Automated Ball Launcher for Alleviation of Pet Canine Separation Anxiety

Applications of Bioelectrical Programming of Cell Morphology in Cancer Treatment: A Prediction of Societal Influence on Bioelectrical Applications for Cancer Treatment

A Thesis Prospectus
In STS 4500
Presented to
The Faculty of the
School of Engineering and Applied Science
University of Virginia
In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Electrical Engineering

By
Alexander Byrd

November 1, 2021

Andrew Childers, Ji Sun Hong, Alexander Byrd, Hayden Sarpong, Austin Turner

On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

ADVISORS

Bryn Seabrook, Department of Engineering and Society

Harry Powell, Department Electrical and Computer Engineering

Introduction:

Regenerative abilities to heal any wound, remodel any deformed feature, and replace any lost appendage have long been powers exclusive to comic book characters and a select few organisms, but what if such a power was lying dormant within every complex life form? We can already regenerate lost skin, heal bruises, and close cuts; however, repairing more complex structures has one major complication: the potential to cause cancer. The morphology of a group of cells characterizes its geometric organization and is maintained, and regenerated, through the exchange of bioelectrical signals within the cell group and with neighboring cellular systems (Levin, 2021). Cancer can be modeled as the manifestation of a morphology that does not properly communicate with any cells outside of the tumor (Chernet, 2013). Recent discoveries indicate the potential for certain bioelectric signals to treat cancer by reintegrating the tumor into neighboring morphologies (Levin, 2021). The STS research project aims to predict how factors within the scientific, medical, and broader communities will influence the development of bioelectrical methods to manipulate cell morphology for cancer treatment.

During Covid-19 pandemic, pet dogs spent most of quarantine in the company of their owners, but now that quarantine is lifted pet dogs will be subject to emotional pain induced by the sudden drop in attention and time with their owners (Jezierski et al, 2021; Martos Martinez-Caj, 2021). The goal of the technical project is to alleviate separation induced emotional pain experienced by dogs through the production of an automated ball launcher to play fetch with the dog while its owner is away. The capstone project is motivated by a strong affection towards pets and an interests in gaining hands on experience designing a machine that incorporates motors.

Both the STS research project and the technical project are motivated by a curiosity to explore applications of electrical engineering outside of my field of expertise and by a desire to provide people with new methods of alleviating unnecessary suffering of their loved ones.

Technical Topic (Capstone):

The end of quarantine poses a new risk for the mental health of pet dogs within the United States. Quarantine altered the behavior of pet dogs in a manner that indicates increased dependence upon attention from their owners (Jezierski et al, 2021). Separation from their owners due to the end of quarantine subjects pet dogs to an increase in separation induced anxiety (Martos Martinez-Caj, 2021). The American Kennel Club recommends that as a general guideline, most dogs need at least two hours of social time with either humans or other dogs every day (Kearl, 2019). While two hours seems like a manageable amount the busy nature of life sometimes makes it difficult to achieve this daily necessity for your pet, which can lead to problems at home. Dogs with too much alone time may be destructive, pace or pant uncontrollably, urinate or defecate in the house or excessively bark or howl due to boredom, lack of social stimulation, incomplete training, or more serious conditions like separation anxiety ("Separation Anxiety"). Studies on the behavior shaping methods for dogs indicates that automated devices can have a positive effect for reducing stress in dogs (Mundell, 2020). Therefore, this capstone project aims to design an automated ball launcher capable of playing fetch with a dog while its owner is away.

The automated ball launcher will incorporate analog and digital circuit design, embedded software development, electromechanical energy conversion, closed loop control circuitry, CAD design techniques, Bluetooth communication protocols, and web service design. The chassis of the ball launcher will be designed in CAD; it will consist of a launching tube for the ball to exit, a funnel for the god to return the ball into, a detached base to allow for rotation, and a main body responsible for housing the motors and circuitry. Electromechanical energy conversion will be

implemented to power and control the two motors responsible for launching the ball and the servo responsible for rotating the launcher. Analog circuitry will be implemented in the form of filters to reduce electrical noise in the circuit produced by the motors and circuitry to prevent unintended electrostatic build up on the analog circuit components, such as the capacitors. A Printed Circuit Board, or PCB, will be responsible for distributing power from a wall adapter to the electronics within the device as well as connecting the components to the microcontroller. The microcontroller will be responsible for controlling the speed of the motors, the direction the launcher is facing, when the ball is launched, and storing data from the user-tailored schedule. Personal devices will then connect over Bluetooth with the automated ball launcher via an amazon web service application, which allows the user to enter the range of distance and direction they'd like the ball to launch, the variation between launches, the period over which it will launch, and the frequency of ball launches. The range and variation of distance and direction between launches provides a controlled sense of variability aimed to keep the dog engaged instead of boring it with the repetitive launch of the ball in a predictable location.

STS Topic:

The ability for complex organisms to repair or replace damaged cellular structures in their body implies that something within the body recognizes the injury, replaces the missing cells, and knows once it has completed rebuilding the structure. The structure, shape, orientation, and location that cells arrange themselves into is referred to as their morphology, which also usually indicates the functionality of those cells (Levin, 2021). Previous studies have identified that all cells, not just neural cells, communicate with each other through bioelectric signals (Blackiston et al, 2009). Therefore, it is implied that all cells can create networks analogous to neural networks, which will be referred to as bioelectrical network in the context of non-neural

cells. The state of a cell within a bioelectrical network is partially represented by its membrane potential, and bioelectrical signals between cells is observed through the flow of ions between them. Evidence suggests that bioelectrical networks are responsible for how cells know their current morphology, intended morphology, and how to approach the intended morphology (Pinet et al, 2019). Furthermore, it has been identified that a cells' intended morphology can be altered by manipulating the bioelectrical signals within a bioelectrical network (Yang et al, 2020).

A novel way to view cancer is not just as a malfunctioning cell, but as a cell that rejects the network it was a part of and attempts to produce a new one. Tumors essentially act like a separate organism from the one they were once a part of. Since cancer cells no longer share a morphology with their previous bioelectrical network, they can often be identified by irregularities in their membrane potential (Kuwahara et al, 2021). Experiments have also shown that introducing certain bioelectrical signals to cancerous cells can inhibit their proliferation (Lansu, 2013). Additionally, it has been observed introduction of bioelectrical signals to cancerous cells can cause the cancerous cells to reintegrate, or normalize, into the organism they previously diverged from (Chernet, 2013). A more disturbing discovery Chernet made was that some electrical signals could induce cancer in previously healthy cells, or force cells neighboring a tumor into joining it rather than vice versa. This obviously poses safety concerns, but the prospect of treating cancer cells without needing significant radiation or surgery is still very promising.

The examination of bioelectric treatment of cancer cells will be done through the framework of Social Construction of Technology, or SCOT. The premise of SCOT is that the design process of a technology depends on its social environment and relevant social groups, and that feedback from social groups allows for continual modification of the technology until it

meets the satisfactions of all relevant groups. SCOT was chosen as the framework because its interpretive flexibility component applies well to the young field of bioelectrical research since it will likely be redirected by societal influence as it matures. However, Klein (2001, pp 30-31) critiques that the relevant social groups component of SCOT makes the fallible assumption that all groups contribute equally to the design process. Furthermore, the wider context component of SCOT suffers from the same critique as it adds more social groups to the picture (Klein, 2001, 40-42). However, the relevant social groups component is advantageous for focusing on only groups that intend to utilize bioelectrical research for medical purposes as opposed to algorithm modelling or the production of synthetic lifeforms, which can be addressed in the wider context component.

Research Question:

How will the interests in the scientific and medical communities, as well as the regulatory and ethical concerns of society, influence the development of bioelectrical methods to manipulate cell morphology for cancer treatment?

Research Methods:

The research will be performed primarily through documentary research methods, and then analyzed using literary analysis and historical case studies. The literary analysis will be to examine trends in recent research in applications of bioelectric morphology manipulation, specifically as a means for cancer treatment. Since ongoing research in bioelectric morphology manipulation is not very widely known, the historical case study will provide an approximation for the societal response to this new potential for cancer treatment by analyzing the response society had when other dangerous forms of cancer treatment were widely practiced, such as chemotherapy. Publications in scientific and medical journals that record the observations of

their experiments will be utilized as primary sources; others that elaborate on previous experimental observations will serve as secondary sources for the literary analysis. Documentation of past and present medical practices regarding cancer treatment will be used as secondary sources for the historical case study. Finally, surveys, policies, or reports that indicate society perception and expectation for previously cutting-edge cancer treatments will be analyzed in the historical case study. The keywords for finding research in relevant bioelectric applications will be morphology, bioelectric, membrane voltages, ion channels, cell communication, cell networks, cancer reintegration, endogenous. The keywords for finding information for the historical case study are chemotherapy supportive care, chemotherapy risks, cancer poison, cancer treatment procedures, chemotherapy regulation, etc.

Conclusion:

The capstone project will result in a prototype ball launcher that can launch the ball a configurable distance on a user made schedule. The base of the launcher will allow it to rotate 180 degrees from its starting position to achieve a diverse selection of launch directions. The time when the ball launcher is active, the frequency of the launches, and the direction of launches can be configured in a user made schedule via its amazon web service application. The expected outcome of the STS research project will be a report that predicts the trajectory of ongoing bioelectric research into morphology manipulation for the purposes of cancer treatment. The historical case study will be used to justify expectations of regulatory influence from communities outside of the researchers. Additionally, the ongoing trends with research into bioelectric applications for morphology manipulation will be analyzed to predict the proportion of researchers interested in finding applications useful to cancer treatment.

References:

Amat, Marta, et al. “Separation-Related Problems in Dogs: A Critical Review.” *Advances in Small Animal Care*, vol. 1, Nov. 2020, pp. 1–8. *ScienceDirect*, https://doi.org/10.1016/j.yasa.2020.07.001.

Ashmore, Jonathan, et al. “Wnts Control Membrane Potential in Mammalian Cancer Cells.” *The Journal of Physiology*, vol. 597, no. 24, 2019, pp. 5899–914. *Wiley Online Library*, https://doi.org/10.1113/JP278661.

Bartel, Karin, et al. “V-ATPase Inhibition Increases Cancer Cell Stiffness and Blocks Membrane Related Ras Signaling - a New Option for HCC Therapy.” *Oncotarget*, vol. 8, no. 6, Dec. 2016, pp. 9476–87. *PubMed Central*, https://doi.org/10.18632/oncotarget.14339.

Blackiston, Douglas J., et al. “Bioelectric Controls of Cell Proliferation: Ion Channels, Membrane Voltage and the Cell Cycle.” *Cell Cycle*, vol. 8, no. 21, Taylor & Francis, Nov. 2009, pp. 3527–36. *Taylor and Francis+NEJM*, https://doi.org/10.4161/cc.8.21.9888.

Chernet, Brook, and Michael Levin. “Endogenous Voltage Potentials and the Microenvironment: Bioelectric Signals That Reveal, Induce and Normalize Cancer.” *Journal of Clinical & Experimental Oncology*, vol. Suppl 1, 2013, pp. S1-002. *PubMed Central*, https://doi.org/10.4172/2324-9110.S1-002.

DeVita, Vincent T., and Edward Chu. “A History of Cancer Chemotherapy.” *Cancer Research*, vol. 68, no. 21, American Association for Cancer Research, Nov. 2008, pp. 8643–53. *cancerres.aacrjournals.org*, https://doi.org/10.1158/0008-5472.CAN-07-6611.

Dowsett, Elisha, et al. “Adult Separation Anxiety Disorder: The Human-Animal Bond.” *Journal of Affective Disorders*, vol. 270, June 2020, pp. 90–96. *ScienceDirect*, https://doi.org/10.1016/j.jad.2020.03.147.

Ebrahimkhani, Mo R., and Joshua Hislop, editors. *Programmed Morphogenesis: Methods and Protocols*. Springer US, 2021. *DOI.org (Crossref)*, https://doi.org/10.1007/978-1-0716-1174-6.

Ebrahimkhani, Mo R., and Michael Levin. “Synthetic Living Machines: A New Window on Life.” *IScience*, vol. 24, no. 5, Elsevier, May 2021. *www.cell.com*, https://doi.org/10.1016/j.isci.2021.102505.

Jezierski, Tadeusz, et al. “Changes in the Health and Behaviour of Pet Dogs during the COVID-19 Pandemic as Reported by the Owners.” *Applied Animal Behaviour Science*, vol. 241, Aug. 2021, p. 105395. *ScienceDirect*, https://doi.org/10.1016/j.applanim.2021.105395.

Kearl, Mary. “Alone Time for Dogs: How Much Is Too Much?” *American Kennel Club*, 4 Sept. 2019, https://www.akc.org/expert-advice/training/alone-time-dogs-much-much/.

Klein, Hans K., and Daniel Lee Kleinman. “The Social Construction of Technology: Structural Considerations.” *Science, Technology, & Human Values*, vol. 27, no. 1, SAGE Publications Inc, Jan. 2002, pp. 28–52. *SAGE Journals*, https://doi.org/10.1177/016224390202700102.

Kuwahara, Yoshikazu, et al. “Decreased Mitochondrial Membrane Potential Is an Indicator of Radioresistant Cancer Cells.” *Life Sciences*, vol. 286, Dec. 2021, p. 120051. *ScienceDirect*, https://doi.org/10.1016/j.lfs.2021.120051.

Lansu, K., and S. Gentile. “Potassium Channel Activation Inhibits Proliferation of Breast Cancer Cells by Activating a Senescence Program.” *Cell Death & Disease*, vol. 4, no. 6, June 2013, pp. e652–e652. *www.nature.com*, https://doi.org/10.1038/cddis.2013.174.

Levin, Michael. “Bioelectric Signaling: Reprogrammable Circuits Underlying Embryogenesis, Regeneration, and Cancer.” *Cell*, vol. 184, no. 8, Apr. 2021, pp. 1971–89. *PubMed*, https://doi.org/10.1016/j.cell.2021.02.034.

Martos Martinez-Caj, A., et al. “Pets and Their Owners during the First COVID-19 Lockdown Period: Perceived Changes in Routines and Emotions – an Exploratory Study.” *Journal of Veterinary Behavior*, Oct. 2021. *ScienceDirect*, https://doi.org/10.1016/j.jveb.2021.09.009.

Mundell, Paul, et al. “An Automated Behavior-Shaping Intervention Reduces Signs of Separation Anxiety–Related Distress in a Mixed-Breed Dog.” *Journal of Veterinary Behavior*, vol. 37, May 2020, pp. 71–75. *ScienceDirect*, https://doi.org/10.1016/j.jveb.2020.04.006.

Nanos, Vasilios, and Michael Levin. “Rewiring Endogenous Bioelectric Circuits in the Xenopus Laevis Embryo Model.” *Methods in Molecular Biology (Clifton, N.J.)*, vol. 2258, 2021, pp. 93–103. *PubMed*, https://doi.org/10.1007/978-1-0716-1174-6_7.

Nishimura, Osamu, et al. “Unusually Large Number of Mutations in Asexually Reproducing Clonal Planarian Dugesia Japonica.” *PLOS ONE*, vol. 10, no. 11, Public Library of Science, Nov. 2015, p. e0143525. *PLoS Journals*, https://doi.org/10.1371/journal.pone.0143525.

Pai, Vaibhav P., et al. “Transmembrane Voltage Potential Controls Embryonic Eye Patterning in Xenopus Laevis.” *Development*, vol. 139, no. 2, Jan. 2012, pp. 313–23. *Silverchair*, https://doi.org/10.1242/dev.073759.

Pietak, Alexis M., et al. “Planarian Regeneration as a Model of Anatomical Homeostasis: Recent Progress in Biophysical and Computational Approaches.” *Seminars in Cell & Developmental Biology*, vol. 87, Mar. 2019, pp. 125–44. *ScienceDirect*, https://doi.org/10.1016/j.semcdb.2018.04.003.

Pinet, Kaylinnette, et al. “Adaptive Correction of Craniofacial Defects in Pre-Metamorphic Xenopus Laevis Tadpoles Involves Thyroid Hormone-Independent Tissue Remodeling.” *Development*, vol. 146, no. 14, July 2019. *Silverchair*, https://doi.org/10.1242/dev.175893.

Prehn, R. T. “Cancers Beget Mutations versus Mutations Beget Cancers.” *Cancer Research*, vol. 54, no. 20, Oct. 1994, pp. 5296–300.

Protections (OHRP), Office for Human Research. “Federal Policy for the Protection of Human Subjects ('Common Rule’).” *HHS.Gov*, 23 June 2009, https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html.

Regulski, Matthew J. “Cellular Senescence: What, Why, and How.” *Wounds: A Compendium of Clinical Research and Practice*, vol. 29, no. 6, June 2017, pp. 168–74.

Rose, Christopher S., et al. “Deconstructing Cartilage Shape and Size into Contributions from Embryogenesis, Metamorphosis, and Tadpole and Frog Growth.” *Journal of Anatomy*, vol. 226, no. 6, 2015, pp. 575–95. *Wiley Online Library*, https://doi.org/10.1111/joa.12303.

Rouleau, Nicolas, et al. “Learning and Synaptic Plasticity in 3D Bioengineered Neural Tissues.” *Neuroscience Letters*, vol. 750, Apr. 2021, p. 135799. *ScienceDirect*, https://doi.org/10.1016/j.neulet.2021.135799.

“Separation Anxiety.” *ASPCA*, https://www.aspca.org/pet-care/dog-care/common-dog-behavior-issues/separation-anxiety. Accessed 1 Nov. 2021.

Stephan, Gerrit, et al. “Pet Dogs Home Alone: A Video-Based Study.” *Applied Animal Behaviour Science*, vol. 244, Nov. 2021, p. 105463. *ScienceDirect*, https://doi.org/10.1016/j.applanim.2021.105463.

Vandenberg, Laura N., et al. “Normalized Shape and Location of Perturbed Craniofacial Structures in the Xenopus Tadpole Reveal an Innate Ability to Achieve Correct Morphology.” *Developmental Dynamics*, vol. 241, no. 5, 2012, pp. 863–78. *Wiley Online Library*, https://doi.org/10.1002/dvdy.23770.

Yang, Chih-Yu, et al. “Encoding Membrane-Potential-Based Memory within a Microbial Community.” *Cell Systems*, vol. 10, no. 5, May 2020, pp. 417-423.e3. *ScienceDirect*, https://doi.org/10.1016/j.cels.2020.04.002.