

BRAINZOOM: High Resolution Reconstruction from Multi-modal Brain Signals

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Abstract

How close can we zoom in to observe brain activity? Our understanding is limited by the resolution of imaging modalities that exhibit good spatial but poor temporal resolution, or vice-versa. In this paper, we propose BRAINZOOM, an efficient imaging algorithm that cross-leverages multi-modal brain signals. BRAINZOOM (*a*) constructs high resolution brain images from multi-modal signals, (*b*) is scalable, and (*c*) is flexible in that it can easily incorporate various priors on the brain activities, such as sparsity, low rank, or smoothness. We carefully formulate the problem to tackle nonlinearity in the measurements (via *variable splitting*) and *auto-scale* between different modal signals, and judiciously design an *inexact alternating optimization*-based algorithmic framework to handle the problem with provable convergence guarantees. Our experiments using a popular realistic brain signal simulator to generate fMRI and MEG demonstrate that high spatio-temporal resolution brain imaging is possible from these two modalities. The experiments also suggest that smoothness seems to be the best prior, among several we tried.

1 Introduction

Research in neuroimaging have resulted in the development of several techniques, viz., Electroencephalograms (EEG) [1], functional Magnetic Imaging (fMRI) [16], Magnetoencephalograms (MEG) [7], etc. These uni-modal techniques use different mechanisms to measure human brain activity. While EEG measures electrical activity of the brain, MEG measures magnetic fields generated by electric currents in the brain, and fMRI measures metabolic response due to neural activation through

a blood oxygen-level dependent (BOLD) signal. Due to the diversity in the sources of these measurements, different neuroimaging techniques often have complementary strengths. For instance, while EEG and MEG have low spatial but high temporal resolution, fMRI posses just the opposite – high spatial but low temporal resolution.

Combining two or more of such complementary signals to overcome limitations posed by individual modalities has resulted in the development of several multimodal neuroimaging techniques — see [3] for a recent review. Multi-modal neuroimaging techniques have been of great interest in the brain imaging community — see [3] for a recent review. They have been used for source localization and for learning commonalities across multiple modalities, with many of these methods targetted at reducing the dimension of the brain image data, or studying specific hypotheses about relationships between imaging modalities.

However, our interest in this paper lies in reconstructing *super-resolution* images of activity across the brain – that is capturing the union of the information derived from each modality, not their intersection. While super-resolution algorithms have been applied in uni-modal settings [22], they have not been widely explored for multi-modal neuroimaging. We fill this gap by introducing BRAINZOOM, a novel method for super-resolution reconstruction of brain activity by combining different modalities of brain imaging. A snapshot of BRAINZOOM’s capabilities is shown in Figure 1. Our long term goal is to complement the missing information of each modality, to ultimately construct the richest possible spatial-temporal summary of the underlying neural activity.

For the experiments in this paper, we employ BRAINZOOM to produce super-resolution brain images by combining MEG/EEG and fMRI. However, we note that BRAINZOOM is more widely applicable and may be used to create super-resolution images from other modalities as well. We make the following contributions:

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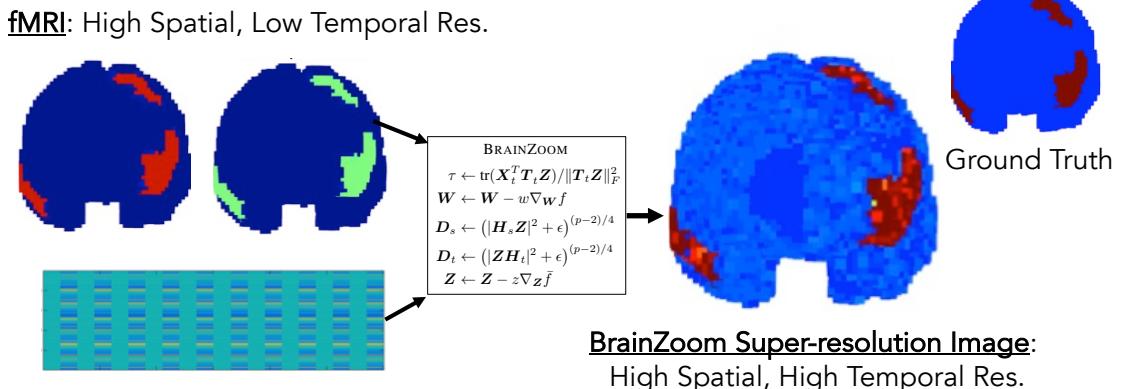


Figure 1: BRAINZOOM effectively reconstructs. BRAINZOOM effectively combines different brain measurement modalities with complementary strengths with respect to temporal and spatial resolution into a *super-resolution, whole-brain image*.

- **Novel Problem Formulation:** In Section 3 we formulate and solve the problem of generating a super-resolution brain image by combining different modalities (e.g., fMRI and MEG/EEG measurements). To the best of our knowledge, this is the first work to rigorously formulate this task as we have, as an optimization problem with this specific optimization objective, which takes into account the non-linearity in the fMRI measurements. Our formulation is also flexible in that it can easily incorporate a variety of priors that can help enhance the quality of reconstruction – so that one can seamlessly try out different hypotheses and pick out the one that gives the best performance.
- **Efficient Algorithm:** BRAINZOOM, introduced in Section 3, uses a novel modified alternating optimization method to solve the optimization problem mentioned above with high scalability. Through variable splitting, BRAINZOOM is able to handle nonlinear measurements. We also provide rigorous convergence analysis of the proposed method.
- **Evaluation:** Since the ground truth, high-resolution brain activity is not known, we cannot test the performance of our method on real brain data. Instead, in Section 4 we use simulated brain signals in order to test the ability of our method to recover the true solution. We generate synthetic brain activity using the Virtual Brain (TVB) [12] simulator. TVB is an open-source platform that creates brain activity simulations using biologically realistic assumptions, relying on well-known neuroscience models. With TVB, we can simulate synthetic brain signals with similar patterns as real brain data, as well as generate multi-modality observations such as fMRI, MEG, or EEG, at different sampling rates.
- **Reproducibility:** We will make our methods, code, and simulator scripts publicly available upon publication.

Property	Localization	CCA, ICA	BRAINZOOM
Hi-resolution imaging	✗	✗	✓
Scalability	✓	✓	✓
Quadratic modeling	✗	✗	✓
Convergence proof	N/A	✓	✓
Auto-scaling	✗	✓	✓
Generality	✗	✗	✓

Table 1: Comparison between BRAINZOOM and other related methods along various properties. We observe that BRAINZOOM overcomes limitations of competing methods.

tion of the paper.

2 Background and Related Work

fMRI and MEG: The exact relationship between neural activity, observed fMRI, and observed MEG signals is not fully understood. It is known that fMRI measures the ratio of oxygenated to deoxygenated hemoglobin in the blood, at a spatial resolution of approximately 1 mm, and it is widely accepted that this oxygen fluctuation is related to the convolution of local neural activity with an impulse response that lasts for 8- 10 seconds. It is also believed that fMRI corresponds more closely to local field potentials in the brain than to actual spiking [14]. In contrast, the MEG device measures magnetic fields emanating from the brain, at 1 msec temporal resolution. These magnetic fields are generated from neural currents, and are especially strong when many neurons are spatially aligned and fire synchronously. MEG signals also depend, unlike fMRI, on the direction of the neural currents generating these magnetic fields. There have been several studies of

the exact relationship between MEG and fMRI measures of neural activity. For example, Kujala et al. [11] provide evidence that fMRI correlates with source-localized MEG activity in many regions of the brain, that the exact nature of this correlation varies somewhat across the brain, and that fMRI typically correlates best with the high frequency components of MEG.

Multi-modal Methods: In the literature, there are two main classes of methods for analyzing multi-modal brain imaging data: those that aim to localize a few dominant ‘point’ sources of brain activity using inverse imaging or high-resolution methods; and those that target the recovery of a few dominant ‘latent’ components. The latter include popular multi-modal fusion techniques that rely on factor analysis tools, such as Independent Component Analysis (ICA) which aims to recover statistically independent latent sources of brain activation; and Canonical Correlation Analysis (CCA) which aims to unravel sources of co-variation in multiple ‘views’ of the brain stemming from the different modalities. Variants of PCA [6], ICA [5], and CCA [8] have been studied for multi-modal fusion of various brain imaging modalities. See [2,3,9,10,13,20,21] for additional background on existing localization and common component extraction methods.

The main difference between our approach and the aforementioned two broad lines of work is that we aim to reconstruct a high spatio-temporal resolution image of the entire brain – not just a few point or dominant sources / components.

Super-resolution in Image Processing: Super-resolution via fusing multi-modal data is also an active research area in image processing. Specifically, fusion of remotely sensed hyper-spectral and multi-spectral images is of great interest [15]. Both hyper- and multi-spectral images are special images whose pixels span many frequency bands and can provide spectral information of the materials contained in the pixels – which finds many applications in geoscience, mineral detection, and food safety. Hyper-spectral images have very high spectral resolution but very coarse spatial resolution, and the situation of the multi-spectral images is exactly the opposite. Much effort has been spent on fusing these two types images that captured on the sites, to create super-resolution data in both space and frequency. The task is very similar to ours, except that the transformation from the virtual super-resolution image (i.e., \mathbf{Z}) to hyper- and multi-spectral images are both linear (to be precise, sub-sampling) [19,23]. But in our problem, the transformation from \mathbf{Z} to fMRI is nonlinear – which poses a much more challenging optimization problem.

3 Proposed Method

In this section, we first present assumptions behind our modeling of entire brain super-resolution image construction from multi-modal neuroimaging data, and then formulate it as an optimization problem. Subsequently, we discuss various priors we can add to the optimization objective. Then we propose BRAINZOOM, a highly scalable and flexible algorithmic framework that solves the above optimization problem, while provably converging to a stationary point at least sub-linearly, despite the fact that the problem is non-convex and possibly NP-hard.

3.1 Notations & Modeling Assumptions We start by denoting the complete brain activity as matrix \mathbf{Z} , where each column of \mathbf{Z} is the (vectorized) 3D brain activity at a particular time tick, and the brain activity is recorded within some time frame to form the matrix \mathbf{Z} . However, we are not able to observe \mathbf{Z} directly, and resort to fMRI and MEG/EEG images as inputs. The goal of this paper is to reconstruct the high-resolution brain activity matrix \mathbf{Z} in *both* spatial and temporal domain, given the MEG and fMRI measurements.

Given the different phenomena observed by MEG and fMRI, what shall we define as the units of our latent neural activity \mathbf{Z} ? In this paper, we assume \mathbf{Z} is a measure of the intensity of neural activity that is linearly related to MEG activity. Let \mathbf{X}_t denote the high temporal-resolution image given by MEG or EEG. It is related to \mathbf{Z} through a linear operator \mathbf{T}_t that operates on the spatial domain, possibly corrupted with noise.

$$(3.1) \quad \mathbf{X}_t = \mathbf{T}_t \mathbf{Z}$$

Notice that the temporal resolution of \mathbf{Z} is the same as that of the given MEG/EEG measurements, since there is no way we can go beyond them in this dimension.

To capture the fact that fMRI is insensitive to the direction of the activity that MEG observes, we model fMRI as dependent on a linear function of the *square* of the \mathbf{Z} activity. Although this is at best an approximation of the unknown, complex relationship between neural spiking, local field potentials, neural currents, and observed fMRI and MEG, this model does capture some basic properties, and it enables us to frame a well-posed problem of solving for high spatial and temporal resolution measure of neural activity. The success of our method in a simulator [12] of brain activity suggests this approximation is reasonable. Let \mathbf{X}_s be the high spatial resolution image captured by fMRI. We model the dependence between \mathbf{X}_s and \mathbf{Z} through a linear operator \mathbf{T}_s as shown below, again possibly corrupted with noise.

$$(3.2) \quad \mathbf{X}_s = \sigma |\mathbf{Z}|^2 \mathbf{T}_s,$$

Here, $\sigma|\mathbf{Z}|^2$ is the element-wise square of \mathbf{Z} with an unknown scaling factor σ . We note that the spatial resolution of \mathbf{Z} is the same as that of the given fMRI images.

Reconstructing high-resolution brain activity matrix \mathbf{Z} in *both* the spatial and temporal domains, given the fMRI measurements \mathbf{X}_s and MEG/EEG measurements \mathbf{X}_t , and their corresponding sensing matrices \mathbf{T}_s and \mathbf{T}_t , is a highly ill-posed inverse problem, since the number of measurements we are given is much smaller than the number of unknowns we want to estimate. One has to impose additional assumptions onto brain activities to make the problem well-defined, which will be discussed in detail in the sequel. Furthermore, when simultaneously considering fMRI and MEG/EEG imaging, the fMRI measurements are *nonlinear* with respect to \mathbf{Z} , which makes the problem even harder to deal with.

3.2 Problem formulation According to the physics of multi-modal brain imaging measurements described in equations (3.1) and (3.2), the problem of inferring the super-resolution description of neural activity Z can be formulated naively as the following optimization problem,

$$(3.3) \quad \min_{\mathbf{Z}, \sigma} \|\mathbf{X}_t - \mathbf{T}_t \mathbf{Z}\|_F^2 + \|\mathbf{X}_s - \sigma|\mathbf{Z}|^2 \mathbf{T}_s\|_F^2 + r(\mathbf{Z}),$$

where $r(\mathbf{Z})$ is some regularization function we put on \mathbf{Z} to make the estimation problem well-defined. Before we dive into different assumptions on the brain activities, let us first focus on the second term that tries to fit the fMRI data, which is a six-order polynomial with respect to σ and \mathbf{Z} together, and makes the problem highly non-convex and seemingly difficult to tackle.

In terms of σ , we notice that it is just an unknown scaling factor, and we can equivalently put it into the first term in (3.3)

$$\min_{\mathbf{Z}, \tau} \|\mathbf{X}_t - \tau \mathbf{T}_t \mathbf{Z}\|_F^2 + \|\mathbf{X}_s - |\mathbf{Z}|^2 \mathbf{T}_s\|_F^2 + r(\mathbf{Z}),$$

resulting the optimal solution \mathbf{Z} to be just a scaled version of that of (3.3), which is usually inconsequential in practice. With respect to the term that involves $|\mathbf{Z}|^2$, we invoke the *variable splitting* trick by introducing another variable \mathbf{W} , and at the same time try to minimize the difference between \mathbf{Z} and \mathbf{W} in the following way

$$(3.4) \quad \begin{aligned} \min_{\mathbf{Z}, \mathbf{W}, \tau} & \|\mathbf{X}_t - \tau \mathbf{T}_t \mathbf{Z}\|_F^2 + \|\mathbf{X}_s - (\mathbf{Z} * \mathbf{W}) \mathbf{T}_s\|_F^2 \\ & + \mu \|\mathbf{Z} - \mathbf{W}\|_F^2 + r(\mathbf{Z}), \end{aligned}$$

where $*$ denotes Hadamard (element-wise) multiplication. Although the resulting formulation (3.4) is still non-convex, the idea is to alternatingly update \mathbf{Z} , \mathbf{W} , and τ ,

so that the cost decreases monotonically. With careful design of the algorithm, we can even claim stronger convergence results, which will be shown in the sequel.

There exist a lot of commonly used priors that can be used to help reconstruct high-resolution brain signals in our formulation (3.4). In this work we consider the following possibilities:

- minimum energy: $r(\mathbf{Z}) = \rho \|\mathbf{Z}\|_F^2$;
- sparsity: $r(\mathbf{Z}) = \rho \|\mathbf{Z}\|_1$, the sum of absolute values;
- low rank: $r(\mathbf{Z}) = \rho \|\mathbf{Z}\|_*$, the sum of singular values;
- smoothness: $r(\mathbf{Z}) = \rho (\|\mathbf{H}_s \mathbf{Z}\|_F^2 + \|\mathbf{Z} \mathbf{H}_t\|_F^2)$, where matrices \mathbf{H}_t and \mathbf{H}_s have the form [4]

$$(3.5) \quad \begin{bmatrix} -1 & 2 & -1 & 0 & \dots \\ 0 & -1 & 2 & -1 & \dots \\ \vdots & & \ddots & & \\ & & -1 & 2 & -1 \end{bmatrix},$$

with appropriate sizes.

- total variation: $r(\mathbf{Z}) = \rho (\|\mathbf{H}_s \mathbf{Z}\|_{p,\epsilon}^p + \|\mathbf{Z} \mathbf{H}_t\|_{p,\epsilon}^p)$, similar to the smoothness regularization, but in this case the matrices \mathbf{H}_s and \mathbf{H}_t have the form

$$(3.6) \quad \begin{bmatrix} 1 & -1 & 0 & \dots \\ 0 & 1 & -1 & \dots \\ \vdots & & \ddots & \\ & & & 1 & -1 \end{bmatrix},$$

with appropriate sizes and $\|\cdot\|_{p,\epsilon}^p$ denotes the ℓ_p quasi-norm defined as

$$\|\mathbf{A}\|_{p,\epsilon}^p = \sum_{i,j} (|a_{ij}|^2 + \epsilon)^{p/2}, \quad 0 < p \leq 2.$$

For $p = 2$, this norm reduces to the normal ℓ_2 norm that is used in the smoothness regularization; for $0 < p \leq 1$, this regularization encourages the solution to be piecewise constant, which is something we want to promote in this case.

In the rest of this section we will design an algorithm based on the latter two regularizations, which have similar forms but only differ in the definitions of the \mathbf{H} matrices, for the following reasons:

1. Because fMRI measures convolutions of $|\mathbf{Z}|^2$, there is an inherent sign ambiguity in the entries of \mathbf{Z} that are not sampled by the \mathbf{T}_t matrix using the first three regularizations, whereas by enforcing elements that are spatially and temporally close to each other to have similar values, this inherent sign ambiguity can

be resolved. Therefore, before real validations, our conjecture is that the latter two regularizations seem to be better models.

2. Computationally, the first three regularizations can be handled by very simple *proximity operators* [17], thus it will be easy to modify the forth-coming algorithm to accommodate them. The smoothness and total-variation regularization, on the other hand, are more complicated to deal with—this is partly why we choose to use the ℓ_p quasi-norm rather than the more commonly used ℓ_1 norm to promote the effect that we want in \mathbf{Z} .

Toward this end, we formalize the problem formulation as

$$\begin{aligned} \min_{\mathbf{Z}, \mathbf{W}, \tau} \quad & \|\mathbf{X}_t - \tau \mathbf{T}_t \mathbf{Z}\|_F^2 + \|\mathbf{X}_s - (\mathbf{Z} * \mathbf{W}) \mathbf{T}_s\|_F^2 \\ (3.7) \quad & + \mu \|\mathbf{Z} - \mathbf{W}\|_F^2 + \rho (\|\mathbf{H}_s \mathbf{Z}\|_{p,\epsilon}^p + \|\mathbf{Z} \mathbf{H}_t\|_{p,\epsilon}^p), \end{aligned}$$

and we denote the cost function in (3.7) as $f(\mathbf{Z}, \mathbf{W}, \tau)$.

3.3 Proposed method Based on the formulation, we propose BRAINZOOM, a highly scalable and flexible algorithmic framework for the brain super-resolution problem based on alternating optimization.

Let us start with the update of τ , which is independent of \mathbf{W} , and by fixing \mathbf{Z} , the conditionally optimal update of τ is

$$(3.8) \quad \tau \leftarrow \text{tr}(\mathbf{X}_t^T \mathbf{T}_t \mathbf{Z}) / \|\mathbf{T}_t \mathbf{Z}\|_F^2.$$

As for the update of \mathbf{W} , to avoid heavy computations, we propose to perform just one simple gradient step, where the gradient with respect to \mathbf{W} can be calculated as

$$(3.9) \quad \nabla_{\mathbf{W}} f = \mathbf{Z} * \left[(\mathbf{Z} * \mathbf{W}) \mathbf{T}_s \mathbf{T}_s^T \right] - \mathbf{Z} * (\mathbf{X}_s \mathbf{T}_s^T) + \mu(\mathbf{W} - \mathbf{Z}).$$

To ensure decrease of the cost function value, we need to make sure that the step-size is less than one over the Lipschitz constant of \mathbf{W} conditioned on \mathbf{Z} . Our selection is

$$(3.10) \quad w = 1 / \left(\lambda_{\max}(\mathbf{T}_s \mathbf{T}_s^T) \max(|\mathbf{Z}|^2) + \mu \right),$$

where $\lambda_{\max}(\cdot)$ computes the largest eigenvalue of the argument matrix, and in Appendix A we prove that it ensures decrease. Notice that $\lambda_{\max}(\mathbf{T}_s \mathbf{T}_s^T)$ only needs to be computed once, can then be saved for subsequent iterations.

Now we turn to the update of \mathbf{Z} , and we again propose to go just a similar gradient step to avoid heavy computations. However, the regularization terms $\|\mathbf{H}_s \mathbf{Z}\|_{p,\epsilon}^p + \|\mathbf{Z} \mathbf{H}_t\|_{p,\epsilon}^p$ are non-differentiable. To compensate this, we first invoke the following property for the ℓ_p quasi-norm:

$$\|\mathbf{A}\|_{p,\epsilon}^p \leq \sum_{i,j} \frac{p}{2} (|\tilde{a}_{ij}|^2 + \epsilon)^{(p-2)/2} |a_{ij}|^2 + \text{constant},$$

for all $\tilde{\mathbf{A}}$, and the equality holds when $\mathbf{A} = \tilde{\mathbf{A}}$. Using this property, we define $\bar{f}(\mathbf{Z}; \mathbf{W}, \tau)$ as

$$\begin{aligned} \bar{f}(\mathbf{Z}; \mathbf{W}, \tau) = & \|\mathbf{X}_t - \tau \mathbf{T}_t \mathbf{Z}\|_F^2 + \|\mathbf{X}_s - (\mathbf{Z} * \mathbf{W}) \mathbf{T}_s\|_F^2 \\ (3.11) \quad & + \rho (\|\mathbf{D}_s * (\mathbf{H}_s \mathbf{Z})\|_F^2 + \|\mathbf{D}_t * (\mathbf{Z} \mathbf{H}_t)\|_F^2) \\ & + \mu \|\mathbf{Z} - \mathbf{W}\|_F^2, \end{aligned}$$

where

$$\begin{aligned} (3.12) \quad \mathbf{D}_s &= \left(|\mathbf{H}_s \tilde{\mathbf{Z}}|^2 + \epsilon \right)^{(p-2)/4}, \\ \mathbf{D}_t &= \left(|\tilde{\mathbf{Z}} \mathbf{H}_t|^2 + \epsilon \right)^{(p-2)/4}, \end{aligned}$$

and $\tilde{\mathbf{Z}}$ is from the previous iteration. Notice that when $p = 2$, i.e., in the smoothness case, the \mathbf{D} matrices are simply the all one matrices, which makes $\bar{f} = f$. In the total variation case when $0 < p \leq 1$, function $\bar{f}(\mathbf{Z}; \mathbf{W}, \tau)$ is a smooth upperbound function for $f(\mathbf{Z}, \mathbf{W}, \tau)$ with respect to \mathbf{Z} while fixing \mathbf{W} and τ . Then we can apply a similar gradient descent step with gradient calculated as

$$\begin{aligned} \nabla_{\mathbf{Z}} \bar{f} = & \tau^2 \mathbf{T}_t^T \mathbf{T}_t \mathbf{Z} - \tau \mathbf{T}_t^T \mathbf{X}_t + \mu(\mathbf{Z} - \mathbf{W}) \\ (3.13) \quad & + \mathbf{W} * \left[(\mathbf{Z} * \mathbf{W}) \mathbf{T}_s \mathbf{T}_s^T \right] - \mathbf{W} * (\mathbf{X}_s \mathbf{T}_s^T) \\ & + \mathbf{H}_s^T [\mathbf{D}_s^2 * (\mathbf{H}_s \mathbf{Z})] + [\mathbf{D}_t^2 * (\mathbf{Z} \mathbf{H}_t)] \mathbf{H}_t^T, \end{aligned}$$

and step size chosen as

$$\begin{aligned} (3.14) \quad z = 1 / & \left(\tau^2 \lambda_{\max}(\mathbf{T}_t^T \mathbf{T}_t) + \lambda_{\max}(\mathbf{T}_s \mathbf{T}_s^T) \max(|\mathbf{W}|^2) \right. \\ & \left. + \mu + \rho (\max(\mathbf{D}_s^2) c_H^2 + \max(\mathbf{D}_t^2) c_H^2) \right), \end{aligned}$$

where c_H is a sharp upperbound on the maximum singular value of the \mathbf{H} matrices

$$(3.15) \quad c_H = \begin{cases} 4, & \text{for smoothness (3.5),} \\ 2, & \text{for total variation (3.6).} \end{cases}$$

Again, in Appendix A we prove that this choice of step size guarantees decrease of the cost function.

Summarizing (3.8)-(3.14), we propose BRAINZOOM

as the following iterative update rule

$$\begin{aligned}
& \text{BRAINZOOM} \\
& \tau \leftarrow \text{tr}(\mathbf{X}_t^T \mathbf{T}_t \mathbf{Z}) / \|\mathbf{T}_t \mathbf{Z}\|_F^2 \\
& \mathbf{W} \leftarrow \mathbf{W} - w \nabla_{\mathbf{W}} f \\
& \mathbf{D}_s \leftarrow (|\mathbf{H}_s \mathbf{Z}|^2 + \epsilon)^{(p-2)/4} \\
& \mathbf{D}_t \leftarrow (|\mathbf{Z} \mathbf{H}_t|^2 + \epsilon)^{(p-2)/4} \\
& \mathbf{Z} \leftarrow \mathbf{Z} - z \nabla_{\mathbf{Z}} \bar{f}
\end{aligned} \tag{3.16}$$

3.4 Convergence Properties Although BRAINZOOM is a very simple algorithm that blends alternating optimization with gradient descent, it has very nice convergence properties, as we show here.

Theorem 1 *Let $\{(\mathbf{Z}^{(r)}, \mathbf{W}^{(r)}, \tau^{(r)})\}_r$ be the solution sequence produced by the proposed BRAINZOOM (3.16). We have*

- 1) *Every limit point of $\{(\mathbf{Z}^{(r)}, \mathbf{W}^{(r)}, \tau^{(r)})\}_r$ is a stationary point of Problem (3.7).*
- 2) *The optimality gap between $\{(\mathbf{Z}^{(r)}, \mathbf{W}^{(r)}, \tau^{(r)})\}_r$ and a stationary point is at most $\mathcal{O}(1/r)$; i.e., the algorithm approaches a stationary point at least sub-linearly.*

The proof of Theorem 1 is relegated to Appendix B.

Remark. The proposed BRAINZOOM is a flexible combination between alternating optimization and gradient descent. A clear advantage is that all the variations that people have been using to modify the algorithm to accommodate constraints and non-linearities, by simply putting an additional projection or proximal step. This includes the first three regularizations that we discussed in Section 3.2, namely, minimum energy, sparsity, and low rank. Moreover, if we have the prior knowledge that the underlying signal \mathbf{Z} is non-negative, we could also add a simple projection step to zero out the negative entries. All the convergence results can be similarly applied.

4 Experiments

We evaluate BRAINZOOM on realistic simulated data. Since in real neuroscience data we do not have access to the ground truth, super-resolution brain activity, it is difficult to assess the performance of our algorithm. Instead of using unattainable ground truth super-resolution brain images, we generate realistic brain signals using an open source framework, the Virtual Brain (TVB) [12], which is able to simulate brain networks with biologically realistic connectivity. TVB implements several well-known neuroscience models, and can produce brain signals with similar patterns as real brain data, as well as generate multi-modal observations such as fMRI, MEG, or EEG, at different sampling rates.

In the following few lines, we describe details of the simulation. First, we select a type of stimulus, and apply it to the brain at a location and time of choice. In this experiment, we use a 3s pulse stimulus, with 3s delay. TVB records the response of the brain to this stimulus, at a very high frequency, with an integration step size of 0.0625ms. From this response we generate our \mathbf{Z} as the temporal average of this raw data, sampled at 200ms.

We show \mathbf{Z} in matrix form in Figure 2, where the horizontal axis represents time (we get 300 samples in time, over a total of 60s), and the vertical axis represents 16384 voxels (vectorized). Next, TVB can create multi-modality observations of this underlying signal. We sample MEG data at 200ms, and fMRI data at 1000ms. The MEG data is produced by TVB by projecting the underlying signal to the surface of the brain, at the predefined location of 248 MEG sensors. This projection is also encoded in our \mathbf{T}_t matrix. The fMRI data is obtained by convolving the brain signal with a hemodynamic response function (hrf) of choice. Here, we chose the Gamma hrf that is given by $f(t) = (\frac{t}{\tau})^{(n-1)} * \frac{\exp(-\frac{t}{\tau_{\text{hrf}}})}{\tau_{\text{hrf}}(n-1)!}$ with the default parameters suggested by TVB. We also encode this hrf in our \mathbf{T}_s matrix. Note that TVB applies this convolution directly on underlying signal \mathbf{Z} , resulting in a simple linear transformation. Since in our method we can model a more complex relationship between fMRI and \mathbf{Z} than TVB does not capture, and we want to test if our algorithm can recover the underlying signal under this condition, we modify fMRI's generative process to capture this non-linearity – i.e., we set the fMRI signal to be the convolution of $|\mathbf{Z}|^2$ and the hrf described above.

Using the fMRI, MEG, \mathbf{T}_s and \mathbf{T}_t thus constructed, we apply our algorithm to recover the super-resolution brain \mathbf{Z} . We show \mathbf{Z} , MEG, and fMRI as space \times time matrices in Figures 3 and 4, respectively. Figure 2 shows our reconstructed \mathbf{Z} , using the smoothing regularizer. One can see that the reconstructed \mathbf{Z} matches the ground truth very well, although the recovering problem is a challenging under-determined non-linear inverse problem. This suggests that the proposed algorithm combined with the smoothness regularization is effective in fusing MEG and fMRI data.

We also map the above space \times time matrices back to brain manifolds at different time points and show some interesting results in Figure 5. Here, we present two fMRIs as in the right column, which are recorded at time points 38.0s and 40.0s, respectively. Before 38.0s, there was no activity in the brain (cf. the upper-left subfigure). At time point 38.0s, a stimulus is presented at three regions of the brain, and the activity spans a duration starting from 38.0s across 40.0s. Our recovered \mathbf{Z} 's at 37.9s and 39.9s – when fMRI are not recorded

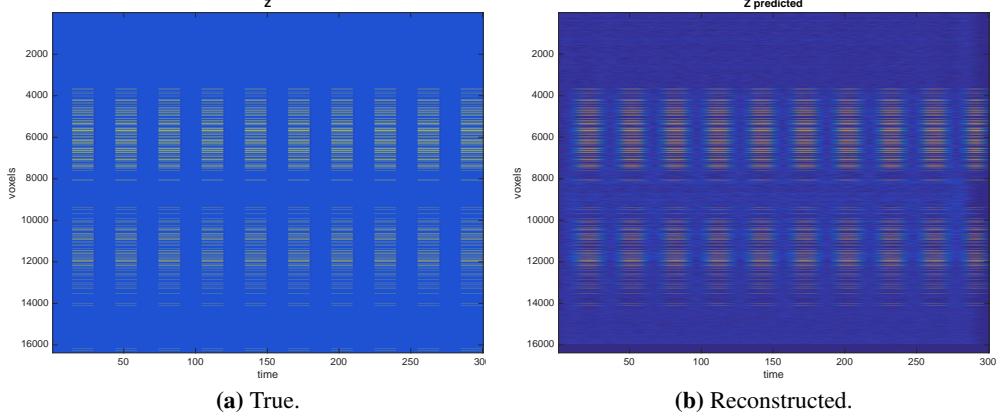


Figure 2: Reconstructed Z matches the ground truth. True Z vs reconstructed Z .

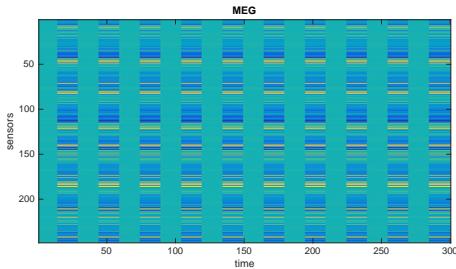


Figure 3: MEG for 248 sensors \times 300 time points, across 60s of simulation.

– are presented in the middle column. One can see that the recovered Z 's match the true Z 's very well. This indicates that our approach correctly interpolate the time points by using the information provided by MEG, thereby achieving temporal super-resolution.

We also show the results obtained by using the minimal energy regularization in Figure 6. It can be seen that the interpolation between 39.0s and 40.0s is not as clear as we have seen in Figure 5. In addition, at the time point prior to the stimulus being present, there is an obvious artifact (bright spot) near the right edge of the estimated brain. This suggests that under the considered signal model, smoothness is a more promising regularizer.

5 Conclusions

Estimating high spatial-temporal neural activity in the brain from multiple imperfect imaging methods is a key to studying and understanding brain function. In this paper we introduce BRAINZOOM, a principled algorithmic tool to address the brain activity super-resolution problem.

Our contributions are as follows:

- **Novel Problem Formulation:** We formulate the problem of recovering a super-resolution image from multi-modal brain signals. To the best of our knowledge, this work is the first to directly address the reconstruction

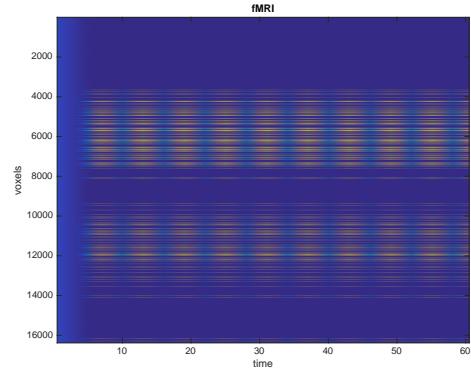


Figure 4: fMRI for 16384 voxels \times 60 time points, across 60s of simulation.

of a *super-resolution brain image for the whole brain*.

- **Efficient Algorithm:** We propose BRAINZOOM, an algorithmic framework that

- handles non-linearity through variable splitting
- learns the unknown scaling between multi-modal signals
- incorporates a large number of regularizations
- admits simple and efficient iterative updates
- provably converges

- **Evaluation:** Our experimental results on the realistic simulated data matches with intuition. Both the space \times time plots of the estimated super-resolution matrices and the brain-manifold illustration show that our recovered space-time super-resolution brain matches with the ground-truth very well.

- **Reproducibility:** We are planning to release our source code and data upon publication. Furthermore, in order to foster and encourage reproduction and extension of our work, we describe in detail how we generate realistic data using an open source brain simulator which is widely used by neuroscientists.

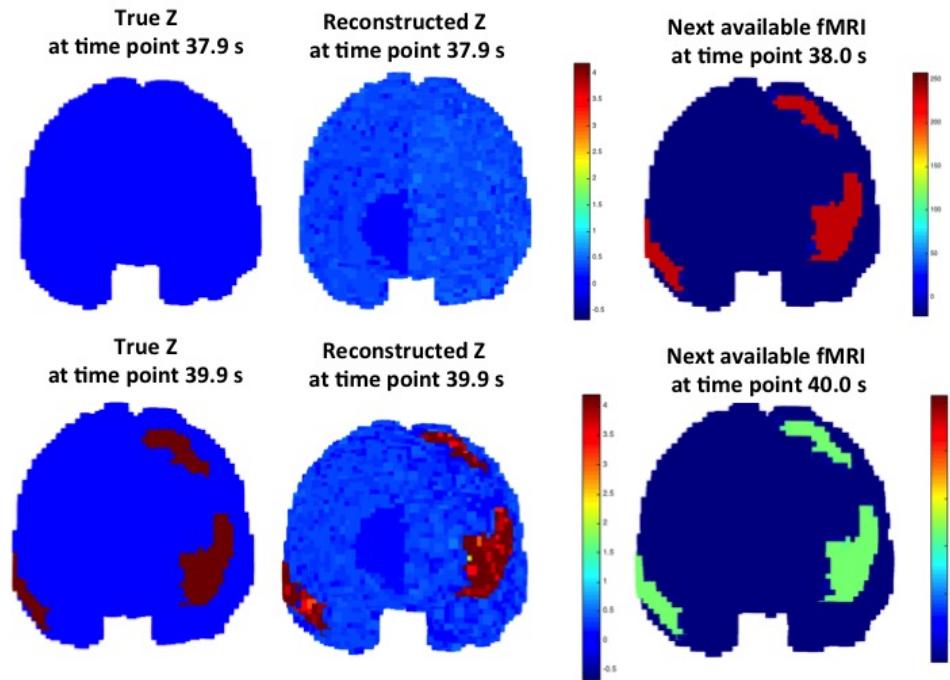


Figure 5: Smoothness regularizer recovers well. True brain activity, predicted brain activity and fMRI at two time points: when the stimulus is present (top row), and when it is absent (bottom row). Reconstructed Z is by using the smoothness regularizer and $\lambda = 1,000$.

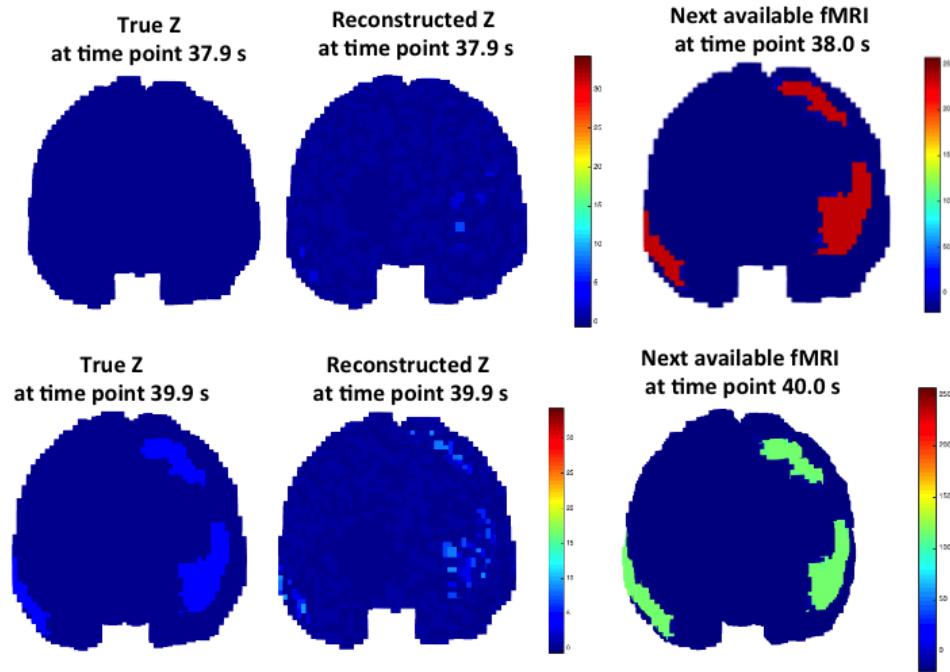


Figure 6: Minimal energy regularizer fails to recover. True brain activity, predicted brain activity and fMRI at two time points: when the stimulus is present (top row), and when it is absent (bottom row). Reconstructed Z is by using the minimal energy regularizer.

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