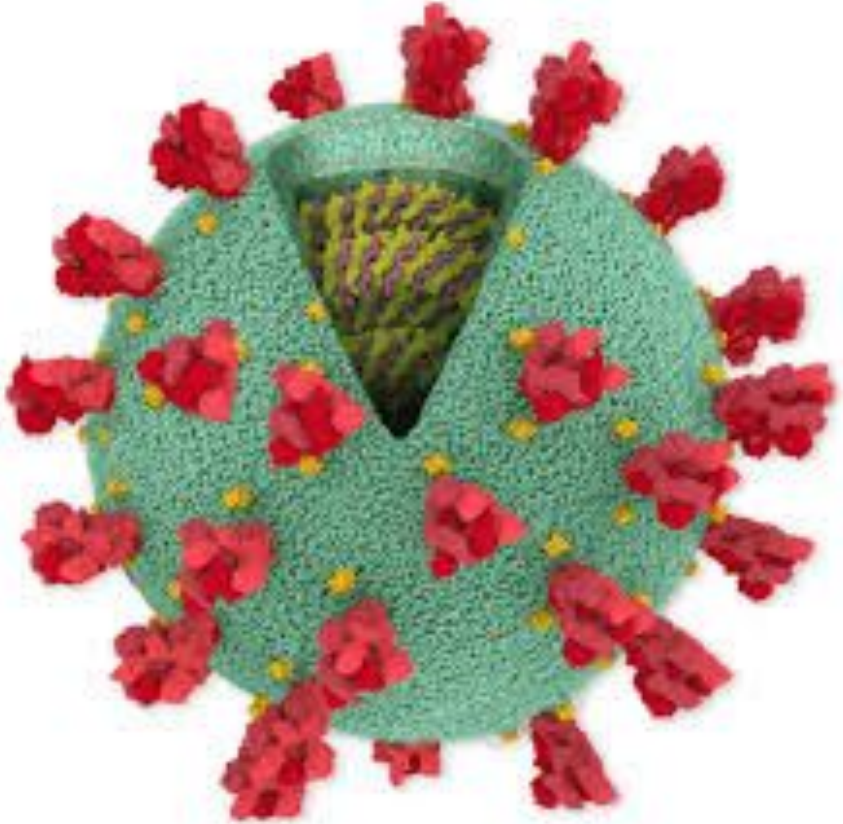
COVID-19 High-Throughput Serologic Chip

Group 6
Dylani, Jacob, John, Paul

Outline

- Background
  - What is COVID-19
  - Current crisis
  - Current detection methods
- Individual Sensor
  - Transducer
- High-Throughput Format
  - Electrical Logic
  - Fluid Delivery
- Innovation
- Summary



Background: What is COVID-19?

- Coronavirus disease 2019 (COVID-19) is a viral respiratory illness [1]
- Symptoms of COVID-19
  - Shortness of Breath
  - Fever
  - Cough

- These symptoms may be mild or severe
- No current anti-viral treatment for COVID-19
- Treatment only available for relief of symptoms

Background: Prevalence of COVID-19

Total Cases: Worldwide

2,119,333

Total Cases: USA

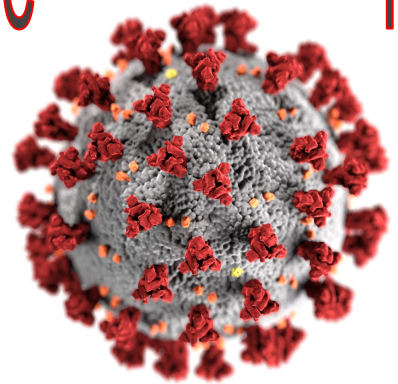
653,397

Total Deaths: Worldwide

141,956

Total Deaths: USA

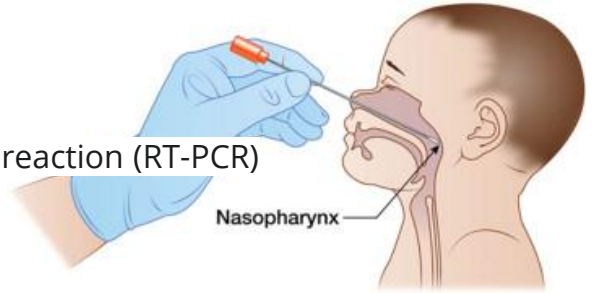
33,405



210 countries and territories affected

Background: Current COVID-19 Detection Methods

- Detection During First Week of Infection[3]
  - Nasopharyngeal swab collected
  - Virus detected using real-time reverse transcription polymerase chain reaction (RT-PCR)
  - Results within a couple hours to a few days

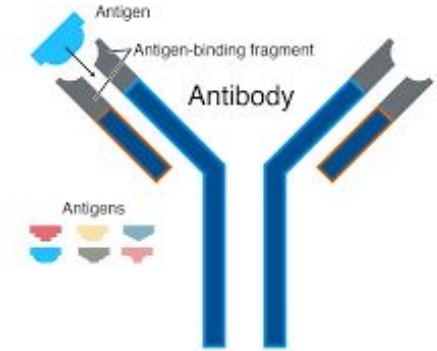


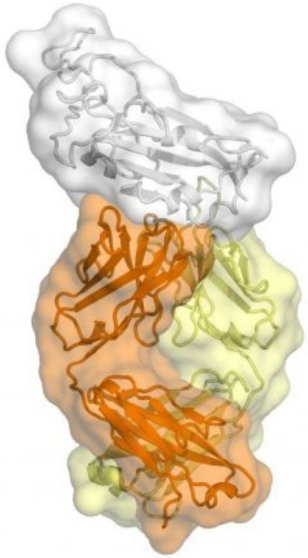
- Detection During Second Week of Infection
  - Virus disappears from the nose and multiplies in the lungs instead
  - Samples collected from deep airways using a suction catheter
  - Tested using RT-PCR to detect live COVID-19
  - Results within a couple hours to a few days

- Detection Methods Post-Illness [4]
  - Detection of antibodies
  - Requires a blood sample
  - Lateral flow immunoassay that detects antibodies of immunoglobulin M and G against COVID-19
  - Results within 15 minutes

Our Device Detection Method

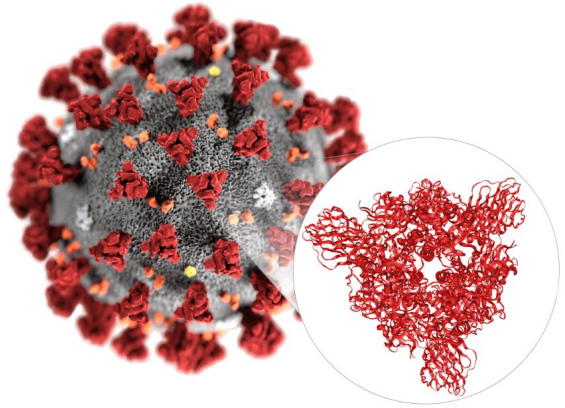
- This device is for mass detection of COVID-19 for those who believe they may have had this illness previously
- Antibody detection method
  - Still present in the blood post-recovery
- Allows all individuals to test for COVID-19 immunity

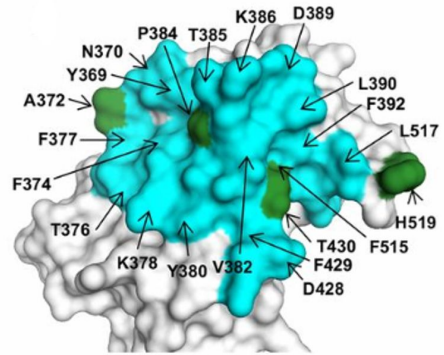




Antibody/Virus Binding

- Receptor-Binding Domain (RBD) present on Spike Protein (S) trimer.
- Largely hydrophobic interactions with IgG.
- 917 $Å^2$ interaction area between antibody/antigen.
- Cell membrane (ACE2) and Antibody bind to different virus RBDs.

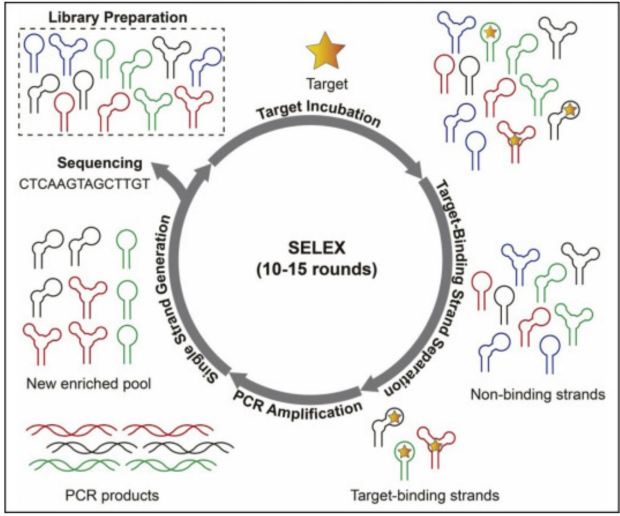




[4]

Aptamer Engineering

- SELEX method to find best “fit” to SARS-CoV-2 Specific Immunoglobulin-G.
- Result would share similar RBD nucleotide sequence shown below.
- Additional sequencing needed for conformation and glutaraldehyde cross-linking.

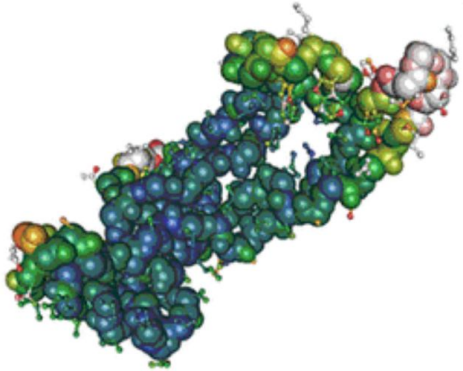


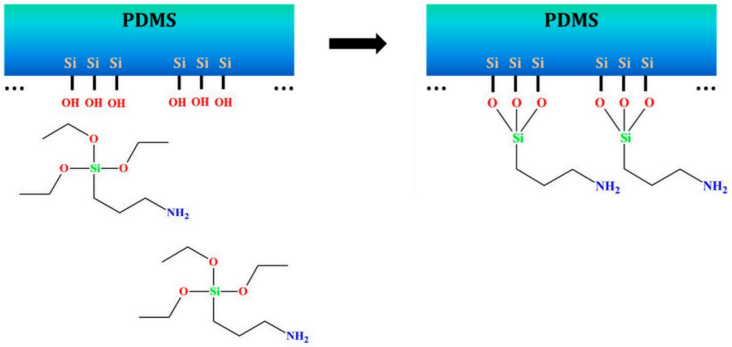
[5]

```
SARS-CoV-2 RBD   319 RVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVL 368
                 369 YNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTGKI 418
                 419 ADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDI 468
                 469 STEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELL 518
                 519 HAPATVCGPKKSTNLVKNKCVNFS  542
```

Aptamer Immobilization on Sensor

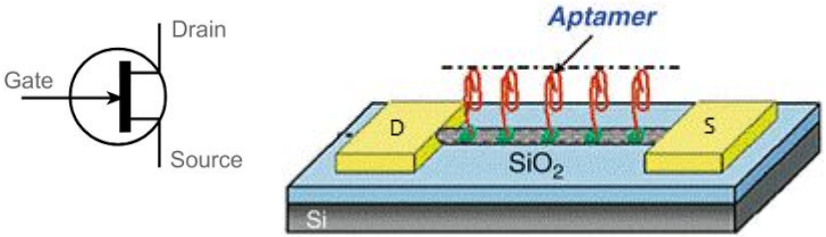
- PDMS Substrate.
- Silicon Electrode.
- APTES-GA Aptamer Immobilization.
  - Hydroxyl Surface Functionalization.
  - Silanization.
  - Glutaraldehyde Cross-Linker.
- Aptamer Bio-Recognition Element



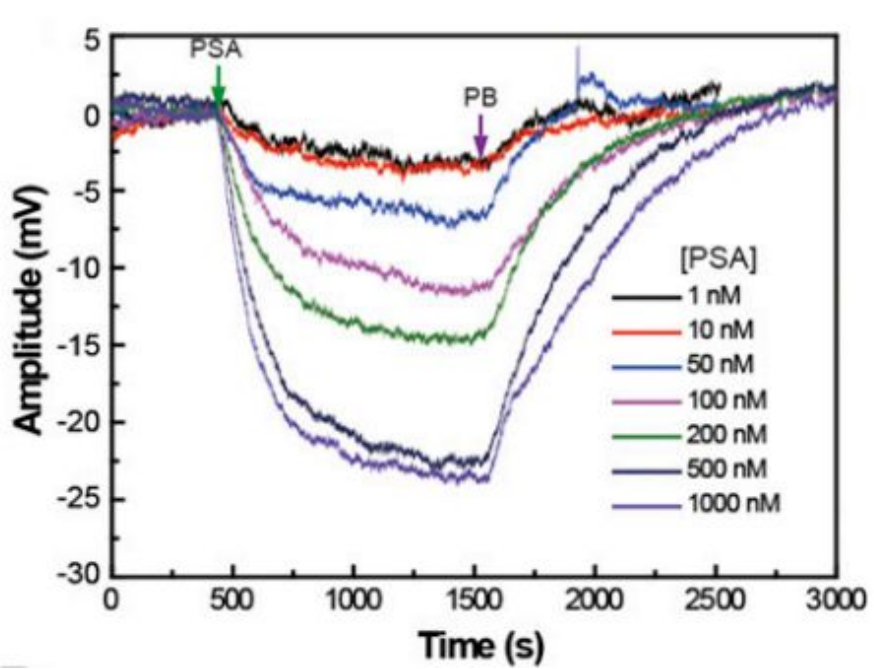


Individual Sensor: FET Configuration

- Aptamer-antibody interaction creates a small electrostatic potential
- As more aptamers bind the gate is saturated



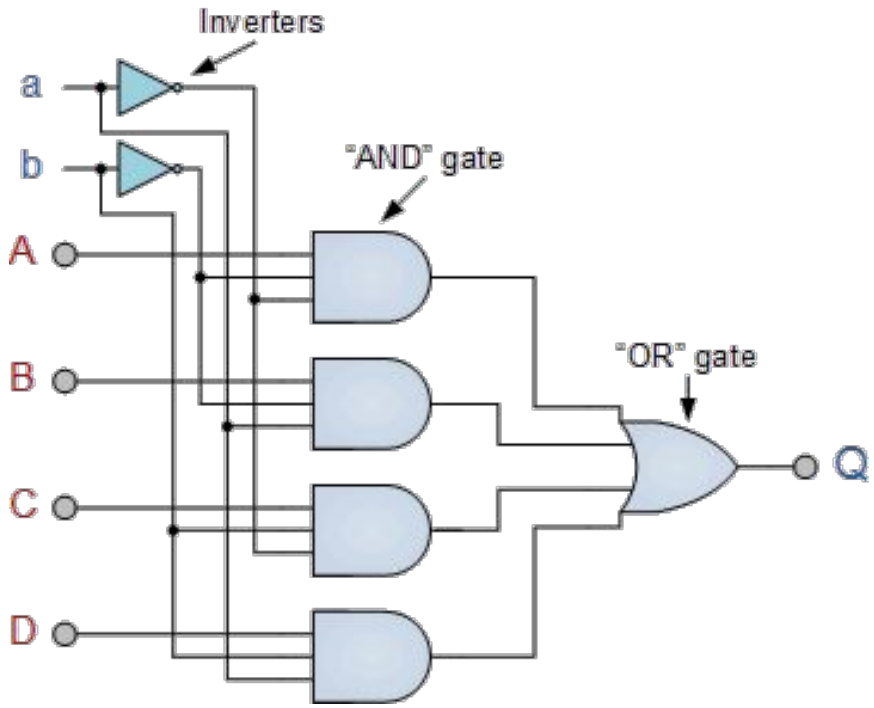
[7]



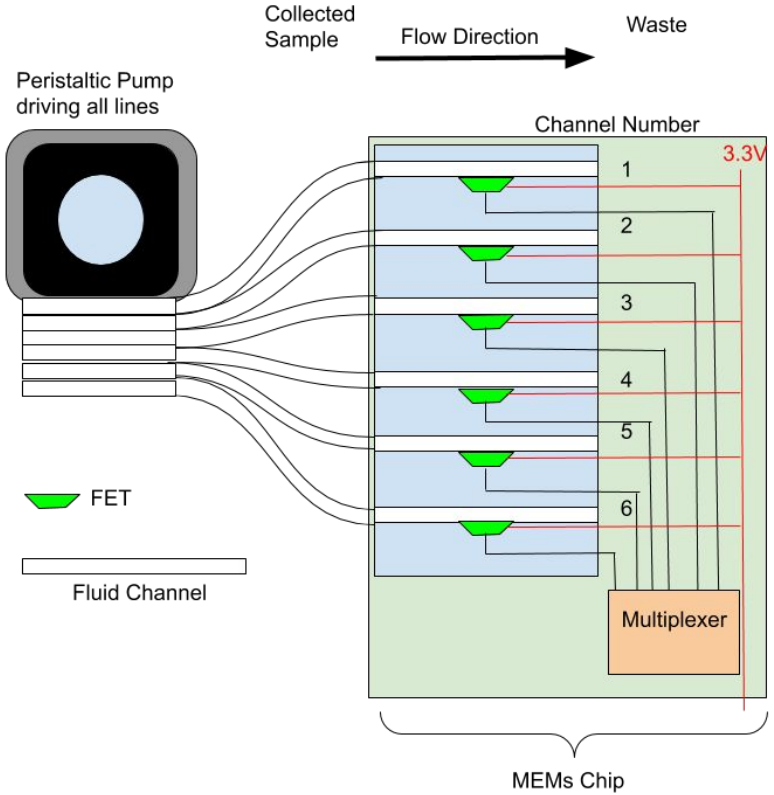
[8]

High-Throughput Format: Electrical Output

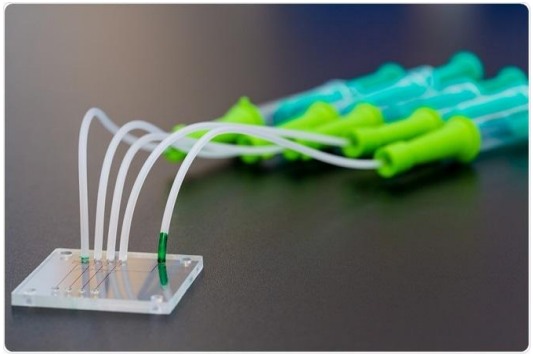
- Allows selection of which sensor is being read at a given time
- Use of multiplexer to require 8 content points with a computer rather than 128
  - 1 Output
  - 7 Input
- Scalable
- Existing tech can be applied



High-Throughput Format: Fluid Delivery



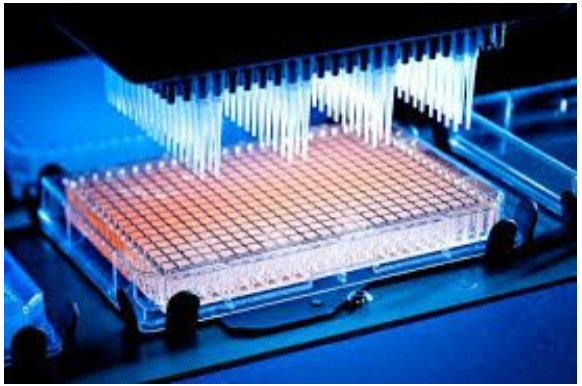
- Tubing from collected samples attached to chip
- Flow provided by external pump
- 128 total lines



Innovation

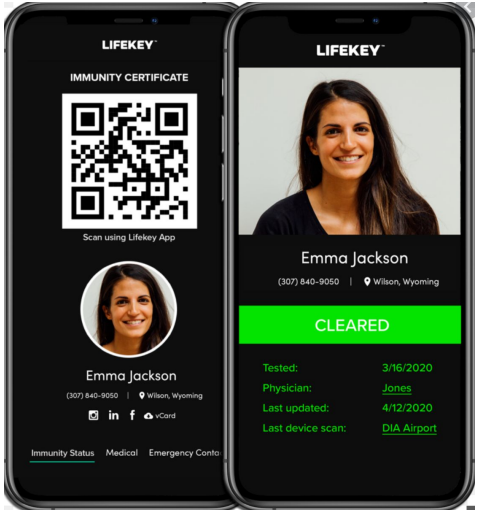
- High-throughput technology allows testing thousands of patient samples at once

- <8 minutes per batch

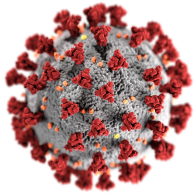


Benefits

- Rapid high-throughput testing allows for mass testing.
- Allows us to determine spread and population immunity
- Minimize travel delays if immunity requirement is implemented



Summary



- We proposed a high-throughput aptamer-based antibody sensing device
- Signal is transduced by voltage generated across an FET transistor
- Useful for identifying who has COVID-19 immunity at a population scale

Resources

1. “What You Need to Know About Coronavirus Disease 2019 (COVID-19).” Centers for Disease Control and Prevention, 8 Apr. 2020, www.cdc.gov/coronavirus/2019-ncov/communication/factsheets.html.
2. “Coronavirus Cases: Live Update.” *Worldometer*, 2020, www.worldometers.info/coronavirus/.
3. “Clinical Specimens: Novel Coronavirus (2019-NCoV).” Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 8 Apr. 2020, www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html.
4. Li, Zhengtu, et al. “Development and Clinical Application of a Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis.” *Wiley Online Library*, John Wiley & Sons, Ltd, 13 Apr. 2020, onlinelibrary.wiley.com/doi/full/10.1002/jmv.25727?casa_token=Ylp9EtaDoj8AAAAA%3AiyotiL5aU5c3Pplk2PFZUqnTuw0rvxqLGcMnmTgK5z3fnBUo64Juqps8k5mSqElAYq6sqqaJvtX7Lg.
5. Yuan, M., Wu, N., Zhu, X., Lee, C., So, R., & Lv, H. et al. (2020). A highly conserved cryptic epitope in the receptor-binding domains of SARS-CoV-2 and SARS-CoV. *Science*, eabb7269.
6. Kaiser, L., Weisser, J., Kohl, M., & Deigner, H. (2018). Small molecule detection with aptamer based lateral flow assays: Applying aptamer-C-reactive protein cross-recognition for ampicillin detection. *Scientific Reports*, *8*(1).
7. Ren, Y., Huang, S., Mosser, S., Heuschkel, M., Bertsch, A., & Fraering, P. et al. (2015). A Simple and Reliable PDMS and SU-8 Irreversible Bonding Method and Its Application on a Microfluidic-MEA Device for Neuroscience Research. *Micromachines*, *6*(12), 1923-1934.
8. H. Chen, J. Huang, A. Palaniappan, Y. Wang, B. Liedberg, M. Platt, and A. ling Yoong Tok, “A review on electronic bio-sensing approaches based on non-antibody recognition elements,” Royal Society of Chemistry, 2013.
9. N. Gao, T. Gao, X. Yang, X. Dai, W. Zhou, A. Zhang, and C. M. Lieber, “Specific detection of biomolecules in physiological solutions using graphene transistor biosensors,” Proceedings of the National Academy of Science of the United States of America, vol. 113, no. 15, Dec. 2016.