Point of Care Diagnostic Device for Early Detection of Osteoarthritis

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Osteoarthritis

Definition	Irreversible degradation of protective cartilage in the joints
Symptoms	Pain, swelling, stiffness, tenderness loss of flexibility, grating sensation
Risk Factors	Older age, sex, obesity, joint injuries, genetics, deformaties, repeated stress

Current Treatments

Medications

- Acetaminophen
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Cymbalta

Therapy

- Physical Therapy
- Occupational Therapy
- Transcutaneous Electrical Nerve Stimulation (TENS)

Procedures

- Cortisone Injections
- Lubrication Injections
- Realigning Bones
- Joint Replacement

Limitations of Current Technology

1. **No devices for early detection**

Earlier treatment can reduce pain and discomfort.

2. **Cartilage loss revealed by X-rays**

Loss of space between bones revealed by imaging.

3. **Joint fluid analysis to test for inflammation**

Fluid extracted from affected joint to determine if cause is infection or OA.

Design Proposal

Combining biomarker counting and a sensor to confirm biomarker type for the most accurate and earliest detection of OA via synovial fluid

Targeted OA Biomarkers

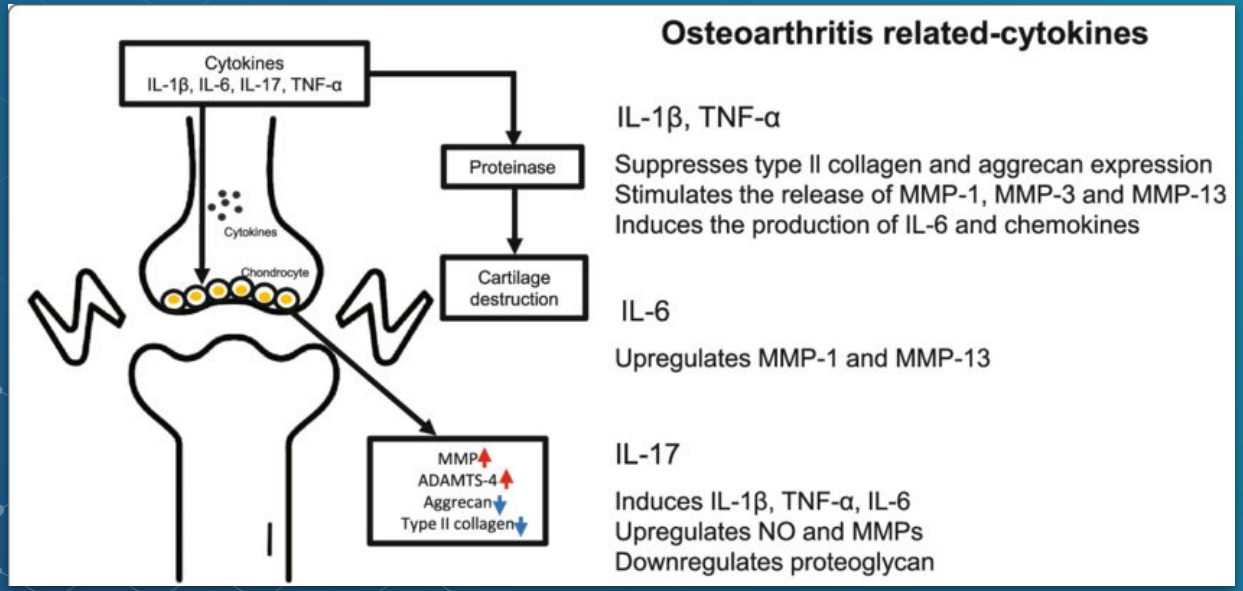
Cytokines

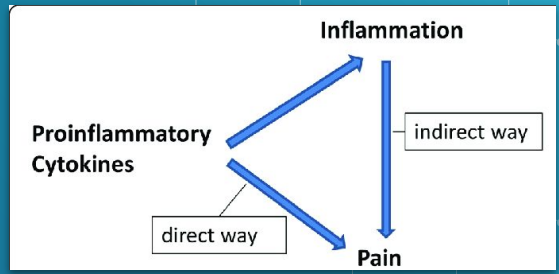
- Proteins secreted by immune cells
- Bind to synovial macrophages
- Leads to degradation of collagen that maintains joint structure

hYKL-39 Antibody

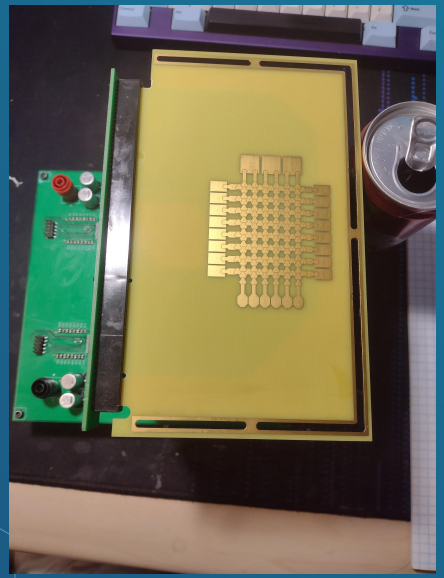
- Binds with YKL-39 antigen
- Synthesises chondrocytes & synovial cells in inflammation or remodels the cell matrix
- Important for cartilage remodelling & degradation in OA joints

Biological Targets for Device Design

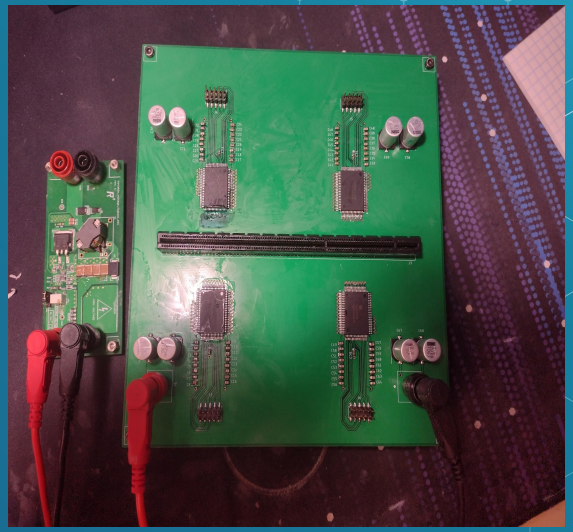




Digital Microfluidics to Manipulate Discrete Droplets



DMF Platform on Riser

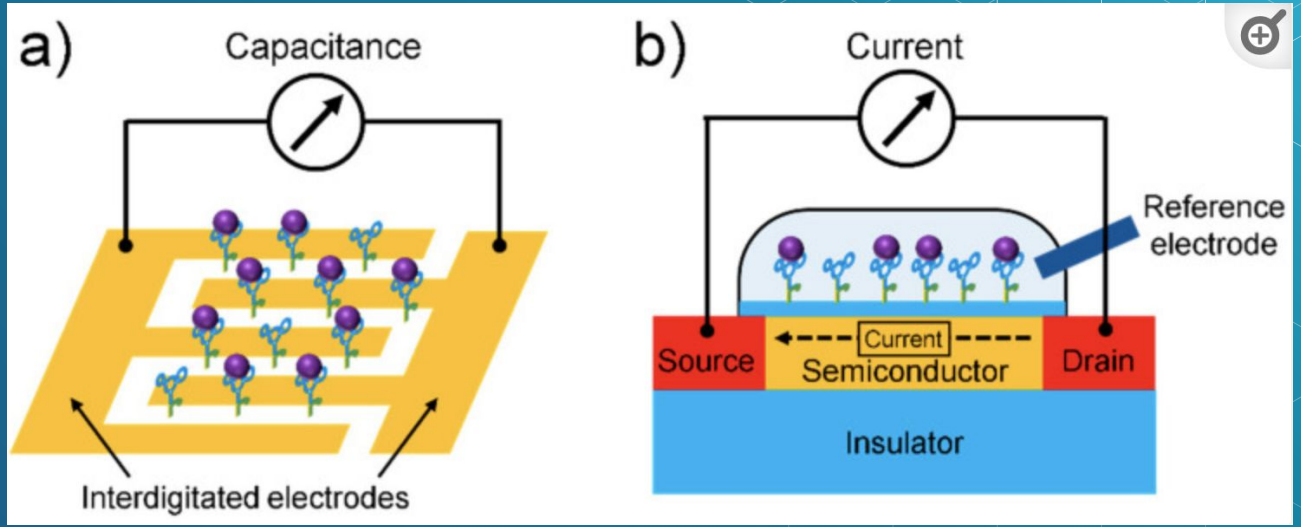


Driver PCB with High Voltage Power Supply

Digital Microfluidics to Manipulate Discrete Droplets

Principles of Device Operation

- Electrowetting Dielectric Principle
- Time Constant Capacitive Measurement
- Receptor Placed on top of SIO_2



Device Material Selection

AlN Ceramic PCB: Excellent thermal conductivity, high insulation resistance, mass production

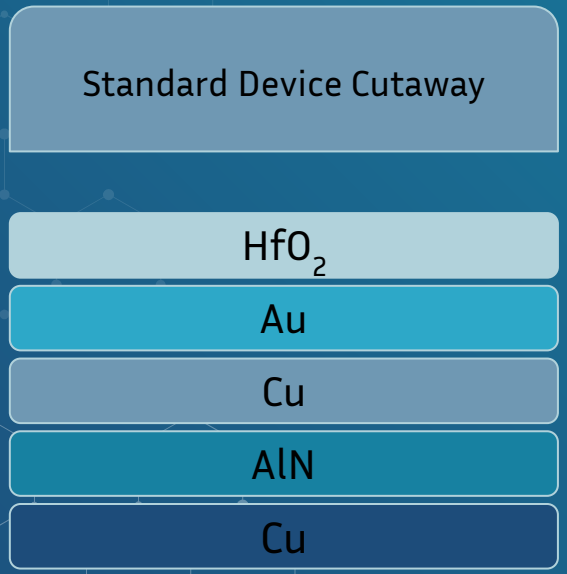
ALD of HfO_2: Excellent dielectric constant to reduce operation voltage.

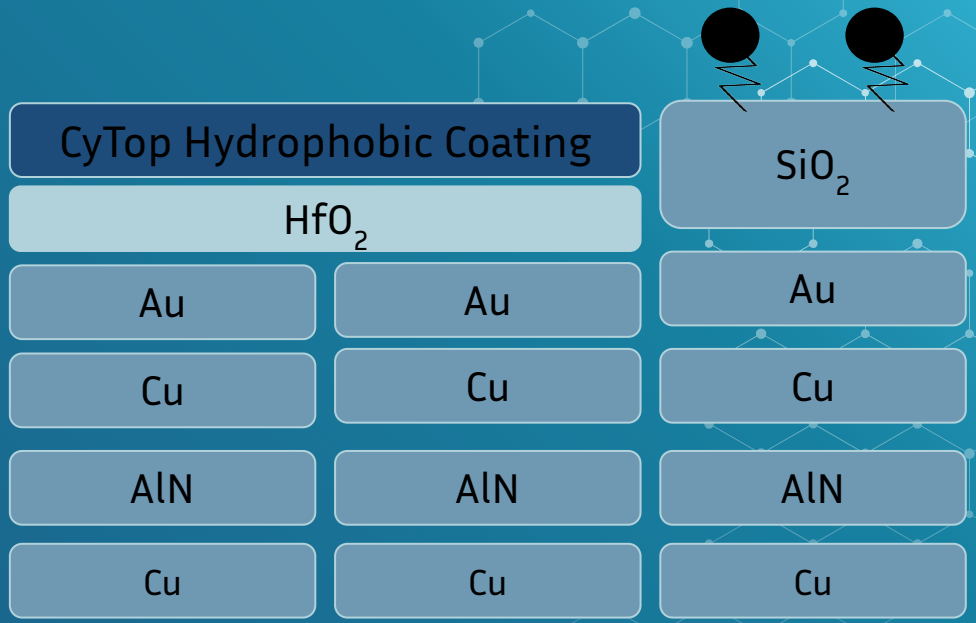
Cy Top: Hydrophobic coating

SiO_2: Surface to grow aptamer

Device Stackup

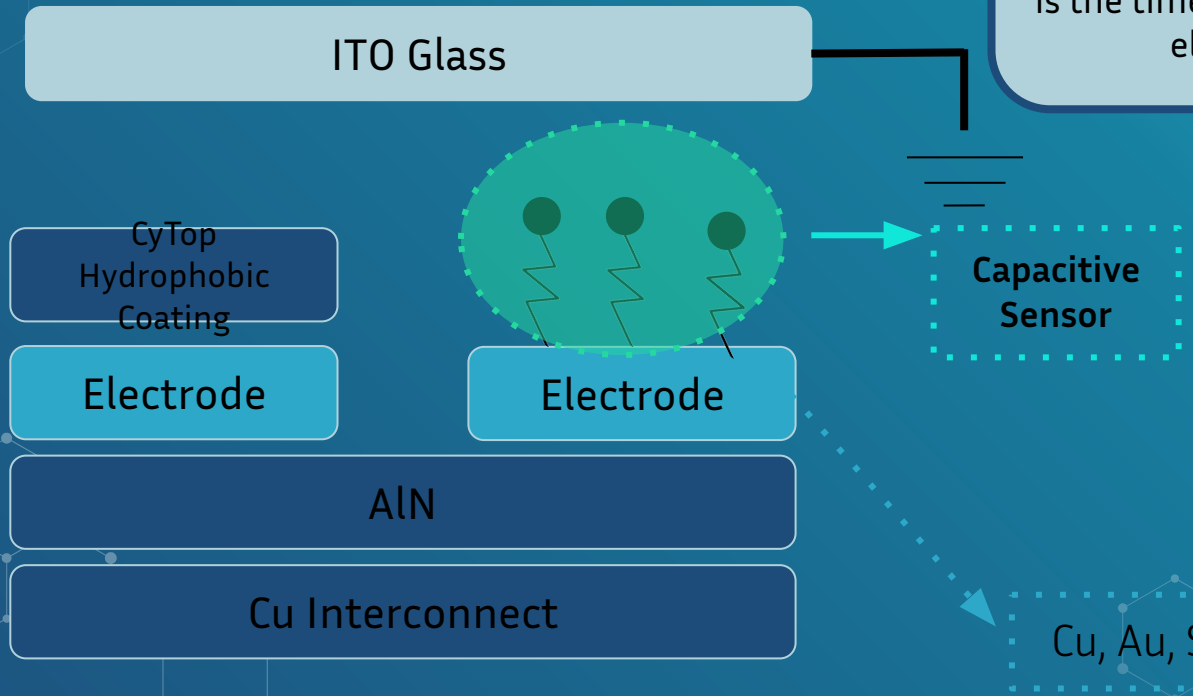
Standard Device Cutaway



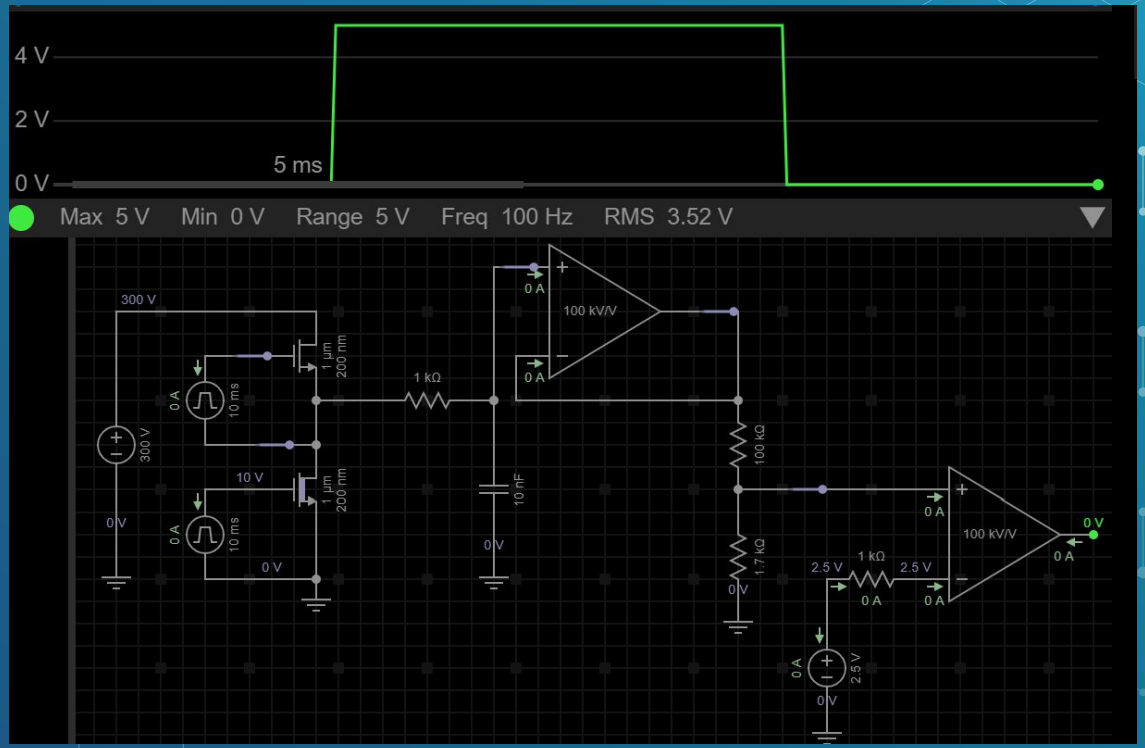


Device Fabrication

Our method of employing capacitive measurement is to apply a DC voltage into the electrode and measure the T=RC constant where T is the time where the voltage at the electrode is ½ VDD.



Signal Acquisition



Testing and Validation

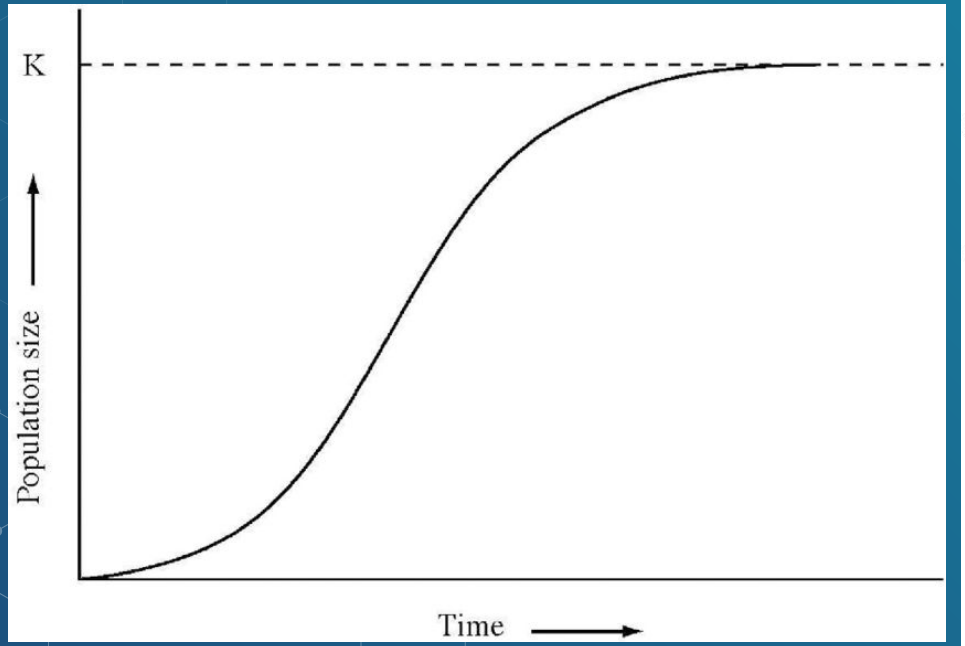
Quantitative characterization of capacitive versus concentration curves.

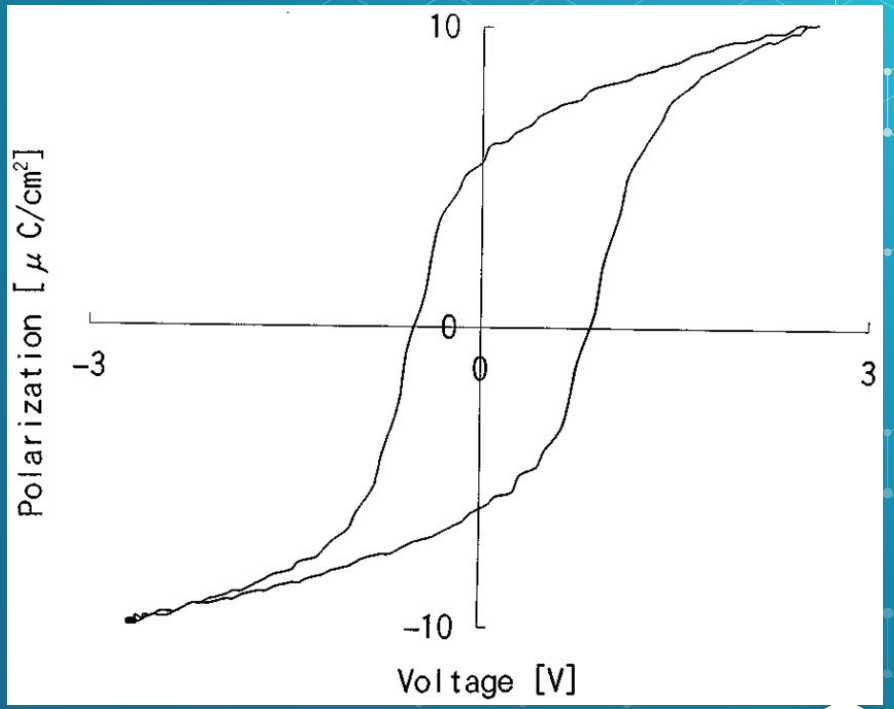
Unbinding method between proteins and antibody for reusability.

Hysteresis characterization of binding events

Overall precision and accuracy

Expected Result



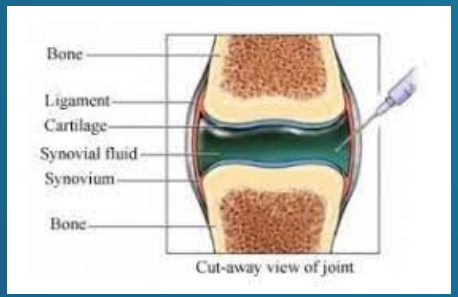


Limitations & Challenges

Early Detection ≠ Cure

Invasive to get appropriate sample

Concentration of biomarker may not be enough to signal OA



Future Directions

- Potential for drug modeling purposes?
- Improving quality of analytical biomarkers
- Could be generalized to other joints to expand diagnostic capabilities
- As with most new technology, increasing accessibility by decreasing cost and size

Conclusions

- Osteoarthritis is a degenerative disease that occurs when the flexible tissue at the end of the bones wears down
- Our device aims to be able to more accurately and efficiently diagnose the disease using bioMEMS technology
- There are certainly limiting factors, but it has exciting prospects for the future of early diagnosis

Thank you!

Questions?

References

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