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Formal modeling with multistate neurones and multidimensional synapses

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Abstract

Multistate neurones, a generalization of the popular McCulloch–Pitts binary neurones, are described; they are intended to model the fact that neurones may be in several different states of activity, while McCulloch–Pitts neurones model two states only: active or inactive. We show that as a consequence, multidimensional synapses are necessary to describe the dynamics of the model. As an illustration, we show how to derive the parameters of formal multistate neurones and their associated multidimensional synapses from simulations involving Hodgkin–Huxley neurones. Our approach opens the way to solve in a more biologically plausible way, two problems that were addressed previously: (1) the resolution of 'inverse problems', i.e. the construction of formal networks, whose dynamics follows a pre-defined spatio-temporal binary sequence, (2) the generation of spatio-temporal patterns that reproduce exactly the 'code' extracted from experimental recordings (olfactory codes at the glomerular level).

Keywords: Multistate neurones; Multidimensional synapses; Neural coding; Spatio-temporal patterns; Hodgkin–Huxley model; Formal neural network

1. Introduction

The present study is a step in the modeling of the relations between the anatomical and biophysical *structure* of biological neural networks and their signal processing and encoding *function*. More precisely, we suggest a new tool that may bring a contribution to the following general question: what can we infer about the connectivity of a neural network just by looking at the neuronal activity? Answering that question quantitatively amounts to solving an "inverse problem", which was addressed before (Quenet et al., 2000, 2002) by making the drastic assumption that neurones can have only two states of activity, hence can be modeled as binary elements.

In a first step, that simplification allowed the computation of the appropriate synaptic weights such that the resulting neural network exhibited precisely the spatio-temporal experimentally recorded code[1] (Quenet et al., 2000). In a second step, a network of Hodgkin–Huxley

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[1] By "spatio-temporal pattern", we mean the activity of a set of neurones during a period of time. Such an activity can be

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(HH) spiking neurones having the connectivity derived in the first step was simulated; it was shown that if (i) an appropriate synchronization mechanism is implemented, and if (ii) synaptic efficacies and delays are appropriately defined, then the network of HH neurones exhibits *exactly* the same spatio-temporal activities as the network of McCulloch–Pitts (McCulloch and Pitts, 1943) (McCP) neurones defined in the previous step. This proves that the *analytic* construction of networks of McCP neurones can serve as a guide to more biologically relevant models, since HH neurones can mimic, sometimes with a wealth of details (Mainen and Sejnowski, 1996; Santamaria et al., 2002), the features and the activities of single biological neurones.

Therefore, it can be conjectured that in order to make progress in the direction of solving inverse problems with bio-inspired models, it would be useful to design models of neurones that like binary neurones, have analytically tractable dynamics, but unlike McCP neurones, can model more complexity. In the present paper, we show how to extend McCP neurones to multistate units with multidimensional synapses, which (i) can take into account the fact that a neurone can have several states of activity (e.g. can generate, zero, one or two spikes in a given time interval, depending on the state of its presynaptic neurones), and that (ii) can take into account several types of synapses (e.g. involving different neurotransmitters, or with different locations on the dendritic tree) as well as multiple contacts between two neurones.

Finally, we show how to derive the states of the multistate neurones, and the elements of the multidimensional synapses, from simulations of HH neurones. It constitutes also a step to bring together two models of a neurone, a biologically plausible one, the HH neurone and an analytically tractable one, the McCP-like neurone, using an example of the former in order to define, in an ad hoc manner, the latter.

experimentally recorded or computed, for biological or formal neurons, respectively. If time bins can be defined, the number of spikes emitted in each time bin by the recorded neurones may be used to define a "spatio-temporal code" (see, for instance, Wehrt et Laurent, 1994) that can be reproduced with discrete time formal neurones, *provided the resolution of an inverse problem*.

2. Direct and inverse problems in a network of binary units

In the present section, we recall briefly the notations that are used in the analysis of binary (McCP) neurones, and we outline the resolution of inverse problems with such model neurones.

2.1. The dynamic neural filter: a network of McCulloch and Pitts binary units

In its deterministic version, a dynamic neural filter (Quenet and Horn, 2003; Quenet et al., 2000) is a network of binary units with exogeneous inputs and arbitrary connectivity, whose dynamics is defined in discrete time. Let us consider a network of N McCP units, where the activity $s_i(t)$ of each unit i, $i \in \{1,\ldots,N\}$; at discrete time t can be either 0 or 1. The general term of the synaptic matrix $\boldsymbol{W}$ of the network is $w_{ij} \in \mathbb{N}$, that term corresponds to the weight of a single synaptic contact from neurone j to neurone i. We consider here a model, in which each neurone receives an external input $R_i \in \mathbb{N}$, the vector $\vec{R}$ defined by the N coordinates R_i is the input vector to the network. The dynamics of the network is defined by:

$$h_i(t) = R_i + \sum_{j=1}^{N} w_{ij} s_j (t-1) \tag{1}$$

$h_i(t)$ is the potential of neurone i at discrete time t and $s_j(t-1)$ the state of neurone j at time $t-1$, which takes its value in $\{0,1\}$.

$$s_i(t) H\left(h_i(t) - \frac{1}{2}\right)$$

$$\text{with} \quad H(x) = \begin{cases} 1 & \text{if } x > 0 \\ 0 & \text{otherwise} \end{cases} \tag{2}$$

Such a network exhibits a discrete-time dynamics whose major property is to respond to any stable input $\vec{R}$ with a spatio-temporal activity pattern: a sequence of 0 and 1 for each neurone. Given an initial state of the network, the binary spatio-temporal patterns evolve towards a fixed point or toward a cycle whose length[2]

[2] This length may become very large at the edge of chaos under some conditions on $\boldsymbol{W}$ and $\vec{R}$ (Gutfreund et al., 1988; Kliper et al., 2003, in press).

depends on the values of $\boldsymbol{W}$ and $\vec{R}$. Ranking the neurone activities in a row for each time step, a spatio-temporal pattern of length T can be denoted a $[(T+1)\times N]$ matrix $\boldsymbol{P}$, whose general term P_{ti} is the activity $s_i(t)$ of neurone i at time t: the first row of $\boldsymbol{P}$ is the initial state of the network, i.e. at time $t=0$, row $(t+1)$ of $\boldsymbol{P}$ is the state of the network at time t, and the column i is the sequence of activity of neurone i.

2.2. Direct and inverse problems

The direct problem can be defined as follows: given $\boldsymbol{W}$ and $\vec{R}$, what is the spatio-temporal behaviour of the network, i.e. what pattern, or code, does it exhibit as a response to the input $\vec{R}$? The coding properties of the DNF are described in (Quenet and Horn, 2003); it is shown that they are robust to synaptic noise.

Given a matrix $\boldsymbol{P}$ of a spatio-temporal pattern, an inverse problem consists in finding $\boldsymbol{W}$ and $\vec{R}$ such that the network exhibits the activity described by matrix $\boldsymbol{P}$.[3] The conditions on the terms w_{ij} and R_i can be written as N sets of T inequalities, one set per neurone; such an inequality is given for time discrete t and neurone i in Eq. (3).

$$(2P_{ti}-1)\left(\sum_{j=1}^{N} w_{ij}P_{(t-1)j}+R_i\right)>0 \tag{3}$$

3. Multidimensional synapses in a formal multistate neural network

In the present section, a network of multistate neurones with multidimensional synapses is defined as an extension of the model neurones and synapses defined above. The purpose of that extension is to model different states of activity of a neurone, while retaining the topological equivalence of the states, which allows addressing an inverse problem by solving sets of linear inequalities.

Since the state of a McCP neurone is defined by a scalar that can take on two values; a straightforward extension consists in encoding the state of the neurone by a scalar that can take on K different values. Such an approach, however, cannot be valid since the three states are not topologically equivalent. In that representation, state K is separated from state $K+2$ by state $K+1$.

The standard way of achieving complete topological equivalence of the states of a multi-state system consists in using a one-out-of-K encoding; each state of the system is represented in K-dimensional space as a vector belonging to a basis of that space. Complete topological and metric equivalence between the states is achieved if the basis is orthonormal: state k of the system is described as a vector, whose kth component is equal to 1, all other components being equal to 0.

Equivalently, the state can be represented by a vector in $K-1$ dimensional space where the possible states are described by K vectors, provided that $K-1$ vectors provide a complete basis of $K-1$ dimensional space. The relation between the above representations is described in Appendix 1.

As an example, the state of a three-state neurone can be represented as one vector out of three vectors $\vec{A}$, $\vec{B}$, $\vec{C}$ in two-dimensional space, if two vectors among the three possible vectors are not collinear. Topological and metric equivalence of the states is achieved if the three vectors $\vec{A}$, $\vec{B}$, $\vec{C}$ have the same length and are at 120° angular separation (Fig. 1). That is identical to a three-state Potts neurone (Kanter, 1988; Wu, 1982), but with synapses defined in a very different way.[4]

In that framework, the potential of formal neurone i is a vector in $K-1$ dimensional state, which is obtained by a *linear transformation* of the vector states of all presynaptic neurones: hence information transfer between each pair of neurones $\{i, j\}$ is described by a $(K-1, K-1)$ *matrix* W_{ij}.

In the case of a three-state neurone, the potential of the neurone is defined by

$$\vec{h}_i(t)=\sum_{j=1}^{N} W_{ij}(\vec{S}_j(t-1))+\vec{R}_i \tag{4}$$

[3] The inverse problem was solved for several P-patterns in response to several inputs to a given network (Quenet et al., 2002, 2000).

[4] Another three-state neuron has been described by Silverman, Shaw and Pearson (Silverman et al., 1986), where these three states are ranked on a one-dimensional space. In this model, the synapses are scalar.

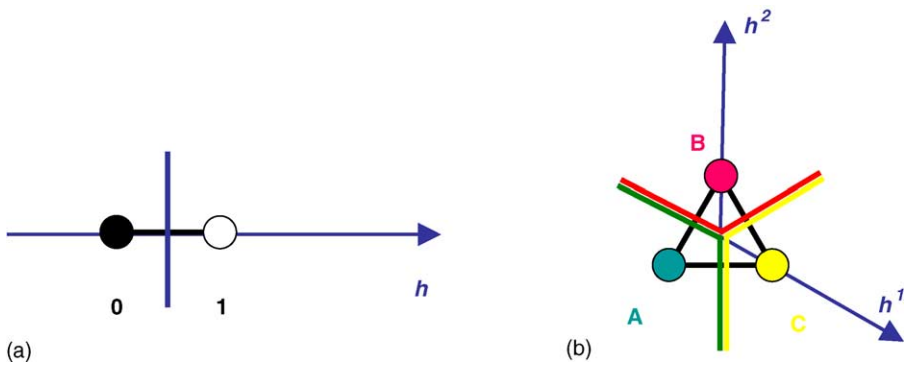

Fig. 1. (a) A single dimension is sufficient to represent two independent states of a binary unit; they can be seen as a dumb-bell with one state at each extremity. They are perfectly symmetric with respect to their centre of gravity. The membrane potential h is a one-dimensional object. (b) A two-dimensional space is necessary to represent three states without any order relationship between them; the potential $\vec{h}$ is a bidimensional object.

$\vec{h}_i(t)$ is the potential of neurone i at discrete time t and $\vec{S}_j(t-1)$ the state of neurone j at time $(t-1)$, which takes its value in $\{\vec{A}, \vec{B}, \vec{C}\}$.

In the deterministic case, the state $\vec{S}_i(t)$ of neurone i at time t is the state among $\{\vec{A}, \vec{B}, \vec{C}\}$ that *is closest to* $\vec{h}_i(t)$, since $||\vec{A}|| = ||\vec{B}|| = ||\vec{C}||$:

$$\vec{s}_i(t) = \vec{A} \Leftrightarrow \vec{h}_i(t)\vec{A} > \vec{h}_i(t)\vec{B} \text{ and } \vec{h}(t)\vec{A} > \vec{h}(t)\vec{C} \quad (5)$$

Similar conditions hold for $\vec{B}$ and $\vec{C}$.

Given a $[(T+1) \times N]$ matrix $\boldsymbol{P}$ of a spatio-temporal ternary pattern, solving an inverse problem consists in finding a tensor $\boldsymbol{W}$ (of size $2 \times 2 \times N \times N$ and general term w_{ij}^{ab}) and a matrix R (of size $2 \times N$ and general term) such that the network exhibits the spatio-temporal pattern defined by matrix $\boldsymbol{P}$. The conditions on the terms w_{ij}^{ab} and R_i^a can be written as N sets of $2T$ inequalities, one set per neurone; a couple of inequalities can be written for time t and neurone i. In order to write these inequalities, it is necessary to assign to $\vec{h}$ some components in the two-dimensional space, for instance, $\vec{h} = h^1\vec{B} + h^2\vec{C}$. Since $\vec{A} \cdot \vec{B} = \vec{B} \cdot \vec{C} + \vec{A} \cdot \vec{C} = \frac{1}{2}||\vec{A}||^2$ and $\vec{h}$ is defined by Eq. (4), the conditions are given in Eq. (6).

$$\begin{aligned}
\text{If } \vec{P}_{ti} = \vec{A} \quad & \begin{cases} \sum_{j=1}^{N} \left[w_{ij}^{11} P_{(t-1)j}^1 + w_{ij}^{12} P_{(t-1)j}^2 \right] + R_i^1 < 0 \\ \sum_{j=1}^{N} \left[w_{ij}^{21} P_{(t-1)j}^1 + w_{ij}^{22} P_{(t-1)j}^2 \right] + R_i^2 < 0 \end{cases} \\
\text{if } \vec{P}_{ti} = \vec{B} \quad & \begin{cases} \sum_{j=1}^{N} \left[w_{ij}^{11} P_{(t-1)j}^1 + w_{ij}^{12} P_{(t-1)j}^2 \right] + R_i^1 > 0 \\ \sum_{j=1}^{N} \left[(w_{ij}^{11} - w_{ij}^{21}) P_{(t-1)j}^1 + (w_{ij}^{12} - w_{ij}^{22}) P_{(t-1)j}^2 \right] + (R_i^1 - R_i^2) > 0 \end{cases} \\
\text{if } \vec{P}_{ti} = \vec{C} \quad & \begin{cases} \sum_{j=1}^{N} \left[(w_{ij}^{21} - w_{ij}^{11}) P_{(t-1)j}^1 + (w_{ij}^{22} - w_{ij}^{12}) P_{(t-1)j}^2 \right] + (R_i^2 - R_i^1) > 0 \\ \sum_{j=1}^{N} \left[w_{ij}^{21} P_{(t-1)j}^1 + w_{ij}^{22} P_{(t-1)j}^2 \right] + R_i^2 > 0 \end{cases}
\end{aligned} \quad (6)$$

4. Modeling a Hodgkin–Huxley neurone as a multistate neurone with multidimensional synapses

Let us suppose that we want to reproduce neuronal recordings that can be considered as a sequence of synchronised three-state data. Applying the same strategy as described for binary data, we take advantage of the possibility of solving the inverse problem for a McCP-like three-state neural network in order to define synaptic connections and inputs. Nevertheless, the three neuronal states identified in some experimental recordings are not necessarily in a *symmetric configuration*. It means that we need first to define appropriate McCP-like neurones before solving the inverse problem for a network of such neurones. A HH model of neurone exhibiting three types of activities may be helpful. Indeed, it is possible to perform numerical experiments on such a model, i.e. simulations with the software NEURON, in order to build an ad hoc *three state McCP-like unit*, where not only the *states* must be defined and their components assigned, but also the potential $\rightarrow h_i$ and the two functions f_1 and f_2 that describe respectively the *potential-states* relation ($\vec{h} = f_1$(states), as in Eq. (4) and the *state-potential* relation ($\vec{s} = f_2$(potential), as in Eq. (5). We will describe how the three state McCP-like units can be derived from numerical experiments performed on HH neurones.

4.1. The Hodgkin–Huxley model

The HH model considered here is made of two compartments: a soma and a dendrite where an inhibitory synapse and an excitatory synapse are located; a diagram of this neurone is represented in Fig. 2. Using the NEURON software, this simple model was constructed with a minimal number of ionic currents. The nonlinear nature of calcium dynamics enable cells to generate a wide repertoire of spatio-temporal patterns; therefore, in addition to the somatic sodium and potassium currents, a low-threshold calcium current (*T*-current) and the mechanism for decay of internal calcium concentration due to calcium currents and pump were introduced in the somatic and dendritic membrane in order to facilitate the generation of double spikes (Destexhe et al., 1998).

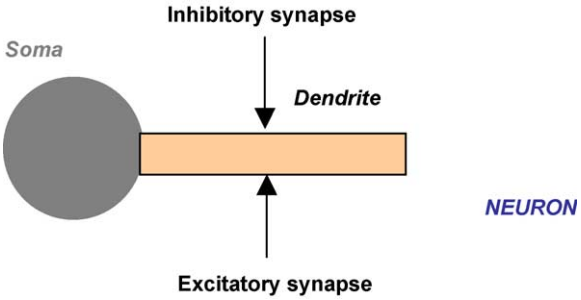

Fig. 2. The Hodgkin–Huxley formal neurone is made of two compartments: a somatic compartment and a dendritic one, which receives an inhibitory synapse and an excitatory one located in the middle of the dendrite. A table with the values of the geometrical and biophysical parameters is given in Appendix 2.

4.2. The synapses, delays and temporal behaviours

The temporal evolution of the synaptic conductances are modeled by *alpha functions* with different time constants for the inhibitory synapse and for the excitatory one. The activity of such a unit is simulated with the software NEURON; the parameters of the neuronal model are such that a typical behaviour of the model is indicated in Fig. 3 where three types of activity appear: no spike, one spike and two spikes. It is thus possible to define the three states *A*, *B* and *C* that encode the generation of zero,

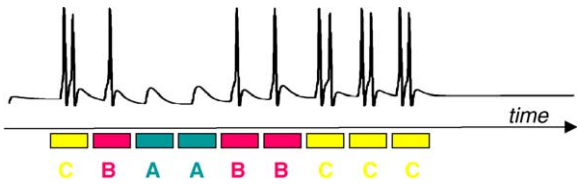

Fig. 3. As a response to a regular couple of external stimuli applied with varying amplitudes to both the excitatory and the inhibitory synapses, the typical temporal behaviour of the HH neurone described in Fig. 2 exhibits three different patterns of activity that can be considered as *three different states*; we assign state *A* to the state were the neurone emits no spike as a response to a stimulus, state *B* to the emission of a simple spike, and *C* to the emission of a double spike. The definition of the states relies on a sampling of the continuous time into bins: the activity of the HH neurone in each time bin corresponds to the state of a McCP-like neurone updated at one time step.

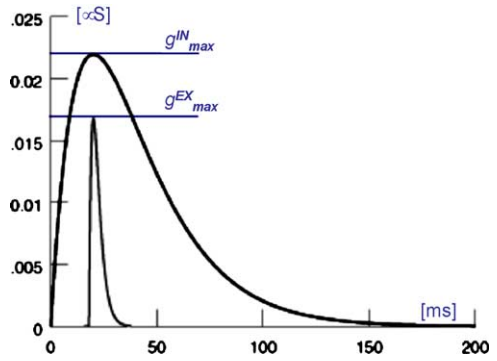

Fig. 4. Alpha functions describing the temporal evolution of inhibitory and excitatory synaptic conductances. The corresponding equation is $(g = g_{\max}\ (t/\tau)\exp^{(1-t/\tau)})$ with $\tau = \tau^{\mathrm{IN}}$ and τ^{EX}, respectively. The stimuli applied to the neurone are delayed in such a way that the conductances reach their maxima simultaneously. The time course of the synaptic conductances is smaller than the time bin mentioned in Fig. 3.

one or two spikes in a given time bin.[5] Such activities are responses to short pulses (Dirac) applied to each synapse with adapted delays such that the peaks of the synaptic conductances occur simultaneously as indicated in Fig. 4; they depend on the values of the two activity-dependent quantities $g^{\mathrm{IN}}_{\max}$, and $g^{\mathrm{EX}}_{\max}$.

We define the '*potential*' $\vec{h}$ as the two-dimensional vector whose components are *the maximal synaptic conductances*:

$$\vec{h} = \begin{pmatrix} g^{\mathrm{IN}}_{\max} \\ g^{\mathrm{EX}}_{\max} \end{pmatrix}$$

4.3. Numerical experiments

Having defined the states and the potential, we show how simulations performed with the HH neurone can be used in order to define the dependence of the potential of a McCP-like neurone on the state of activity of the network (f_1) and the dependence of the state of this neurone on its potential (f_2). Since function f_2 is easier to construct, we describe it first.

4.3.1. Construction of the state of the neurone from its potential (function f_2)

The function we are looking for should assign to any, i.e. to any couple of values $(g^{\mathrm{IN}}_{\max}, g^{\mathrm{EX}}_{\max})$, a state of the neurone, i.e. an activity as a response to the presynaptic stimulus: no spike, one spike or two spikes. The following numerical experiment was performed: the number of spikes generated by the neurone shown on Fig. 2 was recorded in response to the simultaneously stimulation of both its excitatory and its inhibitory synapses (Fig. 5), as a function of the potential $(g^{\mathrm{IN}}_{\max}, g^{\mathrm{EX}}_{\max})$; the results are displayed on Table 1.

The number of spikes observed in the simulations defines sub-regions of this potential space, clearly separated by linear boundaries, whose equations are of the type $g^{\mathrm{EX}}_{\max} = m\, g^{\mathrm{IN}}_{\max} + \theta$.

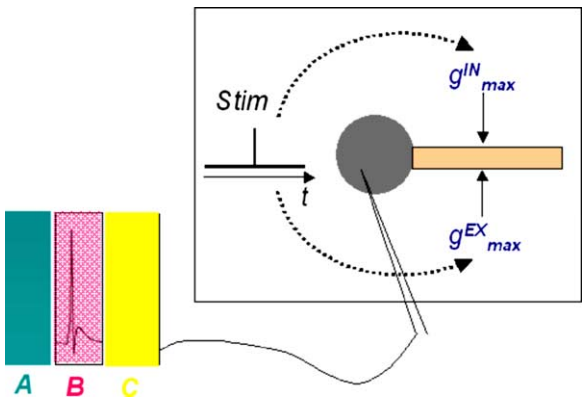

Fig. 5. Schematic representation of the numerical experiments performed with the HH neurone of Fig. 3 in order to define f_2. By incrementing the weights of the inhibitory and the excitatory synapses between a stimulating element (Stim) and the neurone, we modify the conductances $g^{\mathrm{IN}}_{\max}$ and $g^{\mathrm{EX}}_{\max}$ and we measure the effect of the simultaneous input of both excitation and inhibition by looking at the somatic response which is no spike (state *A*), one spike (state *B*) or a double spike (state *C*). The results are given in Table 1.

[5] The formalism introduced here to describe a three-state neurone can be extended to other behaviours than the triplet "no spike, one spike, two spikes": for instance, it is possible to introduce a bursting state as one of such states. Our approach is useful to define the dynamics of a neural network with multistate neurones *if these states can be defined within short fixed time bins*, which is not the case for more complex neuronal behaviours like poissonian firing or oscillatory firing for instance. Such long-term behaviours may *emerge* as temporal patterns exhibited by some neurones in a multistate neural networks.

Table 1
Table of the state-potential relation for the HH neural model of Fig. 2

	0	0.0032	0.0064	0.0096	0.0128	0.016	0.0192	0.0224	0.0256	0.0288	0.032	0.0352	0.0384	0.0416	0.0448	0.048	0.0512	0.0544
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.0018	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.0036	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.0054	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.0072	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.009	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
0.0108	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
0.0126	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0
0.0144	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0
0.0162	2	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0
0.018	2	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0
0.0198	2	2	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
0.0216	2	2	2	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0
0.0234	2	2	2	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0
0.0252	2	2	2	2	1	1	1	1	1	1	1	1	1	1	0	0	0	0
0.027	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	0	0	0
0.0288	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	0	0
0.0306	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	0
0.0324	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1
0.0342	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1
0.036	2	2-	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1
0.0378	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1
0.0396	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1
0.0414	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1

On the horizontal axis, the value of the inhibitory maximal conductance $g_{\max}^{\mathrm{IN}}$ is increased from 0 to 0.0644 μS by steps of 0.0032, while on the vertical axis, $g_{\max}^{\mathrm{EX}}$ is increased from zero to 0.0414 μS, by steps of 0.0018 (a fixed excitatory additional input is applied to the neurone, which corresponds to a maximal conductance of 0.0114 μS). We observe here that the regions defined by the states of the neurone are separated by linear boundaries.

In the present case, f_2 can be expressed in the following way (Eq. (7)), with $h^1 = g_{\max}^{\mathrm{IN}}$ and $h^2 = g_{\max}^{\mathrm{IN}}$.[6]

$$\begin{aligned}
&\text{If } h^2 - m_{AB}h^1 - \theta_{AB} < 0 \qquad s = A \text{ (no spike)}\\
&\text{If } h^2 - m_{AB}h^1 - \theta_{AB} > 0 \quad \text{and}\\
&\quad h^2 - m_{BC}h^1 - \theta_{BC} < 0 \quad s = B \text{ (1 spike)}\\
&\text{If } h^2 - m_{BC}h^1 - \theta_{BC} > 0 \qquad s = C \text{ (2 spikes)}
\end{aligned} \tag{7}$$

The parameters of the boundary between regions of data A and B are estimated to be $m_{AB} = 0.56$ and $\theta_{AB} = 0.0132$ μS; similarly, $m_{BC} = 1.02$ and $\theta_{BC} = 0.0274$ μS.

4.3.2. Construction of the potential of the neurone from the state of activity of the network (f_1)

The function we are looking for should assign to each state s_j of neurone j, presynaptic to neurone i, a value of

$$\vec{h}_{ij} = \begin{pmatrix} g_{ij}^{\mathrm{IN}}\max \\ g_{ij}^{\mathrm{EX}}\max \end{pmatrix},$$

due to the contribution of neurone j to the potential of neurone i. According to Eq. (4), such a contribution can be written as indicated in Eq. (8).[7]

$$\begin{aligned}
\vec{h}_{ij} = \begin{pmatrix} g_{ij}^{\mathrm{IN}}\max \\ g_{ij}^{\mathrm{EX}}\max \end{pmatrix} &= W_{ij}\vec{s}_j \begin{pmatrix} w_{ij}^{11} & w_{ij}^{12} \\ w_{ij}^{21} & w_{ij}^{22} \end{pmatrix} \begin{pmatrix} x_j^s \\ y_j^s \end{pmatrix}\\
&= \begin{pmatrix} w_{ij}^{11}x_j^s + w_{ij}^{12}y_j^s \\ w_{ij}^{21}x_j^s + w_{ij}^{22}y_j^s \end{pmatrix}
\end{aligned} \tag{8}$$

[6] Provided h^1 and h^2 are in the range of values defined by the numerical experiments.

[7] Time is not included in this equation, as we look for a relationship, which is time-independent. Nevertheless, when this potential-state relation is a part of the updating rules, time appears in the states, as in Eq. (4).

where the components $\begin{pmatrix} x_j^s \\ y_j^s \end{pmatrix}$ of state s_j, are $\begin{pmatrix} x_j^A \\ y_j^A \end{pmatrix}$, $\begin{pmatrix} x_j^B \\ y_j^B \end{pmatrix}$ or $\begin{pmatrix} x_j^C \\ y_j^C \end{pmatrix}$. Since synaptic conductances add, we can consider that the potential $\vec{h}_t$ at the level of neurone i is the sum of the contributions of all presynaptic neurones j, and of an external stimulus $\vec{R}_i$:

$$\vec{h}_i = \sum_{j=1}^{N} \vec{h}_{ij} + \vec{R}_i. \tag{9}$$

Let us assume that neurone j has *two* types of synaptic contacts on neurone i[8]: one inhibitory synapse with *weight* G_{ij}^{IN} and one excitatory synapse with *weight* G_{ij}^{EX}, where these weights are the maximal conductance of the synpases when they are activated by a single presynaptic spike. We are looking for a relation between the elements of the formal multidimensional synapse W_{ij} and the weights G_{ij}^{IN} and G_{ij}^{EX}. Such a relation depends on the values of the components assigned to states A, B and C; the latter are still to be defined. In other words, if we want to derive the contribution of neurone j to the potential of neurone i in Eq. (9), we need to estimate the values of 10 *unknown quantities*: the 3×2 components of the states and the four components of the multidimensional synapse. They can be estimated from numerical experiments as follows: a stimulus that mimics[9] a presynaptic state A, B or C, can be generated, and its effect on the values of the potential ($g_{\max}^{\mathrm{IN}}$, $g_{\max}^{\mathrm{EX}}$) of a postsynaptic HH neurone can be computed for different values of G^{IN} and G^{EX} (Fig. 6).

When the stimulating element is *silent* (state A), *whatever the value of* G^{IN} (respectively G^{EX}) the value of $g_{\max}^{\mathrm{IN}}(0)$ is 0 (respectively $g_{\max}^{\mathrm{EX}}(0)$ is 0). In this case, Eq. (8) becomes Eq. (10)[10]

$$\begin{pmatrix} g_{\max}^{\mathrm{IN}}(0) \\ g_{\max}^{\mathrm{EX}}(0) \end{pmatrix} = \begin{pmatrix} w^{11}x^A + w^{12}y^A \\ w^{21}x^A + w^{22}y^A \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \quad \forall w^{11}, w^{12}, w^{21}, w^{22} \tag{10}$$

Eq. (12) is trivially verified if we choose the components of state A to be zero:

$$\begin{pmatrix} x^A \\ y^A \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}.$$

When the stimulating element emits *one spike* (state B), by definition, *for each value of* G^{IN} (respectively G^{EX}) the value of $g_{\max}^{\mathrm{IN}}(1)$ is G^{IN} (respectively $g_{\max}^{\mathrm{EX}}(1)$ is G^{EX}). In this case, Eq. (10) becomes Eq. (11)

$$\begin{pmatrix} g_{\max}^{\mathrm{IN}}(1) \\ g_{\max}^{\mathrm{EX}}(1) \end{pmatrix} = \begin{pmatrix} w^{11}x^B + w^{12}y^B \\ w^{21}x^B + w^{22}y^B \end{pmatrix} = \begin{pmatrix} G^{\mathrm{IN}} \\ G^{\mathrm{EX}} \end{pmatrix} \tag{11}$$

If we assign arbitrarily to state B, the following components:

$$\begin{pmatrix} x^B \\ y^B \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

Eq. (11) becomes:

$$\begin{pmatrix} w^{11} \\ w^{21} \end{pmatrix} = \begin{pmatrix} G^{\mathrm{IN}} \\ G^{\mathrm{EX}} \end{pmatrix} \tag{12}$$

We still have two unknown quantities for the multidimensional synapse $\boldsymbol{W}$: w_{12} and w_{22}, and two unknown quantities for the components of state C.

When the stimulating element emits *two spikes* (state C), we measure the values of $g_{\max}^{\mathrm{IN}}(2)$ for some values of G^{IN} and the values of $g_{\max}^{\mathrm{EX}}(2)$ for some values of G^{EX}. The results of these experiments are displayed on Fig. 7, which shows that $g_{\max}^{\mathrm{IN}}(2)$ (respectively $g_{\max}^{\mathrm{EX}}(2)$) is a linear function of G^{IN} (resp. of G^{EX}) with a slope $\alpha^{\mathrm{IN}} = 1.98$ (resp. $\alpha^{\mathrm{EX}} = 1.58$).

[8] Although this assumption may seem unorthodox, the formalism introduced here can include the case of multiple synaptic contacts between two neurones, which may be of opposite signs (i.e., excitatory and inhibitory). Some recent experimental results seem to support the existence of such complex neuronal interactions (Chavas and Marty (2003).

[9] It is also possible to perform simulations where the presynaptic stimulus comes from another HH neurone, however, in so far as the interspike interval of state C is the same, the results of such simulations are similar to those obtained with the "Stim" elements, which mimics such a presynaptic neurone.

[10] The subscripts i and j have been dropped from the equations, as i represents the HH neurone and j the stimulating element. The formal multidimensional synapse from this element to the neurone is $\boldsymbol{W}$.

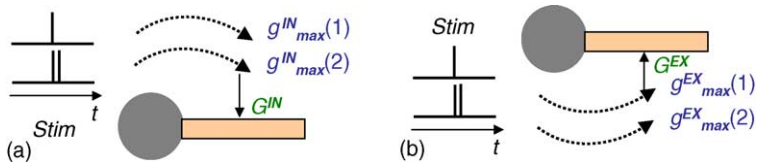

Fig. 6. Schematic representation of the numerical experiments performed on HH neurones in order to define f_1. By changing the state of the Stim element (0, 1 or 2 spikes) and the weights of the inhibitory and the excitatory synapses between it and the neurone, we measure the effects of these changes at the level of the maximal conductances $g^{\mathrm{IN}}_{\mathrm{max}}$(0,1 or 2) and $g^{\mathrm{EX}}_{\mathrm{max}}$(0, 1 or 2) (0 not shown). These experiments are performed on the inhibitory synapse (a) and on the excitatory synapse (b) independently.

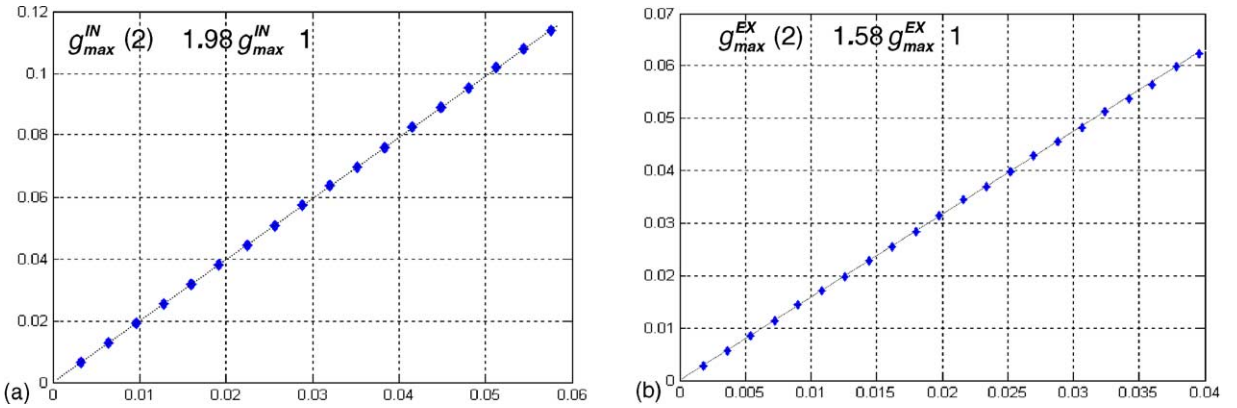

Fig. 7. When the Stim element generates a double spike, the value of $g^{\mathrm{IN}}_{\mathrm{max}}$ varies linearly with the value of G^{IN} (a) (idem for $g^{\mathrm{EX}}_{\mathrm{max}}$ and G^{EX}). The slope is α^{IN}=1.98 for the inhibitory synapse and α^{EX} = 1.58 for the excitatory one. (The unit of the *x*- and *y*-axes is μS; the scales for G^{IN} and G^{EX} are those of Table 1).

In this case, Eq. (8) becomes Eq. (13)[11]

$$\begin{pmatrix} g^{\mathrm{IN}}_{\mathrm{max}}(2) \\ g^{\mathrm{EX}}_{\mathrm{max}}(2) \end{pmatrix} = \begin{pmatrix} G^{\mathrm{IN}}x^C + w^{12}y^C \\ G^{\mathrm{EX}}x^C + w^{23}y^C \end{pmatrix} = \begin{pmatrix} \alpha^{\mathrm{IN}}G^{\mathrm{IN}} \\ \alpha^{\mathrm{EX}}G^{\mathrm{EX}} \end{pmatrix} \quad \forall G^{\mathrm{IN}}, G^{\mathrm{EX}} \tag{13}$$

We have four unknown values for two equations, so that we can *choose two of them arbitrarily*. Once again, let us choose the components of state *C* as: $\begin{pmatrix} x^C \\ y^C \end{pmatrix} = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$. Then Eq. (13) becomes Eq. (14):

$$\begin{pmatrix} g^{\mathrm{IN}}_{\mathrm{max}}(2) \\ g^{\mathrm{EX}}_{\mathrm{max}}(2) \end{pmatrix} = \begin{pmatrix} w^{12} \\ w^{22} \end{pmatrix} = \begin{pmatrix} \alpha^{\mathrm{IN}}G^{\mathrm{IN}} \\ \alpha^{\mathrm{EX}}G^{\mathrm{EX}} \end{pmatrix} \tag{14}$$

[11] Provided G^{IN} and G^{EX} are taken in appropriate intervals (Table 1).

From those numerical experiments, the potential of the neurone can be written down explicitly as a function f_1 of the state of activity of the network:

$$\vec{h}_i = \begin{pmatrix} h^1_i \\ h^2_i \end{pmatrix} = \begin{pmatrix} g^{\mathrm{IN}}_I \max \\ g^{\mathrm{EX}}_I \max \end{pmatrix} = \sum_{j=1}^{N} w_{ij}\vec{s}_j + \vec{R}_i = \sum_{j=1}^{N} \begin{pmatrix} G^{\mathrm{IN}}_{ij} & \alpha^{\mathrm{IN}}G^{\mathrm{IN}}_{ij} \\ G^{\mathrm{EX}}_{ij} & \alpha^{\mathrm{EX}}G^{\mathrm{EX}}_{ij} \end{pmatrix} \begin{pmatrix} x^s_j \\ y^s_j \end{pmatrix} + \begin{pmatrix} R^1_i \\ R^2_i \end{pmatrix} \tag{15}$$

with $\begin{pmatrix} x^A \\ y^A \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$, $\begin{pmatrix} x^B \\ y^B \end{pmatrix} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$ and $\begin{pmatrix} x^C \\ y^C \end{pmatrix} = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$. Eq. (15) describes *the relation between the formal multidimensional synapse W_{ij} and the synaptic weights* of the inhibitory and excitatory connections, given the formal definition of states *A*, *B* and *C*.

5. Generalisation of multidimensional synapses to multisynaptic contacts

The above analysis can be generalized in two respects: one can consider that the neurone exhibits K different states, and that there are L synaptic contact *types* between two neurones.[12] We *define* the potential $\vec{h}$, as being a vector whose length is L, with each of its components corresponding to the maximal conductance of a synaptic type.

Numerical experiments with such a neurone allow, in principle,[13] a mapping of the K states of the post-synaptic neurone as a function of the L values of the maximal synaptic conductances. If the boundaries between regions are linear, i.e. hyperplanes of maximal dimensions $L-1$, function f_2 is simply defined by inequalities as in Eq. (7).

Let us assign to the K states, E^0, $E^1 \ldots$, E^{K-1}, the following components in a $K-1$-dimensional space: the mth component of state E^k is $e^k_m = \delta_{mk}$, where δ_{mk} is the Kronecker symbol and $m \in \{1, \ldots K-1\}$, $k \in \{0, \ldots K-1\}$, which means that all the components of E^0 are zero (silent state), and the only non-zero component of E^k is $e^k_k = 1$. In such a case, W_{ij} is a $L \times (K-1)$ multidimensional synapse whose general term is given in Eq. (16)

$$w^{kl}_{ij} = \alpha^l_k G^l_{ij} \qquad k \in \{1, \ldots, K-1\}, l \in \{1, \ldots, L\} \tag{16}$$

where $\alpha^l_1 = 1\, \forall l$, and $\alpha^l_k = k \in \{2, \ldots, K-1\}$ is the ratio of the maximal conductance measured at synapse type l when the presynaptic neurone is in state k and the maximal conductance of that synapse when the presynaptic neurone is in state 1 (which is, by definition, the weight of the synapse). In other words, each term of the W_{ij} multidimensional synapse is a *synaptic weight*, weighted itself by the influence of the state of the presynaptic neurone on this synapse.

[12] By a "synaptic contact type", we mean a synapse characterised by its *effect* (excitatory or inhibitory), its *dynamics* (time constant of an alpha function for instance) and *its location with respect to the soma of the post-synaptic neurone*. Several contacts of the same type simply sum up their weights.

[13] At least, it is possible theoretically, and practically, if L is not too large to get a map of the states as a function of the maximal synaptic conductances.

6. Conclusion

In an effort towards more insightful mathematical modeling of neurones and networks, discrete-time multistate formal neurones and multidimensional synapses have been defined. The purpose of that approach is to gain biological plausibility while retaining the mathematical simplicity of McCP neurones; that is especially useful when attempting to solve inverse problems, i.e. to infer quantitative hypotheses on the network and its structure from the observation of the activity of a fraction of its neurones.

The multiple states of a neurone can be defined in many different ways: in the present paper, we considered three-state neurones, whose states were "silent", "one spike per time bin" and "two spikes per time bin". Other state definitions can be investigated.

In that framework, the potential of a K-state neurone is a vector in $(K-1)$-dimensional space, which is obtained as a linear transformation, defined by the multidimensional synapses, of the state vector of the neurone; therefore, a synapse between two neurones is no longer defined by a scalar (its efficacy), but by a matrix (hence the term "multidimensional synapse"). That makes modeling very flexible; for instance, the existence of multiple synapses between two given neurones can be taken into account in a model: different types of neurotransmitter, different effects (excitatory or inhibitory) and different locations in the dendritic tree.

As an illustration, we have shown how states and potentials can be defined in that framework, from simulations of "realistic" (HH) neurones; they can be defined similarly from experimental measurements, provided the values of the relevant quantities are available. We have shown how the potential can be derived once the states are defined: in the example addressed in the present paper, the formal potential is defined as the vector of the maximum synaptic conductances. Thus, the results reported here can be expected to open the way to more biologically plausible approaches, within the framework of discrete-time modeling with analytically tractable model neurones.

Appendix A

We show that the state of a K-state neurone can be represented as one among K vectors in $K-1$ dimen-

sional space is equivalent to a one-out-of-K representation in K-dimensional space.

Consider a K-state system described by one vector out of K linearly independent vectors $X_1, \boldsymbol{X}_2, \ldots, \boldsymbol{X}_{\boldsymbol{K}}$. In K-dimensional affine space, the equation of a hyperplane can be written as:

$$\boldsymbol{n}\boldsymbol{X} + 1 = 0,$$

where $\boldsymbol{n}$ is a vector normal to the hyperplane.

If the end points of vectors $\boldsymbol{X}_1, \boldsymbol{X}_2, \ldots, \boldsymbol{X}_{\boldsymbol{K}}$, belong to that hyperplane, then the following set of K linear equations hold:

$$\boldsymbol{n}\boldsymbol{X}_1 = \boldsymbol{n} \cdot \boldsymbol{X}_2 = \cdots = \boldsymbol{n}\boldsymbol{X}_{\boldsymbol{k}} = -1$$

The solution of that set of equations, i.e. the K components of vector n, exists since vectors X_i are assumed to be linearly independent. The orthogonal projection of $\boldsymbol{Y}_i$ of $\boldsymbol{X}_i$ onto the hyperplane is given by: $Y_i = X_i - \frac{X_i n}{\|n\|}\frac{n}{\|n\|} = X_i + \frac{n}{\|n\|^2}$.

Example 1. The state of a two-state system can be represented in two-dimensional state by one of the vectors:

$$\boldsymbol{X}_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} 0 \\ 1 \end{pmatrix}$$

Then

$$\boldsymbol{n} = \begin{pmatrix} -1 \\ -1 \end{pmatrix}, \boldsymbol{Y}_1 = \begin{pmatrix} 1/2 \\ -1/2 \end{pmatrix} \quad \text{and} \quad \boldsymbol{Y}_2 = \begin{pmatrix} -1/2 \\ +1/2 \end{pmatrix}$$

Since $\boldsymbol{Y}_1$ and $\boldsymbol{Y}_2$ are collinear and opposite, the state of the system can represented in one-dimensional space as one of two scalars, e.g. +1 and −1, as usual in a McCP neurone.

Example 2. The state of a three-state system can be represented in three-dimensional space by one of the vectors:

$$\boldsymbol{X}_1 = \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix}, \boldsymbol{X}_2 = \begin{pmatrix} 0 \\ 1 \\ 0 \end{pmatrix}, \quad \text{and} \quad \boldsymbol{X}_3 = \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix}.$$

Then

$$\boldsymbol{n} = \begin{pmatrix} -1 \\ -1 \\ -1 \end{pmatrix}, \boldsymbol{Y}_1 = \begin{pmatrix} 2/3 \\ -1/3 \\ -1/3 \end{pmatrix},$$

$$\boldsymbol{Y}_2 = \begin{pmatrix} -1/3 \\ 2/3 \\ -1/3 \end{pmatrix} \quad \text{and} \quad \boldsymbol{Y}_3 = \begin{pmatrix} -1/3 \\ -1/3 \\ 2/3 \end{pmatrix}.$$

The three vectors have the same module and sum to zero, hence define a two-dimensional subspace and have angular separations of $2\pi/3$ radians.

Appendix B

Hodgkin–Huxley neurones constructed with NEURON

Geometry		
Soma	Diameter	30 μm
	Length	30 μm
	Surface area	2826 μm^2
Dendrite	Diameter	2 μm
	Length	100 μm
	Surface area	628 μm^2

Biophysics	Soma	Dendrite
Membrane conductance (pas) 1/Rm (S/cm^2)	0.0003	0.0001
Axial Resistance (Ra) ohm cm	30	30
Membrane capacitance Cm (μF/cm^2)	1	1
Resting potential (mV)	−59	−70

Ionic conductances

Na^+

Equilibrium potential = 45 (mV)

Maximal conductance (g_{max}) = 0.34 (uS)

K^+

Equilibrium potential = −70 (mV)

Maximal conductance (g_{max}) = 0.1 (uS)

Ca^+

Equilibrium potential = 120 (mV)

Maximal conductance (g_{max}) = 0.0002 (uS)

T-type (low-threshold) calcium current and intracellular calcium dynamics were used according to modelled mechanisms from NEURON (Destexhe et al., 1998)

Synpases (alpha function)	Excitatory synapse	Inhibitory synapses
Equilibrium Potentiel (e) (mV)	45	−90
Maximal Conductance (g_{max}) (uS)	0.0055	0.0022
Time constant (tau) (ms)	2	20

References

Chavas, J., Marty, A., 2003. Coexistence of excitatory and inhibitory GABA synapses in the cerebellar interneuron network. J. Neurosci. 23, 2019–2031.

Destexhe, A., Neubig, M., Ulrich, D., Huguenard, J.R., 1998. Dendritic low-threshold calcium currents in thalamic relay cells. J. Neurosci. 18, 3574–3588.

Gutfreund, H., Reger, J.D., Young, A.P., 1988. The nature of attractors in an asymmetric spin glass with deterministic dynamics. J. Phys. A Math. Gen. 21, 2775–2797.

Kanter, I., 1988. Potts-glass models of neural networks. Phys. Rev. A 37, 2739–2742.

Kliper, O., Horn, D., Quenet, B., 2003. Analysis of Spatio-temporal Patterns in a Model of Olfaction. Neurocomputing 58–60, 1027–1032.

Wehr, M., Laurent, G., 1994. Odor encoding by temporal sequences of firing in oscillating neural assemblies. Nature 384, 162–166.

Mainen, Z.F., Sejnowski, T.J., 1996. Inluence of dendritic structure in firing pattern in model neocortical neurons. Nature 382, 363–366.

McCulloch, W.S., Pitts, W., 1943. A logical calculus of the ideas immanent in nervous activity. Bull. Math. Biophys. 5, 115–133.

Quenet, B., Horn, D., Dreyfus, G., Dubois, R., 2000. Temporal coding in an olfactory oscillatory model. Neurocomputing 38–40, 831–836.

Quenet, B., Sirapian, S., Dubois, R., Dreyfus, G., Horn, D., 2002. Modeling spatio-temporal olfactory data in two steps: from binary to HH neurons. Biosystems 67, 203–211.

Quenet, B., Horn, D., 2003. The dynamic neural filter: a binary model of spatio-temporal coding. Neural Comput. 15, 309–329.

Santamaria, F., Jaeger, D., De Schutter, E., Bower, J.M., 2002. Modulatory effects of parallel fiber and molecular layer interneuron synaptic activity on Purkinje cell responses to ascending segment input: a modeling study. J. Comput. Neurosci. 13, 217–235.

Silverman, D.J., Shaw, G.L., Pearson, J.C., 1986. Associative recall properties of the trion model of cortical organization. Biol. Cybern. 53, 259.

Wu, F.Y., 1982. The potts model. Rev. Mod. Phys. 54, 235–268.