Energy efficiency of information transmission by electrically coupled neurons

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Abstract

The generation of spikes by neurons is energetically a costly process. This paper studies the consumption of energy and the information entropy in the signalling activity of a model neuron both when it is supposed isolated and when it is coupled to another neuron by an electrical synapse. The neuron has been modelled by a four dimensional Hindmarsh-Rose type kinetic model for which an energy function has been deduced. For the isolated neuron values of energy consumption and information entropy at different signalling regimes have been computed. For two neurons coupled by a gap junction we have analyzed the roles of the membrane and synapse in the contribution of the energy that is required for their organized signalling. Computational results are provided for cases of identical and nonidentical neurons coupled by unidirectional and bidirectional gap junctions. One relevant result is that

there are values of the coupling strength at which the organized signalling of two

neurons induced by the gap junction takes place at relatively low values of energy

consumption and the ratio of mutual information to energy consumption is relatively

high. Therefore, communicating at these coupling values could be energetically the

most efficient option.

Key words:

neurons, coding energy, mutual information energy

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1 Introduction

The relation between cerebral energy consumption and neuronal activity was

first suggested by Roy and Sherrington (Sherrington 1890). A neuron transmits

information by depolarizing and repolarizing its membrane to generate action

potentials, what requires energy obtained from ATP produced from glucose

in the mitochondria. The rate of ATP generation depends on multiple factors

and if any of them causes the replenishment of ATP supplies not be enough to

satisfy the demand from the neuron its refractory period will increase and the

information will be altered. The generation of actions potentials, or spikes, is

metabolically costly with energy demands tightly coupled to spiking frequency

(Lennie 2003, Smith et al. 2002) what makes the metabolic energy required

to maintain neural activity in a global scale very high (Clarke & L.Sokoloff

1999, Attwell & Laughlin 2001, Laughlin 2001, Siekevitz 2004). In humans,

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for instance, the brain has only 2% of the body mass and consumes 20% of the human metabolic energy (Clarke & L.Sokoloff 1999) being a large fraction of this total energy expended in the generation of the firing sequences of action potentials that neurons use to represent and transmit information (Attwell & Laughlin 2001). The demand of energy to generate these sequences of action potentials is so high that energy supply seems to be a real constraint for neural coding (Laughlin 2001) and, it has been suggested that nature, searching a compromise between energy consumption and representational capacity, might have developed energy efficient codes, that is, codes that maximize the ratio of representational capacity to energy expended (Levy & Baxter 1996, 2002, Schreiber et al. 2002). For instance, in the early visual system energy efficient coding could be a real biologically-based justification for sparse coding in the cortex and retinal ganglion cells (Vincent et al. 2005).

This paper approaches the problem of whether biological computation optimizes energy use in the way neurons communicate. The evaluation of the energy efficiency of the transmission requires both, calculation of the amount of information transmitted and calculation of the energy cost of the transmission. Quantitative mathematical models have proved to be an indispensable tool in pursuing the goal of understanding neuron dynamics (Herz et al. 2006) and the study of models showing the irregular spike bursting characteristic of real neurons (Hodgkin & Huxley 1952, FitzHugh 1961, Hindmarsh & Rose 1984, Rose & Hindmarsh 1985) has received much attention (Rulkov 2001, Monte et al. 2003, Ivanchenko et al. 2004, Venaille et al. 2005, Abarbanel et al. 1996, Huerta et al. 1997, Rosenblum & Pikovsky 2004, I. Belykh & Hasler 2005, Hayashi & Ishizuka 1991, Lago-Fernandez et al. 2000, Yoshioka 200, Hasegawa E 70, 066107 2004, Nagai et al. 2005). As these models are kinetic models

with no energy considerations, it could be of interest to further develop them in such a way that they could be used to study the relation between the dynamical properties of a neuron and its energy implications. In Refs. (Torrealdea et al. 2006, 2007) we deduced for a three dimensional Hindmarsh-Rose neuron (Hindmarsh & Rose 1984, Rose & Hindmarsh 1985) a function of its variables and parameters that can be associated to the neuron as a real electrical energy. This energy function was used to evaluate the energy consumption of the neuron during its signalling activity. Our procedure to find a physical energy compatible with the dynamics of a dynamical system described by differential equations can be used to associate energies to many of the generally used models of neurons. Simple models with polynomial derivatives such as FitzHugh-Nagumo or Hindmarsh-Rose models are particularly apposite to associate to them an electrical energy function. Most of these models have been inspired in the work of Hodkking and Huxley but they do not conserve the clear physical meaning of the original work making it difficult to associate to them a physical energy. It is precisely here where our method can help. In this paper we deduce an energy function for a four dimensional Hindmarsh-Rose model. It is remarkable that this four dimensional energy turns out to be a natural extension of the one we found for the three dimensional case, what enhances the confidence in our result.

Energy efficient information transmission from the point of view that inputs are optimally encoded into Boltzmann distributed output signals has been analyzed in (Balasubramanian et al. 2001). An open question is the determination of the energy cost of generating the spike trains that codify each of the different output symbols. Our approach could provide a way to determine the energy cost of the generation of these spike trains.

Most of the cells in the nervous system are interneurons, that is, neurons that communicate only to other neurons and provide connection between sensory and motor neurons. Signals are transferred from one neuron to another through synaptic junctions which can be chemical or electrical. The rate of information transmitted between two neurons can be quantified calculating the mutual information between the corresponding trains of spikes of the presynaptic and postsynaptic neurons (Rieke et al. 1999). Electrical synapses are considered to be frequent and, it is believed, that they provide a flexible mechanism for modifying the behavior of an oscillatory neural network (Connors & Long 2004, Kepler et al. 1990). Most of the electrical synapses are formed by gap junctions between neurons of the same type, homologous gap junctions. Heterologous gap junctions are less frequent (Galarreta & Hestrin 2001). In this paper we analyze model neurons of the same type and we refer to two neurons as identical when they share the same set of parameter values and as nonidentical when they differ in the value of some parameter.

A neuron responds to income signals from other neurons with changes in its firing regime that modify its information capacity as well as its average energy consumption. A natural way to propagate information through a channel of neurons could be via partial or total synchronization of the postsynaptic neuron to the signalling pattern it receives from its presynaptic neighbor. For instance, electrical synapses between AII amacrine cells and ON-cone bipolar cells are considered essential for the flow of visual signals in the retina (Kolb & Flamiglietti 1974) and temporally precise synchronization between them of subthreshold membrane potential fluctuations has been demonstrated (Veruki & Hartveit 2002b). The degree of synchronization reached by the neurons conditions their capacity to transmit information and the energy con-

sumption of their signalling activity. As the degree of synchronization is highly dependent on the coupling some coupling conditions may be more favorable than others for an energetically efficient transmission of signals. In this work we investigate how this efficiency depends on the type of coupling, unidirectional and bidirectional, and on the values of the coupling strength when both neurons are coupled electrically. We also investigate the role of the electrical junction in the provision of the energy that the neurons require to maintain their synchronized regime.

In Sec. 2 we summarize a procedure to find an energy function that quantifies the physical energy associated to the states of a generic model neuron described by differential equations. This function can be used to quantify the consumption of energy of the neuron in its different possible signalling regimes. We also discuss the balance of energy when two generic neurons are coupled electrically and quantify the contribution of the synapse to the total energy required for both neurons to maintain the synchronized signalling activity. This discussion is particularized to the case of a four dimensional Hindmarsh-Rose model of thalamic neurons for which analytical expressions of energy consumption and synapse contribution are given. In Sec. 3 we present some considerations relative to the way we have computed the information entropy and the mutual information of two electrically coupled neurons. In Sec. 4 we present computational results. Firstly, results are given for the information entropy rate and energy consumption of the different patterns of spike trains that are generated by an isolated neuron at different values of the applied external current. Secondly, results are given for two neurons coupled electrically. Four cases have been studied. Identical and nonidentical neurons coupled with unidirectional coupling and with bidirectional symmetrical coupling. For each studied case results of mutual information rates, energy consumption, ratios of mutual information to energy consumption, and relative weight of the synapse contribution of energy are presented and discussed. Finally in Sec. 4 we give a brief summary and present our conclusions.

2 Energy considerations

In this section we quantify the energy required by a model neuron to maintain its signalling activity. We analyze the energy requirements when the neuron acts as an isolated oscillator and also the energy aspects linked to the synaptic junction when two neurons are electrically coupled. In order to quantify theoretically the energy consumption of a model neuron we require an analytical expression of the energy of the neuron in its different possible states. In Ref. (Sarasola et al. 2004) we described how to associate to a chaotic system a function of its dynamical variables that can be formally considered a real physical energy of the system. By real physical energy we mean that if a set of kinetic equations is considered a good model for the dynamical behavior of, for instance, a thalamic neuron, then we must consistently consider the energy associated to it a good model for the energy implications of that dynamical behavior. We have tested the procedure with many electrical and mechanical systems always obtaining the correct energy. In (Sarasola et al. 2004) an example is given for an oscillatory electric circuit. In the following section we very quickly summarize the procedure described in Ref. (Sarasola et al. 2004) which can be used to find an energy function for a model neuron.

2.1 Energy function associated to a model neuron

Let us consider an oscillatory autonomous dynamical system represented by $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$, where $\mathbf{x} \in \mathbb{R}^n$ and $\mathbf{f} : \mathbb{R}^n \to \mathbb{R}^n$ is a smooth function, as the mathematical model of a generic neuron. The velocity vector field $\mathbf{f}(\mathbf{x})$ can be expressed as sum of two vector fields $\mathbf{f}(\mathbf{x}) = \mathbf{f}_c(\mathbf{x}) + \mathbf{f}_d(\mathbf{x})$, one of them, $\mathbf{f}_c(\mathbf{x})$, conservative containing the full rotation and the other, $\mathbf{f}_d(\mathbf{x})$, dissipative containing the divergence (Donald 1986). Taking the conservative vector field, the equation

$$\nabla H^T \mathbf{f}_c(\mathbf{x}) = 0, \tag{1}$$

where ∇H^T denotes the transpose gradient of function H, defines a partial differential equation from which a function $H(\mathbf{x})$ can be evaluated. This function $H(\mathbf{x})$ is a generalized Hamiltonian for the conservative part $\dot{\mathbf{x}} = \mathbf{f}_c(\mathbf{x})$ as long as it can be rewritten in the form $\dot{\mathbf{x}} = J(\mathbf{x})\nabla H$ where J is a skew symmetric matrix that satisfy Jacobi's closure condition (Olver 1993, Morrison 1998). If that is the case, we consider $H(\mathbf{x})$ as an energy associated to the original system $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$. This energy is dissipated, passively or actively, due to the dissipative component of the velocity vector field according to the equation,

$$\dot{H} = \nabla H^T \mathbf{f}_d(\mathbf{x}). \tag{2}$$

In Ref. (Torrealdea et al. 2006) we used this procedure to find an energy function for the well-known three variable Hinmarsh-Rose thalamic model of a neuron. In the last part of this section we apply the same procedure to find and energy function for the four dimensional version of the model that was introduced by Pinto et al. in Ref. (Pinto et al. 2000). This energy function is used to evaluate the energy consumption of the neuron in isolation and also

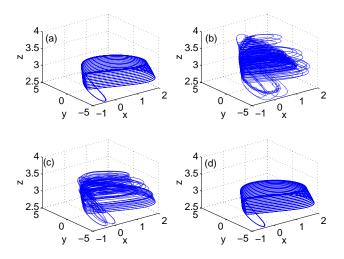


Fig. 1. Projection on the x, y, z axes of the attractor of a postsynaptic four dimensional Hindmarsh-Rose neuron forced by an electrical unidirectional synapse, Eqs. 15, to follow another identical neuron. Values of the coupling strength (a) k = 0, (b) k = 0.25, (c) k = 0.7, (d) k = 1. when it is connected to other neurons through electrical synapses. It provides the basis for all the computational results presented in this work.

2.2 Electrically coupled neurons. Energy contribution from the synapse

In this section we analyze the balance of energy required to maintain the signalling activity of two model neurons coupled by an electrical synapse. Let us consider the oscillating neurons $\dot{\mathbf{x}}_1 = \mathbf{f}_1(\mathbf{x}_1)$ and $\dot{\mathbf{x}}_2 = \mathbf{f}_2(\mathbf{x}_2)$ coupled electrically according to the scheme,

$$\dot{\mathbf{x}}_1 = \mathbf{f}_1(\mathbf{x}_1) + \mathbf{K}_1(\mathbf{x}_2 - \mathbf{x}_1)$$

$$\dot{\mathbf{x}}_2 = \mathbf{f}_2(\mathbf{x}_2) + \mathbf{K}_2(\mathbf{x}_1 - \mathbf{x}_2),$$
(3)

where $\mathbf{f}_1, \mathbf{f}_2 : \mathbb{R}^n \to \mathbb{R}^n$ are smooth functions, $\mathbf{K}_1, \mathbf{K}_2 \in \mathbb{R}^n \times \mathbb{R}^n$ are diagonal matrices representing the coupling strength with entries $k_1^i, k_2^i \geq 0$

i=1,...n, and $\mathbf{x}_1, \mathbf{x}_2 \in \Re^n$ indicate the state of the coupled neurons. Note that the terms $\mathbf{K}_1(\mathbf{x}_2 - \mathbf{x}_1)$ and $\mathbf{K}_2(\mathbf{x}_1 - \mathbf{x}_2)$ represent the gap junction that connects both neurons. These two terms, taken together, represent a potentially bidirectional electrical junction with selective ion channels of different conductances depending on the coupling matrices \mathbf{K}_1 and \mathbf{K}_2 .

The signalling activity of a neuron consists of the generation of action potentials with different patterns of repetitive firing or bursting. This oscillatory behavior, when represented in the phase space, makes the temporal evolution of the neuron remain confined to an attractive region which is characteristic of its dynamics. When two neurons are coupled their respective dynamics change although still remaining confined to attractive regions in the phase space, see Fig. 1 for the particular case analyzed in Section 2.3.2 of the paper. The nature of the coupled oscillatory regime of each neuron depends on the particular values of the coupling matrices \mathbf{K}_1 and \mathbf{K}_2 . As the temporal trajectory $\mathbf{x}_1(t)$ remains confined to an attractive region of the phase space, the long term net average energy variation along that trajectory of the system $\dot{\mathbf{x}}_1 = \mathbf{f}_1(\mathbf{x}_1) + \mathbf{K}_1(\mathbf{x}_2 - \mathbf{x}_1)$, neuron and synapse, is zero. That is,

$$\langle \nabla H_{f_1}^T \mathbf{f}_1(\mathbf{x}_1) \rangle + \langle \nabla H_{f_1}^T \mathbf{K}_1(\mathbf{x}_2 - \mathbf{x}_1) \rangle = 0, \tag{4}$$

where the brackets represent averaging on the attractor and $\nabla H_{f_1}^T$ denotes the transpose gradient of the energy function of the neuron $\dot{\mathbf{x}}_1 = \mathbf{f}_1(\mathbf{x}_1)$. The same argument applies to system $\dot{\mathbf{x}}_2 = \mathbf{f}_2(\mathbf{x}_2) + \mathbf{K}_2(\mathbf{x}_1 - \mathbf{x}_2)$.

The first term of Eq. (4) can be associated with the variation of the energy of the first neuron through its membrane and the second term with the variation of its energy through the synapse. Thus, for each of the coupled neurons, i = 1, 2, the following balance of energy applies on average,

$$\langle \dot{H} \rangle_m^i + \langle \dot{H} \rangle_s^i = 0, \tag{5}$$

where $\langle \dot{H} \rangle_m^i$ and $\langle \dot{H} \rangle_s^i$ stands for the average energy variation of neuron *i* through its membrane and synapse respectively.

According to Eq. (4), if $\mathbf{K}_1 = 0$, the average energy variation of the energy of neuron one through its membrane is zero, $\langle \dot{H} \rangle_m^1 = 0$. The same applies to neuron two if $\mathbf{K}_2 = 0$. In other words, if a neuron does not receive signals from any other neuron the energy it obtains through the membrane, $\langle \dot{H}^+ \rangle_m^i$, is perfectly balanced by its dissipation of energy through the membrane, $\langle \dot{H}^- \rangle_m^i$. Nevertheless, according to Eq. (5), if a neuron is signalling forced by signals arriving from another neuron through a gap junction, it is the global average, membrane plus synapse, what is zero. The average variation of energy through the membrane is no longer zero. Therefore, when two neurons are coupled a contribution of energy from the synapse is required to maintain their cooperative behavior. This fact is a consequence of the forced oscillatory regime induced by the synapse and it is to be expected that the relative weight of the contribution of energy from the synapse to the energy balance of the coupled neuron be dependent on the strength of the synapse itself.

For each of the neurons, i = 1, 2, Eq. [5] can be rewritten as,

$$\langle \dot{H}^{+}\rangle_{m}^{i} = -\langle \dot{H}^{-}\rangle_{m}^{i} - \langle \dot{H}\rangle_{s}^{i}, \tag{6}$$

where $\langle \dot{H}^{+}\rangle_{m}^{i}$ stands for the average of the positive part of the energy derivative, i.e., the energy income rate through the membrane, and $\langle \dot{H}^{-}\rangle_{m}^{i}$ for the average of the negative part of the energy derivative, i.e., the energy dissipation rate through the membrane. Equation [6] emphasizes the fact that the

total average income of energy through the membrane of the neuron equals its dissipation trough the membrane plus a net flow of energy in the synapse. From Eq. [6] the relative weight, Sw, of the contribution of the synapse to the total energy income would be,

$$Sw = \frac{\langle \dot{H} \rangle_s^i}{\langle \dot{H}^i \rangle_m^i}.$$
 (7)

This expression will be used later on in the paper to quantify the relative contribution of the synapse in the different coupling conditions studied in this work.

For the particular case of identical neurons and bidirectional gap junctions $\mathbf{f}_1 \equiv \mathbf{f}_2 = \mathbf{f}$ and $\mathbf{K}_1 \equiv \mathbf{K}_2 = \mathbf{K}$, the total average energy variation of neurons one and two in the synapse is,

$$\langle \dot{H} \rangle_s = \langle \dot{H} \rangle_c^1 + \langle \dot{H} \rangle_c^2, \tag{8}$$

where

$$\langle \dot{H} \rangle_s^i = \langle \nabla H_f(\mathbf{x}_i)^T \mathbf{K} (\mathbf{x}_j - \mathbf{x}_i) \rangle,$$
 (9)

with i, j = 1, 2; $i \neq j$. Equations (9) are symmetrical with respect to an exchange of variables \mathbf{x}_i and \mathbf{x}_j and as both neurons are identical and undistinguishable $\langle \dot{H} \rangle_s^1$ and $\langle \dot{H} \rangle_s^2$ must be equal and, therefore, the total energy variation in the synapse is $2 \langle \nabla H_f^T \mathbf{K}(\mathbf{x}_j - \mathbf{x}_i) \rangle$. On the other hand, as both neurons are identical and the gap junction bidirectional and symmetrical, they are energetically identical with relation to the synapse and, on average, there cannot be any net flow of energy from one neuron to the other through the synapse. As the net average energy variation at the synapse site is not zero the gap junction itself must act as a source or sink of energy for both neurons.

Note that the degree of synchronization reached, measured in terms of the norm of the error vector $\mathbf{e} = \|\mathbf{x}_j - \mathbf{x}_i\|$, will condition the magnitude of this contribution of energy. If the two neurons are identical, and the strength of the coupling large enough, the synchronization error goes to zero and, therefore, signalling transmission between identical neurons in complete synchrony occurs with no energy contribution on average from the synaptic junction.

2.3 The four dimensional Hindmarsh-Rose neuron

The Hindmarsh-Rose model of a thalamic neuron (Hindmarsh & Rose 1984, Rose & Hindmarsh 1985) is a qualitative three dimensional model which is widely used in the study of neuron dynamics because it can produce several modes of spiking-bursting activity, including a regime of chaos, that appear similar to those seen in biological neurons. The model, although qualitative, is not unrealistic. Rose and Hindmarsh in a series of papers (Rose & Hindmarsh 1989a,b,c) showed how a Hodking-Huxley like model, based on ionic currents that can be related to experimental recordings, is derived from it. However its parameter space for chaotic behavior is much more restricted than what is observed in real neurons (Selverston et al. 2000, Pinto et al. 2000). The chaotic behavior is greatly expanded by incorporation of a fourth slow variable that increases the realism of the description of slow Calcium currents. This four dimensional model produces simulations of intracellular activity which are even more similar to the biological observations (Selverston et al. 2000, Pinto et al. 2000). In this paper we represent a single neuron by the four dimensional extension of the original Hindmarsh-Rose model which is described by the following equations of movement:

$$\dot{x} = ay + bx^2 - cx^3 - dz + \xi I,$$

$$\dot{y} = e - fx^2 - y - gw,$$

$$\dot{z} = m(-z + s(x + h)),$$

$$\dot{w} = n(-kw + r(y + l)).$$
(10)

In the model variable x is a voltage associated to the membrane potential, variable y although in principle associated to a recovery current of fast ions has been transformed into a voltage, and variable z is a slow adaptation current associated to slow ions. These three first equations constitute the standard three dimensional model. Variable w represents an even slower process than variable z and was introduced because a slow process such as the calcium exchange between intracellular stores and the cytoplasm was found to be required to fully reproduce the observed chaotic oscillations of isolated neurons from the stomatogastric ganglion of the California spiny lobster Panulirus interruptus (Pinto et al. 2000). Parameter I is a external current input. The time variable of the model is dimensionless. For the numerical results of this work we fix the parameters to the values a = 1, $b = 3.0 \, (mV)^{-1}$, $c = 1 \, (mV)^{-2}$, $d = 0.99 \, M\Omega$, $\xi = 1 \,\mathrm{M}\Omega, \; \mathrm{e} = 1.01 \,\mathrm{mV}, \; \mathrm{f} = 5.0128 \,(\mathrm{mV})^{-1}, \; \mathrm{g} = 0.0278 \,\mathrm{M}\Omega, \; \mathrm{m} = 0.00215,$ $s = 3.966\,\mu\text{S},\, h = 1.605\,\text{mV},\, n = 0.0009,\, k = 0.9573,\, r = 3.0\,\mu\text{S},\, l = 1.619\,\text{mV}.$ These numerical values refer to cm² and are the same that have been used in Ref. (Pinto et al. 2000). Both the three dimensional and four dimensional models have regions of chaotic behavior, but the four dimensional model has much larger regions in parameter space where chaos occurs (Pinto et al. 2000).

2.3.1 Energy consumption when signalling in isolation

In the Hindmarsh-Rose model given by Eq. (10) the vector field $\mathbf{f}(\mathbf{x})$ can be expressed as sum of the following vector fields,

$$\mathbf{f}_{c}(\mathbf{x}) = \begin{pmatrix} ay - dz \\ -fx^{2} - gw \\ msx \end{pmatrix} \quad \text{and} \quad \mathbf{f}_{d}(\mathbf{x}) = \begin{pmatrix} bx^{2} - cx^{3} + \xi \mathbf{I} \\ e - y \\ msh - mz \\ nrl - nkw \end{pmatrix}. \tag{11}$$

As it can be observed $\mathbf{f}_c(\mathbf{x})$ is a divergence free vector that accounts for the whole rotor of the vector field $\mathbf{f}(\mathbf{x})$, and $\mathbf{f}_d(\mathbf{x})$ is a gradient vector that carries its whole divergence. Consequently, the energy function H(x, y, z, w) will obey the following partial differential equation,

$$(ay - dz)\frac{\partial H}{\partial x} - (fx^2 + gw)\frac{\partial H}{\partial y} + msx\frac{\partial H}{\partial z} + nry\frac{\partial H}{\partial w} = 0,$$
 (12)

which has the cubic polynomial solution

$$H(x, y, z, w) = \frac{p}{a} \left(\frac{2}{3} fx^3 + \frac{msd - gnr}{a} x^2 + ay^2 \right) + \frac{p}{a} \left(\frac{d}{ams} (msd - gnr) z^2 - 2dyz + 2gxw \right)$$

$$(13)$$

where p is a parameter. As in the model time is dimensionless and every adding term in Eq. (13) has dimensions of square voltage, function H is dimensionally consistent with a physical energy as long as parameter p has dimensions of conductance. In this paper we fix parameter p to the arbitrary value p = -1 S. The minus sign has been chosen to make consistent the outcome of the model with the usual assumption of a demand of energy associated with the

repolarization period of the membrane potential and also with its refractory period (see Fig. 2).

Note that if parameter g is set to zero the four dimensional system given by Eqs. (10) reduces itself to the standard three dimensional model, as variable w becomes uncoupled, and Eq. (13) reduces to,

$$H(x, y, z) = \frac{p}{a} \left(\frac{2}{3} fx^3 + \frac{msd}{a} x^2 + ay^2 + \frac{d^2}{a} z^2 - 2 dyz \right)$$

which is the expression for the energy of a three dimensional model that we reported in Ref. (Torrealdea et al. 2006).

It can be easily checked that the energy derivative $\dot{H} = \nabla H^T \mathbf{f}_d(\mathbf{x})$, that is,

$$\dot{H} = \frac{2p}{a} \begin{pmatrix} fx^2 + \frac{msd-gnr}{a}x + gw \\ ay - dz \\ \frac{d}{ams}(msd - gnr)z - dy \\ gx \end{pmatrix} \begin{pmatrix} bx^2 - cx^3 + \xi I \\ e - y \\ msh - mz \\ nrl - nkw \end{pmatrix}, (14)$$

is also dimensionally consistent with a dissipation of energy. As the states of an isolated Hindmarsh-Rose neuron are confined to an attractive manifold the range of possible values of its energy is recurrent and the long term average of its energy derivative is zero. However, it has to be considered that the average involves a global balance of energy. The model itself incorporates, in a non explicit way, components which are responsible of the energy consumption together with others which are the energy suppliers.

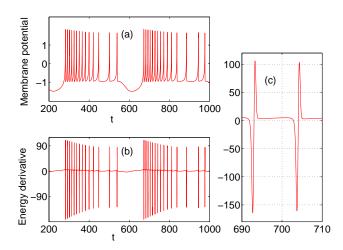


Fig. 2. (a) Action potentials and (b) energy derivative for the Hindmarsh-Rose model neuron. (c) Detail of the energy derivative associated to two spikes showing the dissipation of energy during the depolarization of the membrane potential (negative area) and its ulterior demand of energy during its repolarization period (positive area).

Figure 2(a) shows a series of action potentials (variable x in the model neuron) and Fig. 2(b) shows the energy derivative \dot{H} corresponding to that series. In Fig. 2(c) a detail of the energy derivative corresponding to a train of two action potentials is also shown. For each action potential it can be appreciated that the energy derivative is first negative, dissipation of energy while the membrane potential depolarizes during the rising period of the spike, and then positive, contribution of energy to repolarize the membrane potential during its descending period. During the refractory period between the two spikes the energy derivative remains slightly positive, still demanding energy, until the onset of the following action potential. To link the demand of energy to the repolarizing process is in agreement with the results about the energetics of neural activity in rat brain by Attwell and Laughlin (Attwell & Laughlin 2001) who found that, for spiking frequencies of 4 Hz, 15% of the energy is used to maintain resting membrane potentials in non firing epochs while the

remaining 85% is used to restabilize membrane potentials in firing epochs. We calculate the average energy consumption per unit time of the neuron, that is, the metabolic energy that has to be supplied to the neuron to maintain its activity, evaluating the long term average of the negative component of the energy derivative, that is the energy that is dissipated in the process of spike generation.

2.3.2 Two electrically coupled neurons

Let us consider two Hindmarsh-Rose neurons electrically coupled according to the following equations,

$$\dot{x}_{i} = a y_{i} + b x_{i}^{2} - c x_{i}^{3} - d z_{i} + \xi I_{i} + k_{i}(x_{j} - x_{i}),$$

$$\dot{y}_{i} = e - f x_{i}^{2} - y_{i} - g w_{i},$$

$$\dot{z}_{i} = m(-z_{i} + s(x_{i} + h)),$$

$$\dot{w}_{i} = n(-k w_{i} + r(y_{i} + l)),$$
(15)

where $k_i \geq 0$ is the coupling strength and i, j = 1, 2; $i \neq j$ are the indices for the neurons. Note that the coupling affects only to their respective first variables x_1 and x_2 . This kind of coupling between neurons has been very often reported (Pinto et al. 2000, Abarbanel et al. 1996, Huerta et al. 1997, Rosenblum & Pikovsky 2004, I. Belykh & Hasler 2005, Hansel & Sompolinsky 1992, Dhamala et al. 2004).

Considering the energy of a neuron given by Eq. (13) and also Eqs. (4) and (5) we have for the average energy variation through the membrane of neuron of index i,

$$\langle \dot{H} \rangle_{m}^{i} = \frac{2p}{a} \begin{pmatrix} f x_{i}^{2} + \frac{\text{msd-gnr}}{a} x_{i} + g w_{i} \\ a y_{i} - d z_{i} \\ \frac{d}{\text{ams}} (\text{msd-gnr}) z_{i} - d y_{i} \\ g x_{i} \end{pmatrix} \begin{pmatrix} b x_{i}^{2} - c x_{i}^{3} + \xi I_{i} \\ e - y_{i} \\ \text{msh-m} z_{i} \\ \text{nrl-nk} w_{i} \end{pmatrix}, \quad (16)$$

where i, j = 1, 2; $i \neq j$. As it has been said, the energy consumption of neuron i corresponds to the average of the negative component of this derivative.

The average energy variation at the synapse site of neuron i is given by,

$$\langle \dot{H} \rangle_s^i = \frac{2p}{a} \left(f x_i^2 + \frac{\text{msd-gnr}}{a} x_i \right) k_i (x_j - x_i),$$
 (17)

These equations are used in what follows in the different circumstances in which the computation of energy is required.

3 Information considerations

A neuron responds to changes in the applied external current and to inputs from other neurons with changes in its firing regime that modify its information capacity as well as its average energy consumption. Shannon's information theory (Shannon & Weaver 1949) provides a framework to quantify the amount of information that neurons can convey during its signaling activity. The first application of Shannons theory to estimate the information entropy of spike trains was due to MacKay and McCulloch (Mackay & McCulloch 1952). A comprehensive approach to understanding the information content of neural spikes, together with a review of some important contributions to

this area of research can be found in Ref. (Rieke et al. 1999).

The information entropy S of a discrete distribution of probability p_i is defined by $S = -\sum_i p_i log_2 p_i$. This entropy is usually contemplated as a measure of the average uncertainty of occurrence of events that have a probability of occurrence p_i . Although the information entropy of a discrete probability distribution is well defined, the situation is less clear when what is sought is the information entropy of a train of spikes emitted by a neuron. A long spike train emitted by a neuron can be observed as a succession of windows of spike trains of T ms length which are partitioned into bins of $\Delta \tau$ ms length each. The presence or absence of a spike inside one of these bins can be codified as 1 or 0 respectively, so that each window of spikes can be contemplated as a particular symbol from a binary alphabet of $2^{\frac{T}{\Delta \tau}}$ different symbols. We suppose $\Delta \tau$ small enough as to count no more than one spike per bin.

Let us suppose that two interneurons are coupled by an electrical synapse according to Eq. (15). Let T_1^i and T_2^i represent symbols of the grammar of the different possible symbols that can be coded with the spike trains of the presynaptic and postsynaptic neurons respectively. The information entropy rate S_j of neuron j = 1, 2 will be,

$$S_j = -\sum_i p(T_j^i) log_2 p(T_j^i). \tag{18}$$

The mutual information, I_m , between the spike trains of both neurons can be defined as

$$I_{m} = -\sum_{i} p(T_{2}^{i}) log_{2} p(T_{2}^{i})$$

$$+ \sum_{i} p(T_{1}^{j}) \sum_{i} p(T_{2}^{i}/T_{1}^{j}) log_{2} p(T_{2}^{i}/T_{1}^{j}),$$

$$(19)$$

that is, the entropy of the postsynaptic train minus the average of its condi-

tioned entropies. This formulation emphasizes the fact that the mutual information between the two trains of spikes can be contemplated as the reduction in entropy that would take place in the postsynaptic train if the presynaptic one was known.

According to (Nemenman et al. 2004), since the maximum likelihood estimate of the probabilities $p(T_i)$ is given by the frequencies, Eq. 18 provides an estimate of maximum likelihood of the real entropy. This estimator is biased and underestimates the entropy. With good sampling, $N \gg K$ with K possible neuron responses and N number of samples, the estimate deviates from the correct value in an additive error (K-1)/2N plus a term proportional to 1/N.

It has to be noted that the mean firing rate of a train of spikes conditions the probabilities of occurrence of the different symbols of the alphabet making their distribution not uniform on the set of bins. This fact reduces the variability of the signal and the actual value of entropy do not reach its maximum possible limit of $T/\Delta\tau$ bits per window. The maximum entropy rate that can be measured with time precision $\Delta\tau$ from a spike train of mean firing rate \bar{r} is given by (Rieke et al. 1999),

$$S_{max} = \frac{-\bar{r}\triangle\tau\log_2(\bar{r}\triangle\tau) - (1 - \bar{r}\triangle\tau)\log_2(1 - \bar{r}\triangle\tau)}{\triangle\tau}$$
 (20)

That is, the firing rate imposes a limit to the maximum entropy rate of a given signal. At a given mean firing rate the maximum entropy is reached when the presence or absence of spikes in a time bin $\Delta \tau$ is independent of all other time bins, that is, when there are no temporal correlations in the timing of the spikes. If in addition to the absence of temporal correlations the spike train is perfectly reproducible across repetition of the same stimulus,

that is, if there is no noise, this maximum entropy rate sets an upper limit on the information that can be transmitted at the observed spike rate which is termed coding capacity. The actual information transmitted by the spike train compared with its coding capacity provides a measure of the efficiency of the coding.

In this work we have performed a naive estimate (Strong et al. 1998) of the information entropy, generating successive windows of spikes of 25 ms length which are partitioned into 5 bins of 5 ms length each. The presence or absence of a spike inside one of these bins is codified as 1 or 0 respectively, so that each window of spikes represents a symbol from a binary alphabet of K=32different symbols. To estimate entropies in coupled neurons we have generated N = 10000 samples. According to Eq. 20 the maximum entropy rate that we could measure is S=5 bits per average 25 ms window in case we had a long spike train firing at 100 Hz mean rate and with no time correlations. In practice, for the cases of coupled neurons we have studied, the active leading neuron is activated with an external current I = 3.024 what makes the neuron fire at a mean firing rate $\bar{r} = 39$ Hz. At this firing rate, according to Eq. 20, the corresponding maximum entropy is $S_{max} = 3.65$. Using Eq. 18, we have estimated S=3.15 with an additive error (K-1)/2N=0.007. Thus, for the studied cases, windows of spike trains of T=25 ms partitioned into bins of $\Delta \tau = 5$ ms provide enough variability for the observed neuron responses as to obtain, with no significant error, an information entropy near to its maximum value.

Extrapolation of the windows to larger word length only imply very small corrections that have no incidence in our conclusions. On the other hand, the value of the information entropy rate that is obtained when calculating the

entropy of a given spike train is very dependent on the size of the time bin $\Delta \tau$ used for its calculation. The entropy increases as $\Delta \tau$ decreases illustrating the increasing capacity of the train to convey information by making use of the spike timing (Rieke et al. 1999). The value $\Delta \tau = 5$ ms used in this work corresponds to timing each spike to within 20 % percent of the typical interspike interval of the leading neuron which fires at a mean rate $\bar{r} = 39$ Hz. This value of time resolution and the window length used in this work are frequently used with empirical and simulated data. They are computationally appropriate and are used in Ref. (Koch et al. 2004) to explore retinal ganglion cells. Also in Ref. (Strong et al. 1998) similar values are used to analyze responses of a motion sensitive neuron in the fly visual system. For our purpose changing the time resolution $\Delta \tau$ supposes a scale change in the calculated amount of information transmitted between two coupled neurons at different values of their coupling gain and therefore has no effect on the form of the curves ratio of information to energy.

4 Computational results

In this section we present results firstly for the neuron considered as an isolated oscillator and secondly for two neurons coupled electrically. For the isolated neuron results of energy consumption and information entropy at different values of the applied external current I are analyzed. For neurons coupled electrically, unidirectional and bidirectional couplings have been studied for identical and nonidentical neurons and results relative to mutual information, energy consumption, information to energy ratio and synapse contribution of energy are given.

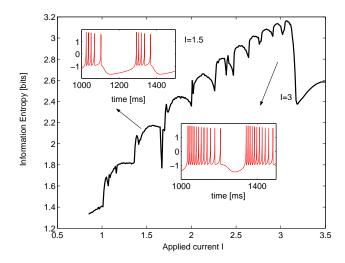


Fig. 3. Information entropy per 25 ms spike train of an isolated neuron at different values of the external applied current I. Computation has been performed generating 2000 spike trains of 25 ms at each value of the external current I. In the insets bursting regimes corresponding to $I = 1.5 \,\mathrm{nA}$ and $I = 3 \,\mathrm{nA}$.

4.1 Information entropy and energy consumption in the isolated neuron

To study the relationship between information entropy and energy consumption in the different possible oscillatory regimes of an isolated neuron we have computed its information entropy and average energy consumption at different values of the applied current I. To quantify the information capacity of the neuron in its different signalling regimes we have used Eq. (18). The computation has been performed generating 2000 different spike trains of $25\,ms$ length at every value of the external current. As it can be seen in Fig. 3, the information entropy increases in plateaus corresponding to progressively richer signalling activity. This is so because the bursting regime of the isolated neuron is very sensitive to its applied external current I. Increasing I gives rise to subsequent bursting regimes of an increasing number of spikes per burst (Pinto et al. 2000, Hansel & Sompolinsky 1992). The two insets to Fig. 3 show two examples of bursting regimes corresponding to $I = 1.5\,\mathrm{nA}$ and $I = 3\,\mathrm{nA}$.

Average energy consumption has been computed averaging over sufficiently large periods of time the negative part of the energy derivative given by Eq. (14). Results for consumption are displayed as positive, i.e. we define consumption as the absolute value of the energy dissipated. Figure 4 shows the results. The energy consumption of the neuron increases in steps with I, being very sensitive to the different firing regimes. The different plateaus correspond to the subsequent bursting regimes of increasing number of spikes per burst. Figure 4 also shows, in dots, the average number of spikes that the isolated neuron emits per unit length at different values of the applied current I. As it can be appreciated the energy consumption is more or less proportional to the average number of spikes per unit time. In the range of values of I between 2.5 nA and 3 nA the linearity is remarkable. A linear relation between energy consumption and frequency of spikes is what should be expected as energy consumption is basically linked to the generation of action potentials. This linear relation has been sometimes hypothesized in theoretical studies of energy efficiency in the signal transmission by neurons (Laughlin 2001, Levy & Baxter 1996, 2002). Our results show that this simple law does not apply exactly to every signalling regime in the isolated neuron and, as we show later on, it is not going to be followed when two neurons are coupled.

4.2 Two electrically coupled neurons

In this section we consider two neurons coupled electrically. We suppose that the presynaptic neuron always signals in a chaotic regime corresponding to a external current $I_1 = 3.024$. As we have seen, in this chaotic regime the neuron signals at its maximum information capacity. In the identical cases

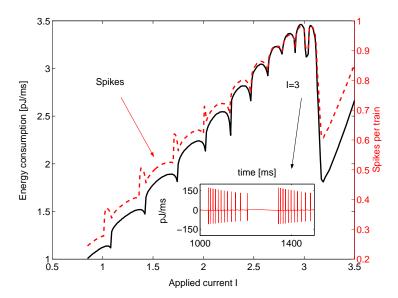


Fig. 4. Energy consumption rate, left vertical axis, and average number of spikes per train, right axis, of an isolated neuron at different values of the external applied current I. Computation has been performed generating 2000 spike trains of 25 ms at each value of the external current I. In the inset temporal energy derivative corresponding to $I = 3 \,\mathrm{nA}$.

the receiving neuron also signals at I = 3.024. For the nonidentical cases we have set the postsynaptic neuron close to its quiescent state at a low value, $I_2 = 0.85$, of its external current. We have analyzed the unidirectional case setting the gain parameters between both neurons as $k_1 = 0$, $k_2 = k$ and the bidirectional case setting $k_1 = k_2 = k$. Computation has been performed, in every case, generating 10000 different spike trains of $25 \, ms$ length at every value of the gain parameter k.

4.2.1 Mutual information

Using Eq. (19) and the coding explained before, we have computed the mutual information between the trains of spikes of the pre and postsynaptic neurons at different values of the coupling strengths k_1 and k_2 . The mutual infor-

mation between both neurons as well as the information entropy rate of the presynaptic and postsynaptic spike trains are shown in Fig. 5.

When the two neurons are identical, sufficiently large values of the coupling strength lead both neurons to complete synchronization and, therefore, to a noiseless channel where no loss of information takes place. For two identical neurons with unidirectional coupling results are displayed in Fig. 5(a). At k=1 the two neurons are completely synchronized and their mutual information reaches its maximum value that corresponds to the noiseless channel. The constant value of the entropy of the sending neuron serves as reference. The highest value measured for the entropy rate of the receiving neuron is 0.18 bits per second that corresponds to an entropy of 4.5 bits per average 25 ms train which is very near to the maximum possible entropy value, 5 bits per 25 ms train, that our procedure can detect. Figure 5(b) shows the mutual information rate between two identical neurons bidirectionally coupled and the information entropy rate of the sending and receiving neurons at different values of the coupling gain k. Due to the symmetry of the coupling the information entropy of both neurons is identical. At k = 0.5 the two neurons are completely synchronized and the mutual information reaches its maximum value that corresponds to the noiseless channel.

In practice actual channels are always noisy and neurons nonidentical and it is of practical interest to know about the efficiency of the signal transmission in these circumstances. For nonidentical neurons with unidirectional coupling results are shown in Figure 5(c). As it can be appreciated, the information entropy of the receiving neuron increases rapidly with k reflecting the fact that the signalling activity of the postsynaptic neuron becomes more complex due to the coupling. Eventually, at larger values of k, the information entropy

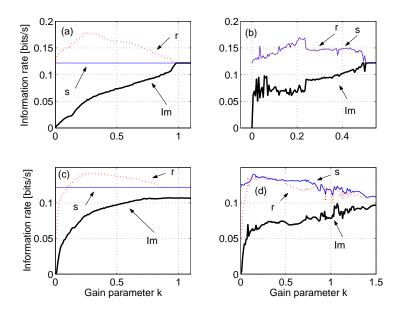


Fig. 5. Mutual information, Im, and information entropies of the sending, s, and receiving, r, neurons at different values of the coupling strength k. (a) Identical neurons and unidirectional coupling. (b) Identical neurons and bidirectional coupling. (c)Nonidentical neurons and unidirectional coupling. (d) Different neurons and bidirectional coupling.

of the receiving neuron equals the entropy of the sender in spite of the fact that both neuron are nonequal and complete synchrony does not take place. The mutual information also starts a slower and progressive increase from being zero when both neurons work independently, at k=0, to its maximum value slightly larger than $0.1\,bits/ms$ which is reached at about k=0.7. As the channel is noisy the mutual information never reaches the information entropy of the presynaptic signal. Finally, Fig. 5(d) shows the mutual information rate and the entropy rates of two nonidentical neurons coupled bidirectionally. The dynamics of the neurons is now more complex. The information entropy of the receiving neuron soon reaches a relatively high value and progressively diminishes with subsequent increment of the coupling strength k. The information entropy of the sender also experiences a slight decline as both neurons mu-

tually synchronize. The channel is noisier than in the unidirectional case and the values reached by the mutual information are now lower and more erratic.

4.2.2 Average energy consumption

We have calculated the average energy consumption per unit time that is required to maintain the organized bursting of two electrically coupled neurons. To produce these results the negative component of the energy variation given by Eq. (16) has been averaged over 10000 different spike trains of $25 \, ms$ length. Figure 6 shows the results at different values of the coupling strength k.

Results for two identical neurons when the coupling is unidirectional are shown in Fig. 6(a). It becomes apparent that there is a region of values of the coupling parameter, around k=0.6 where signalling occurs at minimum values of energy consumption by the receiving neuron. The energy consumption of the sending neuron remains constant because its dynamics is not affected by the unidirectional coupling. In Fig. 6(b) we can see what happens to the same identical neurons when the coupling is bidirectional. Due to the symmetry of the coupling the energy average consumption of the sending and receiving neurons are practically the same. It is remarkable the very neat reduction of energy consumption that takes place between values of the gain parameter k in the interval 0.2 < k < 0.25. Subsequent increases in the value of the gain maintain the consumption in a flat plateau at high values of energy consumed. At values of the gain parameter close to k=0.5 the consumption of energy falls to its initial uncoupled level as complete synchronization takes place.

For nonidentical neurons Fig. 6(c) displays the energy consumption of the receiving neuron when the coupling is unidirectional. The constant energy

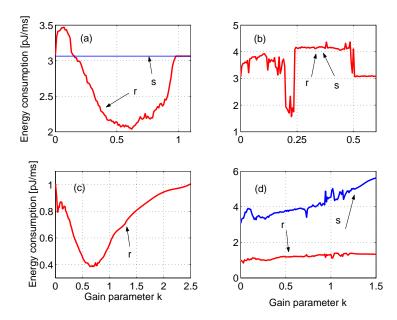


Fig. 6. Average energy consumption through the membrane of the sending s and receiving r neurons at different values of the coupling strength k. (a) Identical neurons and unidirectional coupling. (b) Identical neurons and bidirectional coupling, both consumptions are equal. (c)Nonidentical neurons and unidirectional coupling. (d)Nonidentical neurons and bidirectional coupling.

consumption of the sending neuron is not displayed for scale reasons. The energy consumption of the receiving neuron also exhibits a clear minimum that occurs for a value of the coupling strength around k = 0.6. Subsequent increase in he gain k leads to higher and higher levels of energy consumption. Finally, in Fig. 6(d) we can see the same two nonidentical neurons when the coupling is bidirectional. As it can be appreciated, the signaling of the sending neuron takes place at higher values of average energy consumption than the ones of the receiving neuron. This result is quantitatively consistent with the data of average consumption of energy at different values of the external current I that we have presented in Fig 4. Despite the unidirectional case, where the average consumption of energy of the sending neuron remains constant, in the bidirectional case the coupling also affects the sending neuron and makes it

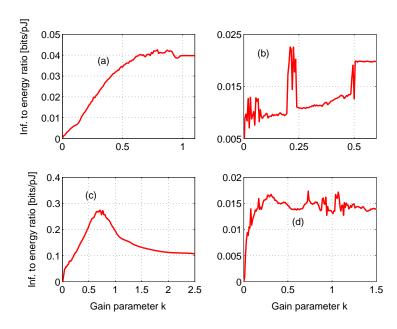


Fig. 7. Mutual information to energy consumption ratio at different values of the coupling strength k. In the unidirectional coupling the computed energy consumption refers to the energy consumed through the membrane exclusively by the receiving neuron. In the bidirectional cases the consumption of energy refers to the summation of the energy consumed through the membrane by each of the neurons (a) Identical neurons and unidirectional coupling. (b) Identical neurons and bidirectional coupling. (c) Nonidentical neurons and unidirectional coupling. (d) Nonidentical neurons and bidirectional coupling.

modify its energy consumption as a function of the coupling strength k. The average energy consumption of both neurons follows quite an irregular pattern which can not be clearly appreciated due to the scale of the figure.

4.2.3 Mutual information to average energy consumption ratio

Figure 7 shows the ratio of mutual information to average energy consumption rate at different values of the coupling gain k, and Fig. 8 their corresponding averaged synchronization errors measured as the norm of the error vector $\mathbf{e} = \|\mathbf{x}_2 - \mathbf{x}_1\|$, for the same neurons and couplings presented before. In Fig.

7(a) the neurons are identical and the coupling unidirectional. As it can be appreciated, from k = 0.6 the information to consumption ratio reaches values even higher than the one that corresponds to identical synchronization at k = 1.0. As it can be seen in Fig. 8, identical unidirectional coupling neurons at values of the coupling around k = 0.6 have still a high synchronization error and it is remarkable that transmitting information at values of the coupling where the channel remains noisy is energetically more efficient than transmitting with the noiseless channel that would correspond to complete synchronization at k = 1. Figure 7(b) shows the same identical neurons coupled bidirectionally. In this case both neurons respond to changes in the coupling k with changes in their energy consumption, see Fig. 6(b), and the ratio has been computed adding the consumptions of the sending and receiving neurons. As it can be appreciated, between k = 0.2 and k = 0.25 the information to consumption ratio has a neat peak with very high relative values. In this region of the coupling strength, the information to consumption ratio reaches values even higher than the one that corresponds to identical synchronization at k = 0.52. Noticeably enough, at those values of the coupling strength the synchronization error is maximum, Fig. 8. This is due to the fact that in that region of values of the coupling strength both neurons synchronize in anti-phase producing large synchronization errors and maximum correlation values (Torrealdea et al. 2006). Moreover, anti-phase synchronization occur at the least possible values of energy consumption, Fig. 6(b), what altogether produces the highest efficiency of the transmission from the point of view of its energy cost.

Figure 7(c) shows the mutual information rate to average energy consumption ratio between two nonidentical coupled neurons with unidirectional coupling.

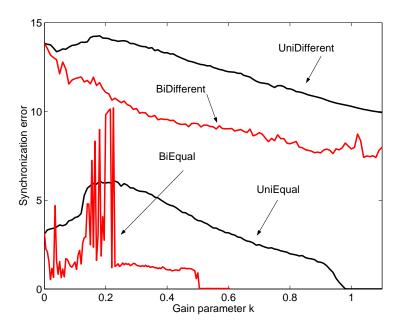


Fig. 8. Average synchronization error between two coupled neurons at different values of the coupling gain k. The synchronization error has been measured as the norm of the error vector $\mathbf{e} = \|\mathbf{x}_2 - \mathbf{x}_1\|$ and the average has been done, for each value of k, over 10000 trains of $25\,ms$ length. The curves labelled UniEqual and BiEqual show results for the case of identical neurons with coupling respectively unidirectional and bidirectional and the curves labelled UniDifferent and BiDifferent show the respective results for nonidentical neurons. The external applied current is always I=3.024 for the sending neuron and I=3.024 or I=0.85 for the receiving neuron in the identical and nonidentical cases respectively.

As we have seen before, there is a region of values of the coupling strength, at about k = 0.8, where the consumption of energy is minimum, Fig. 6(c), and the mutual information has already reached its maximum possible value, Fig. 5(c). This fact is reflected in Fig. 7(c) where the maximum value of the mutual information to consumption ratio occurs at k = 0.8. Further increase in the coupling strength does not lead to any improvement in the information transmission rate but to a loss in the energy efficiency of the transmission. As it can be appreciated in Fig. 8, the synchronization error for this case at

k=0.8 remains high but has no particular influence in the information to consumption ratio. Figure 7(d) presents the bidirectional nonidentical case. In this bidirectional case, the energy consumption corresponds to the total average energy consumed by both neurons. The ratio of the mutual information to the total energy consumption of both neurons soon reaches a kind of uneven plateau with many peaks. All these peaks represent relative maxima of the information to energy ratio which provide plenty of room for energy efficient information transmission.

4.2.4 Relative weight of the contribution from the synapse to the average income of energy through the membrane

When a neuron is signalling in isolation the average energy dissipated through the membrane, energy consumption, is perfectly balanced by its average income of energy, that is the long term temporal average of Eq. (14) is zero. Nevertheless, when the neuron receives a synaptic junction its oscillatory regime is altered influenced by the synapse. The new oscillatory regime requires the synapse to play a role in the energy balance that makes the new regime possible.

Figure 9 (a) shows for two identical unidirectionally coupled neurons the average energy derivative, that is the long term average of Eq. (14), of the postsynaptic neuron at different values of the coupling gain k. At k = 0, when the neuron is still uncoupled, the average energy derivative is zero, reflecting the fact that the neuron is signaling according to its natural isolated dynamics. In that conditions, the average energy received through the membrane is perfectly balanced by its average dissipation of energy. As soon as the coupling

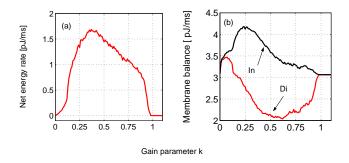


Fig. 9. (a) For two identical coupled neurons net average energy rate of the receiving neuron at different values of the coupling gain k. The coupling is electrical and unidirectional. (b) Balance of energy in the receiving neuron. Curve Di, average of the negative part of its energy derivative, that is, the energy consumption rate of the neuron, energy that is dissipated through its membrane. Curve In average of the positive part of the energy derivative, that is, the total income of energy trough the membrane of the cell. Computation has been performed generating 10000 spike trains of 25 ms at each value of the coupling gain k

is working the dynamics of the neuron changes and this balance is broken. As shown in Fig. 9(a) the average energy derivative at each value of k is positive indicating that there is a net and sustained increase in time of the energy of the neuron or, in other words, that the average income of energy is larger than the average energy dissipated trough the membrane. To make more visible the unbalance of the flow of energy through the membrane that takes place when a gap junction is present Fig. 9 (b) shows both the average energy rate dissipated trough the membrane by the postsynaptic neuron, that is its consumption of energy, and its average income of energy trough the membrane. As it can be appreciated, the average power dissipated through the membrane only equals the average power received trough it when both neurons are isolated at k = 0 or when both neurons are completely synchronized at $k \ge 1$. When synchronization is not complete the average power dissipated through the membrane is always larger than the average power dissipated through it.

However, the dynamics of the coupled neuron returns again and again to the same recurrent regions of the phase space, see Fig. 1, what means that its average energy does not increase in time. This energetically sustained signalling regime is possible because the average increase of energy of the receiving neuron is compensated by a net outflow of energy through the synapse. Accordingly with Section 2.2 of this paper, our interpretation is that this energy is somehow transformed and contributed again as part of the total income of energy trough the membrane, i.e., the synapse must be energetically active during the synchronized behavior. Figure 10 shows for every studied case, at different values of the coupling strength k, the relative weight of the contribution of the synapse to the total energy income of the receiving neuron through its membrane. For identical unidirectional neurons, Fig. 10(a), the contribution from the synapse increases smoothly reaching its maximum contribution, forty percent of the total at k = 0.4, and then smoothly decreasing towards zero as the neurons completely synchronize. In the bidirectional case, Fig. 10(b), there is no substantial contribution from the synapse except in the region of values of the gain parameter $0.2 \le k \le 0.25$ where the maximum information to energy ratio takes place. In this region the contribution from the synapse is as high as sixty percent of the total income rate of energy to the neuron through its membrane. For the nonidentical case, Figs. 10(c) and 10(d), the contribution of the synapse reaches a plateau and becomes independent of the gain k. In both cases the synapse contributes nearly ninety percent of the total income of energy through the membrane.

These results show that some production of energy at the synaptic site seems to be necessary for the neuron to keep its coordinated signalling regime. Nevertheless, there is biological evidence that links the generation of metabolic

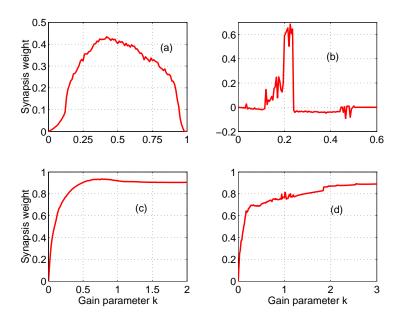


Fig. 10. Relative weight of the contribution of the synapse to the total income of energy through the membrane of the receiving neuron at different values of the coupling strength k. (a) Identical neurons and unidirectional coupling. (b) Identical neurons and bidirectional coupling. (c) Nonidentical neurons and unidirectional coupling. (d) Nonidentical neurons and bidirectional coupling. energy to the inflow of glucose through the membrane to produce ATP. Both facts could be reconcile assuming that the electrical energy produced at the synaptic site is conveniently transformed and reabsorbed by the neuron through its membrane for the generation of new spikes. Our proposed global flow of

5 Discussion and conclusions

energy has been schematized in Fig. 11.

Since the work of Hodgkin and Huxley (Hodgkin & Huxley 1952), who where able to describe the membrane currents of the squid axon via a quantitative model in differential equations, models of that type are frequently used (Rulkov 2001, Monte et al. 2003, Ivanchenko et al. 2004, Venaille et al. 2005,

Abarbanel et al. 1996, Huerta et al. 1997, Rosenblum & Pikovsky 2004, I. Belykh & Hasler 2005, Hayashi & Ishizuka 1991, Lago-Fernandez et al. 2000, Yoshioka 200, Hasegawa E 70, 066107 2004, Nagai et al. 2005) to generate and analyze spike trains with temporal characteristics similar to the ones emitted by real neurons. We have shown in Refs. (Torrealdea et al. 2006, 2007), that this type of models can also tell us about the energy implications of producing spike trains. In this work we have assigned an energy function $H(\mathbf{x})$ to a four dimensional Hindmarsh-Rose neuron. This function has the characteristics of a real physical energy and, therefore, it can be used to estimate the energetic cost of any particular signalling regime, providing the basis for all the computations involving energy provision or consumption. We do not imply that this energy function is quantitatively and accurately describing the changes in energy associated to the dynamics of a real neuron. What we imply is that if a particular kinetic model is considered able to describe some dynamical aspects of the signaling patterns of real neurons and we can associate to it a function that satisfies some required conditions, this function represents a physical energy for the model able to describe the energy implications of its dynamics and, consequently, able to describe some energy implications of the signalling patterns of real neurons. Our approach is valid for many of the frequently used models of neurons in continuous differential equations. In principle the approach is not applicable to models of the type integrate and fire as they do not provide any structural hypothesis to support the election of an appropriate energy function. In Ref. (Ozden et al. 2004) the synchronization between an electronic oscillatory circuit and a real neuron from the inferior olivary nucleus of the rat brain has been reported. To accommodate the oscillation between the circuit and the neuron an electronic coupling consisting of adjustable gain amplifiers is used. Experiments of this type seem to support that a flow of en-

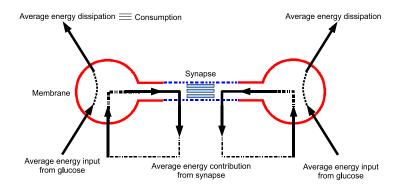


Fig. 11. Average flow of energy through the membranes and at the synaptic sites in two electrically coupled neurons.

ergy must be provided by the coupling mechanism and could be used to obtain information of the energy required for the synchronization of real neurons.

A natural way to propagate information can be through a channel of electrical coupled neurons were signals are transferred from one neuron to another. For instance, electrical synapses between AII amacrine cells and ON-cone bipolar cells are considered essential for the flow of visual signals in the retina under dark-adapted conditions (Kolb & Flamiglietti 1974). In the transmission of information synchronization seems to play a key role. Veruky and Hartveit in Ref. (Veruki & Hartveit 2002a) show that spike generation between pairs of AII amacrine cells can be synchronized precisely and that there is evidence that spikes can be transmitted through electrical synapses between these cells. Also in Ref. (Veruki & Hartveit 2002b) they demonstrate temporally precise synchronization of subthreshold membrane potential fluctuations between amacrine cells and ON-cone bipolar cells. Identical neurons can always reach precise synchronization at sufficiently large values of the gain parameter. Thus, a channel of identical neurons at large enough values of the synaptic coupling constitutes a noiseless channel where mutual information reaches its maximum rate and maximum efficiency in the transmission could be expected. Nevertheless, our results show that the information to consumption ratio reaches high values, even higher than the one that corresponds to identical synchronization, for values of the coupling strength below the ones producing identical synchronization. Transmitting at these conditions is energetically advantageous without implying a significant loss in the information rate. At these values of the coupling strength the synchronization error is still high and it is remarkable that transmitting information at values of the coupling where the channel remains noisy is energetically more efficient than transmitting with a noiseless channel. If the neurons are nonidentical synchronization is never complete and the channel is always noisy independently of the value of the coupling strength. Our results show that there is a region of values of the coupling strength where the mutual information is high and the consumption of energy is still relatively low. Further increase in the coupling strength does not lead to any improvement in the information transmission rate but to a loss in the energy efficiency of the transmission.

The existence of regions of high mutual information rate with relatively low consumption of energy can be linked to the appearance of temporal antiphase synchronization. In these regions cross correlation of instantaneous values shows that the consumption of energy of both neurons is basically incoherent Torrealdea et al. (2006) what could facilitate a cooperative behavior, especially in a large net of assembled neurons, and questions the point raised by (Lennie 2003) relative to the severe limitations that the high cost of a single spike imposes on the number of neurons that can be substantially active concurrently.

For the central nervous system it has been proposed the existence of a specialized structural site, for glycolytic generation of ATP, localized at the postsynaptic site (Wu et al. 1997, Siekevitz 2004). According to Ref. (Kasischke & Weebb 2004) the temporal pattern of the presumed glycolytic response would directly follow the presynaptic input in order to meet metabolic needs induced by the processing of nerve signal transduction. We have found that the synapse must be energetically active during the synchronized behavior. On average, there is no flow of energy through the synapse from one neuron to the other but a flow of energy leaving the neuron at the synaptic site. It can certainly be instantaneous flows of energy from one neuron to the other, in fact, it is believed that the electrical coupling itself is caused by flow of current through gap junctions (Veruki & Hartveit 2002b), but the net average flow of energy between the two neurons is zero. The average income of energy through the membrane exactly matches the average output of energy through the membrane, energy consumption, plus the average energy leaving the neuron at the synaptic site. We hypothesize that the energy leaving the neuron at the synaptic site to the extracellular medium does not substantially degrade and it is somehow fed back again into the neuron through its membrane, Fig. 11. The Hindmarsh-Rose model of the dynamics of the neuron does not provide enough biological information as to be able to decide which terms in the energy derivative should be considered energetically conservatives. We have assumed that the net energy contributed from the synapse does not imply a net energy consumption and that it is in some way recovered an indefinitely reused for the generation of new spikes. It could be well the case that part of the synapse energy also degraded. In that case, the consumption of energy of the neuron to maintain its signalling activity would have to include the dissipation of energy in the synapse.

Energy efficient information transmission from the point of view that inputs

are optimally encoded into Boltzmann distributed output signals has been analyzed in (Balasubramanian et al. 2001). An open question is the determination of the energy cost of generating the spike trains that codify each of the different output symbols. Our approach provides a way to determine the energy cost of the generation of different spike trains. It is to be emphasized that the distribution of energy cost of a set of symbols can be very dependent on the particular coupling conditions of the signalling neuron.

When the availability of energy is a significant constraint a trade-off between the transfer rate of information between neurons and its energetic cost is to be expected in order to obtain an efficient use of energy by the neurons. Our results, obtained from a comprehensive single model of neuron that links information and energy, provide room for such a kind of trade off and suppose a novel approach to the open problem of whether biological computation optimizes the use of energy in the generation and transmission of neural codes. It seems likely that real neurons use energy efficient circuits to generate and transmit information. It has been reported (Vincent et al. 2005) that the neural organization observed in the early visual system is compatible with an efficient use of metabolic energy. The center surround organization of retinal ganglion cells optimizes the use of energy when encoding natural images. Other aspects of the organization such as the higher densities of receptive fields in the fove athat decrease in the periphery could also be in an attempt to optimize the use of metabolic energy (Vincent et al. 2005). In order to test their energy efficient coding hypothesis Vincent et al. use a model where the metabolic cost of the synaptic activity and firing rates can be fully manipulated. In the retinal stage, a cost that increases in proportion to synaptic activity is imposed while in the cortical stage they suppose a cost proportional to the firing rate of neurons. Although this is certainly a plausible hypothesis it is not based on any comprehensive model of energy linked to the true dynamics of the firing regime of the neurons. We think that models of energy like the one described in this paper could provide support to empirical studies to ascertain if neurons really are taking advantage of efficiency savings.

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