Fabrication & Optimization of a Wearable Microneedle Patch Sensor for Cardiac Biomarker Detection

Amy Luo[1], Yuanwen Jiang[2]

[1]School of Engineering and Applied Science, University of Pennsylvania Class of 2027, [2]Dept. of Materials Science Engineering, University of Pennsylvania

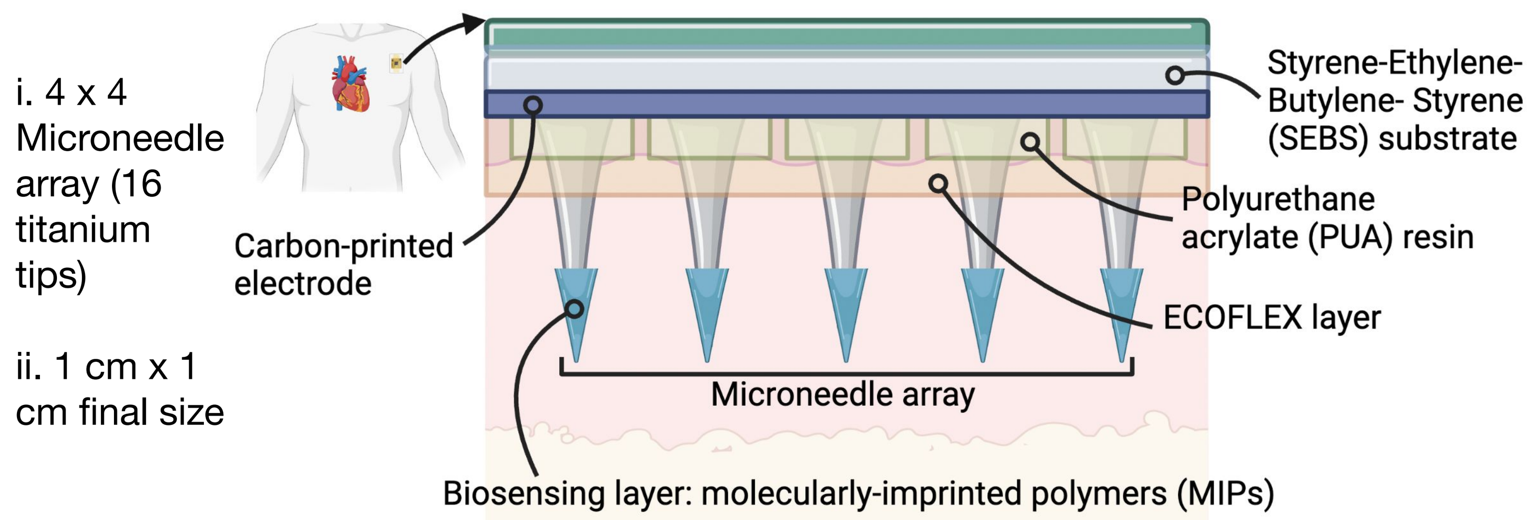
Introduction

Microneedle biosensors are an emerging innovative technology designed for minimally invasive diagnostics, offering the potential for continuous monitoring of conditions such as cardiac health. This research project focuses on developing and optimizing a wearable microneedle patch sensor for detecting cardiac biomarkers, integrating advanced materials science and fabrication techniques. Wearable electrochemical sensors, particularly those utilizing microneedle arrays, enable noninvasive, real-time monitoring of clinically relevant biomarkers across various biofluids, such as sweat, tears, and interstitial fluid.

The primary objective addressed in this research project is how to optimize the design and functionality of microneedle-based sensors to improve the accuracy and reliability of biomarker detection through the integration processes of the multidimensional sensor components, particularly the microneedle array, substrate, electrode, and sensing layers.

Design & Methods

Schematic of biosensor design



1. Fabrication of Microneedle Tips using Electrochemical Etching

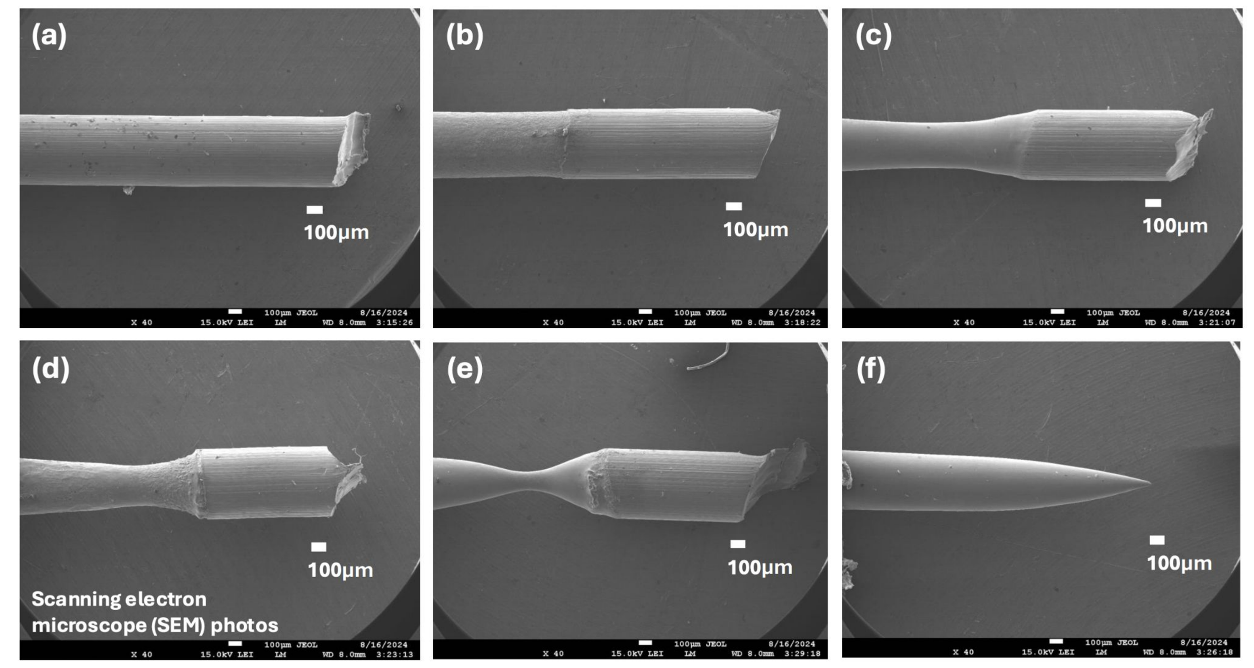
- Electrochemical etching procedure involves the dissolution of metal soaked in an electrolyte under an electric current
- Needle selection: stainless steel vs. tungsten vs. titanium
  - When experimentally testing with stainless steel, initially used electroplating used to deposit gold nanoparticles onto needles to increase biocompatibility
  - Titanium wire selected for etching due to intrinsic biocompatibility

2. Elastomer Substrate Synthesis

- Substrate selection: Polyurethane acrylate (PUA) resin vs. ClearFlex 50/95 resin vs. Styrene-Ethylene-Butylene-Styrene (SEBS) resin
  - UV curing of PUA lead to strong adhesion to the glass substrate; irremovable
  - EcoFlex elastomer was not compatible with carbon ink — when stretched, cured ink would peel off — due to low surface energy
  - SEBS provided the most optimal material nature; however, due to being a thermoplastic, the heating required for skin-compatibility modification would result in permanent deformation of the substrate
- Optimization of substrate fabrication:
  - Added layer of water-soluble polysaccharide solution Dextran for ease of removal of ClearFlex resin
  - Plasma etching applied onto ClearFlex substrate before printing to increase compatibility with carbon ink
- Final design utilizes PUA to fix microneedle tips onto carbon electrode, ECOFLEX for flexibility and encapsulation, and SEBS as the primary sensor substrate

Results

1. Microneedle etching progression

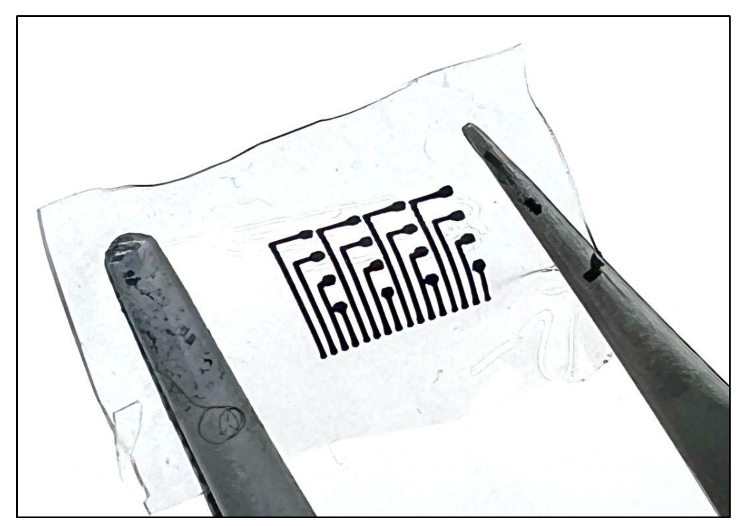


Etching conducted at 20V in solution of 1 M NaCl and ethylene glycol

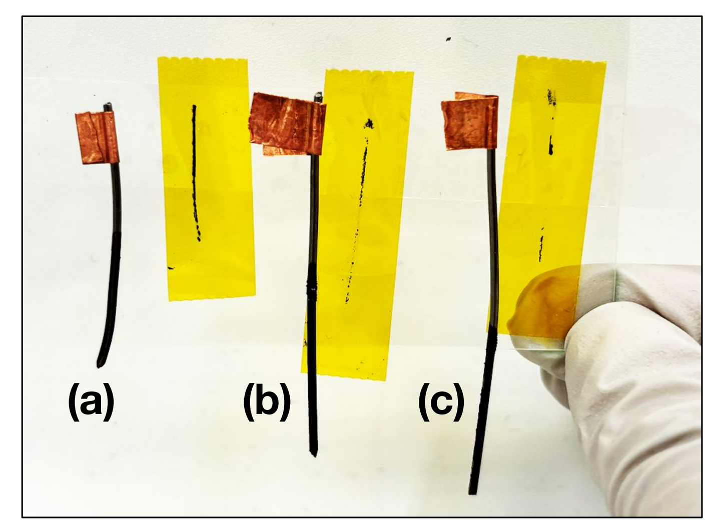
(a) Raw wire
(b) 30 min. of 0.01A
(c) 30 min of 0.1 A
(d) 15 min of 0.2 A
(e) 30 min of 0.2 A
(f) Tip drop off from 0.2A

Needle diameter: 20μm

2. Printed electrode & substrate

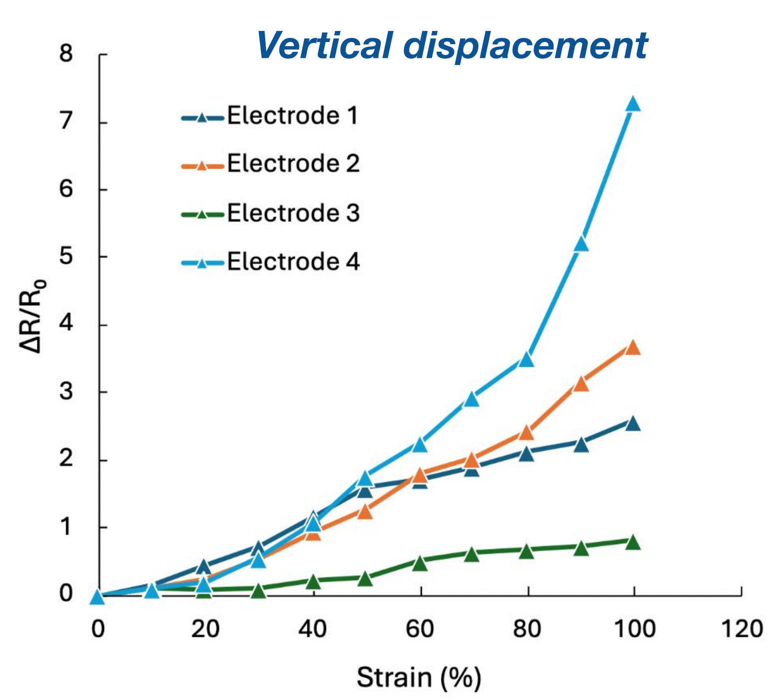


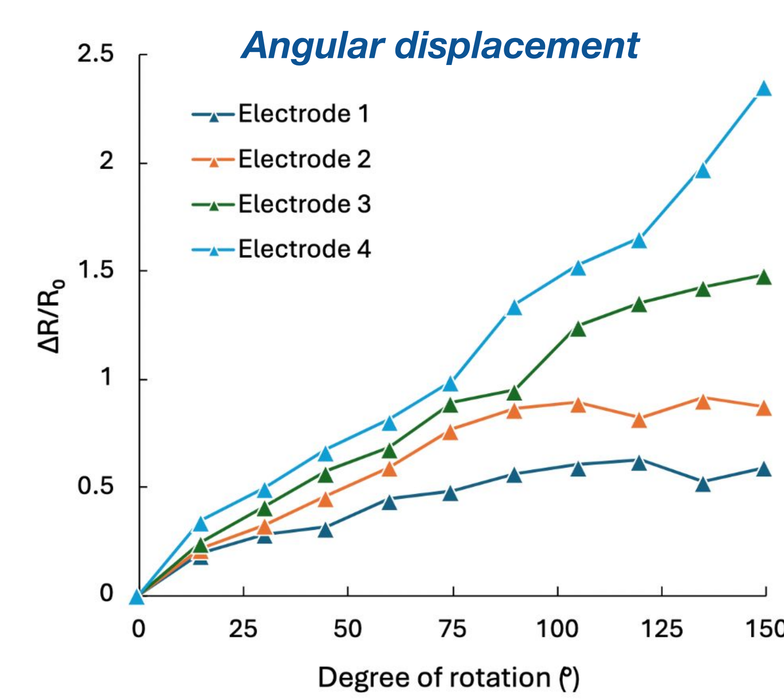
3. MIP adhesion tests



(a) No treatment
(b) No plasma etching
(c) Plasma etching

4. Resistance retention of sensor electrode when stretched





1. Etching of titanium wire under given procedure produces 20μm microneedle tip
2. Current resolution of carbon electrode still in need of improvement due to overlap of electrode nodes
3. Plasma-etched needle retains highest adhesion quality, followed by no plasma etching, and needle with no treatment has lowest adhesion retention
4. Electrode 1 is the most sensitive while Electrode 4 is the least sensitive to resistivity change due to stretching and twisting of substrate
   i. Resistivity change dependent on size and distribution of electrode on film

Methods cont.

3. Direct-Ink Electrode Printing

- Voltera PCB Electronic Printer and carbon conductive ink
  - Optimization of printing procedure primarily focused on adjustment of probing & dispensing heights based on substrate type
- Ink selection: Carbon vs. Poly(3,4-ethylenedioxythiophene) (PEDOT) vs. silver ink
  - Silver has highest conductivity, but carbon is both conductive and stretchable
- Silver epoxy applied to each electrode node to increase microneedle tip connectivity

4. Molecularly-Imprinted Polymer (MIP) Integration

- MIP-Making Protocol
  - Electropolymerization in PBS containing target biomarker molecule solution, 50 mM pyrrole, 5 mM $FeCl_3$, 5 mM $K_3[Fe(CN)_6]$ and 0.1 M HCl
- Adhesion Testing Protocol
  - Mix 10 mL ethanol, 100 µL ammonia, and 100 µL Triethoxyvinylsilane, then stir at 50°C for 1 hour; plasma treat the titanium wire for 5 minutes on both sides; stir the treated titanium wire in Solution 1 at 50°C overnight and treat with diazirine
  - Diazirine type: BXW-202 dissolved in cyclohexane
- Deposition onto Titanium Wire
  - Deposit the MIP layer using constant voltage (10V) with a current of ~2-3 mA for 10 minutes. Cure the MIP layer under UV light for 10 minutes.
  - Differs for needle deposition: instead, cyclic voltammetry from 1-3V for 20 cycles, or until MIP layer is uniformly deposited

Conclusion

Future Steps & Applications

- Full integration and connection of sensor components, increase resolution of sensing circuit
- Add targeted receptor molecule cavity to MIP sensing layer for effective biomarker recognition

The integration of high-resolution carbon electrodes and optimal substrate materials, particularly SEBS, ensures the reliability and efficacy of the microneedle sensor. Further research will explore the targeted application of this technology to cardiac biomarkers and beyond. Additionally, this biosensor may be integrated with drug delivery functionality along with wireless communication applications and algorithmic data analysis to form a closed-loop treatment device.

References / Acknowledgements

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