Towards a synthetic model for cortical spreading depolarization

Srini Venkatramanan[1*], Aniruddha Adiga[1], Srikar Mutnuri[1,2], Madhav Marathe[1,2], Andrew Carlson[3]

[1]Biocomplexity Institute, UVA

[2]Department of Computer Science, UVA

[3]Department of Neurosurgery, UVA

*srini@virginia.edu



iCSD 2026

UVA Biocomplexity Institute

UVA Health

Introduction

- Computational models of SD have predominantly focused on detection algorithms on ECoG and scalp-EEG datasets

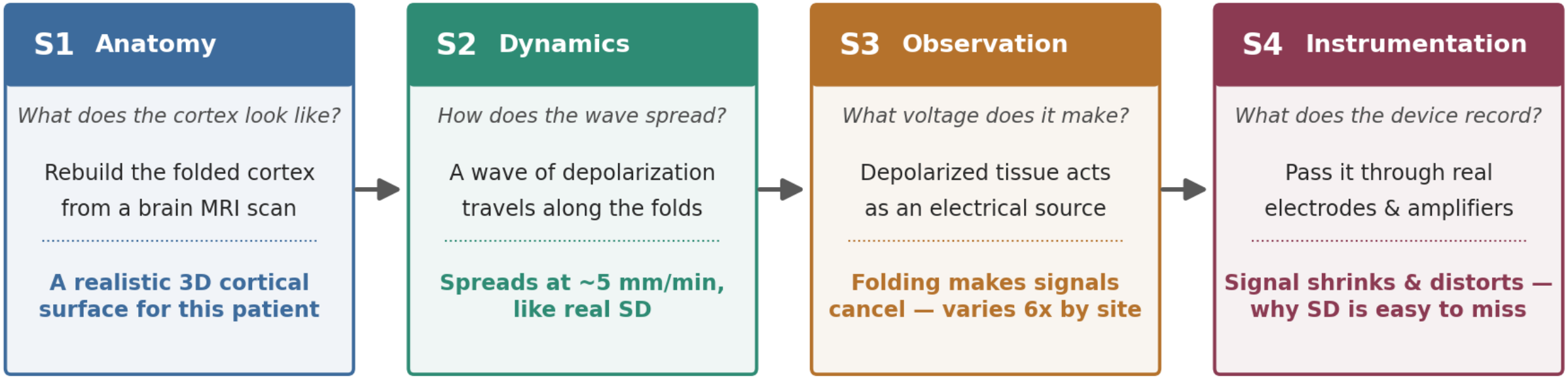
- Virtual Patient paradigm[1] can provide a testbed for developing personalized strategies towards therapy and intervention

- Synthetic models of SD[2] will need to account for structural variability, underlying biophysics, as well as signal characteristics

How do we make meaningful advances towards a synthetic model for cortical spreading depolarization?

Methods – Overview of the Pipeline

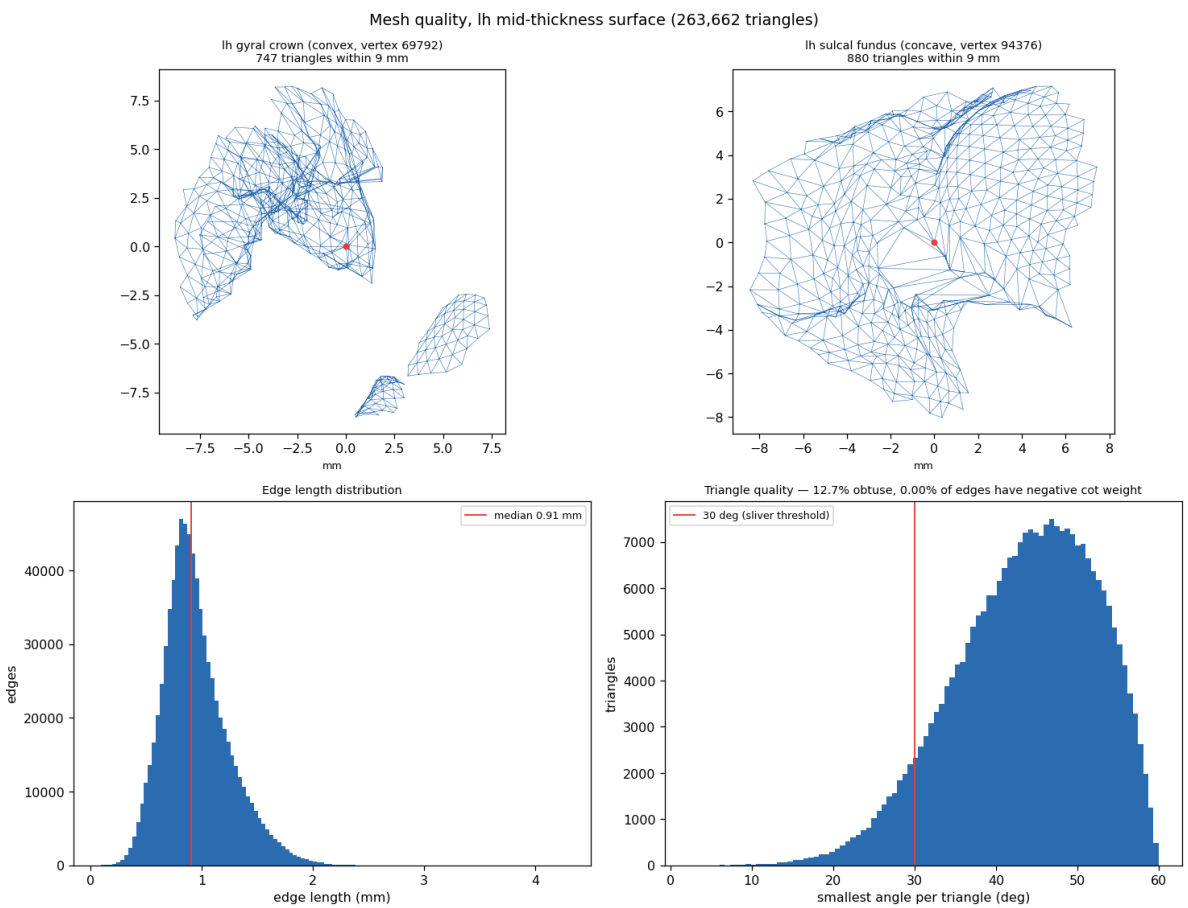
Synthetic forward model for spreading depolarization: anatomy → dynamics → observation → instrument

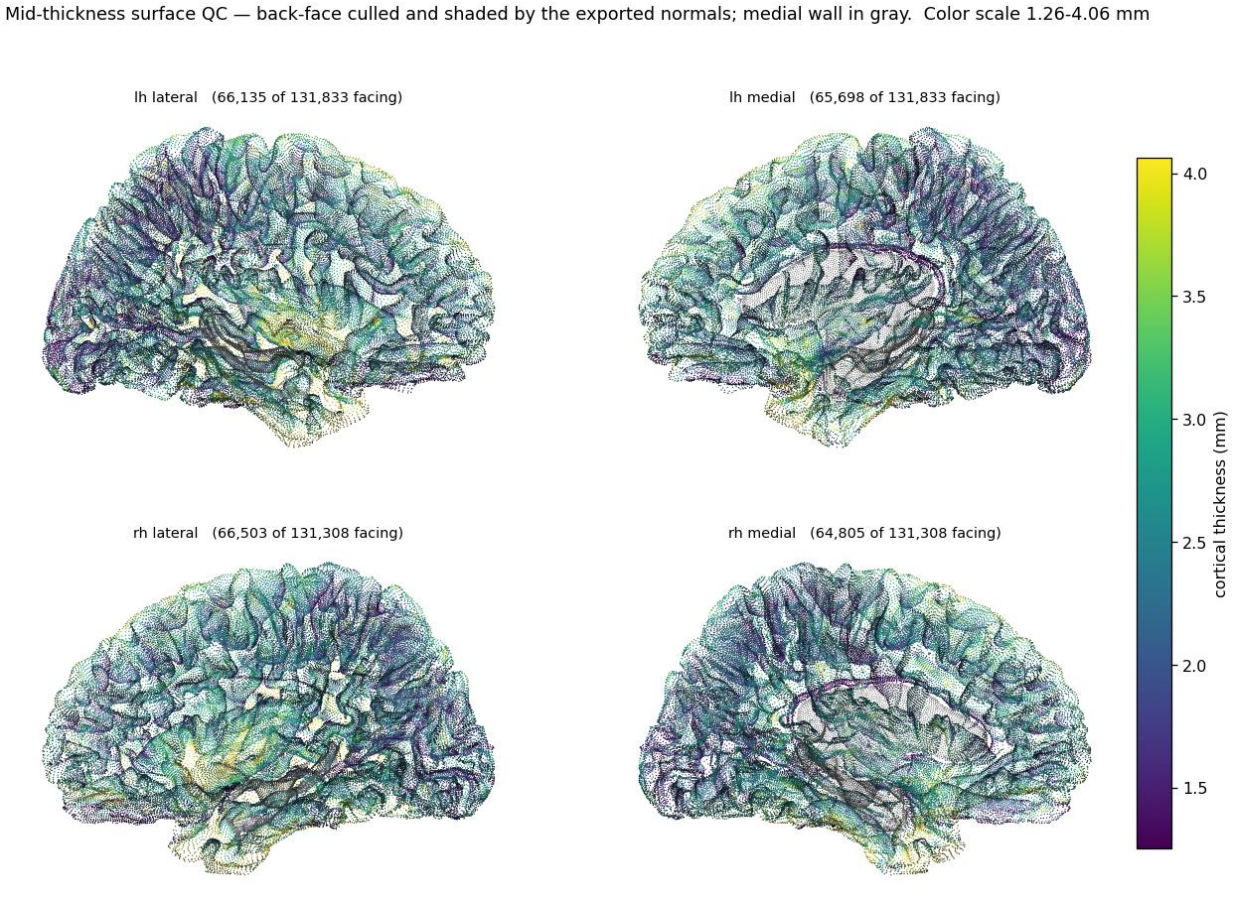


Results – 1. Structural Representation

Structural MRI data was transformed[3] into a triangulated mesh so that wave propagation respects geodesic distance

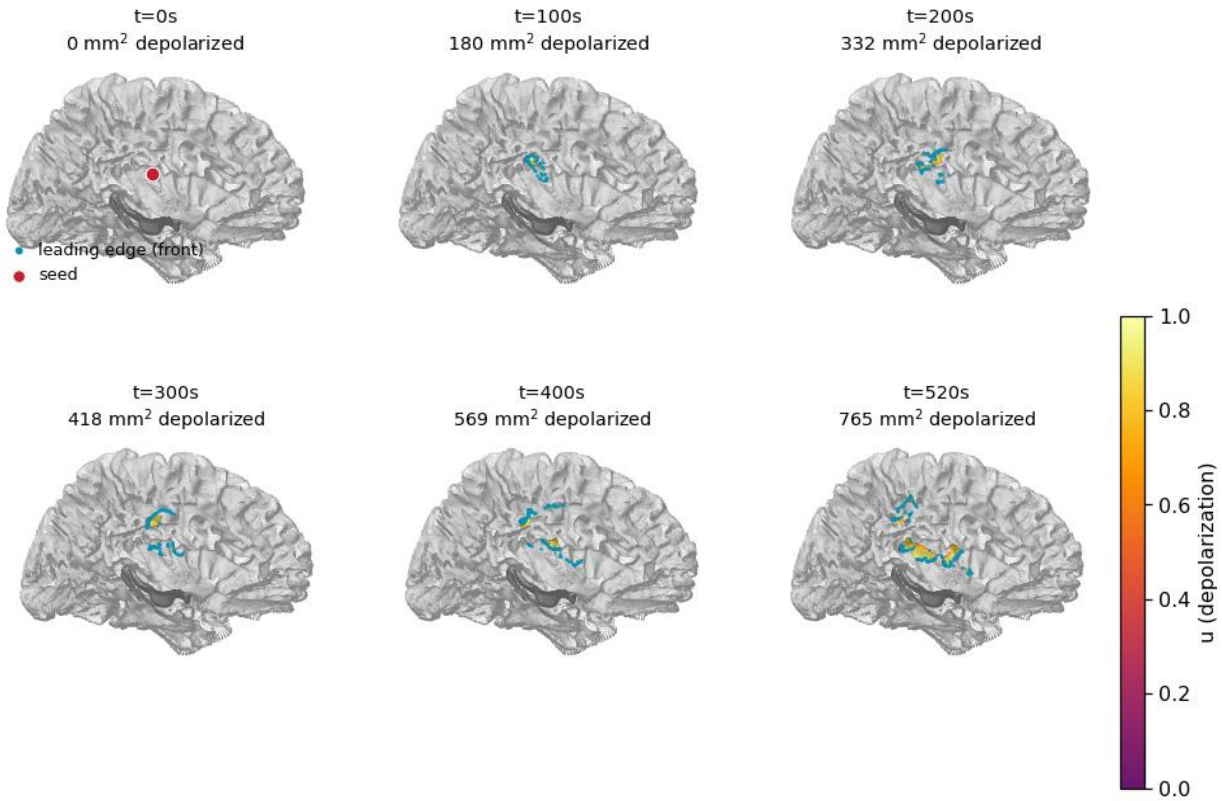
Delaunay flipping removes obtuse triangles that result in negative weights for tangential differential operators

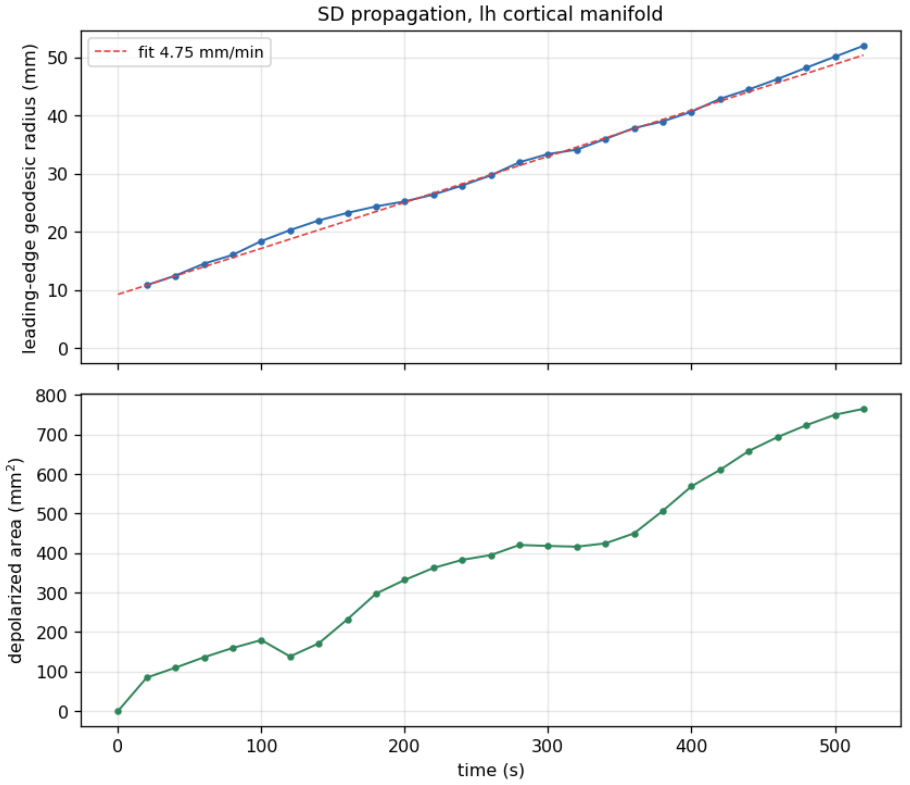




Results – 2. Spreading dynamics

Two variable reaction-diffusion on excitable media with inhibitor (FitzHugh – Nagumo model) [4] used for dynamics
~4.8 mm/min propagation speed. Reaches 52mm geodesic and 765mm^2 depolarized area by 520s

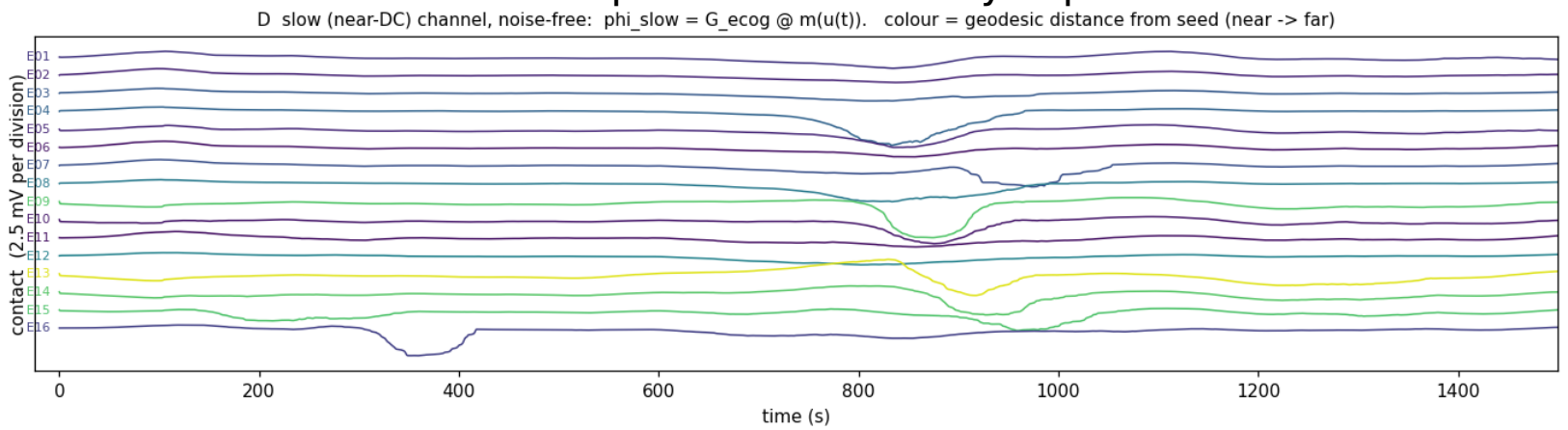


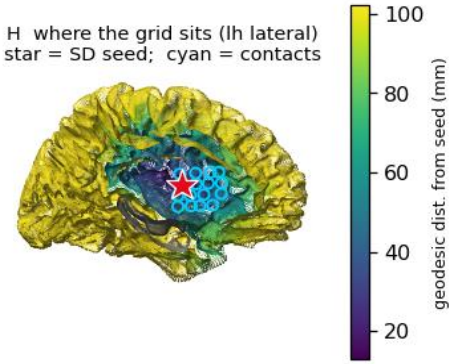


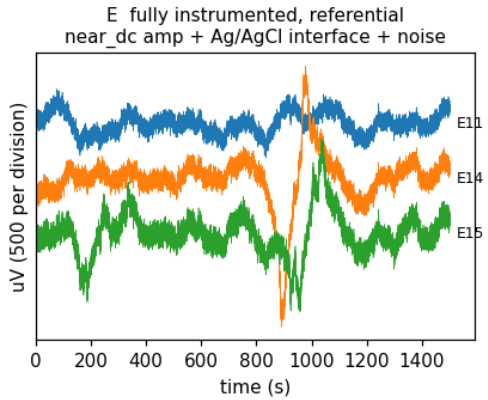
Results – 3. Virtual ECoG (16-contact subdural grid)

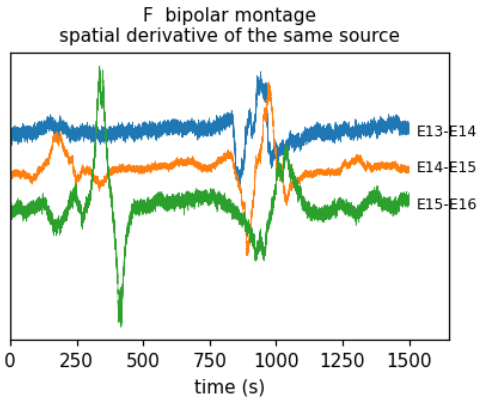
All 16 contacts show a complete waveform – arrival, 1-4.5min plateau and recovery.

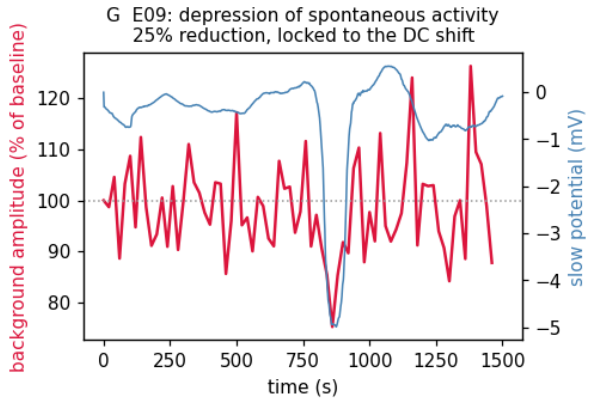
Spontaneous activity depression reaches ~25-28%

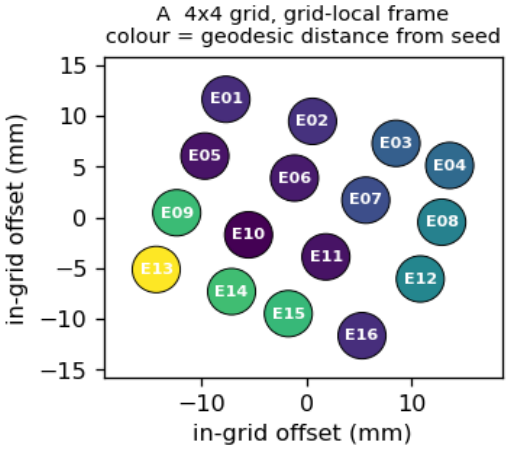












Conclusion & Future Research

- Current model is phenomenological and capable of producing plausible ECoG observations
  - Highlights parameters and assumptions that can significantly affect observed dynamics

- Comprehensive calibration yet to be performed
  - Requires skull conductivity, dipole gain, and contact impedance to be treated as separate parameters

Next steps: Improve calibration and create consistent scalp-EEG

References

1. Jirsa, Viktor K., et al. "The virtual epileptic patient: individualized whole-brain models of epilepsy spread." *Neuroimage* 145 (2017): 377-388. https://www.sciencedirect.com/science/article/pii/S1053811916300891
2. Gerardo-Giorda, Luca, and Julia M. Kroos. "A computational multiscale model of cortical spreading depression propagation." *Computers & Mathematics with Applications* 74.5 (2017): 1076-1090. https://www.sciencedirect.com/science/article/pii/S0898122117303024
3. Fischl, Bruce. "FreeSurfer." *Neuroimage* 62.2 (2012): 774-781. https://surfer.nmr.mgh.harvard.edu/
4. Tuckwell, Henry C., and Robert M. Miura. "A mathematical model for spreading cortical depression." *Biophysical Journal* 23.2 (1978): 257-276. https://pubmed.ncbi.nlm.nih.gov/687764/

Acknowledgments

R01NS128006 (Clinical Stimulation and Spreading Depolarization)

Thank you