

# **BIOMEDICAL** ENGINEERING

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**Carnegie Mellon University**

**2020 Biomedical Engineering  
Summer Undergraduate Research Symposium**

**July 31, 2020  
9:00 AM to 10:30 AM**

### **Biomedical Engineering at Carnegie Mellon University**

Biomedical engineering education at Carnegie Mellon reflects the belief that a top biomedical engineer must be deeply trained in both a traditional engineering practice and biomedical sciences. The unique additional major program leverages extensive collaborations with sister departments in the College of Engineering and with major medical institutions in Pittsburgh. This collaborative approach, combined with a rigorous engineering education, confers unique depth and breadth to the education of Biomedical Engineering graduates.

### **Biomedical Engineering Summer Undergraduate Research Program (BME SURP)**

This program allows students to spend a ten-week period on a project that combines translational research and clinical exposure at a local medical center. Hundreds of students have participated in BME-SURP since its introduction in 1980. The experience has played a major role in helping students choose their career paths and obtain positions in industrial or academia. This program is supported by grants from the CMU College of Engineering. This program is supported by grants from the CMU College of Engineering and the CMU University Research Office (URO).

### **Presentation Schedule**

9 to 9:15: Lynn Rushkin

9:15 to 9:30: Dilara Ozdoganlar

9:30 to 9:45: Madeline Davis

9:45 to 10:00: Daniel Thomeer

10:00 to 10:15: Rylee Wayand

## Mathematical Modelling of Urea Transport Across a Hollow Fiber Dialyzer

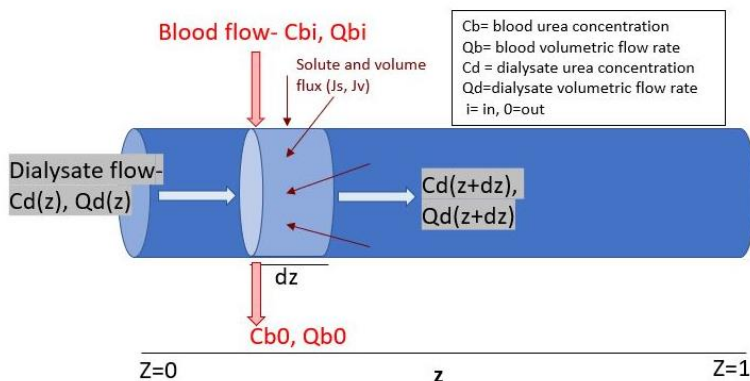
Lynn Rushkin, Keith Cook

Carnegie Mellon University, Pittsburgh PA

**Introduction:** The development of a wearable artificial kidney (WAK) would drastically improve the quality of life for patients with chronic kidney disease on dialysis<sup>2</sup>. Most WAKs being developed are a smaller version of a conventional dialysis circuit, which includes a hollow fiber dialyzer that uses countercurrent flow of blood and dialysate where blood flows inside hollow fiber capillaries and dialysate flows outside. This project aims to increase urea transport by utilizing cross-current flow with blood flowing external to the dialyzer fibers. In this study, a mathematical model of urea transport specific to this dialyzer design was developed so that the concentration profile of urea across a fiber can be predicted theoretically.

**Materials and Methods:** Carnegie Mellon University Library databases were used to perform a literature search on existing mathematical models for solute transport in hemodialysis. Applicable equations for urea transport across a single fiber of a hemodialyzer with external and cross current blood flow were synthesized into a preliminary mathematical model. MATLAB was used for initial simulations of the model.

**Results:** The One-Dimensional Theory of Hemodialysis, which includes the Kedem-Katchalsky equations for volume and solute flux across a membrane was found to be a commonly applied model for countercurrent flow in a flat plate dialyzer<sup>3</sup>. These equations assume transport properties are constant across the membrane and neglects the effect of boundary layers at the borders of the membrane. This simplified model works best for small solutes. These equations were adapted to model concentration and volume profiles across the length of a single fiber for a dialyzer with cross current, external blood flow:



Correlations of the Sherwood, Reynolds and

Schmitt numbers have been developed to determine the mass transport coefficients across boundary layers surrounding the membrane on the dialysate and blood side of the dialyzer. These correlations were used to solve for the mass transport coefficient and subsequently the mass flux at the boundary layers. One correlation was found for laminar, parallel flow which can be applied to the dialysate flow and another correlation can be applied for the blood side correlation as it assumes orthogonal flow outside fibers<sup>1</sup>.

**Conclusion:** A mathematical framework was developed for modeling urea transport in an external blood cross flow dialyzer with and without boundary conditions. The next step for this study is to compare predicted urea transport with and without boundary conditions using MATLAB.

### References:

- [1] Fukuda M, Namekawa K, Sakai K. Identical Dependence of Dialysate-side Mass Transfer Coefficient on Reynolds Number Using Dimensionless Correlation Based on the Mass Transfer Model in Newly Developed Dialyzers and a Downsized Dialyzer. *Advanced Biomedical Engineering*. 2016. 5:118-123. doi:10.14326/abe.5.118.
- [2] Salani M, Roy S, Fissell WH 4th. Innovations in Wearable and Implantable Artificial Kidneys. *Am J Kidney Dis*. 2018;72(5):745-751. doi:10.1053/j.ajkd.2018.06.005
- [3] Waniewski J. Mathematical modeling of fluid and solute transport in hemodialysis and peritoneal dialysis. *Journal of Membrane Science*. 2006; 274(1-2):24-27. doi:10.1016/j.memsci.2005.11.038.

## **Biotechnology for COVID-19 Diagnosis**

Authors: Dilara Ozdoganlar, Anushree Gupta, Kaylee Liang, Siyang Zheng, PhD.

**Introduction:** Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The recent outbreak has been classified as a global pandemic by the World Health Organization (WHO) and there are still no approved drugs or vaccines available for the disease. As a result, early detection and diagnosis is crucial to managing and containing the outbreak. Emerging biosensors and other biotechnologies present many opportunities for improving SARS-CoV-2 detection by providing faster, cheaper, and more accurate alternatives to the current gold standards. In this context, we review the most promising emerging technologies for COVID-19 diagnostics and highlight current challenges hindering the implementation of these devices.

**Materials and Methods:** To produce a thorough and relevant literature review, ample research and background knowledge is necessary. Every week each team member read 4-5 published or preprint papers regarding current biotechnology related to COVID-19 diagnostics and prepared a presentation outlining the motivation, results, and conclusions of each paper. Weekly meetings were held in order to discuss and evaluate the quality and pertinence of each paper. Conflicting and corresponding evidence across literature sources were identified and data were re-organized in an understandable manner. In the end, over 120 papers will have been reviewed and discussed to produce a comprehensive summary and synthesis in a publishable format.

**Results and Discussion:** We are continuing the review and critical analysis process and have already collected an abundance of results through the papers analyzed so far. Our literature reviews indicate that nucleic acid detection technologies and immunoassays are the most common methods used and researched for COVID-19 diagnostics. We have also analyzed additional technologies related to COVID-19 diagnostics including new biosensors, SARS-CoV-2 fecal viral activity, water research, and infection classifiers. Each of these additional technologies provides new ways to evaluate the spread of pandemics. It can also be seen that certain avenues, including CRISPR-Cas12- based detection and the Wantai Ig serological assay, are more popular and effective than others. We have identified some of the most important considerations for these biotechnologies including sensitivity, specificity, positive and negative predictive values (PPV & NPV), qualitative versus quantitative results, cost, speed, accuracy, and mass manufacturing capabilities.

**Conclusions:** Emerging biotechnologies such as biosensors, immunoassays, and nucleic acid detection methods, are innovative and promising tools that have the potential to be lifesaving during pandemics. Especially during the COVID-19 pandemic, the development of highly sensitive and rapid diagnostic tools has become increasingly important. This literature review serves to provide a comprehensive summary and synthesis of the most important information regarding these tools to help expedite various elements of diagnostics research. This research is not only pertinent to the current pandemic but will also be imperative in improving outcomes for future pandemics by providing faster and more accurate testing mechanisms that contribute to better containment and management of infections.

**Acknowledgements:** I would like to thank Dr. Zheng for guiding me through this project. I would also like to thank students Anushree Gupta and Kaylee Liang who I am working with to complete this literature review.

### **References:**

Giwan Seo, ACS Nano 2020, 14, 535-5142  
James P. Broughton, Nature Biotechnology 2020, 38, 870-847

## Methods for Neural Spike Data Visualisation

### Introduction

High Density Neural Recordings provide insight into the function and formation of neural circuits, particularly to understand brain function and dysfunction in the context of neurological disorders.

In the presence of stimuli, neurons communicate via patterns of action potentials or spikes. In an experimental context, these spikes can be detected as patterns of electrical activity via an implantable recording electrode. The characteristic pattern of a neural action potential, called a waveform, is determined by the neuron cell type and location. Spike sorting algorithms can be used to cluster spikes with similar waveforms in order to isolate and classify the activity of a single neuron. Current methods to visualise raw neural data and isolated waveforms involve manual curation by a trained electrophysiologist. Oftentimes, this time-consuming analysis can only be performed after-the-fact, so experimental procedures cannot be changed based on the data in real-time. This project aims to improve neural data visualisation methods achievable in real-time by automating the plotting of filtered/sorted neural waveforms and exploring the data visualization of real-time neural data.

### Methods and Materials

The data analysis and software construction was completed using Python 3.7.2 and Scipy 1.2.1. The electrophysiological data sampled was collected from rodent cortical spheroids utilising microelectrodes modified with PEDOT:PSS, and Intan Acquisition software.

#### Automated Waveform Plotting Function

Prior to use in the automated plotting project, the SpikeInterface Library and MountainSort4 algorithm were applied to the raw neural data to automatically detect and sort spikes without manual curation. Additionally the data was filtered in the frequency domain to remove unwanted artefacts.

#### Real Time Neural Data Visualiser

Raw neural data was processed from Intan .rhd files and displayed utilising the GUI development module PyQt 5.15.0 and its associated plotting package pyqtgraph 0.11.0. This data was used for testing during the development of the software, however the programs are designed to be compatible with real-time acquisition using an Intan neural recording amplifier system.

### Results

#### Automated Waveform Plotting Function

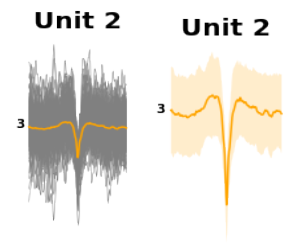
Neural Waveforms were displayed using overlaid plots of different occurrences of waveform, as well as the average waveform shape. The first iteration enabled the user to sort plots by specific microelectrode channels and units (neurons), as well as specified the number of waveforms displayed. The utilisation of SciPy libraries permitted faster visualisation than pre-existing functions built into spike sorting packages.

Furthermore, a custom option was added to display the standard deviation of the occurrences. Additionally, the visualisation was augmented to reject outlier waveforms. The neural data was filtered by calculating the maximum error for each waveform occurrence to establish a threshold to remove data several standard deviations outside this limit.

#### Real Time Visualiser

PyQt was used to build a desktop application displaying the variation in amplitude values of neural recordings in real-time to allow the quality of neural data to be assessed as it is recorded.

The application extrapolates raw neural data and plots 30,000 samples of raw neural data per second across multiple electrode channels. Additionally, playback controls were incorporated, allowing the user to play, pause, rewind and skip through the data, as well as change display speed. An event detection module was added to permit users to isolate repeating instances of specific neural waveforms by setting custom threshold and sample size parameters.



*Figure 1: Automated waveform plot of Glutamate-induced activity of a cortical neuron. Left – Plot of 700 random occurrences with average. Right – Plot of Standard Deviation*

### **Conclusion and Future Work**

The project adequately demonstrated several methods to automate and improve the visualisation of sorted and raw neural data. The automated waveform plotting function provided a novel approach to comparing waveform characteristics of different neurons and allowed custom neural data figures to be generated efficiently for use in research papers. Likewise, the real-time neural data visualiser will improve the ability of researchers to assess the quality of neural data. In the future, further capabilities will be incorporated into the real-time data visualiser including frequency-domain filtering techniques, and additionally module that plots signal to noise ratio. The GUI functionality will be expanded to allow more in-depth interactive data exploration in real time.

### **Acknowledgements**

I would like to thank my graduate student advisor Jay Reddy and Maysam Chamanzar for their invaluable guidance and support throughout the duration of the project. I would also like to thank the Carnegie Mellon BME department for providing funding and resources.

## **Effects of Wind Shear on Plants**

Authors: Daniel Thomeer (Cook Lab)

**Introduction:** Polycarboxybetaine (PCB) surface coatings using 3,4-dihydroxyphenylalanine (DOPA) surface linkages are used in artificial lungs to reduce protein adsorption, platelet adhesion, and clot formation. However, with flowing blood, the coating does not reach its full potential due to shear induced degradation. The flow of blood over the coating is similar to wind flow over crops. Therefore, an investigation was conducted into how height of crops and planting density affect shear stress on plants. The goal of this investigation is to determine if any structural changes to the surface coating might help to reduce shear stress and possibly improve function.

**Materials and Methods:** In order to examine the wind shear on plants previous studies were examined to learn any trends and data that could be useful for the current investigation.

**Results and Discussion:** Results of the research show shear stress increases with the height with the maximum shear stress at the top of the plant. A mathematical model derived to calculate shear stress profiles. The results of the calculations show the relative shear stress versus the relative height of the plant, therefore while it shows general trends it does not explicitly show how shear stress changes due to changing heights of plants. Although mechanically it does make sense that a shorter plant would experience less shearing than a taller one. Two experiments conducted in wind tunnels confirm and expand on the mathematical model. The first again shows the shear stress increasing with height. The second experiment examined looks to explore the effect of density more clearly. This experiment shows the surface shear stress around a small circular patch of grass cut to the same length. The results show that perpendicular to the direction of flow there is little variation on the surface shear. However, in the direction of flow on the surface in front of and especially behind the plant, the surface shear stress drops. This suggests that while little effect would be expected when changing planting density in the direction perpendicular to flow, increasing planting density in the direction of flow would decrease the shear stress on the plants.

**Conclusion:** As expected, the results of this examination showed that wind shear on plants increases along the height of the plant. This would mean there is a similar effect on the surface coating due to blood flow shear, meaning the highest shear stress is along the top of the PCB coating. Additionally, while it was unable to be shown explicitly that a shorter height leads to a lower shear, it appears to be a relatively good assumption from the data. Finally, increasing planting density in the direction of flow would also decrease shear on the plants. These findings are a step in the right direction in order to make a more efficient PCB coating that functions better under blood shear. However, more studies are needed with the coating itself to be able to optimize the length and surface density of the coating for maximum functionality.

## **References:**

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- Seginer, I., et al., *Boundary-Layer Meteorology* (1976) 10.4: 423-453
- Walter, et al. *Boundary-layer meteorology* (2012) 144.2 : 217-241

## Effects of Subjected Patient Population on Cardiovascular Diagnostic Testing

Authors: Rylee Wayand (Carnegie Mellon University), Mark Doyle (Allegheny General Hospital)

**Introduction:** Heart disease is the number one cause of death in the United States, with over 12% of the adult population<sup>1</sup> diagnosed with heart disease and over 6.5 million people reporting to emergency rooms with chest pain in a year<sup>2</sup>. With such a large effect on the American population, it's important to be able to diagnose heart diseases and the level of blockage in the coronary arteries with high accuracy. However, the patient population subjected to these diagnostic tests can change how accurate the tests are and should be considered carefully so as to minimize false positive and false negative rates. We hypothesize that the usage of older tests become less accurate over time, as the risk level of patients subjected to these tests is not sufficiently considered. Bayes theorem provides a solution to avoid testing an excessive number of low-risk patients in diagnostic tests.

**Methods:** Baseline data from the ISCHEMIA trial was used as it reflects current usage of diagnostic tests in ischemic heart disease. In the ISCHEMIA trial, patients were tested for a moderate to severe level of ischemia and excluded if left-main coronary artery disease was present or if level of ischemia was not of sufficient intensity to allow randomization. Patients were first tested with either 1) nuclear stress test, 2) echo stress test, or 3) cardiac magnetic resonance imaging (CMR) myocardial perfusion imaging. Following this entry test they were all tested with coronary computed tomography, so as to reject patients not suitable for the trial. Percentage of patients rejected from each test was examined and compared to the age of the test.

**Results:** 33% of patients subjected to nuclear stress tests were rejected, 39% of those subjected to echo stress tests were rejected, and 17% of those subjected to CMR were rejected (Figure 1). The nuclear is the oldest, closely followed by echo, with CMR being about two decades younger. There is a significant difference between the percent of patients rejected between the nuclear and echo tests compared to CMR. This result aligns with our hypothesis that the older a test is, the less accurate it becomes, as both nuclear and echo tests are older than CMR. There is a slight difference between nuclear and echo stress tests (33% v. 39% rejected) that disagrees with our hypothesis (the nuclear stress test is the oldest test).

**Conclusions:** The adverse effect of subjected patient populations on diagnostic test accuracy can be improved by using Bayes theorem with patient data. If Bayes theorem is applied to patient symptom data and other tests performed, diagnostic tests can be applied to a more specific and relevant patient population. Limiting the number of low-risk patients who are subjected to these diagnostic tests will reduce the adverse effect on test accuracy. To implement Bayes in more clinical settings, education of healthcare professionals is necessary. Future study is required to examine the full effect that Bayes theorem can have when used on patients. Ideally, studies actually limiting the patient population subjected to these tests, and further exploring effects on patients and diagnostic tests will be conducted.

### References:

1. Villarroel MA, Blackwell DL, Jen A. Tables of Summary Health Statistics for U.S. Adults: 2018 National Health Interview Survey. National Center for Health Statistics. 2019. Available from: <http://www.cdc.gov/nchs/nhis/SHS/tables.htm>.
2. Rui P, Kang K. National Hospital Ambulatory Medical Care Survey: 2017 emergency department summary tables. National Center for Health Statistics. Available from: [https://www.cdc.gov/nchs/data/nhamcs/web\\_tables/2017\\_ed\\_web\\_tables-508.pdf](https://www.cdc.gov/nchs/data/nhamcs/web_tables/2017_ed_web_tables-508.pdf).