MEASUREMENT SYSTEM FOR THE ACQUISITION, VISUALIZATION, AND ANALYSIS OF THE CARDIAC ELECTRIC NEAR-FIELD

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Abstract: We present a measurement system for the highly resolving evaluation of the local cardiac electric near-field (CNF) from the surface of isolated autorhythmic animal hearts or electrically stimulated heart tissue preparations. Four electric potentials are measured very close to the surface of the specimen using a flexible sensor. By means of digital signal processing, the CNF is reconstructed and characteristic parameters of the cardiac excitation spread, namely direction and magnitude of conduction velocity, and vector-loops of the cardiac electric near-field strength are calculated in real-time and displayed online. The hardware and software concept based on a client-sever architecture permits analysis and monitoring in a beat-to-beat manner. We evaluate the system performance for the use of a single computer in stand-alone mode and a configuration with separate client and server computers. The given results demonstrate the outstanding performance of the presented measurement system, which makes it a powerful tool for the investigation of the cardiac electrical excitation spread at a microscopic size scale.

Introduction

The analysis of electrical excitation spread throughout the heart muscle at a microscopic size scale is expected to gain deeper insight into the factors of structure-caused arrhythmias. One approach to get this information of local conduction is to capture the gradient of epicardial potentials Φ at a given site by means of four recording electrodes in quadratic arrangement, spaced with less than $200\,\mu$m. Assuming conduction velocities of $0.7\,$m/s, latencies between the four signals are expected to be less than $300\,\mu$s. We have shown by computer simulations, that from these recordings of Φ, the surface gradient of Φ, namely the two dimensional representation of the cardiac electric near-field (CNF) oriented parallel to the tissue surface can be computed [1]. We developed suchlike sensors earlier [2, 3] and modified ones recently [4, 5]. During depolarization, the cardiac electric near-field strength $\mathbf{E}$ describes a vector-loop pointing opposite to the direction of excitation spread [4].

The purpose of the work was to develop and implement a concept of data acquisition and signal analysis, which allows the continuous recording of the signals as well as the beat-to-beat monitoring of the vector-loop of $\mathbf{E}$ and the values of local conduction velocity $\boldsymbol{\theta}$. The technological challenge arises from two facts. First, sampling rates have to be higher than 100 kHz to resolve the small latencies and to estimate $\boldsymbol{\theta}$ properly. Second, the signal window of 5 to 20 ms length around the depolarization phase has to be analyzed and displayed before the subsequent heartbeat occurs (heartbeat intervals range from 100 to 1000 ms). The following work describes the measurement system, and in particular the developed software application, which is capable of analyzing and monitoring the CNF in a beat-to-beat manner.

Materials and Methods

Measurement Chain: We use a flexible sensor of four electrodes with $50\,\mu$m spacing connected to a custom-designed amplifier system including analog 4^{th} order Bessel low-pass filters with a cut-off frequency of 20 kHz. The measured electrode voltages allow defining the four extracellular potentials $\Phi_1 \ldots \Phi_4$ with respect to a reference potential. The four signals are digitized simultaneously (NI PXI-6120, National Instruments, Texas) using a data logging system (PXI-1002, National Instruments, Texas) with sampling rates of up to 800 kHz per channel and a quantization with a resolution of 16 Bit.

Software Application: A major component of the described measurement system is the custom-designed software application, which controls the signal acquisition process and provides beat-to-beat analysis and visualization of the CNF, as well as safe data storage for subsequent off-line analysis. An additional software module allows the remote acquisition of images from the investigated preparation with a digital camera. The large amount of data arising from the high sampling rates make the online evaluation of the excitation spread computationally expensive. Beat-to-beat analysis requires the following tasks to be performed within one heartbeat cycle (100 to 1000 ms): A section of 5 to 20 ms length around the depolarization phase of $\Phi_1 \ldots \Phi_4$ has to be acquired. Then the desired excitation spread parameters have to be extracted by signal processing and the necessary diagrams

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and values for the on-line monitoring have to be visualized. For autorhythmic hearts from species with high heart rates like the mouse or for high frequency pacing of tissue preparations, this beat-to-beat analysis is an extremely time-critical task.

We have developed the software application in LabVIEW 7.1 [6], based on a client-server architecture, which separates and parallelizes the data acquisition task and the data display and analysis tasks (see Figure 1).

The server application performs the time-critical data acquisition and writes the acquired data into a FIFO buffer in the computer's internal memory. An in parallel running thread continuously reads out the content of this buffer and transmits it via TCP/IP to the client.

The client application including the graphical user interface launches and controls the server, and performs the data analysis. Signal data received from the server are written into a FIFO buffer. This buffer is read out by another thread for data processing and visualization.

Server and client exchange data via three communication channels, each of them using a separate TCP/IP port: The command channel to exchange commands and status information, the data channel to transmit acquired data from server to client, and the synchronization channel for handshaking purposes.

Due to the described architecture, client and server can be either run on a single computer or on two separate computers connected by Ethernet. Server and client applications themselves are designed to take advantage of the inherent parallelism of the LabVIEW programming language [6]. Apart from its effectiveness, the developed software application has an easy-to-use graphical interface with intelligent instrumentation [5].

Signal Processing: The on-line digital signal processing of the four acquired waveforms includes FIR lowpass filtering with selectable filter characteristics and calculation of parameters, which describe the cardiac excitation spread. A spatially discrete approximation of $\mathbf{E}$ is determined by the extracellular potentials $\Phi_1 \ldots \Phi_4$ and the distance *DD* between two diagonal electrodes.

$$\mathbf{E} \approx -\frac{1}{DD}\begin{bmatrix}\Phi_2 - \Phi_1 \\ \Phi_4 - \Phi_3\end{bmatrix} \tag{1}$$

The local conduction velocity $\boldsymbol{\theta}$ is calculated according to [1]. The local activation times $t_1 \ldots t_4$ of the tissue beneath the four electrode tips are obtained by temporally differentiating $\Phi_1 \ldots \Phi_4$ and determining the instant of the maximum negative peak in each of the derivatives. At the center of the electrode arrangement the gradient of t_A is computed using a finite difference approach.

$$\nabla t(x,y) = \begin{bmatrix}t_x \\ t_y\end{bmatrix} \approx \frac{1}{DD}\begin{bmatrix}t_2 - t_1 \\ t_4 - t_3\end{bmatrix} \tag{2}$$

Vector and magnitude of $\boldsymbol{\theta}$ are expressed as follows.

$$\boldsymbol{\theta} = \begin{bmatrix}\theta_x \\ \theta_y\end{bmatrix} = \frac{1}{t_x^2 + t_y^2}\begin{bmatrix}t_x \\ t_y\end{bmatrix}, \quad \theta = \sqrt{\theta_x^2 + \theta_y^2} \tag{3}$$

The direction of propagation is determined by inverting the angle of the peak magnitude of $\mathbf{E}$.

Monitoring: The signal window around the depolarization phase is obtained by triggered signal acquisition (analog hardware triggering) on any of the four input signals or an external source, with adjustable level, slope, and pretrigger or posttrigger time. A strip-chart-like display of the signals (untriggered acquisition) is available to get an overview of signal characteristics and to adjust the trigger. During an experiment the four electrode signals $\Phi_1 \ldots \Phi_4$, their temporal derivatives, and the calculated vector-loop of $\mathbf{E}$ are displayed in separate diagrams. The determined values for direction and velocity of the depolarization wave are plotted in a trend-chart, to observe their development from beat to beat.

Storage: Signal data can be recorded either continuously (streaming) to one file or by cyclic writing of a defined number of heartbeats each in a separate file. The signal files have defined data format and header part to allow further off-line analysis using the viewer functionality of the described software application or other appropriate data analysis software.

Image Acquisition: Furthermore, we have developed a software module for the remote control of a digital camera (Olympus C5060-WZ, Japan) via USB interface. It allows adjusting the camera settings like focal distance and exposure time and capturing images of the investigated tissue section with 5.1 Mpixel in super macro mode. Acquired images are immediately transferred to the computer, displayed on the screen, and stored in the structured experiment database on the hard disk.

Results

We have successfully used the described measurement system in several electrophysiological in-vitro experiments with either isolated autorhythmic hearts from mouse or guinea pig in a Langendorff perfusion system, or electrically stimulated heart tissue preparations. The on-line analysis and monitoring functionality as well as the facilities for signal recording have led to increased scientific outcome of each experiment and reduced demand for isolated entire hearts and tissue preparations.

Performance Limitations: The critical factors for the beat-to-beat analysis to succeed are the heartbeat or stimulation interval T_{stim} and the number of acquired samples (arising from the sampling rate f_S and the window length T_w to be processed). We have carried out the following performance tests using a PXI embedded controller (NI 8175, P3 866 kHz, 512 MB RAM) as standalone system as well as in combination with a client PC (Dell Inspiron 8200, P4m, 1.8 GHz, 256 MB RAM), and a function generator as signal source. We have investigated the lower limit for the stimulation period $T_{stim,min}$ above which the reliable beat-to-beat analysis can be guaranteed, for different sampling rates f_S and window sizes T_w (see Table 1). Table 2 shows the results for the maximum T_w at given stimulation periods of $T_{stim} = 250$ ms and

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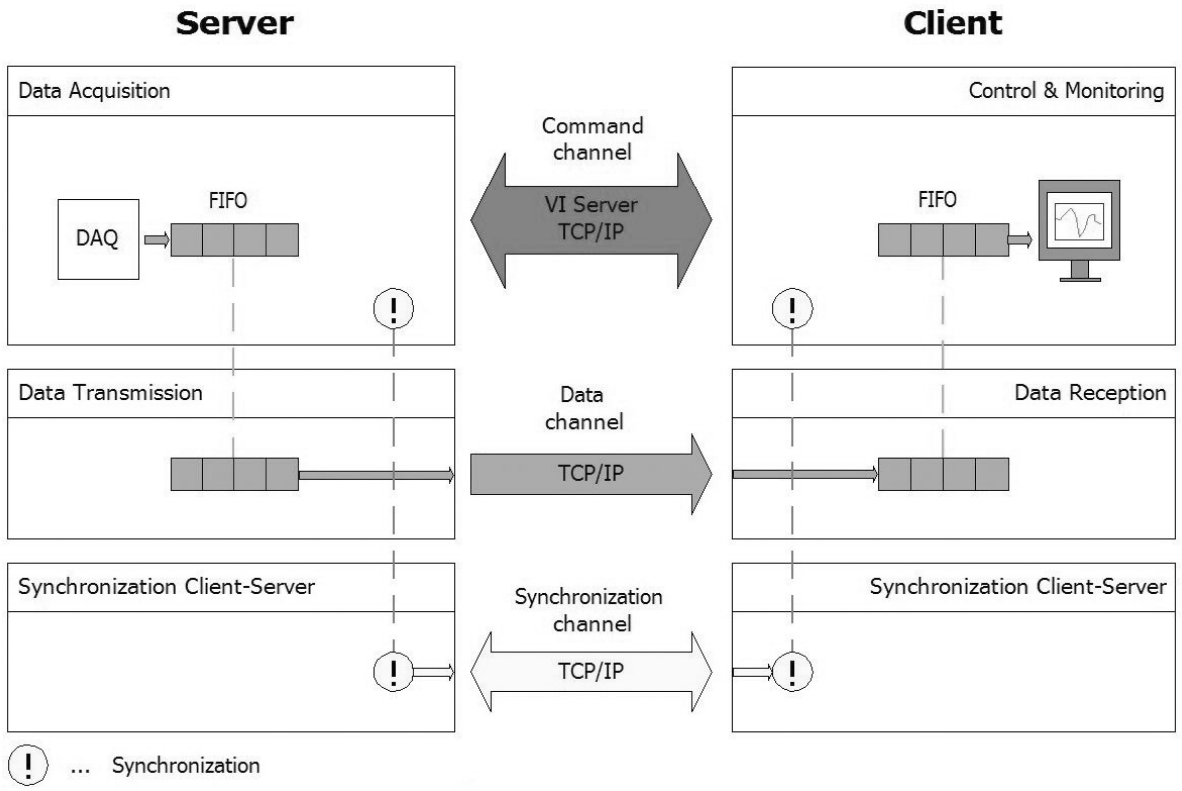

Figure 1: The basic architecture of the application: The server exchanges data with the client via three communication channels. The boxes within the client and server applications symbolize different program parts which are executed in parallel.

$T_{stim} = 100\,\text{ms}$ (corresponding to typical minimum heartbeat intervals of guinea pig and mouse, respectively). Beyond the denoted limits, the trigger may miss the subsequent heartbeat or one of the FIFO buffers may be filled faster than emptied.

Table 1: Results for $T_{stim,min}$ in *ms*, for given f_S and T_w.

	PXI		**PC/PXI**	
$T_w[ms]$	10	20	10	20
$f_S[kHz]$	$T_{stim,min}$	$T_{stim,min}$	$T_{stim,min}$	$T_{stim,min}$
10	28	36	18	26
100	58	98	40	48
200	94	150	75	115
800	230	600	230	400

Table 2: Results for $T_{w,max}$ in *ms*, for given f_S and T_{stim}.

	PXI		**PC/PXI**	
$T_{stim}[ms]$	250	100	250	100
$f_S[kHz]$	$T_{w,max}$	$T_{w,max}$	$T_{w,max}$	$T_{w,max}$
10	185	81	238	91
100	66	21	90	33
200	36	12	45	15
800	9	2	11	3

Discussion

Sampling Rate: The accuracy of the magnitude of conduction velocity θ, calculated with the above described algorithm is determined by f_S. Even for $f_S = 100\,\text{kHz}$, already unusually high for biosignal processing applications, the uncertainty of θ is in the range of 10% (assuming $\theta = 0.7\,\text{m/s}$, electrode distance $DD = 70\,\mu\text{m}$). This justifies a further increase of the sampling rate.

Interpretation of the Results: Tables 1 and 2 illustrate the high system performance. Accordingly, the reliable beat-to-beat analysis is possible for heartbeat intervals below 50 ms which corresponds to tachycardia of the mouse heart.

The results show only a moderate increase in performance when using a separate computer as client for signal processing and visualization. We have observed that for the PC/PXI combination, the bottleneck of the overall system is on one hand the embedded controller working as server and on the other hand the data transmission via TCP/IP. The use of a more powerful server computer may lead to a further increase in performance. A faster client computer may allow applying further on-line signal processing methods. Moreover, the results of the performance tests show that there is no global limit of acquired samples per heartbeat of stimulation interval.

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Conclusions

Due to the microscale electrode-array and the highly resolving data acquisition, the overall measurement system achieves highest resolution in time and in space for measuring the local CNF. The smart hardware and software concept of the developed application allows the beat-to-beat analysis and real-time visualization of important parameters during electrophysiological experiments. Even highly dynamic excitation scenarios like tachycardia of the mouse heart can be successfully evaluated. The continuous monitoring of slight trends in local conduction velocity and small beat-to-beat alterations of direction of the propagating cardiac impulse becomes possible with the presented system.

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