Model of traveling waves in a coral nerve network

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Abstract

Coral polyps contract when electrically stimulated and a wave of contraction travels from the site of stimulation at a constant speed. Models of coral nerve networks were optimized to match one of three different experimentally observed behaviors. To search for model parameters that reproduce the experimental observations, we applied genetic algorithms to increasingly more complex models of a coral nerve net. In a first stage of optimization, individual neurons responded with spikes to multiple, but not single pulses of activation. In a second stage, we used these neurons as the starting point for the optimization of a two-dimensional nerve net. This strategy yielded a network with parameters that reproduced the experimentally observed spread of excitation.

Keywords

Genetic algorithm (GA); Neuron; Network; Coral

Introduction

Corals, members of the phylum coelenterata, are the simplest organisms with a nervous system. Depending on the symmetry of their body plans, hexacorals (class Anthozoa, subclass Zoantharia, order Scleratinia, including the reef-building species) and octacorals (class Anthozoa, subclass Alcyonaria, order Alcyonacea), are distinguished (Veron 2000; Fabricius and Alderslade 2001). What all of these species have in common is a structure composed of multiple polyps embedded in a common body. Each polyp consists of a tube with tentacles at its upper margin, which it uses to catch plankton. The individual polyps are similar to sea anemones (class Anthozoa, subclass Zoantharia, order Actiniaria, Fig. 1a), to which corals are related. The body tube consists of endodermal tissue on the inside and ectodermal tissue on the outside. These organisms, in contrast to all higher metazoans, lack a mesoderm. A cell-free substance, the mesogloea, is located between the endo- and ectoderm. The mouth of coral polyps is both the entry and exit point into their intestine. Many species of corals contain such

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actively feeding polyps, called autozooids and non-feeding, supporting polyps, called siphonozooids. In addition to feeding on plankton, many corals harbor photosynthetic symbionts, the zooxanthellae. Despite their otherwise rather simple Bauplan, the ectoderm already contains a network of nerve cells (neurons), which are relatively unspecialized when compared to the neurons of higher animals (Bullock and Horridge 1965). After the initial settlement of a larva, a single organism contains anywhere between a single polyp to hundred of thousands (*Acropora*) of polyps. The nervous system is continuous between the individual polyps, and Horridge (1957) and we have observed the spread of activity across many polyps in response to repetitive electrical stimulation. The response of coral colonies was varied between species of corals. In *Palythoa* (Fig. 1b), the diameter of the area of contracted polyps increased in a linear fashion. The pattern we fit our model to was the average response and we omitted the variation from this study. This is related to, but distinct of the study by Horridge, where a sublinear, linear or supra-linear spread of excitation as a function of stimuli, not time, was observed.

One of us (THB) has worked for over 40 years to model the spread of contractions in a coral nerve net. The long process of finding an appropriate set of parameters proceeded by trial and error. This process was greatly speeded up using a genetic algorithm (GA), an optimization procedure that is analogous to the selection for fitness that occurs during biological evolution (Mitchell 1998). The model of a coral nerve net was optimized to match experimental observations of corals that were electrically perturbed. There are three levels of complexity that can be distinguished and are biologically motivated: the individual neuron, the single polyp containing many neurons, and the colonial organism containing many polyps. We sequentially optimized models of the first two of these three levels. We omitted an explicit simulation of the polyp structure within the colony level and collapsed the complete coral nervous net into one layer of neurons. The polyps are implicitly modeled by the layer of neurons within the structure closest in proximity to the interconnective tissue between polyps. A model based on individual neural elements as opposed to a mean-field model was chosen as it more realistically models the structure of the nervous system.

In GAs, first a population of candidate solutions (in our case coral nerve net models) is constructed from a population of parameter sets. Then an alternation of rounds of selection and the introduction of variation mimic the natural selection process, which leads to the successively better adaptation of natural organisms to their environment. It is important to point out that although GAs mimic the algorithmic structure of biological evolution, they are not meant as a model of evolution, but merely as an optimization strategy.¹ In this paper, we improve the basic genetic algorithm concept by mimicking another feature of biological evolution, its modularity. We do this by first optimizing the parameters of the individual neuron models that compose the nerve net. In a second step, we use these values as starting points and additionally optimized the parameters of the connections between neurons. In this manner, we obtained the parameter values of a model of a coral nerve net reproducing the experimentally observed spread of excitation.

Methods

Coral nerve net model

We modeled the nervous system of a coral as a homogenous network of connected single-compartment neurons. Each neuron contained the classical fast Na^+ , delayed rectifier K^+ and

¹In the same sense, the terminology used here, such as “genome” for the parameters to be optimized and “generation” for a round of optimization do not reflect a claims about modeling biological evolution but merely follow GA terminology.

leak Hodgkin–Huxley ion channels (Hodgkin and Huxley 1952). We chose the Hodgkin–Huxley model of neural excitability as it represents a well-characterized description of neural spiking, and although the precise parameter values are likely to be different, we assume that spiking in corals is equally mediated by depolarization-activated de- and hyperpolarizing channels. Unfortunately, there are no intracellular voltage recordings of coral neurons extant. This did not allow us to model the electrical behavior of coral neurons with kinetical parameters specific to these organisms. We also lack specific information on the details of synaptic transmission in coelenterates, so we used a generic chemical model of an excitatory synapse in our model. By generic model we mean that we do not make any assumptions about the nature of the involved neurotransmitters and receptors. Rather, we assume chemical transmission with an excitatory reversal potential at the postsynaptic side. The experimental electrical stimulation was simulated as synaptic potentials in the neurons.

The network is an extension of the model of a coral nerve net simulated in Josephson et al. (1961) and is oriented in a two-dimensional grid with Hodgkin–Huxley neurons positioned at a uniform distance from all nearest neighbors. Neurons are bi-directionally connected to their eight nearest neighbors in the horizontal, vertical, and diagonal directions of the grid. A refractory period is applied to each neuron following an action potential to prevent reverberatory activity.

Genetic algorithm

The GA was used to optimize the parameters of first the model neurons, then the model nerve net so that the models performed the desired behaviors. During the single-cell simulations, a single EPSP was elicited in the neuron. This was followed by a second simulation where it was stimulated by three consecutive impulses 2 ms apart. The single cells were optimized to spike in response to repeated stimulation, but not a single stimulus. During the network simulations, a single neuron in the center of the network was stimulated by either one or three consecutive impulses 2 ms apart. The networks were optimized for a propagation of the edge of activation linear in time in response to the triple stimulation.

The parameters specifying the models were contained in a list of parameters called “genomes” in the GA literature. A genome for a neuron contained three parameters: maximum sodium and potassium conductances, and leakage reversal potential.

Only the conductance densities and not the kinetic parameters were varied in order to keep the search-space low dimensional. For the network, it additionally contained parameters for the connection delay and the connection weight. Cell body dimensions, stimulus strength, and duration, and the interval between consecutive stimuli were held constant.

There were 32 models in the population, each with a different set of parameters. After each round of simulations, the performance of each model network was evaluated and assigned a fitness value. The networks were then ranked according to their fitness values. The next generation of models was drawn from the top scoring 70% of the population, eliminating the possibility of selection from the lowest ranking 30% of the population. The selection probability of a genome was scaled according to the ranking of its fitness value, so that the networks with the highest fitness were the most likely to survive in the next generation. The three best scoring network genomes were carried over to the subsequent generation without alteration, a process called elitism. This process was used to avoid the loss of favorable genes through the stochastic selection process.

Two sources of variability were used to alter the genomes: mutation and recombination. During mutation, a small random number was added to each parameter with a mutation probability of

89%, and individual parameters from two different genomes were swapped representing the same network parameter with a crossover probability of 45%. We first optimized the parameters of individual neurons to respond to the single perturbation with no action potentials fired, but to fire once in response to the multiple perturbations. Neurons were also selected to have a resting voltage of close to -60 mV.

The single neuron fitness function was:

$$f = 200x + 5|1 - y| + |-60 - v_0|/2 + |v_0 - v_1|/2, \quad (1)$$

where x is the number of action potentials fired following the single perturbation, y is the number of action potentials fired following the multiple perturbations, v_0 is the resting voltage (before perturbation), and v_1 is the voltage 370 ms after perturbation.

The GA procedure was repeated to optimize the five parameters: maximum sodium and potassium conductances, leakage reversal potential, connection weight, and delay multiplier. All parameters were the same for all neurons in the network. Default Hodgkin–Huxley parameters were used as initial values for the conductance and leakage reversal potential parameters and the connection weight, and delay multiplier were also assigned initial values. The fitness function selected for a radial spread of firing throughout the network with a constant velocity. In addition, the fitness function required no action potentials in response to the first perturbation and a single action potential in response to the second perturbation from all neurons in the network. A resting voltage of approximately -65 mV was also required with a smaller contribution to the fitness value than the firing behavior.

The network fitness function thus was:

$$f = |-65 - v_0| + \sum_i (5x_i + 10|y_i - 1| + |t_{\text{avg}} - t_i|) + z(x, y), \quad (2)$$

where x_i is the average number of action potentials fired by the i th order neighbors following the single perturbation, y_i is the average number of action potentials fired by i th order neighbors following the multiple perturbations, t_i is the average time elapsed from first spike from i th to $(i+1)$ th order neighbors, t_{avg} is the average time elapsed between first spikes of adjacent neighbors, v_0 is the resting voltage, and z is the additional cost for having too few or too many action potentials fired.

All simulations and optimizations were carried out in the neuronal simulation language NEURON (version 5.7, Hines and Carnevale 1997). A single generation of the GA, an iteration of the optimization routine, which includes the construction of 32 networks, electrophysiological simulations (200 and $\sim 4,000$ ms) and selection, mutation, and recombination of genes, required approximately 1.5 min on four parallel Opteron AMD 2.4 GHz processors. The simulation code is available upon request and will be submitted to the Yale Sense Lab Model Database (<http://senselab.med.yale.edu/modeldb/>).

All experiments comply with the “Principles of animal care”, publication No. 86-23, revised 1985 of the National Institute of Health, and also with the current laws of the country in which the experiments were performed (Table 1).

Results

The patterns we aimed to replicate were observed by T.H.B. in *Palythoa* in the Sea of Cortez, Mexico and in the Enewetok Atoll in the Republic of the Marshall Islands (then a UN trusteeship of the USA). Screenshots from video footage of the observed propagation patterns in response to repetitive electrical stimulation are shown in Fig. 1b.

In a first step to achieve this goal, we optimized single neurons so that they would respond with a spike to three but not to one stimulation pulse. The reasoning behind this step is that a network, which responds to repetitive stimulation in an interesting manner, is most likely composed of subunits, which perform some kind of integration.

The single neuron parameters were found after 43 generations and were shown in Table 2

A single perturbation caused a small subthreshold increase in voltage, while two or more perturbations caused a single firing in the single neuron, from the resting potential of -65 mV (Fig. 2).

As a second step, we took these parameters as a starting value and optimized for a linear spread of excitation. The network parameters for this behavior were found after 13 generations and were shown in Table 3

The first perturbation caused a small subthreshold increase in the voltage of the center (perturbed) neuron and two or more perturbations caused a single firing from all neurons in the network. Firing was simultaneous in neurons equidistant from the center neuron and spread radially with an approximately constant velocity of 1 neuron/s (Fig. 3). We initially assumed that -60 mV was a reasonable resting potential for the parameter search. After the single neuron optimization, we found that the Hodgkin–Huxley neurons in the NEURON program environment favor a resting potential of -65 mV for a range of maximum sodium conductances (approximately 0.09 – 0.17 S/cm²) while the maximum potassium conductance is held constant at the default value. The network fitness function favored -65 mV as the ideal resting potential rather than -60 mV in the single neuron fitness function; however, the difference in fitness punishment between these two selected resting potentials is marginal.

Discussion

The model coral nerve network with the parameters found by optimizing first the single neuron, then the single neuron and network parameters, reproduced experimentally observed behavior. In response to repetitive stimulation, the diameter of the activity increased in a linear manner, as experimentally observed in *Palythoa* (Fig. 1b).

GAs were previously been used for optimizing only single-cell parameters (Stiefel and Sejnowski 2007; Achard and De Schutter 2006). We have successfully extended this approach to optimize the parameters of a model coral neural net. This successful optimization shows that the behavioral output of an animal's complete nervous system can be modeled with a few assumptions and that all parameters of such a model can be found within reasonable computing time. The relatively simple structure of the coelenterate nervous system makes this possible for the linear radial spread of firing behavior.

The optimized network tended to exhibit a radial spread of excitation with constant velocity for a variety of connection weight and delay parameters. Holding the conductance and delay parameters constant and decreasing the connection weight resulted in a marginal decrease in velocity of spread between only the stimulated neuron and the first order neighbors on the order

of a few milliseconds. The velocity of spread between successive neighbors was not affected. Systematically varying the delay parameter while holding the conductance parameters constant showed that the velocity of spread remained constant, but was linearly related to the magnitude of the delay parameter for a variety of connection weights. These results suggest that the radial spread of firing with constant velocity is robust and preserved for a variety of connection weights and delay parameters. Optimizing for a radial spread of firing with acceleration of velocity is a future direction of this work.

In the future, we will include additional biological detail in the simulations of coral nervous systems, such as the separation of the network into polyps and interpolypoidal neurons. We will also aim to delimit the parts of the parameter space giving rise to all three observed modes of the spread of excitation.

We hope that more empirical details of the physiology of coral nervous systems will emerge in the near future and that these data will shed more light and allow more biologically realistic modeling of these fascinating animals at the base of the metazoan phylogenetic tree.

Theodore H. Bullock: personal reflections

This collaboration with Ted Bullock grew out of a long-term interest that he had in modeling the nervous networks of coral. We have old movies of him out in the Marshall Islands stimulating corals with a Grass stimulator. His early programming efforts were in FORTRAN and with other colleagues he had developed a simulation environment that allowed him to explore the behavior of models with different parameters for the neurons and networks. His notebook was filled with attempts to search for a combination of parameters that would match his behavioral data. In an earlier collaboration with Ted, we had developed a computational model of the pacemaker nucleus of electric fish (Moortgat et al. 2000), another field that he pioneered. We teamed up with Ted again in 2005 for this project, applying genetic algorithms to the problem of how waves of activity travel in coral using a technique that allowed the search to be carried out rapidly and automatically. We had used this technique before to explore the complexity of single neurons and this was our first foray into the complexity of networks. We learned from Ted a great deal about corals and he inspired us to learn more from the literature. He shared with us stories about his coral expeditions and regaled us with other stories behind the many artifacts in his office, from dolphin and bull shark brains to Amazonian natives' bows and arrows. One of us (KS) has since moved to Okinawa and through Ted's influence has become a computational coral neuroscientist. Ted's personality and scientific achievements have inspired generations of neuroscientists to take up their life's work.

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Fig. 1.

Structure of a polyp and observed patterns of the spread of excitation across polyps. **a** Schematic drawing overlayed onto photograph of a polyp. **b** Spread of polypal contraction activity at the indicated times in a *Xenid* soft coral collected in the Sea of Cortez. The polyps are stimulated with consecutive pulses through a suction electrode and neighboring polyps contract in a radially expanding pattern at a rate of approximately 1 polyp/s

Fig. 2. Single neuron model simulations. Membrane potential traces in response to **a** a single stimulation and **b** to three stimuli

Fig. 3. Network model simulations. Spread of excitation in an 11×11 array of polyps in response to triple stimulation of the center neuron. Time since the stimulation is shown to the left of each array. Excited neurons in *yellow* and inactive neurons in *violet*

Table 1

Model parameters

Parameter	Description	Units	Single neuron initial value	Network initial value
gnabar_hh	Maximum sodium channel conductance	S/cm ²	0.12	0.161203
gkbar_hh	Maximum potassium channel conductance	S/cm ²	0.036	0.036
el_hh	Leakage reversal potential	mV	-54.3	-54.3
Delay multiplier	Multiplier which scales delay in conduction of excitation between neurons			100
Connection weight	Weight of connection between neurons			0.1

Table 2

Optimized neuron parameters

gnabar_hh (S/cm ²)	0.161203
gkbar_hh (S/cm ²)	0.036
el_hh (mV)	-54.3

Table 3

Optimized network parameters

Delay multiplier	200.598
Connection weight	2.04033