Electrical stimulation with burst-modulated pulse waveforms improves efficiency and fiber-selectivity.

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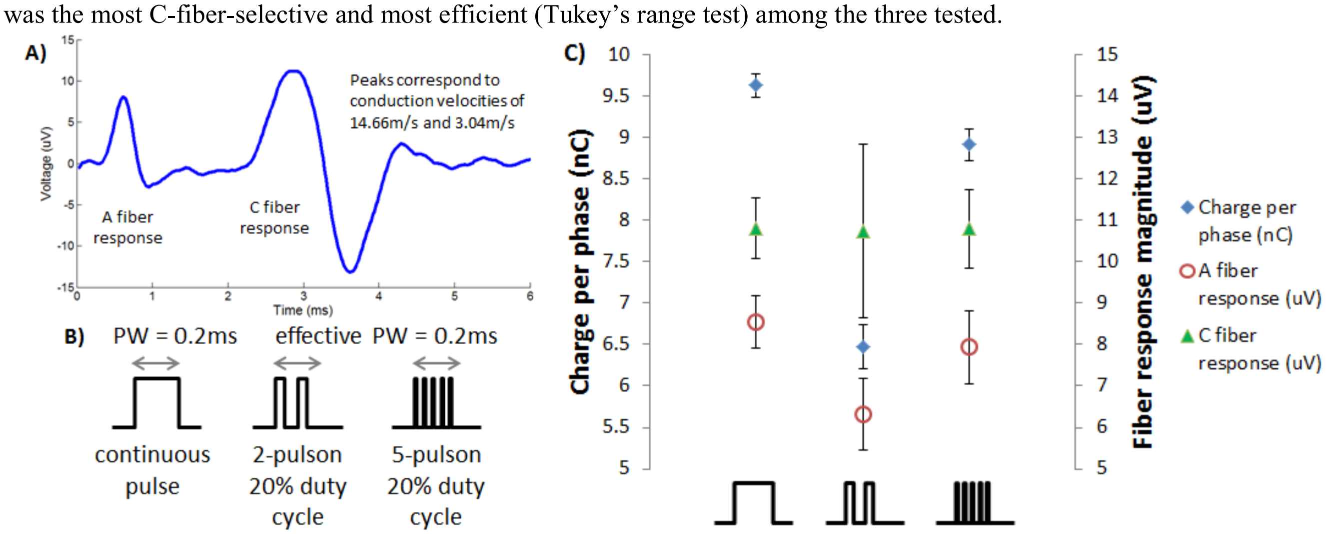
ELECTRICAL stimulation of neural tissue is an effective treatment for various neuropsychiatric disorders. By applying electrical currents that depolarize the neuron membrane, stimulators are capable of driving action potentials and altering normal or pathological behavior. The stimulus waveforms used typically consist of a train of short rectangular pulses. While effective at eliciting action potentials, these pulses preferentially activate fast-conducting axons—axon fibers with larger diameter and more myelin are activated more easily. This feature is not always desirable and can pose a challenge to therapy as well as research, and different stimulation strategies have been proposed to selectively target different axon populations. However, with electrical stimulation (as opposed to optogenetic methods), these attempts have only limited success.

As a different approach, we developed a stimulation system that replaces each pulse with a burst of smaller pulses, which are referred to here as "pulsons". By adjusting the parameters of these burst-modulated pulse waveforms, we were able to alter the fiber-selectivity of the stimulus. In addition, we found that the burst-modulated pulse waveforms tend to have significantly better efficiency than the conventional pulse waveforms, that is, lower electrical charge needs to be delivered to elicit the same level of response (sample nerve response shown in **Figure A** below). These findings have important implications for nerve stimulation and deep brain stimulation systems.

I. Sample results

Vagus nerve stimulation experiments with different waveforms were conducted in anesthetized Long-Evans rats. Other than the pulse itself, all other parameters were the same: 1 second pulse train, 20 Hz pulse repetition, 0.2 ms pulse width, balanced cathode-leading biphasic pulsing with interphasic interval of half the period. The stimulus charge per phase and *in vivo* vagus nerve response data from one animal are shown in **Figure C** below (each data point represents the mean ± standard deviation of 20 separate trials). In this particular experiment, 2-pulson and 5-pulson waveforms (**Figure B**) were chosen for comparison against the continuous pulse (choices were based on prior data, not included). All three waveforms maintained the same level of C fiber response (ANOVA p-value = 0.9938) but resulted in different levels of A fiber response (p-value = 1.893E-11) and required different amounts of charge per phase (p-value = 1.210E-47). The 2-pulson waveform was the most C-fiber-selective and most efficient (Tukey's range test) among the three tested.



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