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Decoding stimulation intensity from evoked ECoG activity using support vector regression

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Abstract. One of the unsolved problems of the application of cortical stimulation for therapeutic means is the selection of optimal stimulation parameters. Using support vector regression, we demonstrate that the intensity of single pulse electrical stimulation can be decoded from the waveform of the evoked electrocorticographic (ECoG) activity, even if intensities used for training and testing of the regression model are disjoint. This was most effective when stimulation was applied directly over the motor cortex, less so for premotor and sensory cortex. Thus, if the optimal shape of the evoked neural response to stimulation is known, a regression model trained on the responses to a small set of stimulation intensities could be sufficient to determine the optimal stimulation intensity.

1 Introduction

Cortical stimulation is a means of treating for example epilepsy, central pain [1] or movement disorders [2]. While these treatments seem to be beneficial for many patients, the exact mechanisms why they work are not fully understood. In particular, the question of how to select optimal stimulation parameters is unanswered [3]. One approach for optimization could be to use the stimulation-evoked neural response as a target by first determining the shape of the response most beneficial for the treatment of the patient. Secondly, one would need to find stimulation parameters best suited to evoke this target waveform.
We investigated in this work the second part of this parameter-selection problem. We conducted experiments with 2 chronic stroke patients with implanted epidural electrocorticography (ECoG) electrodes who participated in a study on the use of brain-computer interfaces and cortical stimulation for stroke rehabilitation [4]. Using support vector regression (SVR), models were trained to decode the stimulation intensity from the evoked neural responses for a small set of intensities. The models were validated by applying them to the waveforms evoked from intensities not used during training, thus treating them as possible target waveforms.

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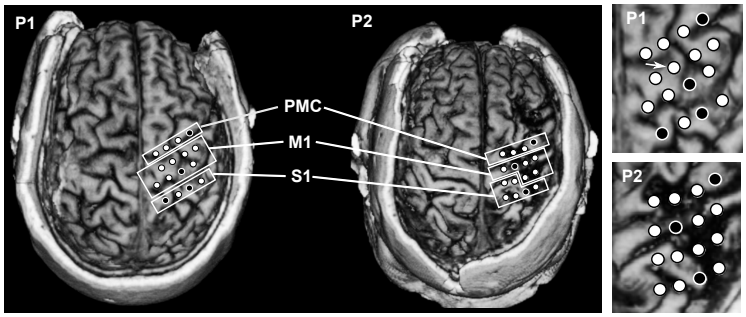

Fig. 1: ECoG electrode positions for P1 and P2. Electrodes are roughly grouped by cortical areas: somatosensory cortex (S1), primary motor cortex (M1) and premotor cortex (PMC). The location of electrodes used at least in one session for stimulation are marked as black circles, electrodes used only for recording as white circles. Right: Zoom on the electrode positions. Arrow: position of channel 10 shown in figure 2.

2 Methods

2.1 Patients

Two chronic stroke patients (both male, ages 52 (P1) and 56 (P2), 80 and 159 months after a stroke in the right hemisphere) participated in this study. None of the patients was able to produce voluntary movements of the left hand. The patients were implanted with 16 epidural electrodes with a diameter of 4 mm. These electrodes were arranged in a 4x4 grid (see figure 1), centered on the hand area of the right motor cortex as identified by pre-surgical evaluation of TMS mappings and intraoperative cortical stimulation and covered parts of premotor and sensory areas as well. All procedures were approved by the local ethics committee of the faculty of medicine of the university hospital in Tübingen.

2.2 Experimental setup

The patients were lying in bed throughout the experiment with open eyes. We conducted 2 sessions with patient P1 and 3 with P2. In each session, 3 electrodes were used for the delivery of single pulse stimulation, one located on the somatosensory, one on the primary motor and one on the premotor cortex. All other electrodes were used to record the evoked neural responses.

2.2.1 ECoG recording

We recorded the ECoG signals with a monopolar amplifier (BrainAmp MR plus, BrainProducts, Munich, Germany) with a sampling rate of 5000 Hz and a built-in low-pass filter at 1000 Hz. No high-pass filter was used to ensure that hardware filters do not interfere with the shape of the stimulation artefact and the evoked

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neural potentials. The signal was monitored and the built-in DC-correction of the amplifier was used if the recorded signal threatened to exceed the operating range of the amplifier (± 3.27 mV). The ECoG data was referenced to the electrode at the fronto-medial corner of the grid.

2.2.2 Electrical stimulation

For epidural stimulation we used monopolar biphasic symmetric pulses with a length of 500 μs that were applied to one electrode on the grid with a STG4008 stimulus generator (MultiChannel Systems, Reutlingen, Germany) with a 50x90 mm adhesive electrode placed under the left clavicle of the patient acting as the antipole. This electrode also served as the ground electrode for recording. Stimulation intensities were varied in steps of 1 mA between 1 and 8 mA for P1 and the first session of P2 and between 5 and 12 mA for the second and third session of P2. The highest intensities per patient were sufficient to evoke small muscle twitches in the paralyzed left hand of P1 and sometimes P2 when stimulating over M1. We applied anodal pulses in the first sessions of both patients and the third session of P2 and cathodal pulses in the second sessions. Per session, 100 pulses were given for each intensity in randomized order, in total 800 pulses. The inter-stimulus interval was set to 1 second.

2.3 Feature extraction

Channels with excessively long (> 20 ms) and pronounced stimulation artifacts were removed from further analysis. A bandpass filter (cutoff: 5 and 500 Hz) and a notch filter at 50 Hz were applied anti-causally to the data to avoid contamination of the evoked response with the stimulation artifact. The time window between 5 and 155 ms after each stimulation pulse (figure 2) was extracted and divided in 30 bins of length 5 ms to capture the shape of the early evoked response. A semi-automatic trial rejection using the variance of the post-stimulation data was employed to remove trials with channel-specific artifacts, amplifier saturation or artefacts of the DC correction.

2.4 Support vector regression (SVR)

For each recording channel, SVR was used to infer the applied stimulation intensity from the 30 bins of the poststimulus activity. SVR is a method for sparse regression based on support vector machines. Following Brugger et al. [5], the regression model $g(x) = \sum_{i=1}^{m} \beta_i k(x, x_i) + b$ for a set of training patterns $\{(x_i, y_i)\}_{i=1}^{m} \in \mathbb{R}^d \times \mathbb{R}$ for primal SVR is found by

$$\min_{\beta, \mathbf{b}} \left(L_\epsilon(\beta, \mathbf{b}) = \frac{1}{2} \sum_{i=1}^{n} l_\epsilon(\mathbf{K}_i \beta + b - y_i) + \frac{\lambda}{2} \beta^{\mathbf{T}} \mathbf{K} \beta \right)$$

where l_ϵ is the ϵ-insensitive loss function, k is the kernel function, K_i the i-th row of the kernel matrix K, β are the coefficients in the solution, b is the bias

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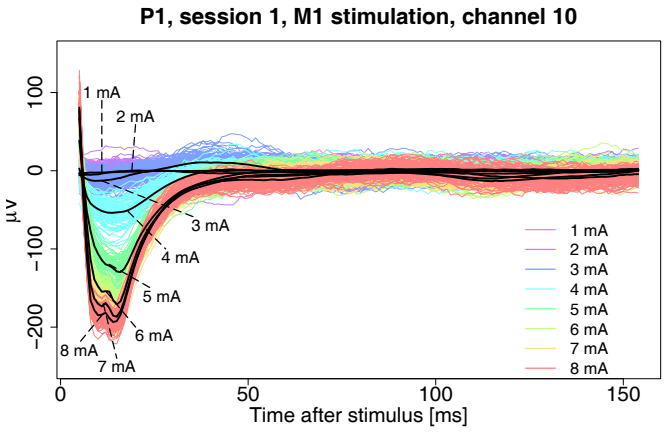

Fig. 2: Evoked activity on channel 10 (arrow in figure 1) after anodal pulses were applied to the motor cortex of P1. Colored lines: Single trials color-coded by intensity. Black solid lines: Mean evoked activity per intensity.

term and $\lambda = \frac{1}{C}$ is the regularization parameter. This SVR implementation was used because it yielded better results for this problem than the libSVM SVR implementation [6]. We used an RBF kernel and employed span bound optimization [7] to determine C, the width ϵ of the loss function and the kernel parameter σ.
For P1, the SVR was trained on the trials with intensities of 1, 3, 5 and 8 mA for training and tested on 2, 4, 6 and 7 mA. This was also done for the first session of P2, whereas for the second and third session, 5, 7, 9 and 12 mA were used for training and 6, 8, 10 and 11 mA for testing. The size of the training and the test set was 365.6 ± 47.4 and 365.9 ± 45.9 instances, respectively (mean $\pm$ std). The quality of the intensity decoding was quantified with the root mean squared error (RMSE) and the squared correlation coefficient r^2 between the decoded and the actual intensities. Models with an RMSE smaller than our step size of 1 mA were considered to be successful.

3 Results

The dependency of evoked responses on stimulation intensity can be seen in figure 2, demonstrating that there is a non-linear relationship between the amplitude of the evoked activity and the intensity. For the depicted channel, the strongest differences are found in the first 50 ms after the stimulus. We tested whether this dependency can be captured by a regression model by training the SVR only on half of the intensities and testing it on the remaining half. We found that the specificity of the differences between intensities depends on the position of the recording channel in relation to the stimulation channel. For

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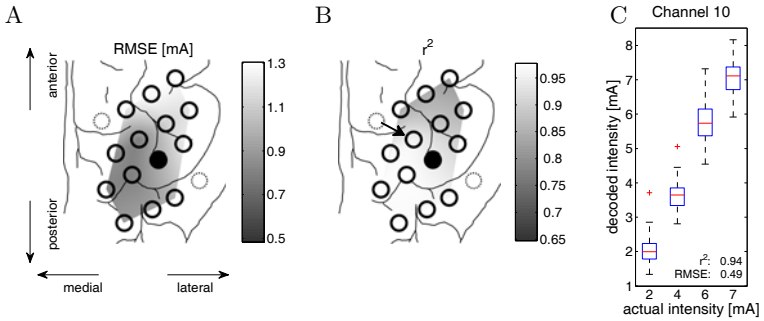

Fig. 3: Results for session 1 of P1, stimulation over M1. Spatial interpolation of RMSE (**A**) and r^2 (**B**) with sulci denoted by black lines. The stimulation electrode is marked by a black, recording electrodes by open circles. Dotted electrodes were excluded from the analysis. **C**: Results for the channel with lowest RMSE (arrow in B). Boxes encompass the 25th-75th percentile, whiskers extend up to 1.5 times the interquartile range. Plus signs denote outliers.

the example in figure 3, after stimulation on M1, the smallest error is found for the channels on the somatosensory cortex and the channels on the motor cortex medial to the stimulation electrode. For many of these channels, such as the example given in figure 3 C, the RMSE is smaller than the intensity step size of 1 mA, indicating a very good separability of the evoked responses for different intensities. Table 1 lists the average RMSE and r^2 for all channels grouped by their position (M1, S1 or PMC). When stimulating on S1 for P1, no recording was possible on the other channels on S1 due to strong stimulation artifacts.

4 Discussion and Conclusion

For patient P1, the results are in general better than for P2. Interestingly, stimulation on PMC is decoded worse on S1 than vice versa, indicating that either S1 is better excitable than PMC or that the stimulus itself is relayed better from somatosensory cortex towards premotor areas. For patient P2 it is clear that the intensity can be best decoded from stimuli applied to the motor cortex, where in all sessions and in all recording areas average $r^2 > 0.5$ are reached. For stimulation on the other brain areas, no meaningful decoding was achieved. This might be due to the cortical lesion in the sensorimotor area of P2 within the electrode grid (figure 1) which possibly disrupts the effective transmission of the stimulation to other brain areas.
In conclusion we have found that, depending on the position of the recording and stimulating electrodes, using SVR, a regression model can be constructed that generalizes from the evoked response of a few training intensities well enough to find the proper parameter setting for responses from novel intensities. Thus, a rough sampling of the range of intensities could be enough to predict the intensity best suited to evoke the target evoked response. Although this analysis

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	Session	Stim	Recording area					
			S1		M1		PMC	
			RMSE	r^2	RMSE	r^2	RMSE	r^2
P1	1	S1			0.65	0.91	0.88	0.82
		M1	0.79	0.92	0.77	0.88	1.24	0.69
		PMC	2.06	0.00	1.36	0.49	0.69	0.88
	2	S1			0.74	0.90	1.20	0.66
		M1	0.89	0.91	0.84	0.82	1.08	0.75
		PMC	1.52	0.39	0.90	0.77	0.64	0.91
P2	1	S1	2.02	0.02	1.77	0.20	1.83	0.07
		M1	1.55	0.43	1.32	0.48	0.80	0.83
		PMC	2.00	0.01	2.04	0.00	2.16	0.02
	2	S1	1.92	0.10	2.02	0.02	2.06	0.01
		M1	1.23	0.58	0.77	0.85	0.95	0.79
		PMC	2.03	0.04	1.95	0.10	1.72	0.26
	3	S1	2.00	0.04	1.83	0.16	1.82	0.19
		M1	1.16	0.66	1.26	0.58	1.35	0.56
		PMC	2.03	0.03	1.99	0.05	1.65	0.27

Table 1: Average RMSE and r^2 over all channels recording from M1, S1 or PMC for different positions of the stimulation electrode (Stim).

was performed on a single channel basis, it would be straightforward to extend it to multichannel data by using the concatenated evoked activities of the single channels as input to the regression model. The use of specialized spatial filters in data preprocessing could improve the decoding performance further by directly extracting the spatiotemporal patterns most sensitive to changes in stimulation intensity.

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