Fully computer-controlled Patch Clamp Amplifiers

Introduction

HEKA is very proud to release the EPC 10 USB - the newest member of the EPC 10 family of fully computer-controlled patch clamp amplifiers. The EPC 10 USB continues the HEKA commitment to provide the most up-to-date and technologically advanced products for scientific research. The EPC 10 USB is the successor to the revolutionary EPC 9 patch clamp amplifier, which was introduced in 1990\cite{1,2,3}, as well as the renowned EPC 10.

The EPC 10 USB patch clamp amplifier is available with either one (EPC 10 USB), two (EPC 10 USB Double), three (EPC 10 USB Triple) or four (EPC 10 USB Quadro) integrated amplifier modules.

The EPC 10 USB is fully integrated with HEKA’s new LIH 8+8 data acquisition interface. The LIH 8+8 is a high resolution, low noise scientific data acquisition interface that utilizes the latest Analog to Digital, Digital to Analog, USB 2.0 and high-speed processor technologies. This powerful hardware combination in conjunction with PATCHMASTER or PATCHMASTER NEXT software provides a highly-integrated system that will minimize total recording noise, eliminate compatibility problems, reduce additional equipment expense, and most importantly, set-up time.

There are many advantages to a fully digitally-controlled patch clamp amplifier. Three major advantages employed in the design of the EPC 10 USB are:

- First, since all of the functions of the amplifier are controlled by a data acquisition program all of the amplifiers hardware settings can be stored along with the data. Not only is this capability important when reviewing and analyzing the data but also for complete and thorough experimental book-keeping.
- Second, computer control allows a number of operations to be fully automated. These can include automatic mode switching (e.g. switching between the settings for establishing a seal or those for single-channel recording), automatic capacitance neutralization of C-Fast and C-Slow, and series resistance compensation. In fact, digital control of every adjustable parameter in the amplifier circuitry is implemented including full functionality test and calibration.
- Finally, the integration of the amplifier, data acquisition interface and software allows experiments to be easily replicated to exact details.

Applications

The EPC 10 USB family of amplifiers can be used, for example, for any of the following applications:

- Low noise single-channel recordings
- Low noise whole-cell patch clamp recordings: voltage clamp and current clamp/Low Frequency Voltage Clamp (LFVC)
- Measurements of fast action potentials (AP), fast switching between voltage and current clamp and vice versa.
- Loose-patch recordings⁴.
- Intracellular voltage recordings with high resistance electrodes.
- Field potential recordings.
- Recordings from artificial membranes (Bilayer Recordings) and nanopores.
- Study Synaptic Transmission by simultaneous stimulation/recording from multiple cells (e.g. pre- and post-synaptic cells).
- Study of Long Term Potentiation (LTP) and Long Term Depression (LTD).
- Study of Exocytosis/Endocytosis or Synaptic Transmission by
  - Measurement of whole-cell membrane capacitance
  - Measurement of on-cell membrane capacitance
  - Detection of released substances (amperometry with e.g. carbon fiber electrodes)
  - Detection of released substances under a patch (patch amperometry)
  - Combined membrane capacitance measurements with amperometry (using EPC 10 USB Double)
  - Combined patch amperometry and on-cell capacitance measurements (using EPC 10 USB Double)
- All above mentioned methods can be combined with photometric determination of e.g. the internal calcium ion concentration.

Revision “T” Improvements

With the latest EPC 10 USB Revision “T” amplifiers we added new hardware features:

Extended Stimulus Range

The extended stimulus range:

- increases the voltage stimulus range from ± 1 V to ± 2 V in voltage clamp mode.
- increases the voltage measuring range from ± 1 V to ± 5 V in current clamp mode.
- increases the current injection capability in current clamp mode by factor of 5.

Filter 2 Bypass

An option for using the “Filter” on the current or the voltage signal. This new feature e.g. allows filtering of the voltage signal in a current clamp measurement using the Filter 2. If Filter 2 is set to “V_ Bessel” or “V_Butterworth”, then the current signal is filtered by Filter 1 only.

Models and Features

The EPC 10 USB is a complete data acquisition system, which can be used with HEKA’s PATCHMASTER or PATCHMASTER NEXT software. A DLL (dynamic link library) is available for software developers who are interested in writing their own Windows data acquisition software.

The EPC 10 USB patch clamp amplifier, combined with a computer and PATCHMASTER / PATCHMASTER NEXT software is equivalent to a fully-equipped recording setup, which includes a patch clamp amplifier, a digital storage oscilloscope, a variable analog filter, a sophisticated pulse generator, and a full featured data acquisition and analysis system.

EPC 10 USB Patch Clamp Amplifier family

Common Features

- Fully computerized patch clamp amplifier that has a built-in data acquisition interface.
- The integration of the built-in low noise LIH 8+8 data acquisition interface and the amplifier provides optimal grounding, removes external connections and only requires a single USB 2.0 (Hi-speed) port connection.
- Compatible with either Windows or Mac OS systems, fully controlled via the PATCHMASTER / PATCHMASTER NEXT software
- Software testing and calibration routines allows the user to verify the working condition of the instrument within minutes. Calibration, which typically required that the amplifier be taken out of service can be performed in-house, within a few minutes, with no additional expense, and more importantly no downtime to the recording setup. In addition, if needed, the headstage can be easily replaced and calibrated by the user.
- The EPC 10 USB features C-Slow compensation in the high gain range (50 GΩ feedback resistor) for low noise whole-cell measurements.
- Ultra slim low noise headstage design is optimized for single-channel, whole-cell and loose-patch current recordings
- Resistor switching headstage with three gain ranges can be switched during an experiment
- True Current Clamp capabilities
- A “Low Frequency Voltage Clamp”(LFVC) mode is provided to automatically inject an appropriate amount of current to preserve the membrane potential, at a desired level during current clamp measurements.
- Gentle Switch option from voltage clamp to current clamp (injection current is equal to the current monitor in voltage clamp mode)
- Automatic or manual C-Fast and C-Slow capacitance neutralization
- Capacitance tracking
- Hardware leak compensation for non-voltage gated channels
- True noise measurements from 100 Hz to 15 kHz
- Built-in tone generator fully controlled by software
- 16 Digital-In and 16 Digital-Out connections at the rear panel. Three of the Digital-Out connectors are also provided via BNC on the front panel.
- All amplifier settings and parameters are stored with the data.
- EPC DLL (dynamic link library) for controlling the EPC 10 USB is available for writing custom Windows applications

EPC 10 USB AMPLIFIERS

Our classic packages starting with an EPC 10 USB Single up to our workhorse, the Quadro.

<table>
<thead>
<tr>
<th>Order #</th>
<th>Product Name Description</th>
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<tbody>
<tr>
<td>895277</td>
<td>EPC 10 USB System w/ S-Probe Headstage</td>
</tr>
<tr>
<td>895278</td>
<td>EPC 10 USB Double System w/ S-Probe Headstages</td>
</tr>
<tr>
<td>895279</td>
<td>EPC 10 USB Triple System w/ S-Probe Headstages</td>
</tr>
<tr>
<td>895280</td>
<td>EPC 10 USB Quadro System w/ S-Probe Headstages</td>
</tr>
</tbody>
</table>

Further configurations are available. For more information see our product overview.
The EPC 10 USB Double, Triple and Quadro amplifiers are the optimal instruments for performing multiple patch/cell experiments. Although two, three or four amplifiers are combined in a single housing, along with the built-in LIH 8+8 interface, each amplifier is completely independent. The amplifiers and headstages are clearly identified, so the user can immediately assign the amplifiers to particular patched cells.

The PATCHMASTER / PATCHMASTER NEXT software can simultaneously stimulate and acquire the response from each amplifier. Current and/or voltage signals from all of the amplifiers can be recorded, displayed and analyzed online.

The EPC 10 USB Double, Triple and Quadro amplifiers also provide an economical solution in comparison to a combination of several individual instruments. They also have advantages of optimized noise performance, grounding, data acquisition and data storage, convenience and ease of integration over multiple external amplifiers.

Extending an EPC 10 USB

with an LIH 8+8

The number of input and output channels available on the front panel of the EPC 10 USB family of amplifiers can be extended by combining an EPC 10 USB amplifier with an additional LIH 8+8 interface. This may be especially useful when using an EPC 10/n USB amplifier in which the number of available outputs is decreased because of internal usage to stimulate the additional amplifiers.

with a second EPC 10 USB

The number of recording channels and the number of amplifiers can be increased by connecting two EPC 10 USB amplifiers. On the rear panel of the EPC 10 USB there are “Slave Sync” and “Master Sync” CAT5 connectors. EPC 10 USB amplifiers can be connected in such a way to create 8 parallel patch clamp amplifiers. This type of connection can be applied to either the single, double, triple and quadro versions of the amplifier.

For example, an 8-channel parallel patch clamp amplifier can be configured by connecting two EPC 10 USB Quadro. These 8 independent patch clamp amplifiers can be controlled by one copy of PATCHMASTER. Expandability to a 16-channel parallel patch clamp amplifier can be done by connecting four EPC 10 USB Quadro. In this case the amplifiers are controlled by two copies of PATCHMASTER that are synchronized and data can be automatically transferred to a single data file.

Example 1
EPC 10 USB Double + EPC Single Amplifier
3 Probes

Example 2
EPC 10 USB Triple + LIH 8+8 Interface
3 Probes + 9 A/D In +5 D/A Out

Example 3
2 x EPC 10 USB Quadro Amplifier
8 Probes
Software Control Options

PATCHMASTER NEXT

The EPC 10 USB family of amplifiers can be controlled with PATCHMASTER NEXT software on either Windows (10 (64-bit)) or Mac (OS X 10.6+) platform. PATCHMASTER NEXT is a multi-channel stimulation/acquisition and control software. For more details please refer to the PATCHMASTER NEXT brochure or contact us.

A Amplifier Window
Each amplifier control can be accessed through the software and all hardware parameters can be accessed. This window is customizable in respect to displayed and required hardware parameters.

B Control Window
The control center of the PATCHMASTER NEXT software. Here, you start, break and or pause your experiments. Further, you have access to all main windows and the configuration of PATCHMASTER NEXT.

C Test Pulse Window
This window is essential for the patch process itself. A running test pulse is necessary to estimate important cell parameters like membrane resistance or offset currents. Further, one can easily detect changes in patch clamp conditions during an ongoing experiment. Each amplifier board has its own test pulse view pane.

D Oscilloscope Window
All acquired and replayed data will be displayed in this window.

E Data Tree
Shows all the acquired data of the currently loaded data file. The tree-like organization of the data enables fast and easy data screening.

F Notebook Window
All relevant software information is plotted into the Notebook which can be stored along with the data itself. Further, the Notebook Window is an important place to write on- and offline analysis results.

G Graph Layout
Analysis results can be plotted on- or offline in analysis graphs which are displayed in the Graph Layout window.
Stimulus Editor

In this editor you define the pattern of the stimulation sequence. You have access to all output and input channels of the EPC 10 USB amplifier. Numerous different segment classes, an Increment Editor and a File Template Editor allows you to create almost every possible stimulation sequence.

Protocol Editor

The Protocol Editor allows to create experimental protocols via an event list which is processed in the given order. In addition to data acquisition one can now control or interact with external devices, react to analysis results or create conditional loops including break conditions or assigned keys. The predefined protocol lines allow a highly standardized and automated experimental procedure.
Headstages

Red Star Headstage

The Red Star Headstage is used with the EPC 10, EPC 10 USB or the EPC 800 USB Patch Clamp Amplifiers. It offers excellent noise levels in the most important 1 - 10 kHz bandwidth. Further, it has three feedback resistors (50 GΩ, 500 MΩ, 5 MΩ) for three gain ranges which are switchable during the measurement. The Red Star Headstage is also noise-optimized for demanding single-channel recordings. The amplifier (EPC 10 USB) and the headstage need to be calibrated using PATCHMASTER NEXT or EPCMaster software.

<table>
<thead>
<tr>
<th>Order #</th>
<th>Product Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>895008</td>
<td>Red Star Headstage</td>
<td>Red Star Headstage with 240 cm flexible connection cable (LxWxH: 90x17x14.5 mm, Weight: 42 g)</td>
</tr>
</tbody>
</table>

S-Probe Headstage

The unique feature of the S-Probe is the significantly reduced size and weight compared to our standard headstages. This allows for compatibility with a wider range of applications, especially when experimental space is limited or where the weight of the headstage itself matters. The electrical specifications of the S-Probe are identical to our standard Red Star Headstage, with the added feature of an optional bath sense connection enabling operation in 3-Electrode mode (with EPC 10 USB only). It is compatible with a new EPC 10 USB or EPC 800 USB amplifier and is also available as an upgrade. Check with our support team to find out if this headstage is supported by your HEKA patch clamp amplifier. The amplifier (EPC 10 USB) and the headstage need to be calibrated using PATCHMASTER NEXT or EPCMaster software.

<table>
<thead>
<tr>
<th>Order #</th>
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</thead>
<tbody>
<tr>
<td>895137</td>
<td>S-Probe Headstage</td>
<td>S-Probe Headstage with 248 cm flexible ribbon cable and a BNC to SMA connector (LxWxH: 49x17x14.5 mm , Weight: 24 g)</td>
</tr>
</tbody>
</table>

Model Circuits

Model Cells for Patch Clamp Amplifiers

<table>
<thead>
<tr>
<th>Order #</th>
<th>Product Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>895013</td>
<td>MC 10</td>
<td>The model cell “MC 10” mimics a model circuit of a biological cell with 500 MΩ membrane resistance, 5 MΩ access resistance and 22 pF cell capacitance. It is essential for testing and calibrating the EPC 10 USB Patch Clamp Amplifiers.</td>
</tr>
<tr>
<td>895014</td>
<td>MC-TESC1</td>
<td>Model circuit for two recordings (VC/CC) of one cell mimicking 10 MΩ and 20 MΩ access resistance, 500 MΩ membrane resistance and 22 pF membrane capacitance.</td>
</tr>
<tr>
<td>895140</td>
<td>MC-TETC3</td>
<td>Model circuit for two recordings from two cells, which are coupled by a gap-junction. Both cells have 500 MΩ membrane resistance, 22 pF membrane capacitance. The access resistance is either 10 or 20 MΩ. There is an additional switch to mimic a gap-junction conductance by a 10 or 100 MΩ series resistance.</td>
</tr>
</tbody>
</table>
Technical Specifications

General

Number of Amplifiers/Headstages

<table>
<thead>
<tr>
<th></th>
<th>Single</th>
<th>Double</th>
<th>Triple</th>
<th>Quadro</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPC 10 USB Single</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPC 10 USB Double</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPC 10 USB Triple</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPC 10 USB Quadro</td>
<td>4</td>
<td></td>
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</table>

Amplifier Control

Fully software controlled patch clamp amplifier featuring e.g. direct access to all amplifier settings, automatic calibration and self testing/diagnosis procedures.

Host Interface

USB 2.0

Dimensions Main Unit

<table>
<thead>
<tr>
<th></th>
<th>Single</th>
<th>Double</th>
<th>Triple</th>
<th>Quadro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth x Width</td>
<td>31.1 x 48.3 cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>14.5 cm</td>
<td>18.0 cm</td>
<td>26.9 cm</td>
<td></td>
</tr>
</tbody>
</table>

mounts in a 19” rack

Weight Main Unit

<table>
<thead>
<tr>
<th></th>
<th>Single</th>
<th>Double</th>
<th>Triple</th>
<th>Quadro</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.4 kg</td>
<td>12.2 kg</td>
<td>15.3 kg</td>
<td>16.5 kg</td>
</tr>
</tbody>
</table>

Dimensions Headstage

D x W x H: 90 x 17 x 14.5 mm

Power Supply

Power requirements are 100 Watt. The logic controlled power supply automatically switches the voltage range. It operates in the range 85 V to 250 V at line frequencies of 50 or 60 Hz. A shielded transformer minimizes noise pickup from power line frequencies.

Ground Lines

A Signal ground is accessible via a Banana plug on the front panel of the main unit and via a connector pin on the headstage. In case of EPC 10 USB Double, Triple and Quadro, all amplifiers share the same ground.

A Chassis ground is accessible via a Banana plug on the front panel of the main unit. Chassis and Signal ground are connected via a 10 MΩ resistor.

Voltage Clamp Mode

Current Measuring Resistors

The headstage provides three feedback resistors. The gain ranges can be switched during the experiment.

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<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Low gain range (5 MΩ)</td>
<td>± 2 µA current range</td>
<td></td>
</tr>
<tr>
<td>Medium gain range (500 MΩ)</td>
<td>± 20 nA current range</td>
<td></td>
</tr>
<tr>
<td>High gain range (50 GΩ)</td>
<td>± 200 pA current range</td>
<td></td>
</tr>
</tbody>
</table>

Current Gain Settings

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low gain range</td>
<td>0.005, 0.01, 0.02, 0.05, 0.1, 0.2 mV/pA</td>
<td></td>
</tr>
<tr>
<td>Medium gain range</td>
<td>0.5, 1, 2, 5, 10, 20 mV/pA</td>
<td></td>
</tr>
<tr>
<td>High gain range</td>
<td>50, 100, 200, 500, 1000, 2000 mV/pA</td>
<td></td>
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</table>

Input Capacitance

< 1 pF

Noise Performance

Measured with open input via external 8-pole Bessel filter.

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<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Medium gain range</td>
<td>up to 1 kHz:</td>
<td>~ 180 fA rms (theoretical limit)</td>
</tr>
<tr>
<td></td>
<td>up to 3 kHz:</td>
<td>~ 320 fA rms (theoretical limit)</td>
</tr>
<tr>
<td></td>
<td>up to 10 kHz:</td>
<td>~ 580 fA rms</td>
</tr>
<tr>
<td>High gain range</td>
<td>up to 1 kHz:</td>
<td>~ 31 fA rms</td>
</tr>
<tr>
<td></td>
<td>up to 3 kHz:</td>
<td>~ 72 fA rms</td>
</tr>
<tr>
<td></td>
<td>up to 10 kHz:</td>
<td>~ 350 fA rms</td>
</tr>
</tbody>
</table>

Bandwidth

100 kHz (low and medium gain range), > 60 kHz (high gain range)

Current Filter

Filter 1 is a 6-pole Bessel pre-filter with 10 kHz, 30 kHz, 100 kHz, and HQ 30 kHz. The EPC 10 USB Single, Double, and Triple allow to directly sample the current signal of Filter 1.

Filter 2 is a 4-pole filter with 100 Hz to 15 kHz bandwidth with selectable Bessel or Butterworth characteristics. Filter 2 is usable in series with Filter 1 or as separate filter for external signals.

Holding Potential

Software controlled holding within a ± 2000 mV range.

External Stimulus Input (VC)

Via a BNC connector at the front panel an external stimulus input can be added to the internal set holding potential. An external stim scaling circuit allows scaling of the external stimulus with a factor in the range of ~ 1.0 to + 1.0.
**Technical Specifications**

**Compensations in Voltage Clamp Mode**

**Pipette Offset Potential Compensation**
Automatic or manual adjustment of the offset potential in the range ± 200 mV.

**Injection Capacitors**
The C-Fast compensation signal is injected via a 1 pF capacitor. The C-Slow compensation signals are injected via a 10 pF capacitor in medium and low gain and via a 1 pF capacitor in high gain range.

**C-Fast Compensation**
Automatic or manual compensation in all gain ranges:
- 0 to 15 pF, 0 to 8 μs τ (calibrated)
- 0 to ~ 80 pF (Extended C-Fast)

**C-Slow Compensation**
Automatic or manual compensation in all gain ranges:
- 0.2 to 1000 pF (low and medium range), 0.2 to 100 pF (high range).
- Rs range 1 MΩ to 1 GΩ.

**Synchronous C-Slow Compensation**
The EPC 10 USB Double, Triple and Quadro provide the option for synchronous C-Slow compensation pulses on multiple cells. This is essential for using the C-Slow compensation when measuring on multiple electrically connected cells.

**Series Resistance Compensation**
Maximal compensation is 95% with the optimal setting being dependent on the cell capacitance.
Equivalent time constants: 2 μs, 5 μs, 10 μs, 100 μs

**Hardware Leak Subtraction**
Automatic or manual linear leak subtraction in all gain ranges:
- 0 to 2 nS (high range), 0 to 200 nS (medium range), 0 to 20 μS (low range).
- Injection time constant: 100 μs

**Software Leak Subtraction**
A versatile p/n leak subtraction is provided in combination with the PATCHMASTER / PATCHMASTER NEXT software.

**Other VC Features**

**Zap Pulse**
Provided by the PATCHMASTER / PATCHMASTER NEXT software. The amplitude (up to ± 1 V) and duration is programmable.

**Audio Resistance Monitor**
A 3.5 mm jack is provided at the rear panel for connecting phones or speakers. Volume and Resistance/Frequency ratio can be adjusted by the PATCHMASTER / PATCHMASTER NEXT software. Frequency range: 1 Hz to 10 kHz.
Current Clamp Mode

Current Injection
Four current injection gains are selectable:
- 0.1 pA/mV range: ± 1 nA
- 1 pA/mV range: ± 10 nA
- 10 pA/mV range: ± 100 nA
- 100 pA/mV range: ± 1 µA

In the “Extended Stimulus Range” the current injection capability in current clamp mode is increased by factor of “5”.

Voltage Gain
Two gains are selectable: Bit resolution:
- V-mon x 10: ± 1000 mV 30 µV
- V-mon x 100: ± 100 mV 3 µV

Voltage Filter
Filter 2 setting do also allow the filtering of the voltage signal in a current clamp measurement.

Voltage Measuring Range
The voltage measuring range is ± 1 V (± 5 V when using the “Extended Stimulus Range”) in current clamp mode.

External Stim Input (CC)
Via a BNC connector at the front panel an external stimulus input can be added to the internally set holding current. The scaling factor is determined by the selected current injection gain.

C-Fast in CC Mode
C-Fast is active in current clamp mode to allow voltage recordings at high bandwidth.

Bridge Mode
The voltage drop across the pipette resistance can be compensated.

Low Frequency Voltage Clamp (LFVC)
Automatic current tracking readjusts the holding current to fix any slow voltage drift while in current clamp mode.

Gentle Switch
When switching from voltage to current clamp, the holding current is automatically set to the “I-mon” in voltage clamp mode.

Fast Mode Switching
The PATCHMASTER / PATCHMASTER NEXT software allows to rapidly switch between current and voltage clamp mode and vice versa during data acquisition.

DA/AD Converter

Stimulation
- Number of DA-converters: 4
- Settling Time: 1 µs
- DA output voltage range: ± 10 V
- Number of AD-converters: 2
- DA/AD resolution: 16 bit
- Fastest Sampling Rate:
  - 2 channels 200 kHz
  - 8 channels 50 kHz

Free DA channels
- EPC 10 USB Single: 3
- EPC 10 USB Double: 2
- EPC 10 USB Triple: 1
- EPC 10 USB Quadro: 0

Free AD channels
- EPC 10 USB Single: 5
- EPC 10 USB Double: 3
- EPC 10 USB Triple: 1
- EPC 10 USB Quadro: 0

Digital Input/Output
- Digital I/O: 16 digital in and 16 digital out channels are provided on a 40 pin male connector on the rear panel.
- Digital In: 16 channels provided at the Digital In connector on the rear panel.
- Digital Out: 16 channels provided at the Digital Out connector on the rear panel, three of them are also provided via BNC on the front panel.
- Trigger In: Via 1 BNC connector on the front panel data acquisition can be triggered externally.

Master/Slave Sync
2 CAT5 connectors for synchronization of a second amplifier/interface system are provided at the rear panel.
The Smart Source for All Your Ephys Needs

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