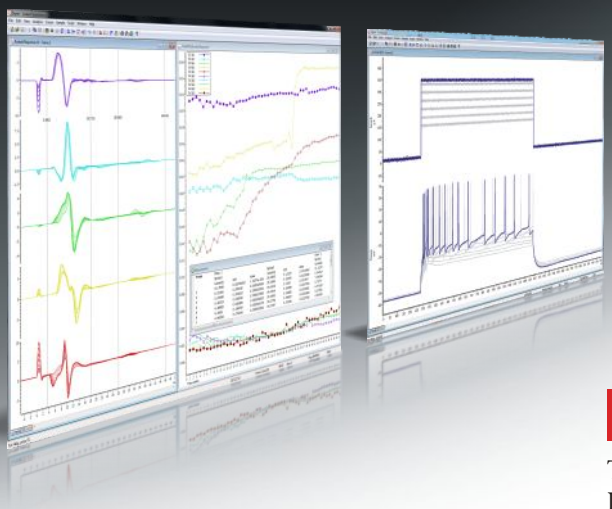


Signal

Sweep-based data acquisition & analysis system

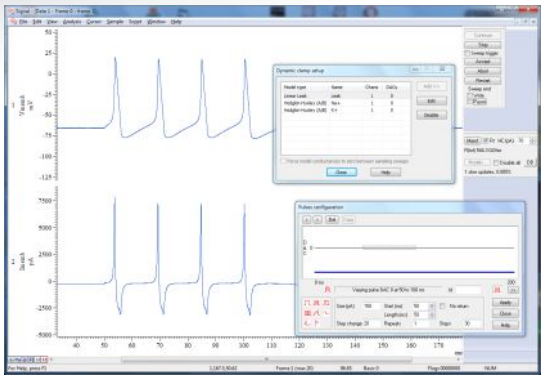
Dynamic clamping

The Signal for Windows application from CED is well known for its extensive Patch and Voltage clamp recording and analysis capabilities. From Signal version 5 we implement extensive dynamic clamp support to augment this flexible program. Used in conjunction with the CED Power1401-3 or mk II and your existing current-clamp amplifier, no special hardware is required.

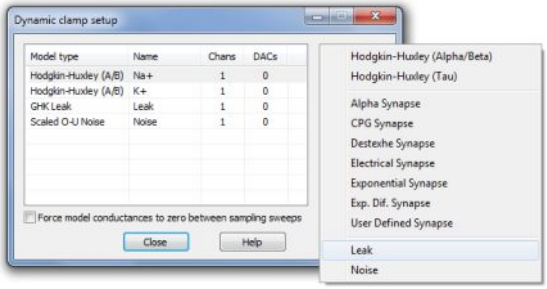
Signal includes a fully integrated, easily configurable, high-performance dynamic clamping system. This advanced feature makes the technique readily available to researchers who do not have access to complex customised hardware and software by providing a professionally designed, maintained and supported package that is usable by all at a low cost.

In the dynamic clamp technique[1], a typically nonlinear feedback system delivers current to a cell to represent the actions of virtual ion channels, allowing ion channels or synapses to be simulated, or the actions of existing channels to be cancelled[2].

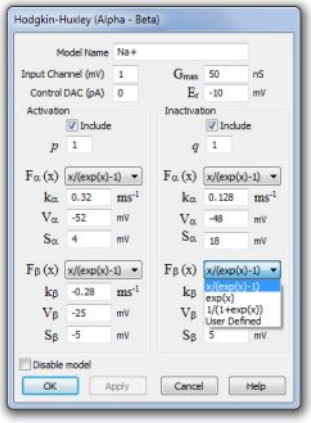
- Execute up to 15 models to generate outputs on up to 8 DACs; multiple models driving one DAC are automatically summed
- Very fast update rates: over 300 kHz with one Hodgkin-Huxley model and 270 kHz with two models (see table below)
- Detection of overload in hardware gives confidence in your results
- Ergonomic dialogs to view and edit the model parameters
- Modify model parameters and apply your changes while sampling
- Switch automatically between multiple parameter sets during sampling
- Pulse and waveform outputs defined by the user can be summed with the outputs generated by dynamic clamping
- Output sequencer can enable and disable individual models dynamically during a single sampling sweep



Dynamic clamp simulating action potentials with model parameter access during sampling



Adding and selecting models



Setting parameters for a Hodgkin-Huxley model

The Power1401-3, as used for dynamic clamping

Currently available models and speeds

Model class	Type
Hodgkin-Huxley	Alpha/Beta *, Tau*
Synapse	Alpha, Central pattern generator, Destexhe, Electrical, Exponential, Exponential difference, User defined *
Leak	Linear, GHK, Boltzmann, User defined *
Noise	Ornstein-Uhlenbeck, Scaled Ornstein-Uhlenbeck *

H-H Models	x1	x2	x4	x8
Power1401-3	320 kHz	270 kHz	175 kHz	105 kHz
Power 1401 Mk II	100 kHz	85 kHz	60 kHz	45 kHz

** These models can be customised or extended by replacing numerical parameters with user generated tables of values*

Embedded hardware-based dynamic clamp systems offer feedback that is fast and precisely timed, but these systems are often expensive and sometimes inflexible. PC-based systems, on the other hand, allow more complex feedback, but real-time performance can be poor[3].

The CED Signal dynamic clamp system gives you the best of both worlds. All real-time aspects of the system are executed by the Power1401's fast embedded processor using pre-calculated lookup tables and optimised floating-point arithmetic, with the feedback calculations triggered by the ADC sampling for maximum stability. This software-based design is fast yet still provides great flexibility. The non-real-time aspects of the system are handled by the controlling PC to allow simplicity and ease of use. The result: a dynamic clamp system integrated into the standard Signal data acquisition software that greatly outperforms generally-available dynamic clamp systems.

It has been shown[3] by simulations and experiment that the performance of dynamic clamp systems is strongly affected by the update rate and latency of updates. The very high-speed methods used by CED provide the superior update rates with low latencies that allow you to undertake the most demanding experiments. The mechanism incorporates a hardware based overflow detector so that you can be sure that the required update rates have been achieved and that your data is trustworthy.

[1] Sharp AA, O'Neil MB, Abbott LF, Marder E (1993) Dynamic Clamp: Computer-Generated Conductances in Real Neurons. *J Neurophysiol* 69: 992-995 †

[2] Prinz AA, Abbot LF and Marder E. The dynamic clamp comes of age. *Trends Neurosci.* 2004 Apr;27(4):218-24 †

[3] Bettencourt JC, Lillis KP, Stupin LR and White JA. Effects of Imperfect Dynamic Clamp: Computational and Experimental results. *J Neurosci Methods*. 2008 April 30; 169(2):282-289 †

Voltage and patch-clamp features

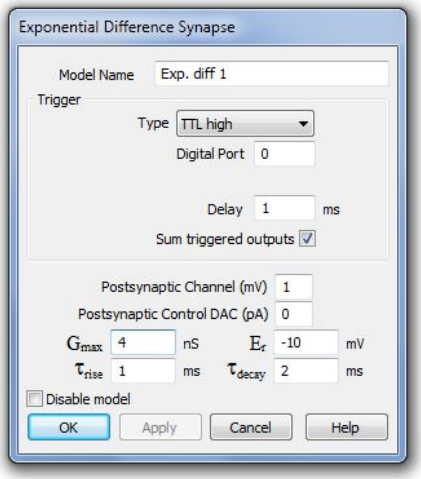
In addition to the integrated dynamic clamp features, Signal also provides support for standard clamping experiment methodologies:

Voltage and current clamp Generates all of the stimuli needed, including pre-recorded waveforms. Multiple sets of stimuli can be stored in one sampling configuration and selected manually or automatically sequenced. On-line measurement of seal and membrane resistance. Leak-subtraction and I/V plots online and offline. Curve fitting to waveform data and I/V plots.

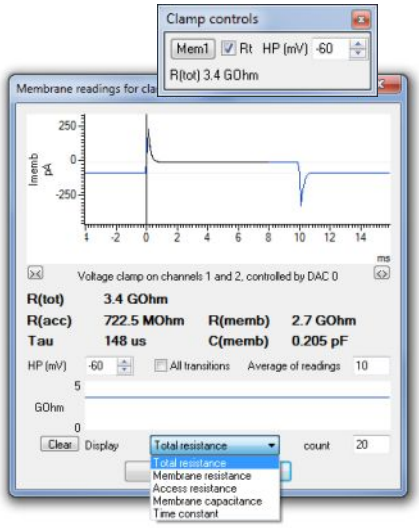
Single channel patch clamp Produces idealised current traces from patch data showing detected transition events either by thresholding or SCAN analysis. The idealised trace is editable by dragging open/closed times and amplitudes, splitting and combining events. Amplitude histograms and dwell time histograms can be produced.

System requirements

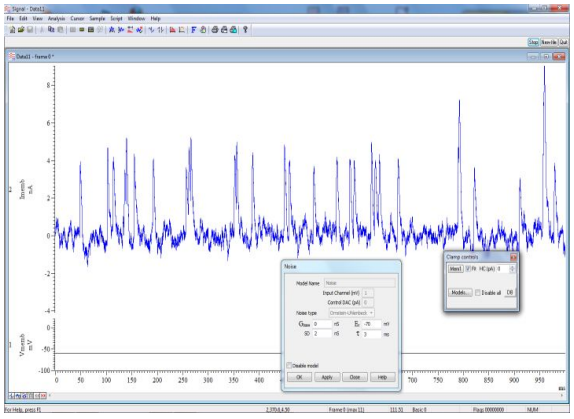
Signal Dynamic clamping requires a CED Power1401-3 or mk II laboratory interface and a PC with Windows XP, Windows Vista, Windows 7, Windows 8 or Intel Macintosh running Windows. Both 64-bit and 32-bit OS versions are supported. We recommend the computer has a minimum of 2GB of RAM.



Setting parameters for exponential difference synapse model



Membrane test during sampling



Exponential difference synapse model with superimposed noise, triggered internally at randomised intervals

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