Arguments in Favor of HEKA EPC 10 based Patch Clamp System

This document highlights features that are in favor of a HEKA system compared to systems of competitors. This document is by far not a complete feature list, please refer to the corresponding product brochures and related documents for additional features.

A typical system consists of a patch clamp amplifier of the **EPC 10 USB** or **EPC 10 PLUS** family and **PATCHMASTER** software.

Hardware Features of EPC 10 family patch clamp amplifier

The only really digitally controlled patch clamp amplifier with built-in AD/DA converter interface (see Ref 1, 2, 5, and 6) is perfectly software controlled.

Self-testing and self-calibration functions allow easy test and calibration of the patch clamp amplifier by the user in their own laboratory (see Ref 1 and 2). This is of very importance since electronic parts will alter with time. Therefore, manually calibrated amplifiers have to be sent in for re-calibration in regular intervals whereas digitally controlled amplifiers such as EPC 10 type amplifiers can be easily re-calibrated by the user.

The headstage can be replaced and calibrated by the user. No shipment to the service center is required for re-calibration of the amplifier. The replaced headstage works with the same quality as a complete new instrument.

The EPC 10 USB is available with one to four independent headstages, each which contains circuitry for voltage clamp (resistor-feedback) AND fast current clamp (voltage follower). This allows a wide range of experiments, including patch clamp, sharp electrode, voltammetry and bilayer recording.

A wide current measuring range in voltage clamp from +/-200 pA to +/-2 µA is covered by three feedback-resistor ranges (5 MOhm – 50 GOhm).

Ten fold higher current passing capabilities of the EPC 10 headstage in current clamp (+/- 2 µA) than amplifiers from competitors.

Mode to preserve the membrane potential at a desired level during current clamp measurements: The so-called "Low Frequency Voltage Clamp" (LFVC) mode automatically injects an appropriate amount of current to preserve the membrane potential at a desired level during current clamp measurements.

Only 1 USB or PCI connection to computer. Data acquisition and amplifier are controlled through a single USB 2.0 connection or a fast PCI-bus interface card (option for EPC 10 Plus). The amplifier is completely and perfectly controlled by the software. Configurable Hot Keys allow a direct access to all amplifier settings. No additional knobs and switches are required.

Choice between PCI or USB connection. The EPC 10 USB is connected through a high speed USB 2.0 interface with the computer. The EPC 10 Plus in addition offers the possibility to connect the amplifier through a PCI-bus card with the computer.

Hot Keys allow direct access to all hardware functions. No knobs and switches are necessary.

Optimal grounding configuration. The factory-site integration of the DA/AD interface and corresponding internal shielding/grounding provide an optimal grounding and noise configuration for all measuring configurations and eliminates compatibility problems. No external BNC connections are required.

Low noise of complete acquisition system. The noise values specified by HEKA always include both devices, amplifier and interface whereas the noise specifications of AXON's amplifiers relate to the amplifier only. The noise values of the HEKA system can be easily checked by the user.

Lowest Noise. In medium and high gain mode the noise of EPC 10 amplifiers is about 15-20% lower than comparable modes of competitive systems (medium gain 500 fA, high gain: 125 fA (at 5 kHz bandwidth, rms).

No bandwidth-filtering errors due to automatic filter adjustment. The amplifier provides two low pass current output filters. However, the overall bandwidth is not just given by the lowest frequency of the two filters! With a HEKA system, the user always specifies the overall bandwidth of the combination of both filters! The secondary filter is then set automatically to the appropriate cut-off frequency to yield the requested bandwidth.

Automatic prevention of aliasing artifacts. An AutoFilter function prevents aliasing artifacts due to violation of the Nyquist Theorem (sampling theorem).

Three scaled outputs. The amplifier provides three scaled outputs for membrane current (after filter 1), membrane current (after filter 2), and membrane voltage.

CSlow compensation in high gain range. The amplifier features CSlow compensation in high gain range (50 GOhm feedback resistor) for low noise whole-cell measurements.

High resolution voltage recordings. Selectable voltage gain of x10 and x100 to allow e.g. high resolution recording of field potentials.

Gain range switching without loosing the cell. The “Gentle CC Switch” function allows seamless transition between Voltage Clamp and Current Clamp and vice versa.

Sound device. A ToneGenerator allows translation of membrane/pipette resistance values into audio signals.

Digitization

Optically isolation. All inputs/outputs are optically isolated.

4 DA converters. Analog Outputs: 4 DA converters with 16 bit (EPC 10 USB) or 18 bit (EPC 10 Plus) resolution.

8 analog inputs share 2 AD converters with 16 bit resolution. Maximal membrane voltage resolution 30.5 µV (EPC 10 USB).

8 AD converters with 18 bit resolution. Maximal membrane voltage resolution 3.05 µV (EPC 10 Plus).

Cophasic acquisition for 2 channels and double staggered acquisition for more than 2 channels (EPC 10 USB). The EPC 10 Plus features cophasic acquisition of all 8 channels. All competitors acquisition systems work in the so-called interleaved mode: The individual AD- and DA-channels are sampled/set sequentially. This results in a time delay between the acquisition/setting of different AD- and DA-channels. The delay is calculated by dividing the sampling interval by the number of AD- or DA-channels. E.g. if 2 channels are acquired with a sampling frequency of 10 kHz using a Digidata interface, then the samples of the two channels are separated by 50 µs although the software claims that they are sampled simultaneously.

200 kHz for 2 channels, 100 kHz for 4 channels or 50 kHz for 8 channels. is the max. acquisition frequency (EPC 10 USB):

Extendibility

Two EPC 10 USB amplifiers under control of one Software. Parallel Patch Clamp: A system based on a Patch Clamp Amplifier of the EPC 10 USB family (EPC 10 USB Single, Double, Triple and Quadro) can be extended in parallel by a second amplifier of the EPC 10 USB family or an LIH 8+8 acquisition interface. Both devices are connected to the computer and a hardware connection between them synchronizes the clocks of the data acquisition boards. (see Ref. 7)

Headstage Multiplexing Device. Serial Patch Clamp: Each patch clamp amplifier of EPC 10 USB and EPC 10 PLUS family can be extended by a headstage multiplexing device. The concept of “digitally controlled” patch clamp amplifier allows to use different headstages with the same patch clamp amplifier. When switching the probe all calibration settings (e.g. high frequency boost) will be digitally adjusted on the main amplifier board with respect to the calibration performed with the corresponding headstage. (see brochure “EPS 16 Probe Selector”)

Standardization and Automation

User defined actions can be recorded and stored as a macro. These macros can be used i.e. to adjust the system for a specific experimental recording. Macros can be automatically executed before or after a recording.

The Protocol Editor allows standardization and automation of complete experimental procedures. Within the procedure, the system can get feedback from external inputs, amplifier controls, online analysis results or user inputs and experimental parameters can be adjusted. This adaptive feedback is possible by introducing:

> **Conditional statements:** With so called “IF-Then” events a protocol can react on either results from measurements or external input, making the procedure more intelligent and powerful.
>
> **Complex calculations** can be done with a set of “global values” to allow adaptive adjustment of e.g. amplifier controls. Acquisition parameters can be automatically adjusted by setting the global variables “pgf-parameters”.

The complete system can be controlled from another application in a platform independent manner. The user can write their own application with a custom tailored user interface but still benefit from the advanced features of the HEKA system.

Use in GLP Environment

HEKA provides PATCHMASTER PRO software to run manual patch clamp systems in a GLP (Good Laboratory Practice) environment. (see PATCHMASTER PRO brochure or Ref 8)

General System Features

Supported Operating Systems: Mac OS X, Windows 2000/XP and Vista

Host interface: **PCI-bus** and **PCI-X-bus** as well as **USB 2.0** supported

Cophasic Acquisition Mode: For GAP junction measurements two headstages can be controlled absolutely simultaneously with identical stimuli. Auto CSlow compensation can be used in GAP junction studies.

Data Integrity: Due to the complete software control, a complete set of parameters describing the state of the amplifier and other recording conditions is stored with the data. This allows detailed reconstruction of the experiment for exact analysis at later times. (No telegraphing necessary!)

Acquired data are organized and stored in a data tree. Multiple data packages are usually stored in one data file and organized in levels of Groups/Experiments/Series/Sweeps and Traces to allow easy review, selection and analysis of all data in that data file.

Software LockIn: The system features a software Lock-In amplifier for time resolved measurements of membrane capacitance. (see Ref 3)

Photometry Extension: Different fluorescence excitation light sources can be controlled from the system and flexible functions for acquisition and analysis of photometric signals are available.

Data acquisition software features **complete integration of the patch clamp amplifier**.

(Double/Triple/Quadro) Multiple patch clamp **heastages can be stimulated simultaneously with completely independent stimulation protocols**.

Up to 16 data traces can be recorded simultaneously.

Mathematical processing of incoming data. The virtual trace feature allows online mathematical processing of incoming data.

Automatic Break will stop the acquisition. For each acquisition channel a break criteria can be defined. An Automatic Break will stop the acquisition whenever one of break criteria becomes true.

References and related documents

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2. Design of the EPC-9, a computer-controlled patch-clamp amplifier. 2. Software, Sigworth, F.J., Affolter H., Neher E. Journal of Neuroscience Methods 56 (1995) 203-215

3. Admittance-based measurement of membrane capacitance using the EPC-9 patch-clamp amplifier. Gillis K.D., Pflügers Archiv (2000) 439:655-664

4. Technical Information: Acquisition Modes EPC 9, EPC 10 and EPC 10 PLUS, HEKA brochure

5. The Stone Age of Patch Clamp Amplifiers, Neher E., HEKA *impulse* 01

6. The HEKA History, HEKA *impulse* 01

7. Amplifier Cluster under Control of PATCHMASTER, HEKA *impulse* 02

8. PATCHMASTER PRO supports GLP and FDA Regulations, HEKA *impulse* 03