

THE SPECTRAL CONTROL FEATURES OF A BIPOLAR ECoG BCI IMPLANT OVER PRIMARY HAND MOTOR CORTEX

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ABSTRACT: Both Low Frequency Band (LFB) and High Frequency Band (HFB) features of the electrocorticography (ECoG) signal have been described and explored in the context of BCI. In literature, HFB power is emerging as a dominant control feature. However, the recently published Utrecht Neural Prosthesis (UNP) showed that HFB power from a bipolar electrode pair over the hand motor area alone was not good enough for stable high performance click-based BCI control [1]. Instead, a combination of LFB and HFB signals was optimal for click-based control. Here, we explore the spectral features that make up the LFB and HFB features of the bipolar ECoG signal used in the UNP. We demonstrate that the LFB of the bipolar signal is a combination of mu and low and high beta rhythms with independent functional and temporal characteristics.

INTRODUCTION

For continuous real-life use of a BCI implant, the standards of performance are much higher than those needed for proof of concept in a controlled lab setting. Optimal neural control signals in real-life use can differ significantly from those established for short experiments in the lab given the requirement for reliable and robust decoding for daily use.

The Utrecht Neural Prosthesis (UNP) is a fully implanted communication BCI based on bi-polar electrocorticography (ECoG) signals recorded from the primary motor cortex (subdural Resume II electrodes, Investigational Activa® PC+S and Nexus System, Medtronic). We recently demonstrated that a subject with late-stage ALS is able to use the UNP system to generate reliable brief neural events to control a spelling device at home [1].

Initial tests with a standard BCI cursor control task [2] showed high performance using the High Frequency Band (HFB) signal that has been most commonly used in human ECoG BCI studies [1, 3-7]. The HFB signal has been shown to be ubiquitous to human neocortex [8] and has been associated with increased asynchronous neural activity in the cortical tissue directly underneath an ECoG electrode [8-11].

However, in the case of the UNP it was also demonstrated that reliable click-based spelling control

was dependent on a combination of the HFB signal and a Low Frequency Band (LFB) signal, the spectral range of which (indicate frequency band we use in LFB) is consistent with that of the classic LFB spectral feature of motor cortex reported in ECoG literature [6, 12]. The LFB signal overlaps the mu-band (6-12 Hz) motor rhythm often used in EEG-based motor BCI [13], in addition to other oscillatory features commonly reported in EEG and ECoG literature such as the theta (4-7Hz) [14], and beta (12-30Hz) [15] bands.

A number of factors make the UNP control signal unique among human BCI systems. First, the chronic use click-based control requires precise control of the timing of control features derived from cognitive tasks. Second, the UNP has a bi-polar ECoG signal source (as opposed to the generally reported Common Average Referenced (CAR) signals). Third, the signals are gathered from a subject with late stage ALS, who has been paralyzed for years. Hence, in this work we explored the temporal and spectral characteristics of the UNP control signal to gain a better understanding of the underlying neural features that compose the bipolar control signal.

MATERIALS AND METHODS

UNP ECoG signal: The primary control signal of the UNP device is recorded using a bi-polar electrode pair implanted over the ‘hand knob’ within the primary motor cortex of a subject suffering from late-stage ALS. (see Fig. 1 in [1]). Each electrode was 4 mm in diameter and the center-to-center separation was 1 cm. The cognitive strategy used to control the UNP signal is attempted movement of the contralateral hand. In addition to the online control mode of the UNP device, in which analog filtered spectral amplitude signal is relayed to the receiving tablet at 5Hz (see [1] Methods for details), non-filtered ‘raw’ time domain signals can be transmitted at 200Hz. This work uses off-line analysis of the time domain signal recorded during several types of research tasks. This raw signal is used to compute Event-Related Potential (ERP) responses, time-locked to cued attempted hand movements, in addition to time-locked responses in the frequency domain (see sections *Spectral analysis* and *Spectral band analysis*).

Attempted hand movement screening task: Signal

properties during repetitive attempted hand movements were assessed using time domain data from a screening task in which the subject was cued to make repetitive attempted hand movements or relax for periods of 15s each. In total 46 runs consisting of either 10 (17 runs) or 3 (29 runs) alternated rest and attempted movement trials were used.

Short activation feedback task: In addition data from a task that cue the user to make brief 1s attempted hand movements was analyzed. This task also provided feedback to the user using the UNP control signal to control the vertical position of ball centered on the screen while alternating blocks of sky and grass scrolled from right to left across the top and bottom of the screen respectively. The blocks of sky were timed so that they took 1s to move pass the ball. The subject was instructed to make brief attempted hand movements to hold the ball at the top of the screen during the sky blocks and rest to allow the ball to reach the bottom of the screen during the grass blocks.

2-Target BCI control task: The signal properties during successful online BCI control were evaluated using time domain signal data from a subset of runs of a standard 2-target BCI control task (see [2] for details). In short, the subject was instructed to use attempted hand movements to control the vertical position of a ball moving at a constant speed from the left towards either an upper or lower target on the right of a screen. The task was administered using the BCI200 software package [ref] and used elevated power in the HFB (60-90Hz) to drive the ball up and relaxation (inducing a decrease in HFB power) to drive the ball down. A 1s cue, indicating either the top or bottom target, was presented before the ball appeared and began to move for a 2-4s period towards the right. Task performance was high (95%) for 2 runs with 3s movement periods.

Spectral analysis: The amplitude for each frequency bin from 1 to 90Hz (in steps of 1Hz) was computed offline for every time sample of each time domain data file using the real component of the convolution with a complex Gabor wavelet (span 4 cycles at full width half maximum) [16].

Spectral band analysis: In order to access the contributions of known distinct spectral bands to the UNP control signal, the Delta (1-4Hz), Theta (5-7Hz) Mu (8-12Hz), Low Beta (13-20Hz), and High Beta (21-31Hz) in addition to the HFB (41-90Hz) were analyzed. Each band's amplitude trace was computed for the duration of each data set by summing the mean normalized 1Hz bin amplitude traces over the above ranges. The amplitude trace of each band was then z-score normalized.

RESULTS

The bi-polar spectral profile for attempted hand movements during the screening task closely matched the classic ECoG spectral profile for M1 activity [6, 12] (Fig. 1). The range of 1-4Hz and 41 to 90Hz showed an

attempted movement related increase in amplitude. A decrease in amplitude during attempted movement compared to relaxation was seen from 9 to 34 Hz. While the magnitude of the HFB increase is relatively uniform after 50 Hz, the LFB decrease shows a trough centered at 25 Hz and approximately covering the high Beta (21-31Hz) range.

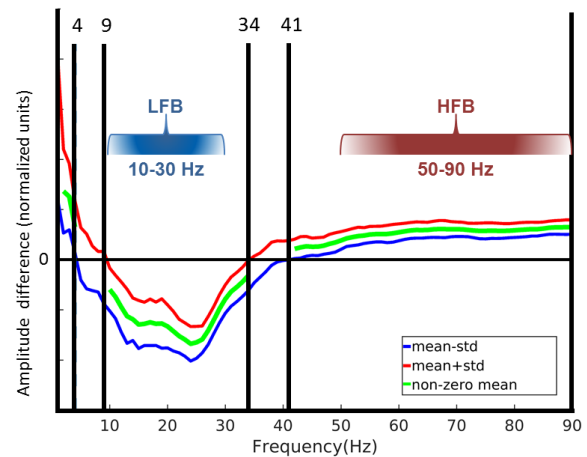


Figure 1: Attempted hand movement vs. rest condition spectral contrast. The classically reported HFB and LFB ranges [6, 12] are indicated with the red and blue highlights respectively. The mean + 1 standard deviation and mean - 1 standard deviation spectral contrast (attempted hand - rest condition) profiles (over trials and runs) are plotted in red and blue respectively. The green trace indicates the regions of the mean profile that are 1 std above or below 0.

Inspection of the mean spectrogram of the attempted movement and rest periods of the screening task (Fig. 2) shows that the decrease in High Beta amplitude parallels the increase in HFB and Delta band amplitude, which starts at attempted movement onset and continues until offset. In addition, a relative increase in amplitude in the High Beta range during the duration of the rest condition parallels the general decrease in the HFB and Delta ranges that begin at approximately 2s after the rest cue. However, it can also be seen in Fig. 2 that the lower portion of the LFB (9-20Hz) which consists of the mu and Low Beta bands has a pronounced initial drop in amplitude in the period after attempted movement onset (compared to the period prior to the offset). Furthermore, this lower LFB range shows a very pronounced increase (referred to hereafter as a rebound) in amplitude just after attempted movement offset. This rebound last for 3-4 seconds and does not continue for the duration of the rest periods. Strikingly, the rebound not only includes a peak in High Beta amplitude in the first 2s after attempted movement offset, it is accompanied by increased HFB amplitudes during the beginning of the rebound period.

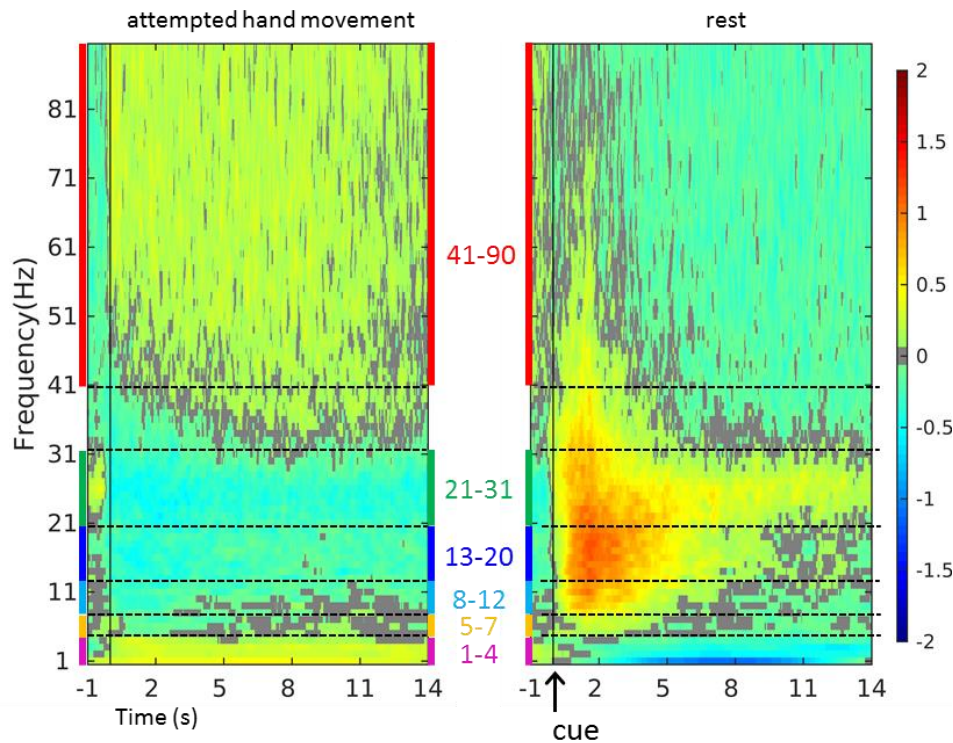


Figure 2: Mean attempted hand movement and rest condition responses. A) Mean spectrograms for -1 to 14s periods centered on movement onset (left) and offset (right) cues (note: trials were 15s, meaning that last 1s of each trial is analogous to the -1 to 0 second periods in plots). The colors indicate positive (yellow to red) and negative (turquoise to blue) mean z-scores. In addition the HFB, High Beta, Low Beta, Mu, Theta, and Delta bands are highlighted in red, green, blue, cyan, orange, and magenta respectively.

Fig. 3 depicts the temporal response patterns of the separate frequency bands (colored traces) to a series of short impulse like attempted hand movements made in the context of visual feedback (see section: *Short activation closed loop feedback task*). As with the repetitive attempted hand movements, a clear increase in HFB power (red trace) with a parallel decrease in High Beta (green trace) power can be seen. Likely due to the anticipation facilitated by the feedback the coupled HFB and High Beta response starts approximately 1s before the cue. In addition, the same decoupling between the Mu/ Low Beta bands on the one hand, and the High Beta band on the other, that is seen in the sustained movement response, is seen in the short attempted movement response. Notably, the Low Beta band trace increases past zero and begins the rebound period just before the offset cue. This rebound period is also seen to continue to increase till past the cessation of the HFB increase and High Beta decrease. However, the short attempted movements also reveal that the Mu band response has a later negative peak and subsequent later rebound onset than the Low Beta band. The Theta band has a similarly timed decrease in amplitude as that of the Mu band, but does not show a post offset rebound.

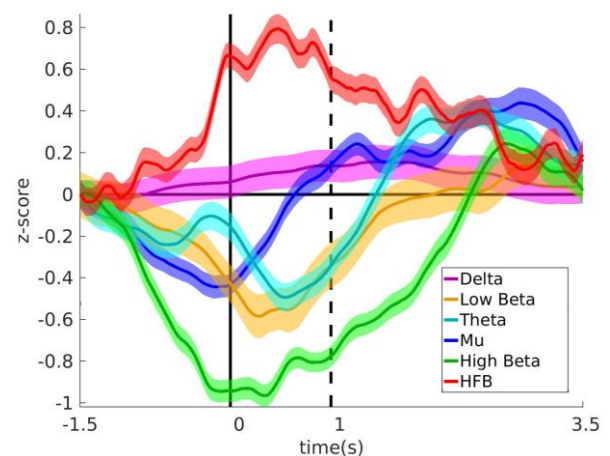


Figure 3: Spectral band responses to brief attempted hand movements during a feedback task. The mean z-scored traces and standard error margins (indicated by the shaded regions) are plotted (see legend for color indications) for the period of -1.5s to 3.5s time-locked to the onset of the sky blocks in the *Short activation feedback task* (see section *Short activation feedback task*).

Given the separate temporal profiles of individual bands, it is interesting to consider the full range (1-90Hz) spectral response to the traditional 2-Target BCI control

task (Fig.4). As expected, the HFB increase used to drive the feedback is well timed to the up trials' movement cue (vertical black line, left plot). Again this HFB increase is paralleled by a High Beta band decrease and a broad spectrum rebound after the target feedback cue which includes the Mu and Low Beta bands. However, the expected lack of HFB increase during the down trials (right plot) is not coupled by an increase in High Beta band amplitude. In fact, the High Beta band

shows a decrease in amplitude coupled by a marked increase in the Low Beta band towards the end of the down trials. Furthermore, the rebound in amplitude seen after target feedback offset in the up trails is much diminished after the down trials. Another interesting features is the increase in Mu band amplitude just before and around the down trail movement cues which is clearly not present in the up trials.

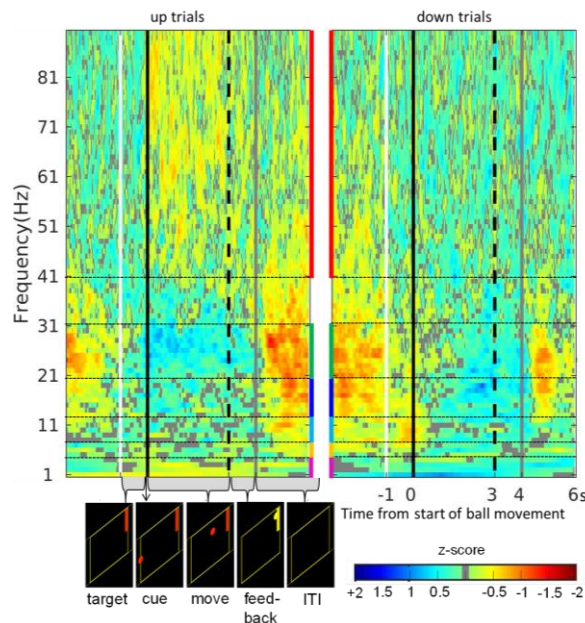


Figure 4: Mean up (attempted hand movement) on the left and down (rest) condition spectrograms on the right. The colors indicate positive (yellow to red) and negative (turquoise to blue) mean z-scores. The visual feedback corresponding to the successive periods of the task are depicted under the x-axis of the left plot. See Fig. 3 for explanation of color colored highlights.

DISCUSSION

The bi-polar signal used with the UNP has 3 main distinguishable frequency bands. A 41-90Hz HFB which is well matched to the traditional HFB [6], and a 9-34 Hz LFB (matched to the traditional LFB [6]) that is made up of distinguishable Mu/Low Beta and High Beta band features.

The results presented here indicate that the HFB is likely a segregate for the broadband component of the ECoG signal described by Miller et al. [8-9]. Since the HFB has been linked to synaptic mechanisms and irregular firing of single neurons [9-12] bi-polar referencing should only serve to strengthen its presence as a functional feature. If there is an increase broad band activity in one of the two neural populations under electrode pair then an increase in the differential bi-polar signal will be observed. In addition, due to the irregular or asynchronous nature of the broad band feature in the raw potential signal, if there is an increase in both neural populations then the broad band (and hence HFB) component of the differential signal will be even further increased in amplitude. However, this does lead to more possible functional variance since two neuronal populations that are on a scale at which they are likely to be functionally

independent [17] are reflected in the signal. This could have advantages and disadvantages. One advantage is the possibility for more distinct functional states. However, this also implies that larger range of cognitive tasks could affect the signal and lead to false positives in simple single click based system like the UNP.

We also show that LFB is clearly present in the bi-polar signal. Since this range has traditionally been associated with synchronized neural population oscillation effects [18] and the LFB has been reported to be anatomically broader than the 1 cm separation of the electrode pair [6, 12], it could be expected that synchronized suppression of the neural populations under the electrodes could lead to the LFB amplitude responses being subtracted out of the differential signal. However, the results presented here suggest that either the LFB is not synchronized across the covered populations or that a large enough phase shift in this range between the two populations exists to prevent this. This concept is exemplified by considering the subtractions of two signals with equal amplitude oscillations at the same frequency that are exactly out of phase. In this situation the amplitude of the differential signal would be doubled.

In addition the LFB band can be divided into distinct oscillatory bands with distinct temporal function

response patterns. The High Beta (21-31Hz) component of the LFB shows task suppression consistent with hypothesized release of inhibition during cortical processing associated with the motor Mu rhythm [18]. On the other hand, the Mu/Low Beta component is also suppressed during attempted movement, but is not directly anti correlated with HFB. The rebound affect that has been reported for the Beta band [15] is most prominent in this range.

CONCLUSION

In addition to a clearly present HFB component, a multi-faceted LFB component made up of distinct High Beta and Mu/Low Beta components is present in the to the bipolar signal. This LFB component is not only suppressed during attempted movements, it also shows a large post neural activation rebound affect. The combination of these effects helps improve robustness of HFB feature and leads to the stable single cognitive event features [1].

REFERENCES

- [1] Vansteensel MJ, Pels EGM, Bleichner MG, Branco MP, Denison T, Freudenburg ZV, Gosselaar P, Leinders S, Ottens TH, Van Den Boom MA, Van Rijen PC, Aarnoutse EJ, Ramsey NF. Fully Implanted Brain-Computer Interface in a Locked-In Patient with ALS. *N Engl J Med* 2016;375(21): 2060-66
- [2] Schalk G, McFerland DJ, Hinterberger T, Birbaumer N, Wolpaw JR. BCI2000: a general-purpose brain-computer interface (BCI) system. *IEEE Trans Biomed Eng* 2004;51: 1034-43.
- [3] Buzsáki G, Wang XJ. Mechanisms of Gamma Oscillations. *Annu Rev Neurosci* 2012; 35: 203–25.
- [4] Leuthardt E, Miller K, Anderson N, Schalk G, Dowling J, Miller J, Moran D, Ojemann J. Electrographic frequency alteration mapping: a clinical technique for mapping the motor cortex. *Neurosurgery* 2007; 60: 260.
- [5] Leuthardt, E, Schalk, G, Wolpaw, J, Ojemann, J, Moran D. A brain-computer interface using electrocorticographic signals in humans. *J Neural Eng* 2004; 1: 63.
- [6] Miller KJ, Schalk G, Fetz EE, den Nijs M, Ojemann JG, Rao RPN. Cortical activity during motor execution, motor, imagery, and imagery-based online feedback. *PNAS* 2010;107(9): 4430-35.
- [7] Vansteensel M, Bleichner M, Freudenburg Z, Hermes D, Aarnoutse E, Leijten F, Ferrier C, Jansma J, Ramsey N. Spatiotemporal characteristics of electrocortical brain activity during mental calculation. *Hum Brain Mapp* 2014;35: 5903–20.
- [8] Miller KJ, Honey CJ, Hermes D, Rao RPN, Nijs M, Ojemann JG. Broadband changes in the cortical surface potential track activation of functionally diverse neuronal populations. *NeuroImage* 2014;85: 711-20.
- [9] Miller K, Sorensen L, Ojemann J, Nijs M. Power-Law Scaling in the Brain Surface Electric Potential. *PLoS Computational Biology* 2009;5(12).
- [10] Hermes D, Miller K., Vansteensel M, Aarnoutse E, Leijten F, Ramsey N. Neurophysiologic correlates of fMRI in human motor cortex. *Hum Brain Mapp* 2012; 33: 1689–99.
- [11] Hermes D, Siero J, Aarnoutse E, Leijten F, Petridou N, Ramsey N. Dissociation between Neuronal Activity in Sensorimotor Cortex and Hand Movement Revealed as a Function of Movement Rate. *J Neurosci* 2012; 32: 9736–44.
- [12] Miller KJ, Leuthardt E, Schalk G, Rao RPN, Anderson N, Moran D, Miller J, Ojemann JG. Spectral changes in cortical surface potentials during motor movement. *J. Neurosci.* 2007; 27(9): 2424-32.
- [13] Wolpaw J, Wolpaw EW. *Brain-Computer Interfaces: Principles and Practice*. Oxford University Press, Oxford, England (2012)
- [14] Canolty RT, Edwards E, Dalal SS, Soltani M, Nagarajan SS, Kirsch HE, Berger MS, Barbaro NM, Knight RT. High gamma power is phase-locked to theta oscillations in human neocortex, *Science* 2006, 313(5793), 1626-28
- [15] Miller K, Hermes D, Honey C, Hebb A, Ramsey NF, Knight RT, Ojemann J, Fetz E. Human motor cortical activity is selectively phase-entrained on underlying rhythms. *PLoS Comp Bio* 2012; 8(9).
- [16] Bruns A. Fourier-, Hilbert- and wavelet-based signal analysis: are they really different approaches? *J Neurosci Methods* 2004;137.
- [17] Leuthardt EC, Schalk G, Roland J, Rouse A, Moran DW. Evolution of brain-computer interfaces: going beyond classic motor physiology. *Neurosurg Focus*. 2009; 27(1).
- [18] Amzica F, da Silva FL, Schomer DL. *Basic Principles, Clinical Applications, and Related Fields*. Lippincott Williams & Wilkins, Philadelphia, Pa, USA (2010)