Full-Stack Optimization of a Multi-State Software System to Support Novel Clinical Electroporation Devices

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Introduction: Electroporation

- Electroporation is the targeted delivery of high-voltage fields to a biological area to either permeate or rupture cells
- The effects are reversible or irreversible and can treat inoperable cancers or deliver novel genetic and electrochemical therapies[1]

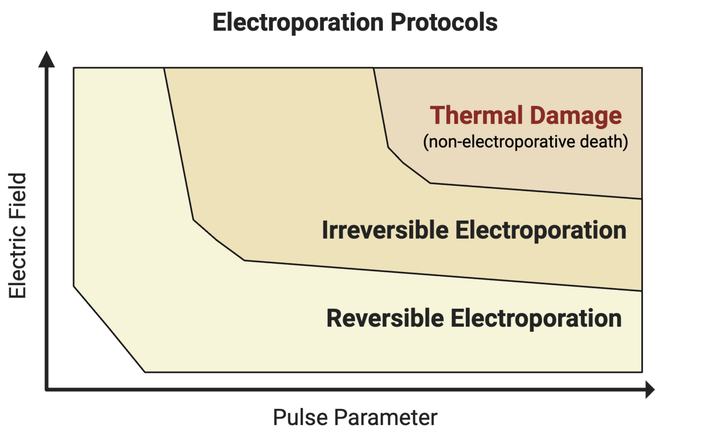

Image inspired by Tabaja et al., 2023.[2] Made with BioRender.com

Figure 1. Electroporation protocols and parameters
- As electric field strength, pulse width, length, and duration increase, electroporation results increase in severity
- If electric field and/or the pulse parameter are too high, thermal damage may occur, resulting in cell death that is considered non-electroporative

Irreversible electroporation can be used to treat inoperable tumors by continuing the application of electric fields past the critical threshold

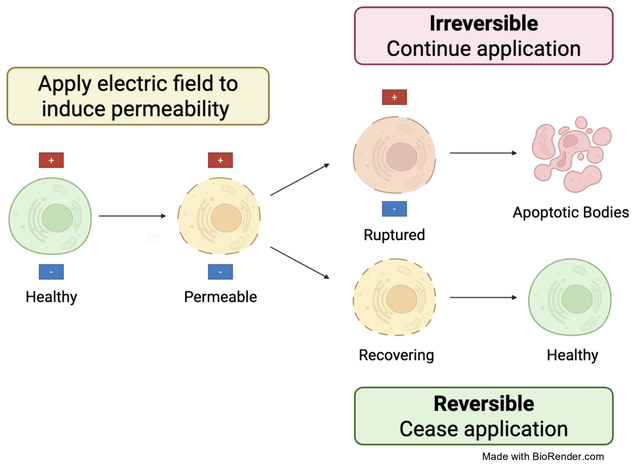

Figure 2. Reversible versus irreversible electroporation
- An electric field is applied to a healthy cell, moving it into a permeable state
- If the field is sustained, the cell reaches a critical threshold and ruptures, forming apoptotic bodies and releasing immunostimulants
- If the field is removed, the cell recovers, and reversible electroporation is achieved
- Reversible electroporation is utilized for electrochemotherapy and has promise for DNA vaccine delivery

Case Study: Canine Soft Tissue Sarcoma

H-FIRE and ECT Provide a Synergistic Anti-Tumor Effect

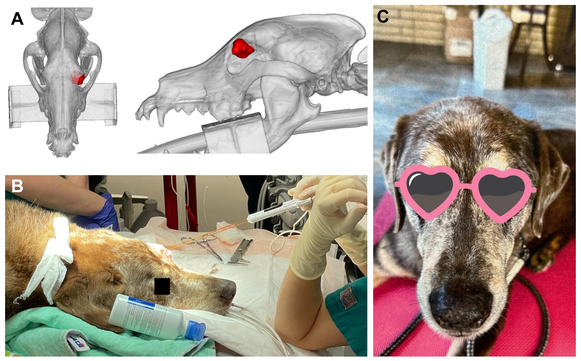

Figure 3. Case study of a ~2cm canine soft tissue sarcoma impacting the left orbit that was treated using combined H-FIRE and ECT. **A** shows a CT construction of the mass, **B** demonstrates the H-FIRE and ECT being utilized ablate the mass and increase chemotherapy penetration to induce apoptosis in cancer cells, and **C** is a post-operative image of the patient.

- The patient was at risk of losing their left orbit due to a soft-tissue sarcoma posterior to the socket
- H-FIRE was used in combination with ECT to ablate the mass and ensure clean margins
- The patient was able to enter remission and retain their left orbit

Software: Multithreading Security

Novel Fail-Safe Protocols Secure Multi-State System

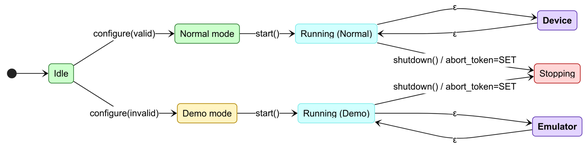

Figure 4. State diagram for expected system behavior with security emulator added. The system will run in normal mode when connected to a valid device, and if ever a valid device fails to configure, a fail-safe emulator system prevents unexpected behavior.

- Potential failure if faulty device configuration causes valid system to run as invalid
- Emulator system provides a safe pathway for valid devices running demo mode

Multithreading Error Could Cause Unexpected Behavior

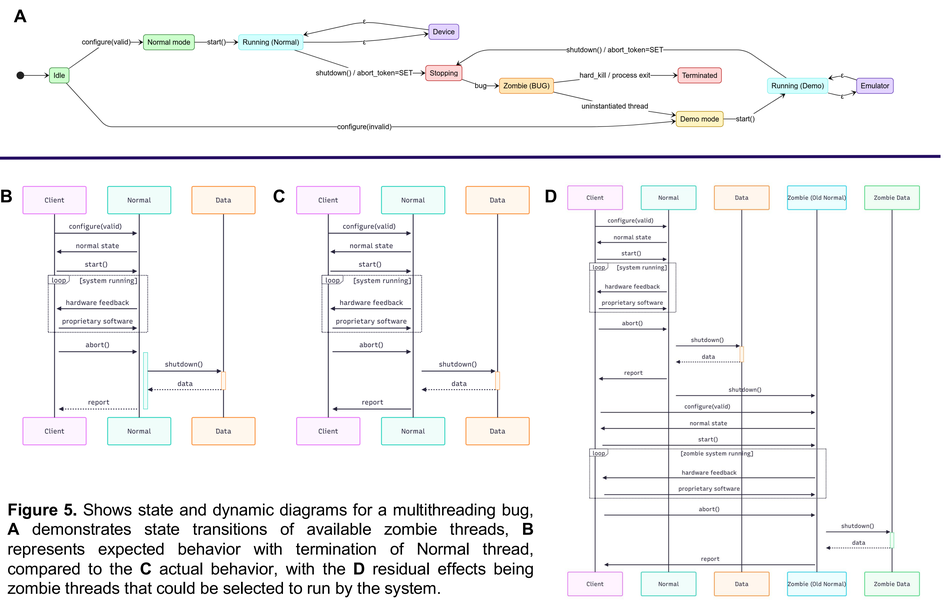

Figure 5. Shows state and dynamic diagrams for a multithreading bug, **A** demonstrates state transitions of available zombie threads, **B** represents expected behavior with termination of Normal thread, compared to the **C** actual behavior, with the **D** residual effects being zombie threads that could be selected to run by the system.

Software: Frontend Optimization

Previous Design

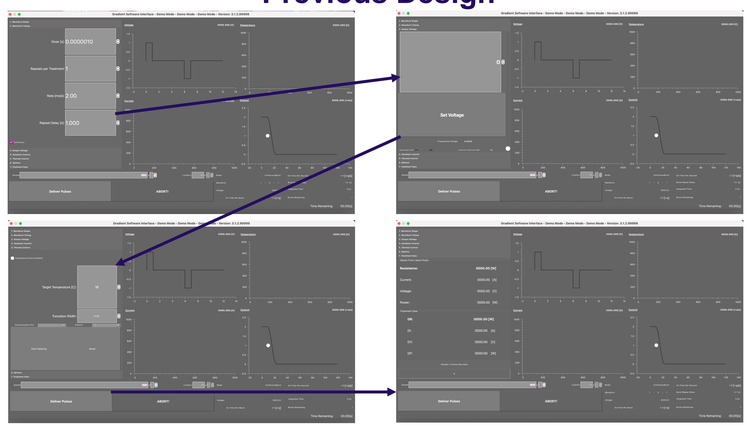

Figure 6. Previous frontend with collapsed menus, unclear click points, no safety checks, and information irrelevant to clinicians.

- **Safety Optimization:** requires value check, gridlines show clinicians safe bounds, only relevant metrics shown
- **Ease of Use:** 3 vs 12 clicks to select and begin treatment
- **Enhancement:** separate roles, generates patient report

New: Researcher

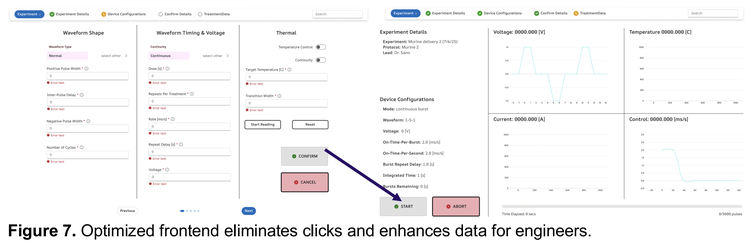

Figure 7. Optimized frontend eliminates clicks and enhances data for engineers.

New: Clinician

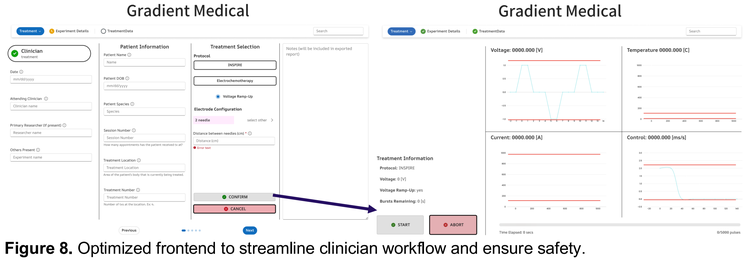

Figure 8. Optimized frontend to streamline clinician workflow and ensure safety.

References and Acknowledgements

[1] Weaver, J. C., Smith, K. C., Esser, A. T., Son, R. S., & Gowrishankar, T. R. (2012). A brief overview of electroporation pulse strength-duration space: a region where additional intracellular effects are expected. *Bioelectrochemistry (Amsterdam, Netherlands)*, *87*, 236–243. https://doi.org/10.1016/j.bioelechem.2012.02.007

[2] Tabaja, Chadi, Arwa Younis, Ayman A Hussein, Tyler L Taigen, Hiroshi Nakagawa, Walid I Saliba, Jakub Sroubek, Pasquale Santangeli, and Oussama M Wazni. "Catheter-Based Electroporation." *JACC. Clinical Electrophysiology* 9, no. 9 (September 1, 2023): 2008–23. https://doi.org/10.1016/j.jacep.2023.03.014.

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