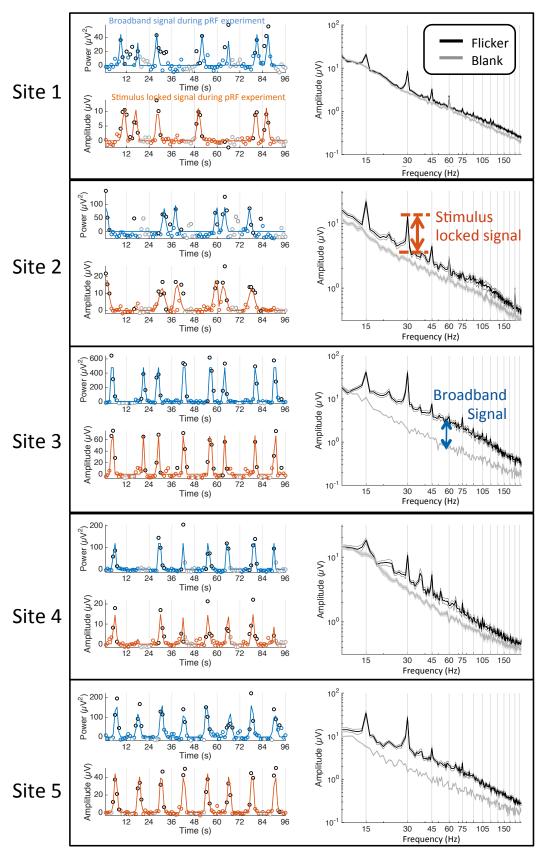
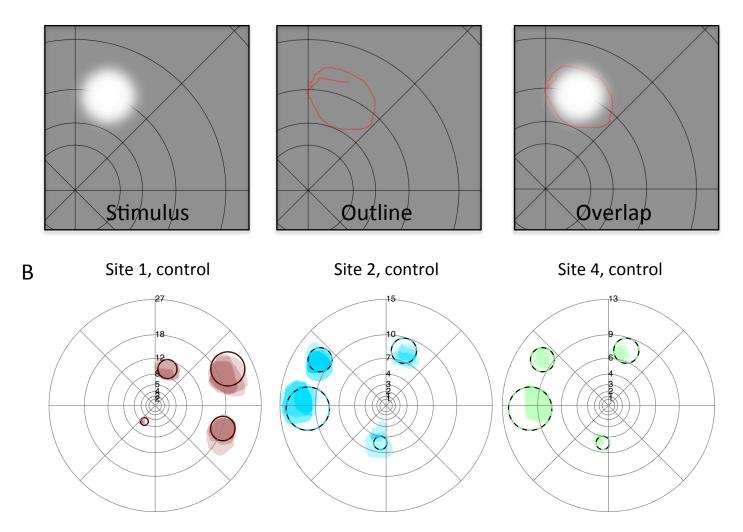
Figure S1. Related to Figure 1.



**Figure S1. Separation of ECoG signal into stimulus-locked and broadband components.** Broadband and stimulus locked responses for each of 5 sites. See Figure 1C,D for details.

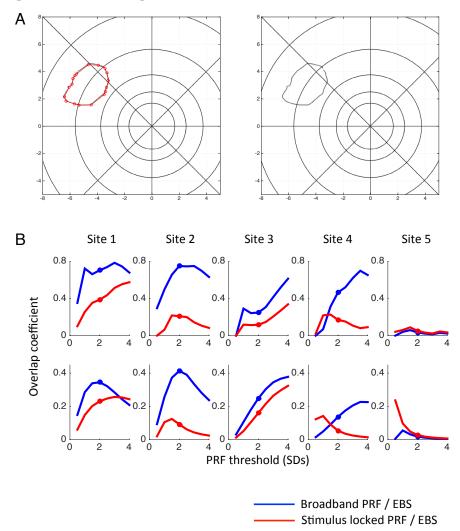
## Figure S2. Related to Figure 2.

# A Example control trial, for site 1



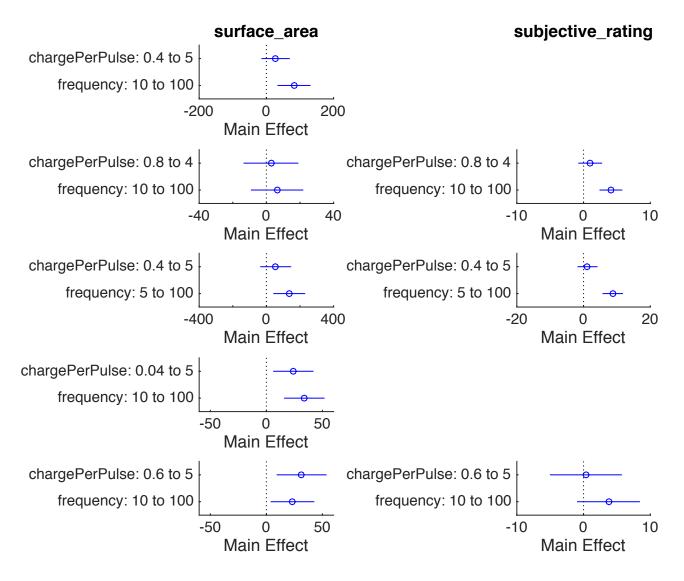
**Figure S2. Drawing reliability on control trials.** To assess whether subjects could reliably outline visual sensations, control trials were conducted in which subjects marked the locations of briefly viewed stimuli. (A) The stimuli were white circles with a smoothed edge on a gray background with a black, polar grid (left). The visual stimuli were presented for one second while the subject fixated the center of the grid. Immediately after the stimulus disappeared, the subject outlined the region where it was presented (middle). The overlap for this trial (control for site 1) shows excellent overlap between stimulus and outline (right). (B) Stimuli were presented in 4 locations 3 times each in random order for each subject. Stimuli close to fixation were smaller than those in the periphery. Each panel shows all 12 control trials from one subjects. The locations of the stimuli are schematically indicated as dashed outlines. The subjects' drawings are shown as partially transparent shaded regions for consistency with Figures 3 and 4. The three subjects tested in the control trials are the subjects with electrodes at sites 1, 2, and 4 for ECoG and EBS trials. (The subject with EBS/ECoG sites 3 and 5 was not tested in this control procedure.) Overall there is good agreement between the stimulus locations (outlines) and the subject drawings (shaded regions), indicating that subjects understood and could do the task.

#### Figure S3. Related to Figure 2.



**Figure S3. Related to Figure 2. Overlap between phosphenes and pRFs.** (A) An example screen capture of a phosphene drawn by S3 is shown on the left. The polar grid was seen during the EBS trial to facilitate accurate encoding and reproduction of the phosphene. On the right is the manual digitization of the phosphene, indicated in red. (B) For each of 5 sites, two pRFs were obtained, one from the ECoG broadband signal and one from the ECoG stimulus locked signal. For each site there were multiple EBS trials, with 9 to 21 phosphenes per site. Overlap between the phosphenes and the pRFs was summarized by the Sørensen-Dice coefficient (2 times the area of overlap divided by the sum area of the two areas). The upper plots show the overlap computed between the pRF at each site with the average phosphene from that site, and the lower plots show the average of the overlap between the pRF from a site and each of the separate phosphenes from that site. For the upper plot, the average of the phosphenes was defined by first averaging the binarized phosphene images (1s inside the outline, 0s outside), and then thresholding the resultant image. The threshold value was

expressed in standard deviations: A threshold of *n* STDs was defined as a Gaussian with height 1 evaluated at radius *n* STDs:  $e^{-\frac{n^2}{2}}$ . The pRFs were also thresholded at *n* STDs. The x-axis indicates different thresholds in units of STDs. The y-axis is the overlap coefficient. A threshold of 2, indicated by a circle on each plot, was used to summarize the data in the main text and in Supplementary table 1. The lower panels plot the overlap by computing the Sørensen dice coefficient for the thresholded pRF and each phosphene separately, yielding 9 to 21 overlaps for each site. The mean of these overlaps is plotted. For sites 1-4, the overlap is higher for the broadband pRFs than the stimulus locked pRFs at nearly any threshold evaluated by either method (overlap between pRF and mean of phosphenes, or mean overlap between pRFs and phosphenes). For site 5, the overlap was higher for the stimulus locked pRF, although the overlap coefficient was low for both kinds of pRFs.



**Figure S4: Model fits for Figure 4E**. Plots show the parameter fits for a linear model in which either phosphene surface area (left) or subjective rating (right) were predicted by the charge per pulse and the frequency of stimulation, corresponding to Figure 4E. Each row is one site. Circles indicate the mean and the line indicates the 95% parameter fit. For example, for site 5, varying the frequency from 10 to 100 Hz caused an increase in surface area of about  $25\pm20 \text{ mm}^2$ , and varying the charge per pulse caused an increase from 0.6  $\mu$ C to 5  $\mu$ C caused an increase in surface area of about  $35\pm25 \text{ mm}^2$ . In 4 of 5 sites, the effect of frequency on phosphene surface area was greater than 0 (95% CI), and in 2 of 5 sites, the effect of charge per pulse on surface area was greater than 0. For subjective rating, frequency had a clear effect in 2 of 3 sites, and a marginal effect in the third. Charge per pulse did not have a significant effect on the subjective rating in any of the three sites.

### Table S1. Related to Figure 1.

Site #	Subject number	Hemi	Gender	Age	Electrode Diameter (mm)	Diameter of exposed electrode (mm)	Spacing between electrodes (mm)	Recording frequency (Hz)	Seizure Zone (Pathology)
1	1	L	М	24	4	2.3	5	1525.88	Posterior collateral sulcus (cortical dysplasia)
2	2	R	М	36	2	1.2	4	1000.00	Lateral occipital (not resected, pathology unavailable)
3	3	R	М	40	4	2.3	5	3051.76	Medial fusiform gyrus (cortical dysplasia)
4	4	R	F	36	4	2.3	5	1525.88	Medial temporal lobe (gliosis)
5	3	R	М	40	4	2.3	5	3051.76	Medial fusiform gyrus (cortical dysplasia)

**Table S1. Participant details.** The study comprised of 5 V1 sites (column 1) in 4 subjects (column 2). Participant details in columns 3-5 indicate the hemisphere of the implantation, the gender, and the age at the time of the experiment. The electrode diameter (column 6) is defined in terms of the region of exposed platinum. Spacing (column 7) is the center-to-center spacing on the strip or grid. The recording frequency (column 8) was several times above the high end of the band pass filter (column 9).

# Table S2. Related to Figure 2.

Site	Trial #	Current (mA)	Frequency (Hz)	Pulse Width (µS)	Duration (S)	Charge per Pulse (µC)	Charge per Trial (µC)	Rating (1-10)	Phosphene Area (deg <sup>2</sup> )	Cortical Area, Individual V1 (mm <sup>2</sup> )	Cortical Area, Formula (mm <sup>2</sup> )
1	1	5	50	200	1	1	50	-	45.0	22.5	20.4
1	2	5	10	1000	1	5	50	-	15.0	4.1	4.7
1	3	5	50	1000	1	5	250	-	61.6	74.4	74.3
1	4	2	10	1000	1	2	20	-	35.3	14.5	14.1
1	5	2	50	1000	1	2	100	-	6.9	0.0	2.9
1	6	2	10	200	1	0.4	4	-	0.5	0.0	0.2
1	7	5	10	200	1	1	10	-	26.1	9.3	9.1
1	8	2	50	200	1	0.4	20	-	23.0	7.8	7.7
1	9	2	10	1000	1	2	20	-	32.3	11.1	12.2
1	10	2	50	200	1	0.4	20	-	4.6	0.0	1.7
1	11	2	50	1000	1	2	100	-	127.9	43.2	45.3
1	12	5	50	1000	1	5	250	-	124.1	74.9	82.0
1	13	5	10	1000	1	5	50	-	25.0	13.5	11.7
1	14	2	10	200	1	0.4	4	-	9.2	2.9	3.6
1	15	5	10	200	1	1	10	-	106.1	42.1	44.7
1	16	5	50	200	1	1	50	-	167.4	69.1	76.2
1	17	2	100	200	1	0.4	40	-	108.1	40.1	43.9
1	18	5	100	200	1	1	100	-	286.3	153.8	146.7
2	1	2	50	400	0.5	0.8	20	-	10.0	48.0	36.3
2	2	4	50	1000	0.5	4	100	5	4.6	55.0	37.0
2	3	4	10	1000	0.5	4	20	2	1.6	4.5	5.5
2	4	2	50	1000	0.5	2	50	6	5.9	28.6	20.4
2	5	4	10	400	0.5	1.6	8	-	7.3	27.4	20.8
2	6			Sha	m			-	-	_	_
2	7	4	50	400	0.5	1.6	40	6	10.0	46.4	35.2
2	8			Sha	m			-	-	_	_
2	9	4	100	400	0.2	1.6	32	6	5.3	14.1	12.6
2	10	2	10	1000	0.5	2	10	2	1.9	11.1	8.5
2	11	2	10	400	0.5	0.8	4	1	2.2	12.0	8.4
2	12	4	10	1000	0.5	4	20	2	3.4	23.3	20.2
2	13	2	50	400	0.5	0.8	20	5	5.4	27.7	19.9
2	14	2	100	400	0.5	0.8	40	5	4.0	20.1	16.0
2	15			Sha	m			-	-	-	_
2	16	2	10	1000	0.5	2	10	1	3.3	23.7	17.9
2	17	4	10	400	0.5	1.6	8	1	2.4	20.0	16.7
2	18	2	10	400	0.5	0.8	4	1	2.8	18.0	15.5
2	19	2	50	1000	0.5	2	50	5	4.7	18.9	15.4
2	20			Sha	m			-	—	-	_

2	21	4	50	400	0.5	1.6	40	4	4.8	22.9	17.5
2	22	2	50	1000	0.2	2	20	4	3.9	19.4	14.5
2	23	2	100	400	0.2	0.8	16	4	6.4	29.5	22.0
2	24	4	50	1000	0.2	4	40	4	6.0	26.2	19.6
2	25	4	100	400	0.2	1.6	32	5	4.2	21.5	15.9
3	1			Shai	n			_	-	-	_
3	2	5	10	1000	1	5	50	2.5	0.6	11.9	7.1
3	3	5	50	1000	1	5	250	10	13.3	235.3	159.1
3	4	5	5	1000	1	5	25	1	0.3	0.0	5.8
3	5	5	100	1000	1	5	500	10	15.2	200.3	123.9
3	6	5	100	200	1	1	100	7	-	-	—
3	7			Shar	n			_	_	-	-
3	8	5	50	200	1	1	50	8	7.2	75.0	45.0
3	9	5	10	200	1	1	10	1	_	-	-
3	10			Shai	n			—	-	-	-
3	11	5	5	200	1	1	5	1	2.0	25.4	16.5
3	12	1	5	200	1	0.2	1	1	-	-	-
3	13	2	100	200	1	0.4	40	8	4.4	58.7	33.3
3	14	2	50	200	1	0.4	20	7	2.2	39.9	24.4
3	15	2	10	200	1	0.4	4	1	2.9	69.9	41.5
3	16	2	10	1000	1	2	20	2	1.2	17.6	10.7
3	17	2	100	1000	1	2	200	10	20.8	294.0	194.5
3	18			Shar				-	—	-	_
3	19			Shai	n			-	-	_	-
3	19 20	2	5	Shai 1000	n 1	2	10	- 1	- 0.6	- 8.6	- 5.7
3 3 3	19 20 21	2	5 50	Shar 1000 1000	n 1 1	2	100		- 0.6 6.7	- 8.6 81.1	- 5.7 49.5
3 3 3 4	19 20 21 1	2	5 50 50	Shar 1000 1000 200	n 1 1 1	2 0.4	100 20	- 1		- 8.6 81.1 13.7	- 5.7 49.5 10.5
3 3 3 4 4	19 20 21 1 2	2 2 2	5 50 50 10	Shar 1000 1000 200 200	n 1 1 1 1	2 0.4 0.4	100 20 4	- 1 8 - -	- 0.6 6.7 0.2 0.1	- 8.6 81.1 13.7 7.8	- 5.7 49.5 10.5 5.0
3 3 3 4 4 4 4	19         20         21         1         2         3	2 2 2 2 2	5 50 50 10 10	Shar 1000 200 200 200 200	n 1 1 1 1 1	2 0.4 0.4 0.4	100 20 4 4	- 1 8 - - -	- 0.6 6.7 0.2 0.1 0.02	- 8.6 81.1 13.7 7.8 0.0	- 5.7 49.5 10.5 5.0 1.3
3 3 3 4 4 4 4 4	19         20         21         1         2         3         4	2 2 2 2 2 2 2	5 50 50 10 10 50	Shar           1000           200           200           200           200           200           200	n 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4	100 20 4 4 20			- 8.6 81.1 13.7 7.8 0.0 10.0	- 5.7 49.5 10.5 5.0 1.3 8.7
3 3 4 4 4 4 4 4	19           20           21           1           2           3           4           5	2 2 2 2 2 2 2 2 2	5 50 50 10 10 50 100	Shar           1000           200           200           200           200           200           200           200           200           200           200           200	n 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 0.4	100 20 4 4 20 40	- 1 8 - - - - -	- 0.6 6.7 0.2 0.1 0.02 0.1 0.5	- 8.6 81.1 13.7 7.8 0.0 10.0 21.3	- 5.7 49.5 10.5 5.0 1.3 8.7 21.1
3 3 4 4 4 4 4 4 4	19           20           21           1           2           3           4           5           6	2 2 2 2 2 2 2 2 2 2	5 50 50 10 10 50 100 10	Shar           1000           200           200           200           200           200           200           200           200           200           200           200           200           200           200           200           200	n 1 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 2	100 20 4 4 20 40 20		- 0.6 6.7 0.2 0.1 0.02 0.1 0.5 0.02	- 8.6 81.1 13.7 7.8 0.0 10.0 21.3 0.0	- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6
3 3 4 4 4 4 4 4 4 4 4	19           20           21           1           2           3           4           5           6           7	2 2 2 2 2 2 2 2 2 2 2 2	5 50 50 10 10 50 100 10 50	Shar           1000           1000           200           200           200           200           200           1000           1000           1000	n 1 1 1 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 2 2 2	100           20           4           20           4           20           40           20           100	- 1 8 - - - - - - - - -	- 0.6 6.7 0.2 0.1 0.02 0.1 0.5 0.02 0.5	- 8.6 81.1 13.7 7.8 0.0 10.0 21.3 0.0 14.8	- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8
3 3 4 4 4 4 4 4 4 4 4 4	19           20           21           1           2           3           4           5           6           7           8	2 2 2 2 2 2 2 2 2 2 2 2 2	5 50 50 10 10 50 100 10 50 10	Shar           1000           200           200           200           200           200           200           1000           1000           1000	n 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 2 2 2 2 2	100           20           4           20           4           20           40           20           100           20		- 0.6 6.7 0.2 0.1 0.02 0.1 0.5 0.02	- 8.6 81.1 13.7 7.8 0.0 10.0 21.3 0.0 14.8 0.0	- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2
3 3 4 4 4 4 4 4 4 4 4	19         20         21         1         2         3         4         5         6         7         8         9	2 2 2 2 2 2 2 2 2 2 2 2 2 0.2	5 50 50 10 10 50 100 10 50 10 50	Shar           1000           200           200           200           200           200           200           1000           1000           1000           1000           200	n 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 2 2 2 2 0.04	100           20           4           20           40           20           100           20           20           20           20           20           20           20           20           20           20           20           20	- 1 8 - - - - - - - - -		 8.6 81.1 13.7 7.8 0.0 10.0 21.3 0.0 14.8 0.0 No phosphene	- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2
$     \begin{array}{r}       3 \\       3 \\       3 \\       4 \\     $	19           20           21           1           2           3           4           5           6           7           8	2 2 2 2 2 2 2 2 2 2 2 2 2	5 50 50 10 10 50 100 10 50 10 50 50	Shar           1000           1000           200           200           200           200           200           200           1000           1000           1000           1000           1000           1000           1000	n 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 2 2 2 2 2	100           20           4           20           4           20           40           20           100           20	- 1 8 - - - - - - - - - - - -	- 0.6 6.7 0.2 0.1 0.02 0.1 0.5 0.02 0.5 0.04 0.3		- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 2 18.7
$     \begin{array}{r}       3 \\       3 \\       3 \\       4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5 50 50 10 10 50 100 10 50 10 50	Shar           1000           200           200           200           200           200           200           1000           1000           1000           1000           200	n 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2 0.4 0.4 0.4 0.4 0.4 2 2 2 2 0.04 2	100           20           4           20           40           20           100           20           100           20           100           20           100           20           100           20           100	- 1 8 - - - - - - - - - - - - - - - -		 8.6 81.1 13.7 7.8 0.0 10.0 21.3 0.0 14.8 0.0 No phosphene	- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2
$     \begin{array}{r}       3 \\       3 \\       3 \\       4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10         11	2 2 2 2 2 2 2 2 2 2 2 2 2 0.2 2 5	5 50 50 10 10 50 100 10 50 50 50 10	Shar           1000           1000           200           200           200           200           200           1000           1000           1000           1000           200           200           200           200           200           1000           1000           200           200	n	2 0.4 0.4 0.4 0.4 2 2 2 0.04 2 1	100           20           4           20           40           20           100           20           100           20           100           20           100           10		0.6 6.7 0.2 0.1 0.02 0.1 0.5 0.02 0.5 0.04 0.3 0.1		- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 2 18.7 3.2
$     \begin{array}{r}       3 \\       3 \\       3 \\       4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10         11         12	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5           50           50           10           10           50           100           10           50           100           10           50           10           50           10           50           10           50           50           10           50           50	Shar           1000           1000           200           200           200           200           200           200           200           1000           1000           1000           1000           200           200           200           200           200           1000           200           200           200           200	n	$ \begin{array}{c} 2\\ 0.4\\ 0.4\\ 0.4\\ 0.4\\ 2\\ 2\\ 2\\ 0.04\\ 2\\ 1\\ 1\\ 1 \end{array} $	100           20           4           20           40           20           100           20           100           20           100           20           100           50		$\begin{array}{c} - \\ 0.6 \\ 6.7 \\ 0.2 \\ 0.1 \\ 0.02 \\ 0.1 \\ 0.5 \\ 0.02 \\ 0.5 \\ 0.04 \\ \hline \\ 0.3 \\ 0.1 \\ 0.6 \\ \end{array}$		- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 2 8 2 18.7 3.2 25.9 52.7
$     \begin{array}{r}       3 \\       3 \\       3 \\       4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10         11         12         13	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5           50           50           10           10           50           100           10           50           100           10           50           10           50           10           50           10           50           10           50           10           50           100	Shar           1000           1000           200           200           200           200           200           200           200           200           200           200           200           200           1000           1000           200           200           200           200           200           200           200           200           200           200           200	n	$\begin{array}{c} 2 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 2 \\ 2 \\ 2 \\ 0.04 \\ 2 \\ 1 \\ 1 \\ 1 \\ 1 \end{array}$	100           20           4           20           40           20           100           20           100           20           100           20           100           20           100           20           100           10           50           100		$\begin{array}{c} - \\ 0.6 \\ 6.7 \\ 0.2 \\ 0.1 \\ 0.02 \\ 0.1 \\ 0.5 \\ 0.02 \\ 0.5 \\ 0.04 \\ \hline \\ 0.3 \\ 0.1 \\ 0.6 \\ \end{array}$		- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 2 8 2 18.7 3.2 25.9 52.7
$   \begin{array}{c}     3 \\     3 \\     3 \\     4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10         11         12         13         14	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5           50           50           10           10           50           100           10           50           100           50           10           50           10           50           10           50           10           50           10           50           100           10	Shar           1000           200           200           200           200           200           200           200           200           200           200           200           200           200           1000           1000           200           200           200           200           200           200           200           200           200           200           200           200	n	$\begin{array}{c} 2 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 2 \\ 2 \\ 2 \\ 0.04 \\ 2 \\ 1 \\ 1 \\ 1 \\ 5 \\ \end{array}$	100           20           4           20           40           20           100           20           100           20           100           20           100           50           50		- 0.6 6.7 0.2 0.1 0.02 0.1 0.5 0.02 0.5 0.04 0.3 0.1 0.6 1.2		- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 25.9 52.7 2
$   \begin{array}{c}     3 \\     3 \\     3 \\     4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10         11         12         13         14         15	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5           50           50           10           10           50           100           10           50           100           50           100           50           10           50           10           50           100           50           100           50           100           50           50	Shar           1000           200           200           200           200           200           200           200           200           200           200           200           200           1000           1000           200           200           200           200           200           200           200           200           200           200           1000           1000	n	$\begin{array}{c} 2 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 2 \\ 2 \\ 2 \\ 0.04 \\ 2 \\ 1 \\ 1 \\ 1 \\ 5 \\ 5 \\ 5 \\ \end{array}$	100           20           4           20           40           20           100           20           100           20           100           20           100           50           100           50           250		$ \begin{array}{c} -\\ 0.6\\ 6.7\\ 0.2\\ 0.1\\ 0.02\\ 0.1\\ 0.5\\ 0.02\\ 0.5\\ 0.04\\ \hline 0.3\\ 0.1\\ 0.6\\ 1.2\\ \hline 1.9\\ \hline $		- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 25.9 52.7 2 78.5
$     \begin{array}{r}       3 \\       3 \\       3 \\       4 \\     $	19         20         21         1         2         3         4         5         6         7         8         9         10         11         12         13         14         15         16	$     \begin{array}{r}       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       2 \\       5 \\     $	5           50           50           10           10           50           100           10           50           100           50           100           50           10           50           10           50           10           50           10           50           100           10           50           10	Shar           1000           1000           200           200           200           200           200           200           200           200           200           200           200           200           1000           1000           200	n	$\begin{array}{c} 2 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 0.4 \\ 2 \\ 2 \\ 2 \\ 0.04 \\ 2 \\ 1 \\ 1 \\ 1 \\ 5 \\ 5 \\ 1 \\ \end{array}$	100           20           4           20           40           20           100           20           100           20           100           20           100           50           100           50           100           50           100				- 5.7 49.5 10.5 5.0 1.3 8.7 21.1 1.6 13.8 3.2 25.9 52.7 2 78.5 1.1

4	19	5	10	1000	1	5	50	-	0.02	0.0	1.0
4	20	5	50	1000	1	5	250	-	1.4	67.4	78.4
5	1	<i>1</i> 50 200 <i>1</i> 0.2 10						-	No phosphene		
5	2	3	50	200	1	0.6	30	8	0.1	7.2	5.5
5	3	3	10	200	1	0.6	6	2	Phosphene	seen, drawing	not obtained
5	4	3	100	200	1	0.6	60	10	Phosphene	seen, drawing	not obtained
5	5	3	20	200	1	0.6	12	2	Phosphene seen, drawing not obtained		
5	6			Shar	m			-	_	—	_
5	7	Sham						-	-	-	-
5	8	3	20	1000	1	3	60	9	0.1	14.1	12.8
5	9	3	100	1000	1	3	300	10	0.2	37.2	26.1
5	10			Shar	m					—	_
5	11	3	10	1000	1	3	30	3	0.1	13.4	10.1
5	12	3	50	1000	1	3	150	9	0.1	11.2	7.8
5	13	5	50	1000	1	5	250	9	0.4	62.0	47.2
5	14	5	50	1000	1	5	250	-		No phosphene	
5	15	Sham						-	-	-	-
5	16	5	10	1000	1	5	50	5	0.1	16.5	10.9
5	17	5	20	1000	1	5	100	9	0.2	30.3	31.7
5	18	4.84	100	1000	1	4.84	484	9	0.7	74.6	54.4

**Table S2. EBS results in all trials.** EBS results are listed by site (1-5) and by trial number. For each trial we indicate the current (mA), frequency (Hz), pulse width ( $\mu$ S) and duration (S). The charge per pulse, in  $\mu$ C, is the product of pulse width in ms and current in mA. Charge deposited per trial in  $\mu$ C is the product of charge per pulse in  $\mu$ C, frequency in Hz, and duration in seconds. The subjective rating on a 1-10 scale was obtained for sites 2, 3, and 5. For sites 2 and 3, the subject separately rated the intensity of color, brightness, and motion, each on a 1-10 scale. But since the three values were almost always the same, we collapsed them into 1 (using the median if the three were not identical). The phosphene area (deg<sup>2</sup>) was computed by digitizing the points on the subject's outline and measuring the area within the outline. The cortical area for individual V1 (mm<sup>2</sup>) is the projection of the phosphene onto the subject's V1 map. The cortical area by formula was computed by assuming a standard formula for cortical magnification (see Methods). Of the 102 trials, there were 13 sham trials (no stimulation) and there were no false positives. Of the 89 trials with stimulation, there were 4 trials in which no phosphene was reported. There were 3 trials in which phosphenes were reported but no drawing was obtained.

### Table S3. Related to Figure 2.

	pRF variance explained		Sørensen–Dice between ECo mean of pho	G pRF and	Mean Søren coefficient bety pRF and in phosph	ween ECoG dividual	Bootstraps in which Broadband Sørensen–Dice coefficient is higher than SL coefficient	
Site	Broadband	Stimulus-	Broadband	Stimulus-	Broadband	Stimulus-	fraction	p-value
		locked		locked		locked		
1	64.0	83.3	0.70	0.39	0.34	0.23	0.0093	0.0186
2	81.8	74.3	0.75	0.21	0.41	0.09	0.0000	0.0000
3	87.9	86.2	0.25	0.12	0.25	0.16	0.0000	0.0000
4	84.9	68.6	0.46	0.17	0.14	0.05	0.0030	0.0060
5	85.0	89.0	0.03	0.05	0.02	0.03	1.0000	0.0000

**Table S3. EBS and ECoG overlap.** For each of 5 sites, a pRF was measured from the ECoG broadband time series and the ECoG stimulus-locked time series. The table show the variance explained in these time series by the pRF model (columns 2-3). The Sørensen-Dice coefficient was computed in two ways. First, it was computed as the overlap between the thresholded pRF and the thresholded and averaged phosphene for that site (columns 4 and 5). Second, it was computed as the average overlap between the thresholded pRF and each separate phosphene, and then averaged across phosphenes for that site (columns 6 and 7). The first method yields higher overlap values, but it provides only one overlap coefficient per site for broadband and one for the stimulus locked signal. The second method results in multiple overlap coefficients at each site (9-21 phosphenes per site, each compared with the broadband pRF and the stimulus locked pRFs, the paired overlap coefficients for each site (9-21) were bootstrapped 10,000 times, and the mean of the differences between the pairs was computed 10,000 times. The 8<sup>th</sup> column shows the fraction of bootstraps for which the overlap between broadband pRF and phosphenes was higher than stimulus-locked pRF and phosphenes. The 9<sup>th</sup> column converts this fraction into a two-tailed *p-value* by the formula,  $1 - 2 \times abs(0.5 - fraction)$ .

## Table S4. Related to Figure 4.

	S4. Related to Figure 4.			
Site	Figure 5a	Figure 5b	Figure 5c	Figure 5d
	Phosphene area $(deg^2) v$	Cortical area $(mm^2)$ v charge	Cortical area $(mm^2)$ v	Subjective rating v Charge
	charge deposited per trial(µC)	deposited per trial(µC)	Phosphene area (deg <sup>2</sup> )	deposited per trial (µC)
1	General model:	General model:	General model:	General model:
	$f(x) = b^*x^m$	$f(x) = b^* x^m$	$f(x) = b^*x^m$	$f(x) = b^*x^m$
	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):
	b = 3.609 (-4.598, 11.82)	b = 17.62 (-19.69, 54.94)	b = 0.5213 (-0.1538, 1.196)	$b = 0.8658 \ (0.1519, \ 1.58)$
	m = 0.5709 (0.1032, 1.039)	m = 0.358 (-0.1094, 0.8254)	$m = 0.9901 \ (0.7412, 1.239)$	m = 0.4495 (0.2222, 0.6768)
	sse: 1.6569e+04	sse: 7.7123e+04	sse: 2.8954e+03	sse: 23.9083
	rsquare: 0.3648	rsquare: 0.1834	rsquare: 0.8890	rsquare: 0.6045
	dfe: 16	dfe: 16	dfe: 16	dfe: 16
	adjrsquare: 0.3251 rmse: 32.1803	adjrsquare: 0.1323 rmse: 69.4275	adjrsquare: 0.8821 rmse: 13.4522	adjrsquare: 0.5797 rmse: 1.2224
2	General model:	General model:	General model:	
	$f(x) = b^* x^m$	$f(x) = b^*x^m$	$f(x) = b^*x^m$	
	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):	
	b = 11.24 (1.846, 20.64)	b = 2.638 (0.2192, 5.058)	b = 8.406 (3.981, 12.83)	
	m = 0.2577 (0.01383, 0.5015)	m = 0.1921 (-0.08092, 0.4652)	m = 0.714 (0.4226, 1.005)	
	sse: 2.0083e+03	sse: 94.9695	sse: 1.0152e+03	
	rsquare: 0.2030	rsquare: 0.1208	rsquare: 0.5971	
	dfe: 19	dfe: 19	dfe: 19	
	adjrsquare: 0.1610	adjrsquare: 0.0745	adjrsquare: 0.5759	
	rmse: 10.2810	rmse: 2.2357	rmse: 7.3098	
3	General model:	General model:	General model:	General model:
	$f(x) = b^*x^m$	$f(x) = b^*x^m$	$f(x) = b^*x^m$	$f(x) = b^*x^m$
	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):
	b = 6.636 (-6.022, 19.29)	b = 0.5586 (-0.3825, 1.5)	b = 10.26 (2.999, 17.53)	b = 1.288 (-0.01894, 2.595)
	m = 0.5624 (0.217, 0.9077)	m = 0.5678 (0.2632, 0.8724)	m = 1.046 (0.7889, 1.303)	m = 0.3589 (0.1607, 0.5571)
	sse: 2.6131e+04	sse: 150.6532	sse: 3.8607e+03	sse: 62.7857
	rsquare: 0.6473	rsquare: 0.7090	rsquare: 0.9479	rsquare: 0.6582
	dfe: 11	dfe: 11	dfe: 11	dfe: 11
	adjrsquare: 0.6152	adjrsquare: 0.6825	adjrsquare: 0.9431	adjrsquare: 0.6271
	rmse: 48.7395	rmse: 3.7008	rmse: 18.7342	rmse: 2.3891
4	General model:	General model:	General model:	
	$f(x) = b^*x^m$	$f(x) = b^* x^m$	$f(x) = b^* x^m$	
	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):	
	b = 0.417 (-0.3412, 1.175) m = 0.8684 (0.5138, 1.223)	b = 0.01028 (-0.007065, 0.00765)	b = 31.64 (27.34, 35.95)	
	$\mathbf{m} = 0.8684 \ (0.5138, 1.223)$	0.02763) m = 0.0227 (0.5061, 1.240)	$\mathbf{m} = 0.8123 \ (0.5716, 1.053)$	
	sse: 1.6760e+03	$\mathbf{m} = 0.9227 \ (0.5961, 1.249)$	sse: 618.1507	
	rsquare: 0.7082 dfe: 18	sse: 1.3659 rsquare: 0.7740	rsquare: 0.8924 dfe: 18	
	adjrsquare: 0.6919	dfe: 18	adjrsquare: 0.8864	
	rmse: 9.6493	adjrsquare: 0.7614	rmse: 5.8602	
	111150. 7.0775	rmse: 0.2755	11150. 5.0002	
5	General model:	General model:	General model:	General model:
	$f(x) = b^* x^m$	$f(x) = b^*x^m$	$f(x) = b^* x^m$	$f(x) = b^* x^m$
	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):	Coefficients (with 95% CI):
	b = 0.7267 (-1.205, 2.659)	b = 0.0004315 (-0.00124, 0.00124)	b = 62.28 (47.97, 76.59)	b = 3.382 (0.02973, 6.735)
	$\mathbf{m} = 0.6657 \ (0.1967, 1.135)$	0.002103)	m = 0.6905 (0.4908, 0.8901)	m = 0.1792 (-0.01639,
	sse: 576.8872	m = 1.195 (0.542, 1.848)	sse: 143.3675	0.3749)
	rsquare: 0.7000	sse: 0.0684	rsquare: 0.9254	sse: 24.7070
	dfe: 7	rsquare: 0.8373	dfe: 7	rsquare: 0.4239
	adjrsquare: 0.6571	dfe: 7	adjrsquare: 0.9148	dfe: 7
	rmse: 9.0781	adjrsquare: 0.8141	rmse: 4.5256	adjrsquare: 0.3416
		rmse: 0.0989		rmse: 1.8787

**Table S4. Power function model fits for Figure 4A-D.** The table shows model fits for each of 5 sites for plots in Figure 4A-D (with only 3 sites for 4d). Data were fit with a power law of the form,  $f(x) = b^*x^m$ . The table shows the estimated coefficients (*b* and *m*)

and 95% CI, the sum of squared error (sse), rsquare, degrees of freedom (dfe), adjrsquare, and root mean squared error (rmse). Importantly, when the lower end of the 95% CI of the *m* parameter is positive, the fit indicates a significantly positive slope (indicated in **bold**).

## **Supplemental Experimental Procedures**

### Participants

Four adult patients with focal epilepsy were implanted with intracranial electrodes unilaterally for clinical reasons to localize the source of seizures. There were 3 male patients and 1 female (age 24 to 40; Table S1). All subjects had normal or corrected-to-normal vision. Prior to implantation of electrodes, patients performed structural MRI as well as functional MRI, and after surgery, patients were monitored with implanted electrodes during the same visual mapping task (see below). Patients signed informed consent for participation in our study, which was approved by the Stanford University Institutional Review Board. In each patient, V1 and adjacent cortex was outside the seizure onset zone and void of epileptiform activity.

## **Electrode localization**

Electrodes were implanted as either strips or grids (AdTech Medical Instrument Corp, Racine, Wisconsin, USA). Five electrodes were used for analysis in this study from the four patients, all recording from primary visual cortex (Table S3). Each electrode was a platinum plate, either 2.3-mm or 1.15 mm in diameter (exposed recording area) with center-to-center spacing of 4-10 mm between adjacent electrodes on the grid or strip. The electrode positions were identified on post-operative computed tomography (CT) images. The CT images were aligned with the preoperative anatomical MRIs. We compensated for discrepancies between the two types of brain images caused by shifts in brain structure from electrode implantation using a method described in [ref (Hermes et al., 2010)]. When compared to ground truth, as established by intrasurgical photography of exposed electrodes, this method has an average error of 2.6 mm (distance between location computed by alignment and location measured by photography).

### **Anatomical and Functional MRI**

MRI sessions were conducted to localize visual field maps and electrode positions. The MRI session took place prior to electrode implantation. In two subjects, we acquired both functional and anatomical MRI (S1 and S3). For S2 and S4, we acquired only anatomical MRI, and derived retinotopic maps from the subject's individual anatomy using a published retinotopic template(Benson et al., 2014; Benson et al., 2012).

The procedures for MRI acquisition have been described previously(Winawer et al., 2013), and are briefly summarized here. The MRI sessions took place at the Center for Neurobiological Imaging (CNI) or the Lucas Center, both at Stanford University using a GE 3T scanner. We acquired T1-weighted anatomical scans (3D SPGR) of the whole brain at 1-mm resolution. The T1-weighted images were segmented into gray/white voxels using FreeSurfer's autosegmentation algorithm (http://surfer.nmr.mgh.harvard.edu/(Dale et al., 1999)). Functional MRI scans were acquired as echo planar images using gradient echo. In addition, a separate T1-weighted anatomical scans was acquired in conjunction with fMRI scans that matched the slice prescription of the functional scans. This 'inplane' anatomical scan was used to co-register the functional images with the whole-brain T1 image. Visual field maps were identified based on fMRI data as described in previous work(Winawer et al., 2010). The field of view for fMRI was 192 x 160 mm, with 2.5 mm isotopic voxels (TR = 1.5 s, TE = 29 ms). Data were pre-processed via field map correction, slice time correction, motion compensation, and then projected from the EPI space to the whole brain anatomy, as described previously (Winawer et al., 2010; Winawer et al., 2013). Both pre-processing and pRF analysis code are part of the in-house written, freely available vistasoft toolbox (https://github.com/vistalab/vistasoft). Because data were not averaged across subjects, all analysis took place in the native space of the individual subjects.

## Localization of primary visual cortex

To verify that each of the electrodes under study was located in V1, two methods were used. First, a V1-V3 atlas was applied to the T1-weighted whole brain anatomy, using publicly available software (), based on work by Noah Benson and colleagues . Using the Benson atlas, it is clear that the electrode positions are in V1 and not V2 (Figure 1a). Second, a V1 probabilistic atlas was derived from the same T1-weighted anatomy using Freesurfer (). The files used for this are called 'lh.v1.prob' and 'rh.v1.prob', and are produced by the *recon-all* command. This probabilistic atlas was created by Hinds et al . They used MRI based anatomical alignment tools (FreeSurfer) combined with high resolution imaging of ex vivo brains. They were able to define the full extent of V1 based on the Stria of Genari, enabling the probabilistic atlas to extend from the central fovea to the far periphery. We applied this probabilistic atlas to all of our subjects and show that all of our 5 electrodes are located in high probability regions of V1 (Figure 1b).

## **Electrophysiological Recording and Artifact Rejection**

We recorded signals with a 128-channel recording system made by Tucker Davis Technologies (<u>http://www.tdt.com/</u>). Off-line, data were re-referenced to the common average, excluding channels with large artifacts or epileptic activity, as determined by the patient's neurologist (author JP).

#### Stimuli for ECoG experiments

*Display.* Methods for ECoG visual field mapping experiments were reported previously in detail(Winawer et al., 2013). Here we summarize the methods and note a few differences. ECoG data for S3 comprise a subset of those published in ref(Winawer et al., 2013), and were re-analyzed here. Experiments were conducted in the subject's hospital room using a 15-inch MacBook Pro (S3) or a 13-inch MacBook Air (S1, S2, S4) for stimulus presentation, placed at a distance to the subject close enough to ensure a sufficient field of view to map the receptive fields of pre-selected electrodes, based on the electrode anatomical location (range: 30 cm – 61 cm), with the center of the screen at eye level. If the electrode was over an anterior part of V1, then its receptive field was assumed to be peripheral, and a closer viewing distance was needed. All stimuli were confined to a circular aperture whose diameter was equal to the screen height, corresponding to a visual angle of 19.2 - 32.9 deg. For S1, the fixation dot was on the left side of the screen, rather than in the center, in order to maximize the field of view in the right hemifield because the electrode of interest (site 1) was anterior with a

very peripheral receptive field. The display had a resolution of 1440 x 900 pixels and a nominal refresh rate of 60 Hz. The refresh rate was measured by the Psychoolbox function 'FrameRate'. The frequency of the square-wave patterns (see below) was adjusted slightly to be an integer multiple of the measured refresh rate (7.466 Hz rather than 7.5 Hz). Display luminance was measured with a Minolta Color Meter II in the patient rooms to quantify image contrast. Minimum and maximum luminance were approximately 24.6 and 203 cd/m^2 for S1, S2, and S4, and 2.4 and 24.7 cd/m^2 for S3, who requested reduced screen and room illumination for comfort.

The moving bar stimuli were identical to those used previously for fMRI experiments(Amano et al., 2009; Dumoulin and Wandell, 2008; Winawer et al., 2010). A contrast pattern was viewed through a bar aperture that swept across the visual field in 12 1-second steps. There were 8 sweeps across the visual field, including 4 cardinal directions (left to right, right to left, top to bottom, and bottom to top) interspersed with four diagonals (see Figure 3 for the sequence). The cardinal sweeps consisted of 12 discrete steps whereas the diagonals sweeps consisted of 6 steps (from the screen corner to the screen middle) followed by a 6-second blank (zero-contrast, mean luminance); the blanks help to estimate the baseline response level. For all subjects, the bar width was 1/8 the maximum bar height.

The contrast of the checkerboard pattern within the moving bars was the maximum afforded by the display given the ambient illumination in the hospital room (78%-82%).

*Fixation task.* During the experiments, participants viewed a small central fixation dot, which alternated between red and green at random intervals (average once per 3 s). Participants pressed a button on an external number pad to indicate a change in fixation color. The purpose of the fixation task was to ensure central fixation. All participants responded to the fixation color changes with high accuracy.

Visual stimuli were generated on a Macintosh MacBook Pro in the Matlab programming environment using in-house software, made freely available (<u>http://vistalab.stanford.edu/software/</u>). The software tools are built on functions from the Psychtoolbox (Brainard, 1997; Pelli, 1997).

## **PRF** model fitting

The pRF models were computed as described previously, using a 'Compressive Spatial Summation' variant of the linear pRF model , of the form,

$$r(t) = g \times \left( \int S(x, y, t) P(x, y) dx dy \right)^{n}$$
  

$$P(x, y) = e^{-\frac{(x - x_{0})^{2} + (y - y_{0})^{2}}{2\sigma^{2}}}$$
(Eq S1)

where the pRF is P(), the receptive field center is  $(x_0, y_0)$ , the amplitude is scaled by gain factor (g), and the apparent receptive field is  $\sigma/\sqrt{n}$ , which corresponds to the receptive field of the response when the stimulus is a point.

In this model, the stimulus (S) is represented as a series of 2D contrast images, the spatial receptive field (P) is represented as a 2D circularly symmetric Gaussian, and a static nonlinearity (n; power-law function) is applied to the output. When the power-law exponent is one, the model is linear, like the pRF model introduced for fMRI measurements by Dumoulin and Wandell . When the exponent is less than one, the model predicts compressive (subadditive) spatial summation. The CSS model was developed to account for a range of fMRI data in visual cortex .

As in our previous work, the output nonlinearity, *n*, was a free parameter for the broadband models, and was forced to be exactly 1 for the stimulus-locked model. Hence the stimulus-locked model was linear, and the broadband model was not.

The pRF models were fit to each of the 5 electrode's broadband and stimulus-locked time series separately (5x2 models) by minimizing the difference between the predicted response and the observed response, according to a least squares metric using nonlinear optimization (MATLAB Optimization Toolbox). Before fitting the model, data were preprocessed and averaged across repeated experiments with the identical stimulus.

The models were seeded with a Gaussian centered at the image center, *sigma* equal to the maximum stimulus extent, and n=1. To reduce the chance of finding a local minimum, the model was solved stepwise. In the first iteration, *n* was fixed at 1 and the x,y, sigma, and gain parameters were optimized. In the second iteration, applied only to the broadband data, *n* was allowed to vary.

The code to solve the pRFs is included in our repository. The wrapper function is *ebs\_solve\_PRF\_models.m*.

## Stimuli for fMRI experiments

Stimuli were presented using a Samsung SyncMaster 305T LCD monitor positioned at the head of the scanner bed. Subjects viewed the monitor via a mirror mounted on the RF coil. The monitor operated at a resolution of 1280 x 800 at 60 Hz, and the luminance response of the monitor was linearized using a lookup table based on spectrophotometer measurements. The minimum and maximum luminance was 1.4 cd/m<sup>2</sup> and 121 cd/m<sup>2</sup>, respectively. Stimuli subtended 12.5–12.8° of visual angle. A button box recorded behavioral responses.

The bar stimuli used in fMRI experiments were the same as those used in ECoG experiments except for two differences: the duration of each aperture position was 1.5 s rather than 1 s; the number of discrete steps in one sweep of the visual field was 16 rather than 12; the contrast pattern within the aperture drifted rather than flickered (2 Hz temporal frequency) (see (Dumoulin and Wandell, 2008) and (Winawer et al., 2010)). Between 2 and 4 fMRI bar scans were conducted, and the time series were averaged from repeated scans prior to further analysis. The fixation task was identical to the ECoG fixation task.

## Broadband and Stimulus-locked ECoG Responses

The time series of the broadband and stimulus-locked responses to bar stimuli were constructed by short-time Fourier analysis. The window for Fourier analysis was the duration that a stimulus aperture remained in a position (1 second). The time series from the one-second window was multiplied by a Hann window (raised cosine) to reduce edge artifacts.

For the broadband data, a line was fit in log-log space to the signal power (squared amplitude) of Fourier components from 8 Hz to 150 Hz, excluding values within 2 Hz of even harmonics of the stimulus frequency (15, 30, 45, 60, 75, 90, 115, 120, 135, and 150 Hz). The slope of the line was forced to be the same for all stimulus positions for a given electrode. The height of the line at 30 Hz was taken as the broadband signal for that time point.

Because the stimulus contrast reversed 15 times per second, a stimulus locked signal is found at multiples of 15 Hz (Figure 1). Of these harmonics, we found that the response at 30 Hz was most reliable, and we defined the stimulus-locked as the amplitude at 30 Hz, after subtracting the broadband fit. In previous work, we defined the stimulus locked response as the amplitude at 15 Hz for the same stimulus (Winawer et al., 2013). The reason we chose 30 Hz here is that the response at 15 Hz can be obscured by non stimulus-locked oscillations near this frequency (alpha oscillations). The pattern of results in terms of overlap between pRFs and EBS phosphenes was the same whether we defined the stimulus-locked signal as the amplitude at 15 Hz, 30 Hz, or the sum of the two, but 30 Hz yielded pRF models which explained highest variance in the time series.

As in our previous work (Winawer et al., 2013), spectral power was used to measure the broadband response. We use power rather than amplitude because when the temporal frequency phases are random signal superposition is additive with respect to power. Specifically, if the phases are random the sum of the power spectrum of signal X and the power spectrum of signal Y is on average the power spectrum of signals X + Y. Amplitude was used as the dependent measure for the stimulus-locked signal because the phase of the response at stimulus harmonics (e.g., 30 Hz) were roughly constant across trials; if the phase is constant, amplitude rather than power is additive.

## **Electrical Brain Stimulation**

Electrical brain stimulation is a safe procedure used routinely in clinical neurology practice. Electrical biphasic and rectangular pulses were delivered at different frequency, pulse width, amplitude, and durations (Table S2). These pulses were current-regulated and charge balanced (i.e., no charge accumulation with toxic effect on the tissue). For each site, one electrode was in V1 and the other channel was in a non-visually responsive region, remote from V1. Occasional sham trials were intermixed with stimulation trials. The subjects were not informed which trials were sham and which contained stimulation. The neurologist (author JP) was aware of the stimulation conditions, so the study was single blind rather than double blind. EBS trials took place 1-2 days after ECoG visual mapping experiments. In each experiment, the charge density per pulse was kept within the recommended limits (~50  $\mu$ C/ pulse, see Table S2 for more information about EBS safety). In our analysis, we relied on the accumulated charge during a stimulus trial rather than the analysis of charge density per pulse because we noticed that subjects' rating of phosphenes not only depended on the amplitude and width of single pulses but also their frequency (i.e., the total number of pulses delivered per unit of time). Calculations of stimulation parameters were as follows: *Electrical charge* = time (s) \* current (A); *Charge per pulse* ( $\mu$ C) = pulse width (ms) \* current (mA); *Charge density per pulse* ( $\mu$ C/cm<sup>2</sup> per pulse) = charge per pulse/ electrode surface area (cm<sup>2</sup>), Electrode surface area (cm<sup>2</sup>) =  $\pi$ r<sup>2</sup> (3.14 \* (0.2 or 0.1cm)<sup>2</sup> = 0.126 cm<sup>2</sup> or 0.063 cm<sup>2</sup>; *Pulses per stimulation trial* = frequency (Hz) \* duration (s); *Charge per trial* ( $\mu$ C) = charge per pulse ( $\mu$ C) \* pulses per stimulation trial.

Electrical brain stimulation in patients with implanted electrodes is applied routinely for the purpose of functional mapping with great safety profile. The limit of  $\sim 50 \mu C/cm^2/pulse$  was chosen as a guide based on our reading of the recent literature, but we are mindful that the current guidelines were established on the basis of studies of <u>continuous</u> electrical stimulations i.e., for hours or days of non-stop electrical charge delivery (Agnew et al., 1983; Babb and Kupfer, 1984). EBS is often applied to a small region of the brain in patients with Parkinson disease continuously with frequencies in the range of 200-300 electrical pulses per second for years without harmful effects.

## **Phosphene recordings**

During the EBS sessions, subjects viewed the same laptop used for the ECoG visual mapping experiments, viewed from the same distance. The screen was blank other than a polar grid (Figure 3b). Subjects were instructed to fixate the center of the grid prior to EBS, and to draw the outline of their visual percept on the screen using the laptop touchpad immediately following stimulation. The purpose of the polar grid was to provide a spatial reference so that the subjects could accurately encode and then reproduce the location of the phosphene. Immediately after the subject drew the phosphene outline, we recorded the image via screen capture. Offline, the phosphene images were loaded into Matlab, and digitized by marking approximately 20 points along the phosphene outline (Figure S3).

On a few trials, the subject reported seeing two distinct phosphenes, approximately symmetric above and below the horizontal midline, and drew the outline of both. One was always much larger than the other. We interpreted this as charge spreading across the

banks of the calcarine sulcus, as the dorsal and ventral banks are close together and represent approximately symmetric positions in the visual field. On these trials, we analyzed only the larger phosphene.

## Subjective ratings

Subjective ratings of phosphene intensity were obtained immediately after drawing the phosphene outline for sites 2, 3, and 5 (and not for sites 1 and 4). For site 3 and 5 (S3), the subject was instructed to indicate on a scale from 1-10 how much motion, color, and brightness was in each phosphene. Specifically, the instructions were one of three questions, '*Was it colorful?*', '*Did it move?*', or '*Was it bright?*', followed by '*Please give a number from zero to ten, zero being the least, ten being the most.*' It appeared that the subject did not use the ratings independently, as the three ratings were almost always the same for a given phosphene. Hence we collapsed the three ratings per trial into one (using the median if the three were not identical). For S2, whose experiment took place later, we asked for only a single rating of 1-10 to indicate the intensity of the percept. For this subject, we asked, '*How intense was it? Please give a number from zero to ten, zero being the most.*'

For some trials, the subject offered a spontaneous description. Descriptions of phosphene appearance could not be quantified and were not produced on every trial, so we do not report them in the results. Some examples are below. See Table S2 for stimulation parameters on these trials.

- Site 5, trial 2: It had the illusion of motion, but went nowhere unless I move my eyes.
- Site 5, trial 3 (phosphene seen but no drawing): Very faint dot right here. [In response to, 'Did it move?':] All look like they are moving, but it wasn't moving.
- Site 5, trial 4: Lots of splattering and flickering
- Site 5, trial 6 (sham): Nothing.
- Site 5, trial 9: Oh wow! I think that one might have left an afterimage for a second. It was loud and noisy.
- Site 5, trial 10 (sham): Nothing.
- Site 5, trial 11: I saw that here- was a 3 in color. I guess a 3 in motion and Brightness- a 3. It was one of those wimpy ones. If I was driving down the street I might be able to see that. The one before it I would have to pull over.
- Site 5, trial 17: Looks like someone is having a party and opens the windows for a second.
- Site 3, trial 9 (no drawing): Can barely make them out. I'm not sure where they are, but they were very faint. But I definitely saw them.

## Computation of phosphene cortical area

Phosphenes were projected to the surface of V1 based on the subject's retinotopic map in order to infer the area of activated cortex resulting from EBS. The projection was defined as the set of voxels in V1 whose retinotopic coordinates (x,y) were within the polygon defined by the digitized phosphene. These voxels formed a region of interest, and the surface area of this region of interest was computed on the 3D cortical manifold using methods described previously (Dougherty et al., 2003). The Matlab function used for this computation is 'roiSurfaceArea', part of the freely available in-house vistasoft software (https://github.com/vistalab/vistasoft).

The calculations above have the advantage of relying on the individual subject's retinotopic maps, thereby respecting individual differences in the size and cortical magnification of V1. To confirm that these methods gave reasonable results, we also computed the surface area using a standard formula for cortical magnification(Horton and Hoyt, 1991). For this calculation, we found the eccentricity of the centroid of the digitized phosphene and then multiplied the area of the phosphene by the cortical magnification according to the formula,  $M_{area} = 300/(E + 0.75)^2$ , where *M* is the cortical magnification and *E* is the eccentricity(Horton and Hoyt, 1991). The two calculations of surface area were very highly correlated ( $R^2 = 0.994$ , 0.980, 0.996, 0.968, 0.966 for sites 1-5), with some variability in slope (0.986, 0.680, 0.658, 1.100, 0.737) when plotting the surface area from the formula as a function of the surface area computed from the individual subject data. A slope of <1 indicates that the standard formula underestimates the area relative to the area from the individual subject map.

Because the surface area of the individual subject is based on a discrete list of cortical nodes (those whose pRF center was within the phosphene drawn by the subject), this estimate could be inaccurate for small phosphenes. In particular, for small phosphenes sometimes there were 0 vertices with pRFs inside the phosphenes. On the other hand, the surface area computed from the standard formula for cortical magnification is continuous and can therefore estimate arbitrarily small cortical areas. In order to respect individual differences in cortical magnification, while at the same time avoiding the pitfalls of computing surface area based on a discrete list of cortical nodes, we derived surface areas by predicting the individually fit values from the standard formula for each subject.

## Statistics and model fitting

*Overlap coefficients*. Overlap between phosphenes outlined by the subjects and the pRFs measured by ECoG was summarized by the Sørensen-Dice coefficient, where the overlap coefficient, O, between region A and region B is 2 times the area of overlap divided by the sum of the two areas:

$$O(A,B) = 2 \times \left[\frac{area \ (A \cap B)}{area(A) + area(B)}\right]$$
(Eq S2)

For pRFs, the area was defined as the region within 2 standard deviations of the center. For each site and on each trial, two Sørensen-Dice coefficients were computed, one between the broadband pRF and the phosphene, and one between the stimulus-locked pRF and the phosphene. To assess whether the coefficients from the broadband pRFs differed significantly from the coefficients from the stimulus-locked pRFs for a given site, a bootstrapping procedure was used: for *n* paired coefficients (18, 21, 16, 18 or 9 for sites 1-5), *n* pairs were drawn at random with replacement, 10,000 times. For each of the 10,000 bootstraps, the mean of the *n* differences was computed. The fraction of these *n* differences greater than 0, ' $\mu$ ', is used to derive a 2-sided *p-value*:

$$p_{value} = 1 - 2 \times abs(0.5 - \mu) \tag{Eq S3}$$

A bootstrapping test was used rather than parametric statistics because there is no assumption that the data are normally distributed. Both the *p*-value and the fraction  $\mu$  are reported in Table S3.

*PRF fits.* PRF models were fit to the broadband and stimulus-locked time series using nonlinear optimization, as described previously(Winawer et al., 2013). The accuracy of the pRF models fit to each of the 5 sites for each of the two signals (broadband and stimulus-locked) was computed as the coefficient of determination (Table S3), as previously(Kay et al., 2013):

$$R^{2} = 100 \times \left[ 1 - \frac{\sum (MODEL - DATA)^{2}}{\sum DATA^{2}} \right]$$
(Eq S4)

*Effects of stimulation parameters.* The effects of charge deposited per trial on the size of phosphenes in visual space, on the size of phosphenes projected to the cortex, and on subjective numerical ratings, were summarized by the best fitting power function of the form  $y=b^*x^m$  (Figure 4a-d). The fits were obtained in Matlab using the function 'fit.m', using the method of nonlinear least squares. The parameters of the fits and goodness of fit values are reported in Table S4. For modeling the cortical area of phosphenes and subjective rating linear regression was computed using the Matlab function 'fitlm.m', with the parameters plotted in Figure S4.

#### **Data Availability**

In the interest of reproducible computation in neuroscience, the full set of Matlab code and data needed to reproduce all plots and analyses will be made publicly available via the Open Science Framework (<u>https://osf.io/pz42u/</u>, DOI 10.17605/OSF.IO/PZ42U).

### **Supplemental References**

Agnew, W.F., Yuen, T.G., and McCreery, D.B. (1983). Morphologic changes after prolonged electrical stimulation of the cat's cortex at defined charge densities. Exp Neurol 79, 397-411.

Amano, K., Wandell, B.A., and Dumoulin, S.O. (2009). Visual field maps, population receptive field sizes, and visual field coverage in the human MT+ complex. Journal of neurophysiology 102, 2704-2718.

Babb, T.L., and Kupfer, W. (1984). Phagocytic and metabolic reactions to intracerebral electrical stimulation of rat brain. Exp Neurol 86, 183-197.

Benson, N.C., Butt, O.H., Brainard, D.H., and Aguirre, G.K. (2014). Correction of distortion in flattened representations of the cortical surface allows prediction of V1-V3 functional organization from anatomy. PLoS Comput Biol 10, e1003538.

Benson, N.C., Butt, O.H., Datta, R., Radoeva, P.D., Brainard, D.H., and Aguirre, G.K. (2012). The retinotopic organization of striate cortex is well predicted by surface topology. Curr Biol 22, 2081-2085.

Brainard, D.H. (1997). The Psychophysics Toolbox. Spat Vis 10, 433-436.

Dale, A.M., Fischl, B., and Sereno, M.I. (1999). Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage 9, 179-194.

Dougherty, R.F., Koch, V.M., Brewer, A.A., Fischer, B., Modersitzki, J., and Wandell, B.A. (2003). Visual field representations and locations of visual areas V1/2/3 in human visual cortex. J Vis 3, 586-598.

Dumoulin, S.O., and Wandell, B.A. (2008). Population receptive field estimates in human visual cortex. Neuroimage 39, 647-660.

Hermes, D., Miller, K.J., Noordmans, H.J., Vansteensel, M.J., and Ramsey, N.F. (2010). Automated electrocorticographic electrode localization on individually rendered brain surfaces. Journal of neuroscience methods 185, 293-298.

Horton, J.C., and Hoyt, W.F. (1991). The representation of the visual field in human striate cortex. A revision of the classic Holmes map. Archives of ophthalmology 109, 816-824.

Kay, K.N., Winawer, J., Mezer, A., and Wandell, B.A. (2013). Compressive spatial summation in human visual cortex. Journal of neurophysiology 110, 481-494.

Pelli, D.G. (1997). The VideoToolbox software for visual psychophysics: transforming numbers into movies. Spat Vis 10, 437-442.

Winawer, J., Horiguchi, H., Sayres, R.A., Amano, K., and Wandell, B.A. (2010). Mapping hV4 and ventral occipital cortex: the venous eclipse. Journal of vision 10, 1.

Winawer, J., Kay, K.N., Foster, B.L., Rauschecker, A.M., Parvizi, J., and Wandell, B.A. (2013). Asynchronous broadband signals are the principal source of the BOLD response in human visual cortex. Curr Biol 23, 1145-1153.