A One-Chip Solution for Automated Prediction of Atrial Fibrillation after Cardiac Surgery

Mario Schlosser
Institute for Microelectronic Circuits and Systems
University of Hannover
schlosser@ims.uni-hannover.de

Carsten Malonnek
Institute for Microelectronic Circuits and Systems
University of Hannover
malonnek@ims.uni-hannover.de

Erich Barke
Institute for Microelectronic Circuits and Systems
University of Hannover
barke@ims.uni-hannover.de

Max Pichlmaier
Hannover Medical School
pichlmaier@thg.mh-hannover.de

ABSTRACT

Atrial fibrillation following routine cardiac surgery is a major cause of post-operative patient morbidity. Reliable prediction of the imminent onset of atrial fibrillation can be achieved by monitoring and analyzing electrical signals from the patient's heart, thus allowing prophylactic treatment of those patients at risk. However, predicting atrial fibrillation manually remains a complicated and daunting task. We have therefore developed a chip which is capable of predicting the onset of atrial fibrillation automatically, based on the monitoring of the monophasic action potential recorded from the patient's heart. Our system operates fully autonomously and it is stable, resource-conserving and extensible.

Keywords

Atrial fibrillation, monophasic action potential, prediction algorithm, chip design

1. INTRODUCTION

Rhythm disturbances, mainly atrial fibrillation (AF) represent the major cause of patient morbidity and raise hospital cost following routine cardiac operations [1]. The incidence averages around 27% after coronary bypass surgery [2]. The physician needs to be able to identify those patients that will develop arrhythmias and to implement a specific prophylactic treatment to reduce morbidity and cost at the same time as avoiding side effects of drugs in those patients who do not need them. The chip that is presented in this paper addresses this challenge by providing clinical staff with an automated prediction of the onset of atrial fibrillation after cardiac surgery. Our chip performs an on-line analysis of the so-called monophasic action potential recorded from a patient's heart to estimate the probability of atrial fibrillation to develop within the following hours. The system operates in an entirely autonomous manner, not requiring initialization or manual intervention, while ensuring stability and reliability of its analysis results. Our chip implements an analysis algorithm that we designed based both on results from theoretical and empirical studies of atrial fibrillation and pathological changes in the propagation of electrical activity on the heart. The latter were obtained from the clinical study with an early recording device for monophasic action potentials [4]. Our chip design can be accommodated on a re-programmable logic circuit, an FPGA, saving costs and guaranteeing easy extensibility and upgradeability. As of now, there is no automatic AF prediction system with these characteristics available: The analysis of MAP signals yields deeper insights into the processes causing atrial fibrillation than the use of an electrocardiogram (ECG), and our one-chip solution integrates very well into standard monitoring procedures following cardiac surgery.

In Section 2, we provide an introduction to the medical background of our analysis algorithm. We examine the task the algorithm has to perform more closely in Section 3,. In Section 4, the algorithm's operations are discussed. Section 5 explains the chip design which performs on-line interpretation of MAP signals. Results and experiments are discussed in Section 6. We conclude in Section 7.

2. MEDICAL BACKGROUND

Atrial fibrillation following cardiac surgery has been shown to result from different forms of so-called re-entry mechanisms in the myocardium. The atrial myocardium is specifically susceptible to invoking these re-entry mechanisms following cardiac surgery, resulting in atrial fibrillation as a common incidence. Re-entry mechanisms severely affect the regular propagation of electrical activity within the myocardium: In the normal case, action potentials disseminate in a geometrically regular manner over the surface of the heart, conceivable as isotropic action potential wave fronts. They cause the myocardium to contract and relax in a steady-going rhythm.

However, upon entering a state of atrial fibrillation, the regu-

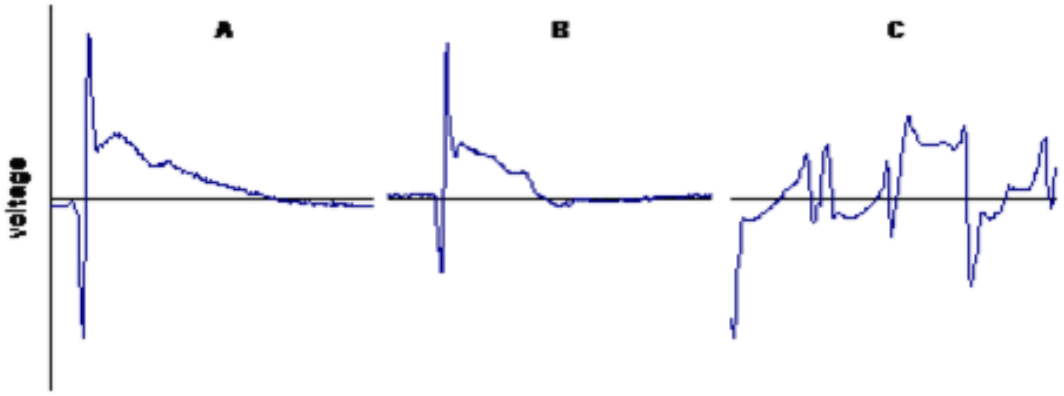

Figure 1: Post-operative, pre-AF and AF MAP events

lar propagation of action potentials within the myocardium is replaced by irregular and chaotic electrical propagation patterns. In this case, rotor-shaped patterns (also referred to as re-entrant wavelets) wander around on the atrium, re-entering recently depolarized and already repolarized heart cells (myocytes) frequently and thus preventing them from regular contraction and relaxation. Due to the coordinating function of the atria, the heart's ability to pump blood is seriously hampered and the patient suffers discomfort and a serious limitation of physical ability. The electrical alterations cumulating in the occurrence of postoperative atrial arrhythmias are reflected by gradual changes of the local electrical activity of the myocytes. In order to predict the onset of arrhythmias a more detailed instantaneous knowledge of the electrical activity of the myocytes other than the surface electrocardiogram (ECG) is thus required. We record the monophasic action potential (MAP) from the patient's heart surface: The MAP represents a summed signal of cellular action potentials from a comparatively small number of cells and closely mimics the ion currents across the cell membrane of a myocyte. Fractally coated electrodes with low impedance, no frequency-dependent damping, and a low polarisability allow to record the MAP reliably over a period of at least 14 days.

3. AUTOMATED PREDICTION OF AF

The time course of morphological changes of the MAP recorded from human epicardium may be used to predict the imminent onset of AF following cardiac surgery. The results obtained from a clinical study, are supported by theoretical results obtained from modeling and simulating the electrical stimuli propagation [3]. We shall consider three excerpts from an MAP recording to track down gradual changes that reflect the atrial myocardium's electrical activity deteriorate into a state of atrial fibrillation.

Post-operative MAP. The MAP signal can be decomposed into several so-called MAP events. An MAP event mimics the depolarization and repolarization cycle of a myocyte, i.e. a myocyte's reaction to electrical stimulus. The series of MAP events reflects a regular rhythm, ranging between 40 and 140 beats per minute (bpm). An MAP event is represented by an initial upstroke, a prominent plateau phase (typically, a plateau will resemble a round hilltop) and a repolarization phase, in which the signal returns to its baseline. Figure 1A shows a normal MAP event, recorded a few hours after the cardiac surgery.

Pre-AF MAP. Figure 1B depicts an MAP event, recorded 2.5 hours prior to the onset of atrial fibrillation. The morphology of the event has changed, MAP events are now of triangular shape: The plateau phase has diminished and the MAP signal almost immediately returns to the baseline after the initial onset.

MAP during AF. Figure 1C shows an MAP record during ongoing atrial fibrillation. MAP events are almost indistinguishable in the signal. AF is marked by a very high atrial rhythm, ranging between 250 and 600 bpm.

4. MAP ANALYSIS ALGORITHM

The algorithm that is presented in this section performs an automated analysis and interpretation of MAP signals. The algorithm's main objective is to predict an imminent onset of atrial fibrillation by considering information that is gathered from analyzing MAP signals from the patient's heart. The descriptions in Section 3 show that the electrical alterations which are associated with the formation of atrial fibrillation affect morphological and structural properties of the MAP signal over time. Automated prediction of AF therefore requires these properties be extracted from the signal and monitored constantly.

The algorithm consists of five main steps which are executed in an interleaved fashion. These steps shall be described in this section:

1. Signal preprocessing
2. Event segmentation
3. Event parameter extraction
4. Parameter interpretation
5. Verification and self-adjustment

4.1 Signal Preprocessing

To facilitate the algorithm's operations and to lay a common ground for parameter interpretation, the MAP signal will be preprocessed before it is fed into subsequent steps. During preprocessing, the signal is normalized and smoothed, its signal-to-noise ratio is computed, and the current heart rate is determined.

Signal normalization. The average amplitude of the MAP plateau is used to normalize the signal. Our interest focuses on the morphology of the MAP events, therefore no absolute voltage levels are examined. This value is obtained by applying a median filter to a 3.2 sec long signal excerpt, with a window size chosen such that only low-frequency plateaus prevail. A 3.2 sec long window is guaranteed to contain at least two MAP events, assuming a minimum heart rate of 40 bpm.

Signal-to-noise ratio. Straight lines are contiguously fit into a 3.2 sec long signal window by linear regression. The median value of the regression approximation errors is regarded as the current SNR.

Heart rate. The current heart rate is extracted from the signal by identifying maxima in the autocovariance function that is calculated in a 3.2 sec long window. The window is moved along the MAP signal in overlapping 1.6 sec long intervals, results are median-filtered to prevent errors.

Signal smoothing. Smoothing operations are applied to certain parts of the signal (see below).

4.2 Event Segmentation

As an MAP event (Section 4) closely resembles the electrical activity of a myocyte, its morphology can be expected to bear a strong indication on the state of stimuli propagation on the atrium. In a first step, the algorithm will identify MAP events and segment them from the MAP signal. Two approaches are used. Both results are used in parallel to verify the correctness of segmented MAP events.

Threshold-based segmentation. A point in the signal at which the first derivation of the signal is larger than the average plateau amplitude is considered as possible event upstroke.

Adaptive matched filter segmentation. A template of a typical MAP event is used to segment MAP events in the MAP signal by running signal and template through a matched filter. Starting from the last known and verified MAP event, the current event template is moved over the MAP signal. At each step, the convolution of MAP signal and time-inverse event template is computed. The matching quality at each template position n* is computed as

$$Q[n^*] = \frac{\sum_{m=0}^{templatewidth} x[n^* + m] \cdot t[m]}{\sum_{m=0}^{templatewidth} t[m]^2}$$

where x[n] denotes the MAP signal and t[m] the MAP event template. In each segmentation step, the most recent verified MAP event is adaptively used to detect the next MAP event in the signal.

4.3 Event Parameter Extraction

Each detected MAP event is analyzed to extract parameters that will be evaluated during interpretation, the last step in the algorithm. Figure 2 depicts the parameters that describe the morphology of an MAP event sufficiently. The parameters are listed and described in Table 1. Parameter CL is omitted in the figure, it represents the time difference between two consecutive MAP events.

Baseline, upstroke and MAP event end position. The algorithm detects baseline and upstroke of an MAP event by approximating the event with straight lines, employing linear regression. Starting at the initially detected event start position, the algorithm fits straight lines of iteratively increasing length into the MAP signal. Event upstroke, pre-event baseline and the offshoot of the previous MAP event are detected as approximation lines of a certain minimum length and a particular gradient. Baseline and upstroke amplitude are determined thereafter. The start position of the event analysis area is calculated by adding a constant blanking time to the position of the event upstroke to ignore noise which follows the swift electrical stimulus due to electrical processes in the MAP electrode.

Plateau detection. An MAP event plateau actually appears as a rounded hilltop in the MAP signal - this deformation is due to properties of the signal measurement. Plateau candidates are searched in the MAP event analysis area. Zero-crossings and zero dwellings of the signal's first derivation are considered as plateau candidates. Position, amplitude and curvature of each plateau candidate are extracted and calculated and mapped to quality values. The plateau candidate that yields the highest overall quality value is chosen as plateau. In case the quality values of all candidates are too low, or no candidates can be found at all, the algorithm decides that the event does not contain a plateau (which will be the case prior to AF).

Repolarisation analysis. The analysis detects the signal positions at which the MAP signal returns to (100-N)% of the plateau value. These parameters are referred to as MAPdN, they indicate an N% repolarisation of the monitored myocytes after the initial electrical stimulus. If the MAP event does not contain a plateau, the MAPdN positions are computed based on the maximum signal value in the event analysis area, which will most likely mark the beginning of the triangular phase in the event.

4.4 Interpretation

In its interpretation stage, the algorithm considers all previously extracted MAP event parameters. The parameters are combined into features whose evolution over time is correlated with the formation of atrial fibrillation. Two groups of features are formed, morphological features and rhythm features.

The morphological features compute to

$$nMAPGradient = MAPd75 - MAPd25$$

and

$$nMAPdN = \frac{MAPdN}{CL}$$

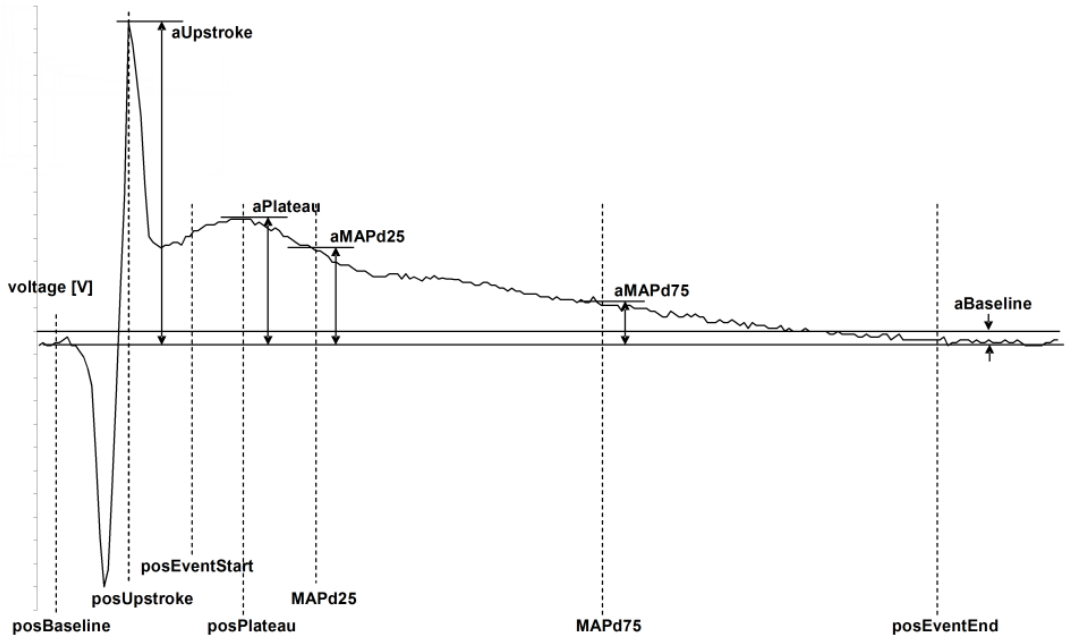

Figure 2: MAP event

The current values of nMAPdN and nMAPGradient are normalized by their initial values, obtained shortly after the cardiac surgery. A decreasing nMAPd75 and an increasing nMAPGradient reflect a possible formation of atrial fibrillation, a 20% decrease of nMAPd75 and a 20% increase of nMAPGradient can be seen as imminent threat. These feature changes describe the formation of a triangular phase in MAP events, an indication for upcoming atrial fibrillation (Section

The rhythm features are calculated as

$$\Delta MAPd75 = MAPd75_i - MAPd75_{i-1}$$

and

$$\Delta CL = CL_i - CL_{i-1}$$

Increasing values of ΔCL and $\Delta MAPd75$ yield increasing threat values. An increase of ΔCL above 75 ms and an increase of $\Delta MAPd75$ above 20 ms is regarded as imminent threat. Increasing rhythm features denote increasing stimuli irregularity, an indication for pathological changes in the stimuli propagation on the atrium. Threat values are computed and outputted independently for the morphological and rhythm features.

4.5 Validation and Self-adjustment

To work fully autonomously and without intervention by clinical or technical staff, the algorithm must feature high stability and reliability.

Specifically, this includes minimized vulnerability against measurement errors (e.g. signal noise) and against misinterpretations of the signal during analysis (e.g. choosing the wrong plateau candidate as plateau). and against wrong assumptions on signal parameters (e.g. outdated MAP template for event detection).

All these issues are efficiently addressed by validating and self-adjustment loops in the algorithm. Parameters guiding the matching process are always adapted to the current signal situation. Results are double-checked, e.g. the heart rate is validated by comparing it to the MAP event cycle lengths. Furthermore, the evolution over time of all extracted parameters is monitored to detect outliers, i.e. possible mistakes committed by the analysis. Parameter series are median-filtered and checked for physiological feasibility.

5. MAP INTERPRETATION ENGINE

We took the MAP analysis and interpretation algorithm to the next stage of its evolution by creating a chip design that implements the algorithm, dubbed MAP Interpretation Engine.

5.1 Features

The chip design accepts MAP signals in a digital form, analyzes them and generates a prediction on the likelihood of imminent onset of atrial fibrillation. The MAP Interpretation Engine is capable of performing all algorithmic steps as described in Section 4. Its main benefits include:

- On-line analysis: The digital design is able to execute an on-line analysis of MAP signals.
- Minimized equipment expense: An external computer or larger device is not required.
- FPGA technology: A modern field-programmable gate array accommodates our design, no static and expensive application-specific silicon is produced.

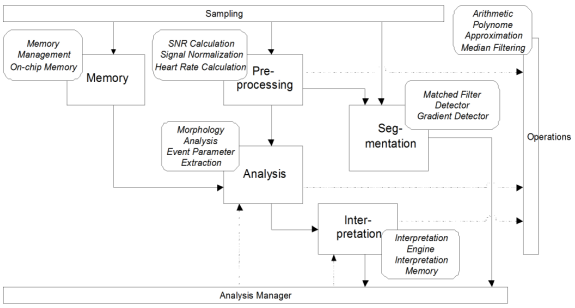

Figure 3: Block diagram for the MAP interpretation engine

- Modular and reprogrammable architecture: The design's functional block structure permits module-contended functional upgrades, greatly facilitating re-use and extensibility.

5.2 Architecture

The design's internal architecture, depicted in Figure 3, features rigid functional modularization. Module organization Figure 3 shows that all modules belong to 8 different categories:

1. Sampling: Sampling Manager module - receives and forwards signal samples from the logic design's signal interfaces
2. Preprocessing: SNR Calculation, Signal Normalization, Heart Rate Calculation modules - implement the algorithm's preprocessing steps
3. Segmentation: Matched Filter Detector, Gradient Detector modules - detect MAP events in signal
4. Analysis: Morphology Analysis, Event Parameter Extraction modules - analyze events
5. Interpretation: Interpretation Engine and Memory modules - interpret MAP parameters
6. Operations: Arithmetic, Polynome Approximation, Median Filtering modules - provide operations needed by other modules
7. Control: Analysis Manager module - imposes global scheduling on data and control flow
8. Memory: Memory and Management modules - buffer signal values and manage memory access

Solid lines indicate data flow, dotted lines denote control flow between modules.

Module management. The design's central Control module, termed Analysis Manager, serves as a central scheduling instance. It performs three basic tasks: Firstly, it manages the data and control flow between modules, e.g. the analysis of an event is always scheduled to take place after event segmentation. Secondly, it resolves resource contention: Modules in the category Operations are used in a shared fashion, i.e. their services are employed by several other modules. Thus, accesses to them have to be managed. The Memory modules maintain their own fair access allocation. Finally, the Analysis Manager handles external events such as resets and maintains global status information.

Parallel execution. Within the scheduling framework imposed by the Analysis Manager, the design is signal-driven: As a new signal sample is published by the Sampling modules, all modules in the design process it. This is largely happening concurrently; for example, the preprocessing modules constantly update their results, and the Segmentation modules check each sample for its likelihood to mark the start of a new MAP event. Samples are recorded with a sampling frequency of 500 Hz and a signal resolution of 8 bit, since the interesting information in the signal is located between 0 and 200 Hz in the spectrum.

Signal buffer. Several modules require the processing of more than one sample at a time. For example, the module Morphology Analysis calculates regression lines in the opposite time direction of the signal flow to detect an MAP event's baseline. The design always buffers 4K signal samples in an on-chip memory to capture around 3.5 MAP events at a time.

6. RESULTS AND EXPERIMENTS

Algorithm and chip design were tested with real data.

Algorithm. We used MAP recordings from an earlier clinical study to assess the quality and reliability of our algorithm. In this study, 22 patients were monitored for a period of up to 14 days. During the cumulative recording period of 170.1 days, 7 episodes of AF were observed. In 5 of 7 cases, the MAP event morphology changed as predicted (Section

Chip design. Our design comprises 50K of gate equivalents and 32Kbit on-chip RAM. In this form, it is able to process MAP signals from one patient. Our design can be compiled to different technologies, in particular it can be accommodated on an FPGA. The module netlists are simulated and verified. We are performing top-level simulations and an emulation of the design. Moreover, the MAP Interpretation Engine is additionally integrated into a deployable MAP prediction system. During cardiac surgery, MAP measurement electrodes will be attached to the atrium, in simple addition to standard heart wires that are stitched on the heart per default. An analog circuit that is under development amplifies and digitizes the MAP signal, the chip interprets them. In addition, it is able to maintain a wireless Bluetooth connection to a central workstation, even permitting wireless algorithm upgrades. The lightweight system itself can be easily carried on the patient.

7. CONCLUSION

We have described an algorithm and a chip design for automated prediction of atrial fibrillation based on the on-line analysis of the monophasic action potential following cardiac surgery. The device provides an accurate and reliable assessment of pathological action potential formation and propagation on the atrium, operates autonomously, integrates with standard post-operative monitoring procedures and requires low equipment overhead. It is currently advanced into

a full-fledged prediction system.

8. REFERENCES

[1] S.F., Shaw D.P., Adams D.H. et al. *Predictors of atrial fibrillation after coronary artery surgery.* Current trends and impact on hospital resources, Circulation 1996;94(3):390-397.

[2] Andrews T.C., Raimold S.C., Berlin J.A. et al. *Prevention of supraventricular arrhythmias after coronary artery bypass surgery.* Circulation 1991;84(III):236-244.

[3] Lang, V. *Entstehung und Stabilitaet von Rotoren in erregbaren Medien.* Dissertation, Zentralinstitut fÃijr Biomedizinische Technik, University of Erlangen, 1999.

[4] Pichlmaier, A. M. et al. *Prediction of the onset of atrial fibrillation after cardiac surgery using the monophasic action potential.* Heart 80.5 (1998): 467-72.