Published in final edited form as:

J Neurosci Methods. 2011 October 30; 202(1): 87–98. doi:10.1016/j.jneumeth.2011.08.032.

Evaluation of Techniques Used to Estimate Cortical Feature Maps

Nalin Katta¹, Thomas L. Chen², Paul V. Watkins³, and Dennis L. Barbour¹

¹Laboratory of Sensory Neuroscience and Neuroengineering, Campus Box 1097, One Brookings Drive, Washington University in St. Louis, St. Louis, Missouri 63130, U.S.A.

²Tulane University School of Medicine, 1430 Tulane Ave. New Orleans, LA 70112

³University of Maryland, College Park, MD 20742

Abstract

Functional properties of neurons are often distributed nonrandomly within a cortical area and form topographic maps that reveal insights into neuronal organization and interconnection. Some functional maps, such as in visual cortex, are fairly straightforward to discern with a variety of techniques, while other maps, such as in auditory cortex, have resisted easy characterization. In order to determine appropriate protocols for establishing accurate functional maps in auditory cortex, artificial topographic maps were probed under various conditions, and the accuracy of estimates formed from the actual maps was quantified. Under these conditions, low-complexity maps such as sound frequency can be estimated accurately with as few as 25 total samples (e.g., electrode penetrations or imaging pixels) if neural responses are averaged together. More samples are required to achieve the highest estimation accuracy for higher complexity maps, and averaging improves map estimate accuracy even more than increasing sampling density. Undersampling without averaging can result in misleading map estimates, while undersampling with averaging can lead to the false conclusion of no map when one actually exists. Uniform sample spacing only slightly improves map estimation over nonuniform sample spacing typical of serial electrode penetrations. Tessellation plots commonly used to visualize maps estimated using nonuniform sampling are always inferior to linearly interpolated estimates, although differences are slight at higher sampling densities. Within primary auditory cortex, then, multiunit sampling with at least 100 samples would likely result in reasonable feature map estimates for all but the highest complexity maps and the highest variability that might be expected.

Keywords

Functional map; cortical topography; topographical map; auditory cortex; frequency map; tonotopy

© 2011 Elsevier B.V. All rights reserved.

Please send correspondence to: Dr. Dennis Barbour, Campus Box 1097, One Brookings Drive, Washington University in St. Louis St. Louis, Missouri 63130, U.S.A. Tel. 314-935-7548, Fax. 314-935-7448, dbarbour@biomed.wustl.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

Mapping physiological features in individual brain areas represents a powerful tool for understanding how brain function is organized and for elucidating the neural circuitry underlying information processing. Nonrandom distribution of neuronal features within a cortical area is common, and the nature of the maps that typically form as a result (relatively smooth or “topographic” maps) is used by neuroscientists to infer functional neuronal organizations. Within cat primary auditory cortex (A1), for example, numerous features appear to be topographically mapped at various levels of organization. Some of these features include characteristic sound frequency or CF (Merzenich et al., 1973, 1975; Schreiner and Mendelson, 1990), bandwidth (Cheung et al., 2001; Philibert et al., 2005; Read et al., 2001; Recanzone et al., 1999; Schreiner and Mendelson, 1990), threshold (Cheung et al., 2001; Esser and Eiermann, 1999; Philibert et al., 2005; Schreiner et al., 1992), latency (Cheung et al., 2001; Mendelson et al., 1997; Philibert et al., 2005), modulation frequency (Langner et al., 1997; Schulze and Langner, 1997a, b), binaural dominance (Imig and Adrian, 1977; Kelly and Judge, 1994; Reale and Kettner, 1986; Rutkowski et al., 2000), sound source location (Clarey et al., 1994; Middlebrooks et al., 1998), rate-level monotonicity (Clarey et al., 1994; Schreiner et al., 1992), FM sweep rate and direction (Godey et al., 2005; Mendelson et al., 1993; Shamma et al., 1993; Zhang et al., 2003), dynamic range (Schreiner et al., 1992) and maximum response level (Schreiner et al., 1992). The appearance of these maps varies greatly: maps like CF, for example, are organized at a relatively low spatial frequency, while other features such as binaural dominance appear to be mapped at a higher spatial frequency. We refer to maps containing relatively low spatial frequencies as “low-complexity” and maps containing relatively high spatial frequencies as “high-complexity.”

Multiple techniques have been developed to extract feature map structure in cortical areas. These techniques can be categorized generally into two distinct groups: single unit and multiunit recording techniques. The single unit recording techniques, such as single-cell electrode recordings and optical imaging with multiphoton microscopy and Oregon-Green BAPTA (Bandyopadhyay et al., ; Ohki et al., 2005; Rothschild et al., 2010), map only one neuron at each location. Multiunit techniques record simultaneously from a group of neurons, so each location (or map pixel) can be viewed as the average response of a group of neurons. Techniques that record multiunits or derivative physiological markers include multiunit electrode recording, local field potential recording, intrinsic optical imaging and functional magnetic resonance imaging.

Physiological and anatomical properties of the brain can hinder the ability of these imaging techniques to map features at a high enough spatial resolution in order to resolve the maps. Variability within cortical columns and across cortical space has been observed in auditory cortex that may interfere with the accuracy of the mapping in addition to estimation errors themselves (Atencio and Schreiner, 2010; Phillips and Irvine, 1981). Threshold maps in A1, for example, have been observed to change between individual animals and between species (Schreiner et al., 1992). The geometry of the brain may prevent recordings of the entire cortical area as areas may fold into gyri and sulci, making it difficult to sample an entire area uniformly. Our previous modeling study has demonstrated that the shape of a cortical area can have a substantial effect on cortical feature maps and that the map structure at the area border may influence the rest of the map (Watkins et al., 2009). Furthermore, invasive techniques such as electrode recordings may need to avoid certain areas to prevent damaging blood vessels. Despite these particular issues, a fundamental limiting factor in mapping cortical areas is likely to be limitations on the spatial resolution of the sampling itself (Chen et al., 2010).

This study examines the sampling resolution necessary for estimating feature maps for the two general types of mapping techniques: single unit and multiunit measurements. We used previously devised computational techniques to create plausible feature maps of a cortical area such as A1 (Watkins et al., 2009). We then conducted studies upon these maps to determine the effects of sampling resolution, measurement averaging, nonuniform sampling and map variability upon the quality of map estimates. The result is a series of guidelines for how best to estimate cortical feature maps using a variety of techniques under a range of assumptions, as well as the degree of inaccuracy that might be expected with a given sampling protocol. While these guidelines are general, they may be particularly relevant for auditory cortical areas, where topographic map estimation faces unique challenges (Chen et al., 2010).

Materials and Methods

Self-Organizing Feature Maps

The self-organizing feature map (SOFM) is a dimensionality-reduction algorithm that projects n feature dimensions, such as physiological features, onto the two anatomical dimensions of the cortical surface. The SOFM model assumes that neurons with similar characteristics are more likely to be connected with one another than with neurons having less similar characteristics. Under the principle of wiring-length minimization, connected neurons should be physically located closer together than unconnected neurons. Using these assumptions, the SOFM implements a competitive Hebbian learning algorithm that has been employed experimentally to generate spatial arrangements of neuronal properties well-matched to topographies observed in functional imaging studies of primary visual cortex (V1) (Farley et al., 2007; Obermayer and Blasdel, 1993; Obermayer et al., 1992; Yu et al., 2005). The principles of SOFMs have also been applied to maps relevant to primary auditory cortex or A1 (Chen et al., 2010; Watkins et al., 2009). One finding from these studies was that higher weightings of a feature lead to greater preservation of mapping uniformity and compactness of that feature. In this study, SOFM models were used to create plausible neuronal maps in order to test how accurately different maps could be estimated using different neurophysiological recording methodologies. To model cortical feature maps, SOFMs were used to define the position and the properties of each unit in each map. All SOFMs in this study were confined to square grids with 150×150 units. A particular 4-feature SOFM with a relative feature weighting of 10:4:2:1, which can be seen in Figure 1, was selected for analyzing the estimation of cortical maps. These weightings were chosen empirically to create a variety of feature topographies in the maps and to provide a reasonable representation of the types of maps that might be expected in A1. The first feature map exhibits relatively low spatial frequencies while maps of the second, third, and fourth features exhibit progressively higher spatial frequencies. In other words, the complexity of the maps increases with increasing feature number.

Auditory neurons are organized within cortical columns, but the properties of neurons estimated within a given column can vary somewhat either from the underlying physiology or the estimate or both (Atencio and Schreiner, 2010; Phillips and Irvine, 1981), just as is the case with primary visual cortex (Hubel and Wiesel, 1974). In the present study, all sources of variability within cortical columns affecting the estimation accuracy at a particular sampled location were modeled by stacking multiple similar but slightly varied SOFMs. Mapping variability was generated by using the SOFM to represent the arithmetic means of spatial probability distributions instead of deterministic values. The particular feature value of any given unit (or map pixel) for any given map was drawn from this distribution. To quantify cortical and estimation variability, each feature map was assigned a two-dimensional Gaussian distribution with standard deviations defined as a percentage of the total range of values for that given feature. Each layer of the model stack contained values

that were varied independently from the mean, but the locations of each unit and the underlying SOFM were the same between stack layers. Figure 2 shows the effect of introducing two levels of variability in a map of feature 1. Larger variability in the SOFM simulates cortical maps with larger variability in their columnar structure. A variability of 0, on the other hand, represents deterministic mapping with no variability in columnar map structure, as seen in the maps of Figure 1.

Topographic Map Estimation

To determine experimental and analytical practices useful for elucidating map structure, SOFM were originally created at a resolution of 150×150 for a total of 22,500 total samples, and then probed with lower sampling densities. These probed samples were used to reconstruct the original SOFM with either an averaged or an unaveraged procedure. The resolution of sampling for map estimation is indicated either by referring to sampling densities of $n \times n$ or a total number of samples of n^2 , where n is a small integer. Samples taken using the averaged procedure were obtained by calculating the arithmetic mean of all the unit feature values within a sampled pixel. For the purpose of this study, sample pixels were composed of all the original pixels in the original map that were closer to the sampled point than to any other sampled point. The averaged sampling procedure was intended to simulate a multiunit, local field potential, electrocorticographic, or functional imaging experiment where the average activity of a local group of neurons (or a derivative physiological marker) is recorded in each measurement. Samples taken using the unaveraged procedure were obtained from the individual SOFM values that corresponded to the location of each sample. This condition was intended to simulate a single-unit sampling experiment.

Sampling locations in unaveraged experiments were spaced either uniformly across the array in a lattice or randomly sampled without replacement. The nonuniform sampling procedure reflects the worst-case scenario for penetrating microelectrode experiments where sampling locations usually cannot be placed precisely on a grid due to obstructions. These obstructions can include blood vessels that must be avoided or areas that are unreachable due to the geometry of the brain. For the averaged estimations, sampling locations were always uniformly spaced across the array, reflecting imaging experiments with a uniform grid of imaging elements. An example of the different sampling methodologies can be seen in Figure S01.

The number of samples taken for any experiment in this study was always the square of an integer between 2 and 25. Uniform sampling locations were selected so that centers of the unaveraged experiments matched centers of sample pixels from the averaged experiments. By using only squares of integers, the number of samples from a uniformly sampled array that form square lattices match the number of samples from nonuniformly sampled maps. Thus, an experiment used to estimate the underlying map by sampling on a 5×5 square lattice can be compared to a nonuniformly sampled experiment that estimates the map with 25 samples.

The topographic map sampling techniques described so far assume that the nature of the underlying map can be estimated perfectly at each sampled point and all estimation error lies in the interpolation process. Multiple factors could contribute to actual sampled values also containing some estimation error, including measurement error of the underlying physiological variable as well as some intrinsic variability in the neuron-by-neuron manifestation of the underlying map.

To simulate the contribution of all sources of variability to the feature value estimates at the sampled locations (including variability in the cortical column structure and in the estimates

themselves), ten independent instantiations of SOFM maps with variability were superimposed upon each other before averaging. This procedure was only necessary for experiments in which averaging took place, because a single-variable SOFM would be sufficient for a trial making use only of direct measurement, such as a single-unit study. In the averaging experiments, if a sample pixel corresponded to a 2×2 square of original map pixels, for example, that sample pixel would be assigned the arithmetic mean of 40 different units, 4 from each of the ten model instantiations. Once a sparse map was assembled, it was resampled back to 150×150 pixels using zeroth-order (nearest-neighbor) or first-order (linear) interpolation. For zeroth-order interpolation a popular method called Voronoi tessellation was used to recreate the maps (Cheung et al., 2001; Godey et al., 2005; Kilgard and Merzenich, 1998; Read et al., 2001). Voronoi tessellations are created by assigning the value of the sampled point to a surrounding polygon defining the local region for that sample point. For the estimated maps that were resampled with linear interpolation, units outside the border created by the extracted points were not extrapolated or used for later analysis, thereby creating a fairer comparison between the two methods of estimation.

Estimated maps were created with a variety of sampling densities and cortical variability percentages. Twenty-four different sampling densities were selected, ranging from 4 to 625 samples, and seven different variability percentages were used, ranging from 0% to 30% variability. For each combination of sampling density and variability percentage, the estimations were repeated 100 times.

Analysis

The accuracy of each estimated map was quantified relative to the model maps using a coefficient of determination (R^2). This metric measures how well the estimated maps fit the underlying SOFM maps relative to the overall mean value of the SOFM map. R^2 is derived from a ratio between the sum-of-square error and the total sum of squares:

$$R^2 = 1 - \frac{\sum_i (y_i - f_i)^2}{\sum_i (y_i - \bar{y})^2},$$

where y represents the SOFM feature values prior to adding cortical variability, $\bar{y}$ represents the mean of all the SOFM feature values, f represents the interpolated feature values, and i indexes the set of interpolated values and their associated non-randomized values. R^2 values of 1 represent perfect fits with no error while R^2 values of 0 represent fits that have summed squared error equivalent to fitting with the mean feature value of the map. Positive R^2 values are typically reported in the literature because better models will have R^2 approaching 1. Mathematically, however, if the model generates more error than simply using the mean value of the data, the R^2 will be negative. One intuitive situation in which this occurs is when a signal is undersampled. Figure 3 demonstrates how an undersampled 10 Hz sine wave results in negative R^2 values. As the sampling rate decreases, the R^2 values diminish, and once the sampling rate drops below the Nyquist rate (20 samples/s), the R^2 values become erratic and ultimately negative. The lower bound of the R^2 values for the averaged map estimates is at or near zero because the estimated maps with low sampling densities have predictive power similar to the mean value of the SOFM due to the averaging. The unaveraged estimates, however, may have negative R^2 values because estimates at low sampling densities can be arbitrarily worse than the map average.

An alternative analysis intended to determine minimum sampling densities for accurately reconstructing maps involved assessing the spatial frequency distribution of the maps and

estimating the corresponding Nyquist frequency. In two dimensions this analysis turned out not to be straightforward, in that the estimated Nyquist frequencies were extremely sensitive to the magnitude threshold criteria selected, and off-axis map features did not contribute to this estimate in obvious ways. For this reason the model approach described previously was adopted, and the utility of this methodology relative to a simple Nyquist estimation is illustrated for the one-dimensional case in Figure 3.

To examine the effects that 1) different cortical map variability percentages, 2) different sampling distributions and 3) different extraction methods have on the ability to estimate accurate maps, the mean and the standard deviation of the R^2 were found for each distribution set. A Wilcoxon rank-sum test was used to compare the different methods of estimating maps and to determine which method produced more accurate interpretations of the underlying SOFM maps. A two-tailed Chi-squared test (two-sampled F -test) was used to compare the variance in R^2 values for each estimation method.

Results

Sampling Density and Averaging

For the four-feature maps depicted in Figure 1, we created a total of 67,200 different map instantiations at 24 different sampling densities, 7 different variability percentages and 4 SOFM features. Maps for each combination of parameters were randomized 100 times for both the averaged and unaveraged estimation conditions. Each map was sampled at the appropriate resolution and then interpolated back to 150×150 pixels in order to visually compare the quality of estimation between maps of different sampling densities. As the sampling density of the estimation increased, the overall structure of the map became more apparent visually, and the R^2 value increased. Figure 4 shows a series of unaveraged, uniformly sampled maps of feature 3 as sampling density increased, and demonstrates that the quantified improvement in map quality (indicated by R^2 values) tracked closely with the visible map quality. Estimated feature values were only interpolated, not extrapolated, which resulted in an unestimated bounding area that was largest for the lowest sampling densities. These unestimated areas were excluded from coefficient of determination calculations and all other calculations. Map estimation with averaging can be seen for all four features in Supplementary Figure S02.

Estimated maps for features with low spatial frequencies, such as feature 1, had relatively high R^2 values even at relatively low sampling densities. For maps with higher spatial frequencies and more global disorder, however, a higher sampling density was required to determine the general structure of the maps. This trend is quantified in the upper row of panels in Figure 5 for uniformly sampled maps. Maps estimated using averaging (see Methods) showed a steady trend of increasing R^2 as sampling density increases. For example, estimates of feature 4 require a sampling density of at least 100 points (10×10) in the averaged sampling condition to produce map estimates with a mean R^2 of 0.30. The lower row of panels in Figure 5 indicates that the averaging condition provides the substantial benefit of eliminating virtually all variability in the estimates, even at extremely low sampling densities. In most cases variability was reduced over an order of magnitude simply by averaging.

Some of these trends also persisted when maps were estimated without averaging. Notably, greater sampling densities tended to improve map estimates, as seen by the generally increasing R^2 values as a function of increasing sampling density. Just as with the averaging case, low sampling densities tended to undersample high-complexity maps. One substantive difference, however, is that undersampled maps in the unaveraged case could have very negative coefficients of determination, implying that the reconstructed map was less

accurate than an estimate consisting simply of the mean feature value across all the pixels. This result is equivalent to saying that the estimated map is aliased. In such a case, the resulting maps can actually be quite misleading when analyzed either visually or computationally, as can be seen for one example in Figure 6. The oscillations in R^2 values seen for unaveraged samples at low sampling densities of features 3 and 4 mirror the oscillations seen in the undersampled sine function (Figure 3), implying aliasing. When variability was present, unaveraged maps also demonstrated standard deviations of R^2 values that were about three orders of magnitude higher than the averaged maps, particularly at lower sampling densities where the sampling locations exhibited a larger influence upon the estimated maps. This variability was not seen in the averaged sampling case because the sample means are better estimates of the real feature values in general than any individual value. This same phenomenon leads to a greater influence of map variability upon unaveraged estimate quality than for averaged estimate quality, resulting in a greater spread among the family of curves in the former case. While increasing sampling density in the unaveraged case did decrease map variability for all maps, it did not result in smooth convergence toward arbitrarily accurate maps, even for low-complexity maps such as feature 1. Feature extraction without averaging can be seen for all four features in Supplementary Figure S03.

The unaveraged estimations often produced better estimates for lower complexity maps such as feature 1 because averaging acts as a lowpass filter. This filtering smooths maps containing variability, which benefits estimates of lower complexity maps. On the other hand, at low sampling densities this filtering lowers the R^2 value for higher complexity maps. In these cases the averaged maps more closely reflect simply the overall mean feature value. At the same time, averaging prevents the R^2 from falling much below 0. At an R^2 of 0, the sum-of-square error of the estimated map is equal to the sum-of-square error for the mean feature value the SOFM. The unaveraged map estimates, however, can fall well below zero, as seen in the R^2 values for the feature 4 in Figure 6. As noted previously, however, at higher map variabilities this filtering effect cannot fully compensate the estimation errors that result from single neuron sampling without averaging.

Averaging generally resulted in a smaller range of map quality variation, as seen in the reduced R^2 standard deviations for averaging in the bottom panels of Figure 5. Out of 672 total parameter combinations (100 trials each), 625 exhibited significantly lower R^2 standard deviations for the averaged estimations, 30 exhibited significantly lower R^2 standard deviations for the unaveraged estimations, and 17 exhibited an insignificant difference in R^2 standard deviations between the two types of estimations ($p < 0.01$, Chi-squared test). These results indicate that collectively over all the conditions tested, averaging resulted in significantly less map estimate variability ($p = 0$, binomial test). The averaging procedure removed much of the estimate variability because of the law of large numbers and thereby increased the accuracy of the estimation.

To examine the differences between mapping estimations simulating single-unit recordings and mapping estimations simulating multiunit recordings, we sampled individual points spaced uniformly through the map and averaged the surrounding values into a single pixel on the map, as described in the *Map Estimation* section of Methods. The R^2 value of each estimation and the Wilcoxon Rank-Sum Test for each combination of variability and sampling density were used to compare the averaged and the unaveraged estimations directly. The resulting R^2 values suggested that the averaged points provided better estimations for maps with low spatial frequencies, large variability, and low sampling densities (Figure 7). As the spatial densities of the maps increased or the variability percentage decreased, unaveraged estimations produced higher R^2 values than the averaged

estimations. For maps with high spatial frequencies like the map of feature 4, however, averaged estimations provided better estimations at lower sampling densities.

Estimations with Nonuniform Sampling and Visualization Techniques

We next examined the effects of random versus uniform sampling on the map estimation accuracy and found that in most cases, uniform sampling yielded a small but significant improvement in accuracy over nonuniform sampling (Figure 8). Out of 672 total parameter combinations (100 trials each), 627 exhibited significantly higher R^2 values for uniform sampling, 35 exhibited significantly higher R^2 values for nonuniform sampling and 10 exhibited no significant difference in R^2 values ($p < 0.01$, Wilcoxon rank-sum test). Uniform sampling also resulted in a somewhat smaller range of map quality variation than nonuniform sampling, with 664/672 parameter combinations exhibiting significantly lower R^2 standard deviations for uniform sampling, 0/672 parameter combinations exhibiting significantly lower standard deviations for nonuniform sampling and 8/672 parameter combinations exhibiting insignificant differences ($p < 0.01$, Chi-squared test). These results indicate that collectively over all the conditions tested, uniform sampling resulted in significantly less map estimate variability ($p = 0$, binomial test). Nonuniform sampling provided better map estimation when the sampling density was low because variation in local sampling density can reveal map features missed by uniform sampling. As the sampling density increased, however, this effect was diminished, and performance tended to equalize between the two methods. The maximum R^2 value did not seem to be affected by sampling nonuniformly, as R^2 values approached similar asymptotic values at high sampling densities for both approaches. A summary of some estimation quality values for uniform versus non-uniform sampling and averaged versus unaveraged maps is given in Table 1.

A popular method to visualize estimated features maps with randomly sampled points is with a zeroth order interpolation known as a Voronoi tessellation plot (Figure 9) (Cheung et al., 2001; Godey et al., 2005; Kilgard and Merzenich, 1998; Read et al., 2001). A Voronoi plot is generated by assigning all the points within a nonuniform pixel the same value, and pixel shapes are determined by assigning territory based upon the local sampling density. Voronoi plots allow the reader to identify both the sampling density and the interpolated feature values in the same image. As seen in Figure 9, however, the estimates for feature 3 derived from linear interpolation produced consistently higher R^2 values than estimates derived from zeroth order interpolation, but this difference is diminished at higher sampling densities. One advantage of Voronoi plots, on the other hand, is to be able to extend estimates outside the sampled territory without explicitly extrapolating.

Even when maps are uniformly sampled, linear (first-order) interpolation allows for the visualization of features that might not normally be visually apparent otherwise (Figure 10). Particularly at lower sampling densities, first-order interpolations provide a clearer and more accurate depiction of the map than zeroth-order interpolations. Unlike with Voronoi plots, however, sampling density information is obscured on a first-order interpolation and would be indiscernible if not reported. Nonetheless, increased resolution and feature visualization appear to outweigh the loss of this information on the plot. Additional examples of zeroth-order interpolation on Voronoi maps can be seen in Figures S4–S7. Figure 10 further demonstrates undesirable effects from poorly chosen colormaps. The spurious apparent spatial frequencies introduced in the estimated map of feature 4 using a rainbow colormap obscure the detection of spatial frequencies in the map itself. This phenomenon is particularly prominent in the zeroth-order interpolation case (middle), but can also be seen somewhat in the original map (left). Such problems introduced by rainbow colormaps can potentially be overcome using higher sampling densities and/or linear interpolation. A simpler solution, however, is to use an appropriate colormap suited to the data. The grayscale colormaps in Figure 10 all reveal visually the structure of the underlying map

more accurately than the rainbow case, which is only successful in this particular case because this map has a bimodal, nearly symmetric distribution of values around 0, thereby allowing hue transitions in the colormap to fortuitously segregate peaks and troughs visually. Spurious spatial frequencies are still introduced by zeroth-order interpolation with a grayscale colormap (middle bottom), but the effect is not compounded by the hue transitions of the rainbow colormap (middle top).

Discussion

Mapping studies of cortical areas elucidate the physical arrangement of neurons performing particular processing tasks. Topographic functional maps are revealed by sampling a subset of neurons across the area of interest, normally accomplished through either recording the activity from a succession of single neurons or recording the averaged activity over a number of neurons at each location of interest. The locations and the values of these samples are then combined together to create a map of activity across the cortical area. This study sought to identify the conditions under which either of the two methods provides a more accurate estimation of underlying feature maps and to determine the conditions that affect estimation accuracy. The computational model assumes perfect sampling in that unaveraged units represented accurate estimates of single neuron features while averaged units represented the accurately estimated but averaged neuronal features over a small local area. Variability in the actual maps themselves (i.e., the physical locations of neurons with particular feature values) and feature estimation errors would both introduce estimated map variability, which was accounted for by analyzing variable feature maps.

Methods for Estimating Unit Features

Neurons within a cortical column have been shown to display varying physiological characteristics (Atencio and Schreiner, 2010; Hubel and Wiesel, 1974; Phillips and Irvine, 1981). These varying characteristics were modeled in this study as map variability. Modeling results showed that averaged estimations performed better than unaveraged estimations when a substantial amount of map variability was present. Estimated map quality generally improved in all cases when sampling density increased, but unaveraged estimations showed significantly greater variation in estimate quality upon repeated trials as well as lower estimate quality than averaged estimations for most cases. These results suggest that single-unit studies may lead to less accurate estimated maps than multiunit studies at all but the lowest map variabilities. On the other hand, recording techniques that average neuronal activity together are likely to be relatively resistant to the effects of cortical map variability. One important way in which single-unit studies can be modified in the face of substantial map variability that would likely improve estimated maps would be to average multiple single unit measurements taken in close proximity. Suppose, for example, that time limitations on a physiological mapping experiment permit only a limited number of neuronal measurements, say 400. A more accurate estimated map is likely to result if those 400 measurements are made as 4 single unit measurements in 100 separate penetrations and averaged together to obtain an averaged 10×10 map compared to an unaveraged 20×20 map. In some cases, particularly for some neuronal features in the auditory system, single unit as opposed to multiunit measures are desirable in and of themselves because of issues related to neuronal selectivity (Chen et al., 2010), making successive single-unit measurements the only reasonable approach to take to achieve accurate map estimation.

To provide a specific context for the consideration of columnar variability, a published single-unit electrophysiology data set from 149 marmoset monkey A1 electrode penetrations (Watkins and Barbour, 2011) was reexamined to quantify the variability recorded. Using the same metrics employed for the computational maps, characteristic frequency exhibited a relatively low variability of 0.7%. On the other hand, monotonicity index (i.e., the degree to

which neuronal responses are tuned to sound intensity) has a relatively high variability of 21%. Both of these features are nonrandomly distributed across cortex, as can be seen in Figure 10 of (Watkins and Barbour, 2011); monotonicity index, however, is considerably more variable than frequency. Response threshold also exhibits a relatively high variability of 15%. Therefore, 0–30% apparently encompasses a reasonable range of columnar variability to test. While an accurate map of frequency could likely be constructed adequately using any of a variety of techniques, maps of monotonicity would likely benefit from mapping techniques that average neuronal responses together.

For high-complexity maps containing high spatial frequencies, unaveraged (single-unit) studies could perform better than averaged approaches at higher sampling densities as long as map variability is not too high. This effect comes about because of the low-pass filtering that accompanies averaging, which smoothes map estimates and thus inappropriately obscures the higher spatial frequencies present in the actual map. At high sampling densities, this effect is diminished because the smoothing occurs over a smaller spatial area. At lower sampling densities, averaged maps converge to the mean feature value measured and would thus produce an experimental result likely to be interpreted as no map for that particular feature. This effect occurs at all map variabilities. So while unaveraged sampling might be more likely to reveal the presence of an underlying map than averaged sampling, the ability of that methodology to obtain accurate map estimates is dependent upon both the sampling density used and the inherent map variability. A reasonable estimate of underlying map variability would therefore be a parameter useful for deciding an appropriate sampling density for a given anticipated map complexity.

Sampling Locations and Display of Estimated Maps

For unaveraged single-unit mapping studies, the locations of the sampled units plays an important part in creating accurate map estimates. It is possible under some conditions for nonuniform sampling to create more accurate map estimates than uniform sampling because local sampling densities may be higher where the feature gradient is the greatest. Overall, however, the accuracy of estimated maps in this study was significantly greater with uniform sampling under most conditions. Keeping the sampling uniform will both improve the accuracy of estimated maps and lower the variability between different estimates. The geometry of the brain, the need to avoid blood vessels and other potential factors may prevent mapping cortical areas in a uniform manner, however. In such cases, it is worth noting that as long as sampling density is sufficiently high, uniform and nonuniform sampling both result in similar estimation quality.

Voronoi tessellation or zeroth-order interpolation plots have a distinct advantage of allowing readers to identify both the sampling density and the mapped feature values at the same time in the same image. While linear interpolation on its own obscures the sampling density, it does result in a more accurate estimation by smoothing out the estimated maps between sampling locations. A disadvantage of this process, however, is the lack of an explicit map estimate of feature values at locations outside the convex boundary of sampled points. This shortcoming could be rectified by adding extrapolation outside this area or perhaps performing a zeroth-order interpolation at the boundary. Within this boundary, linear interpolation combined with adequate sampling consistently yields a more accurate estimation of the underlying feature map in comparison to zeroth-order interpolation. Neither method of interpolation can counteract undersampling of the map and the aliasing that results, however. At higher sampling densities, the performance of both types of interpolation nearly equalizes, leaving Voronoi tessellation with a relative advantage. Additionally, tessellation plots are perhaps the closest visual display methodology to simply presenting the sampled feature values at their physical locations, which adds the least processing and interpretation to the measured data. Finally, colormaps poorly matched to the

underlying feature map data, which usually includes rainbow colormaps, can contribute to visual misinterpretations about the nature of the map. In most cases a grayscale or other monochromatic colormap introduces the least spurious spatial frequencies into the visualization.

Mapping Features in Auditory Cortex

The utility of the methodological assessments presented here can be readily seen when considering historical attempts to determine functional organization in auditory cortex. Variations in experimental and analytical methods led to considerable debate over the existence of functional auditory maps in the cortex for over three decades. The first published evidence for functional organization in cat auditory cortex was given by Woolsey and Walzl in 1942 (Woolsey and Walzl, 1942). While electrically stimulating points along the cochlea of an anesthetized cat, Woolsey and Walzl systematically measured surface potentials along the contralateral cortex. They identified three regions for which distance along the cochlea (equivalent to sound frequency) was mapped. Despite being successful, this technique would be considered coarse by modern electrophysiological standards because the large electrodes used were sensitive to neuronal activity over a fairly wide area of cortex and were stepped in 1 mm increments. This technique was successfully extended to anesthetized monkeys shortly thereafter (Woolsey and Walzl, 1944), leading to a generalized understanding of frequency or tonotopic organizations in multiple cortical fields in multiple species.

Later experimenters extended this work with steadily improving methods. Hind, for example, also examined functional organization in the auditory cortex of anesthetized cats by measuring “strychnine spikes” over constrained 1 mm² patches in response to acoustic stimulation at defined frequencies (Hind, 1953). The results agreed well with those of Woolsey and Walzl, showing low-frequency localization at the dorsal ends of the posterior ectosylvian sulcus and anterior ectosylvian gyrus as well as high-frequency localization at the dorsal-anterior of the middle ectosylvian gyrus and the lower posterior ectosylvian gyrus. This study also confirmed previous work in primates and cats showing a consistent organization of frequency in several auditory cortical areas (Bailey et al., 1943; Licklider, 1942; Rose and Woolsey, 1949).

As physiological methods improved further and investigators began to study individual neurons in awake animals, however, the issue of cortical tonotopy became less clear. Studies began to report that any neuronal preferred frequency could essentially be found throughout primary auditory cortex (Erulkar et al., 1956; Evans et al., 1965; Evans and Whitfield, 1964; Goldstein et al., 1970). The detailed study conducted by Goldstein, *et al.*, (1970) using single-unit data collected from 21 awake cats. These authors presented single-unit data collected in auditory cortex of 21 awake cats. Despite a high collective sampling density, the pooled data revealed no clear frequency organization. This finding obviously surprised the authors given prior research history, but they were unable to reconcile the single-unit data with the surface recordings from previous decades.

The issue of tonotopy in auditory cortex was ultimately resolved by Merzenich, Knight and Roth (Merzenich et al., 1973, 1975). The authors of this study used anesthetized cats, recording in auditory cortex from penetrating electrodes but selected for multiunit data from middle (input) layers and sampled at a high density in individual animals. Their finding of clear tonotopy in primary auditory cortex mirrored the earliest physiological studies using surface potentials. While other factors could be involved (such as how preferred frequency is estimated for each neuron or the effects of anesthesia on neuronal responses), three factors most likely lowered the effects of underlying map variability to the point where the underlying frequency map could be seen readily: the precise combination of input layer bias,

multiunit averaging and high intrasubject sampling density. This point was essentially conceded by Goldstein and Abeles (Goldstein and Abeles, 1975) and is consistent with our own theoretical findings that for the purposes of estimating maps, physiological methods that average neuronal features can in many instances provide superior inferences about the physiological map structure of a cortical area.

Once tonotopy was firmly established to be a trait of primary auditory cortex, other potential feature maps received renewed interest, though their higher-complexity nature made visualizing any trends more challenging. Maps were initially visualized by showing penetration sites on a photograph with the relevant neuronal characteristic listed near each penetration. While perhaps suitable for low-complexity maps such as preferred frequency, better visualization and presentation methods would be necessary for displaying higher complexity feature maps. To overcome this problem, researchers began experimenting with other display methods, such as three-dimensional projections and contour maps. While the projection provided a high level of interpolated data, this method alone led to perceptual distortions of the underlying map. The addition of contour lines to map estimates provided a less distorted view, although the penetration sites had to be explicitly included to convey sampling density accurately (Schreiner et al., 1992). A practical and useful alternative was the use of Voronoi tessellation plots to present recordings from the cortex (Kilgard and Merzenich, 1998). The polygon shapes in such maps confer the location and shape over which the estimate is applied, while the colors or grayscale depict the particular value of the feature at that location, eliminating the necessity for a perception-distorting third dimension.

Frequency maps produced by Kilgard and Merzenich were generated from 70–110 probes. With the level of map variability expected in primary auditory cortex, this sampling density is likely more than sufficient to estimate frequency maps accurately. This number of samples is at the lower end to begin seeing an accurate map of a complex feature, however. The sampling density required to successfully estimate a map is determined partly by the spatial frequencies present in the map itself. Feature 1, a low-complexity map, could be estimated relatively accurately at even the lowest sampling densities tested. Feature 4, on the other hand, required a sampling density of over $15 \times 15 = 225$ to produce estimations with R^2 higher than 0.7. Electrophysiology studies in primary auditory cortex (A1) sometimes sample at or near these densities: for example, 179 (Cheung et al., 2001), 289 (Bonham et al., 2004) and 352 penetrations (Philibert et al., 2005). The average number of penetrations per experimental animal appears to be considerably lower, however, ranging from 80 to 100 penetrations. Studies with such sampling densities may be able to adequately resolve lower complexity maps but may have difficulty resolving higher complexity maps, depending upon the amount of map variability and how the maps are visualized. Imaging studies generally map with sampling densities in excess of 80×80 points (Ojima et al., 2005; Petkov et al., 2006); however, difficulty still exists in reliably reproducing many maps obtained from electrophysiology. Since the resolution of the imaging studies generally exceeds the necessary sampling density needed to accurately resolve maps, a fundamental limitation within the neural circuitry and stimulus response may exist that hinders imaging studies relative to electrophysiology studies (Barbour, 2011; Chen et al., 2010).

To put these findings into an appropriate physical context, 100 penetrations spread uniformly across a $\sim 25 \text{ mm}^2$ cortical area such as cat A1 (Merzenich et al., 1973, 1975) would result in map “pixels” approximately $500 \mu\text{m}$ on a side, 200 penetrations would lead to $250 \times 250 \mu\text{m}$ pixels, and so forth. Sampling densities in this range would therefore potentially sample individual cortical columns of the classically defined size of $200 - 800 \mu\text{m}$ (Horton and Adams, 2005; Hubel and Wiesel, 1977; Mountcastle, 1997), but would be considerably coarser than the $30 - 70 \mu\text{m}$ size of minicolumns (Mountcastle, 1997; Winer, 1984). The simulated model areas used in this study were composed of $150 \times 150 = 22,500$

pixels and would therefore yield cat A1 pixel sizes of 30×30 µm, which would be a sufficient resolution to represent feature maps where spatial feature variations were limited to minicolumns (Swindale, 2004).

Armed with the guidelines presented here, we anticipate that ongoing studies estimating higher complexity feature maps in auditory cortex and other cortical areas can be made with greater confidence using a variety of physiological measurement and analytic techniques.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by National Institutes of Health grant R01-DC009215.

References

- Atencio CA, Schreiner CE. Laminar diversity of dynamic sound processing in cat primary auditory cortex. *J Neurophysiol.* 2010; 103:192–205. [PubMed: 19864440]
- Bailey P, von Bonin G, Garol HW, McCulloch WS. Functional organization of temporal lobe of monkey (*Macaca mulatta*) and chimpanzee (*Pan satyrus*). *Journal of Neurophysiology.* 1943; 6:121–7.
- Bandyopadhyay S, Shamma SA, Kanold PO. Dichotomy of functional organization in the mouse auditory cortex. *Nat Neurosci.* 2010; 13:361–8. [PubMed: 20118924]
- Barbour DL. Intensity-invariant coding in the auditory system. *Neurosci Biobehav Rev.* 2011 (in press).
- Bonham BH, Cheung SW, Godey B, Schreiner CE. Spatial organization of frequency response areas and rate/level functions in the developing AI. *J Neurophysiol.* 2004; 91:841–54. [PubMed: 14534283]
- Chen TL, Watkins PV, Barbour DL. Theoretical limitations on functional imaging resolution in auditory cortex. *Brain Res.* 2010; 1319:175–89. [PubMed: 20079343]
- Cheung SW, Bedenbaugh PH, Nagarajan SS, Schreiner CE. Functional organization of squirrel monkey primary auditory cortex: responses to pure tones. *J Neurophysiol.* 2001; 85:1732–49. [PubMed: 11287495]
- Clarey JC, Barone P, Imig TJ. Functional organization of sound direction and sound pressure level in primary auditory cortex of the cat. *J Neurophysiol.* 1994; 72:2383–405. [PubMed: 7884466]
- Erulkar SD, Rose JE, Davies PW. Single unit activity in the auditory cortex of the cat. *Bulletin of the Johns Hopkins Hospital.* 1956; 99:55–86. [PubMed: 13356091]
- Esser KH, Eiermann A. Tonotopic organization and parcellation of auditory cortex in the FM-bat *Carollia perspicillata*. *Eur J Neurosci.* 1999; 11:3669–82. [PubMed: 10564374]
- Evans EF, Ross HF, Whitfield IC. The spatial distribution of unit characteristic frequency in the primary auditory cortex of the cat. *Journal of Physiology.* 1965; 179:238–47. [PubMed: 5853890]
- Evans EF, Whitfield IC. Classification of unit responses in the auditory cortex of the unanaesthetized and unrestrained cat. *Journal of Physiology.* 1964; 171:476–93. [PubMed: 14193935]
- Farley BJ, Yu H, Jin DZ, Sur M. Alteration of visual input results in a coordinated reorganization of multiple visual cortex maps. *J Neurosci.* 2007; 27:10299–310. [PubMed: 17881536]
- Godey B, Atencio CA, Bonham BH, Schreiner CE, Cheung SW. Functional organization of squirrel monkey primary auditory cortex: responses to frequency-modulation sweeps. *J Neurophysiol.* 2005; 94:1299–311. [PubMed: 16061492]
- Goldstein MH Jr, Abeles M, Daly RL, McIntosh J. Functional architecture in cat primary auditory cortex: tonotopic organization. *J Neurophysiol.* 1970; 33:188–97. [PubMed: 5411513]
- Goldstein MH Jr, Abeles M. Note on tonotopic organization of primary auditory cortex in the cat. *Brain Research.* 1975; 100:188–91. [PubMed: 1182512]

- Hind JE. An electrophysiological determination of tonotopic organization in auditory cortex of cat. *J Neurophysiol.* 1953; 16:475–89. [PubMed: 13097196]
- Horton JC, Adams DL. The cortical column: a structure without a function. *Philos Trans R Soc Lond B Biol Sci.* 2005; 360:837–62. [PubMed: 15937015]
- Hubel DH, Wiesel TN. Ferrier lecture. Functional architecture of macaque monkey visual cortex. *Proc R Soc Lond B Biol Sci.* 1977; 198:1–59. [PubMed: 20635]
- Hubel DH, Wiesel TN. Uniformity of monkey striate cortex: a parallel relationship between field size, scatter, and magnification factor. *J Comp Neurol.* 1974; 158:295–305. [PubMed: 4436457]
- Imig TJ, Adrian HO. Binaural columns in the primary field (A1) of cat auditory cortex. *Brain Res.* 1977; 138:241–57. [PubMed: 589474]
- Kelly JB, Judge PW. Binaural organization of primary auditory cortex in the ferret (*Mustela putorius*). *J Neurophysiol.* 1994; 71:904–13. [PubMed: 8201431]
- Kilgard MP, Merzenich MM. Cortical Map Reorganization Enabled by Nucleus Basalis Activity. *Science.* 1998; 279:1714–8. [PubMed: 9497289]
- Langner G, Sams M, Heil P, Schulze H. Frequency and periodicity are represented in orthogonal maps in the human auditory cortex: evidence from magnetoencephalography. *J Comp Physiol [A].* 1997; 181:665–76.
- Licklider, JCR. An electrical investigation of frequency-localization in the auditory cortex of the cat. University of Rochester; Rochester, New York: 1942.
- Mendelson JR, Schreiner CE, Sutter ML. Functional topography of cat primary auditory cortex: response latencies. *J Comp Physiol [A].* 1997; 181:615–33.
- Mendelson JR, Schreiner CE, Sutter ML, Grasse KL. Functional topography of cat primary auditory cortex: responses to frequency-modulated sweeps. *Exp Brain Res.* 1993; 94:65–87. [PubMed: 8335076]
- Merzenich MM, Knight PL, Roth GL. Cochleotopic organization of primary auditory cortex in the cat. *Brain Res.* 1973; 63:343–6. [PubMed: 4764302]
- Merzenich MM, Knight PL, Roth GL. Representation of cochlea within primary auditory cortex in the cat. *J Neurophysiol.* 1975; 38:231–49. [PubMed: 1092814]
- Middlebrooks JC, Xu L, Eddins AC, Green DM. Codes for sound-source location in nontotopic auditory cortex. *J Neurophysiol.* 1998; 80:863–81. [PubMed: 9705474]
- Mountcastle VB. The columnar organization of the neocortex. *Brain.* 1997; 120 (Pt 4):701–22. [PubMed: 9153131]
- Obermayer K, Blasdel GG. Geometry of orientation and ocular dominance columns in monkey striate cortex. *J Neurosci.* 1993; 13:4114–29. [PubMed: 8410181]
- Obermayer K, Blasdel GG, Schulten K. Statistical-mechanical analysis of self-organization and pattern formation during the development of visual maps. *Phys Rev A.* 1992; 45:7568–89. [PubMed: 9906831]
- Ohki K, Chung S, Ch'ng YH, Kara P, Reid RC. Functional imaging with cellular resolution reveals precise micro-architecture in visual cortex. *Nature.* 2005; 433:597–603. [PubMed: 15660108]
- Ojima H, Takayanagi M, Potapov D, Homma R. Isofrequency band-like zones of activation revealed by optical imaging of intrinsic signals in the cat primary auditory cortex. *Cereb Cortex.* 2005; 15:1497–509. [PubMed: 15659656]
- Petkov CI, Kayser C, Augath M, Logothetis NK. Functional imaging reveals numerous fields in the monkey auditory cortex. *PLoS Biol.* 2006; 4:e215. [PubMed: 16774452]
- Philibert B, Beitel RE, Nagarajan SS, Bonham BH, Schreiner CE, Cheung SW. Functional organization and hemispheric comparison of primary auditory cortex in the common marmoset (*Callithrix jacchus*). *J Comp Neurol.* 2005; 487:391–406. [PubMed: 15906314]
- Phillips DP, Irvine DR. Responses of single neurons in physiologically defined primary auditory cortex (AI) of the cat: frequency tuning and responses to intensity. *J Neurophysiol.* 1981; 45:48–58. [PubMed: 7205344]
- Read HL, Winer JA, Schreiner CE. Modular organization of intrinsic connections associated with spectral tuning in cat auditory cortex. *Proc Natl Acad Sci U S A.* 2001; 98:8042–7. [PubMed: 11438747]

- Reale RA, Kettner RE. Topography of binaural organization in primary auditory cortex of the cat: effects of changing interaural intensity. *J Neurophysiol.* 1986; 56:663–82. [PubMed: 3783214]
- Recanzone GH, Schreiner CE, Sutter ML, Beitel RE, Merzenich MM. Functional organization of spectral receptive fields in the primary auditory cortex of the owl monkey. *J Comp Neurol.* 1999; 415:460–81. [PubMed: 10570456]
- Rose JE, Woolsey CN. The relations of thalamic connections, cellular structure and evocable electrical activity in the auditory region of the cat. *J Comp Neurol.* 1949; 91:441–66. [PubMed: 15409490]
- Rothschild G, Nelken I, Mizrahi A. Functional organization and population dynamics in the mouse primary auditory cortex. *Nat Neurosci.* 2010; 13:353–60. [PubMed: 20118927]
- Rutkowski RG, Wallace MN, Shackleton TM, Palmer AR. Organisation of binaural interactions in the primary and dorsocaudal fields of the guinea pig auditory cortex. *Hear Res.* 2000; 145:177–89. [PubMed: 10867291]
- Schreiner CE, Mendelson JR. Functional topography of cat primary auditory cortex: distribution of integrated excitation. *J Neurophysiol.* 1990; 64:1442–59. [PubMed: 2283536]
- Schreiner CE, Mendelson JR, Sutter ML. Functional topography of cat primary auditory cortex: representation of tone intensity. *Exp Brain Res.* 1992; 92:105–22. [PubMed: 1486946]
- Schulze H, Langner G. Periodicity coding in the primary auditory cortex of the Mongolian gerbil (*Meriones unguiculatus*): two different coding strategies for pitch and rhythm? *J Comp Physiol [A].* 1997a; 181:651–63.
- Schulze H, Langner G. Representation of periodicity pitch in the primary auditory cortex of the Mongolian gerbil. *Acta Otolaryngol Suppl.* 1997b; 532:89–95. [PubMed: 9442850]
- Shamma SA, Fleshman JW, Wiser PR, Versnel H. Organization of response areas in ferret primary auditory cortex. *J Neurophysiol.* 1993; 69:367–83. [PubMed: 8459273]
- Swindale NV. How different feature spaces may be represented in cortical maps. *Network.* 2004; 15:217–42. [PubMed: 15600232]
- Watkins PV, Barbour DL. Rate-level responses in awake marmoset auditory cortex. *Hear Res.* 2011; 275:30–42. [PubMed: 21145961]
- Watkins PV, Chen TL, Barbour DL. A computational framework for topographies of cortical areas. *Biol Cybern.* 2009; 100:231–48. [PubMed: 19221784]
- Winer JA. Anatomy of layer IV in cat primary auditory cortex (AI). *J Comp Neurol.* 1984; 224:535–67. [PubMed: 6725630]
- Woolsey CN, Walzl EM. Topical projection of the cochlea to the cerebral cortex of the monkey. *Amer J Med Sci.* 1944; 207:685–6.
- Woolsey CN, Walzl EM. Topical projections of nerve fibers from local regions of the cochlea to the cerebral cortex of the cat. *Bulletin of the Johns Hopkins Hospital.* 1942; 133:315–44.
- Yu H, Farley BJ, Jin DZ, Sur M. The coordinated mapping of visual space and response features in visual cortex. *Neuron.* 2005; 47:267–80. [PubMed: 16039568]
- Zhang LI, Tan AY, Schreiner CE, Merzenich MM. Topography and synaptic shaping of direction selectivity in primary auditory cortex. *Nature.* 2003; 424:201–5. [PubMed: 12853959]

Research Highlights

- 100 samples is sufficient to accurately estimate most functional auditory maps
- Averaging improves estimates of disordered maps better than taking more samples
- Undersampling can lead to poor map estimates or false conclusions of no map
- Uniform sampling always yields better map estimates than nonuniform sampling

Figure 1. Deterministic self-organizing feature maps (SOFMs) showing different degrees of organization. In this model, four arbitrary neuronal features are mapped with a 10:4:2:1 weighting. The nature of SOFMs ensures that maps with higher weightings are more highly organized and more nearly uniform than maps with lower weightings. Variants of these four maps were used for all the analyses in this study.

Figure 2.
Two randomized maps of feature 1 with different amounts of variability.

Figure 3.

The effect of sampling rate on R^2 values for a sinusoid. The R^2 values were found for a 10 Hz sine wave sampled at a range of sampling rates. The estimated sine waves were resampled back to 1 kHz using linear interpolation before the R^2 values were calculated. Top panel: A 12.5 Hz sampling rate of the 10 Hz sine wave produces a R^2 value of -0.727 , while a 25 Hz sampling rate produces a R^2 value of 0.729 . Bottom panel: At sampling rates below the Nyquist rate (marked with a vertical line), the sine wave is undersampled. Negative R^2 values indicate that the sine wave is severely undersampled and the mean of the function (indicated by horizontal line in the top panel) would generate an estimate with less error.

Figure 4. Unaveraged estimates of a deterministic feature 3 map at different uniform sampling densities. As the sampling density of this map increased, the R^2 values using linear interpolation steadily increased (bottom 4 panels).

Figure 5.

Effect of sampling density on random maps. Averaged and unaveraged estimations at different uniform sampling densities were compared. The mean R^2 values of 100 runs for each scenario are shown in the upper panels, while the standard deviations of the R^2 values are shown in the lower panels. Each family of curves represents different degrees of map variability in the amounts (from top to bottom in the upper panels and from bottom to top in the lower panels) 0.0, 0.05, 0.10, 0.15, 0.20, 0.25 and 0.30. Oscillations in R^2 values at low unaveraged sampling densities for features 3 and 4 are consistent with undersampling and aliasing.

Figure 6.

Unaveraged estimates of a randomized feature 4 map at different sampling densities. As the sampling density of this map increased, the R^2 values using linear interpolation oscillated for values below zero before steadily increasing at positive values (bottom 4 panels). The oscillation is consistent with undersampling and aliasing.

Figure 7.

The Wilcoxon rank-sum test was used to examine in which cases the averaged or unaveraged estimation provided better estimates of the underlying map. Blue shades represent cases where the unaveraged estimates produced higher R^2 values, and red shades represent cases where the averaged estimates produced higher R^2 values. Z scores greater than 2.58 or less than -2.58 represent significant differences (uncorrected $p < 0.01$). Averaged sampling typically performs better for maps with any amount of variability.

Figure 8.

Effect of sampling methodology on unaveraged maps. Uniform and nonuniform sampling approaches were compared. The mean R^2 values of 100 runs for each scenario are shown in the upper panels, while the standard deviations of the R^2 values are shown in the lower panels. Each family of curves represents different degrees of map variability in the amounts (from top to bottom in the upper panels and from bottom to top in the lower panels) 0.0, 0.05, 0.10, 0.15, 0.20, 0.25 and 0.30. Oscillations in R^2 values at low uniform sampling densities for features 3 and 4 are consistent with undersampling and aliasing.

Figure 9.

Estimates are shown of a deterministic feature 3 map using zeroth-order (top row) and first-order interpolation (bottom row) for nonuniform sampling. In the first-order interpolated maps, the white pixels denote locations outside the convex boundary that were not interpolated or used to compute R^2 . The locations of the nonuniform sampling points and the tessellation boundaries are shown on all estimated maps for comparison. Linear interpolation yields higher R^2 values in all cases.

Figure 10.

A deterministic feature 4 map (left column) was estimated with averaged uniform sampling and a sampling density of 20×20 . Zeroth-order interpolation (center column) does not reveal underlying map trends visually as well as linear interpolation (right column). This trend holds true generally as long as the map is not undersampled. Furthermore, the use of a rainbow colormap with zeroth-order interpolation (top middle) introduces spurious spatial frequencies that visually obscure the underlying map. This phenomenon is muted in the grayscale maps (bottom row).

Table 1

Summary of R^2 values for map estimations using various combinations of sampling, averaging and interpolation. In this comparison, all maps exhibited 5% variability and were probed with 100 total samples.

Feature	Uniform, Unaveraged	Uniform, Averaged	Nonuniform, Unaveraged, Voronoi	Nonuniform, Unaveraged, Linear Interp
1	0.99	1.0	0.96	0.98
2	0.98	0.98	0.92	0.96
3	0.92	0.91	0.74	0.83
4	0.34	0.34	-0.14	0.08