

2011/12

Digitimes

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Acquisition Amplification Anti-vibration Cell Injection Iontophoresis Manipulation Manometry Micro-incubation
Noise Elimination Patch-clamp Perfusion Pipette Manufacture Software Stimulation Urodynamics

Welcome to the 2011/12 issue of our Digitimes newsletter, bringing you the latest news relating to the Digitimer research and clinical neurophysiology product ranges, including our NeuroLog System.

As an established world leader in the design and manufacture of biological signal amplifiers, electrical stimulators and other electronic instruments for life science and clinical markets, we hope our current product range will be of interest to you.

Inside this Issue:-

Product Focus - Taking a closer look at the features of our DS4 Biphasic Stimulus Isolator, which can be controlled by a DAQ system.

Clinical Neurophysiology - Additions to our range of electrodes, new software control options for our D360 amplifier and DS5 stimulator. Plus, a preview of our new D440 isolated EMG amplifier, which is currently in development.

News from our Partners - Including novel brain slice chambers from Scientific Systems Design and 64 bit drivers from HEKA.

Research News - New accelerometer/interface package for our Neurolog System, plus details of our other research products.

NEW Corkscrew & Disposable Adhesive Electrodes added to our Neurodiagnostics Range



As part of our expanding range of neurodiagnostic accessories, we now offer disposable corkscrew electrodes for transcranial electrical stimulation and EEG recording applications as well as packs of prewired self adhesive electrodes. The corkscrew electrodes are constructed from stainless steel and are supplied individually packed in boxes of 24 electrodes (4 x 6 colours). The electrodes are fitted with 1.2m long lead wires which terminate in 1.5mm touch proof (DIN 42802) plugs, compatible with Digitimer D185 electrode connection headboxes as well as our amplifier inputs.



The self adhesive electrodes are supplied in boxes of 10 sealed pouches, each containing four 20mm disk electrodes. Individually packed ground electrodes are also available in boxes of 20. The self adhesive electrodes are prewired with 1m or 2m leads terminating in 1.5mm touch proof plugs. If you would like a copy of our Neurodiagnostic Accessories brochure, please contact us.



Shake, Rattle 'n' Roll - NEW NeuroLog System Accelerometer & Interface

Designed for use with our Neurolog System NL109 Bridge Amplifier, the NL261 Accelerometer and Interface Module (NL260) were developed in collaboration with Dr Justin Kanavagh (Griffith University, Australia) so that he could record finger tremor in combination with ECG recordings made with the Neurolog System. Digitimer engineers produced a small box which acts as an interface between a single axis accelerometer and our NL109 Bridge Amplifier. The interface box can be used with 2 or 3 axis accelerometers (one NL109 required for each axis).

Kavanagh, J.J, Grant, G.D, and Anoopkumar-Dukie, S. Low dosage Promethazine and Loratadine negatively affect neuromotor function. Clinical Neurophysiology. In press.



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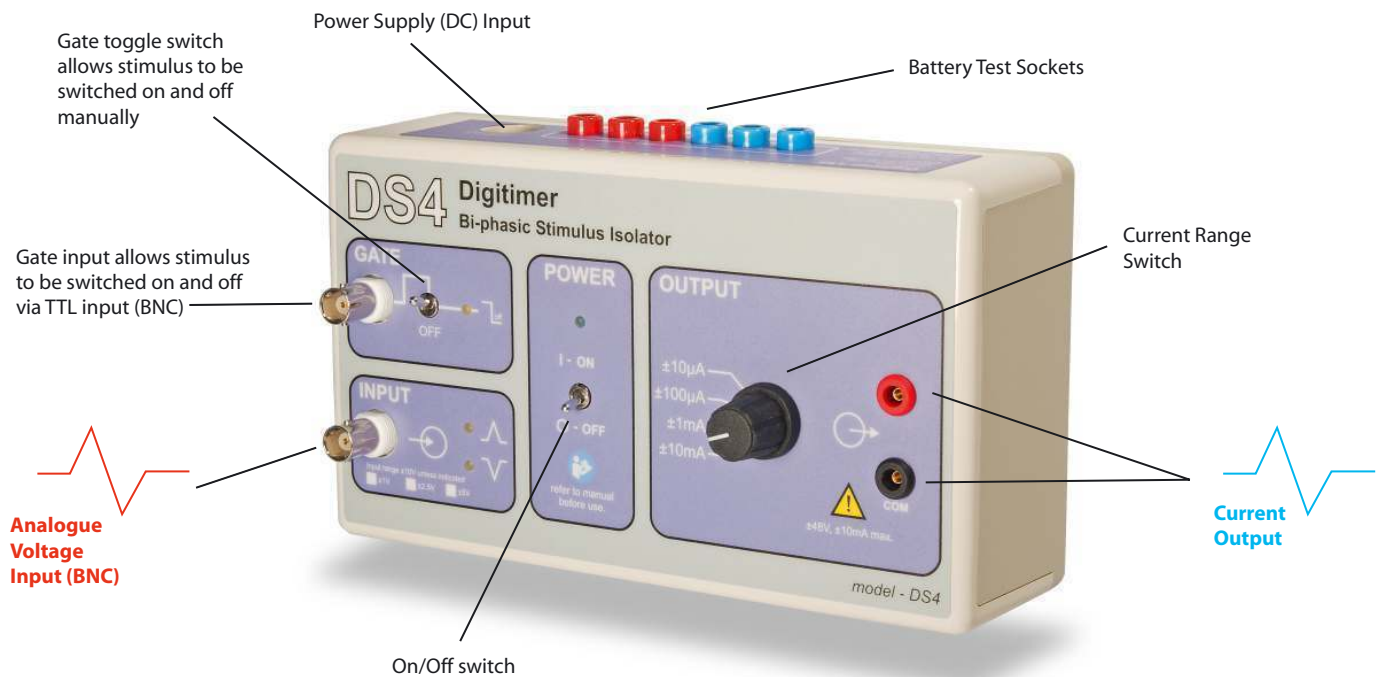
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DS4 Bi-phasic Stimulus Isolator

Stimulation with arbitrary waveforms using your DAQ

PRODUCT
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External Control - Voltage In, Current Out

If you want greater control over stimulus shape than our DS2A or DS3 stimulators allow, perhaps the DS4 is what you need. The DS4 accepts a biphasic analogue "command" voltage and uses this waveform to define the shape of a biphasic constant current output, allowing DS4 users to deliver stimuli of any shape with external control of the stimulus parameters. This means that any user with a computer and data acquisition system (which has an analogue output) can control their stimulation parameters via their acquisition software. The DS4 is recommended over our clinical DS5 stimulator for non-human and in vitro threshold tracking nerve excitability studies which use QtracW software.

Versatile - Wide Input and Output Ranges

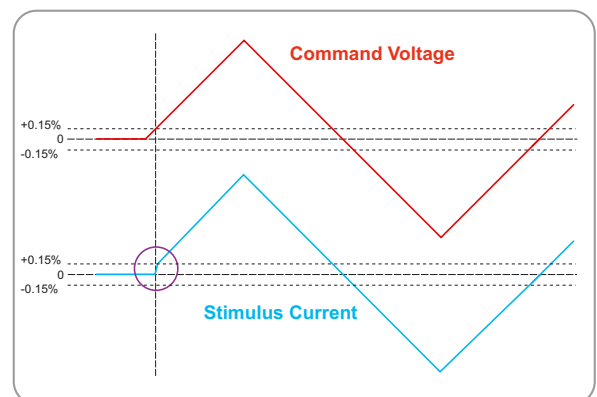
The DS4 accepts a variety of voltage input ranges ($\pm 1V$, $\pm 2.5V$, $\pm 5V$ and $\pm 10V$) and produces a constant current stimulus output in 4 overlapping ranges ($\pm 10\mu A$, $\pm 100\mu A$, $\pm 1mA$ and $\pm 10mA$) from a compliance voltage of $\pm 48V$. In addition, the DS4 has a GATE input which allows multiple DS4's to be connected to a single analogue voltage source, with each DS4 being digitally enabled, separately.

Unique - Inactivity Sensor Reduces Leak Currents

One of the problems with stimulators that make use of an external voltage source to define a stimulus waveform is that small offsets or noisy baseline signals from the DAC's used to drive them can result in unwanted battery drain or perhaps worse, low amplitude stimulation. The DS4 uses a special "inactivity sensor" to monitor the input voltage

and disable the DS4 output if this voltage drops to $0 \pm 0.15\%$ of the full scale value for a user selectable time period of 100ms, 200ms, 1s or 2s. Unlike other devices which only produce an output when the input voltage exceeds a threshold value, this "inactivity sensor" reduces battery usage and damaging "leak currents" during infrequent stimulation, while at the same time maintaining low levels of zero crossing distortion for repetitive waveforms. The figure below illustrates how the DS4 inactivity sensor "wakes up" the DS4 output in tens of microseconds, when the input voltage exceeds $0 \pm 0.15\%$ of the full scale value, thereby initiating stimulation. The DS4 output remains active unless the input voltage drops below this threshold for a period longer than that set by the user selectable internal jumper.

The DS4 uses a DC power supply for the control circuitry and readily available/inexpensive batteries to provide the opto-isolated stimulus voltage source.



The inactivity sensor clamps the output current (blue) to zero until the command voltage (red) reaches a level greater than 0.15% of the full scale value, whereupon it rapidly increases the current to reach the requested level.

Recent Publications

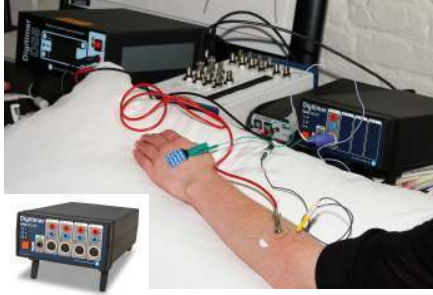
Jiruska P, Csicsvari J, Powell AD, et al. High-frequency network activity, global increase in neuronal activity, and synchrony expansion precede epileptic seizures in vitro. *Journal of Neuroscience*. 2010; 30(16): 5690-5701.

Moldovan M, Alvarez S, Pinchenko V, et al. Nav1.8 channelopathy in mutant mice deficient for myelin protein zero is detrimental to motor axons. *Brain*. 2011; 134(2): 585-601.

Sittl R, Carr RW, Grafe P. Sustained increase in the excitability of myelinated peripheral axons to depolarizing current is mediated by Nav1.6. *Neuroscience letters*. 2011; 492(3): 129-33.

Soteropoulos DS, Edgley SA, Baker SN. Lack of Evidence for Direct Corticospinal Contributions to Control of the Ipsilateral Forelimb in Monkey. *Journal of Neuroscience*. 2011; 31(31): 11208-11219.

Prototype Amplifier Debuts at Nerve Excitability Workshop



A recent nerve excitability workshop, held at the Royal Society's Chicheley Hall and sponsored by Digitimer (see www.nerveexcitability.org.uk), allowed neurologists and clinical neurophysiologists from around the world to receive hands-on training in nerve excitability testing, using the QtracW automated threshold tracking software developed by Prof Hugh Bostock FRS. During this intensive three day course, five EMG setups each including a Digitimer DS5 Bipolar Stimulator and prototypes of our new D440 clinical amplifier, were used to train the delegates in nerve excitability testing and operation of the specialist QtracW software.

The prototype D440 amplifiers supplied by Digitimer performed admirably and proved capable of making small amplitude recordings crucial for this technique. We still have plenty of work to do, but this successful trial means that we can progress with development of the amplifier, the intention

being to officially launch the amplifier during 2012.

The D440 amplifier will be controlled from a Windows PC using a USB connection and we plan to offer it in two or four channel versions. Ultimately, we expect that the D440 will be certified to meet the requirements of the European medical device directive (CE) and the United States FDA, for patient use. Digitimer will keep you updated with the development of the D440 amplifier via our website and Facebook page, but if you would like to register an interest or even pre-order, please contact us directly.

Take Control Your D360 Amplifier from within CED Software

Until recently the only way to change the settings on the D360 8 Channel Patient Amplifier was to use the Digitimer D360 Control Software which runs in the background when the amplifier is operating. We are pleased to announce that software engineers at Digitimer and Cambridge Electronic Design (CED) have collaborated to implement support for D360 control within the Signal acquisition software. Support for Spike2 is in progress as we go to press, please contact CED or Digitimer for the latest news.



Ultimately, all CED Spike2 and Signal applications will be able to interface with the Digitimer D360 amplifier control software, allowing these applications to alter input modes, signal gains or filtering before or during sampling. All settings are stored as part of the application sampling configurations. The tight integration of amplifier support into these applications means that changes made to the amplifier settings are compensated for by automatic adjustments to the channel scalings, ensuring that signal calibrations remain correct.

Need to Stimulate with Alternating Polarity? It's an Optional Feature of the DS7A/DS7AH

Our DS7A and DS7AH High Voltage Constant Current Stimulators are used all over the world for nerve and muscle stimulation. We periodically receive requests for modifications to our standard devices and the DS7A/AH stimulators are no exception. One of the most frequently requested modifications for the DS7A and DS7AH is affectionately known by our engineers as "M288A"! This modification adds an extra toggle switch to the front panel of the stimulator, the purpose being to allow the DS7A/AH to deliver pulses of positive, negative or alternating polarity.



M288A relies upon use of a mechanical relay which takes several milliseconds to switch the electrode polarity between pulses. Because of this, the alternating mode will only work correctly if the inter-stimulus interval is >10ms. If the pulse frequency is too high, a warning LED illuminates on the front panel of the stimulator and stimulation is terminated.

If you are interested in purchasing a new DS7A or DS7AH with this modification, please contact us in advance so we can provide you with a price and delivery estimate.

Data Translation DT9812/18- Simple Computer Control of the Digitimer DS5 Stimulator

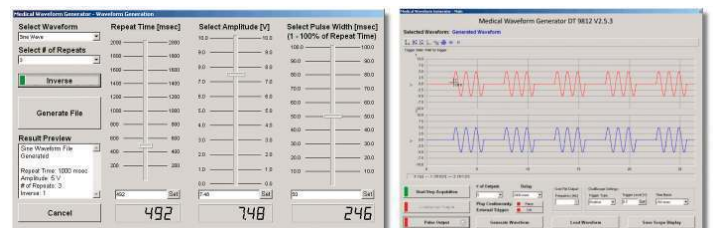


DT9818

Our DS5 Bipolar Constant Current Stimulator is controlled by an analogue voltage waveform which is typically produced by a DAQ system and compatible software. Some DS5 users write or purchase specialist software packages to control the DS5 and acquire responses, such as QtracW for threshold tracking nerve excitability studies. However, for users who want a simple method to control a DS5 with a computer and do not have any experience of DAQ system usage, we offer a straightforward solution. The Data Translation DT9812 and DT9818

are two USB DAQ units which are supplied along with Waveform Generator software which runs on Windows-based computers. The Waveform Generator software allows the user to define a stimulation template that can include biphasic sine waves, triangles, ramps and square pulses.

Waveforms can even be assembled in a spreadsheet package and saved as an ASCII file for later use. Stimulus waveforms can be triggered by TTL input to either unit, however only the DT9818 features a "hardware trigger" which prevents CPU processing time from delaying the waveform output following a TTL trigger event. The software also features an oscilloscope function which allows the user to monitor the current and voltage output from the DS5 on their computer screen, if required.



Due for Release in November 2011

New Slice Incubation Chambers from Scientific Systems Design



Membrane Chamber for Upright or Inverted Microscopy - Let Your Slices Breathe!

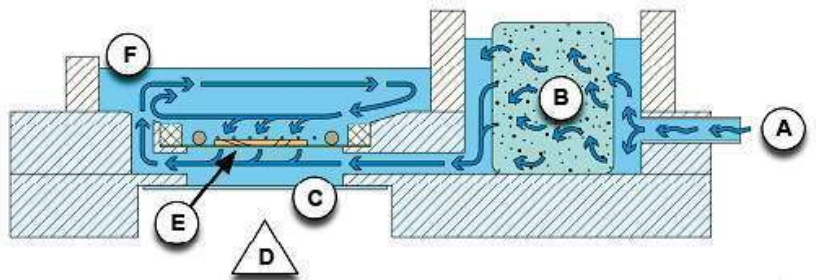
The Membrane Chamber (MC) is a new design of in vitro slice recording chamber (Hill & Greenfield 2010). Brain slices are submerged on a completely flat, transparent semi-permeable membrane. This offers for the first time ideal conditions for inverted microscopy of in vitro preparations. The utilisation of a membrane with a high molecular weight cut off ensures all nutrients and oxygen can flow freely for optimum perfusion. The design of the flow path is such that rates up to 20ml/min can be used without inducing mechanical noise. A further advantage is that the high speed flow of oxygenated aCSF directly underneath and across the semi-permeable membrane exerts a Bernoulli effect, resulting in a pressure difference between the upper and lower surfaces of the membrane. This in turn causes a significant



movement of nutrients and oxygen downwards through the semipermeable membrane, increasing the availability to the slice especially on the underside and thereby surpassing passive slice perfusion techniques. The active flow downward through the membrane keeps the slice from floating and makes it mechanically stable. The transparent membrane offers ideal conditions for imaging through a glass coverslip window on the underside of the chamber with an inverted microscope whilst the upper chamber is exposed for microelectrode access. Alternatively there is sufficient access from above for upright microscopes to allow immersion objectives to be used and allow access with microelectrodes from the front and sides.

So How Does it Work?

A peristaltic pump delivers pulsatile flow at high speed in the range 15ml / min (A) into a reservoir containing a buffer (B) which induces turbulence and reduces pulsation. Smoothed laminar flow passes through the infra chamber (C) directly below the surface of the semipermeable membrane (E) carrying the slice preparation. A Bernoulli effect produces a pressure difference between the upper and lower surfaces resulting in a net movement downwards (arrows) through the membrane and also increases access to slice preparation. A glass coverslip window allows for optical access (D) from below. Fluid exits into the supra chamber and leaves from the chamber through a buffered exit for smooth outflow with a pump or vacuum line.



Hill, M.R.H. & Greenfield, S.A., 2011 *The Membrane Chamber: A new type of in vitro recording chamber* *Journal of Neuroscience Methods*, 195 (1), pp. 15-23.

BSK5 "Interface Mode" Brain Slice Keeper (Pre-chamber)

The BSK5 Brain Slice Keeper has been designed to pre-incubate a large number of brain slices prior to transfer into recording chambers. Based on the BSK4, it consists of two (BSK5-2, pictured) or four (BSK5-4) closely fitting acrylic rings, located in a half cylinder manifold.

The close fitting rings allow a removable sheet of nylon netting to be wedged and held in place. Unlike the BSK1 and BSK4, where the slices are submerged, the slices in this incubator are maintained at an interface between the



incubation medium and a humidified, high oxygen atmosphere within the holding vessel. Furthermore the slices can be maintained on a flat porous membrane attached to the nylon netting in order to maintain the underside of slices perfectly flat for subsequent experiments utilizing microscope techniques.

For more information on these new products, please contact us or use our Digitimes feedback form on our website.

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Please Contact Us to Arrange a No Obligation Evaluation Loan

Thorlabs Add a Faraday Cage to their High Performance Range ScienceDesk of Anti-vibration Tables

The ScienceDesk™ series is a modular system designed to provide an ergonomic alternative to conventional anti-vibration tables. This high quality, modular workstation is ideally suited to a range of vibration-sensitive applications, including confocal microscopy, laser scanning microscopy, biotechnology and electrophysiology.

An array of accessories, including Faraday cage, shelving options, keyboard holder, monitor mount, mounting posts and castors are available to allow customization of the table. Three standard sizes are available: 30" x 36" (750 mm x 900 mm), 30" x 48" (750 mm x 1200 mm), and 36" x 48" (900 mm x 1200 mm), all at a standard desk height of 30.6" (765 mm).

- The welded steel construction of the frame provides a durable work platform; the breadboard is inset into the frame to avoid incidental contact.
- Frames are available with three levels of vibration isolation: Active, Passive and Rigid.
- Each is designed to accept a breadboard from our Performance™ or PerformancePlus™ Series.
- Models are available with or without tapped holes (imperial or metric).
- The combination of frame and breadboard allows flexibility in creating a work space with an array of vibration-isolation possibilities.

Of course, experiments in electrophysiology, confocal microscopy and other sensitive applications must often be shielded from external interference such as electrostatic fields and high-frequency electromagnetic waves. The NEW ScienceDesk Faraday cage protects against these external sources of interference, and fits the 750 mm x 900 mm ScienceDesk base.

The range of ScienceDesk post-mounted accessories can be installed inside the enclosure, providing a variety of shelving and equipment mounting options. The Faraday cage features two cable entry ports (more can be added). All side panels are held in place magnetically and can be removed if required. Digitimer can offer special pricing for customers in the UK willing to act as reference sites, please contact us for details.



Air - The New Sensation from Japan

NARISHIGE



The new IM-11 from Narishige takes microinjection to a new level of simplicity. The IM-11 requires minimal setup as it does not use an oil or gas source, however, it provides performance comparable with oil filled injectors. Air pressure is perfectly controlled with large and small movement control dials. Even tube replacement is made simple, as the IM-11 features a tool-free push in/out tube replacement mechanism.

As if these features weren't enough of an incentive to buy one, until the end of July 2012, the IM-11 is available from us with a **15% introductory discount**.

Don't forget that as an official representative of Narishige, we are able to offer their complete range of electrophysiology, microinjection and sterotaxic equipment. Please contact us for a full price list.

HEKA ITC Driver Now Supports 64-bit Operating Systems

HEKA

HEKA Elektronik are now able to offer 64-Bit drivers for Windows 7 64-Bit and Vista 64-Bit operating systems. These drivers support ITC-16, ITC-18, ITC-1600, LIH-1600 data acquisition interfaces and EPC 9, EPC 10, and EPC 10 Plus patch clamp amplifiers. The newer LIH 8+8 and EPC 10 USB amplifiers can be used on 64-Bit operating systems already and do not require any driver installation.

However, potential users of 64-Bit operating systems should note that Patchmaster 2.60 or newer is required for these drivers to work correctly. They should not be used with older Patchmaster versions or with PULSE. We would like to remind all Pulse users that Digitimer can offer a discounted PatchMaster upgrade license as well as the opportunity to exchange existing parallel port dongles for a more versatile USB equivalent.

If you are based in the UK and interested in upgrading to Patchmaster or would like to find out more about the range of HEKA patch/voltage clamp amplifiers, please contact Digitimer.



EPC800-USB



EPC10-USB



NeuroLog System - The Modular Electrophysiology Workstation

The NeuroLog System is a modular and versatile rack-based system for making electrophysiological recordings, delivering electrical pulses & stimuli or conditioning pre-amplified signals. If we look at amplification functions alone, the NeuroLog System incorporates modules for microelectrode, extracellular, intracellular, isolated EMG/EEG and transducer recording. The range of modules is always expanding and this issue of Digitimes introduces a new accelerometer and interface compatible with our NL109 Bridge Amplifier.

As it can support multiple functions or several channels of recordings in a single rack, the NeuroLog System evolves with the direction of your research and provides a long term solution to your electrophysiological hardware needs.

Multi-channel High Current/Voltage Stimulation for Organ Baths and Cultured Cells

The D330 MultiStim System is a modular and versatile multi-channel stimulator for biomedical scientists requiring accurate in vitro stimulation of multiple low impedance tissue preparations with different stimulating voltages or currents. Timing modules are available to generate pulses, variable in frequency and duration, which can be controlled as trains using a gating waveform, variable in repetition rate and duration or pulse count. Sockets are fitted to allow full external control and synchronisation if required. The D330 MultiStim System comes as a 19" rack-mountable unit that can house up to ten stimulation channels - along with the pulse train generator, gating and meter modules. In order to help with module selection, a number of application diagrams are downloadable from the Support section of our website.



The DG2A - An Easy to Use, Inexpensive TTL Trigger Source for Our Stimulators

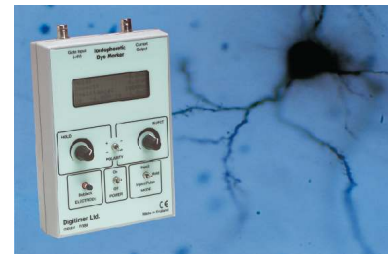


The DG2A Trigger Generator is a compact, free-standing, battery powered device which can be used to generate trigger pulses necessary for repetitive stimulation. Also featuring DELAY controls, it can be used for determining nerve or axonal Effective Refractory Period (ERP) through the production of a delayed second pulse.

Various modes allow output pulses to be produced singularly, continuously or in a burst, with the burst/train duration and pulse frequency determined by the front panel controls. In each of the modes (except FREE-RUN), outputs can be initiated either by the front panel push button, a TTL compatible trigger/gating pulse or a suitable foot switch. The unit is especially suitable for use with our range of isolated stimulators.

Simple & Cost Effective Anatomical Dye Labelling by Iontophoresis

The D380 Iontophoretic Marker provides a compact and easy to use solution for dye labelling of cells or injection of pharmacological agents. Electrophysiologists often use an existing patch clamp amplifier to provide current to carry out such tasks, however, if these techniques are not already being used in the laboratory, alternative iontophoretic devices are often prohibitively expensive. The D380 provides a cost effective answer, delivering currents of up to $\pm 12\text{nA}$, with a holding current of up to $\pm 6\text{nA}$. A deblock button provides a means of removing blockages from the end of electrodes and an LCD display allows continuous monitoring of several parameters.



Compact Constant Current (DS3) or Constant Voltage (DS2A) Stimulus Isolators

The Digitimer DS2A (constant voltage) and DS3 (constant current) Isolated Stimulators are popular in electrophysiology laboratories all over the world. Their compact and user friendly design has generated a loyal following amongst researchers wishing to precisely stimulate nerve or muscle from an isolated power source. They can be triggered manually using the front panel single-shot button or automatically in response to TTL compatible trigger pulses. In addition, pulse duration can be defined by (i) the settings of the front panel control dials (ii) the duration of the incoming trigger pulse or (iii) the length of time that the single-shot button is held down. Power for both stimulators is derived from eleven standard 9V batteries, which offer low noise and long life. Power is only drawn from the batteries when a stimulation pulse is given. The DS2A, DS3 or DG2A Trigger Generator (see above) can be 19" rack mounted using our D121-11 mounting frame which will support up to two of these instruments.



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