SpikeGadgets

Two-way Neural Interrogation System

All channels capable of recording and electrically stimulating





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Technical Overview

- The Headstage Combiner Unit pulse train generator receives high-level commands and parameters from the Trodes software suite. These commands define the detailed characteristics of a stimulation pulse train. The generator will store these parameters and run them with high temporal precision when a trigger command is received.
- High-level stimulation commands originate from the Trodes software. Users
 can use commands on python to define, upload, and trigger the stimulation
 pulse programs. The same interface can be used for closed-loop protocols
 where the stimulation triggers are contingent on real-time detection of
 neural recording patterns.
- All channels can independently switch between stimulating and recording with low delay, enabling two-way electrical interrogation of neural circuits.
- Up to eight 32-channel headstages can be used simultaneously (256 channels).



UH32stim Headstage

The 32 Channel Upright Record/Stim Headstage (UH32stim) amplifies and digitizes 32 neural channels during record mode. The UH32stim samples at a rate of up to 30 samples/second. Each channel can independently switch to stimulation



mode to source or sink programmatically defined current that can be updated at the sampling frequency. The headstages are generally used during head-fixed experiments and plugged into the SpikeGadgets Headstage Combiner Unit (HCU). Up to eight UH32stim headstages can be used concurrently with a single HCU, enabling up to 256 channels of two-way neural interrogation.

The UH32stim headstage uses two Intan Technology RHS2116 16-channel stimulator/amplifier chips, which are designed to output programmable amounts of electrical current on any channel and perform all required analog functions, such as amplification, multiplexing, and digitizing. The chip can source and sink currents ranging from 10 nA to 2.55 mA, enabling precise biphasic stimulation. Each channel can guickly switch back to

recording after a stimulation event using fast amplifier artifact recovery circuitry. For more information on the specifications of these chips, please see the RHS2116 datasheet.



UH32stim specifications

| Channel count | 32 |
|------------------------------------|--|
| Intended experimental applications | headfixed |
| Connector to electrode array/probe | 36-pin Omnetics with 4 guide pins |
| Sampling rate | Up to 30 kHz |
| Bit depth (ADC's) | 16-bit |
| Connector to system | Flat ribbon cable |
| Input range | ± 5 mV |
| Dimensions | 26 x 16 x 5 mm |
| Noise floor | 2.4 μV rms typical |
| Stimulation current range | Source and sink between 10nA to 2.55 mA over an 18V range. |
| Stimulation current step size | Between 10nA to 10 $\mu A.$ Full range divided into 256 steps. |
| Stim-to-record switch time | 1-2 ms typical. Depends on the specific artifact recovery method used during the stimulation presentation. |

UH32stim connectors

An Omnetics 36-pin female connector with four guide pins (two one each end) is used to connect to various types of electrode arrays. Below is a pin hardware map for the UH32stim Omnetics connector. G stands for system ground and R stands for amplifier reference. In the default headstage configuration, reference is tied to ground. Please see the Trodes documentation on how to order and organize the channels according to what makes most sense for your specific electrode array.







The connection to the Headstage Combiner Unit uses a ZF5S series zero insertion force connector from Samtec. A 0.5 mm pitch ribbon cable routes to signals to an HDMI adaptor that plugs into the HCU. To replace the ribbon cable, the connector has a black cam that can be pulled out to release the hold on the cable. When inserting the replacement cable, it must be aligned and fully inserted before the cams are pushed back down.

Replacement cables can be purchased from SpikeGadgets in various lengths (up to 100 cm supported).



Headstage Combiner Unit (HCU) and Main Control Unit (MCU) and Environmental Control Unit (ECU)

Detailed documentation on the HCU, MCU, and ECU are located in the SpikeGadgets Control Units manual. Details on system setup and general usage is given there and will not be covered in this documentation. While the HCU and MCU are required for the two-way neural interrogation system, the ECU is an optional add-on for environmental control. The scheduling of stimulation pulse patterns is carried out by the HCU. The combined data from all headstages plugged into the HCU (up to eight) is streamed to the MCU. The MCU, in turn, is responsible for all communication with the computer and Trodes software.

Pulse Train Generator

Commands to define stimulation patterns originate from the computer (Trodes software). The commands will be parsed on the control hardware and translated into an event queue of low-level commands going to the stim/record chips. The HCU translates the command into a buffered array of low-level commands going to the target stim/record chip. Once triggered, these buffered low-level commands will be sent to the chips at the sampling rate of the headstage (30 kHz) until the entire pulse train is completed or a stop command is given. In between pulses in the train, the target channel(s) will switch back to recording mode.

Parameters used to define a pulse train

The commands used to define a pulse train have ten main parameters. With these parameters, users can define a biphasic stimulation train using 1 or 2 channels (the anode and cathode channels, which can be the same channel for monopolar stimulation). See the figure below for an illustration of a pulse train and the parameters.

- 1. Leading pulse width (samples). Note: the leading pulse can be cathodic or anodic.
- 2. Leading pulse amplitude (256-step resolution divided across the set amplitude range)



- 3. 2nd (charge balance) pulse width
- 4. 2nd pulse amplitude
- 5. Interphase dwell (samples)
- 6. Pulse period (samples)
- 7. Delay before the first pulse (samples)
- 8. Number of pulses in train
- 9. Anode channel
- 10. Cathode channel (can be the same as the anode channel)



Triggering a defined pulse train

The control hardware is able to execute multiple pulse train commands simultaneously. When a train definition is sent, it is added to a user-defined "slot" and "group". Multiple trains can be added to a group. A stimulation train is started by triggering either the slot (just one train) or the group (multiple trains triggered



simultaneously). If the stimulation train needs to be aborted before it has completed, a stop command can be applied to either the slot or an entire group.

Charge balancing

Deep-brain stimulation combined with simultaneous recording presents multiple challenges. Problems that may arise include tissue damage, electrode degradation, and stimulation artifacts on recording channels. To curtail these potential problems, one of the most important factors to consider is how electric charge is balanced on the stimulation electrodes when the pulses are presented. For most applications, it is critical that the total amount of charge sourcing and sinking is balanced between the anode and cathode. Any unbalanced charge can create dangerous tissue heating, damage to electrodes, and for experiments with simultaneous stimulation and recording, any residual charge will cause spikes in the recorded voltage that persists long after the pulse. If the anode and cathode are selected to be on different electrodes in the recording array, you must make sure they are nearby each other. Distant anode/cathode pairs will not allow adequate charge balancing and may result in tissue damage or electrode degradation. If you are using different pulse amplitudes for the anode and cathode, the pulse widths that balance total charge must be used.

Global settings

Some stimulation parameters apply to all channels and cannot be set independently for individual channels. The most important global parameter is the range of the stimulation amplitudes. A small range means that the 256 step sizes are high-resolution steps, whereas a big range allows large stimulation currents to be used. The set range applies to both the cathode and anode. Allowed range values are:

max10nA, max20nA, max50nA, max100nA, max200nA, max500nA, max1uA, max2uA, max5uA, and max10uA

The rest of the global stimulation settings are used to fine-tune how the system performs artifact recovery. It is recommended that users start with the default settings before attempting to modify the artifact recovery settings.



Trodes Software

General information about Trodes is located in the online Wiki manual. This document will cover information specific to stimulation setups.

https://bitbucket.org/mkarlsso/trodes/wiki/Documentation

Workspaces

Please see the Trodes documentation on how to create a workspace for you specific headstage and recording array:

https://bitbucket.org/mkarlsso/trodes/wiki/Workspace

One important note about stimulation capable systems is that any channel that will stimulate must be given permission to be stimulation capable in the workspace. The cooresponding <SpikeChannel> element for that channel in the workspace must be given a stimCapable="1" setting. The default is 0.

Visualizing stimulation trains

You can visualize the timing of the stimulation pulses in Trodes by clicking on the "Filter Band" drop down menu and selecting "Stimulation". If you only want to visualize the stimulation pulses for a subset of nTrodes while the others continue to show neural data, you can right-click on the nTrode ID number next to the traces and selected the display setting independently for any nTrode.

Digital referencing limitations

Trodes allows users to set up complex digital referencing patterns, where any recording channel can be used as a reference for any other recording channel. Furthermore, users can set up common average referencing (CAR) calculations using defined sets of channels. Channels that can switch between stimulation and recording should not be used as reference channels, because it would create confusing results when the channel is not recording (in stimulation mode). Therefore, any channel that has been designated as a stimulation capable channel is excluded from the list of allowed reference channels in Trodes. If you are using hardware where all channels are stimulation capable, you will need to remove the stim capable designation for the channels that you intend to use as references.



Accessing stimulation information from a recording

Trodes uses a suite of export programs to extract specific types of data from the recording file, such as spike waveforms, LFP traces, or environmental events. Stimulation information can be extracted using these programs and imported into Python or Matlab. Details about these programs are provided here:

https://docs.spikegadgets.com/en/latest/basic/ExportFunctions.html?highlight=ex

port

Stimulation Programming Interface

The creation of stimulation pulse trains relies on the Trodes Network API, which allows users to write and execute scripts in python. Detailed general documentation on the API is located in the Trodes online documentation.



About SpikeGadgets

SpikeGadgets is trying something new. Our hybrid approach is to design and sell powerful hardware that interfaces with an open-source software platform supported by a large community of scientists and developers. Our goal is to support the efforts of the open-source community in a commercially-sustainable way.

Technical Support

If you would like technical support, please email us at support@spikegadgets.com.