Semi-supervised low-rank logistic regression for high-dimensional neuroimaging data

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Abstract

Imaging neuroscience links human behavior to aspects of brain biology in ever-increasing datasets. Existing neuroimaging methods typically perform either discovery of neurobiological structure or evaluation of explicit hypotheses on mental tasks. Modelling mental tasks however hinges on the pertinence of the assumed neurobiological structure. We therefore propose to solve the unsupervised dimensionality reduction and supervised task classification in an identical statistical learning problem. We show that this approach yields more accurate and more interpretable neural models of psychological tasks in a reference neuroimaging dataset.

keywords: dimensionality reduction; semi-supervised learning; bioinformatics; fMRI; systems neuroscience

1 Introduction

Methods used in neuroimaging research can be grouped by discovering neurobiological structure or revealing the neural correlates associated with mental tasks. To discover coherent distributions of activation structure across time, independent component analysis (ICA; [6]) is often used to decompose the BOLD (blood-oxygen level-dependent) signals into the important modes of variation. The ensuing spatial activation patterns are believed to represent brain networks of functionally interacting brain regions. Similarly, sparse principal component analysis (SPCA; [21]) has been used to separate brain activity signals into parsimonious network components. Thus extracted brain networks have been shown to be manifestations of electrophysiological oscillation frequencies [13]. Their fundamental role in brain organization is attested by continued covariation during sleep and anesthesia. Network discovery is typically performed by applying ICA or SPCA on unlabeled "resting-state" data. These capture brain dynamics during ongoing random thought without controlled environmental input. The biggest fraction of the BOLD signals are known not to correlate with a particular behavior, stimulus, or experimental task.

On the other hand, to investigate the neural correlates underlying mental tasks, the general linear model (GLM; [10]) is the dominant approach. The contribution of individual brain voxels is estimated according to a design matrix of experimental tasks. Alternatively, psychophysiological interactions (PPI; [9]), elucidate the functional interactions between voxels as a function of experimental tasks. Dynamic causal modeling (DCM; [19]), in turn, quantifies directed, task-driven influences between regions by treating the brain as a nonlinear dynamic system with unknown neuronal states. As a last example, always more neuroimaging studies model experimental tasks by training classification algorithms on brain signals [17]. All these methods are applied to labeled task data that capture brain dynamics during stimulus-guided behavior. Two important conclusions can be drawn. First, the mentioned supervised neuroimaging analyses operate without exception in a single-voxel space. This ignores the fact that the BOLD signal exhibits coherent spatial activation patterns. Second, existing neuroimaging analyses do not acknowledge the fact that the task-induced changes of the BOLD signal amount to less than 5% of baseline activity [8]. They do thus not exploit the high similarity of BOLD dynamics in the human brain at rest and during experimental tasks. Indeed, very similar brain networks were observed when applying ICA separately on rest and task data [18].

Both biological properties can be conjointly exploited in a semi-supervised (i.e., use rest and task data) low-rank (i.e., perform network decomposition) approach. The integration of brain-network discovery in a supervised classification goal should identify the neurobiological structure that allows for the best predictive models. Autoencoders suggest themselves because they can emulate variants of most nonsupervised learning algorithms, including PCA, SPCA, and ICA. Autoencoders are one-layered learning models that condense the input data to local and global representations by improving reconstruction from them [12]. They behave like a PCA in case of one linear hidden layer and a squared error loss [3]. This architecture yields a convex optimization objective with unique global minimum. Autoencoders behave like a SPCA if shrinkage terms are added for the matrix weights in the optimization objective. In turn, they behave like an ICA in case of a nonlinear convex function of the first-layer activation and tied weights [15]. These authors further demonstrated that ICA, sparse autoencoders, and sparse coding are mathematically equivalent under mild conditions. In this way, autoencoders can flexibly project the neuroimaging data onto the axes of main variation and thus reverse-engineer properties of the data-generating neural processes [16].

In the present investigation, an autoencoder will be fed by (unlabeled) rest data and integrated as bottleneck into a low-rank logistic regression fed by (labeled) task data. Using the chain rule in back-propagation, we can then solve the unsupervised data representation and a supervised classification in an identical statistical learning problem. From the perspective of dictionary learning, the first layer can be viewed as a learned set of basis functions whose linear combinations are learned in the second layer [16]. Neurobiologically, this allows delineating a low-dimensional manifold of brain network patterns and then distinguishing mental tasks by their most discriminative linear combinations. Theoretically, a big reduction of the model variance is expected by regularization using resting-state autoencoder to put probability mass on the most neurobiologically valid members of the model space. The generalization performance should consequently be improved due to much reduced Vapnik-Chervonenkis dimensions of the classification estimator. Taken together, the important modes of variation in brain dynamics and the neural correlates subserving mental operations have mostly been studied in isolation. We provide a principled computational framework to link these previously unconnected domains of systems neuroscience.

2 Methods

Using Human Connectome Project (HCP) data (n=500), optimal low-rank projections and logistic-regression models are identified in a same gradient descent. Brain network decompositions are thus exposed that explain task-descriminative spatial patterns.

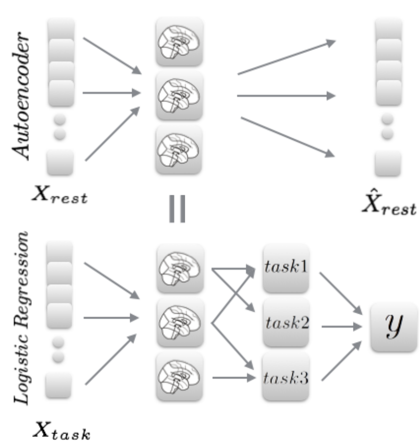


Figure 1: **Architecture**

Data was drawn from 498 unrelated, healthy HCP participants. All provided informed consent to the Washington University in St. Louis institutional review board. HCP tasks were selected that feature known suitability as localizers and reliability across participants [4]. Mostly block-design, but also event-related, paradigms were administered on 1) working memory/cognitive control processing, 2) incentive processing, 3) visual and somatosensory-motor processing, 4) language processing (semantic and phonological processing), 5) social cognition, 6) relational processing, and 7) emotional processing. All data were acquired on the same Siemens Skyra 3T scanner. Whole-brain EPI acquisitions were acquired with a 32 channel head coil (TR=720ms, TE=33.1ms, flip angle=52, BW=2290Hz/Px, in-plane FOV=280 $\times$ 180mm, 72 slices, 2.0mm isotropic voxels). The minimally preprocessed pipeline [11] includes gradient unwarping, motion correction, fieldmap-based EPI distortion correction, brain-boundary-based registration of EPI to structural T1-weighted scan, non-linear (FNIRT) registration into MNI space, and grand-mean intensity normalization. Activation maps were spatially smoothed by a Gaussian kernel of 4mm (FWHM). A general linear model (GLM) was implemented by FILM from the FSL suite with model regressors from convolution with a canonical hemodynamic response function and from temporal derivatives. HCP tasks were conceived to modulate activation in a maximum of different brain regions and neural systems. Indeed, at least 70% of the participants showed consistent brain activity in contrasts from the task battery, which certifies excellent coverage [4]. In sum, the HCP task dataset incorporated 8650 first-level activity maps from 18 diverse paradigms administered to 498 participants. All maps were downsampled to a common 36x43x36 space of 5mm isotropic voxels and gray-matter masked (at least 10%). All analyses were based on task maps of 13,657 voxels representing Z values in gray matter.

Unsupervised and supervised learning were combined into a low-rank logistic regression problem. The 13,657 z values from each activity map were subject to a first linear projection into Z latent components (i.e., 1, 5, 10, .., 100). These hidden brain networks loadings were subsequently projected into the 18 class space for multinomial logistic regression. The goal was to find the two weight matrices (input-to-hidden: 13,657 x Z and hidden-to-output: Z x 18) and their corresponding bias vectors. Non-linearities were not applied on the transformation results. Weights and biases were initialized by Gaussian random noise. Gradient descent updated these matrices and vectors in each iteration (100 samples per batch, 250 epochs). Using the chain rule, the partial derivates for the update were computed for the transformation into the latent space and the subsequent transformation into the class space. We choose the RMSprop algorithm [20] with an initial learning rate of 0.01. Early stopping ensured that the best weight matrices/vectors were retained in each epoch cycle. This was evaluated by the prediction accuracy on a validation set (10% of the training data) at each iteration.

This approach was benchmarked against independent dimensionality reduction and learning of a classification function. Data reduction was performed on one half of the data by ICA and SPCA. ICA unmixed the BOLD signals into separate spatial components by minimizing their mutual information [14]. This iterative blind source separation was realized by a parallel FASTICA implementation (200 maximum iterations, per-iteration tolerance of 0.0001, initialized by a random mixing matrix, preliminary whitening). SPCA separated the BOLD signals into network components with few regions, which scales well to large datasets [21]. This regression-type optimization problem constrained by ℓ_1-penalty in an implementation without orthogonality assumptions (1000 maximum iterations, per-iteration tolerance of $1 * 10^{-8}$, sparsity alpha=1, ridge-shrinkage at 0.01, Lasso path computed with coordinate descent). Each linear decomposition revealed the specified number of latent network components in one half the HCP data. The extracted hidden network components were subsequently used to reduce the remain half of task maps to a considerably smaller number of component loadings. 13,657 voxels were thus condensed into 1, 5, 10, .., 100 measures of network involvement using ridge regression (regularization alpha parameter=0.001, using Cholesky solver). Multinomial logistic regression was finally performed on the brain network loadings to learn classifying the 18 cognitive tasks. Importantly, in all approaches, the final classification models were tested on an unseen test set (10% of data).

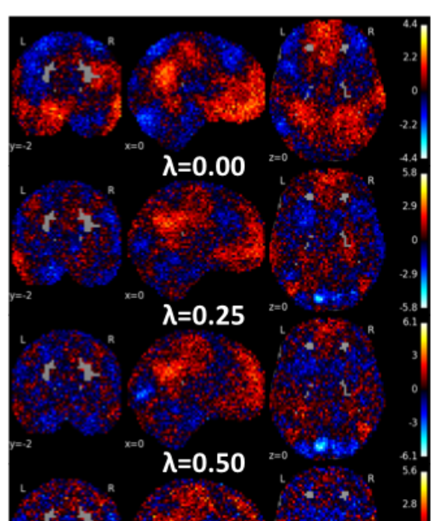
linear decomposition + elastic net penalty -¿ has characteristics of a sparse PCA

Learning of the identity function as trivial solution is avoided by the both bottleneck and the sparsity-enforcing ElasticNet penalty.

o maximize intranetwork homoge- neity and between-network heterogeneity.

AE: coordinate system for points on the manifold low-dimensional bottleneck layer

FORMULA 'reconstruction error' criterion encoder: input -¿ hidden reprsentation where b0 and b1 are biase



vectors average reconstruction error pen. avoids learning trivial soutoin - identitiy

coompute the error derivates of the weights gradually modified according to possible compression algorithms

affine autoencoder with squared error loss X hat is a dterministic function of X It can thus be said that training an autoencoder to minimize reconstruction error amounts to maximizing a lower bound on the mutual information between input X and learnt repre- sentation Y .

rest data is already compressed to a sparse PCA remote form of pretraining of the first layer bottleneck -¿ untercomplete representing, i.e. lossy compression

as a pretraining strategy

are decomposed into d networks, in a way that maximizes the homogeneity of function within each network while maximizing the heterogeneity between them.

output is vector-valued -¿ generative properties? optimal transformation matrix

forward propegation: input through architecture to generate output reconstruction cost backward propegation: generate the deltas for all units / model paramters corresponds to the derivative of the cost function with respect to the parameters

100 components close to sparse over-complete representation because Xrest contains only 20 components

whereas elasticnet on the model paramters is regulization

Hints. In fact, the constraint by a rest-data autoencoder qualifies as a *hint* rather than regularization [2]. Its purpose is not to prevent overfitting but to introduce prior knowledge on known properties of the unknown target function f. Rather than relying only on input-output pairs in the learning process, we thus narrow our hypothesis set to the biologically most plausible solutions. That is, we reduce the search space in a way that is compatible with the expected representation of BOLD activity signals.

FORMULA

$$\begin{aligned} arg\,min_\theta \;\; \mathcal{L}(\theta,\lambda) = \lambda \frac{1}{N_{X_{task}}} &\sum_{i=0}^{N_{X_{task}}} \log(P(Y=y^{(i)}|x^{(i)};W,b)) \\ + \;\; (1-\lambda)&\frac{1}{N_{X_{rest}}}\|X_{rest}-\hat{X}_{rest}(W,b)\|^2 \end{aligned} \tag{1}$$

mutiple output units aCcording to equation (1) As solver, we chose *rmsprop* [20], a mini-batch version of rprop. This procedure dictates an adaptive learning rate for each model parameter by scaled gradients from a running average. Gradient normalization by RMSprop is known to effectively exploit curvature information. We opted for a small batch size of 100, given the high degree of redundancy in X_{rest} and X_{task}. The matrix parameters were initalized by Gaussian random values multiplied by a gain of 0.004. The bias parameters were initalized to be zero.

With a slight abuse of notation, let θ denote a component of θ. The normalization factor and the update rule for θ are given by

$$
\begin{aligned}
v^{(t+1)} &= \rho v^{(t+1)} + (1-\rho)\left(\frac{\partial f}{\partial \theta}\right)^2 \\
\theta^{(t+1)} &= \theta^{(t)} + \alpha \frac{\nabla f(\theta^{(t)})}{\sqrt{v^{(t+1)} + \epsilon}},
\end{aligned}
\tag{2}
$$

where $0 < \rho < 1$ constitutes the decay rate. ρ was set to 0.9 to deemphasize the magnitude of the gradient. Further α is the learning rate and ϵ a global damping factor. The hyper-parameter α was set to 0.00001 by prior manuel cross-validation and ϵ was set to 1^{-6}. Note that we have also experimented with other solvers (stochastic gradient descent, adadelta, and adagrad) but found that rmsprop converged faster and with higher generalization performance.

20 components: high bias/low variance 100 compoentens: low bias/high variance

Generating samples from the learned statistical model

minimizing the discrepancy between the orig- inal data and its reconstruction. The required gradients are easily obtained by using the chain rule to backpropagate error derivatives first through the decoder network and then through the encoder network

theanopython The analyses were performed in Python. We used *nilearn* to handle the high-dimensional neuroimaging data [1] and *theano* for automatic differentiation of symbolic computation graphs [5, 7]. All Python scripts that generated the results are accessible online for reproducibility and reuse `http://github.com/banilo/nips2015`.

3 Experimental Results

all vectors are column vectors

affine encoder and decoder

Low-rank regression outperformed serial ICA/SparsePCA and logistic regression.

reduction of n gray-matter voxels to n components

Modifications of the mode that di not improve the genralization performacne: dropo-out, input corruption, addining non-linearities (sigmoid, tanh),

introducing a nonlinearity (sigmoid, tanh) into the system did not improve predictive accuracy but elastic did -¿ most useful decomposition has characteristics of a SPCA and not PCA or ICA

outperforms plain vanilla LR inject prior domain knowledge into the learning process

4 Discussion and Conclusion

There is an increasing occurrence of high-dimensional problems in the neuroimaging domain. This calls for new statistical learning algorithms that behave well in large-cohort settings. Ideally, they should acknowledge and exploit existing widely-accepted neuroscientific knowledge. In the present work, we propose such an estimator that learns dimensionality reduction in a neurobiologically valid and interpretable fashion.

-hypothesis space includes sparse PCA and PCA but not ICA since no linearity

respect structure in the fMRI data

- if linearity, then would be closer to the notion of 1-hidden layer neural network rather than low-rank logistic regression

We hope that these results stimulate the development of even more powerful semi-supervised classification methods

improve computational tractability, prediction accuracy, and interpretability neuroimaging datasets does it produce testable predictions? -¿ we can test predictive value of network-network architectures across mental domains.

open window to study the correspondence between brain dynamics during every-day mind-wandering and task-focused brain states.

classifier that operates in a (sparse) network space, rather than in a voxel space. domain-specifc classification algorithms

repertoire of mental operations that the human brain can perform

large quantities of neuroimaging data logistic regression in an autoencoder paradigm

automatically learn a mapping to and from a brain-network space

statistical structure

PCA: captures structure in the data that is well described by Gaussian clouds, linear pair-wise correlations are most important form of statistical dependence/orthongonal components

-¿ BOLD images can readily be reduced to linear combinations of sparse spatial structures

scale different classificatiuon architectures to large neuroimaging data

task data might concentrate near a low-dimensional manifold of brain networks

neurobiolgocial fidelity

entities of the neuroimaging domain

There is much uncertainty about the most pertinent representation of neural activation information put probability mas shwere we expeted neurobiological strucuture

canonical set of brain networks

FUTURE link the restings-tate component to the pattern sof cognitive proceses reduce information von resting-state data in neurological and psychiatric populations for discovery of neurobiological sub-groups as well as prediction of disease trajectories and drug responses

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