Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Velocity-Selective Recording from Frog Nerve Using a Multi-Contact Cuff Electrode

Martin Schuettler, *Member, IEEE* , Vipin Seetohul, *Member, IEEE* , John Taylor, *Member, IEEE* and Nick Donaldson

***Abstract*—Obtaining neural information from nerve cuff recordings for use as feedback signals for neural prostheses is slowly becoming state-of-the-art. Traditional tripolar cuff recordings cannot provide information on the fiber type contributing to the compound electro neurogram. In order to get this data we employed a novel nerve cuff carrying eleven electrode contacts equally distributed along its axis. Connecting this cuff to a custom made low-noise ten-channel amplifier, a data acquisition system and applying some basic data processing routines, we were able to generate profiles that show, for the first time, the different propagation velocities that contribute to the whole nerve signal.**

I. Introduction

SINCE Erlanger and Gasser published their work on the relationship of fiber diameter and action potential propagation velocity it is known that neural signals travel at different velocity, depending on the type of information they are transmitting [1].

Investigating velocities and the direction of propagated action potentials within a peripheral nerve gives an overview of the fiber type (fiber diameter, afferent or efferent fiber) that conducts the action potentials. This information allows purpose or meaning of the neural communication to be determined, e.g. intention to activate strong muscle units, signals that indicate the relative change of the orientation of a joint, pain signals from skin, or temperature.

In previous publications, the theoretical feasibility of a method to investigate propagation velocity profiles using a multi-contact cuff was discussed [2]. It is based on an interlinked arrangement of tripolar (or: double-differential) amplifiers that obtain nine signals from eleven contacts of a nerve cuff electrode. Depending on the propagation speed, an action potential is picked up by neighbouring electrode contacts with a velocity (and contact pitch) specific delay *dt*. Delaying the signal from the first contact relative to the second contact and adding these two together results in an action potential of twice the amplitude, when the time delay matches *dt*: the signals of the two contacts add constructively. Time delays longer or shorter than *dt* cause summation of the signals that is not constructive. Instead of using only two signals coming from two contacts as described above, we used nine signals originating from eleven contacts (Fig.1). This means, a constructive summation of matched time delays increases the signal amplitude by a factor of nine compared to the output of a single tripolar amplifier. Rieger et al. showed that this method can be used to determine the propagation velocity of a single population of fast fibers in a frog peripheral nerve [3]. In contrast to that, the work presented here focuses on detecting the activity of more than one fiber population. Furthermore we carried out hook electrode recordings in the manner of Erlanger and Gasser [1] in order to validate our results.

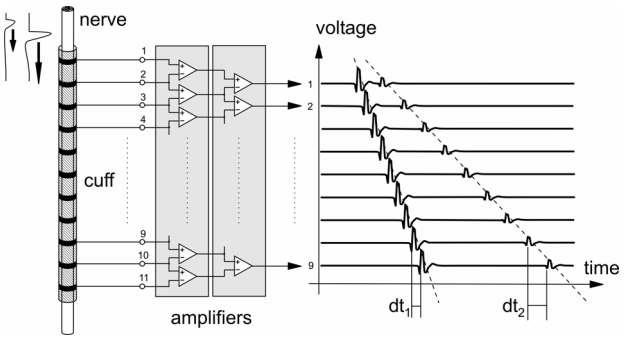

Fig. 1. Two action potentials with different velocities and their electro neurogram as recorded by an eleven contact cuff connected to a bank of tripolar amplifiers.

II. Materials and Methods

A. Nerve Preparation

Four sciatic nerves were obtained from two decapitated adult *Xenopus Laevis* frogs. The nerves were handled by sutures that were tied to the nerve endings. After explanting, the nerves were transferred to the basin of our setup and immersed in amphibian Ringer's solution at room temperature. The nerves had a total length of typically 8 to 9 cm and varied in diameter from 0.5 mm distally to 2 mm close to the spinal cord. The data shown in this publication are representative results from an experiment with one of the four nerves. The other nerves gave comparable data.

Manuscript received March 30, 2006. This work was supported in part by the German Academic Exchange Service (DAAD).

M. Schuettler is with the Laboratory for Biomedical Microtechnology, Institute of Microsystems Engineering, University of Freiburg, Germany (tel: +49 761 203 -7433; fax: -7472; e-mail: schuettler@imtek.de).

V. Seetohul and J. Taylor are with the Department of Electronic and Electrical Engineering, University of Bath, United Kingdom (e-mail: v.r.k.seetohul@bath.ac.uk, j.t.taylor@bath.ac.uk).

N. Donaldson is with the Implanted Devices Group, Department for Medical Physics & Bioengineering, University College London, United Kingdom (e-mail: nickd@medphys.ucl.ac.uk).

B. Neural Electrodes

Polyimide thin-film technology was employed for producing the multiple contact cuff electrodes. These electrodes consist of a 300 nm film of sputtered platinum sandwiched between two 5 µm layers of spin-coated polyimide (Pyralin 2611, HD-Microsystems, Bad Homburg, Germany). The area of the contact pads and recording sites was opened by dry-etching the top polyimide sheet using an oxygen plasma. A detailed description of the manufacturing process can be found in [4]. The planar polyimide substrate was transferred to the three-dimensional cuff shape by keeping it curled in a metal tube while annealing the mechanical stress by heat treatment (2 h at 300 °C). The now self-curling cuffs were connected to screen printed alumina ceramic adapters by a gold-bond technique which rivets the thin-film contacts through a hole to the screen printed gold tracks of the ceramic substrate [4]. Enameled copper wires were then soldered to the screen printed tracks. All contacts and tracks of this adapter were insulated with medical grade silicone adhesive. The final electrode is 1.5 mm in diameter, 40 mm long and carries eleven 0.5 mm wide, ring-shaped platinum contacts that are equally distributed along the cuff at a pitch of 3.5 mm (Fig. 2). The stimulation electrodes were fabricated in the same way as the recording electrodes. They have a diameter of 1.0 mm and carry three ring-shaped platinum contacts (0.2 mm wide) at a longitudinal pitch of 5.0 mm [5].

A bipolar hook electrode was manufactured from 0.127 mm diameter platinum wire. It was used to record the electro neurogram the same way as Erlanger and Gasser described it and allowed validation of the propagation velocity profiles based on the multi-contact cuff recordings.

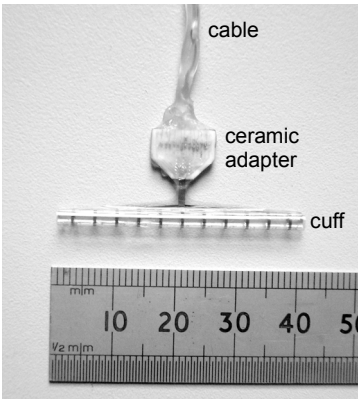

Fig. 2. The eleven-contact polyimide thin-film cuff electrode.

C. Neural Recording and Data Acquisition

The contacts of the recording cuff were connected directly to the inputs of a custom-built low-noise neural amplifier bank, a developed version of an ASIC described in [6]. This amplifier bank provides ten channels of differential amplifiers with a pass band of 310 Hz to 3.3 kHz, a voltage gain of 10,100, and an input-referred voltage noise density of 3.8 nV/√Hz at 1 kHz. The hook electrode was connected to an instrumentation amplifier with a gain of 500 and a band pass of 17 Hz to 8.8 kHz. The outputs of the amplifiers were fed into a data acquisition system, based on a NI DAQ Card-6062E (National Instruments, Austin, TX, USA), that allowed sampling at 40 kHz and a dynamic range of 12 bit for the ten nerve signals, the stimulation signal, and the hook electrode signal. The setup was controlled by a laptop computer via a LabView 7.1 user interface (National Instr.). Fig. 3. gives a schematic overview of the setup.

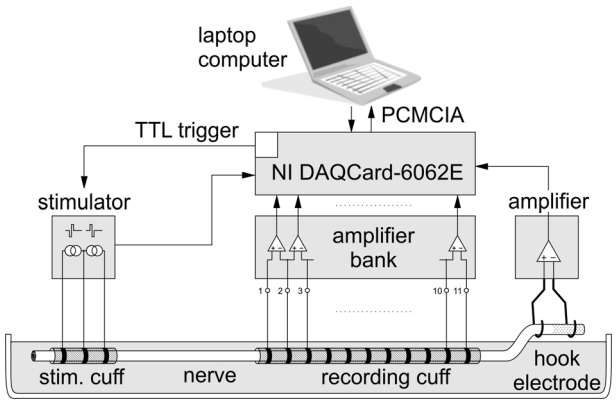

Fig. 3. Setup for recording electrically evoked compound action potentials from frog nerve in Ringer's solution using an eleven contact recording cuff and a hook electrode (for validation purposes).

D. Neural Stimulation

The stimulation was triggered by the LabView program via the NI DAQ Card. A custom made nerve stimulator was used that generates current controlled, charge balanced, rectangular shaped pulses on two latched channels. The stimulating pulse was adjustable in amplitude and pulse width, while the amplitude of the charge recovery phase was set to 20 µA, which was found to be below excitation threshold. The stimulation amplitude and pulse width were gradually increased, until a single population of large fibers was excited, resulting in a simple-shaped biphasic compound action potential recording picked up the hook electrode. Further increase of amplitude and pulse width resulted in a hook electrode neurogram, which suggested the presence of at least one additional fiber population, slower in propagation than the first one.

E. Data Processing

Data processing was carried out offline using Matlab R12 (The Mathworks Inc., Natick, MA, USA). The Matlab routine calculated nine tripolar signals from the ten outputs of the bipolar amplifiers. Then, the signal of tripole number two was delayed in time by *dt* relative to the signal of tripole number one and added to it. The signal from tripole number three was added to this sum after delaying it by 2x *dt*. Signal number four was delayed by 3x *dt* and added, and so on.

After summation, the signal was full-wave rectified and its maximum voltage peak was detected. A delay profile was generated by plotting the maximum voltage peak as a function of the delay time *dt*.

III. Results

A. Hook Electrode Recordings

Stimulating at low intensity (rectangular pulse shape: 1.3 mA x 100 µs = 0.13 µC) caused the hook electrode to detect a compound action potential (CAP) that has a pronounced positive phase followed by a much weaker negative phase. Employing larger charges (1.5 mA x 675 µs = 1.01 µC) for stimulation changed the shape of the recorded trace. The pronounced positive phase now peaked later in time and during its decay, another positive phase appeared (Fig. 4). This behavior was expected and known in electrophysiology as "inverse recruitment": the stimulation threshold of the fast and large diameter fibers is lower than that of the slow and small ones.

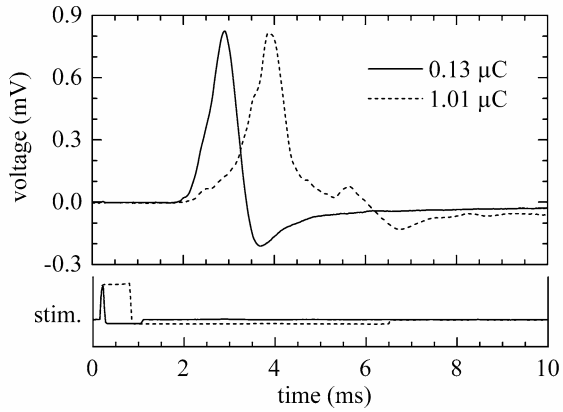

Fig. 4. Hook electrode recordings (top) and the stimuli that evoked them (bottom). Solid line: only one fast fiber population was excited. Dotted line: Two positive peaks indicate the activity of two populations.

The distance between the anodal contact of the hook electrode and the cathode of the stimulation cuff was 68 mm. The onset of stimulation took place at 0.15 ms (according to Fig. 4), the stimulus duration was set to 0.1 ms, which was just above stimulation thresholds of the large fibers. The positive slope of the CAP started at 2.075 ms, which gives a latency of 2.075 ms – (0.15 ms + 0.1 ms) = 1.825 ms. Therefore, the propagation velocity of this CAP was 68 mm / 1.825 ms = 37.3 m/s.

A larger stimulation pulse width was chosen in order to introduce enough charge for additionally exciting smaller fibers. The onset of the stimulus was at 0.15 ms, the pulse width was now 0.675 ms, and the CAP of the first positive phase of the hook electrode recordings begins at 2.125 ms. Assuming that this first phase was excited by the same charge as in the case described earlier, the calculated velocity is 68 mm / (2.125 ms – 0.15 ms – 0.1 ms) = 36.3 m/s. The onset of the second phase of the recordings was at 5.325 ms. It took all the charge provided by the pulse to excite this fiber population. Therefore the latency is 5.325 ms - (0.15 ms + 0.675 ms) = 4.5 ms. The propagation velocity calculates to 68 mm / 4.5 ms = 15.1 m/s.

B. Cuff Electrode Recordings

The nerve cuff recordings are smaller in amplitude than the hook electrode signals; interference and noise are more pronounced. Fig. 5 and Fig. 6 show the amplified bipolar signals after converting them to tripolar signals using Matlab. The y-axis shows the position of the tripole along the cuff. The further distant the tripole, the longer the time the signal needs to appear. Fig. 6 shows the effect of higher level of stimulation intensity than in Fig. 5. In this case the dispersion of two different CAPs can be seen.

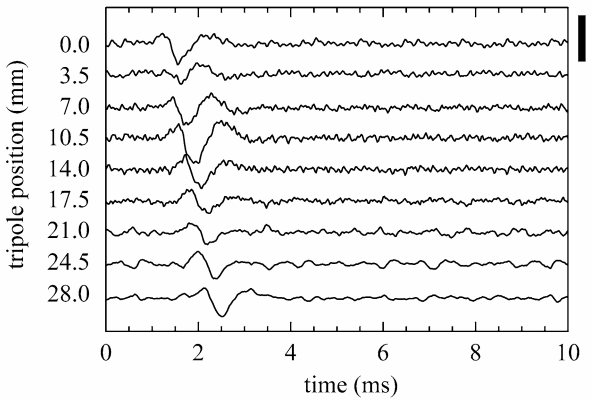

Fig. 5. Tripolar recordings of electrically evoked potentials, recorded with the eleven-contact cuff. The stimulation intensity was 0.13 µC. The black bar to the right shows the amplitude scale: 50 µV.

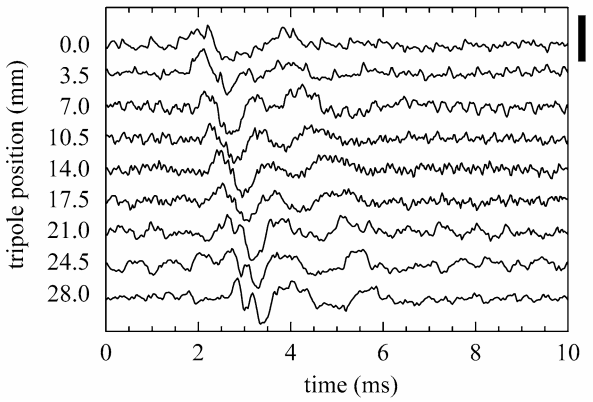

Fig. 6. Tripolar recordings of electrically evoked potentials, recorded with the eleven-contact cuff. The stimulation intensity was 1.01 µC. The black bar to the right shows the amplitude scale: 50 µV.

Processing the cuff data as described earlier results in a time delay – peak amplitude profile for each of the two stimulation intensities as shown in Fig. 7. At low stimulation intensities a single distinct peak can be found at a delay of *dt* = +125 µs. The contact pitch of the cuff electrode is 3.5 mm, therefore the propagation velocity of this fiber

population is 3.5 mm / +125 µs = +28 m/s. The plus sign indicates the direction the recorded nerve signals (away from the stimulation electrode towards the recording cuff). At high stimulation charges, we find two peaks, one at +100 µs that corresponds to a velocity of +35 m/s and smaller one at +250 µs, which relates to a speed of +14 m/s.

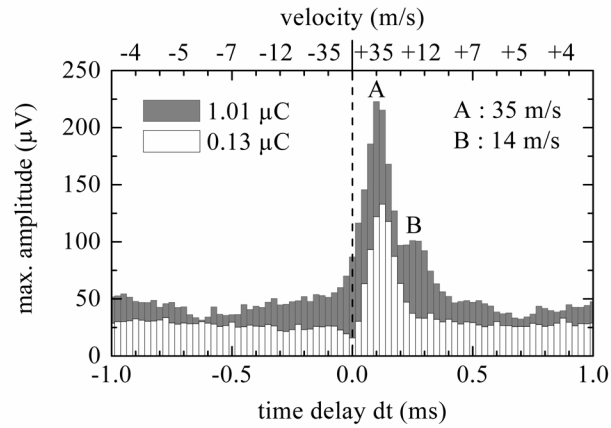

Fig. 7. Two delay profiles corresponding to two different stimulation intensities: gray: 1.01 µC, white: 0.13 µC. The bars have a width of 25 µs which is the reciprocal value of the sampling frequency.

IV. Discussion

Comparing the propagation velocities obtained with the two different methods (cuff and hook), it is clear that the results of both are in the range described in the literature for frog nerve at room temperature: normally up to about 42 m/s [1]. However, the actual values differ, depending on the applied method as shown in Table I.

TABLE I
PREDOMINANT PROPAGATION VELOCITIES OBSERVED WITH TWO DIFFERENT METHODS USING A HOOK AND A CUFF ELECTRODE

Stimulus Charge	Hook Electrode	Cuff Electrode
Q_{stim} = 0.13 µC	v_1 = 37.3 m/s	v_1 = 28.0 m/s
Q_{stim} = 1.01 µC	v_1 = 36.3 m/s	v_1 = 35.0 m/s
	v_2 = 15.1 m/s	v_2 = 14.0 m/s

Possible errors are inherent to both methods. For the hook method the exact determination of timing and distance is crucial, but fine measurement of the distance between the hook and the stimulation cathode is difficult and also relating the onset time of a positive slope to the time during a long stimulation pulse when the stimulation threshold reached is a matter of guessing. The main problem of the cuff method is the minimum delay time *dt*, which is the reciprocal value of the sample frequency. Setting the sampling frequency to 40 kHz leads to a coarse resolution of the velocity profile at higher speeds, as shown in Table II. Clearly, the use of a NI DAQ Card with a higher sampling rate would remove this difficulty.

TABLE II
TIME DELAY *dt* IS RESTRICTED TO MULTIPLES OF THE SAMPLE INTERVAL; THE VELOCITY *v* PROFILE HAS A LOW RESOLUTION AT HIGH SPEEDS.

dt (µs)	25	50	75	100	125	150	175
v (m/s)	140	70	47	35	28	23	20
dt (µs)	200	225	250	275	300	325	350
v (m/s)	18	15	14	13	12	11	10

V. Conclusion

Using explanted nerves we were able to demonstrate that the method of multi-contact cuff recording is easily applicable to *in vitro* setups and provides information in shape of a profile about the conduction velocity of the active fibers as well as their direction of propagation. In contrast to this, calculating propagation velocities from a hook electrode recording is not only difficult (you have to guess the exact moment of fiber excitation during long pulses) but also cannot be transferred to neural prosthetic applications. In those, nerve traffic is macroscopically chaotic and bi-directional. Multi-contact cuff recordings are very easy to interpret and we are optimistic that this method works as well *in vivo*, where bi-directional, chaotic neural traffic is present. However, this has to be investigated in future experiments.

Acknowledgment

This work was supported in part by the German Academic Exchange Service (DAAD) and by the Engineering and Physical Sciences Research Council (EPSRC) UK.

References

[1] J. Erlanger and H. S. Gasser, "The Comparative Physiological Characteristica of Nerve Fibres," in *Electrical Signs of Nervous Activity*. The Eldridge Reeves Johnson Foundation for Medical Physics, Philadelphia: University of Pennsylvania Press, pp. 34-78, 1937.

[2] J. Taylor, N. d. N. Donaldson, and J. Winter, "Multiple-Electrode Nerve Cuffs for Low-Velocity and Velocity-Selective Neural Recording," *Medical and Biological Engineering and Computing*, vol. 42, pp. 634-643, 2004.

[3] R. Rieger, J. Taylor, E. Comi, N. d. N. Donaldson, M. Russold, C. M. O. Mahony, J. A. McLaughlin, E. T. McAdams, A. Demosthenous, and J. C. Jarvis, "Experimental Determination of Compound Action Potential Direction and Propagation Velocity from Multi-Electrode Nerve Cuffs," *Medical Engineering & Physics*, vol. 26, no. 6, pp. 531-534, 2004.

[4] T. Stieglitz, H. Beutel, M. Schuettler, and J. U. Meyer, "Micromachined Polyimide-Based Devices for Flexible Neural Interfaces," *Biomedical Microdevices*, vol. 2, no. 4, pp. 283-294, 2000.

[5] F. J. Rodriguez, D. Ceballos, M. Schuettler, A. Valero, E. Valderrama, T. Stieglitz, and X. Navarro, "Polyimide Cuff Electrodes for Peripheral Nerve Stimulation," *J. Neurosci. Methods*, vol. 98, pp. 105-118, 2000.

[6] R. Rieger, J. Taylor, A. Demosthenous, N. Donaldson, and P. J. Langlois, "Design of a Low-Noise Preamplifier for Nerve Cuff Electrode Recording," *IEEE Journal of Solid-State Circuits*, vol. 38, no. 8, pp. 1373-1379, 2003.