OPTIMIZING A CORAL NERVE NET

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Eugenia J. Chen

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The Undersigned Faculty Committee Approves the

Thesis of Eugenia J. Chen:

OPTIMIZING A CORAL NERVE NET

_____

Peter Blomgren, Chair
Department of Mathematics and Statistics

_____

Antonio Palacios
Department of Mathematics and Statistics

_____

Forest Rohwer
Department of Biology

_____

Approval Date

DEDICATION

In memory of Dr. Theodore H. Bullock.

ABSTRACT OF THE THESIS

Optimizing a Coral Nerve Net
by
Eugenia J. Chen
Master of Science in Computational Science
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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 2-dimensional nerve net. This strategy yielded a network with parameters that reproduced the experimentally observed spread of excitation.

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CHAPTER 1

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 octocorals (class Anthozoa, subclass Alcyonaria, order Alcyonacea), are distinguished (Veron 2000; Fabricius and Alderslade 2001). What 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 are used to catch plankton. The individual polyps are similar to sea anemones (class Anthozoa, subclass Zoantharia, order Actiniaria, Figure 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 actively feeding polyps, called autozoids and non-feeding, supporting polyps, called siphonozoids. In addition to feeding on plankton, many corals harbour 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 hundreds of thousands (*Acropora*) of polyps. The

nervous system is continuous between the individual polyps, and Horridge (1957) and Chen et al. (2008) 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* (Figure 1b), the diameter of the area of contracted polyps increased with a constant velocity. The model was optimized to fit the average response and the variation is omitted from this study. This is related to, but distinct from the study by Horridge, where a sublinear, linear or superlinear spread of excitation as a function of stimuli, not time, was observed.

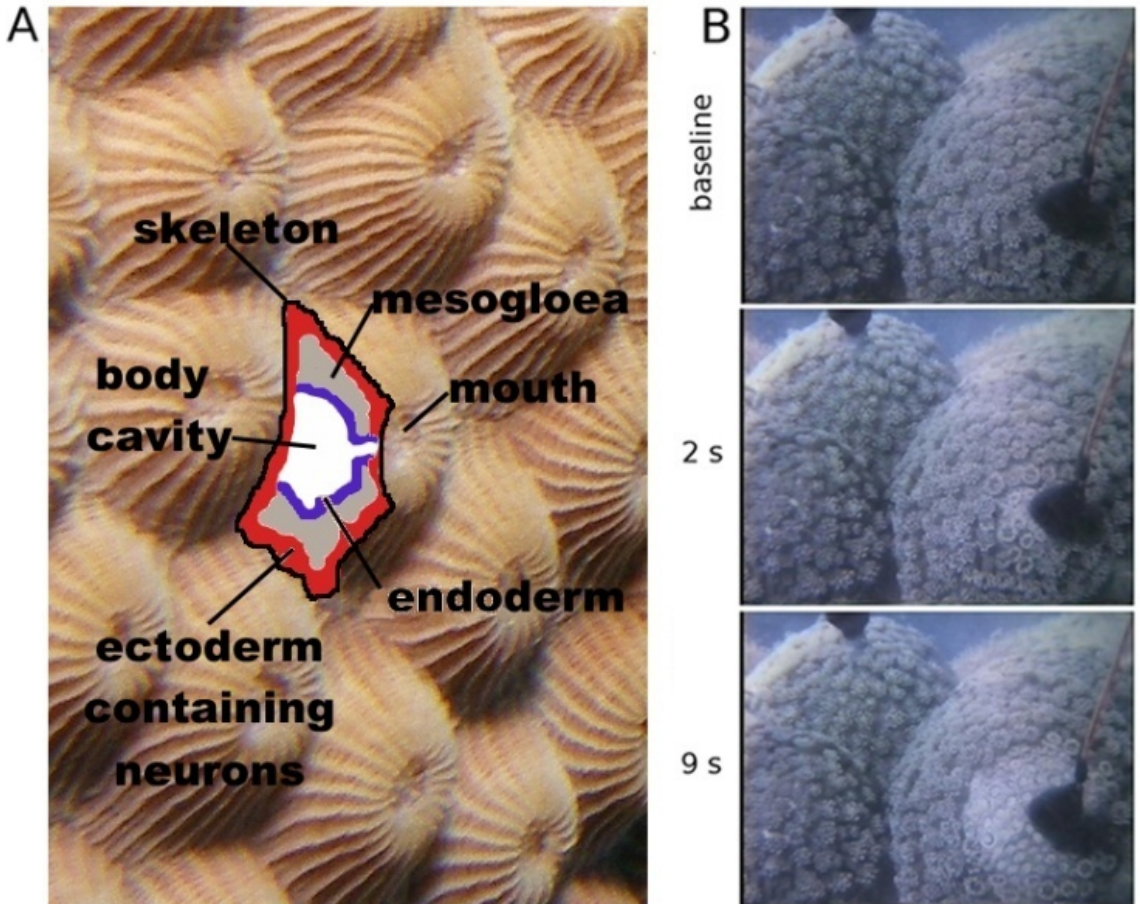


Figure 1. Structure of a polyp and observed patterns of the spread of excitation across polyps. A: Schematic drawing overlayed onto photograph of a polyp. B: Spread of polypal contraction activity at the indicated times in a Xenid soft coral collected in the Sea of Cortez. The polyps are stimulated with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

Theodore H. Bullock 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 is greatly sped up by 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 coral nervous net into one layer of neurons during the optimization procedure. 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 process, leading 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, merely an optimization strategy[1]. In this thesis, 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. During a second step, we use these values as starting points and additionally optimize 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.

[1]In 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.

CHAPTER 2

METHODS

We model the nervous system of a coral as a homogenous network of connected single-compartment neurons. Each neuron contains the classical fast Na^+, delayed rectifier K^+ and leak Hodgkin-Huxley ion channels (Hodgkin and Huxley 1952). The Hodgkin-Huxley equations are implemented by using equations (1) – (16).

$$I_{tot} = I_{Na} + I_K + I_l + I_{app} \quad (1)$$

The total current across the cell membrane (I_{tot}) is the sum of the ionic currents (I_{Na}, I_K, I_l) and the applied current (I_{app}) from the stimulus or network connections.

$$I_{Na} = g_{Na}(v - e_{Na}) \quad (2)$$

The sodium current results from the potential difference across the cell membrane (v) and the sodium equilibrium potential (e_{Na}).

$$g_{Na} = \overline{g_{Na}} m^3 h \quad (3)$$

The sodium conductance depends on the maximum sodium conductance ($\overline{g_{Na}}$), the probability of a sodium channel activation gate being in an open state (m), and the probability of a sodium channel inactivation gate being in a open state (h).

$$I_K = g_K(v - e_K) \quad (4)$$

The potassium current results from the potential difference across the cell membrane (v) and the sodium equilibrium potential (e_K).

$$g_K = \overline{g_K} n^4 \quad (5)$$

Sodium conductance depends on the maximum sodium conductance ($\overline{g_K}$) and the probability of a potassium channel activation gate being in an open state (n).

$$I_l = g_l(v - e_l) \tag{6}$$

Leakage current results from the potential difference across the cell membrane (v) and the leakage equilibrium potential (e_l).

$$\frac{dm}{dt} = \frac{(m_\infty - m)}{m_\tau} \tag{7}$$

$$\frac{dh}{dt} = \frac{(h_\infty - h)}{h_\tau} \tag{8}$$

$$\frac{dn}{dt} = \frac{(n_\infty - n)}{n_\tau} \tag{9}$$

The respective rates of change of the sodium activation variable (m), sodium inactivation variable, and the potassium activation variable (n) are time and voltage dependent.

$$m_\infty = \frac{0.1 * vtrap[-(v+40),10]}{[0.1 * vtrap[-(v+40),10] + 4\exp\left[\frac{-(v+65)}{18}\right]} \tag{10}$$

$$m_\tau = \frac{1}{[0.1 * vtrap[-(v+40),10] + 4\exp\left[\frac{-(v+65)}{18}\right]} \tag{11}$$

$$h_\infty = \frac{0.07\exp[\frac{-(v+65)}{20}]}{0.07\exp[\frac{-(v+65)}{20}] + \left[\exp\left(\frac{-(v+35)}{10}\right)+1\right]^{-1}} \tag{12}$$

$$h_\tau = \frac{1}{0.07\exp[\frac{-(v+65)}{20}] + \left[\exp\left(\frac{-(v+35)}{10}\right)+1\right]^{-1}} \tag{13}$$

$$n_{\infty} = \frac{0.1 * vtrap[-(v+55),10]}{[0.1 * vtrap[-(v+55),10] + 0.125\exp\left[\frac{-(v+65)}{80}\right]} \quad (14)$$

$$n_{\tau} = \frac{1}{[0.1 * vtrap[-(v+55),10] + 0.125\exp\left[\frac{-(v+65)}{80}\right]} \quad (15)$$

Rate constants for the sodium activation variable (m_{∞}, m_{τ}), the sodium inactivation variable (h_{∞}, h_{τ}), and the potassium activation variable (n_{∞}, n_{τ}) are fit to HH empirical data.

$$vtrap(x,y) = \begin{cases} y\left[1 - 0.5\left(\frac{x}{y}\right)\right] & \left(\frac{x}{y}\right) < 1\times10^{-6} \\ \frac{x}{\exp\left(\frac{x}{y}\right) - 1} & \left(\frac{x}{y}\right) \geq 1\times10^{-6} \end{cases} \quad (16)$$

The function vtrap(x,y) is used to avoids division by zero in the rate equations.

Table 1. Hodgkin-Huxley Parameters Held Constant

Parameter	Description	Units	Value
e_{Na}	Sodium Reversal Potential	mV	50
e_K	Potassium Reversal Potential	mV	-77
g_l	Leakage Conductance	S/cm^2	0.0003

We use 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 kinetic parameters specific to these organisms. We also lack detailed 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 2-dimensional grid with Hodgkin-Huxley neurons positioned a uniform distance from all nearest neighbors (Figure 2). Neurons are connected bidirectionally in the horizontal and vertical directions with the NEURON[2] function NetCon. Diagonal connections occur only in the corners of the squares formed by the neurons with respect to the center polyp in order to connect all neurons with the same number of incoming connections (Figure 3). A refractory period is applied to each neuron following an action potential to prevent reverberatory activity.

[2] http://neuron.yale.edu/

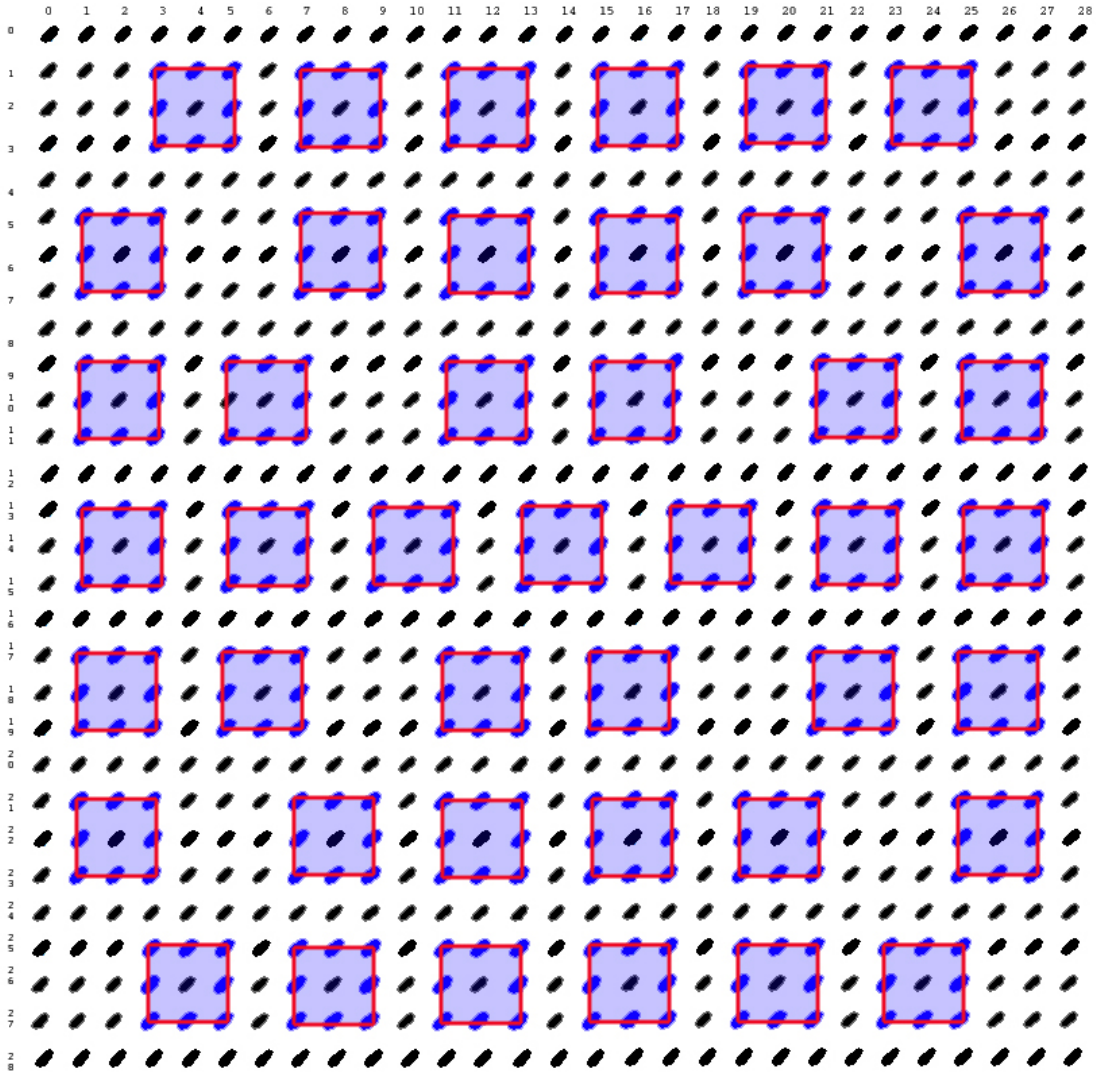


Figure 2. 2D projection of the coral network. 29x29 neurons in the xy-plane shown as black ellipses with polyps outlined in red and polyp neurons colored in blue.

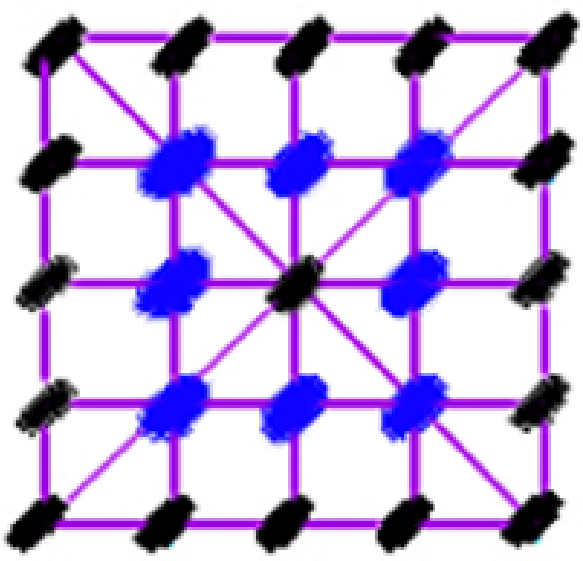


Figure 3. Network Connectivity. Center polyp (blue) and nearest neighbor neurons (outer polyp neurons in black) with connections shown in purple.

A NEURON function called NetCon connects a source (neuron) with a target synapse belonging to a neighboring neuron. At each time step, NetCon oversees a connection by applying the current from the source neuron onto the target synapse if the source neuron voltage crosses threshold. The connection weight parameter scales the strength of the current applied to the target neuron and a delay parameter determines the onset of the current. A connection threshold value of 0 mV is held constant while connection weight and delay are varied in the optimization. Current from a source neuron is applied to the target neuron 5λ milliseconds after the membrane voltage of the source neuron membrane voltage exceeds threshold, where λ is the value of the delay multiplier. The delay multiplier scales the modeled distance (5 μm) between neurons linearly.

Each neuron is associated with a single synapse. The synapse has a discontinuous change in conductance when excitation from a neighboring neuron is received through the

function NetCon and undergoes exponential decay according to the time constant τ. The time constant is fixed and the synaptic current is given by the following equations:

$$i = g(v - \theta) \tag{17}$$

$$g = weight \cdot e^{-t/\tau} \tag{18}$$

where $\theta = 0$ mV (synaptic threshold) and $\tau = 1$.

A second network is a 3-dimensional extension of the first network with polyps positioned a uniform distance from the center of the grid based on connection order and a polyp is positioned in the center of the grid. The polyp neurons form 3x3 squares in the xy plane of the network and layers of neurons are positioned in the z direction to form a total polyp height of four layers of neurons (Figure 4). In the connective layer (z = 0) there is a neuron in the center of the 3x3 polyp square. Layers above this square (z > 0) do not contain a neuron at the center, corresponding to the ectodermal placement of neurons in the polyp body. There are 43 polyps positioned in the grid. During the 3D network simulations, the neurons on the $z = 4$ plane of the center polyp are stimulated whereas during the 2D network simulation, a 3x3 square of neurons in the center of the grid are stimulated.

The program first loads a setup file which creates the neurons, synapses, and specifies parameters held constant throughout the optimization (Appendix A). A file containing the genome, the parameters varied during the optimization, loads and Hodgkin-Huxley dynamics are added to the neurons with the conductance parameters specified in the genome. The network is positioned in the xy plane and in the positive z direction in the 3D network. This positioning is used for visualization purposes only and does not affect the dynamics of the

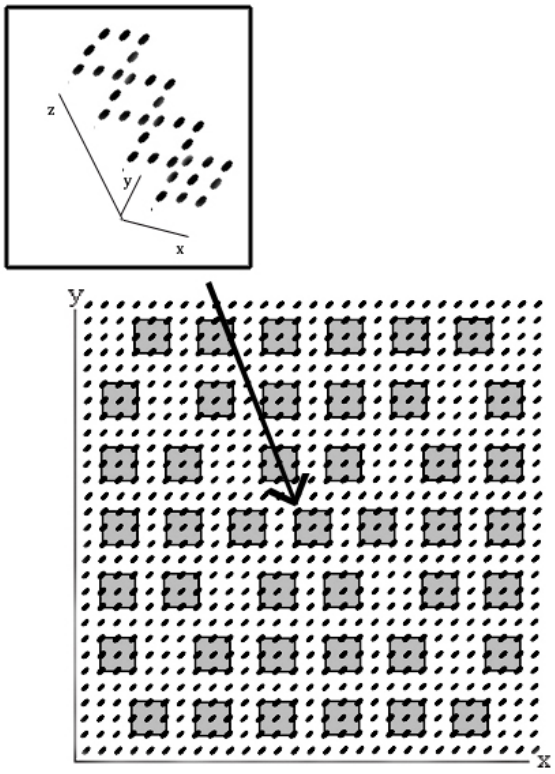


Figure 4. Mapping a polyp to the 2D grid. Each model polyp, composed of four layers of neurons, corresponds to a 3x3 square in the XY projection of the 3D network.

network. However, the dimensions of the neurons are specified during this loop. Each neuron is simulated as an approximately elliptical cell body. Several connection subroutines are loaded to connect neurons horizontally, vertically, and diagonally. The stimulus is coded in a subroutine that specifies the neurons to be stimulated, the time intervals between impulses, and the strength of the stimulus, all of which are held constant throughout the optimization.

Two simulations are conducted after the network is formed. The first simulation runs for 200 ms. The resting voltage of the center neuron at 50 ms is recorded and the simulation a

single stimulus is applied at 60 ms. After the simulation, the number of firings and spike times of each neuron is recorded.

The second simulation runs for a length of time proportional to the size of the delay parameter. Simulation length is calculated as follows for the second simulation.

$$t_{end} = 200 + \frac{3}{2}(delay * netsize) \quad (19)$$

Resting voltage of the center neuron is recorded after 50 ms and stimulation begins at 60 ms, where three impulses are applied in 2 ms intervals. The number of firings and spike times of each neuron are also recorded. Following the second simulation, the fitness score is calculated and recorded in an output file. Other recorded network output information, including number of firings, resting voltage, and difference in firing times between the perturbed neurons and neighboring neurons are recorded in the file along with the genome used to create the network.

The GA is used to optimize the parameters of first the model neurons, then the model nerve net so that the models perform the desired behaviors (Figure 5). During the single-cell simulations, a single action potential is elicited in the neuron. This is followed by the second simulation where it is stimulated by 3 consecutive impulses. The single cells are optimized to spike in response to the repeated, but not the single stimulation. During the network simulations, a 3x3 square of neurons in the center of the network are stimulated by either 1 or 3 consecutive impulses. The networks are optimized for a propagation of the edge of activation linear in time in response to the triple stimulation.

A list of parameters called a “genome” in the GA literature contains the parameters specifying the models. A neuron genome contains 3 parameters: maximum sodium and potassium conductance and leakage reversal potential. Only the conductance densities and not the kinetic parameters are varied in order to keep the search-space low-dimensional. For the network, it additionally contains parameters for the connection delay and the connection weight. Cell body dimensions, stimulus strength and duration, and the interval between consecutive stimuli are held constant.

There are 32 models in the population, each with a different set of parameters (Table 2). After each round of simulations, the performance of each model network is evaluated and assigned a fitness value. The networks are then ranked according to their fitness values. The generation of models is drawn from the top scoring 70% of the population, eliminating the possibility of selection from the lowest ranking 30% of the population. Probability of selecting a given genome is scaled according to the ranking of its fitness value, so that genomes corresponding to higher scoring networks are more likely to appear in the next generation. The two best scoring network genomes are carried over to the subsequent generation without alteration, a process called elitism. This process is used to avoid the loss of favorable genes through the stochastic selection process.

Table 2. Model Parameters

Parameter	Description	Units	Initial Value	
			Single Neuron	2D Network
$\overline{g_{Na}}$	Maximum sodium channel conductance	S/cm^2	0.12	0.161203
$\overline{g_K}$	Maximum potassium channel conductance	S/cm^2	0.036	0.036
e_l	Leakage reversal potential	mV	-54.3	-54.3
λ	Multiplier scaling delay in conduction of excitation between neurons			50
weight	Weight of connection between neurons			0.01

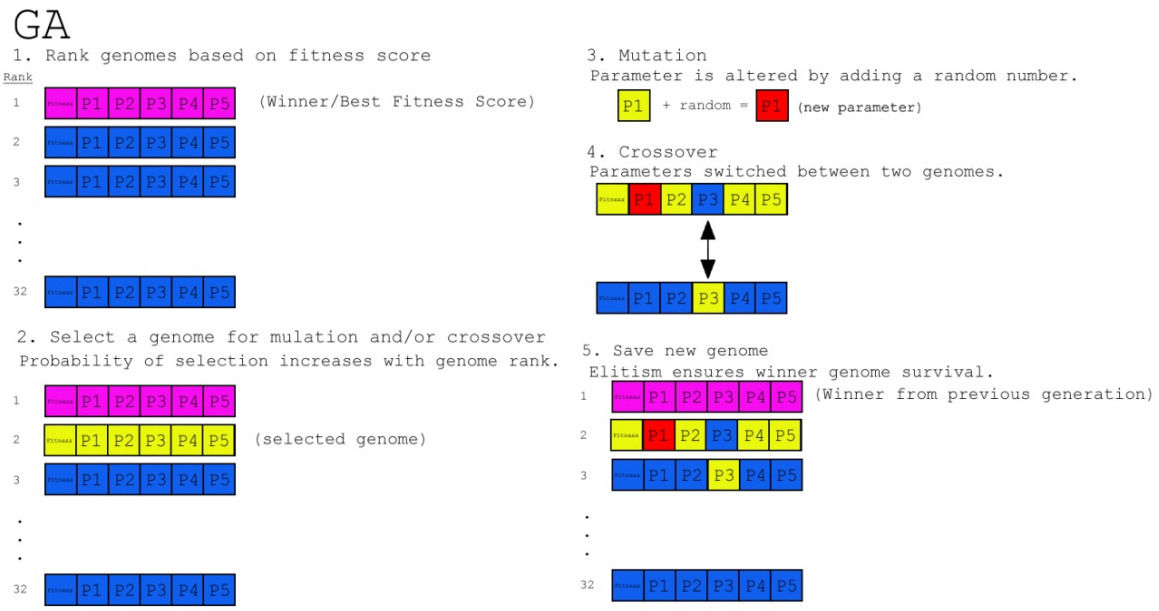


Figure 5. GA optimization steps. The selection, mutation, and crossover (steps 2-4) are iterated 32 times each generation. Once the 32 iterations are complete, the new genomes are used to build the next generation of neurons or networks. Elitism is implemented by copying the top two ranking genomes of the previous generation over two of the genomes saved during the GA process.

Two sources of variability are used to alter the genomes: mutation and recombination. During mutation, a small random number is added to each parameter with a mutation probability of approximately 90% for connection parameters and approximately 20% for conductance parameters. Mutation rates for connection parameters are chosen to be much higher for connection parameters since the conductance parameters were already tuned during the single neuron optimization and the connection parameters are generally less sensitive to small perturbations. The random number is drawn from a normal distribution with a mean of zero and standard deviation scaled to suit the parameter based on sensitivity to small perturbations and initial value (Table 3). If sodium conductance, potassium conductance, connection weight or connection delay parameters are mutated to negative values, the absolute value of these parameters were used in the simulation and the reflected positive values are recorded in the output file when writing the genome.

Conductance parameters and the leakage reversal potential mutation standard deviations are between approximately 2% and 6% of their respective initial values. The standard deviation of the delay mutation parameter is set to 0.2% in order to allow the GA to make small adjustments to firing velocity. The connection weight mutation standard deviation is set very high since the network fitness value is insensitive to larger fluctuations in connection weight. Individual parameters representing the same network parameter from two different genomes are swapped with a crossover probability of 45%. We first optimize the parameters of individual neurons to respond to the single perturbation with no action potentials firing, but to fire once in response to the multiple perturbations (Figure 6). Neurons are also selected to have a resting voltage close to -60 mV.

Table 3. Mutation Parameters

Parameter	Standard Deviation	Initial Value
Maximum Sodium Conductance $\left(S/cm^2\right)$	0.01	0.161203
Maximum Potassium Conductance $\left(S/cm^2\right)$	0.001	0.036
Leakage Reversal Potential $\left(mV\right)$	1	-54.3
Delay multiplier	0.1	50
Connection weight	0.1	0.01

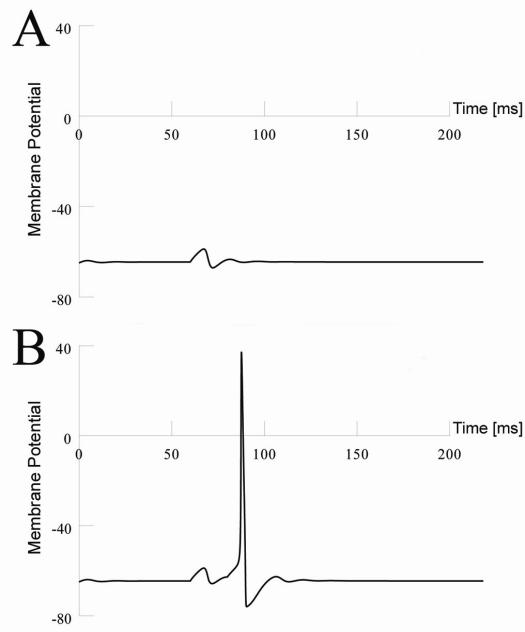


Figure 6: Single neuron model simulations. Membrane potential traces in response to A: a single stimulation and B: to three stimuli.

The single neuron fitness function is:

$$f = 200 \cdot x + 5 \cdot |1-y| + |-60 - v_0| / 2 + | v_0 - v_1 | / 2, \quad (20)$$

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 conductance, 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 (Figure 7). In addition, the fitness function requires 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 is also required with a smaller contribution to the fitness value than the firing behavior. The network fitness function is:

$$f = \left|- 65 - v_0\right| + z(x, y) + \left|250 - w_{avg}\right| + \sum_i (5 \cdot x_i \cdot i + 10 \cdot | y_i - 1 | + | t_{avg} - t_i |) \quad (21)$$

where x_i is the average number of action potentials fired by the ith order neighbors following the single perturbation, y_i is the average number of action potentials fired by ith order neighbors following the multiple perturbations, t_i is the average time elapsed between the firing times of the first spikes from ith and $(i+1)$th order neighbors, t_{avg} is the average time elapsed between the first spikes of adjacent neighbors, v_0 is the resting voltage, $z(x,y)$ is the

additional cost for having too few or too many action potentials fired, and w_{avg} is the average velocity of the spread of firing.

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 construction of 32 networks, electrophysiological simulations (200 ms and ~4000 ms) and selection, mutation and recombination of genes required approximately 1.5 minutes on 4 parallel Opteron AMD 2.4 GHz processors. The simulation code is available upon request[3] and will be submitted to the Yale Sense Lab Model Database (http://senselab.med.yale.edu/modeldb/).

[3] Email eugeniajchen@gmail.com for requests.

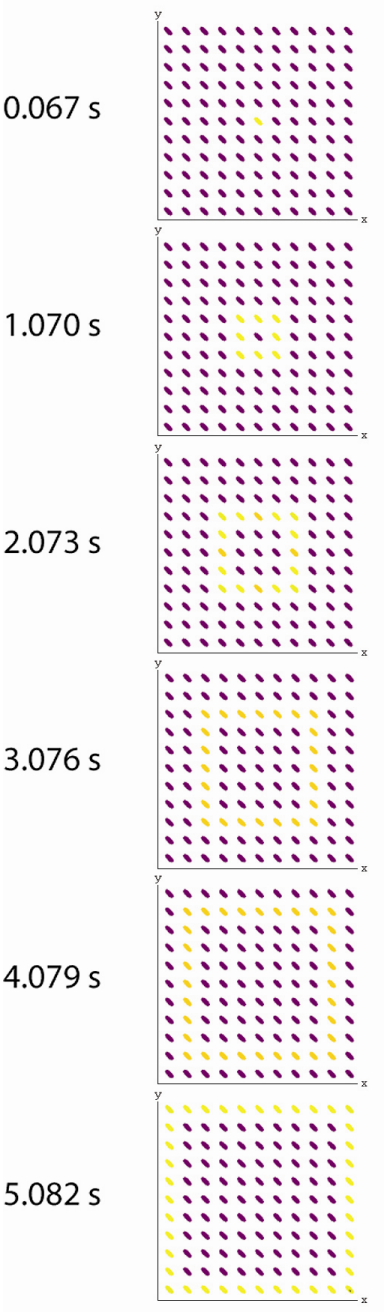


Figure 7: 2D Network model simulations. Spread of excitation in an 11x11 array of polyps in response to triple stimulation of the center neuron. Time since the stimulation is shown to the left of each array. Excited neurons are shown in yellow and inactive neurons in violet.

CHAPTER 3

RESULTS

The patterns we aimed to replicate were observed by T.H. Bullock in *Palythoa* in the Sea of Cortez, Mexico and in the Enewetok Atoll in the Republic of the Marshall Islands, which was then a UN trusteeship of the USA (Chen 2008). Screenshots from video footage of the observed propagation patterns in response to repetitive electrical stimulation are shown in Figure 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:

Table 4. Optimized Neuron Parameters

gnabar_hh $\left(S/cm^2\right)$	0.161203
gkbar_hh $\left(S/cm^2\right)$	0.036
el_hh $\left(mV\right)$	-54.3

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 (Figure 6).

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 26 generations and were:

Table 5: Optimized Network Parameters.

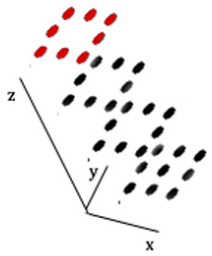
gnabar_hh $\left(S/cm^2\right)$	0.215724
gkbar_hh $\left(S/cm^2\right)$	0.043386
el_hh $\left(mV\right)$	-54.198300
Delay multiplier	49.986900
Connection weight	0.545957

The first perturbation caused a small subthreshold increase in the voltage of the center polyp neurons and two or more perturbations caused a single firing from all neurons in the network. Firing was simultaneous in neurons equidistant from the center polyp and spread radially with an approximately constant velocity of 1 neuron/250 ms (Figure 7). 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 to 0.17 S/cm^2) 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.

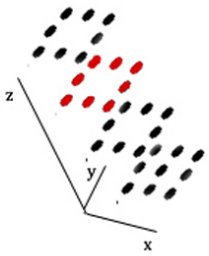
The 3D network was constructed and run with the parameters optimized for the 2D network. Firing spread with the same constant velocity of 1 neuron/250 ms and firing within polyps of similar order occurred simultaneously (Figure 8). The linear radial spread of firing solution was preserved between the 2D network and 3D polyp network (Tbl. 6). Stimulated neurons are of order 0. The first 3 orders of neurons in the 3D network (highlighted) are polyp neurons, which have fewer nearest neighbors than neurons in the xy plane. Spike times are similar between the linear and 2D networks and the 3D network spike times are similar to the latter two networks after the excitation spreads outside of the stimulated polyp (order 3 and greater).

Table 6. Spike times of neurons by order relative to stimulated neuron(s).

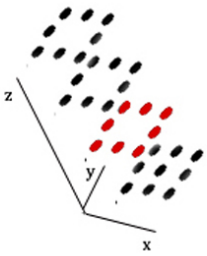
	Spike Times (ms)		
Neuron Order/Network Type	Linear	2D	3D
0	0.065144	0.065144	0.065188
1	0.377664	0.377664	0.377708
2	0.690171	0.690171	0.690223
3	1.002678	1.002678	1.002738
4	1.315185	1.315185	1.315254
5	1.627692	1.627692	1.627769
6	1.940199	1.940199	1.940284
7	2.252706	2.252706	2.252799
8	2.565213	2.565213	2.565314
9	2.87772	2.87772	2.87783
10	3.190227	3.190227	3.190345
11	3.502734	3.502734	3.50286
12	3.815241	3.815241	3.815375
13	4.127748	4.127748	4.127891
14			4.440406
15			4.752921
16			5.065436



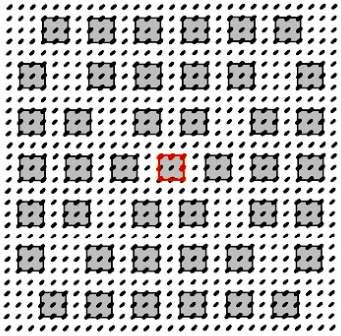
A 4.70934 ms



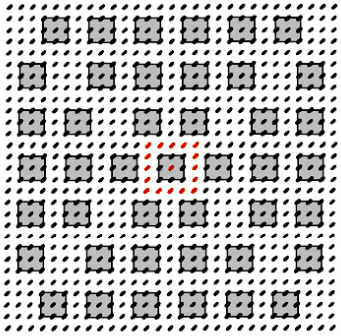
B 254.7084 ms



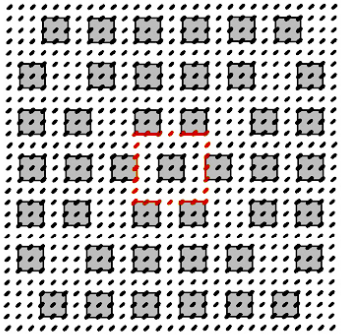
C 504.6952 ms



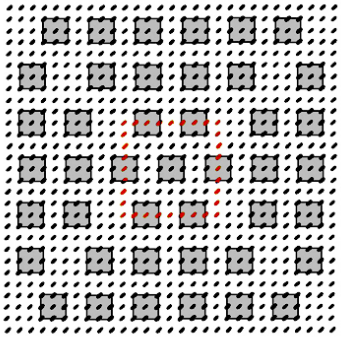
D 754.682 ms



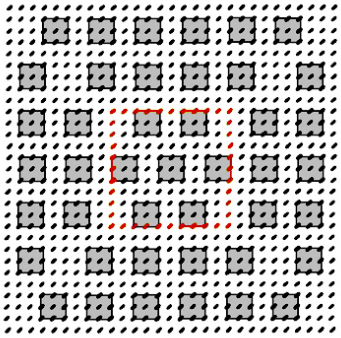
E 1004.669 ms



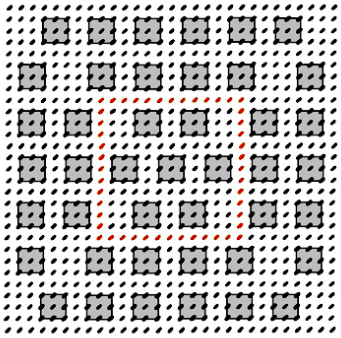
F 1254.656 ms



G 1504.642 ms



H 1754.629 ms



I 2004.616 ms

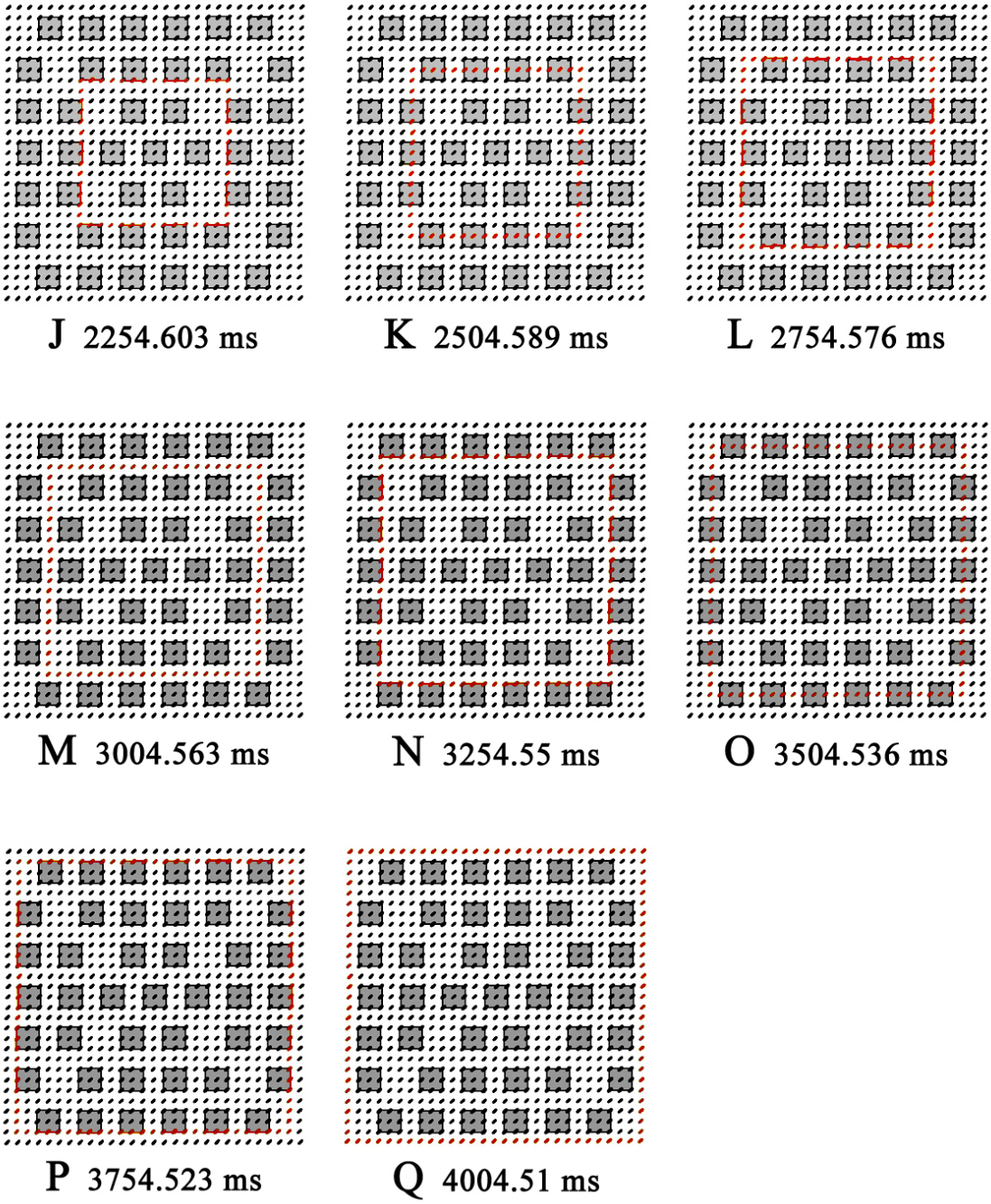


Figure 8. Firing spread in the optimized 3D network. Activated neurons are shown in red and inactivated neurons are shown in black. Parts A-C show the center (stimulated polyp) activation. Neurons outside of the center polyp are at rest in parts A-C. The times elapsed since the onsets of the stimuli are shown below.

CHAPTER 4

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* (Figure 1b).

GAs were previously been used for optimizing only single-cell parameters (Stiefel and Sejnowski 2007; Achard 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 tends 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 result 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. Velocity of spread between successive neighbors is not affected. Systematically varying the delay parameter while holding the conductance parameters constant shows that the velocity of spread is linearly related to the

magnitude of the delay parameter (Figure 9) 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.

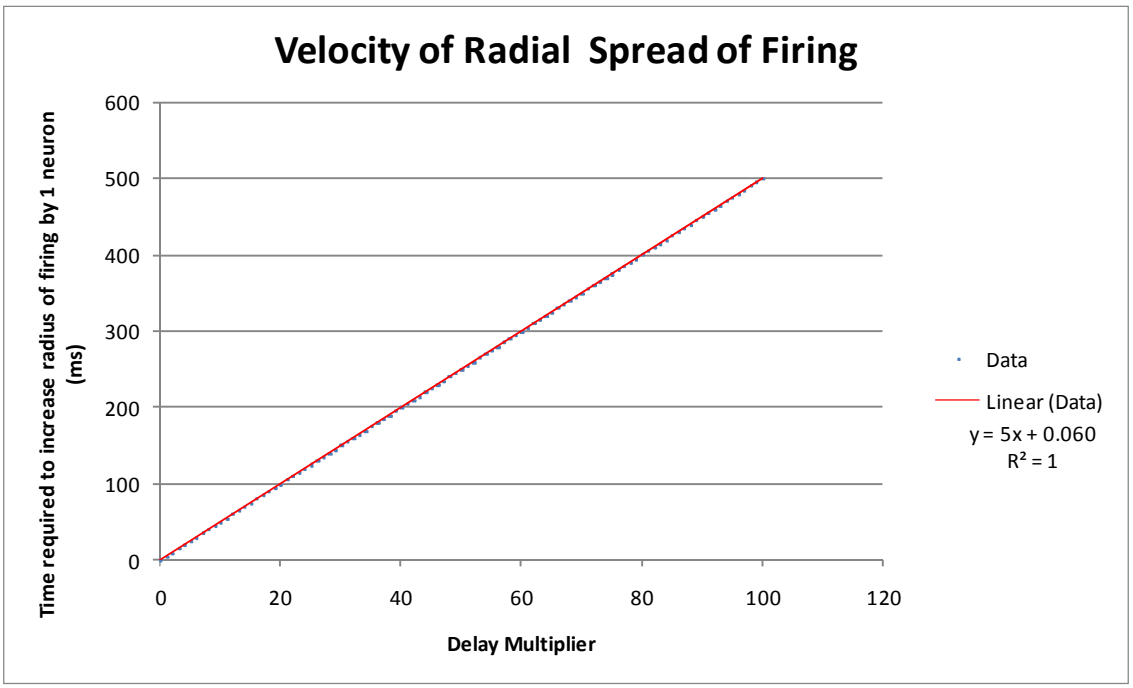


Figure 9. Velocity of Spread of Firing. Data collected from 2D network (11x11) with delay multiplier varied from 0 to 100 in increments of 1. The rate of increase in velocity of spread with respect to the delay multiplier is equal to the modeled distance between neurons (5 µm).

In the future, we will 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.

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APPENDIX A

PROGRAM CODE: SETUP.HOC

```
// Parameters, create neurons

xdist=5                        // distances between neurons in polyps
ydist=5
zdist=5
center=5

netsize=11              // size of network inside polyps
popsize=netsize^2

numstats=12
numgenes=5

//--------------------------- load genome from file
objref genomefile, netparm
netparm =  new Vector(numgenes)
genomefile = new File()
genomefile.ropen("cellgenome.txt")
for z=0, numgenes-1 {
     netparm.x[z]=genomefile.scanvar()
     if (netparm.x[z]<0 && z!=2) {netparm.x[z]=0 }
}

k=abs(netparm.x[3])
pweight=abs(netparm.x[4])

stimint=2   // Stimulus parameters held constant
stimtau=1

//--------------------------------neurons
objref apc[netsize][netsize], spiketimes[netsize][netsize]
objref connection[netsize][netsize][8]
objref synapse[netsize][netsize]
create neuron[netsize][netsize]     // polyp network

forall {                // every cell has HodginHuxley currents
      insert hh
      gnabar_hh=netparm.x[0]
      gkbar_hh=netparm.x[1]
      el_hh=netparm.x[2]
      nseg=1
}

radius=8.2981221/2
setlength=8.2981221
setdiam=3.1925001
```

ABSTRACT OF THE THESIS

Optimizing a Coral Nerve Net
by
Eugenia J. Chen
Master of Science in Computational Science
San Diego State University, 2008

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 2-dimensional nerve net. This strategy yielded a network with parameters that reproduced the experimentally observed spread of excitation.