**A WEARABLE SYSTEM FOR WIRELESS AND MULTIPLEXED MOLECULAR SENSING VIA SOLID MICRONEEDLES**

**Novelty / Progress Claim(s)**

**Here we present the most compact wireless and multiplexed potentiostat (Fig. 1) and its integration with a multielectrode microneedle array (MNA) (Fig. 2) for continuous, real-time, wearable, intracutaneous electrochemical sensing. The solid polymer MNAs are fabricated by a novel multi-step laser-micromachining process. The multiplexed MNAs responded selectively to concentrations of their respective targets, and were also demonstrated *in vivo*, showing potential for real-time wearable monitoring of multiple endogenous and exogenous molecules with minimal invasiveness.** Background / State of the Art

EAB sensors can selectively and reversibly bind to molecules with seconds time resolution (Fig. 3) making them an appealing option for monitoring biomarkers and exogenous targets [1]. To date, *in vivo* EAB sensing commonly involves invasive surgical implantation of wires into vein or subcutaneous space . Solid microneedles offer a minimally invasive alternative,placing sensing electrodes directly in interstitial fluid of the skin. Benchtop potentiostats typically used to interrogate electrochemical sensors limit potential applications, but the development of potentiostat systems on a chip (SoC) allows drastic decrease in size for wearable monitoring.

Description of the New Method or System

The YAMstat has been configured into a wristwatch format housing the PCB and a 3.7 V battery with the MNA held in place under the case (Fig. 1). The PCB consists of an ADuCM355 SoC for 2 multiplexed sensing channels and a nRF52840 SoC for Bluetooth low energy (BLE). Open-source firmware was modified to run square wave voltammetry (SWV) on the ADuCM355 for interrogating functionalized MNAs [2]. The two chips communicate via UART protocol and data is sent via BLE to a computer or phone running custom software whichcontrols the YAMstat and processes the data (Fig. 4).

PEEK was selected as the microneedle substrate for its mechanical properties, biocompatibility, and gold adhesion which is necessary for aptamer immobilization [3]. Each microneedle is1400 µm long and 250 µm wide with a 30° tip(Fig. 5B). MNAs are fabricated by machining a 250 µm thick PEEK sheet and beveling the tips via laser. The microneedles are then bent out of plane in a single step by pressing the array between a silicone sheet and custom jig. Ti/Au is deposited through a shadow mask to define two sets of working electrodes (WE) and counter electrodes (CE), a shared reference electrode (RE) later coated with Ag/AgCl ink, and contact pads which interface with off-the-shelf connectors (Fig. 5A) (Fig. 6). Independent functionalization of the WEs to address different targets was accomplished via incubation in a custom microfluidic fixture.

Experimental Results

The MNAs consistently pierced rat skin leaving behind visible punctures (Fig. 7). When challenged with phenylalanine and vancomycin, the MNA’s electrodes responded only to their corresponding target, demonstrating its multiplexing capability (Fig. 8). *In vivo* function was demonstrated in an anesthetized rat using a MNA and subcutaneous wire sensor in parallel, showing an observable response to injected target (Fig. 9). Differences in sensor signal gain may be a result of differences in transport kinematics of the subcutaneous and upper cutaneous spaces. Data was also collected using the YAMstat with functionalized gold wires to test multiplexing and sensing capabilities (Fig. 10). An expected signal gain was achieved using the YAMstat comparable to results with benchtop testing (Fig. 7).

The ADuCM355 is capable of many common electrochemical techniques, such as cyclic voltammetry and electrochemical impedance spectroscopy, expanding the possibilities of integrated sensors using the YAMstat. Future work entails continued *in vivo* sensing with MNAs integrated with the YAMstat and mechanical characterization of the MNAs.

**Word count: 633**

**References**

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