

A high-pass pole shifting technique for bidirectional electrophysiological interfaces using a novel tunable analogue filter block

Konstantinos Petkos, and Emmanuel M. Drakakis

Abstract— This paper details the design of a high-pass pole shifting technique, which can achieve a rapid recovery of the analogue front-end electronics from strong stimulation pulses and electrochemical DC offsets in bidirectional electrophysiological interfaces. The technique is implemented by making use of a novel continuous-time analogue filter block that offers tunability in the applied cut-off frequency, scalability, real-time and low-noise recording capabilities, along with the capability of interfacing with various types of sensors. The measurement results of this work prove that the proposed technique can offer low integrated noise values ($<2 \mu\text{Vrms}$ from 0.5 Hz up to 4 kHz) and immediate recording of the biosignal of interest after the stimulation pulse, when implemented with the specific tunable filter. The recorded biosignals are free from undesired ringing oscillations or phase shifts. All those merits render this technique as a versatile and reliable solution to be utilized in a wide range of applications and environments.

Index Terms— Analogue filtering, analogue front-end (AFE), bidirectional systems, bioelectrical signals, bioinstrumentation, concurrent stimulation and biosignal recording, high-pass pole shifting, rapid recovery, tunable filter.

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I. INTRODUCTION

HIGH fidelity recording of weak bioelectrical activity necessitates the design of high-performance biopotential acquisition systems that are capable of detecting biosignals down to microvolt amplitudes [1], [2]. So far, implantable analogue front-end (AFE) designs have primarily focused on optimizing power efficiency to extend battery life and minimize heat dissipation. As biopotential recording circuits scale to higher channel counts (>1000), power-efficient AFE design is further exacerbated, due to tight area constraints and high communication data rates.

Due to these constraints, most existing biopotential recording devices have not been designed to achieve simultaneous sensing and stimulation and are thus vulnerable to artefacts [3]. For instance, power-efficient AFEs typically apply a large gain on the recorded signals to maximize their sensitivity. Hence, the power requirements of subsequent processing stages, such as

the analog-to-digital converter (ADC), are relaxed. In bioelectrical signal acquisition, the signal of interest is superimposed on large DC offset voltages, such as electrode contact potentials [4]. As a result, this high amplification is not only applied on the bioelectrical signals, but both on the stimulation artefacts and the DC offsets, which often leads to the saturation of the front-end amplifier [5]. In addition, conventional AFEs use an analogue high-pass filter (HPF) with a low corner frequency to block DC offsets. This design decision results in slow recovery from saturation due to the large, rapid transient voltage of a stimulation artefact [3].

As a result, very short latency (<1 millisecond) evoked activity is often not investigated in the clinic due to the presence of those large stimulation artefacts [6]. Indeed, various implantable bidirectional electrophysiological interfaces that apply different types of stimulation (e.g. deep brain stimulation, cardiac stimulation, spinal cord stimulation etc) necessitate the design and delivery of versatile, low-noise and low-power analogue front-ends that are robust to strong stimulation interference [3], [7]. Achieving fast recording of the biosignal of interest after the stimulation pulse is pivotal for minimizing biosignal loss and thus maximizing the efficiency of implantable closed-loop bidirectional devices. Depending on the application, the targeted neural signals can be electrocorticographic signals, local field potentials, evoked and/or spontaneous action potentials.

Various anti-artefact technologies were developed in the past decades. Those approaches are characterized by distinct application contexts addressing a range of artefact problems. However, despite the differences in application background, the consistent nature of the artefact issue calls for the development of unified approaches to alleviate its negative effects on the recorded signal quality.

A common approach for artefact elimination is to apply (usually high-order) digital filtering techniques [8]. Nevertheless, such a strategy may lead to significant delays in data processing, especially in the case of high-channel-count and high sampling rate recording systems. These delays could risk the real-time operation of the system, which is particularly important in neuromodulation because the stimulation must change instantaneously based on the measured state of the neural network [9], [10].

An alternative approach is to use a series switch at the input to disconnect the AFE when stimulation is applied in order to prevent artefacts from reaching the recording electronics [11], [12], [13], [14], [15]. Unfortunately, this technique often suffers from slow transient settling once reconnection occurs [9], [16]. While action potentials may be detected and analyzed even

when superimposed on the long decays following amplifier saturation, these settling responses severely degrade local field potentials and electrocorticographic signals [3].

To solve the amplifier saturation issue during stimulation, some bidirectional systems make use of adaptive gain control technologies, which allow the instrumentation amplifier to perform varying gain adjustments based on the input signal amplitude [17]. Such an approach has two main limitations: a) the larger the range of the programmable gain amplifier's gain, the more complex the digital reconstruction algorithm becomes, and b) different gains lead to different programmable gain amplifier input-referred noise levels and bandwidth settings, which deteriorate the recorded signal quality.

Other anti-artefact techniques that have been proposed in the literature [17]: a) combine a low-gain front-end recording amplifier with a high-resolution ADC to increase the input dynamic range, or b) sense, inversely amplify and sum common-mode signals of the two recording electrodes to remove common-mode artefacts (CM cancellation path), or c) make use of current compensation techniques, combined with rail-to-rail topologies, to enhance the input common-mode range and linearity, or d) deploy direct conversion topologies to directly distinguish neural signals from artefacts. Those approaches either require high dynamic range front-ends (i.e. low-gain front-end gain approach and direct conversion topology), or high current demanding ADC blocks (i.e. low-gain front-end approach), or suffer from distortion when used in systems requiring low noise and low power consumption (i.e. current compensation technology), or do not fully address the artefact issue (i.e. CM cancellation path strategy). Therefore, they are not ideal for implantable closed-loop systems.

Another recently proposed strategy [16] is to introduce a high-order analogue notch filter in the front-end electronics in order to increase the available bandwidth by suppressing the artefact originating from the stimulation frequency and apply high-order low-pass filtering to reject the higher-frequency harmonics. This implementation was successfully validated in a non-human primate animal model. The circuit architecture presented in that work is an application specific solution that can effectively suppress deep brain stimulation (DBS) pulse trains, which are generally characterized by small duty cycles ($\sim 2\%$). However, in applications where pulses of higher duty cycles are applied (e.g. up to 20% duty cycle is used in research diagnostic cardiac stimulation protocols [7], [18] and in spinal cord stimulation procedures [19]), ringing oscillations may be induced in the biosignals of interest due to the notch operation.

Reconstruction methods remove samples contaminated with artefacts and replace them with interpolated values in real time. However, they are implemented by DC-coupled systems [20] which are more susceptible to prolonged saturation issues due to the large electrochemical DC offsets. Hence, such methods can be considered as application-specific techniques for DBS,

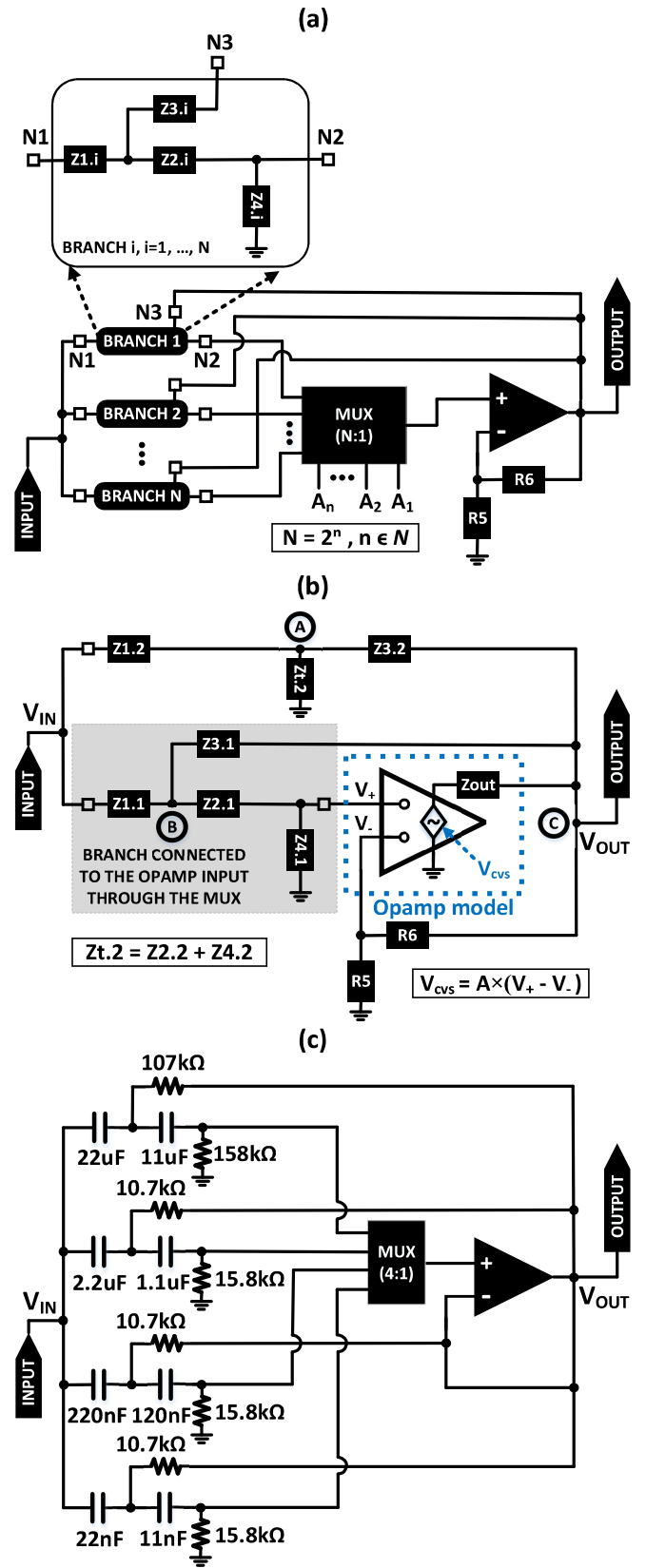


Fig. 1. Tunable filter block based on the Sallen-Key topology. (a) Block diagram of the generic filter block. (b) Simplified equivalent circuit for $N=2$ branches, where branch 1 is selected to be connected to the output of the tunable filter through the multiplexer (MUX). (c) Block diagram of the artefact suppression block presented in this work, which is based on the high-pass filter variation of the generic tunable filter block shown in Fig. 1 (a).

where the typical offset values are tens of mV [16], [21], [22], [23]. Furthermore, template subtraction techniques can be implemented with low latency, but they often suffer from varying artefact morphology stemming from undersampling the artefact [3], [24]. To avoid signal distortion, templates must be regularly updated to track any changes in artefact shape or stimulation waveform. However, estimated templates often take time to converge, resulting in varying levels of cancellation over time. Finally, high dynamic range front-ends are required, since the undistorted artefact waveform has to be recorded [3].

This paper presents a novel, tunable and multi-function filter topology that can be used in various stimulation and recording setups to achieve rapid recovery of the front-end electronics from the strong stimulation pulses. Before and after the application of the stimulation train, the corner frequency of the tunable filter can be instantaneously adjusted so that slow transient settling is avoided (the abrupt increase of the high-pass filter's corner frequency aims at decreasing the associated time constants) and amplifier saturation issues are alleviated.

II. SYSTEM ARCHITECTURE

A. Implementation of the tunable filter

To achieve on-the-fly configuration of the high-pass characteristics of an AFE, we designed the tunable filter block shown in Fig. 1(a). This implementation, which is based on the 2nd order Sallen-Key filter, makes use of a multiplexer that allows the user to switch between different cut-off frequencies for a given filter approximation. In the HPF implementation, Z1 and Z2 are capacitors, whereas Z3 and Z4 are resistors. In the low-pass filter topology, Z1 and Z2 are resistors, whereas Z3 and Z4 are capacitors. The gain of the filter is determined by the resistors R5 and R6.

The novel property of this topology is that all branches shown in Fig. 1(a) are directly connected to the output of the operational amplifier. It is important to note here that each of these branches can be configured to provide a different corner frequency and/or filter approximation. In other words, the overall filter topology can contain a number of embedded (low-and/or high-pass) filters/branches, whose characteristics are dictated by the bandwidth specifications of the intended application. At any time, any one of these filters/branches can be selected by the multiplexer in order for it to be connected to the positive input of the operational amplifier and determine the response of the overall filter block.

B. Equivalent circuit analysis

To analyze the effect of the parallel branches on the operation of the Sallen-key filter, we deduce and present in Fig. 1(b) a simplified equivalent of the architecture shown in Fig. 1(a), when there are only two branches ($N=2$); one that has been selected and one that has not been selected by the multiplexer. To apply circuit analysis, the equivalent model of the operational amplifier was incorporated in Fig. 1(b).

The derivation of the overall filter block's transfer function can be found in the Appendix. As shown in the circuit analysis, the transfer function of the proposed tunable filter block (Fig. 1(b)) is the same with the transfer function of a classic 2nd order Sallen-Key topology. In other words, branch 2 (which is the one

that has not been selected by the multiplexer) in Fig. 1(b) does not affect the operation of the 2nd order active filter formed by the selected branch (branch 1). The application of the same circuit analysis for the case where the number of branches/embedded filters is higher than 2 ($N>2$) yields the same result, as confirmed with appropriate simulations in a commercially available software package (MATLAB Simulink, Mathworks Inc, USA).

To reach this outcome, we based our analysis on the fact that the operational amplifier is characterized by a very low output impedance value (in the Ω range), especially in the frequency range of the signals we study in this work (<10 kHz). For instance, the output impedance of the ADA4528 chip is less than 0.1Ω up to 10 kHz and becomes equal to 10Ω at 1 MHz.

C. Fabricated artefact suppression block

In Fig. 2, a fabricated tunable second order HPF, which was designed in accordance with the schematic shown in Fig. 1(c), is exhibited. This block is used in this work to achieve rapid recovery of the front-end electronics from the strong stimulation artefacts. It contains four Bessel high-pass filters that offer unity gain and corner frequencies 0.1, 10, 100 and 1000 Hz. The nominal values of the capacitors and resistors used in this design are presented in Fig. 1(c) and their tolerances are 10% and 0.1%, respectively. Finally, the 4:1 multiplexer ADG1404 and the operational amplifier ADA4528 (Analog Devices, USA) were used for building the filter topology.

III. RESULTS

A. Measured frequency and time-domain responses

Frequency responses corresponding to the four possible corner frequencies (0.1, 10, 100, and 1000 Hz) were measured (Fig. 3(a)) using the fabricated tunable HPF shown in Fig. 2. A commercial oscilloscope and network analyzer (Analog Discovery 2, Digilent Inc.) was used to perform the frequency sweeps and acquire the Bode plots of the four filter branches.

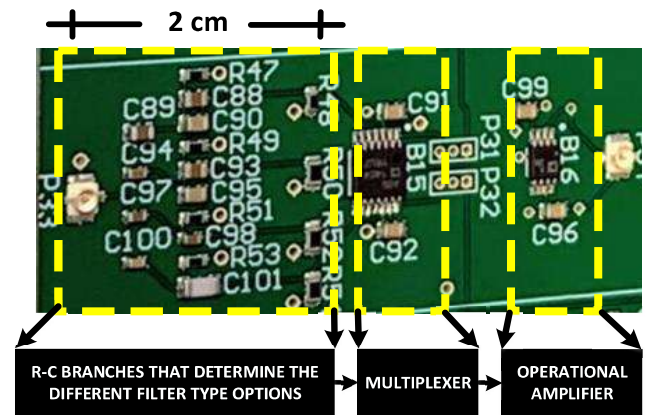


Fig. 2. Structure of a fabricated tunable HPF with ± 2.5 V dynamic range.

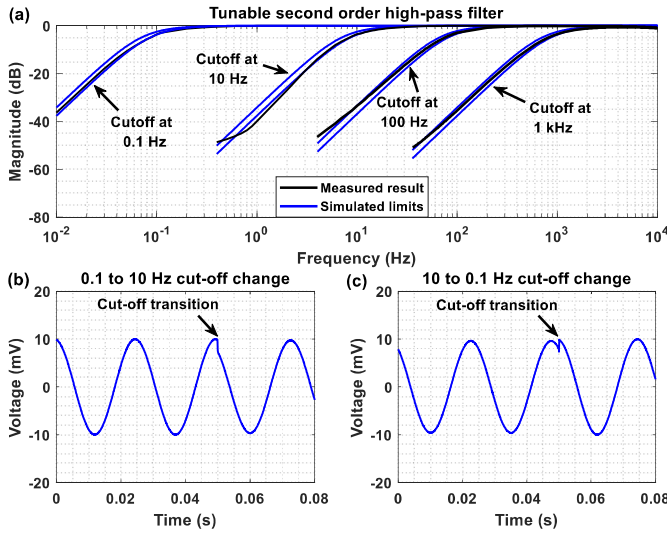


Fig. 3. (a) Measured frequency responses vs simulated worst-case limits (based on the resistor/capacitor tolerances) of a tunable high-pass filter providing four different corner frequencies (0.1, 10, 100, and 1000 Hz). (b) Impact of an on-the-fly cut-off frequency increase on the recorded sinusoidal signal (40 Hz tone). (c) Impact of an on-the-fly cut-off frequency decrease on the recorded sinusoidal signal (40 Hz tone).

Moreover, simulations on a commercial software package (Tina, Texas Instruments, USA) were performed using the border-values of all components based on their tolerances. More specifically, for each filter branch, the two extreme values (based on the tolerance) per resistor along with ten values per capacitor were selected, resulting in a simulation that provides the frequency responses of 400 combinations of component values. From all those combinations, only the two extreme limits are presented in Fig. 3(a). The above analysis shows that the corner frequencies of the four branches can range from 0.09 Hz to 0.11 Hz (0.1 Hz nominal), 9.12 Hz to 11.20 Hz (10 Hz nominal), 86.10 Hz to 104.70 Hz (100 Hz nominal) and 912.00 Hz to 1.10 kHz (1 kHz nominal), due to the component (resistor/capacitor) tolerances. Those frequency ranges are typically acceptable in most biomedical applications since a more accurate bandwidth definition can occur in the digital domain (e.g. through a digital filter on the microcontroller).

Based on Fig. 3(a), the measured cut-off (-3 dB) frequencies of the four branches (~ 0.11 Hz, ~ 11.00 Hz, ~ 99.00 Hz, ~ 1.10 kHz) reside within the simulated worst-case limits. In Fig. 3(b), the impact of a sudden transition between two high-pass cut-off frequencies on a recorded signal is assessed. The on-the-fly shifting of the high-pass pole does not induce any spikes in the recorded sinusoidal signal (10 mV peak, 40 Hz) and the transition is fast and fairly smooth.

B. AC-coupling during monophasic stimulation

Pulse distortion is a significant problem that impedes the accurate recording of biosignals in the interstimulus interval. As shown in Fig. 4, typical monophasic stimulation pulse profiles recorded by a HPF set at a relatively high cut-off frequency (e.g. 10 Hz) lead to significant signal distortion in the interstimulus interval. Moreover, the negative peaks (along with the signal that is superimposed on them in a typical concurrent biosignal recording and stimulation setup) shown in Fig. 4 are vulnerable

to saturation at later gain stages of a recording AFE. On the contrary, when the same stimulation profiles are recorded by a HPF set at a relatively low cut-off frequency (e.g. 0.1 Hz), the signal in the interstimulus interval is superimposed on a DC level with its morphology remaining unaffected (Fig. 4). On the other hand, a low HPF cut-off frequency leads to a slow transient settling to zero level after the last stimulation pulse, whereas a high HPF cut-off frequency allows for a fast transient settling to zero after stimulation.

The strategy followed in this work is to make use of the tunable HPF shown in Fig. 2 in order to combine the desirable features associated with two HPF corner frequencies; one low cut-off (e.g. 0.1 Hz) during stimulation to achieve high-quality recording in the interstimulus intervals, and one high cut-off (e.g. 10 or 100 Hz) after the last pulse to accomplish a fast transient settling to zero level after the stimulation has ended.

Referring to Fig. 4, different stimulation profiles yield different levels of down-shift applied on the input monophasic pulse train, and thus different levels of front-end saturation risk during stimulation. Indeed, the application of an ideal HPF on a monophasic pulse train shifts down the signal at the output of the filter (V_{OUT}) by its DC component. More specifically, a monophasic pulse train with amplitude A_{STIM} (which is superimposed on a DC offset V_{OFFSET} that represents the DC offset voltage originating from the electrode-tissue interface) entering the input of an ideal HPF, is described by the following equations [25]:

$$V_{IN} = V_{OFFSET} + A_{STIM} V(t) \quad (1)$$

$$V(t) = m + \sum_{n=1}^{\infty} \frac{2 \sin(n\pi m) \cos(2n\pi f t)}{n\pi} \quad (2)$$

where m and f are the duty cycle and the frequency of the pulse train, respectively.

In this case, the signal at the output of the HPF is the following:

$$V_{OUT} = A_{STIM} (V(t) - m) \quad (3)$$

since the parameters $A_{STIM} \times m$ and V_{OFFSET} are removed by the HPF.

From Equation (3):

$$V_{OUT} = A_{STIM} V(t) - A_{STIM} m \Rightarrow$$

$$V_{OUT} = V_{PULSE_TRAIN} - A_{STIM} m \quad (4)$$

where V_{PULSE_TRAIN} is the original monophasic pulse train (without the DC offsets originating from the electrode-tissue interface). After examining Equation (4), it becomes clear that the extent of the original pulse train's down-shift at the output of the HPF depends on both the duty cycle and the amplitude of the stimulation pulses.

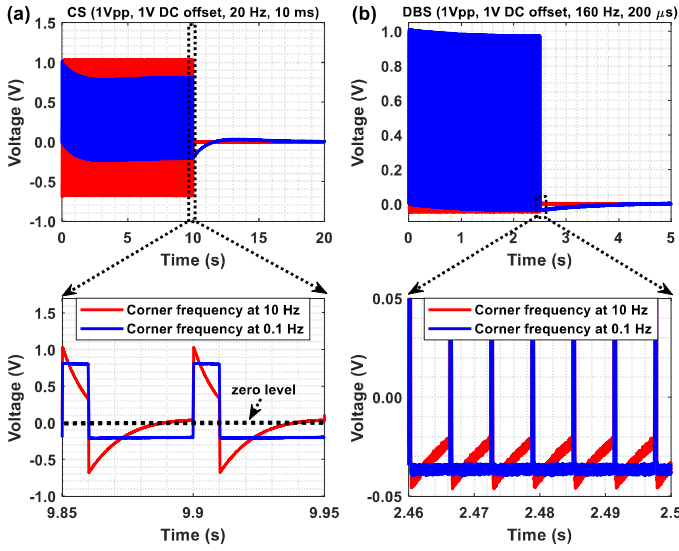


Fig. 4. Profile of the monophasic stimulation pulses recorded by a 2nd order HPF when the cut-off frequency is set at 0.1 Hz and 10 Hz. (a) Cardiac stimulation (CS) profile. (b) Deep brain stimulation (DBS) profile.

C. High-pass pole shifting in monophasic stimulation

To examine the efficacy of the high-pass pole shifting technique implemented using the proposed tunable HPF, a sinusoidal signal ($1.5 \text{ mV}_{\text{peak}}$, 500 Hz), which was superimposed on monophasic pulses (with frequency and pulse width characteristics that are commonly used in bidirectional cardiac and DBS setups), was directly injected to the input of the tunable HPF presented in Fig. 2. The analogue output of the channel was connected to the Powerlab 16/35 (ADInstruments) data acquisition system and sampled at 100 kSPS using a 16-bit resolution. A relatively high sampling frequency was selected in order to achieve a better representation of the signals recorded in the short cut-off frequency transition time windows. In this study, the (DC-coupled) AFE of the Powerlab system plays the role of the analogue gain in stages that should be placed after the proposed tunable HPF in a recording device in order to amplify the biosignals of interest prior to digitization.

In the cardiac stimulation setup, a transition from a high (10 Hz) to a low (0.1 Hz) cut-off frequency before the onset of stimulation was applied. At the end of stimulation, the opposite transition (i.e. from 0.1 Hz to 10 Hz) was applied to achieve a fast recovery of the filter from the strong pulses. This strategy is presented in Fig. 5 and is compared against the case where a fixed HPF is used. The tunable HPF: a) provides immediate biosignal recording in the interstimulus intervals when compared to a fixed 10 Hz corner frequency, and b) recovers from the strong cardiac stimulation pulses (amplitude $0.2 \text{ V}_{\text{pp}}$, 1 V DC offset, 20 Hz, 10 ms pulse width), which are directly injected to its input, in 90 ms, whereas the fixed HPF at 0.1 Hz is characterized by a slow transient settling of about 8 s. In these tests, the dynamic range of the Powerlab's AFE was set at $\pm 50 \text{ mV}$ in order to adequately amplify the biosignal of interest, which is in the mV range (normally less than $2 \text{ mV}_{\text{peak}}$). In the DBS setup a transition from a low (0.1 Hz) to a high (100 Hz) cut-off frequency takes place within a small time-window

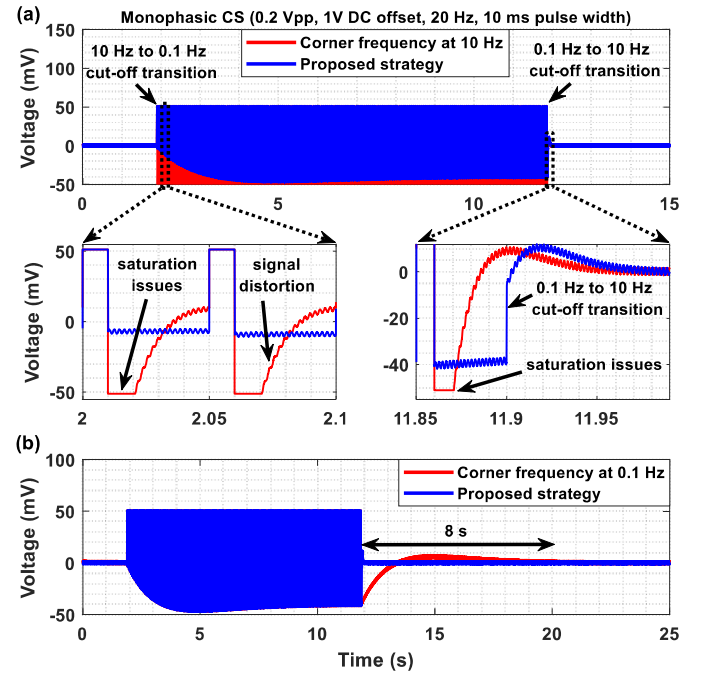


Fig. 5. (a) Comparison of the proposed technique with the case where a fixed HPF at 10 Hz is used. (b) Comparison of the proposed technique with the case where a fixed HPF at 0.1 Hz is used. The dynamic range of the AFE was set at $\pm 50 \text{ mV}$.

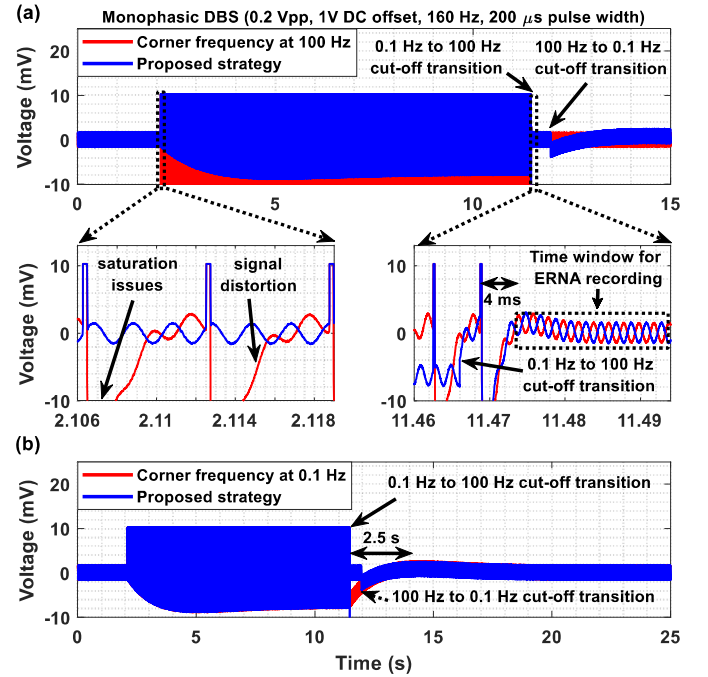


Fig. 6. (a) Comparison of the proposed technique with the case where a fixed HPF at 100 Hz is used. (b) Comparison of the proposed technique with the case where a fixed HPF at 0.1 Hz is used. The dynamic range of the AFE was set at $\pm 10 \text{ mV}$.

before the last DBS pulse (amplitude $0.2 \text{ V}_{\text{pp}}$, 1 V DC offset, 160 Hz, 200 μs pulse width) has been applied (Fig. 6). The application of the 0.1 Hz HPF cut-off frequency during stimulation allows for instantaneous recording of biosignals after the artefact. Hence, evoked compound action potentials, which provide insight into the activity of neurons directly affected by stimulation and are characterized by a frequency

content ranging from 100 Hz to 4 kHz [26], could be recorded. Before the end of stimulation, a 0.1 to 100 Hz cut-off transition allows the tunable HPF to recover in approximately 4 ms, and thus record evoked resonant neural activity, which appears 4 ms after the last DBS pulse and lasts for ~ 20 ms [6]. On the contrary, the fixed HPF at 0.1 Hz is characterized by a slow transient settling of about 2.5 s.

Since the bandwidth of interest in local field potential recording ranges from 0.5 to 500 Hz, the successful recording of evoked neural activity should be immediately followed by an HPF cut off frequency transition from 100 Hz back to 0.1 Hz. As shown in Fig. 6, this cut-off transition introduces a small delay in the transient response of the system. However, this delay may be considered tolerable taking into account that this strategy can enable an AC-coupled recording system to record evoked resonant neural activity.

Indeed, the systems that have been used so far for recording evoked resonant neural activity are DC-coupled [6] in order to avoid the interference of the slow transient responses originating from the filtering operation (bear in mind the slow recovery of the fixed HPF at 0.1 Hz in Fig. 6), with the decaying oscillatory activity that characterizes this physiological signal. In these tests, the dynamic range of the Powerlab's AFE was set at ± 10 mV to adequately amplify local field potentials with amplitudes ranging from $1 \mu\text{V}$ to $10 \mu\text{V}$ when measured from DBS electrodes [9].

D. High-pass pole shifting in biphasic stimulation

To examine the efficacy of the high-pass pole shifting technique implemented using the proposed tunable HPF, a sinusoidal signal ($1.5 \text{ mV}_{\text{peak}}$, 500 Hz), which was superimposed on biphasic pulses (with frequency and pulse width characteristics that are commonly used in bidirectional cardiac and DBS setups), was directly injected to the input of the tunable HPF presented in Fig. 2. The recording setup was kept the same with the one used in the case where monophasic stimulation pulses were applied.

After examining Fig. 7 and Fig. 8, the same conclusions with the case where monophasic pulses were applied are drawn here. Indeed, the application of a HPF at 0.1 Hz during stimulation allows for instantaneous and high-quality biosignal recording, while the immediate transition to a higher cut-off at the end of stimulation enables the AFE to settle significantly faster compared to a fixed HPF at 0.1 Hz. However, it should be highlighted here that, as anticipated, for the same dynamic range of the AFE (± 50 mV and ± 10 mV for the CS and DBS setup, respectively), in biphasic stimulation stronger stimulation pulses can be tolerated by the AFE without facing prolonged saturation issues during stimulation. Indeed, in the monophasic stimulation setup, the maximum pulse amplitude that could be tolerated by the ± 50 mV (CS) and ± 10 mV (DBS) AFEs was $0.2 V_{\text{pp}}$, whereas in the biphasic stimulation setup, pulse amplitudes of $5 V_{\text{pp}}$ and $3 V_{\text{pp}}$ were successfully handled by the ± 50 mV (CS) and ± 10 mV (DBS) AFEs, respectively.

Higher pulse amplitudes in the cardiac biphasic stimulation experiment were not applied since each phase of the pulse was

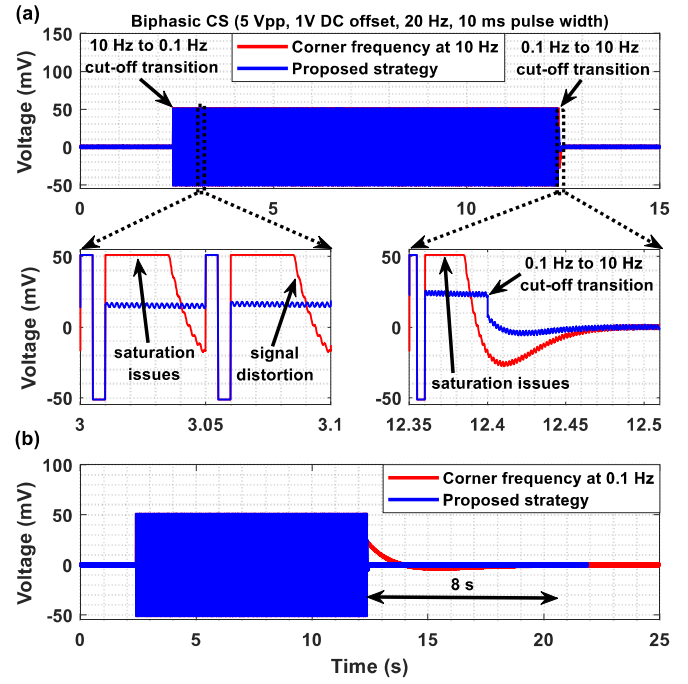


Fig. 7. (a) Comparison of the proposed technique with the case where a fixed HPF at 10 Hz is used. (b) Comparison of the proposed technique with the case where a fixed HPF at 0.1 Hz is used. The dynamic range of the AFE was set at ± 50 mV.

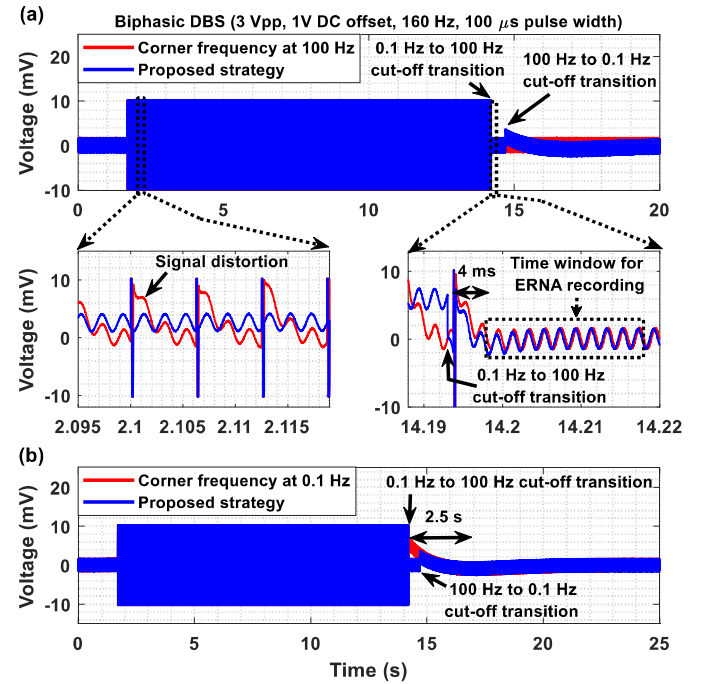


Fig. 8. (a) Comparison of the proposed technique with the case where a fixed HPF at 100 Hz is used. (b) Comparison of the proposed technique with the case where a fixed HPF at 0.1 Hz is used. The dynamic range of the AFE was set at ± 10 mV.

already equal to the rail of the operational amplifier (± 2.5 V). However, if higher pulse amplitudes are anticipated to reach the AFE, the AFE dynamic range should increase and the operational amplifier used in this work should be replaced by another low-noise one that provides overvoltage protection (e.g.

ADA4177, Analog Devices). On the other hand, in the DBS biphasic stimulation setup, pulse amplitudes that are higher than $1.5 V_{\text{peak}}$ were not tested because in an actual *in vivo* setup the stimulation artefact reaching the AFE is anticipated to have an amplitude that is in the range of hundreds of mV [21], [27].

E. Noise considerations

In the experimental setup used in this paper to evaluate the robustness of the proposed filters, a weak sinusoidal signal ($1.5 \text{ mV}_{\text{peak}}$, 500 Hz), which represents the signal of interest that is superimposed on the stimulation pulses, was injected to the inputs of the proposed topologies. To examine the noise performance of the tunable filters which were tested during electrical stimulation in this paper (high-pass filters at 0.1 Hz, 10 Hz, and 100 Hz), input-referred noise tests were conducted. To acquire these noise measurements, the input of each filter was connected to the ground of the system and the output was recorded at 200 kSPS using the Powerlab 16/35 system.

As shown in Fig. 9, the integrated noise values characterizing the proposed filtering architecture are $1.6 \mu\text{V rms}$ for a 0.5 Hz to 4 kHz bandwidth, $1.1 \mu\text{V rms}$ for a 10 Hz to 4 kHz bandwidth, and $1.5 \mu\text{V rms}$ for a 100 Hz to 4 kHz bandwidth. Those integrated noise levels: a) are sufficient for recording weak (μV -scale) neural signals, and b) are better or comparable to the ones accomplished by amplifier architectures that are widely used in the field of local field potential and action potential recording [22], [28].

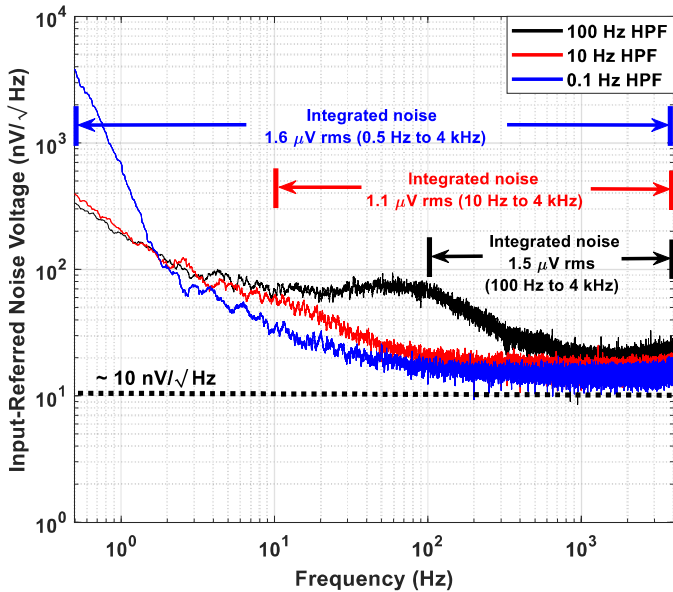


Fig. 9. Measured input-referred noise of the tunable HPF block shown in Fig 1 (c). Noise power spectral density estimate in the passband is above $10 \text{ nV}/\sqrt{\text{Hz}}$.

IV. DISCUSSION

This work proposes an alternative strategy for building resilient recording front-ends that are able to both rapidly recover from strong stimulation pulses and provide continuous and high-quality recordings of bioelectrical signals. It is

important to note that the tunable 2nd order filter block presented here avoids using a multiplexer for each capacitor and resistor of the active topology (i.e. 4 multiplexers in total), which is the typical approach that someone would follow to build a tunable filter based on the Sallen-Key architecture. It is thus a small, simple and practical topology that: 1) requires just one digital line for controlling its response, and 2) can be easily incorporated in the AFE of a device in order to add flexibility and adjustability in various applications and environments.

Taking into consideration that an AC-coupled system removes the strong DC offsets generated on the electrode-tissue interface in the presence of stimulation [22], [29], it is less susceptible to saturation compared to a DC-coupled one. Thus, the implementation of the proposed strategy could: 1) alleviate amplifier saturation problems during stimulation that have not been fully addressed yet by the approaches proposed so far [30], and 2) allow the recording of the evoked neural activity of interest, which is a readily utilizable electrophysiological signal and a target-specific biomarker that could potentially be used for guiding electrode implantation surgery and optimizing DBS therapy to improve patient outcomes [6].

In this study, the tunable HPF was placed at the first stage of the AFE architecture and the gain was applied at a later stage (in the DC-coupled AFE of the Powerlab system, which is connected to the output of the tunable HPF). Since the operational amplifier used for building the tunable HPF (ADA4528) is characterized by a very low and flat noise floor ($\approx 7 \text{ nV}/\sqrt{\text{Hz}}$) ranging from 1 Hz to 100 kHz, weak (μV -scale) biosignals can be successfully recorded in the bandwidth of interest (0.1 Hz - 4 kHz). In applications where high-quality recording of very weak bioelectrical signals is required (e.g. in DBS, where the minimum detectable biosignal is specified as $1 - 3 \mu\text{V}_{\text{rms}}$ [10]), a 20 dB increase in the current voltage gain (0 dB) of the tunable HPF (accompanied by a 20 dB decrease in the gain of subsequent stages – Powerlab's AFE in this work) can minimize the effects of noise generated in subsequent stages of the AFE [31]. In this way, the sensitivity of the front-end tunable HPF can increase without changing the AFE dynamic range values specified in this paper.

In the experiments conducted in this work, the minimum AFE dynamic range values that ensure biosignal recording without saturation in the interstimulus intervals were specified. For the pulse amplitudes specified in our experiments, lower AFE dynamic range values than the ones applied here can lead to saturation in the interstimulus intervals and subsequent loss of clinical information. All the pulse amplitudes and DC offsets applied in this work are realistic parameters that are expected to appear at the input of a recording device in most bidirectional electrophysiological interfaces [16], [21], [22], [23], [27].

It should be highlighted here that in the case where higher pulse amplitude values have to be tolerated by the front-end electronics, AFE dynamic range values that are higher than the ones proposed here have to be set. In this case, on-the-fly adjustability on both the bandwidth and the set gain could be applied. As a result, the Sallen-Key filter block used in this work could be replaced by the multiple-feedback filter topology. Indeed, after applying the single-multiplexer approach on a multiple-feedback filter, the equivalent circuit structure is the same with the one presented in Fig. 1 (b). Since

each branch in a multiple-feedback filter can apply a different gain, a tunable multiple-feedback topology implemented using the proposed approach would not only offer tunability on the bandwidth and filter approximation, but also on the gain of the overall filter block. This merit is crucial in concurrent stimulation and recording setups because, in addition to the bandwidth, the gain of the filter can also be adjusted within a small time-window before the onset (gain decrease) and after the termination (gain increase) of stimulation in order to increase the dynamic range of the AFE and thus avoid signal loss (due to AFE saturation) in the interstimulus interval and in the interval after the last pulse.

Another important observation is that the quality of the biosignal recording offered by the proposed technique in the intervals that are not directly affected by the artefact (i.e. interstimulus intervals and interval after the last pulse) does not deteriorate when the duty cycle of the pulses increases. Indeed, the results presented in this work indicate that the tunable filter can be used in various setups (DBS and CS with duty cycles 3.2% and 20%, respectively, were used as examples in this work) to provide high-quality biopotential recording that is free from ringing or phase distortion in both the interstimulus intervals (where the cut-off is placed at 0.1 Hz to avoid signal distortion/saturation issues) and in the interval after the last pulse (where the cut-off is placed at a high value, e.g. 10 or 100 Hz, in order to achieve a fast recovery of the AFE). This is a significant advantage compared to our analogue notch filtering methodology presented in [16]. Therefore, the proposed tunable filters can be used in various stimulation setups (e.g. DBS, spinal cord stimulation and recording of local field potentials and action potentials, cardiac stimulation etc) to offer biosignal recording during stimulation. Clearly though, the proposed technique yields the best outcome when the applied duty cycle is very small (which is the case in DBS and many spinal cord stimulation setups) since in this case saturation during the artefact does not lead to significant information loss.

The above analysis reveals that the proposed technique is an analogue AC-coupling approach that prevents saturation in the interstimulus intervals by offering adjustability in the applied cut-off frequency and/or gain. Indeed, this strategy is less vulnerable to drifts and prolonged saturation issues compared to approaches based on DC-coupled systems. Having achieved minimal contamination of the recorded signal in the time domain, the next step is to eliminate the spectral contamination of the recordings due to the presence of stimulation-induced artefacts. This can be accomplished by combining the front-end artefact suppression technique shown in this work with a back-end artefact cancellation strategy, e.g. the linear interpolation technique, which has been shown to eliminate spectral contamination in DBS setups [20]. Indeed, this combination would allow the linear interpolation technique, which is currently applied by DC-coupled recording systems [20] (that avoid using filtering blocks in order to obtain recordings that are free from slow transient responses to stimulation pulses) in application-specific (DBS) experimental setups, to be used in a wider range of bidirectional electrophysiological interfaces.

V. CONCLUSION

This work presents a high-pass pole shifting technique for stimulation artefact suppression, which is conveniently

implemented by an innovative tunable filter architecture. The performance evaluation (using various stimulation protocols) conducted in this work confirms that the combined action of the proposed method and filter block can alleviate problems commonly encountered in bidirectional electrophysiological interfaces due to the presence of strong stimulation-induced artefacts. It has been proven that the proposed front-end technique can: a) provide high fidelity biosignal recording in the interstimulus intervals that is free from ringing oscillations or phase shifts, thus allowing the recording of short latency (e.g. 0.1 ms after the application of each DBS pulse [26]) evoked compound action potentials, and b) offer an immediate recovery of the front-end amplifier from strong stimulation pulses and electrochemical DC offsets so that continuous biosignal recording is achieved. Future developments on this work could include ex-vivo and in-vivo testing of the presented method and device, aiming at verifying its artefact suppression capabilities under various application specifications and requirements.

All in all, the use of the method presented in this paper in a multi-channel recording system could: a) save space on the printed circuit board of the device, b) reduce the overall power consumption of the system, c) preserve the real-time operation of the system, d) reduce the number of digital lines that are needed in order to control the filter response, and e) prevent high-frequency switching noise from being coupled into the analogue biosignals of interest (since it is a continuous-time and not a switched-capacitor filter implementation). Hence, a tunable filter block consisting of a moderate number (e.g. 2) of branches/embedded filters could be introduced into implantable recording and stimulation devices to offer real-time and adjustable artefact suppression so that reliable biosignal recordings can be acquired directly from the stimulation site.

APPENDIX

DERIVATION OF THE SYSTEM TRANSFER FUNCTION

The application of Kirchhoff's current law on the circuit shown in Fig. 1(b) leads to the following equations:

$$\text{Node A: } \frac{V_{IN}-V_A}{Z_{11}} = \frac{V_A-V_{OUT}}{Z_{31}} + \frac{V_A}{Z_{21}+Z_{41}} \quad (5)$$

$$\text{Node B: } \frac{V_{IN}-V_B}{Z_{12}} = \frac{V_B}{Z_{22}} + \frac{V_B-V_{OUT}}{Z_{32}} \quad (6)$$

$$\text{Node C: } \frac{V_B-V_{OUT}}{Z_{32}} + \frac{V_A-V_{OUT}}{Z_{31}} = \frac{V_{OUT}-A(V_+-V_-)}{Z_{OUT}} + \frac{V_{OUT}}{R_5+R_6} \quad (7)$$

$$V_+ = \frac{Z_{41}}{Z_{21}+Z_{41}} V_{OUT} \quad (8)$$

$$V_- = \frac{R_5}{R_5+R_6} V_{OUT} \quad (9)$$

The incorporation of Equations (8) and (9) into Equation (7) yields the following result:

$$\left[\frac{1}{Z_{31}} + \frac{A Z_{41}}{Z_{OUT} (Z_{21}+Z_{41})} \right] V_A + \frac{1}{Z_{32}} V_B - \left(\frac{1}{Z_{31}} + \frac{1}{Z_{OUT}} + \frac{1}{Z_{32}} + \right.$$

$$+ \frac{1}{R_5 + R_6} + \frac{A R_5}{Z_{OUT} (R_5 + R_6)}) V_{OUT} = 0 \quad (10)$$

In Equation (10), the $\frac{1}{Z_{31}}$ term is much smaller than the $\frac{A Z_{41}}{Z_{OUT} (Z_{21} + Z_{41})}$ term, and it can thus be omitted. In addition, the terms $1/Z_{31}$, $1/Z_{OUT}$, $1/Z_{32}$, and $1/(R_5 + R_6)$ are much lower than the term $\frac{A R_5}{Z_{OUT} (R_5 + R_6)}$, and thus they can also be omitted. The above approximations hold because the value of the parameter A (open-loop gain of the operational amplifier) is very high and the value of the parameter Z_{OUT} (output impedance of the amplifier) is very low.

Further processing of Equations (5) & (6) yield:

$$V_A = \frac{(Z_{21} + Z_{41}) (Z_{31} V_{IN} + Z_{11} V_{OUT})}{Z_{11} Z_{21} + Z_{11} Z_{41} + Z_{11} Z_{31} + Z_{21} Z_{31} + Z_{41} Z_{31}} \quad (11)$$

$$V_B = \frac{Z_{22} Z_{32} V_{IN} + Z_{22} Z_{12} V_{OUT}}{Z_{12} Z_{32} + Z_{22} Z_{32} + Z_{12} Z_{22}} \quad (12)$$

After incorporating Equations (11) and (12) into Equation (10) and taking into account the approximations described above, the following result is deduced:

$$\frac{V_{OUT}}{V_{IN}} = \frac{\frac{A Z_{41} P}{Z_{OUT} (Z_{21} + Z_{41})} + \frac{M}{Z_{32}}}{\frac{A R_5}{Z_{OUT} (R_5 + R_6)} - \frac{K A Z_{41}}{Z_{OUT} (Z_{21} + Z_{41})} - \frac{N}{Z_{32}}} \quad (13)$$

where:

$$P = \frac{Z_{21} Z_{31} + Z_{41} Z_{31}}{Z_{11} Z_{21} + Z_{11} Z_{41} + Z_{11} Z_{31} + Z_{21} Z_{31} + Z_{41} Z_{31}} \quad (14)$$

$$M = \frac{Z_{22} Z_{32}}{Z_{12} Z_{32} + Z_{22} Z_{32} + Z_{12} Z_{22}} \quad (15)$$

$$K = \frac{Z_{21} Z_{11} + Z_{41} Z_{11}}{Z_{11} Z_{21} + Z_{11} Z_{41} + Z_{11} Z_{31} + Z_{21} Z_{31} + Z_{41} Z_{31}} \quad (16)$$

$$N = \frac{Z_{22} Z_{12}}{Z_{12} Z_{32} + Z_{22} Z_{32} + Z_{12} Z_{22}} \quad (17)$$

Referring to Equation (13), since the ratio A/Z_{OUT} is very high, the terms M/Z_{32} (in the numerator) and N/Z_{32} (in the denominator) can be omitted from the calculated transfer function of the system.

As a result, Equation (13) can be reduced as follows:

$$\frac{V_{OUT}}{V_{IN}} = \frac{Z_{41} P (1 + \frac{R_6}{R_5})}{Z_{21} + Z_{41} - K Z_{41} (1 + \frac{R_6}{R_5})} \quad (18)$$

The incorporation of parameters P and K into Equation (18) yields the following result:

$$\frac{V_{OUT}}{V_{IN}} = \frac{1 + \frac{R_6}{R_5}}{\frac{Z_{11} Z_{21}}{Z_{31} Z_{41}} + \frac{Z_{11}}{Z_{41}} + \frac{Z_{21}}{Z_{41}} + 1 - \frac{Z_{11} R_6}{Z_{31} R_5}} \quad (19)$$

which is the transfer function of a classic 2nd order Sallen-Key filter.

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