

Design and Implementation of a Multi-Channel Field-Programmable Analog Front-End For a Neural Recording System

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Bahareh Ebrahimi Sadrabadi

Abstract

Neural recording systems have attracted an increasing amount of attention in recent years, and researchers have put major efforts into designing and developing devices that can record and monitor neural activity. Understanding the functionality of neurons can be used to develop neuroprosthetics for restoring damages in the nervous system. An analog front-end block is one of the main components in such systems, by which the neuron signals are amplified and processed for further analysis.

In this work, our goal is to design and implement a field-programmable 16-channel analog front-end block, where its programmability is used to deal with process variation in the chip. Each channel consists of a two-stage amplifier as well as a band-pass filter with digitally tunable low corner frequency. The 16 recording channels are designed using four different architectures. The first group of recording channels employs one low-noise amplifier (LNA) as the first-stage amplifier and a fully differential amplifier for the second stage along with an NMOS transistor in the feedback loop. In the second group of architectures, we use an LNA as the first stage and a single-ended amplifier for implementing the second stage. Groups three and four have the same design as groups one and two; however the NMOS transistor in the feedback loop is replaced by two PMOS transistors.

In our design, the circuits are optimized for low noise and low power consumption. Simulations result in input-referred noise of $6.9 \mu V_{\text{rms}}$ over 0.1 Hz to 1 GHz. Our experiments show the recording channel has a gain of 77.5 dB. The chip is fabricated in AMS 0.35 μm CMOS technology for a total die area of 3 mm \times 3 mm and consumes 2.7 mW power from a 3.3 V supply. Moreover, the chip is tested on a PCB board that can be employed for in-vivo recording.

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Dedication

I would like to dedicate this thesis to my parents, and my husband for their endless love, limitless encouragement, and sacrifice throughout my Masters.

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Nomenclature

ADC	Analog to Digital Converter
BMR	Beta Multiplier Reference
CM	Common Mode
CMFB	Common Mode Feedback
CMRR	Common Mode Rejection Ratio
DAC	Digital to Analog Converter
LNA	Low Noise Amplifier
PSRR	Power Supply Rejection Ratio
SNR	Signal to Noise Ratio
THD	Total Harmonic Distortion

Chapter 1

Introduction

1.1 Motivation

Recent decades have seen growing interest in understanding how the human brain and the nervous system operate. With the rapid advance in neural science, much information has been learnt about human neural networks and the neuron as its basic component. Neurons are excitable cells that collect, process and transmit information through neural systems by the aid of chemical signals [58]. Therefore, further observation of reactions happening in neurons can improve our knowledge about the functionality of the nervous system. A better understanding of neurons may enable us to address a wide range of neurological symptoms and disorders, such as Epilepsy and Parkinson's disease [33].

Epilepsy covers a group of long-term neurological disorders that affect around one percent of people [40]. The disease is characterized by epileptic seizures that are typically

caused by abrupt and excessive electrical discharge in a group of neurons. Such seizures are recurrent and may vary from brief lapses of attention to severe and prolonged seizure activities [46]. The unexpected nature of most seizures introduce significant trouble into patients' lives and impact their families. Unfortunately, there is no permanent cure for epilepsy, but it can be controlled by medications or surgery. Around thirty percent of patients do not have access to these methods [15]. However, electrically stimulating certain parts of the brain may considerably reduce the frequency and intensity of seizures [20].

Parkinson's is another common nervous system deficiency, and is known to be a degenerative neurological disorder of the central nervous system. Parkinson's affects the motor control of the brain [46]. Its symptoms usually include tremors at rest, difficulty in initiating movement, uncontrolled movements, and muscle stiffness to name a few. To date [46], the main cause of Parkinson's disease is not known, although some atypical cases have a genetic origin [46]. As such, no definitive cure has been found, but it is shown that stimulating the brain decreases the tremors [32].

Electrically stimulating the brain to mitigate neurological symptoms requires accurate understanding of neurons and their performance. For this purpose, we should record and analyze neural activities in their normal and excited modes. The detail of this analysis helps us to determine a proper pattern for stimulating the brain [9][20]. Moreover, we may be able to restore neurons' functions in parts of the nervous system damaged by different diseases or paralysis.

Scientists carried out initial attempts to explore neurons' activities by observing animals' neural networks, and they gained invaluable information about the nervous system

and its operations [13][54]. For example, they detected and recorded the action potentials of many neurons corresponding to motor planning or control to develop analytic models that predict hand trajectories in real time [60]. They were eventually able to use the model in prosthetic devices and simulate hand movements in humans [28]. Furthermore, recent clinical experiments with paralyzed human volunteers have demonstrated that it is feasible to develop prosthetic devices that are controlled directly by thoughts, if the activity of multiple neurons can be observed [28]. Therefore, researchers try to record and process the neural activities in human brains to facilitate controlling different devices with human thoughts. This technology has a significant impact on people with disabilities as it offers the hope of restoring their abilities in the near future.

Neural recording systems have attracted an increasing amount of attention in recent years, and researchers have put major efforts into designing and developing devices that can record and monitor neural activities. One of the core components in such systems is known as the analog front-end block. The neural signals are entered into this block after recording by electrodes. The analog front-end block then amplifies the signals to make them suitable for further processing.

In this thesis, we aim to design and implement a mixed-signal field-programmable analog front-end block using AMS 0.35 μm CMOS technology. The chip is comprised of 16 recording channels with the ability to tune the low corner frequency response digitally to cope with process variation. To examine various architectures, the recording channels are designed using four different configurations. Our experiments show promising results and prove the design's potential as one of the initial works in the area of neural recording systems. Based on our results, we intend to use the design in an up coming set of in vivo

experiments, led by our clinical partners.

1.2 Thesis Organization

This chapter presents the motivation for this work. The organization of the thesis chapters is as follows.

- Chapter 2 presents the background related to neuron functionality. The different recording techniques and the characteristics of a neural recording system are then explained. A review on the works of different research groups involved in the design of neural recording systems are described next.
- The design details of an analog front-end for neural recording systems is described in Chapter 3. Preferred architectures for each block will be discussed based on the system specification, and then the circuit of interest, with its design details, will be provided.
- Chapter 4 includes our experiments and demonstrates the simulation results. Then, the design of a PCB, used for testing our chip design, will be discussed. The chapter ends with our the test results.
- Chapter 5 summarizes the work to date and the suggested work that can be done in the future.

Chapter 2

Background

2.1 Characteristics of Neural Signals

Neuron cells are the most fundamental elements in the nervous system as they transfer information throughout the body [58]. Anyone working on neural recording systems requires an understanding of neurons. This section presents relevant background about neurons and their activities.

2.1.1 Resting Potential

Neurons, like all other cells in the body, have a cell membrane with various ions distributed around it. Table 2.1 shows the distribution of the ions across the membrane in a neuron cell in a resting state [8]. These ions are distributed unequally around the membrane. Concentrations of K^+ ions are mostly inside the cell (intracellular), and Na^+ ions are

mostly concentrated outside the cell (extracellular). There also exist other ions such as Ca^{2+} and Cl^- , in lower concentrations [8].

An ion-pump comprised of protein in the cell membrane pumps different ions into or out of the neuron. It also helps to keep the concentration of intracellular and extracellular ions in their resting state values [58]. The Na^+ - K^+ pump, which uses ATP to operate, is one of the most important mechanisms that preserves the high concentration of K^+ and Na^+ inside and outside of the cell, respectively. The pump acts by pumping two K^+ ions into the cell and three Na^+ outside the neuron. These two ions are uninterruptedly diffused across the membrane [58].

Table 2.1: Distribution of ions around a neuronal membrane.

Ions	extracellular value (mM)	intracellular value (mM)
Na^+	155	20
K^+	3	140
Cl^-	130	8
A^-	25	162
Ca^{2+}	1.2	10^{-4}

It can be observed that the electric charge across a membrane in the resting state is not zero, and thus a so-called resting potential exists inside the neuron with respect to the outside of the neuron. The net flow of each ion across the membrane is zero at a particular voltage. At this voltage, the concentration gradient and electrical gradient of the ion reach equilibrium, so we call this voltage equilibrium potential [8]. The voltage is calculated using Nernst's equation (2.1). For instance, the equilibrium potentials calculated for Na^+

and K^+ at $37^\circ C$ are equal to $+55 mV$ and $-103 mV$, respectively [8].

$$E_x = \frac{RT}{Z_x F} \ln \frac{[X]_o}{[X]_i}, \quad (2.1)$$

where R is the universal gas constant, T is the temperature in K , F is the Faraday Constant, and Z_x is the valency of ion x . $[X]_o$ and $[X]_i$ are the external and internal concentrations of the ion x , respectively.

The resting potential depends on the permeability and equilibrium potential of all different ions across the membrane. If the permeability of K^+ and Na^+ are equal, the resting potential will be in between their equilibrium potential and equal to $-48 mV$. In the resting state, the K^+ ion permeability is dominant; thus, the resting potential would be close to the equilibrium potential of K^+ ions than that of Na^+ . Calculations show that the resting potential is typically around -60 to $-70 mV$ [8][58].

2.1.2 Action Potentials

Neurons are known as excited cells and can generate spikes at the time of stimulation [58]. These spikes are called action potentials and can be produced with the aid of ion channels, which are macromolecular pores made from protein in the cell membrane. They control the flow of ions by opening and closing the gate to shape electrical signals in neurons, and create an action potential, which is the response in the nervous system. Each channel is ion-specific and lets only one ion flow through it [27].

The ion channels existing in neurons are voltage-gated ion channels, meaning that these

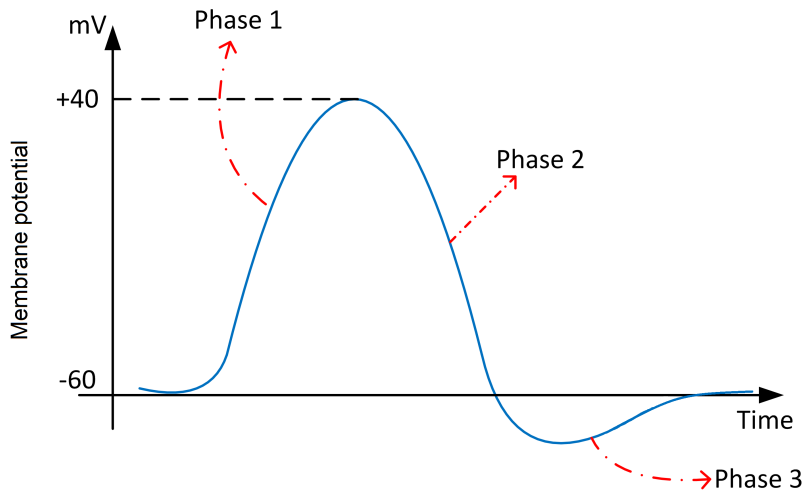


Figure 2.1: Functionality of an action potential

ion channels will open if stimulation is large enough to exceed their threshold potential. Figure 2.1 illustrates the different phases of an action potential occurrence. When a neuron is sufficiently stimulated, the Na^+ ion channels open and diffuse Na^+ ions through the cell, causing increased potential (phase1). The potential required for opening K^+ ions is larger than that needed for Na^+ ions. Therefore, when the membranes' potential is high enough, the K^+ channels open. The Na^+ channels close after 1ms. These two incidents produce phase 2, which decreases the membrane potential toward the resting potential level. The K^+ ion channel will be closed for a period after that of Na^+ , resulting in an undershoot in phase 3. Eventually, the membrane potential will reach the resting state with the help of ion pumps [58]. Experiments show that the action potentials in humans are typically pulses with a duration of approximately 1 msec and amplitude of 100 mV [8].

2.2 Neural Recording Techniques

The neural signals that are recorded by arrays of micro-electrodes can be categorized into two major groups: action potential and field potential [43]. The neural signals in these two groups differ mainly in their characteristics, such as signal bandwidth, amplitude and function.

The action potential signals can be obtained by either intracellular or extracellular method. In order to do intracellular recording, a sharp micro-electrode is typically inserted inside the cell. Using this method, we are able to measure up to 100 mV. However, the micro-electrode penetrates the cell causing cell death within a few minutes, and thus such electrodes are not appropriate for chronic implants [26]. To avoid penetrating cells, a micro-electrode with a sufficiently small tip is used for extracellular recordings [43]. In this method, the micro-electrode is placed adjacent to the neuron, and so the neuron action potential or spike is much smaller than that obtained with intracellular recording. Usually, the amplitude of the neural signals using extracellular recording is around $50 \sim 500 \mu\text{V}$, with a bandwidth of 100 Hz to 6 kHz [39]. Extracellular recording is sometimes a challenging task. For example, recording the activities of multiple neurons located in a single region of the brain often requires an array of recording electrodes. Moreover, two or more independent neurons may contribute to the output of a single recording electrode, and thus they should be differentiated according to the action potential waveform using signal processing software [43]. This is often called multi-unit recording.

One common neural recording approach is known as a field potential. In the nervous system, individual neurons produce an electric field. The integration of these fields results

in a local field potential [43]. The activities of the neurons can be recorded by interacting with these fields and with the aid of three major methods: local field potential (LFP), electrocorticograms (ECoG) and non-invasive scalp-recorded electroencephalograms (EEG) [4]. In LFP, the electrophysiological signal generated by a local field is recorded with a low impedance extracellular micro-electrode. The micro-electrode is located far from local neurons to alleviate the domination of any particular cell in measuring the electrophysiological signal [34]. The recording in ECoGs is done by an electrode implanted inside the skull yet outside the brain, providing an invasive method while preserving signal quality [55]. A method is called invasive when the neuron activity is recorded directly from the cortex under the skull. Such methods require surgery and provide high spatial and time resolution at the same time. An EEG is a non-invasive approach in which the electrical field changes are recorded by placing electrodes on the scalp [4]. The LFP method is preferred to record the activity of a group of neurons located within millimeters of the recording electrode in the tissue of interest. In contrast, ECoGs and EEGs collect the neural signals over much larger areas, such as several square centimeters at the cortical surface and scalp, respectively [4]. In addition, unlike the other two methods, which focus on specific neural signals, EEGs can provide a big picture of the brain that is quite helpful in many applications [43]. In general, electrodes on the brain, cortex or scalp surface provide signals that have a far lower amplitude than action potential recordings, and thus they have much less specific-time resolution.

2.3 Characteristics of Neural Recording Systems

A neural recording system should have various characteristics. To reduce the possibility of infection during clinical experience, having a fully implantable system is one of the key factors in the design of neural recording devices [22]. Therefore, wireless features are appealing for neural recording systems. The use of wireless communication for such systems enables patients to have free movement and avoids the typical difficulties arising with wired systems [31]. Moreover, wireless systems let researchers carry out their tests on various animals.

A wire line supply voltage cannot be used in fully implantable circuits due to the high risk of infection [31]. One of the best options is to use a battery as the power supply. The battery should be rechargeable, since repeated surgeries are not desirable. Finding appropriate small-size and long-lifetime batteries is a challenge. A wireless power circuit is also an option [22] for overcoming power-supply issues.

The power dissipation of implants causes heat, which kills the tissues surrounding electrodes. Research shows that an increase of even 1°C in temperature equals $80\text{ mW}/\text{cm}^2$ power density dissipation, which puts healthy cells in severe danger [50]. The higher power dissipation also causes a shorter battery lifetime and requires a larger size battery; thus, the power consumption of the device should be small enough to prevent damage to human tissues. Last but not least, the battery should preferably work for eight to ten years.

The extracellular potential recorded from neural signals is very small, typically in the range of $50\ \mu\text{V}$ to $500\ \mu\text{V}$ [26], and so it is necessary to have very small input-referred noise in the interface of such recording systems.

A neural recording chip should also have small enough dimensions in the order of millimetres, as it is feasible to implant small chips in the body [14]. Small size chip also considerably decreases damage to human tissues. The maximum size of a chip varies based on the position of the implant in the body. Smaller chips also reduce the fabrication cost.

Typically, a human body treats any implanted device as a foreign substance. Thus, bio-compatibility plays a core role in device implementation and is very important for realizing a clinically implantable device. It is essential to design and develop implants in a way that introduces minimal intrusion to the body. Protecting the implant itself is a separate major challenge, that is beyond the scope of this thesis.

2.4 State-of-the-Art Neural Recording

In 1952, Hodgkin and Huxley [29] pioneered a model for generating action potential and understanding how neurons work using intracellular recording. Great interest has been shown in the neural recording field from that time, and several research groups have been working on this area. Major progress has been achieved in the analog front-end circuits of neural recording systems. Recent state-of-the-art methods will be discussed in this section.

The initial neural recording circuits were developed using discrete components in the 1970s [59][17][62] due to difficulties in integrating circuits and problems in fabrication. These circuits were not implantable because of their large sizes and high power consumption. Some sensors like blood-pressure and flow meters were also introduced between 1960 and the 1970s [45][49][47][19][16].

For the first time, in 1986, K. Najafi and K. D. Wise proposed an IC-compatible multichannel recording array using an on-chip circuitry [39]. The circuit included amplifiers with a gain of 100, an analog multiplexer and a unity gain output buffer. Moreover, it performed with a 5V supply voltage. The chip was 1.3 mm² in size and dissipated 5 mW of power. The group tried to extend their work, and in 1992, J. Ji and K. D. Wise [30] introduced an analog front-end with a second-generation of their probes. The proposed circuit includes an amplifier with higher gain (300) than the previous one, as well as a band-pass filter for limiting the low and high frequency to 15 Hz and 7 kHz, respectively. The die area of the circuit is 2.5 mm² and its equivalent input noise integrating from 100 Hz to 10 kHz is 15 μ V_{rms}. It works with a 5V voltage and dissipates 2.5 mW. T. Alun and K. Najafi [1] developed a telemetrically powered neural recording system with multichannel, fully integrated circuitry in a bipolar CMOS process in 1998. The front-end includes 100 Hz to 3.1 kHz band limited amplifiers, a multiplexer, and an ADC and RF interface circuitry. The front-end operates with a 5V supply and dissipates 10 mW of power. Its size is 4x4 mm². In 2003, R. H. Olsson et al. [42] designed a fully integrated band-pass amplifier for neural recording systems. It uses diode-connected NMOS transistors that are biased in the sub-threshold region in the feedback loop of the amplifier as we will use in our work. The AC gain of the amplifier equals 38.2 dB, and it has low and high cut-off frequencies of 66 mHz and 24 kHz, respectively. The circuit works with a 1.5V supply, and it dissipates 92 μ W. The input-referred noise of the circuit integrated from 100 Hz-10 kHz is 16.6 μ V_{rms} and has a 0.82 mm² area. The aforementioned group have also worked on wireless blocks of the system and has introduced different circuits [52][10]. Finally, in 2009, A. M. Sodagar et al. developed the most recent implantable neural recording system to date from this group

[53]. The 64-channel neural recording system sends spike data to an external interface wirelessly. The system operates with a 1.8 V supply and consumes 14.4 mW. It takes 2170 mm^2 of die area, and its input-referred noise is $8 \mu V_{\text{rms}}$. The analog front-end part was implemented in a commercial 0.5 μM CMOS process and includes 64 amplifier channels. The amplifier gain and high-frequency cut-off equal 59.5 dB and 9.1 kHz, respectively. The low frequency corner of the amplifier can be adjusted from sub-Hertz to a few hundred Hertz. The amplifier dissipates $75 \mu\text{W}$, and the size of each channel is 0.072 mm^2 . In 2010, G. E. Perlin and K. D. Wise [44] proposed a new probe and 64-channel analog front-end with the ability of programmable gain from 40 dB to 60 dB digitally. The equivalent input noise of opamp from 10 Hz to 10 kHz is $4.8 \mu V_{\text{rms}}$. The low-frequency cutoff is adjustable from 10 Hz to 100 Hz and the high cutoff frequency is 9.1 kHz. The circuit is fabricated in 0.5 μm with 14.88 mm^2 die area. It also dissipates $50 \mu\text{W}$ power.

In [24], R. R. Harrison and his colleagues at the University of Utah developed a low-noise and low-power bio-amplifier for neural recording systems. The topology has a MOS-bipolar pseudo-resistor in the feedback loop. The gain of the amplifier is equal to 39.5 dB, and it rejects all DC offset. The low and high corner frequencies of the amplifier are 0.025 Hz and 7.2 kHz, respectively, and the input-referred noise over the band is $2.2 \mu V_{\text{rms}}$. The chip has 0.16 mm^2 of die area and is built in a standard 1.5 μm CMOS process. It dissipates $80 \mu\text{W}$ at 2.5 V supply voltage. In 2006, P. T. Watkins et al. introduced a wireless multichannel, fully implantable neural recording system [56]. The chip contains amplifiers, ADC and circuitry for spike detection as well as FSK data transmission. The 88-channel chip contains a 60 dB amplifier in the frequency range of 1 kHz to 5 kHz and input-referred noise of $5.1 \mu V_{\text{rms}}$. The total chip dissipates 13.5 mW of power and has a 27.3

mm² area. In 2007, R. R. Harrison designed a 16-channel front-end for neural recording systems with a tunable high frequency [23]. This chip has the ability to record different types of bioelectrical signals such as EEG, EMG, ECG, etc. Each channel consists of two amplifiers, with the gain of each amplifier equal to 46 dB, and its low-frequency cutoff is 0.05 Hz. The high frequency of the amplifier can be adjusted in the range of 10 Hz to 10 kHz according to the type of signal by using two off-chip resistors. The input-referred noise for each amplifier is $2 \mu\text{V}_{\text{rms}}$. The chip is built using a $0.6 \mu\text{m}$ CMOS process, and the total dissipated power with $f_H = 10 \text{ kHz}$ is 41 mW. Finally, in 2009, R. R. Harrison et al. proposed a 100-channel integrated circuit for wireless neural recording systems [25]. The chip contains amplifiers, 10-bit ADC and a transmitter for sending out the data. The amplifier has a 60 dB gain with programmable low and high cut-off frequency.

Another group working in the design of neural recording systems is at the University of Toronto under the supervision of R. Genov. In 2007, J. Aziz et al. [5] designed a 256-channel analog front end for neural recording systems. The chip was fabricated in $0.35 \mu\text{m}$ and has a 13.5 mm^2 size. Each channel has a two-stage amplifier with band pass filter with a sub-hertz low cutoff frequency and tunable high cutoff frequency from 1 kHz to 10 kHz. The amplifiers used in the chip are single-ended, with sample and hold cells. The gain of the channel is also programmable with values of 200,1000,2500,5000. The chip operates at 3.3V, with a power dissipation of 6 mW and input-referred noise of $13 \mu\text{V}$ integrating from 10 Hz to 10 kHz. R. Shulyzki et al. reported a closed-loop neural recording and stimulation system in 2011 [51]. The chip records the extracellular neurons' potential using 256 channels. Then, based on the given data taken from the recording channels, it generates stimulation signals for 64 channels. The analog front-end of the recording part

is comprised of two-stages fully differential with a adjustable low cutoff frequency. It also has a sample-and-hold cell and an ADC. The gain of the channel is programmable in 8 modes from 54 dB to 72 dB. The chip is in 0.35 μm technology and dissipates an overall power of 13.5 mW. The input-referred noise of one recording channel is $7.99 \mu\text{V}_{\text{rms}}$.

In 2006, Liu et al. from the the University of California at Santa Cruz designed a wireless system for recording the neural activity of sharks. The chip consists of amplifiers, a multiplexer and an off-chip ADC and telemetry circuit [36]. It is fabricated in a 0.18 μm process and consumes 18 μW , and the input-referred noise is equal to $8.5 \mu\text{V}_{\text{rms}}$. To have a high CMRR, a wide swing current mirror is used in OTA. The designed amplifier has 100 dB voltage gain, with the corner frequency of 1 Hz to 10 kHz. In 2011, the same group developed a 64-channel fully integrated analog front-end [37]. Every channel has a two-stage amplifier with adjustable gain and corner frequency. Each of the 32 recording channels then has a 32X1 MUX and an ADC. The chip is fabricated in 65 nm technology and operates at 1.2V. The overall power consumption of the chip is equal to 2.56 mW, and the input-referred noise is $3.8 \mu\text{V}_{\text{rms}}$ integrating from 30 Hz to 100 kHz. The gain of the amplifier is tunable in the range of 47 to 59 dB. Table 2.2 shows a comparison between some of the state-of-the-art works mentioned here.

Table 2.2: Comparison of state-of-the-art analog front-ends for neural recording systems

Ref.	[42]	[24]	[23]	[53]	[44]	[51]	[37]	This work
Number of Channels	1	1	16	64	64	256	64	16
Gain	38.2	39.5	46	59.5	40-60	53-72	47-59	77.5
Input-referred noise	16.6	2.2	2	8	4.8	7.99	3.8	6.9
Power Supply	± 1.5	± 2.5	5	1.8	± 1.5	3	1.2	3.3
Power Dissipation for one channel	92	80	460	75	50	52	-	125
Low Cut-off Frequency	66m	0.025	0.05	0.1-100	10-100	0.5-10	0.5-300	0.1 to 1k
High Cut-off Frequency	24k	7.2k	10-10k	9.1k	9.1k	10k	500-12k	2.5k
Front end Area for one channel	0.082	0.16	0.37	0.072	0.098	0.035	-	-
Chip Area	-	-	4.3×3.1	-	3.1×4.8	-	3×4	3×3
Total Power Dissipation	-	-	41m	14.4	-	13.5 m	2.56 m	2.7 m
Technology	3	1.5	0.6	0.5	0.5	0.35	.065	0.35
Year	2003	2003	2007	2009	2010	2011	2011	2013

Chapter 3

Design and Simulation of Neural Recording Analog Front-End

This chapter presents different architectures and circuits designed for an electrical neural recording front-end chip (AF5). This chip is a 16-channel mixed-signal neural recording analog front-end, in which the frequency response of the amplifiers can be tuned according to digital signals. It is fabricated in AMS 0.35 μm CMOS technology and has an area of 3 mm \times 3 mm. The design of circuits described in this chapter is done in collaboration with Brendan Crowley, a doctoral student in our research group.

3.1 Recording Channel Architecture

As we mentioned, neural signals have a small amplitude, around 100~500 μV , and so the signals need to be amplified to larger values to make them suitable for data conversion

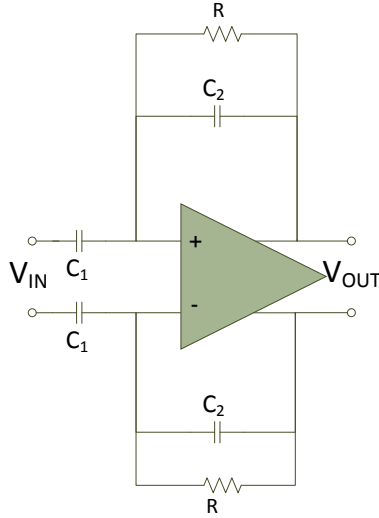


Figure 3.1: Band-pass filter for rejection of electrode DC offset

and signal processing. Therefore, two-stage amplifiers were used to obtain a high gain and good linear performance.

Electrochemical effects at the electrode-tissue interface typically introduce a DC offset of 1~2 V across differential recording electrodes [18]. An offset that is larger than the neural signals, will cause the amplifiers to be saturated. To eliminate the DC offset and amplify only small neural signals, an amplifier with large DC offset rejection is required. One solution is to use a capacitive feedback amplifier as shown in Figure 3.1. This circuit has a band-pass filter characteristic, which rejects the DC offset. The corner frequencies of the filter are given by Eq. 3.1 through 3.2.

$$f_L = \frac{1}{2.\pi R.C_2} \quad (3.1)$$

$$f_H = \frac{G_m}{A_V \cdot C_{load}}, \quad (3.2)$$

where, in the high corner frequency equation, G_m is the trans-conductance of the amplifier, C_{load} is the equivalent capacitors of node V_{OUT} , and A_V is the mid-band gain of the filter given by

$$A_v = \frac{C_1}{C_2}. \quad (3.3)$$

The recording channel needs to have the smallest possible noise contribution. Therefore, the channel must be comprised of low noise blocks. In addition, the amplifier's bandwidth should be limited to desired range to filter out the noise that exists outside of the bandwidth. In our design specification, the range of the desired frequency responses for each channel is between 750 Hz to 7.5 kHz. The equivalent capacitor load of the circuit (depicted in Figure 3.1) is small parasitic capacitors in node V_{OUT} , so the high corner frequency will be very high. By adding a load capacitor, C_L , at V_{OUT} of the first stage amplifier, C_{load} will be increased and consequently, the high corner frequency will be decreased. We select a proper value for the C_L to achieve the high cut-off frequency at 7.5 kHz.

According to Eq. 3.1, the resistor R should be set to a very large value to obtain the 750 Hz as low cut-off frequency. In our proposed design, R is implemented using MOS transistor that is biased in the sub-threshold region. The MOS biased in sub-threshold has a large resistance while it occupies a small layout area. Moreover, by controlling the bias voltage of the transistor the resistor, R , will be tuned. This approach is used to tune the

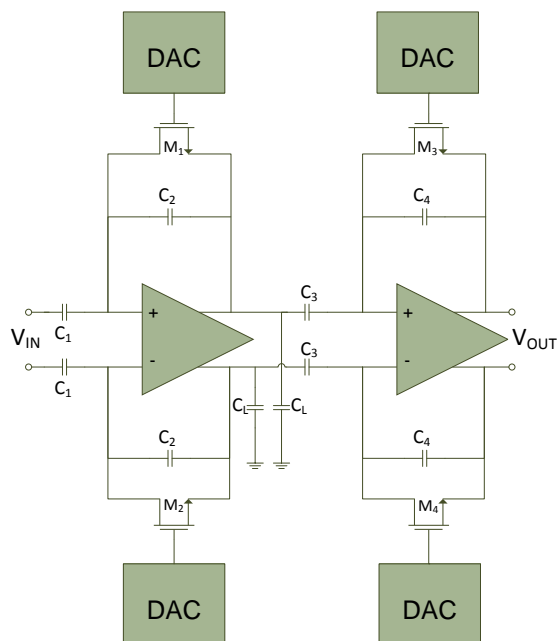


Figure 3.2: Architecture of block 1 of recording channel's front-end.

frequency response of the recording channels and will be described in the following sections in more detail.

The 16 channels of the AF5 chip are divided into 4 blocks of 4 different channel types. Figure 3.2 shows the architecture of the channels in block 1, which contains a low noise amplifier (*LNA*) as the first-stage and a fully differential amplifier as the second. Eventually, the same filter circuits described above will be used with an NMOS as a replacement of R in feedback.

Fully differential amplifiers have a higher common mode noise rejection than single-ended amplifiers. On the other hand, single-ended amplifiers have less power dissipation and occupy a smaller area; moreover, these amplifiers can be simply designed and do not

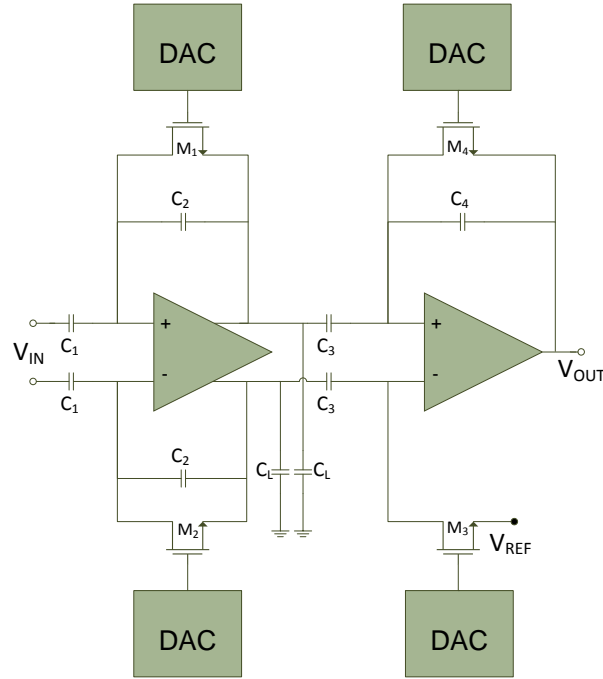


Figure 3.3: Architecture of block 2 of recording channel's front-end.

need common-mode feedback circuits. For all these reasons, a single-ended amplifier is used for the second stage in block 2 (Figure 3.3).

As previously mentioned, the resistors are implemented using PMOS and NMOS transistors. The PMOS transistor has higher equivalent resistance than NMOS with the same size. They are also preferred in terms of their fabrication process, since the bulk of PMOS can be connected to source. Thus, NMOS transistors in block 1 and 2 are replaced with two PMOS transistors in series in blocks 3 and 4, respectively. Using two PMOS transistors in series provides better linearity. The architecture of these two blocks can be seen in Figures 3.4 and 3.5. The design detail of capacitors in feedback will be determined when the two-stage amplifiers are designed.

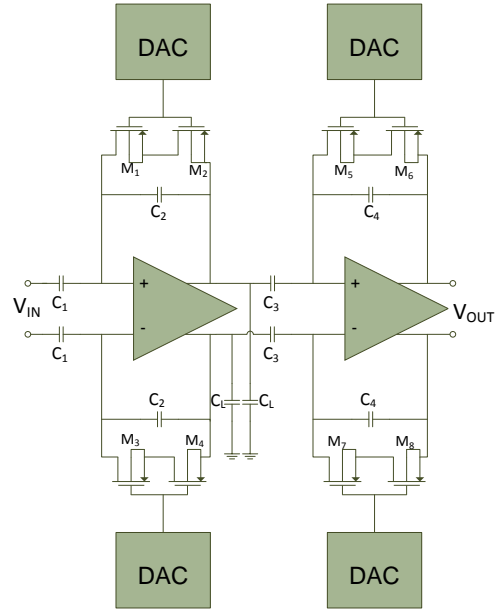


Figure 3.4: Architecture of block 3 of recording channel's front-end.

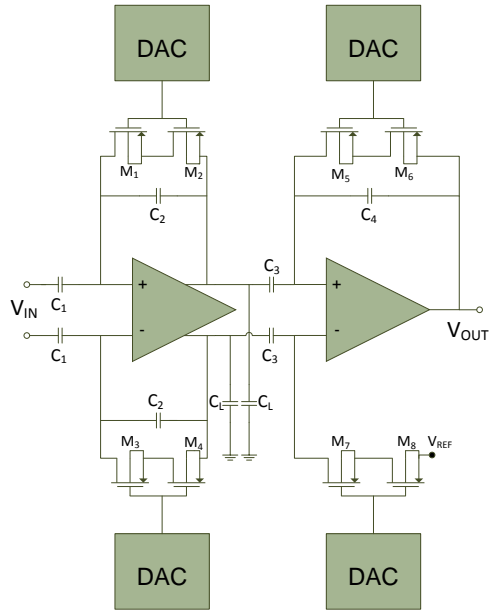


Figure 3.5: Architecture of block 4 of recording channel's front-end.

3.2 Design of LNA

As mentioned, one of the key requirements of a neural recording system is to have good noise performance. The first stage of the front-end, which interfaces with neural signals, contributes the most noise. Thus, it should be an LNA, that consumes low power. These trade-offs make the LNA the most important block in our design. The electrode impedance is high [41], so we need to have high input impedance for the LNA to ensure the input signal is not attenuated. Since the overall gain is provided by both amplifiers, the LNA block does not need to have high gain and a large output swing.

Table 3.1, taken from [48], shows overall comparisons among different op-amp topologies. The telescopic op-amp is a good match for first-stage. This topology leads to low noise and low power dissipation. The telescopic op-amp used in our design is a fully differential amplifier, and so it needs a common-mode feedback (CMFB) circuit. Figure 3.6 shows the schematic of a telescopic amplifier with its CMFB circuit. The transistor sizes of such op-amps is shown in Table 3.2.

Table 3.1: Comparison of different op-amp topologies. Adapted from [48]

	Gain	Output Swing	Speed	Power Dissipation	Noise
Telescopic	Medium	Medium	Highest	Low	Low
Folded-Cascode	Medium	Medium	High	Medium	Medium
Two-Stage	High	Highest	Low	Medium	Low
Gain-Boosted	High	Medium	Medium	High	Medium

The channels operate at low frequencies in which two types of noise are more common: flicker and thermal noise. Eq. 3.4 and 3.5 show the overall input-referred noise of the circuit for thermal and flicker noise, respectively [48].

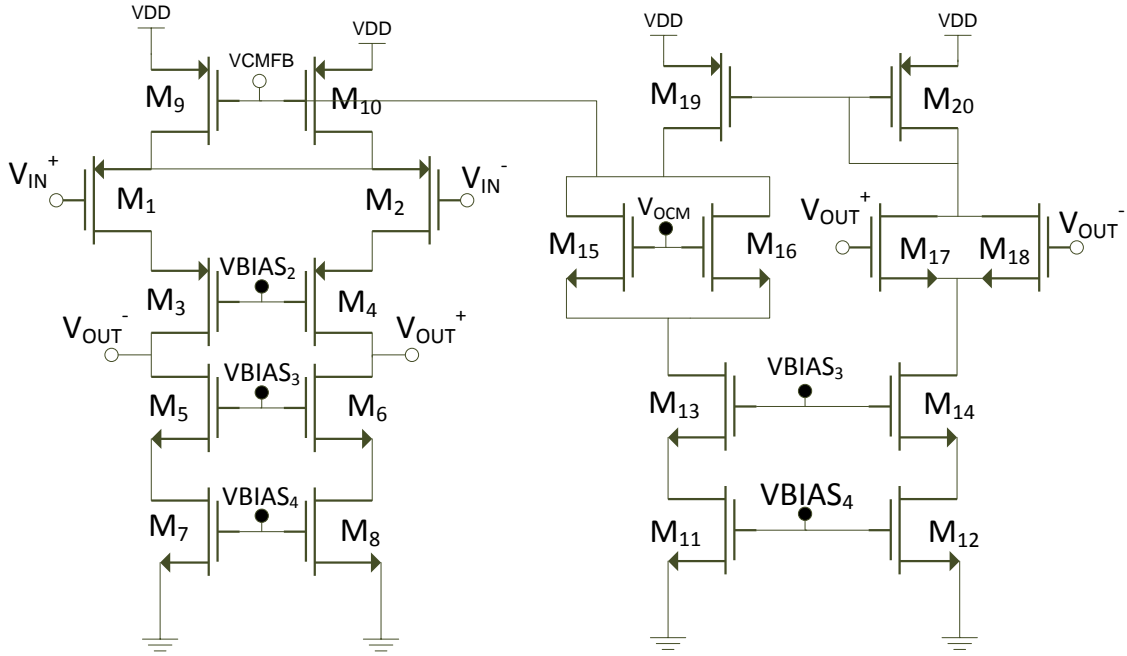


Figure 3.6: Schematic of LNA circuit and its CMFB circuit.

Table 3.2: Transistor sizing of LNA and its CMFB circuit.

Transistor	W/L(μm)
$M_{1,2}$	40/20
$M_{3,4}$	8/10
$M_{5,6}$	2/10
$M_{7,8}$	4/20
$M_{9,10}$	8/10
$M_{11,12}$	4/20
$M_{13,14}$	2/10
$M_{15,16}$	4/10
$M_{17,18}$	4/10
$M_{19,20}$	8/10

$$\bar{V}_n^2 = 4KT(2 * \frac{2}{3g_{m1}} + 2\frac{2}{3g_{m7}}) \quad (3.4)$$

$$\bar{V}_n^2 = 2\frac{K_p}{w_1L_1C_{ox}f} + 2\frac{K_n}{w_7L_7C_{ox}f}\frac{g_{m7}^2}{g_{m1}^2} \quad (3.5)$$

where in the thermal noise, K is the Boltzmann's constant, T is the temperature, and g_m is the trans-conductance of the transistor. In the flicker noise equation, W and L are the width and length of the transistor, C_{OX} is the MOS oxide capacitance, f is the working frequency, and K_N and K_P are the flicker noise coefficients of NMOS and PMOS transistors, respectively.

From the above-mentioned equations, we realize that the pairs M1, M2 and M7, M8 govern the input-referred noise, and other transistors have only a negligible effect in the noise component. Since the sizing of transistors on the left branch is the same as for their corresponding transistors on the right branch, the noise of M1 and M2 are equivalent. This statement is true for M7 and M8 as well.

The PMOS transistor has less flicker noise than NMOS [48] [2]. M1 and M2 have the most contribution in input-referred noise, and thus we select PMOS transistors for M1 and M2 to alleviate the flicker noise. According to Eq. 3.5, for low flicker noise, the sizing of M7 and M8 should be smaller than that of M1 and M2. Equivalently, g_{m7} becomes smaller than g_{m1} , resulting in less thermal noise in Eq. 3.4.

The amplifier gain is also an important factor in the design of low-noise amplifiers. In our circuit, the gain is defined by

$$A_v \simeq g_{m1}[(g_{m3} \cdot r_{o3} \cdot r_{o1}) \parallel (g_{m5} \cdot r_{o5} \cdot r_{o7})] \quad (3.6)$$

where, r_o is the output resistor of MOS.

High open-loop gain is needed in LNA, to increase the linearity of the amplifier. Thus, the transistor sizes should be chosen in a way that meets the constraints for low noise and desirable high gain. The transistors M9 and M10 provide the current source for our LNA. Power consumption strongly depends on the current value. Therefore, the current should be as small as possible.

In our circuit, the V_{CMFB} needs to be set to a required voltage value for common mode output voltage. There are many approaches to develop Common Mode Feedback (CMFB) circuits. We utilize the one presented in [2]. Transistors M17 and M18 produce a current based on the common-mode (CM) voltage of V_{OUT}^+ and V_{OUT}^- . This current will be mirrored, I9, and will be compared with the current created in M15 and M16 (I_{OCM}). Having the same current in the branches of the current mirror is desirable. The sizes of M15-M18 are consequently chosen to be exactly the same. The same procedure is followed to provide identical currents in M19 and M20. If the common mode (CM) voltage of V_{OUT}^+ and V_{OUT}^- matches V_{OCM} , currents I19 and I_{OCM} become the same, and thus V_{CMFB} will be fixed. On the other hand, the larger CM voltage in V_{OUT} nodes than in V_{OCM} causes I19 to be greater than I_{OCM} , which decreases V_{CMFB} . As a result, the voltage of V_{OUT} decreases until its CM voltage equals V_{OCM} . This procedure also happens if the CM voltage of V_{OUT} becomes lower than V_{OCM} due to increased DC levels in V_{CMFB} . Finally, the sizing of other transistors is determined based on the biasing voltages needed for our circuit.

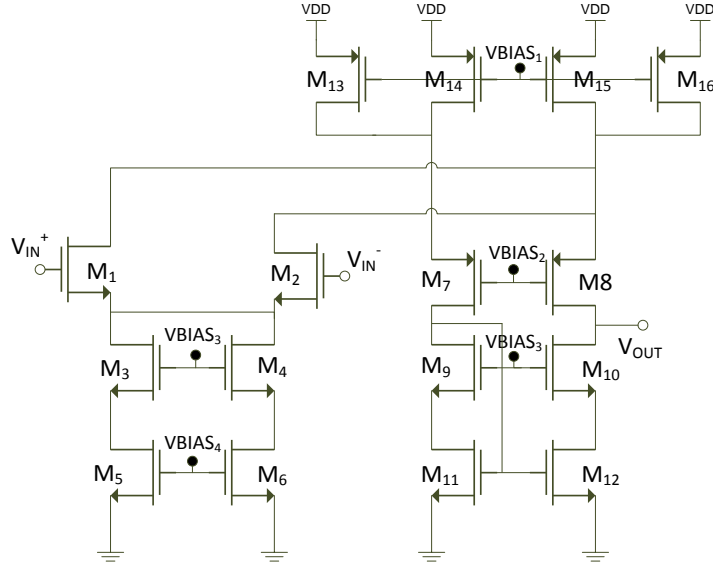


Figure 3.7: Schematic of single-ended folded-cascode amplifier circuit.

3.3 Design of Second-Stage Amplifier

To compute the impact of the second stage on the total input-referred noise of our recording system, the input-referred noise of the second-stage is divided by the gain of the first-stage in the proposed circuit [48]. It can be concluded that the second stage does not have as much effect as the first stage in the overall input-referred noise. However, the second stage amplifier needs to have fairly high gain and a high output swing. Moreover, the power dissipation of this stage should be low. The single-ended folded-cascode configuration shown in Figure 3.7 is selected to implement the second stage.

An NMOS transistor has a larger g_m than a PMOS transistor of the same size does. This fact motivated us to use NMOS transistors for M1 and M2 in the folded-cascode amplifier to provide high gain. The gain of the second stage is defined by Eq. 3.7.

$$A_v \simeq g_{m1}[(g_{m10} \cdot r_{O10} \cdot r_{O12}) \parallel (g_{m8} \cdot r_{O8} \cdot (r_{O16} \parallel r_{O15}))], \quad (3.7)$$

The output swing of a folded-cascode is equal to that shown in Eq. 3.8, where V_{OV} denotes the overdrive voltage of a transistor. It can be shown that the swing of such amplifiers is one overdrive voltage larger than that of a telescopic amplifier. This circuit also has a good Power Supply Rejection Ratio (PSRR) [2]

$$\max V_{O(PP)} = VDD + VSS - 4|V_{OV}|. \quad (3.8)$$

As mentioned, half of the proposed recording channels use a fully differential amplifier in their second stage instead of a single-ended amplifier. The swings of fully differential amplifiers are about two times larger than those of single ended amplifiers, resulting in a higher signal-to-noise ratio (SNR). Furthermore, they have better common-mode noise rejection. The symmetric configuration of fully differential amplifiers eliminates even-order types of distortion, introducing less non-ideality in the amplifier characteristics. In contrast, single-ended amplifiers have all orders of distortion [21]. Figure 3.8 shows a fully differential schematic. The sizing of transistors for a folded-cascode amplifier is given in Table 3.3.

On the other hand, the fully differential amplifiers need a CMFB circuit. Using an extra CMFB circuit makes the fully differential amplifiers consume more power and require more area. The CMFB circuit for a folded-cascode circuit [7] is shown in Figure 3.9.

The common mode voltage of the output generates a voltage at the node at which

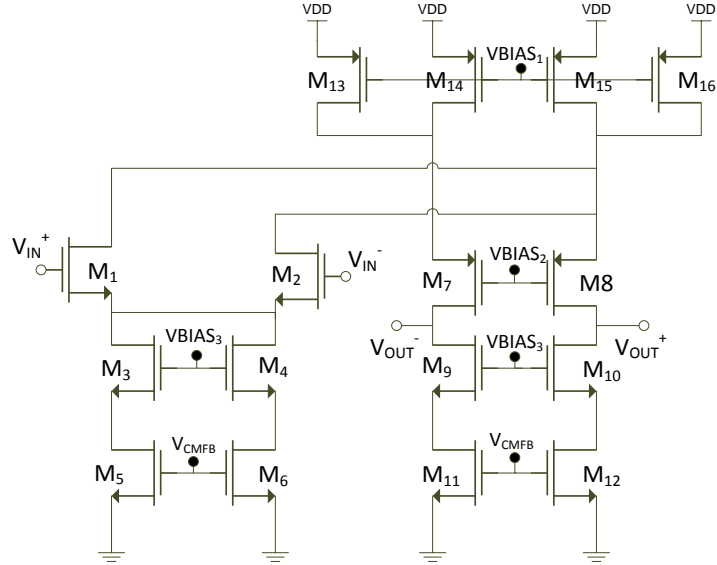


Figure 3.8: Schematic of fully differential folded-cascode amplifier circuit.

Table 3.3: Transistor sizing of folded-cascode amplifier circuit.

Transistor	$W/L(\mu m)$
M_{1-6}	1/1
M_{7-8}	4/1
M_{9-12}	1/1
M_{13-16}	4/1

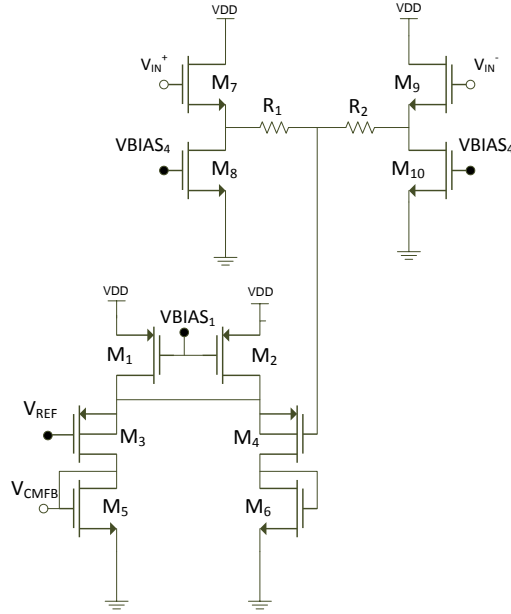


Figure 3.9: Schematic of CMFB circuit for fully differential folded-cascode amplifier.

two resistors are connected. This voltage is compared with V_{REF} , and thus the V_{CMFB} is adjusted based on the voltage. The implementation details of the CMFB circuit of the folded-cascode can be seen in Table 3.4.

Table 3.4: Transistor sizing of CMFB Circuit for fully-differential folded-cascode amplifier.

Transistor	W/L(μm)
M_{1-4}	4/1
M_{5-10}	1/1
$R_{1,2}$	166.6 K

The capacitor values in feedback can be defined, after designing of two-stage amplifiers. The capacitor C_1 to C_4 will be determined to obtain the desired mid-band gain in each

stage, based on Eq. 3.3. The overall gain of two-stage amplifier is then determined by

$$A_V = \frac{\text{maximum swing of the output}}{\text{the amplitude of input signal}}, \quad (3.9)$$

where maximum swing of the output is equal to maximum swing of the folded-cascade amplifier, which defined in Eq. 3.8. The amplitude of input signal is the neural signals whose amplitudes are around $100\sim 500\ \mu\text{V}$. From Eq. 3.9 the overall gain of two-stage amplifier is set to be 78.27 dB. Consequently, the mid-band gain of 38.27 dB for the first stage and 40 dB for the second stage was chosen.

There are some constraints that should be considered in the process of finding proper value for capacitors. It is important to have as small as possible area in the chip. This fact will limit the capacitor values that can be chosen for feedback. The capacitor with value around 10 pF is the highest value that can be chosen to have reasonable area. The load capacitor (C_L) value is determined based on the G_m value of the first stage amplifier to provide desired high cut-off frequency around 7.5 kHz (from Eq. 3.2). The G_m of first stage amplifier is equal to gm1. The capacitor C_3 should be chosen in a way that doesn't have loading effect on the first stage. The capacitor values are shown in table 3.5.

Table 3.5: Capacitor values for channel architecture (F)

C_1	10.6p
C_2	129f
C_3	1p
C_4	10f
C_L	3.18p

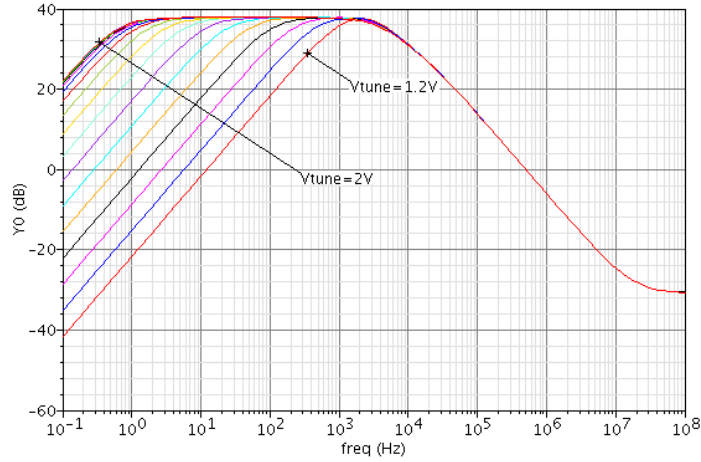


Figure 3.10: Frequency response of LNA with a varying bias voltage from 1.2 V to 2 V with 25 mV steps.

3.4 Design of DACs

The MOSFET transistors in feedback operate in the sub-threshold region. These devices suffer from especially significant process variation and mismatch, which cause change in the frequency response of the recording channel. Changing the gate voltage of the MOS transistor in feedback varies the equivalent resistance of the MOS device. This feature enables us to tune the frequency response of recording channels. Figure 3.10 shows the frequency response of LNA with a bias voltage (V_{TUNE}) varying from 1.2V to 2 with 25mV steps. Using a digital to analog converter (DAC), we may digitally control the gate voltages of transistors. A 5-bit DAC is sufficient to change the V_{TUNE} in the range of 1.2V to 2V with 25mV steps.

One of the simplest architectures for building a DAC uses a Kelvin Divider circuit [38]. An N-bit Kelvin divider DAC is a 2^N stack resistor in series with each other, with two

references, V_{LOW} and V_{HIGH} , as supplying the voltage at either end. Each node of the circuit is connected to a digital switch used to select the desired node voltage and connect that to V_{OUT} . The voltage of the i_{th} node from the 2^N nodes of the resistors is equal to 3.10, where N is the bits number of DAC

$$V_i = V_{low} + [(V_{high} - V_{low}) * \frac{i}{2^N}]. \quad (3.10)$$

Figure 3.11 shows the 5-bit DAC implemented in the chip. The resistors have a value of 6.6 k Ω , and a 32 \times 1 MUX was used as a digital switch to select the desired voltage node. The design of MUX will be shown in the following sections.

3.5 Testability

It is essential to access some important nodes of blocks for testing purpose. The most important node to monitor in LNA is V_{CMFB} . Because of fabrication constraints, all 16 V_{CMFB} of the recording channels cannot connect to the output port directly. Therefore, we utilize two 8 \times 1 MUXs to access the V_{CMFB} of the desired channel.

The V_{CMFB} of the amplifier in the second stage must also be probed during testing. Since only 8 channels of the second stage amplifiers are fully differential, using one 8 \times 1 MUX to connect this node to an output pad of AF5 chip is enough.

Every recording channel has 4 DACs, for tuning the frequency response. The 4 DACs in the first recording channel were chosen for probing, and thus the output of this DAC was connected to a tri-state buffer (or transmission gate) and the output pad. Using the

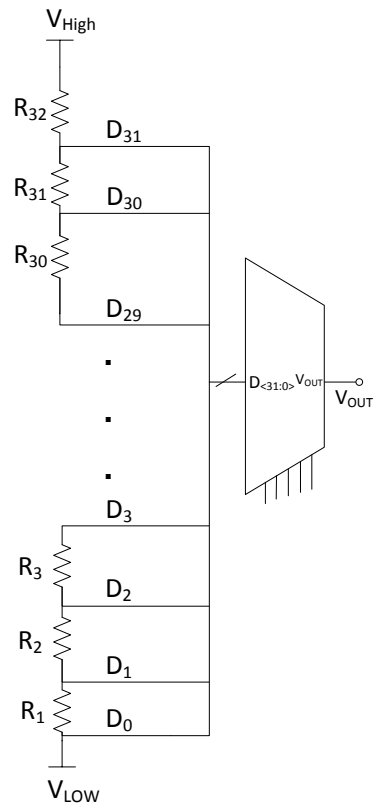


Figure 3.11: Architecture of 5-bit DAC circuit.

tri-state buffer, the DACs output is connected to the output port only when the buffer is enabled during testing. The rest of the time, the buffer is disabled, and the output is in a high Z state.

It was mentioned that 16 channels were divided into four different blocks. Figure 3.12 shows the architecture of one of these blocks.

To access the outputs of LNAs and second stages, the output of the first recording channel in each block is directly connected to an output pin. Two 4×1 differential MUX blocks were also used for each stage amplifier. Therefore, by enabling different selecting inputs, we obtain the output of each amplifier for a desired recording channel. To reduce the loading effect, each MUX's output was connected to an amplifier with a unity gain feedback as a buffer. The buffer needs to have a high gain with a fairly high swing. A basic two-stage amplifier, shown in Figure 3.13, was used for the buffer. The gain equation for the two-stage amplifier is given by

$$A_v \simeq g_{m1}[(r_{O2}) \parallel (r_{O4})]g_{m7}(R_{out}) = g_{m1}[(r_{O2}) \parallel (r_{O4})]g_{m7}[(r_{O7}) \parallel (r_{O8})]. \quad (3.11)$$

Table 3.6 demonstrate the design details of the buffer.

Table 3.6: Transistor sizing of Miller amplifier.

Transistor	W/L(μm)
$M_{1,2}$	4/0.5
$M_{3,4}$	1/0.5
$M_{5,6}$	4/0.5
M_7	6.65/0.5
M_8	5* 4/0.5

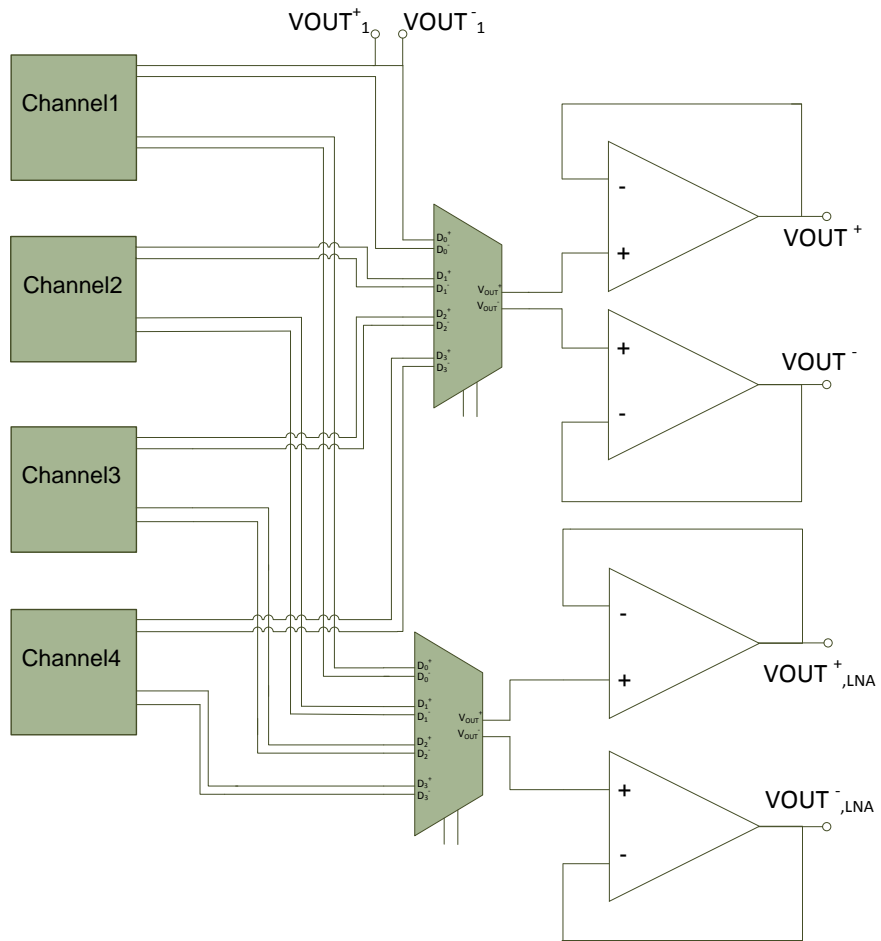


Figure 3.12: Architecture of one block

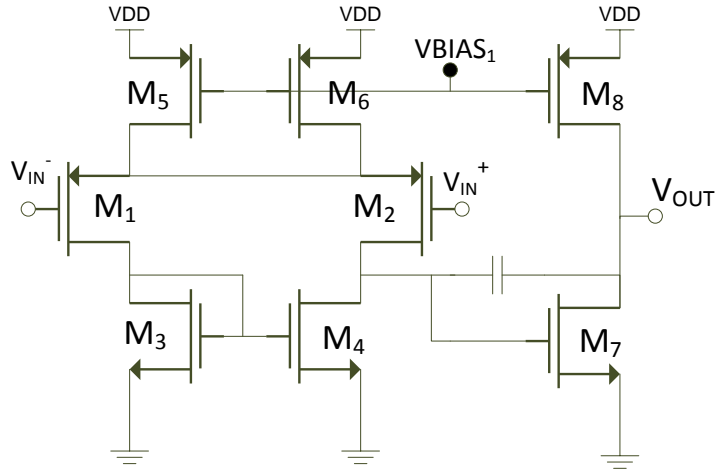


Figure 3.13: Schematic of Miller Amplifier circuit

3.6 Design of MUXs

The Tri-state Buffer or transmission gate is one of the components in integrated circuits such as MUX [61]. Figure 3.14 is a schematic of a transmission gate in which the circuit works as a switch. When $B_0=1$ ($\overline{B_0}=0$), the two transistors are ON, and so, the V_{IN} signal can be transferred to V_{OUT} . At $B_0=0$ ($\overline{B_0}=1$) state, the two transistors are off and the output will be in a high Z state.

Figure 3.15 shows a schematic of the 8x1 circuit used in the chip. It can be seen that MUX is built upon the transmission gate cell of Figure 3.14. It can be seen that the inputs of each transistor pair are compared, and one of them is selected according to the enabling signals. As a result, 4 of the 8 inputs will be selected in the first stage based on B_0 . Then, in the second stage two of these 4 inputs will be selected (based on B_1). Finally, the desired input is connected to the output by B_2 .

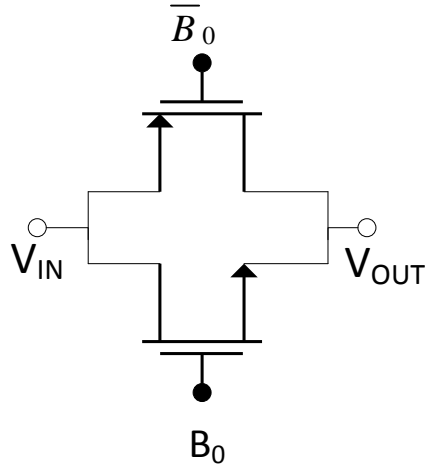


Figure 3.14: Schematic of Fully differential MUX cell

As previously stated, the DAC has a 5-bit MUX in its architecture. Figure 3.16 shows the architecture of a 5-bit DAC. The pass transistor is used instead of a transmission gate as a building block in this MUX. Figure 3.17 shows the 3-bit MUX that is used in 5-bit DAC.

The MUXs and DACs that are used in the chip have enabling inputs that use digital signals. Thus, a digital block comprised of two serial shift registers is used for biasing enabling inputs. One of shift registers is used for MUXs and the other is used for DACs. The architecture of digital block is shown in Figure 3.18. The digital values are sent to the input of the chip, then shifted inside, and then the last bit in the shift register will be connected to the outside pin of the chip to make sure the data is being sent correctly. The MUXs and DACs are also connected to the desired bit of the shift registers to get the proper value. The shift registers are the standard ones from the library of technology.

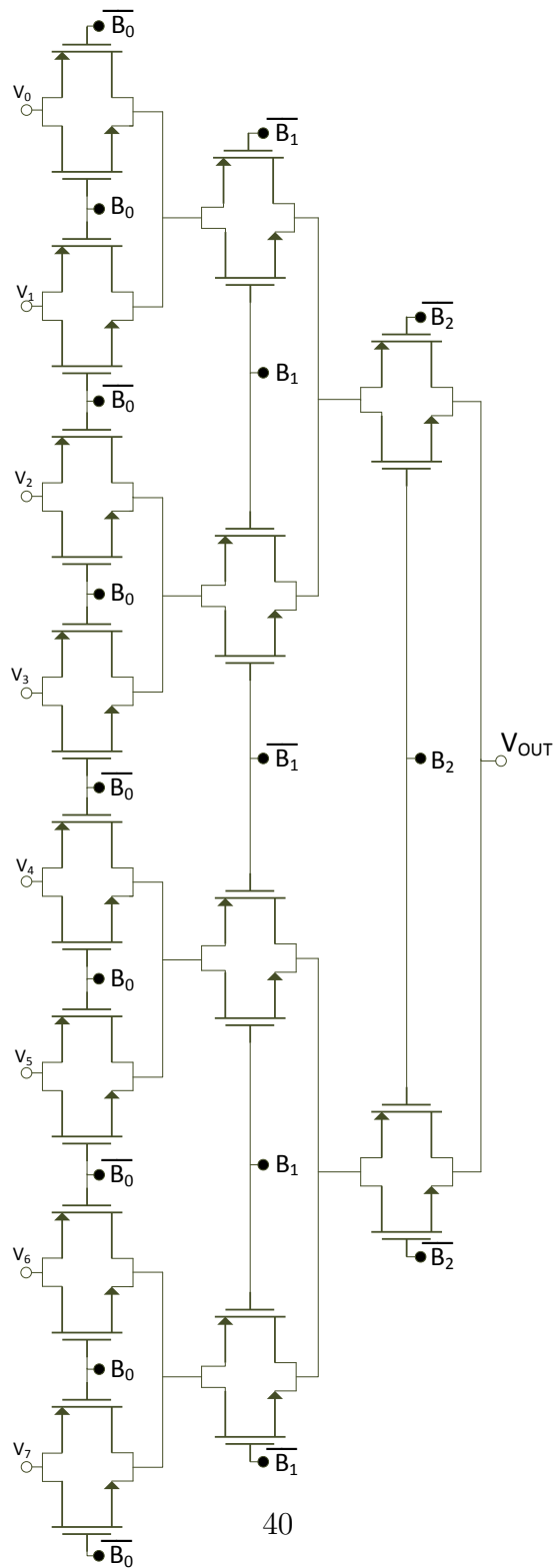


Figure 3.15: Schematic of 8X1 MUX circuit

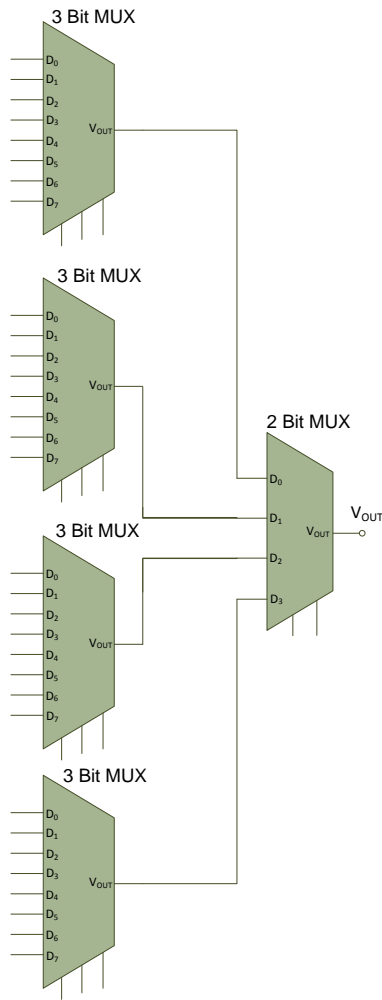


Figure 3.16: Architecture of 32X1 MUX (5-bit) circuit for DAC

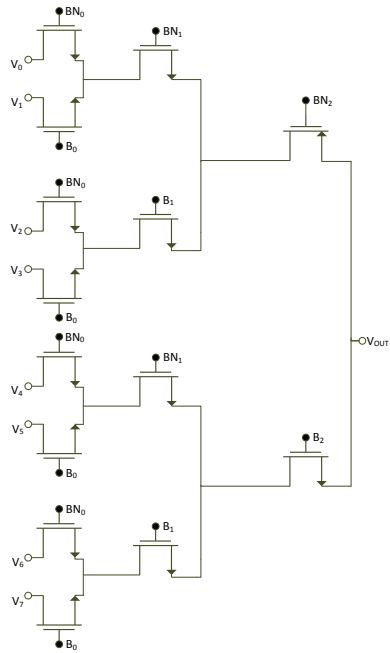


Figure 3.17: Schematic of 8X1 MUX circuit for DAC

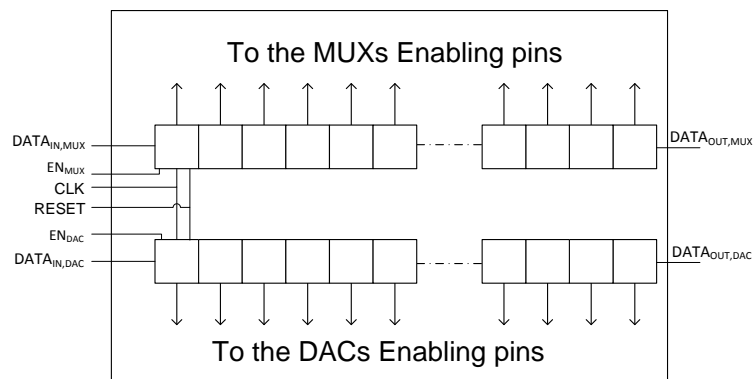


Figure 3.18: Architecture of digital block

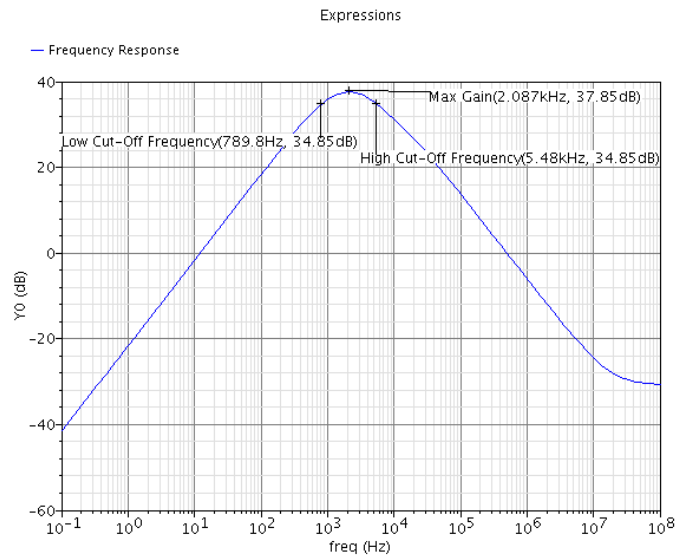
Chapter 4

Simulation and Measurement Results

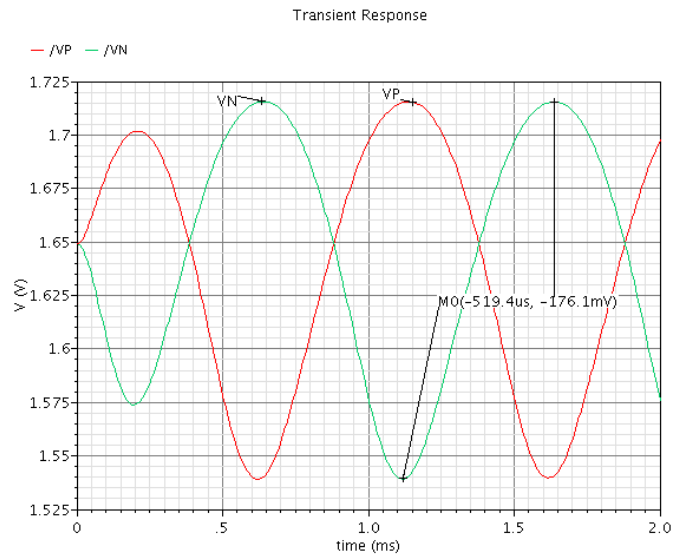
During chip implementation, evaluation must be performed to ensure the designed circuit works appropriately. The first form of evaluation is to simulate the designed circuits. If the simulation results are as expected, then the chip can be sent out for fabrication. The fabricated chip should then be tested to verify whether it meets all the desired specifications. In this chapter, the simulation results of different circuits related to block 3 (fully differential amplifiers with PMOS transistors in its feedback) will be presented first, and then the test results of the chip. The simulation results of other blocks will be shown in Appendix B.

4.1 Simulation Results

The most important circuit in the design of an analog front-end for a neural recording system is the LNA. Figure 4.1 shows the AC and transient simulation results of the LNA



(a)



(b)

Figure 4.1: (a) Frequency response (b) Transient simulation of the LNA with PMOS transistor in feedback (blocks 3 & 4) with an input signal of 3 mV at 1 kHz

with PMOS transistors in its feedback, with the input signal of 3 mV at 1 kHz. It can be seen that the gain of the LNA is 37.85 dB and the corner frequencies are 789 Hz and 5.48 kHz. Moreover, the transient simulation demonstrates the good performance of our circuit. The noise simulation result of the LNA is also shown in Figure 4.2. The input-referred noise of the LNA integrating from 0.1 Hz to 1 GHz is equal to $6.9 \mu\text{V}_{\text{rms}}$.

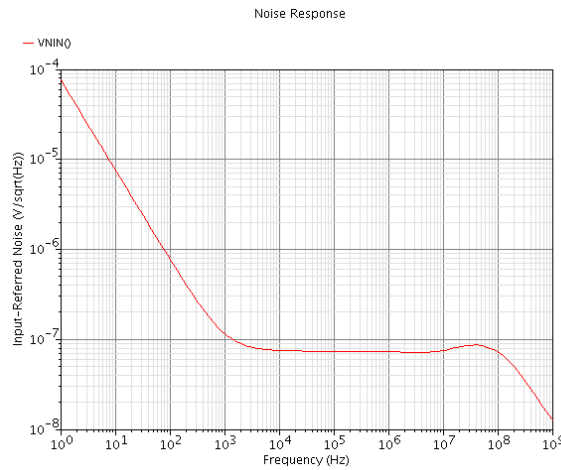


Figure 4.2: Noise simulation of LNA with PMOS transistor in feedback (blocks 3 & 4).

Gain is an important factor in the design of second-stage amplifiers. In our design, we set the gain of the second-stage amplifier to 40 dB. Figure 4.3 shows the frequency response of the fully differential amplifier with PMOS transistors in feedback. It can be seen that the gain is 38.92 dB.

Figure 4.1 shows the AC simulation of the whole recording channel for the fully differential amplifiers with PMOS transistors in feedback. The total gain of the channel is 76.7 dB, and the low and high corner frequencies of the channel are 778 Hz and 5 kHz, respectively. The input-referred noise of the recording channel integrating from 0.1 Hz to 1

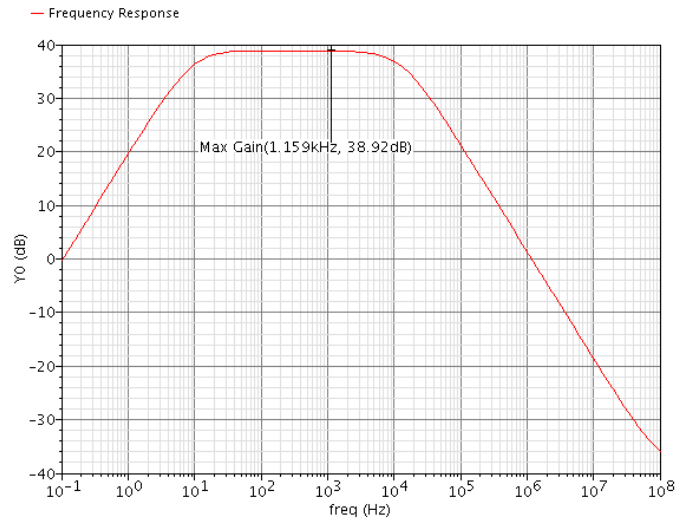


Figure 4.3: Frequency response of the second-stage amplifier with PMOS transistor in feedback (blocks 3).

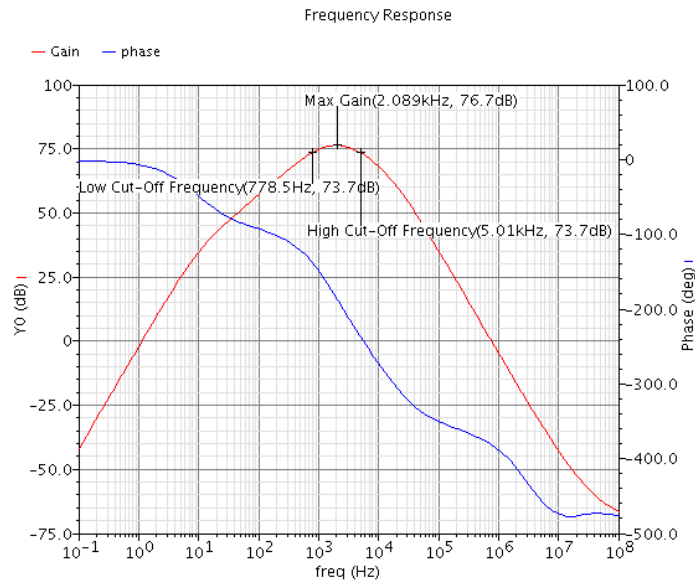


Figure 4.4: Frequency response of the recording channel with PMOS transistor in feedback (block 3).

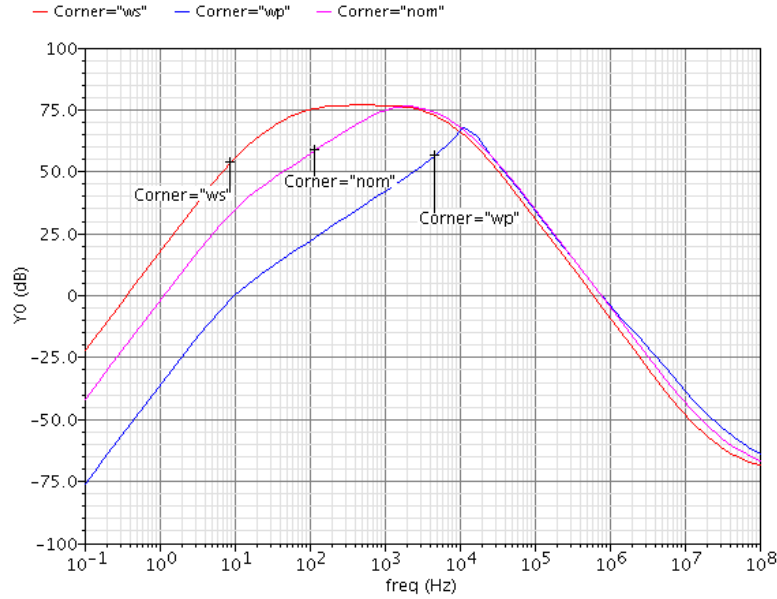


Figure 4.5: AC simulation of the recording channel (blocks 3) for process variation.

GHz is $6.9 \mu V_{\text{rms}}$. Figure 4.5 shows the AC simulation of the channel for process variation. As mentioned in the previous chapter, DACs are used to control the gate voltages of these devices, enabling us to compensate for the mismatches and process variations.

The Total Harmonic Distortion (THD) of block 3 is simulated and is illustrated in Figure 4.6. In our simulations, we assume that the fundamental frequency is 100 Hz and the range of input voltage is from $200 \mu V$ to $600 \mu V$.

Table 4.1 provides simulation results for different blocks. In the table, FDNMOS and SENMOS represent block 1, and 2, respectively. Also, FDPMOS and SEPMOS stand for block 3 and block 4, respectively.

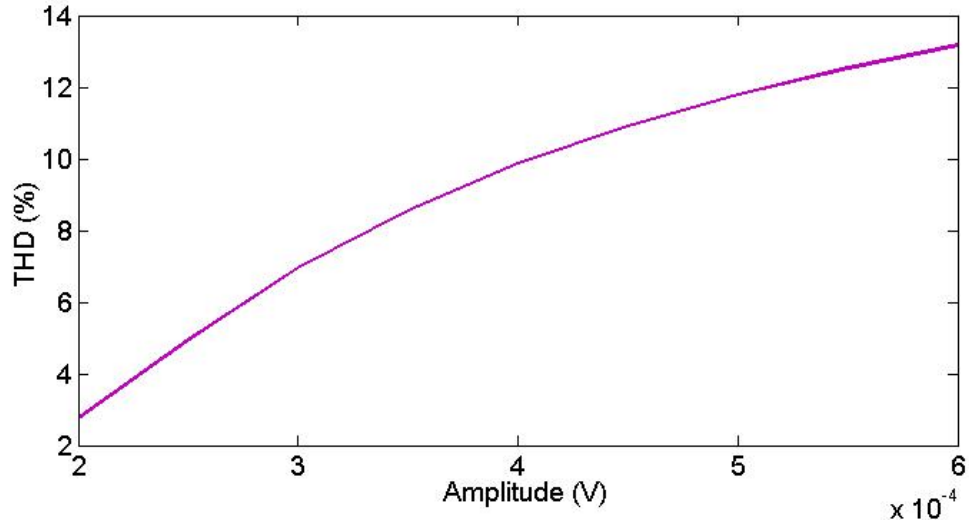


Figure 4.6: Simulated total harmonic distortion of recording channel (block 3) with a input voltage varies from $200 \mu\text{V}$ to $600 \mu\text{V}$

Table 4.1: Simulation results for different blocks.

Block	Gain (dB)	Noise (μV_{rms})	Power Dissipation (μW)	THD @ $200 \mu\text{V}$ (%)
FDNMOS (1)	77.55	6.9	150	11.31
SENMOS (2)	77.4	7.2	125	15.59
FDPMOS (3)	76.7	6.9	150	2.76
SEPMOS (4)	77.3	7.2	125	2.6

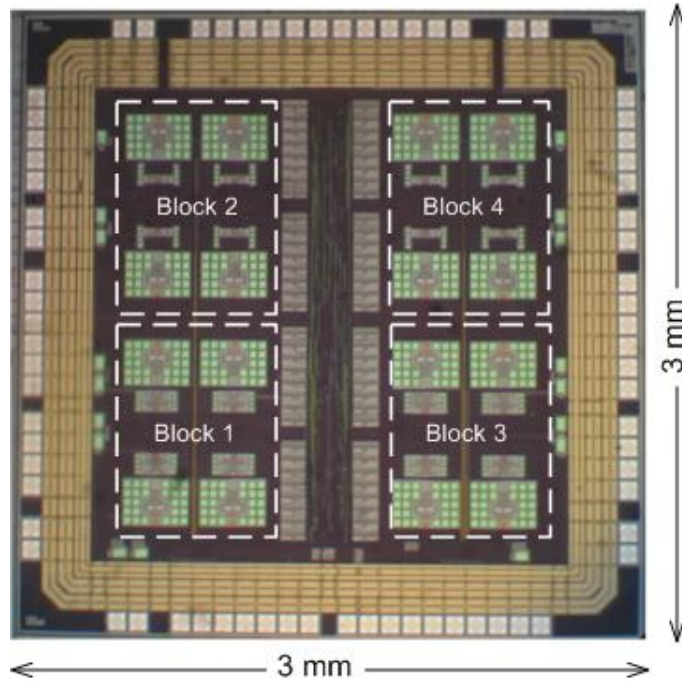


Figure 4.7: Die Photo of 16-channel neural recording

4.2 Design of AF5 PCB

The AF5 analog front-end was fabricated in AMS 0.35 μm CMOS technology. Figure 4.7 shows a die photo of the AF5 chip.

A four-layer PCB (AF5PCB) using Altium software was designed to test the chip, and is shown in Figure 4.8. The two inner layers are used for the ground and power supply. Each layer is also split into analog and digital sides for high-speed performance and the noise reduction. The PCB has four separate 3.3V regulators for analog supply of the board, analog supply of the AF5 chip, the digital supply of the board and digital supply of the AF5 chip.

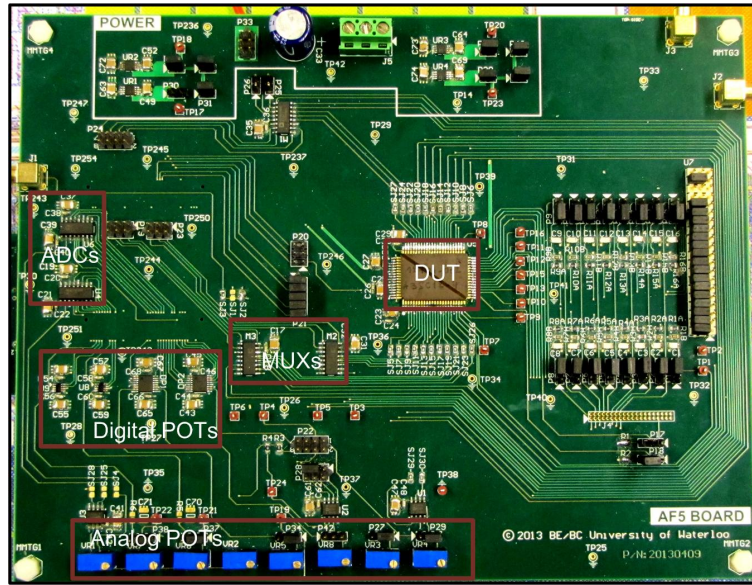


Figure 4.8: AF5PCB board

The chip must be tested with a simple signal generator before live recordings. To simulate neural signals, we need to attenuate the outputs of signal generators as the real neural signals have very small amplitude. Thus, a simple resistor divider is used. The resistor values were chosen so as to imitate the electrodes' impedance. A capacitor is placed parallel to the outputs of resistor dividers to filter excess noise. To use the input signals coming from electrodes in live recordings, the PCB includes a connector for interfacing with the Cerebus, which is a commercial system for recording and analysing the nervous network of animals brain [57]. Thus, the board can be used in live experiments.

An Opal-Kelly XEM6010 board with XC6SLX45 Xilinx FPGA is used to provide the digital data needed for the digital part of the chip as well as for getting the digital output data of the AF5. The DC voltages required by by DACs and CMFB circuits in the chip are provided by either the digital or analog potentiometer (POT). The output signals of

the recording channels in the chip are connected to the MUXs in the PCB. If a digital output signal is needed, then the MUX's output can be connected to a buffer and then an ADC. The digital output of the ADC is then connected to the Opal-Kelly module for signal processing.

4.3 Test Results

The first step in testing the chip is to provide the required digital data for the shift-registers in the chip. A code was written for the Opal-Kelly module and then loaded into it. The Opal-Kelly sends the data to the chip. Measurements show that the output signal of serial shift register is similar to the input signal of that, but with a delay, and so the digital part of the chip works correctly.

Next, we program the chip to test the recording channels. Figure 4.9 illustrates the output signals of the LNA for a 3 mV input signal at 1 kHz frequency. It can be seen that the LNA has a gain of 34.9 dB. The outputs of the recording channels were also probed. Figure 4.10 shows the output signals of a fully differential recording channel with PMOS in feedback (block 3), with an input signal of 200 μ V at 1 kHz frequency.

It was mentioned that the DACs were used to control the channels' frequency response by controlling the transistors' gate voltages. The frequency response of the LNA with different DAC values is demonstrated in Figure 4.11, and it confirms that the channels work as expected.

Figure 4.12 demonstrates the measured noise of channel 10 in the range of frequency

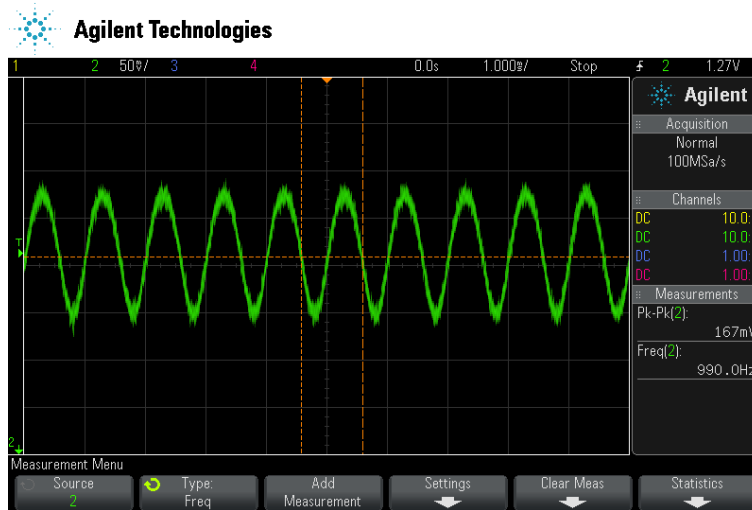


Figure 4.9: Output signal of the LNA with PMOS in feedback (channel 10).

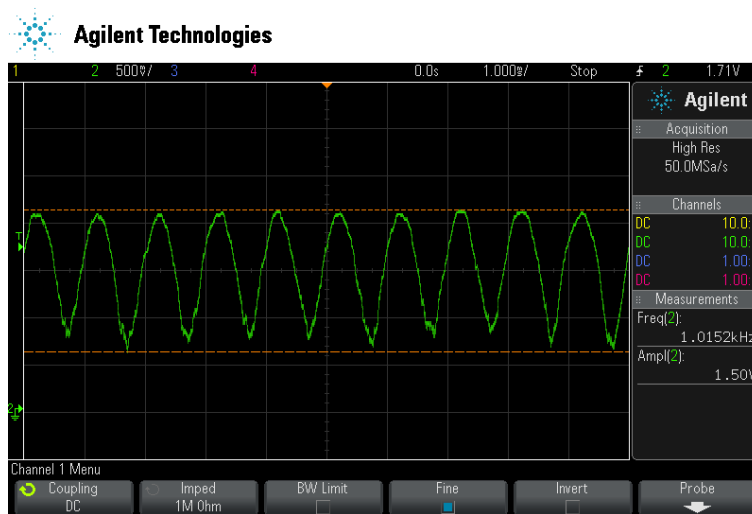


Figure 4.10: Output signals of a fully differential recording channel with PMOS in feedback (channel 10).

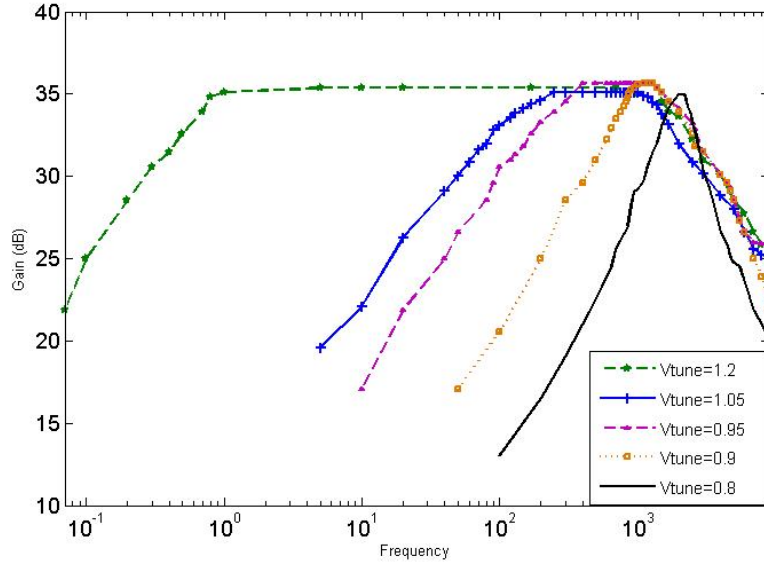


Figure 4.11: Measured frequency response of the LNA with PMOS in feedback (channel 10) with different DAC values.

from 1 Hz to 50 kHz. By using this, the input referred noise integrated from 1 Hz to 50 kHz equals 1.4 mV. Unfortunately, the noise of the testing board is much higher than the chip noise, and thus the measured input referred noise is mainly due to noise of the board.

The power consumption of the chip is 2.7 mW, which is close to the simulation result (2.6 mW).

Table 4.2 shows that what channels are functional in our experiments, and Table 4.3 provides the test results of different parameters for the working blocks. An overall summary on our chip and its characteristics is given in Table 4.4.

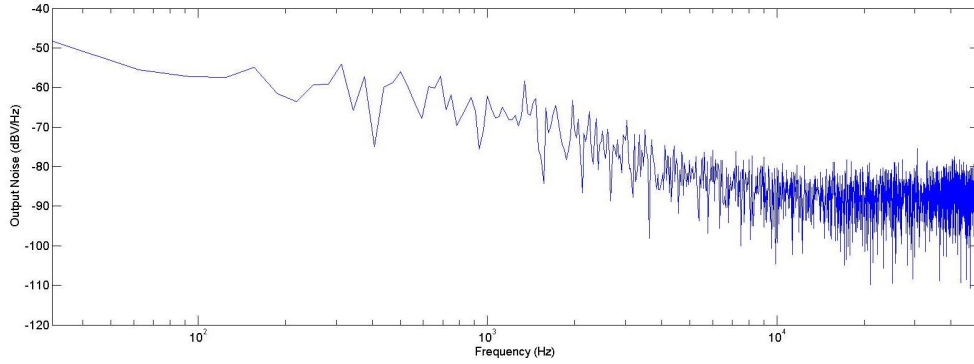


Figure 4.12: Measured noise of recording channel for block 10

Table 4.2: Functionality of different recording channels

Block	Channel NO.	Tested	Functional	Low cut-off Frequency
FDNMOS (1)	1	Y	NO	-
FDNMOS (1)	2	Y	NO	-
FDNMOS (1)	3	Y	NO	-
FDNMOS (1)	4	Y	NO	-
SENMOS (2)	5	Y	NO	-
SENMOS (2)	6	Y	NO	-
SENMOS (2)	7	Y	NO	-
SENMOS (2)	8	Y	Y	0.1 Hz to 600 HZ
FDPMOS (3)	9	Y	NO	-
FDPMOS (3)	10	Y	Y	0.1 Hz to 1kHz
FDPMOS (3)	11	Y	Y	0.1 Hz to 1kHz
FDPMOS (3)	12	Y	Y	0.1 Hz to 1kHz
SEPMOS (4)	13	Y	Y	0.1 Hz to 1kHz
SEPMOS (4)	14	Y	Y	0.1 Hz to 1kHz
SEPMOS (4)	15	Y	NO	-
SEPMOS (4)	16	Y	NO	-

Table 4.3: Test and Simulation results for different blocks

Block	Test Results		Simulation Results	
	Gain (dB)	THD @ 200 μ (%)	Gain (dB)	THD @ 200 μ (%)
SENMOS(2)	74.7	9.4	77.4	15.5
FDPMOS(3)	77.5	3.76	76.7	2.76
SEPMOS(4)	71.2	1.9	77.3	2.6

Table 4.4: Measurement results of the AF5 chip

Number of Channels	16
Gain	77.5 dB
Power Supply	3.3V
Low cut-off Frequency	Adjustable from 0.1 Hz to 1kHz
High cut-off Frequency	2.5 kHz
Total Power Dissipation	2.7 mW
Chip Area	3 mm \times 3 mm
Technology	0.35 μ m

Chapter 5

Conclusions

5.1 Summary of the Work and Contributions

This work focuses on the design and implementation of a field-programmable 16-channel analog front-end for the neural recording systems. Each recording channel contains two-stage amplifiers, as well as DACs, which are used for controlling the low corner frequency response of each channel digitally to overcome process variation, and other mismatches. The circuits of the chip are designed for good noise performance and power consumption.

The 16 recording channels are divided into four different blocks to evaluate the performances of different architectures. The first block includes one LNA as the first stage amplifier and a fully differential amplifier as the second stage. An NMOS transistor is used in the feedback loop of the amplifier. Block 2 uses a single-ended amplifier instead of the fully differential amplifier as a second stage. Block 3 and 4 are similar to blocks 1 and 2,

respectively, with small differences where blocks 3 and 4 use two PMOS in series instead of an NMOS transistor in feedback.

Neural recording systems should be fully implantable, and thus they need to be tuned automatically. This chip is programmable so that we can ultimately implement a self-tuning feature on chip. We aim to digitally tune the frequency response of the channels with the aid of DACs. Specifically, there exist FPGA and ADCS on the board to drive the DACs for the purpose of self-tuning.

The chip is fabricated in AMS 0.35 CMOS technology and is tested on an AF5PCB board, which was designed for this purpose. The board has the ability to be used for in-vivo recording. Unfortunately, in-vivo testing could not be done due to the limited time available. However, our clinical colleagues in Alberta will start live testing in the near future.

5.2 Future Work

- Four different architectures have been used in the design of our recording channels. These architectures will be evaluated and compared completely in in-vivo testing, and the best architecture will be chosen for future designs.
- A better understanding of how each circuit works in the chip may be obtained after testing the chip. This knowledge can be used in designing different circuits for the next chip. As an example, the transistors' sizing can be changed so as to be optimized for design specifications.

- Although the chip and the board are designed to provide the circuits required to perform self-tuning feature, this feature was not implemented because of limited time. The algorithms needed to evaluate this feature will be implemented in the near future.
- In order to have all the systems on our chip and have a fully-implantable device, the on-chip analog-to-digital converter and the circuitry for sensing the frequency response will be included in the next chip.

APPENDICES

Appendix A

Current and Voltage Reference

A.1 Design of Current Reference

The current and voltage references are among the most important blocks in every design, as they provide biasing voltages for the circuits. An ideal voltage reference block should be independent of any fluctuations in power supply and temperature.

Using bipolar transistors, the band-gap circuits are designed to make stable and reliable reference voltages. However, the architecture is not preferred in our design since its implementation by CMOS technology is cumbersome. Therefore, we use a beta multiplier reference (BMR) suggested in [6] for CMOS technology. Figure A.1 shows a schematic for this circuit with its start-up circuit. Table A.1 shows the transistor sizing for the BMR circuit.

In this circuit the W/L ratio of transistors M3 and M4 are equal, so they have the same

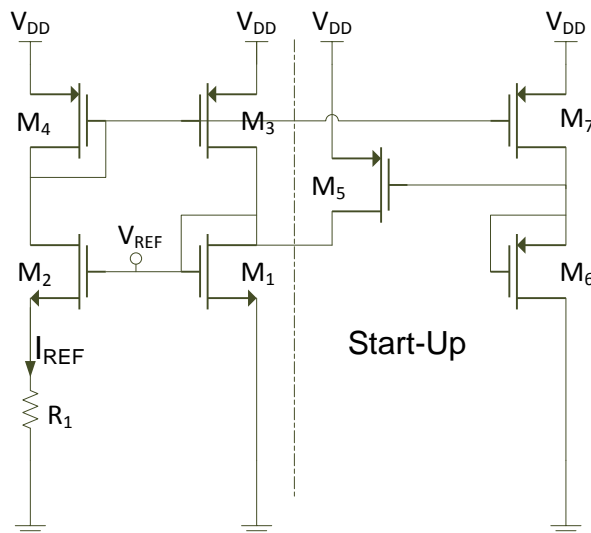


Figure A.1: Schematic of Beta multiplier reference circuit

current for each branch. We have

$$V_{GS1} = V_{GS2} + I_{REF} \cdot R_1, \quad (\text{A.1})$$

where V_{GS} is the voltage between the gate and source of the transistor. To ensure that the circuit works correctly, V_{GS1} should be greater than V_{GS2} . This condition is satisfied by making the W of transistor M2, K time larger than that of M1, while K is greater than 1. Furthermore, K greater than 1 guarantees positive feedback in the circuit, resulting in a stable circuit. Using Eq. A.1 and the current equations of transistor M1 and M2, we can derive the I_{REF} and V_{REF} values as below

$$I_{REF} = \frac{2}{R_1^2 K \mu_n C_{OX} \frac{W_1}{L_1}} \left(1 - \frac{1}{\sqrt{K}}\right), \quad (\text{A.2})$$

Table A.1: Transistor sizing of BMR circuit.

Transistor	W/L(μm)
M_1	2/2
$M_{2,3,4}$	4* 2/2
M_5	2/1
M_6	1/80
M_7	2* 4/1

$$V_{REF} = \frac{2}{R_1 K \mu_n C_{OX} \frac{W_1}{L_1}} \left(1 - \frac{1}{\sqrt{K}}\right) + V_{thn}, \quad (\text{A.3})$$

where V_{thn} is the threshold voltage of the NMOS transistor. It can be seen that both V_{REF} and I_{REF} values are independent of power supply.

Since the resistor, R_1 , has a positive temperature coefficient, a rise of temperature increases the voltage drop across R_1 . On the other hand, V_{GS2} has an inverse response since V_{th} has negative temperature coefficients. In other words, increasing the temperature reduces V_{GS} . Therefore, by finding a proper value for R_1 , these two voltages can compensate for each other and produce a voltage that is not a function of temperature [35]. Eq. A.4 and A.5 show the temperature coefficients of I_{REF} and V_{REF} , respectively.

$$\frac{\partial I_{REF}}{\partial T} = I_{REF} \cdot \left[\frac{-2}{R_1} \frac{\partial R_1}{\partial T} - \frac{1}{K \mu_n C_{OX}} \frac{\partial K \mu_n C_{OX}}{\partial T} \right], \quad (\text{A.4})$$

$$\frac{\partial V_{REF}}{\partial T} = \frac{\partial V_{thn}}{\partial T} - \frac{2}{R_1 K \mu_n C_{OX} \frac{W_1}{L_1}} \left(1 - \frac{1}{\sqrt{K}}\right) \cdot \left(\frac{1}{R_1} \frac{\partial R_1}{\partial T} + \frac{1}{K \mu_n C_{OX}} \frac{\partial K \mu_n C_{OX}}{\partial T} \right). \quad (\text{A.5})$$

It can be concluded from the equation that the I_{REF} and V_{REF} temperature coefficients depend on W/L , R_1 and K , and so proper values for these parameters results in the desired reference values. The K value is set to 4 in most designs, and is called a constant-gm bias circuit. By choosing $K=4$, gm is equal to A.6. It can be seen that, g_m is not a function of MOSFET process shifts, and is a constant value [6].

$$g_m = \sqrt{2K\mu_n C_{OX} \frac{W_1}{L_1} \cdot I_{REF}} = \frac{1}{R_1} \quad (\text{A.6})$$

The BMR circuit is a self-biased circuit, and so it is essential to use a start-up circuit that prevents circuits working at zero current values. If a circuit works in this situation, transistors M1-M4 are off at time zero. The voltage gate of M1 and M2 is zero, while the voltage at the gate of M3 and M4 is V_{DD} , causing M7 and then M6 to be turned off. Consequently, the gate-source voltage of M6 is less than V_{thn} , causing M5 to be ON, which runs the current flow through M1 and M2. The voltage of gate M1 and M2 keeps increasing until all 4 transistors are ON. When the circuit works at the desired biasing points, M6 turns OFF.

As seen in previous sections, different biasing voltages are needed to bias the telescopic and Folded-Cascode amplifiers. The circuit shown in Figure A.2 is used to provide the required voltages for both amplifiers [6]. Since the bias voltages are different for these amplifiers, the sizing of transistors for each amplifier is different, to reach the desired bias voltages. Tables A.2 and A.3 show the transistor sizing for the telescopic and folded-Cascode amplifiers, respectively.

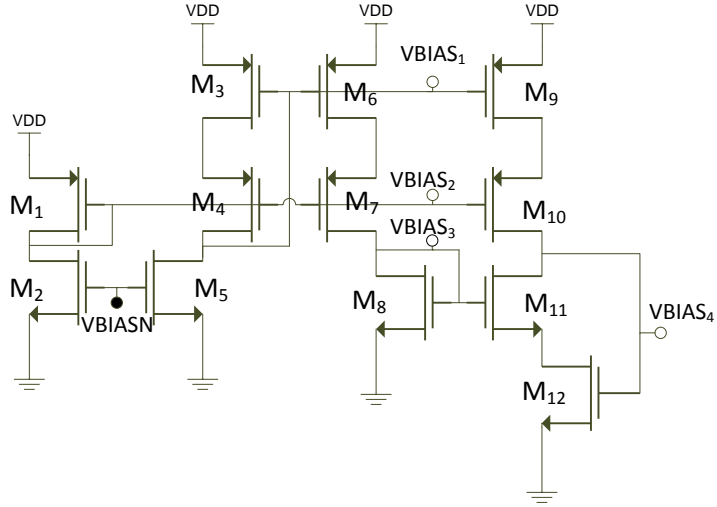


Figure A.2: Schematic of biasing circuit for telescopic and folded-cascode amplifier

Table A.2: Transistor sizing of LNA-biasing

Transistor	W/L(μm)
M_1	1/16
$M_{2,5}$	2/2
$M_{3,6,9}$	8/10
$M_{4,7,10}$	4/1
M_8	1/40
M_{11}	1/1
M_{12}	2/10

Table A.3: Transistor sizing of folded-cascode biasing

Transistor	W/L(μm)
M_1	4/20
$M_{2,5}$	1/1
$M_{3,6,9}$	4/1
$M_{4,7,10}$	4/1
M_8	1/20
$M_{11,12}$	1/1

A.2 Simulation and Test Results

The V_{REF} of BMR circuit as well as the 4 V_{BIAS} voltages provided for each amplifier should be probed to ensure the circuit is biased at the preferred bias points. The V_{REF} is connected directly to the output pad. The 8 V_{BIAS} points for each amplifier stage were connected to an 8×1 MUX, while the output of the MUX is connected to one output pad. The reference and biasing voltages were probed. Table A.4 shows the simulation and measurement results of these testing points. It can be seen that the measured value of voltages are close to what we expected from simulation.

Table A.4: Simulation and test results of biasing voltages

Biasing Voltage	Simulations	Measurements
V_{REF}	0.673	0.67
V_{BIASL_1}	2.298	2.22
V_{BIASL_2}	1.298	1.27
V_{BIASL_3}	1.709	1.56
V_{BIASL_4}	0.891	0.88
V_{BIASF_1}	2.439	2.42
V_{BIASF_2}	1.984	1.92
V_{BIASF_3}	1.308	1.15
V_{BIASF_4}	0.678	0.67

Appendix B

Simulation Results of Other Blocks

The simulation results of block 3 was shown in chapter 4. The simulation results of the other blocks are presented here. Figure [B.1](#), [B.2](#) and [B.3](#) show the AC simulation of blocks 1, 2, 4, respectively. Figure [B.4](#) shows the simulated THD for each block.

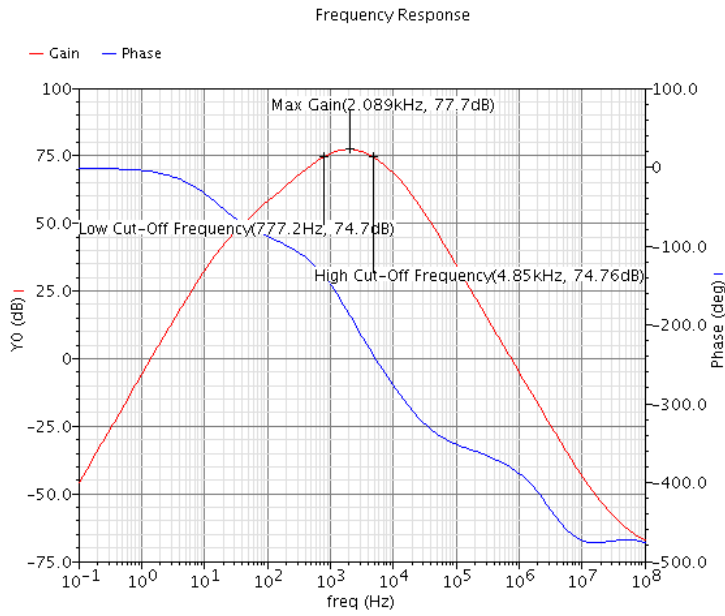


Figure B.1: Frequency response of the recording channels for block 1

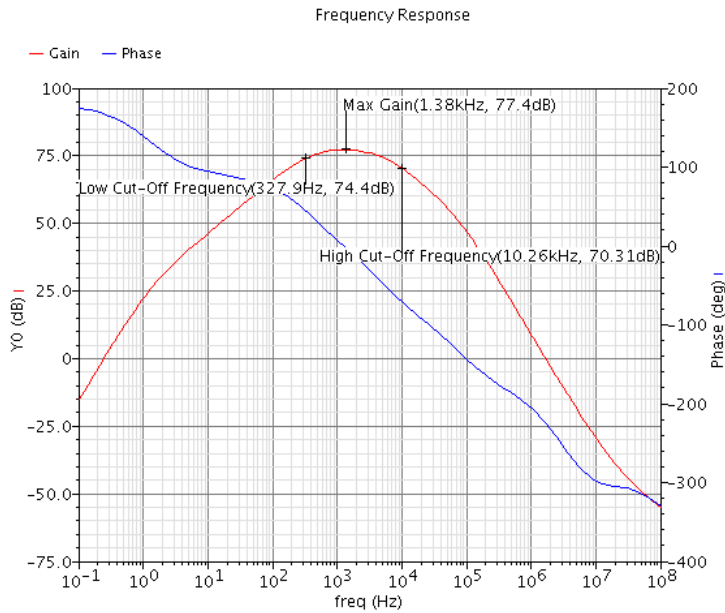


Figure B.2: Frequency response of the recording channels for block 2

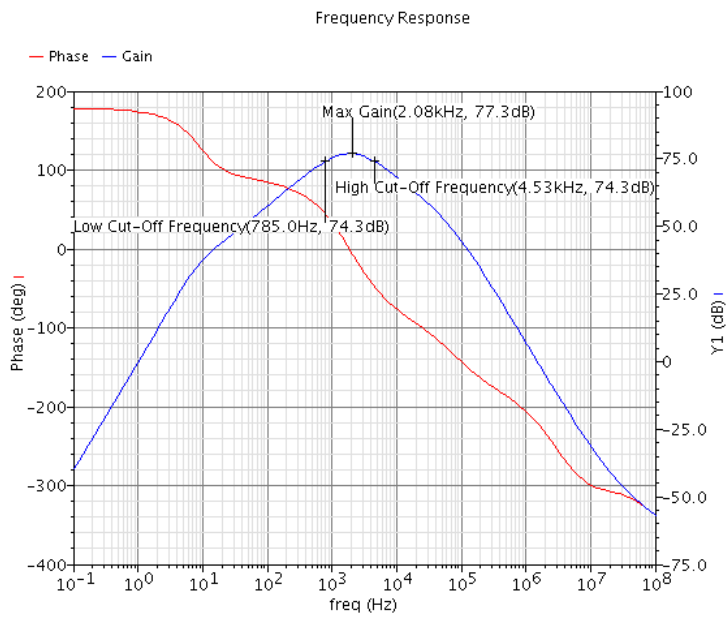


Figure B.3: Frequency response of the recording channels for block 4

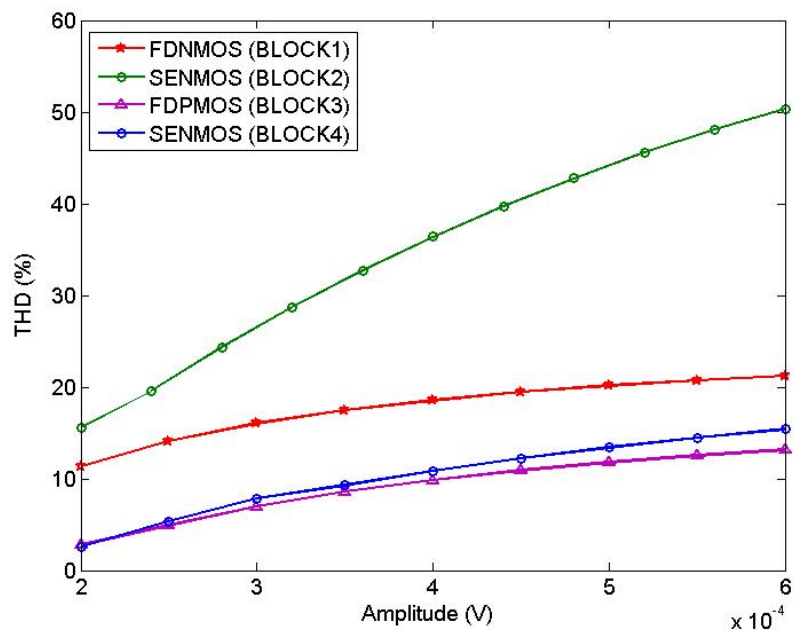


Figure B.4: Simulated total harmonic distortion for each block

References

- [1] T. Akin, K. Najafi, and R. M. Bradley. A wireless implantable multichannel digital neural recording system for a micromachined sieve electrode. *IEEE Journal of Solid-State Circuits*, 33(1):109–118, 1998.
- [2] P. E. Allen and D. R. Holberg. *CMOS analog circuit design*. Oxford University Press, second edition, 2002.
- [3] B. Aouizerate, E. Cuny, C. Martin-Guehl, D. Guehl, H. Amieva, A. Benazzouz, C. Fabrigoule, M. Allard, A. Rougier, B. Bioulac, J. Tignol, and P. Burbaud. Deep brain stimulation of the ventral caudate nucleus in the treatment of obsessive-compulsive disorder and major depression: Case report. *Journal of neurosurgery*, 101(4):682–686, 2004.
- [4] M. A. Arbib. *The handbook of brain theory and neural networks*. MIT Press, second edition, 2003.
- [5] J. N. Y. Aziz, R. Genov, B. L. Bardakjian, M. Derchansky, and P. L. Carlen. Brain-silicon interface for high-resolution in vitro neural recording. *IEEE Transactions on Biomedical Circuits and Systems*, 1(1):56–62, 2007.
- [6] R. J. Baker. *CMOS: Circuit Design, Layout, and Simulation: Third Edition*. John Wiley & Sons, 2011.
- [7] M. Banu, J. M. Khoury, and Y. Tsvividis. Fully differential operational amplifiers with accurate output balancing. *IEEE Journal of Solid-State Circuits*, 23(6):1410–1414, 1988.
- [8] M. W. Barnett and P. M. Larkman. The action potential. *Practical Neurology*, 7(3):192–197, 2007.

- [9] A. Bernyi, M. Belluscio, D. Mao, and G. Buzski. Closed-loop control of epilepsy by transcranial electrical stimulation. *Science*, 337(6095):735–737, 2012.
- [10] A. Borna, T. Marzullo, G. Gage, and K. Najafi. A small, light-weight, low-power, multichannel wireless neural recording microsystem. *Conference proceedings : Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, 2009:5413–5416, 2009.
- [11] T. C. Carusone, D. A. Johns, and K. W. Martin. *Analog integrated circuit design*. John Wiley & Sons, second edition, 2012.
- [12] M. S. Chae, W. Liu, and M. Sivaprakasam. Design optimization for integrated neural recording systems. *IEEE Journal of Solid-State Circuits*, 43(9):1931–1939, 2008.
- [13] J. K. Chapin, K. A. Moxon, R. S. Markowitz, and M. A. L. Nicolelis. Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex. *Nature neuroscience*, 2(7):664–670, 1999.
- [14] C. T. Charles. Wireless data links for biomedical implants: Current research and future directions. In *Conference Proceedings - IEEE Biomedical Circuits and Systems Conference Healthcare Technology, BiOCAS2007*, pages 13–16, 2007.
- [15] O. Devinsky. Patients with refractory seizures. *New England Journal of Medicine*, 340(20):1565–1570, 1999.
- [16] D. M. Di Pietro and J. D. Meindl. Optimal system design for an implantable cw doppler ultrasonic flowmeter. *IEEE Transactions on Biomedical Engineering*, 25(3):255–264, 1978.
- [17] H. Eichenbaum, D. Pettijohn, A. M. Deluca, and S. L. Chorover. Compact miniature microelectrode-telemetry system. *Physiology and Behavior*, 18(6):1175–1178, 1977.
- [18] C. D. Ferris. *Introduction to bioinstrumentation : with biological, environmental, and medical applications*. Humana Press, 1978.
- [19] T. B. Fryer, H. Sandler, W. Freund, E. P. McCutcheon, and E. L. Carlson. A multichannel implantable telemetry system for flow, pressure, and ecg measurements. *Journal of applied physiology*, 39(2):318–326, 1975.
- [20] P. R. Gigante and R. R. Goodman. Alternative surgical approaches in epilepsy. *Current Neurology and Neuroscience Reports*, 11(4):404–408, 2011.

- [21] P. R. Gray, P. J. Hurst, S. H. Lewis, and R. G. Meyer. *Analysis and design of analog integrated circuits*. Wiley, 5th edition, 2009.
- [22] R. Harrison, P. Watkins, R. Kier, R. Lovejoy, D. Black, R. Normann, and F. Solzbacher. A low-power integrated circuit for a wireless 100-electrode neural recording system. In *Digest of Technical Papers - IEEE International Solid-State Circuits Conference*, 2006.
- [23] R. R. Harrison. A versatile integrated circuit for the acquisition of biopotentials. In *Proceedings of the Custom Integrated Circuits Conference*, pages 115–122, 2007.
- [24] R. R. Harrison and C. Charles. A low-power, low-noise cmos amplifier for neural recording application. *IEEE Journal of Solid-State Circuits*, 38(6):958–965, 2003.
- [25] R. R. Harrison, R. J. Kier, C. A. Chestek, V. Gilja, P. Nuyujukian, S. Ryu, B. Greger, F. Solzbacher, and K. V. Shenoy. Wireless neural recording with single low-power integrated circuit. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 17(4):322–329, 2009.
- [26] R. R. Harrison, P. T. Watkins, R. J. Kier, R. O. Lovejoy, D. J. Black, B. Greger, and F. Solzbacher. A low-power integrated circuit for a wireless 100-electrode neural recording system. *IEEE Journal of Solid-State Circuits*, 42(1):123–133, 2007.
- [27] B. Hille. *Ion Channels of Excitable Membranes*. Sinauer Associates, Sunderland, Massachusetts, 2001.
- [28] L. R. Hochberg, M. D. Serruya, G. M. Friehs, J. A. Mukand, M. Saleh, A. H. Caplan, A. Branner, D. Chen, R. D. Penn, and J. P. Donoghue. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature*, 442(7099):164–171, 2006.
- [29] A. L. Hodgkin and A. F. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of physiology*, 117(4):500–544, 1952.
- [30] J. Ji and K. D. Wise. An implantable cmos circuit interface for multiplexed microelectrode recording arrays. *IEEE Journal of Solid-State Circuits*, 27(3):433–443, 1992.
- [31] S. Kim, R. A. Normann, R. Harrison, and F. Solzbacher. Preliminary study of the thermal impact of a microelectrode array implanted in the brain. In *Proc. Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Conference*, 1:2986–2989, 2006.

- [32] A. E. Lang and A. J. Lees. Management of parkinson's disease: An evidence-based review. *Movement Disorders*, 17(SUPPL. 4), 2002.
- [33] M. A. Lebedev and M. A. L. Nicolelis. Brain-machine interfaces: past, present and future. *Trends in neurosciences*, 29(9):536–546, 2006.
- [34] H. Li. A neural recording front end for multi-channel wireless implantable applications. Master's thesis, Michigan State University, 2011.
- [35] S. Liu and R.J. Baker. Process and temperature performance of a cmos beta-multiplier voltage reference. in *Proc. IEEE Int. Midwest Symp. Circuits and Systems (MWS-CAS)*, pages 33–36, 1998.
- [36] W. Liu, M. Sivaprakasam, W. Gang, and S. C. Moo. A neural recording system for monitoring shark behavior. In *Proceedings - IEEE International Symposium on Circuits and Systems*, pages 4123–4126, 2006.
- [37] Y. Lo, W. Liu, K. Chen, M. . Tsai, and F. Hsueh. A 64-channel neuron recording system. In *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, pages 2862–2865, 2011.
- [38] F. Maloberti. *Data Converters*. Springer, 2007.
- [39] K. Najafi and K. D. Wise. An implantable multielectrode array with on-chip signal processing. *IEEE Journal of Solid-State Circuits*, SC-21(6):1035–1044, 1986.
- [40] A. K. Ngugi, C. Bottomley, I. Kleinschmidt, J. W. Sander, and C. R. Newton. Estimation of the burden of active and life-time epilepsy: A meta-analytic approach. *Epilepsia*, 51(5):883–890, 2010.
- [41] C. T. Nordhausen, E. M. Maynard, and R. A. Normann. Single unit recording capabilities of a 100 microelectrode array. *Brain research*, 726(1-2):129–140, 1996.
- [42] R. H. Olsson, M. N. Gulari, and K. D. Wise. A fully-integrated bandpass amplifier for extracellular neural recording. *Proc.1st Int.IEEE EMBS Conf.Neural Engineering*, pages 165–168, 2003.
- [43] P. G. Patil and D. A. Turner. The development of brain-machine interface neuroprosthetic devices. *Neurotherapeutics*, 5(1):137–146, 2008.

- [44] G. E. Perlin and K. D. Wise. An ultra compact integrated front end for wireless neural recording microsystems. *Journal of Microelectromechanical Systems*, 19(6):1409–1421, 2010.
- [45] K. G. Plass. A new ultrasonic flowmeter for intravascular application. *IEEE Transactions on Biomedical Engineering*, 11(4):154–156, 1964.
- [46] D. Purves, G. J. Augustine, D. Fitzpatrick, L. C. Katz, A. LaMantia, J. O. McNamara, and S. M. Williams. *Neuroscience*. Sinauer Associates, Sunderland, Massachusetts, second edition, 2001.
- [47] R. D. Rader, J. P. Meehan, and J. K. C. Henriksen. An implantable blood pressure and flow transmitter. *IEEE Transactions on Biomedical Engineering*, BME-20(1):37–43, 1973.
- [48] B. Razavi. *Design of Analog CMOS Integrated Circuits*. McGraw-Hill, 2001.
- [49] H. Sandler, T. B. Fryer, and B. Datnow. Single-channel pressure telemetry unit. *Journal of applied physiology*, 26(2):235–238, 1969.
- [50] T. M. Seese, H. Harasaki, G. M. Saidel, and C. R. Davies. Characterization of tissue morphology, angiogenesis, and temperature in the adaptive response of muscle tissue to chronic heating. *Laboratory Investigation*, 78(12):1553–1562, 1998.
- [51] R. Shulyzki, K. Abdelhalim, A. Bagheri, C. M. Florez, P. L. Carlen, and R. Genov. 256-site active neural probe and 64-channel responsive cortical stimulator. In *Proceedings of the Custom Integrated Circuits Conference*, 2011.
- [52] A. M. Sodagar and K. Najafi. Wireless interfaces for implantable biomedical microsystems. In *Midwest Symposium on Circuits and Systems*, volume 2, pages 265–269, 2006.
- [53] A. M. Sodagar, G. E. Perlin, Y. Yao, K. Najafi, and K. D. Wise. An implantable 64-channel wireless microsystem for single-unit neural recording. *IEEE Journal of Solid-State Circuits*, 44(9):2591–2604, 2009.
- [54] D. M. Taylor, S. I. H. Tillery, and A. B. Schwartz. Direct cortical control of 3d neuroprosthetic devices. *Science*, 296(5574):1829–1832, 2002.
- [55] G. Wang. *An Integrated, Low Noise Neural Recording System*. PhD thesis, University Of California Santa Cruz, 2009.

- [56] P. T. Watkins, R. J. Kier, R. O. Lovejoy, D. J. Black, and R. R. Harrison. Signal amplification, detection and transmission in a wireless 100-electrode neural recording system. In *Proceedings - IEEE International Symposium on Circuits and Systems*, pages 2193–2196, 2006.
- [57] Cerberus website. <http://www.blackrockmicro.com/content.aspx?id=13>.
- [58] J. G. Webster. *Bioinstrumentation*. John Wiley & Sons, 2004.
- [59] R. Wertz, G. Maeda, and T. J. Willey. Design for a micropowered multichannel pam/fm biotelemetry system for brain research. *Journal of applied physiology*, 41(5), 1976.
- [60] J. Wessberg, C. R. Stambaugh, J. D. Kralik, P. D. Beck, M. Laubach, J. K. Chapin, J. Kim, S. J. Biggs, M. A. Srinivasan, and M. A. L. Nicolelis. Real-time prediction of hand trajectory by ensembles of cortical neurons in primates. *Nature*, 408(6810):361–365, 2000.
- [61] D. Money Weste, N. H. E. Harris. *CMOS VLSI design : a circuits and systems perspective*. Addison-Wesley, 4th edition, 2011.
- [62] Y. Yonezawa, I. Ninomiya, and N. Nishiura. A multichannel telemetry system for recording cardiovascular neural signals. *The American Journal of Physiology*, 236(3):H513–518, 1979.