An Izhikevich simple model of a hippocampal OL-M interneuron

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Abstract

We adapt the Izhikevich simple model neuron formalism to simulate a hippocampal oriens/alveus interneuron with lacunosum-moleculare axon (OL-M interneuron). This neuron species is of a type not simulated to date within the formalism: it is spontaneously active in the absence of synaptic input, but also shows post-inhibitory rebound. We modify the Izhikevich approach to include two dominant currents, one of which de-activates. The resulting simple model captures the spontaneous activity, linear f-I curve, and post-inhibitory rebound properties of the OL-M interneuron.

1 Introduction

Recent models of hippocampus CA1/CA3 networks have shown how both theta and gamma frequencies of oscillation can emerge together, and in coherent cell assemblies, from the interactions of a particular microcircuit (Rotstein et al., 2005; Tort et al., 2007). These models show great promise as the basis for understanding a wide range of experimental data obtained from the hippocampus. Unfortunately, these models use multiple micro-circuits comprised of multiple-compartment pyramidal neuron models and complex single-compartment models of fast-spiking (FS) and oriens lacunosum-moleculare (OL-M) inter-neurons, and so are costly to run. Thus, we would like to greatly simplify these model neurons, so that we can properly explore the properties of the networks.

The recent simple model of Izhikevich (2006) is capable of re-producing a wide variety of spiking neuron behaviour. Further, pyramidal and FS inter-neuron versions already exist (Izhikevich, 2006). Here we establish an OL-M model within the Izhikevich approach, as the first step in replicating the network models.

2 A model of the OL-M interneuron

The OL-M interneuron *in vitro* is both spontaneously active in the absence of synaptic input (Maccaferri and McBain, 1996), and fires a post-inhibitory rebound spike after release from hyperpolarising current injection (Lacaille and Williams, 1990). This combination of properties has, as far as we know, not yet been modelled within the Izhikevich frame-work. In particular, no Izhikevich model we are aware of is able to fire spontaneously.

In their 196-compartment model of the OL-M neurons, Saraga et al. (2003) identify four main currents found in the soma: the two standard Hodgkin-Huxley action potential generation channels I_{Na} and I_K; an A-type potassium current I_A, similar to the one found in pyramidal neurons; and an inward-rectifying, non-specific cation, current I_h, responsible for the spontaneous activity of the OL-M interneuron (Maccaferri and McBain, 1996). The design question for us is: which current do we chose for u?

We can immediately ignore the I_{Na} and I_{K} currents, as their effects are contained within the existing form of the Izhikevich model's equations. We instead find that we need to model both I_{h} and I_{A} as separate u contributions, that we shall label u_{h} and u_{A}. The corresponding parameters we shall also label with the same subscripts, $a_{\text{A}}, a_{\text{h}}, \dots$ etc. The basic Izhikevich simple model is a two-dimensional ordinary differential equation system, one for the membrane potential v, and one for the phenomenological variable u that describes the effect of the dominant active current in the neuron. Thus, we extend this here to a three-dimensional model with two dominant currents.

The membrane potential v is as given by Izhikevich (2006), but with two u contributions

$$C\dot{v} = k(v - v_{\text{r}})(v - v_{\text{t}}) - (u_{\text{A}} + u_{\text{h}}) + I \tag{1}$$

where C is capacitance, v_{r} and v_{t} are the resting and threshold potentials, and I is a current source (external or synaptic). Parameter k is derived from known passive properties of the OL-M neuron (see below).

The I_{A} phenomenological variable u_{A} is also in the standard form

$$\dot{u_{\text{A}}} = a_{\text{A}} \left[b_{\text{A}}(v - v_{\text{r}}) - u_{\text{A}} \right], \tag{2}$$

where a_{A} is the time constant of activation of I_{A}. For many Izhikevich neuron models, b can be determined from a simple equation, but for the OL-M neuron, with two active currents, this is not possible; however, we know that $b_{\text{A}} < 0$ because I_{A} is an 'amplifying' (additive/subtractive) current.

We find that a useful form for u_{h} is

$$u_{\text{h}} = \begin{cases} 0, & \text{if } v > E_{\text{h}} \\ a_{\text{h}} \left[b_{\text{h}} \left(v - E_{\text{h}} \right) - u_{\text{h}} \right], & \text{otherwise} \end{cases}, \tag{3}$$

which models the activation of the I_{h} current by hyperpolarisation, its de-activation above some potential E_{h}, and its positive contribution to the membrane potential when activated. Note we know that $b_{\text{h}} > 0$ because I_{h} is a 'resonant' current.

The OL-M model has the standard reset condition

$$\text{if } v \geq v_{\text{peak}} \text{ then } v \leftarrow c;\ u_{\text{A}} \leftarrow u_{\text{A}} + d_{\text{A}};\ u_{\text{h}} \leftarrow u_{\text{h}} + d_{\text{h}}, \tag{4}$$

where c is the reset potential (i.e. the value of the membrane potential immediately after an action potential is fired); and $d_{\text{A}}, d_{\text{h}}$ are tuned to achieve the desired spiking behaviour.

2.1 Parameter values

The values of the OL-M neuron model parameters are given in Table 1, along with notes on their origins. The value of k can be found from

$$k = \frac{g_{\text{in}}(v_{\text{max}} - v_{\text{r}}) - I_{\text{r}}}{(v_{\text{max}} - v_{\text{r}})^2}, \tag{5}$$

where g_{in} is the input conductance (reciprocal of the input resistance), and I_{r} is the rheobase current — the minimum current needed to make the neuron fire.

For the OL-M interneuron, input resistance when the membrane is held at 'resting' potential is $R \sim 215$ MΩ (Morin et al., 1996), and so we take $g_{\text{in}} = 4.65$ nS. The notion of I_{r} is a little strange for the OL-M interneuron, as it is spontaneously active. However, if we take $I_{\text{r}} = -25$ nA, the smallest value of the injection current that will suppress spontaneous activity (Maccaferri and McBain, 1996), then (5) gives sensible answers with the other parameters from Table 1.

Table 1: OL-M interneuron model parameter values and their origins

| Parameter	Value	Notes and references
C	120 pF	found from $C \simeq \tau_m/R$, given $\tau_m \sim 23$ ms (passive membrane time constant) and $R \sim 215$ MΩ (Morin et al., 1996)
k	1.2	approximate value given by (5)
v_t	-55 mV	value given by Lacaille and Williams (1990) for approximate firing threshold
v_r	-70 mV	difficult to place a value for a spontaneously active neuron, but we know it must be close to c because of the mostly linear trajectory of the membrane potential between spikes.
c	-75 mV	the reset potential estimated from (Maccaferri and McBain, 1996)
v_{peak}	40 mV	approximate height of action potential (Lacaille and Williams, 1990)
a_A	0.2	corresponds to ~ 5 ms time constant of activation (Saraga et al., 2003)
b_A	2	tuned for best fit
d_A	100	tuned for best fit
a_h	0.005	corresponds to ~ 200 ms time constant of activation (Saraga et al., 2003)
b_h	5	tuned for best fit
d_h	-35	tuned for best fit
E_h	-50 mV	approximate de-activation potential of I_h (Maccaferri and McBain, 1996)
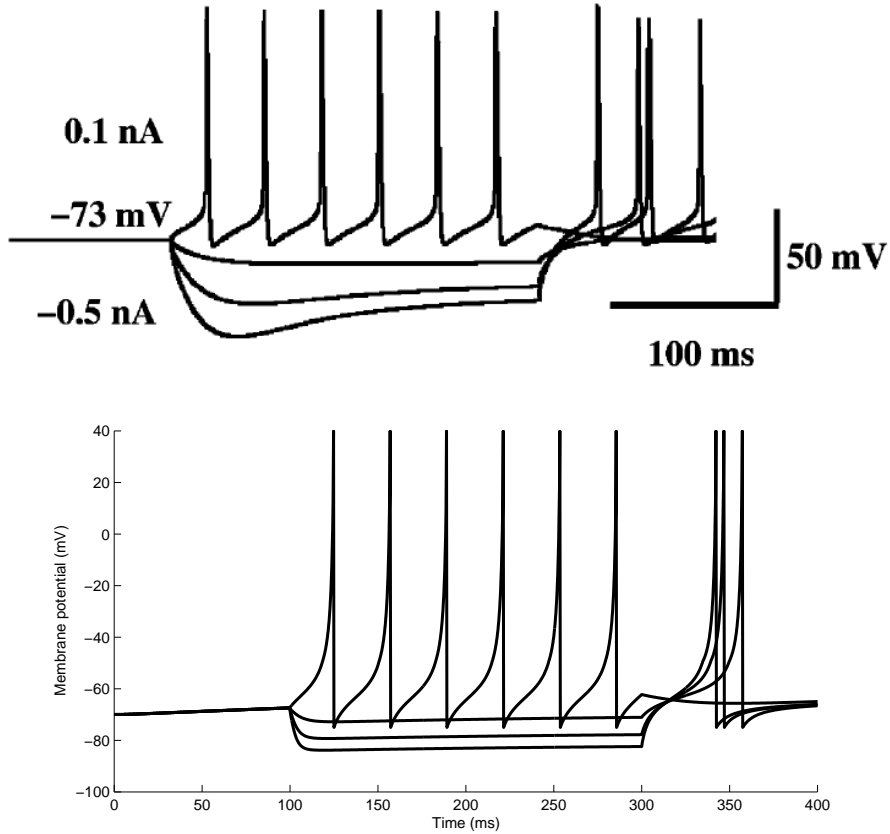
Figure 1: Responses of OL-M neuron models to 200ms current steps (of -0.5, -0.3, -0.1, and 0.1 nA). Top, the membrane responses of the Saraga et al. (2003) compartmental OL-M model. Bottom, the membrane responses of the Izhikevich-style OL-M model using the parameters in Table 1. The Izhikevich-style model reproduces both the post-inhibition rebound spike, and the firing patterns induced by the positive current step, but has a barely discernible voltage-sag after the onset of the inhibitory current step.

3 Results

The tuned values in Table 1 were found by trying to replicate both the f-I (current-frequency) curve of an example OL-M interneuron (Maccaferri and McBain, 1996), and the post-inhibitory rebound behaviour (Lacaille and Williams, 1990). The two fits were mutually constraining, and clearly limited the possible range of values.

Figure 1 shows that our OL-M interneuron model's responses to 200ms current injection steps (of -0.5, -0.3, -0.1, 0.1 nA) captures the essential characteristic of a rebound spike elicited by the offset of the current step. Our OL-M model does not have a pronounced voltage sag after the onset of a strong inhibitory current step. However, we feel this is a minor problem, as such phenomena are useful for deducing the channel composition of a neuron species, but do not in themselves strongly influence its behaviour in a network. The comparison in Figure 1 is to the somatic voltage of the Saraga et al. (2003) compartmental model, also used in (Tort et al., 2007): note the good qualitative agreement in the models' responses.

Figure 2 shows that the fit to the f-I curve is excellent, when using the parameters in Table 1. Only the exponential rise to the linear portion of the f-I curve from -30 nA to -10 nA is missing: the model could reproduce this behaviour, but required that the time constant for u_h was even longer ($a_h \leq 0.001$) — in this case, the model no longer showed rebound spikes after 200ms of hyperpolarising current.
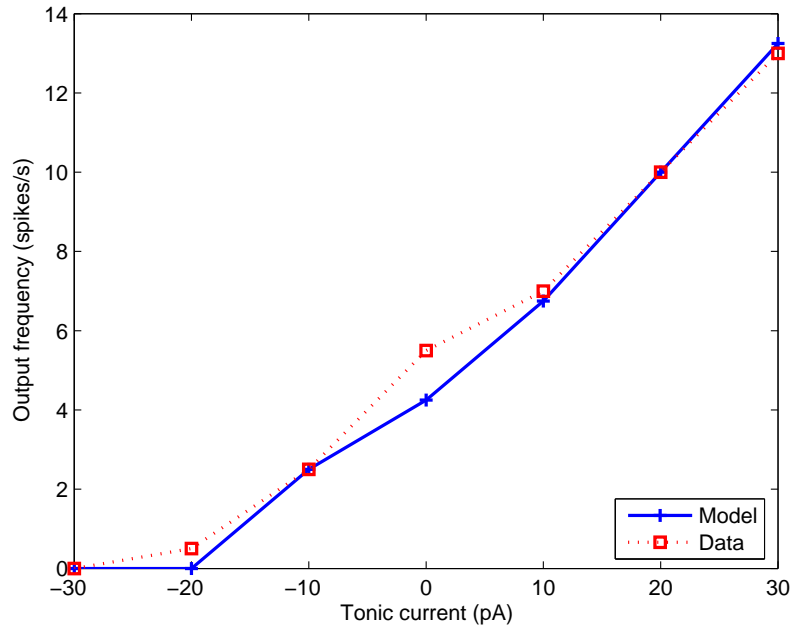
Figure 2: The f-I curve of an example OL-M interneuron from the *in vitro* study of Maccaferri and McBain (1996), and the f-I curve of the Izhikevich-style OL-M model using the parameters in Table 1. The fit is excellent, with only the small exponential rise to the linear portion missing.

4   Conclusion

The Izhikevich-style neuron model captures the principal properties of the OL-M neuron model: spontaneous firing in the absence of synaptic input; linear f-I curve over most of its tested input range; and post-inhibitory rebound spikes. Using the parameters in Table 1, the model cannot capture the small exponential rise at the start of the f-I curve, nor show a voltage sag after the onset of hyperpolarising current step. However, we believe these properties are of minor importance, particularly in the context of a network of these neurons. Finally, it is instructive to consider the computational cost of the Izhikevich neuron: it has 3 differential equations (1)-(3), with one auxiliary equation (4), and the differential equations can be solved stably using the simplest possible numerical method (forward Euler); the Saraga et al. (2003) model has, in its somatic compartment, 7 differential equations, with 11 auxiliary equations. The computational trade-off against the loss of some detail in the neuron's behaviour is, we feel, in favour of the Izhikevich neuron model.

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