

Real-Time Development of Data Acquisition and Analysis Software for Hands-On Physiology Education in Neuroscience: g-PRIME

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Abstract— We report on the real-time creation of an application for hands-on neurophysiology in an advanced undergraduate teaching laboratory. Enabled by the rapid software development tools included in the Matlab technical computing environment (The Mathworks, Natick, MA), a team, consisting of a neurophysiology educator and a biophysicist trained as an electrical engineer, interfaced to a course of approximately 15 students from engineering and biology backgrounds. The result is the powerful freeware data acquisition and analysis environment, “g-PRIME.” The software was developed from week to week in response to curriculum demands, and student feedback. The program evolved from a simple software oscilloscope, enabling RC circuit analysis, to a suite of tools supporting analysis of neuronal excitability and synaptic transmission analysis in invertebrate model systems. The program has subsequently expanded in application to university courses, research, and high school projects in the US and abroad as free courseware.

I. INTRODUCTION

FOR over three decades, the Department of Neurobiology and Behavior at Cornell University has offered a one semester neurophysiology laboratory course to upper level undergraduate and graduate students. The course is primarily based on the red swamp crayfish (*Procambarus clarkii*) model system but includes exploration into other invertebrate models such as the fruit fly larvae (*Drosophila melanogaster*), the large brain cells of the great pond snail (*Lymnaea stagnalis*), and even the electrically active plant cells of *Chara corallina* [1]. Students explore membrane and synaptic dynamics in systems similar to mammalian brain synapses (crayfish neuromuscular junctions), where they compare extracellular nerve recordings to intracellular signals in the muscles that they innervate. The students explore ion currents, how electrolytic balance forms the membrane voltage, the behavior of synapses in response to neuromodulators, and other topics of modern neurophysiology.

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In order to interface the model systems, the students utilize research grade hardware such as extracellular electrode amplifiers, National Instruments data acquisition hardware (National Instruments, Austin, TX), and feedback based two-electrode voltage clamp systems. As the course and available technology have evolved, the software to connect the students to the physiology has evolved as well. In 2001, a Matlab based software oscilloscope program was developed parallel to an offline analysis tool [2]. These tools were powerful additions to the course and served the needs of the laboratory exercises for approximately 6 years. In the spring of 2007, one of us (GKL), while a graduate student in the field of biophysics (specializing in neuroscience instrumentation development), was hired to assist in the evolution of the course.

During the semester, a close collaboration between neuroscience faculty, 15 students, and an electrical engineering trained teaching assistant (GKL) produced g-PRIME, a freeware data acquisition and analysis tool specifically designed to meet the needs of this laboratory course. The Matlab based software oscilloscope utilizes the Matlab Data Acquisition Toolbox, and the Handle Graphics user interface design system (Fig 1). The tool allows for real-time amplitude threshold based event detection, cross-

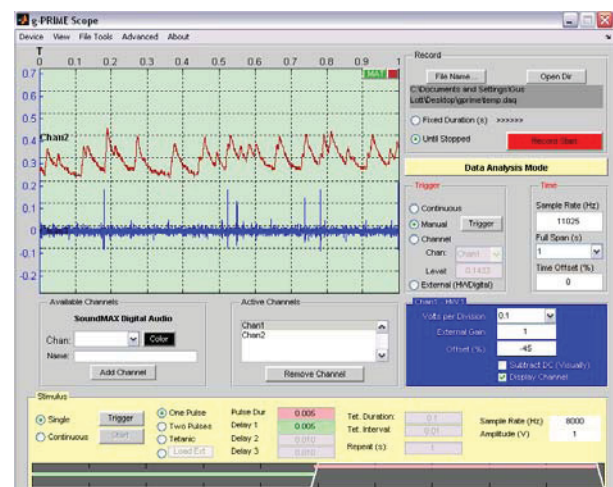


Fig. 1. g-PRIME scope graphical interface. The bottom channel is an extracellular recording from a nerve bundle in the Crayfish tail periphery and the second (top channel) is an intracellular recording from the muscle that the nerve innervates. Stimulus generation tools and data logging controls are visible.



Fig. 2. Spike detection from a 6-unit tonic nerve in the crayfish tail (superficial flexor system). All six units can be clearly discerned in this energy density vs. time representation. The brief suppression period of the largest amplitude spike corresponds with an increase in activity of the 5th amplitude spike (the inhibitory neuron in this system).

channel correlations (event triggered averages), offline cluster analysis, and report generation. The power of the tool and the rapid adaptability enabled by the Matlab development environment caught the attention of research faculty, and the development of g-PRIME moved into both the educational and research realm.

Features in the program were added from week to week as the students required them for laboratory exercises. Students would discover limitations or logical errors in the program, and we responded with rapid updates (frequently within the same laboratory period). Student feedback was crucial to the development of a transparent and intuitive interface to connect the user to the biology. This project illustrates an effective coupling between neurobiological education and electrical engineering (hardware interface & software design), mediated by the rapid prototyping environment of Matlab, to mold future generations of neuroscience researchers and biomedical engineers.

II. SOFTWARE CONSTRUCTION

g-PRIME is a software oscilloscope wrapping the Matlab Data Acquisition Toolbox in an intuitive interface and adding online and offline analysis and report generation features. The software is “compiled” to a stand-alone executable for license free distribution to researchers and educators. The program consists of approximately 5000 lines of Matlab code.

The software leverages the Matlab “handle graphics” system of user interface design tools and implements all live video updates (10Hz) and analysis functions in an event driven fashion based on a number of samples being available on the data acquisition interface (the “samples

acquired function”). Much thought was put into reducing “option overload” for non-technical users. For example, many options for scaling of visualization axes permit only discrete values from a drop down list (Fig 1). Code was optimized for speed and efficiency using the integrated Matlab Profiler tool. A large portion of the Matlab source code (including the GUI design and the analysis functions) has also been released to guide future projects at other institutions [3].

III. APPLICATIONS & STUDENT RESULTS

One of the focal preparations in the course is the crayfish superficial flexor neuromuscular junction. A small bundle of neurons diverges from the ventral nerve cord in each tail segment of the animal. This nerve contains six motor neuron axons of a variety of sizes and functions (including a single inhibitory neuron), and exhibits tonic activity [4, 5]. An extracellular suction electrode [6, 7] attached to the nerve easily reveals the tonic activity in the six neural units (Fig 2).

The students may also record intracellularly from the muscle which this nerve innervates. This allows the students to observe input/output characteristics of the synapse itself by time-correlating post-synaptic membrane potentials with the pre-synaptic spike that elicit them (Fig 3).

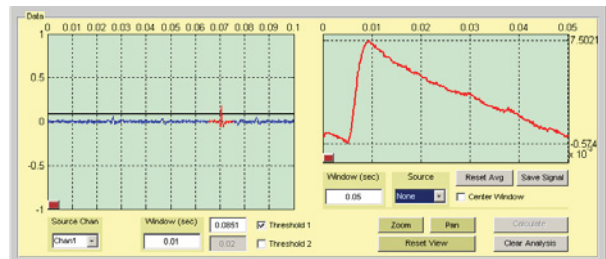


Fig. 3. Spike triggered average between two channels. A single spike class from a multi-unit nerve in the crayfish can be selected via amplitude thresholds and the corresponding intracellular muscle potentials can be averaged. Uncorrelated post-synaptic-potentials (PSPs due to multi-terminal innervation) average away and only the PSP elicited by the specifically selected neuron remains. One can clearly see the propagation delay, membrane depolarization rate, and PSP amplitude associated with a single synapse.

Students in the course use g-PRIME to complete a variety of exercises including:

- Generation of square wave stimuli to a simple RC filter to visualize the integrating behavior of a simulated cell membrane.
- Data logging from extracellular and intracellular recordings in sensory neurons, motor neurons, and muscle cells in the crayfish as well as brain cells in the pond snail.
- Event cross correlation on simultaneously acquired data channels for synaptic dynamics analysis (Fig 3)

- JPEG/TIFF generation of publication quality graphics for inclusion in their lab reports.
- Exploration of their own research project including topics such as neuromodulatory effects on synaptic dynamics, and spike conduction velocity as a function of temperature.

IV. DISCUSSION & FUTURE DEVELOPMENT

As the software developed through the course, neuroethological research groups in the department took notice and began to request features and to guide the software's growth. By the end of the term, the software was rapidly adapted to projects ranging from the acquisition and analysis of fruit fly courtship song to mildly electric fish aggression and mating displays and mosquito wing vibrations [8].

The tight closed loop between engineering instrumentation software development and the needs of the neurobiological research community illustrates a cross disciplinary project enabled by the rapid prototyping tools of the Mathworks' suite of tools. Fundamentally, neural circuits are no different than circuits created by electrical engineers. The basic tools of signals and systems analysis extend readily to biological neural networks and the field of neuroscience benefits greatly when electrical engineering tools and methods are effectively coupled into biological preparations.

APPENDIX

The software is released as free courseware on the Crawdad web site: <http://crawdad.cornell.edu/gprime/>. A software manual and further instructions to use g-PRIME are also on this web site. The tool is currently expanding to applications in research and education at levels from high schools [9] to universities. g-PRIME continues to evolve as the project "Spike Hound" in the instrumentation development group supporting basic neurobiology research at the Howard Hughes Medical Institute's Janelia Farm Research Campus (<http://www.hhmi.org/janelia/>) in response to cutting edge basic brain circuit research in models systems from fruit flies to mice.

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