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# The role of electrical coupling in generating and modulating oscillations in a neuronal network

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ABSTRACT

A simplified model of the crustacean gastric mill network is considered. Rhythmic activity in this network has largely been attributed to half center oscillations driven by mutual inhibition. We use mathematical modeling and dynamical systems theory to show that rhythmic oscillations in this network may also depend on, or even arise from, a voltage-dependent electrical coupling between one of the cells in the half-center network and a projection neuron that lies outside of the network. This finding uncovers a potentially new mechanism for the generation of oscillations in neuronal networks.

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## 1. Introduction

Networks of neurons display a variety of oscillatory behaviors. For example, oscillations in the levels of calcium concentrations, gene expressions and in the membrane voltage across cell membranes are all commonly found in neuronal systems. Often these oscillations are rhythmic in that they display a consistent pattern at a prescribed frequency [1]. Central pattern generating (CPG) networks provide several examples that exhibit rhythmic activity. CPGs refer to networks of neurons in the central nervous system that produce patterned (usually oscillatory) activity in the absence of patterned sensory input. These networks play a critical role in generating a diverse array of motor functions such as digestion, locomotion, respiration and regulation of heartbeat in invertebrates [2]. A central question in the study of neural oscillations is what are the mechanisms that underlie the generation of rhythmic activity and how that activity is regulated. This study will focus on this general question in the context of the gastric mill rhythm (GMR; frequency 0.1 Hz) that arises in the stomatogastric ganglion (STG) in the crustacean central nervous system. In particular, we will show the existence of a new mechanism based on voltage-dependent electrical coupling for generation of oscillations within a neuronal network.

The gastric mill network consists of a small number of neurons in the STG that control muscles that move teeth to provide grinding of food (chewing) within the gastric mill stomach of crustaceans [3]. In the Jonah crab, a pair of neurons, the lateral gastric (*LG*) and Interneuron 1 (*INT*1) form a half-center oscillator (HCO) and are primary contributors to the GMR. These neurons are connected by reciprocally inhibitory synapses and, during gastric mill activity, display anti-phase bursting oscillations. They also receive input from various parts of the stomatogastric nervous system (STNS). In particular, *INT*1 receives rhythmic inhibition from the pacemaker anterior burster neuron (*AB*) of the pyloric CPG. Because the pyloric rhythm (frequency 1 Hz) is much faster than the gastric mill, the *AB* to *INT*1 input produces pyloric timed patterns in the *INT*1 bursting activity. Both *LG* and *INT*1 receive excitatory input from the modulatory commissural neuron 1 (*MCN*1) with *INT*1 receiving fast excitation and *LG* receiving slow modulatory excitation. Additionally, the *MCN*1 axon terminals are electrically coupled to *LG* in a manner that is dependent on the voltage of *LG* [5]. It is the role of this electrical coupling that is of particular interest to us in this paper.

Neurons that lie within an HCO typically utilize reciprocal inhibition to generate oscillations [6]. In particular, in a two cell HCO, when one of the cells is active, its inhibitory synapse suppresses the other. At some later time, the silent cell escapes or is released from inhibition and the roles of the two cells switch [7]. In the gastric mill network, *LG* and *INT*1 can oscillate in this manner with the ability to escape inhibition and generate oscillations,

*Abbreviations:* CPG, central pattern generating; GMR, gastric mill rhythm; STG, stomatogastric ganglion; HCO, half-center oscillator; LG, lateral gastric; INT1, interneuron 1; STNS, stomatogastric nervous system; AB, anterior burster; MCN1, modulatory commissural neuron 1.

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but only in the presence of the excitatory input provided by *MCN*1 [5,8].

Although a number of modeling studies have explored the generation of oscillations in the gastric mill network [8–11,13], the role of the strong electrical coupling between the *MCN*1 axon terminals and the *LG* neuron has not been previously explored. In this study, we will show that voltage-dependent electrical coupling can provide an alternative mechanism for the generation of oscillations when the inhibition based HCO mechanism is incapable of doing so. In particular the $LG-INT1$ HCO can be rendered ineffective if (1) the inhibitory synapse form *INT*1 to *LG* is inactivated, or (2) if the excitability property of *LG* is reduced. In order to fully understand how electrical coupling affects this network, we will first consider a simple model to see how electrical coupling between *LG* and *MCN*1 axon terminals affects the ability of oscillations to be created through the standard HCO inhibition based mechanism. We will discuss how the electrical coupling modulates the rhythmic properties of this oscillation. We will then remove the *INT*1 to *LG* synapse and show that rhythmic oscillations can still arise through the electrical coupling between *LG* and *MCN*1 axon terminals, but only if this coupling is voltage dependent, as has been reported experimentally [5]. We will then demonstrate the same in a biophysical model based on the Morris–Lecar equations [15]. For both models, we derive conditions on parameters showing why the electrical coupling must be voltage dependent to produce oscillations.

The modeling and analysis in this paper is based on the use of geometric singular perturbation theory. Exploiting inherent differences in timescales, we will derive sets of fast and slow equations that can be studied in the relevant phase space. For the simple model, this can be done on a two-dimensional phase plane and is the focus of Sections 3.1–3.4. The analysis in those sections follows the tradition of using relaxation oscillators with the individual neurons modeled as passive elements. The relaxation oscillations in this case arise due to the method of model reduction that incorporates a slow synaptic variable. In Section 3.5, the fast–slow analysis allows us to project the relevant dynamics onto two different phase planes to facilitate understanding of the model.

## 2. Model

### 2.1. Simple passive cell network model

We describe the simple network that we shall initially consider. A key assumption for this model is that *INT*1 and *LG* are modeled as passive cells with no active currents or excitable properties. Thus if oscillations are to be generated, they must arise as a direct result of network interactions. By identifying variables that evolve on different time scales and by making a few other assumptions, we can use geometric singular perturbation theory to focus on the analysis of a reduced two-dimensional system of equations. These variables correspond to the voltage of *LG* and to the synaptic input that *LG* receives from MCN1 and are shown in solid in Fig. 1. The electrical coupling is also shown in solid in Fig. 1 as it can be defined in terms of the reduced quantities including the voltage of *LG*. Shown with dotted lines/circles are the other variables that we will incorporate into the solid variables and thus will not need to explicitly track.

Let $V_L$ and $V_I$ denote the voltages of *LG* and *INT*1 respectively. We will not model individual spikes but instead keep track of when a cell is above (active) or below (silent) threshold. These voltages will evolve on a fast time scale. Notice that *AB* and *MCN*1 do not receive synaptic input from any other cells in the circuit. Thus we do not explicitly model either but instead need only keep track of their synaptic and electrical output. The equations that describe the relevant voltages are:

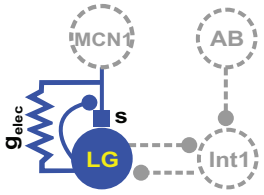


**Fig. 1.** Schematic diagram of the modeled network.Solid elements are explicitly represented in the reduced two-dimensional model whereas dashed elements are defined as functions of the explicit variables. Filled small circles indicate synaptic inhibition, solid box is synaptic excitation and the resistor symbol indicates electrical gap junction coupling between the *MCN*1 axon terminals and *LG*.

$$\epsilon\frac{dV_L}{dt} = -I_{rest,L}(V_L) - I_{syn,I\to L}(V_I,V_L) - I_{syn,M\to L}(V_M,V_L,s) - I_{elec}(V_L,V_M) \tag{1}$$

$$\epsilon\frac{dV_I}{dt} = -I_{rest,I}(V_I) - I_{syn,L\to I}(V_I,V_L) - I_{syn,AB\to I}(V_I,s_{AB\to I}) \tag{2}$$

The intrinsic current $I_{rest,x}(V_x) = g_{rest,x}[V - E_{rest,x}]$ where $g_{rest,\,x}$ and $E_{rest,\,x}$ are the passive rest conductance and reversal potentials. Notice that in the absence of any other currents, the value $V = E_{rest,x}$ is a stable rest point. For *LG*, $E_{rest,\,L} < V_T$ while for *INT*1, $E_{rest,\,I} > V_T$ for a fixed threshold $V_T$. *MCN*1 is assumed to be tonically active which we model by setting its voltage to a value $V_M > V_T$. The synaptic currents obey an equation of the form $I_{syn,x\to y} = g_{x\to y}s_{x\to y}[V_y - E_{inh}]$ where $x$ and $y$ are the pre- and post-synaptic cells. The variables $s_{AB\,\to\,I}$, $s_{L\,\to\,I}$ and $s_{I\,\to\,L}$ are straight forward to understand and are instantaneous. The synaptic variable $s_{AB\,\to\,I}$ provides the input due to *AB* activity and is modeled using a periodic, half-sine function with an amplitude of 1 and period of 1 s. This synapse takes on the value one when the sine function is greater than a threshold, set here to 0.5, and is zero otherwise. The synapses between *LG* and *INT*1 are also instantaneous and we utilize the fact that these cells are always out-of-phase with one another.

$$s_{AB\to I}(t) = \mathrm{Heav}\left(\sin\left(\frac{2\pi(t)}{1000}\right) - 0.5\right) \tag{3}$$

$$s_{L\to I}(V_L) = \left[1+\exp\left(\frac{\nu_1 - V_L}{k_1}\right)\right]^{-1} \tag{4}$$

$$s_{I\to L}(V_I) = \left[1+\exp\left(\frac{\nu_2 - V_I}{k_2}\right)\right]^{-1} \tag{5}$$

The remaining synaptic variable $s$ requires some explanation. In the biological system, *MCN*1 exerts a slow excitatory effect on *LG* that is modulated by pre-synaptic inhibition from *LG* onto the *MCN*1 to *LG* synapse. Thus when *LG* is active, this excitation is slowly removed; when *LG* is silent, the excitation slowly builds. This is modeled by the variable $s$ that evolves on a slow time scale and is the only slow variable in our model. Equations governing this variable are:

$$\frac{ds}{dt} = \begin{cases} (1-s)/\tau_r & V_L \le V_T \\ -s/\tau_f & V_L > V_T \end{cases} \tag{6}$$

In equation (1), the synaptic current is then given by

$$I_{syn,M\to L} = g_{M\to L}s[V_L - E_{exc}]. \tag{7}$$

Fig. 1 shows an electrical coupling between *LG* and the *MCN*1 axon terminals. The electrical current is given by

$$I_{elec}(V_L,V_M) = g_{elec}(V_L)[V_L - V_M]. \tag{8}$$

This coupling is dependent on the voltage of *LG* and *MCN*1 in two different ways. First, the strength is an increasing function of $V_L$.