the fluctuation parameter \( \sigma_{E,sp} \) can be read from figure 3, since we know that the diamonds in that figure provide a lower bound for memory activity. For example, memory activity can be lowered by up to 8 Hz for \( \sigma_{E,sp} = 1 \) mV, 12 Hz for \( \sigma_{E,sp} = 2 \) mV and about 25 Hz if \( \sigma_{E,sp} = 5 \) mV. Thus, this lower bound increases as the fluctuations around the mean synaptic input (either external or due to recurrent collaterals) increase. The value of the reset potential \( V_r \) relative to the firing threshold \( \theta \) also has an effect on the minimal working memory activity. For \( \sigma_{E,sp} = 2 \) mV, \( V_r = 5 \) mV above resting potential leads to a minimal \( \nu_{\text{onset}} \) of about 10 Hz, while if the reset potential is closer to threshold, \( \nu_{\text{onset}} \) increases (e.g. for \( V_r = 15 \) mV, \( \nu_{\text{onset}} \) cannot be lower than 22 Hz).

**Basins of attraction of spontaneous and working memory states and transitions between states**

The basins of attraction of the spontaneous and working memory states are defined by the unstable intermediate fixed point \( \nu_* \) shown in figures 4 and 5. After a stimulus is shown to the network, two scenarios might occur. If the firing rate of cells activated by that stimulus is driven below \( \nu_* \) by the end of the presentation, the network will eventually return to the spontaneous activity state in the delay period following the stimulus presentation, indicating failure of maintenance of working memory. If the firing rate is driven above \( \nu_* \) during the

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**Figure 5.** Minimal memory activity decreases when spontaneous activity is increased. Left: bifurcation diagram when spontaneous activity is increased to \( \nu_{E,sp} = 7.5 \) Hz. Other parameters as in figure 4. Rates in spontaneous (full curve, lower branch) and memory activity (full curve, upper branch) versus synaptic potentiation parameter \( L \). The dashed curve indicates the unstable, intermediate solution. Right: minimal memory activity versus spontaneous activity: \( \nu_{\text{onset}} \) (dashed curve) as a function of \( \nu_{E,sp} \) (full curve). Other parameters are as in figure 4.
presentation of the stimulus, the network will go to the memory state corresponding to that stimulus. In other words, the activity of activated cells tends towards $v_{\text{w,m}}$. Both figures 4 and 5 show that, at the onset, the basin of attraction of the memory state is small, but it increases as the ‘potentiation strength’ $L$ is increased, at the expense of the basin of the spontaneous activity state. As $L$ is increased, the basin of attraction of the spontaneous activity state shrinks, until the second bifurcation occurs, at which the spontaneous activity state becomes unstable.

In networks of excitatory and inhibitory neurons of finite size, fluctuations of the global activity can be large (Amit and Brunel 1997b, Brunel and Hakim 1999). Thus, one might expect fluctuation-driven transitions between spontaneous and selective states to occur: the mean transition time from one state to another will be given by the interplay between the characteristics of the fluctuations and the size of the basin of attraction. Close to the bifurcation where working memory occurs, $v_*$ is close to $v_{\text{w,m}}$, indicating a small basin of attraction of working memory states. Therefore, these states can be expected to have short lifetime. The lifetime of working memory states increases as the basin of attraction increases. Then, close to the second bifurcation, $v_*$ becomes close to $v_{\text{E,sp}}$, and the spontaneous activity state is likely to destabilize towards one of the memory states. After this point, the only players left in the game are the working memory states. When working memory and spontaneous activity are very close to each other, both types of state have lifetimes of the order of seconds or less, resulting in erratic jumps between states.

**Full mean-field analysis and numerical simulations**

The results obtained with the simplified analysis have been confirmed both in the full mean-field analysis, i.e. by solving the full system of equations (1)–(3), and in numerical simulations of the system.

As an example, the results obtained with a network of 20 000 cells (16 000 excitatory and 4000 inhibitory), with connection probability 0.1, storing $p = 5$ patterns with a coding level $f = 0.1$ are shown in figures 6 and 7. Two synaptic parameter sets with different spontaneous activity levels have been chosen to make the point that working memory activity can reach lower levels when spontaneous activity is higher. In the first parameter set, spontaneous activity is 2.6 Hz for pyramidal cells and 5.2 Hz for interneurons. The bifurcation diagram obtained for such a cortical network module is shown in figure 6. Note the similarity with the diagram obtained using the simplified analysis, figure 4. The bifurcation at which working memory appears takes place around $g_* = 1.75$, for which memory activity is about 20 Hz. There is good agreement between simulations and the theory. Increasing spontaneous activity to $v_{\text{E,sp}} = 4$ Hz moves the bifurcation point to $g_* = 1.9$, for which the onset memory activity has decreased to about 15 Hz. In the simulations, the spontaneous activity is only stable up to $g_* = 1.95$. This is due to the fact that at this point its basin of attraction becomes very small, and fluctuations of the global network activity drive the network spontaneously to one of the memory states after a time of the order of one second.

The operation of the network before, during and after presentation of the stimulus in a typical simulation is illustrated in figure 7. Before presentation of the stimulus, the network is in its unstructured spontaneous activity state. Pyramidal cells fire at about 4 Hz and interneurons at about 8 Hz. During presentation of the stimulus, neurons selective to that stimulus experience a fast increase of their activity to about 50 Hz. In the delay period, they show persistent activity at about 17 Hz. The behaviour of other cells in the delay period is also instructive. Neurons selective for other stimuli fire at rates which are slightly lower than spontaneous (3 Hz), while other neurons (pyramidal as well as interneurons) slightly increase their rates.
Visual response versus delay activity

A striking phenomenon observed in figure 7 is that delay activity of cells activated by the stimulus is much lower than the ‘visual response’. This is due to the fact that the ‘contrast’ used in that simulation is relatively high (0.1). Figure 8 shows that the visual response of activated cells is effectively controlled by the contrast. Cells receiving selective external inputs with a low contrast have a visual response which is typically lower than their delay activity. Note that in the lower panel the contrast is very low (0.0025). It is the presence of spontaneous activity, that places cells very close to their firing threshold, that enables the network to detect such low-contrast stimuli, before maintaining them in active memory.

Inhomogeneous networks

The effect of inhomogeneities on network behaviour has been checked by analysing and simulating a network in which single-cell thresholds have a variability from neuron to neuron. The threshold of each cell is drawn randomly, and independently from cell to cell, from a Gaussian distribution $Pr(\theta)$ with mean 20 mV and standard deviation 1 mV. The effect of inhomogeneities on the collective behaviour has been investigated by both analysis and simulations. The mean-field equations (1) are easily generalized to describe networks with such inhomogeneities. Equations (1) have to be replaced by

$$\nu_{act} = \int Pr(\theta) \phi_E(\mu_{act}, \sigma_{act}), \quad \nu_s = \int Pr(\theta) \phi_E(\mu_s, \sigma_s),$$
Figure 7. Pre-stimulus (0–1000 ms), stimulus (1000–1500 ms) and delay activity (1500–2500 ms) in a simulation of a network of 20,000 cells (16,000 excitatory and 4,000 inhibitory), with \( g_+ = 1.9 \).

Other parameters correspond to the set \( \nu_E, \nu_I = 4 \text{ Hz} \) in figure 6. Top: raster file showing the firing times of (from top to bottom) ten interneurons (I), ten non-selective pyramidal cells (E0), 20 pyramidal cells which are selective for other stimuli (E+) and five pyramidal cells which are selective for the shown stimulus (Eact). The mean activity of each of these four populations in bins of 2 ms is shown below in separate graphs, together with the mean-field prediction (dashed curves).

\[
\nu_0 = \int \Pr(\theta) \phi_E(\mu_0, \sigma_0), \quad \nu_1 = \int \Pr(\theta) \phi_E(\mu_1, \sigma_1),
\]

where \( \Pr(\theta) \) is the distribution of thresholds, and the f–I curve \( \phi \) depends on \( \theta \) via equation (3). The distribution of firing rates in each population is given by

\[
\Pr_x(v) = \int \Pr(\theta) \delta(v - \phi_x(\mu_x, \sigma_x))
\]

where \( x \) is the population index.

The results of both analysis and simulations in the inhomogeneous case are illustrated in figure 9. It shows that the inhomogeneity affects only mildly the average firing rates obtained.
Figure 8. Visual response depends on the ‘contrast’ of visual stimuli, shown between $t = 500$ and 1500 ms. Top panel: 10% contrast. Bottom panel: 0.25% contrast.

Figure 9. Analysis and simulation of an inhomogeneous network. Left panel: spontaneous and working memory activity as a function of synaptic potentiation parameter $g_+$. Parameters as in figure 6, second set. Full curves represent spontaneous and persistent activity branches of the homogeneous network. Dashed curves indicate average spontaneous and persistent rates of the inhomogeneous network (thresholds randomly distributed with a Gaussian distribution with mean 20 and SD 1 mV). Right: the theoretical distributions of firing rates in spontaneous activity (full curve) and persistent activity (dashed curve), for $w_+ = 1.97$, are compared with simulation results (histograms).

in the homogeneous network. On the other hand, it produces wide distributions of firing rates in both spontaneous and persistent activity, as shown in the right-hand panel of figure 9.
Discussion

This paper demonstrates, using both simulations and analysis, that coexistence of spontaneous and working memory activity at physiological rates can be achieved in a cortical network model. The arguments presented here indicate that, to sustain working memory activity at rates close to spontaneous activity, both should be close to the frontier between sub- and supra-threshold firing modes. As memory and spontaneous rates become closer, the range of values of the synaptic potentiation factor for which both memory and spontaneous activity coexist becomes narrower. In the light of this result, one might speculate that experimentally observed ratios between persistent and spontaneous activity result from a compromise between the need to minimize the metabolic cost of maintaining working memory activity with a persistent firing mechanism, and robustness with respect to variation of synaptic parameters.

Qualitatively, these considerations apply for any f–I curve, provided it has the two aforementioned firing regimes: a sub-threshold regime in which the transfer function is convex, and a supra-threshold one in which the transfer function is concave. In areas expressing memory activity such as PF or IT cortex, persistent activity is not much higher than spontaneous activity. The present model predicts that the operating regime of neurons in these areas should be close to the frontier between the two regimes of the f–I curve. In spontaneous activity, cells would be in the sub-threshold mode, with mean inputs just below threshold. In persistent activity, cells would be in the supra-threshold mode, but with mean inputs bringing cells just above threshold. In the presence of noise, the hypothesis that the transfer function of real neurons has the properties described above seems reasonable. Quantitatively, the picture may change as more details are incorporated in the model neuron. In particular, the behaviour of the f–I curve near threshold is critical for quantitative predictions. Further studies are therefore needed to check that the picture obtained in this paper is valid in a network of more realistic model neurons.

Low persistent firing can be achieved in a network with only fast synapses, corresponding to AMPA-type synapses. This stands in contrast to the recent study of Wang (1999), which showed that slow synapses were necessary to sustain low persistent firing rates. The requirement of slow synapses in that study arises from stability of the asynchronous persistent state in the face of synchronized oscillations that arises when AMPA synapses have faster dynamics than GABA synapses. In our study, we chose for simplicity AMPA and GABA synapses to have identical time constants. Thus, it is likely that more detailed synaptic models yield additional constraints to the stability of the persistent state. In addition, rate control mechanisms such as those studied by Wang (1999) are likely to enlarge the parameter region where spontaneous activity and persistent activity at realistic rates coexist.

The magnitude of the memory activity has been related to the single-cell f–I curve using a graphical analysis. The analysis shows that both spontaneous and working memory activity correspond to intersections of a straight line with the f–I curve. The idea of obtaining graphically the firing rates in stationary states of the network is quite old (see e.g. Amit and Tsodyks 1991, Gerstner and van Hemmen 1992b, Wang 1999 for a recent application of this idea). However, previous studies investigated networks with no spontaneous activity, and bistability occurred between a silent state and a persistent state. In this paper, it is shown that using the magnitude of spontaneous activity and the ‘learning level’ to manipulate the position of a straight line, any level of persistent activity can be stabilized, provided it is in the region of the f–I curve that is concave. Thus, the lowest stable working memory activity that can be achieved in a network storing memories in recurrent collaterals is determined by the characteristics of the single-pyramidal-cell f–I curve. Measurements of f–I curves in areas where working memory activity is observed would thus provide a test of the hypothesis that
such an activity stems from recurrent feedback interactions.

Frequency–current curves are usually measured in slice preparations using constant input currents (see e.g. McCormick et al. 1985). The present analysis emphasizes the importance of using noisy rather than constant inputs, since the model predicts that spontaneous activity would be in the region where firing is due to fluctuations in the synaptic input. Such measurements could be made in vitro, injecting a current with an artificial source of noise to the cell, rather than constant currents. The ideal way to obtain the frequency–current curve however would be using intracellular recordings in vivo, in the same animal and in the same area in which the delayed response tasks are performed. The advantage would be of providing an f–I curve in which the noise is due to the synaptic environment of a spontaneously active network, rather than to an artificial source. Unfortunately, such an experiment would be difficult if not impracticable using current recording techniques.

The model discussed in this paper reproduces two landmarks of recordings in areas where persistent activity is observed: spontaneous activity, and selective persistent activity, both at physiological rates. These results are obtained with plausible anatomical and physiological parameters, and both kinds of state are stable with respect to synchronized oscillations. The analysis provided in this paper proposes further tests and predictions of the recurrent hypothesis, but it certainly does not rule out other mechanisms for maintenance of working memory, such as bistability at the single-cell level.

The model has other interesting properties that reproduce features observed in neurophysiological experiments. (i) Cells which experience persistent activity show a highly irregular firing. This irregularity is due to the fact that even in the persistent state, mean inputs to a cell are close to threshold, and therefore fluctuations have a strong influence on firing behaviour. (ii) Cells that are selective to stimuli other than the shown stimulus have lower firing rates in the delay period than in the spontaneous activity state, as do many cells in the temporal lobe (Nakamura and Kubota 1995). This is due to the fact that they receive depressed synapses from the subset of cells that have persistent activity, and inhibition has increased in order to control the activity of the network. (iii) Cells that are not selective to any of the stimuli typically have slightly enhanced rates in the delay period. Cells with non-selective delay period activity are observed in many recordings from IT cortex and PF cortex (see e.g. Funahashi et al. 1989, Fuster 1990). (iv) Cells active in the delay period have a visual response which can be either lower or higher than delay activity, depending on the ‘contrast’ of the stimulus. Both types of cell are observed in both IT cortex (Fuster 1990) and PF cortex Funahashi et al. (1989).

In the model described in this paper, interneurons have no selective delay activity. There have been reports of tuned delay activity in interneurons during spatial working memory tasks (Rao et al. 1999). However, no such selectivity seem to have been reported in working memory tasks involving object identity. Additional modelling studies are needed to investigate the possible roles of interneuron selectivity in working memory networks.

The model described here concerns object memory and as such could apply to IT cortex (Miyashita 1993) as well as ventral areas of PF cortex (Wilson et al. 1993). The range of spontaneous and working memory firing rates exhibited by the model is compatible with experimental data in both areas, though often cells in IT cortex show persistent rates below 8 Hz, that would be hard to account for with the present model unless the excitatory membrane time constant is increased. An alternative is that persistent activity in IT cortex is the result of back-projections from PF cortex (Miller et al. 1996). Another possibility is that more realistic models of synaptic transmission, in particular of NMDA channels, or including synaptic depression, introduce rate control mechanisms enabling one to stabilize lower working memory rates (Wang 1999). Last, it would be interesting to investigate whether these findings are also applicable to network models of spatial working memory (Camperi and Wang 1998, Compte et al. 2000),
or to parametric working memory (Romo et al. 1999).

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