Microelectronics Journal 42 (2011) 1305–1312

Contents lists available at SciVerse ScienceDirect

Microelectronics Journal

journal homepage: www.elsevier.com/locate/mejo

A dual band-pass amplifier-filter circuit for simultaneous recording of spikes and local field potentials from live neuronal tissue using multielectrode arrays

W. Dąbrowski *, T. Fiutowski, P. Rydygier, P. Wiącek

Faculty of Physics and Applied Computer Science, AGH University of Science and Technology, Krakow, Poland

ARTICLE INFO

Article history:
Received 10 May 2011
Received in revised form
1 September 2011
Accepted 5 September 2011
Available online 15 September 2011

Keywords:
Low-noise amplifier
Neural recording
Band-pass filter
CMOS amplifier

ABSTRACT

The paper presents the design and test results of a novel circuit with dual band-pass filter for simultaneous recording of Local Filed Potentials and spikes from individual neurons. Single readout channel is built of an input AC-coupling circuit with the cut-off frequency below 0.1 Hz, a low noise preamplifier and two parallel band-pass filters with nominal bandwidths from 2 Hz to 100 Hz and from 200 Hz to 2 kHz. The design is optimized for low noise, high dynamic range, and low power dissipation. The circuit has been designed and manufactured in a 0.35 μm CMOS process as a multichannel chip comprising also an analog multiplexer for serialization of the analog output signals.

1. Introduction

There is a growing interest in system neuroscience to record simultaneously from many neurons and possibly also from multiple regions of brain. Recent developments in high-density implantable silicon probes make it also possible to explore deeper regions of brain, not accessible with other techniques [1]. In such experiments one would like to look at the coherent activity of large assemblies of neurons resulting in Local Field Potentials (LFPs) and simultaneously at spikes generated by individual neurons. The LFPs and individual neuron spikes form two distinct classes of signals with respect to their amplitudes and frequency spectrum.

In the paper we report on the design and performance of a prototype integrated circuit, which is foreseen to be used as a building block in a multichannel system for simultaneous stimulation and recording from cortical tissue of small animals. Building such a system is feasible only by employing multichannel Application Specific Integrated Circuits (ASICs). Our approach is based on successful development of a 61-electrode system, which has been used for simultaneous stimulation and recording from identified retinal ganglion cells [2]. The key components of the system are high density multielectrode array and two 64-channel ASICs: Stimchip [3] and Neuroplat [4]. A similar system suitable for in-vivo recording from the brains of small animals requires a new generation of ASICs, which will cover the frequency spectra of LFP signals and of spikes. Furthermore, the performance of the new ASIC is expected to be improved with respect to the dynamic range and the power consumption.

Combining electrical stimulation of individual neurons and recording from the same or nearby neurons imposes additional requirements on the dynamic range of the recording amplifier. Artifact signals related to stimulation can drive the input amplifier into saturation lasting typically a few milliseconds. However, as far as the artifact parasitic signal does not drive the amplifier out of the linear range one can record elicited spikes superimposed on the artifact signals and remove the artifacts in data processing. A simple subtraction of the artifact level averaged over many repetitions has been applied and allowed recording elicited spikes with latencies shorter than 0.15 ms [5]. The method employing subtraction of the averaged artifact from the recorded signals can be applied provided the total signal composed of an artifact and a neuronal signal remains within the linear range of the amplifier. Therefore, in the experiments employing electrical stimulation much larger dynamic range of the recording amplifier is required compared to the experiments recording spontaneous neural activity only, especially if one aims at recording elicited spikes with very short latencies after stimulations.

In order to address these requirements, a novel concept of the recording amplifier has been developed and realized in a 0.35 μm technology.

2. Recording channel

A functional block diagram of the recording channel is shown in Fig. 1. The input stage comprises a high-pass filter built of

* Corresponding author. Tel.: +48 12 617 2959; fax: +48 12 634 0010.
E-mail address: w.dabrowski@ftj.agh.edu.pl (W. Dąbrowski).

0026-2692/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.mejo.2011.09.002

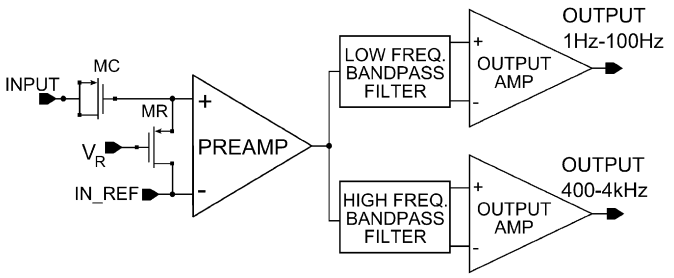

Fig. 1. Schematic diagram of the recording channel comprising two parallel band-pass filters.

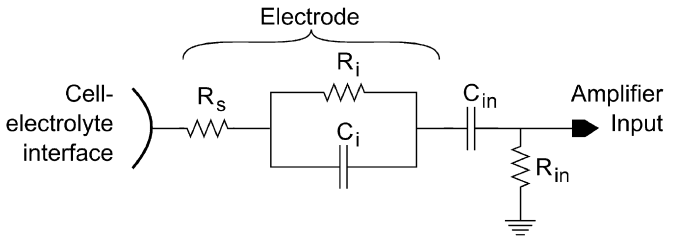

Fig. 2. A simplified electrical model of the interface between the neural cell membrane and the input of the recording amplifier.

transistors MC and MR, and a low noise preamplifier. At the preamplifier output the signal path is split into two sub-channels, each one comprising a tunable band-pass filter and an output amplifier with variable gain. The low frequency circuit with the nominal passband 2 Hz to 100 Hz passes low frequency LFP signals. The high frequency circuit with the nominal passband 200 Hz to 2 kHz passes spikes generated by individual neurons. The two filter outputs are foreseen to be sampled at different rates, about 1 kHz for the low-frequency output and 40 kHz for the high-frequency output, depending on settings of the filter passbands. The output signals from both sub-channels will be combined onto single output line using an analog multiplexer.

2.1. Input coupling circuit

One of the problems in extracellular recording from alive neural tissue is the DC offset voltage at the recording electrode. Due to electrochemical processes electrical potentials are generated at the metalized electrodes immersed in the physiological solution. These potentials are of the order of hundreds of millivolts and vary from electrode to electrode while the extracellular neural signals to be recorded are in the range of hundreds of microvolts. To avoid saturation of the preamplifier by the offset one has to introduce AC-coupling between the electrode and the recording amplifier or provide some means to compensate this offset. Frequency spectrum of the signals generated by the neurons covers a range from of about 1 Hz so that the lower cut-off frequency of the input coupling circuit must be below 1 Hz.

A simplified equivalent circuit diagram of the electrode and the preamplifier input circuit is shown in Fig. 2. The electrode model includes capacitor C_i and resistor R_i, which represent the electrode interface, and resistor R_s representing the spreading resistance of the conductive solution. Both resistances, R_i and R_s, are inversely proportional to the surface area of the electrode while the capacitance C_i is directly proportional to the electrode surface area. In more accurate models the interface capacitance is described by a constant phase impedance component. The detail model of the interface between the cell membrane and the electrolyte, known as the electrical double layer, is not important for the considered input coupling circuit.

From the point of view of minimizing the silicon area occupied by the input AC-coupling circuit one should aim at a resistance as large as possible and minimize the capacitance. This approach has been used in several designs of CMOS amplifiers for recording spikes, e.g. [6–8]. However, when recording the spikes only one usually does not require extremely low cut-off frequency below 1 Hz as it is needed for recording the LFP signals. A large input resistance, in the order of tens GΩ, can be realized relatively easily in the CMOS technology using a properly sized and biased MOSFET, though one has to keep in mind that modeling of unusually devices biased in the weak inversion may be not accurate.

In the process of maximizing the input resistance and minimizing the coupling capacitance one has to take into account the noise generated by the input resistance, which becomes dominant in the low frequency range. Fig. 3 shows the noise spectra at the preamplifier input due to the resistive components of the electrode and the input resistance for the same value of the lower cut-off frequency of 1 Hz while using different combinations of the coupling capacitance and the input resistance. The spectra have been generated with the SPECTRE simulator so they include only the contributions from the thermal noise sources associated with the resistors in the circuit. The model does not take into account possible excess noise sources associated with the electrode and the PMOS transistor used for defining the input resistance. The simulations have been performed for typical parameters of the electrodes used for recording from retina tissue [9]: $R_i = 1.65\ \mathrm{M\Omega}$, $C_i = 1.4\ \mathrm{nF}$, and $R_s = 64\ \mathrm{k\Omega}$. A relatively low value of the electrode resistance R_s is achieved by electroplating with platinum, which forms a granular structure increasing the effective area of the interface. In order to illustrate how critical is a low value of the spreading resistance, simulations have been performed also for a large value $R_s = 640\ \mathrm{k\Omega}$, which can occur in experimental conditions.

One can see that in the low frequency range 2 Hz to 100 Hz the noise spectra are determined entirely by the parameters of the AC-coupling circuit, i.e. the thermal noise of resistance R_{in} integrated on capacitance C_c, according to following formula:

$$\frac{d\langle v_n^2\rangle}{df} = \frac{4kTR_{in}}{1+(2\pi f R_{in}C_c)^2} \tag{1}$$

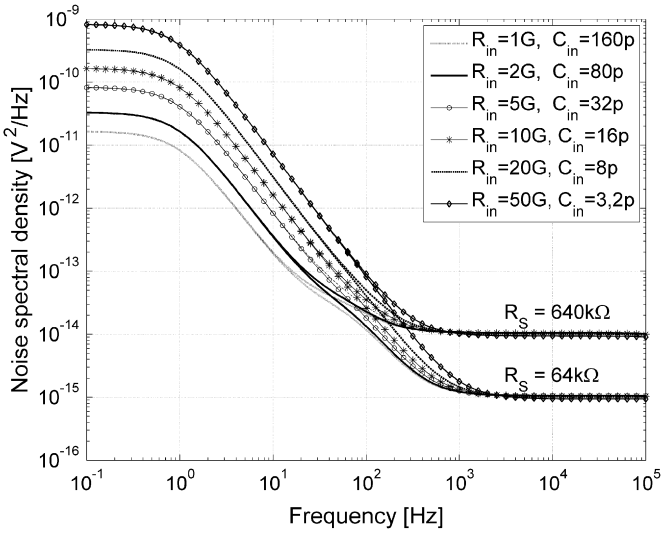

Fig. 3. Noise spectra at the preamplifier input due to resistance of the input C_c–R_{in} coupling circuit and the equivalent resistance of the electrode for different combinations of C_c and R_{in} values giving the lower cut-off frequency of 1 Hz, and for two different values of the electrode spreading resistance.