Software Experiment #5

HOW DO TETRAPODS DECIDE WHEN TO WALK, TROT OR GALLOP

Content areas: Basic neuroscience covered in biology, physiology, psychology, and engineering courses

Pre-requisite knowledge: Cell biology, basics of neurophysiology (action potentials, synapse), human nervous system

Learning Objectives: After this lesson, students should be able to:
- how neurons can interact to implement functions
- oscillators in the nervous system
- how the human heart, breathing, digestion, etc. work

Time Required:

Keywords central pattern generators, rhythmic activity in neurons

Summary This lesson is focused on one mechanism of generating rhythm in multiple neurons connected using synapses. Again, this builds on the concepts of AP and synaptic transmission developed in the previous lessons.

INTRODUCTION / MOTIVATION

Excerpted from the Book of GENESIS (pages 131-133)
Chapter 8, Central Pattern Generators by SHARON CROOK and AVIS COHEN
http://www.genesis-sim.org/GENESIS/iBoG/iBoGpdf/index.html

8.1 Introduction

Many organisms exhibit repetitive or oscillatory patterns of muscle activity that produce rhythmic movements such as locomotion, breathing, chewing and scratching. Examples include the escape swimming of the mollusc *Tritonia diomedia*, the digestive rhythms of the lobster, the undulatory swimming movements of the fish or the lamprey, the stepping movements of the cockroach, the rapid wing motion of the locust during flight, and the more complicated locomotion of a quadruped mammal such as the domestic cat. The neuronal circuits that give rise to the patterns of muscle contractions which produce these movements are referred to as *central pattern generators*, or CPGs. Various experimental preparations in which the CPG is isolated from external influence demonstrate that these circuits require no external control for the generation of temporal sequences of rhythmic activity. However, these animals move through the world in an adaptive manner where the same motorneurons are involved in the production of a variety of rhythmic behaviors. Thus, many CPGs are capable of producing multiple patterns of activity in the intact behaving animal (Getting 1989). The ability to switch between different motor behaviors and blend different rhythms relies on feedback from proprioceptors and influence from higher centers of the nervous system; therefore, it is most appropriate to view every CPG as one piece of a distributed control system (Cohen 1992).

One would like to understand how the neurons in a CPG interact and influence one another, how the underlying circuitry of the network produces the collective behavior of the cells, what mechanisms might allow the network to switch among various patterns of activity, and whether the oscillatory patterns are due primarily to the activity of individual intrinsically oscillatory neurons or to oscillations that are a product of the entire network. The number of cells composing a network that functions as a CPG often determines the manner in which the CPG is studied and the choice of a modeling strategy. Some CPG circuits are anatomically localized and contain a small number of neurons. This occurs most often in CPGs that produce rhythmic behaviors in invertebrates. In these small networks, neurons can be individually identified from animal to animal, permitting detailed circuit descriptions that include cellular and synaptic properties. In contrast to these invertebrate CPGs, there are possibly millions of neurons involved in the production of rhythmic patterns of motor activity in most vertebrates (Murray 1989). In this case, modelers often categorize the neurons into classes that share similar properties so that large networks can be simulated by relatively few cell types (Getting 1989).

The small localized CPGs that occur in invertebrate preparations make it possible to study the relationship between the emergent collective behavior of the biological network and the network's underlying circuitry (Getting 1989). The dynamical properties of many invertebrate CPGs have been analyzed using such techniques as experimental manipulations of cellular, synaptic, and connectivity properties, detailed simulations of the cell interactions within the network, and analytical studies of equations that might describe the network dynamics. For example, Getting created a network simulation of the escape swimming rhythm of the mollusc *Tritonia diomedia* (Getting 1989). This simulation relies on a compartmental model of the network cells with appropriate passive membrane properties, repetitive firing characteristics, and synaptic actions. In addition, the input to the model corresponds to the normal sensory activation of the actual CPG. Some of the properties of Getting's model are demonstrated in the GENESIS simulation *Tritonia*. Another example of an invertebrate CPG that has been studied and modeled extensively is the lobster stomatogastric ganglion. This region contains the neurons that are involved in the generation of the slow rhythm that fires the muscle contractions of the lobster gastric mill and also those that generate the rhythm that controls the muscles of the pyloric region of the lobster stomach (Shepherd 1994). Experimentation with this system has shown that even when a detailed study of the network circuitry provides a qualitative description accounting for the presence of a given motor pattern, there is often no precise explanation for the mechanisms that control the frequency, duration, and phase relations of the motor pattern (Marder and Meyrand 1989). Studies of the invertebrate CPGs mentioned above show that the generation of these rhythms is a complicated process involving the influence of multiple neurotransmitters and modulators that modify the output of the circuit (Marder and Meyrand 1989). Due to the large number of neurons present in most vertebrate CPG circuits, models of CPGs in vertebrates often involve simplified mathematical representations where a single oscillator may represent many neurons. For example, most models of mammalian locomotion attempt to create an oscillatory network that can account for the production of the alternating flexor-extensor activity responsible for limb coordination during locomotion (Grillner 1981). In such models, the step cycle of each single limb is represented by the cyclic behavior of an oscillator intended to abstractly represent the collective output of the neurons controlling that limb. Examples of such models include Szekely's model for the locomotion of the salamander (Szekely 1968), and the models of Lundberg and Phillips (1973) and Grillner (1981) for cat locomotion. The lamprey and various types of fish have also been used extensively in studies of vertebrate CPGs. These organisms propel themselves through water by a sequence of rhythmic body undulations caused by traveling waves of contractions that progress down the axial muscles from head to tail. Their swimming patterns have led to models of locomotion consisting of chains of coupled oscillators that represent the state of the oscillatory cells that occur in segments along the spinal cord and control the sequence of muscle contractions along the body during locomotion (Rand, Cohen and Holmes 1988, Cohen and Kiemel 1993, Kopell and Ermentrout 1986). For an overview of such models, see Murray (1989) or Cohen, Ermentrout, Kiemel, Kopell, Sigvardt and Williams (1992).

Suggestions of simulation parameters that provide illustrative behaviors for various models are given throughout the remaining sections of this chapter (Chapter 8, provided for you from The Book of Genesis). In the event that the mathematical description of the behavior of a particular model seems unclear, it may be useful to run the simulations before attempting a more detailed study of the mathematical treatment.

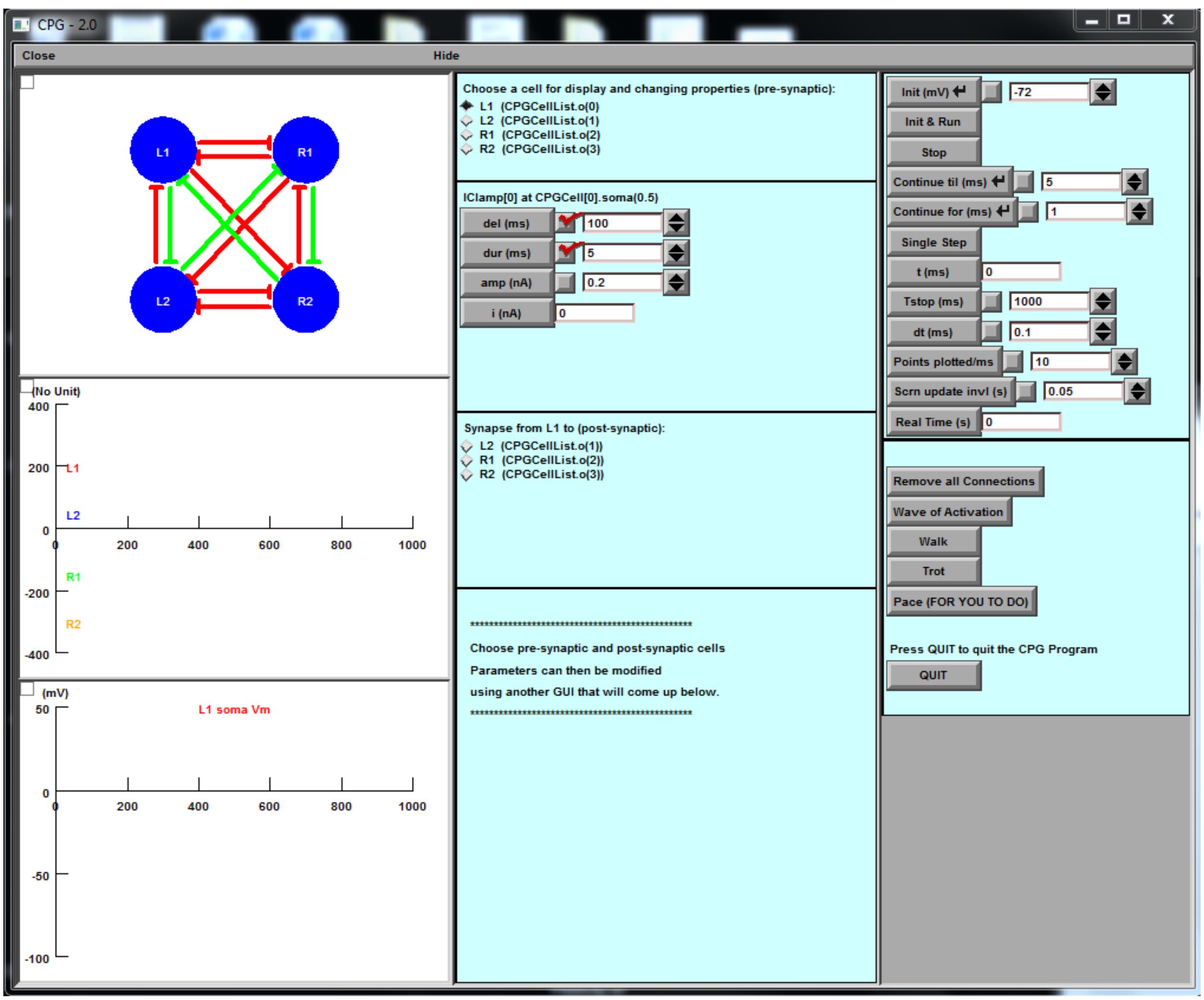
SOFTWARE EXPERIMENT #5 ASSIGNMENT

CPG Tutorial [adapted from a similar GENESIS tutorial (Bower and Beeman, 2007) by Henry Chen and John Ball]

Use the tutorial **S5 CPG.hoc** to learn how neurons can be coupled via excitatory and inhibitory connections to burst rhythmically and function as central pattern generators to control muscles and implement diverse 'functions' such as locomotion, breathing, chewing, and scratching. Examples include digestive rhythms of the lobster (STG ganglion that you have been measuring from in the bio labs), "...the undulatory swimming movements of the fish or the lamprey, stepping movements of the cockroach, the rapid wing motion of the locus during flight, and the more complicated locomotion of a quadruped mammal such as the domestic cat.

INSTRUCTIONS TO RUN THE CPG SIMULATION

Assuming that NEURON is already installed on your computer, go to the folder where you saved your scripts and open the **S5 CPG.hoc** file. This will open the NEURON software and start the CPG tutorial. A screen similar to the one below will pop up.



Input: coupling of multiple cells via excitatory and inhibitory synaptic inputs to dendrites (and current injection also if needed)

Output: rhythmic spiking of the central pattern generator (which is connected to appropriate muscles)

When you run the simulation, a window comes up with four large circles representing the four cells in the oscillator. L1 and R1 represent the front limbs of the animal while L2 and R2 represent the hind limbs. The lines between the cells show the synaptic connection between them. Green connections are excitatory, red are inhibitory, and if it is not visible then there is no connection. To change the synaptic connections you choose a pre-synaptic cell in the top Details window of the middle column, and a post-synaptic cell in the Synapse window below. This allows you to make the connections inhibitory or excitatory, and to control their strengths. A weight of zero will make the connection disappear to show that it is not affecting the model. To change current injections to the cells choose the appropriate cell under the **IClamp** window.

Click on the **Init&Run** button to run the simulation. Under the multi-cell graph window you will see a plot of the output of each of the four cells. Notice that the default architecture produces a walking gait. This is easier to see towards the end of the simulation as the phases lock into the gait. The right hind leg (R2) is followed by the right front leg (R1), then the left hind leg (L2), and finally left front leg (L1), and the process repeats itself – the tetrapod is walking!

QUESTIONS

1. First remove all connections and convince yourself that the firing patterns of all the four neurons are identical. Next, click on 'Walk', and then 'Init & Run'. Explain how the synaptic connections implement the walk gait. Also, explain how the signal propagates. How will you slow down the pace of walking – only explain, no plot needed for this.

2. Now explain how the synaptic connections implement the “Wave of Activation”. What is the logic to speed it up or slow it down?

3. Now explain how the synaptic connections implement the “Trot” gait, in a similar manner.

4. Finally, using the ideas from above, you are to design the connections for the 'Pace' gait. Use a weight of 100 for all the connections you make. Explain your LOGIC clearly (important) and include a plot of connections and of the spiking patterns of all four neurons (one of the plots on the screen).