Supervised Autoencoders Learn Robust Joint Factor Models of Neural Activity

Austin Talbot¹, David Dunson¹, Kafui Dzirasa²,⁴, and David Carlson³,⁵

¹Department of Statistical Science
²Department of Psychiatry
³Department of Biostatistics and Bioinformatics
⁴Department of Neurobiology
⁵Department of Civil and Environmental Engineering

Abstract

Factor models are routinely used for dimensionality reduction in modeling of correlated, high-dimensional data. We are particularly motivated by neuroscience applications collecting high-dimensional ‘predictors’ corresponding to brain activity in different regions along with behavioral outcomes. Joint factor models for the predictors and outcomes are natural, but maximum likelihood estimates of these models can struggle in practice when there is model misspecification. We propose an alternative inference strategy based on supervised autoencoders; rather than placing a probability distribution on the latent factors, we define them as an unknown function of the high-dimensional predictors. This mapping function, along with the loadings, can be optimized to explain variance in brain activity while simultaneously being predictive of behavior. In practice, the mapping function can range in complexity from linear to more complex forms, such as splines or neural networks, with the usual tradeoff between bias and variance. This approach yields distinct solutions from a maximum likelihood inference strategy, as we demonstrate by deriving analytic solutions for a linear Gaussian factor model. Using synthetic data, we show that this function-based approach is robust against multiple types of misspecification. We then apply this technique to a neuroscience application resulting in substantial gains in predicting behavioral tasks from electrophysiological measurements in multiple factor models.

1 Introduction

Analyzing and interpreting neural dynamics involves finding patterns in large datasets, both in terms of the dimensionality of the measurements as well as the number of observations [1]. Neuroscientists often resort to dimensionality reduction to make sense of their data. This is commonly done through factor models [2, 3, 4], in which a small number of latent variables explain the variance of the high dimensional data. Modeling the data this way has several benefits. First, lower dimensional representations can increase statistical power by ameliorating issues stemming from multiple hypothesis testing [5]. Second, carefully designed factors in neuroscience can have intuitive biological meaning as “networks” [6]. Third, the loadings from some factor models can be interpreted to generate new biological hypotheses for further experimentation [7]. Commonly
used factor analysis-type approaches include principal component analysis (PCA) [8], non-negative matrix factorization (NMF) [9], latent Dirichlet allocation [10], independent component analysis (ICA) [11], and many other techniques.

In our motivating applications, the data quantify electrophysiological signals, such as electroencephalograms (EEG) [12], local field potentials (LFPs) [13], or neuron firing (spiking) [14]. While finding networks that explain brain activity is important, it is not sufficient. To answer relevant scientific questions, the networks must both explain observed patterns in the activity data and relate to a specific 'outcome', such as behavior [15], genotype [16], or experimental condition [17]. It is well known that the factors explaining most of the variability in a set of predictors are commonly not the most predictive of an outcome [18]. This is certainly true in neuroscience; for example, the leading factors underlying activity may relate to motion but not to a specific neuropsychiatric disorder of interest.

In order to target learning of factors more to prediction, joint models have been widely used. In a joint factor model, unobserved latent variables give rise to both the outcome and predictors, usually with the assumption of conditional independence given the factors. One example is supervised probabilistic PCA [19], which corresponds to probabilistic PCA [8] with distinct variances for the predictors and outcome. Such models are appealing in neuroscience by providing an explicit relationship between electrophysiological data and outcomes. In addition, prediction is straightforward; for test individuals, we simply learn the posterior distribution of the latent factors given only the predictors, and then use the predictive distribution of the outcomes given the inferred latent factors. When the model is well specified, such an approach leads to Bayes optimal predictions.

However, misspecifying a joint model can severely impact the model’s utility for prediction. In particular, it has been documented that underestimating the number of latent factors can destroy predictive ability [20]. The intuitive cause is that when fitting the model jointly, the variance of the predictors often vastly outweighs the variance of the outcome. Hence, if factors are a scarce resource, they will be used to improve characterization of the predictor distribution at the expense of predictive accuracy.

In practice, all models of neural dynamics are merely approximations to the true brain mechanics. Neural dynamics are notoriously complex, which is not surprising given the large amount of work needed for the body to simultaneously maintain homeostasis, move, analyze sensory inputs, make decisions, and so on. It is reasonable to assume that any factor model substantially underestimates the number of true factors underlying neural activity. Thus, any model seeking to predict behavior using neural dynamics must be robust to this type of misspecification.

We provide a new inference method for factor models based on supervised autoencoders [21], a technique used with great success in image recognition, especially in the context of semi-supervised learning [22, 23, 24]. An autoencoder is a method for dimensionality reduction that maps inputs to a low dimensional space using a neural network known as an “encoder.” These latent spaces are then used to reconstruct the original observations by a neural network called a “decoder” [?]. Both the encoder and the decoder are learned simultaneously to minimize the reconstructive loss. Supervised autoencoders add another transformation from the latent factors to predict the outcome of interest, thus encouraging the latent factors to represent the outcome well [25, 26, 27]. While autoencoders are deterministic, variational autoencoders [28] use a stochastic mapping to approximate the conditional distribution of the scores given the predictors, and can approximate posterior distributions and yield statistical interpretations.

Our modified inference method, which we call encoded supervision, yields substantially better
predictions of the outcome under model misspecification. This robustness to misspecification is demonstrated on synthetic data. We also show substantial gains in predictive performance of behavioral tasks from electrophysiology in applied neuroscience datasets. We provide some technical support for encoded supervision, showing the estimator is distinct from previous estimators, and giving analytic solutions when both the predictors and outcome are normally distributed in a linear factor model.

In Section 2 we introduce the data motivating this study, as well as highlighting the deficiencies of existing methods in analyzing these data. In Section 3 we introduce the proposed encoded supervision approach. Section 4 provides simulation studies assessing the performance under misspecification. In Section 5 we demonstrate improvements for our motivating data. Finally, in Section 6 we provide a discussion of our method and further directions.

The codes to implement the methods we describe below are publicly available at [https://github.com/carlson-lab/encodedSupervision](https://github.com/carlson-lab/encodedSupervision).

## 2 Data and Scientific Motivation

### 2.1 Electrophysiology: Tail Suspension Test

Our motivation comes from recent applications in neuropsychiatric research with the explicit goal of characterizing the brain dynamics responsible for mental illnesses at a network level [29, 7, 30]. In these examples, the data come from mouse models of neuropsychiatric disease performing behavioral tasks. During these tasks the electrical activity is measured in multiple brain regions through implanted electrodes [31]. The measured signals are known as Local Field Potentials (LFPs) and are believed to reflect the aggregate behavior of hundreds of thousands of neurons [32]. Compared to individual neurons, LFP signals have been found to be more consistent between individuals, motivating their use to find common patterns of neuropsychiatric disorders in a population. Our goal is to model this electrical activity (the predictors) with factor models and relate the factors to behavior (the outcome), which could potentially be used to develop new treatments [29].

We focus on using our methods to identify a whole brain network associated with stress [29]. In this experiment, 26 mice were recorded from two genetic backgrounds (14 wild type and 12 genetically modified CLOCKΔ19). The CLOCKΔ19 genetic modification is a mouse model of bipolar disorder [33]. Each mouse was recorded for 20 minutes across 3 behavioral contexts: 5 minutes in its home cage (non-stressful), 5 minutes in an open field (arousing, mildly stressful), and 10 minutes suspended by its tail (highly stressful). For our purposes, we want to determine a network that predicts stressful activity, so we consider all data from the home cage as the negative label (stress-free condition) and all data from the other two conditions as the positive label (stressed condition). A second prediction task is to determine brain differences between the genetic conditions (i.e., what underlying differences are there between the wild type and bipolar mouse model?). Data were recorded from 11 biologically relevant brain regions with 32 electrodes (multiple electrodes per region) at 1000 Hz. Data from faulty electrodes were removed, and the time series were averaged per region to yield an 11-dimensional time series per mouse. A visualization of these data can be seen in Figure 1.

There is strong evidence to support the belief that the behaviorally relevant aspects of electrophysiology are frequency-based power within brain regions, as well as frequency-based coherence between brain regions [34, 35]. To characterize the dynamics in the LFPs we discretized the time
For our purposes any model must: (1) characterize the powers and coherences in terms of latent factors, (2) relate these factors to the observed behavior, and (3) yield interpretable loadings that can be used to construct testable hypotheses to establish causality in follow-up experiments. Following our recent work [7, 30], we will use a factor modeling framework and will explore how our proposed model fitting helps satisfies these conditions.

First, we previously proposed a latent function factor model called Cross-Spectral Factor Analysis (CSFA) [7]. This approach modeled the observed time series as a weighted superposition of Gaussian processes with a Cross-Spectral Mixture (CSM) kernel [36]. This kernel is constructed to capture power and coherence properties of the data, yielding interpretable networks that were previously called electrical connectome (electome) networks [30]. We denote this approach as CSFA-CSM in the rest of the manuscript. The mathematical framework of this model has been previously published and we give critical mathematical details in Appendix D.

Instead of directly modeling the time series, a second approach is to first extract the relevant quantities from the recorded data prior to modeling. Specifically, we first calculated the spectral power from 1 Hz to 56 Hz in 1 Hz bands using Welch’s method [37], which is recommended in the neuroscience literature [38]. Prior literature has demonstrated that most of the important information is in lower frequencies, so we only used information up to 56Hz. Mean squared coherence was calculated in the same frequency bands for every pair of brain regions [39]. After these preprocessing steps, each window of data was converted to 3696 non-negative power and coherence features. A visualization of what these features look like can be found in Figure 2.

Given these spectral estimates, we then can use a non-negative matrix factorization approach to extract the electome networks and feature scores, which we denote as CSFA-NMF. The non-negative formulation provides a better biological interpretation: individual features are only positive (e.g. power and coherence) and the networks are either active or inactive in the measured data. We provide additional details on the model and inference in Appendix C.

While both CSFA-CSM and CSFA-NMF are useful in these neuroscience applications in their own right, we want to encourage the learned representations to be predictive of our outcome of interest. This motivates our interest in supervised factor modeling (or supervised dimensionality reduction) approaches to improve the scientific utility.

Figure 1: On the left we show example LFP recordings in a subset of the regions measured. The LFPs were divided into one second windows to yield discrete observations. On the right we provide a simple diagram of the TST experiment. The mice were recorded in the home cage as a non-stressful environment. They were then recorded for 5 minutes in a mildly stressful open field test (OFT) and then 10 minutes in a highly stressful tail suspension test (TST).
Figure 2: A visualization of the features used for CSFA-NMF. On the left we show a 1-second window for the LFPs in two brain regions. The middle shows the power spectra for each LFP from 1-56 Hz estimated using Welch’s method. The right shows the mean squared coherence, which we used to quantify the coherence between the two LFPs. We show two channels for clarity, in practice we have many channels and calculate all pairwise coherences.

2.2 Difficulties with Existing Methods

There is a substantial literature on estimating latent spaces predictive of an outcome. Joint modeling and supervised autoencoders are two of the most prominent methods for this objective. Joint modeling methods have had successes \[19\], but are unfortunately not robust. In particular, since the variance of the outcome is generally small relative to the predictors, it is often necessary to increase the importance of the outcome in order to make it influence the estimated model. As the relative importance of the outcome increases, however, it makes the posterior estimation of the factors highly dependent on the knowledge of the outcome. At test time, when the outcome is unknown, the inferred factors have greatly changed estimates, an effect we refer to as factor dragging. We detail this effect in our simulations in Section 4. This creates a challenging situation, where we must choose between making the outcome irrelevant for estimating the model or making the estimation of the factors rely on knowledge of the outcome. Several techniques have been explored to address these issues.

One widely studied approach is sufficient dimensionality reduction (SDR), which exploits the assumption that the response is conditionally independent of the predictors given a projection of the predictors to a lower dimensional subspace. Sliced inverse regression provides one popular example of an SDR approach \[40\]. A related statistical technique is to first use some form of regularized regression to find a subset of the predictors related to the outcome, and then learn a factor model on the reduced set \[41\]. A major issue with SDR-type methods in our motivating neuroscience applications is that the focus is entirely on prediction and not on simultaneously providing an accurate lower-dimensional characterization of the predictors (in our case, brain activity dynamics, or the electome networks).

In an attempt to improve upon robustness to misspecification in joint modeling, “cutting the feedback” approaches have been proposed \[42, 43, 44\]. When used in an MCMC method, the samples on the latent variables are estimated using only the predictors (hence the influence from the outcome is cut). A variety of justifications have been given including when the model is flawed \[42\], the outcome is unreliable \[43\], or for handling missing data in meta-analysis \[45\]. While these approaches have been successful for some applications in joint modeling, they yield subpar results as we later show in Section 5. The primary issue is that the methods require that the relevant information for the classification is captured in the highest variance components. Unfortunately, in our application the factors that explain the largest amount of variance are relatively unpredictable.
(a common issue in statistics [18]), as networks related to motion [46] or even blinking [47] can be particularly dominant.

3 Encoded Supervision

3.1 Joint Modeling

Before introducing our model fitting framework, we first introduce a standard joint modeling approach. We denote \( \{x_i\}_{i=1}^{N} \in \mathcal{X} \) as the measured predictors and \( \{y_i\}_{i=1}^{N} \in \mathcal{Y} \) as the corresponding outcome. The latent factors are denoted \( \{s_i\}_{i=1}^{N} \in \mathcal{S} \). A generic objective function to fit a joint factor model is

\[
\max_{\Phi, \Theta, \{s_i\}_{i=1}^{N}} \sum_{i=1}^{N} \log p(x_i | s_i, \Theta) + \mu \log p(y_i | s_i, \Phi). \tag{1}
\]

In this model, \( \Theta \) corresponds to the parameters relating the factors to \( x \) and \( \Phi \) corresponds to the parameters relating the factors to \( y \). A standard maximum likelihood approach would use \( \mu = 1 \); however, in practice \( \mu \) is often modified to upweight the importance of predicting the outcome by taking \( \mu > 1 \). Given this objective function, we find the optimal values of the latent factors, \( \Theta \), and \( \Phi \), which can be effectively done through stochastic gradient methods [48]. Because the latent variables are referred to as “local” variables for these stochastic methods, we denote this strategy as “local supervision,” and we modify this approach below.

As mentioned in the introduction, this approach is successful when the model is properly specified. Unfortunately, though, it is not robust to model misspecification, which is prevalent in our application.

3.2 Encoded Objective Function

Our primary modification to Equation 1 is that we require that latent variables to be estimated exclusively by the information given in \( x \), which would enforce that our latent variable estimates are the same whether or not \( y \) is observed. However, we still want \( y \) to influence how we learn our model parameters. Our strategy to accomplish this is to require that \( s = A(x) \), where \( A : \mathcal{X} \to \mathcal{S} \) is a function that maps the predictors to the latent factors, which we call the “encoder.” The encoder ensures that the latent variables are only determined by \( x \), but we want the encoded values to still be predictive of \( y \). These modifications yield our novel objective function of

\[
\max_{\Phi, \Theta, A} \sum_{i=1}^{N} \log p(x_i | s_i = A(x_i), \Theta) + \mu \log p(y_i | s_i = A(x_i), \Phi). \tag{2}
\]

While the encoder can take any functional form, it is often useful to limit the complexity to address overfitting concerns. The simplest useful encoder is an affine transformation \( A(x) = Ax + b \). As in Equation 1, \( \mu \) is a tuning parameter that controls the relative focus on predicting \( y \) from the latent space.

At first glance, Equations 1 and 2 seem trivially different; however, despite superficial similarities, this inference approach results in different behavior under model misspecification. To help
understand why, we can think of Eq. 2 as a Lagrangian relaxation of a constrained optimization objective,

\[
\max_{A, \Theta, \Phi} \sum_{i=1}^{N} \log p(x_i | s_i = A(x_i), \Theta) \\
\text{s.t.} \sum_{i=1}^{N} \log p(y_i | s_i = A(x_i), \Phi) \geq C.
\]

(3)

In this formulation, it is clear that our method is finding a latent representation of \( x \) that requires \( y \) be predictable by using the information in \( x \) alone. This contrasts to the effects happening in Eq. 1, where the factors are dragged by the information in \( y \), especially as \( \mu \) increases. This property will make the solution found in this approach much more robust to model mismatch, and also decreases the sensitivity to whether the information pertinent to classification is a dominant source of variance in \( x \).

### 3.3 Analytic solutions with a \( L_2 \) Loss

Most encoded supervision and joint models do not have analytic solutions, but we can obtain analytic solutions to Equations 1 and 2 in specific scenarios. One such case is when the likelihood is replaced with an \( L_2 \) loss. This yields a form similar to PCA, which can be viewed as the limiting case of probabilistic PCA as the variance of the conditional distribution goes to 0 \[49\].

We define the encoder as a linear transformation \( s_i = Ax_i \) in the encoded inference strategy. For convenience, we will define matrix forms of the data and factors:

\[
X = \begin{bmatrix} x_1, \ldots, x_N \end{bmatrix} \in \mathbb{R}^{p \times N}, \quad Y = \begin{bmatrix} y_1, \ldots, y_N \end{bmatrix} \in \mathbb{R}^{q \times N}, \quad S = \begin{bmatrix} s_1, \ldots, s_N \end{bmatrix} \in \mathbb{R}^{L \times N}.
\]

We let the model parameters \( \Theta = W \) and \( \Phi = D \) for matrices \( W \in \mathbb{R}^{p \times L} \), \( D \in \mathbb{R}^{q \times L} \) and \( \|X\|_F \) be the Frobenius norm.

First, we focus on the solution that comes from the “local” approach in which \( s \) is learned from both \( x \) and \( y \). This decomposition and its solution are well-known except for the minor extension due to the \( \mu \) term. Following simplifications, the objective is

\[
\max_{W, D, S} \sum_{i=1}^{N} \frac{1}{2} \|x_i - WS_i\|_F^2 - \mu \frac{1}{2} \|y_i - WS_i\|_F^2.
\]

Rewriting the above objective in matrix form as a minimization problem yields

\[
\min_{W, D, S} \|X - WS\|_F^2 + \mu \|Y - DS\|_F^2.
\]

The solution for the concatenation of \( W \) and \( D \), \( \begin{bmatrix} W \\ D \end{bmatrix} \), can be found as an eigendecomposition of the matrix

\[
B = \begin{bmatrix} XX^T & \mu X Y^T \\ Y X^T & \mu Y Y^T \end{bmatrix}.
\]

(4)

Predicting \( S \) when \( Y \) is unknown is a simple projection of the data onto the latent space, \( S = (WW^T)^{-1}WX \). This solution form is well-known from PCA except for the minor extension with \( \mu \). The derivation of Equation 4 is given is Appendix A.1.

Next, we will focus on deriving the solution for encoded supervision, which can be similarly rewritten in terms of minimizing an \( L_2 \) loss. We assume a linear encoder, \( A(x) = Ax \). Once again,
we start with the $L_2$ loss corresponding to Equation \[2\] as

$$
\max_{\mathbf{W}, \mathbf{D}, \{s_i\}_{i=1,...,N}} \left\{-\sum_{i=1}^{N} \frac{1}{2} \left\| x_i - \mathbf{W} \mathbf{A} x_i \right\|_2^2 - \mu \frac{1}{2} \left\| y_i - \mathbf{W} \mathbf{A} x_i \right\|_2^2. \right\}
$$

(5)

This can be rewritten as a minimization in matrix form as

$$
\min_{\mathbf{W}, \mathbf{D}, \mathbf{A}} \left\| \mathbf{X} - \mathbf{W} \mathbf{A} \mathbf{X} \right\|_F^2 + \mu \left\| \mathbf{Y} - \mathbf{D} \mathbf{A} \mathbf{X} \right\|_F^2.
$$

The solution for the concatenation of $\mathbf{W}$ and $\mathbf{D}$ is also an eigendecomposition, but with a different matrix

$$
\mathbf{B} = \begin{bmatrix}
\mathbf{X}^T & \mu \mathbf{Y}^T \\
\mu \mathbf{Y} \mathbf{X}^T & \mu \mathbf{Y} \mathbf{P} \mathbf{X} \mathbf{Y}^T
\end{bmatrix},
$$

(6)

where $\mathbf{P}_\mathbf{X} = \mathbf{X}^T(\mathbf{X} \mathbf{X}^T)^{-1}\mathbf{X}$ is the projection matrix on $\mathbf{X}$. In contrast to the local supervision approach, the mapping to the latent factors is the same regardless of whether $\mathbf{Y}$ is observed. We provide the derivation of Equation \[6\] in Appendix A.2.

While finding an analytic solution is helpful computationally when using these models, it also provides insight as to practical differences between the two forms. When $\mu = 1$, the solution for Equation \[4\] is easily recognizable as the solution for PCA on the predictors and outcome jointly. The solution for Equation \[6\] is different due only to the addition of the term $\mathbf{P}_\mathbf{X}$. In this case it maximizes the variance explained by $\mathbf{x}$ and the variance of $\mathbf{y}$ to the extent that it is linearly predictable by $\mathbf{x}$. This makes sense in terms of the original objectives of the learning and inference strategy because the estimated scores are unaffected when $\mathbf{y}$ is unknown.

3.4 General Inference

The encoded supervision formulation given in Equation \[2\] can be used with many different modeling formulations. A more general form is

$$
\min_{\mathbf{A}, \mathbf{\Theta}, \Phi} \sum_{i=1}^{N} \mathcal{L}(\mathbf{x}_i|s_i = \mathbf{A}(\mathbf{x}_i), \mathbf{\Theta}) + \mu \mathcal{L}(\mathbf{y}_i|s_i = \mathbf{A}(\mathbf{y}_i), \Phi),
$$

(7)

where $\mathcal{L}$ is a loss measuring the distance between the estimated value of $\mathbf{x}$ or $\mathbf{y}$ to the observed value. This loss can easily be minimized by stochastic gradient descent, facilitating easy scalability to large datasets. This is of vital importance as our datasets contain millions of high-dimensional observations. Stochastic gradient descent has rigorous convergence proofs under mild conditions \[50\] and adaptive learning methods can improve computational efficiency and decrease parameter tuning \[51, 52\]. When used with packages such as Tensorflow \[53\] that allow for automatic differentiation, a unique statistical model can be implemented with a few lines of code and inference performed in a matter of minutes.

4 Simulation Study

The two main types of model misspecification that concern us are using fewer latent factors than are truly needed to represent the data, as well as an incorrect latent distribution. Prior to analyzing
our data of interest, we use synthetic data to illustrate that encoded supervision is robust to both of these difficulties.

We also found that the encoded supervision was comparatively robust to the chosen $\mu$ even when all other properties are properly specified. Since that value can be cross-validated, this is a practical advantage, but less important in these studies. A visualization of this property is shown in Appendix E.

4.1 Misspecified Number of Latent Factors

We first examine misspecification in the number of latent factors. We synthesized data with the generative model corresponding to Supervised Probabilistic PCA [19], which is a joint linear latent factor model. We set the number of predictors to 20 with a single outcome and the latent dimensionality was 3. The largest factor was unpredictive of the outcome. Additionally, we limited the inferred dimensionality to 2. This mimics our biological models that under-specify the true number of brain networks.

We fit a locally supervised and encoded supervised PCA model with 2 components over a range of supervision strengths using the formulas derived in Section 3.3 and show the results in Figure 3.

Both the local and encoded supervision methods yield worse reconstructions of the data when the model is forced to be predictive (high $\mu$), which is expected as the highest variance component is unpredictive of outcome. In the local supervision approach, though, the improved prediction of $y$ is contingent upon knowing $y$. Specifically, when $y$ is known the model overfits, forcing the prediction loss to vanish. However, when $y$ is unknown there are only slight initial gains in predictive ability before overfitting actually leads to worse predictions. In contrast, the ability to predict $y$ does not depend on the observation of $y$ in the encoded scenario, so it is more robust and predicts better.
Additionally, because the encoded supervised approach only uses \( x \) to predict \( y \), it corresponds to better reconstruction of the predictors when the outcome is unknown.

### 4.2 Unknown Latent Distribution

We chose NMF with a binary classification problem to illustrate the impact of an unknown latent distribution and unknown number of factors. For this example we wanted the data to be more complex but still know the true model behind the system. To illustrate this, we created a pseudo-synthetic dataset from the Fashion-MNIST dataset by fitting a 40 component NMF model from the data and then generating the synthetic data as the reconstruction of the original data plus noise. Thus the synthetic data come from a known NMF model with 40 components. However, the distribution on the latent scores needed to create a probabilistic model is still unknown, making this an ideal demonstration of the utility of encoded supervision and contrasts to the situations above where the latent scores were generated from a known Gaussian distribution.

To simplify our synthetic example, we limited ourselves to three binary classification problems. For each classification problem we selected the relevant observations and trained a supervised model and evaluated the AUC on a hold-out test set. We trained a locally supervised and encoded supervision model with 5 components, creating an analogous situation where the fitted model severely underestimates the true dimensionality of the data. As comparison methods, we also fit logistic regression on the original NMF features used to generate the data. We compared local and encoded supervision to a sequentially fit model. The sequential model first fits an NMF to the images and then applies a logistic regression model.

Table 1 shows the results of the different prediction methods. Encoded supervision matches the performance from logistic regression on every classification task and dramatically improves upon the local supervision. The sequentially fit model matches the performance on a single category but lags substantially on the other two classification tasks. The case in which the performance is the same corresponds to when one of the highest variance components is predictive of the outcome, so the NMF captures this feature. However, encoded supervision is able to provide consistently good predictions irregardless of the relative importance of the predictive features in the generative model.

| Method                     | Pullover/Shirt | T-shirt/Shirt | T-shirt/Coat |
|----------------------------|----------------|---------------|--------------|
| Linear model on ground truth NMF | 0.84           | 0.90          | 0.90         |
| Sequential NMF             | 0.78           | 0.90          | 0.76         |
| Local Supervision NMF      | 0.76           | 0.82          | 0.71         |
| Encoded Supervision NMF    | 0.85           | 0.89          | 0.89         |

Table 1: A comparison of supervision methods in the synthetic Fashion-MNIST dataset. The top row gives the AUCs generated using logistic regression on the “true” 40-component NMF model. We then compare competing supervision methods for sequential, local supervision, and encoded supervision. Encoded supervision consistently matches the best linear predictions using the true model. While sequential training matches the performance in one case because a predictive factor happened to explain a high amount of variance, encoded supervision is consistent even when this is not the case.
5 Learning Relevant Electome Networks

We now evaluate the performance of encoded supervision on data described in Section 2. There are two classification tasks, differentiating between the two genotypes and differentiating between the experimental conditions (stress biomarker). All models were implemented in Tensorflow and fit with the NADAM stochastic gradient method [52]. Previously, the local supervision solution was referred to as discriminative CSFA (dCSFA) [7], so we denote local supervised approaches as dCSFA in the tables.

First, we evaluated the different fitting approaches on CSFA-NMF using the derived power and coherence features to learn 5 networks. The loadings were constrained to have unit norm. We also placed an $L_1$ penalty on the supervision coefficients to encourage sparsity and prevent overfitting. All network details can be found in Appendix C. We compared a sequential method, local supervision, and then our encoded supervision approach. In our experiments, 18 mice were used for training the model and a set of 8 mice was reserved for testing.

For our applications, it is imperative that networks both predict outcome and use relevant neural activity so that they are biologically meaningful. Thus, we care both about the outcome prediction metrics and the reconstruction ability. In these experiments, cross-validating over $\mu$ is computationally expensive, so we chose $\mu$ such that the reconstruction log-likelihood and the supervision log-likelihood had similar magnitudes. The results are shown in Table 2. In our case, the encoded supervision pays only a small penalty on the reconstruction for a vast and meaningful improvement to the prediction. Notably, the local supervision approach drastically overfits with the chosen value of $\mu$. These results match the same patterns as the synthetic data. We note that if the value of $\mu$ were fully cross-validated, we would expect that the local supervision should at least match the same performance as the sequential method; however, that is not tractable. Instead, it is preferable in practice on large-scale data to have a method that is fairly robust to this chosen value. The most predictive brain network from the encoded CSFA-NMF is shown in Figure 4.

| Method            | Genotype | Condition |
|-------------------|----------|-----------|
|                   | Predictive AUC | Generative $L_2$ Loss | Predictive AUC | Generative $L_2$ Loss |
| CSFA-NMF          | 0.57 ± 0.02 | 0.21 ± 0.001 | 0.77 ± 0.01 | 0.21 ± 0.001 |
| dCSFA-NMF         | 0.54 ± 0.001 | 0.21 ± 0.01 | 0.78 ± 0.01 | 0.21 ± 0.03 |
| Encoded CSFA-NMF  | 0.66 ± 0.02 | 0.29 ± 0.01 | 0.93 ± 0.002 | 0.28 ± 0.01 |

Table 2: A comparison of supervised CSFA-NMF models in the TST dataset. We compare sequential fitting, local supervision and encoded supervision, where the local and encoded supervision use a single chosen value of $\mu$. Once again, encoded supervision matches the performance of logistic regression and substantially outperforms sequential and local supervision, particularly for predicting genotype.

As a demonstration of the general applicability of encoded supervision, we next applied encoded supervision on the same dataset using the CSFA-CSM algorithm [7]. For the encoder we use an affine transform with a softplus activation to ensure non-negativity of the factors. While the log-likelihood uses the original data, we used the same power features derived used in CSFA-NMF as input to the encoder (directly using the time series data would require the development of a more complex convolutional neural network encoder). To reflect a common goal in neuroscience, we induce sparsity by limiting a single network to be predictive, which also addresses the multiple
Figure 4: A brain network negatively associated with the CLOCKΔ19 genotype as found by encoded CSFA-NMF. The colored bands on the rim indicate power in the particular brain region at a given frequency. The spokes on the wheel indicate coherence between the regions. This network is characterized by power in the dorsal hippocampus at 3-8 Hz and power at the 10-30 Hz range in the VTA and medial substantia nigra. This provides a useful network for neuroscientists to explore the relationship between neural dynamics and bipolar disorder.

comparisons problem. Our CSFA models for the encoded, local and generative models included 25 networks. Computational limitations precluded cross-validating over supervision strength for local supervision, hence we set $\mu = 10.0$, where the supervision loss was approximately 10 percent of the total loss.

The classification results comparing the different approaches using the CSM kernel are given in Table 3. As we can see, the encoded supervision dramatically outperforms local supervision and the sequential method on both classification tasks, likely due to the fact that dominant brain networks in variance are rarely directly related to neuropsychiatric disorders. For CSFA-NMF, the estimated network from encoded CSFA-CSM is visualized in Figure 5.

| Method            | Predictive AUC | Negative Log Likelihood | Predictive AUC | Negative Log Likelihood |
|-------------------|----------------|-------------------------|----------------|-------------------------|
| CSFA-CSM          | 0.49 ± 0.3     | 98.1 ± 0.8              | 0.54 ± 0.01    | 98.1 ± 0.8              |
| dCSFA-CSM         | 0.53 ± 0.1     | 94.0 ± 0.9              | 0.53 ± 0.1     | 92.8 ± 1.0              |
| Encoded CSFA-CSM  | 0.63 ± 0.1     | 89.7 ± 0.3              | 0.94 ± 0.01    | 90.7 ± 0.24             |

Table 3: A comparison of supervised CSFA-CSM models with the TST dataset. Notably, neither CSFA-CSM nor the local supervision approach, dCSFA-CSM, capture the genetic differences in the electrophysiological signals. In stark contrast, the encoded supervision approach easily captures useful signals in both contexts, providing huge gains in the predictive task.
Figure 5: The CSFA network negatively correlated with stress. Bands on the edges indicate the network involves power in the specific brain region, while spokes indicate coherence between two regions. Thus, this network is characterized by power at 50 Hz in the basal lateral amygdala as well as the nucleus acumbens. This is accompanied by greater coherence between these regions as well as the ventral tegmental area, prefrontal cortex, and thalamus.

While these approaches have differences in the way that they model the data, the encoded supervision uniformly provides gains in predictive accuracy. In our experience, in these real datasets, the methodology was reliable and robust to the exact setting of the supervision strength, mirroring the synthetic examples.

Finally, the encoded supervision was much faster, and a single model was trained in approximately half an hour for CSFA-NMF and one hour for CSFA-CSM using a single NVIDIA 2080 Ti GPU, while the local supervision took roughly 10 hours for CSFA-NMF and 16 hours for CSFA-CSM. The NMF models were initialized to the learned parameters from the NMF implementation in scikit-learn \cite{54} to both have a robust initialization and save time. While both the CSFA-CSM models and CSFA-NMF models are non-convex, we empirically found that the results were robust to different random initialization, yielding similar predictive performance and a similar predictive factor.

6 Discussion

Supervised dimension reduction is useful in neuroscience, as most datasets involve explaining variance in high-dimensional observations. Reducing the dimensionality can increase statistical power, and carefully designed factor models can have useful biological interpretation as networks. However, these benefits are contingent upon capturing the information related to outcome in the latent space. A joint factor model fit by maximum likelihood has been shown to be susceptible to mis-specification, a common occurrence in neuroscience and many other fields.
Our formulation for supervised factor models, based on supervised autoencoders, differs from previous methods in that we maximize a constrained optimization, yielding a latent representation that explains the variation in the observed predictors while requiring that the factors estimated from the observed predictors alone give good predictive performance. We find that our model formulation is substantially more robust to misspecification than approaches that maximize a joint likelihood. In our practical real-data experiments, this led to significant gains in predictive performance. These gains appear for multiple generative models with vastly different likelihoods.

This work can be easily extended in several new directions. Replacing a deterministic mapping with a stochastic one similar to a variational autoencoder could help with our potential for overfitting the predictions and quantify our uncertainty in the network scores. Additionally, combining the developed approach with missing data models would increase practical utility, as different experiments often focus on different subsets of brain regions.

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A Proof of Analytic Solutions in Linear Factor Models

Below we give the accompanying proofs for Section 3.3, which focus on PCA-like solutions for the local and encoded supervision models.
A.1 Local Supervision

We first restate the optimization goal from Equation 4 showing that local supervision with linear models can be rewritten in matrix form as

$$\min_{W,S,D} \|X - WS\|^2_F + \mu \|Y - DS\|^2_F.$$  

This is equivalent to the trace representation of

$$\min_{W,S,D} \text{Tr}((X - WS)^T(X - WS)) + \mu \text{Tr}((Y - DS)^T(Y - DS))$$

$$\min_{W,S,D} \text{Tr}(X^TX - 2X^TWS + S^TWTWS) + \mu \text{Tr}(Y^TY - 2Y^TDS + S^TD^TDS).$$

We now compute the partial derivatives with respect to $W$, $S$ and $D$ using standard techniques with the aim to find the fixed points where each partial derivative vanishes. First, the partial derivative with respect to $W$ is

$$0 = \frac{\partial F}{\partial W} = -2XS^T + 2WSS^T,$$

$$2XS^T = 2WSS^T,$$

$$W = XTS^T(SS^T)^{-1}. \quad (8)$$

The derivative with respect to $D$ is

$$0 = \frac{\partial F}{\partial D} = -2YS^T + 2DSS^T,$$

$$2YS^T = 2DSS^T,$$

$$D = YS^T(SS^T)^{-1}. \quad (9)$$

And the derivative with respect to $S$ is

$$0 = \frac{\partial F}{\partial S} = -2W^TX + 2W^TWS - 2\mu DT^TY + 2\mu DT^DS,$$

$$2W^TX + 2\mu DT^TY = 2W^TWS + 2\mu DT^DS,$$

$$S = (W^TW + \mu DT^TD)^{-1}(W^TX + \mu DT^TY). \quad (10)$$

We need these conditions to all be satisfied at the fixed point solution to this problem. We will first solve for a single latent feature, so the matrices $W$, $D$, and $S$ are vectors denoted as $w$, $d$, and $s$, respectively. With that, we can rewrite Equation 10 as

$$s = (\|w\|^2 + \mu \|d\|^2)^{-1}(w^TX + \mu d^TY). \quad (11)$$

We denote $\alpha = (\|w\|^2 + \mu \|d\|^2)^{-1}$ and $\gamma = (SS^T)^{-1}$. Since $s$ is a vector both $\alpha$ and $\gamma$ are scalars in this case. Thus, in the single feature case the fixed point equations of 8, 9, and 10 can be written concisely as

$$w = \gamma Xs^T,$$

$$d = \gamma Ys^T,$$

$$s = \alpha(w^TX + \mu d^TY). \quad (12)$$

When we substitute $s$ into the previous equations we end up with

$$w = \alpha\gamma X(X^Tw + \mu Y^Td), \quad (12)$$

$$d = \alpha\gamma Y(X^Tw + \mu Y^Td). \quad (13)$$
Because $\alpha$ and $\gamma$ are scalars, we note that the solution to Equations 21 and 22 must be an eigenvector of

$$B = \begin{bmatrix} XX^T & \mu XY^T \\ YY^T & \mu YY^T \end{bmatrix},$$

where the first part of the eigenvector corresponds to solution of $w$ and the second part corresponds to the solution of $d$. In practice, we have always found that the solution corresponds to the largest eigenvector. Finding further dimensions can be done iteratively by subtracting out the previous variance explained then repeating the procedure. In practice we have found these to be equivalent to the $L$ largest eigenvalues of $B$, which is supported by the fact that when $\mu = 1$ this yields the classic PCA solution.

### A.2 Encoded Supervision

We use a similar procedure as before. Rewriting the encoded supervision objective in matrix form in Equation 6 is

$$\min_{W, D, A} \|X - WAX\|^2_F + \mu \|Y - DAX\|^2_F.$$

Here, the matrix $A$ functions as our linear encoder, with $D$ and $W$ retaining their meaning as the loadings for the outcome and predictors respectively.

We can rewrite this objective in terms of traces as

$$\min_{W, A, D} \text{Tr}((X - WAX)^T(X - WAX)) + \mu \text{Tr}((Y - DAX)^T(Y - DAX))$$

Next, we will find the fixed points by determining when the partial derivatives are 0. The partial derivative for $W$ is

$$0 = \frac{\partial F}{\partial W} = -2XX^T A^T + 2WAXX^T A^T,$$

$$2XX^T A^T = 2WAXX^T A^T,$$

$$W = XX^T A^T (AXX^T A^T)^{-1}. \tag{14}$$

The partial derivative of $D$ is

$$0 = \frac{\partial F}{\partial D} = -2\mu YX^T A^T + 2\mu DAXX^T A^T,$$

$$2YX^T A^T = 2DAXX^T A^T,$$

$$D = YX^T A^T (AXX^T A^T)^{-1}. \tag{15}$$

The partial derivative of $A$ is

$$0 = \frac{\partial F}{\partial A} = -2W^T XX^T + 2W^T WAXX^T - 2\mu D^T YX^T + 2\mu D^T DAXX^T,$$

$$2W^T XX^T + 2\mu D^T YX^T = 2W^T WAXX^T + 2\mu D^T DAXX^T],$$

$$(W^T X + \mu D^T Y)X^T = (W^T W + \mu D^T D)AXX^T,$$

$$A = (W^T W + \mu D^T D)^{-1}(W^T X + \mu D^T Y)X^T (XX^T)^{-1}. \tag{16}$$

We begin by finding the solution when only a single latent variable is used, and can rewrite Equation [16] as

$$a = (\|w\|^2 + \mu \|d\|^2)^{-1}(w^T X + \mu d^T Y)X^T (XX^T)^{-1}.$$
We define the scalars $\alpha = (\|w\|^2 + \mu \|d\|^2)^{-1}$ and $\gamma = (aXX^Ta^T)^{-1}$. Thus, our fixed points in the univariate case are the solutions to the system of equations given as

$$
\begin{align*}
\mathbf{w} &= \gamma X X^T a^T \\
\mathbf{d} &= \gamma Y X^T a^T \\
\mathbf{a} &= \alpha (w^T X + \mu d^T Y) X^T (XX^T)^{-1}.
\end{align*}
$$

Substituting $a$ yields a similar form to the local supervision case, with

$$
\begin{align*}
\mathbf{w} &= \alpha \gamma X X^T (XX^T)^{-1} X (X^T w + \mu Y^T d), \\
\mathbf{d} &= \alpha \gamma Y X^T (XX^T)^{-1} X (X^T w + \mu Y^T d).
\end{align*}
$$

Because $\alpha$ and $\gamma$ are scalars, we note that the solution to Equations 17 and 18 must be an eigenvector of $B = \begin{bmatrix} XX^T & \mu XY^T \\ YX^T & \mu XP Y^T \end{bmatrix}$.

where the first part of the eigenvector corresponds to solution of $\mathbf{w}$ and the second part corresponds to the solution of $\mathbf{d}$. In practice, we have always found that the solution corresponds to the largest eigenvector. Once again, the full solution with $L$ latent variables can be found iteratively, which in practice we have found these to be the $L$ largest eigenvalues of the previous matrix.

### B Implementation of supervised NMF

Our encoded supervision version of NMF was implemented in Tensorflow. The encoder was a neural network with a single hidden layer with a softplus activation function, 30 latent features, and a softmax output layer for classification. The loadings $\mathbf{W}$ were optimized by learning an unconstrained matrix $\mathbf{W}_u$ which was put through a softmax activation function to ensure both non-negativity and normalization such that $\|\mathbf{W}_i\| = \sqrt{p}$. The parameters were learned using Adam with Nesterov momentum (NADAM) as our optimization algorithm with $1 \times 10^5$ iterations. We set $\mu = 10$.0. We used an $L_1$ penalty to regularize the predictive coefficients.

### C Cross Spectral Factor Analysis: Non-Negative Matrix Factorization (CSFA-NMF)

The CSFA-NMF algorithm is based upon the motivation for the originally proposed CSFA algorithm [7]. However, instead of using a Guassian process formulation, the Electrical Connectome Networks are learned by NMF over extracted features that capture relevant properties. In this case, we use Power and Coherence features defined immediately below, and then use our inference strategy to learn a supervised NMF model. Note that it would be natural to extend this strategy with Granger causality features as well.

#### C.1 Generating Power and Coherence Features

The electrophysiological features of interest for these experiments are frequency based power within the brain regions as well as the coherence between the brain regions. While the periodogram, the squared coefficients of a Fourier transform, yields an unbiased estimate of the power spectrum, it is an inconsistent estimator with a fixed variance. There are multiple methods for overcoming this issue, such as spline smoothing or using a parameterized autoregressive model [38]. We instead chose to use Welch’s method [37], which breaks up the signal into subsections and averages the periodogram for each segment, which denoises the estimator. We quantified the coherence using the metric of mean squared coherence [39, 56]. This computes the power
and cross-spectra using Welch’s method and scales the cross-spectrum by the power spectrum of each signal. This yields a value between 0 and 1. The power and coherence were estimated in Matlab using the functions pwelch and mscohere respectively with the default parameters at 1 Hz intervals.

C.2 Integrating with Supervised NMF

After extracting the relevant features, the approach outlined in the manuscript and in Appendix B are used to learn a supervised NMF model. Each learned component corresponds to a defined brain network, and the extracted features are related to behaviors of interest.

D Implementation of Supervised Cross Spectral Factor Analysis: Cross Spectral Mixture (CSFA-CSM)

Below, we give a brief description of the CSFA generative model [7] using the Cross-Spectral Mixture (CSM) kernel, and then we discuss how it can be combined with the supervised framework we developed.

D.1 The CSFA-CSM Generative Model

Cross-Spectral Factor Analysis (CSFA) is designed specifically to model brain networks in an interpretable manner. It uses Gaussian processes to characterize the power and cross spectra through a carefully designed kernel. Let the data be composed of \( N \) observations, from \( C \) distinct brain regions. We let window \( w \) be represented by \( Y^w = [y^w_1, \ldots, y^w_N] \in \mathbb{R}^{C \times N} \). \( N \) is determined by the sampling rate and the duration of the window. The complete dataset is represented by the set \( \mathcal{Y} = \{ Y^w \}_{w=1}^W \). The CSM kernel, designed by [36], is given as

\[
K_{CSM}(t, t'; B_q, \mu_q, \nu_q) = \text{Real} \left( \sum_{q=1}^Q B_q k_q(t, t'; \mu_q, \nu_q) \right),
\]

(19)

where the matrix \( K_{CSM} \in \mathbb{C}^{C \times C} \). This is the real component of a sum of \( Q \) separable kernels. Each of these kernels is given by the combination of a cross-spectral density matrix, \( B_q \in \mathbb{C}^{C \times C} \), and a stationary function of two time points that defines a frequency band, \( k_q(\cdot) \). Representing \( \tau = t - t' \), as all kernels used here are stationary and depend only on the difference between the two inputs, the frequency band for each spectral kernel is defined by a spectral Gaussian kernel,

\[
k_q(\tau; \mu_q, \nu_q) = \exp \left( -\frac{1}{2} \nu_q \tau^2 + j \mu_q \tau \right),
\]

(20)

which is equivalent to a Gaussian distribution in the frequency domain with variance \( \nu_q \), centered at \( \mu_q \).

The matrix \( B_q \) is a positive semi-definite matrix with rank \( R \). This is also known as coregionalization matrix in spatial statistics [57]. Choosing \( R \) to be smaller than \( C \) induces a low-rank approximation that can help prevent overfitting. This relationship is maintained and \( B_q \) is updated by storing the full matrix as the outer product of a tall matrix with itself:

\[
B_q = \tilde{B}_q \tilde{B}_q^\dagger,
\]

(21)

where \( \tilde{B}_q \in C \times R \).

Phase coherence between regions is given by the magnitudes of the complex off-diagonal entries in \( B_q \). The phase offset is given by the complex angle of those off-diagonal entries.

CSFA creates a factor model by relating each factor to the data through a CSM kernel. Let \( t_n \) represent the time point of the \( n^{th} \) sample in the window and \( t \) represent \([t_1, \ldots, t_N]\). Each window is modeled as

\[
y^w_n = f_w(t_n) + \epsilon^w_n, \quad \epsilon^w_n \sim \mathcal{N}(0, \eta^{-1} I_C),
\]

(22)

\[
F_w(t) = \sum_{l=1}^L s_{wl} F^l_w(t), \quad F_w(t) = [f_w(t_1), \ldots, f_w(t_N)],
\]

(23)
where $F_w(t)$ is represented as a linear combination functions drawn from $L$ latent factors, given by \( \{ F^l_w(t) \}_{l=1}^L \). The $l$-th latent function is drawn independently for each task according to

\[
F^l_w(t) \sim \mathcal{GP}(0, K_{CSM}(\cdot; \theta_l)),
\]

(24)

where $\theta_l$ is the set of parameters associated with the $t^{th}$ factor (i.e. \( \{ B^l_q, \mu^l_q, \nu^l_q \}_{q=1}^Q \)).

The factors are all constrained to be non-negative, and thus treats the brain dynamics as a linear sum of non-negative brain networks.

D.2 Implementing Encoded CSFA-CSM

Implementing CSFA for the local and unsupervised models follow the developments of [7], although we reimplemented the technique in Tensorflow and used stochastic gradient descent with Nesterov momentum as the optimizer rather than using the originally proposed learning strategy. At each step in our algorithm a small batch of data was selected, the factors were trained to convergence, and then a single update on the CSFA parameters was performed given the factors.

We modified the method described in Equation 7 as well as the training algorithm for encoded CSFA. Rather than using the time series for our encoder, we used the power features used for the CSFA-NMF model as inputs to our encoder. This was done because the features of interest are spectral based, thus any encoder relying on the original time series would require a convolutional encoder, which has high potential to overfit. The original time series was used however, to evaluate the likelihood from the CSFA-CSM model.

Due to the vast differences in size of the likelihood during training, we incorporated an additional step optimizing the encoder solely with respect to the predictive loss at each iteration. Thus, the encoder was constrained to be predictive at each step of the training. This was done implemented in Tensorflow version 1.9 with Adam as the optimization method.

E Robustness to Supervision Strength

Here we examine the sensitivity of both encoded and local supervision to the parameter $\mu$ when the other parameters are known and given. We only fit the model using 200 samples. Here, we use the derived PCA-like analytic solutions for the local and encoded supervision models. We choose to use this assumption on the variances because it is common in practice (e.g., the prevalence of PCA for data analysis) and allows us to compare model parameters without future consideration of model settings. Also, note that while this assumption impacts the eigenvalues, and hence the latent factors, the eigenvectors indicating the directions of maximum variance remain unchanged [8].

Figure 6 visualizes how model performance changes as we change the value of $\mu$ from the local and encoded supervision. When $\mu$ is small, the impact of the supervised task is small, and the solution from the local and encoded methods are very similar. However, as $\mu$ increases, the fit model from the local and encoded supervised inference strategies diverge. Specifically, the local supervised approach is greatly impacted by the knowledge of $y$ that appears as a large discrepancy in the latent factors when $y$ is observed or not (factor dragging). Note that the model does not predict $y$ well when it is unobserved. In direct contrast, the encoded supervision model is comparatively less unaffected and is substantially more robust to the value of $\mu$, which is visible as the predictive performance is better for large values of $\mu$ and the learned parameters reconstruct $X$ better.
Figure 6: An illustration of the comparative sensitivity of local and encoded supervision to the values of $\mu$ with a synthetic example. The two methods are given the correct number of latent factors. With local supervision as $\mu$ increases $y$ becomes increasingly dominant, and substantially overfits, as shown by the large discrepancy between the factors estimated with and without knowledge of $y$. This also leads to worse reconstructions of the predictors. Encoded supervision also eventually overfits, but substantially lower than the local adversary indicating substantial robustness to the choice of $\mu$. 