Spatiotemporal Analysis of Cardiac Electrical Activity

Robert S. MacLeod Quan Ni Richard O. Kuenzler
Bruno Taccardi and Robert L. Lux
NEH Cardiovascular Research and Training Institute
University of Utah, Salt Lake City, Utah

Dana H. Brooks
Center for Communications and Digital Signal Processing
Northeastern University, Boston, MA

Abstract

Electric measurements from the heart are a valuable source of information in both normal and pathological electrophysiology. They also present special signal processing challenges to the researcher or clinician intent on extracting this information. For example, spatial sampling is often limited and almost always irregularly organized. Sources of cardiac signals are time varying, distributed within a complex, anisotropic excitable medium. The goal of cardiac signal analysis is to describe spatial and temporal features of activation and relaxation of the heart tissue; both spatial and temporal views have importance and in many cases merging of the two is necessary to reveal the relevant information.

In this presentation, we cover some of the techniques that electrophysiologists have developed to analyze and interpret cardiac electric potentials. Specific examples include interpolation and statistical estimation, time and space based methods for locating the cardiac wavefront, and the use of explicit solutions of boundary value problems to predict cardiac sources from ECG measurements. We will also outline some of the challenges remaining in cardiac signal processing.

1. Introduction

Electrocardiographic mapping consists of a family of measurement techniques in which multiple electrodes are used to sample electric potentials from the heart or the thorax. The history of this approach is perhaps 35 years old and its progress closely parallels that of digital electronics and computers. When combined with scientific visualization, a geometric model of the measurement sites, and signal processing techniques such as filtering, interpolation, feature extraction, and decomposition, mapping becomes an imaging modality that reveals the spatiotemporal distribution of bioelectric potential in, on, or around the heart.

It is this ability to capture both the temporal and the spatial features of the bioelectric fields originating in the heart that characterizes mapping and also suggests its value. The heart is an irregularly shaped piece of muscle consisting of a variety of cell types connected in a complex, three-dimensional arrangement of fibers. Contraction of the heart is driven by a wave of local electrical activity that moves in a systematic sequence through the tissue, generating time-varying extracardiac currents as it moves. Descriptions based on simple source models are very limited in their ability to encompass this spatial and temporal complexity, just as measurements based only a small number of signals, as in the standard electrocardiogram (ECG), are incapable of acquiring the necessary information. Electrocardiographic mapping offers a much richer image by measuring with higher spatial sampling density.

The extraction of useful information from this ensemble of spatially organized signals, however, presents interesting challenges, many of which lie in the field of signal processing. In this paper we will discuss some of these challenges, what makes them different from those that arise in most other multichannel measurement situations, and a few of the clinical and experimental applications in which signal processing plays a significant role. More extensive reviews of mapping and signal processing can be found in, for example, [3] and [13].

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2. Measurement and Applications

2.1. Mapping Techniques

Cardiac mapping usually refers to measurements of electric potential from the heart[7], while *body surface potential mapping* (BSPM) is the term reserved for recording from the surface of the chest. While a standard ECG consists of measurements from 3–10 electrodes—which are subtracted to generate 3–12 potential differences or *leads*—BSPM requires 32–200 electrodes referenced to a common potential[10].

In clinical cardiology, the cost and additional time required to acquire the signals in BSPM have so far limited its use largely to research applications. Cardiac mapping, on the other hand, has a rich history of clinical use, initially applied during open-chest surgery to the outer surface (epicardium) of the heart by means of an array of electrodes sewn into a flexible nylon sock[7]. With the development of narrow, flexible electrode catheters, cardiac mapping has shifted from the outer to the inner surfaces (endocardium) of the heart chambers and from invasive surgery to percutaneous application. The most recent generations of catheters even allow the recording of signals from veins that lie on the epicardium and—by means of multielectrode "basket" catheters—from the endocardial surfaces of the heart. The major application area of cardiac mapping is in the detection of irregular heart rhythms (arrhythmias) and their interruption by means of radio frequency ablation of abnormal tissue.

Experimental cardiac mapping has an extremely diverse range of applications, including heart surface measurements but also recordings from electrodes embedded in needles that traverse the walls of the heart. Numbers of signal channels vary from tens to thousands of individual leads recorded using acquisitions systems capable of up to 2000 simultaneous channels at sampling rates of 500–2000 samples/s. The goals of such experiments include not only the development of clinical techniques, but also fundamental research into the electrophysiology of normal and abnormal hearts under a variety of interventions.

2.2. Application Examples

To illustrate the use of signal processing techniques in electrocardiographic mapping, we introduce a few specific applications, which will also form the basis of further discussion below.

Potential mapping: The spatial distribution of electric potential and its evolution over time are valuable markers of the underlying electrophysiologic events in the heart. Potential polarity can indicate the coarse orientation of the bioelectric source and the transition from positive to negative potential is a reflection of a wave of activation (depolarization of the cardiac cells) passing near the recording electrode. The potential amplitude indicates proximity to the source, but also reflects the influence of source configuration and the shape and conductivity of the conducting volume between source and electrode. As an example of potential changes characterizing physiology, in the case of reduced blood supply, the affected cells exhibit a slightly positive shift in the cellular potential at rest but then a negative shift in the amplitude during the subsequent action potential. These shifts results in dynamic, regional imbalances of potential within the heart, which then produce elevations and depressions of potentials recorded from heart and body surfaces that vary with time and electrode location. Proper interpretation of these potential deviations can identify the site and to some extent the degree of "ischemia" that results from such compromised blood flow and help diagnose patients with angina or a heart attack.

Activation/recovery mapping: *Activation*, the transition from resting to excited states, spreads like a propagating wave within the heart as depolarized cells excite neighboring cells, which excite their neighbors, and so on. Detecting the path of activation—activation mapping—is a frequent goal in cardiac electrophysiology. While the sequence is normally fairly consistent from beat to beat and to a lesser extent from heart to heart, variations in this sequence arise, often as a result of disease. Ideally, one would like to know the path of activation throughout the heart volume and then be able to capture and describe abnormal situations in which, for example, activation originates not in the atria, but from the ventricles themselves (ventricular ectopic activation). Another goal is to detect reentry conditions, *i.e.*,, in which instead of passing once through the heart during each beat, activation traces self-initiating recurrent loops at a frequency much faster than that of the healthy heart, leading to reduced pumping efficiency. *Recovery* is the complement of activation and marks the much less coordinated return of the heart tissue to rest. Abnormalities in recovery are thought to precipitate the leading acute cause of death in the West, the complete disruption of regular cardiac rhythm, known as fibrillation, and the resulting sudden cardiac death.

Inverse problems: Clinical cardiologists use the ECG to infer information about the state of the heart, a task that can be formulated as an electrocardiographic inverse problem. There are actually other formulations of electrocardiographic inverse problems, for example, one might wish to predict the potential distribution on the endocardial surfaces of the heart from potentials measured within the blood-filled volume of the heart chambers, based on the shape of the heart and the location of the measurement sites. The great utility of inverse solutions lies in the fact that they extract information about the heart from largely non-invasive measurements, hence they are of immense interest in clinical cardiology.

3. Biophysical Assumptions

There are a number of biophysical features of cardiac electrical activity, some of which are familiar from other domains, but there are also others that make the application of signal processing techniques more challenging than might be immediately apparent. Familiar features include the presence of reasonably localized sources that generate electrostatic currents in a volume conductor, resulting in measurable electric fields. Furthermore, one can formulate the time sequence of these sources as a moving wave that propagates in a volume and there exist candidate parametric models for the propagation of activation. As with other applications, one of the goals is to characterize and parameterize this source in time and space based on measurements from an array of sensors.

Associated with these familiar features, however, are a number of restrictions that contradict the assumptions of many standard signal processing approaches. These restrictions include:

- measurements from regularly spaced sites are seldom possible;
- the shapes of both the source region and the volume conductor are often complicated;
- the source region and volume conductor are often inhomogeneous, attenuating, even anisotropic;
- the sources are poorly represented as points, instead they have complex shape and may have multiple, simultaneous components;
- the sources produce highly nonlinear potentials;
- the resulting wavefronts are therefore neither planar nor stationary, but instead have complex curvature and can merge or annihilate each other and diverge into multiple wavelets;
- propagation velocity is constant only over small regions;
- measurement sites often lie close to the wavefronts so that simplifying far-field assumptions are problematic.

4. Signal Processing Approaches

In the face of the restrictive conditions imposed by the biophysics of electrocardiographic mapping, investigators have taken two different paths to extracting useful information with signal processing. The first is either to assume some simplifying conditions or to use only data acquired under simplified conditions and then apply general methods. The main advantage of this approach is that it allows the use of well developed and understood methods. The important disadvantage, however, is that the method is not suited to the data, or, at best, is appropriate only to a small subset of data, and thus lacks general utility. This limitation is especially problematic when the errors resulting from unfulfilled assumptions are not known, or there is no obvious way to tell how well data are suited to the method. Another weakness of applying general methods is that there is often ambiguity about the meaning of the extracted parameters and their link to physiology.

Examples of the application of general methods to electrocardiography include the Fourier decomposition of either temporal or spatial content of map data. While changes in frequency content may correlate with disease state, the lack of direct link between spectral profile and electrophysiological mechanisms reduce the specificity of discrimination. Simulation studies have attempted to establish such links, but results to date indicate that the connections are often multifaceted, complex and ambiguous[8]. Another approach that takes into account a simplified (planar wave) model of the spread of activation is the Zero-Delay Wavenumber Spectrum (ZDWS) method[17], which has been applied to differentiate normal from ischemic tissue using epicardial mapping data[19]. Decomposition techniques based on the Karhunen-Loeve[11] and wavelet methods[4] have also been used successfully as means of discrimination and signal parameterization, but without establishing clear links to physiology.

The second path for analyzing mapping signals is to develop specific methods that are explicitly suited to the prevailing conditions. Many of these methods tend to be *ad hoc* rather than firmly grounded in theory but their use is often widespread. One example are the methods used in activation mapping to detect the passing of a wavefront near an electrode. When recorded by unipolar leads (*i.e.*, relative to a remote, common potential), the time of maximum negative slope of the electrogram indicates the instant at which the wavefront passes close to the electrode. This observation has been well supported by both experimental and theoretical studies[15], but there are many practical problems with identifying the correct instant of maximum negative deflection, especially under conditions of disease[2]. One attempt at a solution has been to use bipolar leads measured from two closely spaced electrodes for activation detection. Although widely used, the theoretical underpinnings for this method are sparse and even the practical implementation is disputed[15].

Interpolation in mapping also has many examples of specific, *ad hoc* approaches that have shown practical merit. Bi- or tri-linear methods have long been considered the least biased of interpolation methods but have significant weaknesses, especially when applied to signals from the heart. We have recently introduced a new approach based on features of activation that has shown greatly improved performance, especially in regions of high spatial gradient[16]. This "wave equation based" (WEB) approach accommodates the highly nonlinear distribution of potential in the heart by resolving a single interpolation of potential into a sequence of two interpolations of variables that vary more smoothly. The method consists of interpolating the activation times from nearby electrograms, then time aligning those electrograms according to the interpolated activation time, and finally interpolating the time aligned signals. Figure 1 illustrates a performance comparison of linear and WEB interpolation from epicardial maps.

Another signal processing approach in mapping is to use statistical estimation techniques based on previously recorded maps. We have developed electrocardiographic leadset selection strategies[12] and more recently a means of estimating cardiac activation time maps from very limited leadsets[14] based on this approach. Measuring activation time from cardiac signals has great clinical significance in characterizing arrhythmias, yet requires open-chest surgery for recording from the epicardial surface. An alternative route is to insert multielectrode catheters into the coronary veins that run along the epicardium and record potentials from these locations. The signal processing challenge is to determine a complete map from this relatively small set of measurements. We have used a database of experimentally obtained epicardial activation maps from animal hearts to generate a linear estimator between subsets of electrodes that lie along coronary veins and the entire epicardial map. In one

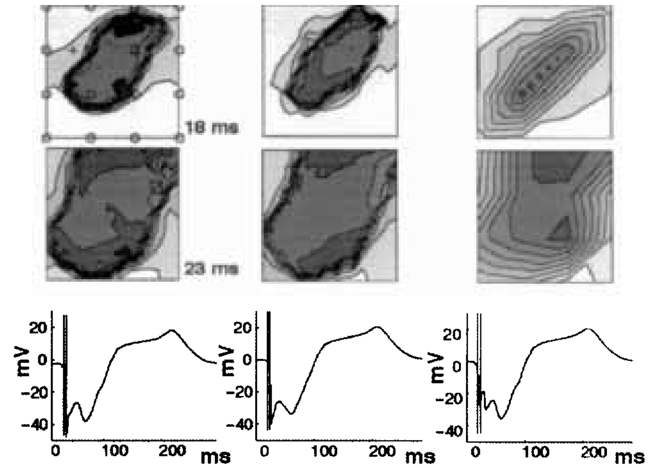

Figure 1. A comparison of standard linear and wave equation based interpolation for two time instants. Contour spacing is 6.7 mV and the vertical line in the time signals indicate the time instants of the maps above.

set of experiments, we reconstructed epicardial activation time maps originally recorded with 490-electrode arrays using only 21 electrodes arranged in five strands corresponding to the major coronary veins. We computed an estimator based on a training set of 122 maps from five separate experiments, then applied it to 31 different maps from a separate experiment. The resulting mean correlations between estimated and measured maps were 0.90 ± 0.08 and the root mean squared errors in activation time were 11.27 ± 3.89 ms[9].

A final example of a specific signal processing approach to electrocardiographic mapping is finding solutions to electrocardiographic inverse problems. The standard approach is to solve either a Poisson's or Laplace's equation (depending on the boundary conditions) based on a discrete geometric model of the heart and thorax. There have been many approaches to finding inverse solutions (see, *e.g.*, [5, 18, 13, 6]) but the main challenge lies in the physically ill-posed nature of the problem itself. Usable solutions require the application of constraints based on *a priori* knowledge of some aspect of the result typically using a method known as regularization. Clinical applications of the inverse solution have so far been quite rare, in large part because of a lack of adequate methods for computing stable solutions. Our own work has concentrated on developing novel means of applying multiple constraints to the electrocardiographic inverse problem[1], and also in developing clinical and experimental means of validating the results of inverse problems[13].

5. Concluding Remarks

This brief overview of spatiotemporal signal processing as it applies to electrocardiographic mapping has outlined some motivation and methods as well as the obstacles involved in this field. We have also highlighted a few of the specific solutions that have evolved in response to these needs. It is important to conclude with a summary of some of the major outstanding challenges in order to illustrate the critical role that signal processing can play in future research. Foremost of these is the need for better techniques for representation of mapping signals that reflect both their spatial and temporal nature. A great deal of the important information lies in the interplay between time and space, yet few contemporary techniques are capable of adequately capturing this relationship. Special challenges in this regard include the non-planar, irregular arrangement of measurements sites dictated by the complex geometry of the underlying anatomy. Any useful approaches should not only discriminate disease states, but also have well defined links to the underlying physiology. The area of inverse problems should have special appeal to signal processors, both because of its immense clinical potential but also because of the strong role that signal processing has played in many other types of inverse problems such as tomography, source localization, and image deblurring. By combining current and future measurement capabilities, signal processing techniques, and electrophysiological knowledge, it will be possible to advance mapping to the status of a medical imaging modality and provide largely non-invasive access to a wealth of electrical information from the human body.

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