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Review

Patient-specific flexible and stretchable devices for cardiac diagnostics and therapy

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ABSTRACT

Advances in material science techniques and pioneering circuit designs have led to the development of electronic membranes that can form intimate contacts with biological tissues. In this review, we present the range of geometries, sensors, and actuators available for custom configurations of electronic membranes in cardiac applications. Additionally, we highlight the desirable mechanics achieved by such devices that allow the circuits and substrates to deform with the beating heart. These devices unlock opportunities to collect continuous data on the electrical, metabolic, and mechanical state of the heart as well as a platform on which to develop high definition therapeutics.

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1. Introduction

High-density cardiac mapping has been an important experimental and clinical tool for the identification and the evolution of the understanding of normal conduction and arrhythmia mechanisms. The first electrode heart "socks" were developed in the 1980s for global epicardial electrical mapping. As basic research tools, many of the first sock devices were handmade designs with recording electrodes mounted on synthetic fabric, sewn to loosely fit a ventricle (Harrison et al., 1980; Paul et al., 1990; Wit et al., 1982; Worley et al., 1987). These devices provided an effective tool to increase the spatial resolution of recording propagation patterns. Studies using similar devices have been used to investigate local potential heterogeneities in ischemia transition regions (Swenson et al., 2009), to visualize atrial activation patterns including preferential pathways with temporary silicon sheets of unipolar electrodes (Derakhchan et al., 2001), and a nylon sock has even been used to test cardiac resynchronization therapy (CRT) pacing sites for mechanical resynchronization (Helm et al., 2007). However, due to the dynamic contours of the beating heart, it is difficult to achieve quality contact across the whole epicardial surface with these devices. Although still used frequently in the research setting, these

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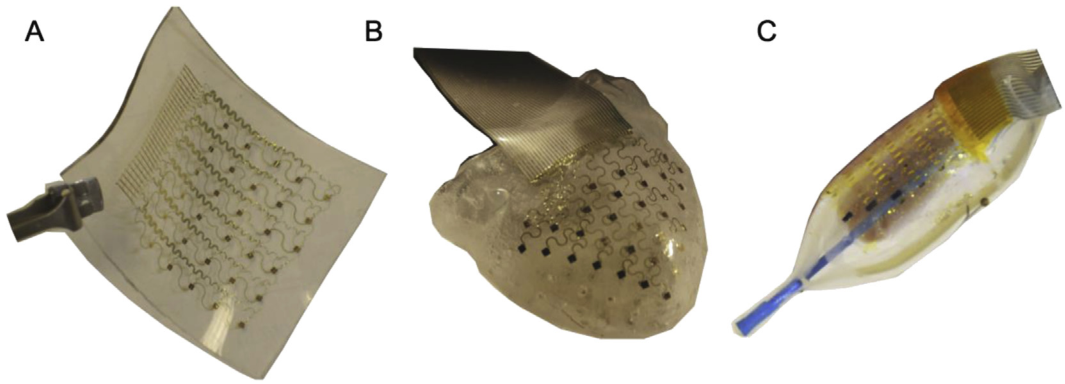

Fig. 1. Custom Design Option. Sample geometries for stretchable membrane devices. **A** planar sheet with gold recording electrodes. **B** Epicardial membrane custom design for rabbit heart geometry with gold recording electrodes. **C** Endocardial balloon with gold recording electrodes and IRO_2 pH electrodes.

devices have not transitioned to clinical applications and the assembly of the socks still presents limitations including the density of electrode arrays, spatial coverage, and scalable manufacturing. Additionally, it is becoming increasingly evident that the electrical, mechanical and energetic states of the heart should not be studied only in isolation. The interplay of pathophysiological remodeling across many disciplines of cardiac research compels the development of research and clinical tools that can extend beyond high-resolution electrical signals.

Taking advantage of recent advances in materials science fabrication technology and innovative circuit design, a novel platform has emerged for the development of such devices that can monitor multiple parameters simultaneously with high spatial resolution and follow the curvilinear surface of the beating heart (Xu et al., 2014). These devices are built on stretchable contour-fitting membranes custom designed to the geometry of the heart. A diverse array of multiparametric sensors can be placed in custom orientations across the membrane, spanning the entire epicardial surface. The design process can also be tailored to different shapes depending on the intended implementation. Planar sheets, epicardial socks, and balloons have all been tested in the research setting (Fig. 1).

Feasibility tests for these sensors have been executed in ex vivo environments for a variety of cardiac applications and have demonstrated the success of such a platform at simultaneously interrogating many cardiac states for research, diagnostic, or therapeutic use (Chung et al., 2014; Kim et al., 2011a; Xu et al., 2014). Therapeutic electrical stimulation paradigms have long been restricted to 1 or 2 electrode sites. CRT was a sizable step forward with the introduction of simultaneous pacing at two separate sites (Lattuca et al., 1990). However, not all patients respond equally to CRT in its current form (Auricchio and Prinzen, 2011). The devices reviewed here offer a platform for access to an enormous increase in pacing sites and a shift from low definition to high definition electrical therapies. With future development, these membranes can be implemented as near-continuous monitors of cardiac performance, providing clinicians with a set of internal eyes guarding patients' progression into or from disease states by tracking improvement following therapeutic intervention.

1.1. Device fabrication

Device fabrication has been discussed in detail previously (Kim et al., 2012, 2011b; Rogers et al., 2010) and here we give an overview of the process. The current cardiac specific membranes build upon previous work at the University of Illinois-Urbana Champaign (UIUC) on soft-contact sensors for epidermal applications (Khang et al., 2006; Kim et al., 2011b). The Rogers' group mastered the art of bonding ultrathin sensors to a substrate with mechanics that match the two-dimensional biological tissue with which it interfaces. The elastomer substrate and the circuits are designed to stretch, twist, and bend to great extremes while maintaining the integrity of the circuit (Fig. 2). Experimental tests illustrating consistent I–V characteristics in a variety of deformed states have been conducted. Furthermore, Finite Element Modeling has been used to study the distributions of strain to guide the design and fabrication of these circuits. Representative examples of such

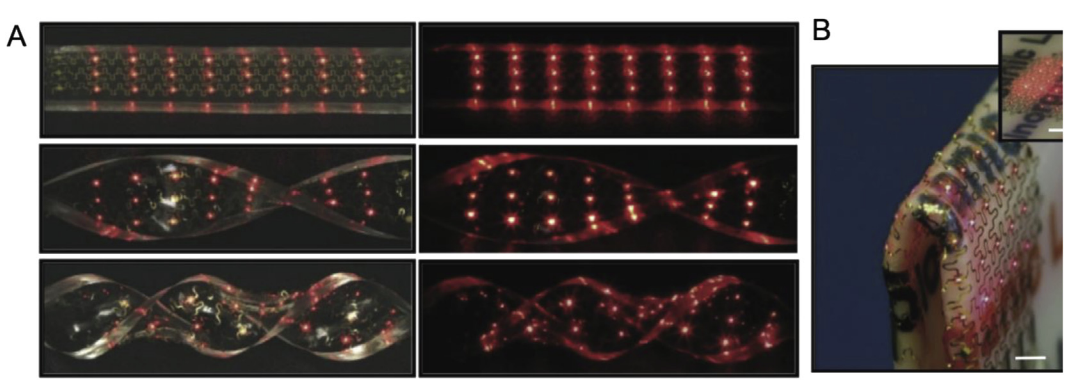

Fig. 2. Conformability of circuits. **A** LED circuit in the flat configuration and various degrees of twisting the substrate. Illumination demonstrates integrity of circuit is maintained. **B** LED circuit is bent around a corner. Illumination demonstrates integrity of circuit is maintained. This figure is modified from Kim et al., 2010.