SILENCE: On-Demand Seizure Suppression via Closed-Loop Sonogenetics

Morris, Evan (School: Saint Paul Academy and Summit School)

Epilepsy affects over 50 million people, and one in three cannot stop their seizures with medication. Neuromodulatory therapies are the leading alternative, but development has been bottlenecked by experiments that are slow and expensive. To overcome this constraint, I developed SILENCE: the first low-cost sonogenetic platform to rapidly optimize neuromodulatory therapies in vivo. SILENCE operates across three parametrizable layers in the acr-2(n2420) Caenorhabditis elegans seizure model. MscL(G22S), a gain-of-function bacterial mechanosensitive channel, was integrated into GABAergic neurons via CRISPR/FLInt safe-harbor knock-in under unc-47p. This step converts low-intensity ultrasound (US) into a circuit-restricted inhibitory signal. A custom RF-amplified transducer rig delivers US trains with tunable control of parameters relevant to therapeutic neuromodulation. A Python controller computes a motion-energy seizure index and fires US only when clustered events cross an adaptive threshold. Under a factorial US × actuator design (n = 12 per condition), post-trigger seizure recurrence dropped 70.1% (Mann-Whitney $p = 0.00000074$) and seizure rate dropped 29.8% (US × MscL interaction $p = 0.000469$). Sweeping US train duration from 100 to 2000 ms, SILENCE identified stimulation optima. An orthogonal levamisole assay confirmed the effect was driven by sonogenetic activation rather than baseline strain differences ($p < 0.0001$). Each run costs under 2 dollars and takes 5 minutes. At that throughput, SILENCE can compress months of neuromodulation research into hours of benchtop science, accelerating therapy development across neuromodulatory modalities. SILENCE unlocks therapeutic neuromodulation for nonspecialist labs worldwide and for the patients waiting for effective options.

Awards Won:

First Award of $6,000

Mary Sue Coleman Award

Herschbach SIYSS Award