On-line 32 channel signal processing and integrated database improve navigation during cranial stereotactic surgeries

K.M.L. Menne[1]*, C.K.E. Moll[2], S. Kondra[1], M. Bär[3], P. Detemple[3], A.K. Engel[2], U.G. Hofmann[1]

[1]*Institute for Signalprocessing, University of Lübeck, Lübeck, Germany*
[2]*Institute for Neurophysiology, University-Hospital Hamburg-Eppendorf, Hamburg, Germany*
[3]*Institut für Mikrotechnik, Mainz, Germany*

Abstract. Target point accuracy is a main issue in functional stereotactic procedures for the implantation of deep brain stimulators. Next to standard stereotactic methods, intraoperative microelectrode recordings help to reach the target point. While currently up to 5 electrodes are used, we introduce a new 32-channel system. Our probes allow for recording 32 neural signals alongside up to 1 cm of the planned trajectory simultaneously. The signal evaluation is supported by customized analysis and visualization tools contained in our navEgate DAQ software. The acquisition software has access to the navEbase database that holds characteristic signal features with respect to their anatomic origin. Currently recorded signals can be compared against nominal values from the database. While preclinical studies of our system are on the way, we are convinced that the possibility to record neural depth profiles will fasten intrapoerative microelectrode recordings, and that the feedback from navEbase will assist teams in questionable cases.

Keywords: surgical navigation, microelectrode recording, on-line signal processing, database, histogram flatness measure

1. Introduction

We present preliminary results achieved in the framework of the German BMBF-funded navEgate project. The ultimate goal of this project is to give revolutionary new inputs to the field of computer-aided navigation in functional neurosurgery. Our medical application area is the implantation of deep brain stimulators for the treatment of patients suffering from Parkinson's disease. Deep brain stimulation (DBS) is currently the method of choice to treat patients that were formerly medicated with L-Dopa but do not respond to L-Dopa anymore or suffer from severe adverse effects, respectively [1]. The deep brain stimulator is preferably implanted into one of the target regions subthalamic nucleus (STN) or internal pallidum (GPi). Since the size of both deep brain structures does not exceed a few hundred mm^3, target point accuracy is a crucial issue for DBS [2]. Currently high accuracy is sought to be reached by preoperative trajectory planning on the basis of patients' CT and MRI images, framebased stereotaxy, and intraoperative

* Corresponding author. *E-mail address*: menne|hofmann@isip.uni-luebeck.de.

stimulations. This approach would suffice to reach the target point, if there were no errors intrinsic to stereotactic procedures, if there was no brain-shift, if there were no interindividual morphometric differences in the deep brain anatomy, and if the target regions could be better seen on the standard image material [3]. Since these requirement are in no way fulfilled, microelectrode recordings seem to be mandatory during the surgery [3]. Currently up to 5 electrodes are used. Microrecordings help to identify different brain regions since each elicits characteristic activity pattern. We describe in the following how intraoperative mircrorecordings can be much more exploited. In Section 3 we introduce a novel 32-channel probe together with the needed acquisition hardware that allows to record at 50 kHz. The 32-channel data acquisition software "navEgate DAQ" will be described in Section 3 as well. This software calculates different signal features online in order to fasten and simplify the process of assigning recorded signals to different brain regions. Resulting features are stored with respect to an anatomical reference coordinate system into our "navEbase" database that communicates with "navEgate DAQ", and constitutes an ever-growing knowledge base that gives additional support in future surgeries and shall assist especially less experienced teams. As of this writing, pre-clinical and clinical studies of the complete system are on the way. Shown data analysis results are gained from data recorded as described in the next section.

2. Materials and methods

2.1 Data Acquisition

.Signals analyzed and presented in this study originate from recordings performed during stereotactic implantations of electrodes for deep brain stimulation in the subthalamic nucleus of patients suffering from Parkinson´s disease at the University-Hospital Hamburg-Eppendorf.

Ongoing neural activity was recorded using a 4 channel microelectrode-recording unit (Leadpoint ; Medtronic Inc., Minneapolis, MN, USA) with conventional tungsten single-electrodes (microtargeting electrode 291A; FHC, Bowdoinham, ME, USA; impedance 0.5-1.5 M). Signals were amplified, bandpass-filtered (500-5000Hz) and digitized (sampling rate: 24 kHz). Artifact-free and stable activity was stored for offline-analysis. All patients gave free and informed consent. For ethical reasons, the duration of the recording sessions was made as short as possible. Typical recording sequences lasted between 30 and 300 seconds.

2.2 Data Analysis

Before integrating any new algorithms into thenavEgate DAQ software, we test their suitability with the help of MATLAB (The Mathworks, Inc.). The results presented in the following section were generated with MATLAB. We analyzed data gained in two different surgeries. Signals have a duration of 30 seconds. In the following we limit the presented results to spikerate calculation and inter-spike interval (ISI) histograms. Spikerates were calculated within a sliding window of 1 second duration. The mean spikerate was calculated for each signal from analysis windows, shifted by 0.25 seconds, thus overlapping by 75%. Spike detection was performed by means of threshold detection, where the threshold was chosen to be 2.5 times the root mean square value of

data contained in the analysis window. The ISI histograms were calculated as a sum of occurrences from non-overlapping windows.

We introduce a new measure that we call histogram flatness measure (hfm) according to the spectral flatness measure (sfm) that is used for power spectral densities. hfm and sfm, respectively, are defined as geometric mean/ arithmetic mean [4].

3. Results

3.1 New Type of Probes

The Institut für Mikrotechnik Mainz (IMM) fabricated a novel type of probe within the framework of the navEgate project [5]. The most outstanding feature of these probes is, that they allow for recording from 32 electrodes simultaneously on one trajectory track. One electrode is located at the tip of the probe, the remaining 31 electrodes are distributed either linearly or helically on the shaft, see Fig. 1 for prototypes. Helical design probes and linear design probe differ in the way how they are manufactured. Table 1 lists some technological specifications of the probes.

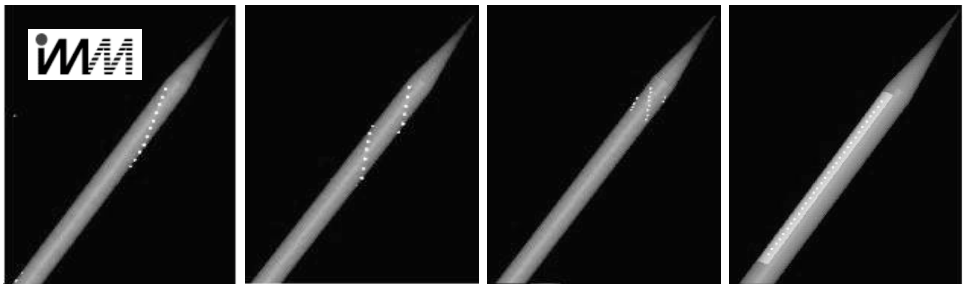


Fig. 1 Prototypes of IMM-probes. One recordingsite is at the tip each case, the remaining 31 recordingsites are arranged on the shaft in a single helix (A), a double helix (B), a quad helix (C), or linearly (D).

Table 1
Technical specifications of IMM-probes. "Pitch" denotes the center-to-center electrode distance of the 31 probes on the shaft.

	Simple Helix	Linear
Length	340 mm	340 mm
Diameter	530 μm	650 μm
Tip Angle	15°	15°
Electrode Diameter	20 μm	42 μm
Pitch	typically 100 μm	typically 100 μm
Array Length	about 3 mm	about 3 mm

Especially the manufacturing process for the helical design probes allows for producing different array lengths. The array length denotes the distance between the first electrode on the shaft, which is next to the tip and the last of the 31 electrodes on the shaft. Thus it is a measure on how long a stretch of brain tissue neuronal activity can be recorded from. Table 1 lists a rather small array length, depending on the center-to-center electrode distance, but an array length of more than 1 cm is also achieved. The impedance of the electrodes is on average 0.66M at 1 kHz. Probes are introduced into the brain with the help of a guide tube, which enlarges the diameter by 150 μm.

3.2 32-channel Acquisition Hardware

The signals are amplified by 32 channel preamplifier and main amplifier that were built according to medical security standards by Thomas Recording GmbH, Gießen. The amplification factors for the main amplifier can be set via the control panel of the main amplifier itself or through the data acquisition software.

Thomas Recording also fabricates a computerized microdrive that controls the feed of the probe for 2 cm around the planned target point. Adjustments of the stereotactic frame and tracking of the penetration depth of the probe allow to calculate the actual position of the probe tip at each time.

We employ an off-the-shelf DSP board from Innovative Integration featuring Texas Instruments digital signal processor (C6701) to communicate the signals to a PC (Windows 2000) where the acquisition software is running. Digitization is performed by A/D modules that are mounted on the digital signal processor board. The sampling frequency is 50 kHz for all channels, and the data resolution equals 16 bit.

3.3 navEgate DAQ & navEbase

Our data acquisition software navEgate DAQ stores, visualizes and analyzes the data. navEgate DAQ is based on software that was originally developed within the framework of the EU project VSAMUEL, the purpose of which was to provide a 128-channel data acquisition system for animal experiment applications. navEgate DAQ is developed according to European Medical Standards EN 60601-1-4. The acquisition software has access to our database called navEbase. Recording set-ups, patient information, and characteristic signal features are stored in navEbase. Signal features are stored together with the 3D coordinates of the position at which they were gained. We employ the freely available MySQL 4.0.17 database management system.

There are three different operator modi, among which the user can choose. In the online-mode during a surgery, 32-channal data is stored to hard-disk in binary format. Online analysis tools provide for signal features that are conveniently visually presented next to the raw signals. In addition, the signal features get stored into navEbase. Vice versa it is also possible to recall information from navEbase. A typical query is to get some characteristic signal features that were recorded at a position from which is currently recorded as well. Thus nominal value and actual value can be compared.

In offline-mode, data stored in previous procedures can be reinvestigated by means of the same analysis and visualization tools that are available in online-mode. It is also possible to store data into or retrieve data from navEbase.

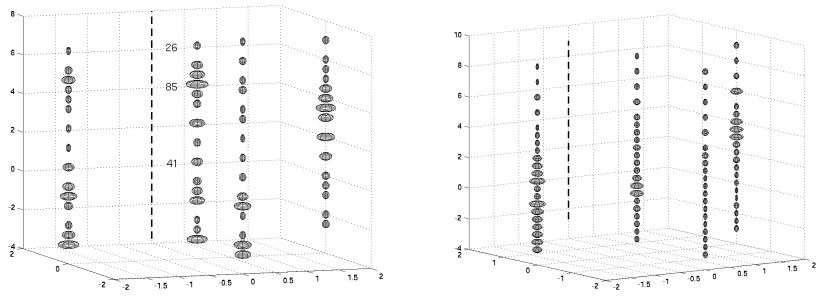
The third mode allows for performing database queries independent of any selected dataset.

Data analysis tools include spikerate estimation, inter-spike interval histogram calculation, Fast Fourier Transformation and Wavelet Analysis, with their respective feature extraction schemes.

3.4 Data Analysis

For up to 5 channels, it is feasible, that neurophysiologists look at the raw signals presented in kind of oscilloscope presentation or listen to them. The observation of 32 raw signals is rather demanding. Therefore we are currently investigating signal features that characterize signals originating from different brain regions uniquely. The easiest

feature might be the spikerate [6]. Figures 2A and 2B qualitatively illustrate the mean spikerates as calculated for the two analyzed datasets. The bigger the ellipsoid, the more spikes were detected in the signal at the respective penetration depth.



A **B**

Fig. 2 Spikerates of two different datasets. Anterior, central, lateral, and posterior trajectory are presented from left to right. Anterior, posterior, and lateral trajectories have a distance of 2mm from the central one. The dashed lines indicate where a medial trajectory would be situated. Numbers indicate exemplary spikerates.

Work done by others [6] shows, that spikerates do not characterize distinct brain regions uniquely. The next possible feature might be the distribution of interspike interval frequencies. Fig.3 presents the ISI histograms for the left-most trajectory in Fig. 2A. By looking at the raw signals, we contributed the activity from –1000µm of the target point to +500µm after the planned target point to the STN, whereas we characterize the activity at +2500 and +3000µm after the target point as originating from substantia nigra (SNR). Fig. 2 and 3 indicate high activity in both regions, but the falling slope of the ISI histogram is steeper for SNR activity. In order to grasp this observation quantitatively, we used the histogram flatness measure. The hfm is close to 0dB for random signals, about –0.97dB for STN-activity and about –1.55dB for SNR activity. These results were affirmed by all other investigated trajectories but one.

4. Discussion

Neurological practitioners as well as patients will benefit from the improved electrophysiological navigation possibilities. 32 electrodes on one shaft mean for the patient that ideally only one penetration is necessary resulting in minimal damage of brain tissue. With only one trajectory there are of course two spatial dimensions missing. This is however compensated by the fact that a neural signal depth profile is available, revealing at one glance the length of stretches where similar activity pattern are found [7].

Not only the tissue damage is reduced, but also the required time forintrapoerative recordings, and thus the discomfort of the patient and the working hours of personell involved with the surgery. The speed-up arises from the possibility to record at different depth simultaneously. That makes it possible to bring the probe closer to the target point before starting to record.

Off-line analysis and the seamless integration of knowledge from the navEbase database will clearly support medical research.

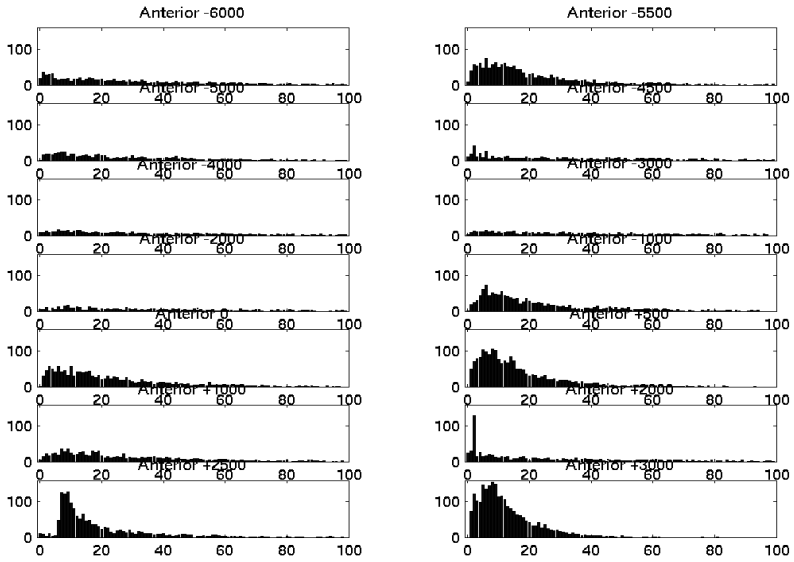


Fig. 3 ISI histograms for anterior trajectory of Fig. 2A. Anterior –6000 denotes the recording position 6000 µm of the planned target point.

The navEbase database will also be a most useful component for less experienced neurological practitioners. The possibility to compare currently recorded data against descriptive features from the database gives valuable feedback in the target localization process.

More work has to be done concerning the analysis tools. We are currently working on descriptive signal features that are gained by Fast Fourier Transformation and by Wavelet analysis. Our hypotheses have to be tested for more signals, which not only arise from STN trajectories.

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