Real-time, Autonomous Bladder Event Classification and Closed-Loop Control from Single-Channel Pressure Data

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Abstract— **Urinary incontinence, or the loss of bladder control, is a debilitating condition affecting millions worldwide, which significantly reduces quality of life. Neuromodulation of lower urinary tract nerves can be used to treat sensations of urgency in many subjects, including those with Spinal Cord Injury (SCI). Event driven, or conditional stimulation has been investigated as a possible improvement to the state-of-the-art open-loop stimulation systems available today. However, this requires a robust, adaptive, and noise-tolerant method of classifying bladder function from real-time bladder pressure measurements. Context-Aware Thresholding (CAT) has been previously shown to work well on prerecorded single contraction urodynamic data. In this work, for the first time, we present real-time detection of multiple serial bladder contractions using urodynamic recordings from human subjects with SCI and Neurogenic Detrusor Overactivity (NDO). CAT demonstrated a high degree of accuracy and noise tolerance on prerecorded data from 15 human subjects, with a mean accuracy of 92% and average false positive rate of 0.3 false positives per contraction. Analysis of event detection latencies showed that CAT identified and responded to events 1.4 seconds faster than the original human experimenter. Finally, we present a case study in which CAT was used live for real-time autonomous, closed-loop bladder control in a single human subject with SCI and NDO, successfully inhibiting four consecutive unwanted bladder contractions and increasing bladder capacity by 40%.**

I. Introduction

Urinary incontinence, or the loss of bladder control, is one of the leading causes of morbidity following Spinal Cord Injury (SCI). It also leads to decreased quality of life [1] and high financial costs [2] for millions worldwide. Neuromodulation, including Genital Nerve Stimulation (GNS), can be used to artificially restore bladder control by applying patterned electrical stimulation to nerves that supply sensory input to the spinal circuits that control the lower urinary tract, inhibiting unwanted bladder contractions [3]. State-of-the-art neuromodulation devices, such as the Interstim (Medtronic, Minneapolis, MN) operate under an open-loop stimulation paradigm, where relatively low levels of stimulation are applied constantly, helping to reduce feelings of urgency in some subjects [4]. However, open loop, or *always-on* stimulation has several major disadvantages, including reduced battery and electrode life and the potential for habituation. The former translates to more frequent recharges and replacement electrodes, driving up the cost of this treatment modality, and the latter can result in the lower urinary tract nerves becoming desensitized to the stimulator, eventually requiring increased power to maintain treatment efficacy.

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Closed-loop, or *event-driven* stimulation has been shown to be at least as effective as open-loop stimulation [5], and has been investigated as an attractive alternative to mitigate issues of power consumption, electrode life, and habituation. In this case, stimulation occurs only when required, so this method has the potential to greatly increase the life of the stimulator battery and electrodes, while reducing the risk of habituation. However, to be viable, a closed-loop stimulator requires a means of determining in real time whether or not stimulation is required. For chronic monitoring and treatment systems, implantable pressure sensors under development may be used [6]. The ability to detect different events consequently enables the system to *respond* specifically to various bladder events, providing fine-grained control and individualized treatments. Furthermore, a high degree of noise tolerance is required, as is the ability to accurately discriminate among the various events visible in the sensor output, including pressure rises caused by movement (coughs, laughs, sneezes, etc.) or those caused by bladder contractions (both voiding and non-voiding). Finally, the system must be adaptive and flexible, able to classify events as they begin whether they occur seconds or hours apart.

Previous work in bladder event detection has demonstrated the feasibility of such a system, successfully discriminating between bladder contractions and motion artifacts using Context-Aware Thresholding (CAT) [7]. CAT is a parameterized, tunable framework for real-time classification of bladder events from a single bladder pressure sensor. Optimal tuning is achieved by maximizing the *Conditional Stimulation Score* (CSS), a metric which combines detection accuracy, false positive rate (FPR), and the effective stimulator duty cycle. CAT was previously tested on 64 clinical urodynamics recordings, each containing a single contraction event, and no stimulation was applied during data acquisition. In this work, we make the following novel contributions:

1) Design and implementation of a real-time, closed-loop neurostimulation system for autonomous bladder control using the CAT algorithm.
2) Retrospective analysis on multi-contraction recordings during which GNS was applied, demonstrating highly accurate, automatic event detection that is significantly faster than a human experimenter.
3) Successful demonstration, for the first time, of using CAT for autonomous, closed-loop bladder control in a human study participant, inhibiting numerous unwanted bladder contractions and significantly increasing bladder capacity.

Section II presents a brief overview of the CAT algorithm; Section III describes the dataset, data acquisition methodology, and the real-time hardware/software bladder event detection system. Section IV, provides results from the retrospective analysis of multi-contraction recordings using this system; Section V, presents the real-time, autonomous bladder control case study on a human

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subject; finally, Section VI concludes with future directions for the research.

II. Context-Aware Thresholding

Typical clinical urodynamics procedures require two separate catheter sensors, one measuring vesical pressure (P_{ves}) from the bladder, and the other measuring abdominal pressure (P_{abd}), usually with a rectal or vaginal catheter. The simultaneous difference $P_{ves} - P_{abd}$ yields detrusor pressure (P_{det}), which is the pressure generated independently by the bladder organ when contracting. CAT operates on vesical pressure only, which is highly desirable for subject comfort and clinical utility. However, this single-channel approach requires discrimination between increases in bladder pressure caused by the detrusor muscle (e.g. bladder contractions), and those caused by the abdominal muscles (e.g. coughs, laughs, or sneezes). To achieve this classification, a series of parameterized processing stages first filter out noise, then separate the abdominal and detrusor muscle contributions. Two separate adaptive thresholds operate on each signal independently, resulting in a classification of current bladder state. The *Smoothing*, *WindowSize*, and *Sensitivity* parameters can be adjusted to modify algorithm performance [7].

This system was previously implemented in Matlab (Mathworks, Natick, MA) to emulate a real-time environment. A total of 64 urodynamics recordings from 14 individuals with SCI and NDO were tested. CAT outperformed the other thresholding methods, achieving an accuracy of $96 \pm 2\%$ and a false positive rate of 9.2 ± 7.3 false positives per event using general parameters [7].

While the single contraction results were promising, it remained to be seen how the system would perform when presented with multiple contractions in series from an extended urodynamics recording during which conditional GNS had been manually applied. For example, a sliding window that was large enough to ensure a low false positive rate for single contraction recordings could be too long to detect multiple events in sequence. Additionally, if the algorithm detection latency is higher than the experimenter's, the algorithm may not be able to detect contractions before the manually triggered GNS inhibits them. Therefore, successful detection of events under these conditions would have far-reaching implications for the use of this technology beyond conditional stimulation for treatment. Potential applications include computer aided diagnostic systems for urologists, or a monitoring system that acts as a controlled method for testing the efficacy of pharmaceuticals designed to treat Over Active Bladder (OAB) or other lower urinary tract dysfunctions.

III. Methods

In this section, we describe the data acquisition and the system for real-time bladder pressure data processing.

A. Data Acquisition

Experiments were conducted at the Louis Stokes Cleveland VA Medical Center and approved by their Institutional Review Board. Fifteen male subjects with SCI and NDO, confirmed with urodynamics examinations, were included. A total of 58 trials from these subjects, testing manual stimulation on condition of a bladder contraction, were included in this analysis.

Data were collected during serial cystometrograms (CMGs) (Fig. 1). In the clinic, subjects lay on a padded testing table with a balloon catheter inserted into the rectum to measure abdominal pressure and a dual lumen intraurethral catheter inserted into the bladder to infuse saline for bladder filling and measure bladder pressure. In addition, two surface patch electrodes 2 cm in diameter (Natus, Middleton, WI) were applied to the dorsum of the penis approximately 3 cm apart and connected to a stimulator (DS7A, Digitimer, Welwyn Garden City, UK). Bladder and abdominal pressure signals, as well as the stimulation trigger signal and saline infusion, were recorded via a data acquisition system (Labview SC-2345) and custom LabVIEW software (National Instruments, Austin, TX).

Subjects' bladders were filled at a rate of 50 mL/min. Bladder contractions were defined as a precipitous rise in bladder pressure 10 cmH_2O over the baseline. When the experimenter identified a bladder contraction, GNS was applied to inhibit bladder activity and reduce bladder pressure. Alternatively, if the subject reported strong feelings of bladder urgency, stimulation was applied to reduce those feelings of urgency. GNS was applied as biphasic, cathodic-leading square-wave pulses delivered at 20 Hz with a leading pulse width of 0.2 ms. Effective and comfortable stimulation settings were determined for each subject.

B. Real-Time Processing

In order to analyze the full-speed performance of automated closed-loop GNS on these recordings, a custom hardware/software platform was developed. It was designed such that it could be used both with prerecorded data and during a real-time experiment.

1) Hardware: A custom CAT module was designed to plug into the expansion slots within a National Instruments SC-2345 DAQ unit to provide software/hardware compatibility with the Labview software (Fig. 1). The module consisted of a low-power Freescale K20 microcontroller, status LEDs, and a 3.3 V linear regulator. A USB connector permitted microcontroller programming and serial communication of algorithm status during operation. Vesical pressure data were sent to the CAT module via an analog output channel of the DAQ and acquired by the K20 using an onboard, 12-bit analog-to-digital converter. Pressure data were scaled by Labview before analog output such that pressures ranging from 0-100 cmH_2O produced voltages from 0-3 V at the CAT module. The CAT module was also wired to the trigger input of the neurostimualtor to directly control when stimulation was applied. An analog input channel of the DAQ measured the stimulator status, so that stimulation was logged synchronously.

The hardware platform remained the same for offline simulations using pre-recorded data and real-time closed-loop stimulation studies. In offline simulations, recordings were loaded into Labview and pressures were scaled as previously described. Data were then played back in real-time through a DAQ analog output channel for processing by the CAT module. The CAT module triggered the stimulator as if it were connected to a subject, and corresponding stimulation triggers were recorded by Labview. In real-time experiments, vesical bladder pressures were immediately sent to the CAT module after acquisition into Labview, and the real-time CAT algorithm continuously monitored pressure signals to determine when to trigger GNS.

2) Software: The software flow is shown in Fig. 2. Pressure data were sampled at 10 Hz using a high precision interval timer. New samples were passed directly to the EMA filter, and the output was enqueued to a custom data structure implementing a fixed-size queue. When sufficient samples were acquired (as defined by the *WindowSize*), an array copy of the structure was obtained for use in a custom *db2* lifting wavelet implementation [8]. This routine operates on the data in-place, efficiently interleaving the computations for the approximation and detail coefficients.

Results were saved to two instances of a *SortedList* structure, which maintained a linked list sorted by value in ascending order for both sets of coefficients. Due to the downsampling operation in

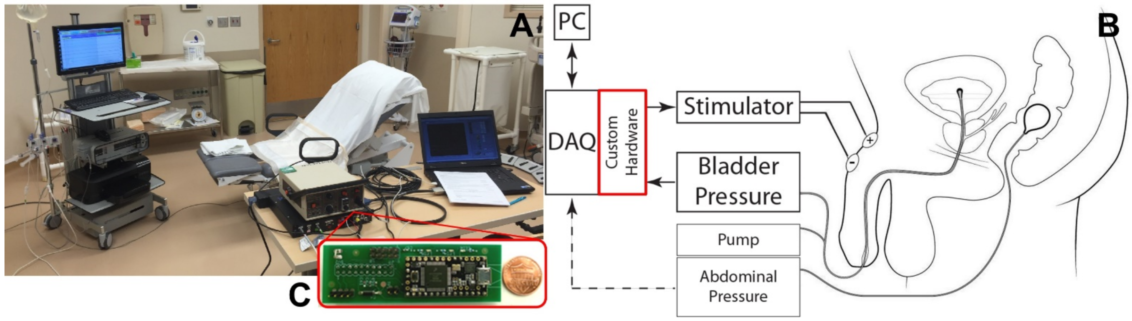

Fig. 1. Acute Urodynamics and Closed-Loop GNS Setup: (A, left) Urodynamics is conducted using a clinical system (left) with the subject sitting on a bed. Equipment (right, foreground) acquire data in parallel with the clinical system without additional catheters. (B) Urethral and anal catheters measure bladder and abdominal pressures while a pump infuses saline into the bladder. A computer (PC) communicates with data acquisition (DAQ) to acquire bladder and abdominal pressure signals. Custom hardware (C) running our detection algorithm analyzes bladder pressure data continuously and triggers the stimulator when it detects a bladder contraction. The stimulator provides electrical stimulation to surface electrodes placed on the dorsum of the penis, targeting the genital nerves.

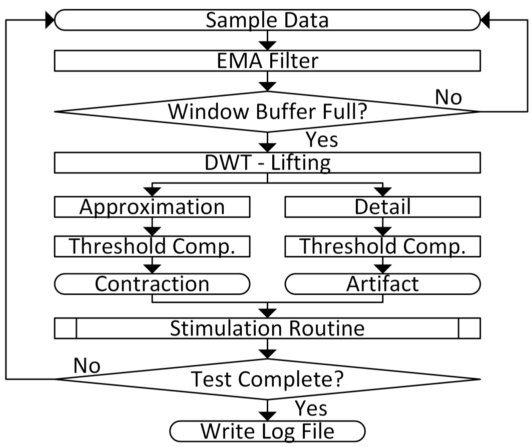

Fig. 2. Context-Aware Thresholding software flow, as implemented for the real-time analysis platform.

each stage of the transform, the number of elements was reduced by 2^L, where L is the number of transform levels, reducing the time complexity of the following processing stages. The individual thresholds were computed as percentiles using the *SortedList* structures and the *Sensitivity* parameters. Finally, the output was used to control the stimulation routine.

IV. Results with Prerecorded Data

Using the dataset and platform described in Section III, we obtained algorithm stimulation signals using the same, general parameters for all subjects to observe the untuned algorithm performance on multi-contraction data (Table I). Algorithm signal event detections were successful when one of the following conditions were met: detection within 5 seconds before, or 1 second after, the manual stimulation start time, or after a precipitous rise in bladder pressure 10 cmH_2O over the baseline. Note that the manual trigger did not represent contraction onset, but rather a time at which GNS successfully inhibited an unwanted contraction. Therefore, the first case dealt with the fact that early detection is beneficial, but late detection is increasingly likely to result in unsuccessful contraction inhibition, despite stimulation. The latter case dealt with situations where manual stimulation was left ON during multiple subsequent events, and therefore could not be used to define target detection times. False positives were counted when they occurred more than 5 seconds prior to any contraction event.

TABLE I
CAT Results Per-Subject with Untuned General Parameters
(F_c = 0.11 Hz, *WindowSize* = 160, *Sensitivity* = 90%)
(Standard Deviation Shown)

Subject ID	# Trials	# Events	Acc. (%)	FPR
1	7	30	100	1.0
2	2	17	88	0.1
3	2	6	100	0.2
4	4	24	96	0.2
5	4	24	88	0.3
6	2	12	100	0.2
7	4	16	94	0.1
8	6	22	82	0.4
9	10	92	91	0.4
10	2	10	90	0.5
11	3	9	89	0.1
12	1	3	100	0.0
13	1	4	75	0.3
14	3	17	94	0.2
15	7	43	93	0.2
		Avg.	**92±7%**	**0.3±0.2**

Several examples of event detection on prerecorded data are shown in Fig. 3, and results using general parameters are shown per-subject in Table I. A total of 329 events are present in the dataset. The average per-subject detection rate was $92 \pm 7\%$, with an average FPR of 0.3 ± 0.2 per contraction in a given recording. As sensations of urgency were not necessarily reflected in the vesical pressure, they could not detected by the algorithm.

Retrospectively, we estimated the event onset times, which enabled us to measure both the experimenter reaction latencies and the algorithm detection latencies, with medians and standard deviations of 6.0 ± 2.0 s and 4.6 ± 2.2 s, respectively. The CAT algorithm detection latencies were significantly less than the experimenter reaction latencies (Wilcoxon signed-rank test, $N = 161$, $p < 0.001$). For the same events, the algorithm detected and responded before the experimenter. Despite experimenter?s longer response latency, experimenter-triggered stimulation was successful. Therefore, the CAT algorithm latency does not have to be minimized in favor of modifying parameters to reduce the false positive rate. Indeed, this trend may arise naturally as an outcome of subject-specific parameter tuning.

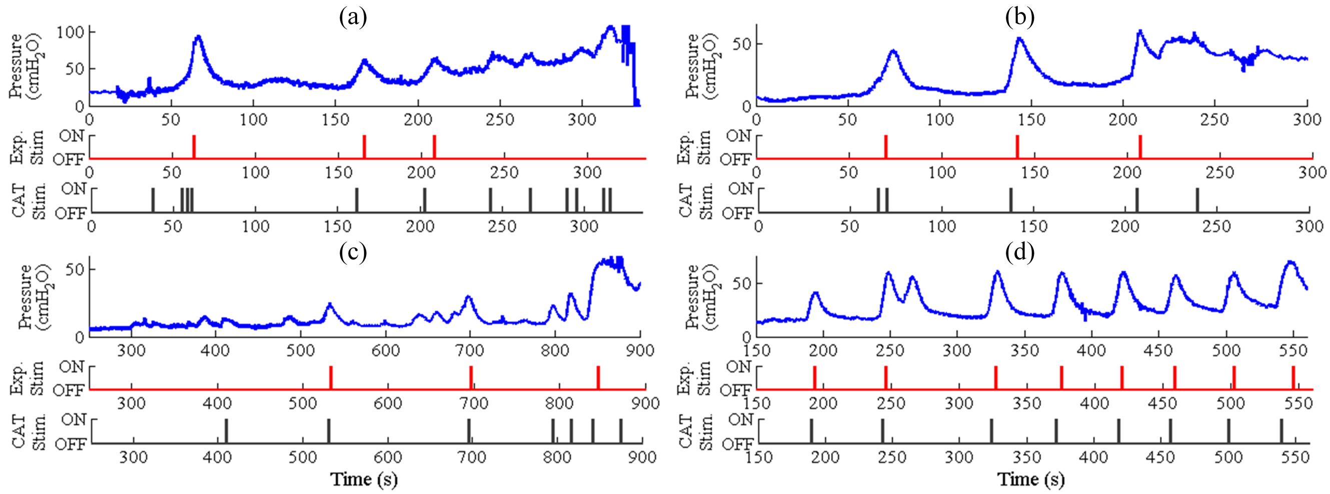

Fig. 3. Example outputs showing original pressure and both the manual (Exp Stim) and algorithm (CAT Stim) signals indicating detection of contraction onset. CAT generally detects contractions before manual stimulation begins, and very soon after contraction onset despite sensor noise and artifacts.

V. Real-Time, Autonomous Bladder Control

This system was employed for a case study using catheter-based bladder measurements to demonstrate the feasibility of automated closed-loop GNS in a 62 year old human subject with SCI and NDO. This subject experiences sensations of bladder urgency, which often results in urinary leakage. Data were collected in a single urodynamics session involving 6 CMGs (Fig. 1). The first CMG was conducted without stimulation to confirm NDO. Subsequent CMGs were conducted with or without closed-loop GNS. The real-time CAT algorithm monitored only the vesical pressure and determined when to apply stimulation without experimenter input. CAT-controlled closed-loop GNS inhibited the unwanted bladder contractions and significantly increased bladder capacity, from 320 ± 78 ml to 520 ± 91 ml (Fig. 4).

Stimulation typically lasted for 3 s, usually turning on and off twice within that duration. The subject reported that feelings of urgency vanished immediately after stimulation and that the sudden stimulation onset was not painful or disturbing. It is important to note that successful closed-loop GNS was achieved with only bladder pressure data, and that abdominal pressure data were not required. This is contrary to the standard urodynamics practice of using multiple sensors to derive detrusor pressure. It remains to be seen whether modifying one or more of the parameters or adjusting the tuning for multi-contraction data may have resulted in fewer false positives or faster and more accurate event detection [7].

VI. Conclusion

In this work, we have shown that CAT is capable of identifying multiple sequential contractions in a urodynamics experiment using only intravesical pressure. Because it can detect both isolated contractions and multiple serial contractions, CAT can be used for automated long-term urodynamic data analysis. This has diverse applications, including use as a diagnostic aid for urologists, or as a controlled method for testing the efficacy of pharmaceutical treatments for urinary incontinence. In future work, we will test the algorithm using tuned parameters to determine the effect of tuning on the accuracy and false positive rates in multi-contraction data. We will also conduct additional real-time testing of the closed-loop GNS system to investigate the tuning sensitivity and robustness to noise. Finally, we will design custom hardware implementing this algorithm for use in an ultra low-power implant device.

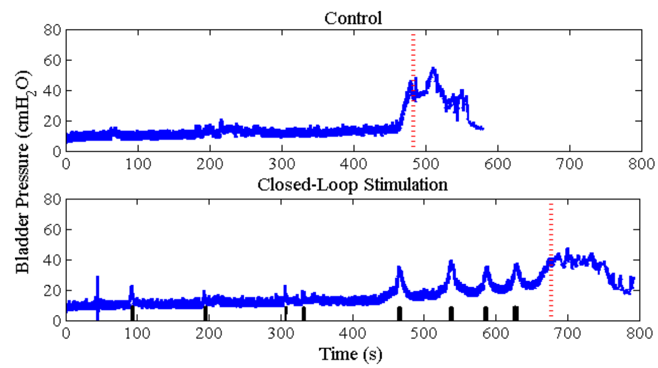

Fig. 4. Autonomous, closed-loop GNS inhibited bladder activity and increased bladder capacity. (A) A hyper-reflexic contraction occurred at 480 seconds after 400 mL of saline was infused into the bladder, resulting in urine leakage (long vertical dashed line). (B) Automatic conditional GNS controlled by CAT (short vertical lines) increased bladder capacity by 40% after inhibiting 4 unwanted contractions in this example.

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