Latent Factor Regression Models for Grouped Outcomes

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Outline

1. Overview
2. Modeling Grouped Outcomes
3. Simulation Study
4. Study for Future Families
5. Conclusions
Multiple-outcome regression models pool information across outcomes, for higher power to detect a covariate effect.

Two traditional approaches:

- **Random effect models**: random effects induce correlations between outcomes (cf. Sammel, Lin, & Ryan 1999; Roy, Lin, & Ryan 2003)
- **Latent factor models**: continuous latent variables manifested by outcomes (cf. Muthén 2002; Sanchez et al. 2005)

Our focus: **Multiple outcomes nested in domains** such as motor function, intelligence, and attention.

Motivating example: Relating sexually dimorphic traits in male infants to factors including exposure to phthalates (industrial chemicals).
Overview

- We show **the random effect models are a special case of the continuous latent factor framework, even when the multiple outcomes are nested in domains**

- Not surprising since the continuous latent factor framework is extremely general, and non-identifiable in unrestricted case.

- Allows us to view modeling options as a spectrum between parsimonious random effect models and flexible latent factor models

- We **introduce a set of models along this spectrum, and show that they are identifiable**
Overview

- Gives a set of general-purpose tools for modeling and sensitivity analysis in the case of outcomes nested in domains

- Yields estimates of the exposure/covariate effect both at the domain and outcome levels

- Shares information across outcomes, in part by **shrinkage of the estimated effect across outcomes**.

- Models **differ in degree of shrinkage**
Modeling Grouped Outcomes

Random effect regression model for outcomes nested in domains

(Thurston, Ruppert, Davidson 2009). Subjects $i \in \{1, \ldots, n\}$, (standardized) outcomes $j \in \{1, \ldots, p\}$:

$$Y_{ij} = (b_{o,j} + b_{D,d(j)} + b)X_i + \phi_i + \psi_{i,d(j)} + \epsilon_{ij}$$

$d(j) \in \{1, \ldots, D\}$: domain of outcome $j$

$b$: common covariate effect

$b_{D,d(j)}$: random domain-level covariate effect

$b_{o,j}$: random outcome-level covariate effect

$\phi_i$: subject random effect

$\psi_{i,d(j)}$: subject-domain random effect
Modeling Grouped Outcomes

\[ Y_{ij} = (b_{o,j} + b_{D,d(j)} + b)X_i + \phi_i + \psi_{i,d(j)} + \epsilon_{ij} \]

- Captures positive correlation between outcomes even after accounting for covariates
- Shrinks covariate effect across domains and across outcomes within a domain
Modeling Grouped Outcomes

**Continuous latent factor framework** (non-identifiable)
(cf. Sammel & Ryan 1996; Muthén 2002; Sanchez et al. 2005)

\[
Y_i = \alpha + \beta_o X_i + \Lambda \xi_i + \epsilon_i \\
\xi_i = \beta_D X_i + B \xi_i + \zeta_i.
\]

- \(Y_i\): outcomes vector
- \(\beta_o, \beta_D\): regression coefficients matrices
- \(\Lambda\): factor loadings matrix
- \(\xi_i\): latent factors vector
- \(B\): matrix relating latent factors
- \(\epsilon_i, \zeta_i\): independent residuals
Modeling Grouped Outcomes

- Take the # latent factors = $D$
- Take nonzero elements of $\Lambda$ to be the $(j, d(j))$ elements. E.g., with $D = 2$ and $p = 4$ where $d(1) = d(2) = 1$ and $d(3) = d(4) = 2$ then

$$\Lambda = \begin{pmatrix} \lambda_1 & \lambda_2 & 0 & 0 \\ 0 & 0 & \lambda_3 & \lambda_4 \end{pmatrix}^T.$$  

- Induce $B$ by setting $\xi_i = \beta_D X_i + \phi_i + \psi_i$

Yields

$$Y_{ij} = \alpha_j + \beta_{o,j} X_i + \lambda_j \xi_i, d(j) + \epsilon_{ij}$$

$$\xi_{ik} = \beta_{D,k} X_i + \phi_i + \psi_{ik}$$
Modeling Grouped Outcomes

\[ Y_{ij} = \alpha_j + \beta_{o,j} X_i + \lambda_j \xi_{i,d(j)} + \epsilon_{ij} \]
\[ \xi_{ik} = \beta_{D,k} X_i + \phi_i + \psi_{ik} \quad (1) \]

- This model is identifiable so long as \( \beta_{o,j} \) are random effects and \( \lambda_j = 1 \) for the first outcome in each domain.

- Additionally taking \( \lambda_j = 1 \) for all \( j \) and making \( \beta_{D,k} \) random effects yields the random effect model of Thurston et al. (2009).

- We investigate models of the form (1)
Modeling Grouped Outcomes

\[ Y_{ij} = \alpha_j + \beta_{o,j}X_i + \lambda_j \xi_{i,d(j)} + \epsilon_{ij} \]

\[ \xi_{ik} = \beta_{D,k}X_i + \phi_i + \psi_{ik} \]

We obtained this from the latent factor framework by making assumptions about \( \Lambda \) and \( B \)

Contrast our choice of \( B \) (induce via subject random effect \( \phi_i \)) with more standard choice: assign latent factors particular interpretations, like “motor function” and “intelligence”, then manually select a small number of nonzero elements in \( B \) corresponding to hypothesized associations among the factors
Modeling Grouped Outcomes

\[ Y_{ij} = \alpha_j + \beta_{o,j} X_i + \lambda_j \xi_{i,d(j)} + \epsilon_{ij} \]
\[ \xi_{ik} = \beta_{D,k} X_i + \phi_i + \psi_{ik} \]

Our models (identifiable):

A. As above

B. Make \( \beta_{D,k} \) random effects

C. Like A but sets \( \beta_{o,j} = 0 \)

D. Like C but sets \( \lambda_j = 1 \) for all \( j \)

Use Bayesian inference and MCMC computation
Simulation Study

Vary:

- Models used to simulate & fit data
- sample size $n$
- # outcomes per domain
- factor loading ($\lambda_j$) values
- ...

Evaluate bias and RMSE for:

- domain-specific covariate effects $\beta_{D,k}$
- outcome-specific covariate effects $OS_j \triangleq \beta_{o,j} + \lambda_j \beta_{D,d(j)}$
Simulation Study

<table>
<thead>
<tr>
<th>$\lambda_j$ Simulated Estimation</th>
<th>Some $\lambda_j = 0.5$ Model A</th>
<th>Model A</th>
<th>All $\lambda_j = 1$ Model B</th>
<th>Model D</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{bias } \beta_{D,k}$</td>
<td>$-0.011$</td>
<td>$-0.041$</td>
<td>$-0.014$</td>
<td>$-0.002$</td>
</tr>
<tr>
<td>$\text{bias OS}_j$</td>
<td>$-0.001$</td>
<td>$0.002$</td>
<td>$-0.005$</td>
<td>$0.001$</td>
</tr>
<tr>
<td>$\text{RMSE } \beta_{D,k}$</td>
<td>$0.054$</td>
<td>$0.063$</td>
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<td>$\text{RMSE OS}_j$</td>
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<td>$0.061$</td>
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</table>

Even when the model is misspecified:

RMSE is an order of magnitude smaller than the parameter range (.5) for $\text{OS}_j$, and $\approx 5 \times$ smaller than the range (.2) for $\beta_{D,k}$.

Bias is 2 orders of magnitude smaller than the range for $\text{OS}_j$ and $5-25 \times$ smaller for $\beta_{D,k}$.
## Simulation Study

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The highest error occurs if we fit too simple of a model (D) when the data are simulated from a more complex model (A).

The lowest error occurs if the model is simple (D) and we fit the simple model (D).

Fitting Model B does not yield lower error than fitting Model A, even if the data are from Model B.
Study for Future Families:

Relate sexually dimorphic traits in male infants to factors including phthalate exposure.

7 outcomes, in 3 domains:

- 4 skinfold thickness metrics
- body mass index and weight percentile-for-age
- head circumference percentile-for-age

Predictors including:

- phthalate score
- infant age
- gestational age
- mother’s age & race
Study for Future Families

- Applied Models A, C, and D (Model B not appropriate because phthalate effect not hypothesized to be similar, or even have the same sign, in all domains)
- Find no evidence of a phthalate effect in any model
- Estimated covariate effects show differences between models
Model D coefficient estimates (common within a domain):

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Domain 1</th>
<th>Domain 2</th>
<th>Domain 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant Age</td>
<td>$-28.0 \ (-41.5, -14.9)$</td>
<td>$-19.5 \ (-36.0, -3.3)$</td>
<td>$16.1 \ (-2.7, 34.9)$</td>
</tr>
<tr>
<td>Mother’s Age</td>
<td>$-11.3 \ (-24.9, 1.9)$</td>
<td>$0.13 \ (-13.2, 13.4)$</td>
<td>$9.97 \ (-9.4, 29.5)$</td>
</tr>
<tr>
<td>Gestational Age</td>
<td>$8.36 \ (-4.9, 21)$</td>
<td>$18.1 \ (2.0, 34.1)$</td>
<td>$10.4 \ (-8.3, 29.1)$</td>
</tr>
<tr>
<td>Race (Cauc./Non)</td>
<td>$5.06 \ (-7.9, 18.0)$</td>
<td>$4.56 \ (-8.1, 17.3)$</td>
<td>$-12.3 \ (-31.1, 6.4)$</td>
</tr>
</tbody>
</table>

- Positive relationship between gest. age and BMI/weight
- Negative relationship between infant age and both skinfold thickness and BMI/weight
Model A estimates are shrunk relative to separate regressions, and Model D estimates are shrunk relative to Model A. Model C estimates are very different.
Although interval estimates get wider Model D → C → A, there are as many significant covariate effects in Models C & A as in D.

Slightly different set in Model A, which allows covariate effects to have different significance within a domain
Conclusions

- Showed that random-effect models for multiple outcomes nested in domains are a special case of the continuous latent factor framework.

- Introduced identifiable models extending the random-effect models.

- Simulations show excellent accuracy in point estimation of outcome-specific and domain-specific covariate effects, even in misspecified cases.

- Applied to the Study for Future Families to understand factors relating to sexually dimorphic traits in male infants.

- We recommend the use of Models A & D, which showed complementary strengths in the simulation study and different degrees of shrinkage in the data analysis.

Paper available at: http://people.orie.cornell.edu/woodard/