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Numerical Modeling to Optimize Treatment Protocols in Neuromodulation and Electroceuticals

Jeffrey E. Arle, MD, PhD [(1)] and Kristen W. Carlson * [(1)]
(1) Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, 02215, *e-mail: kwcarlso@bidmc.harvard.edu; carlsonkw@gmail.com

Extended Abstract. Neuromodulation and electroceuticals apply electromagnetic fields to the nervous system to restore healthy states from diseased states. Despite widespread use — for example, over 100,000 vagus nerve implantations for seizure to date and over 60,000 spinal cord stimulators implantations per year — typically the mechanism of action (MoA) is unknown [1, 2]. Yet to optimize efficacy and minimize side effects, we must identify the neural elements responsible for each effect.

Toward identifying which biological protein structures are involved in the MoA of two very different forms of neuromodulation, we present novel numerical models of spinal cord stimulation (SCS) for chronic neuropathic pain and vagus nerve stimulation (VNS) for seizure [3, 4].

Low frequency SCS (210 μs pulses at 40 – 180 Hz) produces paresthesia, a vibrating feeling that can be uncomfortable, along with highly effective chronic pain relief for pharmaco-resistant patients. Finite element models (FEM) predict electric field strength in inhomogeneous complex protein tissues, and nerve fiber models predict different fiber types' responses to the fields based on the field effects on complex protein sub-components such as nodes of Ranvier and ion channel gates [5]. These models predict which fibers are responsible for pain relief and paresthesia. New techniques using higher frequencies — 30 μs pulses at 10 KHz — and bursts — 1 ms pulses at 500 Hz intra-burst and 40 Hz inter-burst — both produce pain relief, but without paresthesia. Numerical models based on *in vivo* data predict that the threshold of vibration-causing fibers rises faster than that of the efficacy fibers and can explain lack of paresthesia in high frequency and burst SCS [4].

Similarly, numerical models of vagus nerve stimulation for seizure, grounded in empirical studies, have produced a theory of which fibers produce efficacy and which produce the side effects of hoarseness, cough, and tightness in the chest. Our models predict that 8 μm efferent recurrent laryngeal fibers produce hoarseness, 5 μm aortic baroreceptor fibers stimulating the locus coeruleus likely produce reduction of seizure, and 3 μm P2ylr efferent pulmonary fibers produce cough and chest tightness [3]. We estimate the excitation and blocking thresholds of these fibers, and the numbers that are recruited by VNS.

FEM of new directional electrode arrays and closed-loop neuromodulation permit identifying fibers responsible for efficacy and side effects and their location in the dorsal column and vagus nerve. The expanded MoA knowledge of which biological structures are affected leads to optimized efficacy and reduced side effects.

References

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