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Mixed-Signal Front-End Design for Concurrent Acquisition of Electrophysiological and Hemodynamic Brain Signals

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Abstract

Based on experimental evidence, multimodal neuro engineering applications in the case of electrophysiological monitoring and hemodynamic monitoring of a brain region demands simultaneous functionality, but is difficult because of the difference in signal amplitude, bandwidth and noise specifications that is very high indeed. Electrophysiological signals are microvolt-scale amplitude and bandwidth (KHz) signals, and hemodynamic signals are millivolt-scale amplitude and sub-10-Hz signals, so attempt to record both simultaneously is likely to be saturation artefact, crosstalk, and or timing error. The paper will discuss a mix signal front-end system that allows simultaneous capture of both modalities with a single and time synchronized signal chain. The proposed design uses dual analogue conditions along conditions along with modality selective gain and bandwidth isolation, and then an identical mixed-signal conversion stage, to synchronise sampling. To suppress inter-path interference and at the same time maintain sensitivity to low-amplitude electrophysiological signals a noise-optimised low-noise amplifier and frequency-selective filtering strategy is adopted. Noise in Analytical Noise Analytical noise models are developed to design circuits and choice parameters. Sub-microvolt input-referred noise Experimental validation of synthesised brain-signal emulation containable levels in combination with reliable concurrent acquisition of the electrophysiological path, low inter-modal crosstalk, and stable tracking of hemodynamic signals under simultaneous operation have been demonstrated. The findings affirm that, the proposed mixed-signal front-end offers scalable and low-energy efficient model of deployed multimodal brain-monitoring systems and facilitates compact and synchronised acquisitions architectures of next-generation neuro interface systems.

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Introduction

The brain system Multimodal brain monitoring Multimodal brain monitoring systems are electrophysiological and hemodynamic systems used to complement each other in terms of fast electrical activity and slow vascular dynamism.[4-7] These systems are also becoming applicable in brain-computer interface applications, in cognitive workload assessment, and closed loop neuro stimulation platforms.[4, 6, 7] But simultaneous acquisition of all these heterogeneous signal modalities is demanding at the circuit-level in the front end, requiring immense signal-to-noise ratio variations, bandwidth variations, and variation of noise tolerance over the compression limits to be accommodated in a very compact and energy dissipative circuit.[1, 3, 8, 9] Electrophysiology signals (e.g. electroencephalography) have micro volt amplitude and bandwidth of nanophase range with noise requirements in the kilohertz range.[1-3], [10, 12] Hemodynamic signals, which are generally the product of optical or bio impedance-based sensing, have amplitudes a few millivolts and below a few hertz dynamics.[4-7] In the traditional way of acquisition, different front-end chains are used by each modality and this causes complexity of the system, higher power consumption and accuracy of the synchronisation.[4, 6, 9] In other cases, shared front-end designs have gain

saturation, crosstalk between inter-modes, and low-amplitude insensitivity.[1, 8, 10, 11] To overcome these deficiencies, the current work proposes a mixed-signal front-end architecture which is specifically meant to be employed in the simultaneous acquisition of both electrophysiology and hemodynamic brain signals. The suggested design is a dual analogue conditioning paths design with modality-specific gain and bandwidth isolation then sharing a common stage of mixed-signal conversion synchronised by time.[3, 8, 9, 12] The architecture has the ability to optimise noise performance, dynamic range and crosstalk suppression jointly allowing reliable simultaneous acquisition without distorting signal quality.[1, 2, 10, 11] It is experimentally proven that the presented front-end offers low input-referred noise, efficient inter-modal isolation, and robust simultaneous operation, so it is qualified to be implemented in multi-scale multimodal brain-monitoring systems.[5-7]

System Requirements and Design Constraints

This simultaneous acquisition of the electrophysiological and hemodynamic brain signals makes highly conflictual demands on the circuitry in the front-end by the extreme disparities in the nature of the signals. Such modalities are orders of magnitude different in amplitude, band width, and noise sensitivity, and have a direct effect upon gain allocation, filtering strategy and mixed-signal resolution. The amplitude of the electrophysiological signals is generally within 1 and 100 kilometres V and has frequency content that extends to the kilohertz range, making them need large programmable gain, high input impedance, and ultra-low input-referred noise to maintain signal fidelity. Conversely, hemodynamic signals have kilohertz spectral occupancies at this location with significant amounts above 10 Hz spectral content which imposes less strict noise requirements but large dynamic range management is required to avoid over saturation when sharing analogue or mixed signal resources.

This scale difference creates basic architectural issues with coherent front-end architectures. Optimisation of excessive gain to electrophysiological acquisition may readily oversaturate the signal chain with hemodynamic modulations but assume a much lower signal-to-noise ratio of low-amplitude neural signals is when gain is reduced to allow larger signals to pass. Equally, a single-bandwidth front-end can at any one time neither support within the electrophysiological dynamics nor across the hemodynamic variations on a kilohertz scale, without disrupting the information in inter-modal interactions or distortion. Such conflicting demands also apply to the analogue-to- digital conversion phase as high resolution is needed to meet micro volt contribution requirements and sampling rates need to be chosen to meet high-frequency neural activity requirement and low-frequency hemodynamic requirement. Table 1 provides the summarised signal characteristics and front-end design requirements of an electrophysiological and hemodynamic modality. The comparison reveals the need to have modality specific gain staging, bandwidth isolation and precisely orchestrated sampling strategies. These limitations are directly the motivation behind the dual-path analogue conditioning and synchronised mixed-signal acquisition design in the next section which is developed specifically to permit good simultaneous acquisition in a manner that signal integrity is not compromised.

Table 1.Signal and Front-End Design Requirements

Parameter	Electrophysiological	Hemodynamic
Amplitude	1-100 µV	1-100 mV
Bandwidth	0.5-1 kHz	DC-10 Hz
Required gain	40-60 dB	10-20 dB
Noise floor	<1 µVrms	<50 µVrms
Sampling rate	≥2 kS/s	100-500 S/s

Proposed Mixed-Signal Front-End Architecture and Methodology

Architecture Overview

The proposed mixed-signal front-end architecture is successfully intended to support simultaneous recording of electrophysiological and hemodynamic brain signals

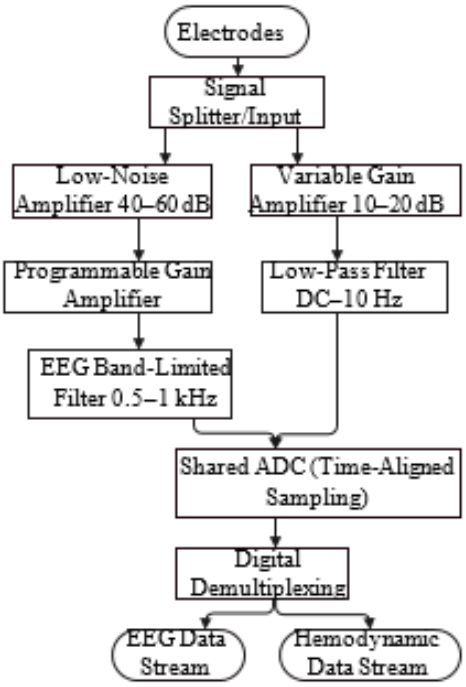

Fig. 1: Proposed Mixed-Signal Front-End Architecture

whilst maintaining signal integrity between modalities with enormous difference in amplitude and bandwidth properties. The architecture, as shown in Figure 1, uses a common electrode interface, with a buffered signal-splitting stage which is a high-input impedance and controlled-/buffered-/fan-out signal stage, but does not load sensing electrodes. This design has the benefit that, the two modalities will be launched at the same sensing point and avoid the inter-path interference at the input stage.

The signal is fragmented at the input buffer and spread to two special purpose analog conditioning paths that are conditioned to the modality of the signal. The programmable gain control, Low-noise amplification stage and band limited filtering is part of the electrophysiological path and supports signals down to the level of microvolts but with a band width of kilohertz. Simultaneously, the hemodynamic path uses lower gain amplification and low-pass filtering to acting on the signals in the millivolts range that are dominated by sub-10-Hz dynamics. This isolation by separation of gain and bandwidth between the two paths makes it possible to isolate them effectively and to operate simultaneously. Both conditioned analogue signals are sent to the common analogue-to-digital conversion stage which runs on common clock. Synchronous sampling of both modalities is achieved by use of a common time-aligned ADC to avoid timing skew normally caused by the use of multi-converter systems. Digital DE multiplexing is then used to decouple the electrophysiological and hemodynamic output data streams of the digitised data streams, producing independently processed electronics and hemodynamic outputs. This mixed-Signal platform offers a small and extensible platform to acquire multimodal brain signals and satisfy noise, dynamic range, and synchronisation constraints.

Analog Front-End Circuit Design and Analysis

Low-Noise Amplifier Design

The inherent noise limitations of the electrophysiological acquisition path are the input-referred noise of the first amplification stage, thus, the low-noise amplifier (LNA) is aimed at maximising the sensitivity to microvolt-level signals but requires resistance to the electrode offsets and low-frequency offset. This is a topology of chopper-stabilised, capacitive coupled instrumentation amplifier that is used to eliminate flicker noise, DC offsets, as well as high input impedance. The capacitive coupling used in this structure rejects large components of DC elements of the electrodes, whereas the chopper modulation of the noise and baseband offset are repositioned to allow lower filtering to reject the up-modulated artefacts. This is especially efficient when operating EEG-bands, in which 1/f noise can prevail when not remedied. The biasing has been chosen to work in the low-noise regime to reduce the power of the input devices, as further current increases power but do not give equal noise reduction. Biasing of the input transistors is made to minimize the contribution of thermal noise and provide control over input-referred current noise, and make the operation of common-mode constant over different electrode impedances. Gain programmability An interface to inter-subject and inter-electrode variability Gaining programmability gain programmability is provided by a programmable gain amplifier stage prior to the LNA (or switched-capacitive bits of instrumentation amplifier) to achieve the necessary dynamic range at a low noise floor. Noise of the input-referred noise of the front-end may be described as a sum of electrode resistance thermal noise and amplifier noise mechanisms. In line with this the overall input-referred noise is modelled as:

$$v_{n,in} = \sqrt{4kTR + \frac{e_n^2}{G^2} + i_n^2 R^2}, \quad (1)$$

Where Boltzmann is's constant, is absolute temperature, R represents the effective source/electrode resistance, and are the noise densities of the input-referred voltage and current to the amplifier and G is the closed-loop gain. The three key design levers that have been employed in this work as shown by equation (1) include: (i) minimising the effective noise bandwidth of a band-limited filtering, (ii) minimising. via chopper stabilization and low-noise input device sizing/biasing, and (iii) limiting the impact of by ensuring high input impedance and careful bias current management so that the term does not grow at increased electrode impedances. Moreover, the choice of gain allocation is made to provide enough early-stage gain in order to damp off the relative importance of the contributions of noise in the down-stream approach and yet not to be saturated by any offset and motion artefacts. Combined, these options reduce the predominant noise terms and allow credible acquisition in terms of electrophysiology to take place when multimodal operation is running.

Bandwidth Isolation and Crosstalk Mitigation

Accurate simultaneous recording of electrophysiological and hemodynamic brain signals has to be comparatively suppressed by the presence of inter-modal interference due by the shared input interface, near-proximate physical location of analogue circuit boards and mixed-resource reuse. The clear difference in the signal bandwidth and amplitude between the two modalities implies that bandwidth isolation is set as the most important

method to reduce crosstalk in the suggestive front-end architecture. Each analogue path has frequency-selective filtering used to concentrate the signal energy to its spectral band before digitization. A cut-off band filter, centered on the EEG frequency band, inserted into the electrophysiological path, rejects the low frequencies of a hemodynamic signal, drift in electrodes. On the other hand, low-pass philtre is used in the hemodynamic path to cut high-frequency electrophysiological information and switching artefacts. This spectral isolation gives residual coupling between the paths a large attenuation factor even at the other operating bands, even when the two modalities are simultaneously acquired. Physical separation and differential routing are also implemented on the layout level in addition to filtering to minimise capacitive and inductive coupling. Sensitive high-gain electrophysiological nodes are physically separated not only by hemodynamic circuitry of lower gain and sub digital switching areas, but also by the use of differential signal paths, to enhance common-mode noise rejection and reduce the effects of substrate and supply-induced circuit coupling. These are especially relevant within a mixed-signal implementation whereby shared clock and transitioning between digital data can otherwise serve to add spurious coupling to low-amplitude analog data. An extra degree of isolation is given by gain partitioning over the two paths. The gain that is high in the electrophysiological path is localized only where needed and the hemodynamic path functions with much lower gain eliminating large amplitude signals reaching shared common nodes. This controlled allocation of gain minimises the possibilities of coupling and nonlinear mixing between gain saturation due to simultaneous operation. A crosstalk coupling ratio (CTR) is used to measure the effectiveness of the proposed isolation strategy where:

$$CTR = 20\log_{10}\left(\frac{V_{interference}}{V_{signal}}\right), \quad (2)$$

where $V_{interference}$ represents the undesired coupled voltage from the opposite modality and V_{signal} represents the desired signal strength. Reduced values of CTR are related to better isolation as the equation below, Equation (2), outlines. The proposed front-end is by far characterised by low inter-modal crosstalk, achieved through frequency-selective filtering, physical and differential layout approaches, as well as physical modality-specific gain partitioning, where concurrent acquisition of electrophysiological and hemodynamic signals is possible with no signal fidelity degradation.

ADC and Mixed-Signal Timing Strategy

A single shared analog-to-digital converter (ADC) is used by the proposed front-end architecture to digitize electrophysiological and hemodynamic signals to allow time-aligned inherent sampling of both modalities. The architecture eliminates inter-channel timing skew which is common in systems that use more than one independent ADC because of the common conversion clock. The synchronisation is especially necessary in multimodal brain monitoring applications, in which the temporal association of fast electrophysiological processes and slower hemodynamic processes are essential to obtain accurate data incorporation and analysis.

Although timing can be easily controlled by using only a single ADC, and area and power overhead are minimised because the two modalities are characterised by different amplitudes, there is a fundamental trade-off between resolution and dynamic range between the modalities in the former case. Electrophysiological signals need high effective resolution to see the difference between variations of microvolt and the hemodynamic signals need high effective resolution to see the difference between variations of millivolts without saturation. To cope with this issue, the suggested architecture will assume the use of modality-specific scaling of analogue gain before digitization, where again both types of signals are efficiently scaled to the range of the ADC input. This gain normalisation enables the ADC to work within its optimal signal-to-noise-and-distortion ratio in both directions even though their amplitude levels are at different levels. The ability to solve the ADC when it is operating with a second item is measured as the number of effective bits (ENOB), which is the sum total of the quantization noise, thermal noise, and distortion. ENOB is expressed as:

$$ENOB = \frac{SNDR - 1.76}{6.02}, \quad (3)$$

Where SNDR represents a ratio of signal-to-noise-and-distortion of the ADC output. When it is desired to have a large ENOB, both analogue front-end noise and nonlinear distortion have to be controlled before conversion, as indicated by Equation (3). In the proposed design, a suitable gain partitioning, bandwidth constrained filtering and synchronised sampling will ensure the ADC is being used in its linear regime without loss of adequate resolution to detect low-amplitude electrophysiological signals. The mixed-signal timing approach presented is one of the approaches that allow heterogeneous brain signals to be digitized reliably and simultaneously with compact conversion architecture consume minimal power.

Experimental Setup and Measurement Protocol

The experimental aspect of the proposed mixed-signal front-end was tested through diffusion of the

controlled laboratory experiment based on the ability to simulate real operating conditions and concurrently electrophysiological and hemodynamic signal acquisition. In order to measure front-end performance without any interference due to biological variability, there was the production of EEG-like and hemodynamic-like signals with well-known amplitude and spectral properties, synthetically. Low-amplitude sinuoidal and broadband waveforms in the frequency range of the EEG were used to simulate electrophysiological measures and low-frequency deviations were simulated as hemodynamic signals that would represent slow vascular dynamics. The two types of signals were used at the same time which tested the robustness of the architecture when in parallel use. Electrode-skin impedance was modelled using a phantom-based electrode interface, and to provide repeatable and constant input conditions, precision networks of resistive networks were used. In this method, the input-referred noise, gain accuracy and crosstalk were controllably evaluated with no confounding effects due to motion artifacts or electrode polarization. Calibrated lab equipment was used to measure the responses of the front-end working under nominal operating conditions in time-domain and frequency-domain.

Table 2 condenses the major parameters of measurements utilised during the evaluation of the experiment. The front-end was driven at 1.8 V, as would be the case with a low-power mixed-signal implementation. The amplitude of test signals and the sampling rate was chosen such that both modalities have realistic operating limits, and the performance of concurrent acquisition of both modalities in the desired operating range of their applications can be directly evaluated.

Table 2: Measurement and Test Parameters

Parameter	Value
Supply voltage	1.8 V
Technology	CMOS / Prototype
EEG test signal	10–50 µV
Hemodynamic signal	5–50 mV
Sampling rates	2 kS/s / 200 S/s

Results and Performance Evaluation

The proposed mixed-signal front-end was tested in the concurrent acquisition case to confirm that the device could communicate electrophysiological and hemodynamic signals without their reduction in signal fidelity. The experimental setup in Section 4 was used to measure key performance indicators such as noise floor, inter-modal crosstalk, dynamic range and power consumption. This electrophysiological path has a low input-referred noise floor and allows, despite the fact that simultaneously-recorded higher-amplitude hemodynamic components are present, to reliably detect signals of microvolt scale. The experimental noise performance of the low-noise amplifier ascertained that the gain partitioning strategy and low-noise amplifier are able to substantially reduce the overwhelming noise sources due to thermal noise and flicker noise with a stable acquisition of the EEG with simultaneous operation. No increase of noise could be observed with the hemodynamic path active and this means that there is isolation between the two analogue paths.

Inter-modal Crosstalk was considered by injecting high amplitude low frequency hemodynamic signals with the electrophysiological response observed. The experiment shows that crosstalk is low throughout the EEG band indicating that frequency-selective filtering, physical isolation, and gain separation have been successfully used to prevent interference. The fact that the EEG signal shows no sign of visible distortion or baseline modulation, when it is being obtained concurrently, is an additional confirmation that there is a strong crosstalk suppression. The front-end has a dynamic range that is non-saturating enough to record electrophysiology of that range (when in microvolt range) and hemodynamic signals of that range (when in millivolt range). This makes sure that the common ADC resolution is efficiently utilised, and sensitivity of the common signal amplitude disparities is maintained. The overall power of the front-end is also within the limits of low-power mixed-signal operation, which enables the implementation to be compared with multi-channel implementations. Figure 2 is a time-domain description of the electrophysiological and hemodynamic responses that were simultaneously obtained. The high-speed EEG-band signal is superimposed with a low-frequency hemodynamic change on a shared time scale, which clearly shows simultaneous acquisition without saturation, inter-modal distortion, or signal detail degradation. This finding empirical data of the

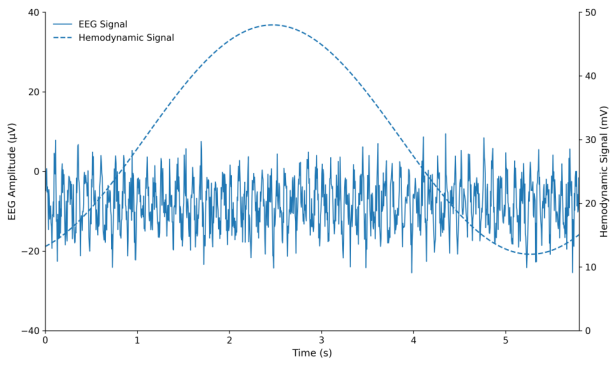

Fig. 2: Concurrent Acquisition Results

front-end to acquire multimodal brain signals in sync.

Discussion

The development of mixed-signal front-end illustrates that simultaneously measuring electrophysiological and hemodynamic brain signals can be developed with a single architecture without any signal degradation. A major design trade-off is offered by the commonness of an analogue-to-digital converter. Although one of the advantages of using one ADC is intrinsic time resolution and a lower area and power cost than a multi-converter implementation, ADC results cause significant burdens on analogue gain partitioning and dynamic range control. In practise modality-specific amplification and bandwidth isolation are effective in eliminating these limitations, but systems that demand much larger numbers of channels or larger amplitude range probably need much more expensive conversion schemes. It has a naturally scalable architecture based on replicate of the analog conditioning paths, but shared mixed-signal resources. This will substantially decrease the per-channel overhead of the multimodal acquisition system when it is large. However, the shared ADC can be used as a throttle neck in a channel-arbitration delay as the number of channels escalates and especially with electrophysiological signals, which might need high sampling rates. It may be considered to implement time-division multiplexing or hierarchical ADC architecture in order to overcome this drawback in future designs. Although the given design has its benefits, there are limitations to it. Simultaneous sampling is limited by the single use of an ADC only to those cases where effective gain normalisation may precede conversion. Moreover, experimental validation uses synthetic and phantom based signals; although this can be used to control concurrency and isolation; there are other artefacts that can occur in in vivo measurements including motion induced coupling or changes in electrode impedance. Improving such aspects as well as considering adaptive gain control and multi-ADC extensions is one of the promising avenues of future research.

Conclusion

The paper provided a mixed-signal front-end architecture of simultaneous acquisition of electrophysiological and hemodynamic brain signals, including the issues of the different amplitude, and bandwidth of the signals as well as their different noise levels. The proposed design is able to support synchronized multimodal acquisition with signal fidelity intact by employing a shared electrode interface, modality-sensitive analog conditioning paths and a time correlated shared analog-to-digital conversion stage. Experimental measures reveal very good input-referred noise in the electrophysiological chain, good inter-modal crosstalk rejection and the dynamic range to support simultaneously in the microvolt and millivolt range. The time-domain results assure that there is quality simultaneous operation that proves the success of the suggested gain partitioning, bandwidth separation, and mixed-signal timing plan. These findings underscore the feasibility of adopting a cohesive front-end design in small and low-energy multimodal systems of monitoring the brain. Although introduced trade-offs are encountered in scalability and throughput with the usage of a common ADC, the architecture presented here forms a good basis of future scale/adaptive systems extensions to multi-channel systems. On balance, this paper proves that front-end architectures based on mixed-signalling can be used to provide synchronised acquisition of heterogeneous neural signals, making it possible to scale and integrate to provide solutions to the next-generation neuro engineering and brain-computer interface applications.

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