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Robustness of implantable algorithms to detect epileptiform activity in the presence of broad-spectrum background noise

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Abstract—**Detection of epileptiform activity is of interest for responsive stimulation and diagnostic or monitoring devices in epilepsy; some implantable systems use low-computational-complexity algorithms such as line length trending and half-wave detection. Broadband noise was added to recorded electrocorticographic signals in order to model the potential impact of factors such as electrode-tissue interface properties and distance from the epileptic focus on these detection tools. Simulation demonstrated that half-wave and line length tools can yield consistent results in the presence of moderate amounts of noise.**

I. Introduction

EPILEPSY is a relatively common neurological disorder affecting up to 3% of the population [1]. At least 30% of these patients are not adequately treated with antiepileptic drugs, meaning that seizures are not entirely suppressed, and in an additional fraction of patients seizures are suppressed at the cost of adverse drug effects such as cognitive impairment and fatigue [2]. Even infrequent seizures in refractory (uncontrolled or poorly controlled) epilepsy can greatly impact quality of life for patients, affecting for instance the ability to qualify for a driver's license.

Furthermore, approximately 60 percent of epilepsy cases are localization-related, meaning that seizures can be attributed to one or more specific anatomical foci, and the majority of these patients experience complex partial seizures [3]. A minority of these patients with refractory, localization-related epilepsy are candidates for resective surgery [4], which under optimal conditions yields a one-year seizure freedom rate of 56 - 77% [5], but is not acceptable to many patients [6] and is accompanied by drawbacks such as surgical risk and potential of functional deficits. Vagal nerve stimulation provides an additional option and has been shown to yield a median seizure reduction of 25 to 30% [7], but rarely results in freedom from seizures [8].

The motivation for developing new treatments, thus, is clear, and in localization-related epilepsy there is great interest in interventions that specifically target the epileptic focus. Over the long history of surgical procedures for epilepsy – including intracranial mapping and resective surgery – it has been observed that cortical electrical stimulation can disrupt epileptiform activity [9][10] and terminate seizure-like afterdischarges caused by cortical mapping [11][12]. Focal hippocampal stimulation [13] has shown some success in reducing seizures. Non-responsive and non-focal stimulation, while outside the scope of this paper, is also a promising area of research for both focal and non-focal epilepsies and has been the subject of a major clinical trial [14].

Because seizures are episodic and associated with electrographic changes, responsive electrical stimulation holds particular promise, and researchers over the past decade have undertaken to "close the loop" [15][16] and stimulate in response to epileptiform activity. Preliminary studies using a bedside device [17]-[19] led to development of the first fully-implantable responsive neurostimulator for epilepsy as part of the NeuroPace RNS® System (NeuroPace, Inc., Mountain View, CA), which is currently being evaluated for safety and efficacy in clinical trials.

Work toward closed-loop stimulation as well as efforts to detect seizures for diagnostic and warning purposes [20]-[22] have driven development and optimization of methods to detect epileptiform activity using electrocorticographic (ECoG) data, and this is now a somewhat mature field [23]. Specifically, power and size constraints on implantable systems require the use of algorithms having relatively low computational complexity, such as line length [24] and half-wave detection [25][26].

These tools are dependent on epileptiform signals being discernable in the electrographic data, and detection performance has been well-characterized using both real and simulated epileptiform activity. However, the actual prominence of epileptiform activity will depend on factors such as the functional synchrony and amount of tissue generating the activity, the distance between the electrodes and the focus, the amount and character of spontaneous activity in the region, the electrical and geometric properties of the surrounding tissue, and the electrical properties, such as impedance, of the electrode-tissue interface.

In this paper, we assume that the cumulative effect of these factors may be approximated as the effect of broad-spectrum background noise. Using electrographic data previously recorded by the RNS System, we simulated changes in detection performance while varying the relative amount of real signal versus broad-spectrum noise.

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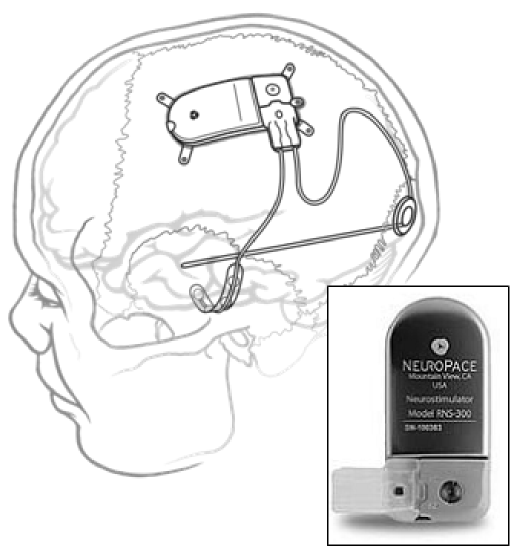

Fig. 1. Typical NeuroPace RNS® System implant configuration is shown in schematic view, with inset showing the implantable neurostimulator. Up to two leads may be connected to the neurostimulator; either may be a depth lead or cortical strip lead with electrodes placed at or near the seizure focus.

II. Methods

A. System overview

The RNS® System (Fig. 1) consists of a cranially-implanted neurostimulator and leads, a physician programmer and wand capable of wireless communication with the implanted device, a data transmitter used by the patient to upload recorded data, and a Patient Data Management System (PDMS) which receives and provides access to these data.

The neurostimulator is 28 mm wide, 60 mm long, and 7.7 mm thick and is shaped to approximate the typical curvature and thickness of the calvarium. At implant, a section of skull is removed that corresponds to the size and shape of the neurostimulator. A titanium ferrule (a tray that is similar to a skull plate) is inserted in the resulting opening, and attached to its perimeter using standard bone screws. The neurostimulator is then inserted into the ferrule.

Either one or two leads are implanted to situate electrodes as close as possible to the epileptic focus or foci, and the leads are routed to the neurostimulator through burr holes or through the craniectomy. Both depth leads, similar in geometry and construction to those commercially available for deep brain stimulation, and cortical strip leads, similar to those commercially available for intracranial monitoring, are provided with the system. The distal end of each lead bears four platinum/iridium electrodes of surface area 7.9 mm^2 apiece. The neurostimulator continuously analyzes incoming ECoG data and delivers electrical stimulation when the patient's characteristic epileptiform activity is detected.

In addition to its detection and stimulation capabilities, the neurostimulator can be configured to record up to four channels of ECoG activity in response to detected electrographic events or patient activation using a magnet, or according to a predefined schedule. All data are appropriately pre-filtered before digitization at a sampling rate of 250 Hz.

B. Simulated noise and detection

To provide a realistic basis for the stimulation, ECoG records were selected from three patients, all with mesial temporal foci. All records were greater than 20 seconds long (32 to 180 s, median duration 90 s) and were collected between 7 and 139 days (inclusive) after initial implant. Records including artifact due to neurostimulator-delivered stimulation were excluded; this yielded 305, 43, and 112 ECoG records respectively for the three patients.

Broad-spectrum noise was generated with a typical power spectrum individualized for each patient's data (Fig. 2). For

TABLE I
Detection Tools Used in Simulation

Parameter	**HW1** (8-25 Hz, moderate amplitude)	**HW2** (2-125 Hz, spike)
Min HW amplitude (arb. units)	80	400
Hysteresis threshold (arb. units)	50	32
Min HW duration (ms)	16	0
HW count threshold (arb. units)	7 in 440 ms	4 in 1000 ms
Analysis window thresh.	8 of 8 windows	2 of 4 windows
Persistence (s)	1	1

Parameter	**LL1** (% threshold)	**LL2** (fixed threshold)
Short-term window (ms)	4096	4096
Long-term window (ms)	16384	16384
Sampling interval (ms)	4096	4096
Threshold	6.25%	40 units
Persistence (s)	1	1

Simulated detection tools, including an alpha/beta band half-wave detector **HW1**, a spike (half-wave) detector **HW2**, and line length detectors with percentage threshold **LL1** and fixed threshold **LL2**.

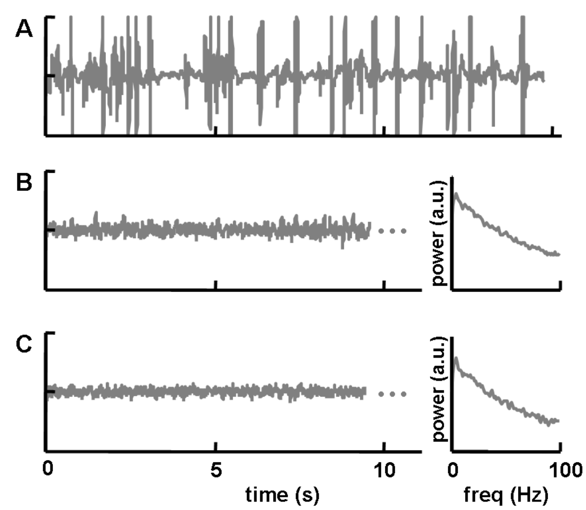

Fig. 2. Typical data for patient 1, including epileptiform activity recorded from hippocampus (A), the ECoG record and its power spectrum selected as a basis for noise generation (B and inset), and simulated broad-spectrum noise and its power spectrum (C and inset). Power spectra are in arbitrary units.

each patient, we identified an ECoG record believed to be characteristic of the patient's non- or less-epileptiform activity, insofar as possible in a system where all electrodes are placed near the focus. Noise segments used in the simulation were generated by taking the fast Fourier transform of the patient's exemplary non-epileptiform record, randomly shuffling phase values between frequency bins, and reconstituting a time-domain signal using the real component of the inverse fast Fourier transform. This shuffling and reconstitution was done 25 times, yielding 25 segments of individualized noise, for each patient.

Four detection tools, labeled HW1, HW2, LL1, and LL2, were chosen for simulation (Table I). Each detection tool was exemplary of its class, and each was an appropriate detector for interictal epileptiform activity in one of the three patients. Specifically, HW1 was a typical half-wave algorithm programmed to detect alpha- and beta- band oscillations, HW2 was a typical half-wave-based spike detector, and LL1 / LL2 were programmed to identify increases in line length compared to a 16-second-long trend. Detection parameters were adjusted to be fairly sensitive and to give similar detection rates for each detector (see Table II). Details regarding detector operation may be found in the references cited previously [24]-[26].

ECoG records for each of the three patients were passed through the detection tool appropriate to that patient to determine "baseline" (no added noise) detection behavior (Fig. 3). This yielded a list of time windows (with 128 ms granularity) at which the detection tool would either trigger (output = 1, indicating detection) or not (output = 0). Then,

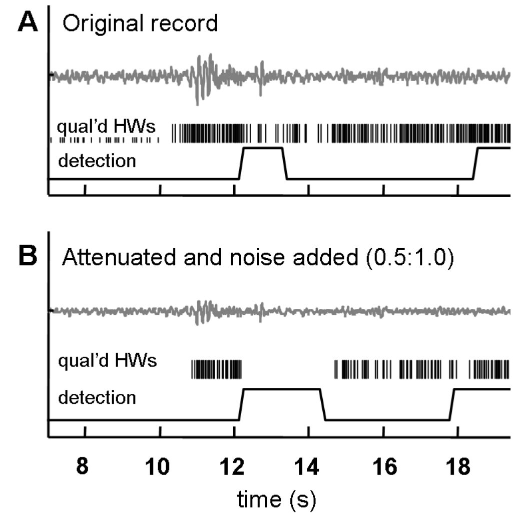

Fig. 3. Operation of alpha/beta detector **HW1**, including original ECoG record (A) and ECoG record with 50% attenuation and full-amplitude noise added and half-wave parameters adjusted appropriately (B). Some effect on qualified half-waves (black ticks below ECoGs) is apparent, but detection results (black traces, higher value indicates detection) are quite similar.

new records were created by additively combining individualized broad-spectrum noise segments with attenuated versions of the original ECoG records. Scaling factors used for original ECoG data and noise, respectively, were 0.9:0.2, 0.8:0.4, 0.7:0.6, 0.6:0.8, and 0.5:1.0. This was repeated 25 times for each ECoG record, applying each of the 25 noise segments in turn.

Finally, since tools HW1, HW2, and LL2 involve threshold parameters related to the absolute magnitude of ECoG features, these tools were re-run while appropriately scaling these parameters by the signal attenuation factor.

Similarity of detection output between the noise-added and baseline records was quantified (see below) and averaged across the multiple ECoGs and 25 noise segments to yield an overall value for each detection tool and each amount of noise.

TABLE II
STABILITY OF DETECTION TOOLS IN THE PRESENCE OF NOISE

	HW1	**HW1** scaled	**HW2**	**HW2** scaled
Initial detections per 30 sec in baseline data	3.13		2.32	
Signal : noise scaling factors				
0.9 : 0.2	0.75	0.93	0.84	0.96
0.8 : 0.4	0.60	0.87	0.70	0.93
0.7 : 0.6	0.46	0.83	0.52	0.90
0.6 : 0.8	0.32	0.77	0.33	0.85
0.5 : 1.0	0.19	0.64	0.21	0.81

	LL1	**LL2**	**LL2** scaled
Initial detections per 30 sec in baseline data	2.30	2.33	
Signal : noise scaling factors			
0.9 : 0.2	0.99	0.97	0.99
0.8 : 0.4	0.97	0.93	0.97
0.7 : 0.6	0.95	0.88	0.96
0.6 : 0.8	0.91	0.80	0.93
0.5 : 1.0	0.86	0.70	0.90

Values shown indicate the fraction of detections that are stable (see text); higher values indicate less change in detection compared to the no-added-noise case. "Initial detections" means the number of transitions from no-detection to detection.

III. RESULTS

Results are shown in Table II. Values in this table indicate the fraction of detections that remained stable in the presence of noise; specifically, the number of timepoints marked as "detections" in *both* the baseline *and* noise-added records, divided by the total number of timepoints marked as detections in *either* the baseline *or* noise-added records. Thus, values approaching 1 indicate similar detection behavior in the baseline and noise-added conditions, while values approaching 0 indicate dissimilar detection behavior.

As expected, before parameter scaling the half-wave detector **HW1** was most affected by the presence of broad-spectrum noise and by signal attenuation. Examination of intermediate results showed that attenuation of the original signal meant that half-waves due to alpha/beta band oscillations – already of moderate amplitude – were less likely to meet the amplitude and hysteresis criteria. In practice, however, the amplitude and hysteresis parameters can be adjusted to compensate for lower-amplitude signals, and when this rescaling was applied (see column for **HW1** scaled, Table II) detection was shown to be relatively stable. 64% of detection timepoints were identical to the baseline case, even in the worst case tested (50% signal attenuation and full-amplitude noise).

The spike detector **HW2** was less affected for low noise amplitudes, even without parameter adjustment. This is consistent with the fact that spikes are highly detectable events and a threshold can easily be set to distinguish them from broadband noise and background ECoG. However, increases in signal attenuation eventually mean that even large spike-related half-waves do not meet the amplitude criterion, so parameter adjustment is of value here as well. With appropriate scaling, 81% of detection timepoints were identical to the baseline case in the worst case tested.

The line length detector **LL1** was least affected by signal attenuation and moderate amounts of broadband noise; this is consistent with expectations for a detector using a percentage threshold and relatively long short-term window (4096 ms), since relative changes in line length will not be affected by attenuation, and brief fluctuations in noise characteristics will not affect even the short-term trend. 86% of detections were identical to baseline in the worst case tested.

Finally, before parameter scaling the line length detector **LL2** was moderately affected by the presence of large amounts of broadband noise, as expected for a detector using a fixed-value threshold. Appropriate parameter adjustment yielded a stable detector with 90% of detections identical to baseline in the worst case tested.

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