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**AN FPGA SYSTEM FOR REAL-TIME  
SENSOR-ARRAY DATA PROCESSING**

Ph.D. Programme: Electrical Engineering and Information Technology  
Branch of study: Measurement and Instrumentation

Doctoral thesis statement for obtaining the academic title of “Doctor”,  
abbreviated to “Ph.D.”

Prague, August 2012

The doctoral thesis was produced in full-time manner Ph.D. study at the Department of Measurement of the Faculty of Electrical Engineering of the CTU in Prague.

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# 1 CURRENT SITUATION OF THE STUDIED PROBLEM

## 1.1 MICROELECTRODE ARRAYS

Microelectrode arrays (MEA) are sensors designed for extracellular recordings of action potentials generated by electrogenic cells (neurons and cardiomyocytes). The first microelectrode arrays were designed in early 1970's [1]. They were passive, manufactured by means of a standard lithography process, with only a few tens of electrodes. Nowadays, they are even available commercially<sup>1</sup>, but the limitation of low electrode count and low spatial resolution remains. Their biggest advantage is the simple manufacturing process which allows to create 3D structures to mechanically constrain the growing cells [2, 3].

In the past few years a new type of so-called active MEAs is being developed, based on the standard CMOS process. The complexity of the integrated electronics may differ, but even the simplest arrays contain an output multiplexer, sequentially connecting the individual electrodes to only a few output ports. In such configuration, arrays with tens of thousands electrodes can be manufactured, allowing measurements with sub-cellular resolution [4]. Moreover, the signal conditioning channels can be integrated together with the electrode array, minimizing the amount of noise added by an external acquisition system and cabling. But the ultimate solution is to integrate the A/D converters at the same die [5]. In such case, the analogue signal does not leave the chip and the amount of noise coupled into the converted signal is minimized.

Wide range of experiments is performed with these sensors including detailed analysis of signal propagation within a single cell [6], investigation of neural plasticity [5] and high throughput drug screening [7]. A special class of the active MEAs are the implantable sensors for in vivo experiments [8].

This thesis is focussed on the high-density planar active MEA [6] with on-chip A/D conversion, designed at Physical Electronics Laboratory, ETH in Zurich. This array uses a novel approach of electrode to readout circuitry interconnection. Programmable routing matrix inspired by similar structures in the field programmable gate arrays (FPGA) is manufactured beneath the array of more than 11 thousand electrodes. Through this matrix an arbitrary subset of 126 electrodes can be permanently connected to dedicated readout channels

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1. Multi Channel Systems GmbH, Germany, [www.multichannelsystems.com](http://www.multichannelsystems.com)  
Panasonic, Japan, [www.med64.com](http://www.med64.com)  
Plexon Inc., USA, [www.plexoninc.com](http://www.plexoninc.com)

implemented around the array. In such configuration, continuous readout and stimulation is possible from any electrode on the chip allowing the array to adapt to any type of measured sample.

## **1.2 MEA RECORDINGS PROCESSING ALGORITHMS**

Extracellularly recorded signals generated by the electrogenic cells are called spikes and the ultimate goal for the neural-recordings processing algorithms is to detect these spikes and classify them (assign them to a particular neuron). A good overview of the spike sorting methods is given in [9], summarizing the state of the art in 1998. Since then, several new approaches were introduced, employing wavelet transformation [10, 11] and artificial neural networks [12].

Most of the standard spike sorting algorithms follow the same scheme [13]. A threshold is applied to the raw data and the potential spikes are extracted. Distinctive features are extracted from the detected spikes and upon these features the spike is classified and assigned to a particular neuron or discarded as a false match. There are many different approaches to perform these three steps optimized for different cell cultures and recording setups.

All these algorithms, have to be performed off-line, due to the calculation complexity of the classification phase. Raw data have to be provided to these algorithms in order to detect all spikes, even the overlapping ones. A loss-less or a near loss-less compression algorithm may be required in order to deliver the raw data. In case the loss-less compression is not sufficient in terms of data reduction, a partial classification has to be performed on-line, resulting in very high compression ratios [14], but also a very high signal distortion. In such applications, only partial spike sorting is possible, as most of the less pronounced and overlapping spikes are destroyed during the compression process. Furthermore, such algorithms require a learning phase performed off-line on the raw data. Wavelet-based multiresolution analysis was reported to be a suitable replacement [15] for these methods, as it uses standardized base vectors and does not require the off-line training phase.

## 2 AIMS OF THE DOCTORAL THESIS

The primary goal of this thesis is to design a modular hardware platform for multi-chip recording from a high density MEA [6]. This acquisition system should allow several chips to be connected at the same time and simultaneously recorded from. The system must provide a simple and transparent interface to the connected MEA chips, allowing the software running on a supervising computer to easily configure them and record raw data from them. In addition, it should support real-time spike detection and spike sorting, allowing complex bio-feedback experiments to be carried out without any interaction with the supervising PC. The system must be designed as an open platform allowing new signal processing modules to be added with minimal effort.

To achieve the main goal, several tasks, listed below, have to be solved:

- **Source data analysis** - better understanding of the processes behind the actual spike generation, and its recording, is required to evaluate the properties of different signal processing algorithms currently used.
- **Optimal algorithms selection** - upon the initial signal properties evaluation, a few general algorithms should be selected, providing means for recorded signal compression, spike detection and sorting.
- **Data acquisition system design** - there is currently no hardware platform allowing the newly designed high-density active MEAs to be used in bio-labs. A simple acquisition system has to be designed first to acquire real data required for the initial signal analysis. After the processing algorithms are chosen, the system should be modified to support them.
- **Implementation of the selected algorithms** - based on the initial evaluation, several algorithms should be implemented in form of a hardware module and included into the final acquisition system.
- **Real measurements** - the functionality of the whole system should be confirmed by series of measurements performed at a different state of the design process. The minimal functionality required is recording from a limited number of electrodes on a single MEA chip, to provide data for the algorithm evaluation, but the ultimate goal is the parallel recording from all electrodes on several chips with real-time compression and cell stimulation.

## **3 WORKING METHODS**

### **3.1 SIGNAL ANALYSIS**

In parallel with this thesis, an off-line spike sorter is being developed at PEL [6]. When applied on the recorded data it is able to detect and classify the spiking activity of the individual neurons and generate so-called *cell footprints*, a set of averaged spike shapes detected at the individual electrodes. First experiments will be carried out with Purkinje cells from rat's cerebellum, neurons with planar topology and well described process of spike generation [16]. Combining the raw data and the extracted cell footprints, the process of signal propagation in the system can be evaluated, and the sources of noise and other interfering signals localized.

In order to confirm or disprove the usability of the blind source separation (BSS) algorithms, the spike shape properties and signal propagation delays have to be investigated. For all the detected cells, the strongest spike can be chosen and compared with the other spikes within the particular footprint and with the strongest spikes of other cells within the sample. As a part of this process, the propagation delay can be evaluated by means of cross-correlation between all the spikes within the footprint.

Based on the results, the usability of the Independent Component Analysis (ICA) BSS algorithm can be evaluated.

### **3.2 DISCRETE WAVELET TRANSFORMATION**

Successful application of the wavelet transformation (WT) was reported in literature, but in most cases only in form of third-party tools without deeper understanding of the processes behind. In order to design a high throughput discrete wavelet transformation (DWT) based spike system, full understanding of the underlying processes is required.

Custom designed tool performing the lifting scheme filter decomposition may reveal structures more suitable for hardware implementation, than the ones provided by standard tools (e.g. Matlab). Additionally, the original decomposition algorithm [17] can be modified to produce causal structures in contrast to the commonly used non-causal decompositions, that need to be artificially causalized before the hardware implementation. Software simulation tool have to be provided in order to test the designed structures prior to the final hardware implementations.

Once the possibility of parallel DWT processing is confirmed and resource requirements evaluated, more complex structures can be constructed,

including hardware support for further DWT analysis, denoising and compression. One important property of the DWT, the signal shift dependency should be studied further and hardware structures for shift-invariant DWT calculation designed.

Wavelet for the final hardware implementation has to be chosen upon both, the hardware complexity and spike separation capability.

### **3.3 LOSS-LESS COMPRESSION**

In order to recover the overlapping spikes, the off-line analysis has to be performed on raw data. A loss-less compression algorithm has to be provided in order to support these applications, while allowing the system to record from several MEA chips in parallel.

As the first step, the a priori knowledge of the data structure should be employed in order to reduce the redundant information in the data. After that, an optimal encoding scheme have to be found providing high compression ratios with minimal hardware requirements. Different types of compression methods should be tested, including the three main families, dictionary-based, run length encoding (RLE) and entropy based.

The designed algorithm should be first tested in form of software utility and once its functionality is confirmed, it can be included into the designed acquisition system in form of a hardware module.

### **3.4 ACQUISITION SYSTEM DESIGN**

There is currently no acquisition system allowing the newly developed active MEAs to be used in the bio-lab environment. Therefore as the first step, a simple system should be designed in order to record data from a single chip and forward them to the supervising PC without any additional processing. Based upon the analysis of these data, the final system should be designed, capable of recording from several MEA chips in parallel. The multichannel nature of the source data clearly suggests the use of a field programmable gate array (FPGA), but a dedicated signal processor will be also required in order to provide the PC connectivity and support for the real-time feedback stimulation tasks.

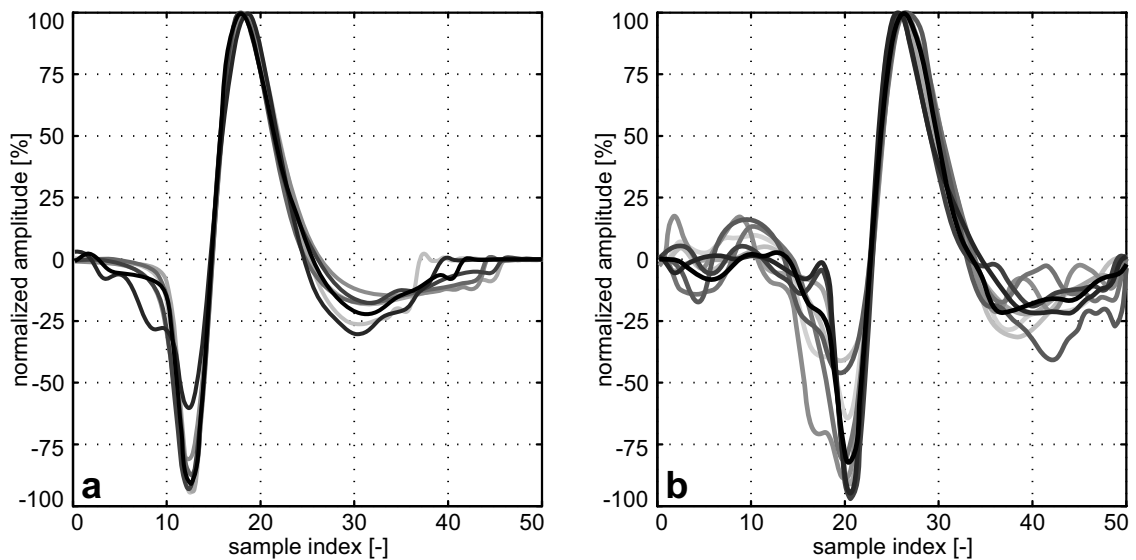
New MEA data processing algorithms may be designed in future, the system must be conceived as a modular platform in order to allow their simple integration. To prove the concept right, the advanced signal processing algorithms designed within this thesis should be implemented in form of hardware modules and integrated into this system.



## 4 RESULTS

### 4.1 MEA SIGNAL PROPERTIES

The initial signal analysis was performed as outlined in Chapter 3.1. High similarity in shape among different cells within a single culture was confirmed as demonstrated in Fig. 4.1a.



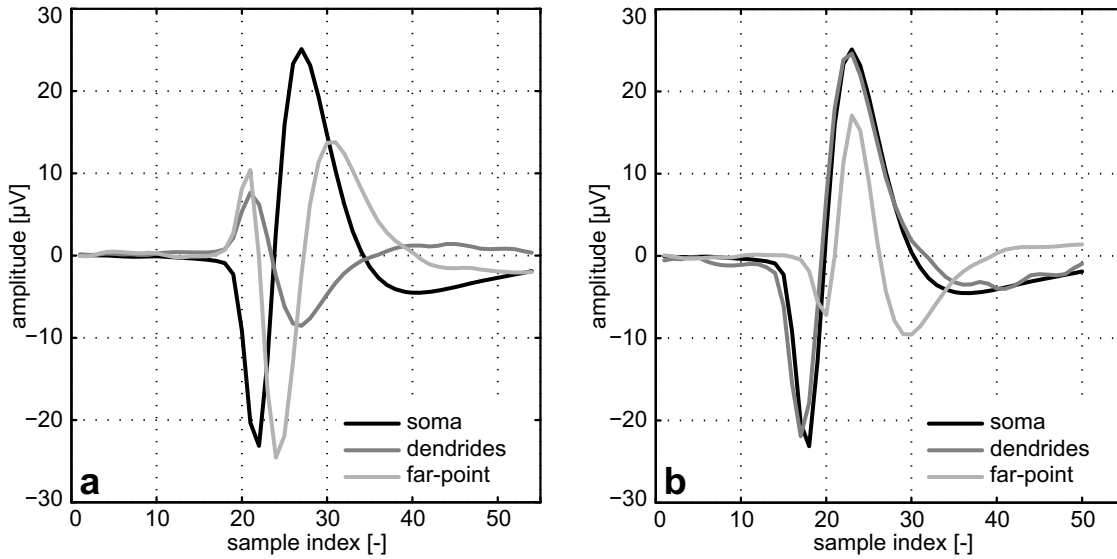
*Fig. 4.1: Normalized and aligned spikes from seven different cells within the sample (a) and from a single cell measured on different electrodes (b).*

In order to make this plot, the extracted spikes were aligned in time and rescaled. In order to provide better alignment, the number of recorder data points was increased 5 times by means of interpolation. The higher difference in shape among spikes recorded from a single cell, shown in Fig. 4.1b, is mostly caused by their lower amplitude, resulting in higher amount of noise and other interferences.

In addition to these standard-shaped spikes, also spikes with different shape demonstrated in Fig. 4.2 were detected.

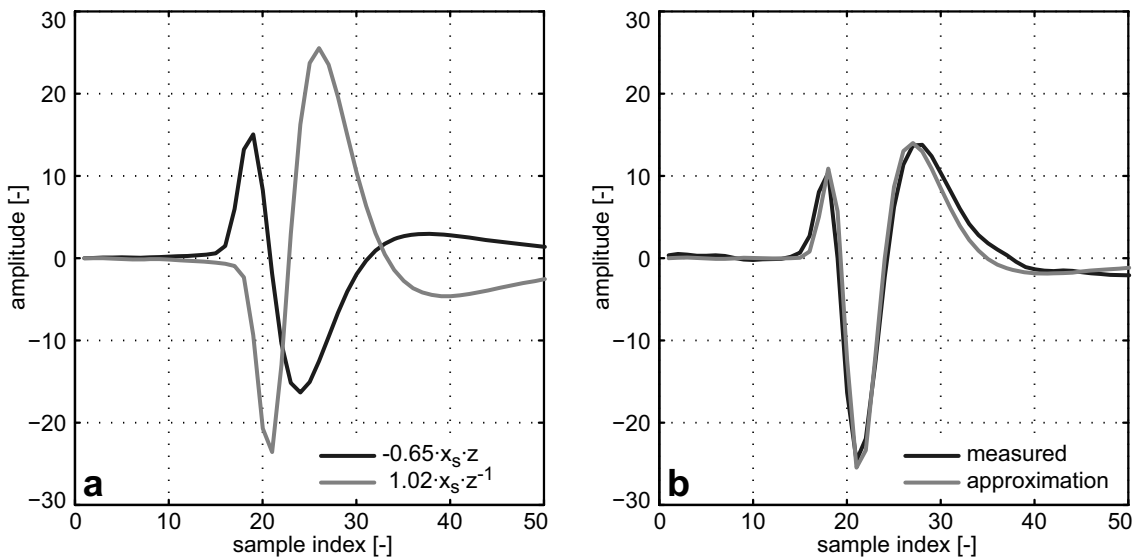
The origin of this signals is further discussed in [6] and the measurement validity confirmed by comparison with an extensive numerical model of the Purkinje cell on a simplified model of the MEA chip. It was confirmed that the strongest spike was recorded from the cell soma and that the signal from its dendrite tree is in terms of shape very similar, only with smaller and opposite amplitude.

The shape of the spike measured further away from the soma can be explained only when a nonzero signal propagation delay is taken into account.



*Fig. 4.2: Spikes recorded at three different points of the Purkinje cell (a) and comparison of their shape by means of a minimal error fitting (b).*

Fig. 4.3 confirms that this signal can be approximated by a combination of differently delayed and scaled signals from the cell soma and dendrite tree.



*Fig. 4.3: Approximation of the signal measured further away from the cell (b) by a sum of shifted and scaled typical-shape spikes (a).*

Further experiments were performed in order to evaluate the propagation delay within the system and to compensate for it, in the ICA algorithm. But even in case of the convolved ICA, modified for systems with nonzero propagation delay, the individual independent components still contain spikes from several neurons and a real-time spike sorting based on the ICA algorithm is highly improbable.

## 4.2 DISCRETE WAVELET TRANSFORMATION

Based on a thorough analysis of the DWT structures, a novel method for causal lifting decompositions of the DWT filter banks was designed. Further analysis were performed in order to identify wavelets most suitable for the MEA signals processing. Wavelets sym4 and bior5.5 were able to localize most of the spike energy within two decomposition details and were chosen for further tests. Thanks to the lower expected hardware complexity, wavelet sym4 was converted into the improved lifting structure depicted in Fig. 4.4.

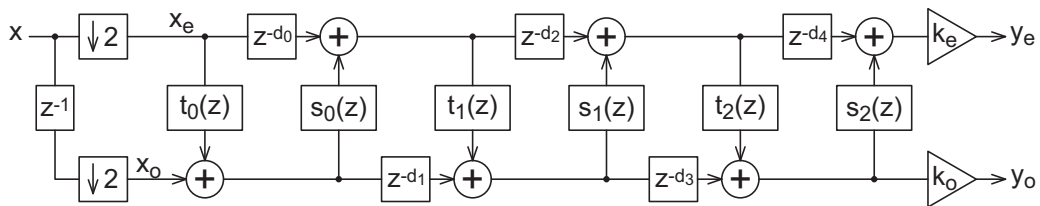


Fig. 4.4: General 6<sup>th</sup> order lifting decomposition structure with correction elements.

The actual filter coefficients obtained from the decomposition algorithm are listed in Fig. 4.5.

```

----- decomposition 1 -----
step 1: t = [-0.391147]
step 2: s = [0.339244 0.124390]
step 3: delay of 1 on odd branch
step 4: t = [-0.162031 -0.899146]
step 5: delay of 1 on even branch
step 6: s = [0.431283 -0.230469]
step 7: delay of 1 on odd branch
step 8: t = [0.664617]
step 9: scaling = [1.250082, 0; 0, 0.799948]
-----
totally 3 independent memory elements required
totally 8 coefficients with dynamic range of 2.85 bits
scaling coefficients dynamic range: 0.64 bits

```

Fig. 4.5: Optimal sym4 lifting decomposition.

One of the big advantages of the proposed algorithm is the inherent causality of the generated structures. In contrast to the lifting structures generated by other tools (e.g. Matlab, see *doc lifting*), the correction delay elements introduced, allow all the individual update filters to be causal (expressed in negative orders of  $z$ ). As result, the filters allow a straightforward hardware implementation in contrast to the structures based on

the standard decompositions [15]. To further highlight the benefits of the proposed algorithm, a causal decomposition of the sym4 wavelet with filter coefficients equal to the commonly used ones was located in the generated structures and is listed in Fig. 4.6.

```

----- decomposition 10 -----
step 1: s = [0.391147]
step 2: delay of 1 on odd branch
step 3: t = [-0.124390 -0.339244]
step 4: delay of 1 on even branch
step 5: s = [-1.419515 0.162031]
step 6: t = [0.431283 0.145983]
step 7: delay of 1 on even branch
step 8: s = [-1.049255]
step 9: scaling = [0, 1.570700; -0.636659, 0]
-----
determinant of the scaling matrix is 1.00000000
totally 4 independent memory elements required
totally 8 coefficients with dynamic range of 3.51 bits
scaling coefficients dynamic range: 1.30 bits

```

*Fig. 4.6: Causalized common sym4 lifting decomposition.*

The rank assigned to this decomposition is 10 which means, there are 9 other structures (including Fig. 4.5) more suitable for the hardware implementation. Twice higher scaling coefficients dynamic range results in faster growth of the intermediate signal precision with growing decomposition depth. The higher filter coefficients dynamic range leads to one bit higher precision required for the individual filter coefficients. But the most important difference is the number of memory elements needed to store the signal previous values (corresponding to the  $z^{-1}$  operator). Both decompositions contain three first order update filters and three delay elements. In case of the optimal structure, all the correction delays can be shared with the previous update stages, while in case of the common structure, the first delay element requires its own memory. The structure presented in [15], based on the common decomposition, requires also at least four memory elements.

In case of single-channel systems, a single memory element does not make a big difference. But for system with hundreds of channels (630 in this system) processed in parallel, the 25 % memory requirements reduction became an important factor.

Fig. 4.7 shows the block diagram of an actual hardware implementation of the sym4 lifting structure, based on identical building blocks. In comparison to [15], the implementation is absolutely straightforward. But sym4 is just an

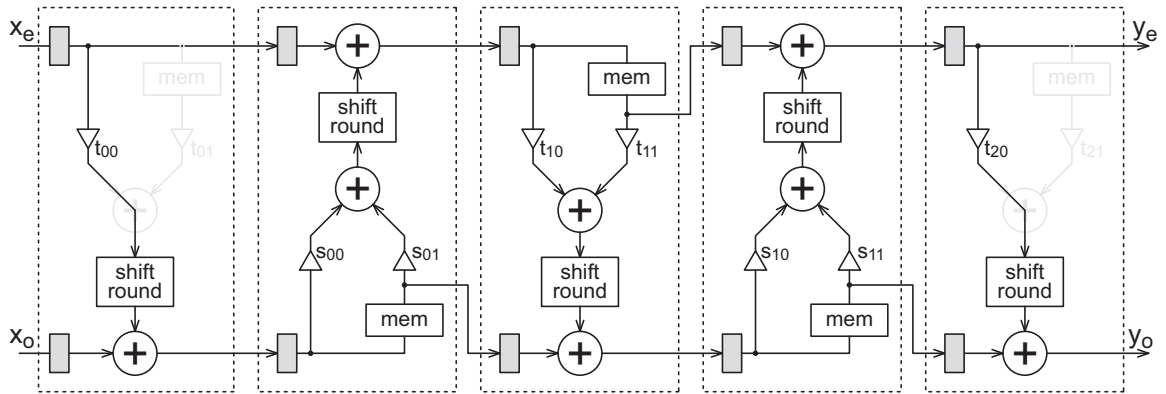


Fig. 4.7: Hardware optimal structure for causal sym4 lifting decomposition.

example, the proposed algorithm is able to decompose any wavelet, even a custom designed one.

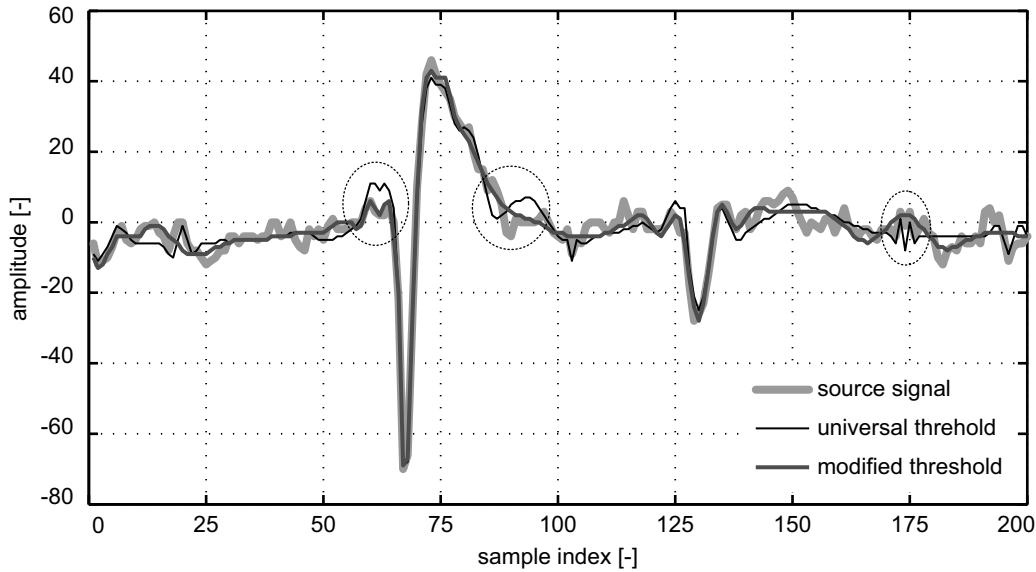
A software simulation tool was designed in order to test the designed structures and the influence of filter coefficient and the intermediate results rounding. In addition to the rounding error tests, this library allows real-time streamed data processing to be performed in Matlab. In contrast to the standard batch functions available, this tool supports short data chunks (down to a single word) processing with no artefacts created at the chunk boundaries.

Based on this library, complex structures for DWT-based denoising and compression were constructed. An improved method of dynamic threshold calculation was designed to support these tasks. It offers better performance with much lower hardware complexity comparing to the commonly used *universal threshold* algorithm, based on the Median Absolute Deviation (MAD) operator. Fig. 4.8 demonstrates the performance of this algorithm on a section of the real data with a well pronounced spike.

In both cases, 10 % of nonzero DWT coefficients were preserved and while the denoising based on the modified threshold calculation algorithm results in nicely smoothed signal, the universal threshold selection causes unexpected artifacts highlighted by the dotted line.

A lossy compression algorithm was designed upon the denoising structures and a customized RLE encoder, providing compression ratios corresponding to the amount of nonzero DWT coefficient preserved. But as a result of the denoising process, the off-line spike sorter [6] was not able to recover as many overlapping spikes as before. This topic was not pursued any further.

Instead, the possibility of a shift-invariant DWT decomposition was analyzed in order to improve the spike detection capability of the standard DWT. The real-time denoising system based on these structures was confirmed to provide the same results as the common cycle-spinning approach



*Fig. 4.8: Real MEA recording trace containing a well pronounced spike denoised by means of the fourth order bior5.5 DWT and different threshold calculation methods.*

with much lower hardware complexity. For an arbitrary decomposition depth  $d$ , the number of filter blocks is reduced from  $d \cdot 2^d$  to  $2^d - 1$ .

### 4.3 LOSS-LESS COMPRESSION

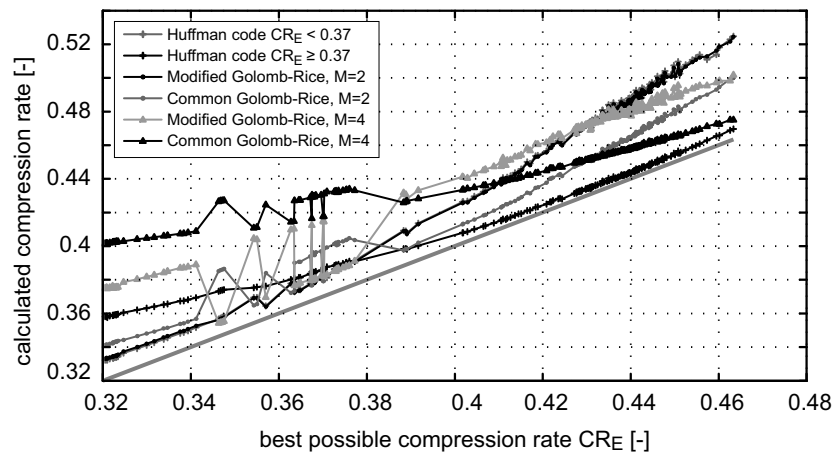
The reduction of redundant information within the individual channels and in the recordings as whole may prove to be the key for the loss-less compression of MEA recordings. Due to the programmable nature of the sensor array, no analytical algorithms can be implemented, based on based on the geometrical arrangement of the individual electrodes. Partial success was achieved with blind deconvolution based on the principal component analysis (PCA) but only for the price of a very high computational complexity. Instead the data properties within the individual channels were analyzed resulting in a simple predictor based on the signal last value. Shannon entropy was used as the measure of information content, suggesting the possibility of compression ratios from 1:2 down to 1:4 with this predictor applied.

The three major compression algorithm families were tested in order to evaluate their hardware complexity and achievable compression ratios. The RLE encoding, successfully applied to the DWT preprocessed data, is unusable in this case as there are almost no strings of constant value present in the data. Due to its higher hardware complexity, the dictionary based approach was tested only through a third-party implementation in form of an universal

file compressor ZIP, but the achieved results were more than 10% worse than suggested by the signal entropy.

Instead, the entropy coding schemes were further investigated resulting in a fast compressor based on the Huffman codes [18]. Based on the real data counting more than 400 files, the statistical properties of neuronal recordings were analyzed in order to define several statistical models covering all the available data. With an adaptive best-model selection algorithm added, the achieved compression ratios in most of the useful signal range were less than 1 % worse than the best achievable ones (calculated from the signal entropy).

Further hardware complexity reduction was pursued resulting in compression algorithm with analytically expressed conversion function, based on a modified Golomb-Rice [19] code. In both cases the original algorithms had to be modified in order to ensure deterministic timing of their hardware implementations. Fig. 4.9 shows the results achieved for all the individual compression algorithms (based on different statistical models). In the real application, the best-model selection chooses the optimal encoding scheme for the particular data resulting in ratios even closer to the best achievable one plotted in the thick grey line.



*Fig. 4.9: Compression ratios provided by the individual encoding schemes prior to the best-model selection.*

Encoders based on the Huffman codes offer in general better compression ratios especially for data with higher entropy. But due to the lower hardware complexity, the algorithm based on G-R codes was implemented in the final version of the acquisition system, in form depicted in Fig. 4.10.

Both algorithms were also implemented in form of software compression utilities in order to compare the achieved compression ratios and execution times with the general purpose file compressors. Even though these programs

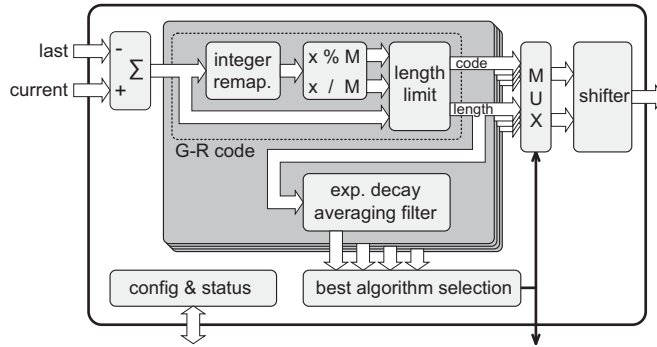


Fig. 4.10: Streamed data compression core based on the modified G-R algorithm.

were not optimized for best performance, the measured compression times were in general more than 10 times lower, while the compression ratios were comparable, if not better.

Fig. 4.11 shows the compression ratios achieved by the designed compression algorithm on recordings from different cell cultures, most of which were not available during the algorithm design phase. The best theoretically possible compression ratio, including the file structure overhead is plotted in dashed line. In order to make this test, more than 24 hours of recordings totaling more than 200 GB were processed, (the actual number of files is indicated in brackets). The designed algorithm provides good compression ratios even for data not available during its design. The suboptimal performance on cardiomyocytes is acceptable as the main goal of data rate reduction to less than 50 % is achieved, allowing the acquisition system to record from all connected MEA chips in parallel.

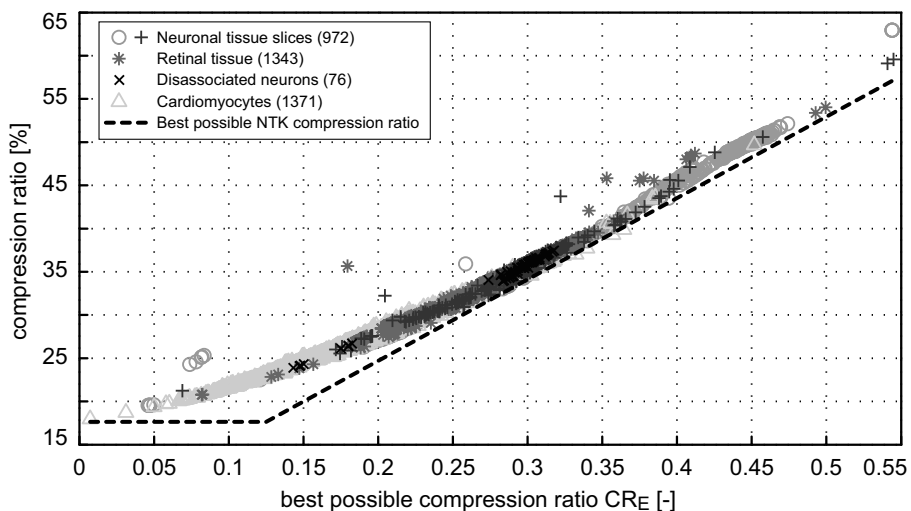
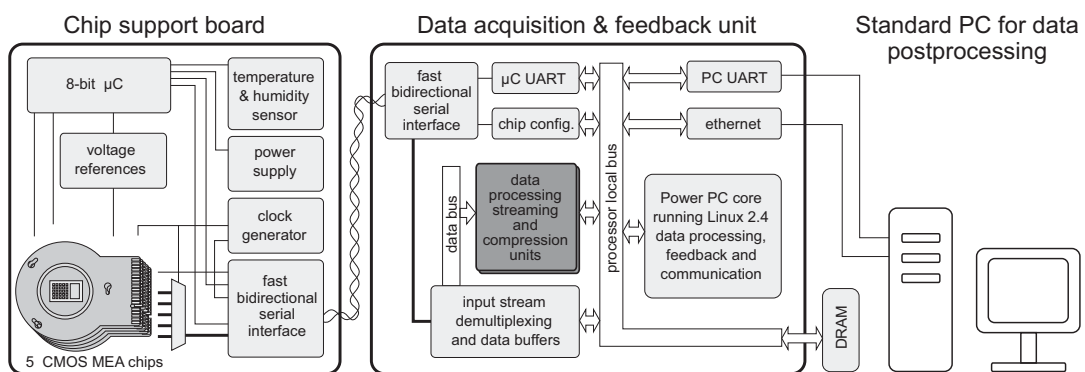


Fig. 4.11: Compression ratios achieved by the modified Golomb-Rice coder on almost 4000 recordings from five different cell cultures.



## 4.4 ACQUISITION SYSTEM

Fig. 4.12 shows a block diagram of the designed acquisition system. The system is composed of two interconnected hardware modules, the chip support board and the data acquisition and feedback unit. Together they allow five independent MEA chips to be connected at a time and simultaneously recorded from. The chip support board is fully custom made, including a solid metal case required for better protection against the bio-lab environment. The data acquisition unit is based on a third-party hardware, the Xilinx XUP evaluation board, with just a simple interfacing board attached to it, hosting the LVDS transceivers for communication with the chip support board and the GPIO level buffers and shifters for the experiment control.



*Fig. 4.12: The Neurolizer MEA acquisition system block diagram.*

The core of the acquisition system is a Virtex II Pro FPGA with hardwired PowerPC processor core. MEA signal processing framework was designed for this platform, providing several levels of hardware abstraction and all required support for bidirectional communication with living cells on the attached MEA chips. Besides the main infrastructure on both, the FPGA itself and the PowerPC core (linux kernel mode driver) a simple user application was implemented in order to provide the access to all system functionality.

The standard 100 Mb ethernet was chosen as the main communication interface in order to galvanically separate the system and simplify the user software design. A simple text-based user interface was implemented for the system and experiments control. Once the system is configured, the recorded data are transferred through a dedicated binary stream. Another binary stream is used to deliver the chip configuration commands. The measured data throughput is approximately 6.8 MB/s. The compression algorithm described in the previous section has to be included in order to simultaneously record from more than two chips (one chip generates 2.68 MB/s of raw data).

## 5 CONCLUSION

The main aim of this thesis was to design an acquisition and signal processing system capable of parallel processing of data recorded from microelectrode arrays. This goal was successfully accomplished and a modular system capable of simultaneous recording and processing of data from up to five active MEA chips (totaling 630 electrodes) was developed. While all the algorithms designed are optimized for signals recorded from the MEAs, several partial results and implemented tools are applicable generally to a broad variety of signal processing tasks.

An overview of the sub-tasks solved in order to achieve the main goal is given in the following list:

- **Source data analysis:**

Various properties of the source signal were investigated in order to evaluate the usability of blind source separation techniques such as independent component analysis. Propagation delay in order of 1 to 5 samples together with the high similarity in the spike shape among cells within the sample render these methods unusable for real-time data processing. Off-line methods may still benefit from these algorithms but only in form of preprocessing stages improving the performance of the standard spike sorting and classification algorithms [6].

- **Optimal algorithms selection:**

Based on the performed signal studies and unsatisfactory results of the complex blind separation algorithms, a deterministic approach was chosen in order to provide a general set of tools for neural data processing. Considering the successful application of the discrete wavelet transformation reported in literature, hardware-friendly DWT decomposition structures were investigated. As a result, an improved algorithm for the hardware DWT blocks construction was designed. A set of tools *liftDecomp* and *liftFilter* was implemented, supporting the construction of these structures and their real-time software emulation. Further study of the DWT suitability for the MEA data processing was performed with these tools, resulting in a shift-invariant DWT analysis, improved denoising algorithm and the DWT-based lossy compression.

Two loss-less compression algorithms were designed in order to deliver raw data from all the chips connected to the supervising PC. Consisting of carefully chosen predictor block followed by two different entropy coders, these algorithms provide compression ratios close to the best achievable ones calculated from the signal entropy as demonstrated in

Fig. 4.11. The expected hardware complexity of both algorithms is very low and their performance in form of software utility exceeds the standard data compressors more than 10 times in terms of speed while providing comparable or better compression ratios.

- **Data acquisition system design:**

In a close cooperation with the MEA chip author at the Physical Electronics Laboratory, ETH Zurich a modular acquisition system depicted in Fig. 4.12 was designed. Implemented as an open modular platform, new signal processing modules can be simply added, based on the templates provided.

- **Implementation of the selected algorithms:**

The designed real-time loss-less compression algorithm based on the modified Golomb-Rice codes was successfully included into the acquisition system, providing the means for simultaneous recording from all the connected chips.

The proposed DWT structures were not included in the actual design mainly due to the lack of time. But a full analysis of their hardware complexity was performed and several possible implementations suggested. With the tools provided, spike sorting algorithms based on the wavelet transformation may be defined and implemented as hardware modules.

- **Real measurements:**

The functionality of the designed system was tested during many experiments carried out at PEL and closely cooperating laboratories. The data acquired during these experiments helped to further investigate the source data properties and to improve the overall functionality of the system. Thanks to the data recorded over several years, the performance of the designed compression algorithm was confirmed even on recordings from cell cultures not available at the time of its design.

After the testing phase more than 10 systems were distributed to cooperating laboratories in Switzerland, Germany, USA and Japan, where they are still being used.

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For all publications listed bellow, the contributions of all authors are equal.

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## SUMMARY

This thesis deals with the analysis and design of algorithms suitable for the microelectrode array (MEA) data processing. MEA is a bio-sensor designed to record weak electrical signals generated by some types of living cells. The modern active MEAs, designed within past several years are manufactured mostly in a standard CMOS process and offer more than ten thousand electrodes with spatial resolution high enough to record the activity of a single cell on tens of electrodes.

The actual sensor used in the designed acquisition system is a high-density active MEA with more than 11 thousand metallic electrodes and 126 readout channels, designed at Physical Electronics Laboratory, ETH Zurich. The technical part of the acquisition system design was also realized at this laboratory during a one year internship.

Based on the existing algorithms and the preliminary analysis of the data recorded with the designed acquisition system, two main tasks were defined. Discrete wavelet transformation (DWT) was reported to be a useful tool for MEA recordings analysis, but its suitability for real-time hardware processing of hundreds of channels is questionable. The designed acquisition system allows simultaneous recording from 630 electrodes with sampling frequency of 20 kSa/s. Besides the DWT analysis, a hardware-friendly algorithm for MEA data loss-less compression was required, maximizing the system throughput and reducing the storage requirements for the recorded data.

In addition to the acquisition system itself, the most important achievements are the novel method of hardware-friendly DWT decomposition structures design and the neural signal properties analysis, resulting in a fast loss-less compression algorithm. DWT structures generated by the proposed algorithm allow a straightforward hardware implementation in both, recurrent and full-speed, pipelined forms. Compared to the structures reported in literature, the improved DWT blocks save up to 25 % of hardware resources.

The designed loss-less compression algorithm allows to compress the recorded data with ratios from 1:2 down to 1:4, better or comparable to ratios achieved by the common file packers. In software implementation, this algorithm offers considerably faster execution than the standard file packers, but the main advantage is its very low hardware complexity.

While all the algorithms were primarily designed for the MEA data processing, most of them (especially the tools for DWT decomposition) can be applied other type of signals as well.

## RESUMÉ

Práce se zabývá analýzou a vývojem metod pro zpracování signálů z tzv. micro-elektrodoých polí (MEA), senzorů určených pro měření elektrické aktivity živých buněk. Obzvláště aktivní MEA, vyráběné z velké části ve standardním CMOS, procesu prošla v posledních několika letech bouřlivým vývojem. Existují již pole s více než deseti tisíci elektrod a prostorovým rozlišením umožňujícím zaznamenat aktivitu jediné buňky na desítkách elektrod.

Právě pro tato aktivní pole byly určeny algoritmy vyvíjené v rámci práce a komplexní měřicí systém umožňující jejich praktické použití. Konkrétně se jedná o aktivní MEA s 11 tisíci elektrod a 126 nezávislými vyčítacími kanály vyvinutá v Physical Electronics Laboratory, ETH Zurich, ve Švýcarsku. V této laboratoři byla též, v rámci stáže, realizována technická část vývoje měřicího systému.

Na základě studia existujících řešení a předběžné analýzy signálů zaznamenaných zvoleným senzorem byly vybrány dva základní směry, kterými se práce dále zabývala. Byly prostudovány možnosti zpracování signálu z nervových buněk za pomoci diskrétní vlnkové transformace (DWT). Primárně byly posuzovány možnosti hardwarového výpočtu DWT rozkladu v reálném čase pro systém s velkým množstvím kanálů zpracovávaných naráz. V případě navrženého systému jde o data z 630 elektrod vzorkovaných s frekvencí 20 kSa/s. Zároveň bylo nutné implementovat algoritmus bezztrátové komprese signálů z MEA umožňující záznam z většího počtu senzorů naráz a podstatnou úsporu místa v případě ukládání záznamů pro off-line zpracování.

Mezi nejdůležitější dosažené výsledky patří, kromě realizovaného měřicího systému, hlavně návrh algoritmu pro automatický návrh struktur hardwarově optimálního DWT rozkladu a vyvinutí algoritmu pro bezztrátovou kompresi signálů z MEA v reálném čase. DWT filtry generované navrženým algoritmem dosahují úspory až 25 % systémových prostředků oproti stávajícím řešením a umožňují přímočarou realizaci v podobě rekurentních i plně paralelizovaných pipelined struktur.

Navržený bezztrátový kompresní algoritmus pak nabízí kompresní poměry v řádu 1:2 až 1:4, srovnatelné či lepší než nabízí běžné kompresní programy. V případě softwarové implementace je ale navržený algoritmus podstatně rychlejší. Jeho hlavní předností je pak minimální hardwarová náročnost.

Přesto že primární vývoj byl zaměřen na zpracování dat z MEA, velkou část dosažených výsledků a implementovaných nástrojů (obzvláště ze sekce DWT) lze použít i pro jiné typy signálů.