

**MEA recordings from acute heart slices from adult rats and guinea pigs**H. Lohmann<sup>1</sup>, A. Bussek<sup>2</sup>, M Meier<sup>1</sup>, M. Schmidt<sup>2</sup>, E. Wettwer<sup>3</sup>, U. Ravens<sup>3</sup>

<sup>1</sup> Lohmann Neuropharmacological Consulting, Am Förderturm 9, 44575 Castrop-Rauxel, Germany

<sup>2</sup> Allg. Zool. & Neurobiol., Ruhr-University, Universitätsstr. 150, 44780 Bochum, Germany

<sup>3</sup> Inst. Pharmacol. & Toxicol., Med.Fac.Carl-Gustav-Carus,TU-Dresden, Germany

Acute tissue slices from the brain have been extensively studied with the multielectrode array technique in neuroscience research. Comparable studies on tissue slices from the heart, however, are only rarely encountered. Here we describe the preparation, maintenance of slices from heart tissue of adult rats and guinea pigs and the evaluation of signal propagation on standard planar MEAs.

All experiments were carried out according to the guidelines for animal welfare. The heart was carefully removed under deep anaesthesia. After perfusion with oxygenated physiological solution containing 10-15 mM 2,3-butanedione monoxime (BDM), tissue blocks (4 mm x 6-8 mm) were prepared from the left ventricle. A block of tissue was glued to the cutting stage of a precision vibratome (Integraslice, Campden, UK) with cyanoacrylate glue. The cutting stage was mounted in the bath chamber of the vibratome filled with oxygenated physiological solution plus BDM. 300 µm thick transmural longitudinal, transverse slices as well as sagittal slices could be prepared from the tissue blocks by use of ceramic blades. Slices were maintained in a preincubation chamber at room temperature until they were used in the experiment. Slices were positioned on standard planar MEAs with 200 µm interelectrode distance and 30 µm electrode diameter by use of a harp shape specimen holder (Harvard App.). An external stimulation electrode was advanced onto the tissue by means of a manual micromanipulator. Biphasic pulses could be applied over the stimulation electrodes with a STG2004 stimulator. Extracellular field potentials and its propagation throughout the heart slice were recorded with a MEA60 upright system with artifact blanking circuit. Control experiments with intracellular recordings from ventricular cells were performed in order to verify the viability of the heart cells.

Extracellular action potentials (AP) after electrical stimulation correspond well to the first derivative of the intracellular AP and could be recorded from any region of the heart slice for up to 30 hours. The AP size and form was dependent on the heart subregion and animal used. Ventricular AP from rats were much shorter as those from guinea pigs. Pharmacological effects of standard drugs were observed corresponding to the ion current components affected. Application of the  $I_{Kr}$  specific blocker E4031 revealed AP prolongation in accordance with previous results.

Multielectrode experiments demonstrated AP conduction velocities in transverse and sagittal direction in the range of 0.1-0.4 m/s. In order to calculate the spatio-temporal distribution of single AP peaks, time slices were determined and plotted in grey scale in a 8x8 grid. Results from this analysis showed a clear non-isotropic spatial distribution indicating a re-entry path of the signal conduction.

Our results show that standardized acute heart slices with normal physiology and pharmacology can be prepared from adult rat and guinea pig heart and maintained for up to 30 hours. Therefore, the native heart slice will be a valuable new tool in heart research including AP propagation studies for evaluations of heart arrhythmia and risk assessment of QT prolongation.

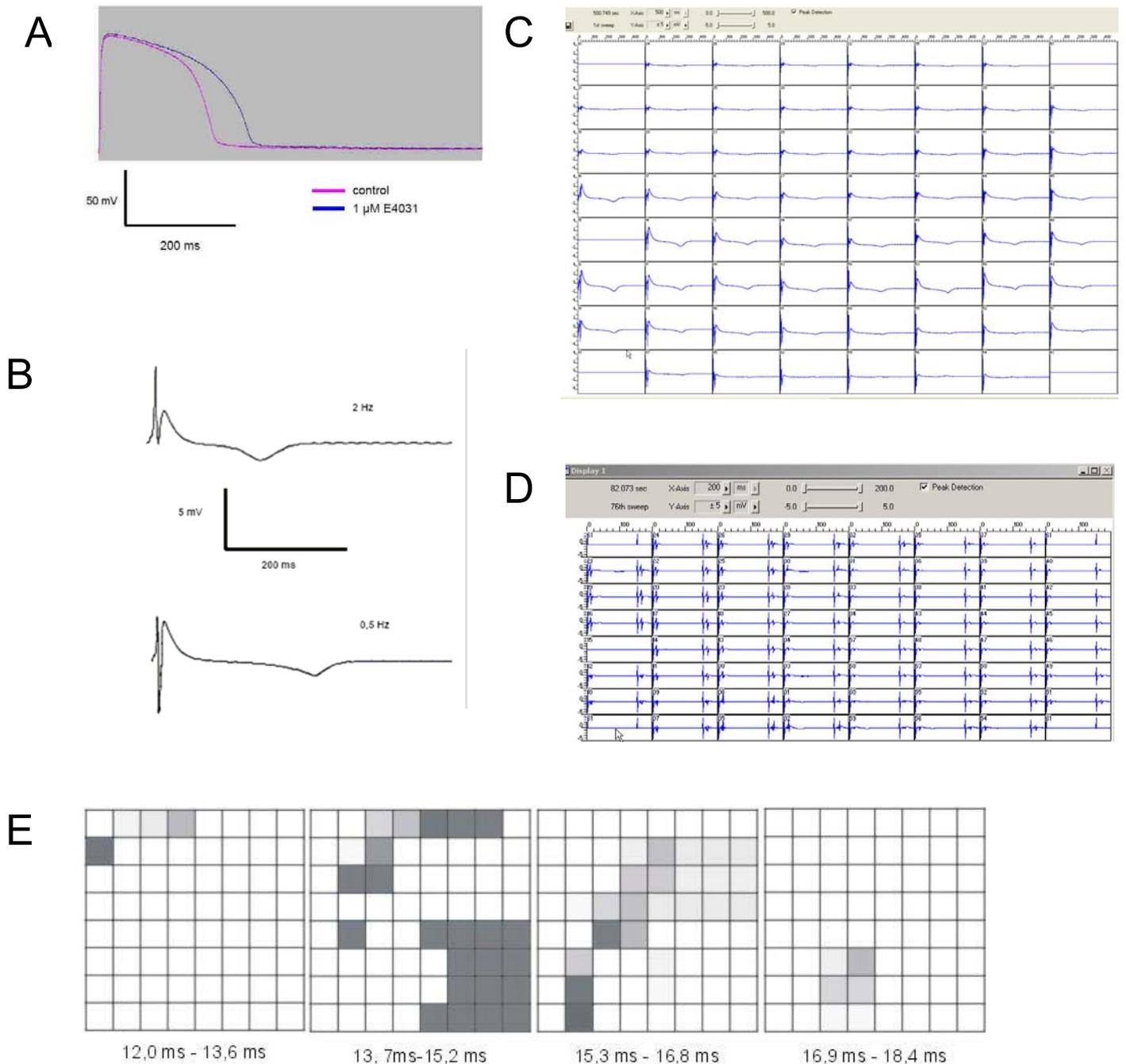


Fig. 1:

- A. Intracellular AP's from guinea pig ventricular cells; violet line: control; blue line: after 1  $\mu\text{M}$  E4031.
- B. Extracellular AP's of guinea pig ventricular tissue slices after electrical stimulation at 2 Hz (upper trace) and 0,5 Hz (lower trace) demonstrating the strong frequency dependence of AP duration.
- C. MEA recording of extracellular potentials from guinea pig ventricular heart slice after electrical stimulation (planar electrodes 200  $\mu\text{m}$  electrode distance),
- D. MEA recording of extracellular potentials from rat ventricular heart slices after electrical double pulse stimulation (planar electrodes 200  $\mu\text{m}$  electrode distance).
- E. Spatio-temporal distribution of neg. AP deflection in guinea pig heart slice (MEA recording) after electrical stimulation; grey scale display: bright: early responses, dark: late responses; propagation of activity grouped into 4 time slices; note the non isotropic distribution of activity and its non-linear propagation throughout the heart tissue.