

<sup>1</sup> A Gaussian process model of human electrocorticographic  
<sup>2</sup> data

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<sup>4</sup> **Abstract**

We present a model-based method for inferring full-brain neural activity at millimeter-scale spatial resolutions and millisecond-scale temporal resolutions using standard human intracranial recordings. Our approach assumes that different people's brains exhibit similar correlational structure, and that activity and correlation patterns vary smoothly over space. One can then ask, for an arbitrary individual's brain: given recordings from a limited set of locations in that individual's brain, along with the observed spatial correlations learned from other people's recordings, how much can be inferred about ongoing activity at *other* locations throughout that individual's brain? We show that our approach generalizes across people and tasks, thereby providing a person- and task-general means of inferring high spatiotemporal resolution full-brain neural dynamics from standard low-density intracranial recordings.

**Keywords:** Electrocorticography (ECoG), intracranial electroencephalography (iEEG), local field potential (LFP), epilepsy, maximum likelihood estimation, Gaussian process regression

<sup>19</sup> **Introduction**

<sup>20</sup> Modern human brain recording techniques are fraught with compromise [33]. Commonly used  
<sup>21</sup> approaches include functional magnetic resonance imaging (fMRI), scalp electroencephalogra-  
<sup>22</sup> phy (EEG), and magnetoencephalography (MEG). For each of these techniques, neuroscientists  
<sup>23</sup> and electrophysiologists must choose to optimize spatial resolution at the cost of temporal reso-  
<sup>24</sup> lution (e.g., as in fMRI) or temporal resolution at the cost of spatial resolution (e.g., as in EEG and  
<sup>25</sup> MEG). A less widely used approach (due to requiring work with neurosurgical patients) is to  
<sup>26</sup> record from electrodes implanted directly onto the cortical surface (electrocorticography; ECoG)

27 or into deep brain structures (intracranial EEG; iEEG). However, these intracranial approaches  
28 also require compromise: the high spatiotemporal resolution of intracranial recordings comes  
29 at the cost of substantially reduced brain coverage, since safety considerations limit the number  
30 of electrodes one may implant in a given patient’s brain. Further, the locations of implanted  
31 electrodes are determined by clinical, rather than research, needs.

32 An increasingly popular approach is to improve the effective spatial resolution of MEG or  
33 scalp EEG data by using a geometric approach called *beamforming* to solve the biomagnetic or  
34 bioelectrical inverse problem [28]. This approach entails using detailed brain conductance mod-  
35 els (often informed by high spatial resolution anatomical MRI images) along with the known  
36 sensor placements (localized precisely in 3D space) to reconstruct brain signals originating from  
37 theoretical point sources deep in the brain (and far from the sensors). Traditional beamforming  
38 approaches must overcome two obstacles. First, the inverse problem beamforming seeks to  
39 solve has infinitely many solutions. Researchers have made traction towards constraining the  
40 solution space by assuming that signal-generating sources are localized on a regularly spaced  
41 grid spanning the brain and that individual sources are small relative to their distances to the  
42 sensors [1, 11, 34]. The second, and in some ways much more serious, obstacle is that the  
43 magnetic fields produced by external (noise) sources are substantially stronger than those pro-  
44 duced by the neuronal changes being sought (i.e., at deep structures, as measured by sensors  
45 at the scalp). This means that obtaining adequate signal quality often requires averaging the  
46 measured responses over tens to hundreds of responses or trials (e.g., see review by [11]).

47 Another approach to obtaining high spatiotemporal resolution neural data has been to col-  
48 lect fMRI and EEG data simultaneously. Simultaneous fMRI-EEG has the potential to balance  
49 the high spatial resolution of fMRI with the high temporal resolution of scalp EEG, thereby,  
50 in theory, providing the best of both worlds. In practice, however, the signal quality of both  
51 recordings suffers substantially when the two techniques are applied simultaneously (e.g., see

52 review by [13]). In addition, the experimental designs that are ideally suited to each technique  
53 individually are somewhat at odds. For example, fMRI experiments often lock stimulus presen-  
54 tation events to the regularly spaced image acquisition time (TR), which maximizes the number  
55 of post-stimulus samples. By contrast, EEG experiments typically employ jittered stimulus pre-  
56 sentation times to maximize the experimentalist’s ability to distinguish electrical brain activity  
57 from external noise sources such as from 60 Hz alternating current power sources.

58 The current “gold standard” for precisely localizing signals and sampling at high temporal  
59 resolution is to take (ECoG or iEEG) recordings from implanted electrodes (but from a limited  
60 set of locations in any given brain). This begs the following question: what can we infer about  
61 the activity exhibited by the rest of a person’s brain, given what we learn from the limited  
62 intracranial recordings we have from their brain and additional recordings taken from *other*  
63 people’s brains? Here we develop an approach, which we call *SuperEEG*<sup>1</sup>, based on Gaussian  
64 process regression [27]. SuperEEG entails using data from multiple people to estimate activ-  
65 ity patterns at arbitrary locations in each person’s brain (i.e., independent of their electrode  
66 placements). We test our SuperEEG approach using two large datasets of intracranial record-  
67 ings [7, 8, 12, 16–19, 21, 23, 30–32, 35, 40]. We show that the SuperEEG algorithm recovers  
68 signals well from electrodes that were held out of the training dataset. We also examine the  
69 factors that influence how accurately activity may be estimated (recovered), which may have  
70 implications for electrode design and placement in neurosurgical applications.

## 71 Approach

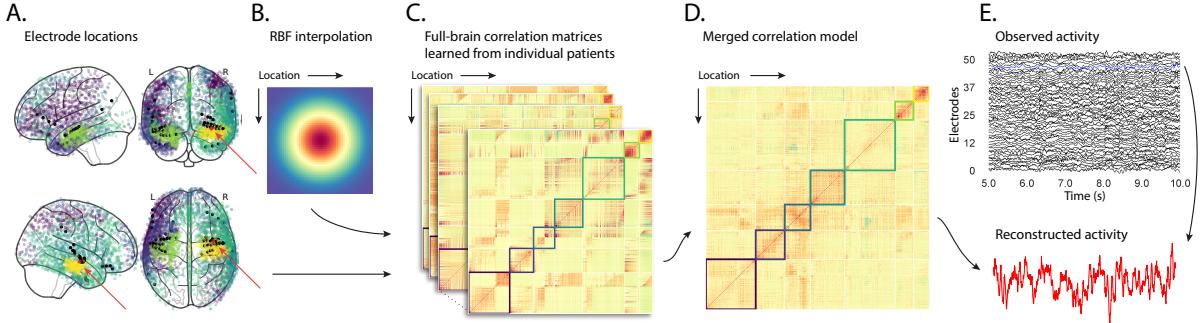
72 The SuperEEG approach to inferring high temporal resolution full-brain activity patterns is  
73 outlined and summarized in Figure 1. We describe (in this section) and evaluate (in *Results*) our

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<sup>1</sup>The term “SuperEEG” was coined by Robert J. Sawyer in his popular science fiction novel *The Terminal Experiment* [29]. SuperEEG is a fictional technology that measures ongoing neural activity throughout the entire living human brain with perfect precision and at arbitrarily high spatiotemporal resolution.

74 approach using a two large previously collected dataset comprising multi-session intracranial  
75 recordings. Dataset 1 comprises multi-session recordings taken from 6876 electrodes implanted  
76 in the brains of 88 epilepsy patients [21, 23, 30–32]. Each recording session lasted from 0.2–  
77 3 h (total recording time: 0.3–14.2 h; Fig. S4E). During each recording session, the patients  
78 participated in a free recall list learning task, which lasted for up to approximately 1 h. In  
79 addition, the recordings included “buffer” time (the length varied by patient) before and after  
80 each experimental session, during which the patients went about their regular hospital activities  
81 (confined to their hospital room, and primarily in bed). These additional activities included  
82 interactions with medical staff and family, watching television, reading, and other similar  
83 activities. For the purposes of the Dataset 1 analyses presented here, we aggregated all data  
84 across each recording session, including recordings taken during the main experimental task  
85 as well as during non-experimental time. We used Dataset 1 to develop our main SuperEEG  
86 approach, and to examine the extent to which SuperEEG might be able to generate task-general  
87 predictions. Dataset 2 comprised multi-session recordings from 4436 electrodes implanted in  
88 the brains of 40 epilepsy patients [7, 8, 12, 16–19, 35, 40]. Each recording session lasted from  
89 0.4–2.2 h (total recording time: 0.4–6.6 h; Fig. S4K). Whereas Dataset 1 included recordings  
90 taken as the patients participated in a variety of activities, Dataset 2 included recordings taken  
91 as each patient performed each of two specific experimental memory tasks: a random word list  
92 free recall task (Experiment 1) and a categorized word list free recall task (Experiment 2). We  
93 used Dataset 2 to further examine the ability of SuperEEG to generalize its predictions within  
94 versus across tasks. Figure S4 provides additional information about both datasets.

95 We first applied fourth order Butterworth notch filter to remove 60 Hz ( $\pm .5$  Hz) line noise  
96 from every recording (from every electrode). Next, we downsampled the recordings (regardless  
97 of the original samplerate) to 250 Hz. (This downsampling step served to both normalize for  
98 differences in sampling rates across patients and to ease the computational burden of our sub-



**Figure 1: Methods overview.** **A. Electrode locations.** Each dot reflects the location of a single electrode implanted in the brain of a Dataset 1 patient. A held-out recording location from one patient is indicated in red, and the patient’s remaining electrodes are indicated in black. The electrodes from the remaining patients are colored by  $k$ -means cluster (computed using the full-brain correlation model shown in Panel D). **B. Radial basis function kernel.** Each electrode contributed by the patient (black) weights on the full set of locations under consideration (all dots in Panel A, defined as  $\bar{R}$  in the text). The weights fall off with positional distance (in MNI space) according to an RBF. **C. Per-patient correlation matrices.** After computing the pairwise correlations between the recordings from each patient’s electrodes, we use RBF-weighted averages to estimate correlations between all locations in  $\bar{R}$ . We obtain an estimated full-brain correlation matrix using each patient’s data. **D. Merged correlation model.** We combine the per-patient correlation matrices (Panel C) to obtain a single full-brain correlation model that captures information contributed by every patient. Here we have sorted the rows and columns to reflect  $k$ -means clustering labels [using  $k=7$ ; 41], whereby we grouped locations based on their correlations with the rest of the brain (i.e., rows of the matrix displayed in the panel). The boundaries denote the cluster groups. The rows and columns of Panel C have been sorted using the Panel D-derived cluster labels. **E. Reconstructing activity throughout the brain.** Given the observed recordings from the given patient (shown in black; held-out recording is shown in blue), along with a full-brain correlation model (Panel D), we use Equation 12 to reconstruct the most probable activity at the held-out location (red).

99 sequent analyses.) We then excluded any electrodes that showed putative epileptiform activity.  
100 Specifically, we excluded from further analysis any electrode that exhibited an average kurtosis  
101 of 10 or greater across all of that patient’s recording sessions. We also excluded any patients  
102 with fewer than 2 electrodes that passed this criteria, as the SuperEEG algorithm requires  
103 measuring correlations between 2 or more electrodes from each patient. For Dataset 1, this  
104 yielded clean recordings from 4168 electrodes implanted throughout the brains of 67 patients  
105 (Fig. 1A); for Dataset 2, this yielded clean recordings from 3159 electrodes from 24 patients.  
106 Each individual patient contributes electrodes from a limited set of brain locations, which we  
107 localized in a common space [MNI152; 10]; an example Dataset 1 patient’s 54 electrodes that  
108 passed the above kurtosis threshold test are highlighted in black and red.

The recording from a given electrode is maximally informative about the activity of the neural tissue immediately surrounding its recording surface. However, brain regions that are distant from the recording surface of the electrode also contribute to the recording, albeit (*ceteris paribus*) to a much lesser extent. One mechanism underlying these contributions is volume conduction. The precise rate of falloff due to volume conduction (i.e., how much a small volume of brain tissue at location  $x$  contributes to the recording from an electrode at location  $\eta$ ) depends on the size of the recording surface, the electrode’s impedance, and the conductance profile of the volume of brain between  $x$  and  $\eta$ . As an approximation of this intuition, we place a Gaussian radial basis function (RBF) at the location  $\eta$  of each electrode’s recording surface (Fig. 1B). We use the values of the RBF at any brain location  $x$  as a rough estimate of how much structures around  $x$  contributed to the recording from location  $\eta$ :

$$\text{rbf}(x|\eta, \lambda) = \exp \left\{ -\frac{\|x - \eta\|^2}{\lambda} \right\}, \quad (1)$$

109 where the width variable  $\lambda$  is a parameter of the algorithm (which may in principle be set  
110 according to location-specific tissue conductance profiles) that governs the level of spatial  
111 smoothing. In choosing  $\lambda$  for the analyses presented here, we sought to maximize spatial

resolution (which implies a small value of  $\lambda$ ) while also maximizing the algorithm's ability to generalize to any location throughout the brain, including those without dense electrode coverage (which implies a large value of  $\lambda$ ). Here we set  $\lambda = 20$ , guided in part by our prior work [22, 24], and in part by examining the brain coverage with non-zero weights achieved by placing RBFs at each electrode location in Dataset 1 and taking the sum (across all electrodes) at each voxel in a  $4 \text{ mm}^3$  MNI brain. (We then held  $\lambda$  fixed for our analyses of Dataset 2.) We note that this value could in theory be further optimized, e.g., using cross validation or a formal model [e.g., 24].

A second mechanism whereby a given region  $x$  can contribute to the recording at  $\eta$  is through (direct or indirect) anatomical connections between structures near  $x$  and  $\eta$ . We use temporal correlations in the data to estimate these anatomical connections [2]. Let  $\bar{R}$  be the set of locations at which we wish to estimate local field potentials, and let  $R_s \subseteq \bar{R}$  be set of locations at which we observe local field potentials from patient  $s$  (excluding the electrodes that did not pass the kurtosis test described above). In the analyses below we define  $\bar{R} = \cup_{s=1}^S R_s$ . We can calculate the expected inter-electrode correlation matrix for patient  $s$ , where  $C_{s,k}(i, j)$  is the correlation between the time series of voltages for electrodes  $i$  and  $j$  from subject  $s$  during session  $k$ , using:

$$\bar{C}_s = r\left(\frac{1}{n}\left(\sum_{k=1}^n z(C_{s,k})\right)\right), \text{ where} \quad (2)$$

$$z(r) = \frac{\log(1+r) - \log(1-r)}{2} \text{ is the Fisher } z\text{-transformation and} \quad (3)$$

$$z^{-1}(z) = r(z) = \frac{\exp(2z) - 1}{\exp(2z) + 1} \text{ is its inverse.} \quad (4)$$

Next, we use Equation 1 to construct a number of to-be-estimated locations by number of patient electrode locations weight matrix,  $W_s$ . Specifically,  $W_s$  approximates how informative the recordings at each location in  $R_s$  are in reconstructing activity at each location in  $\bar{R}$ , where

<sup>132</sup> the contributions fall off with an RBF according to the distances between the corresponding  
<sup>133</sup> locations:

$$W_s(i, j) = \text{rbf}(i|j, \lambda). \quad (5)$$

<sup>134</sup> Given this weight matrix,  $W_s$ , and the observed inter-electrode correlation matrix for patient  
<sup>135</sup>  $s$ ,  $\bar{C}_s$ , we can estimate the correlation matrix for all locations in  $\bar{R}$  ( $\hat{C}_s$ ; Fig. 1C) using:

$$\hat{N}_s(x, y) = \sum_{i=1}^{|R_s|} \sum_{j=1}^{i-1} W(x, i) \cdot W(y, j) \cdot z(\bar{C}_s(i, j)) \quad (6)$$

$$\hat{D}_s(x, y) = \sum_{i=1}^{|R_s|} \sum_{j=1}^{i-1} W(x, i) \cdot W(y, j). \quad (7)$$

$$\hat{C}_s = r\left(\frac{\hat{N}_s}{\hat{D}_s}\right). \quad (8)$$

After estimating the numerator ( $\hat{N}_s$ ) and denominator ( $\hat{D}_s$ ) placeholders for each  $\hat{C}_s$ , we aggregate these estimates across the  $S$  patients to obtain a single expected full-brain correlation matrix ( $\hat{K}$ ; Fig. 1D):

$$\hat{K} = r\left(\frac{\sum_{s=1}^S \hat{N}_s}{\sum_{s=1}^S \hat{D}_s}\right). \quad (9)$$

<sup>136</sup> Intuitively, the numerators capture the general structures of the patient-specific estimates of full-  
<sup>137</sup> brain correlations, and the denominators account for which locations were near the implanted  
<sup>138</sup> electrodes in each patient. To obtain  $\hat{K}$ , we compute a weighted average across the estimated  
<sup>139</sup> patient-specific full-brain correlation matrices, where patients with observed electrodes near a  
<sup>140</sup> particular set of locations in  $\hat{K}$  contribute more to the estimate.

<sup>141</sup> Having used the multi-patient data to estimate a full-brain correlation matrix at the set  
<sup>142</sup> of locations in  $\bar{R}$  that we wish to know about, we next use  $\hat{K}$  to estimate activity patterns  
<sup>143</sup> everywhere in  $\bar{R}$ , given observations at only a subset of locations in  $\bar{R}$  (Fig. 1E).

144 Let  $\alpha_s$  be the set of indices of patient  $s$ 's electrode locations in  $\bar{R}$  (i.e., the locations in  $R_s$ ),  
 145 and let  $\beta_s$  be the set of indices of all other locations in  $\bar{R}$ . In other words,  $\beta_s$  reflects the locations  
 146 in  $\bar{R}$  where we did not observe a recording for patient  $s$  (these are the recording locations we  
 147 will want to fill in using SuperEEG). We can sub-divide  $\hat{K}$  as follows:

$$\hat{K}_{\beta_s, \alpha_s} = \hat{K}(\beta_s, \alpha_s), \text{ and} \quad (10)$$

$$\hat{K}_{\alpha_s, \alpha_s} = \hat{K}(\alpha_s, \alpha_s). \quad (11)$$

148 Here  $\hat{K}_{\beta_s, \alpha_s}$  represents the correlations between the “unknown” activity at the locations indexed  
 149 by  $\beta_s$  and the observed activity at the locations indexed by  $\alpha_s$ , and  $\hat{K}_{\alpha_s, \alpha_s}$  represents the  
 150 correlations between the observed recordings (at the locations indexed by  $\alpha_s$ ).

151 Let  $Y_{s,k,\alpha_s}$  be the number-of-timepoints ( $T$ ) by  $|\alpha_s|$  matrix of (observed) voltages from the  
 152 electrodes in  $\alpha_s$  during session  $k$  from patient  $s$ . Then we can estimate the voltage from patient  
 153  $s$ 's  $k^{th}$  session at the locations in  $\beta_s$  using [27]:

$$\hat{Y}_{s,k,\beta_s} = ((\hat{K}_{\beta_s, \alpha_s} \cdot \hat{K}_{\alpha_s, \alpha_s}^{-1}) \cdot Y_{s,k,\alpha_s}^T)^T. \quad (12)$$

154 This equation is the foundation of the SuperEEG algorithm. Whereas we observe recordings  
 155 only at the locations indexed by  $\alpha_s$ , Equation 12 allows us to estimate the recordings at all loca-  
 156 tions indexed by  $\beta_s$ , which we can define *a priori* to include any locations we wish, throughout  
 157 the brain. This yields estimates of the time-varying voltages at *every* location in  $\bar{R}$ , provided that  
 158 we define  $\bar{R}$  in advance to include the union of all of the locations in  $R_s$  and all of the locations  
 159 at which we wish to estimate recordings (i.e., a timeseries of voltages).

160 We designed our approach to be agnostic to electrode impedances, as electrodes that do not  
 161 exist do not have impedances. Therefore our algorithm recovers voltages in standard deviation  
 162 ( $z$ -scored) units rather than attempting to recover absolute voltages. (This property reflects the

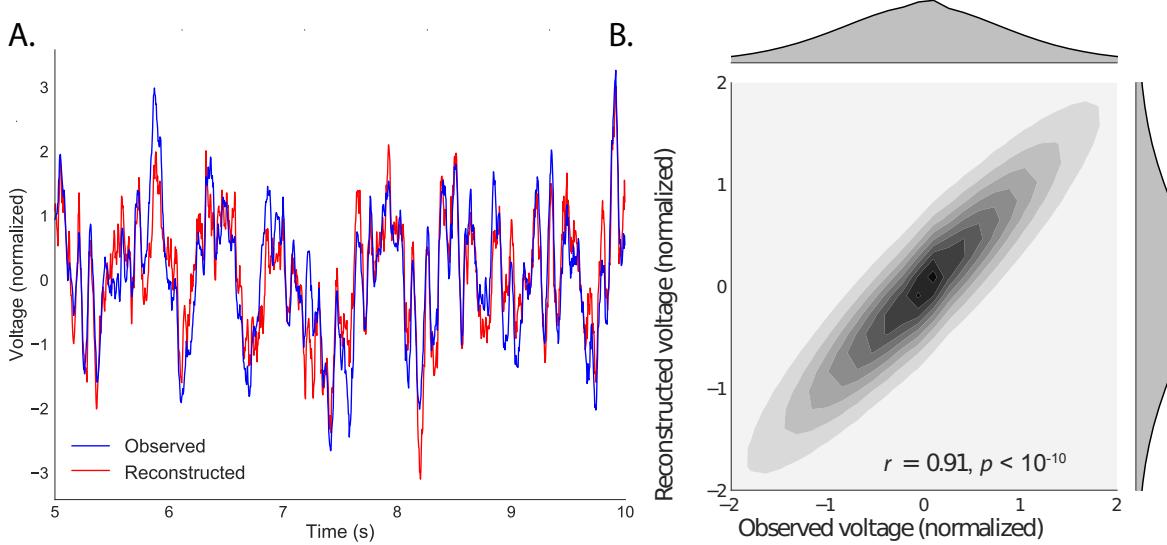
fact that  $\hat{K}_{\beta_s, \alpha_s}$  and  $\hat{K}_{\alpha_s, \alpha_s}$  are correlation matrices rather than covariance matrices.) Also, we note that Equation 12 requires computing a  $T$  by  $T$  matrix, which can become computationally intractable when  $T$  is very large (e.g., for the patient highlighted in Fig. 2,  $T = 12786750$ ). However, because Equation 12 is time invariant, we may compute  $Y_{s,k,\beta_s}$  in a piecewise manner by filling in  $Y_{s,k,\beta_s}$  one row at a time (using the corresponding samples from  $Y_{s,k,\alpha_s}$ ).

The SuperEEG algorithm described above and in Figure 1 allows us to estimate, up to a constant scaling factor, local field potentials (LFPs) for each patient at all arbitrarily chosen locations in the set  $\bar{R}$ , even if we did not record that patient's brain at all of those locations. We next turn to an evaluation of the accuracy of those estimates.

## Results

We used a cross-validation approach to test the accuracy with which the SuperEEG algorithm reconstructs activity throughout the brain. For each patient in turn, we estimated full-brain correlation matrices (Eqn. 9) using data from all of the *other* patients. This step ensured that the data we were reconstructing could not also be used to estimate the between-location correlations that drove the reconstructions via Equation 12 (otherwise the analysis would be circular). For that held-out patient, for each of their electrodes in turn, we used Equation 12 to reconstruct activity at the held-out electrode location, using the correlation matrix learned from all other patients' data as  $\hat{K}$ , and using activity recorded from the other electrodes from the held-out patient as  $Y_{s,k,\alpha_s}$ . We then asked: how closely did each of the SuperEEG-estimated recordings at those electrodes match the observed recordings from those electrodes (i.e., how closely did the estimated  $\hat{Y}_{s,k,\beta_s}$  match the observed  $Y_{s,k,\beta_s}$ ?).

To illustrate our approach, we first examine an individual held-out raw LFP trace and its associated SuperEEG-derived reconstruction. Figure 2A displays the observed LFP from the red electrode in Figure 1A (blue), and its associated reconstruction (red), during a 5 s time window



**Figure 2: Observed and reconstructed LFP from a single electrode.** **A. Example LFP.** A 5 s recording from the red electrode in Figure 1A is displayed in blue, and the reconstructed LFP during the same time window is shown in red. **B. Observed versus reconstructed LFP over 14.2 hours.** The two-dimensional histogram reflects the relation between distributions of observed versus reconstructed voltages from one patient, across the 14.2 hours of recorded data collected over 6 recording sessions. The correlation reported in the panel is between the observed and reconstructed voltages. Both panels: all voltages are represented in standard deviation units (computed within session).

187 during one of the example patient's six recording sessions. The two traces match closely  
 188 ( $r = 0.86, p < 10^{-10}$ ). Figure 2B displays a two-dimensional histogram of the actual versus  
 189 reconstructed voltages for the entire 14.2 total hours of recordings from the example electrode  
 190 (correlation:  $r = 0.91, p < 10^{-10}$ ). This example confirms that the SuperEEG algorithm recovers  
 191 the recordings from this single electrode well. Next, we used this general approach to quantify  
 192 the algorithm's performance across the full dataset.

193 For each held-out electrode, from each held-out patient in turn, we computed the average  
 194 correlation (across recording sessions) between the SuperEEG-reconstructed voltage traces and  
 195 the observed voltage traces from that electrode. For this analysis we set  $\bar{R}$  to be the union of  
 196 all electrode locations across all patients. This yielded a single correlation coefficient for each

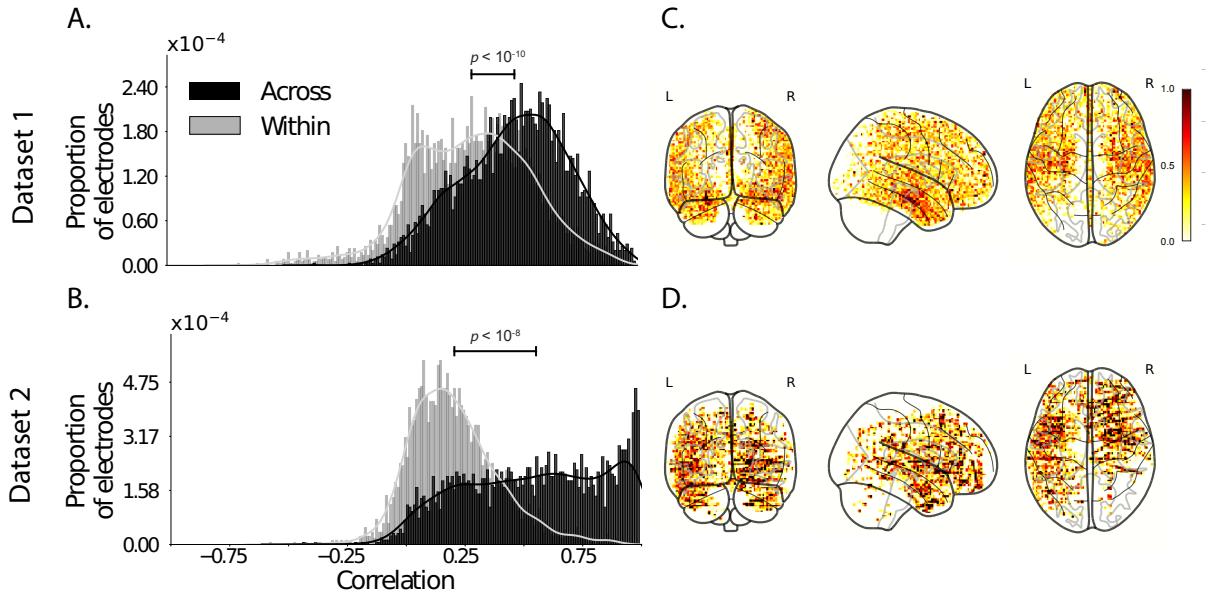
197 electrode location in  $\bar{R}$ , reflecting how well the SuperEEG algorithm was able to recover the  
198 recording at that location by incorporating data across patients (black histogram in Fig. 3A, map  
199 in Fig. 3C). The observed distribution of correlations was centered well above zero (mean: 0.52;  
200  $t$ -test comparing mean of distribution of  $z$ -transformed average patient correlation coefficients  
201 to 0:  $t(66) = 25.08, p < 10^{-10}$ ), indicating that the SuperEEG algorithm recovers held-out activity  
202 patterns substantially better than random guessing.

203 As a stricter benchmark, we compared the quality of these across-participant reconstructions  
204 (i.e., computed using a correlation model learned from other patients' data) to reconstructions  
205 generated using a correlation model trained using the in-patient's data. In other words, for  
206 this within-patient benchmark analysis we estimated  $\hat{C}_s$  (Eqn. 8) for each patient in turn, using  
207 recordings from all of that patient's electrodes except at the location we were reconstructing.  
208 These within-patient reconstructions serve as an estimate of how well data from all of the  
209 other electrodes from that single patient may be used to estimate held-out data from the  
210 same patient. This allows us to ask how much information about the activity at a given  
211 electrode might be inferred through (a) volume conductance or other sources of "leakage"  
212 from activity patterns measured from the patient's other electrodes and (b) across-electrode  
213 correlations learned from that single patient. As shown in Figure 3A (gray histogram), the  
214 distribution of within-patient correlations was centered well above zero (mean: 0.32;  $t$ -test  
215 comparing mean of distribution of  $z$ -transformed average patient correlation coefficients to 0:  
216  $t(66) = 15.16, p < 10^{-10}$ ). However, the across-patient correlations were substantially higher  
217 ( $t$ -test comparing average  $z$ -transformed within versus across patient electrode correlations:  
218  $t(66) = 9.62, p < 10^{-10}$ ). This is an especially conservative test, given that the across-patient  
219 SuperEEG reconstructions exclude (from the correlation matrix estimates) all data from the  
220 patient whose data is being reconstructed. We repeated each of these analyses on a second  
221 independent dataset and found similar results (Fig. 3B, D; within versus across reconstruction

accuracy:  $t(23) = 6.93, p < 10^{-5}$ ). We also replicated this result separately for each of the two experiments from Dataset 2 (Fig. S1). This overall finding, that reconstructions of held-out data using correlation models learned from *other* patient's data yield higher reconstruction accuracy than correlation models learned from the patient whose data is being reconstructed, has two important implications. First, it implies that distant electrodes provide additional predictive power to the data reconstructions beyond the information contained solely in nearby electrodes. (This follows from the fact that each patient's electrodes are implanted in a unique set of locations, so for any given electrode the closest electrodes in the full dataset are likely to come from the same patient.) Second, it implies that the spatial correlations learned using the SuperEEG algorithm are, to some extent, similar across people.

The recordings we analyzed from Dataset 1 comprised data collected as the patients performed a variety of (largely idiosyncratic) tasks throughout each day's recording session. That we observed reliable reconstruction accuracy across patients suggests that the spatial correlations derived from the SuperEEG algorithm are, to some extent, similar across tasks. We tested this finding more explicitly using Dataset 2. In Dataset 2, the recordings were limited to times when each patient was participating in each of two experiments (Experiment 1, a random-word list free recall task, and Experiment 2, a categorized list free recall task). We wondered whether a correlation model learned from data from one experiment might yield good predictions of data from the other experiment. Further, we wondered about the extent to which it might be beneficial or harmful to combine data across tasks.

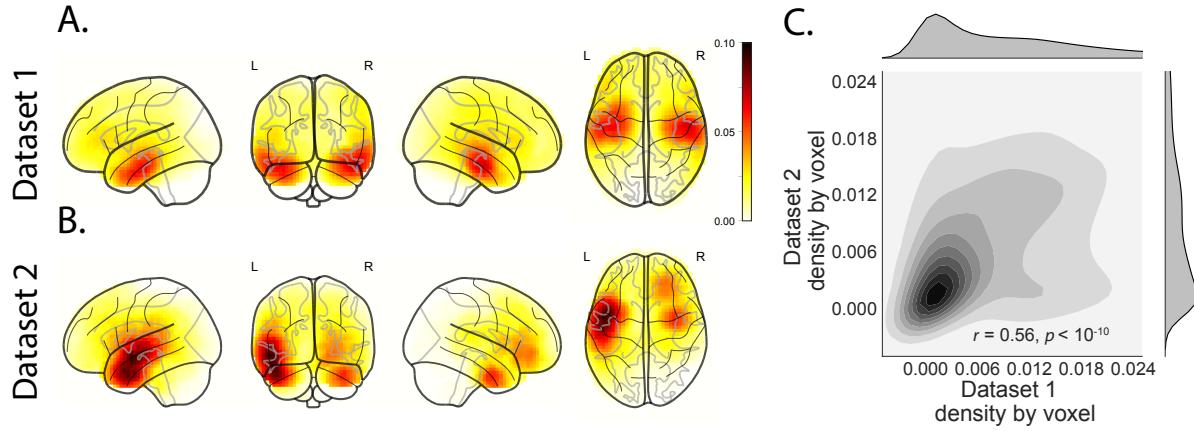
To test the task-specificity of the SuperEEG-derived correlation models, we repeated the above within- and across-patient cross validation procedures separately for Experiment 1 and Experiment 2 data from Dataset 2. We then compared the reconstruction accuracies for held-out electrodes, for models trained within versus across the two experiments, or combining across both experiments (Fig. S2). In every case we found that across-patient models trained using



**Figure 3: Reconstruction quality across all electrodes in two ECoG datasets. A. Distributions of correlations between observed versus reconstructed activity by electrode, for Dataset 1.** The across-patient distribution (black) reflects reconstruction accuracy (correlation) using a correlation model learned from all but one patient’s data, and then applied to that held-out patient’s data. The within-patient distribution (gray) reflects performance using a correlation model learned from the same patient who contributed the to-be-reconstructed electrode. **B. Distributions of correlations for Dataset 2.** This panel is in the same format as Panel A, but reflects results obtained from Dataset 2. The histograms aggregate data across both Dataset 2 experiments; for results broken down by experiment see Figure S3. **C.–D. Reconstruction performance by location.** Each dot reflects the location of a single implanted electrode from Dataset 1 (Panel C) or Dataset 2 (Panel D). The dot colors denote the average across-session correlation, using the across-patient correlation model, between the observed and reconstructed activity at the given electrode location.

247 data from all other patients out-performed within-patient models trained on data only from the  
248 subject contributing the given electrode ( $ts(24) > 6.50, ps < 10^{-5}$ ). All reconstruction accuracies  
249 also reliably exceeded chance performance ( $ts(24) > 8.00, ps < 10^{-8}$ ). Average reconstruction  
250 accuracy was highest for the across-patient models limited to data from the same experiment  
251 (mean accuracy: 0.68); next-highest for the across-patient models that combined data across  
252 both experiments (mean accuracy: 0.61); and lowest for models trained across task (mean  
253 accuracy: 0.47). This result also held for each of the Dataset 2 experiments individually  
254 (Fig. S3). Taken together, these results indicate that there are reliable commonalities in the spatial  
255 correlations of full-brain activity across tasks, but that there are also reliable differences in these  
256 spatial correlations across tasks. Whereas reconstruction accuracy benefits from incorporating  
257 data from other patients, reconstruction accuracy is highest when constrained to within-task  
258 data, or data that includes a variety of tasks (e.g., Dataset 1, or combining across the two Dataset  
259 2 experiments).

260 Although both datasets we examined provide good full-brain coverage (when considering  
261 data from every patient; e.g. Fig. 3C, D), electrodes are not placed uniformly throughout the  
262 brain. For example, electrodes are more likely to be implanted in regions like the medial  
263 temporal lobe (MTL), and are rarely implanted in occipital cortex (Fig. 4A, B). Separately for  
264 each dataset, for each voxel in the 4 mm<sup>3</sup> voxel MNI152 brain, we computed the proportion  
265 of electrodes in the dataset that were contained within a 20 MNI unit radius sphere centered  
266 on that voxel. We defined the *density* at that location as this proportion. Across Datasets  
267 1 and 2, the electrode placement densities were similar (correlation by voxel:  $r = 0.56, p <$   
268  $10^{-10}$ ). We wondered whether regions with good coverage might be associated with better  
269 reconstruction accuracy (e.g. Fig. 3C, D indicate that many electrodes in the MTL have relatively  
270 high reconstruction accuracy, and occipital electrodes tend to have relatively low reconstruction  
271 accuracy). To test whether this held more generally across the entire brain, for each dataset



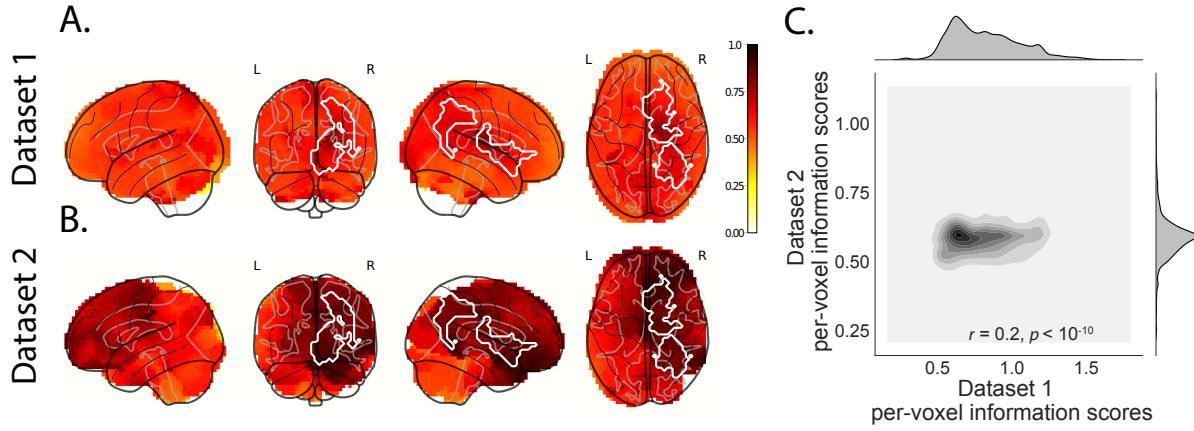
**Figure 4: Electrode sampling density by location.** **A. Electrode sampling density by voxel in Dataset 1.** Each voxel is colored by the proportion of total electrodes in the dataset that are located within a 20 MNI unit radius sphere centered on the given voxel. **B. Electrode sampling density by voxel in Dataset 2.** This panel displays the sampling density map for Dataset 2, in the same format as Panel A. **C. Correspondence in sampling density by voxel across Datasets 1 and 2.** The two-dimensional histogram displays the by-voxel densities in the two Datasets, and the one-dimensional histograms display the proportions of voxels in each dataset with the given density value. The correlation reported in the panel is across voxels in the  $4 \text{ mm}^3$  MNI brain.

we computed the electrode placement density for each electrode from each patient (using the proportion of *other* patients' electrodes within 20 MNI units of the given electrode). We then correlated these density values with the across-patient reconstruction accuracies for each electrode. Contrary to our expectation, rather than positive correlations, we found weak (but reliable) negative correlations between reconstruction accuracy and density for both datasets (Dataset 1:  $r = -0.07, p < 10^{-5}$ ; Dataset 2:  $r = -0.18, p < 10^{-10}$ ). This indicates that the reconstruction accuracies we observed are not driven solely by sampling density, but rather may also reflect higher order properties of neural dynamics such as functional correlations between distant voxels [3].

In neurosurgical applications where one wishes to infer full-brain activity patterns, can our framework yield insights into where the electrodes should be placed? A basic assumption of our approach (and of most prior ECoG work) is that electrode recordings are most informative about

284 the neural activity near the recording surface of the electrode. But if we consider that activity  
285 patterns throughout the brain are meaningfully correlated, are there particular implantation  
286 locations that, if present in a patient’s brain, yield especially high reconstruction accuracies  
287 throughout the rest of the brain? For example, one might hypothesize that brain structures  
288 that are heavily interconnected with many other structures could be more informative about  
289 full-brain activity patterns than comparatively isolated structures.

290 To gain insights into whether particular electrode locations might be especially informative,  
291 we first computed the average reconstruction accuracy across all of each patient’s electrodes  
292 (using the across-patients cross validation test; black histograms in Fig. 3A and B). We labeled  
293 each patient’s electrodes in each dataset with the average reconstruction accuracy for that  
294 patient. In other words, we assigned every electrode from each given patient the same value,  
295 reflecting how well the activity patterns at those electrodes were reconstructed on average.  
296 Next, for each voxel in the 4 mm<sup>3</sup> MNI brain, we computed the average value across any  
297 electrode (from any patient) that came within 20 MNI units of that voxel’s center. Effectively,  
298 we computed an *information score* for each voxel, reflecting the average reconstruction accuracy  
299 across any patients with electrodes near each voxel—where the averages were weighted to reflect  
300 patients who had more electrodes implanted near that location. This yielded a single map for  
301 each dataset, highlighting regions that are potentially promising implantation targets in terms  
302 of providing full-brain activity information via SuperEEG (Fig. 5A, B). Despite task and patient  
303 differences across the two datasets, we nonetheless found that the maps of the most promising  
304 implantation targets derived from both datasets were similar (voxelwise correlation between  
305 information scores across the two datasets:  $r = 0.03, p < 10^{-10}$ ). While the correspondence  
306 between the two maps was not perfect, our finding that there were some commonalities between  
307 the two maps lends support to the notion that different brain areas are differently informative  
308 about full-brain activity patterns. Further, we found the intersection of the top 10% of the



**Figure 5: Most informative electrode locations.** **A. Dataset 1 information score by voxel.** The voxel colors reflect the weighted average reconstruction accuracy across all electrodes from any patients with at least one electrode within 20 MNI units of the given voxel. **B. Dataset 2 information score by voxel.** This panel is in the same format as Panel A. In both panels the contours indicate the intersections between the top 10% most informative voxels in each map. **C. Correspondence in information scores by voxel across Datasets 1 and 2.** Same format as Figure 4C.

most informative voxels between the two datasets (Fig. S5) and found gray matter regions like the right postcentral gyrus, right supramarginal gyrus, and the right nucleus accumbens that exhibited strong information scores in both datasets may be especially promising implantation targets.

## 313 Discussion

Are our brain's networks static or dynamic? And to what extent are the network properties of our brains stable across people and tasks? One body of work suggests that our brain's *functional* networks are dynamic [e.g., 24], person-specific [e.g., 9], and task-specific [e.g., 39]. In contrast, although the gross anatomical structure of our brains changes meaningfully over the course of years as our brains develop, on the timescales of typical neuroimaging experiments (i.e., hours to days) our anatomical networks are largely stable [e.g., 4]. Further, many aspects of brain anatomy, including white matter structure, are largely preserved across

321 people [e.g., 15, 26, 37]. There are several possible means of reconciling this apparent inconsis-  
322 tency between dynamic person- and task-specific functional networks versus stable anatomical  
323 networks. For example, relatively small magnitude anatomical differences across people may  
324 be reflected in reliable functional connectivity differences. Along these lines, one recent study  
325 found that diffusion tensor imaging (DTI) structural data is similar across people, but may be  
326 used to predict person-specific resting state functional connectivity data [2]. Similarly, other  
327 work indicates that task-specific functional connectivity may be predicted by resting state func-  
328 tional connectivity data [5, 38]. Another (potentially complementary) possibility is that our  
329 functional networks are constrained by anatomy, but nevertheless exhibit (potentially rapid)  
330 task-dependent changes [e.g., 36].

331 Here we have taken a model-based approach to studying whether high spatiotemporal  
332 resolution activity patterns throughout the human brain may be explained by a static connec-  
333 tome model that is shared across people and tasks. Specifically, we trained a model to take  
334 in recordings from a subset of brain locations, and then predicted activity patterns during the  
335 same interval, but at *other* locations that were held out from the model. Our model, based on  
336 Gaussian process regression, was built on three general hypotheses about the nature of the  
337 correlational structure of neural activity (each of which we tested). First, we hypothesized that  
338 functional correlations are stable over time and across tasks. We found that, although aspects  
339 of the patients' functional correlations that were stable across tasks, we achieved better recon-  
340 struction accuracy when we trained the model on within-task data [we acknowledge that our  
341 general approach could potentially be extended to better model across-task changes, following  
342 5, 38, and others]. Second, we hypothesized that some of the correlational structure of peo-  
343 ple's brain activity is similar across individuals. Consistent with this hypothesis, our model  
344 explained the data best when we trained the correlation model using data from *other* patients—  
345 even when compared to a correlation model trained on the same patient's data. Third, we

346 resolved ambiguities in the data by hypothesizing that neural activity from nearby sources will  
347 tend to be similar, all else being equal. This hypothesis was supported through our finding that  
348 all of the models we trained that incorporated this spatial smoothness assumption predicted  
349 held-out data well above chance.

350 One potential limitation of our approach is that it does not provide a natural means of  
351 estimating the precise timing of single-neuron action potentials. Prior work has shown that  
352 gamma band and broadband activity in the LFP may be used to estimate the firing rates of  
353 neurons that underly the population contributing to the LFP [6, 14, 20, 25]. Because SuperEEG  
354 reconstructs LFPs throughout the brain, one could in principle use gamma or broadband power  
355 in the reconstructed signals to estimate the corresponding firing rates (though not the timings  
356 of individual action potentials).

357 Beyond providing a means of estimating ongoing activity throughout the brain using al-  
358 ready implanted electrodes, our work also has implications for where to place the electrodes in  
359 the first place. Electrodes are typically implanted to maximize coverage of suspected epilep-  
360 togenic tissue. However, our findings suggest that this approach could be further optimized.  
361 Specifically, one could leverage not only the non-invasive recordings taken during an initial  
362 monitoring period (as is currently done routinely), but also recordings collected from other  
363 patients. We could then ask: given what we learn from other patients' data (and potentially  
364 from the scalp EEG recordings of this new patient), where should we place a fixed number of  
365 electrodes to maximize our ability to map seizure foci? As shown in Figure 5, recordings from  
366 different locations are differently informative in terms of reconstructing the spatiotemporal  
367 activity patterns throughout the brain. This property might be leveraged in decisions about  
368 where to surgically implant electrodes in future patients.

369 **Concluding remarks**

370 Over the past several decades, neuroscientists have begun to leverage the strikingly profound  
371 mathematical structure underlying the brain's complexity to infer how our brains carry out  
372 computations to support our thoughts, actions, and physiological processes. Whereas tradition-  
373 al beamforming techniques rely on geometric source-localization of signals measured at the  
374 scalp, here we propose an alternative approach that leverages the rich correlational structure  
375 of two large datasets of human intracranial recordings. In doing so, we are one step closer to  
376 observing, and perhaps someday understanding, the full spatiotemporal structure of human  
377 neural activity.

378 **Code availability**

379 We have published an open-source toolbox implementing the SuperEEG algorithm. It may  
380 be downloaded [here](#). Additionally, we have provided notebooks for all analyses and figures  
381 reported here.

382 **Data availability**

383 The dataset analyzed in this study was generously shared by Michael Kahana. A portion of  
384 Dataset 1 may be downloaded [here](#). Dataset 2 may be downloaded [here](#).

385 **Acknowledgements**

386 We are grateful for useful discussions with Luke J. Chang, Uri Hasson, Josh Jacobs, Michael  
387 Kahana, and Matthijs van der Meer. We are also grateful to Michael Kahana for generously  
388 sharing the ECoG data we analyzed in our paper, which was collected under NIMH grant  
389 MH55687 and DARPA RAM Cooperative Agreement N66001-14-2-4-032, both to MJK. Our  
390 work was also supported in part by NSF EPSCoR Award Number 1632738 and by a sub-

391 award of DARPA RAM Cooperative Agreement N66001-14-2-4-032 to JRM. The content is solely  
392 the responsibility of the authors and does not necessarily represent the official views of our  
393 supporting organizations.

## 394 **Author Contributions**

395 J.R.M conceived and initiated the project. L.L.W.O. and A.C.H. performed the analyses. J.R.M.  
396 and L.L.W.O. wrote the manuscript.

## 397 **Author Information**

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399 declare no competing financial interests. Readers are welcome to comment on the online  
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401 tional claims in published maps and institutional affiliations. Correspondence and requests for  
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