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Supplementary Materials for

The neural basis of perceived intensity in natural and artificial touch

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SUPPLEMENTARY MATERIALS

MATERIALS AND METHODS

Measuring and modeling threshold adaptation

Extended exposure to stimulation leads to a desensitization (adaptation), characterized by an increase in perceptual thresholds *(44, 45)*. To measure the strength and time course of adaptation, we monitored sensory thresholds in the presence and absence of adapting stimuli. Based on these data, we developed a simple model that allows us to estimate the degree of adaptation caused by different levels of stimulation and the time course of adaptation.

Briefly, we first used a two-alternative, forced-choice tracking paradigm to estimate the perceptual threshold, as is described in the main text, but with the inter-trial interval set at 4 s (for reasons that will soon be clear). After this pre-adaptation threshold measurement, we delivered an adapting stimulus for 120 s, which was either 5, 25, or 50 microseconds above the PW threshold estimated in pre-adaptation measurement. A second threshold was found using the procedure summarized above, except that, during the 4 s inter-trial interval, the adapting stimulus was delivered for 1 s (to maintain the level of adaptation) *(38, 46)*. We ran 3 repetitions of each of the 3 adapting stimulus levels on 2 contacts, where the contacts were alternated and the conditions randomized.

To model the strength of adaptation, we regressed the change in threshold on the ratio of the adapting charge and the baseline threshold charge; the former gauges the degree of adaptation, the latter the strength of the adapting stimulus (Figure S4A). To model how quickly elevated thresholds decay back to baseline, we fit an exponential to the threshold data (Figure S4B). We then used these two functions to correct the thresholds for the experiments described in the main text on a block-by-block basis. That is, we used the mean electrical stimulus delivered on an experimental block as the “adapting” stimulus to estimate how much a threshold would increase given that level of stimulation; we then used the time between successive blocks to estimate how much the elevated thresholds would have decayed back to baseline in the subsequent experiment. For the magnitude scaling experiments, all conditions were interspersed within a single block and the currents delivered were relatively small so no correction was necessary for the resulting data. For the matching experiment, blocks with PW manipulation always followed blocks with PF manipulation. On average, we estimated a 19% change in thresholds for these blocks. Similarly, in all but one discrimination experiment the PW manipulation followed the PF manipulation. Due to the higher currents and shorter pauses between blocks, we estimated threshold changes at 32% on average. Figure S5 shows the data using uncorrected thresholds.

Biophysical model of afferent recruitment

A biophysical model of the human median nerve surrounded by a 36 channel FINE was constructed based on cadaveric cross sections *(47)*. Populations of neurons were simulated within the fascicles according to the approximate axon density of humans within the age range of the two subjects in this study *(48, 49)*. The propagation of current injected from a single cathodal contact to distant return was simulated using Maxwell 3D (Ansys Corporation, Canonsburg, PA).

Activation of each neuron to a single pulse of stimulating current was determined using a linear approximation method in MATLAB (The MathWorks, Inc., Natick, MA) *(50)*. The number of fibers recruited was determined as PW was swept from 0 to 255 microseconds while PA was held at the activation threshold as described in the main text. Following the normalization method proposed in this work, recruitment was plotted as a function of charge above threshold charge for the first fascicle activated by the stimulation. Fig. S7 shows the pattern of recruitment for four stimulating contacts. While all four recruitment curves are well approximated by a sigmoid function, the threshold and slope differ between fascicles. These differences are likely related to differences in contact-fascicle distance and fascicle cross-sectional area, among other factors.

Derivation of activation charge rate (ACR)

Whether a given neuron is activated by electrical stimulation depends on the diameter of the fiber (d), the shape of the voltage field (V) resulting from the pulse amplitude (PA) of stimulation, the properties of the surrounding tissues, and the duration of the stimulation pulse (PW) *(50)*. Therefore, activation of the n^{th} neuron, α_n, is a function of the voltage field experienced by the neuron (V_n), the diameter of the neuron (d_n) and the width of the pulse (PW) (Eq. S1).

$\alpha_n = f(V_n, PW, d_n) \approx f(PA, PW, d_n)$ ....Eq. S1

The pulse amplitude and pulse width can be represented by a single parameter, charge, Q = PA*PW. This is substituted into Eq. S1 to get Eq. S2.

$\alpha_n = g(Q, d_n)$ ....Eq. S2

Activation will either be 1 if the stimulation parameters exceed the threshold for this neuron or 0 if they do not. Extraneural stimulation will activate multiple neurons. Total activation of the population, α_P, is given by Eq. S3, where N is the total number of fibers in the nerve. This equation provides an estimate of the total population or number of fibers activated by a single stimulation pulse.

$\alpha_{Pop} = \sum_{n=1}^{N}[\alpha_n]$ ....Eq. S3

Stimulation typically consists of trains of pulses. Assuming each stimulation pulse, *p*, only elicits a single action potential, Eq. S4 describes the total number of spikes produced by the activated population for *P* pulses.

$\alpha_T = \sum_{p=1}^{P}\left[\alpha_{Pop}\right] = \sum_{p=1}^{P}[\sum_{n=1}^{N} \alpha_n]$ ....Eq. S4

In the present study, we wish to test the hypothesis that total spike rate, α_T, drives perceived intensity. Since the actual number of activated fibers cannot be directly measured, we need to derive an estimate of total activation. Since the recruitment curves are smoothly increasing with an increase in stimulus charge and a value of 0 represents the threshold of recruitment of the first fiber(s), we estimated total number of fibers activated by a single pulse as the charge above threshold (Eq. S5).

$$\alpha_{Pop} \propto (Q_p - Q_{th}) \text{ ......Eq. S5}$$

By substitution of Eq. S5 into Eq. S4, the cumulative numbers of spikes produced for a pulse train is (Eq. S6)

$$\alpha_T \approx \sum_{p=1}^{P} [Q_p - Q_{th}] \text{ ......Eq. S6}$$

Finally, since the pulse rate is constant for these experiments, there are PF pulses per second and we derive our final common factor to represent the cumulative spike rate per second, defined as activation charge rate, ACR (Eq. S7).

$$\sum_{p=1}^{P} [Q_p - Q_{th}] = (Q_p - Q_{th}) * PF$$

$$\therefore ACR = (Q_p - Q_{th}) * PF \text{ ......Eq. S7}$$

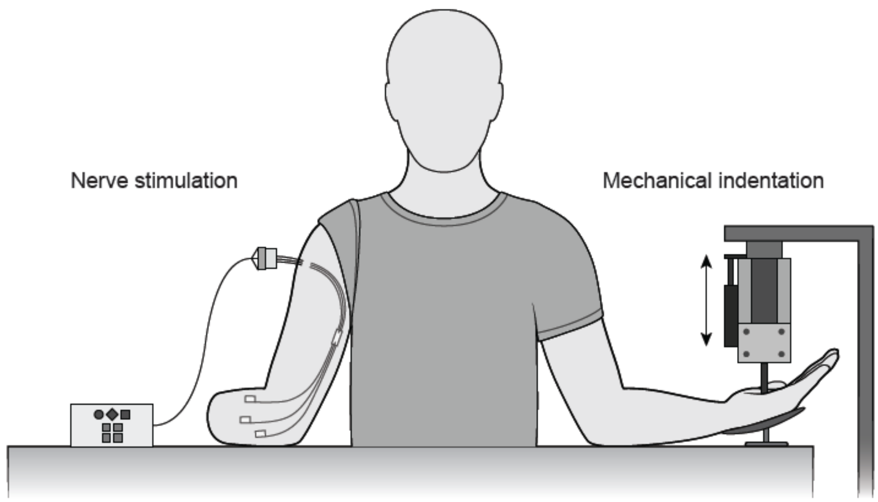

Fig. S1. Matching protocol set-up. The subject matched the perceived intensity of a mechanical skin indentation delivered to the intact (left) hand to that of an electrical stimulus delivered to the nerve of the missing (right) hand. The location of the mechanical stimulation was matched to the perceived location resulting from electrical stimulation.

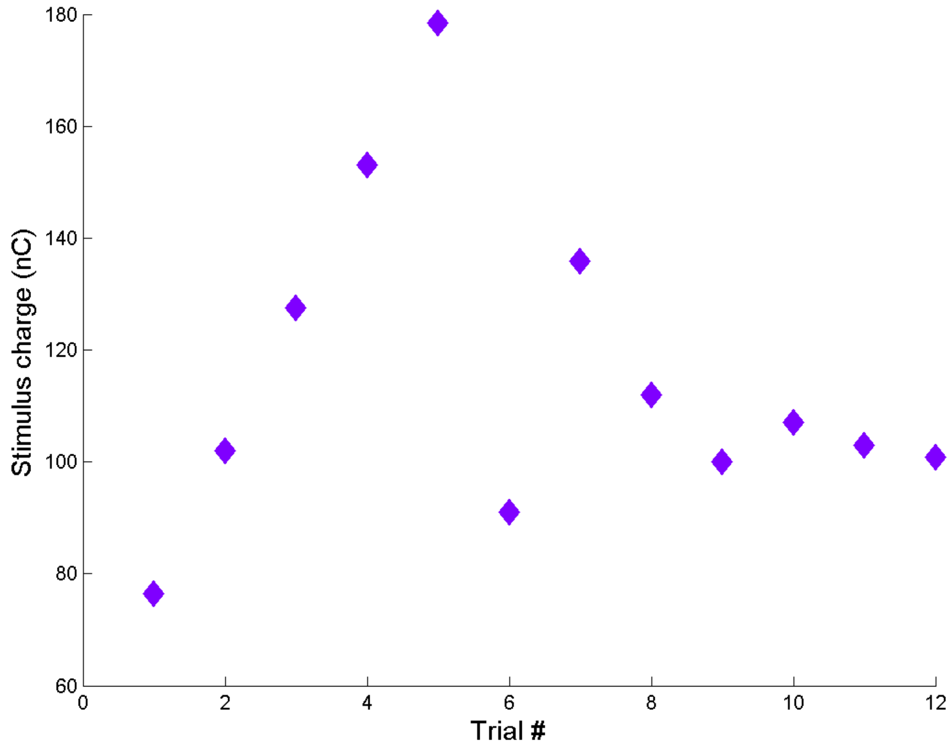

Fig. S2. Threshold search procedure. PW was fixed at 255 μs while PA was increased in steps of 0.1 mA. Once sensation was reported, the PA was fixed at that value and PW threshold was found through a binary search procedure. Threshold was assumed once the PW step size became less than 5 μs.

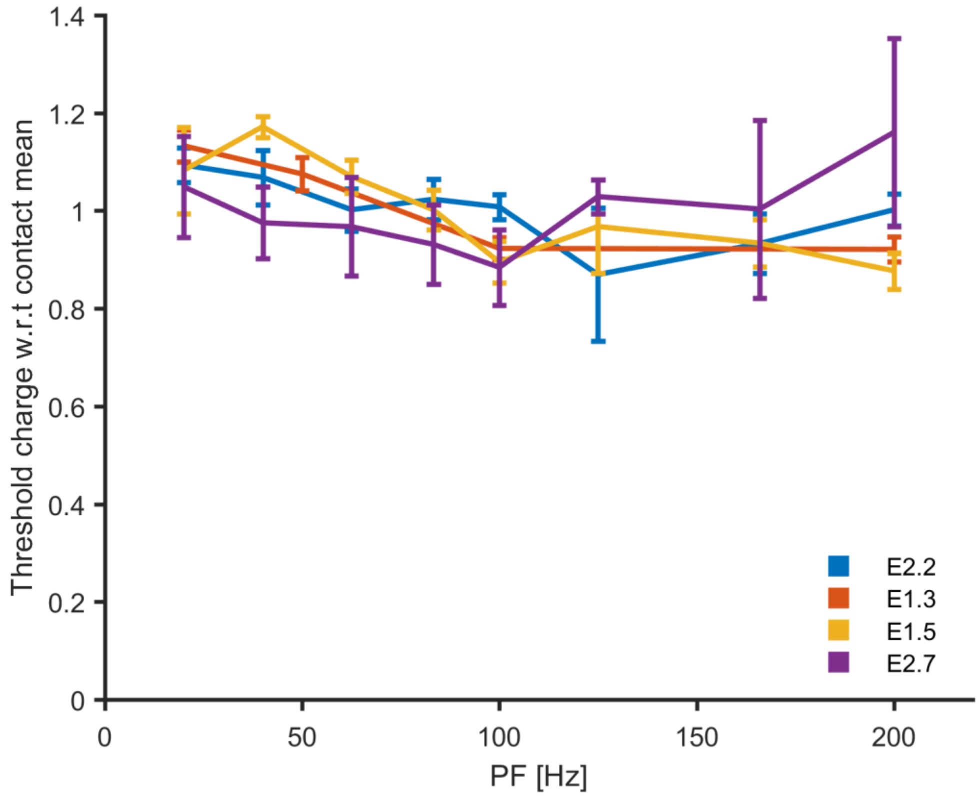

Fig. S3. Detection threshold as a function of stimulation PF. Threshold is relatively flat as a function of stimulation frequency, which supports one of the key assumptions of the threshold correction. Each trace represents a single electrode. In the legend, E*x*.*y* represents the electrode contact *y* of subject *x*.

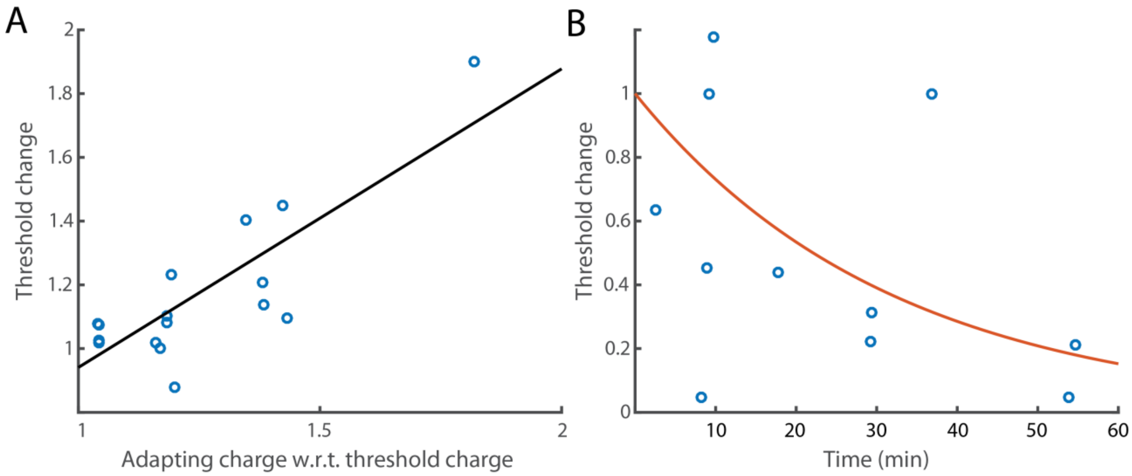

Fig. S4. The effect of adaptation on sensory thresholds. A. Change in threshold charge as a function of the ratio of the adapting charge versus the baseline threshold charge. The more intense the adapting stimulus, the more the thresholds adapt. B. Decay of elevated thresholds back to baseline over time. On average, the decay half-time is around 22 minutes.

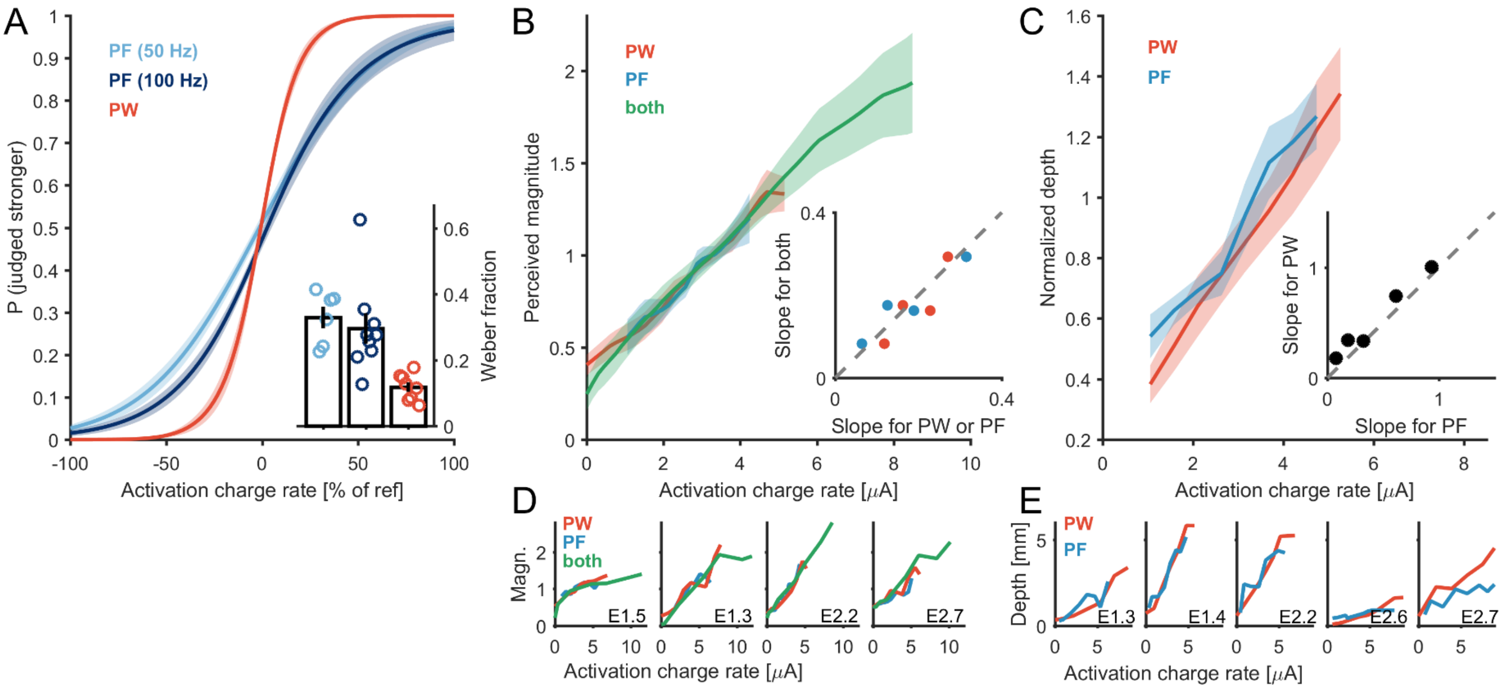

Fig. S5. Charge above threshold determines perceived intensity. Same as Fig. 6 (main text), but not corrected for threshold adaptation.

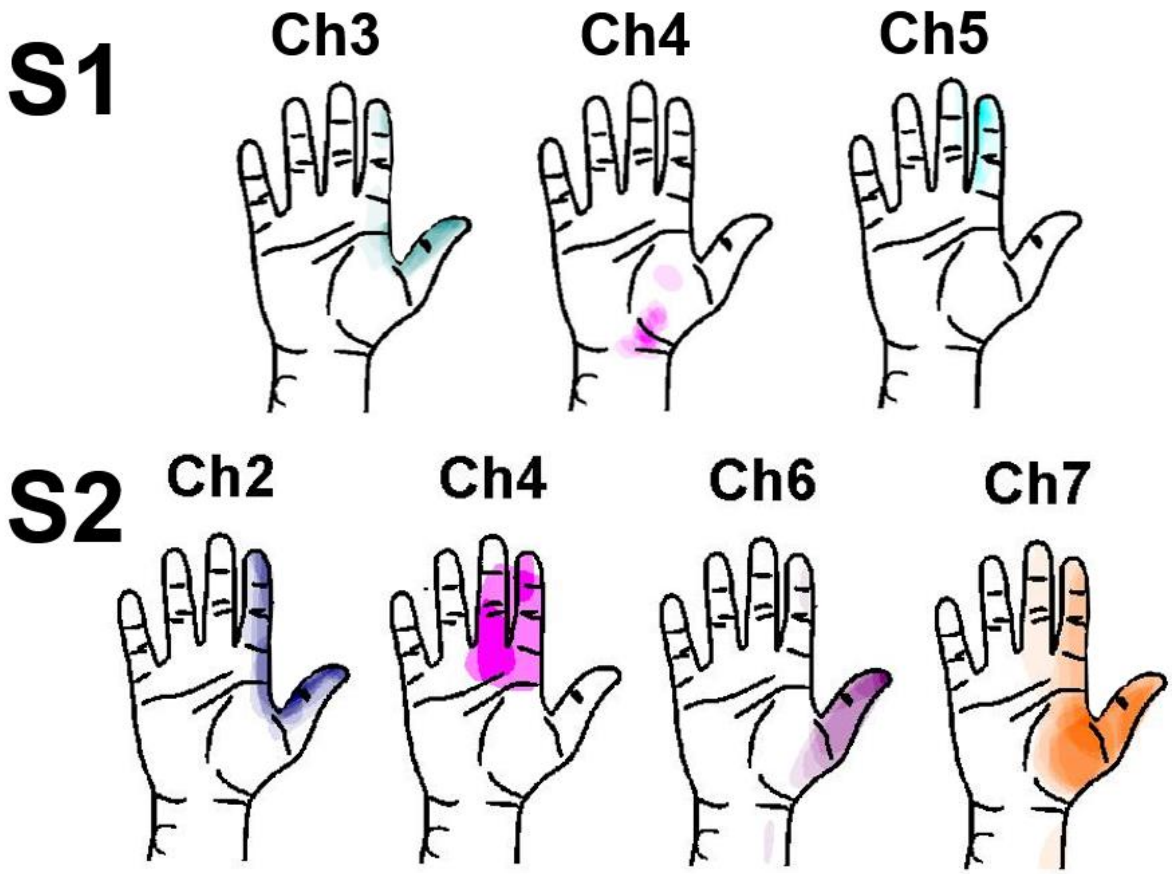

Fig. S6. Projected fields perceived on the missing hand from single-channel stimulation. For each contact, stimulation with parameters across the ranges used in the experimental sessions were presented and the subject was asked to draw each unique location. The fields reported for a given contact across all sessions were then overlaid such that the opacity of the region reflects the frequency of sensation in that region. The projected fields remained highly consistent for each channel across sessions. Subject 1 received stimulation on electrode channels 3, 4, and 5 on the median nerve. Subject 2 receive stimulation on channels 2, 4, 6, and 7 on the median nerve.

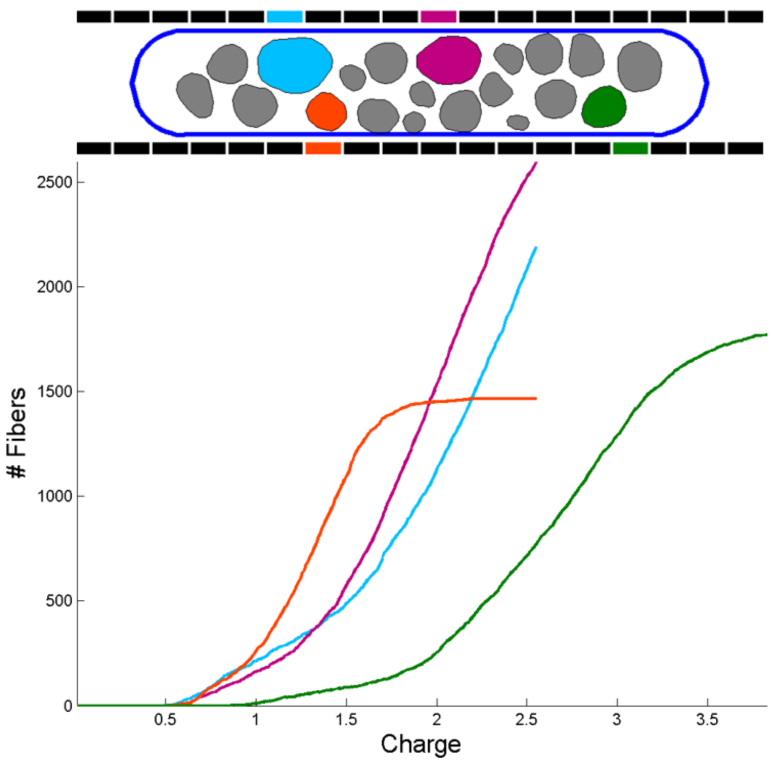

Fig. S7. Recruitment of afferent fibers with increasing charge. The colored lines represent the recruitment curves for the first fascicle activated by electrical stimulation for each of four different electrode contacts (shown in the inset at the top). The size and distance of each fascicle from the stimulating electrode impacts the slope of the recruitment curve. All curves can be well approximated by a sigmoidal function. Inset: The black bars are metal contacts in a theoretical 36-channel FINE surrounding a nerve (epineurium outlined in blue). An active contact and the corresponding fascicle recruited first are highlighted in the same color. Surrounding fascicles in the nerve are shown in grey.