Customized 3D Printing of Live Cells for Novel Bio-Circuitry

Emily E. Scrupps
Advanced STEM Research Laboratory, Odessa High School, Odessa, WA, 99159

Abstract

The revolutionized biomedical industry has a deep connection with the utilization of synthetic biology, to create multi-functional, complex but minimalistic, non-invasive biomedical devices. Bioelectronics have constructed new methods to monitor activity of cells and tissues that will likely advance the medical field to monitor the human body. As a new industry, bio-circuits are faced with emerging problems, this research is focused on the inability to construct and test circuits. This research proposes the implementation of a 3D printer to accurately produce the complexity of a biosensor. The engineering goal was to print 3 dimensional algal biological circuits that would conduct electricity at a 0.4% recovery rate of the controlled circuits voltage. Petroleum based ink cartridges represented the controlled group while being compared to algal bio-ink representing the experimental group. Each ink was printed onto a transparent film sheet and tested for electrical conductivity using a multimeter. The controlled data averaged 28.16mV, 26.77mV, and 5.57mV for one layer and the experimental data averaged 0.1mV, 0.1mV, and 0.0mV for one layer. The experimental data had an average numerical increase of y=3E-5x. With an equalization point at 28.16mV. The algal bio-ink will need 933.33 layers creating a 2.799mm algal layer. The circuit was engineered out of algae which meant that the goal of engineering a completely biological circuit was met. The engineering goal was achieved because the experimental group was able to produce a 0.4% recovery rate as compared to the controlled circuit group.

Research Question

The problem that was chosen to target is the inability to construct and test circuits. The construction of circuits has to be described as complex but in a simple manner; complex in the contents of the biosensors design but created in a simple and attainable procedure.

Engineering Goal

The experimental goal of this project was to have a 99.1% compatibility between both sets of data. The data would be compared using a two tailed TTest to ensure that the compatibility of the data is correct. The 99.1% accuracy ensures that medically there is a difference between the two data sets.

Introduction / Background Research

The revolutionized biomedical industry has a deep connection with the utilization of synthetic biology, to create multi-functional, complex but minimalistic, non-invasive biomedical devices. These devices have created a revolution in medicine to find new ways to solve a situation with minimal invasion and have it serve many functions while it is being used [1]. Many early devices such as the first novel glucose monitor which uses principles of thermal emission spectroscopy to demonstrate glucose measurements with clinically acceptable accuracy, created an even better solution by changing one very like daily calibration[2]. These small but important changes have produced opportunities for others to solve more recent and advanced problems like using nano-electronic brain probes to overcome the mechanical mismatch between soft tissues and hard electronics. As research continues the biomedical industry can potentially be analyzed as the future for all medicine.

A current medical advancement and an emerging method utilizes mathematically advanced optimization of biological circuits or bio-circuits[3]. Bioelectronics have created new ways to monitor the activity of cells and tissues that will likely advance the medical field to monitor anything regarding the human body[4]. These biosensors have begun a new challenge to integrate different modules and create circuits that are progressively more complex. But the problems that synthetic biologists are facing is that each biosensor is rooted with simplistic and uni-functional design flaws, whereas the medical industry needs devices that can carry out multiple functions and produce complex data analysis[5]. This problem on top of two other undisputable problems; the inability to control multiple cellular processes and increasing problems to construct and test circuits, have created a road block for scientists to advance in the bioelectronic field[6].

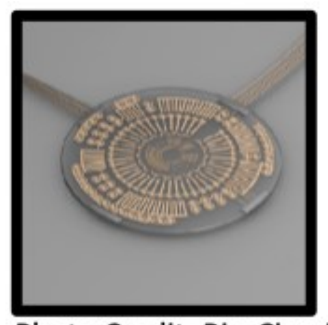
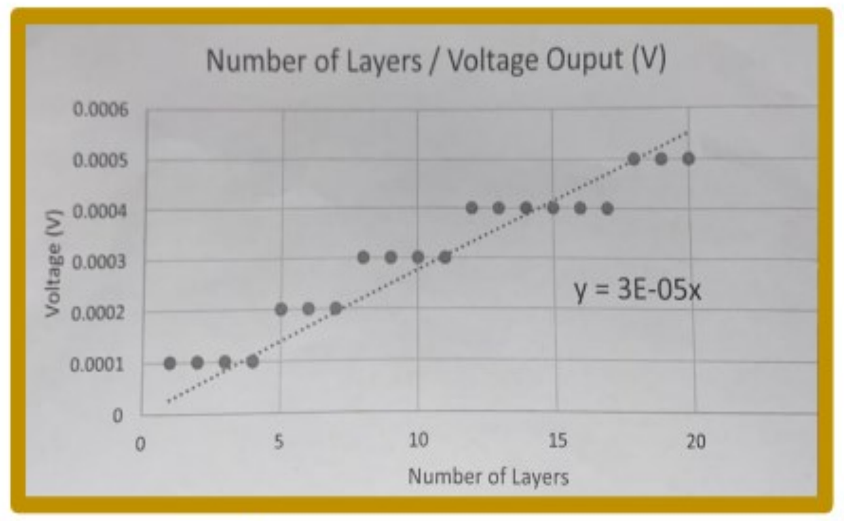



Photo Credit: Bio-Circuit Concept, James Rodney

Photo Credit: *Odessa Record*, 2017

Materials / Methodology

- Bio-Ink Cultivation
- Ink Cartridge Manipulation
- Printer Accuracy Testing
- Circuit Voltage Testing
- Data Analysis

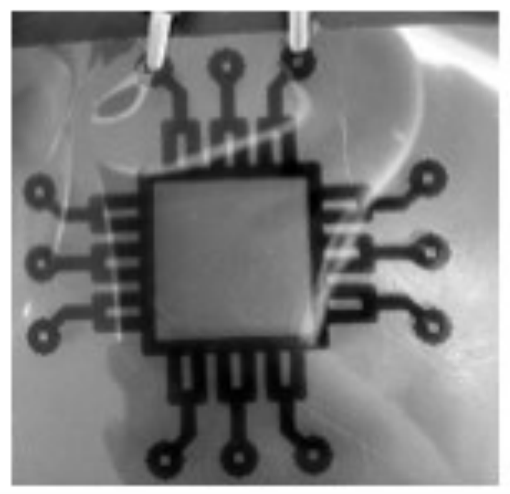





Results

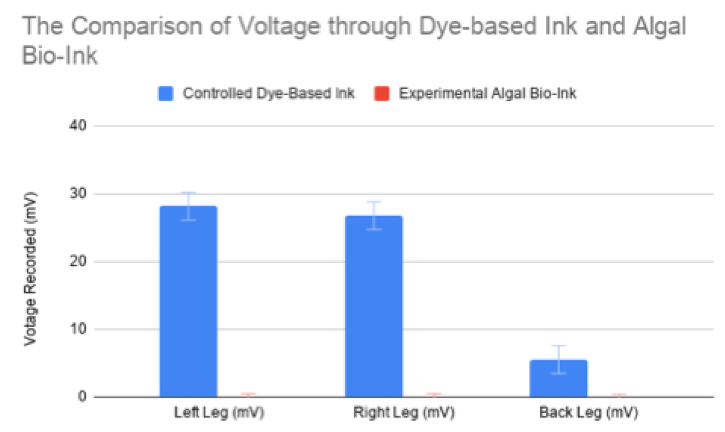
Contolled Group Data (mV) through Dye-Based Ink			
	Left Leg (mV)	Right Leg (mV)	Back Leg (mV)
N	10	10	10
Average	28.16	26.77	5.57
SD±	3.35	2.79	2.042900987

Experimental Group Data (mV) through Biological Ink			
	Left Leg (mV)	Right Leg (mV)	Back Leg (mV)
N	10	10	10
Average	0.1	0.1	0
SD±	0.42	0.03	0

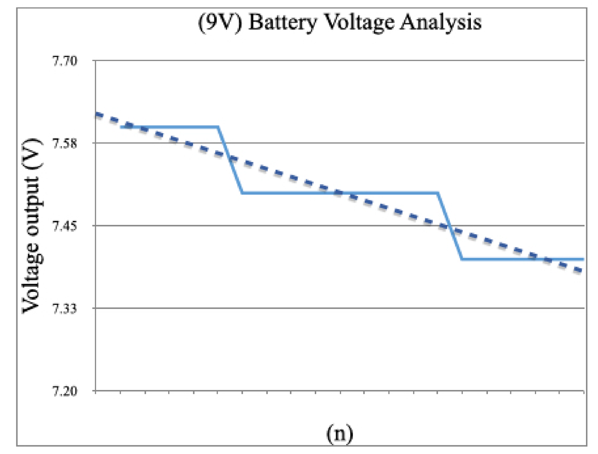


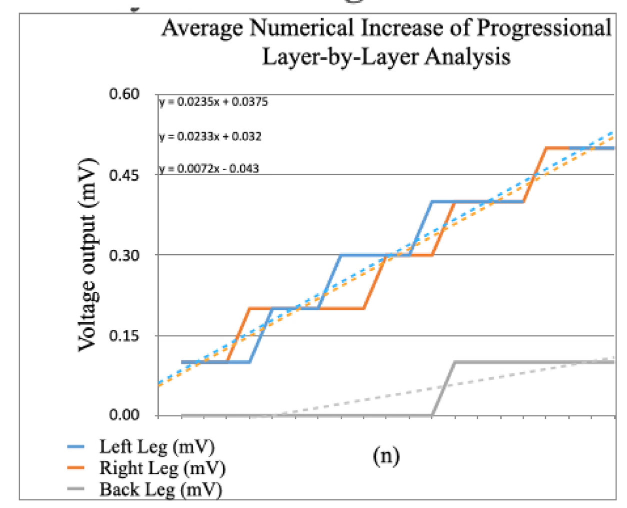

Biological Ink Numerical Increase by Layer				
Layer	Left Leg (mV)	Right Leg (mV)	Back Leg (mV)	Battery (V)
1	0.1	0.1	0	7.6
2	0.1	0.1	0	7.6
3	0.1	0.1	0	7.6
4	0.1	0.2	0	7.6
5	0.2	0.2	0	7.6
6	0.2	0.2	0	7.5
7	0.2	0.2	0	7.5
8	0.3	0.2	0	7.5
9	0.3	0.2	0	7.5
10	0.3	0.3	0	7.5
11	0.3	0.3	0	7.5
12	0.4	0.3	0	7.5
13	0.4	0.4	0.1	7.5
14	0.4	0.4	0.1	7.5
15	0.4	0.4	0.1	7.4
16	0.4	0.4	0.1	7.4
17	0.5	0.5	0.1	7.4
18	0.5	0.5	0.1	7.4
19	0.5	0.5	0.1	7.4
20	0.5	0.5	0.1	7.4

Discussion



- **Engineering Goal**
  - **Accepted**
  - **0.4% Recovery**
- **TTEST: 7.9465e-10**
  - **99.9% Confidence Interval**
  - **Two tailed T-TEST**
  - **p < .001**
  - **18 Degrees of Freedom**

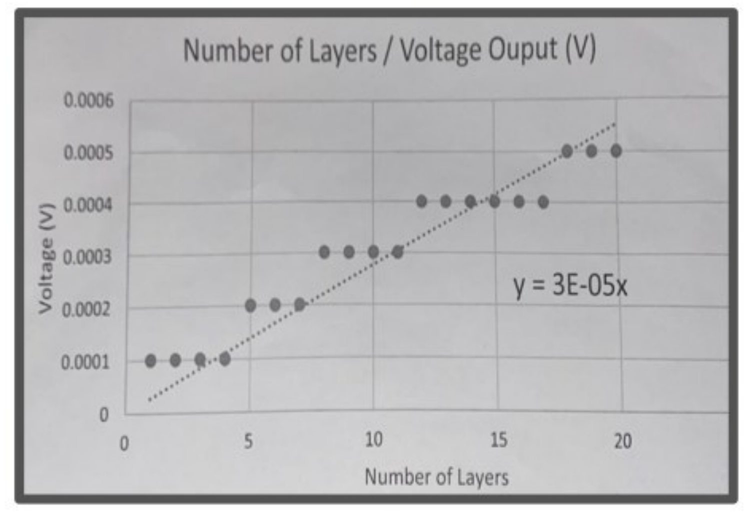




Conclusions

Engineering Goal
- Accepted (0.4% Recovery)

Layer-by-Layer Analysis
- Increasing at a rate of Y=3E-.05X



Equalization Points between the Controlled and Experimental Population				
Leg	Controlled Layers	Experimental Layers	Equalization Point	Algae Equalization Size
Left	1	933.33	28.16mV	2.79999mm
Right	1	892.33	26.77mV	2.67699mm

Future Study

- Growth analysis of printed Bio-Circuits
- Photosynthetic analysis
- Decreasing the size
- Professional laboratory
- Utilization of a hydrogel

Photo Credit: celllink.com [12]

Literature Cited / References

McDermott KW (IBM Watson Health), Freeman WJ (AHRQ), Elixhauser A (AHRQ). Overview of Operating Room Procedures During Inpatient Stays in U.S. Hospitals, 2014. HCUP Statistical Brief #233. December 2017. Agency for Healthcare Research and Quality, Rockville, MD

Sandra I. Berríos-Torres, MD1; Craig A. Umscheid, MD, MSCE2. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, JAMA Surg. 2017;152 (8):784-791. doi:10.1001/jamasurg.2017.0904

"Preventing Surgical Site Infections" The StayWell Company, LLC. Yardley, PA. Retrieved from: https://www.fairview.org/patient-education/89221

Harold C. Neu: The Crisis in Antibiotic Resistance, Science August 21, 1992: Vol. 257, Issue 5073, pp. 1064-1073. DOI: 10.1126/science.257.5073.1064

Solomon SL, Oliver KB. Antibiotic resistance threats in the United States: stepping back from the brink. Am Fam Physician. 2014 Jun 15;89(12):938-41. PMID: 25162160.

Noel, S.P., Courtney, H., Bumgardner, J.D. et al. Chitosan Films: A Potential Local Drug Delivery System for Antibiotics. Clin Orthop Relat Res 466, 1377–1382 (2008). https://doi.org/10.1007/s11999-008-0228-1

Takeuchi, Hirofumi. Yakugaku zasshi : Journal of the Pharmaceutical Society of Japan vol. 140,8 (2020): 1013-1024. doi:10.1248/yakushi.20-00011

Dellinger EP, Gross PA, Barrett TL, et al. Quality Standard for antimicrobial prophylaxis in surgical procedures. Clin Infect Dis 1994; 18: 422–7

Plager, Jessica; Mancini, Christian; Shenoy, Erica; Melnitchouk, Serguei; Collier, Laura; et al.Journal of Allergy and Clinical Immunology; St. Louis Vol. 145, Iss. 2,

Shah, Eric D. MD, MBA1; Hernandez-Barco, Yasmin G. MD2; Beck, Kendall R. MD3; Levy, Benjamin H. III MD4; ACG FDA-Related Matters Committee The American Journal of Gastroenterology: September 2020 - Volume 115 - Issue 9 - p 1351-1352

Mio Endo, Ryohei Hirano, Hiromi Shibasaki, AkitomoYokokawa, Midazolam Intoxication in a Premature Neonate Clinical Therapeutics, Volume 42, Issue 5, 2020, pp. 946-951