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FREQUENCY SHAPES THE QUALITY OF TACTILE PERCEPTS EVOKED THROUGH ELECTRICAL STIMULATION OF THE NERVES

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23 **ABSTRACT**

24 Electrical stimulation of the peripheral nerves of human participants provides a unique
 25 opportunity to study the neural determinants of perceptual quality using a causal manipulation.
 26 A major challenge in the study of neural coding of touch has been to isolate the role of spike
 27 timing – at the scale of milliseconds or tens of milliseconds – in shaping the sensory experience.
 28 In the present study, we address this question by systematically varying the frequency (PF) of
 29 electrical stimulation pulse trains delivered to the peripheral nerves of seven participants with
 30 upper and lower extremity limb loss via chronically implanted neural interfaces. We find that
 31 increases in PF lead to systematic increases in perceived frequency, up to about 50 Hz, at which
 32 point further changes in PF have little to no impact on sensory quality. Above this transition
 33 frequency, ratings of perceived frequency level off, the ability to discriminate changes in PF is
 34 abolished, and verbal descriptors selected to characterize the sensation change abruptly. We
 35 conclude that sensation quality is shaped by temporal patterns of neural activation, even if
 36 these patterns are imposed on a fixed neural population, but this temporal patterning can only
 37 be resolved up to about 50 Hz. These findings highlight the importance of spike timing in
 38 shaping the quality of a sensation and will contribute to the development of encoding
 39 strategies for conveying touch feedback through bionic hands and feet.

40 **SIGNIFICANCE STATEMENT**

41 A major challenge in the study of neural coding of touch has been to understand how temporal
 42 patterns in neuronal responses shape the sensory experience. We address this question by
 43 varying the frequency (PF) of electrical pulse trains delivered through implanted nerve
 44 interfaces in seven amputees. We concomitantly vary pulse width to separate the effect of
 45 changing PF on sensory quality from its effect on perceived magnitude. We find that increases
 46 in PF lead to increases in perceived frequency, a qualitative dimension, up to about 50Hz,
 47 beyond which changes in PF have little impact on quality. We conclude that temporal
 48 patterning in the neuronal response can shape quality and discuss the implications for restoring
 49 touch via neural interfaces.

50 **INTRODUCTION**

51 Physical interactions with our environment give rise to a rich and complex tactile experience.
 52 While a touch can be readily localized to a specific location on the body and described as light
 53 or strong, its sensory quality is multifaceted and often difficult to describe. For example, the
 54 tactile experience of a fabric is different from that of a vibration. Sensory quality does not fall
 55 on one continuum or even a few. Indeed, even a single sensory subspace, such as that for
 56 tactile texture, is complex and can be further broken down into component dimensions and
 57 subspaces (Hollins et al., 1993, 2000; Bergmann Tiest and Kappers, 2006; Lieber and Bensmaia,
 58 2019).

59 The neural underpinnings of sensory quality are also difficult to identify. The perceived location
 60 of a touch is determined by the receptive field location of the activated neural population
 61 (Ochoa and Torebjork, 1983; Schady et al., 1983; Johansson and Flanagan, 2009). The
 62 magnitude of a percept is determined by the overall population spike rate evoked in the
 63 peripheral nervous system (Muniak et al., 2007; Graczyk et al., 2016). Quality, on the other

64 hand, is determined by the specific spatiotemporal pattern of activation elicited in the nervous
 65 system. Some patterns of activation give rise to a texture percept, others to a motion percept,
 66 and these patterns can co-occur and be multiplexed in the nerve (Goodman and Bensmaia,
 67 2018).

68 One determinant of quality is the degree to which each class of tactile nerve fibers is activated
 69 by the stimulus. Indeed, the sensation evoked when an individual nerve fiber is electrically
 70 activated depends on its afferent class – whether it is slowly-adapting or rapidly-adapting, type
 71 I or type II (Ochoa and Torebjork, 1983; Torebjork et al., 1987). As a result, one reason different
 72 tactile stimuli evoke sensations of different qualities is because they differentially activate
 73 different classes of tactile afferent fibers. For example, skin vibrations recruit afferent
 74 populations in a frequency-dependent manner (Talbot et al., 1968; Freeman and Johnson,
 75 1982; McGlone and Reilly, 2010). This differential recruitment accounts in part for the
 76 frequency-dependence of vibrotactile pitch, the qualitative dimension associated with changes
 77 in vibratory frequency (Goff, 1967; Roy and Hollins, 1998; McGlone and Reilly, 2010).

78 Another determinant of quality is the temporal patterning in the spiking response. For example,
 79 the perception of texture is shaped by the millisecond-level timing of sequences of spikes
 80 evoked in nerve fibers (Weber et al., 2013). Similarly, phase-locked responses of nerve fibers to
 81 skin vibrations underlie their perceived vibrotactile pitch, which complements the information
 82 about frequency carried in the pattern of recruitment across classes (Mackevicius et al., 2012;
 83 Birznieks and Vickery, 2017). In natural mechanical touch, the co-occurrence of these coding
 84 principles – differential recruitment and temporal patterning – makes it difficult to disentangle
 85 their respective roles in the determination of sensory quality.

86 Electrical stimulation offers a unique opportunity to examine the contribution of spike timing
 87 on tactile perception independently of the relative recruitment of afferent classes. An electrical
 88 pulse train delivered to the nerve will synchronously activate local neurons regardless of fiber
 89 class, as there are no known class-specific properties to enable preferential recruitment
 90 (Mogyoros et al., 1996; Howells et al., 2012). The impact of stimulation frequency on quality is
 91 thus mediated by the phase-locked spiking response, as all fiber classes are equally likely to be
 92 activated. Thus, by varying stimulation frequency in the peripheral nerve, we can directly
 93 examine the role of spike timing on quality perception.

94 Electrical stimulation of somatosensory peripheral nerves evokes vivid tactile sensations that
 95 are experienced on the hand (Dhillon and Horch, 2005; Ortiz-Catalan et al., 2014; Raspopovic et
 96 al., 2014; Tan et al., 2014; Davis et al., 2016). While increasing stimulation frequency in the
 97 peripheral nerve is known to increase the perceived intensity of the percept, mediated by a
 98 concomitant increase in the population firing rate (Graczyk et al., 2016), the effect on quality is
 99 less clear. To fill this gap, we sought to understand how temporal patterns of activation in the
 100 nerve affect the quality of tactile percepts. We approached this question in two sets of
 101 psychophysical experiments with human amputees implanted with multi-channel nerve cuff
 102 electrodes. First, we investigated how changes in the frequency of electrical stimulation impact
 103 the perceived frequency of the stimulus. In these experiments, participants judged the percept
 104 evoked by a pulse train along a single dimension or discriminated pulse trains that varied in
 105 frequency. Second, we investigated the impact of pulse frequency on a multidimensional space

defined by verbal descriptors to achieve a more holistic understanding of how pulse frequency shapes the quality of an electrically-evoked percept. Understanding how spike timing shapes quality will help unravel the peripheral neural code of touch and will lead to the development of approaches to convey a richer, more natural touch experience to individuals with bionic hands and feet.

METHODS

Participants

Six people, all male, volunteered for this study. Four participants had unilateral acquired amputations of the upper limb below the elbow and two had unilateral acquired amputations of the lower limb below the knee. All participants were implanted with multi-contact peripheral nerve cuff electrodes, either Flat Interface Nerve Electrodes (FINEs) or Composite Flat Interface Nerve Electrodes (C-FINEs)(Freeberg et al., 2017). Upper limb participants (referred to as UL01-UL04) were implanted with 8-channel FINEs or 16-channel C-FINEs around the median, ulnar, and/or radial nerves between 3 and 7 years prior to participation in the present study. Contacts were selected for testing that elicited comfortable sensations on the anterior surface of the hand. Lower limb participants (LL01 and LL02) were implanted with 16-channel C-FINEs around the sciatic and tibial nerves between 1 and 3 years prior to participation in the present study. Contacts were selected for testing that elicited comfortable sensations on the plantar surface of the foot or posterior aspect of the ankle. Percutaneous leads connected the cuff electrodes to an external neurostimulator. Stimulation waveforms were square, biphasic, cathodic-first, and charge-balanced. Stimulation parameters were set in MATLAB (MathWorks, Inc.; Natick, MA, USA) and then sent to a computer running xPC Target (MathWorks, Inc.; Natick, MA, USA), which then drove the stimulator. The stimulator could produce stimulation with PW in the range of 5 to 255 μ s in increments of 1 μ s, PA in the range of 0 to 2 mA in increments of 0.1 mA, and inter-pulse intervals in the range of 1 to 10,000 ms in increments of 1 ms.

The Louis Stokes Cleveland Department of Veterans Affairs Medical Center Institutional Review Board and Department of the Navy Human Research Protection Program approved all procedures. This study was conducted under an Investigational Device Exemption obtained from the United States Food and Drug Administration. All participants provided written informed consent to participate in this study, which was designed in accordance with relevant guidelines and regulations.

Frequency estimation task

In each trial, a 1-second pulse train was delivered and participants estimated the perceived frequency of the evoked sensation. Estimations were made using a visual analog scale displayed on a computer monitor, which displayed “Slowest possible frequency” on the far left of the scale and “Fastest possible frequency” on the far right of the scale. Participants were asked to ignore changes in intensity and location when making frequency estimates. A 3-second inter-trial interval was enforced to minimize the effects of perceptual adaptation (Graczyk et al., 2018).

For each electrode contact, we tested twelve pulse frequencies (PF) and three pulse widths (PW). PFs were set to 2, 5, 10, 20, 35, 50, 65, 80, 100, 200, 500, and 1000 Hz. The three PWs were chosen on a per-contact basis to span the full range of suprathreshold, comfortable intensities. Briefly, we used a staircase procedure to find the minimum PA value that produced a detectable percept at the maximum PW of the stimulator (255 μ s). This PA value was typically between 0.5 and 1 mA. We then used a two-alternative forced-choice tracking paradigm to find the minimum PW value that elicited a detectable percept at this threshold PA (Graczyk et al., 2016). The “Low” PW value in the estimation task was the minimum PW that was reliably perceived at 2 Hz. The “High” PW value was chosen as the maximum PW that was comfortable at 500 Hz. The “Mid” PW value was chosen as the midpoint between the “Low” and “High” values. Preliminary tests with each contact indicated that these PWs resulted in clear differences in perceived intensity. The 36 stimuli were presented in pseudo-random order fifteen times per contact, split into six experimental blocks of 90 trials, all performed on the same day. Five electrode contacts across three participants were included in this analysis.

Frequency ratings were normalized by dividing each estimate by the within-block mean rating. Normalized ratings were then averaged within-contact for each PW and PF condition. We then fit piecewise linear functions to the base-10 logarithm of frequency, separated by PW condition. For each fit, coefficient estimates over their relevant ranges were randomly generated ten times, and the combination with the lowest mean squared error was selected. The transition between the rising and falling phases of the perceived frequency ratings was obtained from the optimized parameters. The transition metric was averaged across participants, contacts, and PWs after first removing two values derived from poor fits ($R^2 < 0.5$) and one outlier that was more than two standard deviations above the mean. Means and standard errors of the frequency estimates were then calculated across participants and contacts within each PW and PF condition.

170 ***Frequency discrimination task***

Each trial consisted of two successive 1-second pulse trains separated by a 1-sec inter-stimulus interval. Participants judged which of the two sequentially presented pulse trains was higher in perceived frequency. In each experimental block, a standard stimulus (at 20, 50, or 100 Hz) was paired with a comparison stimulus whose PF and PW varied from trial to trial. The comparison PFs ranged from 25 to 175% of the standard PF. Specifically, for the 20-Hz reference, the comparison PFs were 5, 10, 16, 18, 20, 22.4, 25, 30, and 35 Hz; for the 50-Hz reference, the comparison PFs were 12.5, 25, 40, 45, 50, 55.55, 62.5, 76, and 90.9 Hz; and for the 100-Hz reference, the comparison PFs were 25, 50, 83, 90, 100, 111, 125, 145, and 166 Hz. The comparison PW took on one of three values: one shorter than, one equal to, and one longer than the standard PW. PWs were based on the same criteria as in the frequency estimation task. All PW values were between 70 to 130% of the standard PW. The standard stimulus was always at the intermediate PW. In each block, each stimulus pair was presented 10 times, and both the order of stimuli within the pair and the order of the pairs varied pseudo-randomly. The inter-trial interval was enforced to be at least 3 seconds long. Thus, each experimental block evaluated one electrode contact and consisted of 270 trials (9 comparison PFs $\times$ 3 comparison PWs $\times$ 10 repetitions). Eight contacts across four participants, six contacts across two

187 participants, and six contacts across two participants were evaluated for the 20, 50, and 100 Hz
188 standard, respectively.

189 Psychophysical performance was calculated as the proportion of trials in which the comparison
190 stimulus was judged to be higher in perceived frequency than the standard stimulus.
191 Psychometric curves were then constructed by fitting a cumulative normal density function to
192 these proportions. Separate psychometric functions were fit for each standard frequency (20,
193 50, and 100 Hz). Just noticeable differences (JNDs) were calculated as the change in frequency
194 required to achieve 75% correct performance. Two JND estimates were obtained from each
195 psychometric function, one above and one below the standard, and these two estimates were
196 averaged. Sessions in which performance did not achieve the 75% threshold performance
197 criterion (above or below the standard) were considered to have an undefined or incalculable
198 JND and were considered to be “poor” performance contacts. These data points were omitted
199 from further analysis. The point of subjective equality (PSE) was defined as the comparison
200 frequency that corresponded to 50% correct performance, as calculated from the fitted
201 psychometric functions.

202 ***Subjective quality description task***

203 On each trial, a 2-second pulse train was delivered and participants were asked to indicate
204 which subset of a list of 30 qualitative descriptors applied to the percept (word list shown in
205 Figure 1d). These words were selected based on prior studies of language associated with
206 natural and artificial somatosensation (Adrian, 1919; Goff, 1967; Tashiro and Higashiyama,
207 1981; Macefield et al., 1990; Kaczmarek and Haase, 2003; Guest et al., 2011; Geng et al., 2012;
208 Perovic et al., 2013). Participants were encouraged to select as many words as necessary to
209 fully describe the sensation. Participants were instructed to use their own definitions for each
210 descriptor, but to maintain consistency throughout each experimental session. For example, if
211 two stimuli felt identical, they were asked to select the same subset of words for both trials.
212 Stimulation was applied at one of 9 PFs and 3 PWs for each stimulus. Stimulation PF was set to
213 2, 5, 10, 20, 50, 100, 200, 500, and 1000 Hz, and PWs were selected in the same manner as in
214 the frequency estimation task. Each stimulus was presented 20 times in pseudo-randomized
215 order. A 2-second inter-trial interval was enforced. A “no sensation” option was provided for
216 trials in which the participant did not feel the stimulus. Eleven electrode contacts were tested
217 across all six participants. Stimulation conditions in which “no sensation” was selected in more
218 than five trials were excluded from the analysis. We computed the proportion of times each
219 descriptor word was selected for each stimulation condition for each contact after “no
220 sensation” trials were removed. The result was a set of 30 proportions for each stimulation
221 condition.

222 To compute within-participant consistency in word selection, we ran a correlation analysis of
223 word proportions between the sets of contacts tested within the same participant. Those
224 participants that only performed the subjective quality test with a single contact were excluded
225 from this analysis. To calculate across-participant consistency in word selection, we first
226 averaged the proportions across contacts for each participant, then computed the correlation
227 in these proportions for each pairing of participants.

228 *Dissimilarity matrices*

229 Having observed that different participants used different words to describe the electrically
 230 evoked sensations, we hypothesized that we could achieve a more generalizable representation
 231 of tactile quality by computing differences in descriptors between stimulation conditions. To
 232 reduce redundant or highly correlated descriptors within each dataset, we ran a principal
 233 component analysis (PCA) on the word proportion vectors across all stimuli (a 30 x 27 data
 234 matrix) on a participant-by-participant basis and retained the components necessary to explain
 235 95% of the variance. We then projected the stimuli onto this reduced dimensionality space and
 236 calculated the pairwise distances between them, resulting in a 27 x 27 distance matrix for each
 237 tested electrode contact (n=11). To remove the influence of the number of dimensions on
 238 calculated distances, we normalized distances to the maximum inter-condition distance (which
 239 was set to 1). For some analyses (e.g. that shown in Figure 6a), we averaged the coordinates for
 240 each PF across PWs and then recomputed the distances, yielding a 9 x 9 distance matrix.

241 To assess the within-participant consistency in dissimilarities, we computed the correlation
 242 between distance matrices obtained from different contacts for each participant. To assess
 243 across-participant consistency in dissimilarities, we first averaged the dissimilarities across
 244 contacts for each participant then computed the correlation in the dissimilarity matrices for
 245 each pair of participants.

246 To examine the quality dissimilarity between successive PF conditions, we computed the
 247 distance between the coordinates of two adjacent PFs in the reduced dimensionality space,
 248 then averaged these distances across PWs and contacts.

249 Finally, we performed a multivariate regression analysis with Δ PF, Δ PW, and their interaction as
 250 factors. We performed this analysis after averaging the 27 x 27 distance matrices across
 251 participants and contacts. The Δ PF and Δ PW factors were z-scored before running the
 252 regression to standardize the regression coefficients. This analysis was also performed with the
 253 data split into two sets: one for PFs below 50 Hz and one for PFs above 50 Hz. We verified that
 254 the regression model fit to the dissimilarity matrix averaged across contacts and participants
 255 yielded the same conclusions as one fit to data pooled across individual contacts and
 256 participants. We also fit regression models to individual participants' dissimilarity matrices, and
 257 verified that the regression coefficients averaged across these models yielded the same
 258 conclusions. We then performed a step-wise regression, in which we assessed whether PF
 259 accounted for a significant proportion of variance in the dissimilarity ratings after differences in
 260 perceived frequency had been regressed out. For this analysis, we first computed differences in
 261 perceived frequency for each stimulus pair from the across-contact averages of perceived
 262 frequency obtained in the first experiment. We then regressed dissimilarity against differences
 263 in perceived frequency ratings and regressed the residuals against z-scored Δ PF. This analysis
 264 was performed separately for stimuli below and above 50 Hz.

265 *Statistics*

266 **Frequency estimation.** We determined the influence of PW on the transition frequency
 267 between the rising and falling regimes of perceived frequency using a one-way ANOVA versus
 268 PW. We then split the data into two regimes: 0-50 Hz and above 50 Hz. For each regime, we ran

a two-way ANOVA on the normalized frequency estimations pooled across contacts and participants with factors of PW and PF. All statistical analyses were performed in Minitab (Minitab, LLC; State College, PA, USA) with an alpha level of 0.05.

Frequency discrimination. We studied the influence of PW on the JNDs and PSEs of the psychometric functions using repeated measures ANOVA with different PWs and different contacts as factors. JNDs and Weber fractions at 20Hz standard were compared to their counterparts at 50Hz using a two-sample t-test. All statistical analyses were performed in MATLAB with alpha level of 0.05.

Subjective quality reports. We ran a linear regression to determine how the number of words selected by each participant changed with PF. We compared within- and across-participant correlations in quality descriptors and dissimilarities using a one-way ANOVA with Tukey pairwise comparisons. We compared quality dissimilarities between successive PFs using a two-way ANOVA with Tukey pairwise comparisons with factors for PF and PW. These analyses, as well as the univariate and multivariate regressions, were performed in MATLAB and/or Minitab with alpha level of 0.05.

RESULTS

Tactile sensations were elicited by delivering electrical pulse trains to the somatosensory nerves, either via Flat Interface Nerve Electrodes (FINEs) or Composite Flat Interface Nerve Electrodes (C-FINEs) (Figure 1a). Four unilateral upper limb amputees and two unilateral lower limb amputees participated in the study.

Perceived frequency increases with pulse frequency up to ~50 Hz

First, we assessed the degree to which changes in frequency can be judged along a single perceptual continuum. To this end, we delivered stimuli that varied in pulse frequency (PF) and asked participants to rate the perceived frequency by positioning a slider along a horizontal bar (Figure 1b). To ensure that participants rated frequency rather than intensity, we varied the stimulation pulse width (PW), which also modulates perceived intensity (Graczyk et al., 2016), from detection threshold to the maximum comfortable level. If frequency estimates were based solely on perceived intensity, then ratings would increase with increases in either PF or PW. PWs were scaled based on the detection threshold, which was measured for each contact separately.

At low PFs, perceived frequency increased logarithmically with PF and was independent of PW (Figure 2). At higher PFs, perceived frequency remained constant or even decreased with increases in PF and was instead modulated by PW (Figure 2b). We fit piecewise logarithmic functions to the relationships between perceived frequency and PF to determine the transition point between the rising and falling (or sustained) portions of the relationships ($R^2 = 0.93 \pm 0.01$, mean $\pm$ SEM) (Figure 2a). We found the transition frequency to be 66.0 ± 1.1 Hz (mean $\pm$ SEM). Transition frequency was highly consistent across participants and contacts and was not significantly modulated by PW (ANOVA, $F(2,11) = 0.43$, $p = 0.66$).

Having identified two different regimes in the PF response characteristic, we then examined the impact of PF and PW on perceived frequency in each regime separately. Below the transition

309 PF, perceived frequency was significantly dependent on PF ($F(5,82) = 27.83$, $p < 0.001$) but not
 310 PW ($F(2,82) = 1.58$, $p = 0.212$). Above the transition PF, perceived frequency ratings depended
 311 on PW ($F(2,82) = 14.08$, $p < 0.001$) but not PF ($F(5,82) = 1.33$, $p = 0.262$). In summary, changes in
 312 PF exert a systematic effect on perceived frequency up to about 60 Hz, and this perceptual
 313 effect can be clearly distinguished from perceived magnitude. Increases in PF beyond 60 Hz do
 314 not change the quality of the percept along the perceived frequency continuum.

315 ***Frequency discrimination is abolished above ~50 Hz***

316 Having found that the effects of PF on electrically evoked tactile percepts occupy two regimes –
 317 one at low and one at high frequencies – we next examined whether these regimes might be
 318 reflected in the participants' ability to discriminate *changes* in PF. To this end, we asked
 319 participants to judge which of two sequentially presented pulse trains was higher in perceived
 320 frequency (Figure 1c). In each experimental block, which consisted of 270 trials, a standard
 321 stimulus (at 20, 50, or 100 Hz) was paired with a comparison stimulus whose PF and PW varied
 322 from trial to trial over a range (25-175% of the standard PF). The comparison PW took on one of
 323 three values: one shorter than, one equal to, and one longer than the standard PW (scaled
 324 based on the threshold PW, see Methods). The variation in PW was intended to reduce or
 325 abolish the informativeness of perceived magnitude, which is modulated by changes in both
 326 PW and PF (Graczyk et al., 2016).

327 ***Discrimination with a constant pulse width***

328 First, we examined participants' ability to distinguish changes in PF independently of PW by
 329 only analyzing same-PW pairs. We found that participants could discriminate on the basis of
 330 frequency on most electrode contacts when the standard PF was set at 20 Hz or 50 Hz, as
 331 evidenced by smooth psychometric functions over the range tested (Figure 3a & b). With the
 332 100-Hz standard, however, PF discrimination performance was very poor on all contacts, and
 333 participants never achieved criterion performance (75% correct, Figure 3c, see Methods). The
 334 just noticeable difference (JND) – defined as the difference in PF that yields 75% correct
 335 discrimination – was 3.867 ± 0.51 Hz and 9.250 ± 0.71 Hz (mean $\pm$ SEM) for the 20- and 50-Hz
 336 standards, respectively, yielding nearly constant and statistically indistinguishable Weber
 337 fractions (0.193 ± 0.03 Hz and 0.185 ± 0.01 Hz) (Figure 3e). In contrast, JNDs were undefined for
 338 the 100-Hz standard for all tested contacts. Note that participants could perceive the stimuli
 339 even when the JND was undefined but they could not discriminate between them.

340 ***Effect of pulse width on frequency discrimination***

341 Second, we examined the degree to which PF could be discriminated independently of changes
 342 in perceived magnitude. Trials with equal-PW pairs were interleaved with trials in which the PW
 343 of the comparison was different from that of the standard stimulus. To the extent that
 344 participants relied on differences in perceived magnitude to make their frequency judgments,
 345 PW would systematically bias participants' frequency judgments, thereby causing lateral shifts
 346 in psychometric functions. Changes in PW may also lead to changes in the clarity or vividness of
 347 the evoked percepts, thereby resulting in changes in the discriminability of PF.

348 We observed systematic leftward shifts in the psychometric functions when the comparison PW
 349 was lower than the standard PW and systematic rightward shifts when the comparison PW was
 350 higher than the standard PW (Figure 4a, b, d & e). In other words, pulse trains with lower PW
 351 tended to be perceived as higher in frequency across PFs. This bias was quantified by
 352 computing the point of subjective equality (PSE) – the PF at which participants were equally
 353 likely to select the standard as they were the comparison stimulus. The PSE increased as the
 354 comparison PW increased for both the 20-Hz and 50-Hz standards (Figure 4b & e, repeated
 355 measures ANOVA, $F(2,16) = 17.34$, $p < 0.001$; $F(2,14) = 17.46$, $p = 0.0012$, respectively). In
 356 summary, the participants exhibited a slight tendency to select the more intense stimulus as
 357 being lower in frequency, consistent with previous findings that the pitch of a vibrotactile
 358 stimulus decreases as the stimulus amplitude increases over this range of frequencies (Roy and
 359 Hollins, 1998; Prsa et al., 2021). Note that this tendency was also observed in the frequency
 360 estimation ratings but was too weak to achieve statistical significance.

361 Next, we investigated the degree to which the comparison PW affected participants' sensitivity
 362 to changes in PF by examining the effect of PW on the JND. For the 20-Hz standard, we found
 363 no systematic effect of PW on JND (Figure 4c, repeated measures ANOVA, $F(2,16) = 1.35$, $p =$
 364 0.3082). For the 50-Hz standard, on the other hand, JNDs increased as PW increased (Figure 4f,
 365 $F(2,14) = 9.58$, $p = 0.0075$). In other words, participants became somewhat less sensitive to
 366 changes in PF at higher PWs, but only for the higher-PF standard.

367 ***Subjective reports of sensory quality depend on stimulation frequency***

368 Given that PF reliably influenced perceived quality along a single frequency continuum, we then
 369 investigated how PF shapes subjective quality more broadly. To this end, participants indicated
 370 which subset of a list of 30 qualitative descriptors pertained to each stimulus. Participants were
 371 encouraged to select as many words as necessary to describe the electrically evoked sensation.

372 ***Qualitative reports***

On average, participants selected 6.5 ± 2.6 words (mean $\pm$ SEM) to describe each sensation. The total number of words chosen to describe a stimulus varied across participants, ranging from 5 to 22.

Examination of the participants' word selections revealed that stimulation PF influenced the descriptors chosen to characterize the stimuli. That is, different sets of words were selected to describe low-frequency stimuli than high-frequency stimuli (Figure 5, Table 1), as has been found with vibrotactile stimulation (Talbot et al., 1968) and intracortical microstimulation (Hughes et al., 2021). For example, descriptors related to periodic sensations, such as 'tapping', 'pulsing', 'twitching', and 'flutter', were commonly selected for low-PF stimuli, whereas continuous sensations, such as 'tingling', 'buzzing', 'electrical', 'pressure', and 'touch', were reported for high-PF stimuli (Table 1). In addition, the total number of reported descriptors increased as a function of stimulation PF (linear regression, $p < 0.001$).

Participants used similar descriptors across electrode contacts, as evidenced by highly correlated descriptor selection within-participants ($R^2 = 0.66 \pm 0.08$, mean $\pm$ SEM). The consistency in reports across electrode contacts indicates that quality is largely independent of which region of the nerve is stimulated. However, the descriptors ascribed to individual stimuli varied widely from participant to participant (Figure 5), yielding weak correlations in descriptor selections across participants ($R^2 = 0.14 \pm 0.04$). These variations likely reflect the participants'

Table 1. The selection rate for perceptual descriptors differed for low frequency and high frequency stimulation conditions. Selection rates are given as the percentage of total trials that each descriptor word was reported across all participants, contacts, and PWs. The top seven most frequently reported words for each frequency regime are shown. Note that since multiple words can be selected for a single trial, the selection rates will not sum to 100%.

Low frequency (<50 Hz)		High frequency (≥ 50 Hz)	
Descriptor	Selection Rate	Descriptor	Selection Rate
Tapping	36%	Tingling	49%
Pulsing	34%	Buzzing	28%
Tingling	29%	Electrical	26%
Twitching	15%	Vibrating	22%
Electrical	14%	Pressure	13%
Flutter	7%	Touch	12%
Vibrating	6%	Movement	9%

idiosyncratic descriptor preferences, since some words, such as tapping and pulsing, may be construed as synonymous.

A robust representation of sensory quality

To overcome participant-specific descriptor choice and assess the effect of PF on quality across participants, we computed differences in descriptor selection between each pair of stimuli. To this end, we first represented quality as a 30-element vector, where each element corresponded to the proportion of trials in which a given descriptor was selected. We then ran a principal component analysis (PCA) on the vectors of individual participants to consolidate

redundant or highly correlated descriptors. Finally, we computed the Euclidean distance between each pair of stimulation conditions (PW and PF combinations) in this reduced dimensional space. These distances represent the perceived dissimilarity between pairs of stimuli, estimated from the differences in descriptor selection (Figure 6a,b).

We found that the resulting dissimilarity matrices were highly consistent across participants and electrode contacts (Figure 6a,b). Indeed, dissimilarity matrices were significantly more similar across participants ($R^2 = 0.81 \pm 0.04$) than were the descriptor selections from which they were derived ($R^2 = 0.14 \pm 0.04$) (One-way ANOVA, $F(3,42) = 35.80$, $p < 0.001$) (Figure 6c, teal bars). The consistency in dissimilarity matrices across participants suggests that the relationship between sensation quality and PF is similar across participants, despite idiosyncratic descriptor usage.

Impact of PF on overall quality

Having established a robust representation of multi-dimensional quality based on dissimilarity, we then assessed the degree to which changes in PF led to changes in the quality of the evoked percept. We found a sharp transition in sensation quality between 20- and 50-Hz for all tested contacts. In fact, the dissimilarity between 20-Hz and 50-Hz stimuli was significantly greater than the dissimilarity between any other pair of adjacent frequencies (ANOVA, $F(7,197) = 16.14$, $p < 0.001$) (Figure 6d). In other words, the perceptual quality was consistent across PFs ranging from 2 to 20 Hz and across PFs from 50 to 1000 Hz, but these two subsets of stimuli felt very different from one another. There was no systematic effect of stimulation PW on the dissimilarities between successive PFs (ANOVA, $F(2,197) = 1.22$, $p = 0.3$).

We then determined the extent to which differences in PF and PW resulted in differences in the evoked sensation. To quantify the impact of PF and PW on quality, we averaged the dissimilarity matrices across contacts and participants (Figure 7a) and regressed the resulting matrix on differences in PF or PW (ΔPF , ΔPW). The regression model that included both ΔPF and ΔPW yielded accurate predictions of dissimilarity ($R^2 = 0.67$, $F(3,725) = 499$, $p < 0.001$) (Figure 7b). While both ΔPF and ΔPW had significant impacts on dissimilarity, the contribution of ΔPF was much higher than that of ΔPW (standardized coefficients: $\beta_{\Delta PF} = 0.17$, $p < 0.001$; $\beta_{\Delta PW} = 0.05$, $p < 0.001$) (Figure 7c). The interaction between ΔPF and ΔPW was significant but weak ($\beta_{\Delta PF * \Delta PW} = -0.04$, $p < 0.001$). We performed the same analyses on individual participants' data and obtained the same results, confirming that these results were not an artifact of pooling (Figure 7d).

Given the sharp transition in perceived quality around 50 Hz, we fit separate regression models for the dissimilarity data below 50 Hz and above 50 Hz. At low PFs, the regression was nearly identical to that obtained using the full dataset ($R^2 = 0.74$, $F(3,221) = 214$, $p < 0.001$; $\beta_{\Delta PF} = 0.18$, $p < 0.001$; $\beta_{\Delta PW} = 0.05$, $p < 0.001$; $\beta_{\Delta PF * \Delta PW} = -0.04$, $p < 0.001$) (Figure 7e). In contrast, at high PFs, the effect of PW dominated that of PF ($R^2 = 0.74$, $F(3,140) = 302$, $p < 0.001$; $\beta_{\Delta PF} = 0.04$, $p < 0.001$; $\beta_{\Delta PW} = 0.11$, $p < 0.001$; $\beta_{\Delta PF * \Delta PW} = -0.03$, $p < 0.001$) (Figure 7f).

Relationship between perceived frequency and dissimilarity

438 Finally, we determined whether the effect of PF on dissimilarity could be explained solely based
 439 on its effect on perceived frequency. That is, we examined whether PF modulates perceptual
 440 quality along a single continuum. To this end, we first regressed dissimilarity on the perceived
 441 frequency ratings obtained in the first experiment, then assessed whether the residuals co-
 442 varied with Δ PF. In the low-frequency regime, we found that differences in perceived frequency
 443 predicted dissimilarity ratings well ($R^2 = 0.71$, $F(1,223) = 545$, $p < 0.001$) (Figure 8a) and that Δ PF
 444 was not significantly predictive of the residuals ($R^2 = -0.004$, $F(1,223) = 0.07$, $p = 0.80$) (Figure
 445 8c). Thus, the effect of PF on quality is confined to a single continuum in the low frequency
 446 regime.

447 In the high-frequency regime, we similarly found that perceived frequency was a significant
 448 predictor of dissimilarity, as it was in the low frequency regime ($R^2 = 0.53$, $F(1,142) = 164$; $p <$
 449 0.001) (Figure 8b). However, Δ PF continued to have a weak but significant effect on dissimilarity
 450 ratings after regressing out the effect of perceived frequency ($R^2 = 0.07$, $F(1,142) = 11$, $p =$
 451 0.001) (Figure 8d). Thus, in the high-frequency regime, the effect of PF on quality dissimilarity
 452 cannot be explained purely on the basis of perceived frequency, consistent with the finding that
 453 perceived frequency is not dependent on PF at those frequencies (see Figure 2). Note, however,
 454 that the overall impact of PF on quality was weak in the high-frequency range (see Figure 7f), so
 455 the magnitude of these effects was small.

456 DISCUSSION

457 *Stimulation frequency shapes sensory quality below 50 Hz*

458 We find that the temporal patterning in the neuronal response, which in this case was periodic
 459 and defined by PF, shapes the perceived quality of electrically-evoked tactile percepts both
 460 along a single continuum – perceived frequency – and across a multi-dimensional space defined
 461 by perceptual descriptors. The effect of PF on quality was most pronounced at low PFs, below
 462 approximately 50 Hz. In this frequency range, increases in PF led to increases in perceived
 463 frequency and systematic changes in verbal reports of sensory quality. In addition, we found
 464 that the impact of PF on verbally reported quality could be accounted for by variations in
 465 perceived frequency, demonstrating that PF modulates quality along a single continuum. The
 466 fact that PW did not have a significant effect on perceived frequency and had a marginal effect
 467 on overall quality in this frequency range indicates that the effect of PF on quality does not
 468 simply reflect a change in perceived magnitude.

469 Taken together, these results show that temporal patterning in the aggregate afferent response
 470 can modulate the quality of tactile percepts at low frequencies, despite the fact that this
 471 temporal patterning is distributed across afferents of all classes. Thus, the differential
 472 recruitment of afferent classes based on their frequency sensitivity profiles is not the only
 473 factor that shapes quality perception, though it likely plays an important role (Ochoa and
 474 Torebjork, 1983; Saal and Bensmaia, 2014; Birznieks et al., 2019).

475 *Changes in PF are indiscriminable at high frequencies*

476 Changing the frequency of vibrations delivered to the skin results in a change in the sensory
 477 experience along a continuum described as ‘vibrotactile pitch,’ underscoring its similarity to the

478 sensory consequences of changes in the frequency of an acoustic tone (Roy and Hollins, 1998;
 479 Yau et al., 2009). Human observers can reliably discriminate a change in vibrotactile frequency
 480 of around 20%, but sensitivity to changes in frequency decreases at higher vibration
 481 frequencies (Goff, 1967; Mountcastle et al., 1969, 1990; LaMotte and Mountcastle, 1975).
 482 Changes in vibrotactile frequency also produce changes in perceived magnitude (Verrillo et al.,
 483 1969). However, human participants can discriminate vibratory frequency in the presence of
 484 concomitant and independent changes in vibratory amplitude (Harvey et al., 2013),
 485 demonstrating that vibrotactile frequency also shapes the quality of the percept.

486 The ability to perceive the frequency of a vibration is thought to be mediated by a timing code
 487 in the nerve (Birznieks and Vickery, 2017; Birznieks et al., 2019). Sinusoidal vibrations delivered
 488 to the skin elicit periodic, phase-locked spiking responses in tactile nerve fibers, and the
 489 frequency of these responses matches the frequency of stimulation (Talbot et al., 1968;
 490 Mackevicius et al., 2012). When this temporal patterning is absent, for example at low stimulus
 491 amplitudes, the ability to discriminate frequency is abolished (Talbot et al., 1968).

492 Pulsed electrical stimulation of the nerve also produces a highly periodic response in the
 493 activated tactile nerve fibers (Formento et al., 2020) and this frequency-dependent temporal
 494 patterning likely mediates the ability to discriminate the perceived frequency of electrical pulse
 495 trains. In fact, sensitivity to changes in the frequency of electrical stimulation is similar to its
 496 vibrotactile counterpart, both yielding Weber fractions of ~ 0.2 . We also demonstrate that
 497 stimulation PF has a larger effect on the quality of an electrically-evoked sensation than it does
 498 on its magnitude: the Weber fraction for PF along the perceived magnitude continuum
 499 (0.3)(Graczyk et al., 2016) is higher than that along the perceived frequency continuum.

500 In contrast to vibrotactile frequency discrimination, which can be achieved over a wide range of
 501 frequencies up to 400 Hz and beyond (Goff, 1967; Harvey et al., 2013), we show that frequency
 502 discrimination of peripheral nerve stimulation is only possible at frequencies below ~ 50 Hz.
 503 Above this point, frequency discrimination falls to near chance. This is surprising in light of the
 504 fact that non-human primates can distinguish the PF of intracortical microstimulation up to
 505 around 200 Hz, though sensitivity to changes in PF decreases at high frequencies (Callier et al.,
 506 2020). While prior studies of electrocutaneous stimulation reported discriminability of pulse
 507 trains up to 100 Hz (Anani et al., 1977; Szeto et al., 1979; Ng et al., 2020, 2021), the
 508 psychophysical tasks in these prior studies were not designed to eliminate intensity cues and so
 509 results therefrom are difficult to compare with those reported here. Indeed, intensity
 510 discrimination of direct nerve stimulation has also been observed up to 100 Hz (Graczyk et al.,
 511 2016). Thus, while changes in PF can be discerned above 50 Hz, this ability may not rely on
 512 perceived frequency.

513 In addition, while our results showed that pulse trains with higher PW tended to be judged as
 514 lower in frequency, prior studies of intracortical microstimulation in non-human primates found
 515 that stimuli with higher pulse amplitude (PA) tended to be reported as being higher in
 516 frequency (Callier et al., 2020). Assuming that PW and PA have similar neural and sensory
 517 correlates, the impact of intensity on frequency discrimination is thus different for the nerve
 518 and cortex. The basis for these differences is unclear, but the neural consequences of

519 stimulation differ between nerve – a bundle of independent channels – and cortex – a densely
520 interconnected circuit.

521 ***Perceived dissimilarity is a robust way to quantify quality***

522 Quality is difficult to quantify because this aspect of a sensory experience occupies a high
523 dimensional space and measuring it relies on verbal reports, which are often highly
524 idiosyncratic. In this study, the specific words chosen to describe the qualitative sensory
525 experiences varied widely across participants. To mitigate this variability in descriptor selection,
526 we developed an approach to represent quality based on *differences* in the descriptors that
527 participants ascribed to the sensations. We found that this representation of quality was very
528 similar across participants, suggesting that tactile sensations evoked from neural stimulation
529 may be approximately equivalent across individuals despite idiosyncratic descriptor usage. We
530 propose that our approach could be used in future studies of quality perception to improve
531 comparisons across participants when the perceptual space is not confined to one or a few
532 experimenter-defined dimensions.

533 ***Quality abruptly changes at 50 Hz***

534 As discussed above, the ability to discriminate PF was abolished beyond about 50 Hz, and the
535 influence of PF on quality was far more pronounced at low PFs. In contrast, PW had a greater
536 impact on quality at high PFs than did PF. Furthermore, multi-dimensional quality also shifted
537 abruptly at ~50 Hz.

538 There are several possible explanations for the transition between the low and high frequency
539 regimes. One possibility is that the tactile nerve fibers cannot, as a population, phase lock to
540 stimulation pulse trains beyond about 50 Hz. Indeed, the temporal patterning in the neural
541 response likely drives the effect of stimulation PF on sensory quality. At high frequencies,
542 stimulation pulses may encroach on the refractory period resulting from the neural response to
543 the previous pulse. This phenomenon might then blur the temporal patterning in the
544 population response. However, given that the refractory period is typically less than 5 ms
545 (Ochoa and Torebjork, 1983) and that pulses are separated by 20 ms at 50 Hz, refractoriness is
546 unlikely to play a critical role in the observed transition in quality.

547 Another possibility is that the spikes evoked in the afferent population by each pulse get
548 desynchronized downstream due to conduction delays, thereby blurring the temporal
549 patterning at the population level. Indeed, neural conduction velocities vary across A β nerve
550 fibers that mediate touch due to the natural variance in fiber diameters (Johansson and Vallbo,
551 1983). In an adult male, the resulting propagation delays for signals to travel from the fingertip
552 to spinal cord range from 11 to 22 ms (J. B. Hursh, 1939). However, this jitter is not observed in
553 the vibrotactile responses of neurons in the somatosensory cortex (Mountcastle et al., 1969;
554 Harvey et al., 2013), which exhibit a high degree of phase locking, suggesting that some
555 compensatory mechanism might eliminate this endogenous jitter along the way to the brain.
556 The synchronized spikes delivered through a nerve cuff might then *become* desynchronized via
557 this compensatory mechanism. Given that the intrinsic delay correction would span about 10
558 ms (to correct for delays ranging from 11 to 22 ms) and that the cuff electrode is positioned
559 approximately halfway between the fingertip and spinal cord, the imposed jitter would span

approximately 5 ms. We might then expect frequency discrimination to break down around 200 Hz. Thus, this conduction delay-mediated desynchronization mechanism is also unlikely to be solely responsible for the transition at 50 Hz.

A more likely possibility is that the unnatural activation of the afferent submodalities by peripheral nerve stimulation obscures the temporal pattern imposed by stimulation at high PFs. Electrical stimulation recruits A β fibers based on their fiber diameter and nodal voltages (Richardson et al., 2000; McIntyre et al., 2002), regardless of their submodality class. In natural touch, the various submodalities of tactile fibers differ in the frequency profiles of their sensitivity to skin vibrations: slowly adapting type 1 (SA1) fibers respond preferentially to low-frequency vibrations, Pacinian corpuscle-associated (PC) fibers respond preferentially to high-frequency vibrations, and rapidly adapting fibers (RA) fibers exhibit intermediate frequency preferences (Talbot et al., 1968; Freeman and Johnson, 1982; McGlone and Reilly, 2010). Given the pulse amplitudes used in this study, tens or hundreds of nerve fibers are likely recruited (Graczyk et al., 2016). A high-PF pulse train will thus activate SA1 fibers, and perhaps RA fibers, to a much greater extent than would a high-frequency vibration delivered to the skin. This large, unnatural signal may obscure the critical signal carried by appropriately responding afferents, especially PC fibers. This phenomenon would be further magnified by the fact that RA1 and SA1 fibers far outnumber PC fibers in the periphery (a ratio of 1:1.6:0.6 for SA1:RA1:PC fibers) (Johansson and Vallbo, 1979).

The hypothesis that over-activation of SA1 and RA fibers could be implicated in poor frequency perception at high PFs is supported by previous studies of intraneural microstimulation: while increases in the PF delivered to individual RA afferents induces increases in perceived frequency at low PFs, further increases only lead to increased intensity (Torebjork et al., 1987). Stimulation of individual SA1 fibers leads to sustained percepts at all but the lowest PFs (Torebjork et al., 1987). The submodality over-activation hypothesis is also bolstered by the previous finding that the impact of peripheral afferent signals on cortical neural activity is highly dependent on the submodality of the peripheral afferents: PC signals in the periphery drive the *temporal patterning* of neural responses in cortex, whereas RA and SA1 signals instead drive the *strength* of the response in cortex (Saal et al., 2015). Thus, the unnatural strength of the SA1 signal (and perhaps the RA signal) evoked via peripheral nerve stimulation may muddle the crucial frequency signal transmitted by PCs to the cortex. This phenomenon would be exacerbated at high PFs, at which SA1 fibers are typically relatively quiescent, consistent with our results. A similar phenomenon, in which RA signals interfere with SA1 signals about local geometric features, has been previously documented (Bensmaïa et al., 2006).

Dependence of quality on PF is consistent across fascicles

We did not observe any electrode-specific differences in the impact of PF on perceived quality, and prior studies similarly found no electrode-specific differences in intensity perception (Graczyk et al., 2016). In contrast, the perceptual correlates of changes in PF of intracortical microstimulation have been shown to vary across electrodes in experiments with human subjects (Hughes et al., 2021) and non-human primates (Callier et al., 2020). These results have been interpreted as reflecting differences in the functions of the stimulated cortical circuits (Sur et al., 1981, 1984; Pei et al., 2009; Saal and Bensmaïa, 2014). Conversely, the fascicles of the

peripheral nerve display only minimal submodality-specific organization (Ekedahl et al., 1997; Wu et al., 1999; Hallin and Wu, 2001), so the submodality composition of the nerve fibers activated through electrical stimulation is likely to be consistent across electrode contacts.

Stimulation frequency can be employed to sculpt artificial touch for bionic limbs

A major challenge facing recent efforts to restore the sense of touch through neural stimulation is to evoke sensations endowed with an appropriate quality. The goal is for contact with a textured surface through a bionic hand to lead to a perceived sensation of the appropriate texture and contact with an edge to lead to the sensation of an edge. In the intact sensory system, the evoked percept and the spatiotemporal pattern of activation elicited in the nerve when interacting with an object depend on the dynamics of contact and the properties of the object. While electrical stimulation of the nerves can reproduce the temporal aspects of this natural neural activity by patterning the pulses, it cannot mimic the complex spatiotemporal patterns due to limitations in the ability to selectively activate individual nerve fibers. Nonetheless, mimicking natural patterns of activation with biomimetic stimulation enables discrimination of textural features (Oddo et al., 2016), confers greater speed to certain sensory discrimination tasks performed with a prosthesis (George et al., 2019), and improves performance on tasks involving object manipulation (Valle et al., 2018). In contrast, the degree to which biomimetic stimulation leads to more natural percepts is inconsistent (Graczyk, 2018; Valle et al., 2018; George et al., 2019). Our results demonstrate that modulating stimulation frequency reliably and systematically modulates sensation quality. This phenomenon can be leveraged to convey information about object and substrate interactions more intuitively for upper and lower extremity neuroprostheses.

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AUTHOR CONTRIBUTIONS

ELG designed the study, collected the data, analyzed the data, interpreted the results, and wrote the manuscript. BPC collected the data, analyzed the data, and wrote the manuscript. QH analyzed the data and wrote the manuscript. DJT advised on result interpretation and revised the manuscript. SJB designed the study, interpreted the results, and wrote the manuscript.

COMPETING INTERESTS STATEMENT

The authors declare no financial competing interests. DJT has patents on the electrodes (US Patent #6456866B1) and stimulation patterns related to sensory restoration (US Patent #9421366B2). ELG, DJT, and SJB also have a patent application on stimulation patterns related to sensory restoration (PCT/US2017/056070).

FIGURE CAPTIONS

Figure 1. Experimental design. a) Electrical stimulation was delivered by an external neurostimulator through percutaneous leads to FINEs or C-FINEs implanted on the residual peripheral nerves of four trans-radial and two trans-tibial amputees. Stimulation consisted of trains of square, biphasic, charge-balanced pulses. b) Frequency estimation task. Three participants were asked to estimate the perceived frequency of an evoked percept by moving a slider along a horizontal bar. Stimuli varied in both stimulation pulse frequency (PF) and pulse width (PW). c) Frequency discrimination task. Four participants judged which of two sequentially-presented pulse trains was higher in perceived frequency, while ignoring any differences in perceived intensity. d) Quality description task. Six participants selected sets of words that described the quality of the evoked percept. Participants could select as many words as they wished to describe each stimulus.

Figure 2. Perceived frequency estimates. a) Perceived frequency versus PF for a representative electrode contact (UL04, contact M2). Filled circles denote average perceived frequency ratings ($n=15$ per condition), normalized to the mean within experimental block (6 blocks). Color denotes the PW level and error bars denote the standard error of the mean. Solid lines represent piecewise logarithmic functions fit to the data. b) Average perceived frequency across all electrode contacts and participants versus stimulation PF ($n=15$). Color denotes the PW level and the shaded region corresponds to the standard error of the mean. The boxplot depicts the transition frequency in the piecewise functions across participants and contacts ($n=12$). The vertical line in the boxplot depicts the median and the shaded region depicts the interquartile range of transition frequency. Note that the abscissa is logarithmic.

Figure 3. PF discrimination performance with constant PW. a) Performance with the 20-Hz standard for participants UL02 (yellow) and UL04 (orange). Each curve denotes the mean performance with a different electrode contact ($n=6$). b) Performance with the 50-Hz standard across contacts ($n=5$) for UL02 (light green) and UL04 (dark green). c) Proportion of stimulation contacts yielding defined JNDs for the three standard frequencies when comparison and standard PWs are equal. Participants achieved threshold performance on 75% (6 out of 8) contacts tested with the 20-Hz standard and 83% (5 out of 6) contacts tested with the 50-Hz standard. Participants never achieved criterion performance (0 out of 7) with the 100-Hz standard. d) Just noticeable differences (JNDs) for the equal PW conditions with the 20-Hz ($n=6$) and 50-Hz ($n=5$) standards. e) The Weber fractions for the 20-Hz ($n=6$) and 50-Hz ($n=5$) standards were statistically indistinguishable.

Figure 4. PF discrimination performance with variable PW. a) Performance with the 20-Hz standard and three comparison PWs, averaged across electrode contacts ($n=6$). b) Point of subjective equality (PSE) vs. PW for the 20-Hz standard ($n=17$). Gray lines denote different contacts, black line denotes the mean across contacts and participants. PSE increases with PW, revealing a PW-dependent bias in PF discrimination performance. Participants exhibited a tendency to perceive higher PWs as being lower in PF. c) JND vs. PW for the 20-Hz standard ($n=17$). There was no significant effect of PW on JND with the 20-Hz standard. d) Performance with the 50-Hz standard and three comparison PWs, averaged across electrode contacts ($n=5$). e) Point of subjective equality (PSE) vs. PW for the 50-Hz standard ($n=15$). PSE was significantly higher at higher PWs. f) JND vs. PW for the 50-Hz standard ($n=15$). JNDs tended to be higher at higher PWs.

Figure 5. Quality descriptors reported for electrically-evoked percepts at each PF, averaged across PWs. Each heatmap corresponds to a participant and contact ($n=11$), and each row corresponds to a descriptor. Color denotes the proportion of times a descriptor was selected at each PF. Participants used different words to describe their sensory experiences. However, descriptors were similar across contacts for each participant.

Figure 6. Perceived dissimilarity estimated from differences in descriptor usage. a) Perceived dissimilarity of stimuli varying in PF for contact M3 of participant UL02. b) Perceived dissimilarity of stimuli varying in PF for contact M5 of participant UL04. Note that the contacts/participants shown in a and b are the same as in Figure 5. c) Within-

participant ($n=8$, purple) and across-participant ($n=15$, teal) pairwise correlations for two metrics of quality. “Descriptors” denotes the words selected by the participant for each stimulus, and “Dissimilarities” denotes the Euclidean distance between pairs of stimulation conditions. Error bars denote the standard error of the mean. Asterisks denote statistically significant differences with $p<0.001$. d) Perceived dissimilarity between successive PF conditions, averaged across PWs ($n=33$). Error bars indicate the standard error of the mean. The asterisk denotes significance at $p<0.001$.

Figure 7. Contribution of stimulation parameters to sensation quality. a) Dissimilarity matrix averaged across participants and contacts ($n=11$). b) Measured dissimilarity vs. prediction from a linear combination of ΔPF , ΔPW , and their interaction. Purple points represent dissimilarities between stimuli at low frequencies (<50 Hz), green points represent dissimilarities between stimuli at high frequencies (>50 Hz), and grey points represent dissimilarities between high and low frequency stimuli. c) Standardized regression coefficients for the model with all data included. d) Regression coefficients for models fit to individual participants’ dissimilarity data. The regression coefficients for individual models are denoted as dark blue filled circles, while the mean coefficients are shown as the light blue bars. e) Regression coefficients for the model with only low frequency data included (<50 Hz). f) Regression coefficients for the model with only high frequency data included (>50 Hz). c,d,e,f) Error bars are standard error of the estimates. Asterisks denote significant contribution to the model at $p<0.001$.

Figure 8. Effect of PF on perceived dissimilarity after removing the influence of perceived frequency. A univariate regression predicting quality dissimilarity based on perceived frequency was performed for low (a) and high (b) frequency stimuli. a,b) Perceived dissimilarity versus a linear prediction based on differences in perceived frequency. c,d) Residuals of the regression (shown in a and b) versus (z-scored) ΔPF . Solid black lines denote the regression of the residuals on to ΔPF . c) At low frequencies, the influence of ΔPF on dissimilarity was not significant after accounting for perceived frequency ($p = 0.8$). d) At high frequencies, ΔPF significantly impacted dissimilarity, even after accounting for perceived frequency ($p = 0.001$), but the effect was modest.

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898

a Extraneural stimulation

b Frequency estimation task

c Frequency discrimination task

d Subjective quality description task

NO SENSATION			FINISHED
Tingling	Stabbing	Pinching	Movement
Prickling	Pressure	Vibrating	Pulling
Electrical	Touch	Pulsing	Twitching
Shocking	Cramping	Buzzing	Contracting
Sharp	Squeezing	Flutter	Tensing
Pricking	Throbbing	Tapping	Tugging
Stinging	Pounding	Fizzing	
Itching	Aching	Tickling