



Finanziato
dall'Unione europea
NextGenerationEU



Ministero
dell'Università
e della Ricerca



Italiadomani
UNIVERSITÀ E RICERCA



ADDRESSING LATENT STATE SEPARATION IN HIDDEN MARKOV MODELS FOR CATEGORICAL DATA WITH COVARIATES: A PENALISED MAXIMUM LIKELIHOOD APPROACH

LUCA BRUSA¹, FULVIA PENNONI¹,
FRANCESCO BARTOLUCCI², ROMINA PERUILH BAGOLINI²
(luca.brusa@unimib.it)

¹University of Milano-Bicocca - Department of Statistics, and Quantitative Methods

²University of Perugia - Department of Economics

Outline

- 1 Hidden Markov models
- 2 Penalized maximum likelihood approach
- 3 Simulation study
- 4 Application
- 5 Conclusions
- 6 References

Hidden Markov model: notation

- **Univariate binary response variables** $\mathbf{Y}_i = (Y_i^{(1)}, \dots, Y_i^{(T)})$, with

$$Y_i^{(t)} = \begin{cases} 1 & \text{if the event of interest is observed at time } t \text{ for unit } i \\ 0 & \text{otherwise} \end{cases}$$

- **Hidden process:** $\mathbf{U}_i = (U_i^{(1)}, \dots, U_i^{(T)})$, following a first-order Markov chain with state-space $\{1, \dots, k\}$, initial probabilities π_u , and transition probabilities $\pi_{u|\bar{u}}$
- **Covariates:** $\mathbf{x}_i = (\mathbf{x}_i^{(1)}, \dots, \mathbf{x}_i^{(T)})$, with $\mathbf{x}_i^{(t)}$ representing the vector of observed individual covariates for unit i at time t
 - **lagged response:** allows for serial dependence between responses over time, thus relaxing the conditional independence of $\mathbf{Y}$ given $\mathbf{U}$ and $\mathbf{x}$

Model formulation

1 **Measurement model** (affected by covariates):

- Conditional distribution of the response variable $Y_i^{(t)}$ given the latent variable $U_i^{(t)}$ and the covariates $\mathbf{x}_i^{(t)}$
- **Conditional response probabilities:**

$$\phi_{u\mathbf{x}}^{(t)} = \mathbb{P} \left(Y_i^{(t)} = 1 | U_i^{(t)} = u, \mathbf{x} \right),$$

such that:

$$\log \frac{\phi_{u\mathbf{x}}^{(t)}}{1 - \phi_{u\mathbf{x}}^{(t)}} = \alpha_u + \mathbf{x}'\beta$$

2 **Latent model** (not affected by covariates):

- Non-parametric distribution of the latent process
- **Unobserved heterogeneity** between individuals, which remains when covariates in the measurement model cannot fully explain the variability

Maximum likelihood estimation

- **Expectation-maximization** (EM) algorithm (Dempster et al., 1977) is often employed to perform **maximum likelihood estimation**
- It maximizes the observed-data log-likelihood function $\ell(\theta)$ relying on the **complete-data log-likelihood** function $\ell^*(\theta)$
- It alternates the following steps until convergence:
 - **E-step: compute the conditional expected value** of $\ell^*(\theta)$ given the value of the parameters at the previous step and the observed data
 - **M-step: update the model parameters** by maximizing the expected value of $\ell^*(\theta)$:
 - explicit solutions are available for π_u and $\pi_{u|\bar{u}}$
 - a Newton-Raphson algorithm is used for updating α and β

Outline

- 1 Hidden Markov models
- 2 Penalized maximum likelihood approach**
- 3 Simulation study
- 4 Application
- 5 Conclusions
- 6 References

Motivation

- When the model is applied to **binary** and categorical response variables with a limited number of categories, the support points α_u may be very large, leading to **widely separated latent states** (**separation problem**)
- This may results in:
 - **excessively higher relevance of one or more latent states** than others
 - **reduced importance of the available covariates** whose estimated effects may become negligible and insignificant
 - **instability of the estimates**

Penalized maximum likelihood estimation

- Proposed **penalty**: to **reduce latent states separation**:

$$\mathcal{A} = \sum_{u=1}^k (\alpha_u - \bar{\alpha})^2,$$

where $\bar{\alpha} = \frac{1}{k} \sum_{u=1}^k \alpha_u$

- Applied to** both the **observed-data log-likelihood** $\ell(\boldsymbol{\theta})$ and the **complete-data log-likelihood** $\ell^*(\boldsymbol{\theta})$:

$$\tilde{\ell}(\boldsymbol{\theta}) = \ell(\boldsymbol{\theta}) - \lambda \mathcal{A} \quad \text{and} \quad \tilde{\ell}^*(\boldsymbol{\theta}) = \ell^*(\boldsymbol{\theta}) - \lambda \mathcal{A},$$

where $\lambda \in \mathbb{R}^+$ is a **tuning parameter** controlling the penalization

- Penalized estimation through the **EM algorithm**:
 - the **E-step** remains unaltered
 - the **M-step** requires to **revise the Newton-Raphson** iteration for α

Outline

- 1 Hidden Markov models
- 2 Penalized maximum likelihood approach
- 3 Simulation study**
- 4 Application
- 5 Conclusions
- 6 References

Simulation study

- **Different scenarios** (40) to explore the performance of the proposal with $k = 3$ hidden states: **sample size** ($n = 250, 500$), **number of time occasions** ($T = 10, 20$), hidden **state persistence** (high or low) and **separation** (five different behaviors: $\alpha^j, j = 1, \dots, 5$)
- **Four covariates** also including the **lagged response variable**; the corresponding vector of regression coefficients is $\beta = (1, -1, 1, 1)'$
- Extensive **Monte Carlo simulation study**; for each scenario:
 - we randomly draw 50 samples
 - we estimate the HM model using both the standard approach and the penalized approach with $\lambda = 0.01$ and $\lambda = 0.05$

Comparison criteria

- **Percentage variation in** the following quantities for both procedures:
 - ① **root mean squared relative error between simulated and estimated model parameters (θ)** defined as:

$$\text{RMSRE} = \sqrt{\frac{1}{M} \sum_{m=1}^M \left(\frac{\hat{\theta}_m - \theta_m}{\theta_m} \right)^2}$$

- ② **standard errors of the covariate regression parameters β** , obtained as minus the second derivative of the expected value of the complete-data log-likelihood
- ③ **computational time**

Results - RMSRE

- In the majority of cases, both values of λ ensure a **lower RMSRE when using the penalized estimation** method. This indicates that the estimated parameters are closer to the true values (**higher estimation precision**)
- The **fourth and fifth scenarios** (characterized by highly separated states) shows the **greatest improvement**; the percentage decreases using penalized estimation are often exceeding 90%
- The penalization approach appears **less effective in the first scenario** (characterized by closely spaced states) and in cases with a high value of T (20 time occasions)
- **Only in two cases** the penalized estimation method exhibits **no improvement** with either value of λ , showing very slight increases in the RMSRE value

Other results

- **Standard errors:**

- In most cases, **penalization reduces the estimated standard errors**
- The proposed approach is **less effective under the first scenario**
- In all other cases, the **percentage decrease is significant**, often reaching very high values

- **Computational time:**

- Estimation with the **penalty** approach often **reduces the average computational time**
- Benefits are **particularly evident in the fourth and fifth scenarios** where hidden states are widely separated

Outline

- 1 Hidden Markov models
- 2 Penalized maximum likelihood approach
- 3 Simulation study
- 4 Application**
- 5 Conclusions
- 6 References

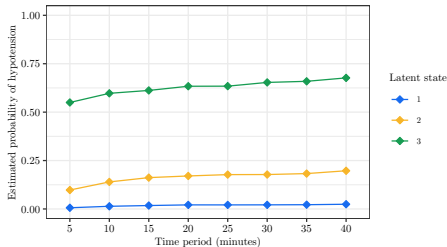
Hypotension during spinal anesthesia

- Data¹ refer to **375 patients** undergoing spinal anesthesia during a surgery; they cover the period **from January 2008 to January 2011**
- Measurements are taken 8 times, at equally spaced intervals over a period of 40 minutes
- Variable $Y_i^{(t)}$ indicates whether or not patient i has experienced **hypotension** (decrease in mean systolic blood pressure) at time t
- Approximately **25% ($n = 94$) of patients** recorded **at least one hypotensive status**
- Time-fixed covariates, time-varying covariates, and lagged response
- Using a **cross-validation approach**, we select **$k = 3$ hidden states** and a **penalization parameter of $\lambda = 0.01$** as optimal

¹Data are freely available at <https://peerj.com/articles/648/>.

Estimated conditional hypotension probability

- Patients in the **first hidden state** ($\hat{\alpha}_1 = -0.827$) have an **almost negligible probability of hypotension** during the surgery
- Patients in the **second hidden state** ($\hat{\alpha}_2 = 3.147$) experience a **low probability of hypotension**, ranging approximately from 0.10 to 0.20
- Patients in the **third hidden state** ($\hat{\alpha}_3 = 7.359$) have a **high probability of hypotension** during surgery, ranging from 0.54 to 0.68



Estimated regression coefficients

Covariate	$\hat{\beta}$	se	p -value
1 $\hat{\epsilon}$ Gender (Female)	1 $\hat{\epsilon}$ 1.541 *	2.032	0.042
Position (Supine)	0.813	1.597	0.110
Operation (Urogoly)	0.363	0.338	0.735
Operation (General surgery)	-0.061	-0.068	0.946
ECG (Normal)	-0.878	-0.978	0.328
2 $\hat{\epsilon}$ Age (year)	2 $\hat{\epsilon}$ 0.037 *	1.967	0.049
3 $\hat{\epsilon}$ DBP	3 $\hat{\epsilon}$ -0.167 **	-7.642	0.000
Pulse rate	-0.002	-0.216	0.829
Marcaïn-heavy	-0.049	-1.235	0.217
4 $\hat{\epsilon}$ Midazolam	4 $\hat{\epsilon}$ 0.243 *	2.104	0.035
Chirocaine	-0.049	-1.346	0.178
Fentanyl	1.215	0.515	0.607
5 $\hat{\epsilon}$ Hypotension ($t - 1$)	5 $\hat{\epsilon}$ 2.675 **	10.289	0.000

- **Gender** (female) has a **significant positive effect** on the response variable, indicating that the conditional **probability of experimenting hypotension** given the latent state is **higher for females**

Estimated regression coefficients

Covariate	$\hat{\beta}$	$\hat{se}$	p -value
1 $\downarrow$ Gender (Female)	1 $\downarrow$ 1.541 *	2.032	0.042
Position (Supine)	0.813	1.597	0.110
Operation (Urogoly)	0.363	0.338	0.735
Operation (General surgery)	-0.061	-0.068	0.946
ECG (Normal)	-0.878	-0.978	0.328
2 $\downarrow$ Age (year)	2 $\downarrow$ 0.037 *	1.967	0.049
3 $\downarrow$ DBP	3 $\downarrow$ -0.167 **	-7.642	0.000
Pulse rate	-0.002	-0.216	0.829
Marcaïn-heavy	-0.049	-1.235	0.217
4 $\downarrow$ Midazolam	4 $\downarrow$ 0.243 *	2.104	0.035
Chirocaine	-0.049	-1.346	0.178
Fentanyl	1.215	0.515	0.607
5 $\downarrow$ Hypotension ($t - 1$)	5 $\downarrow$ 2.675 **	10.289	0.000

- Older individuals exhibit higher log-odds of being diagnosed with hypotension compared to younger individuals

Estimated regression coefficients

Covariate	$\hat{\beta}$	$\hat{se}$	p -value
1 _i Gender (Female)	1 _i 1.541 *	2.032	0.042
Position (Supine)	0.813	1.597	0.110
Operation (Urogoly)	0.363	0.338	0.735
Operation (General surgery)	-0.061	-0.068	0.946
ECG (Normal)	-0.878	-0.978	0.328
2 _i Age (year)	2 _i 0.037 *	1.967	0.049
3 _i DBP	3 _i -0.167 **	-7.642	0.000
Pulse rate	-0.002	-0.216	0.829
Marcaïn-heavy	-0.049	-1.235	0.217
4 _i Midazolam	4 _i 0.243 *	2.104	0.035
Chirocaine	-0.049	-1.346	0.178
Fentanyl	1.215	0.515	0.607
5 _i Hypotension ($t - 1$)	5 _i 2.675 **	10.289	0.000

- **Diastolic blood pressure** has a significant **negative effect** on the log-odds of hypotension: lower pressure is associated with higher probabilities of experiencing hypotension

Estimated regression coefficients

Covariate	$\hat{\beta}$	$\hat{se}$	p -value
1 $\hat{\beta}$ Gender (Female)	1 $\hat{\beta}$ 1.541 *	2.032	0.042
Position (Supine)	0.813	1.597	0.110
Operation (Urogoly)	0.363	0.338	0.735
Operation (General surgery)	-0.061	-0.068	0.946
ECG (Normal)	-0.878	-0.978	0.328
2 $\hat{\beta}$ Age (year)	2 $\hat{\beta}$ 0.037 *	1.967	0.049
3 $\hat{\beta}$ DBP	3 $\hat{\beta}$ -0.167 **	-7.642	0.000
Pulse rate	-0.002	-0.216	0.829
Marcaïn-heavy	-0.049	-1.235	0.217
4 $\hat{\beta}$ Midazolam	4 $\hat{\beta}$ 0.243 *	2.104	0.035
Chirocaine	-0.049	-1.346	0.178
Fentanyl	1.215	0.515	0.607
5 $\hat{\beta}$ Hypotension ($t - 1$)	5 $\hat{\beta}$ 2.675 **	10.289	0.000

- **Midazolam** has a significant **positive effect**, indicating that higher concentration of this drug in the blood is associated with increased odds of experiencing hypotension during surgery. For the other drugs, the estimated coefficients are not significant

Estimated regression coefficients

Covariate	$\hat{\beta}$	$\hat{se}$	p -value
1 Gender (Female)	1 1.541 *	2.032	0.042
Position (Supine)	0.813	1.597	0.110
Operation (Urogoly)	0.363	0.338	0.735
Operation (General surgery)	-0.061	-0.068	0.946
ECG (Normal)	-0.878	-0.978	0.328
2 Age (year)	2 0.037 *	1.967	0.049
3 DBP	3 -0.167 **	-7.642	0.000
Pulse rate	-0.002	-0.216	0.829
Marcaïn-heavy	-0.049	-1.235	0.217
4 Midazolam	4 0.243 *	2.104	0.035
Chirocaine	-0.049	-1.346	0.178
Fentanyl	1.215	0.515	0.607
5 Hypotension ($t - 1$)	5 2.675 **	10.289	0.000

- The **lagged response** has a significant **positive effect on hypotension** indicating serial correlation

Outline

- 1 Hidden Markov models
- 2 Penalized maximum likelihood approach
- 3 Simulation study
- 4 Application
- 5 Conclusions**
- 6 References

Limitations and future works

- **Implementation in C++ to improve computational speed**, particularly for datasets with a large number of repeated measurements and/or a large sample size
- **Evaluation of the model's predictive performance** and comparison with machine learning methods, also in connection with the use of HM models as early warning systems
- **Development of feature selection techniques** to identify relevant covariates, especially when many are available
- **Investigation of methods to achieve scalability**, such as parallel computation and dimension reduction, essential for handling large datasets efficiently

Outline

- 1 Hidden Markov models
- 2 Penalized maximum likelihood approach
- 3 Simulation study
- 4 Application
- 5 Conclusions
- 6 References**

References I

- AKTAS SAMUR, A., COSKUNFIRAT, N., AND SAKA, O. (2014). Comparison of predictor approaches for longitudinal binary outcomes: Application to anesthesiology data. *PeerJ*, **2**, e648.
- BARTOLUCCI, F. AND FARCOMENI, A. (2009). A multivariate extension of the dynamic logit model for longitudinal data based on a latent markov heterogeneity structure. *J. Am. Stat. Assoc.*, **104**, 816–831.
- BARTOLUCCI, F., FARCOMENI, A., AND PENNONI, F. (2013). *Latent Markov models for longitudinal data*. Chapman & Hall/CRC, Boca Raton.
- BARTOLUCCI, F., FARCOMENI, A., AND PENNONI, F. (2014). Latent Markov models: a review of a general framework for the analysis of longitudinal data with covariates. *Test*, **23**, 433–465.

References II

- BATES, D., HASTIE, T., AND TIBSHIRANI, R. (2023). Cross-validation: What does it estimate and how well does it do it? *J. Mach. Learn. Res.*, **24**, 1234–1256.
- DEMPSTER, A., LAIRD, N., AND RUBIN, D. (1977). Maximum likelihood from incomplete data via the EM algorithm (with discussion). *J. R. Stat. Soc. Series B Stat. Methodol.*, **39**, 1–38.
- SMYTH, P. (2000). Model selection for probabilistic clustering using cross-validated likelihood. *Stat. Comput.*, **9**, 63–72.
- WELCH, L. (2003). Hidden Markov models and the Baum-Welch algorithm. *IEEE Inform. Theory Soc. Newsl.*, **50**, 10–13.

Acknowledgments

Acknowledgment: The authors acknowledge the financial support from the grant “Hidden Markov Models for Early Warning Systems” of Ministero dell’Università e della Ricerca (PRIN 2022TZEXKF) funded by European Union - Next Generation EU, Mission 4, Component 2, CUP J53D23004990006.