Standard electrophysiology experiments utilize a technique known as voltage clamping: the surface of the cellular membrane is held constant, or clamped, which allows the researcher to study the membrane permeability and ion exchange.

Currently, this process is usually performed with commercially available analog equipment. While analog circuitry provides an accurate and reliable equipment medium, it does not allow for much in the way of real-time data processing. Additionally, there is still the issue of data acquisition which must be performed using an analog-to-digital converter (A/D). A need exists to resolve these issues in one device. The Universal Clamp, a patent pending electronic device designed and built by Dr. Jiang Wu at the University of Rhode Island, addresses this need. The Universal Clamp, however, does much more than data acquisition (DAQ) and signal processing. As the name implies, it has the capability of performing voltage clamping, current clamping, and dynamic clamping, all in one device, with the aid of a digital signal processing (DSP) chip. This functionality provides researchers greater flexibility in the types of experiments they can conduct, as well as simplifying current standard methodologies. Using the visceral ganglion from Aplysia californica, the Universal Clamp has successfully performed voltage clamping, current clamping and dynamic clamping, while simultaneously executing data acquisition and signal processing algorithms. This paper will present the relevant experimental justification for asserting the effectiveness of the Universal Clamp, the different types of clamping and their purpose, as well as the algorithms employed which make the Universal Clamp such a unique device. The broader impact to the physiological community, including research in neural prostheses, spinal cord injuries, and the brain-machine interface, will also be discussed.

INTRODUCTION

In 1952, A.L. Hodgkin and A.F. Huxley published a series of four landmark papers describing the inward and outward currents of Na+ and K+ through the cell membrane [1]. These papers were the result of experiments with the squid giant axon and the voltage clamp. The invention of the voltage clamp was developed by George Marmont and Kenneth Cole in 1949, has been transformed many times over since its inception, but the fundamental principal remains: understand the ionic currents responsible for action potential behavior. The voltage clamp consists of using a feedback amplifier to keep the voltage across the membrane constant, while the resulting transient must be resolved by the feedforward amplifier, creating a change to the resting membrane potential. But it wasn’t until 1993 when A.A. Sharp et al., introduced a new type of clamping, called dynamic clamping, that the interneuronal communicatory relationships were able to be directly measured and manipulated. The Universal Clamp, a fully digital implementation, is the next in the series of indispensable electrophysiology instrumentation by combining all three types of clamping in one device. In a typical voltage clamp design, this is performed using external switches which are fixed and specific to the device. Because the Universal Clamp uses software to perform the switching, the number of switches is scalable, providing researchers great flexibility in the design of the experiment. Dynamic clamping involves passing current into the cell to change the resting membrane potential. If positive current is passed, this raises the membrane potential, which is usually -40 to -90 mV. Once enough current is passed to raise the membrane potential past the threshold potential, the voltage needed to be reached before any action potential is fixed, the cellular response is to initiate a high frequency volley of action potentials. When the current stimulus is removed, the membrane potential is returned to its original level, but the cell has adapted to the higher potential and it therefore behaves as if the membrane potential is lower than its original level. The Universal Clamp is marketed under the proprietary name Digital Clamp One. The device, the Universal Clamp, provides researchers the ability to perform voltage clamping with one electrode without the need for external switches. Using software to control switching between current injection and voltage measurement, the Universal Clamp eliminates the need for a current injection electrode and a voltage measurement electrode. This is only possible at extremely high sampling rates, in the range of 200k-500k samples per second, since current is passed into the cell and the resulting transient must be resolved by the feedforward amplifier, creating a change to the resting membrane potential. But it wasn’t until 1993 when A.A. 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METHODS

Action Potential Recording Using Microelectrode Methodology

As the goal of this presentation is to illustrate the functionality of the Universal Clamp, only a brief outline of the discussion process will be provided for scientific validation. Further information regarding Aplysia californica can be found in (2). As the Aplysia preparation begins with the administration of approximately 40cs of 0.36M Mg3 to anesthetize the animal. The adult juvenile Aplysia has a mass that ranges from 100 to 200 grams so the anesthetic will vary.) As the Aplysia has a half open circular system, the anesthesia can be injected into the musculature of the foot. Once the drug is dispersed past the heart, it flows through the body and returns through the tissue, not a capillary network. The anesthesia will be taken into the circulation by this process. Filtered sea water is used to rinse and perfuse the animal throughout the dissection process in order to keep the tissues viable for an extended period of time. A two centimeter transverse incision is made across the hind quarter of the foot, providing entry to the abdominal cavity. Care must be exercised so that no internal organs are severed.

REFERENCES


DISCUSSION

The Biomedical Engineering Program at the University of Rhode Island has produced a completely unique digital electrophysiology instrument. The device, the Universal Clamp, provides researchers extremely advanced data acquisition and data processing capabilities previously unavailable in one device. Its efficient design makes it an attractive choice for researchers needing to streamline their instrumentation and concentrate on developing methodologies for physiological understanding. NIH funding has provided the means to improve the design and bring it to market. The partnership with MyNeuroLab, St. Louis, MO, in the SBIR Phase I grant has been a successful one indeed, and has established legitimacy for future grant proposals including the SBIR Phase II grant.

A fully digital implementation of voltage, current, and dynamic clamping methodologies