An Implantable Sacral Nerve Root Recording and Stimulation System for Micturition Function Restoration

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SUMMARY This paper provides a prototype neural prosthesis system dedicated to restoring continence and micturition function for patients with lower urinary tract diseases, such as detrusor hyperreflexia and detrusor-sphincter dyssynergia. This system consists of an ultra low-noise electronic neuronogram (ENG) signal recording module, a bi-phasic electrical stimulator module and a control unit for closed-loop bladder monitoring and controlling. In order to record extremely weak ENG signal from extracellular sacral nerve roots, the system provides a programmable gain from 80 dB to 117 dB. By combining of advantages of commercial-off-the-shelf (COTS) electronics and custom designed IC, the recording front-end acquires a fairly low input-referred noise (IRN) of 0.69 μVrms under 300 Hz to 3 kHz and high area-efficiency. An on-chip multi-steps single slope analog-to-digital converter (ADC) is used to digitize the ENG signals at sampling rate of 10 kSPS and achieves an effective number of bits (ENOB) of 12.5. A bi-phasic current stimulus generator with wide voltage supply range (±0.9 V to ±12.5 V) and variable output current amplitude (0-500 μA) is introduced to overcome patient-dependent impedance between electrode and tissue electrolyte. The total power consumption of the entire system is 5.61 mW. Recording and stimulation function of this system is switched by control unit with time division multiplexing strategy. The functionality of this proposed prototype system has been successfully verified through in-vivo experiments from dogs extracellular sacral nerve roots.

key words: neural prosthesis, functional electrical stimulation, closed-loop bladder control, acute animal experiment, spinal cord injury

1. Introduction

The lower urinary tract has two main functions: the accumulation (continence) and the elimination (micturition) of urine [1]. Spinal cord injury (SCI) and other neurological disorders could cause lower urinary tract symptoms, such as detrusor hyperreflexia (DH) and detrusor-sphincter dyssynergia (DSD). DH is characterized by involuntary reflex detrusor contractions at relatively small urine volume in bladder and results in pathological intravesical pressure. Detrusor-sphincter dyssynergia, also known as bladder-sphincter dyssynergia, is a disorder of the detrusor muscles and the external urethral sphincter muscles. As the symptom of DSD, the urethral sphincter muscle, instead of relaxing completely during urine voiding, dysynergically contracts causing the urine flow to be interrupted and the bladder pressure to rise. Without proper treatment, these two pathological symptoms will cause urinary incontinence, retention, frequent urinary tract infections, renal damage and bladder hypertrophy. Medication is the most commonly used treatment of DH. Surgical augmentation and surgical deafferentation of the bladder are also advocated. But pharmacological and destructive treatments are often unsuccessful and limited due to kinds of side effects [2]–[4]. Urinary catheterization is used to reduce the high bladder pressure caused by DSD. However, patients with ongoing DSD may require continued intermittent self-catheterization which seriously diminishes the quality of life.

Previous clinical experiments as well as animal validation showed that functional electrical stimulation (FES) with selective waveform in specific locations could excite and inhibit detrusor and urethral sphincter [5]–[10]. Great efforts have been done to investigate FES devices in order to control the bladder in paraplegic and quadriplegic individuals. Such devices are still imperfect due to the lack of information about the bladder status, for example, the bladder pressure [11]. Previously, the patients had to empty their bladder at regular intervals, which is discommodious. Consequently, closed-loop feedback system with the ability to monitor the bladder volume and to trigger stimulation is needed. Currently known methods of monitoring the bladder volume change include ultrasound devices, pressure sensors located in the bladder wall [12], [13], body impedance measurement [14], recording electromyogram (EMG) of external urethral sphincter [15], and tracing the bladder activities through its neural pathway [1], [7], [11], [16]. Each one of these techniques has its drawbacks, such as artifacts caused by movements impacting the sensors, electrodes migration and irritation to bladder. In this study, we detect the detrusor contractions and estimate the bladder pressure from recording ENG because the stimulation could be delivered to the nerve in adjacent or same locations. This would allow us to combine FES stimulator and ENG recording circuit into one custom system, and then implant in a single surgery.

Figure 1 shows partial innervation of the detrusor and the urethral sphincter. Three conventional recording sites which could also be used as stimulation locations: sacral nerve roots, pudendal nerves (PN) and pelvic nerves are illustrated in this graph. Many studies demonstrate that ENG signal of all these sites could be used to detect bladder contractions. Boyer [5] demonstrated that detrusor and external urethral sphincter contractions could be inhibited or ex-

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cited respectively by performing stimulation with different amplitudes, pulse widths and frequencies in sacral nerve roots. In contrast, pudendal nerves and pelvic nerves are only innervating detrusor or sphincter, respectively. Which are not appropriate electrode sites for neural prosthesis, as the separation of stimulus and recording positions will lead to additional surgical process. Therefore, we chose sacral nerve root as recording/stimulation sites of our custom implantable neural prosthesis.

Several studies using commercial-off-the-shelf (COTS) electronics or custom integrated circuit (IC) to implement neural interface have been presented [17]–[23], although none of them covered closed-loop control research. The use of COTS electronics is a low-cost, low-noise and easily modified solution. Custom designed ICs, on the contrary, enable the realization of low power consumption device with small size, which is more suitable for chronic implantation. To combine these two approaches’ advantages, we use COTS electronics as a supplement to IC to implement the neural prosthesis system. Consequently, this work represents a useful compromise, in terms of dimensions and capabilities, between the IC and COTS solutions.

In this paper, a sacral nerve root recording and electrical stimulation implantable system is presented. this neural prosthesis system is capable of accomplishing the task of: 1) Acquisition of neural signals from sacral nerve roots; 2) Detecting the contractions of detrusor and estimating bladder pressure from the signals; 3) Generating stimulation signals to control detrusor and the external urethral sphincter according to the bladder status. The core of implantable system is a custom IC designed and fabricated in 0.18-μm CMOS (complementary metal oxide semi-conductor) 1P6M Mix-signal process, with a 1.8 V voltage supply. Compared with traditional stimulation or recording system, the present prototype is also powered by transcutaneous inductive link, but requires no external controller and high-speed information transmission. Moreover, our system is realized by both IC and COTS electronics. Therefore, the proposed neural prosthesis system has advantages in small size, low noise, low power consumption and high flexibility.

![Fig. 1](image_url) Possible recording and stimulation sites.

![Fig. 2](image_url) (a) Architecture of the neural prosthesis system; (b) block diagram of the custom designed IC.

### 2. Overall System Design

The architecture of the neural prosthesis system is shown in Fig. 2 (a), which consists of a custom designed IC chip and several function modules implemented by discrete components. Figures 2 (b) shows block diagram of the IC. The recording pathway contains a fully differential input preamplifier module, followed by a band-pass filter to suppress high frequency noise and baseline drift. The neural signals after pre-amplification are fed to the IC, which consists of 8 alternating current (AC) coupled fully differential secondary amplifiers with tunable low cut-off frequency, an analog time-division multiplexer (MUX), a sample-and-hold (S&H) stage with configurable and a 16-bit differential-inputs multi-steps single slope analog-to-digital converter (ADC).

The neural activity of sacral nerve, which is essentially a kind of extracellular peripheral nervous system (PNS), lies in frequency range of 500 Hz to 7 kHz, peaking at about 2kHz, and the peak-to-peak amplitude of the spikes is about several microvolts [24]. The electrode noise and biological noise mainly from electromyography (EMG) make the overall signal to noise ratio (SNR) very poor. Further, the recording circuit has to account the electrode-electrolyte interface generates direct current (DC) offset and the high impedance of the electrode.

According to the characters of ENG signal, the recording circuit of proposed system provides a gain of 80-115 dB and a frequency bandwidth between 300 Hz to 3 kHz [7],
The gain has been distributed through the neural signal recording pathway, which includes: preamplifier, band-pass filter, secondary amplifier and sample-and-hold stage with configurable gain. The preamplifier cell provides a gain of 10 dB and band-pass filters offer 30 dB. The rest gain will be accomplished by the custom IC. In this way, it could prevent the amplifier saturation caused by high-frequency noise or baseline drift and filter out tampering components of the signal before fully amplifying them. Reduction of input-referred noise (IRN) is realized by allocation small gain (10 dB) at the first stage of the system. The ADC digitizes signals at 10 kSPS sampling rate in order to avoid aliasing (higher than the Nyquist rate for 3 kHz bandwidth) and to satisfy low-power specification of the design. Communication between the IC and control unit is accomplished by using a custom serial interface.

The cathode-leading, charge balanced bi-phasic current pulses with variable amplitude, frequency and pulse width could elicit different muscle reflexes. As a matter of fact, stimulations with mono-phasic lead to charge accumulation at the electrode site and can damage the tissue [25]. The stimulation module in our system generates bi-phasic current pulses (100-300 μs pulse width) at variable amplitude (0-500 μA) and frequency for detrusor/sphincter excitation or inhibition (detrusor: 3-15 Hz for inhibition and 20-33 Hz for excitation; urethral sphincter: 600 Hz for inhibition) [5], [9], [26].

The proposed system supports two control modes: open-loop control for intraoperative application and closed-loop control for implantable application. In the open loop mode, the recorded ENG signals are transferred to instruments outside the body. After processing and analysis of these signals, stimulus pulses will be generated trying to control the bladder. This mode is designed to study the relationship between recording signals and bladder pressure, as well as the detrusors and urethral sphincters responses to various electrical stimulation. The open-loop mode enables evaluating the circuitry performance with bench test and the functionality with in vivo test. In the closed-loop mode, on the contrary, the recording pathway converts the sacral nerve activity into digital signals and transmits these signals to control unit. According to the ENG signals, control unit could determine the bladder status with specific algorithm and make the stimulation module generate FES variable parameters. Closed-loop bladder control will be achieved with the muscles excitement or inhibition by these FES. This mode is suitable for chronic implant and clinical applications.

To avoid artifact issue caused by stimulating, we employ time-division strategy in our system. Specifically, the nerve signal recording path will be blocked during and after the stimulation. This function is simply realized by inserting an analog switch between the recording electrodes and the preamplifier module. It is obvious that the time-division strategy will reduce the sensitivity of closed-loop control. But considering the specific application of our system is bladder function restoration, which needs long-time bladder volume monitoring and occasional FES, this strategy could well satisfy the system requirement.

3. System Implementation

3.1 Preamplifier and Filter Module

The preamplifier and filter module consists of a preamplifier block and a band-pass filter block. The principle circuit diagram of front-end of the recording pathway is shown in Fig. 3.

A precision instrumentation amplifier (Texas Instruments, INA333) offering excellent accuracy with a low noise density (50nV/√Hz) and CMOS operational amplifiers (Texas Instruments, OPA330) which use auto-calibration technique to provide low offset voltage have been employed to implement the circuit.

3.2 Custom Integrated Circuit

3.2.1 AC-Coupled Amplifier

The schematic of the present AC-coupled amplifier is shown in Fig. 4 (a). It is based on operational transconductance amplifier (OTA) and T-capacitor feedback network topology [27]. Common-mode feedback (CMFB) module is employed to retain the DC level of V_on and V_off in this circuit. Figure 4 (b) shows the schematic of OTA1.

The T-capacitor feedback network has equivalent capacitance C_eq, where C_eq = (C_2*C_3)/(C_2 + C_3 + C_4). And the midband gain of the amplifier (A_v) is set to A_v = C_1/C_eq.

The pMOS transistors M1 and M2 controlled by V_res operate in subthreshold condition as a tunable pseudo re-
Fig. 4  Schematic of the AC-coupled amplifier; (b) schematic of the OTA1.

resistor in the feedback network [28]. The equivalent resistor $R_{eq}$ controlled by $V_{res}$, and $C_{eq}$ determine the high-pass pole $f_{HP}$ of the amplifier. Which is $f_{HP} = \frac{1}{2\pi R_{eq} C_{eq}}$. The range of the $V_{res}$ is 0.6 V to 1.6 V, makes the $R_{eq}$ vary from $10^9$ Ω to $10^{13}$ Ω. Therefore, $f_{HP}$ varies between 0.1 Hz and about 300 Hz.

3.2.2 Sample-and-Hold Stage

Programmable gain is significant in our system since the recorded ENG signals character in terms of amplitude is patient and electrode dependent. The sample-and-hold stage circuit with tunable gain was first described in [29], as shown in Fig. 5. A programmable gain ($1/2$, 2, 8 and 32 times) is achieved by the ratio of $A_1$ and $A_2$. In order to calibrate the input offset, a switch-capacitor (SC) chopper network is introduced. To satisfy the requirement of analog-to-digital converter, a level-shifter based on SC network is used to shift the output voltage range to $V_{dd}/2 - V_{dd}$ by injecting a constant amount of charge from level-shifter capacitor $C_{LS}$ to feedback capacitor $C_2$.

3.2.3 Analog-to-Digital Converter

A 16-bit multi-steps single slope ADC is used here to digitize the ENG signal from the sample-and-hold stage, which works similarly to the report voltage-pulse converter [30]. The block diagram in Fig. 6 shows the basic architecture of the ADC, which consists of a sample/hold circuit, a 4-bit quantizer and a $2^4$ residue amplifier. In this paper, FSR means full scale range.

The algorithm of this ADC is illustrated in Fig. 7. There are four phases in one completer measurement cycle. Each phase includes several steps which could be described as follows:

Step 1. The input signal (phase 0) or the amplified residue (phase 1 to phase 3) is sampled as $y_m(0)$, $m = 0,1,2,3$.

Step 2. $y_m(0)$ is subtracted by a constant $\Delta$, where $\Delta = \frac{FSR}{2^4}$. This subtraction operation stops when

$$y_m(n_m + 1) = y_m(n_m) - \Delta < 0 \quad (1)$$

Then the signal $y_m(0)$ is transformed into a 4-bit binary number $n_m$.

Step 3. In the next clock period, the residue of the ramp-down operation $r_m$ could be acquire by add $\Delta$ to $y_m(n_m + 1)$, which is

$$r_m = y_m(0) - n_m \times \Delta = y_m(n_m + 1) + \Delta \quad (2)$$

And the residue of this phase will be amplified by $2^4$ times. The amplified residue will be sampled and feedback to the quantizer for the next phase. This could be expressed as
\( y_{m+1}(0) = 4^4 \times r_m, \quad (m = 0, 1, 2) \) \hspace{1cm} (3)

Step 4. Because of the output hysteresis of the comparator, wrong operation may occur when \( y_m(n_m + 1) \) is slightly smaller than 0, as shown in phase 1 of Fig. 7 (where \( m = 1 \)). This wrong rollover of the comparator results in longer ramp-down operation, which means the subtraction operation stops at \( y_m(n_m + 2) \) instead of \( y_m(n_m + 1) \), and the amplified residue of this phase \( 4^4 \times r_m \) is negative. To rectify this error, we introduce a calibration step in our algorithm. If \( 2^4 \times r_m \) is smaller than 0, the input of the quantizer of the next phase will be calibrated to:

\[
\begin{align*}
    y_{m+1}(0) &= 4^4 \times (r_m + \Delta) \\
    &= 4^4 \times r_m + 4^4 \times \Delta \\
    &= 4^4 \times r_m + \text{FSR}
\end{align*}
\] \hspace{1cm} (4)

The binary number \( n_m \) should be corrected by minus one.

By repeating this steps for four phase, 16-bit binary ADC output from the most to the least significant bits, could be acquired from the single-line digital output of the quantized \( n_m \) (\( m = 0, 1, 2, 3 \)).

The detailed schematic of the proposed ADC is illustrated in Fig. 8. The OTA2-OTA6 employ a folded cascade structure with gain-booster. The open-loop gain of these OTA is larger than 100 dB under a 1.8 V supply.

3.3 Stimulation Module

Figure 9 shows detailed schematic of the stimulation module. An operational amplifier and a PNP bipolar junction transistor (BJT) form a negative feedback system, which steadies the voltage across \( R_s \). Therefore, a referenced current \( I_{\text{ref}} \) is given by

\[
I_{\text{ref}} = \frac{V_{cc} \cdot R_a}{(R_a + R_b) \cdot R_s}
\] \hspace{1cm} (5)

A 4-bit controllable current \( I_{\text{sum}} \) is generated by four groups of current mirrors, which is...
Fig. 9 (a) Current reference $I_{\text{ref}}$; (b) 4-bit controllable current $I_{\text{sum}}$; (c) schematic of the bi-phasic stimulus current generator.

Fig. 10 Sequence diagram of $I_{\text{out}}$

$$I_{\text{sum}} = \sum_{i=1}^{4} S_i \cdot I_i$$

where $I_i = (I_{\text{ref}} \cdot R_0)/R_i$, and $S_i = 1$ or 0.

The bi-phasic stimulus current $I_{\text{out}}$ is formed based on the $I_{\text{sum}}$ and three switches controlled by the FPGA, as is shown in Fig. 10. The anodic and cathodic current path is alternately turned on by switch signals $S_p$ and $S_n$. To prevent the tissues damage caused by charge accumulation on the interface of the electrode and tissue electrolyte, a charge cancellation is needed. This is realized by a charge reduction switch $S_z$. During the interval of stimulation pulses, the charge reduction switch forms a path from the electrode to $V_{\text{cc}}/2$. The accumulated charge on the electrode will be discharged safely.

4. Experiment Results

Figure 11 shows the photography of the fabricated prototype system, which is made of polyimide (PI) flexible printed circuit board (PCB). The shape of the flexible PCB is carefully designed to suit the long-term implantation. Polymerized siloxanes shell is also used to encapsulate this system according to the biocompatible and hermetic consideration. Recording and stimulation electrodes are integrated in the system, as the polyimide thin-film could also be the substrate of flexible belt electrode [31]. The indifferent electrode in Fig. 11 is also shown in Fig. 2 (a) and Fig. 3 (a). This electrode is usually taken as a reference potential in recording circuit. In our system, it is placed at a site remote from the source of recorded activity, and its potential is set to $1/2$ supply voltage. As mentioned above, the substrate of the recording and stimulating electrodes is flexible polyimide (PI). The recording and stimulating sites are gilded to enhance its electrochemical stability. The contact impedances of the electrodes ranges between $2.3 \, \text{k}\Omega$ and $3 \, \text{k}\Omega$ (mean $2720 \, \text{\Omega}$) at $1 \, \text{kHz}$. The total weight of the system is $9.9 \, \text{g}$ ($2.1 \, \text{g}$ without polymerized siloxanes shell).

The micrograph and package of the custom IC is presented in Fig. 12, which is designed and fabricated in UMC $0.18-\mu\text{m}$ CMOS process. The area of the chip is $1.6 \times 1.6 \, \text{mm}^2$ with pads. The fabricated system is subjected to bench tests to evaluate the important electrical characteristics and performance, such as power consumption, input referred noise (IRN) and signal-to-noise and spurious-free dynamic range (SFDR). In-vivo experiment results are also proposed to demonstrate the functionality of the system.
4.1 Bench Test

4.1.1 Amplifiers and Filters

The measured frequency response (dynamic signal analyzer 35670A, Agilent) of the amplifiers (preamplifier and secondary amplifier) is illustrated in Fig. 13. Preamplifier and band-pass filter module has a midband gain of 39.7 dB. The secondary amplifier of custom IC achieves a midband gain of 47 dB with the configurable low cut-off frequency $f_{HP}$ (0.1 Hz to 310 Hz). Therefore, the overall midband gain without S&H stage is 86.7 dB with the pass band from 300 Hz to 3 kHz. The power consumption of this analog front-end is 1.98 mW (DC power analyzer N6705B, Agilent).

Figure 14 shows the input-referred noise (IRN) spectral density curve of the prototype system (35670A, Agilent). The root mean square value of IRN could be calculated by integrating the input-referred noise spectral density curve from 10 Hz to 5 kHz except the 50 Hz point, which is 1.86 $\mu$V$_{rms}$. When it comes to the pass band of our system, 300Hz to 3 kHz, the IRN is low to 0.69 $\mu$V$_{rms}$. The given IRN value has been measured from the fabricated system in an electromagnet shield room.

4.1.2 Analog-to-Digital Converter

For dynamic performance measurements, a 1 kHz sinusoidal wave (arbitrary signal generator 33250A, Agilent) is applied to the ADC. $2^{15}$ sample points has been applied to fast Fourier transform (FFT) analysis. Figure 15 illustrated the measured power spectral density curve under the sample frequency of 6.25 kS/s. The spurious-free dynamic range (SFDR) calculated from this curve is 69.14 dBc. As the input sinusoidal wave is not full-scale signal (200 mV$_{pp}$), the effective number of bits (ENOB) could be calculated by the measured signal to noise and distortion ratio (SINAD$_{measured}$), which is

$$\text{ENOB} = \frac{\text{SINAD}_{measured} - 1.76 + 20 \log(FA/IA)}{6.02}$$

(7)

where FA is full scale amplitude of ADC’s input and IA means actual input signal amplitude. The result of bench test shows that the SINAD$_{measured}$ is 57.8 dB, which corresponds to an ENOB of 12.5. In addition, the current consumption of the proposed ADC is 85 $\mu$A under 1.8 V voltage supply, which achieves a power consumption of 153 $\mu$W.
4.1.3 Stimulation Module

The stimulation waveform (mixed signal oscilloscope MSO-X 3034A, Agilent) generated by the proposed system is shown in Fig. 16. The parameters of the waveform in Fig. 16(a) include: amplitude $I = 100 \mu A$, pulse widths $t_p = t_n = 150 \mu s$, pulse delay $t_d = 150 \mu s$ and frequencies $f = 600$ Hz. Figure 16(b) shows an alternative configuration: amplitude $I = 200 \mu A$, pulse widths $t_p = t_n = 300 \mu s$, pulse delay $t_d = 150 \mu s$ and frequencies $f = 30$ Hz. The quiescent power consumption of this module is measured when no control signal is applied to the circuit, which is 2.31 mW.

4.2 In-vivo Test

Acute animal experiments were performed on adult Beagles to demonstrate the functionality of our design. All animal care and experimental procedures were performed in the department of laboratory animal science at Peking University Health Science Center and Peking University People’s Hospital. All efforts were made to minimize animal suffering.

Figure 17 shows the experimental setup and the in-vivo experiment. Intact adult male dogs ($n=5$, 7.8-10 kg) are anesthetized with pentobarbital sodium (Nembutal, 2.5%). Urinary catheterization with ureter ligated is executed to ensure bladder voiding.

Experiments begin with urodynamic evaluation by inserting a transurethral urethral catheter (dual-lumen, 6 Fr=1.91 mm) into the bladder. The intravesical pressure ($P_{ves}$) is recorded through one lumen of this catheter, which was connected to a solid state pressure transducer of an uro-
dynamic analyzer (Nidoc-970A, Wearnes UEST New Tech). Bladder infusion through the other lumen of the bladder catheter is performed by using a syringe pump of this urodynamic analyzer. Besides, a single-lumen 5 Fr (1.60 mm) catheter is placed through the anus and held in rectum (not be shown in Fig. 17). This catheter is also connected to solid state pressure transducer and used to recorded the abdominal pressure (P_{abdominal}). By monitoring intravesical pressure (P_{ves}) and abdominal pressure (P_{abdominal}), we could calculate detrusor pressure (P_{det}), which is given as P_{det} = P_{ves} - P_{abdominal}.

A limited sacral laminectomy (L7-S3) is performed to expose the extradural sacral nerve roots (S1-S3). After identification of S1-S3 by their anatomical arrangement, recording and stimulation electrodes are placed unilaterally around the S1 or S2 extradural roots. All this procedure is carried out under aseptic techniques. To maintain deep anesthesia, electrocardiogram (ECG) as well as blood pressure are continuously monitored during all experiments.

The bladder is voided and slow filled with room temperature saline (0.9%, 29.8 ml/min) until the onset of hyperreflexia-like bladder contractions are observed by the urodynamic analyzer. To demonstrate the recording function of our system in open-loop mode, the ENG signal of sacral root nerve is recorded and sent out of body during the filling and contraction stages. This experimental configuration is similar to [1], [7]. The nerve signals is preamplified (40 dB), filtered (300 Hz to 3 kHz), further amplified (40 to 77 dB) and digitalized at a sampling rate of 10 kSPS. A graphic user interface (GUI) is developed with LabVIEW to interact with the system in this mode. Figure 18 (a) illustrates the recorded signal of sacral nerve roots during the filling stage for one experiment. The activity of S2 extradural root increases from 10 μV to 14 μV (about 40% above the baseline) during the filling stage. The onset hyperreflexia-like bladder contraction (16 μV, about 60% above the baseline) is recorded at 17:21. Figure 18 (b) shows another onset of bladder contraction at 17:22:41. These contractions correspond to micturition observed by urodynamic analyzer.

The in-vivo experiment results, which are accordant with the prevenient studies [7], [33], demonstrate that the bladder filling and ongoing bladder contraction could be detected by recording ENG signal from sacral nerve roots. Moreover, it proves that our system has the capability of acquiring information about the bladder status, which is significant for closed-loop control of urinary bladder.

On the other hand, bladder pressure is monitored during the electrical stimulation to evaluate the stimulus capability. The method of using urodynamic analyzer to evaluate the electrical stimulator has been previously reported in [5], [9], [26]. Figure 19 shows the pressure curves of bladder (P_{ves}), abdomen (P_{abdominal}) and detrusor (P_{det}) recorded by urodynamic analyzer, where P_{det} = P_{ves} - P_{abdominal}. At T_a = 33:30 and T_c = 33:48, stimuli (amplitude I = 300 μA, pulse widths t_p = t_a = 300 μs, frequency f = 30 Hz and endurance time T = 8 s) were given to S2 roots by the proposed system. Stimuli evoked bladder contractions could be observed by the rapid rises of P_{det}, 2942 Pa to 5884 Pa for the first stimulus and 1961 Pa to 4413 Pa for the second. The result of the stimulation experiments demonstrates that bi-phasic stimulus with specific parameters could obviously excite detrusor.

5. Discussion

5.1 Heating Effect

For the in-vivo electrical systems, one of the biggest problems is the bio-heating effort of the system. Clearly, there are numerous parameters that affect the thermal increase associated with the operation of the implantable system, such as power consumption, implanting location, system size and kind of surrounding tissue.

Heating effect in biological tissue can be computed by means of the bio-heat equation [34]. Taking into account thermal source caused by the implantable systems power consumption, the bio-heat equation can be written as

\[
\rho C \frac{\partial T}{\partial t} = \mathbf{V} \cdot \mathbf{K} \nabla T + \rho_b C_b \omega_b (T - T_b) + \frac{A_0}{V_{tissue}} + P_0 \tag{8}
\]

where \(\rho\) is tissue density (kg/m\(^3\)), \(C\) is specific heat (J/kg), \(T\) is temperature (°C), \(K\) is thermal conductivity (W/m°C), \(\rho_b\) is the blood mass density (kg/m\(^3\)), \(C_b\) is the blood specific heat (J/kg°C), \(\omega_b\) is the blood perfusion rate (l/s), \(T_b\) is the ambient blood temperature(°C), \(A_0\) is the basic metabolic rate (W/m\(^3\)) which is considered insignificant in this study, and \(P_0\) is the power dissipated by the implanted system (W/m\(^3\)). From Eq. (8), it is obvious that the most significant parameter of implantable device in thermal-effect analysis is \(P_0\), which could be given as \(P_0=\text{(power consumption)/(system size)}\).

In order to investigate the thermal effect of our system, we employ finite element analysis and simulation tool COMSOL (COMSOL Inc). The thermal parameters for muscle tissue in the Eq. (8) is directly obtained from [35], [36]. The numeric simulation result shows that the maximum temperature rise of the muscle is lower than 0.04 °C in the worst case of the power dissipated of the implant is 5.61 mW. The similar study in [37] reported a 4×4×0.5mm\(^3\) chip (with 12.4 mW power dissipating) will cause about 0.2 °C temperature rise in ciliary muscle. In view of lower power consumption and larger size result in smaller power dissipated (\(P_0\)) in our implantable system, the simulating result is relatively creditable.

5.2 Noise

In applications that the signals to be acquired are weak biologic voltages, the techniques for low noise is important. In our design, the noise is mainly composed of three sources: the power-supply noise, the thermal noise and the
environmental interference.

The power-supply noise of the analog part in a mixed-signal system is generally introduced from shared power line with digital part. In the proposed system, the power-supply noise is reduced by implementing the system with two distinct power zones. Tow low dropout regulator (LDO) are used in the circuit design to provide analog and digital voltage supply respectively. The copper pour in PCB is also specially designed as the grounds of both power zone are separated but connected with an inductance.

The thermal noise could be given as the power spectral density: \( \sigma_n^2 = 4K_BTR \), where \( K_B \) is Boltzmann’s constant, \( R \) is the value of resistor in circuit, and \( T \) is the resistor’s absolute temperature. As the implantable system is located in a relatively steady thermal environment, \( T \) is unchangeable. In our design, the thermal noise is optimized by minimizing the resistors value in the neural signal recording circuit. The environmental interference in our design is reduced by carefully designing the band-pass filter, which could filter out power-line noise, EMG interference and high-frequency noise such as radio-communication and medical telemetry.

6. Conclusion

A sacral nerve root recording and electrical stimulation implantable system is presented in this paper. As a prototype of a neural prosthesis dedicated to continence and micturition function restoration, a custom designed IC was fabricated in 0.18-\( \mu \)m CMOS process and used to deduce the dimension, power consumption and noise of the implanted system. The main electrical characteristics of the system are investigated by bench tests. The total power consumption of the entire system is 5.61 mW, including the amplifiers, bandpass filters, the single slope ADC, controller and stimulation module. Compared with similar systems reported by other researchers [24], [25], [32] in Table 1, the major characteristics of the present system are superior in input-referred noise, resolution of ADC and configurability of stimulation module. These advantages are significant for ENG signal recording and closed-loop control. Acute experiments are also performed on anesthetized canines to verify the functionality of our system. The results of preliminary in vivo test show that this prototype system meets the requirements.
of implantable experiments.

The future work will focus on the implementation of parallel acquisition of multi-channel neural signal, which could improve the precision and reliability of our system. In addition, clinical experiments are significant for evaluating the biocompatibility and reliability of our design. A chronically implantable neural prosthesis for continence and micturition recovery will be realized in the near future.

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