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AN IMPLANTABLE CMOS SIGNAL CONDITIONING SYSTEM FOR RECORDING NERVE SIGNALS WITH CUFF ELECTRODES

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ABSTRACT
In this paper, we propose a system architecture for recording nerve signals with cuff electrodes and we develop the key component in this system, the small-input, low-noise, low-power, high-gain amplifier. The amplifier is implemented using a mixture of weak- and strong-inversion transistors and a special off-set compensation technique; its performance is validated using Spice simulations.

1. INTRODUCTION
Every year thousands of individuals sustain a spinal cord injury, with a significant impact on patient's life. Recent efforts in biomedical engineering address the issues of electronically monitoring and stimulating paralysed extremities [1, 2, 3, 4]. These techniques are already used in volunteers to regain foot control of early multiple sclerosis patients and to assist the hand grip of tetraplegic persons [2].

Our involvement in this research is to develop implantable devices which will minimize the risk of infections by ensuring skin continuity [5]. In that way a bidirectional inductive link transmits power, control signals and feedback between the external control unit and the damaged nerve. This paper reports a subthreshold approach to biomedical signal amplification and nerve signal recording. An alternative approach to offset cancellation, with minimal impact at the input node, is presented which may find use in other amplifying schemes.

2. IMPLANTED SYSTEM
A special electrode is used in order to establish the necessary electrical contact with the nerve. This so called cuff electrode (figure 1) has a length of 10 – 20 mm and physically connects the nerve to the implanted electronic device [1]. The electrodes are placed around the nerve by use of local anaesthesia. The contact resistance after implantation is about 1 kΩ; the nerve however gradually builds up a protective layer, which increases the resistance to 54 kΩ [1] (aging process). The implanted device (figure 1) consists of an inductive loop around a silicon hip and some discrete components. The control signals and power is needed to operate the circuit are provided by an external control unit through the skin, by the use of an inductive link.

The implanted nerve stimulator has been reported elsewhere [5]. The feedback path must record very small (±10 μV) noisy nerve signals with very tight power requirements (100 μA) posed by the induced power supply. The recording circuit facilitates the identification of the exited nerve state, by comparing the nerve signal to the background activity. Because we are not interested at the absolute value of the input signal, a 10%-15% variation of the gain or harmonic distortion can be tolerated.

Even if it was possible to record the nerve signals with large accuracy, essentially we would be monitoring the thermal noise introduced by the cuff electrode. It therefore makes sense to perform some local signal processing in order to reduce the noise:

3. NOISE AVERAGING

The signal recovery technique [1, 2] is similar to demodulating an amplitude modulated signal. The input is amplified, anti-aliased and sampled at 10kHz. The digitised signal is rectified, low-pass filtered and downsampled thus the output results at a frequency of 20Hz, giving the envelope of the input nerve signal.

The variance of the nerve signal is:

\[
\sigma_n^2 = \text{Var}(V_n) = E((V_n - E(V_n))^2) = E(V_n^2)
\]

where \(V_n\) and \(\mu_n = E(V_n)\) are the (stochastic) nerve signal and its mean respectively.

The rectified signal \(Y^*\) is given by the equation:

\[
Y^* = \sqrt{V_n^2} \quad \text{and} \quad E(Y^*) = E(\sqrt{V_n^2}) = \mu_y
\]

were \(\mu_y\) is the mean of the rectified signal. The variance of \(Y^*\) is given by the equation:

\[
\sigma_y^2 = E((Y^* - E(Y^*))^2) = E((\sqrt{V_n^2} - \mu_y)^2)
\]

\[
= E(V_n^2) + \mu_y^2 - 2\mu_y \sqrt{V_n^2} = \sigma_n^2 + \mu_y^2 - 2\mu_y = \sigma_y^2 - \mu_y^2
\]

If the nerve signal is assumed to be Gaussian then we can find \(\mu_y = \sqrt{2/\pi} \cdot \sigma_n\) and \(\sigma_y^2 = (1 - 2/\pi) \cdot \sigma_n^2\).

After averaging the rectified signal the variance is reduced by 10kHz/20Hz and the overall output has a mean value
and spread given by:

$$\mu_s = 0.798 \cdot \sigma_n, \quad \sigma_s = 0.027 \cdot \sigma_n$$

where we have assumed uncorrelated samples and that the variance does not change during the 500 samples. Thus we have a signal to noise ratio from the envelope detection procedure of 29dB. Such a resolution might seem small for signal processing tasks, however it is adequate to evaluate the state of a human nerve.

4. THE PROPOSED ARCHITECTURE

The overall system architecture is shown in figure 2. A coupling capacitor is used to minimise any DC offsets at the input (which can be hundreds of millivolts from the electrode). The ±10μV input signal is subsequently amplified 10k times to a ±100mV signal, which will be antialiased by the use of a low-pass filter with a cut-off frequency of 5kHz. An Analogue to Digital Converter (ADC) is used to digitise the signal and the digital post-processing will include band-pass filtering [2], rectifying and averaging. The resultant samples will be transmitted by changing the load of the inductive link [6].

![Figure 2. Overall circuit schematic](image)

5. ANTIALIASING

As an antialiasing filter, we use a single capacitor in conjunction with either the cuff electrode resistor or the second amplifier output resistance to achieve a cut-off frequency of 5kHz (see section 6.2). Oversampling is used to suppress high frequency noise folded-down in the signal band. From a power point of view, it often makes more sense to keep low signal-to-noise ratio signal processing in the analogue domain [7]; however the signal processing done after the anti-aliasing filter can be made using very simple digital circuits, so in our case it makes sense to do the A/D conversion here. This also adds to the flexibility of the system.

![Figure 3. Aliasing effects](image)

6. AMPLIFIER

The noise introduced by the amplifier is of prime importance to signal integrity. Because of the minute signal from the electrode, it is crucial that it is amplified as much as immediately, using very few transistors (as these generate noise). The gate referred noise spectral densities of MOSFETs is approximately given by the equation:

$$\frac{\sigma^2}{\Delta f} = 4kT \frac{2}{3} \frac{1}{g_m(W/L)C_{osf}}$$

It is clear that the thermal noise can be reduced by increasing the transconductance ($g_m$) of a transistor and that the flicker ($f/f$) noise can be reduced by increasing the transistor area ($W/L$). The transconductance of a MOSFET for the different modes of operation is given by:

$$g_m = \frac{I_d}{V_{gs} - V_{th}}$$

strong in version saturation:

$$g_m = \frac{2}{L} \cdot g_{os}$$

Where $U_T = 26.7mV$ at $37°C$ (the typical body temperature), $n \approx 1.2$, and the typical effective voltage $V_{eff} = V_{oss} = 200mV$. Thus the transconductance to drain current ratio for a MOSFET is maximised in subthreshold operation and in our case it is about 3 times larger. Furthermore, flicker noise is linked to surface effects in MOSFETs; therefore, the transistor should exhibit lower $f/f$ noise (smaller $K_f$) because subthreshold operation is dominated by diffusion current deep in the substrate [9, 10].

![Figure 4. Amplifying stage](image)
and $M_A, M_S$. These transistors operate in saturation to ensure good operation as current sources and to minimize their contribution to noise [11]. A Common Mode Feed back Circuit (CMFC) is used to bias $M_S$ to stabilize the output common mode voltage to zero. $M_S$ operates in subthreshold and forms the load resistor which controls the gain of the amplifier.

This gain is given by the equation:

$$ A_{1} = g_m \frac{r_{ds}}{2} = \frac{W_1}{L_1} \cdot \frac{1}{2} \cdot n = 100 \quad (1) $$

where $W_1, L_1$ the transistor width and length, $n$ expresses the bulk effect and is given by:

$$ \frac{1}{n} = 1 - \frac{\gamma}{2} \sqrt{V_G - V_T0 + (\gamma/2 + \sqrt{\Phi_n})^2} \approx 1.2 $$

were all the voltages are given with respect to the bulk voltage. Most of the $A_{1}$ mismatch in equation (1) is due to $n$ variations. However, if a maximum 30% variation in all $\gamma$, $V_T0$ and $\Phi_n$ is assumed only by 5%, well within a tolerable variation.

Equation (1) is valid provided that $V_{G1}/nV_{T0} - V_{G2}/nV_{T0} = V_{G0}/nV_{T0}$. The transistors $M_7, M_8$ generate $V_{G0}$ to ensure that this assumption is valid:

$$ I_{ds} = I_{ds0} \Rightarrow I_{ds0} \cdot \frac{V_{G1}+V_{G2}}{V_{T0}} = I_{ds0} \cdot \frac{V_{G0}+V_{G2}}{V_{T0}} $$

where $V_{G0}$, the gate, source voltage of transistor $i$ with respect to the bulk, $I_{ds0}$ is given in [7]. The CMFC ensures that $V_{G0} = V_{G1} = 0V$ and $V_{G0} = V_{G0}$ thus the assumption is valid and $A_{1}$ is given by (1). In practice $I_{ds0}$ is a scaled down version of $I_{ds1}$, to reduce power consumption.

The second amplifier has a similar topology with the first one, though all transistors operate in strong inversion because the signal levels here are too big for the subthreshold version. $M_{16}$ operates in the linear region and its effective voltage defines the dynamic range of the amplifier. The noise of this amplifier referred to the input is divided by the gain $A_{2}$ therefore the bias current can be significantly reduced to $1\mu A$. The gain of the second amplifier is and is given by the equation:

$$ A_{2} = g_m \frac{r_{ds}}{2} = \frac{W_1}{L_1} \cdot \frac{1}{2} \cdot \frac{W_1}{L_1} = 100 \quad (2) $$

A C coupling between the two amplifiers make considered, in order to minimize the effect that offsets might have at the output. In that way an overall gain of $10^6$ is realized in two stages with a gain of 100 each. Therefore the input signal is amplified from $\pm 100V$ to about $\pm 100mV$.

6.1. Offset cancellation

Offsets at the output of the amplifier can be easily removed, since we are only interested at the AC component of the nerve signal. However, the task of cancelling the offset of the first stage is critical. The typical $V_{T0}$ mismatch for a centroid layout of the input transistors, in the process used, is more than an order of magnitude larger than the maximum input signal. Such an offset will force the input transistors out of saturation due to the high gain.

Switching the input will introduce charge feedthrough which will be much larger than the input signal and coupled charge back to the nerve which can easily be damaged. Therefore an alternative offset cancellation technique must be employed. Instead of using switch hysteresis, the current $I_A$ is proposed. A continuous time bias control is applied to regulate the bias current by ensuring that the output of the second amplifier is zero. In this case if the feedback loop is slow, the AC signal component is effectively low-pass filtered. An alternative approach would require a current Digital to Analogue Converter (DAC) and a reset cycle to set the bias current in regular (relatively long) intervals to ensure zero output. This approach offers extended flexibility to the circuit.

This offset cancellation has an effect of introducing current $I_{bias}$ mismatches:

$$ \Delta I_{1,2} = I_{1} - I_{2} = I_{bias} \cdot \frac{V_{G1}-V_{G2}}{V_{T0}} = \frac{3\%}{10} $$

However such a current mismatch will only generate offsets and will not affect the gain to a first order approximation.

Following the method presented above it is possible to realize accurate offset cancellation, without the use of switches which will introducing dynamic input offsets. It is this offset scheme that makes the implementation of such a subthreshold amplifier possible.

6.2. Reducing power consumption

The power is provided by the inductive link, therefore reducing the power consumption of a prime importance. The most energy hungry device is the subthreshold amplifier, which uses 90% of the overall current to suppress the input noise. There are two ways of reducing power consumption of this amplifier.

Figuring the first is to lower the power supply voltage for the first amplifier. This amplifier can operate with very low supply voltage: because the input transistors operate in subthreshold and the signal levels are very small, the overall $V_{ds} - V_{gs} \geq V_{T0} - 100mV + 2V_{eff} \approx 1V$.

**Figure 5. Input filter to reduce switching noise**

An alternative and more power efficient way, is to lower the biasing currents of the subthreshold amplifier in between the sampling intervals. The amplifier needs $1us$ to settle down, therefore a small 5% duty cycle may be used, reducing the overall power consumption. Nevertheless, when the biasing current on $M_1, M_2$ increases (to suppress the input thermal noise), $V_{G1} = V_{G2}$ must decrease (because $V_{G1} \approx V_{G2} \approx 0V$), introducing charge feedthrough (through the relatively large parasitic capacitors $C_{G1}, C_{G2}$) and coupling charge back in the nerve.

The differential input scheme should minimise charge feedthrough effects and a modified input filter arrangement (figure 5) will significantly reduce this noise. The bandpass filter used for AC coupling and antialiasing, ensures that the relatively large an antialiasing capacitance (12nF) provides a large charge reservoir, which holds the gate voltages at the gate of $V_{G1}, V_{G2}$ constant. (Note that when switching the bias current in the amplifier, the antialiasing filter must be placed before the amplifier; external components are necessary for this solution).
7. SIMULATION RESULTS

A subthreshold amplifier has been simulated using the models of a 0.3 μm process. Those simulations demonstrate the applicability of the overall design, with a view to do the layout of a chip to test the circuit. The biasing currents $I_{D3} = I_{D4}$ were designed to be 3.5 μA with an effective voltage of 300 mV; this enables the current sources to be switched down to 1 μA, for saving power, with an effective voltage of about 50 mV. $I_{o} = 250 nA$ for a maximum input voltage. The gain of the amplifier is 103 and the frequency response is shown in figure 6. The amplifier has a 3 dB cut-off frequency at 1.3 MHz. This is due to the large bias currents which are needed for thermal noise suppression.

![Figure 6. Subthreshold amplifier frequency response](image_url)

Figure 6. Subthreshold amplifier frequency response

The offset cancellation is shown in figure 7. A worst case $\Delta V_{TH} = 1 mV$ between $M_1, M_2$ was introduced. This forces the output to become 500 mV. If the current $I_{D4}$ is reduced to 32.7 μA then this offset is cancelled. One can observe that the this cancellation can be made very accurate, as long as the bias control has a sufficient resolution. The current mismatch $\Delta I_{D3,4} = 2.4%$. Because the signal levels are so small, if the offset canceling scheme is capable of keeping the amplifier at the correct bias point, distortion is much lower than what we can tolerate.

8. CONCLUSIONS

In this paper an implantable CMOS system for recording nerve signals was investigated. This device will find use in restoring the mobility of human paralysed extremities. Because the signals are very small ($\pm 10 mV$), the most critical component of the circuit is the amplifying stage. The use of subthreshold circuits, with large transconductance to current ratio, improved noise characteristics and low-voltage properties, operating in a constant temperature environment (37°C body temperature), make our approach feasible for the extremely tight power requirements posed by the nature of the implantable device.

Relatively large offsets, distortion, or mismatches can be cancelled by the digital post processing algorithm. Nevertheless the implementation of such a subthreshold amplifier was made possible by ensuring that an accurate threshold voltage offset cancellation (without the use of switches which will introducing dynamic input offsets) was available. A similar bias current tuning approach may be used for offset cancellation in different amplifying schemes.

The authors finally propose a current reducing technique, to further reduce power consumption. In that way more than one recording circuits may be used in an implantable device to enhance the flexibility of the device. Presently test chips are being fabricated to experimentally verify the designs proposed in this paper.

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