Failure of electrical stimuli to evoke 1:1 axon firing shown in intraneural recordings

Alwin So[1,2], İsmail Devecioğlu[1,2], Felix P Aplin[1,2], Richard M Vickery[1,2], Ingvars Birznieks[1,2]

I. Introduction

Electrical nerve stimulation has been trialed in haptics for conveying shape, movement, and texture percepts. It is often assumed that applied stimuli stably recruit a fixed axon population, with firing rates increasing proportionally with stimulation frequency [1][2]. However, amputees with implanted electrodes in the nerve stump were unable to discriminate frequencies >50Hz [3], despite tactile afferents often responding at several hundred Hz to natural stimuli [4] and mechanical frequencies being discriminable at 200 Hz [5]. We investigated the consistency of intraneural compound action potential (CAP) amplitudes in response to electrical stimulation, using microneurography in healthy participants. Surprisingly, our data suggests tactile afferents fail to respond 1:1 to suprathreshold electrical stimuli even below 50 Hz.

II. Methods

CAP measurements were conducted on 8 fascicles (fingers: 4 index, 2 middle, 2 ring) in 6 healthy participants (2M, 4F), mean age 23 (range 19-26). Experimental protocols were approved by the human research ethics committee of the UNSW Sydney (HC210271) and written informed consent was obtained from all participants.

0.2mm tungsten microelectrodes (impedance 500K-2MΩ at 1000Hz, FHC Inc, USA) were percutaneously inserted into median nerve at the wrist. Electrode position was adjusted with audio feedback to find a population response that avoided single sensory units, palmar innervation, and responses to joint angle changes. Neural signals were amplified 10,000x and bandpass filtered (100Hz-2kHz) through an isolated amplifier (Neuroamp EX, AD Instruments, Australia) and recorded in Labchart (AD Instruments, Australia) at 40,000 samples/s.

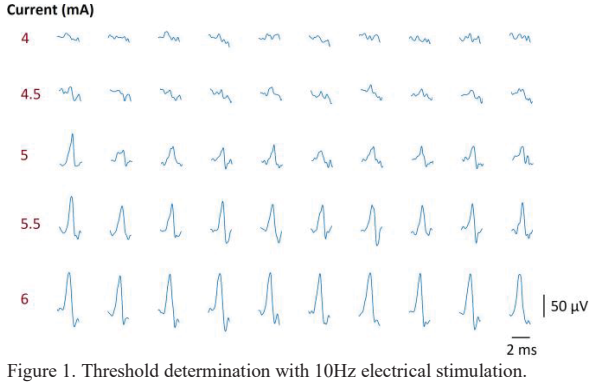

Figure 1. Threshold determination with 10Hz electrical stimulation. Responses to 2-3.5mA (not shown) similar to 4mA. Threshold for this fascicle was 5mA: main protocol used 6mA.

*Research supported by Australian Research Council (DP200100630).

[1]A.S., I.D., F.A., R.V. and I.B. are with UNSW Sydney, NSW, Australia (phone: +61 423 815 831; email: alwin.so@unsw.edu.au).

[2]A.S., I.D., F.A., R.V. and I.B are with Neuroscience Research Australia, NSW, Australia.

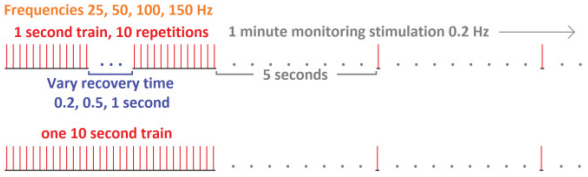

Figure 2. Stimulation parameters for CAP measurements.

Current-controlled electrical stimulation was delivered with a Digitimer DS5 (Digitimer, UK) via Kendall 200 series foam electrodes (Covidien, USA) attached to side of the finger that gave the strongest population response to skin stroking. Electrical stimulation used charge-balanced, asymmetric pulses (0.1ms cathodic followed by 0.9ms anodic). Current was increased in 0.5mA steps, and threshold defined as the current evoking a CAP amplitude >20µV (Fig. 1); with experimental stimulus trains delivered at 1mA above this (range 5-7mA, n=8). Within a given frequency, 10s of stimulation was delivered at each recovery time, in order of 0.2, 1 and 0.5s (10 repetitions of 1s trains), then '0s' (one 10s train). Frequencies were tested in this manner in order of 50, 150, 25, then 100Hz (Fig. 2). Between each combination, 1min 0.2Hz stimuli was delivered to monitor recovery and electrode position.

The initial latency to peak response was used to extract portions of the population activity. CAP amplitudes were measured from this rectified positive signal [6]. Across fascicles, mean response amplitudes during 0.2Hz monitoring stimulation ranged from 9.8 - 25.5x RMS noise. For subsequent analysis, this mean monitoring response amplitude was normalised to 1.0 for each fascicle.

III. Results

CAP amplitudes decreased drastically within 100ms of stimulation onset (Fig. 3: 1 example recording, Fig. 4: mean of 8 fascicles). Amplitudes decreased slightly for each subsequent 1s train (Fig. 4A), and during continuous 10s stimulation (Fig. 4B).

For repetitions of 1s trains, multiple linear regression was performed using frequency, (log of) time in 1s train, repetition number, and recovery time as predictors of mean CAP amplitude, giving R^2 = 0.78. Follow-up ANOVA showed frequency (48.2%, F(1, 9854) = 20950) and (log of) time in 1s train (24.7%, F(1, 9854) = 10719) as main sources of amplitude variation, with minor effects from repetition number (3.3%, F(1, 9854) = 1424). Recovery time and other

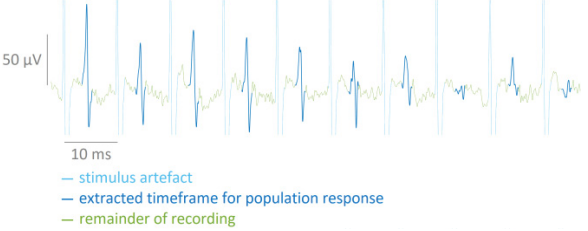

Figure 3. Example of recording. Onset of 100Hz stimulation, 1st repetition.

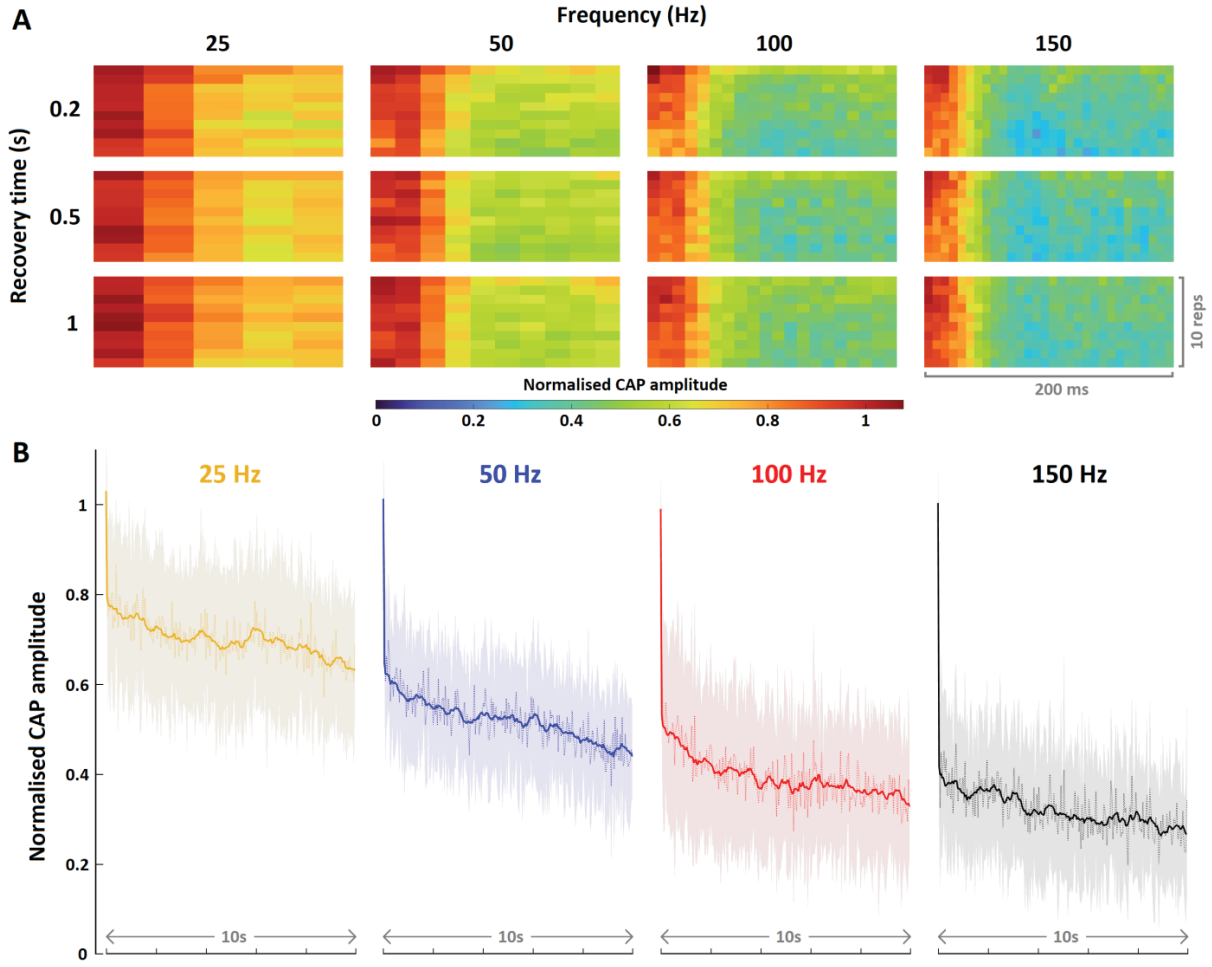

Figure 4. Mean CAP amplitudes (n=8). A: 1s trains, 10 repetitions. First 200 ms of each repetition = 1 row. B: 10s train. After first response, discrete time points of 50-150Hz taken to match 25Hz responses (dotted lines, shaded area 95% CI). Solid lines - smoothed by 10 consecutive values.

interactions contributed to < 1% of amplitude variation.

IV. Discussion

We present preliminary electrophysiological evidence of tactile afferent failure to fire one action potential per suprathreshold stimulus pulse at population level, primarily related to stimulus frequency and time in 1s stimulus train. This failure may contribute to the 50Hz frequency discrimination limit with electrical pulses [3], compared to better than 200Hz for mechanical vibrations [5]. Afferent response failure may also contribute to less than proportional changes in intensity percepts when increasing number of stimulus pulses per burst [7].

Higher currents may improve firing rates in given axons, however, axons with higher threshold (further from electrode, smaller diameter) would likely be recruited and these 'new' axons would then fail to follow. In haptic applications, electrical stimulation patterns are unlikely to evoke the intended precisely planned tactile afferent responses. The fidelity of 1:1 following appears to vary between individual tests, which may affect a variety of perceptual properties of haptic stimulation.

References

[1] D. R. Merrill, M. Bikson, and J. G. Jefferys, "Electrical stimulation of excitable tissue: design of efficacious and safe protocols," Journal of Neuroscience Methods, vol. 141, no. 2, pp. 171-198, 2005.

[2] G. Valle et al., "Biomimetic intraneural sensory feedback enhances sensation naturalness, tactile sensitivity, and manual dexterity in a bidirectional prosthesis,", Neuron, vol. 100, no. 1, pp.37-45, 2018.

[3] E. L. Graczyk, B. P. Christie, Q. He, D. J. Tyler, and S. J. Bensmaia, "Frequency shapes the quality of tactile percepts evoked through electrical stimulation of the nerves," Journal of Neuroscience, vol. 42, no. 10, pp. 2052-2064, 2022.

[4] A. I. Weber et al., "Spatial and temporal codes mediate the tactile perception of natural textures," Proceedings of the National Academy of Sciences, vol. 110, no. 42, pp. 17107-17112, 2013.

[5] D. A. Mahns, N. Perkins, V. Sahai, L. Robinson, and M. Rowe, "Vibrotactile frequency discrimination in human hairy skin," Journal of Neurophysiology, vol. 95, no. 3, pp. 1442-1450, 2006.

[6] M. Baba, S. Simonetti, and C. Krarup, "Sensory potentials evoked by tactile stimulation of different indentation velocities at the finger and palm," Muscle & Nerve, vol. 24, no. 9, pp. 1213-1218, 2001.

[7] K. K. Ng, A. So, J. Y. Fang, I. Birznieks, and R. M. Vickery, "Multiplexing intensity and frequency sensations for artificial touch by modulating temporal features of electrical pulse trains," Frontiers in Neuroscience, vol. 18, p. 1125597, 2024.