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An Implantable Bi-directional Brain-machine Interface System for Chronic Neuroprosthesis Research

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Abstract— An implantable bi-directional brain-machine interface (BMI) prototype is presented. With sensing, algorithm, wireless telemetry, and stimulation therapy capabilities, the system is designed for chronic studies exploring closed-loop and diagnostic opportunities for neuroprosthetics. In particular, we hope to enable fundamental chronic research into the physiology of neurological disorders, define key electrical biomarkers related to disease, and apply this learning to patient-specific algorithms for therapeutic stimulation and diagnostics. The ultimate goal is to provide practical neuroprosthetics with adaptive therapy for improved efficiency and efficacy.

I. Introduction

NEUROMODULATION is approved for the treatment of several neurological disorders including Parkinson's disease, essential tremor, and dystonia. Presently most neuromodulation devices operate in "open-loop," meaning that there is no sensing capability and adjustments require clinician intervention. There is great interest in measuring neurological activity to optimize therapy in real-time based on relevant biomarkers in the spirit of a "closed-loop" neuroprosthesis. In order to explore the feasibility of such systems, a chronic research tool is needed to establish the biomarkers relevant to disease and validate prototype algorithms utilizing these physiological measurements. As illustrated in Fig. 1, at a minimum such a system requires a sensing interface input, a signal processing and algorithm classification system, a stimulation output, and wireless telemetry for data exchange. In addition, indirect monitoring of activity and posture can provide important supplementary data on the patient's state. Such a system that links sensing and stimulation through a control algorithm can be considered a bi-directional brain-machine interface (BMI).

The major challenges to implementing such a system include the chronic measurement of neurological information, the implementation of algorithms within a highly power-constrained environment, and the hurdles of building a safe and reliable system that can withstand the body's harsh environment. By leveraging existing implant technology and adding a carefully partitioned sensing and algorithm system, we were able to balance these constraints to construct a practical bi-directional BMI research system.

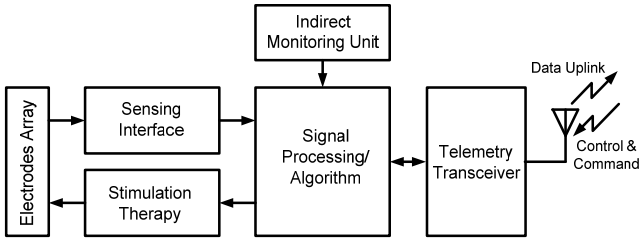

Fig. 1: Functional block diagram for bi-directional BMI.

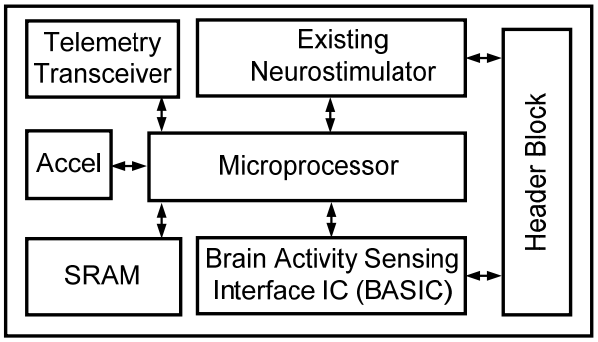

Fig. 2: Electrical system block diagram for implantable BMI.

II. Implantable Bi-directional Brain-machine Interface System Design

A. Overall System Architecture

The overall system architecture of the bi-directional BMI is depicted in Fig. 2. The prototype is built on an existing neurostimulator to leverage proven technology that is viable for chronic implantation. To extract information from the brain, a custom designed Brain Activity Sensing Interface IC (BASIC) is added for sensing neural activity. Connections from the sense and stimulation electronics to electrodes are made through a set of switch matrices and isolation-protection circuitry at the header block of the device; electrode combinations are then attached at this block for flexible BMI architectures. In addition, a custom three-axis accelerometer is included to provide sensing for posture and activity. Sensed signals are passed to a microprocessor for performing control and algorithms. Interactions between the original neurostimulator and the algorithm microprocessor are established by an interrupt vector and I^2C port. An

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SRAM is included for recording events and general data logging. The telemetry subsystem allows for new algorithms to be downloaded into the device and data to be uploaded to an external data logger. The rest of this section highlights the major features of the BMI architecture.

B. *Sensing Strategy and Interface*

The choice of neural recording strategy is a balance of information content and technical feasibility. While single-cell recordings and EEG are viable for many applications, a good balance of trade-offs for our application is provided by the recording and analysis of local field potentials (LFPs). LFPs generally represent the ensemble activity of an *in vivo* neural population around the electrode and are more chronically robust [1]. In addition, LFPs encode highly meaningful data for neurological disease [2], and they are emerging as a viable candidate for BMI applications [1]. In our opinion, LFPs represent the best balance between current technological limitations of electrode systems and meaningful biomarkers correlated with pathological neural activity, especially when restricting ourselves to electrodes available for current neuromodulation devices [3].

High signal resolution and low system power consumption, which are essential for such an implantable BMI, are difficult to achieve even for LFPs with moderate frequency content. However, the band power fluctuations in LFPs are generally at least an order of magnitude slower than the frequencies at which they are encoded. This motivates a BASIC architecture that directly extracts energy in key neuronal bands and tracks the relatively slow power fluctuations prior to digitization and algorithmic analysis, similar to the spectral processing paradigm of AM demodulation to extract the audio signal from a high-frequency carrier signal prior to complex processing [3,4].

The BASIC analog preprocessing block extracts bandpower at key physiological frequencies from LFPs with an architecture that is flexible and low-noise. As described in [3], the signal chain of the BASIC implements a short-time Fourier transform (STFT) by using a modified chopper-amplification scheme. This architecture provides both gain and spectral estimation with power efficient processing. Referring to the die photo in Fig. 3, four sense channels are implemented on the BASIC, two of which can be configured as power sensing channels over a broad range of spectral bands from DC to 500 Hz. The other two channels can be used for recording 200 Hz time domain waveforms. The power channels can sense from the same electrodes to extract two frequency bands simultaneously at the same site.

A custom three-axis accelerometer is also incorporated in the system to provide sensing for posture, tremor and activity. Trends in these states can often provide some insight into the overall health of the patient. The design aims at extremely low power consumption while maintaining acceptable noise performance; details are provided in [5].

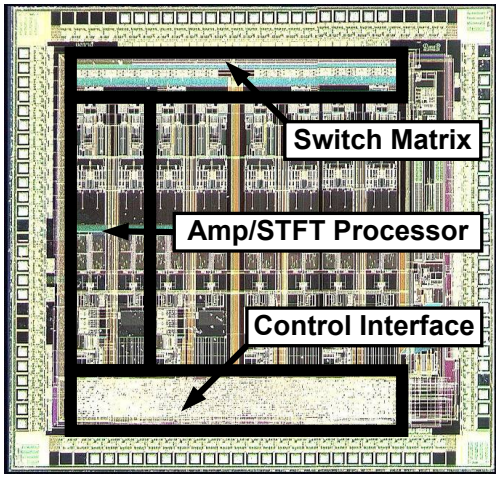

Fig. 3: Brain Activity Sensing Interface IC (BASIC) die photo.

C. *Signal Processing and Algorithm Architecture*

The challenge of processing signals is balancing power consumption, flexibility and performance. Since biomarkers of interest have already had their spectral power extracted by the BASIC's STFT and the spectral power changes vary slowly compared to the LFP frequencies that encode the biomarkers, sampling and processing can be done at sampling rates on the order of Hz. This allows for a system partition (Fig. 4) of analog pre-processing to extract key information and reduce dynamic range, while running complex digital algorithms at slow clock rates. This partition results in an acceptable power budget for a chronic implantable device; similar "neuromorphic" principles are discussed in [4].

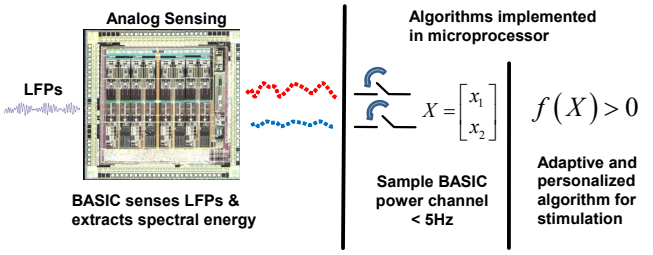

Fig. 4: Partitioning for signal processing and algorithms.

The system is highly configurable. The microprocessor controls the BASIC chip via control registers, enabling adjustments to gain, STFT parameters for spectral estimation, and electrode connectivity through telemetry and algorithm control. To maximize flexibility, algorithms can always be adjusted via telemeterized firmware updates.

The algorithm running in the processor is used to appropriately classify the signal and estimate patient state. This allows the BMI to actuate stimulation therapy appropriately and/or measure key diagnostics. Recent research is demonstrating that patient-specific algorithms can be useful for improving the sensitivity and specificity of this classification. Clinician-supervised machine learning is a good way to accomplish a patient-personalized algorithm, and our system is designed to enable this patient-specific classification in a power-efficient way [6].

D. *Neurostimulator and other System Features*

An existing Medtronic neurostimulator is employed in the system for stimulation therapy, which also serves as a platform for the overall bi-directional BMI system. It communicates through a wireless telemetry link for system configuration, algorithm programming, and data uplink. A 1MB SRAM is included on the platform for recording algorithm-defined or externally-generated events, time-domain waveforms, and general data logging. The data can be downloaded through the wireless link for analysis and investigation at 11.7kbps using the 175kHz ISM band.

III. Stimulation-Sense Interactions

A significant challenge in combining sensing and stimulation in a bi-directional BMI is dealing with signal contamination. The signals we are interested in sensing are on the order of microvolts, while the signals we are injecting (the stimulation) are on the order of volts. The extraction of a biomarker that is six orders of magnitude lower than therapeutic stimulation is a significant challenge.

Several methods are employed in the prototype to allow for coincident sensing and stimulation. One method is simply to have separate leads for each function; but this comes at the cost of increased surgical complexity, and we often want to measure activity in the vicinity of our stimulation target. For simultaneous sensing and stimulation from the same lead, careful placement of the leads and sense-stim configuration can take advantage of the reciprocity theorem of electromagnetism. Stated mathematically, we attempt to design the electrode and anatomical approach such that

$$\phi_A - \phi_B = \frac{\vec{E}_{AB} \bullet I\vec{d}}{I_{AB}} \to 0$$

Intuitively, we can think of this mathematical relationship imposing a symmetry constraint on the sense-stim configuration. Fig. 5 shows an example where the sensing dipole ($A \leftrightarrow B$) is placed symmetrically about a unipolar stimulation electrode ($C \leftrightarrow D$) with far-field return. When the dipole from therapy stimulation is orthogonal to the biomarker sensing vector, our chances for extracting a signal are greatly increased.

Another key method employed in all electrode configurations is to take advantage of the spectral filtering properties of the BASIC. In particular, the architecture of the BASIC is capable of rejecting signals that are out of its tuned band. Saturation is avoided by filtering the signal before significant gain is applied as part of the STFT processing. This allows for the possibility of delivering stimulation therapy in one spectral band and sensing in another at the same time off the same lead; but note, not the same electrode. This constraint is compatible with many deep brain stimulation (DBS) systems which have biomarkers well separated spectrally from therapy stim, and sensing dipoles bounding a unipolar-driven stimulation target [2]. These techniques show promise for simultaneous stimulation and sensing of the same neural circuit, establishing feasibility for real-time adaptive therapy titration.

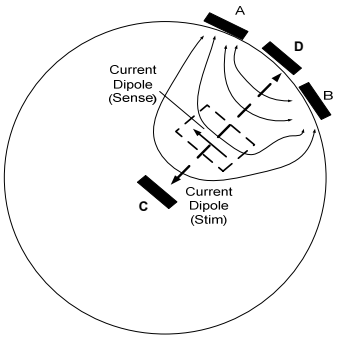

Fig. 5: Diagram of lead placement and stim configuration exploiting the reciprocity relationship.

IV. Prototype System and Measurement Results

A. *Prototype Implantable Bi-Directional BMI System*

A complete implantable BMI system was prototyped using established, but state-of-the-art, medical device technology. The prototype system is shown with a cutaway window in Fig. 6. The BASIC is fabricated using a 0.8µm CMOS process and stacked on the SRAM to provide a module with small form-factor. The electrode-interconnect and algorithm processor are in close proximity to maintain signal integrity. The right side of Fig. 6 is a close-up of the side of the hybrid board containing the new sensing and algorithm electronics (accelerometer not populated in this photo). The other side (not pictured) contains the stim electronics. This device has complete bi-directional BMI functionality and is suitable for chronic preclinical research.

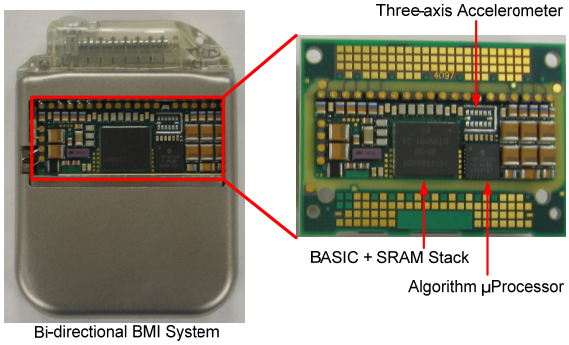

Fig. 6: Prototype implantable Bi-directional BMI system.

B. *General System Characterization*

The prototype system including implantable circuits, electrodes and telemetry was tested in a saline tank with recorded patient data. The BASIC was verified to consume 10µA from a 2V supply, achieving a signal resolution of $<1\mu V_{RMS}$ for a 5Hz power spectral estimation of two channels of operation (one/hemisphere). The linear support vector classification algorithm drew an additional 5µW to classify signals in real-time with 1s estimation updates. In addition to demonstrating basic BMI functionality, the system was also verified to withstand ESD, electrocautery and defibrillation, which is critical for a robust and practical BMI system. The performance is summarized in Table 1.

Table 1: System performance summary

Minimal Detectable Signal Power	$(<0.5\mu Vrms)^2$
Noise Spectral Density (Time Domain)	$150\,nV/\sqrt{Hz}$
Bandpower Center Frequency (δ)	dc to 500Hz, programmable
Bandwidth of Spectral Estimate	1-20Hz, programmable
BASIC + Classifier Algorithm Power	25μW (typical)
Real-time Wireless Uplink	11.7kbps @ 175kHz (ISM)

The ability of the system to perform sensing during the delivery of stimulation was also tested. Fig. 7 shows the results from a test where 145Hz stimulation was delivered between contact 1 and the can. A 24Hz signal, representing typical β band biomarkers, with $10\mu V_{PP}$ amplitude was injected into the tank and sensed across contacts 0 and 2 using the BASIC. This was compared to results obtained using the same stimulation but no test signal. The separation of the two curves indicates a promising ability to sense during delivery of stimulation, especially since most clinical therapy is delivered using 5V of amplitude or less.

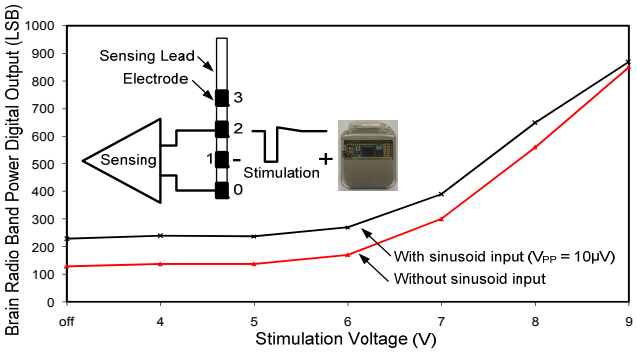

Fig. 7: Sensing capability in the presence of stimulation.

C. *Patient-Specific Algorithms and Classification*

The intent of building this prototype bi-directional BMI is to provide a platform for research that is adaptable to a number of neurological disorders. The common thread for these disorders is that biomarkers are believed to be encoded in LFPs as distinct fluctuations in the frequency spectrum [2, 3]. With appropriate lead placement and BASIC tuning, it is possible to differentiate neural states and use this information for diagnostics and/or therapy titration.

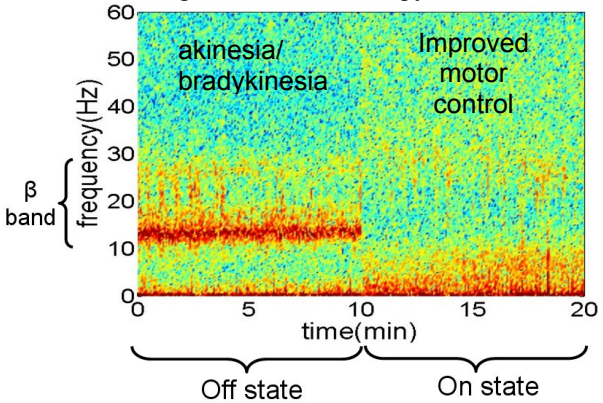

Fig. 8: Spectrogram of LFP data collected from Parkinson's patient.

For example, Fig. 8 shows a spectrogram of LFP data collected from a Parkinson's patient's DBS leads; note the high correlation between energy in the beta band and the pathological symptoms associated with the disorder [2]. Fig. 9 shows how this spectral data can be used to classify the patient's state in real-time with high sensitivity and specificity applying support vector classification on the prototype trained with a supervised learning process similar to that described in [6]. The classified states are then fed to the therapy/diagnostic prototype controller to explore optimizing stimulator settings using algorithms or provide clinician feedback based on quantitative diagnostics.

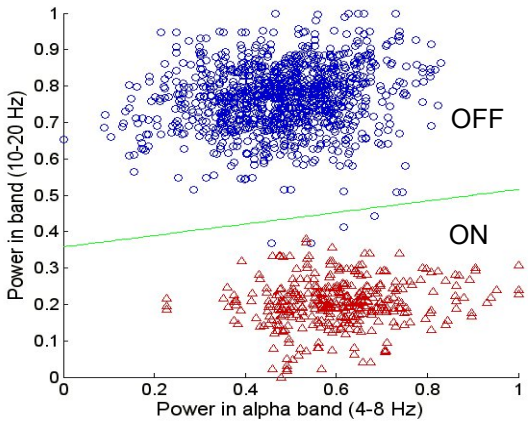

Fig. 9: Classification of Parkinson's patient state based on a supervised, patient-specific machine learning algorithm that is downloaded into the BMI. The classifier for this patient has > 95% sensitivity and specificity.

V. Conclusion

This paper presented a complete prototype bi-directional BMI system suitable for chronic implantation. Using prerecorded signals from DBS electrodes as a test paradigm, we demonstrated the ability to practically measure and classify disease-relevant brain states from derived biomarkers using a custom ASIC and machine learning techniques. The ability to sense meaningful signals in the presence of therapeutic stimulation was also demonstrated as a key to providing closed-loop control. By leveraging existing technology and robust sensing and classification paradigms, this BMI prototype represents a practical milestone towards "closed-loop" neuroprosthesis.

References

[1] A. B. Schwartz, X. T. Cui, D. J. Weber, and D. W. Moran, "Brain-controlled interfaces: movement restoration with neural prosthetics," *Neuron*, vol. 52, pp.205-220, 2006.

[2] A. Kühn, P Brown, et al. "High-frequency stimulation of the subthalamic nucleus suppresses oscillatory β activity in patients with parkinson's disease in parallel with improvement in motor performance," *The Journal of Neuroscience,* 28(24):6165-6173, June 11, 2008.

[3] Avestruz A, et al. "5μW/Channel spectral analysis IC for chronic bidirectional brain-machine interfaces," *IEEE J Solid-State Circuits*, vol. 43, no. 12, December 2008.

[4] R. Sarpeshkar, "Brain power: Borrowing from biology makes for low-power computing," *IEEE Spectrum*, pp. 24-29, May 2006.

[5] T. Denison et al. "A 2μW three-axis MEMS-based accelerometer," *IEEE Instrumentation and Measurement Technology Conference Proceedings*, vol. 1-3, pp. 1-6, May 2007.

[6] A. Shoeb, et al. "A micropower support vector machine based seizure detection architecture for embedded medical devices," to be published in *EMBC 2009*, Minneapolis, MN, September 2009.