NTNU – Trondheim
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Science and Technology

- TFE4520 -
Project Report

Something about an LNA for neural interfaces and shit in the face

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October 4, 2015

Abstract

TheDesignofIntegrated CircuitstoObserve BrainActivity

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I've always wanted an apple corer.

- Shithead

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List of Acronyms

LNA low noise amplifier 1

ECoG electrocorticography 4

EEG electroencephalography 4

iEEG intercranial electroencephalography 4

IC integrated circuit

CMOS complementary metal-oxide-semiconductor 1

LFP local field potentials 4

MEMS microelectromechanical system 1

ADC analog to digital converter

CMRR common mode rejection ration 6

BMI brain-machine interface 1

OTA operational transconductance amplifier

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1 Introduction

The main objective for this report is to propose a low noise amplifier (LNA) front-end for extracellular[1] in-vito[2] neural signal recording electrodes, as well as to research what requirements can be considered critical in achieving such a design. As a natural consequence of the main objective, the project - which this report is a product of - will explore the usage of CMOS technology in neural recording systems. Any findings produced can therefore be used as a preliminary for further research in the authors upcoming graduate thesis. Thus, some basic elaborations on where the design can potentially be situated in a complete brain-machine interface (BMI) - such as a bio-medical IC or a neuro MEMS array with fully integrated electronics, will be undergone.

The rest of this chapter will describe the motivation for initiating this project, provide a rudimentary overview of past work in this area, mention outcomes of the project, and outline the structure of the rest of the report.

1.1 Motivational Background

Technological advances towards a type of electromechanical or biomedical augmentation of the human body which remedies, improves or maybe even grants the user a new set of abilities are intriguing thoughts for anyone with a little *cyberpunk* in them. There is still quite a long way before any such leaps in technology are possible. However, forcing oneself into more pragmatical ways of thinking; there is no doubt that demands for technologies enabling scientists and clinicians to record neural activity from a large number of neurons in a brain is continuously rising. Namely collecting high temporal and spatial resolution neural data from micromachined multielectrode arrays is something that can be regarded standard practice in basic neuroscientifical research [6]. Such research is starting to enable medical, as well as neuroprosthetic applications, and we see that neural recordings can provide scientific insight into the neural correlates of cognitive, sensory and motor processes [14, 1, 4]. Experiments and clinical trials with primates - both human [8] and non-human [21], as subjects have shown that data directly derived from signals - namely action and local field potentialss (which are to be discussed in chapter 2), can be used to control robotic prosthetics.

In the efforts to implement wholly implantable devices for neural recording purposes, microelectromechanical system (MEMS) electrode arrays can be complimented with complementary metal-oxide-semiconductor (CMOS) integrated circuits in such a way that one achieves parallel stand-alone BMIs with on-board wireless data and power transfer, as well as ADCs and a processor [15, 22, 16]. The continuously improving resolutions of MEMS arrays have enabled simultaneous recording of large neuron populations with spatial resolutions down to a single cell activity from populations of neurons [11].

[1] *extracellular* means "outside the cell"
[2] *in-vivo* is Latin for "within the living"

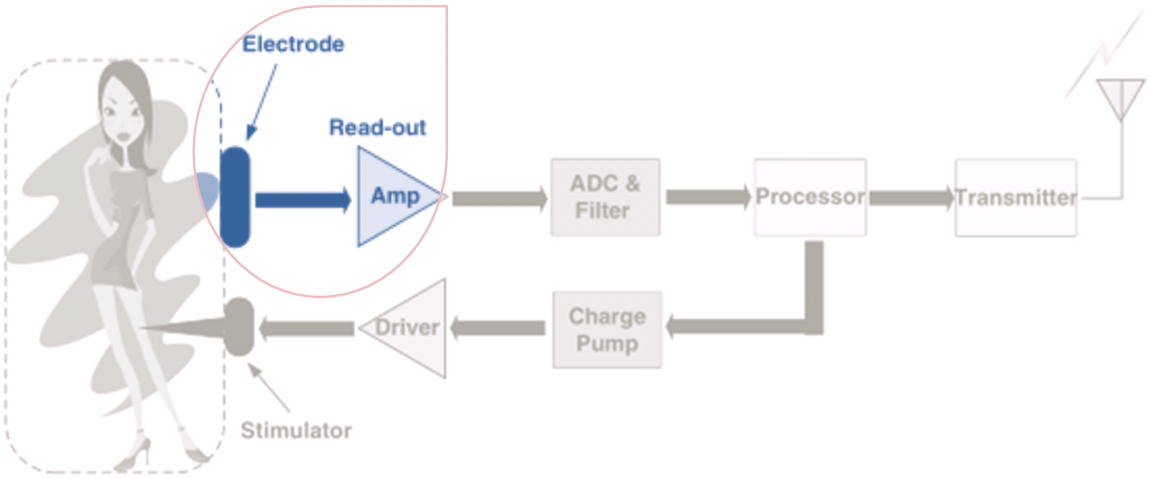
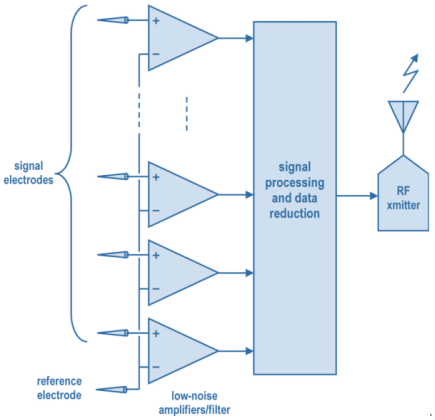


Figure 1.1: `typical architecture of bio-medical IC subsystem [23]`

Studies such as the ones mentioned have shown a promising future for developing BMIs that have practical use for humans. But to reach that point in the future where such systems can be implanted in-vito in humans and function symbiotically with them in their everyday activities, many challenges must be overcome. Even though we are limited to propose a preliminary design for a low noise amplifier front-end for neuro-probes with a type of platinum/iridium based electrodes, we will explore requirements to make the design compatible for integration in a complete in-vito brain-machine interface which utilizes a MEMS electrode array based transducer. The research in this area will ideally continue in the authors upcoming graduate thesis. A block diagram illustrating our focal point in a complete biomedical IC - which also has an interface for stimulation, is shown in figure 1.1. Also, a block diagram depicting the principle for a multielectrode wireless neural interface is given in figure 1.2.

Figure 1.2: `block diagram of a wireless neural recording device`



1.2 Past Work

There is much literature describing both conceptual and physical implementations neural recording systems with varying degrees of practical usability. derpa derp...

1.3 Summary of Authors Contributions

- nada
- nuthin'

1.4 Report Outline

The report is organized in the following manner:

- **Chapter 2** briefly presents the motivational background for neural recording before digging into the relevant theory needed to understand the design itself as well as eventual limitations and difficulties in realizing the best possible specifications. It also provides a basic theoretical understanding of the neural recording principles from an electronic designers point of view - namely how LNA to interface with intercranial electrodes.
- **Chapter 3** TODO
- **Chapter 4** TODO

2 Theoretical Background & Literature Review

As mentioned, this reports main focal point will be on the design of a LNA front-end for a transducer utilizing a type of platinum-iridium based electrodes. As such we will start exploring basic characteristics of neural signals and some practicalities on recording them, before we dig into the electronics theory necessary for us to determine a design methodology for the neural interface front-end. Notice also that remarks about the amplifier design - which is to be fully introduced in later chapters, are made as the theory discussion progresses.

2.1 Neural Recording through Biopotential Acquisition

Neural recording devices basically performs biopotential acquisition using transducers that converts ionic conduction to electronic conduction so that biopotential signals can be stored and viewed. The biopotential signals themselves are generated due to electrochemical activity of electrogenic cells[1] - such as neurons, that are components of muscular, nervous or glandular tissue. There are several measurement variations that are relevant for collecting biopotential data, whereas the ones considered most relevant for the scope of this report are *electroencephalography (EEG)*, *electrocorticography (ECoG)* and *intercranial electroencephalography (iEEG)* (also commonly referred to by the somewhat misleading term *local field potentials (LFP)*).

From a historical perspective one usually refers to surface recording - that is, placing electrodes on top of the scalp - as EEG, while ECoG and iEEG have coined the use of in-vivo intercranial electrodes in order to record electrical activity in the brains cerebral cortex[2]. More specifically on in-vivo recording; iEEG\LFP is usually referred to when recordings are performed using small electrodes placed directly into the cortex from beneath the skull, while with ECoG recordings one places the electrodes on the surface of the cortex.

2.1.1 The Neural Signals

We have have explained that there exists multiple measurement types for recording cortical activity. Biopotential signals generated by electrogenic cells like neurons, produce voltage changes on the order of 100 mV relative to the extracellular fluid [10]. Collecting measurements of this type is possible in brief periods of time by carefully directing individual placement of microelectrodes intracellularly[3]. To get around the limitations of only detecting single cells at a time - and for such short durations, the prime methodology at present is using microelectrode arrays extracellularly (though there exists rudimentary

[1] *Electrogenic cells* refers to cells that exhibit the ability to generate electrical signals[17]

[2] The *cerebral cortex* is the outermost sheet of neural tissue covering the cerebral hemispheres in mammals. [13]

[3] *Intracellular* means "inside the cell"

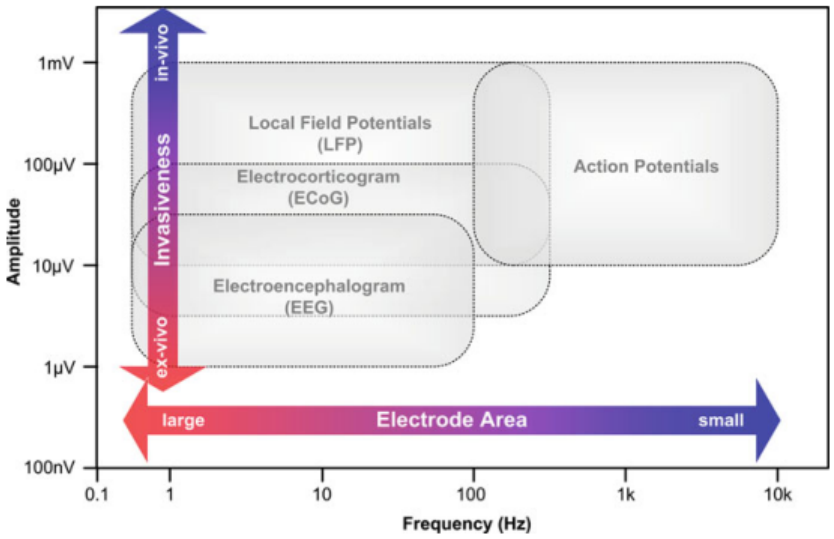
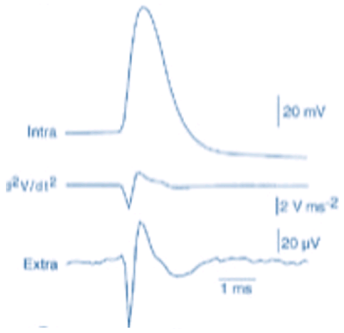


Figure 2.2: `different cortical measurements [23]`

initiatives to merge the advantages of extracellular microelectrode arrays and intracellular microelectrodes, they have still not gained significant usability) [20]. A trade-off here is that we accept "blindness" to potentials generated by single cells as well as a significant reduction in signal amplitude. However, an interesting relationship is shown in figure 2.1 (adapted from [19]); we can see that the shape of the extracellular voltage potential qualitatively matches the second time derivative of the intracellular voltage potential [2]. Note that the resulting variation in cellular potential with time is known as the action potential [17]. Action potentials can be interpreted as "digital" events - neurons normally induce spikes of similar amplitudes and time durations, and information is said to be found in the timing of these "digital" events [5].

Figure 2.1: `Rec. of action potential`



A measurement type can be characterized by their signal strength (which we can see from fig.2.2 is usually in the μ-volts range) and surgical invasiveness versus frequency and electrode area. This is presented in figure 2.2. ECoG signals is measured using subdural surface electrodes (refer to 1. on fig.2.6). This type of measurement is outside of our design scope due to frequency range, but it can be mentioned that the method offers significant increase in spatial and temporal resolutions as well as stronger amplitudes - especially in the high gamma frequency range[4], in contrast to the non-invasive surface based EEG topologies [7]. This leads us to the very similar LFP signals. LFP oscillations differs from ECoG in that LFPs are recorded from within the cortical tissue (illustrated by 2. in fig.2.6). It is considered the internal correlate of ECoG as it registers as the same "crowd noise" - that is synchronous activity of many neurons in one region of the brain, as ECoG recording, only with substantial blurring and attenuations. The signal deterioration happens because LFP oscillations is usually measured using microelectrode arrays [5]. This means LFP spectra is unavoidably detected with microelectrode arrays, even though one might only be after action potentials. It is, however, often beneficial to

[4]Gamma frequency ranges between 70Hz to 110Hz[7]

	Measurement Invasiveness	Electrode Area	Electrode Impedance	Susceptibility to 1/f noise	CMRR Requirement
ECG	− −	+ +	− −	+	+
EMG	− −	+	− −	+	+
LFP	+ +	+	+	+	−
ECoG	+	+	− −	+	+
EEG	−	+	−	++	++
Action potentials	+ +	− −	+ +	−	−

Figure 2.3: `Summary of the considerations during the design of instrumentation amplifiers for different neural signals.`
`(-) indicates a low/small value`
`(+) indicates a high/large value`

record both LFP together with action potential spikes and then apply linear filtering - which should be fairly easy to achieve considering frequency ranges are mostly different for the two signal types. LFPs are interesting for the same reasons that ECoG signals are; they have among other things been especially suitable in understanding motor movements of the body [3] and are consequently very suitable for e.g. neuroprosthetic applications.

We notice from figure 2.2 that the low frequency characteristics and small signal amplitudes poses strict noise requirements on designing a low noise amplifier. In addition we know that CMOS low noise design at such low frequencies will not be a straightforward experience because of CMOS circuitry's susceptibility to flicker noise. For the LNA design - which is to be introduced next chapter, we will focus on action potential measurements. Therefore flicker noise should be a little less of a problem for us as we are in the 100 Hz to 10 kHz frequency range. We will however, have to deal with a larger impedance because smaller electrode area is needed to measure action potentials. Also an important remark to make is about eventual LFP signals; as it is assumed that our LNA will be used for interfacing with a microelectrode array, LFP parts ($< \approx$200 Hz) in the recording would be amplified and they would have be filtered out at a later stage in the system if they are unwanted.

Fig.2.2 also tells us something of what common mode rejection ration (CMRR) we have to expect from the LNA. Again we focus on action potentials and see that the frequency of interest is higher than e.g. the mains frequency for instance, so we can have a much more relaxed CMRR than any other type of neural recording. We still need to try to minimize capacitive and inductive interferences though. In addition; tethering forces introduced by conductors will cause problems for electrodes inserted into the sensitive tissue of the brain. Therefore one should ideally place the amplifier as close to - ideally directly attached to, the transducer. A guideline summary of LNA design considerations in regards to what type of neural signal one seek to record is given in [23] and illustrated in figure 2.3.

2.1.2 Real-life Application of ideal Polarizable & Non-Polarizable Electrodes

To be able pick up biopotential-signals, current should flow from the tissue into the acquisition electronics. As the current is carried by ions in the body of a living being, a

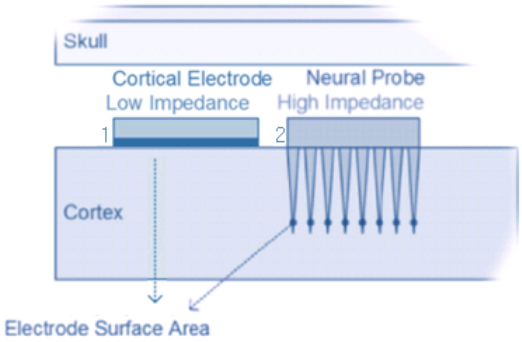


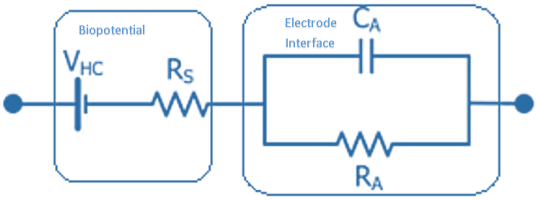
Figure 2.6:

1. Cortical or subdural electrode placed under the skull directly on the surface of the brain.
2. Neuro-probe array placed on the surface of a brain. The recording electrodes are drawn as dots on the array of probes penetrating the cortex

transducer is needed to convert ionic current into electronic current.

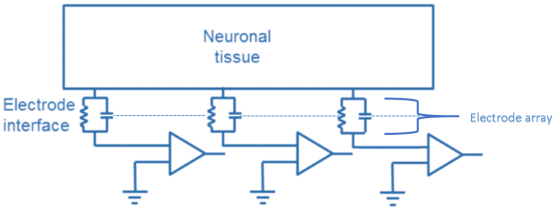
Enter the **electrode**.

Figure 2.4: electrode model



How easily electrons travel through the electrode interface defines if the electrode is considered non-polarizable or polarizable. If current flow happens by very little energy, the electrode is referred to as being non-polarizable. As such the electrode would ideally see no over-potentials and thus, a *perfectly* non-polarizable electrode can be seen as a simple resistor. If no charge crosses the electrode transfer, the electrode is referred to as polarizable and can ideally be seen as capacitor as we only have a displacement current. However, the real world is not so forgiving; no electrode is purely polarizable or non-polarizable, rather something in between. We therefore present a basic electrical model of a single electrode [17] shown in figure 2.4. We see from 2.4 that the source impedance can be modeled by a Thevenin equivalent source with a source impedance of Rs, while the electrode can be modeled by a capacitor C_A in parallel with a resistor R_A.

Figure 2.5: electrode array model



Notice from figure 2.6 how the different electrode placement generally cover different areas. The impedance of an electrode plays an important role during the design of the recording circuit when selecting amplifier design topology. We know that as the electrode surface area decreases, its impedance tends to increase [23]. Thus, the use of probes with high small electrode area forces us to design an amplifier with high input impedance.

2.2 Transistor and Amplifier basics

2.2.1 Designing Low-Noise and Low-Power OTAs

...see [6] section B.

2.2.1.1 MOSFET's and Level of Inversion

New design basis - level of inversion or inversion coefficient (IC)

Work with both region of MOSFET operation and the level of inversion

Use level of inversion as design variable - Replaces conventional approaches involving the bias current and the MOSFET channel width

2.2.2 Noise Performance

2.2.2.1 Noise Figure

2.2.2.2 Noise Efficiency Factor

In order to be able to compare the noise specifications reached with other recently published IAs, a noise efficiency factor (NEF) is introduced. The total equivalent input noise of an ideal bipolar transistor (only thermal noise and no base resistance) is given by

2015HoST Project noise noiseEffFactor

with BW being the frequency bandwidth (for a bipoku transistor this is the ft). The NEF of a system is then defined as

2015HoST Project noise noiseEffFactor

where In, is the total current drain in the system and

Vi. is the total equivalent input noise. The NEF describes how many times the noise of a system with the same current drain and bandwidth is higher compared to the ideal case, e.g., for a CMOS transistor with only white noise, the noise power is given by

2015HoST Project noise noiseEffFactor

3 The LNA front-end

Given that the low noise amplifier makes up the first stage in a neural recording device, it easily becomes one of the most important modules in it. We discovered in chapter 2 that when interfacing with a MEMS array - which has become our transducer of interest, we have the ability to amplify both action potentials and LFPs. We discussed that our design scope will be limited to action potentials and therefore have a more relaxed CMRR than we would have if we were interested in the LFPs. This line of reasoning eventually led us to remark that the amplifier preferably should be attached to the transducer itself. Such a placement compels us to consider another requirement - namely heat dissipation. Findings in [18] tells us that cells exposed to certain temperatures over prolonged periods of time simply dies. Thus, we will have to limit amplifier power usage. [5] claims that modern MEMS arrays might consist of something like 100 electrodes and that for example a 6 x 6 x 2 mm^3 must then consume less than 100μW.

Another consideration we discussed in chapter 2 was a designs potential susceptibility to noise. Even though our bandwidth requirements leave us less vulnerable to flicker noise than designs trying to record any biopotential signals other than action potentials, we still have to maintain a satisfactory suppression of input-referred noise. Minimizing of input-referred noise does often result in a relatively high quiescent current; yet, a contradiction here is that the current that can be supplied to the LNA will be limited by our power consumption requirements. Alas, finding the best noise power trade-off will be one of the main challenges in the design process.

A major drawback in the classical amplifier design topology - e.g. operating transistors in strong inversion, is the fact that transistors in the active region limits a circuits power efficiency. As low-power is critical in a neural recording front-end, an idea is make sure transistors (mainly referring to the input pair the differential stage) operates in weak inversion. Now, as opposed to G_m being proportional to the square root of the drain current, the transconductance G_m will be proportional to the drain current [6] and ergo achieves a better power efficiency. Maximizing G_m in this way will also minimize thermal noise in any CMOS differential amplifier [9] (note that we are aiming for a fixed drain current). Thus, the input pairs in the differential stage will need to have a large W/L ratio. Further on, their lengths should be small so that their widths also will be as small as possible. This way the input capacitance of the LNA does not become problematically large.

In this context, it would be prudent to provide an introduction to the inversion coefficient (IC) relationship:

$$IC = I_D/I_S; \tag{3.1}$$

where I_S is the inversion characteristics current, as given by

$$I_S = \frac{2\mu C_{ox} V_t^2}{\kappa} \cdot W/L; \tag{3.2}$$

In equation 3.2, κ would be the gate coupling coefficient in subthreshold operation, V_t the thermal voltage, C_{ox} the gate capacitance per unit area, and μ the mobility of

electrons near the silicon surface. Lastly W and L is the transistor width and length respectively. We note that [6] claims κ to have a typical value of 0.7. Returning to the inversion coefficient, the same source tells us that IC gives us an understanding of a transistor operating regian, that is IC equates to[1] [2]

- strong inversion if IC $>$ 10;
- medium inversion if 10 $>$ IC $>$ 0.1;
- weak inversion if IC $<$ 0.1 ($V_{GS} - V_{TH}$);

We can summarize design requirements as follows:

1. **Dynamic range** - Fig.2.2 indicates that we must have a dynamic range good enough to convey action potentials as low as $\pm$2mV.
2. **Input Impedance** - Higher input impedance than the transducer as well as negligible dc input current.
3. **Bandwidth** - 100-10kHz to pick up action potentials.
4. **DC offset** - block DC offset at the transducer to prevent unwanted saturation of the amplifier.
5. **Noise** - input noise must be small enough to pick up amplitudes as small as $\simeq 30\mu$V

[1] Notice that the overdrive voltages are given for NMOS

[2] Notice that $\kappa = \frac{1}{n}$ where n is called the subthreshold swing coefficiant (or ideality factor) and is the reciporal of the rate of change in the channel surface potential as a function of gate voltage [12]

4 Design Methodology

This chapter should discuss the details of your implementation for the assignment. Everything related to *how* things were done should go here. Remember to avoid going into too much details, summarize appropriately and try to use figures/charts. Make sure you refer to the figures (such as Figure Avoid putting lots of source code here – small code snippets are fine if you want to discuss something specific.

4.1 Amplifier Topology

Add content in this section that describes how you tested and verified the correctness of your implementation, with respect to the requirements of the assignment.

5 Results

In this chapter, you should discuss the results you have obtained from your implementation. These can be correctness results, i.e whether the implementation behaved as expected, or numerical results that express runtime or energy measurements.

6 Conclusion

This chapter should be a look back at the entire report and summarizing the problem, the solution and the obtained results.

6.1 Evaluation of the Assignment

You can include comments about the assignment itself here. While this part is not obligatory and not graded, it is valuable feedback to the course staff that can be used to improve the exercises in the future.

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