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COI-Wiz: An Interactive Computer Wizard for Analyzing Cardiac Optical Signals

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***Abstract*—A number of revolutionary techniques have been developed for cardiac electrophysiology research to better study the various arrhythmia mechanisms that can enhance ablating strategies for cardiac arrhythmias. Once the three-dimensional high resolution cardiac optical imaging data is acquired, it is time consuming to manually go through them and try to identify the patterns associated with various arrhythmia symptoms. In this paper, we present an interactive computer wizard that helps cardiac electrophysiology researchers to visualize and analyze the high resolution cardiac optical imaging data. The wizard provides a file interface that accommodates different file formats. A series of analysis algorithms output waveforms, activation and action potential maps after spatial and temporal filtering, velocity field and heterogeneity measure. The interactive GUI allows the researcher to identify the region of interest in both the spatial and temporal domain, thus enabling them to study different heart chamber at their choice.**

I. Introduction

EVERY year, in the United States alone, millions of people die suddenly of lethal arrhythmias (sudden cardiac death). A number of structural heart diseases such as ischemic disease and cardiomyopathy can cause such sudden cardiac death. Understanding how these diseases generate lethal arrhythmias is extremely important to develop new therapeutic strategies to treat the patients. To this end, many scientists and physicians have made enormous efforts to develop methods to elucidate the arrhythmia mechanisms in various disease models using animals, tissues, and cell lines [1].

To investigate the underlying mechanisms of arrhythmias, the measurement of electrical activities, action potentials (APs), of the heart is essential. In the traditional methods, APs were measured using glass capillary electrodes such as floating electrode. The combination of the floating electrode method and the coronary arterially perfused wedge preparation using animal hearts has made significant contributions to the better understanding of the correlations of APs and electrocardiogram (ECG) [2]. However, the limited numbers of simultaneous recordings due to the technical difficulties of handling multiple glass electrodes limits the spatial resolution of the AP signals and hampers the understanding of spatial heterogeneity of AP signals that has long been speculated to be able to represent and model different arrhythmia mechanisms. Within the last decade, optical mapping using voltage-sensitive fluorescent dye, optical mapping method, has been established to overcome the difficulty of the electrode based AP recordings [3]. Developing the automatic analysis greatly improves the efficiency of the researchers who use the optical mapping methods in their research. We provide the software from our website at isgrin.tech.uh.edu under Cardiac Optical Imaging section.

In section II, we present the optical mapping system including the data acquisition and components of the computer wizard. In section III, we detail the implementation of each analytic tool available in the wizard and show how users can interactively configure each tool. Section IV gives an example of how cardiac electrophysiology researcher used the wizard to help their research. Finally, in Section V we conclude and point to future direction.

II. Framework of COI-Wiz

Our cardiac optical imaging system has four major components besides cables, power supply, and pacing instruments: perfusion system, light source, CCD (charge-coupled device) camera system, and computer system that have both the data acquisition software and COI-Wiz installed. Fig. 1 shows the setup with one high-speed monochrome CCD camera (TM-6740CL 1/3" Progressive Scan Monochrome CCD Camera from JAI Inc.[4]) and two LED light sources that provide balanced illumination of the heart surface. As shown in Fig.1, the epicardial surface of the rat heart stained with Di-4-ANEPPS and excited at ~532 nm. Fluorescence images were acquired using a high speed CCD camera to produce frames with a spatial resolution of 120x160 at a temporal resolution of 710 frames/s. The set of imaging data we use has up to 1500 frames. On the computer system connected to the hardware runs the data acquisition system based on Labview from National Instrument© and the COI-Wiz for data analysis implemented in Matlab.

Note that we decouple the data analysis from the data acquisition system to take advantage of the existing expertise of the imaging and video analysis within the group [6-8] and enable more flexibility to analyze cardiac optical imaging data from other data acquisition systems by adding file interfacing module to the COI-Wiz. The focus of the paper is the detailed implementation of the various video analytic algorithms in COI-Wiz.

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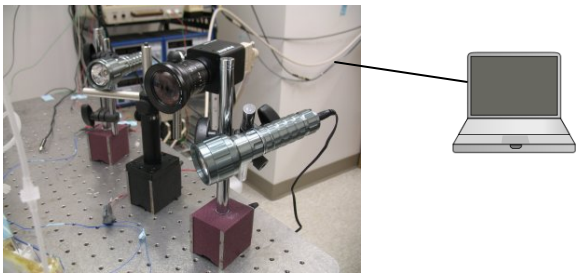


Fig. 1. Hardware setup of cardiac optical imaging system

Fig. 2 shows the flow chart of the COI-Wiz. After the cardiac optical imaging dataset is loaded into the wizard, a file conversion module automatically read the file into the right format based on image resolution selected by the user. Then the cardiac imaging video is displayed with the slide bar showing the video progress and assists the selection of specific frames. The visualization of the difference and the ratio images is a good tool for researchers to identify whether or not the data is usable. The interactive cursors within the waveform analysis tools enable the researchers study AP in detail at the selected spatial position. Before features such as the action potential activation map, duration map, and the velocity field map can be extracted, region-of-interest (ROI) could be selected using mouse. This will make the data analysis algorithms in the following steps computationally efficient. After data analysis, besides displaying the extracted activation map, APD map, and velocity field map, they can be output either in Matlab format, or in excel format for analysis later on.

III. Video Analytic Algorithms

Fig. 3 shows the snapshots from COI-Wiz when it is processing a normal porcine heart cardiac optical imaging data. In this section, we detailed each algorithm that is available in the COI-Wiz.

A. Waveform Visualization and Analysis

As shown in Fig. 3 (orange circle), user can select a reference point and another point to study the difference of action potential signals between two positions. The two action potential waveforms are visualized without any filtering on the right enclosed in a blue circle. The pink waveform shows the AP signal of the reference position, which can be reset. The blue waveform is the AP signal of the position the other cursor selected. The user also can enlarge the selected segment of AP signal from the total frames to be displayed, i.e., the zoom in and out function.

Toward the left bottom are the spatial and temporal filters users can choose to reduce the noise level of the signal. A filtered signal corresponds to the blue AP waveform. User can also choose to show the start time, activation time, peak time, and time for different APD configuration to identify the analysis output desired.

The quality of optical recording depends on the preparation of the heart, the dye, the lighting setup, the location and the positioning of the heart. Sometimes the raw AP signal is so noisy that it is not suitable to study by researchers or extract useful features for automated analysis. We applied spatial and temporal filtering analysis that combines moving average in temporal domain and medium filter in the spatial domain to improve the signal to noise ratio of the AP signal. The result shows significant improvement of the signal to noise ratio (right bottom of Fig. 3). The ***median filter*** considers each pixel in the image in turn and looks at its nearby neighbors to decide whether or not it is representative of its surroundings. Instead of simply replacing the pixel value with the *mean* of neighboring pixel values, it replaces it with the *median* of those values.

B. Waveform Visualization and Analysis

It is important to extract APD information by automating the procedures of region-of-interest identification (ROI), image registration (for reducing the motion artifacts), and spatial-temporal analysis (for characterizing spatial heterogeneity of APD). There are a few important measures used to characterize different arrhythmia mechanisms such as APD restitution, APD accommodations, and various slopes of the time constants. It is quite difficult and time consuming to extract information from hundreds and thousands of cardiac optical mapping positions manually. For example, with moderate spatial resolution of 120x160, there are about 19,200 sites; each has its own activation time within one

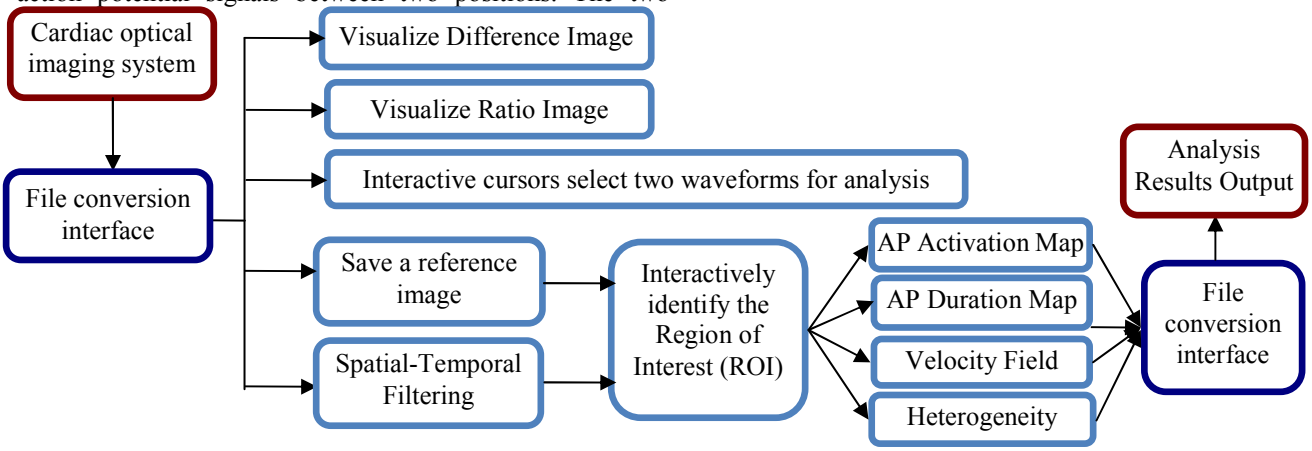


Fig. 2. Flow Chart of the COI-Wiz

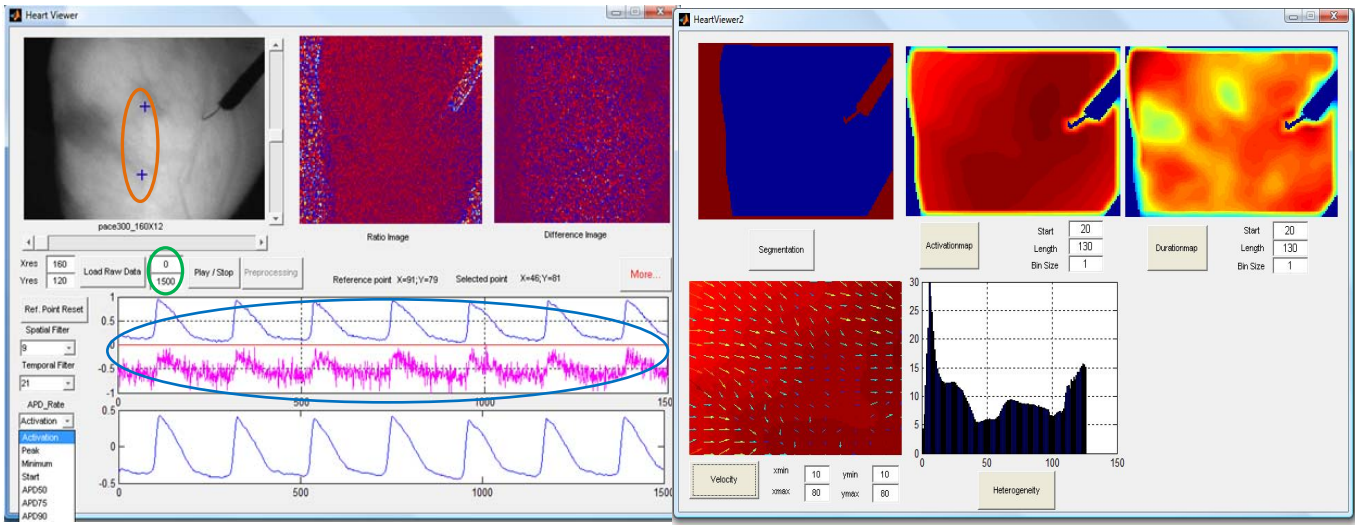


Fig. 3. COI-Wiz is analyzing a normal porcine optical imaging data

cycle.

The activation time is calculated based on the maximum first derivative of the AP signal upstroke, max (dF/dt). We also calculate the real activation time based on Eq. 1.

$$T_{act} = 2 * t(\max(dF/dt)) - t(dF/dt = 0) \quad (1)$$

The peak time can be identified as the time when the first derivative reaches 0 again. Fig. 4 shows the demonstrative AP signal with activation time (T_{act}) and AP duration marked.

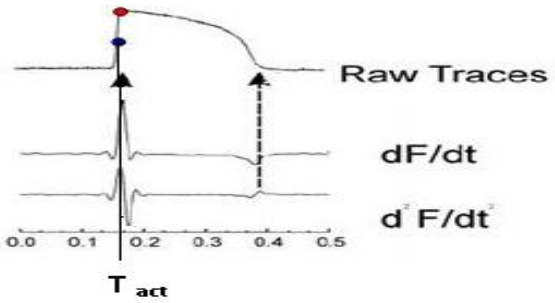


Fig. 4.The definition of activation time and AP duration

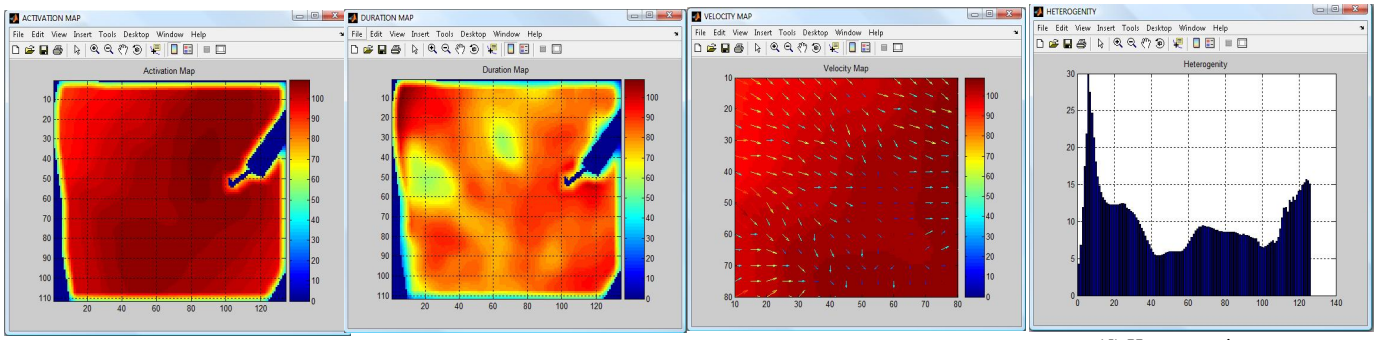
The action potential duration time is calculated by finding the difference between the time with maximum first order deviation ($t(\max \partial F/\partial t)$) and the time when the maximum second order derivative reached ($t(\max \partial^2 F/\partial t^2)$), which equivalent to 97% recovery of the AP back to baseline and coincides with the refractory period of the AP. As shown in Fig. 3, we calculated the APD_{50}, APD_{75}, and APD_{90}, the number represents the percentage of the recovery. For example, APD_{75} represents 75% recovery of the AP back to baseline. Assuming the percentage of the recovery is denoted as α%, the APD_{α} can be calculated based on Eq. 2.

$$APD_{\alpha} = t(F(t(\partial F/\partial t = 0)) * \alpha\%) - T_{Act} \quad (2)$$

Since the activation time and duration time directly associate with a specific polarize-depolarize cycle, the COI-Wiz provides the choice of a window size defined by starting frame number and duration so that user can specify and study the specific cycle.

C. Activation and AP Duration Map Extraction

Once the activation time and AP duration are calculated for each pixel within the Region of Interest (ROI), it is straightforward to generate the isochronal maps with color scale to represent them. These maps are critical in studying the spatial dispersion of restitution kinetics that may indicate intrinsic membrane ionic currents behavior of the heart cells. Fig. 5 (a) and (b) show example of the activation map and APD map for the normal porcine heart cardiac optical imaging data. Note that the maps only contain the identified region of interest which is enlarged back to the original size, i.e., 120x160, for visualization purpose.



(a) Activation Map **(b)** AP Duration Map **(c)** Conduction Velocity Field **(d)** Heterogeneity

Fig. 5. The isochronal maps generated for the normal porcine heart cardiac optical imaging data

D. Conduction Velocity Field Analysis

Conduction velocity vector field describes the local speed and direction of cardiac activity propagation. The magnitude and direction of conduction velocity are especially important during complex arrhythmias, but also difficult to measure. The direction of propagation can be used to describe the path of electrical activity on the epicardium. Isochronal maps (spatial contours of activation time) are popular to show the position of individual wave fronts.

In theory, one can simply measure the location of an activation front at different times, and divide the distance traveled by time interval. In order to describe propagation velocity during complex arrhythmias, a method to estimate the velocity of multiple wave-fronts at different locations and times was developed [9-10] and implemented here. The core of the algorithm is fitting a polynomial function T(x, y) to a set of "active" points in 3-dimension (x, y, z) space, in which z-axis represents the activation time. Fig. 5(c) shows the local conduction velocity field map generated for the normal porcine heart imaging data.

E. Heterogeneity Analysis

Recent theoretical studies have shown that certain dynamic factors are operating synergistically with preexisting tissue heterogeneity to promote wave break [11-12]. The restitution kinetics of action potential duration (APD) is most important among the dynamic factors. Therefore, once APD map is generated, next step is to measure the heterogeneity within the map and between maps. To measure heterogeneity within the map, we use standard deviation to measure dispersion or variability of each column. A low standard deviation in our histogram Fig. 5 (d) shows that the data points tend to be very close to the same value for a normal heart, whereas high standard deviation indicates that the data are "disperse" over a large range of values.

IV. Conclusion

In this paper, we present a computer based cardiac optical imaging analysis tool set, COI-Wiz, that provides the automatic analysis as well as interactive selection for cardiac electrophysiology researchers. The whole framework is open and flexible to have other functions incorporated later and can handle different cardiac imaging datasets by adding new file conversion module in the file conversion interface. The spatial and temporal noise levels are reduced using either default filter configurations or user specified configurations. Tools that extract the most popular analysis matrices such as the activation time map, restitution time map, action potential duration map, and the velocity field map are developed and validated in the advanced cardiac electrophysiology research lab located in the Texas Heart Institute.

A recent abstract about "vasoactive intestinal polypeptide increased action potential spatiotemporal heterogeneity and vulnerability to atrial fibrillation" was accepted by the Heart Rhythm Meeting based on results provided by COI-Wiz. In the future, we plan to extend the COI-Wiz to dual-camera system; add functions to help extract and define the heterogeneity of the APD map; and image registration to handle motion artifacts.

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