No effects of high-rate (multi-kHz) electric fields on brain slice on excitability

Looking for mechanisms of action for kHz therapies

Marom Bikson, PhD
Professor of Biomedical Engineering
The City College of New York. New York, NY, USA

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Slides and References at NeuralEngr.com
What does high-rate (kHz) stimulation challenge conventional models of electrical stimulation mechanisms?

- High-rate neuromodulation apply stimulation a frequencies (1-10 kHz) above conventional techniques (~100 Hz)
- High rate stimulation require short pulse durations (e.g. 10 kHZ : 40 uS)
- Because of the low-pass properties of neuron membranes, high-rate stimulation is ”not effective”?
- We used the most established animal model to detect electrical stimulation effects to measure (any) response to high-rate: acute brain slice
Data from acute rat brain slice model:

- Isolated "column scale", small intact network
- The most studied system to study acute (short term) and lasting (plasticity) changes in synaptic function and neuronal excitability
- Intracellular Recording: membrane polarization by electrical stimulation – primary mode of stimulation transduction
- Extracellular evoked synaptic Current – very broad sensitivity to change in pre or post-synaptic function
- The most studied system for cellular effects of electrical stimulation
- If electrical stimulation does something to cells, it should be quantifiable (detectable) in a brain slice
Neuronal membrane low-pass filter: Shown by Step-response

Stimulation with step-response (long pulse) quantifies membrane time constant result: charging delay

Optical imaging with voltage sensitive dye in rat hippocampal slice:

Effects of uniform extracellular DC electric fields on excitability in rat hippocampal slices in vitro

Marom Bikson¹, Masashi Inoue², Hiroki Akiyama², Jackie K. Deans¹, John E. Fox¹, Hiroyoshi Miyakawa² and John G. R. Jefferys¹

~10 ms time constant
Neuronal membrane low-pass filter: Shown by Step-response

Dual soma and bleb (axon terminal) patch

~1 ms time constant

Neuromodulation of Axon Terminals
Darpan Chakraborty¹, Dennis Q. Truong², Marom Bikson² and Hanoch Kaphzan¹

¹Sagol Department of Neurobiology, University of Haifa, Haifa 3498838, Israel and ²Department of Biomedical Engineering, The City College of New York of CUNY, New York, NY 10031, USA

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Change in synaptic efficacy in response to high-rate stimulation

219 slices: Positive control (DC field) in every slice

Rather than consider action potential generation (supra-threshold stimulation), consider modulation of ongoing activity (sub-threshold stimulation)
Established brain slice model of sub-threshold modulation of excitability via field excitatory post-synaptic potentials (fEPSP)

No evidence (yet) for modulation by high-rate using fEPSP brain slice model
No long term effects
No effects of high-rate (multi-kHz) electric fields on brain slice on excitability

Looking for mechanisms of action for kHz therapies

• Membrane time constant of soma and axons appear too long (1-20 ms) to response to high-rate pulse widths (> 40 us)
• No evidence for change in synaptic efficacy or excitability

• Results limited to cortical slice and short term experiments
• Other novel mechanisms of action (e.g. joule heat) to be explored
Collaborators:

Lucas Parra, Jacek Dmochowski, Asif Rahman, Niranjan Khadka, Mark Jackson, Dennis Truong, Belen Lafon, Gregory Kronberg, Devin Adair, Nigel Gebodh, Zeinab Esmaeilpour, Thomas Radman. John Jefferys

Tianhe Zhang, Brad Hershey, Rosana Esteller, Wendy Gu

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