Development of a Non-Invasive Cortisol Sensor

Natalie Alvarado, Quinn Beato, Hannah Blanchsky, Zoe Bloomfield, Brenna Curvey, Anthony Nguyen, Trey Venners
Introduction
Problem Overview

- Astronauts use heart-rate data to assess stress
  - Microgravity effects cardiovascular system
  - Less accurate understanding of stress
Cortisol

- Hormone released as a parasympathetic response
  - High levels indicative of stress
- Detected in blood, urine, sweat, or saliva
- Until recently, invasively blood testing was only way to test for cortisol levels
Project Overview
Wearables Quest

● **Mission**
  ○ Introduce students to world of wearable technology
  ○ Solve challenges related to engineering, research, health, and more

● **Specific Space Application**
  ○ Task: Create a non-invasive cortisol-based wearable that can be used to assess stress without relying on heart-rate data
Mission Objectives

- Create a non-invasive sensor with the ability to detect cortisol in sweat
- Incorporate sensor into a wearable device designed for use by astronauts
Our Project

- Waistband with the ability to sense cortisol in sweat
  - Fastened on lower back of user
  - Worn during exercise
  - Ability to store user data over time
  - Reliable stress assessment for astronauts at Point-of-Care
Structure of the wearable
Structural Design Requirements

01 Comfortable for user
- Stays in place all day
- Allow full range of motion

02 Allow sweat collection
- Located in an area of heavy perspiration
- Water resistant material

03 Functional for electronics
- Store microcontroller, battery, etc.
- Able to connect wires
Simplified Design
Prototype Design

- Store data via SD card to be read on an external computer
- Connect the wires from the cortisol sensor to the pouch
- Cortisol sensor placed under the band and will stick to the skin with medical grade adhesive
- Electronics pouch holds microcontroller and battery pack
Subsystem Overview
Organic Electrochemical Transistor (OECT)

- Biosensor that measures the concentration of ions in a solution
- Channel changes conductivity depending on concentration of ions
- The change in current ($\Delta I_D$) measures concentration of ions in solution (sweat, in this case)
1) Voltage is applied to gate electrode

2) Voltage is applied to gate electrode

3) Ions in sweat are injected into channel

4) Ions decrease conductivity of channel

5) Change in current measured at source electrode (ΔI_D)

1) Voltage is applied to drain electrode

V > 0

V_d < 0
Molecularly Imprinted Polymer (MIP)

- Cortisol is non-polar
- Placed between sweat reservoir and OECT
- Sponge-like polymer with embedded cortisol binding sites
- Sweat flows through MIP and into the OECT channel
1) Ions in sweat are pulled through MIP into the OECT Channel by the gate electrode

2) Cortisol binds to monomers in MIP

3) Bound cortisol prevents ions from moving into OECT channel

4) Rate of ion flow into channel is measured by OECT ($\Delta I_D$)

- Cortisol
- Ions (Na$^+$ or K$^+$)
- Cortisol Binding Sites
Rational Design/Production of MIPs

![Diagram of MIP synthesis](image)

**Table 1: Optimization conditions.**

| Membrane | Monomer | Cross-Linker | Initiator | Solvent  | Ratio | Conditions          | Sensing factor<br>
|----------|---------|--------------|-----------|----------|-------|---------------------|----------------
| A1010    | MAA     | EDMA         | AIBN      | Acetone  | 1:6:18| UV, 4°C, 30 hours   | 4.2            |
| M1010    | MAA     | EDMA         | AIBN      | Methanol| 1:6:18| UV, 4°C, 30 hours   | 5.1            |
| D1010    | MAA     | EDMA         | AIBN      | DCM      | 1:6:18| UV, 4°C, 30 hours   | 5.4            |
| D1910    | MAA     | EDMA         | AIBN      | DCM      | 1:6:30| UV, 4°C, 30 hours   | 10.1           |
| D1690    | MAA     | EDMA         | AIBN      | DCM      | 1:6:60| UV, 4°C, 30 hours   | 2.2            |
| D1630RT  | MAA     | EDMA         | AIBN      | DCM      | 1:6:30| UV, room temperature, 30 hours | 6.7 |

*Calculated based on each sensor device's performance to express imprinting efficiency.
Electronics & Software
Circuit Design

Circuit designed to power and measure current leaving OECT which is related to cortisol in sweat. Negative voltages used to attract positive ions in the sweat.
Software Flow

Two Potential Angles

- Keep gate voltage constant
  - Determine current through OECT and relate to cortisol
- No gate voltage, rely on ions in sweat
  - Set Vds to constant value by varying output voltage
  - Determine which curve the data lies on

Data Storage

- Both the raw data and the modeled cortisol will be saved
  - SD Card module and prototyping space
Manufacturing and Prototyping
Design Prototyping- OECT Models

- OECTs designed to be laser cut into Kapton tape, applied to glass slides
- Changes made to consider gaps required between individual OECTS and between conductive areas
Manufacturing Procedure

1. OECT Masks
   a. S - Ag⁺/AgCl Paste Electrodes - 6 Masks
   b. G - Evaporated Gold Electrodes - 6 Masks

2. MIP Polymerization Process
   a. M1 - Polymerizing with rational design at 25° C - 4 MIPs
   b. M2 - Polymerizing adjusted rational design at 25° C - 4 MIPs
   c. N1 - Polymerizing without template molecule at 25° C - 2 MIPs

3. Final Configuration and Testing
   a. OM - OECT + MIP - 8 OECTs
   b. ON - OECT + NIP - 2 OECTs
   c. O - OECT alone - 2 OECTs
Manufacturing Procedure
Manufacturing Actuality

1st Production Round:

- 6 Ag⁺/AgCl electrode devices
- 6 Gold Evaporated electrode devices
  - Interrupted by breaking gold devices
  - Transistors short-circuited

2nd Production Round:

- 6 Ag⁺/AgCl devices to save time
- Created more just in case (8 in total)
  - Couldn’t complete
Testing & Analysis
OECT/MIP Subsystem Testing
OECT/MIP Subsystem Testing

B  0.01 μM cortisol

1.0 mM cortisol

D  Molecularly selective membrane

Control membrane

Concentration (μM)
Conclusion
Lessons Learned

- Previous research wasn't entirely practical- manufacturing processes and testing were disorderly
- Testing- a large concern throughout manufacturing- turned out to be relatively quick and easy
- Manufacturing required a lot of lab time, and considerations had to be made for broken devices and other mistakes
- More thought needed to be put into OECT design than originally thought, as room for wires and electrocution mitigation was needed
Conclusions

- A noninvasive wearable cortisol sensor is highly viable for measuring stress in an isolated and high stress environment.
- Applications of device allow personnel, such as astronauts, to easily measure and manage their stress without interrupting their daily workflow.
  - Additionally, with enough data, off site personnel can help diagnose, predict, and address stress related illnesses.
- Wearable sensor is easy to maintain and use, allowing it to be used for extended periods of time.
- More testing is needed to fine tune calibration and overall accuracy.
Acknowledgements

- Special thanks to Dr. Robert McLeod and Megan Renny of McLeod labs
- Additional thanks to Scott Keene, a graduate student in the Salleo Research Group at Stanford University and Kangmin Kim, a graduate student in the Musgrave/Stanbury Research group at the University of Colorado Boulder
- Thank you to the Engineering Excellence Fund for providing additional funding for the project
- Thanks to Sophie Orr and the Colorado Space Grant Consortium for providing resources, support, and advice that was integral to the project and providing this invaluable opportunity
# Contact Information

<table>
<thead>
<tr>
<th>Name</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Project Manager: Natalie Alvarado</td>
<td><a href="mailto:naal2506@colorado.edu">naal2506@colorado.edu</a></td>
</tr>
<tr>
<td>Brenna Curvey</td>
<td><a href="mailto:brcu9113@colorado.edu">brcu9113@colorado.edu</a></td>
</tr>
<tr>
<td>Hannah Blanchard Obolsky</td>
<td><a href="mailto:habl3296@colorado.edu">habl3296@colorado.edu</a></td>
</tr>
<tr>
<td>Trey Venners</td>
<td><a href="mailto:trve5100@colorado.edu">trve5100@colorado.edu</a></td>
</tr>
<tr>
<td>Zoe Bloomfield</td>
<td><a href="mailto:zobl8214@gmail.com">zobl8214@gmail.com</a></td>
</tr>
<tr>
<td>Quinn Beato</td>
<td><a href="mailto:qube1659@colorado.edu">qube1659@colorado.edu</a></td>
</tr>
<tr>
<td>Anthony Nguyen</td>
<td><a href="mailto:anng9781@colorado.edu">anng9781@colorado.edu</a></td>
</tr>
<tr>
<td>Consultant: Megan Renny</td>
<td><a href="mailto:megan.renny@colorado.edu">megan.renny@colorado.edu</a></td>
</tr>
</tbody>
</table>
Thank you!