

Towards human SuperEEG

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Abstract

Human *SuperEEG*¹ entails measuring ongoing neural activity with perfect precision and at arbitrarily high spatiotemporal resolution. Although true SuperEEG is impossible using existing methods, here we present a model-based method for *inferring* 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 spatial correlations, and that (all else being equal) neural activity at nearby locations will tend to be similar. 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 in that individual's brain?

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

Introduction

Modern human brain recording techniques are fraught with compromise [?]. Commonly used approaches include functional magnetic resonance imaging (fMRI), scalp electroencephalography (EEG), and magnetoencephalography (MEG). For each of these techniques, neuroscientists and electrophysiologists must choose to optimize spatial resolution at the cost of temporal resolution (e.g., as in fMRI) or temporal resolution at the cost of spatial resolution (e.g., as in EEG and MEG). A less widely used approach (due to requiring work with neurosurgical patients) is to record from electrodes implanted directly onto the cortical surface (electrocorticography; ECoG)

¹The term "SuperEEG" was coined by Robert J. Sawyer in his popular science fiction novel *The Terminal Experiment* [?]

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

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

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

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

56 The current “gold standard” for precisely localizing signals and sampling at high temporal
57 resolution is to take (ECoG or iEEG) recordings from implanted electrodes (but from a limited
58 set of locations in any given brain). This begs the following question: what can we infer about the
59 activity exhibited by the rest of a person’s brain, given what we learn from the limited intracranial
60 recordings we have from their brain and additional recordings taken from *other* people’s brains?

61 Here we develop an approach, which we call *SuperEEG*, based on Gaussian process regression [?
62]. SuperEEG entails using data from multiple people to estimate activity patterns at arbitrary
63 locations in each person’s brain (i.e., independent of their electrode placements). We test
64 SuperEEG approach using two large datasets of intracranial recordings [? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?].
65 We show that the SuperEEG algorithm recovers signals well from electrodes that were held
66 out of the training dataset. We also examine the factors that influence how accurately activity
67 may be estimated (recovered), which may have important implications for electrode design and
68 placement in neurosurgical applications.

69 Approach

70 The SuperEEG approach to inferring high temporal resolution full-brain activity patterns is
71 outlined and summarized in Figure 1. We describe (in this section) and evaluate (in *Results*) our
72 approach using a two large previously collected dataset comprising multi-session intracranial
73 recordings. Dataset 1 comprises multi-session recordings taken from 6876 electrodes implanted

74 in the brains of 88 epilepsy patients [? ? ? ? ?]. Each recording session lasted from 0.3–14.2
75 hours (Fig. S4A), and includes data recorded roughly from when the patients woke up each
76 morning, to before they went to sleep at the end of each day. In addition to typical bed-ridden
77 hospital patient activities (e.g., lying in bed, reading, watching television, using personal elec-
78 tronic devices, listening to music, visiting with family and friends, etc.), the patients also per-
79 formed a variety of experimental cognitive tasks throughout their day (primarily list-learning
80 memory tasks). For the purposes of the Dataset 1 analyses presented here, we aggregated
81 all data across each recording session, ignoring the particular activities or tasks the patients
82 were performing at any given moment. We used Dataset 1 to develop our main SuperEEG
83 approach, and to examine the extent to which SuperEEG might be able to generate task-general
84 predictions. Dataset 2 comprised multi-session recordings from 3159 electrodes implanted in
85 the brains of 24 epilepsy patients [? ? ? ? ? ? ? ? ?]. Each recording session lasted from
86 .4–6.6 hours (Fig. S4B). Whereas Dataset 1 included recordings taken during a wide variety of
87 behaviors, Dataset 2 included recordings taken as each patient performed each of two memory
88 tasks: a random word list free recall task and a categorized word list free recall task. We used
89 Dataset 2 to further examine the ability of SuperEEG to generalize its predictions within versus
90 across tasks. Figure S4 provides additional details on both datasets.

91 We first applied fourth order Butterworth notch filter to remove 60 Hz ($\pm .5$ Hz) line noise
92 from every recording (from every electrode). Next, we downsampled the recordings (regardless
93 of the original samplerate) to 250 Hz. (This downsampling step served to both normalize for
94 differences in sampling rates across patients and to ease the computational burden of our
95 subsequent analyses.) We then excluded any electrodes that showed putative epileptiform
96 activity. Specifically, we excluded from further analysis any electrode that exhibited an average
97 kurtosis of 10 or greater across all of that patient’s recording sessions. We also excluded any
98 patients with fewer than 2 electrodes that passed this criteria, as the SuperEEG algorithm

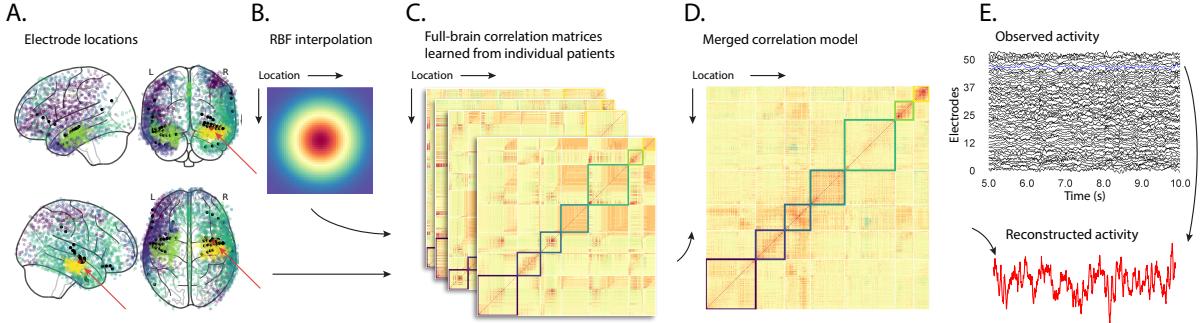


Figure 1: Methods overview. **A. Electrode locations.** Each dot reflects the location of a single electrode implanted in the brain of a Dataset 1 patient. A held-out recording location from one patient is indicated in red, and the patient’s remaining electrodes are indicated in black. The electrodes 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 $k=7$; ?], 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 requires measuring correlations between 2 or more electrodes from each patient. For Dataset
100 1, this yielded clean recordings from 4168 electrodes implanted throughout the brains of 67
101 patients (Fig. 1A); for Dataset 2, this yielded clean recordings from 3159 electrodes from 24
102 patients. Each individual patient contributes electrodes from a limited set of brain locations,
103 which we localized in a common space [MNI152; ?]; an example Dataset 1 patient's 54 electrodes
104 that passed the predefined kurtosis 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 η) depends on the size of the recording surface, the electrode's impedance, and the conductance profile of the volume of brain between x and η . As an approximation of this intuition, we place a Gaussian radial basis function (RBF) at the location η 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 η :

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

105 where the width variable λ is a parameter of the algorithm (which may in principle be set
106 according to location-specific tissue conductance profiles) that governs the level of spatial
107 smoothing. In choosing λ for the analyses presented here, we sought to maximize spatial
108 resolution (which implies a small value of λ) while also maximizing the algorithm's ability
109 to generalize to any location throughout the brain, including those without dense electrode
110 coverage (which implies a large value of λ). Here we set $\lambda = 20$, guided in part by our prior
111 work [? ?], and in part by examining the brain coverage with non-zero weights achieved by

112 placing RBFs at each electrode location in Dataset 1 and taking the sum (across all electrodes)
 113 at each voxel in a 4 mm³ MNI brain. (We then held λ fixed for our analyses of Dataset 2.) We
 114 note that this value could in theory be further optimized, e.g., using cross validation or a formal
 115 model [e.g., ?].

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

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

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

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

125 Next, we use Equation 1 to construct a number of to-be-estimated locations by number of
 126 patient electrode locations weight matrix, W_s . Specifically, W_s approximates how informative
 127 the recordings at each location in R_s are in reconstructing activity at each location in \bar{R} , where
 128 the contributions fall off with an RBF according to the distances between the corresponding
 129 locations:

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

¹³⁰ Given this weight matrix, W_s , and the observed inter-electrode correlation matrix for patient
¹³¹ 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):

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

¹³² Intuitively, the numerators capture the general structures of the patient-specific estimates of full-
¹³³ brain correlations, and the denominators account for which locations were near the implanted
¹³⁴ electrodes in each patient. To obtain \hat{K} , we compute a weighted average across the estimated
¹³⁵ patient-specific full-brain correlation matrices, where patients with observed electrodes near a
¹³⁶ particular set of locations in \hat{K} contribute more to the estimate.

¹³⁷ Having used the multi-patient data to estimate a full-brain correlation matrix at the set
¹³⁸ of locations in \bar{R} that we wish to know about, we next use \hat{K} to estimate activity patterns
¹³⁹ everywhere in \bar{R} , given observations at only a subset of locations in \bar{R} (Fig. 1E).

¹⁴⁰ Let α_s be the set of indices of patient s 's electrode locations in \bar{R} (i.e., the locations in R_s),
¹⁴¹ and let β_s be the set of indices of all other locations in \bar{R} . In other words, β_s reflects the locations
¹⁴² in \bar{R} where we did not observe a recording for patient s (these are the recording locations we
¹⁴³ will want to fill in using SuperEEG). We can sub-divide \hat{K} as follows:

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

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

144 Here $\hat{K}_{\beta_s, \alpha_s}$ represents the correlations between the “unknown” activity at the locations in β_s
 145 and the observed activity at the locations in α_s , and $\hat{K}_{\alpha_s, \alpha_s}$ represents the correlations between
 146 the observed recordings (at the locations in α_s).

147 Let Y_{s,k,α_s} be the number-of-timepoints (T) by $|\alpha_s|$ matrix of (observed) voltages from the
 148 electrodes in α_s during session k from patient s . Then we can estimate the voltage from patient
 149 s ’s k^{th} session at the locations in β_s using [?]:

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

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

156 We designed our approach to be agnostic to electrode impedances, as electrodes that do not
 157 exist do not have impedances. Therefore our algorithm recovers voltages in standard deviation
 158 (z -scored) units rather than attempting to recover absolute voltages. (This property reflects
 159 the fact that $\hat{K}_{\beta_s, \alpha_s}$ and $\hat{K}_{\alpha_s, \alpha_s}$ are correlation matrices rather than covariance matrices.) Also,
 160 note that Equation 12 requires computing a T by T matrix, which can become computationally
 161 intractable when T is very large (e.g., for the patient highlighted in Fig. 2, $T = 20458799$).

162 However, because Equation 12 is time invariant, we may compute Y_{s,k,β_s} in a piecewise manner
163 by filling in Y_{s,k,β_s} one row at a time (using the corresponding samples from Y_{s,k,α_s}).

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

168 Results

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

180 To illustrate our approach, we first examine an individual held-out raw LFP trace and its
181 associated SuperEEG-derived reconstruction. Figure 2A displays the observed LFP from the red
182 electrode in Figure 1A (red), and its associated reconstruction (blue), during a 5 s time window
183 during one of the example patient's six recording sessions. The two traces match closely
184 ($r = 0.869, p < 10^{-10}$). Figure 2B displays a two-dimensional histogram of the actual versus
185 reconstructed voltages for the entire 14.2 total hours of recordings from the example electrode

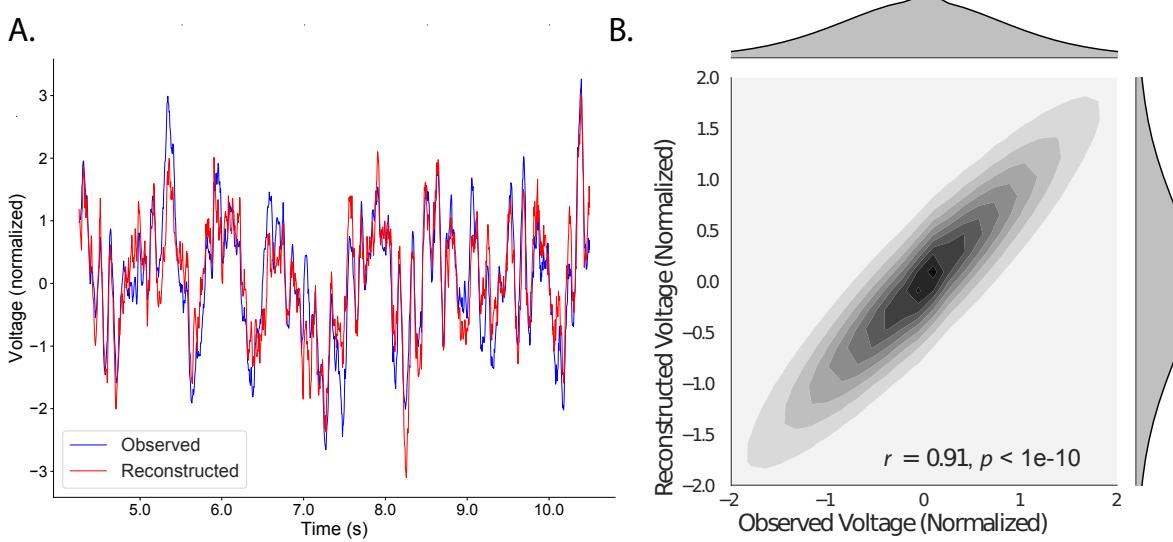


Figure 2: Observed and reconstructed LFP from a single electrode. **A. Example LFP.** A 5 s recording from the red electrode in Figure 1A is displayed in red, and the reconstructed LFP during the same time window is shown in blue. **B. Observed versus reconstructed LFP over 14.2 hours.** The two-dimensional 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).

(correlation: $r = 0.909, p < 10^{-10}$). This example confirms that the SuperEEG algorithm recovers the recordings from this single electrode well. Next, we used this general approach to quantify the algorithm's performance across the full dataset.

For each held-out electrode, from each held-out patient in turn, we computed the average correlation (across recording sessions) between the SuperEEG-reconstructed voltage traces and the observed voltage traces from that electrode. For this analysis we set \bar{R} to be the union of all electrode locations across all patients. This yielded a single correlation coefficient for each electrode location in \bar{R} , reflecting how well the SuperEEG algorithm was able to recover the recording at that location by incorporating data across patients (black histogram in Fig. 3A, map in Fig. 3C). The observed distribution of correlations was centered well above zero (mean: 0.52;

196 t -test comparing mean of distribution of z -transformed per-electrode correlation coefficients to
197 0: $t(66) = 25.08, p < 10^{-30}$), indicating that the SuperEEG algorithm recovers held-out activity
198 patterns substantially better than random guessing.

199 As a stricter benchmark, we compared the quality of these across-participant reconstructions
200 (i.e., computed using a correlation model learned from other patients' data) to reconstructions
201 generated using a correlation model trained using the in-patient's data. In other words, for
202 this within-patient benchmark analysis we estimated \hat{C}_s (Eqn. 8) for each patient in turn, using
203 recordings from all of that patient's electrodes except at the location we were reconstructing.
204 These within-patient reconstructions serve as an estimate of how well data from all of the other
205 electrodes from that single patient may be used to estimate held-out data from the same patient.
206 This allows us to ask how much information about the activity at a given electrode might be
207 inferred through (a) volume conductance or other sources of "leakage" from activity patterns
208 measured from the patient's other electrodes and (b) across-electrode correlations learned from
209 that single patient. As shown in Figure 3A (gray histogram), the distribution of within-patient
210 correlations was centered well above zero (mean: 0.32; t -test comparing mean of distribution of
211 z -transformed per-electrode correlation coefficients to 0: $t(66) = 15.16, p < 10^{-20}$). However, the
212 across-patient correlations were substantially higher (t -test comparing average z -transformed
213 within versus across patient electrode correlations: $t(66) = 9.62, p < 10^{-10}$). This is an especially
214 conservative test, given that the across-patient SuperEEG reconstructions exclude (from the
215 correlation matrix estimates) all data from the patient whose data is being reconstructed. We
216 repeated each of these analyses on a second independent dataset and found similar results
217 (Fig. 3B, D; within versus across reconstruction accuracy: $t(23) = 6.93, p < 10^{-5}$). We also
218 replicated this result separately for each of the two experiments from Dataset 2 (Fig. S1). This
219 overall finding, that reconstructions of held-out data using correlation models learned from
220 *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 data from all other patients out-performed within-patient models trained on data only from the subject contributing the given electrode ($ts(24) > 6.50, ps < 10^{-5}$). All reconstruction accuracies also reliably exceeded chance performance ($ts(24) > 8.00, ps < 10^{-8}$). Average reconstruction

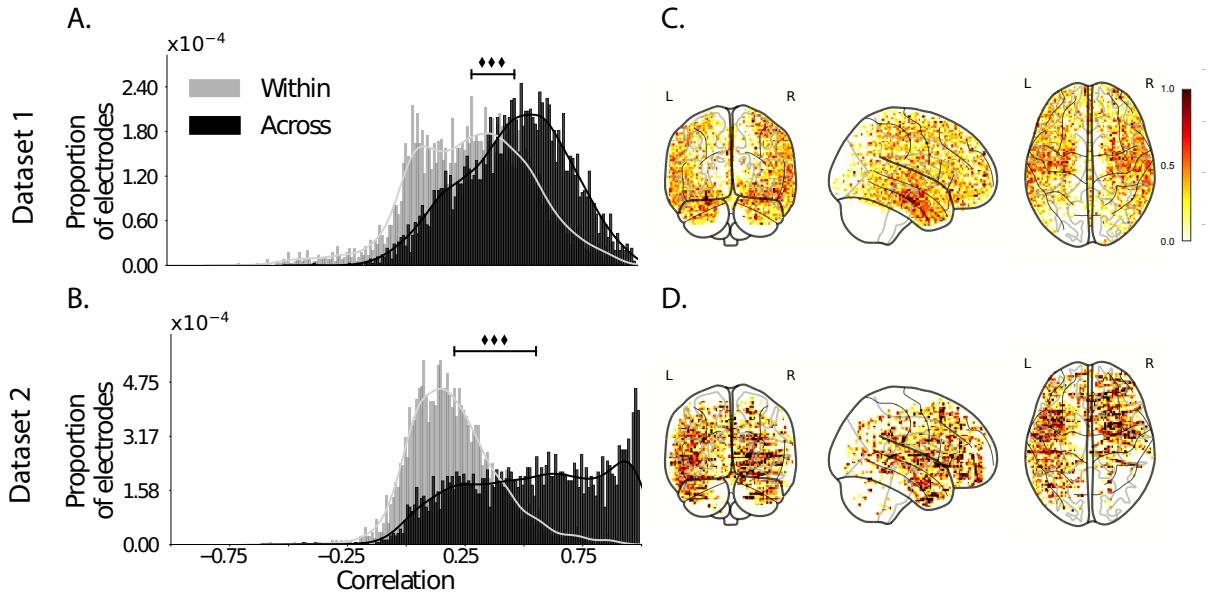


Figure 3: Reconstruction quality across all electrodes in two ECoG datasets. A. Distributions of correlations between observed versus reconstructed activity by electrode, for Dataset 1. The across-patient distribution (black) reflects reconstruction accuracy (correlation) using a correlation model learned 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.

accuracy was highest for the across-patient models limited to data from the same experiment (mean accuracy: 0.68); next-highest for the across-patient models that combined data across both experiments (mean accuracy: 0.61); and lowest for models trained across task (mean accuracy: 0.47). This result also held for each of the Dataset 2 experiments individually (Fig. S3). Taken together, these results indicate that there are reliable commonalities in the spatial correlations of full-brain activity across tasks, but that there are also reliable differences in these spatial correlations across tasks. Whereas reconstruction accuracy benefits from incorporating data from other patients, reconstruction accuracy is highest when constrained to within-task data, or data that includes a variety of tasks (e.g., Dataset 1, or combining across the two Dataset 2 experiments).

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

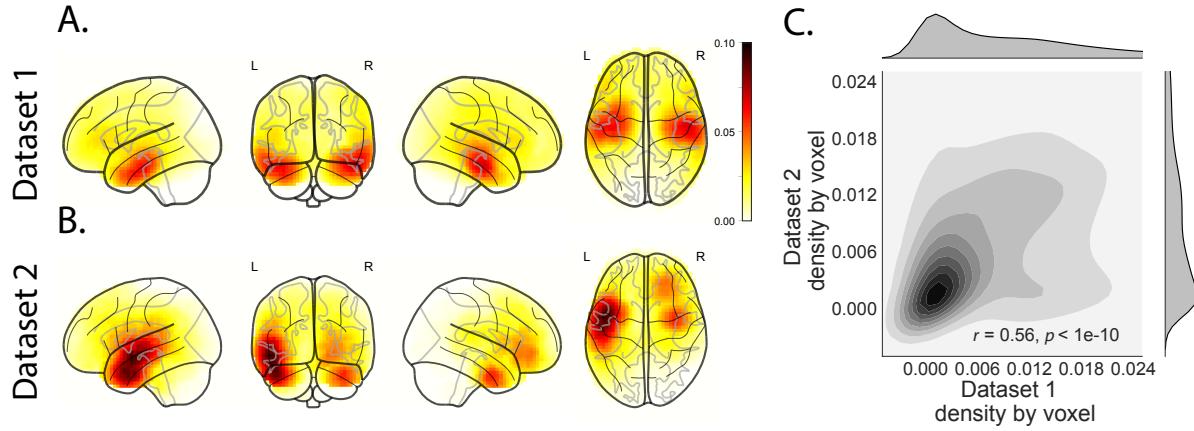


Figure 4: Electrode sampling density by location. **A. Electrode sampling density by voxel in Dataset 1.** Each voxel is colored by the proportion of total electrodes in the dataset that are located within a 20 MNI unit radius sphere centered on the given voxel. **B. Electrode sampling density by voxel 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 mm^3 MNI brain.

271 electrode. Contrary to our expectation, rather than positive correlations, we found weak (but
 272 reliable) negative correlations between reconstruction accuracy and density for both datasets
 273 (Dataset 1: $r = -0.07, p < 10^{-5}$; Dataset 2: $r = -0.18, p < 10^{-10}$). This indicates that the
 274 reconstruction accuracies we observed are not driven solely by sampling density, but rather
 275 may also reflect higher order properties of neural dynamics such as functional correlations
 276 between distant voxels [?].

277 In neurosurgical applications where one wishes to infer full-brain activity patterns, can our
 278 framework yield insights into where the electrodes should be placed? A basic assumption of our
 279 approach (and of most prior ECoG work) is that electrode recordings are most informative about
 280 the neural activity near the recording surface of the electrode. But if we consider that activity
 281 patterns throughout the brain are meaningfully correlated, are there particular implantation
 282 locations that, if present in a patient's brain, yield especially high reconstruction accuracies

throughout the rest of the brain? For example, one might hypothesize that brain structures that are heavily interconnected with many other structures could be more informative about full-brain activity patterns than comparatively isolated structures.

To gain insights into whether particular electrode locations might be especially informative, we first computed the average reconstruction accuracy across all of each patient's electrodes (using the across-patients cross validation test; black histograms in Fig. 3A and B). We labeled each patient's electrodes in each dataset with the average reconstruction accuracy for that patient. In other words, we assigned every electrode from each given patient the same value, reflecting how well the activity patterns at those electrodes were reconstructed on average. Next, for each voxel in the 4 mm³ MNI brain, we computed the average value across any electrode (from any patient) that came within 20 MNI units of that voxel's center. Effectively, we computed an *information score* for each voxel, reflecting the average reconstruction accuracy across any patients with electrodes near each voxel—where the averages were weighted to reflect patients who had more electrodes implanted near that location. This yielded a single map for each dataset, highlighting regions that are potentially promising implantation targets in terms of providing full-brain activity information via SuperEEG (Fig. 5A, B). Despite task and patient differences across the two datasets, we nonetheless found that the maps of the most promising implantation targets derived from both datasets were similar (voxelwise correlation between information scores across the two datasets: $r = 0.23, p < 10^{-10}$). While the correspondence between the two maps was not perfect, our finding that there were some commonalities between the two maps lends support to the notion that different brain areas are differently informative about full-brain activity patterns. Further, regions like the right post central gyrus, right supramarginal gyrus, and the right nucleus accumbens that exhibited strong information scores in both datasets may be especially promising implantation targets.

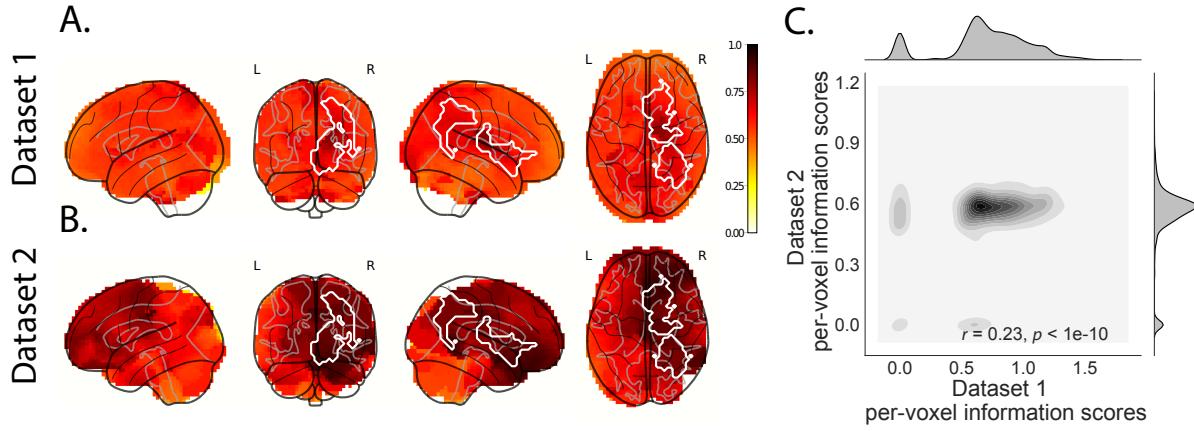


Figure 5: Most informative electrode locations. **A. Dataset 1 information score by voxel.** The voxel colors reflect the weighted average reconstruction accuracy across all electrodes from any patients with at least one electrode within 20 MNI units of the given voxel. **B. Dataset 2 information score by voxel.** This panel is in the same format as Panel A. In Panels A and B 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.

307 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., ?], person-specific [e.g., ?], and task-specific [e.g., ?]. 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., ?]. Further, many aspects of brain anatomy, including white matter structure, is largely preserved across people [e.g., ? ? ?]. There are several possible means of reconciling this apparent inconsistency between dynamic person- and task-specific functional networks versus stable anatomical networks. For example, relatively small magnitude anatomical differences across people may be reflected in reliable functional connectivity differences. Along these lines, one recent study

319 found that diffusion tensor imaging (DTI) structural data is similar across people, but may
320 be used to predict person-specific resting state functional connectivity data [?]. Similarly,
321 other work indicates that task-specific functional connectivity may be predicted by resting state
322 functional connectivity data [? ?]. Another (potentially complementary) possibility is that our
323 functional networks are constrained by anatomy, but nevertheless exhibit (potentially rapid)
324 task-dependent changes [e.g., ?].

325 Here we have taken a model-based approach to studying whether high spatiotemporal
326 resolution activity patterns throughout the human brain may be explained by a static connec-
327 tive model that is shared across people and tasks. Specifically, we trained a model to take
328 in recordings from a subset of brain locations, and then predicted activity patterns during the
329 same interval, but at *other* locations that were held out from the model. Our model, based on
330 Gaussian process regression, was built on three general hypotheses about the nature of the
331 correlational structure of neural activity (each of which we tested). First, we hypothesized that
332 functional correlations are stable over time and across tasks. We found that, although aspects
333 of the patients' functional correlations that were stable across tasks, we achieved better recon-
334 struction accuracy when we trained the model on within-task data [we acknowledge that our
335 general approach could potentially be extended to better model across-task changes, following
336 ? ? , and others]. Second, we hypothesized that some of the correlational structure of peo-
337 ple's brain activity is similar across individuals. Consistent with this hypothesis, our model
338 explained the data best when we trained the correlation model using data from *other* patients—
339 even when compared to a correlation model trained on the same patient's data. Third, we
340 resolved ambiguities in the data by hypothesizing that neural activity from nearby sources will
341 tend to be similar, all else being equal. This hypothesis was supported through our finding that
342 all of the models we trained that incorporated this spatial smoothness assumption predicted
343 held-out data well above chance.

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

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

363 **Concluding remarks**

364 Over the past several decades, neuroscientists have begun to leverage the strikingly profound
365 mathematical structure underlying the brain's complexity to infer how our brains carry out
366 computations to support our thoughts, actions, and physiological processes. Whereas tradi-
367 tional beamforming techniques rely on geometric source-localization of signals measured at the

368 scalp, here we propose an alternative approach that leverages the rich correlational structure
369 of two large datasets of human intracranial recordings. In doing so, we are one step closer to
370 observing, and perhaps someday understanding, the full spatiotemporal structure of human
371 neural activity.

372 **Code availability**

373 We have published an open-source toolbox implementing the SuperEEG algorithm. It may be
374 downloaded [here](#).

375 **Data availability**

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

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³⁸⁷ **Author Contributions**

³⁸⁸ J.R.M conceived and initiated the project. L.L.W.O. and A.C.H. performed the analyses. J.R.M.
³⁸⁹ and L.L.W.O. wrote the manuscript.

³⁹⁰ **Author Information**

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