

[https://doi.org/10.52326/jes.utm.2025.32\(2\).04](https://doi.org/10.52326/jes.utm.2025.32(2).04)
UDC 615.47:611.7/.8



INTERFACE ADAPTATION DESIGN FOR EXTRACELLULAR RECORDINGS FROM EXCITABLE TISSUE

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Received: 05. 12. 2025

Accepted: 06. 21. 2025

Abstract. For a clear and almost exhaustive perspective on the physiology of living organisms, it is important to use the best method to sample the signal and to process it correctly, without affecting the content of information. Therefore, the method must ensure the best possible sensitivity and selectivity. In this work, a device for processing physiological signals is designed. The main component will be an instrumentation amplifier, whose characteristics meet specific requirements. This is an amplifier suitable for high-quality recording of extracellular signals from muscle and nervous tissue. Its characteristics are related to the fact that it has a gain and bandwidth for the signals of interest, a common mode rejection rate, filtering and low internal noise. The input impedance is high, and the consumption is low are other key features of this device. In addition, the component costs are very low, and the design is very compact. Due to the high input impedance of the amplifier, it adapts very easily to different signals. The final experimental results show the viability of the solution chosen by design.

Keywords: *tissue, recording, conditioning, instrumentation amplifier.*

Rezumat. Pentru o perspectivă clară și aproape exhaustivă asupra fiziologiei organismelor vii, este important să se utilizeze cea mai bună metodă de eșantionare a semnalului și de procesare corectă a acestuia, fără a afecta conținutul informației. Prin urmare, metoda trebuie să asigure o sensibilitate și o selectivitate cât mai bună. În cadrul acestei lucrări se proiectează un dispozitiv pentru prelucrarea semnalelor fiziologice. Componenta principală va fi un amplificator de instrumentație, ale cărui caracteristici îndeplinesc cerințe specifice. Acesta este un amplificator potrivit pentru înregistrarea de înaltă calitate a semnalelor extracelulare din țesutul muscular și nervos. Particularitățile lui sunt legate de faptul că are un câștig și o lățime de bandă pentru semnalele de interes adecvat, o rată de rejecție a modului comun, filtrare și zgomot intern mic. Impedanța de intrare este mare și un consum redus sunt alte caracteristici cheie ale acestui dispozitiv. În plus, costurile componentelor sunt foarte mici și design-ul este foarte compact. Datorită impedanței mari de intrare a amplificatorului, se adaptează foarte ușor la semnale diferite. Rezultatele experimentale finale arată viabilitatea soluției alese prin proiectare.

Cuvinte-cheie: *țesut, înregistrare, condiționare, amplificator instrumentațional.*

1. Introduction

To design this kind of device, we must look to three basic functions of any biopotential amplifier: amplifier gain, signal filtering, and which is important when is used to live organisms, protection regarding dangerous potentials. This method can be used as an invasive or non-invasive method. An example of biopotential measurement systems is presented in Figure 1. Main components are electrodes, amplifier, oscilloscope, interface and conversion to connect to a computer. As seen in Figure 1 the performance of this measurement system depends by amplifier stage.

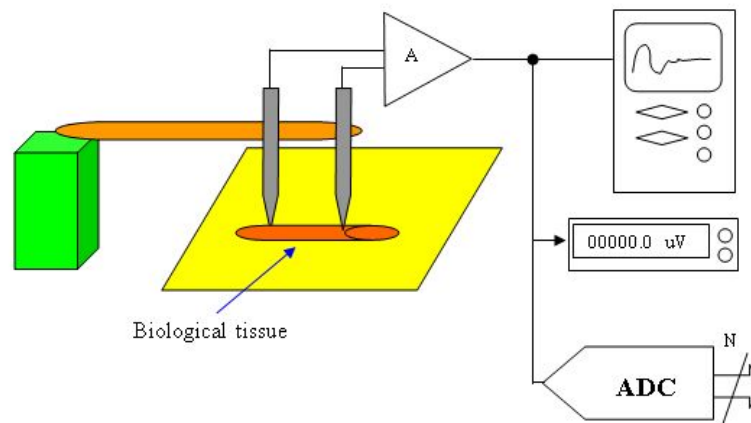


Figure 1. Measurement system for physiological pulses.

Signals can be different types starting with extracellular signals, neuro-physiological signals and brain signals or from muscular activities [1].

On the market are some examples of amplifiers used for physiological signals, like Microelectrode Amplifier (MEA) type 695, COMPEX device and various ECG devices.

The PLUGSYS MEA device is a universal amplifier that samples the signal through microelectrodes, used for physiological and pharmacological research. Using a separate preamplifier (for the first stage), it allows direct measurement of intracellular or extracellular potentials. The PLUGSYS device, even if limited to a single input channel, incorporates advanced technology that requires, in addition to the high performance of the amplifier, other modern additional facilities, such as adjustable output filter, generator for performing a calibration, audio and graphic LED indicators for monitoring the sound and visual signal. The operation of the microelectrodes can also be tested (by measuring contact resistance), tissue capacitance compensation and zero adjustment. Additionally, the PLUGSYS MEA can be equipped with special input stages and a proprietary multifunctional clamp amplifier module for current clamp and voltage clamp applications. The output is made externally via the Bayonet Neill-Concelman (BNC) jack on the front panel, which ensures firm contact and protection against interference. The bandwidth is from DC to 30 kHz (-3 dB). The output signal is ± 10 V for an input signal of ± 1 V. The low-pass filter has 7 steps, from 30 Hz to 30 kHz (-3 dB). The gain is fixed at 10, and the input offset compensation is ± 400 mV [2].

Electrocardiogram (ECG) is an electrical signal present in living organisms with a typical amplitude of 500 μ V and a frequency range of 0.01 to 250 Hz. The desired output signal from the amplifier for the ECG signal is a maximum amplitude signal of 5V, with a frequency range of 0.5 to 100 Hz. Therefore, this amplifier has a gain of 1000, and the filter will have a passband of 0.5 to 100 Hz. Three important and basic functions of any biopotential amplifier must be considered when studying this type of amplifier: patient protection from

non-compliant electrical voltages, signal amplification, and signal filtering. The biopotential amplifier requires an appropriate amplification range, as well as an appropriate frequency range. Noise reduction is another constraint of this amplifier. The basic components of biopotential amplifiers are differential topology amplifiers and instrumentation amplifiers.

COMPEX device is a typical example for a device used to record biological pulses. The basic unit contains an IEEE-488 interface and thus is connected to any computer that is also fitted to this standard. High transfer rates (1 Mb/s) ensure us to be able to connect simultaneously several (up to 16) basic units. Every basic unit is equipped with its own microcontroller that organizes the data exchange with the computer. COMPEX module for analog measurements allows the two-channel recording of extremely fast analog signals. The sampling frequency is 300 kHz maximum, so in this case a resolution of 10 measuring points signals of up to 30 kHz can be recorded per period. To avoid couplings of the earth cables the inputs are designed as earth-free differential voltage inputs so that in each case only the exact voltage difference between two freely selected points is measured and displayed. Therefore, this plug-in module is extremely suitable for representing nerve and sensory, physiological values. It is not necessary to buy and operate a recorder or an expensive storage oscilloscope. The inputs are differential, input resistance is $1\text{M}\Omega$, sensitivity have many values (100 mV, 200 mV, 500 mV, 1 V, 2 V, 5 V, 10 V), sampling frequency: software controlled, 30 Hz, 100 Hz, 300 Hz, 1 kHz, 10 kHz, 30 kHz, 100 kHz, 300 kHz, resolution has 8bit and triggering point of time: software controlled: 0-90 % [3, 4].

From the example above we must take into consideration some aspects regarding proposed device. Briefly, it is about properties that they must fulfill.

Signal amplification is important because of its very low amplitude of its. For signals like EMG, 0,1 mV value can be found. Entire range is around from $10\ \mu\text{V}$ to 5 mV. Signal output value is around 5 V. Necessary gain is x5000. At the same time, with our signal it is other interference signals [5].

Amplifier stages not limited only to simple amplification, but it must be accomplishing others things like accuracy of gain and linearity of signal, current – voltage conversion, decrease noise by increasing signal to noise ratio, and filtering capabilities.

For amplification only function it is thought that we have the following: noise, gain/sensitivity, domain, input signal type (differential or single-ended), common mode rejection rate, input impedance, filtering performance [5].

Noise sources can be from amplifier itself, environment itself (bioelectric sources, heartbeat), cabling effects (power supply at 50Hz), and movement artifact 30Hz. Rejection and attenuation of these noise signals can be done by shielded cable and pre-amplified electrodes.

Gain and sensitivity must vary in a wide range and linearity and gain accuracy must be within reasonable limits.

If it is not choosing an optimal range, for great signals, the device can go in clipped mode and distort the signal. To avoid clipped conditions, there must be the proper gain [5].

Input in amplifier can be done referenced to ground (one working electrode and one reference electrode), differential (two working electrodes and one reference electrode) or double differential (three working electrodes and one reference electrode). The last two electrodes can give better signals and minimum disturbance from common mode signals.

Common Mode Rejection Ratio (CMRR) represents a coefficient which shows how good the amplifier is in eliminating common artifacts regarding useful signals. The great value of

it denotes a very good amplifier. For example, if we have a CMRR ratio $\geq 10000:1$ (or 80 dB) then 99.99% from common signal is rejected or difference of electrode potentials (working electrode and reference electrode) is increased for 10000 times greater than both electrodes common potentials [6].

Input impedance means a quantitative meaning of resistance against current flow. Important is electrodes/site preparation impedance but amplifier input impedance, also. The mutual impact of these both impedances can be reduced to minimum by adaptation.

Practical input impedance of amplifier must be greater than surface contact to avoid signal attenuation. Input impedance can be optimized by setting the place (shave region, abrade, clean with alcohol, use electrolytic gel) and circuit design. For better results, the electrode impedance and surface impedance should be reduced as much as possible, or the input impedance of the amplifier should be increased. Noise reduction is closely correlated with electrode impedance.

Another way to decrease the noise is to shield with a metallic case, the entire measurement system. Using electrochemical batteries, it is a good way to reduce costs of power supply.

Filter types used can be low-pass, notch filter and high-pass. The low-pass filter allows signals with a frequency lower than an upper limit to pass (800-1000 Hz for EMG). Notch filter eliminates a narrow frequency band (50 Hz). The high-pass filter does not allow signals with a frequency lower than a limit to pass (2 Hz for EMG).

Some amplifier has selectable output modes: original signal, RMS: "root mean square" processed signal, and filtered signal. It is recommended to collect raw signals and post-process as needed, to avoid losing information.

The main objective of this work is to develop, with minimal cost, a high-performance amplifier that can bring the low-level signals present in the human body to a convenient level. The output signal of this device can be used, for example, as an input for an acquisition board. This way, the advantages of data processing using a computer system can be used. The fact that the scheme can be easily adapted (by gain and filter options) to any signal is an advantage, ensuring versatility. Avoiding noise that can affect the original signal is done by using shielded cables and protecting the entire device with a metal box.

2. Materials and Methods

The proposed device is a combination of amplifiers-filters, that main purpose is to adapt physiological signal to easy follow by classical measurement methods. This is important when want to connect this device to a data acquisition system for post processing and memorizing them. For the current situation, we have the following parameters considered for the designed device [7]:

- A very high input impedance
- Gain range: 100 - 1000
- Bandwidth, controlled by filtering: 1 Hz – 5 kHz (20 kHz)
- CMRR ~ 100 dB

The general block diagram for this type of measurement system is shown in Figure 2. Components are IA – instrumentation amplifier, A – signal amplification, F – filters.

If the main role of first two stages is to amplifier and to convert from differential signal to ground referenced signal, the filtering stage rejects useless signal (industrial power supply

– 50 Hz) and to superior limiting to avoid overlapping signal spectral components. This last thing is important when it is used an analog to digital converter [8].

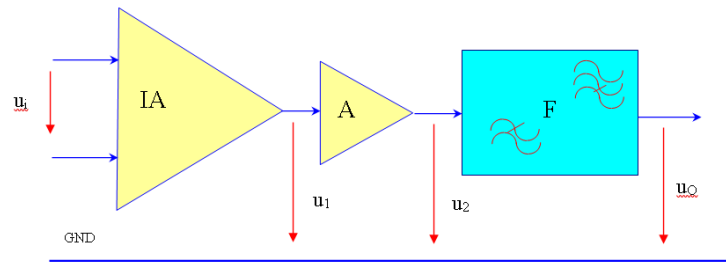


Figure 2. Block diagram of amplification-filtering device.

There are two types of filters: notch filters and low-pass filters. The block diagram is a minimal configuration. Special restrictions must be made to shield the device.

The first stage of this device must be an instrumentation amplifier. The main advantage is common mode rejection rate, very high input impedance and a single adjustable resistor for gain. At the first look, the amplification can be solved from one amplification stage. But it is important to know that the amplification is not constant to any frequency. Here were used LT1920, by Linear Technologies. Two operational amplifiers do the next two amplifier stages from integrated quad circuit LT1079. The preferable solution is this because the interest is to maintain enough bandwidth. The gain and frequency bandwidths are antagonist behavior [9].

A double T network can do a high-quality notch filter. Double T network is one of the RC filtering networks who has a very good characteristic. This RC network is working together with a repeater, which ensures a segregate of output versus network and low output impedance. The high input impedance of repeaters made by operational amplifier has a result in double T network resistor dimensions [10]. Therefore, the capacitors have very low capacitance and low physical dimensions, even if there are low frequency [11]. Quality factor, Q , is about 50. Repeater does not affect double T network parameters, slope and frequency. Figure 3 shows an example of a notch filter [12].

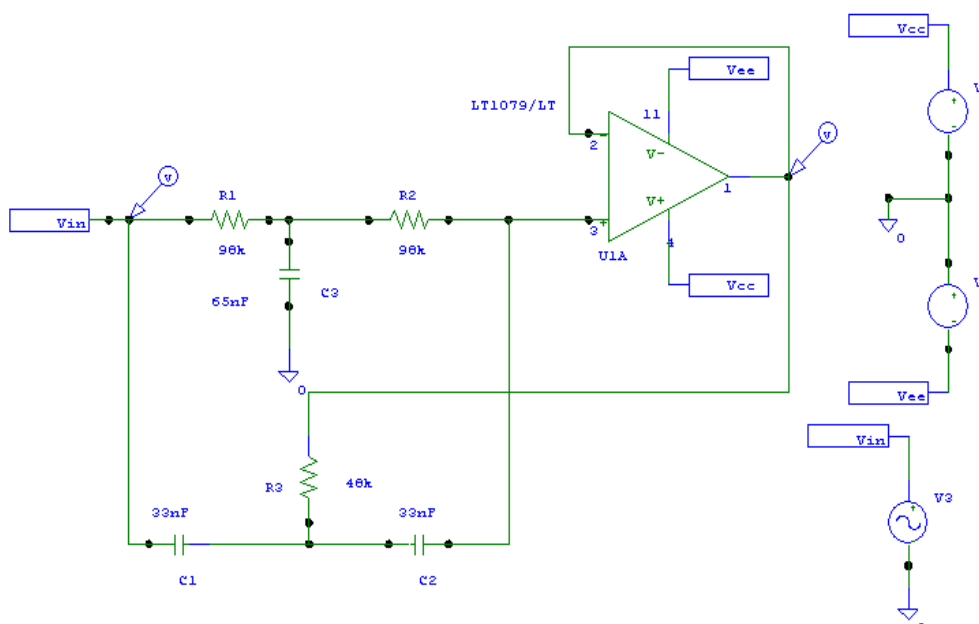


Figure 3. Example of notch filter schematics.

The relationship between capacitor C3 and resistor R3, which usually are linked to ground, is connected to the output of the repeater. This case does not affect the entire functionality of filters because of the very low impedance of output [13].

For interested frequency, $f_t=50$ Hz, the results are pair value: $R_1=98$ k Ω and $C_1=33$ nF or $R_1=318$ k Ω and $C_1=10$ nF. These quantities are for industrial frequency, 50Hz in European countries, rejection.

$$f_0 = \frac{1}{2 \cdot \pi \cdot R_1 \cdot C_1}$$

$$R_1 = R_2 = 2 \cdot R_3 \quad (1)$$

$$C_1 = C_2 = \frac{C_3}{2}$$

The characteristic of the studied notch filter (for 50 Hz) is very well outlined, Figure 4.

If this device is used in a computer aided system, it is not necessary because the industrial frequency is easy to reject by digital filtering. In this case we must use an anti-aliasing filter to avoid false artefacts in signal [14].

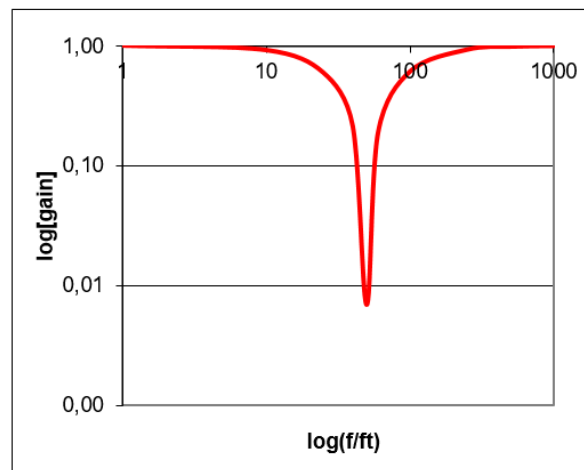


Figure 4. The characteristic of the studied notch filter.

The low-pass filter is depicted in Figure 5. Cut off frequency is around 10kHz. Relation 2 described the cut off frequency by circuit passive elements.

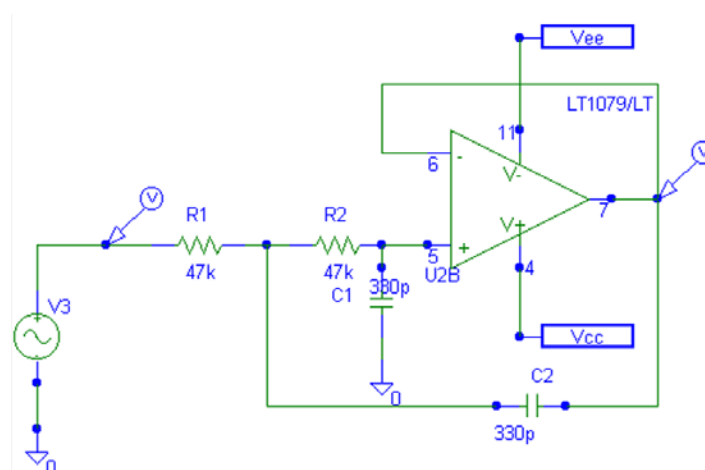


Figure 5. Low-pass filter.

Practical aspects of the device must be according to problems with this type of very low signal device. To shield regarding noise, all printed circuit board must be in metallic box. It is preferable to use connection terminals, because of easy use of connection elements. To select the gain of the device the back panel has a three-position switch. The input in device is done by shielded cable with a minimum length. On the front panel is another three-position switch to select clean signal or filtered signal [15].

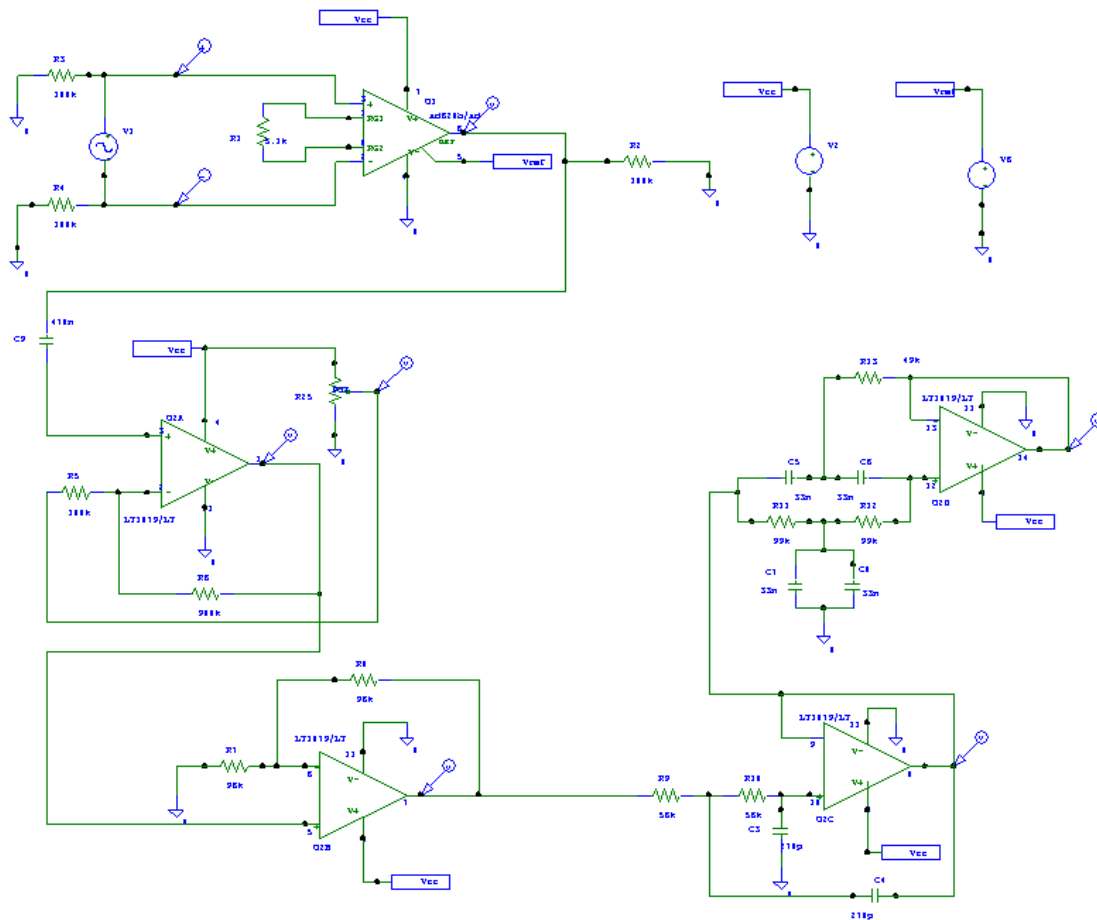


Figure 7. Unipolar power supply, full schematics.

It must be considered that the power supply should be made from chemical sources of continuous current to eliminate any additional interference.

3. Results and Discussion

The amplifier made was tested in signal simulation condition and real condition. One of the first tests is to see the input-output functionality and to determine the characteristics of amplifier. A signal generator and an oscilloscope can be useful at this time. If the generator does not permit low level signals, a signal generator and amplifier is inserted into a voltage divider. Two resistors make it. Oscilloscope must have sensitivity, to represent low level signal. Experiments are made using a non-filtered and filtered signal. Notch filters stage (50 Hz) affects the signal, and the experiment reveals this.

Input signal has a convenient value to oscilloscope (5-10 mV). To avoid clipped mode, at this stage, the gain is reduced to acceptable value. For example, a value of 100 times to gain is enough. Other criterion that must handle are internal noise and common mode rejection rate. Internal noise can be measured connected to the differential input some resistors (0 Ω , 100 k Ω and 1 M Ω). Theoretically, the output must have 0 V. For CMRR the

procedure is to apply both inputs through 100 k Ω two resistors a sinusoidal signal with 1 V amplitude and 50 Hz frequency and follow the output. For this test notch filters (50 Hz) are not used.

For real physiological signals here, sciatic nerves were used from rat or frog. The starting procedure consists of a biological tissue preserve solution. Along with experiments it was finding lose the physiological signal after 1-2 hours (because of nerve fiber drying).

Because of multiple configurations possibilities, this amplifier can be used to ECG or EMG type of signal.

For every working condition, is necessary to modify the amplification, cut off frequency of filters and input configurations.

Signals can be processed after using a plug-in or stand-alone acquisition system. Data from acquisition is saved in file. The software is a simple data transfer from an oscilloscope display and computer. The main component is an oscilloscope. For signal acquisition here there was used serial interface of an oscilloscope. Statistical processing and mathematical transformers can be used to extract utility information from the waveform.

Experiments are done using rat sciatic nerves. Using signal stimulator, the experimental results are present in waveform from Figures 8 and 9. Stimulation is done by one or two pulses. Informative, parameters of these are 0.5 – 5mV amplitude and a pulse width of 1-10 ms.

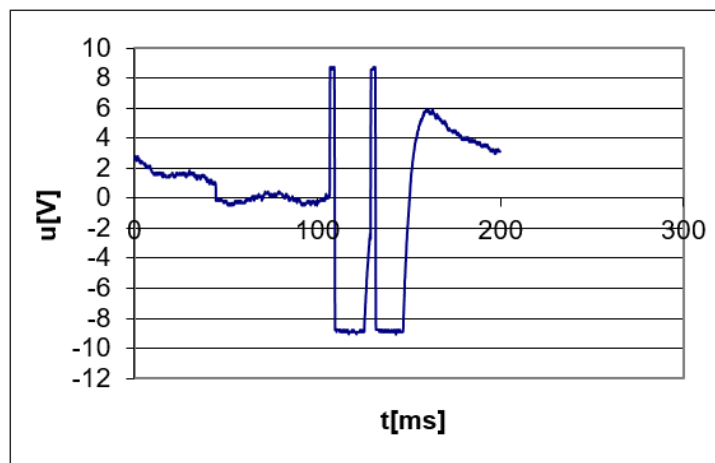


Figure 8. Stimulus signal.

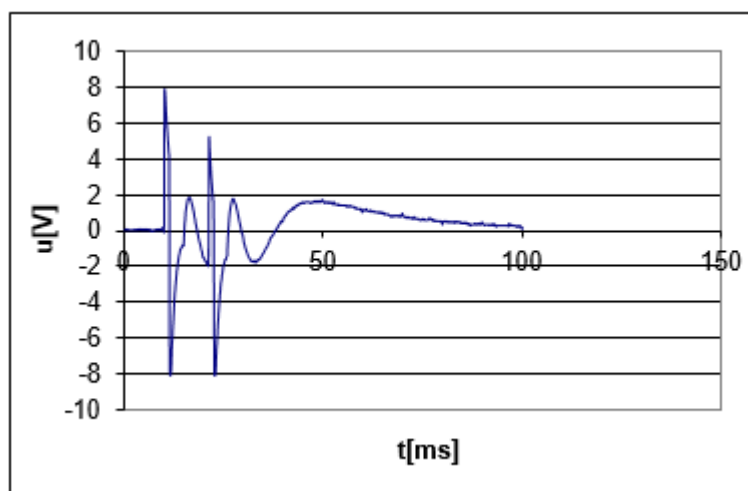


Figure 9. Sciatic nerve signal, excited by stimulus signal.

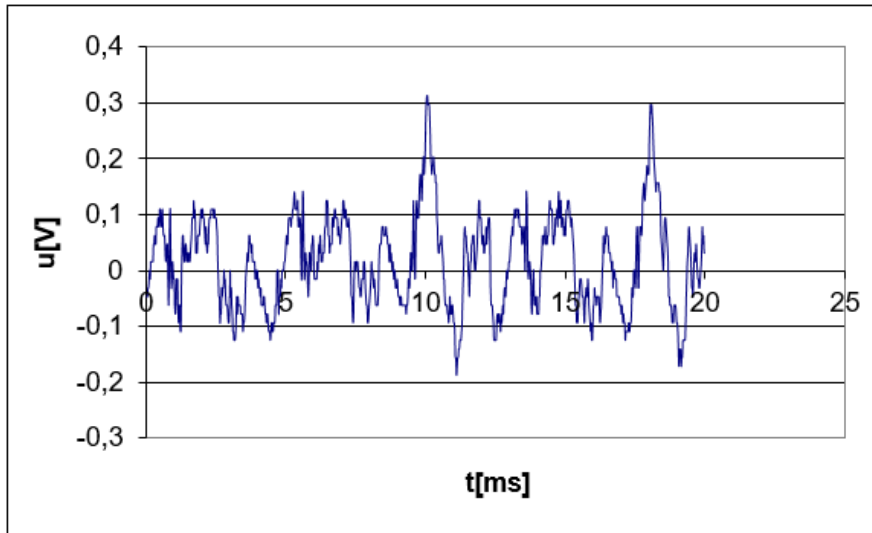


Figure 10. Sciatic nerve signal, without stimulus.

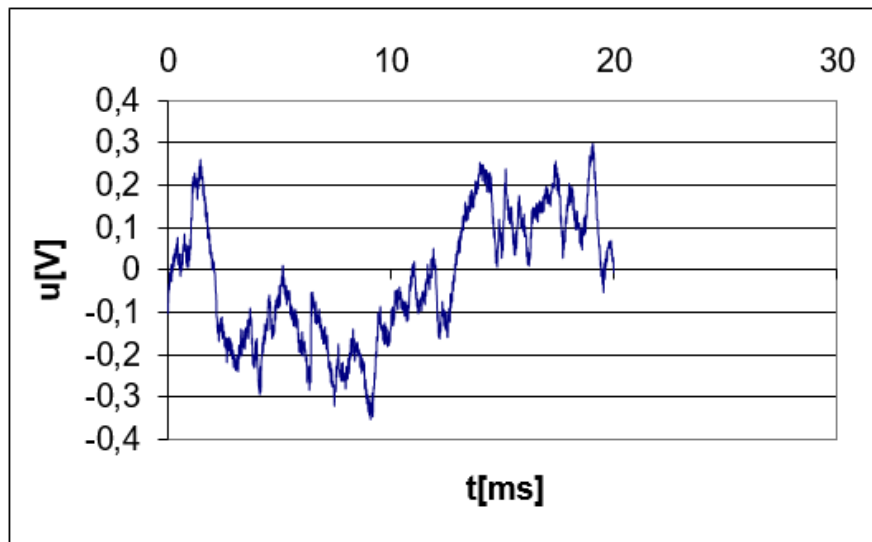


Figure 11. Frequency of 50Hz influence, signal unfiltered.

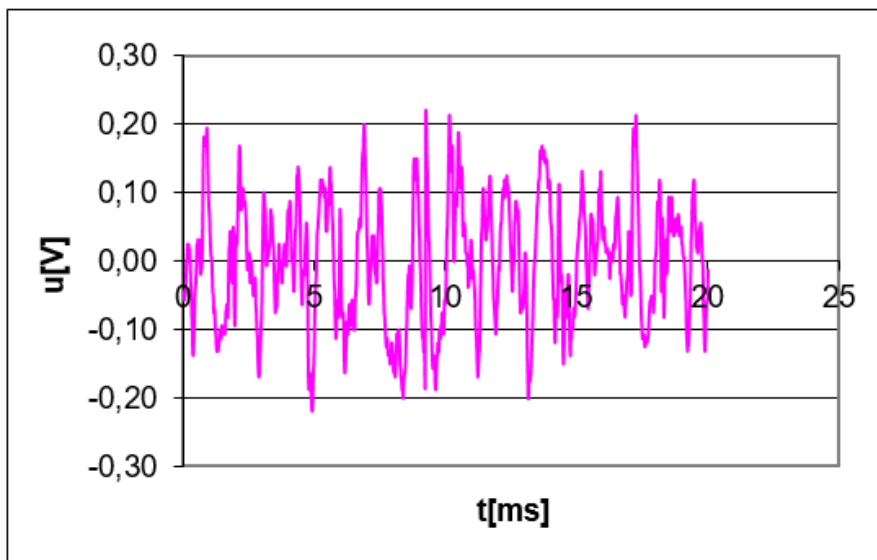


Figure 12. Signal filtered (50 Hz rejected).

Avoid using filters has the result of signal distortion, things shown in Figure 11, where is not use notch filter 50 Hz. The useful signal is modulated by 50 Hz frequency. To compare, in Figure 12 is shown the same signal but filters (50 Hz rejected). The experimental device is depicted in Figure 13.

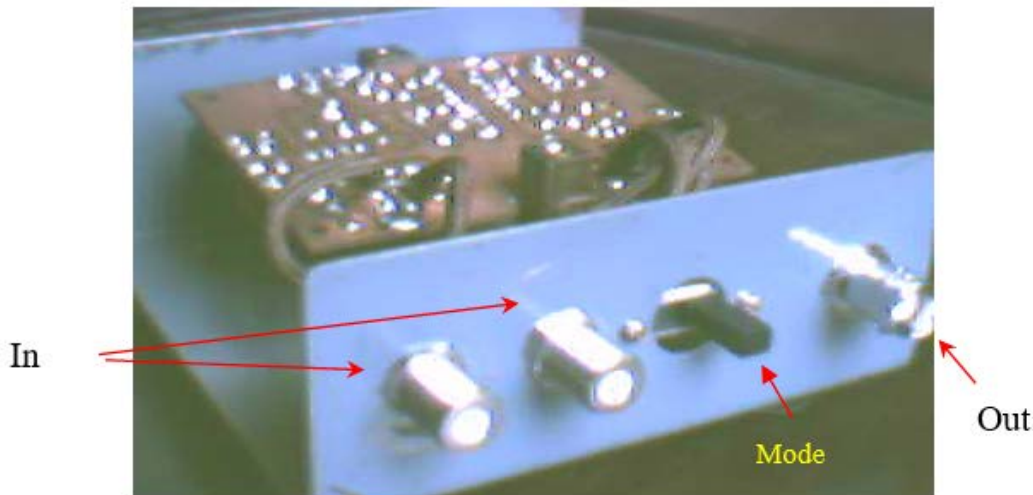


Figure 13. Overview of experimental device.

Considering the results obtained, the designed device, for amplifying low-level signals of a biomedical nature, works according to the proposed objective. Although it is a purely analog implementation, using quality components and considering appropriate technological design of printed circuit board rules, the results confirm a realistic approach.

4. Conclusions

Briefly, the mains accomplish of this paper are:

- Documentation steps consisting in distinguishing parameters of physiological signal amplifiers, displaying some types of this device, which are used in specialty laboratories, research/processing signal methods, using filters and importance of that.
- Designing, according to the block diagram of a physiological signal amplifier, in two alternatives: bipolar and unipolar power supply.
- Schematics functionality by simulation and by experimentation.
- Practical implementation of amplifier, Figure 13.
- Experimental diagram of filters.
- Experimental diagrams of device and reveal unusual state like amplifier saturation.
- Using this device to real physiological signals, from rat nerve.

On all experimental work signals had prevailed through non polarized capacitors. This can affect the output characteristic on the falling edge at very low frequency.

The experiment was done using signal waveform generator and an oscilloscope to determine the output characteristic and using rat sciatic nerve for real physiological signal. Tests can be extended by external signal, for example skin surface. Contact surface must be very clean for a steady connection (using silver electrodes is a good idea).

All connection elements are shielded to avoid additional noise sources. On the front panel of the box are F connector for input signal, BNC coupling for output signal, switch to select type of signal in three steps (only amplifier, low pass filtered signal and notch filtered signal 50 Hz).

In opposite side are gain selection switch (three steps) and power supply connectors. Using power supply from battery instead of real DC power supply. It has no ripple over DC component.

This paper was presented at the scientific event the International Conference on Electronics, Communications, and Computers (ECCO 2024), October 17-18, 2024, Technical University of Moldova, Chisinau.

Conflicts of Interest: The author declares no conflict of interest.

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Citation: Oancea, C.-D. Interface adaptation design for extracellular recordings from excitable tissue. *Journal of Engineering Science*. 2025, XXXII (2), pp. 46-57. [https://doi.org/10.52326/jes.utm.2025.32\(2\).04](https://doi.org/10.52326/jes.utm.2025.32(2).04).

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