Connection Topology Selection in Central Pattern Generators by Maximizing the Gain of Information

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A study of a general central pattern generator (CPG) is carried out by means of a measure of the gain of information between the number of available topology configurations and the output rhythmic activity. The neurons of the CPG are chaotic Hindmarsh-Rose models that cooperate dynamically to generate either chaotic or regular spatiotemporal patterns. These model neurons are implemented by computer simulations and electronic circuits. Out of a random pool of input configurations, a small subset of them maximizes the gain of information. Two important characteristics of this subset are emphasized: (1) the most regular output activities are chosen, and (2) none of the selected input configurations are networks with open topology. These two principles are observed in living
CPGs as well as in model CPGs that are the most efficient in controlling mechanical tasks, and they are evidence that the information-theoretical analysis can be an invaluable tool in searching for general properties of CPGs.

1 Introduction

A central pattern generator is a group of connected neurons that control the activity of a mechanical device by activating muscle groups. CPGs are responsible for activities like chewing, walking, and swimming (Selverston, 1999a, 1999b; Selverston, Elson, Rabinovich, Huerta, & Abarbanel, 1998; Arshavsky, Deliagina, & Orlovsky, 1997). The intrinsic properties of every neuron in the CPG, together with the connection topology between them, determines the phase relationship in the electrical activity. A group of neurons can generate many different spatiotemporal patterns of activity that can control different types of mechanical devices. Only a subset of the possible solutions of activity of the CPG will work for a given mechanical device (see, e.g., Huerta, Sanchez-Montanes, Corbacho, & Sigüenza, 2000). Among the large number of possible spatiotemporal patterns is a subset that efficiently performs the required mechanical functions of the animals. In this work, we intend to determine some generic constraints of a simplified working CPG.

Our motivation is previous work (Huerta, Varona, Rabinovich, & Abarbanel, 2001), where it was shown that the best efficiency of a mechanical pump based in the pyloric chamber and controlled by pyloric CPG of the lobster is achieved by combinations of synaptic connections in sets corresponding to CPGs that oscillate in regular fashion and all of these CPGs have nonopen connection topologies. Here, nonopen topology is defined as a configuration in which every neuron receives synaptic input from at least one other neuron in the CPG (see, e.g., Selverston & Moulins, 1987; Arshavsky, Beloozerova, Orlovsky, Panchin, & Pavlova, 1985; Getting, 1989).

In this letter, we test the use of Shannon and Weaver information (Shannon & Weaver, 1949) as a global measure of the efficiency in the CPG activity. One of the best-known CPGs is the pyloric CPG of the lobster stomatogastric ganglion (Selverston & Moulins, 1987), where the rhythm is achieved by a combination of the intrinsic properties of the neurons connected by many inhibitory and a few electrical synapses. Most neurons isolated from this CPG have been shown to behave in a chaotic way (Rabinovich, Abarbanel, Huerta, Elson, & Selverston, 1997; Selverston et al., 2000), and many ideas for the role of chaos in the neurons of the CPG have been proposed (Abarbanel et al., 1996; Rabinovich et al., 1997). Here we study the behavior of simple CPGs made of either three or four chaotic neurons connected by inhibitory synapses. For simulating the chaotic neuron elements, we use one of the simplest mathematical models that is able
to produce chaotic behavior: the Hindmarsh-Rose model (HR) of a bursting neuron (Hindmarsh & Rose, 1984; Pinto et al., 2000), and the synapses are simulated by a first-order kinetic model of neurotransmitter release (Destexhe, Mainen, & Sejnowski, 1994; Sharp, Skinner, & Marder, 1996; Pinto et al., 2001).

We also included the results from the analysis of CPGs made of three or four electronic neurons (Pinto et al., 2000) based on the HR model (Hindmarsh & Rose, 1984). Our motivation for using analog electronic neurons (ENs) is to include in our experiments more elements of those that a real living CPG is exposed to. Different from mathematical modelling, ENs are made of real components that experience fluctuations in their values (because of changes in temperature, for example) in the same way neurons experience fluctuations in their intrinsic properties due to changes in the temperature or in the ionic concentrations of the saline. ENs are also subject to electronic noise that could be compared to the noise that living neurons receive when embedded in the living tissue. Experiments with ENs produce results that have to be robust to small variations, such as those that can occur in a living CPG, and they can be used to validate the results obtained in ideal systems created by computer simulations.

Information theory has been used to study neural systems (e.g., Deco & Schurmann, 1997; Strong, Koberle, de Ruyter van Steveninck, & Bialek, 1998). However, our approach is different because we consider the input to the CPG as a set of synaptic and conductance configurations. We disregard the effects of neuromodulation on the endogenous properties of the neurons as proposed by Stemmler and Koch (1999). Basically we want to address the generation of information by the CPG due to some given set of synaptic connections.

In order to be able to evaluate the mutual information between the input and the output, three definitions should be given: what the input, the output and the information being conveyed are. First, let us state the definition of the mutual information,

$$MI(I; O) = H(O) - H(O/I)$$

where $I$ and $O$ are the input and the output, respectively; $H$ represents the entropy or the measure of uncertainty or variability. Roughly, the entropy of a system is a measure of how much information we need to be able to predict the system behavior. A low entropy means that the system is very regular and the behavior can be easily predicted. Conversely, a high entropy means that the system behaves in an irregular way, which makes prediction difficult. Our goal is to maximize the mutual information; in the optimal case, this means that the uncertainty of the output $H(O)$ is maximum (meaning that it has a wide range of possible responses), and the uncertainty of the output given the input $H(O/I)$ is minimum, meaning 0. Stated explicitly, we want the response of the system to be as rich as
Figure 1: What is the input and the output? The concentration of the neuromodulators determines the type of connectivity between the neurons (in real CPGs, they also modify the dynamics of every neuron). The connection topology established by the neuromodulators selects a specific phase of bursting electrical activity between the members of the CPG.

possible, and at the same time we want the response of the system to a specific input to be fully determined by this input.

We still need to be more precise about what we call “the input.” In most of the CPGs, the rhythm changes due to neuromodulatory inputs that modify both the synaptic connections between neurons (connection topology) and the kinetics of the ionic channels on the neurons membrane (Harris-Warrick et al., 1998; Brodfuehrer, Debski, O’Gara, & Friesen, 1995; Katz, 1998). To reduce the complexity of the problem, in this letter, we consider only variations in the synaptic connections. As shown schematically in Figure 1, instead of using the neuromodulator concentrations as the input configuration, we choose the connection topology with the assumption that there is a function relating the neuromodulator concentration configuration and the connection topology configuration. Therefore, the input we consider is a specific synaptic configuration, which is given by

\[
I = \{g_{ij}; 0 \leq g_{ij} < g_{\text{max}}, i \neq j; i, j = 1 \ldots N\},
\]

where \(g_{\text{max}}\) is the maximum synaptic conductance and \(N\) is the number of neurons in the CPG.

The output is based on the observation that the electrical activity produced by a neuron is mainly transmitted to the muscles when the burst is on. The spikes are carried through the axons to the muscles, which integrate them to produce an action. Also, there is strong evidence that burst duration can encode information in very different kinds of networks (Kepecs & Lisman, 2003; Lisman, 1997). Thus, for our purposes, we will disregard the frequency of the spike firing, considering that the information is basically carried by the burst start and end times.

A random set of input configurations is used to integrate the CPG so that the conditional distributions and entropies can be calculated. Then the
estimation of the maximum of the mutual information leads us to a subset of configurations in \( I \).

In the next few sections, with an approach independent of the one used by Huerta (Huerta et al., 2001), we show that a subset consisting of 15% of the input configurations is sufficient to obtain the maximum of the mutual information, that all of these configurations lead to regular rhythmic activity, and that all of these are nonopen topology configurations. These last properties are widely observed in living CPGs.

2 Mutual Information Estimation

Let us define the variable \( E(R, t) \) that can assume the Boolean values 0 (no event) or 1 (presence of an event) at time \( t \). The value of \( R \) represents the type of event and is in the range from 1 to \( 2 \cdot N \), where \( N \) is the number of neurons in the CPG. Initially all \( E(R, t) \) are reset to 0. When neuron \( i \) starts a burst at time \( t^* \), we set \( E(R = i, t = t^*) = 1 \), and when neuron \( i \) ends a burst at time \( t^* \), we set \( E(R = N + i, t = t^*) = 1 \). To calculate the joint probability, we integrate the model CPG and obtain \( E(R, t) \) for a given input: a specific synaptic configuration \( G_j \in I \) with \( j = 1, \ldots, M \) and \( M \) is the cardinality of the set \( I \). Setting \( t' = 0 \) when neuron 1 (used as a time reference) started its last burst, we define \( p(R, t'/G_j) \) or \( p_{G_j}(R, t') \) as the conditional probability of observing an event of type \( R \) at time \( t' \) for a given input \( G_j \). The conditional probabilities are calculated as follows. We create a counter-array named \( C_{G_j}(R, t') \), where \( R \) has the previously explained meaning and \( t' \) runs from 0 to a sufficiently large value \( T \).

Starting from \( t = 0 \), we collect the events in \( E(R, t) \) for increasing \( t \):

1. The neuron number 1 is set as the time reference for the rest of the neurons. Every time \( E(R = 1, t = \tau) = 1 \), the reference time \( \tau \) is taken.

2. When an event of type \( i \) is found at time \( t \), the overall counter \( C_{G_j}(R = i, t' = t - \tau) \) is increased by 1.

3. At the end, \( C_{G_j}(R, t') \) is normalized to 1 to yield \( p_{G_j}(R, t') \).

Examples of some typical \( p_{G_j}(R, t') \) obtained for two different input configurations \( G_j \) (corresponding to qualitatively different bursting CPGs made of four neurons) are shown in Figure 2. Note that in both cases, the time probability for all events (\( R = 2 \) to \( 8 \)) was superimposed. For the regular bursting CPG, the \( p_{G_j}(R, t') \) presents well-defined peaks that correspond to the time when each event is expected, while for the irregular bursting CPG, the \( p_{G_j}(R, t') \) is spread to a large extent of time.

Once we have calculated the conditional probabilities, we determine the values of the conditional entropies (defined as the variability of the output
Figure 2: Examples of some typical conditional probabilities obtained in experiments with four analog electronic neuron CPGs. (Top) $p_{G_{251}}(R, t)$ for an irregular bursting CPG. (Bottom) $p_{G_{517}}(R, t)$ for a regular bursting CPG. In each plot, the probabilities of the different events ($R = 2$–$8$) were superimposed.

for a given $G_j$) as follows,

$$H_{G_j} = - \sum_{t=0}^{T} \sum_{R=1}^{2N} p_{G_j}(R, t) \log_2 p_{G_j}(R, t),$$

where the joint probability is $p(R, t, G_j) = p_{G_j}(R, t)p(G_j)$ and $p(G_j)$ is the probability of the configuration $G_j$ in the set $I$. Since during the simulations or experiments, $M$ random synaptic configurations $G_j$ are chosen, $p(G_j) = \frac{1}{M}$.

The marginal probability is

$$p(R, t) = \sum_{j=1}^{M} p_{G_j}(R, t)p(G_j),$$

which is used to calculate $H(O)$ as

$$H(O) = - \sum_{t=0}^{T} \sum_{R=1}^{2N} p(R, t) \log_2 p(R, t).$$
and the conditional entropy

\[ H(O/I) = \sum_{j=1}^{M} p(G_j)H_{G_j}. \]

### 3 The Problem: Maximizing the Mutual Information

We have explained all the elements that we need to calculate the mutual information between the input and the output and therefore are ready to restate the question that we want to address in this work. Which subset of input configurations that belong to \( I \) maximizes the mutual information? To be more specific, What are the values \( p(G_j) \) such that the \( MI(I; O) \) is maximized?

In order to maximize the mutual information as a function of \( p(G_j) \) (we rename \( p(G_j) \equiv x_j \) and \( H_{G_j} \equiv h_j \) for convenience), we calculate the gradient of \( MI(I; O) \) on the \( x_j \) space with restrictions \( \sum_j x_j = 1 \) and \( x_j \geq 0 \). The approach followed to calculate the gradient consists of reducing the space of search from \( M \) to \( M-1 \) by using \( x_M = 1 - \sum_{j=1}^{M-1} x_j \) on the \( MI(I; O) \) formula. The gradient expression used is

\[
\frac{\partial MI(I; O)}{\partial x_\mu} = h_M - h_\mu + \sum_{R=1}^{2N} \sum_{t=0}^{T} \left( p_{x_M}(R, t) - p_{x_\mu}(R, t) \right) \log_2 p(R, t),
\]

with \( \mu = 1, \ldots, M, h_M = \sum_{i \neq \mu} h_i, \) and \( p_{x_M}(R, t) = \sum_{i \neq \mu} p_x(R, t). \) This gradient helps to maximize

\[
\Delta MI(I; O) = \sum_{\mu=1}^{M-1} \frac{\partial MI(I; O)}{\partial x_\mu} \Delta x_\mu.
\]

It is sufficient to change the values \( x_\mu \) by using

\[
\Delta x_\mu = \alpha \frac{\partial MI(I; O)}{\partial x_\mu}
\]

with \( \alpha > 0 \). Another restriction that must be imposed is that if the change of \( x_\mu \) would result in \( x_\mu < 0 \) or \( x_\mu > 1 \), then the modification of the values does not take place.

The idea of using the gradient is to find the direction of \( x_\mu \) that corresponds to bigger values of the mutual information. Then we change \( x_\mu \) in that direction. The process is repeated several times and for all \( x_\mu \) until the gradient approaches zero, close to a maximum. At this point we have the set of \( x_\mu \) that maximizes the mutual information.
Since there are multiple local maxima, the search has to be combined with random hints. The set of \( p(G_j) \) is randomly set at first (we replace the common value \( p(G_j) = \frac{1}{M} \) from the simulations or experiments by randomly choosing each \( p(G_j) \) from a random uniform distribution between 0 and 1). The random set of \( p(G_j) \) is normalized to 1, and the process of finding new \( p(G_j) \)s that maximize the MI described above is repeated until an approximate maximum of the MI is achieved (changes in \( p(G_j) \) become smaller than 1%). The small subset of \( G_j \)s in \( I \) found with maximum \( p(G_j) \) after maximizing the MI is stored, and new random \( p(G_j) \)s are set; the procedure is then repeated.

After enough repetitions (about the number of different configurations in \( I \)) of the process above, we can define \( S \) as the total set of the input configurations found to maximize the mutual information.

Then we define the subset \( s(H_G - \epsilon, H_G + \epsilon) \in S \) as the chosen configurations that generate a conditional entropy \( H_G \), with a value between the numerical values \( H_G - \epsilon \) and \( H_G + \epsilon \). We also define the subset \( i(H_G - \epsilon, H_G + \epsilon) \in I \) of the input configurations that produce an entropy value in \( (H_G - \epsilon, H_G + \epsilon) \). Finally, we can define \( \zeta \) as

\[
\zeta(H_G - \epsilon, H_G + \epsilon) = \frac{\#s(H_G - \epsilon, H_G + \epsilon)}{\#i(H_G - \epsilon, H_G + \epsilon)},
\]

which represents what percentage of the total number of input configurations that generate entropy in a given range is found to maximize the MI.

4 The Model Neurons and Their Synaptic Connections

The single-neuron model is a modified version of the HR model that is known to generate chaotic behavior (Hindmarsh & Rose, 1984). The additional coefficients in the equations were introduced for a more convenient implementation of the analog circuit described in the following sections. The model is made of three dynamical variables comprising a fast subset, \( x \) and \( y \), and a slower \( z \):

\[
\frac{dx(t)}{dt} = 4 \cdot y(t) + 1.5 \cdot x^2(t) - 0.25 \cdot x^3(t) - 2 \cdot z(t) + 2 \cdot e + I_{\text{syn}} \tag{4.1}
\]

\[
\frac{dy(t)}{dt} = b/2 - 0.625 \cdot x^2(t) - y(t), \tag{4.2}
\]

\[
\frac{1}{\mu} \frac{dz(t)}{dt} = -z(t) + 2 \cdot [x(t) + 2 \cdot d], \tag{4.3}
\]

where \( e \) represents a constant injected (DC) current, and \( \mu \) is the parameter that controls the time constant of the slow variable. The parameters are
chosen to set the isolated neurons in the chaotic spiking-bursting regime ($e = 3.281, \mu = 0.0021, b = 1, d = 1.6$). $I_{syn}$ represents the postsynaptic current evoked after the onset of a chemical graded synapse. In this letter, we consider only inhibitory synapses, which is the main type of connection present in the pyloric CPG of the California spiny lobster (*Panulirus interruptus*), and which dominates in most invertebrate CPGs.

The synaptic current has been simulated in a fashion similar to that used in the dynamical clamp technique (Sharp et al., 1996), with minor modifications:

$$I_{syn} = -\overline{g} \cdot r(x_{pre}) \cdot \vartheta(x_{post}),$$  \hspace{1cm} (4.4)

where $\overline{g}$ is the maximal synaptic conductance, $r(x_{pre})$ is the synaptic activation variable that is determined from the presynaptic activity by:

$$\frac{dr}{dt} = \left[ r_{\infty}(x_{pre}) - r \right]/\tau_r$$  \hspace{1cm} (4.5)

$$r_{\infty}(x_{pre}) = \frac{[1 + \tanh((x_{pre} + 1.2)/0.9)]}{2},$$  \hspace{1cm} (4.6)

$\tau_r$ is the characteristic time constant of the synapse ($\tau_r \sim 100$), and $\vartheta(x_{post})$ is a nonlinear function of the membrane potential of the postsynaptic neuron, $x_{post}$:

$$\vartheta(x_{post}) = (1 + \tanh((x_{post} + a)/b)).$$  \hspace{1cm} (4.7)

Parameters for $\vartheta(x_{post})$ ($a = 2.807514$ and $b = 0.4$) were chosen so that this function remained linear for the slow oscillations (subthreshold region for the fast spikes), that is,

$$\frac{dx}{dv}\big|_{a,b} \sim 1$$  \hspace{1cm} (4.8)

$$g(x)\big|_{a,b} \sim 0.$$  \hspace{1cm} (4.9)

The rule used to set the connectivity pattern in the set $I$ is that with a probability of 80%, the connection $g_{ij}$ will range uniformly from 0.0 to 1.0, and with a probability of 20%, it is set to 0. This connectivity pattern rule is chosen in this way because there is no CPG in any animal where all the neurons are connected to all the rest.

After choosing the connectivity of the CPG, we perform the simulation by numerically integrating equations 4.1 to 4.3, plus those for all the active synapses, described by equation 4.5, using a fourth-order Runge-Kutta
algorithm with a fixed step of 0.01 units of time. The bursts are sampled at every two units of time to build the conditional probabilities $p_{G_j}(R, t')$.

5 The Electronic Neuron

We also worked with analog electronic circuits developed to reproduce the observed membrane voltage oscillations of isolated biological neurons from the stomatogastric ganglion of the California spiny lobster. These electronic neurons (ENs) have been successfully used to replace some biological neurons in the stomatogastric ganglion, reestablishing the regular pattern of the oscillations of the lobster pyloric CPG (Szücs et al., 2000).

The block diagram of the simple analog circuit we use to implement the three-dimensional dynamical system of the EN is shown in Figure 3. This circuit integrates equations 4.1 to 4.3. The circuit uses three integrators, one adder, one inverter, two analog multipliers, and one nonlinear amplifier. We used off-the-shelf general-purpose operational amplifiers, National Instruments Model TL082, to build the integrators, adders, inverters, and nonlinear amplifier; and we used Analog Devices Model AD633 as analog multipliers. More details about the analog implementation of the ENs, as well as a four-dimensional EN that is able to reproduce in even more detail the chaotic behavior of the isolated biological neurons, can be found in Pinto et al. (2000).

The ENs were also set a priori in chaotic spiking-bursting regimes as described in section 4 but with different values of the control parameters.
(e ≈ 1.75, b = 0, µ ≈ 0.0022, d ≈ 0.63). The components used in the ENs have a 10% tolerance, and the values indicated for the parameters here are averages of the values set in the ENs. In the experiments, we usually fine-tune e, µ, and d around the values indicated to obtain similar chaotic spiking-bursting patterns among the ENs. There is also an integration time constant that was introduced by means of a capacitor to make the bursts and spikes of the EN have approximately the same average duration presented in time series of the membrane potential of living neurons from the lobster CPG. The time constant relates the real time of the EN to the units of time of the simulations: \( t_{\text{real}} = \frac{t_{\text{units}}}{450} \).

5.1 Implementation of the Analog CPGs Using the DynClamp4, a Dynamic Clamp Program. Our DynClamp4 dynamic clamp program (Pinto et al., 2001) runs on a Windows NT 4.0 platform in a Pentium III computer with an Axon Digidata 1200A ADC/DAC board. DynClamp4 is an implementation of the dynamic clamp protocol (Sharp et al., 1996) that uses an auxiliary analog demultiplex circuit, which we also developed, to generate all the possible combinations of chemical and electrical synapses among up to four living or electronic neurons, as well as several Hodgkin-Huxley voltage-dependent conductances. The DynClamp4 can be used to connect living neurons, electronic neurons, and hybrid circuits, as shown in Figure 4.

The program digitizes the membrane potential of the neurons as it appears at the output of the microelectrode amplifiers; then it calculates the current to be injected in each neuron due to the combination of all synapses and conductances. Then the voltage signals proportional to these currents are generated via digital-to-analog converters. This cycle is repeated with
a frequency of more than 5 kHz so that the neurons are subjected to a continuous current signal, as compared to their intrinsic timescales.

In this work, we used a modified version of the DynClamp4 software for the automatic implementation of the random synapses between the ENs. To facilitate this, we needed to tune the nonlinear amplifiers at the output of the ENs to reshape, rescale, and the offset of the membrane potentials $x_i(t)$ in order to make them resemble the overall and relative amplitudes between slow oscillations and spikes in the signal we have from the biological neurons.

The analog ENs were connected by means of the DynClamp4, so we could repeat the digital computer simulations performed earlier with these analog computers. We used only the chemical synapses of the DynClamp4 program. The model implemented for these synapses is similar to the one described in section 4 for the computer simulations, but it is a closer approximation to the biological graded chemical synapses present in the lobster CPG. The model of the synaptic current is described by the first-order kinetics (Destexhe et al., 1994; Sharp et al., 1996):

$$I_{syn} = g_{syn} S (V_{syn} - V_{post}),$$
$$\left(1 - S_\infty\right) \tau_s \frac{dS}{dt} = (S_\infty - S),$$

where

$$S_\infty (V_{pre}) = \begin{cases} \tanh \left( \frac{V_{pre} - V_{thres}}{V_{slope}} \right) : & V_{pre} > V_{thres} \\ 0 : & \text{otherwise}, \end{cases}$$

$g_{syn}$ is the maximal synaptic conductance, $S$ is the instantaneous synaptic activation, $S_\infty$ is the steady-state synaptic activation, $V_{syn}$ is the synaptic reversal potential, $V_{pre}$ and $V_{post}$ are the presynaptic and postsynaptic voltages, respectively, $\tau_s$ is the time constant for the synaptic decay, $V_{thres}$ is the synaptic threshold voltage, and $V_{slope}$ is the synaptic slope voltage.

The common parameters we used for all synapses were $V_{syn} = -80$ mV (inhibitory synapses), $\tau_s = 100$ ms, $V_{thres} = -40$ mV, and $V_{slope} = 10$ mV. For every trial of synaptic configuration, we chose at random 20% of the synapses to have $g_{syn} = 0$, and the other 80% of the synapses were chosen to have $g_{syn}$ ranging uniformly from 0 to 500 nS. This is similar to what we did in the computer simulations. The output currents generated by the DynClamp4 are in nA, and in the living neurons the microelectrode amplifiers usually use a conversion factor of 50 to 100 mV/nA in their current input. For our ENs, a conversion factor of 200 mV/nA was appropriate to generate the voltage signals to be presented as inputs ($I_{syn}$).

For each synaptic configuration, the dynamic clamp cycle was started; then transients were allowed to dissipate for 60 s before acquiring data.
The bursts of each EN were sampled every 10 ms and detected when the reshaped membrane potential crossed a threshold of $-40 \text{ mV}$. The bursts were recorded for 300 s, and the conditional probabilities $p_{G_j}(R, t')$ for each set of synaptic configuration were calculated in the same way as described in section 2.

6 Results of the Computer Simulations

We performed simulations of CPGs of three and four chaotic neurons where the connections between them were chosen at random according to the rules and methods explained in section 4. For each CPG, a pool of 850 synaptic configurations was tested ($\#I = 850$). For each configuration, 30 random initial conditions were utilized, and a transient time of 10,000 was discarded before the probability distributions were calculated for 40,000 units of time. The bursts were sampled at every 2 units of time, the conditional probabilities and entropies were calculated, and the maximization of $MI(I; O)$ as a function of $p(G_j)$ was carried out.

Once all the numerical calculations were finished, the conditional entropies and probabilities were stored. The maximization of the mutual information was performed using the rules explained in previous sections.

In Figure 5 (left), one can see the distribution of the conditional entropy values for a four-neuron CPG and a random set of $I$, where all the elements were chosen from an uniform distribution. We can see that most of the input configurations are situated in the range of entropy values between 5.5 and 7.5 bits. Those entropy values represent irregular activity (see a time series on Figure 6), whereas values closer to 2 represent regular rhythms. In Figure 5 (right) we show the distribution of the conditional entropy for a four-neuron CPG. In this case, most of the input configurations have conditional entropy between 6 and 9 bits.

![Figure 5](image-url)
Figure 6: (Left) Time series for a configuration $g_{12} = 0.207668, g_{13} = 0.396304, g_{21} = 0.058504, g_{23} = 0, g_{31} = 0.782209, g_{32} = 0.452369$ that generates a conditional entropy with value of 6.64 bits. (Right) Time series for the configuration $g_{12} = 0.110004, g_{13} = 0.253859, g_{21} = 0.700028, g_{23} = 0.152461, g_{31} = 0.772312, g_{32} = 0$ that generates a conditional entropy value of 2.58 bits.

In Figure 7, we can see the ratio $\zeta$ between the number of configurations found to maximize the MI and the number of input configurations for a CPG of three and four neurons. Most of the chosen configurations lie in the lower range of the conditional entropy in both cases ($\zeta$ vanishes for values about 1 or 2 bits higher than the minimum entropies found), which indicates
that a small subset of input configurations is chosen and that most of them behave in a regular manner.

The main results are summarized as follows:

1. A subset of 100 configurations of $I$ accounts for 99% of the configurations that maximize $MI(I; O)$, that is, $\sum_{\mu \in \text{subset}} p(G_{\mu}) \leq 0.99$.

2. The preferred connectivity patterns are the ones with entropy values between 2 and 3 bits. These configurations produced the most regular CPG activity, as can be seen in Figure 6.

3. All of these configurations are nonopen topologies. Most of the known invertebrate CPGs have nonopen topology connections. We have defined nonopen topologies as those in which each neuron receives synaptic input from at least one other neuron. The explanation for the dominance of such topologies is likely because the model neurons are chaotic: any chaotic neuron that does not receive input from any other neuron remains chaotic. The chosen configurations in our experiments are typically nonopen topologies, which produce regular spatiotemporal patterns, while the open topology configurations almost always produce a chaotic pattern.

7 Results of the Analog Computations: ENs + Dynamic Clamp

In the analog computations, we first performed our simulations in a CPG composed of three chaotic neurons, with connections between them chosen at random, as explained in the previous sections. A pool of 500 random synaptic configurations was tested ($#I = 500$). The methods described at the end of section 5 were repeated to obtain the conditional probabilities and the entropies for each synaptic configuration. The maximization of the $MI(I; O)$ as a function of $p(G_{i})$ was carried out in the same way as for the computer simulations (see section 3). The same procedure was repeated for the CPGs composed of four neurons, but we tested a pool of 630 synaptic configurations ($#I = 630$). Figure 8 shows the distribution of the conditional entropy values for random set of $I$ where all the elements were chosen from an uniform distribution for both three- and four-neuron CPGs.

Here we also have most of the input configurations situated in a small but slightly different range of entropy values (between 5.0 and 6.5 bits for three-neuron CPGs and between 5.5 and 7 bits for four-neuron CPGs) as compared to Figure 5. The ranges are shifted about +1 bit in the simulations, because in the analog experiments, the burst sampling rate is about half the sampling rate used in the simulations (when one converts the units of time). However, these values of entropy still represent irregular activity (as in time series in Figure 9, for example) and the values closer to 3 bits represent regular rhythms. Another difference between the results from simulations and the analog experiments is the minimum entropy,
Figure 8: (Left) Distribution of inputs with specific values of the conditional entropy for $\epsilon = 0.225$ in a three-neuron CPG. (Right) Input distribution in a four-neuron CPG for $\epsilon = 0.58$.

Figure 9: (Left) Time series for a configuration $g_{12} = 239 \text{nS}, g_{13} = 374 \text{nS}, g_{21} = 0 \text{nS}, g_{23} = 277 \text{nS}, g_{31} = 217 \text{nS}, g_{32} = 0 \text{nS}$ that generates a conditional entropy with a value of 6.44 bits. (Right) Time series for a configuration $g_{12} = 277 \text{nS}, g_{13} = 0 \text{nS}, g_{21} = 260 \text{nS}, g_{23} = 257 \text{nS}, g_{31} = 0 \text{nS}, g_{32} = 443 \text{nS}$ that generates a conditional entropy with a value of 3.37 bits.

which is smaller in simulations (from 1 to 2 bits) than in the experiments (from 3 to 4 bits), probably because the fluctuations present in the electronic circuits are much higher than the small numerical noise introduced in the simulations.

In order to show that the analog computations also generate the same results pointed out in section 6 for the digital computer simulations, we also calculated the $\zeta$ ratio between the number of configurations found to maximize the MI and the number of input configurations for the analog computations of the three- and four-neuron CPGs. As can be seen in Figure 10, in both cases, most of the chosen configurations have a conditional entropy smaller than 5 bits (the limit is again just about 1 or 2 bits...
higher than the minimum entropies found), which indicates again that the subset of configurations chosen behaves in a more regular way.

8 Discussion

One of the main problems faced by the study of the CPGs in animals is to establish a relationship between the electrical activity of the CPG and the mechanical device that performs a specific function. In the experiments performed in some animals, the CPG is located in a dish without connections to the mechanical device, and hence a measure of the function of the CPG cannot be established. If the motor activity is recorded, there are no means at the present time to introduce electrodes in the neurons of the CPG in the living animal because it moves and breathes. The question we address is, Can we find a general measure that helps us to bound the potential function of a CPG? In this work, we show how, using computer and electronic models, the maximization of the information gives an approximate response that bounds the possible solutions that one can find in the CPG. It is remarkable that regardless of the differences between the computer and electronic implementations, similar results are obtained. It hints at the generality of the phenomenon for simple CPGs made of chaotic neurons.
We must consider that the simplifications imposed on our model CPGs, disregarding intrinsic properties of neurons and including only inhibitory connections, seem to be quite drastic and bring serious limits to the generality of the results, especially when more complex CPGs, such as those found in vertebrates, are considered. However, one should also consider that if even our simple model CPGs were able to show some properties found in living invertebrate CPGs, it could mean that the models were able to express important features. So although these results cannot be claimed to validate the models, they do serve as evidence of the generality of the properties found, at least in small invertebrate CPGs. Several other invertebrate CPGs that have excitatory synapses also present nonopen topologies. For a few examples one can see the CPGs for feeding in Planorbis (Arshavsky et al., 1985), swimming in Tritonia (Getting, 1989), and swimming in Clione (Arshavsky et al., 1998).

From an evolutionary perspective, our results are evidence that one can think that the CPGs are developed following some general rules and then the final adjustments are performed depending on the specific function to be carried out. From this point of view, the application of information theory to CPG selection would be an invaluable tool to perform a first filter of the large number of possible configurations that can occur.

A set of possible experiments to prove whether nature uses the information-maximization principle to evolve would be to let a set of nonspecific neurons develop connections in a culture dish. Once the connections are developed, we should check the configuration obtained. We could repeat the experiments as many times as needed to make the statistic relevant.

The observation that the selected connection topologies are nonopen is also supported in previous work (Huerta et al., 2001), where open topology solutions in the CPG do not provide an efficient function of the pyloric chamber of the lobster. It is interesting to note that information maximization gives a bounded region of configurations where the specificity of a function is included.

Finally, we note that the use of electronic model neurons can be a good tool to check the results obtained from numerical simulations when no better experiments are available, since the results found have to be robust to several kinds of fluctuations the ENs are exposed to.

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