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The emergence of long-lasting transients of activity in simple neural networks

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Abstract. The question was investigated whether long-lasting transients of activity, observed to occur in the intact cerebral cortex (EEG slow (δ) waves and 'K' complexes) as well as in isolated tissues cultured in vitro, can also emerge in a model network of excitatory and inhibitory cells. We show that such transients can indeed occur even if the cells do not have built-in slow kinetics. For certain parameter settings, the network is in a bistable state in which periods of increased activity (long-lasting transients) alternate with minimal activity. Transients are triggered by spontaneously firing cells ('noise'), which, rather than via a build-up of recurrent synaptic inhibition, also initiate their termination. During a transient, the network continually makes transitions from one equilibrium to another as a result of spontaneous firing until it is switched back to the quiescent state, i.e., after a variable period of time of noise-induced transitions the transient is terminated. If the network is small, activity can terminate even without inhibition. In large networks, inhibition keeps the network sensitive to spontaneously firing cells by holding it in the neighbourhood of a critical point between active and quiescent state.

1 Introduction

Bioelectric activity in neural networks depends on both single neuron properties and network organization. Dissociated cerebral cortex cells in vitro, which gradually organize themselves into a synaptically connected network when brought into culture (Van Huizen 1986; Habets et al. 1987; Ramakers et al. 1990), are eminently suitable for studying these dependencies experimentally. These studies have revealed correlations between the developmental stage of the network and single neuron firing patterns. Action potentials in such tissue cultures are often accompanied by field potentials (Crain 1976), which are built up by synchronous activation in a population of neurons. A striking form of field potentials already at early stages of development are long-lasting transients of activity (slow waves) lasting several hundreds of milliseconds. They show a considerable variety of waveforms with respect to polarities, durations and sequences of accompanying action potentials, among various cultures as well as within a given culture (Corner and Crain 1972; Crain 1976). Slow-wave phenomena occur in a wide range of biological neural networks, from dissociated reaggregated spinal cord cells (Crain 1976) to the intact cerebral cortex (EEG δ-waves (Mirmiran and Corner 1982; Ball et al. 1977) and 'K' complexes (Roth et al. 1956)).

Since such slow waves can last as long as several hundred milliseconds, their duration cannot be derived from the classical IPSP (unitary inhibitory input) duration of ca. 100 ms and EPSP (unitary excitatory input) duration of ca. 25 ms, as can be done for EEG fluctuations in the alpha frequency range (Lopes da Silva et al. 1974). Therefore, the question arises whether slow waves basically emerge from interactions in a network of neurons, or are a direct consequence of intrinsic membrane kinetics of single neurons (Steriade et al. 1990). Ion channels with slow kinetics (e.g. a long-lasting (200–500 ms) calcium-mediated potassium conductance (Connors et al. 1982)) may be candidates for such intrinsic kinetics. The possible role of network interactions in generating slow waves will be addressed in this article by means of a simulation model. In particular, it is studied whether a neural network model deliberately devoid of long-lasting membrane processes, is still capable of generating long-lasting transients of population activity.

The model is described in Sect. 2. In Sect. 3 it is shown that the network indeed generates long-lasting transients. Next, the conditions under which they were found to occur are discussed. A qualitative explanation of their emergence is given in Sect. 4, using simplified

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models. Finally, the robustness of the results and similarities with experimentally observed slow waves are discussed.

2 The model

Considering that an assembly of even simple neurons is capable of generating complex behaviour, we have looked for long-lasting transients in a relatively simple distributed model. The model is similar to those found in Harth et al. 1970; Anninos et al. 1970; Anninos 1972; and Clark et al. 1985, with to a large extent deterministic neurons, synchronous dynamics, all-or-none character of the action potential, and an absolute refractory period. Differences include the presence of a relative refractory period, modelling of the membrane potential, and the presence of separate (fast) IPSPs and EPSPs.

2.1 The network

The network is composed of inhibitory (i) and excitatory (e) cells placed at the grid points of a two-dimensional grid, the boundaries of which are connected to each other (torus). The parameters are: *(1)* the total number of cells; *(2)* the fraction of e- and i-cells, which are randomly placed at the grid points; *(3)* strength, length and number of outgoing connections per cell, which may be defined differently according to the type of connection ($e \to e$, $e \to i$, $i \to e$ or $i \to i$). Connection strength is expressed in terms of a conductance change at the postsynaptic membrane (see neuron model). Given the distribution of e- and i-cells, the target cells for the outgoing connections are randomly chosen with equal probability within a circular field, of which the minimum and maximum radius length (range) can be given. Note that a given cell pair can be connected by more than one connection.

2.2 The neuron

The neuron model is based on an electric circuit model (Fig. 1) of the cell membrane (Finkelstein and Mauro 1977). If the capacitance is ignored, the membrane potential is given by

$$V_m = (E_r + S_e \cdot E_e + S_i \cdot E_i)/(1 + S_e + S_i) \quad (1)$$

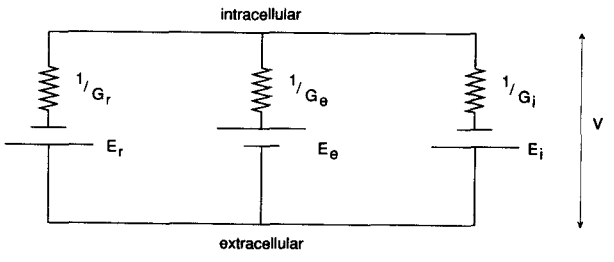

Fig. 1. Electric circuit model of the neuron membrane. E_r is the resting potential; E_e and E_i are the driving potentials of the e- and i-synapses, respectively; G_r is the resting conductance, G_e and G_i are the conductance changes for e- and i-input, respectively; V is the membrane potential

where $S_e = G_e/G_r$ and $S_i = G_i/G_r$ indicate the strengths of the synaptic inputs expressed as ratios of the synaptic conductance to the resting conductance. G_r together with the driving potential E_r generate the resting potential; S_e represents the summed e-input, with E_e as driving potential; S_i represents the summed i-input, with E_i as driving potential. From (1) it can be seen that V_m approaches E_e asymptotically as S_e increases. E_e is the saturation potential of the depolarized state. In analogy, V_m approaches E_i, the saturation potential of the hyperpolarized state, asymptotically as S_i increases. In the simulations we took $E_r = -73$ mV, $E_e = 0$ mV (Na^+ equilibrium potential) and $E_i = -83$ mV (K^+ equilibrium potential), but the results will appear not to be dependent upon the actual choice of these values. Values typical of a particular type of cell might be chosen (e.g., cortical cells: $E_r = -60$ mV, $E_e = 0$ mV and $E_i = -65$ mV (Cl^- equilibrium potential)). Hereafter, all potentials will be expressed relative to the resting potential:

$$V = (S_e \cdot M_e + S_i \cdot M_i)/(1 + S_e + S_i) \quad (2)$$

where $M_e = E_e - E_r$, and $M_i = E_i - E_r$. Equation (2) is used to calculate the instantaneous membrane potential, whereby S_e and S_i are taken to decay according to the time course of EPSP and IPSP, respectively. We take

$$S_e(t+1) = D_e \cdot S_e(t) + I_e(t) \quad (0 < D_e < 1) \quad (3)$$

$$S_i(t+1) = D_i \cdot S_i(t) + I_i(t) \quad (0 < D_i < 1) \quad (4)$$

where D_e and D_i are decay constants; $I_e(t)$ is the summed e-input at time t, and $I_i(t)$ is the summed i-input at time t, with time partitioned into discrete intervals.

The action potential generation is reduced to a threshold rule, with a state variable denoting whether a cell is firing or not. If V exceeds the firing threshold (θ), the cell fires. After firing, θ is put up to M_e for two time intervals (absolute refractory period, see Table 1) and then decreases in two time intervals (relative refractory period) to the default value. Cells are allowed to accumulate input during their refractory period. When not absolutely refractory, each e-cell also has a low probability of firing independent of its membrane potential (this firing will be referred to as spontaneous firing). In this way, the influence of noise sources independent of the network is simulated. Spontaneous firing is random both in time and space, and is initiated by putting V just above θ.

In cortical pyramidal cells, the absolute refractory period lasts 1–2 ms (Abeles 1982, 1991), so each time interval in the model corresponds to about 1 ms. The values of D_e and D_i are such that an IPSP lasts about 35 time intervals (2.5% of original input left) and an EPSP about 10 time intervals.

At each time interval, the state (firing or non-firing) and the membrane potential of all the cells are synchronously updated using the e- and i-inputs from all the firing neurons.

Table 1. Neuron and network parameters used in most of the simulations. Potentials are in mV and relative to the resting potential, the spontaneous firing probability is per time interval, connection ranges are in grid units, and connection strengths are expressed as ratios (S) of the synaptic conductance to the resting conductance

M_e	73	saturation potential depolarized state
M_i	−10	saturation potential hyperpolarized state
θ_0	13	default firing threshold
θ_1	73	threshold one time interval after firing
θ_2	73	threshold two time intervals after firing
θ_3	53	threshold three time intervals after firing
θ_4	33	threshold four time intervals after firing
D_e	0.7	decay constant excitatory input
D_i	0.9	decay constant inhibitory input
sponfire	0.0035	spontaneous firing probability of e-cell
inhpop	0.2	fraction of inhibitory cells
s_x	20	number of cells in x-direction
s_y	20	number of cells in y-direction
n_{ee}	5	number of outgoing $e \rightarrow e$ connections per e-cell
cl_{ee}(min)	1	minimum $e \rightarrow e$ connection length
cl_{ee}(max)	10	maximum $e \rightarrow e$ connection length
w_{ee}	0.15	$e \rightarrow e$ connection strength
n_{ei}	5	number of outgoing $e \rightarrow i$ connections per e-cell
cl_{ei}(min)	1	minimum $e \rightarrow i$ connection length
cl_{ei}(max)	29	maximum $e \rightarrow i$ connection length
w_{ei}	0.05	$e \rightarrow i$ connection strength
n_{ie}	50	number of outgoing $i \rightarrow e$ connections per i-cell
cl_{ie}(min)	1	minimum $i \rightarrow e$ connection length
cl_{ie}(max)	29	maximum $i \rightarrow e$ connection length
w_{ie}	0.014	$i \rightarrow e$ connection strength

3 Results

3.1 Long-lasting transients

In the randomly generated networks (parameter settings of Table 1) transients of activity with a duration on the order of seconds were indeed found to occur. In these networks, there are no $i \rightarrow i$ connections. Of all the cells, 20% are inhibitory. The $i \rightarrow e$ and $e \rightarrow i$ connections extend over the whole network. The $e \rightarrow e$ connections are shorter: 'short range excitation'. The $i \rightarrow e$ connections are numerous and weak, so that inhibition is diffusely spread over the network. The w_{ee} is such that for an e-cell at least 2 simultaneous EPSPs are needed to bring the membrane potential above the firing threshold. At least 5 simultaneous EPSPs ($e \rightarrow i$) are needed for an i-cell.

An example of a series of transients is shown in Fig. 2a. The network is in a bistable state in which periods of increased network activity alternate with periods of minimal activity consisting of spontaneous firing and local responses. The network is near a critical point between the active and quiescent state. A transient is triggered if spontaneous firing occurs in a critical number of cells within a critical period of time. Activity then spreads rapidly throughout the network, as w_{ee} and w_{ei} are strong. Because w_{ei} is strong, the onset of the i-population follows almost immediately that of the e-population. The i-cells are permanently depolarized and fire constantly at a high rate, thereby providing negative feedback to the e-population. There exists a short cycle in the activity pattern within a transient, the exact form of which switches from time to time during the course of a transient (Fig. 3a). The length of this cycle reflects the duration of the refractory period. During a transient, on average around 10% of the e-cells and 25% of the i-cells are firing. At a certain time, the e-population is no longer capable of maintaining its activity and dies out, almost immediately followed by the cessation of activity in the i-population. The network now becomes largely silent except for spontaneous firing, which eventually triggers the next transient. The duration of these transients can clearly be much longer than that of an IPSP or EPSP. The duration varies greatly, both among different random network realizations and within a particular network. In four different random realizations (parameter settings of Table 1) except that *sponfire* = 0.005) the mean and variance of the duration of 10 consecutive transients are: (462, 534), (132, 109), (975, 480), and (1519, 936).

A wide range of firing patterns was found to accompany transients (Fig. 2b–e). There are cells firing only during restricted periods of each transient, cells that fail to fire with every transient, and cells that fire during the entirety of every transient. Variations among cells in terms of the number of receiving excitatory and inhibitory connections accounts for this wide range. An additional source of variation is the trigger zone of network activity, which may change from transient to transient, so that cells behave differently during different transients.

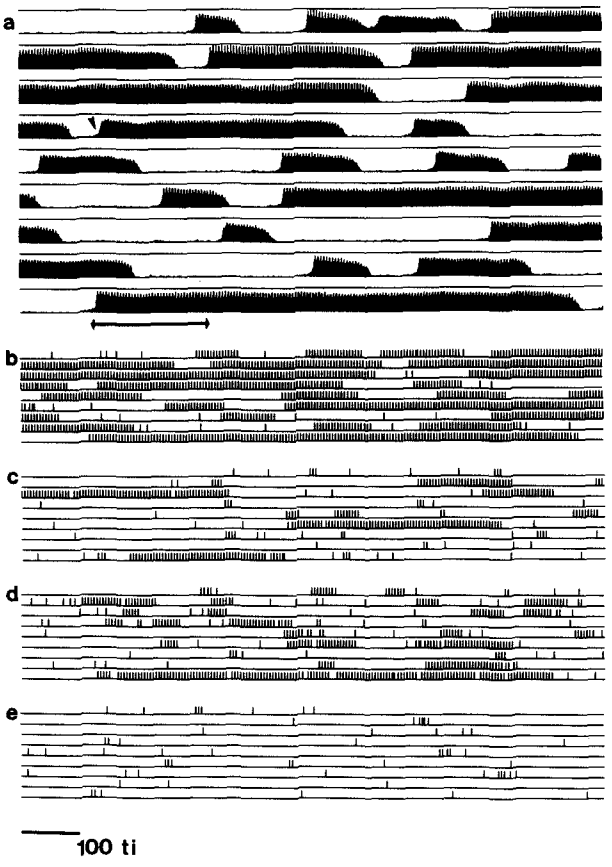

Fig. 2a–e. **a** Series of transients (parameter settings of Table 1). Total number of firing cells plotted against time. A complete episode of 9000 time intervals (ti) is shown, each trace representing 1000 time intervals. The top line of each trace denotes 25% of all cells. Indicated segment in **a** is expanded in Fig. 3a. For the explanation of the arrow in **a**, see Fig. 3c. **b–e** Spike trains of four different excitatory cells accompanying the transients. **b** A cell that fires during the entirety of each transient. **c** A cell firing massively only during some transients. **d** Firing is largely restricted to a few periods of each transient. **e** Sporadic firing

3.2 Parameter sensitivity

In this section, the effect of some parameter variations on the occurrence of long-lasting transients will be described.

Network size. This is not a critical parameter for long-lasting transients to occur, provided that the connection ranges are kept proportional to the network size.

Inhibition. The actual fraction of i-cells is not critical as long as n_{ei} and n_{ie} are adjusted so as to keep the number of incoming $e \rightarrow i$ and $i \rightarrow e$ connections per cell unaltered. An important result is that long-lasting transients can arise in small (up to about 25 cells), purely excitatory networks. If the network becomes bigger, the cells become so strongly depolarized that, once triggered, network activity is not likely to die out. This can be counteracted by decreasing the connection strength. However, this is only possible up to a certain point, below which the chance of triggering network activity becomes extremely small.

Connection range. It is not essential that the $e \rightarrow i$ and $i \rightarrow e$ connections extend over the whole network or that the $e \rightarrow e$ connection range be shorter than the other ranges, as in Table 1. However, if the $e \rightarrow e$ connection range becomes smaller ($cl_{ee}(\max) < 8$), long-lasting transients largely disappear.

Number of outgoing connections. Decreasing n_{ie} while keeping $n_{ie} \cdot w_{ie}$ as before yields longer lasting transients, within which large fluctuations of activity occur. It appears as though different transients blend into one another. Increasing n_{ei} while keeping $n_{ei} \cdot w_{ei}$ as before has no clear-cut effect on the duration of transients.

Connection strength. If w_{ie} or w_{ei} is decreased, c.q. w_{ee} increased, the network moves away from its critical point between active and quiescent state, and, once triggered, activity is not likely to terminate. Transients can be made to reappear, if w_{ie} is increased correspondingly. However, if w_{ei} is either too high or too low, there are no matching w_{ie}.

Saturation potentials. Changing the levels of the saturation potentials (M_e and M_i) does not affect the general outcome of the simulations, provided that the connection strengths are changed accordingly. For example, simulations with $M_e = 60$ and $M_i = -5$ (corresponding to $E_r = -60$ mV, $E_i = -65$ mV and $E_e = 0$ mV) give exactly similar results.

Decay times of excitatory and inhibitory input. Activity will not terminate if D_e is too large relative to the duration of the refractory period. If w_{ie} is increased so that transients reappear, long-lasting transients become rare, with durations mostly in the range from 150 to 250 time intervals. If D_i is made smaller (e.g., $D_i = 0.8$, $w_{ie} = 0.029$) we find long-lasting transients with large fluctuations in activity.

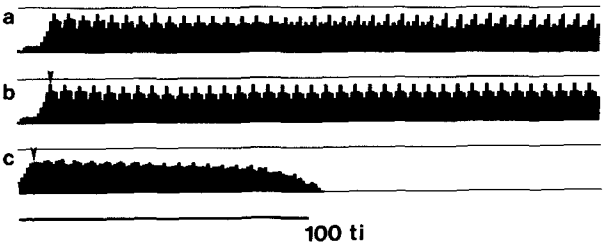

Fig. 3a–c. The effect of stopping spontaneous firing. Total number of firing cells plotted against time. A trace represents 200 time intervals (ti). The top line of a trace denotes 25% of all cells. **a** Expanded segment of the transient indicated in Fig. 2a. **b** Spontaneous firing is stopped (time interval indicated by arrow) in the transient of **a**. After cessation of spontaneous firing, a particular firing pattern is repeated indefinitely. **c** In another transient (See Fig. 2a, transient indicated by arrow), cessation of spontaneous firing (arrow) results in a quicker return to the quiescent state

Probability of spontaneous firing. The duration of the intervals between transients is increased by decreasing *sponfire*. Spontaneous firing also influences the durations of the transients itself. An interesting result is that if *sponfire* is low, it will take a long time for a transient to die out: the activity pattern often becomes trapped in a limit-cycle. If the probability is too high, a transient is also not likely to die out, because new activity is being triggered at a high frequency. If spontaneous firing is stopped shortly after a 'transient' has been triggered, activity will either die out within a short period (up to about 100 time intervals, see Fig. 3c) or will settle into a cyclic mode of activity in which a particular activity pattern is repeated indefinitely (see Fig. 3b).

Refractoriness. If refractoriness is completely removed from the model only short-lasting transients can be generated (provided that w_{ie} is sufficiently increased). All of these last at most about 80 time intervals, among different network realizations as well as within a given network. Upon removing refractoriness, cyclic modes of activity within a transient disappear completely. The duration of the transients is now determined mainly by D_i: the more rapid the decay, the shorter the transients. Long-lasting transients also disappear if the duration of the refractory period is too short relative to D_e.

To stimulate refractoriness after firing, θ is put up to M_e for two time intervals, and is then put back to its original value via two equal steps. An alternative is to let θ decrease exponentially after being put up to M_e, according to

$$\theta(t+1) = D_\theta \cdot (\theta(t) - \theta_0) + \theta_0 \qquad (5)$$

where $\theta(t)$ is the threshold at time t, θ_0 is the default threshold, and D_θ the speed with which the threshold returns to θ_0. With $D_\theta = 0.45$ (same global course of decay) essentially the same results are obtained, i.e., long-lasting periods of activity alternating with periods of minimal activity (Fig. 4). However, there are some important differences. In large networks (>50 cells), a cyclic pattern within a transient reflecting the duration of the refractory period, was not observed. Related to this finding is that, when spontaneous firing is stopped shortly after a transient has been triggered, the activity pattern was never observed to settle into a cyclic mode: the network either became silent after a variable period of time (which might be very long: with $w_{ee} = 0.170$, periods of time even as long as 13000 time intervals have been observed; see also Fig. 4b) or was found to be still active in a non-cyclical fashion.

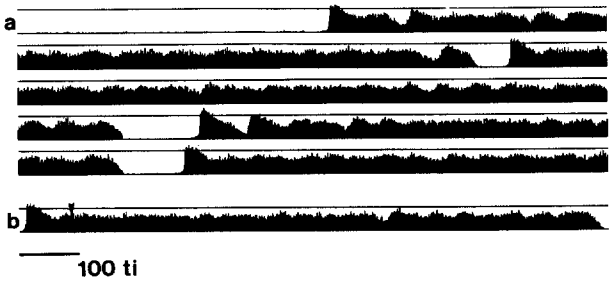

Fig. 4. **a** Series of transients generated using equation (5) for simulating refractoriness. Total number of firing cells plotted against time. A complete episode of 5000 time intervals (ti) is shown, each trace representing 1000 time intervals. The top line of each trace denotes 25% of all cells. Parameters: $w_{ee} = 0.168$, $w_{ie} = 0.009$, *spon fire* $= 0.0025$, $D_i = 0.93$, $D_\theta = 0.45$. The rest of the parameters as in Table 1. **b** Spontaneous firing is stopped (arrow) in the second transient of **a**. The network does not settle into a cyclic mode and remains active for quite a long period of time

4 Analysis of the model

The emergence of long-lasting transients will be qualitatively explained using simplified models. At the same time, the observed effects of parameter changes will be interpreted.

Spontaneous firing, cyclic-mode switching, and transition to quiescent state

Earlier studies showed that if a network of threshold elements with deterministic and synchronous dynamics is activated, it will, after an initial phase of variable length during which no network state is exactly repeated ('wandering' phase), either return to the vacuum state (no activity) or settle into a limit-cycle mode of activity in which a sequence of states is repeated indefinitely (Anninos 1972; Wong and Harth 1973; Choi and Huberman 1983; Caianiello and Marinaro 1988). Any form of stochastic disturbance (e.g., spontaneous firing) will allow the network to exit from the given cycle, so that a new cyclic state becomes accessible. This phenomenon is known as cyclic-mode switching (Clark et al. 1985). Since our model is similar to a network of threshold elements with deterministic (except for spontaneous firing) and synchronous dynamics, cyclic modes of activity and cyclic-mode switching must be expected to occur, as indeed they do. A network of only four e-cells will be used to show that these phenomena underlie the generation of long-lasting transients. Again global activity is triggered by spontaneous firing (Fig. 5), and the network subsequently settles into a cyclic mode, repeating a particular pattern of network states over and over again, until spontaneous firing in one of the cells disturbs the pattern. The network may then switch to a new cyclic mode, or back to the quiescent state. In the latter case, the network is switched into a state that is incapable of sustaining activity due to the particular configuration of refractory cells (after firing spontaneously, a cell goes through the normal sequence of refractory states) and the distribution of membrane potentials. This point can be best illustrated using only two connected e-cells. The sequence of states leading up to the termination of activity is shown in Fig. 6. Spontaneous firing of cell 1 at a point in its cycle just

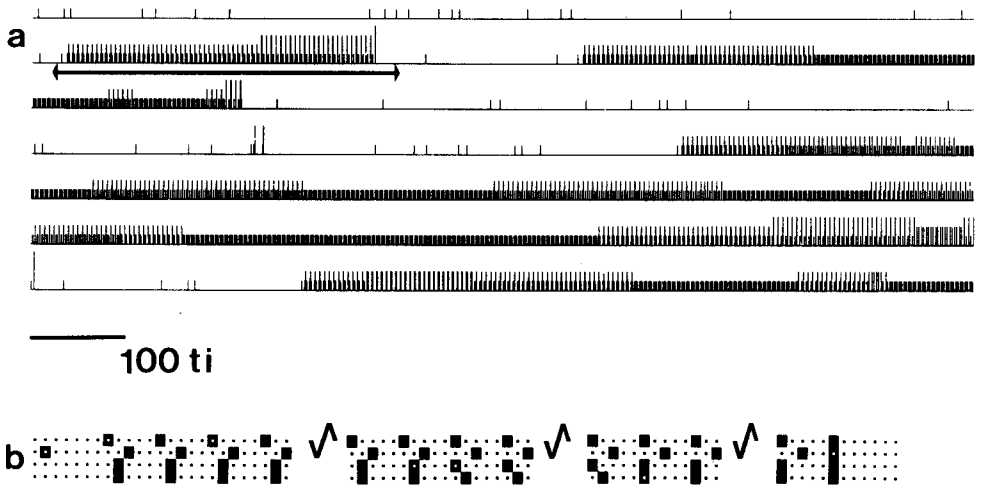

Fig. 5a, b. Transients in a network of four excitatory cells **a** Total number of firing cells plotted against time (the length of the lines found on the first trace corresponds to one firing cell). A complete episode of 7000 time intervals (ti) is shown, each trace representing 1000 time intervals. Parameters: $size_x = 2$, $size_y = 2$, $n_{ee} = 3$ (such that each cell makes exactly one connection to each of the other 3 cells and no connections to itself), $w_{ee} = 0.2$, *sponfire* = 0.006. **b** For the indicated segment in **a**, the firing state of the individual cells are shown. Cells are plotted in a column at each time interval. Horizontal axis represents time. A non-firing cell is indicated by •, a firing cell by ■, and a spontaneously firing cell by ◘

previous to where it would normally have fired, causes the cell to be absolutely refractory. As a result of spontaneous firing of cell 1, the membrane potential of cell 2 is raised earlier and its decay commences earlier than would normally have been the case, so that the membrane potential of cell 2 is sub-threshold where it would normally have fired. Cell 1 receives no input, and the membrane potential of both cells return to their resting level. The activity would not have been terminated had w_{ee} been stronger, or D_e been larger relative to the length of the refractory period. Thus, there exist critical parameter settings of decay time, connection strengths, and refractory period for which system activity is vulnerable to stochastic disturbances. In large networks most of the cells are involved whenever a cyclic mode is present. For certain parameter settings, the network as a whole is susceptible to disturbances by spontaneous firing. The network is in a critical state in the sense that spontaneous firing in only a few cells may be sufficient to bring about the termination of a transient. A small perturbation may produce consequences that propagate throughout the network. Note that it is not stochastic variations in the amount of spontaneous firing that cause the termination. Continuous activity during a transient does not depend on new activity being repeatedly triggered. However, spontaneous firing may also contribute to the maintenance by causing switches from states that would otherwise return to the quiescent state.

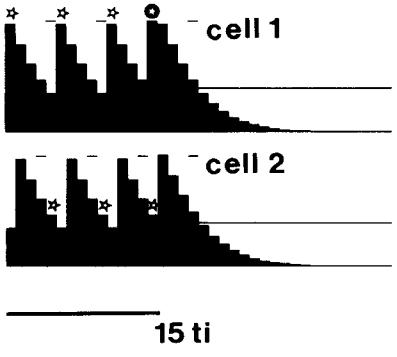

Fig. 6. Spontaneous firing results in the termination of activity in two symmetrically connected *e*-cells. The membrane potential of each cell is plotted against time. Horizontal lines represent firing theshold; only the resting level and level of the last refractory period are visible on this scale. Firing is indicated by ☆, and spontaneous firing by ◘. Parameters: $w_{ee} = 0.65$, *sponfire* = 0.006, $n_{ee}(\min) = n_{ee}(\max) = 1$ (such that each cell makes no connection to itself)

Inhibition and connection strength

If w_{ee} is too strong or w_{ie} too weak, the *e*-population becomes so strongly depolarized that it is less vulnerable to spontaneous firing. Activity, once triggered, is then not likely to terminate.

In a mixed network, the *i*-population follows the *e*-population massively and almost immediately, preventing the latter becoming too strongly depolarized. If the inhibitory connectivity is not sufficiently homogeneous (e.g., n_{ie} too small), there will be some weakly inhibited cells, which may act as seeds for renewed spread of activity. Then, consecutive transients may blend, as it were, into one another and total activity becomes less likely to terminate completely.

If w_{ee} is strong enough to allow triggering of network activity, (large) purely excitatory networks becomes so strongly depolarized that the network is no longer susceptible to small disturbances, accounting for the absence of transients in these networks. In mixed networks, however, subsequent inhibitory feedback keeps the membrane potential within the susceptibility range for termination.

Fig. 7. Spatially restricted transients arise in a purely excitatory, short-range network. Parameters: $size_x = 1$, $size_y = 16$, $l_{ee(\min)} = 1$, $l_{ee(\max)} = 3$, $n_{ee(\min)} = n_{ee(max)} = 5$, $w_{ee} = 0.11$. The firing state of the individual cells are shown against time (time horizontal). A non-firing cell is indicated denoted by •, a firing cell by ■, and a spontaneously firing cell by ◘. Spontaneous firing terminates activity in the upper cells and a few time intervals later also in the bottom cells, while the middle cells continue to be active. Later on, activity in upper and bottom cells is again triggered by spontaneously firing cells

Connection range

With short range $e \rightarrow e$ connections more or less independent local cyclic modes of activity develop, which can give rise to spatially restricted transients, while the activity summed over the whole network shows no prominent transients (Fig. 7). For activity to terminate completely, all local activities have to stop simultaneously; this is less likely an event than the termination of a transient in a long range network, where all the cells are involved in one and the same cyclic mode.

Refractoriness

Using equation (5) with $D_\theta = 0.45$, the global course of decay of the firing threshold is about the same as in the original formulation. However, as a result of the threshold decaying smoothly, the number of refractory states is in fact increased. In small networks, both the cycle within a transient and the 'wandering' phase previous to settling into a cyclic mode (or quiescent state) becomes longer as a result (e.g. cycle lengths of 24 time intervals in a network of 16 cells). In large networks (>50 cells), activity was never observed to settle into a cyclic mode following cessation of spontaneous firing. With the increased number of refractory states, the number of possible network states is also increased, which reduces the accessibility of cyclic modes. As a result, also the length of the initial, wandering phase is greatly increased. Therefore, activity, once triggered can sustain for a (very) long period of time in a non-cyclical fashion and may nevertheless terminate without any disturbances from spontaneous firing (Fig. 4b). That is, the path to the quiescent state has been prolonged (compare Fig. 3c). However, spontaneous firing is still necessary for escaping from (very long) cycles when they are eventually encountered.

In summary, after being triggered by spontaneous firing, the network goes through the following phases. An initial 'wandering' phase, in which no network state is exactly repeated, leading either back to the quiescent state or to an equilibrium in which activity is sustained in a cyclic fastion (cyclical because of the presence of refractory periods). Subsequent spontaneous firing can cause transitions to other equilibrium states or to the quiescent state. During a long-lasting transient, the network makes transitions among different such equilibria. For certain parameter settings, the network will eventually be switched back to the quiescent state. If the network is small, activity can terminate even without inhibition. In large networks, inhibition ensures that the network remains in the neighbourhood of a critical point between active and quiescent state. When the number of refractory states is increased, it is found that both the wandering phase and the duration of the equilibrium cycles is prolonged. In large networks, the wandering phase could be very long while the network was not observed to find equilibrium cycles.

5 Conclusions and discussion

We have demonstrated that long-lasting transients of activity can emerge in a distributed network consisting of cells with only fast intrinsic kinetics. These transients have time characteristics orders of magnitude longer than those of the individual cells. They are triggered by spontaneous firing ('noise'), which eventually also cause their termination by switching network activity, after many transitions among different equilibria, into the quiescent state. Thus, transients do not terminate as a result of a build-up of recurrent inhibition. The role of inhibition here is to keep the network sensitive to spontaneously firing cells, i.e. to keep the network in a critical state between active and quiescent state. The presence of a refractory period is a prerequisite for the existence of cyclic modes of activity as well as for the mechanism by which activity can die out.

The general principle as described here might operate in a large class of neural networks as long as there are different equilibria of activity and paths to the quiescent state. Random perturbations may then cause jumps among these equilibria and the quiescent state. In this respect it is interesting that Nakao et al. (1990) have suggested that wandering among different equilibria as a result of random perturbations can be regarded as the underlying generation mechanism of the $1/f$ power spectral density.

Although all the cells in the model network have identical intrinsic properties, many different firing patterns of individual cells nevertheless occur in association with transients. Therefore, in interpreting spike trains, one should bear in mind the richness of purely network-generated behaviour. Otherwise one will search for differences in intrinsic mechanisms, under the mistaken assumption that such differences must necessarily be present.

The robustness of the results was tested under various alternative formulations of the model. *The neuron model.* The same results are obtained using a model in which the effect of *e*- and *i*-input on the membrane potential is described directly instead of via conductance changes (Van Ooyen et al. 1992). *The nature of spontaneous firing.* Preliminary results indicate that it is not crucial how the stochastic disturbances come about, i.e., whether by synaptic noise, stochastic fluctuations of the firing threshold, or random input to the network. *Asynchronous updating.* It is well known that cyclic behaviour of binary decision elements can be considerably modified under asynchronous updating (Grondin et al. 1983). In preliminary studies with asynchronous updating, long-lasting transients still emerge but cyclic behaviour largely disappears, and, once triggered, activity can be sustained for a long time but still terminate without the need of spontaneous firing.

As the phenomenon studied here seems to be a rather robust one (see also Noest 1988; Kryukov 1990), its underlying mechanism cannot be excluded as a candidate for the generation of slow waves. The duration and variability in duration of long-lasting transients emerging in the model is of the same order of magnitude as those of empirically recorded slow waves (Corner and Crain 1972). Also the spike-train patterns associated with transients resemble those observed to accompany slow waves. Another interesting observation is that in tissue cultures without 'background' unit-spike activity, spontaneous slow waves were absent, even when the threshold for electrically evoking them was low (Corner and Crain 1972). Thus, such background activity may trigger slow waves in tissue cultures just as spontaneous firing triggers transients in the model network.

Long-lasting transients can still emerge in model networks with as few as two *e*-cells. Interestingly, Segal and Furshpan (1990) have demonstrated 'epileptiform' activity bursts (lasting ca. 500 s) in a microculture consisting of only two interconnected excitatory hippo-campal neurons. For the termination of such activity bursts, the presence of repolarization mechanisms such as calcium-mediated potassium currents were suggested, as GABAergic synaptic inhibition could be ruled out in this case. Our results show that it is in principle possible that activity can terminate even without the presence of such intrinsic mechanisms.

Long-lasting transients can also emerge if the neuron model is provided with a mechanism to simulate long-lasting calcium-mediated potassium conductances (Van Ooyen et al. 1992). This conductance slowly hyperpolarizes the cell after repeated firing, so that, once triggered, network activity will terminate after a certain period of time because of accommodation of the cells. Yet another mechanism by which long-lasting transients can in principle be generated is as the result of slow IPSPs.

Traub and Miles (1991) have also studied population activity in model neural networks. Unlike our model, their model is very complex, with intrinsic oscillatory properties of the individual cells, and slow as well as fast inhibition. Large waves of activity lasting about 1 s each were found when slow inhibition was blocked (Traub et al. 1989). These waves, however, may be a direct consequence of the intrinsic burst properties of the individual (model) cells, as the intrinsic burst frequency is of the same order of magnitude as the frequency of the population rhythmicity.

As a next step towards answering the question whether slow waves are essentially network generated, or are a direct result of intrinsic membrane properties, we will test whether slow waves in tissue cultures can still be generated if the slow intrinsic neuron properties are eliminated, i.e., if *(1)* the channels responsible for a long-lasting calcium-mediated conductance are specifically blocked; and *(2)* the slower IPSPs are blocked using $GABA_B$ receptor blockers.

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