Interictal Spike Depolarization in the Neocortex: Relationship to Action Potential Inactivation

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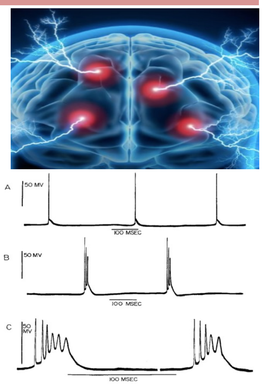
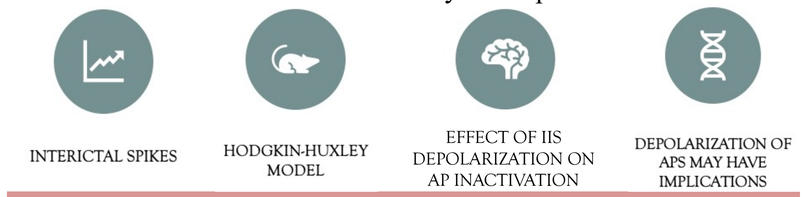
Background

- **Epilepsy:** Neurological condition that affects the nervous system; usually diagnosed after at least two seizures of unknown medical condition
- **Kandel and Spencer**: 1960 publication
  - Classification of spontaneous firing patterns; IIS depolarization occurs and triggers AP firing
- **Hodgkin-Huxley Model**
  - AP inactivation; depolarizations trigger an inward current carried by Na^+ ions followed by an outward current carried by K^+ ions



Research Objective

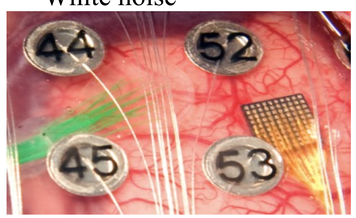
Objective: H-H model utilized to predict pathophysiology of AP inactivation and how it was affected by IIS depolarization



Methods

In Silico:

- Hodgkin-Huxley Model
- Gaussian function: model of interictal spikes
- White noise



Ex Vivo:

- Small block of brain tissue removed and placed into oxygenated slicing solution
- 4/9 neurons analyzed
- Interictal spikes do not occur in excised tissue with normal artificial cerebrospinal fluid

Data and Findings

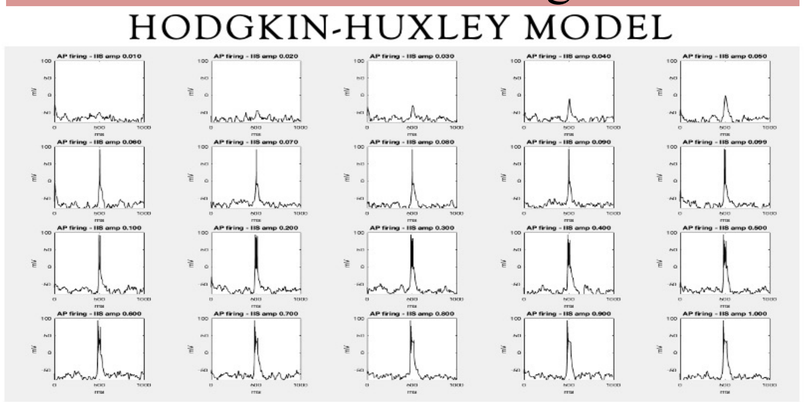


Figure 1: H-H model shows how APs are affected by range of depolarization values. As the amplitude of the depolarizations increased, there was a progression from low firing rate normal APs to higher firing rate normal APs to inactivated APs. Inactivation began at amplitude of 0.200 mV and became more inactivated.

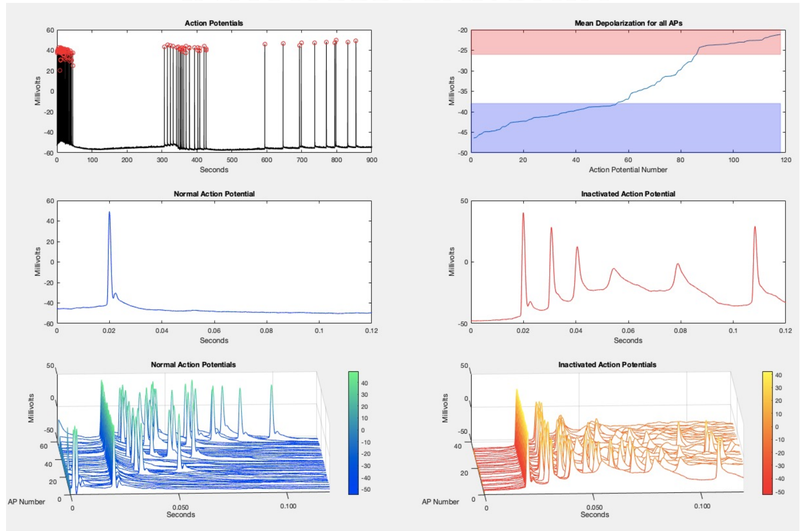
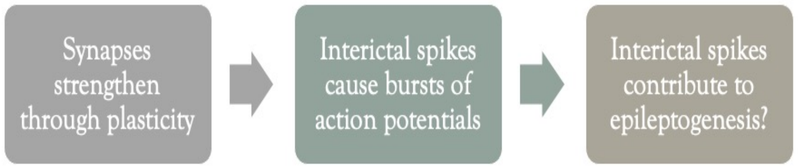


Figure 2: 60 AP peaks found in first neuron. Blue portion shows number of APs that are normal due to low depolarization; red portion shows number of APs that are inactivated due to a higher depolarization. Magnified views of APs. Max threshold: depolarizations could not provide enough stimulation to affect AP firing; Min threshold: depolarizations could provide enough stimulation to affect AP firing.

Conclusions

- AP waveforms displayed increased duration and decreased amplitude during depolarization, consistent with the definition of inactivated action potentials.
- Comparison: As the simulated IIS amplitude increased, AP firing became inactivated
- Hodgkin-Huxley Model was in good agreement in predicting the effect of IIS depolarization on AP inactivation as seen in the intracellular recordings!

Future Work and Implications



- IIS propagation during seizures and the effect of AP firing correlate with synapse strength if cells fire at the same time
- Could provide clinical use for epilepsy treatment

Acknowledgements

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