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Bayesian Group Factor Analysis

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Abstract

We introduce a factor analysis model that summarizes the dependencies between observed variable *groups*, instead of dependencies between individual variables as standard factor analysis does. A group may correspond to one view of the same set of objects, one of many data sets tied by co-occurrence, or a set of alternative variables collected from statistics tables to measure one property of interest. We show that by assuming group-wise sparse factors, active in a subset of the sets, the variation can be decomposed into factors explaining relationships between the sets and factors explaining away set-specific variation. We formulate the assumptions in a Bayesian model providing the factors, and apply the model to two data analysis tasks, in neuroimaging and chemical systems biology.

1 Introduction

Factor analysis (FA) is one of the cornerstones of classical data analysis. It explains a multivariate data set $\mathbf{X} \in \mathbb{R}^{N \times D}$ in terms of $K < D$ factors that capture joint variability or dependencies between the N observed samples of dimensionality D . Each factor or component has a weight for each dimension, and joint variation of different dimensions can be studied by inspecting these weights, collected in the loading matrix $\mathbf{W} \in \mathbb{R}^{D \times K}$. Interpretation is made easier in the sparse variants of FA (Knowles and Ghahramani, 2011; Paisley and Carin, 2009; Rai and Daumé III, 2009) which favor solutions with only a few non-zero weights for each factor.

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We introduce a novel extension of factor analysis, coined *group factor analysis* (GFA), for finding factors that capture joint variability between *data sets* instead of individual variables. Given a collection $\mathbf{X}_1, \dots, \mathbf{X}_M$ of M data sets of dimensionalities D_1, \dots, D_M , the task is to find $K < \sum_{m=1}^M D_m$ factors that describe the collection and in particular the dependencies between the data sets or views \mathbf{X}_m . Now every factor should provide weights over the data sets, preferably again in a sparse manner, to enable analyzing the factors in the same way as in traditional FA.

The challenge in moving from FA to GFA is in how to make the factors focus on dependencies between the data sets. For regular FA it is sufficient to include a separate variance parameter for each dimension. Since the variation independent of all other dimensions can be modeled as noise, the factors will then model only the dependencies. For GFA that would not be sufficient, since the variation specific to a multi-variate data set can be more complex. To enforce the factors to model only dependencies, GFA hence needs to explicitly model the independent variation, or structured noise, within each data set. We use linear factors or components for that as well, effectively using a principal component analyzer (PCA) as a noise model within each data set.

The solution to the GFA problem is described as a set of K factors that each contain a projection vector for each of the data sets having a non-zero weight for that factor. A fully non-sparse solution would hence have $K \times M$ projection vectors or, equivalently, K projection vectors over the $\sum_{m=1}^M D_m$ -dimensional concatenation of the data sources. That would, in fact, correspond to regular FA of the feature-wise concatenated data sources. The key in learning the GFA solution is then in correctly fixing the sparsity structure, so that some of the components will start modeling the variation specific to individual data sets while some focus on different kinds of dependencies.

An efficient way of solving the Bayesian GFA prob-

lem can be constructed by extending (sparse) Bayesian Canonical Correlation Analysis (Archambeau and Bach, 2009) from two to multiple sets and by replacing variable-wise sparsity by group-wise sparsity as was recently done by Virtanen et al. (2011). The model builds on insights from these Bayesian CCA models and recent non-Bayesian group sparsity works (Jenatton et al., 2010; Jia et al., 2010). The resulting model will operate on the concatenation $\mathbf{Y} = [\mathbf{X}_1, \dots, \mathbf{X}_M]$ of the data sets, where the groups correspond to the data sets. Then the factors in the GFA (weight vectors over the dimensions of \mathbf{Y}) become sparse in the sense that the elements corresponding to some subset of the data sets become zero, separately for each factor. The critical question is how well is the model able to extract the correct factors amongst the exponentially many alternatives that are active in any given subset of data sets. We empirically demonstrate that our Bayesian model for group-wise sparse factor analysis finds the true factors even from a fairly large number of data sets.

The main advantages of the model are that (i) it is conceptually very simple, essentially a regular Bayesian FA model with group-wise sparsity, and (ii) it enables tackling completely new kinds of data analysis problems. In this paper we apply the model to two real-world example scenarios specifically requiring the GFA model, demonstrating how the GFA solutions can be interpreted. The model is additionally applicable to various other tasks, such as learning of the subspace of multi-view data predictive of some of the views, a problem addressed by Chen et al. (2010).

The first application is analysis of fMRI measurements of brain activity. Encouraged by the recent success in discovering latent brain activity components in complex data setups (Lashkari et al., 2010; Morup et al., 2010; Varoquaux et al., 2010), we study a novel kind of an analysis setup where the same subject has been exposed to several different representations of the same musical piece. The brain activity measurements done under these different conditions are considered as different views, and GFA reveals brain activity patterns shared by subsets of different conditions. For example, the model reveals “speech” activity shared by conditions where the subject listened to a recitation of the song lyrics instead of an actual musical performance.

In the second application drug responses are studied by modeling four data sets, three of which contain gene expression measurements of responses of different cell lines (proxies for three diseases; Lamb et al., 2006) and one contains chemical descriptors of the drugs. Joint analysis of these four data sets gives a handle on which drug descriptors are predictive of responses in a specific disease, for instance.

2 Problem Formulation

The group factor analysis problem, introduced in this work, is as follows: Given a collection $\mathbf{X}_1 \in \mathbb{R}^{N \times D_1}, \dots, \mathbf{X}_M \in \mathbb{R}^{N \times D_M}$ of data sets (or views) with N co-occurring observations, find a set of K factors that describe the joint data set $\mathbf{Y} = [\mathbf{X}_1, \dots, \mathbf{X}_M]$. Each factor is a sparse binary vector $\mathbf{f}_k \in \mathbb{R}^M$ over the data sets, and the non-zero elements indicate that the factor describes dependency between the corresponding views. Furthermore, each active pair (factor k , data set m) is associated with a weight vector $\mathbf{w}_{m,k} \in \mathbb{R}^{D_m}$ that describes how that dependency is manifested in the corresponding data set m . The $\mathbf{w}_{m,k}$ correspond to the factor loadings of regular FA, which are now multivariate; their norm reveals the strength of the factor and the vector itself gives more detailed picture on the nature of the dependency.

The \mathbf{f} ’s, collected in the matrix \mathbf{F} , have been introduced to make the problem formulation and the interpretations simpler; in the specific model we introduce next they will not be represented explicitly. Instead, the weight vectors $\mathbf{w}_{m,k}$ are instantiated for all possible factor-view pairs and collected into a single loading matrix \mathbf{W} , which is then made group-wise sparse.

3 Model

We solve the GFA problem with a group-wise sparse matrix factorization of \mathbf{Y} , illustrated in Figure 1. The variable groups correspond to the views $1, \dots, M$ and the factorization is given by

$$\mathbf{Y} \approx \mathbf{Z}\mathbf{W}^T,$$

where we have assumed zero-mean data for simplicity. The factorization gives a group-wise sparse weight matrix $\mathbf{W} \in \mathbb{R}^{D \times K}$ and the latent components $\mathbf{Z} \in \mathbb{R}^{N \times K}$. The weight matrix \mathbf{W} collects the factor- and view-specific projection vectors $\mathbf{w}_{m,k}$ for all pairs for which $\mathbf{f}_{m,k} = 1$. The rest of the elements in \mathbf{W} are filled with zeroes.

We solve the problem in the Bayesian framework, providing a generative model that extracts the correct factors by modeling explicitly the structured noise on top of the factors explaining dependencies. We assume the observation model

$$\mathbf{Y} = \mathbf{Z}\mathbf{W}^T + \mathbf{E},$$

where each row of the Gaussian noise \mathbf{E} has diagonal noise covariance $\mathbf{\Sigma}$ with the diagonal of $[\sigma_1^2, \dots, \sigma_M^2]$ where σ_m^2 has been repeated D_m times. That is, every dimension within the same view has the same residual variance, but the views may have different variances.

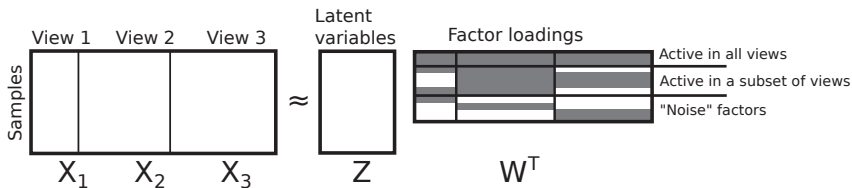


Figure 1: Illustration of the group factor analysis of three data sets or views. The feature-wise concatenation of the data sets \mathbf{X}_i is factorized as a product of the latent variables \mathbf{Z} and factor loadings \mathbf{W} . The factor loadings are group-wise sparse, so that each factor is active (gray shading, indicating $\mathbf{f}_{m,k} = 1$) only in some subset of views (or all of them). The factors active in just one of the views model the structured noise, variation independent of all other views, whereas the rest model the dependencies. The nature of each of the factors is learned automatically, without needing to specify the numbers of different factor types (whose number could be exponential in the number of views) beforehand.

To complete the generative formulation, we assume Gaussian latent variables that are *a priori* independent and specify a Gamma prior for the inverse variances σ_m^{-2} . The full likelihood is hence given by

$$\begin{aligned} p(\mathbf{Y}, \mathbf{W}, \Sigma, \mathbf{Z}) &= p(\mathbf{W})p(\Sigma)p(\mathbf{Z})p(\mathbf{Y}|\mathbf{Z}, \mathbf{W}, \Sigma) \\ &= p(\mathbf{W}) \prod_{m=1}^M \text{Gamma}(\sigma_m^{-2} | a_\sigma, b_\sigma) \\ &\quad \prod_{n=1}^N (\mathcal{N}(\mathbf{z}_n | 0, \mathbf{I}) \mathcal{N}(\mathbf{y}_n | \mathbf{z}_n \mathbf{W}^T, \Sigma)), \end{aligned}$$

where we used $a_\sigma = b_\sigma = 10^{-14}$, $\mathcal{N}(\cdot)$ is the normal distribution, and \mathbf{z}_n denotes the K -dimensional latent variable corresponding to the sample \mathbf{y}_n .

The weight matrix \mathbf{W} is made sparse by a group-wise automatic relevance determination (ARD) prior,

$$\begin{aligned} \alpha_{m,k} &\sim \text{Gamma}(a_0, b_0) \\ p(\mathbf{W}) &= p(\mathbf{W}|\alpha) = \prod_{k=1}^K \prod_{m=1}^M \prod_{d=1}^{D_m} \mathcal{N}(\mathbf{w}_{m,k}(d) | 0, \alpha_{m,k}^{-1}), \end{aligned}$$

where $\mathbf{w}_{m,k}(d)$ denotes the d th element in the projection vector $\mathbf{w}_{m,k}$, the vector corresponding to the m th view and k th factor. The inverse variance of each vector is governed by the parameter $\alpha_{m,k}$ which has a Gamma prior with a small a_0 and b_0 (we used 10^{-14}). The ARD makes groups of variables inactive for specific factors by driving their $\alpha_{m,k}^{-1}$ to zero. The components used as modeling the structured noise within each data set are automatically produced as factors active in only one view.

Since the model is formulated through a sparsity prior we do not explicitly need to represent \mathbf{F} in the model. It can, however, be created based on the factor-specific relative contributions to the total variance of each view, obtained by integrating out both \mathbf{z} and \mathbf{W} . We

set $\mathbf{f}_{m,k} = 1$ if

$$\alpha_{m,k}^{-1} > \epsilon \left(\text{Tr}(\hat{\Sigma}_m) / D_m - \sigma_m^2 \right), \quad (1)$$

where $\hat{\Sigma}_m$ is the covariance and $\text{Tr}(\hat{\Sigma}_m)$ the total variance of the m th view, and ϵ is a small threshold.

The inference is based on a variational approximation

$$\begin{aligned} q(\mathbf{W}, \Sigma, \mathbf{Z}, \alpha) &= \prod_{m=1}^M \left(q(\sigma_m^{-2}) q(\alpha_m) \prod_{d=1}^{D_m} q(\mathbf{W}_m(d)) \right) \\ &\quad \prod_{n=1}^N q(\mathbf{z}_n), \end{aligned}$$

where $\mathbf{W}_m(d)$ denotes the d th row of the part of \mathbf{W} corresponding to the m th view and α_m contains $\alpha_{m,k}$ for all k . The projection matrix is hence factorized over the dimensions of the observed data, but not over the components. The updates for the parameters of the approximation follow closely those provided for Bayesian FA (Lutinen and Ilin, 2010), and are not repeated here. The only differences are that the approximation for α_m needs to be updated for each view separately, σ_m^2 are view-specific instead of feature-specific, and the parts of \mathbf{W} corresponding to different views are updated one at a time.

To solve the difficult problem of fixing the rotation in factor analysis models, we borrow ideas from the recent solution by Virtanen et al. (2011) for CCA models. Between each round of the EM updates we maximize the variational lower bound with respect to a linear transformation \mathbf{R} of the latent subspace, which is applied to both \mathbf{W} and \mathbf{Z} so that the product $\mathbf{Z}\mathbf{W}^T$ remains unchanged. That is, $\hat{\mathbf{Z}} = \mathbf{Z}\mathbf{R}^T$ and $\hat{\mathbf{W}}^T = \mathbf{R}^{-T}\mathbf{W}^T$. Given the fixed likelihood, the optimal \mathbf{R} corresponds to a solution best matching the prior that assumes independent latent components, hence resulting in a posterior with maximally uncorre-

lated components. We optimize for \mathbf{R} by maximizing

$$L = -\frac{1}{2}\text{Tr}(\mathbf{R}^{-1}\langle\mathbf{Z}^T\mathbf{Z}\rangle\mathbf{R}^{-T}) + C\log|\mathbf{R}| - \sum_{m=1}^M \frac{D_m}{2} \log \prod_{k=1}^K r_k^T \langle \mathbf{W}_m^T \mathbf{W}_m \rangle \mathbf{r}_k \quad (2)$$

with the L-BFGS algorithm for unconstrained optimization. Here $C = \sum_m D_m - N$, and \mathbf{r}_k is the k th column of \mathbf{R} , and the $\langle\mathbf{Z}^T\mathbf{Z}\rangle = \sum_n \langle\mathbf{z}_n^T\mathbf{z}_n\rangle$ collects the second moments of the factorization. Similar notation is used for \mathbf{W}_m , which indicates the part of \mathbf{W} corresponding to view m .

3.1 Special Cases and Related Problems

When $D_m = 1$ for all m the problem reduces to regular factor analysis. Then the $\mathbf{w}_{m,k}$ are scalars and can be incorporated into \mathbf{f}_k to reveal the factor loadings.

When $M = 1$, the problem reduces to probabilistic principal component analysis (PCA), since all the factors are active in the same view and they need to describe all of the variation in the single-view data set with linear components.

When $M = 2$, the problem becomes canonical correlation analysis (CCA) as formulated by Archambeau and Bach (2009) and Virtanen et al. (2011). This is because then there are only three types of factors. Factors active in both data sets correspond to the canonical components, whereas factors active in only one of the data sets describe the residual variation in each view. Note that most multi-set extensions of CCA applicable for $M > 2$ data sets, such as those by Archambeau and Bach (2009); Deleus and Hulle (2011), do not solve the GFA problem. This is because they do not consider components that could be active in subsets of size I where $2 \leq I < M$, but instead restrict every component to be shared by all data sets or to be specific to one of them.

A related problem has been studied in statistics under the name multi-block data analysis. The goal there is to analyze connections between blocks of variables, but again the solutions typically assume factors shared by all blocks (Hanafi and Kiers, 2006). The model recently proposed by Tenenhaus and Tenenhaus (2011) can find factors shared by only a subset of blocks by studying correlations between block pairs, but the subsets need to be specified in advance.

Recently Jia et al. (2010) proposed a multi-view learning model that seeks components shared by any subset of views, by searching for a sparse matrix factorization with convex optimization. However, they did not attempt to interpret the factors and only considered applications with at most three views.

Knowles and Ghahramani (2007) suggested that regular sparse FA (Knowles and Ghahramani, 2011) could be useful in a GFA-type setting. They applied sparse FA to analyzing biological data with five tissue types concatenated in one feature representation. In GFA analysis the tissues would be considered as different views, revealing directly the sparse factor-view associations that can only be obtained from sparse FA after a separate post-processing stage. In the next section we show that directly solving the GFA problem outperforms the choice of thresholding sparse FA results.

4 Technical Demonstration

For technical validation of the model, we applied it to simulated data that has all types of factors: Factors specific to just one view, factors shared by a small subset of views, and factors common to most views. We show that the proposed model can correctly discover the structure already with limited data, while demonstrating that possible alternative methods that could be adapted to the scenario do not find the correct result. We sampled $M = 10$ data sets with dimensionalities D_m ranging between 5 and 10 ($\sum_m D_m = 72$), using a manually constructed set of $K = 24$ factors of various types.

For comparing our Bayesian GFA model with alternative methods that could potentially find the same structure, we consider the following constructs:

- FA: Regular factor analysis for the concatenated data \mathbf{Y} . The model assumes the correct number of factors, $K = 24$.
- BFA: FA with an ARD prior for columns of \mathbf{W} , resulting in a Bayesian FA model that infers the number of factors automatically but assumes each factor to be shared by all views.
- NSFA: Fully sparse factor analysis for \mathbf{Y} . We use the nonparametric sparse FA method by Knowles and Ghahramani (2011) which has an Indian buffet process formulation for inferring the number of factors.

With the exception of the simple FA model, the alternatives are comparable in the sense that they attempt to automatically infer the number of factors, which is a necessary prerequisite for modeling collections of several datasets, and that they are based on Bayesian inference.

The solution for the GFA problem is correct if the model (i) discovers the correct sparsity structure \mathbf{F} and (ii) the weights $\mathbf{w}_{m,k}$ mapping the latent variables into

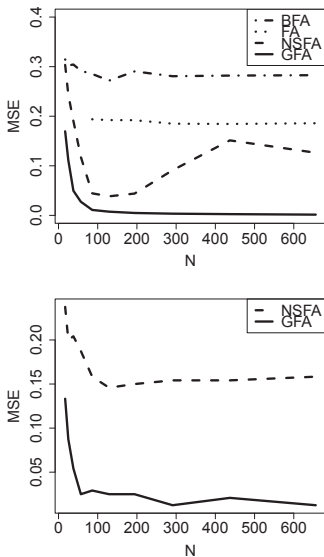


Figure 2: **Top:** Difference (mean square error MSE) between the estimated and true loading matrix \mathbf{W} as a function of the sample size N . Our Bayesian group factor analyzer (GFA) directly solving the GFA problem is consistently the best, beating state-of-the-art non-parametric sparse factor analysis (NSFA), regular factor analysis (FA) and Bayesian FA (BFA). It is worthwhile to notice that increasing the sample size does not help the alternative methods to obtain the correct solution. **Bottom:** Difference between the estimated and true factor activity matrix \mathbf{F} , shown for the two methods providing sparse representations. Again GFA outperforms NSFA.

the observations are correct. Since the methods provide solutions of a varying number of factors given in arbitrary order, we use a similarity measure (Knowles and Ghahramani, 2011) that chooses an optimal re-ordering and sign for the factors found by the models, and then measures the mean-square error.

We start by measuring property (ii), by inspecting the similarity of the true and learned loading matrix \mathbf{W} . The GFA finds the mappings much more accurately than the alternative methods for all of the independent runs with different sample sizes (Fig. 2). Next we inspect the property (i), the similarity of the true and estimated \mathbf{F} , again using the same measure but for binary matrices. Since FA and BFA do not enforce any kind of sparsity within factors, we only compare GFA and NSFA. For GFA we obtain \mathbf{F} by thresholding the ARD weights using (1) with $\epsilon = 10^{-3}$, whereas for NSFA we set $\mathbf{f}_{m,k} = 1$ if any weight within $\mathbf{w}_{m,k}$

is non-zero. GFA again outperforms NSFA which has not been designed for the task. By adaptive thresholding of the weight sets of NSFA it would be possible to reach almost the accuracy of GFA in discovering \mathbf{F} , but as shown by the comparison of \mathbf{W} the actual factors would still be incorrect.

Next we proceed to inspect how well GFA can extract the correct structure from different kinds of data collections, with a particular focus on discovering whether it biases specific types of factors. If no such bias is found, the experiments give empirical support that the method solves the GFA problem in the right way. For this purpose we constructed data sets with a fixed number of samples ($N = 100$) and a varying number of views M that are all $D = 10$ dimensional. We created data collections with three alternative distributions over the different kinds of factors, simulating possible alternatives encountered in real applications. The first distribution type has one factor of each possible cardinality and the second shows a power-law distribution with few factors active in many views and many very sparse factors. Finally, the third type has a uniform distribution over the subsets, resulting in the cardinality distribution following binomial coefficients.

Figure 3 shows the true and estimated distribution of factor cardinalities (the number of active views in a factor, thresholded with $\epsilon = 10^{-3}$) for the different data collections. For all three cases, the model finds the correct structure for $M = 40$ views, and in particular models correctly both types of factors: those shared by several views and those specific to only one or a few. Besides checking for the correct cardinalities, we inspected that the actual factors found by the model match the true ones. We then proceeded to demonstrate (Fig. 3 (d)), for the case with uniform distribution over factor cardinalities, that the finding holds for all numbers of views below $M = 60$ for this case with just $N = 100$ samples; for other distributions the results are similar (not shown).

5 Application Scenarios and Interpretation

Next, we apply the method to brain activity and drug response analysis, representative of potential use cases for GFA, and show how the results of the model can be interpreted. Both applications contain data of multiple views (7 and 4, respectively) and could not be directly analyzed with traditional methods. The number of views is well within the range for which the model was demonstrated above to find the correct structure from the simulated data.

Both applications follow the same analysis procedure,

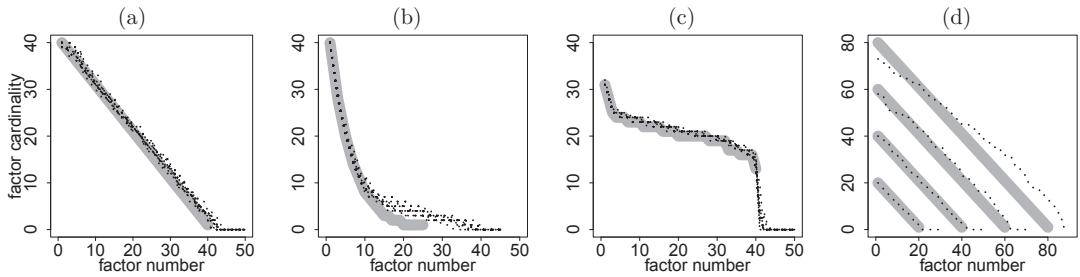


Figure 3: The GFA model finds the correct sparsity structure \mathbf{F} for three very different distributions over different types of factors in the data. The thick grey line shows the true latent structure as the cardinalities (number of active views) of the factors in the decreasing order, and the overlaid curves show results of 10 runs on different simulated data. The first three plots show results for $M = 40$ views with three different distributions of factor types ((a): uniform over the cardinality, (b): power law over the cardinality, (c): uniform over the view combinations), and for all cases the model learns the correct structure. The last plot (d) shows that the behavior is consistent over a wide range of M (the different curves) and only starts to break down when M approaches the sample size $N = 100$. For all cases the model had 10 more components than what were included in the generated data, so the plots also illustrate how the real number of components is inferred automatically.

which can be taken as our practical guidelines for data-analysis with GFA. First, the model is learned with sufficiently many factors, recognized as a solution where more than a few factors are left at zero. Solutions where all the factors are in use cannot be relied upon, since then it is possible that a found factor describes several of the underlying true factors. Consequently, a practical way to choose K is to run with increasing numbers until empty factors are found. After that, the factor activity matrix \mathbf{F} , ordered suitably, is inspected in search for interesting broad-scale properties of the data. In particular, the number of factors specific to individual views is indicative of the complexity of residual variation in the data, and factors sharing specific subsets of views can immediately reveal interesting structure. Finally, individual factors are selected for closer inspection by ordering the factors according to an interest measure specific to the application. We demonstrate that measures based on both \mathbf{Z} and \mathbf{W} are meaningful.

5.1 Multi-set Analysis of Brain Activity

We analyze a data collection where the subject has been exposed to audiovisual music stimulation. The setup is uniquely multi-view; each subject experienced the same three pieces of music seven times as different variations. For example, in one condition the subjects viewed a video recording of someone playing the piece on piano, in one condition they only heard a duet of singing and piano, and in one they saw and heard a person reading out the lyrics of the song.

The $M = 7$ different exposure conditions or stimuli

types were used as views, and we sought factors tying together the different conditions by applying GFA to a data set where the fMRI recordings of the 10 subjects were concatenated in the time direction. Each sample ($N = 1162$) contained, for each view, activities of $D_m = 32$ regions of interest (ROI) extracted as averages of local brain regions. The set of 32 regions was chosen by first picking the five most correlating ROIs for each of the 21 possible pairs of listening conditions and then taking the union of these choices.

The factor-view matrix \mathbf{F} (thresholded with $\epsilon = 10^{-3}$) of a 200-component solution is shown in Figure 4. The number of factors is sufficient, as demonstrated by the roughly 40 empty factors, and we see that the data contain large blocks of view-specific factors suggesting a lot of noise in the data. To more closely examine the factors, we chose to study factors that are coherent over the users. We split the latent variables $\mathbf{z}_k \in \mathbb{R}^N$ corresponding to each factor into 10 sequences corresponding to the samples of the 10 subjects, and measured the inter-subject correlation (ISC) of each factor. The factors were then ranked according to ISC (Fig. 4, bottom), revealing a few components having very high synchrony despite the model being ignorant that the data consisted of several users.

The strongest ISC correlation is for a component shared by all views. It captures the main progression of the music pieces irrespective of the view. A closer inspection of the weight vectors reveals that the responses in the different views are in different brain regions according to the modality; the four conditions with purely auditory stimuli have weights revealing au-

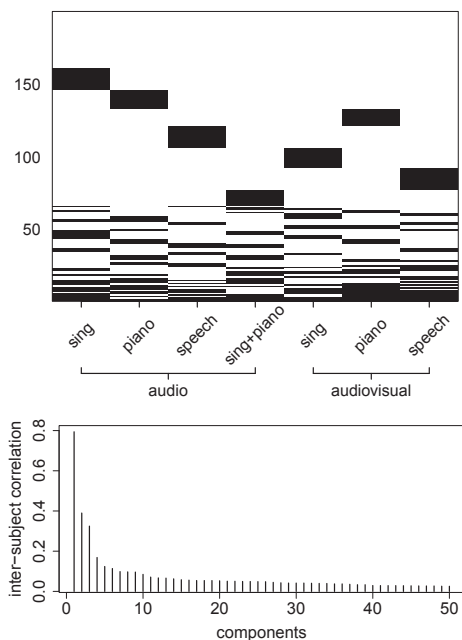


Figure 4: Multi-set analysis of brain activity. **Top:** The matrix \mathbf{F} of factors (rows) across views (columns) indicates the dependencies between the views, different versions of the same songs being played for the subject. **Bottom:** Sorting the factors as a function of inter-subject correlation reveals which factors robustly capture the response to the stimulus.

ditary response, whereas the three conditions with also visual stimulation activate also vision-related regions. The second-strongest ISC correlation is for a component shared by just two views, speech under both audiovisual and purely auditory conditions. That is, it reveals the response to hearing recitation of the song lyrics instead of music as in the other conditions.

In this specific application, it might be useful to additionally apply a model where solutions with similar $\mathbf{w}_{m,k}$ across all m with $\mathbf{f}_{m,k} = 1$ would be favored. The components would then be directly interpretable in terms of specific brain activity patterns, in addition to the time courses.

5.2 Multi-set Analysis of Drug Responses

The second case study is a novel chemical systems biology application, where the observations are drugs and the first $M - 1$ views are responses of different cell lines (proxies to different diseases) to the specific drug. The M th view contains features describing chemical prop-

erties of the drug, derived from its structure. The interesting questions are can GFA find factors relating drug structures and diseases, or relating different cell lines which are here different cancer subtypes.

As the biological views, we used activation profiles over $D_1 = D_2 = D_3 = 1321$ gene sets in three cancer cell lines compared to controls, from (Lamb et al., 2006). The 4th (chemical) view consisted of a standard type of descriptors of the 3D structure of the drugs, called VolSurf ($D_4 = 76$). Observations had been recorded for all cell lines for $N = 684$ drugs.

The factor-view matrix \mathbf{F} (thresholded with $\epsilon = 10^{-6}$) of a 600-component GFA solution is shown in Figure 5 (top). The number of components is large enough since there are over 100 empty factors. Four main types of factors were found: (i) Factors shared by the chemical view and one (or two) cell lines (zoomed inset in Fig 5, top). They give hypotheses for the specific cancer variants. (ii) Factors shared by all cell lines and the chemical space, representing effects specific to all subtypes of cancer. (iii) Factors shared by all cell lines but not the chemical space. They are drug effects not captured by the specific chemical descriptors used. The fact that there is a large block of over 200 of these factors fits well with the known fact that VolSurf features are a very limited description of the complexity of drugs. (iv) Factors specific to one biological view. These represent either “biological noise” or then drug effects specific to that cancer subtype, again not captured by the VolSurf features. Finally, the small set of components active only in the chemical view correspond to structure in VolSurf having no drug effect.

We inspected some of the factors more carefully, and more detailed biological analysis is on-going. The first factor of type (i), shared by one cell line and the chemical descriptors, activates genes linked to inflammatory processes and is active in particular for non-steroidal anti-inflammatory drugs (NSAIDs), especially ibuprofen-like compounds, which are known to have anti-cancer effects (Ruegg et al., 2003). Of the factors shared by all cell lines (type iii), the one with the highest norm of the weight vector shows strong toxic effects on all cell lines, being linked to stopping of cell growth and apoptosis. In summary, these first findings are well in line with established knowledge.

We next validated quantitatively the ability of the model to discover biologically meaningful factors. We evaluated the performance of the factors in representing drugs in the task of retrieving drugs known to have similar effects (having the same targets).

We represented each drug with the corresponding vector in the latent variable matrix \mathbf{Z} , and used correlation along the vectors as a similarity measure when

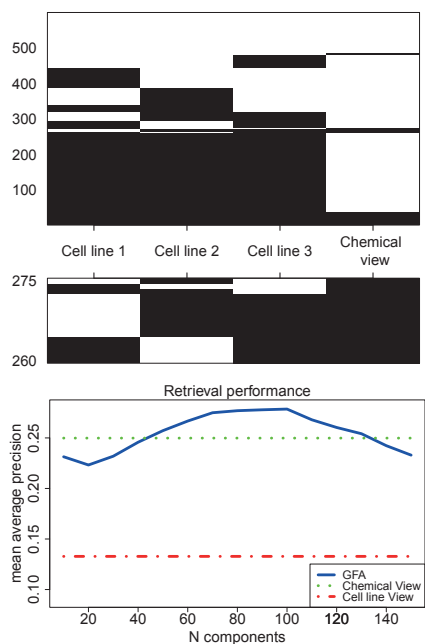


Figure 5: Multi-set analysis of drug responses. **Top:** Factor activity matrix of the factors (rows) against the 3 biological views (columns), cell lines HL60, MCF7, PC3, and the chemical view of drug descriptors. The small matrix at the bottom shows a zoomed inset to an interesting subset of the factors. **Bottom:** Mean average precision of retrieving drugs having similar effects (targets), based on the first N GFA factors. Integration of the data sources gives a significantly higher retrieval performance than any data source separately.

retrieving the drugs most similar to a query drug. Retrieval performance was measured as the mean average precision of retrieving drugs having similar effects (having the same targets). As baselines we computed the similarities in only the biological views or in only the chemical view. Representation by the GFA factors outperforms significantly (t -test, $p < 0.05$) using either space separately (Fig. 5, bottom). The experiment was completely data driven except for one bit of prior knowledge: As the chemical space is considered to be the most informative about drug similarity, the factors were pre-sorted by decreasing Euclidean norm of the weight vectors \mathbf{w}_k in the chemical space.

6 Discussion

We introduced a novel problem formulation of finding factors describing dependencies between data sets or

views, extending classical factor analysis which does the same for variables. The task is to provide a set of factors explaining dependencies between all possible subsets of the views. For solving the problem, coined group factor analysis (GFA), we provided a group-wise sparse Bayesian factor analysis model by extending a recent CCA formulation by Virtanen et al. (2011) to multiple views. The model was demonstrated to find factors of different types, including those specific to just one view and those shared by all views, equally well even for high numbers of views. We applied the model to data analysis in new kinds of application setups in neuroimaging and chemical systems biology.

The variational approximation used for solving the problem is computationally reasonably efficient and is directly applicable to data sets of thousands of samples and several high-dimensional views, with the main computational cost coming from a high number of factors slowing down the search for an optimal rotation of the factors. It would be fruitful to develop (approximative) analytical solutions for optimizing Eq. 2 necessary for the model to converge to the correct sparsity structure, which would speed up the algorithm to the level of standard Bayesian PCA/FA.

The primary challenge in solving the GFA problem is in correctly detecting the sparsity structure. Our solution was demonstrated to be very accurate at least for simulated data, but it would be fruitful to study how well the method fares in comparison with alternative modeling frameworks that could be adapted to solve the GFA problem, such as the structured sparse matrix factorization by Jia et al. (2010) or nonparametric sparse factor analysis (Knowles and Ghahramani, 2011) modified to support group sparsity. It could also be useful to consider models that are group-wise sparse but allow sparsity also within the active factor-view groups or sparse deviations from zero for the inactive ones, with model structures along the lines Jalali et al. (2010) proposed for multi-task learning.

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