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1 Virtual Electrodes by Current Steering in Retinal Prostheses

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24 **Abstract**

25 **Purpose:** Retinal prostheses are an approved treatment for vision restoration in retinal
26 degenerative diseases; however, present implants have limited resolution and simply increasing
27 the number of electrodes is limited by design issues. In cochlear implants, virtual electrodes can
28 be created by simultaneous stimulation of adjacent physical electrodes (current steering). The
29 present study assessed whether this type of current steering can be adapted for retinal implants.

30 **Methods:** Suprachoroidal electrode arrays were implanted in four normally-sighted cat eyes.
31 Electrode pairs were driven simultaneously at different current levels and current ratios. Multiunit
32 spiking activity in the visual cortex was recorded. Spike distribution across channels enabled
33 generation of cortical activation maps and calculation of centroid positions. For each current
34 configuration, centroid shifts between two virtual electrodes were compared to shifts obtained
35 from physical electrode stimulation.

36 **Results:** Using current steering, virtual electrodes with different cortical activation maps could be
37 created. Cortical centroids were found to shift as a function of the current ratio used for virtual
38 electrodes and were similar to the centroid shifts seen when using physical electrodes. In
39 addition, the cortical response to stimulation of a physical electrode could be reproduced by
40 applying current steering to electrodes on either side of the physical electrode.

41 **Conclusions:** These results suggest that current steering can alter activation patterns in the visual
42 cortex and could enhance visual perception in retinal implants by eliciting phosphene percepts
43 intermediate between those elicited by physical electrodes. These results inform development of
44 new electrode arrays that can take advantage of current steering.

45

46 **Introduction**

47 One of the leading causes of blindness is the degeneration of the retina due to a loss of
48 photoreceptors caused by diseases such as retinitis pigmentosa (RP)¹. The prevalence rate for RP
49 is about one in 4000 which results in more than one million people worldwide who are blinded
50 by this disease². Although there are several therapies being investigated, retinal prostheses remain
51 the only approved treatment for RP³. Retinal prostheses aim to restore vision by electrically
52 stimulating the surviving neurons in the inner retina. This is realized by an implantable electrode
53 array which is placed at either one of four locations: epiretinal⁴⁻⁶, subretinal^{7, 8}, suprachoroidal^{9, 10}
54 and trans-scleral^{11, 12}. With the presently available designs, it is possible to regain orientation and
55 mobility of patients to a certain degree^{8, 13} and in some patients even the ability to perform
56 spatio-motor tasks¹⁴ and letter and word reading¹⁵ are possible. Although these results are very
57 promising, more advanced levels of visual perception like sentence reading and face recognition
58 which require higher spatial resolution are still out of reach for most patients^{3, 16}. Hence there is a
59 demand for technologies that can improve the spatial resolution of retinal implants, particularly
60 when the electrode arrays are located hundreds of microns away from the target neurons, for
61 example with the suprachoroidal approach. One strategy is to merely increase the number of
62 physical electrodes which in turn will increase the number of available “pixels”. However, this
63 approach involves engineering and safety challenges¹⁶.

64 Current steering describes numerous stimulation paradigms which are applied in modern
65 neuroprosthetics. In general, current steering refers to the effect of simultaneous stimulation of
66 several electrodes on the overall electric field which is formed by overlapping of individual
67 electrode fields. In neural stimulation, current steering is either used for focusing the current, thus
68 narrowing the area of tissue excited, or for redirecting the current to excite different tissue¹⁷. In
69 the scope of this study, only the latter application will be addressed.

70 Figure 1 shows the principle of the simplest form of current steering where simultaneous current
71 versus a remote return is applied to an electrode pair on a one-dimensional electrode array to
72 create an intermediate “virtual electrode”. When equal current is applied to a pair of electrodes
73 the resultant field peaks at a location mid-way between both electrodes (Fig.1A). When a
74 different current ratio is applied, the peak of the resulting electric field shifts towards the
75 electrode with the higher current (Fig. 1B). Thus the volume of tissue in between the two
76 physical electrodes can be preferentially stimulated. This form of current steering has been
77 successfully used in cochlear implants to produce virtual electrodes that elicit pitch perceptions
78 intermediate to those produced when stimulating physical electrodes. In fact, several studies have
79 shown that it is possible to create on average 4-7 such virtual electrodes between two adjacent
80 physical electrodes in the cochlea¹⁷. Although a similar form of current steering using electrode
81 pairs has been proposed for the retina when placing the electrode array epiretinally¹⁸, the degree
82 to which current steering is useful for other more distant electrode locations like the
83 suprachoroidal placement, and when using a stimulating electrode array that is clinically relevant,
84 is unknown.

85 As a first step towards determining whether current steering using electrode pairs can be usefully
86 applied in suprachoroidal retinal implants, we assessed if it was possible to alter the patterns of
87 evoked activity in the visual cortex by stimulating a pair of suprachoroidal retinal electrodes with
88 different current ratios. A successful implementation of current steering in retinal implants could
89 lead to an increase in effective resolution without an increase in the number of physical
90 electrodes, by producing intermediate phosphene perceptions to those produced by physical
91 electrode stimulation.

92 **Materials and Methods**

93 The procedures for this study were approved by the Animal Research Ethics Committee of the
94 Royal Victorian Eye & Ear Hospital and they complied with the “Australian code of practice for
95 the care and use of animals for scientific purposes” (7th edition 2004), the “Principles of
96 laboratory animal care” (NIH publication No. 85–23, revised 1985), and the ARVO Statement for
97 the Use of Animals in Ophthalmic and Vision Research. The surgical techniques, electrode arrays
98 and general procedures have been described in detail previously^{19,20}, and so will only be briefly
99 described here.

100

101 ***Surgery***

102 Animals were anesthetized using ketamine (Troy Labs, Australia; 20mg/kg, intramuscular) and
103 xylazil (Troy Labs, Australia; 2mg/kg, subcutaneous), and maintained using a continuous
104 intravenous infusion of sodium pentobarbitone (Troy Labs, Australia; 60mg/kg/hr). Core
105 temperature was maintained at 37±1°C. During the study, the eyes were protected against
106 dehydration with hypromellose gel (GenTeal, Novartis Pharmaceuticals, Australia). Fluid
107 replacement was provided by continuous intravenous infusion of compound sodium lactate
108 solution (Hartmann’s solution, 2ml/kg/hr). Respiration rate, CO₂ levels and blood pressure were
109 monitored throughout the experiment. Dexamethasone (Troy Labs, Australia; 0.1mg/kg,
110 intramuscular) was administered for the prophylaxis of brain edema, plus
111 amoxicillin-clavulanate suspension (Clavulox, Pfizer, Italy; 10mg/kg, subcutaneous) as an
112 antibiotic every 24 hours. The experiments were typically conducted over two to three days, after
113 which the animal was terminated.

114 One eye in each of four normally-sighted adult cats (weighting 2.9 – 5.5kg) was implanted with a
115 clinical grade array in the suprachoroidal space. A lateral canthotomy was performed, followed

116 by a full-thickness scleral incision 5mm posterior and parallel to the limbus. A pocket was
117 opened between the sclera and choroid and the electrode array was inserted into this pocket and
118 advanced 17mm posteriorly. Effort was made to place the tip of the array underneath the area
119 centralis as the distance of electrodes to the area centralis has an important influence on evoking
120 cortical responses¹⁹.

121

122 *Suprachoroidal Electrode Array*

123 The design of the suprachoroidal array used for the experiments was similar to what has been
124 applied in previous work²⁰. The array consisted of 21 platinum electrodes (600µm diameter) on a
125 19×8mm silicone substrate. The electrodes were arranged in a hexagonal pattern with a
126 centre-centre spacing of 1mm. Two additional return electrodes with a larger diameter ($\emptyset = 2\text{mm}$)
127 were located distal to the stimulating electrodes.

128

129 *Experimental Setup*

130 After implantation, the animal was transferred to an electrically shielded room and placed in a
131 stereotaxic frame (David Kopf Instruments, Tujunga, CA). A craniotomy was performed to
132 expose the visual cortex. A large surface area platinum ball electrode (1.5mm diameter) was used
133 in order to assess the location with the lowest threshold evoked potential for placement of the
134 60-channel (6x10) recording electrode array (Blackrock Microsystems, Salt Lake City, UT)^{19, 21},
135 ²². The recording array sampled a cortical space area of 2mm in the medio-lateral and 3.6mm in
136 caudo-rostral direction. The penetration depth was approximately 1mm. Multi-unit cortical
137 recordings (band-pass filtered from 0.1 – 7500Hz) were made using the Cerebus system
138 (Blackrock Microsystems, Salt Lake City, UT).

139

140 ***Simultaneous Stimulation for Current Steering***

141 Pairs of electrodes on the suprachoroidal array were stimulated by a custom built constant current
142 source stimulator routed via a cross-point switch matrix²³ that delivered cathodic first biphasic
143 charge-balanced waveforms against a monopolar return electrode. Stimulation pulses had a pulse
144 width of 500µs, an interphase gap of 25µs and a repetition rate of 1Hz. The current between the
145 electrodes in each pair was split according to the following equation 1:

$$I_a = R * I_t \quad (1)$$

146 where I_a represented the current on the first electrode of the pair and I_t the total current. The
147 variable R (current ratio) was varied between 0 and 1 (0.1 steps) and determined the proportion of
148 current which was allocated to the first electrode. The remaining current was delivered to the
149 second electrode of the pair according to following equation 2:

$$I_b = I_t - I_a \quad (2)$$

150 where I_b represented the current for the second electrode. Thus current steering was applied for
151 intermediate current ratios (R = 0.1 to 0.9) whereas single electrode stimulation was applied for
152 the extreme current ratios (R = 0 or 1 respectively). The total current amplitude (I_t) was
153 randomized between 0 and 1.5mA (equating to a maximum charge density of 300µC.cm⁻²) with
154 increments of 50µA (31 different levels). A set of ten repetitions were presented for each current
155 level and current ratio on a given electrode pair. A total of 32 electrode pairs across the four
156 animals were stimulated within this study. The physical distances between the chosen electrodes
157 for each pair were 1mm (13 pairs), 1.7mm (4 pairs), 2mm (6 pairs), 2.6mm (5 pairs) or 3mm (4
158 pairs).

159

160

161

162 ***Data Analyses***

163 Data were cleaned offline as per methods outlined in previous studies^{19, 21, 22} and analyzed by
164 using custom scripts in IgorPro (Wavemetrics, Lake Oswego, OR). Artefacts were removed and
165 multiunit spikes (bandpass filtered, 0.3 – 5kHz) were detected and time-stamped when signal
166 exceeded 4.2 times the root mean square value.

167

168 ***Steering Tuning Curves for Single Channels***

169 Figure 2A shows an example of a recorded signal from one recording channel in response to
170 stimulation. Average spike rates across 10 repetitions were analyzed in the first 20ms from
171 stimulus onset (Figure 2B) at each current level to obtain a current-level versus spike-rate
172 input–output function and a sigmoid curve was fitted (Figure 2C). The threshold current was
173 defined as the current amplitude where the sigmoid curve reached 50% of its maximum saturated
174 spike rate^{21, 22}. Recording channels were analyzed by plotting average spike rates on a contour
175 plot with the total current amplitude on the x-axis and the current ratio on the y-axis (Figure 2D).
176 By joining the thresholds for each cortical site to each applied current ratio a steering tuning
177 curve was computed. Only channels where at least one current amplitude and ratio combination
178 elicited an average of 2 spikes per repetition or higher were included. Steering tuning curves with
179 the lowest threshold for intermediate current ratios ($R = 0.1$ to 0.9) indicated that these recording
180 channels preferred steered current as opposed to current only applied to one of the physical
181 electrodes in the pair ($R = 0$ or 1).

182

183 ***Cortical Spatial Maps and Centroid Shift***

184 For each current ratio, a cortical spatial map was generated by plotting the spike rate across all 60
185 recording channels at the threshold current of the best cortical electrode (BCE; defined as the

186 recording channel with the lowest threshold for that ratio²¹). Spike rates were normalized to the
187 maximum spike rate of each recording site across all measurements (Figure 3A). The centroid of
188 activity for each map was defined as the spike-count-weighted center of mass across all
189 channels²⁴. Centroids for all current ratios of one electrode pair were plotted on a single cortical
190 map to assess the shift between centroids as a function of current ratio (Figure 3B).

191

192 *Cortical Selectivity*

193 As a measure of the spread of cortical activation, a cortical selectivity value was calculated for
194 each spatial map generated at the current level required to reach 90% of the maximum spike rate
195 on the BCE, according to the method described by Cicione et al²¹. The cortical selectivity for
196 each current ratio applied to each pair of retinal electrodes, represented the degree of the drop in
197 spike rate as a function of the distance from the BCE. The drop in spike rate was fitted using an
198 exponential function and the inverse tau used to quantify the cortical selectivity. Cortical
199 selectivity was compared across current ratios for all electrode pairs.

200 **Results**

201 *Steering Tuning Curves for Single Channels*

202 A total of 931 recording channels were analyzed in response to stimulation of 32 electrode pairs.
203 In 8% of the channels, the lowest threshold on the steering tuning curve was found when using an
204 intermediate current ratio indicating that current steering was more effective than single electrode
205 stimulation in activating that recording channel (Figure 2D). In the remaining channels the lowest
206 threshold was found when using single electrode stimulation (i.e. for the extreme current ratios
207 $R=0$ or $R=1$).

208

209 *Cortical Spatial Maps and Centroid Shifts*

210 To quantify centroid shifts between each current ratio applied, the distance between every pair of
211 centroids in the cortex was calculated in mm according to the difference between their
212 corresponding current ratios (ΔR). It was expected that higher ΔR values would result in larger
213 centroid shifts with maximum shifts occurring when $\Delta R = 1$ (i.e. difference between centroid
214 positions when stimulating the two physical electrodes in isolation). Each ΔR value was
215 expressed as a virtual distance in the retina (in mm) by multiplying it by the physical distance
216 separating the two electrodes in the pair. Therefore, when current steering was applied to two
217 electrodes that were physically 1mm apart, a ΔR value of 0.2 would result in a virtual distance of
218 0.2mm, whereas the same ΔR value for a 2mm physical electrode separation would result in a
219 virtual distance of 0.4mm. All virtual distances were rounded to the nearest 0.1mm. To assess the
220 variability in estimating centroid positions from each cortical spatial map, the centroid shifts seen
221 as a result of repeated single electrode stimulation were also estimated and plotted against a
222 retinal distance of 0mm.

223

224 Figure 4A shows the mean cortical centroid shifts as a function of both virtual and physical
225 distances using data from all 32 retinal electrode pairs. Regression lines were fitted to the raw
226 data and showed significant ($p < 0.001$) positive correlation coefficients (Pearson's correlation²⁵)
227 both when using virtual electrodes ($r^2 = 0.14$, Slope = 0.287mm cortical shift per mm retinal
228 distance) and when using single electrodes only ($r^2 = 0.5$, Slope = 0.255mm cortical shift per mm
229 retinal distance). A general linear model on centroid shifts, with the factor set as electrode type
230 (physical or virtual) and the co-variate set as distance, showed that centroid shifts were
231 significantly dependent on the retinal distance ($p < 0.001$) but not on whether they were a result
232 of using virtual electrodes or physical electrodes ($p = 0.529$). While physical and virtual shifts in
233 the retina resulted in similar centroid shifts in the visual cortex as seen in Figure 4A, the only
234 distance for which cortical centroid shifts from physical as well as virtual electrodes could be
235 directly compared was 1mm (Figure 4B). A t-test showed that there was no significant difference
236 in the centroid shift between physical electrodes and virtual electrodes at a retinal distance of
237 1mm ($p = 0.272$).

238

239 ***Cortical Selectivity***

240 Figure 5A shows cortical spatial maps at the current required to reach 90% of the maximum spike
241 rate on the BCE, generated using current steering on a pair of retinal electrodes with the R-value
242 set to 0.5 as well when one of the physical electrodes in the pair was stimulated on its own. The
243 BCE (channel with the lowest threshold, black asterisks in Figure 5A) was the same regardless of
244 using single electrode stimulation or current steering. The drop in spike rate as a function of the
245 distance from the BCE and corresponding inverse tau values of the exponential fits (cortical
246 selectivity) were found to be similar for both modes of stimulation (Figure 5B).

247

248 Figure 6 compares the inverse tau values for all data collected in this study across the different
249 current ratios applied. A one-way ANOVA comparing cortical selectivity across the different
250 R-values and for all electrode pairs used for stimulation, showed no significant difference in
251 cortical selectivity ($p = 0.776$) between physical (R-value = 0 or 1) or virtual (R-values between
252 0.1 – 0.9) electrodes.

253 **Discussion**

254 The aim of this study was to assess if current steering, through simultaneous stimulation of a pair
255 of physical suprachoroidal electrodes, could create virtual electrodes by preferentially activating
256 areas of the retina that lie intermediate to the physical electrodes. We assessed the efficacy of
257 current steering by analyzing data on individual recording channels as well as spatial activation
258 maps across all recording channels in the cortex. We found that a small percentage of individual
259 recording channels showed preference for a steered virtual electrode compared to a physical
260 electrode in terms of requiring a lower threshold of activation. We also demonstrated that the
261 centroid of spatial activation across the cortex could be shifted by varying the current ratio,
262 without affecting the spread of activation.

263 While our results showed that only a small percentage of individual cortical recording channels
264 had a lower threshold for a virtual electrode as opposed to the majority responding with a lower
265 threshold to a physical electrode, this may have been confounded by the relative position of each
266 physical retinal electrode to the location of area centralis. We have previously shown that cortical
267 channels tend to respond with the lowest thresholds to retinal electrodes that are closer to area
268 centralis¹⁹. In all the electrode pairs analyzed, one of the physical electrodes was always closer to
269 the area centralis than the other electrode in the pair; hence the likelihood of paired stimulation
270 giving the lowest threshold was small. Furthermore, the odds of having individual channels from
271 our recording set receiving projections from only areas in between physical electrodes were much
272 lower than the odds of retino-cortical projections originating from areas directly beneath or
273 outside the physical electrodes. Therefore, we also examined cortical spatial activation patterns
274 and estimated the centroid of activation across all recording channels to assess the effectiveness
275 of current steering.

276 The results of analyzing cortical activity maps showed that it was possible to shift the centroid of
277 cortical spike activation by using current steering in the retina on electrode pairs over a range of
278 retinal distances. Generally, larger changes in proportions of current and larger retinal distances
279 (virtual and physical) resulted in larger centroid shifts in the cortex. Moreover, we found no
280 differences in cortical spread of activation between virtual and physical electrodes, which one
281 might have expected if simply a larger area of the retina was being stimulated through an
282 electrode pair compared to the area stimulated by a single electrode. This makes it more likely
283 that the centroid shifts seen in the cortex were a result of localized activation of intermediate
284 areas of the retina that lie in between physical stimulating electrodes as opposed to widespread
285 activation across the two stimulating electrodes.

286 Based on our results, it is expected that current steering will enable the creation of virtual
287 electrodes in a clinical setting, which would elicit phosphene percepts intermediate to those
288 elicited by stimulating single electrodes. At this stage, the number of possible virtual electrodes
289 obtainable clinically is difficult to estimate from our data, however even with one virtual
290 electrode between each adjacent pair of physical electrodes, the overall number of available
291 pixels would be doubled. It has been shown cochlear implant patients can get on average between
292 4-7 virtual pitch channels between each pair of physical electrodes¹⁷, but the total number of
293 available channels could be estimated to be as high as 451 using only 12 physical electrodes²⁶. Of
294 course for a retinal prosthesis, numerous other factors such as electrode size, pulse parameters,
295 proximity of the electrode to excitable tissue, as well as individual phosphene characteristics
296 (shape, size etc.) will also play an important role in determining the overall resolution.

297 It was also possible to mimic the centroid location of cortical activation when stimulating
298 physical electrodes, by applying current steering to an electrode pair with a larger spatial
299 distance. For example by using electrode pairs with a spatial distance of 2mm one could create,

300 using current steering with an R-value of 0.5, a virtual electrode whose position would be 1mm
301 from both electrodes of the pair. Future design of electrode arrays could take advantage of this
302 possibility by spreading electrodes further apart on the array and using current steering to activate
303 intermediate locations. Ultimately this may enable patients to have a wider visual field without a
304 loss in resolution which could significantly improve orientation and mobility. This is of even
305 higher importance when keeping in mind that present commercial retinal implants provide visual
306 fields of only up to 15-20 degrees^{8,13}. Furthermore, current steering could also be used in order to
307 overcome electrode failures (e.g. broken wires) by simultaneously stimulating surrounding
308 electrodes and creating a virtual electrode at the same position as the faulty electrode. Hence a
309 loss in resolution could be avoided.

310

311 *Limitations of the current study*

312 The present study was performed by implanting normally-sighted eyes. However, a previous
313 study performing suprachoroidal stimulation in a blind animal model showed that threshold
314 values and the activated areas in the superior colliculus were approximately doubled compared to
315 the normally-sighted model²⁷. These results emphasize the need to investigate the findings of this
316 study in a blind animal model, although direct testing in patients would provide more concrete
317 evidence of current steering.

318 Although the results of this study suggest that the resolution of retinal implants could be
319 increased by current steering, certain aspects of its impact on visual restoration remain unclear.

320 While cochlear implant patients are able to get additional pitch information from virtual
321 electrodes, a study assessing the effects of current steering on speech performance²⁸ has shown
322 that these additional virtual channels do not provide a significant improvement with speech
323 recognition. For retinal implants this may suggest that while generation of additional intermediate

324 phosphenes may be possible with current steering, it remains unclear whether this will have any
325 impact on visual performance outcomes such as visual acuity. Another question which needs to
326 be addressed is the influence of phosphene overlap on current steering. In the cases of
327 significantly overlapping phosphenes from single electrode stimulation of adjacent electrodes,
328 current steering on an electrode pair would likely provide no additional advantages. However, the
329 use of current focusing techniques to minimize retinal current spread in combination with current
330 steering might be able to overcome this problem. Also, while electrode pairs with different spatial
331 distances were used in this study, based on our results it was not possible to conclusively
332 determine the limit of electrode pitch for effective current steering. In addition, as the method of
333 current steering described in this study will always require pairs of physical electrodes to elicit
334 phosphenes, during this time these physical electrodes will not be available for eliciting their own
335 phosphenes. This may limit the rate at which phosphenes can be presented to the visual system,
336 particularly when using high frame rates. While high frame rates of 50-60Hz have been desirable
337 to avoid flicker perception and convey a quickly changing visual scene, realistic frame rates used
338 in present commercial devices are in the order of 6-8Hz^{8, 29}, mainly because of the problems
339 found with fading of phosphenes³⁰. At these slower frame rates, there should be sufficient time
340 available to interleave stimulation of physical and virtual electrodes within a given video frame
341 by using a short inter-pulse interval. In such situations however, the overall frame rate will also
342 depend on the stimulus parameters used (pulse width, interphase gap and pulse rate per
343 electrode), the time required for charge recovery through electrode shorting, and the number of
344 phosphenes required to be elicited in each video frame. These questions require additional
345 investigation which would best be conducted in the form of psychophysical experiments in
346 retinal prosthesis recipients. Lastly, as one of the next logical steps, two-dimensional current
347 steering should be investigated. Within the present study, current was only divided between two

348 electrodes while using more than two electrodes during simultaneous stimulation could result in
349 additional virtual electrodes whose positions may not be constrained any longer to a linear
350 intermediate space between an electrode pair. Two-dimensional current steering might offer an
351 even more enhanced boost in resolution for retinal prostheses.

352

353 ***Conclusions***

354 The present study provides first *in vivo* proof of principle that current steering on a pair of
355 stimulating electrodes may be beneficial for retinal implants in terms of being able to create
356 virtual electrodes that produce different activation patterns in the cortex. Beneficial effects of
357 current steering were observed in a small number of cortical recording channels as well as a shift
358 of cortical activity centroids was demonstrated with varying current proportions between
359 electrodes. Mimicking of physical electrodes and generation of additional intermediate virtual
360 electrodes may be possible using current steering between two physical electrodes. It remains to
361 be investigated whether the present results can be reproduced in blind animals and enhanced by
362 applying two-dimensional current steering. Finally, the question whether ultimately virtual
363 electrodes and intermediate phosphenes can be evoked by current steering in blind patients, and
364 whether these phosphenes could indeed improve patient performance, needs to be addressed in
365 human trials.

366 **Figure Legends**

367 **Figure 1: The concept of current steering using electrode pairs.**

368 *The electric fields expected from single electrode stimulation (E_5 with solid and E_6 with dotted*
369 *line), and simultaneous stimulation of two adjacent electrodes (dashed line) are shown. Currents*
370 *on each electrode are represented by the relative height of triangles overlaying the electrode*
371 *sites. (A) Dashed line represents cumulative electric field for E_5 and E_6 each stimulated with 50%*
372 *of the total current. (B) Dashed line represents cumulative electric field when E_5 is stimulated*
373 *using 30% and E_6 is stimulated using 70% of the total current.*

374

375 **Figure 2: Generation of steering tuning curves**

376 *(A) Spike recordings on a single cortical recording channel in response to current steering on an*
377 *electrode pair using a total current level of 1.5mA and an R-value of 0.7. A stimulus artifact (red*
378 *asterisk) occurred at time zero followed by a burst of spikes within the first 20ms post-stimulus*
379 *onset. (B) Peri-stimulus time histogram (1ms bin width) for the recording channel in panel A*
380 *across all current levels used with an R-value of 0.7. (C) Spike count (after artifact removal) in*
381 *the first 20ms post-stimulus onset plotted against total current level and fitted using a sigmoid*
382 *curve. (D) Spike activity on the same recording channel in response to current steering using all*
383 *current levels and current ratios. The total current level is depicted on the x-axis and current*
384 *ratios are depicted on the y-axis. A steering tuning curve for the threshold current values was*
385 *appended as a white line. The threshold for this recording channel was lowest when using an*
386 *R-value of 0.8.*

387

388 **Figure 3: Spatial activation maps and centroid determination**

389 *(A) Cortical spatial maps obtained when applying current steering to a pair of retinal electrodes*

390 *(only current ratios between 0.3 and 0.7 are shown). A gradual rostral shift of the cortical*
391 *activity with increasing current ratio is recognizable along with clear shift of the centroids (white*
392 *asterisks). The dotted box in the leftmost panel represents the reduced area represented in panel*
393 *B to show the centroid positions for each R-value. (B) The positions of the centroids of cortical*
394 *activity (marked using x) are depicted on a map for each of the R-values in panel A. Note that*
395 *axes have been readjusted and do not cover the whole range for x and y-coordinates. C =*
396 *Caudal, R = Rostral, M = Medial, L = Lateral*

397
398 **Figure 4: Cortical centroid shift for physical and virtual electrode distances**
399 *(A) Data for all electrode pairs were combined in order to compare virtual with physical*
400 *electrode distances. R-square values of calculated regression lines showed a significant*
401 *correlation between electrode distance and centroid shift. Note: Regression analysis was applied*
402 *to the scatter plot and not to the mean values (individual data points not shown). (B) Centroid*
403 *shifts evoked by physical and virtual electrodes with 1mm distance are compared. No significant*
404 *difference was found indicating the ability of current steering to mimic physical electrodes by*
405 *applying current steering to either side. Error bars indicate standard error.*

406
407 **Figure 5: Measurement of cortical selectivity**
408 *(A) Cortical spatial maps at the current level required to elicit 90% of maximum spike rate on the*
409 *BCE when stimulating a steered pair of electrodes using an R-value of 0.5 (right) and when*
410 *stimulating one of the physical electrodes of the pair (left). Black asterisks denote the BCE. (B)*
411 *Normalized spike rate as a function of the distance from the BCE. Spike rates were normalized to*
412 *each channel's own maximum spike rate. Data points were fitted with a decaying exponential*
413 *and the inverse tau value used as a measure of cortical selectivity²¹.*

414

415 **Figure 6:** *Cortical selectivity as a function of R-value*

416 *Data from all pairs analyzed ($n = 32$) showed no significant difference in cortical selectivity*
417 *(inverse tau) when using current steering on a pair of electrodes ($R = 0.1 - 0.9$) compared to*
418 *when using single electrode stimulation ($R = 0$ or 1). Error bars indicate standard error.*

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