

Bayesian Partition Models for Local Inference in Longitudinal and Survival Data

DISSERTATION DEFENSE

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Acknowledgments

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Outline

Thesis organization:

- I. Locally varying longitudinal mixed models
- II. Drift-diffusion models for tone learning
- III. Bivariate survival regression for current status data

Common features: Partition models that share **dependence** across time (longitudinal data) or across outcomes (survival data)

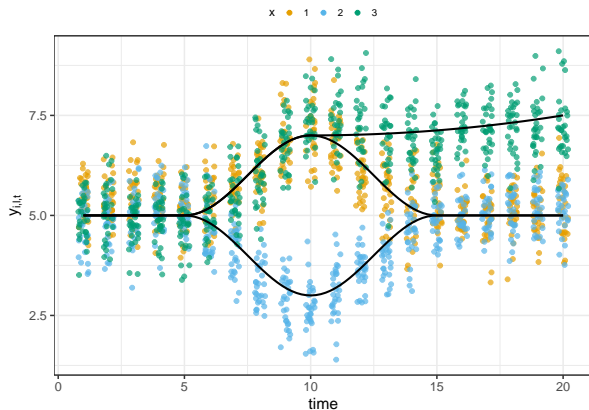
Locally varying longitudinal mixed models

Paulon, G., Llanos, F., Chandrasekaran, B., & Sarkar, A. (2020). Bayesian semiparametric longitudinal drift-diffusion mixed models for tone learning in adults. *Journal of the American Statistical Association*.

Paulon, G., Müller, P., & Sarkar, A. (2021). Bayesian semiparametric hidden Markov tensor partition models for local variable selection in longitudinal data. *Submitted*.

The setting

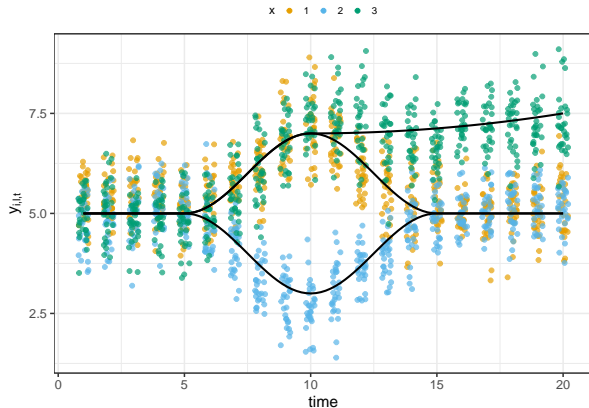
- ▶ Continuous response y varying smoothly over time
- ▶ Associated categorical predictor x which may vary with time
- ▶ The levels of x may affect y differently in the longitudinal stages



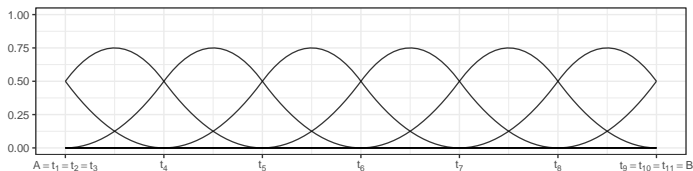
The setting

$$y_{i,\ell,t} \mid (x_{i,\ell,t} = x) = \underbrace{f_x(t)}_{\text{fixed effects}} + \underbrace{u_i(t)}_{\text{random effects}} + \underbrace{\varepsilon_{i,\ell,t}}_{\text{residuals}}, \quad \varepsilon_{i,\ell,t} \sim f_\varepsilon$$

Goal: partition model for the covariate space that evolves dynamically



Penalized B-splines: fixed effects



$$y_{i,l,t} = f_x(t) + u_i(t) + \varepsilon_{i,l,t}$$
$$\{f_x(t) \mid \beta_x\} = \sum_{k=1}^K \beta_{k,x} B_k(t)$$

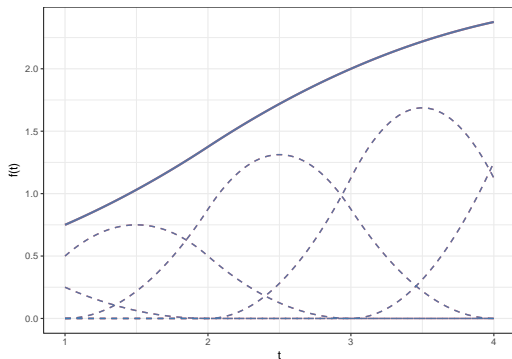
- ▶ Smoothness of curves favored by penalty for 'roughness'
- ▶ B-splines have local support
- ▶ We can cluster the curves by allowing the spline coefficients to have identical values

Local clustering: fixed effects

Curves can cluster 'globally'¹.

$$\beta_1 = (0.5, 1, 1.75, 2.25, 2.5)^\top$$

$$\beta_2 = (0.5, 1, 1.75, 2.25, 2.5)^\top$$



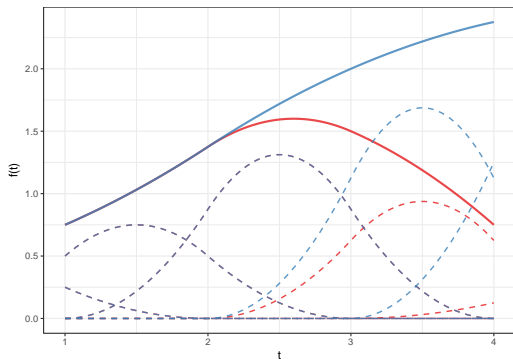
¹Gelfand, A. E., Kottas, A., & MacEachern, S. N. (2005). Bayesian nonparametric spatial modeling with Dirichlet process mixing. *Journal of the American Statistical Association*, 100, 1021–1035.

Local clustering: fixed effects

Curves can merge and branch at knot points, i.e. cluster 'locally'².

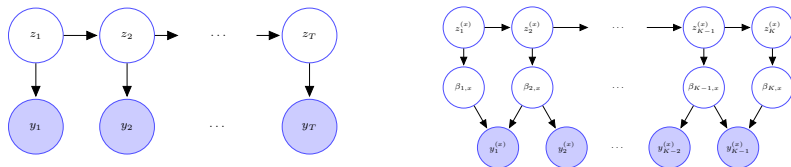
$$\beta_1 = (0.5, 1, 1.75, 2.25, 2.5)^\top$$

$$\beta_2 = (0.5, 1, 1.75, 1.25, 0.25)^\top$$



²Petrone, S., Guindani, M., & Gelfand, A. E. (2009). Hybrid Dirichlet mixture models for functional data. *Journal of the Royal Statistical Society: Series B*, 71, 755–782.

Local clustering: fixed effects



Conventional HMM and proposed HMM

$$y_{i,\ell,t} = f_x(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

$$\{f_x(t) \mid \beta_x\} = \sum_{k=1}^K \beta_{k,x} B_k(t)$$

$$\beta_{k,x} \mid (z_k^{(x)} = z_k) \sim \mathbb{1}\{\beta_{k,x} = \beta_{k,z_k}^*\}$$

- Dynamic clustering given by time evolving latent variables

Local clustering: example

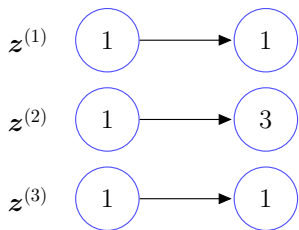
$$z^{(1)} \quad \textcircled{1}$$

$$z^{(2)} \quad \textcircled{1}$$

$$z^{(3)} \quad \textcircled{1}$$

$$\beta_{1,1} = \beta_{1,2} = \beta_{1,3} = \beta_{1,1}^*$$

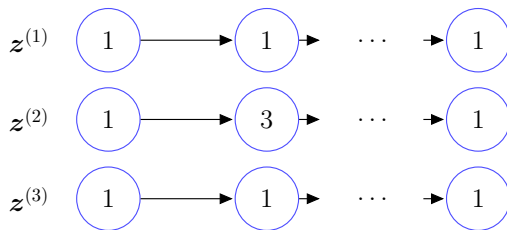
Local clustering: example



$$\beta_{2,1} = \beta_{2,3} = \beta_{2,1}^*$$

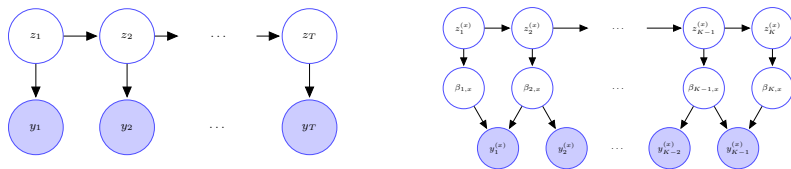
$$\beta_{2,2} = \beta_{1,3}^*$$

Local clustering: example



$$\beta_{K,1} = \beta_{K,2} = \beta_{K,3} = \beta_{K,1}^*$$

Local clustering: fixed effects



Conventional HMM and proposed HMM

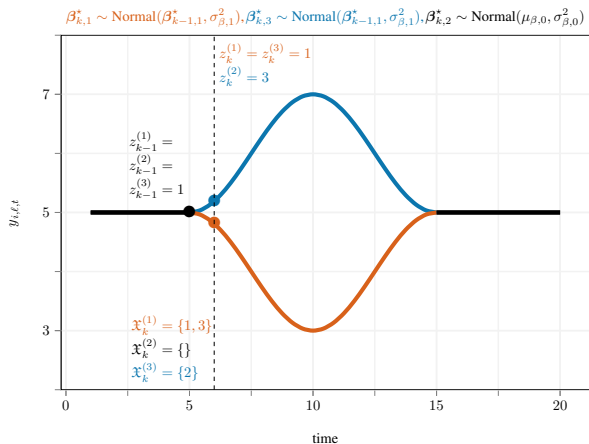
$$y_{i,\ell,t} = f_x(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

$$z_k^{(x)} \mid z_{k-1}^{(x)} = z_{k-1} \sim \text{Mult}(\pi_{z_{k-1},1}, \dots, \pi_{z_{k-1},z_{max}})$$

$$(\pi_{z,1}, \dots, \pi_{z,z_{max}}) \sim \text{Dir}(\alpha/z_{max}, \dots, \alpha/z_{max})$$

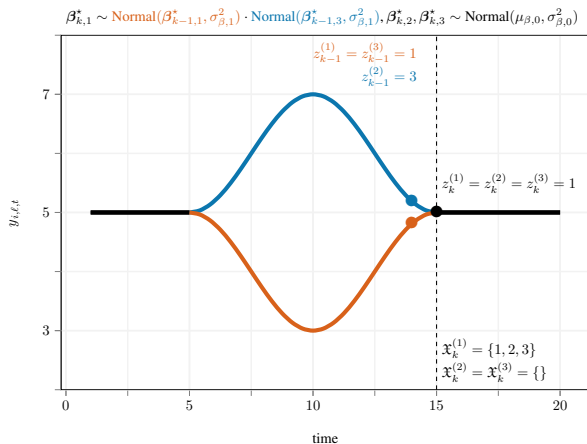
- Each level of the categorical predictor x is associated to a HMM for the group membership variables

Smoothing prior: fixed effects



- Markovian prior on the 'atoms' β_k^* to penalize first-order differences: favor smoothness

Smoothing prior: fixed effects



- ▶ Markovian prior on the 'atoms' β_k^* to penalize first-order differences: favor smoothness

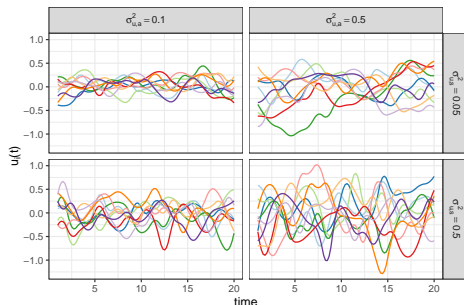
Random effects

$$y_{i,\ell,t} = f_x(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

$$u_i(t) = \sum_{k=1}^K \beta_{k,u,i} B_k(t)$$

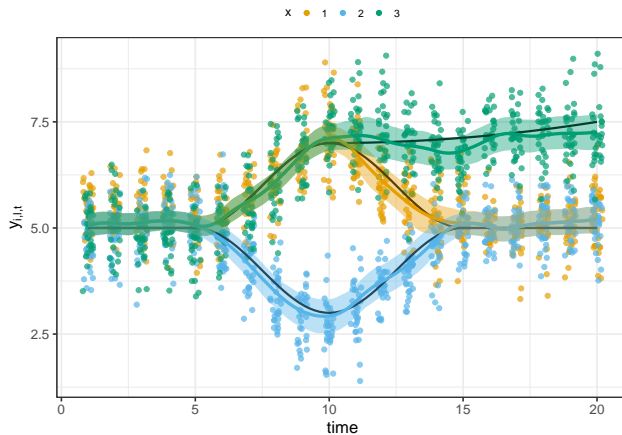
$$\beta_{u,i} \sim \text{MVN}_K\{\mathbf{0}, (\sigma_{u,a}^{-2} \mathbf{I}_K + \sigma_{u,s}^{-2} \mathbf{P}_u)^{-1}\}$$

$$\sigma_{u,s}^2 \sim \mathcal{C}^+(0, 1), \quad \sigma_{u,a}^2 \sim \mathcal{C}^+(0, 1)$$



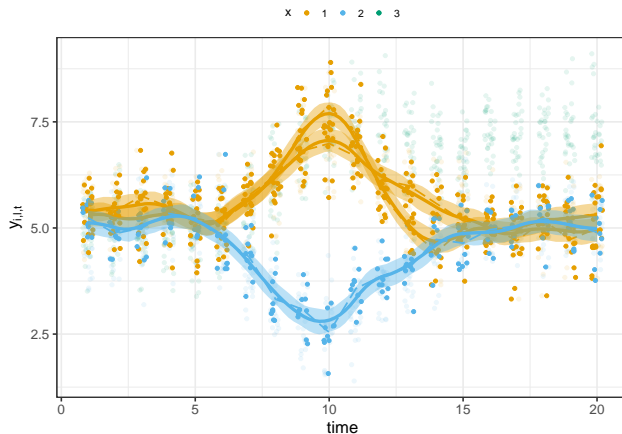
Each panel shows a collection of 10 random draws from the random effects distribution for a combination of $(\sigma_{u,s}^2, \sigma_{u,a}^2)$

Results: fixed effects



$$y_{i,\ell,t} = f_x(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

Results: individual effects



$$y_{i,l,t} = f_x(t) + u_i(t) + \varepsilon_{i,l,t}$$

Possible extensions

How to generalize the previous ideas to multiple predictors x_1, \dots, x_p ?

- ▶ Redefine each combination of the levels of (x_1, \dots, x_p) as a level of a new predictor x^* , and use the model for a single predictor.

Drawbacks: cumbersome computation; impossibility to characterize local and global variable importance of the individual predictors.

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Drawbacks: cumbersome computation; impossibility to characterize local and global variable importance of the individual predictors.

- ▶ Use an additive model: $y_{i,\ell,t} = f_{x_1}(t) + \dots + f_{x_p}(t) + u_i(t) + \varepsilon_{i,\ell,t}$.

Drawbacks: no interactions, no borrowing of information across levels of different predictors.

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Drawbacks: no interactions, no borrowing of information across levels of different predictors.

- ▶ Use a **joint model**: $y_{i,\ell,t} = f_{x_1, \dots, x_p}(t) + u_i(t) + \varepsilon_{i,\ell,t}$.

A joint longitudinal mixed model

- ▶ Multiple predictors $x_j \in \{1, \dots, x_{j,\max}\}, j = 1, \dots, p$

We consider the following generic class of longitudinal mixed models

$$\{y_{i,\ell,t} \mid x_{j,i,\ell,t} = x_j, j = 1, \dots, p\} = \underbrace{f_{x_1, \dots, x_p}(t)}_{\text{fixed effects}} + \underbrace{u_i(t)}_{\text{random effects}} + \underbrace{\varepsilon_{i,\ell,t}}_{\text{residuals}}$$

$$f_{x_1, \dots, x_p}(t) = \sum_{k=1}^K \beta_{k, x_1, \dots, x_p} B_k(t)$$

Proposed model:

- ▶ allows for **dynamic variable selection** and **partitioning** of the levels of the categorical variables
- ▶ accommodates **all order interactions** among the predictors

Why clustering?

Modeling all $K \prod_{j=1}^p x_{j,\max}$ parameters is impractical.

If we allow for identical values in some of the spline coefficients:

- ▶ we can reduce the number of parameters to be modeled
- ▶ we can establish that the some combinations of levels of (x_1, \dots, x_p) have no differential effect on the data generating mechanism
- ▶ we can borrow information across predictors and use more data to estimate the spline coefficients

Example

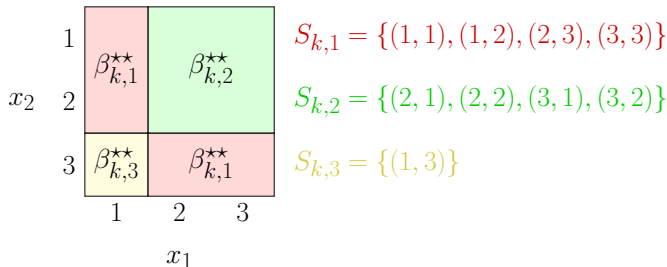
If $\beta_{x_1, \dots, x_{j,1}, \dots, x_p} = \beta_{x_1, \dots, x_{j,2}, \dots, x_p}$ for all combinations of $(x_1, \dots, x_{j-1}, x_{j+1}, \dots, x_p)$, then two levels $x_{j,1}$ and $x_{j,2}$ of x_j have no differential effect on the response.

Local clustering: fixed effects

We introduce local random partitions $\rho_k = \{S_{k,1}, \dots, S_{k,m_k}\}$ of \mathcal{X} , where m_k denotes the cardinality of ρ_k .

$$\{y_{i,l,t} \mid x_{j,i,l,t} = x_j, j = 1, \dots, p\} = f_{x_1, \dots, x_p}(t) + u_i(t) + \varepsilon_{i,l,t}$$

$$\{f_{x_1, \dots, x_p}(t) \mid (x_1, \dots, x_p) \in S_{k,h}, k = 1, \dots, K\} = \sum_{k=1}^K \beta_{k,h}^{**} B_k(t)$$



Local clustering: multiple predictors

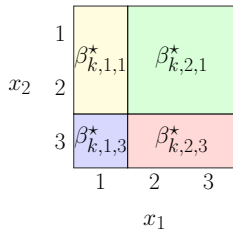
How to induce a partition $\rho_k = \{S_{k,1}, \dots, S_{k,m_k}\}$ of the predictor space \mathcal{X} ?

$$z_{1,k}^{(1)} = 1$$

$$z_{1,k}^{(2)} = z_{1,k}^{(3)} = 2$$

$$z_{2,k}^{(1)} = z_{2,k}^{(2)} = 1$$

$$z_{2,k}^{(3)} = 3$$



Local clustering: multiple predictors

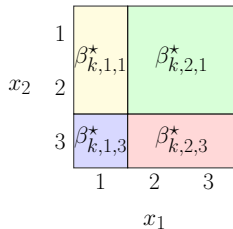
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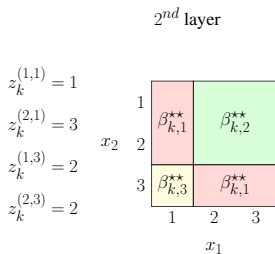
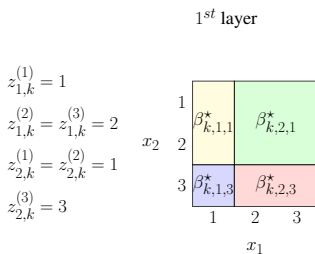


Limitation: joint partition is expressed as the product of p independent marginal partitions.

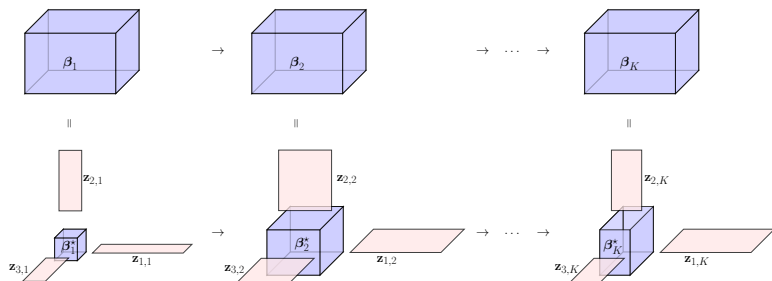
Dynamic partition model

Solution: introduce an additional latent allocation variable $z_k^{(z_1, k, \dots, z_p, k)}$ to make clustering fully flexible. It allows to find coarser partitions by grouping levels across categorical predictors.

$$\{\beta_{k, z_1, k, \dots, z_p, k}^* \mid (z_{1, k}^{(x_1)}, \dots, z_{p, k}^{(x_p)}) = (z_{1, k}, \dots, z_{p, k}), z_k^{(z_1, k, \dots, z_p, k)} = z_k\} = \beta_{k, z_k}^{**}$$



Tensor view



$$\{\beta_{k,x_1,\dots,x_p} \mid z_{j,k}^{(x_j)}, j = 1, \dots, p\} = \sum_{z_{1,k}} \cdots \sum_{z_{p,k}} \beta_{k,z_{1,k},\dots,z_{p,k}}^* \prod_{j=1}^p 1\{z_{j,k}^{(x_j)} = z_{j,k}\}$$

Theoretical properties

Consider $\|f\|_{2,g,loc} = \sum_{\mathbf{x} \in \mathcal{X}} g(\mathbf{x}) \sum_{k=1}^K f_{\mathbf{x}}^2(k)$.

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We can correctly estimate the underlying functions.

Function estimation

For any $\varepsilon > 0$, $\Pi(\|f - f_0\|_{2,g,loc} < \varepsilon \mid \text{data}) \rightarrow 1$.

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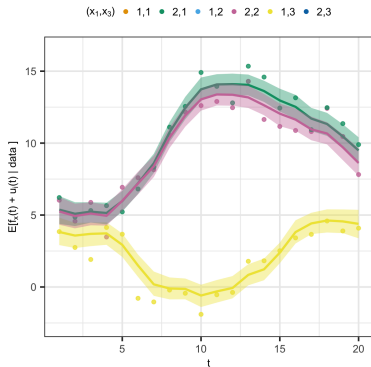
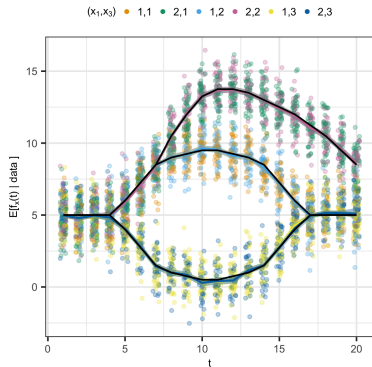
We can also identify the local partitions.

Local partitions

$\Pi(\rho_k = \rho_{k,0} \mid \text{data}) \rightarrow 1$.

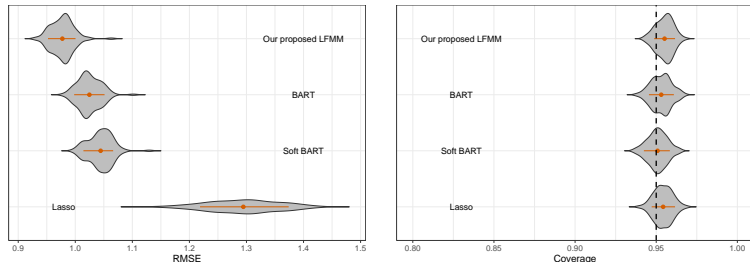
Consistency in recovering the local partitions implies consistency in **local variable selection**.

Results: synthetic data



- ▶ The model correctly identifies the only two important predictors and does not include the eight redundant ones

Results: synthetic data



- ▶ The out-of-sample predictive performance is uniformly better than the one of popular models for nonparametric regression

Drift-diffusion models for tone learning

Paulon, G., Reetzke, R., Chandrasekaran, B., & Sarkar, A. (2018). Functional logistic mixed-effects models for learning curves from longitudinal binary data. *Journal of Speech, Language, and Hearing Research*, 62, 543-553.

Paulon, G., Llanos, F., Chandrasekaran, B., & Sarkar, A. (2020). Bayesian semiparametric longitudinal drift-diffusion mixed models for tone learning in adults. *Journal of the American Statistical Association*.

Roark, C., Paulon, G., Sarkar, A., & Chandrasekaran, B. (2021). Comparing perceptual category learning across modalities in the same individuals. *Psychonomic Bulletin & Review*.

Motivating study

- ▶ Mandarin is a **tonal language**: every syllable has four different tones which convey different lexical meanings



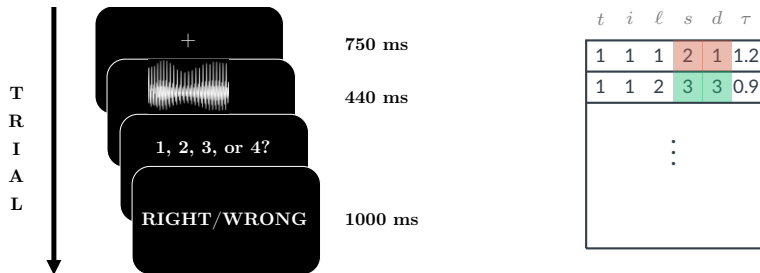
Goal: understand learning of novel speech categories in adulthood

In general: neural commitment to native-language speech sounds may preclude the learning of novel speech categories in adulthood.

Auditory tone learning experiments

Features of **tone learning** experiments:

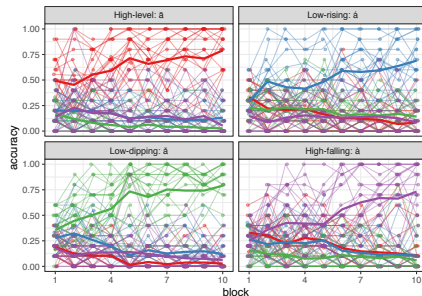
- ▶ exposure to perceptually variable tones
- ▶ trial-by-trial corrective feedback



Improvement of tone categorization within a few hundred trials

Auditory tone learning experiments

- ▶ Learned by 20 non-native speakers over a period of ≈ 20 days
- ▶ We focus on the first two days, when critical differences emerge
- ▶ Data comprise **final responses** and associated **response times**

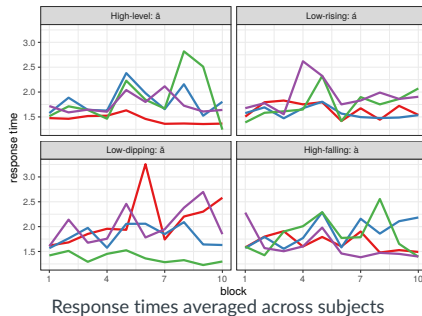


Proportions of times an input tone was classified into different tone categories by different subjects

How do the stimuli affect the perceptual mechanisms at different longitudinal stages?

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How do the stimuli affect the perceptual mechanisms at different longitudinal stages?

Two-choice decision tasks

Neural assumptions of perceptual decision making:

1. evidence is accumulated over time via increased firing of the neurons \Rightarrow multiple racing³ stochastic processes $W(\tau)$
2. a decision is made when firing rates reach a threshold \Rightarrow sufficient evidence has accumulated favoring one alternative over the other

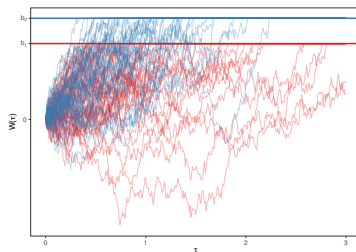
- ▶ Response **category**: first threshold to be reached
- ▶ Response **time** (RT): first-passage time

³Usher, M., & McClelland, J. L. (2001). The time course of perceptual choice: The leaky, competing accumulator model. *Psychological review*, 108.

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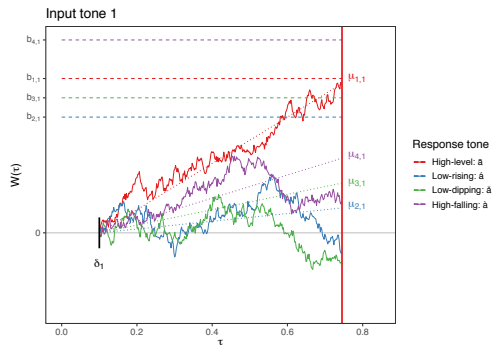
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Our proposal

Extend the existing literature to:

1. multiple-choice tasks
2. dynamic settings: $\theta_{d,s} \rightarrow \theta_{d,s}(t)$
3. subject-specific heterogeneity: $\theta_{d,s}(t) \rightarrow \theta_{d,s}^{(i)}(t)$
4. local clustering

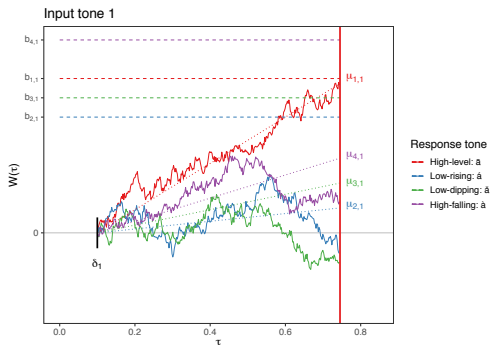
Drift-diffusion models



- When presented with the stimulus s , a decision d is reached at response time τ if the corresponding threshold $b_{d,s}$ is crossed **first**

$$\begin{cases} \tau = \min_{d'} \tau_{d'} \\ d = \arg \min_{d'} \tau_{d'} \end{cases}$$

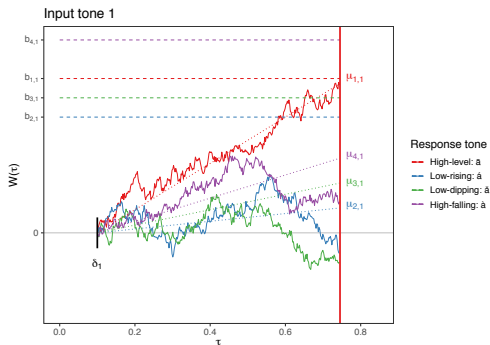
Drift-diffusion models



- δ_s : **offset time** irrelevant to the decision making process (e.g. encode an input signal s before accumulation starts, press a computer key).

Here the auditory stimulus $s = 1$, i.e. we focus on the input tone T1. In our experiment, $s \in \{1, \dots, 4\}$.

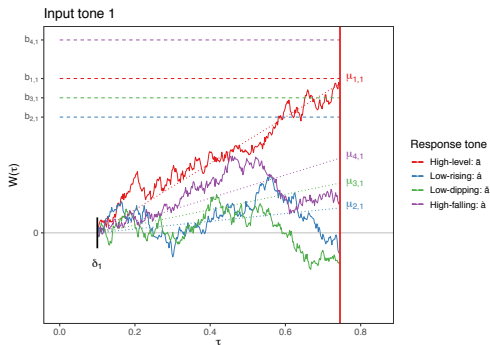
Drift-diffusion models



- $\mu_{d,s}$: **drift rate** at which the brain accumulates evidence in favor of d when the stimulus is s . Related to the firing rate of neurons.

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Drift-diffusion models



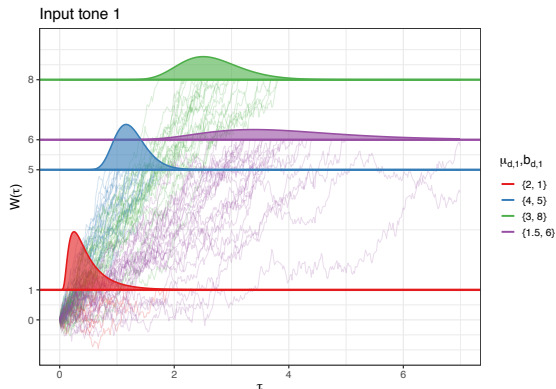
- $b_{d,s}$: **boundary parameter**, i.e. amount of evidence needed to decide in favor of d when the stimulus is s .

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Drift-diffusion models

The time τ_d to reach the d^{th} response boundary under the s^{th} input stimulus is distributed as an inverse-Gaussian with p.d.f.

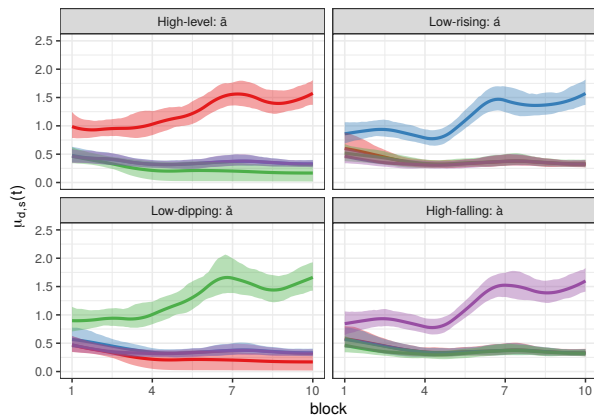
$$g(\tau_d | \theta_{d,s}) = \frac{b_{d,s}}{\sqrt{2\pi}} (\tau_d - \delta_s)^{-3/2} \exp \left[-\frac{\{b_{d,s} - \mu_{d,s}(\tau_d - \delta_s)\}^2}{2(\tau_d - \delta_s)} \right].$$



$$\mathbb{E}[\tau_d | \theta_{d,s}] = b_{d,s} / \mu_{d,s}$$

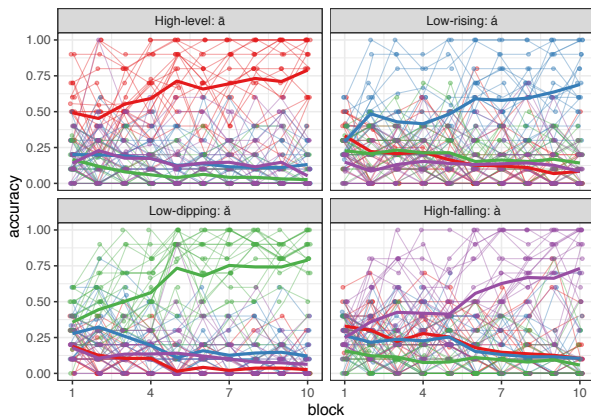
$$\text{var}(\tau_d | \theta_{d,s}) = b_{d,s} / \mu_{d,s}^3$$

Results: drift parameters



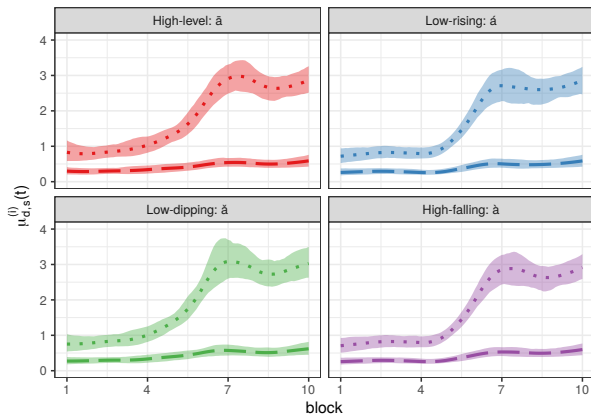
Estimated posterior mean and 95% CI for the population drift parameters $\mu_{d,s}(t)$

Results: drift parameters



Proportions of times an input tone was classified into different tone categories by different subjects

Results: individual level parameters



Estimated posterior mean for the individual drift parameters $\mu_{d,s}^{(i)}(t)$ obtained for two different participants, indicated by different line types

Bivariate survival regression for current status data

Paulon, G., Müller, P., & Sal y Rosas, V. G. (2021). Bayesian nonparametric bivariate survival regression for current status data. *Submitted*.

Motivating study

Randomized controlled trial to assess the effect of partner-notification strategies⁴:

- ▶ **expedited-treatment**: offered medication to give to their partners, or staff members contacted partners and provided them with medication without a clinical examination
- ▶ **standard partner referral**: advised to refer their partners for treatment

Follow-up visits for $n = 1864$ participants treated for recurrent infections:

- ▶ 933 assigned to standard therapy
- ▶ 931 assigned to expedited partner therapy

⁴Golden, M. R., Whittington, W. L., Handsfield, H. H., Hughes, J. P., Stamm, W. E., Hogben, M., ... Thomas, K. K., et al. (2005). Effect of expedited treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection. *New England Journal of Medicine*, 352, 676–685.

Current status data

Primary endpoints of the study: time to symptoms S_i and time to re-infection I_i .

When visiting the hospital at time C_i , two outcomes are recorded:

- ▶ Does the patient test positive for re-infection? $\Delta_{I_i} = \mathbb{1}(I_i < C_i)$
- ▶ Is the patient experiencing symptoms? $\Delta_{S_i} = \mathbb{1}(S_i < C_i)$

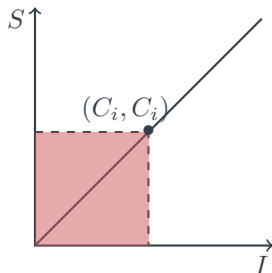
Available information on the outcomes: whether or not they exceed a common monitoring time $C_i \rightarrow$ bivariate current status data.

This is a very common source of data

Current status data

Four possible cases:

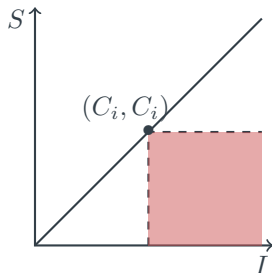
1. $(\Delta I_i, \Delta S_i) = (1, 1)$: positive test and presence of symptoms (symptomatic infections)



Current status data

Four possible cases:

2. $(\Delta I_i, \Delta S_i) = (0, 1)$: negative test but presence of symptoms (due to other causes)

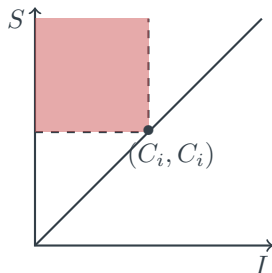


In this case $I_i > S_i$ and the symptoms must be due to other causes.

Current status data

Four possible cases:

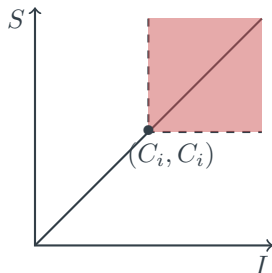
3. $(\Delta I_i, \Delta S_i) = (1, 0)$: positive test but absence of symptoms (asymptomatic infections)



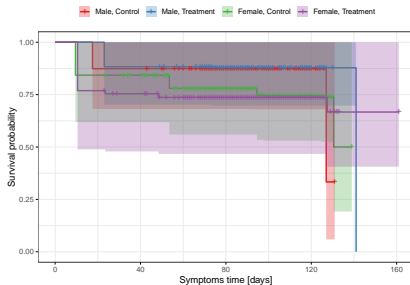
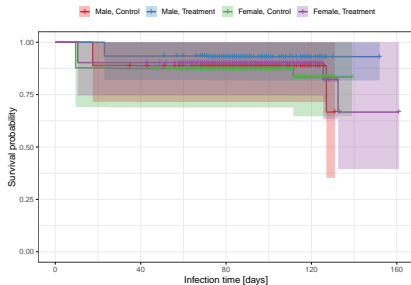
Current status data

Four possible cases:

4. $(\Delta I_i, \Delta S_i) = (0, 0)$: negative test and absence of symptoms



Issue 1: censoring misspecification



Nonparametric MLE

Let us focus on the univariate case:

- ▶ S_i : time to symptoms for patient i
- ▶ Δ_{S_i} : censoring indicator
- ▶ C_i : censoring time
 - ▶ $\Delta_{S_i} = 1$ if $S_i \leq C_i$ (left censoring)
 - ▶ $\Delta_{S_i} = 0$ if $S_i > C_i$ (right censoring)

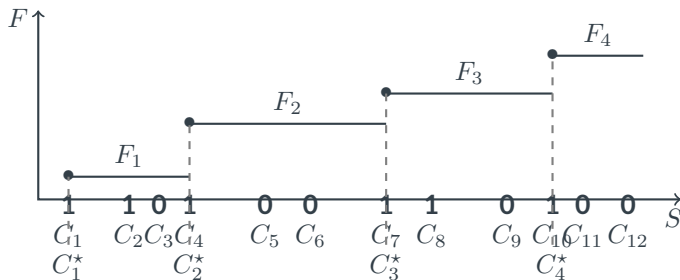
Goal: infer the unknown distribution $f_S(s)$ based on $\{(C_i, \Delta_{S_i})\}_{i=1}^n$, $i = 1, \dots, n$.

W.l.o.g., we assume that the censoring times are ordered, $C_{i-1} \leq C_i$.

Nonparametric MLE

Define $A = \{i > 1 \text{ s.t. } \Delta_{S_i} = 1, \Delta_{S_{i-1}} = 0\} \cup \{1\}$, the set of indices of left censored observations immediately following a right censored observation.

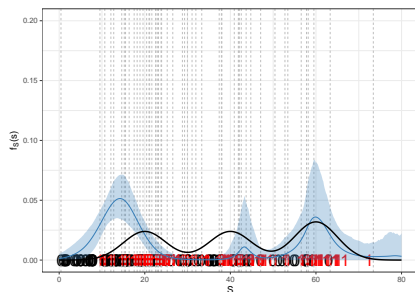
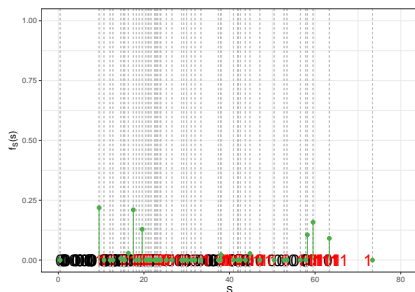
Let $J = |A|$ and $C^* = (C_1^*, \dots, C_J^*) = (C_i, i \in A)$ denote the corresponding censoring times.



Easy to show that $f_S(S) = \sum_{j=1}^{J+1} p_k \delta_{C_j^*}$.

Nonparametric MLE

We can implement a simple EM algorithm⁵.



⁵Groeneboom, P., & Wellner, J. A. (1992). *Information bounds and nonparametric maximum likelihood estimation*.

Proposed solution

Time of visit to the hospital can either occur:

- ▶ **uniformly** in the observation range (visit by protocol)

$$C_i \mid S_i, \lambda = \min\{\text{Unif}(A, B);$$

Proposed solution

Time of visit to the hospital can either occur:

- ▶ **uniformly** in the observation range (visit by protocol)
- ▶ closely **following** the symptoms onset (visit prompted by symptoms)

$$C_i | S_i, \lambda = \min\{\text{Unif}(A, B); S_i + \text{Exp}(\lambda)\}$$

Proposed solution

Time of visit to the hospital can either occur:

- ▶ **uniformly** in the observation range (visit by protocol)
- ▶ closely **following** the symptoms onset (visit prompted by symptoms)

$$C_i | S_i, \lambda = \min\{\text{Unif}(A, B); S_i + \text{Exp}(\lambda)\}$$

The p.d.f. of the conditional distribution of censoring times given the event times is

$$f_{C|S}(c | s) = \frac{\mathbb{1}\{c \leq s\}}{B - A} + \frac{\mathbb{1}\{c > s\}}{B - A} e^{-\lambda(c-s)} \{1 + \lambda(B - c)\}.$$

The setting

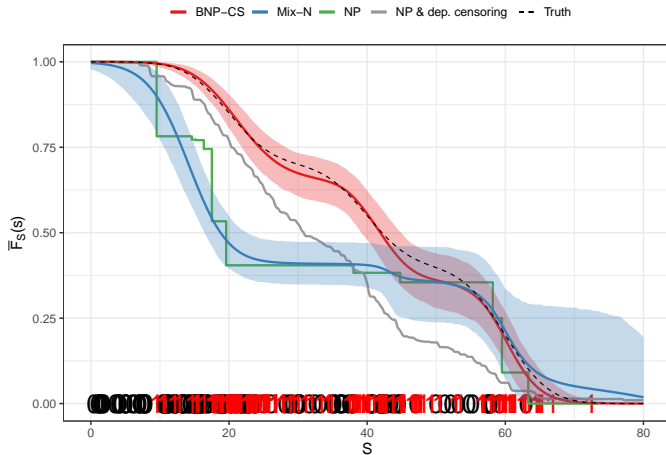
Prior shrinkage via BNP model

$$S_i | H \sim \int \mathbf{N}(S_i | \mu, \sigma^2) dH(\mu, \sigma^2), \quad H \sim \mathbf{DP}(M, H_0)$$

$$\Rightarrow S_i | \{\mu_k, \sigma_k^2, \pi_k\}_{k=1}^{+\infty} \sim \sum_{k=1}^{+\infty} \pi_k \mathbf{N}(S_i | \mu_k, \sigma_k^2)$$

- ▶ Introduce heterogeneity
- ▶ Can include regression on covariates

Results: synthetic data



Issue 2: nonparametric unidentifiability

Back to the bivariate case: we only observe the common monitoring time C_i and the two indicators $\Delta_{I_i} = \mathbb{1}\{I_i < C_i\}$, $\Delta_{S_i} = \mathbb{1}\{S_i < C_i\}$.

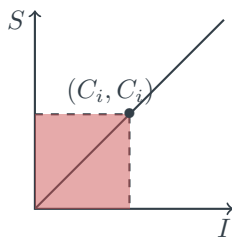
The conditional likelihood only depends on $F_1(c) = P(I_i \leq c)$, $F_2(c) = P(S_i \leq c)$, $F_3(c) = P(I_i \leq c, S_i \leq c)$.

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$$F = \prod_{i=1}^n \{F_3(c_i)^{\Delta_{I_i} \Delta_{S_i}}$$

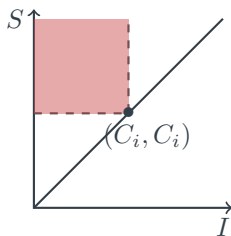


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$$F = \prod_{i=1}^n \{F_3(c_i)^{\Delta_{I_i} \Delta_{S_i}} (F_1 - F_3)(c_i)^{\Delta_{I_i} (1 - \Delta_{S_i})}$$

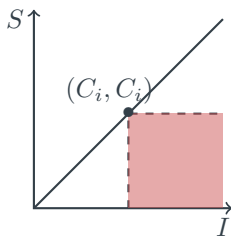


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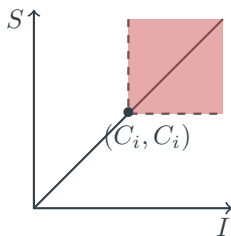


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Possible solutions

Identifiability issues with the nonparametric m.l.e. We can only identify:

- ▶ the marginals $F_1(c)$ and $F_2(c)$
- ▶ the measure of dependence $(F_3 - F_1F_2)(c)$.

Possible strategies:

1. estimate the joint distribution under parametric or semiparametric assumptions
2. build the joint model from the two identifiable marginal distributions and a choice for their dependence structure⁶ that reflects the underlying biology

⁶Wang, W., & Ding, A. A. (2000). On assessing the association for bivariate current status data. *Biometrika*, 87, 879–893.

A bivariate event time model

Two causes of symptoms:

- ▶ due to other causes

- ▶ due to disease

$$f_{IS}(I, S) = wf_{IS}^*(I, S) + (1 - w) \underbrace{f'_{IS}(I, S)}_{\substack{\text{constrained} \\ \text{to } I < S}}$$

A bivariate event time model

Two causes of symptoms:

- ▶ due to other causes \rightarrow time to infection and time to symptoms are independent
- ▶ due to disease \rightarrow time to infection and latency time are independent

$$f_{IS}(I, S) = w \underbrace{f_{IS}^*(I, S)}_{I \perp S} + (1 - w) \underbrace{f'_{IS}(I, S)}_{\substack{I < S \\ I \perp L = S - I}}$$

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- ▶ due to other causes \rightarrow time to infection and time to symptoms are independent
- ▶ due to disease \rightarrow time to infection and latency time are independent

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 &= w f_I(I) f_S^*(S) + (1 - w) f_I(I) f_L(S - I)
 \end{aligned}$$

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 &= w f_I(I) f_S^*(S) + (1 - w) f_I(I) f_L(S - I)
 \end{aligned}$$

Positivity constraint on the latency time:

$$L \mid \lambda_L \sim \text{Exp}(\lambda_L)$$

Building dependence structure

Nonparametric priors:

$$f_S^*(S) = \sum_{k=1}^{+\infty} \pi_k^{(S)} \mathbf{N}(S \mid \mu_k^{(S)}, \sigma_k^{(S)2})$$

$$f_I(I) = \sum_{k=1}^{+\infty} \pi_k^{(I)} \mathbf{N}(I \mid \mu_k^{(I)}, \sigma_k^{(I)2})$$

Building dependence structure

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Dependent censoring on S only:

$$C_i \mid S_i, \lambda = \min\{\mathbf{Unif}(A, B); S_i + \mathbf{Exp}(\lambda)\}$$

Building dependence structure

Nonparametric priors:

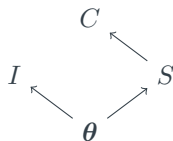
$$f_S^*(S) = \sum_{k=1}^{+\infty} \pi_k^{(S)} \mathbf{N}(S \mid \mu_k^{(S)}, \sigma_k^{(S)2})$$

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Dependent censoring on S only:

$$C_i \mid S_i, \lambda = \min\{\mathbf{Unif}(A, B); S_i + \mathbf{Exp}(\lambda)\}$$

Censoring regularizes inference on both f_I and f_S :



Building dependence structure

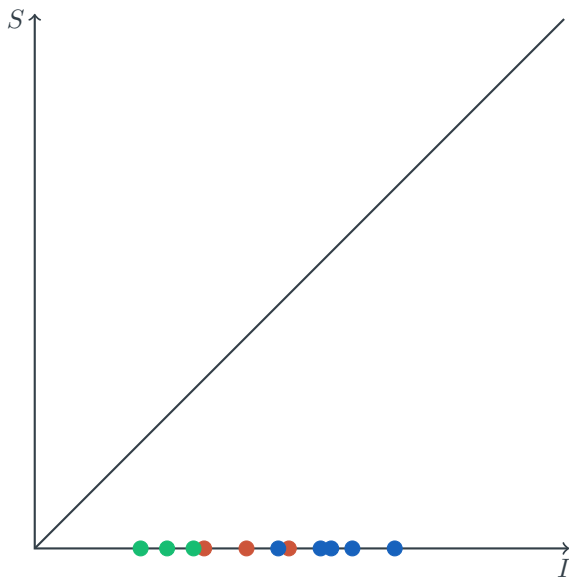
The implied marginal distributions are

$$f_I(I) = \sum_{k=1}^{+\infty} \pi_k^{(I)} \text{N}(I \mid \mu_k^{(I)}, \sigma_k^{(I)2})$$
$$f_S(S) = w \sum_{k=1}^{+\infty} \pi_k^{(S)} \text{N}(S \mid \mu_k^{(S)}, \sigma_k^{(S)2})$$
$$+ (1 - w) \sum_{k=1}^{+\infty} \pi_k^{(I)} \text{EMG}(S \mid \mu_k^{(I)}, \sigma_k^{(I)2}, \lambda_L),$$

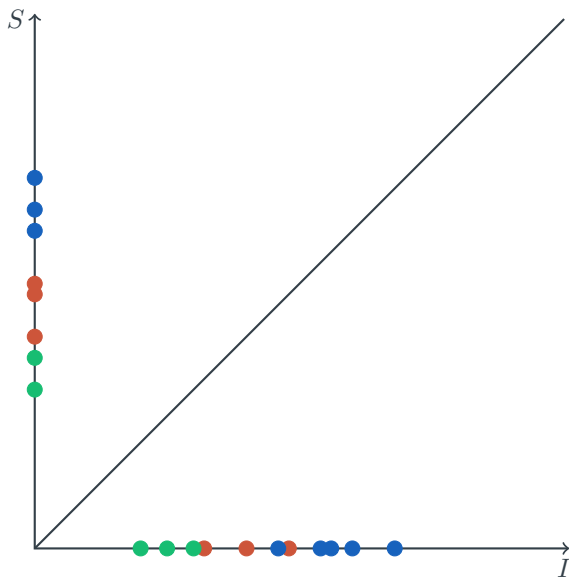
where $\text{EMG}(\mu, \sigma^2, \lambda)$ denotes the exponentially modified Gaussian distribution⁷.

⁷Grushka, E. (1972). Characterization of exponentially modified Gaussian peaks in chromatography. *Analytical Chemistry*, 44, 1733–1738.

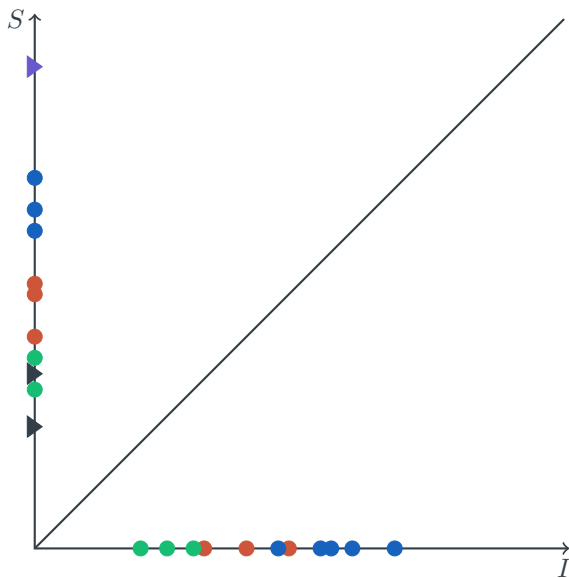
Dependent partitions



Dependent partitions



Dependent partitions



Regression on covariates

- ▶ Predictors: $\mathbf{x}_i = \{gender, arm, age\}$; $\mathbf{d} = (1, x_1, x_2, x_3)^\top$.

Extend the BNP priors to the families of r.p.m.s $\{H_{\mathbf{x}}^{(I)}, H_{\mathbf{x}}^{(S)}, \mathbf{x} \in \mathcal{X}\}$.

Regression on covariates

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Extend the BNP priors to the families of r.p.m.s $\{H_{\mathbf{x}}^{(I)}, H_{\mathbf{x}}^{(S)}, \mathbf{x} \in \mathcal{X}\}$.

We use a dependent DP (DDP) prior with common weights and covariate dependent atoms, i.e.

$$H_{\mathbf{x}} = \sum_k \pi_k \delta_{\mathbf{d}^\top \mathbf{m}_k}$$

where

$$\mathbf{d}^\top \mathbf{m}_k = \delta_k + \alpha_k x_1 + \beta_k x_2 + \gamma_k x_3$$

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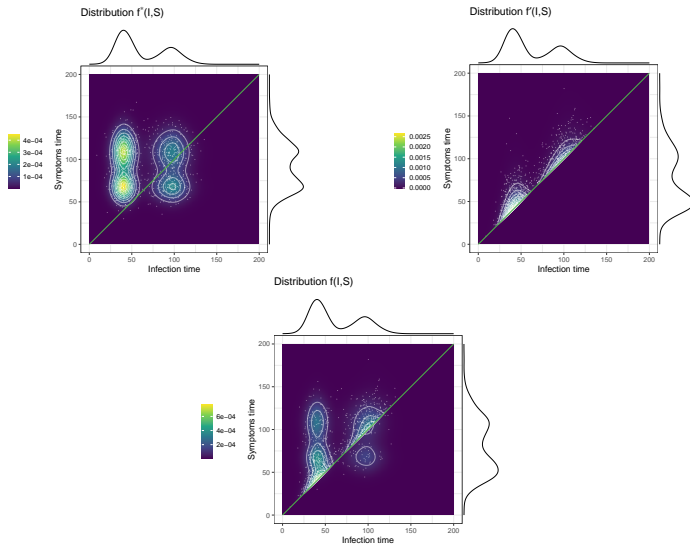
$$H_{\mathbf{x}} = \sum_k \pi_k \delta_{\mathbf{d}^\top \mathbf{m}_k}$$

where

$$\mathbf{d}^\top \mathbf{m}_k = \delta_k + \alpha_k x_1 + \beta_k x_2 + \gamma_k x_3$$

- ▶ **Heterogeneous treatment effect:** $H_{\mathbf{x}}$ implies $H_{\beta} = \sum_k \pi_k \delta_{\beta_k}$

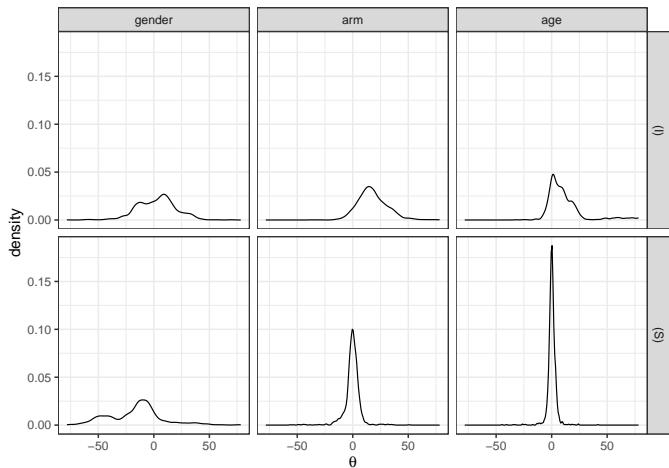
Results: synthetic data



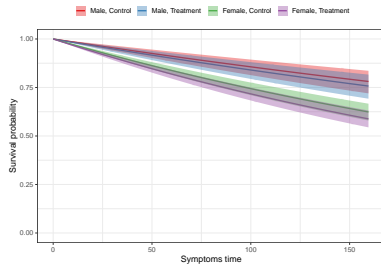
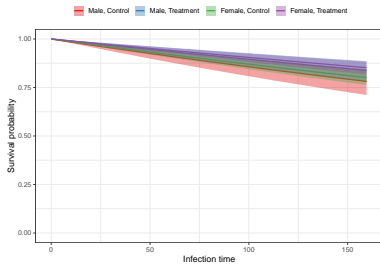
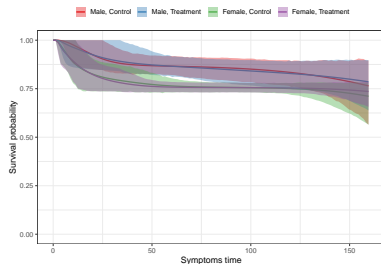
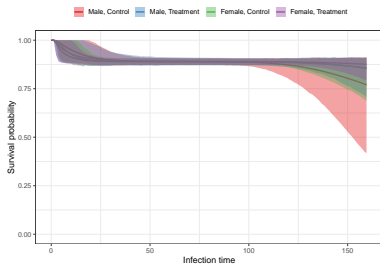
Results: synthetic data

	Sample Size	Distr.	De Iorio et al.	Bivariate Gumbel	Our method
(I)	$n = 250$	Inf.	1.64 (0.92, 3.01)	4.01 (3.14, 5.59)	1.10 (0.09, 2.24)
		Sym.	2.98 (1.11, 5.01)	6.15 (5.31, 8.77)	1.33 (0.18, 3.72)
	$n = 1000$	Inf.	1.32 (0.73, 1.90)	3.76 (3.19, 4.54)	0.50 (0.04, 1.80)
		Sym.	2.32 (1.19, 3.25)	5.99 (5.31, 6.99)	1.30 (0.54, 2.66)
(II)	$n = 250$	Inf.	0.96 (0.74, 1.56)	3.44 (3.08, 4.59)	0.99 (0.13, 2.07)
		Sym.	8.44 (5.21, 12.30)	11.75 (9.18, 18.01)	0.76 (0.22, 2.16)
	$n = 1000$	Inf.	0.80 (0.50, 1.10)	3.12 (3.03, 3.41)	0.19 (0.05, 0.50)
		Sym.	8.18 (6.28, 10.32)	10.74 (9.58, 12.49)	0.12 (0.02, 0.37)
(III)	$n = 250$	Inf.	4.45 (3.00, 6.30)	4.24 (3.09, 5.79)	0.45 (0.08, 1.14)
		Sym.	9.82 (6.70, 13.20)	8.08 (5.72, 12.15)	0.24 (0.03, 0.81)
	$n = 1000$	Inf.	4.10 (3.18, 4.96)	3.96 (3.24, 4.81)	0.13 (0.01, 0.35)
		Sym.	9.94 (8.44, 11.71)	7.98 (6.31, 10.06)	0.05 (0.01, 0.15)

Results: partner notification study



Results: partner notification study



To sum up

Our approach:

- ▶ similar to copula models, with added interpretability, e.g. exponential rates
- ▶ combining BNP model with known structure provides sufficient **regularization**

Work in progress:

- ▶ generalization to different **correlation** structures

Conclusions

Conclusions

► Longitudinal partition models & Auditory neuroscience

Paulon, G., Reetzke, R., Chandrasekaran, B., & Sarkar, A. (2018). Functional logistic mixed-effects models for learning curves from longitudinal binary data. *Journal of Speech, Language, and Hearing Research*, 62, 543-553.

Paulon, G., Llanos, F., Chandrasekaran, B., & Sarkar, A. (2020). Bayesian semiparametric longitudinal drift-diffusion mixed models for tone learning in adults. *Journal of the American Statistical Association*.

Roark, C., Paulon, G., Sarkar, A., & Chandrasekaran, B. (2021). Comparing perceptual category learning across modalities in the same individuals. *Psychonomic Bulletin & Review*.

Paulon, G., Müller, P., & Sarkar, A. (2021). Bayesian semiparametric hidden Markov tensor partition models for local variable selection in longitudinal data. *Submitted*.

Conclusions

- ▶ Longitudinal partition models & Auditory neuroscience
- ▶ Bivariate survival regression & Recurrent hospitalization data

Paulon, G., Müller, P., & Sal y Rosas, V. G. (2021). Bayesian nonparametric bivariate survival regression for current status data. *Submitted*.

Conclusions

- ▶ Longitudinal partition models & Auditory neuroscience
- ▶ Bivariate survival regression & Recurrent hospitalization data
- ▶ Dependent mixture models

Paulon, G., Trippa, L., & Müller, P. (2018). Invited comment on “Bayesian cluster analysis: Point estimation and credible balls”. *Bayesian Analysis*, 13, 590-593.

Pagani Zanini, C. T., Paulon, G., & Müller, P. (2021). Dependent mixtures: Modeling cell lineages. *In preparation*.

Thank you!

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Appendix

Smoothing priors: temporal dynamics

- ▶ HMM for the temporal evolution of the latent local cluster indicators with p independent dynamics:

$$(z_{j,k}^{(x_j)} \mid z_{j,k-1}^{(x_j)} = z_{k-1}) \sim \text{Mult}(\pi_{z_{k-1},1}^{(j)}, \dots, \pi_{z_{k-1},z_{max}}^{(j)})$$

$$\boldsymbol{\pi}^{(j)} = (\pi_{z,1}^{(j)}, \dots, \pi_{z,z_{max}}^{(j)})^\top \sim \text{Dir}(\alpha^{(j)}/z_{max}, \dots, \alpha^{(j)}/z_{max})$$

$$\alpha^{(j)} \sim \text{Ga}(a_\alpha, b_\alpha)$$

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- ▶ Explicit shrinkage priors on the covariate importance indicators:

$$\ell_{j,k} \propto \exp(-\varphi_j \ell_{j,k}) \mathbb{1}_{\{1, \dots, x_{j,max}\}}(\ell_{j,k}), \quad \varphi_j \sim \text{Ga}(a_\varphi, b_\varphi)$$

Smoothing priors: temporal dynamics

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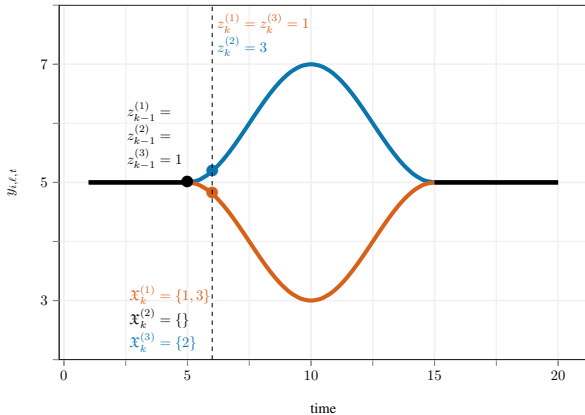
- ▶ Shrinkage priors on the second layer of allocation variables

$$\begin{aligned}(z_k^{(z_{1,k}, \dots, z_{p,k})} \mid \boldsymbol{\pi}^*) &\sim \text{Mult}(\pi_1^*, \dots, \pi_{\ell_k}^*) \\ \boldsymbol{\pi}^* = (\pi_1^*, \dots, \pi_{\ell_k}^*)^\top &\sim \text{Dir}(\alpha^*/\ell_k, \dots, \alpha^*/\ell_k) \\ \alpha^* &\sim \text{Ga}(a_{\alpha^*}, b_{\alpha^*})\end{aligned}$$

where $\ell_k = \prod_{j=1}^p \ell_{j,k}$.

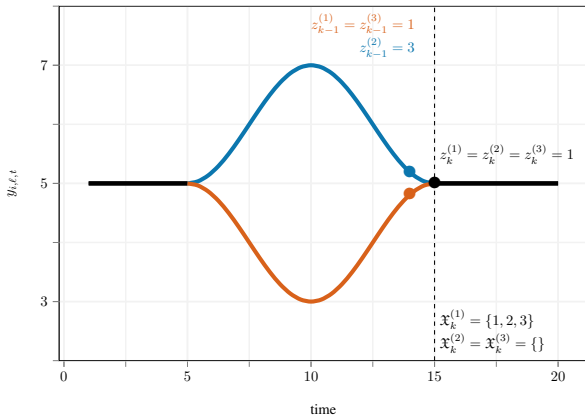
Smoothing prior: fixed effects

$$\beta_{k,1}^* \sim \text{Normal}(\beta_{k-1,1}^*, \sigma_{\beta,1}^2), \beta_{k,3}^* \sim \text{Normal}(\beta_{k-1,1}^*, \sigma_{\beta,1}^2), \beta_{k,2}^* \sim \text{Normal}(\mu_{\beta,0}, \sigma_{\beta,0}^2)$$



Smoothing prior: fixed effects

$$\beta_{k,1}^* \sim \text{Normal}(\beta_{k-1,1}^*, \sigma_{\beta,1}^2) \cdot \text{Normal}(\beta_{k-1,3}^*, \sigma_{\beta,1}^2), \beta_{k,2}^*, \beta_{k,3}^* \sim \text{Normal}(\mu_{\beta,0}, \sigma_{\beta,0}^2)$$



Posterior inference

Varying values of $\ell_{j,k}$ result in varying model dimensions.

Trans-dimensional step to update (ρ_k, β_k^{**}) :

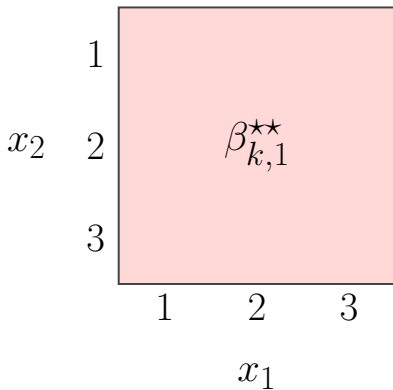
1. propose a change to the partition structure ρ_k
2. conditional on ρ_k , sample from the posterior of the spline coefficients $\beta_k^{**} = \{\beta_{k,h}^{**}\}_{h=1}^{M_k}$

Step 1: for each predictor j , perform the following M-H step

- (i) propose a change to the marginal partition for the levels of x_j (split or merge)
- (ii) propose a corresponding change to the joint partition ρ_k
- (iii) evaluate the acceptance rate, integrating out the curve-specific parameters

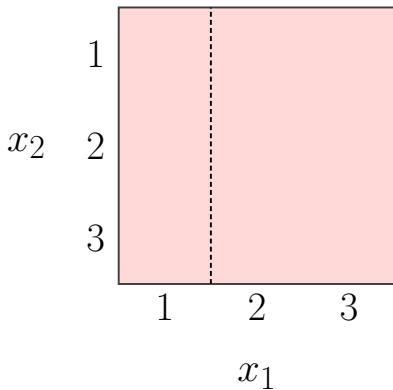
Posterior inference

Initial configuration



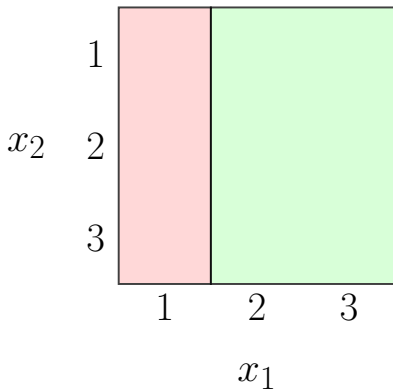
Posterior inference

Propose marginal partition for x_1 : split



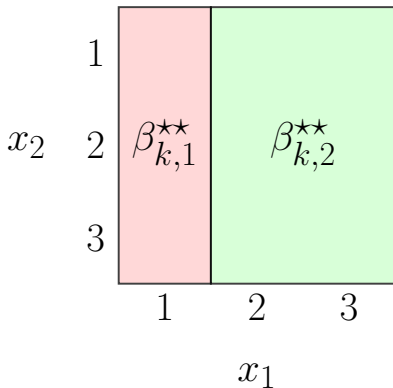
Posterior inference

Conditional on the marginal partition, propose joint partition



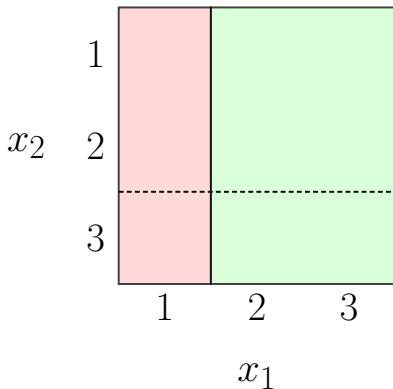
Posterior inference

If accept, update curve-specific parameters



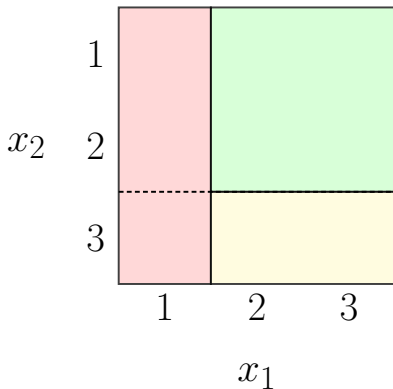
Posterior inference

Propose marginal partition for x_2 : split



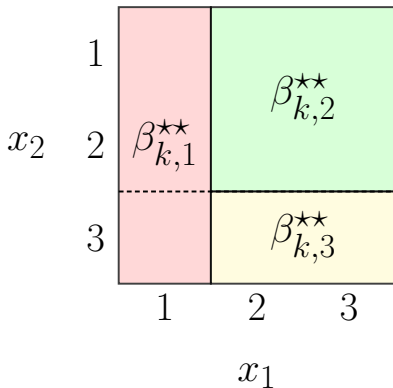
Posterior inference

Conditional on the marginal partition, propose joint partition



Posterior inference

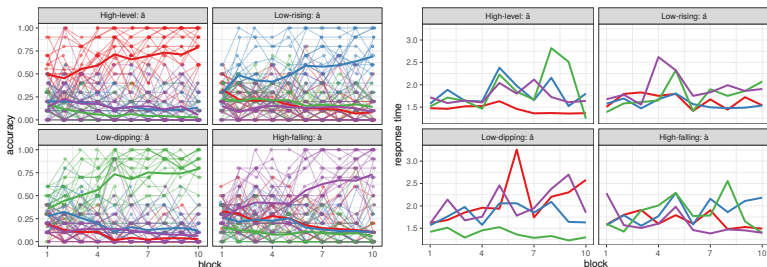
If accept, update curve-specific parameters



Advantages of our approach

Compared to the existing literature, our approach does:

- ▶ introduce a biologically interpretable class of **multi-category** DDM
- ▶ accommodate flexible **random effects** for subject heterogeneity (good vs poor learners)
- ▶ allow to study the **longitudinal** evolution of the parameters as the subjects get trained
- ▶ assess local similarities/**dissimilarities** in the model parameters



Longitudinal drift-diffusion mixed models

Notation:

- ▶ Time points (blocks): $t \in \{1, \dots, T = 10\}$
- ▶ Individuals: $i \in \{1, \dots, n = 20\}$
- ▶ Trials: $\ell \in \{1, \dots, L = 40\}$
- ▶ Observed data: $\mathbf{y}_{i,\ell,t} = (d_{i,\ell,t}, \tau_{i,\ell,t})$

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The likelihood function of the **longitudinal** drift-diffusion **mixed** model is

$$L(\mathbf{d}, \boldsymbol{\tau} \mid \mathbf{s}, \boldsymbol{\theta}) = \prod_{d=1}^{d_0} \prod_{s=1}^{d_0} \prod_{t=1}^T \prod_{i=1}^n \prod_{\ell=1}^L \left[g\{\tau_{i,\ell,t} \mid \boldsymbol{\theta}_{d,s}^{(i)}(t)\} \prod_{d' \neq d} \bar{G}\{\tau_{i,\ell,t} \mid \boldsymbol{\theta}_{d',s}^{(i)}(t)\} \right]^{\mathbf{1}\{d_{i,\ell,t}=d, s_{i,\ell,t}=s\}}$$

where $\boldsymbol{\theta}_{d,s}^{(i)}(t) = (\delta_s, \mu_{d,s}^{(i)}(t), b_{d,s}^{(i)}(t))^{\top}$.

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where $\boldsymbol{\theta}_{d,s}^{(i)}(t) = (\delta_s, \mu_{d,s}^{(i)}(t), b_{d,s}^{(i)}(t))^\top$.

We need to enforce a **positivity constraint** on $\{\mu_{d,s}^{(i)}(t), b_{d,s}^{(i)}(t)\}$

Parameter modeling

With $\mathbf{x} = (d, s)$, we let

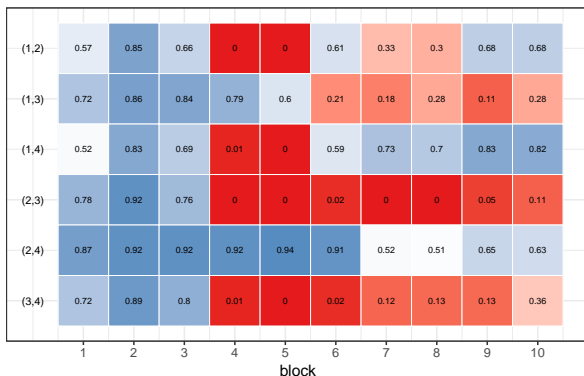
$$\mu_{\mathbf{x}}^{(i)}(t) = \exp\{f_{\mu, \mathbf{x}}(t) + u_{\mu, \mathbf{x}}^{(i)}(t)\}$$

$$\{f_{\mu, \mathbf{x}}(t) \mid z_k^{(\mathbf{x})} = z_k\} = \sum_{k=1}^K \beta_{\mu, k, z_k}^* B_k(t)$$

$$u_{\mu, \mathbf{x}}^{(i)}(t) = \begin{cases} u_{\mu, C}^{(i)}(t) & \text{if } s = d \\ u_{\mu, I}^{(i)}(t) & \text{if } s \neq d \end{cases}$$

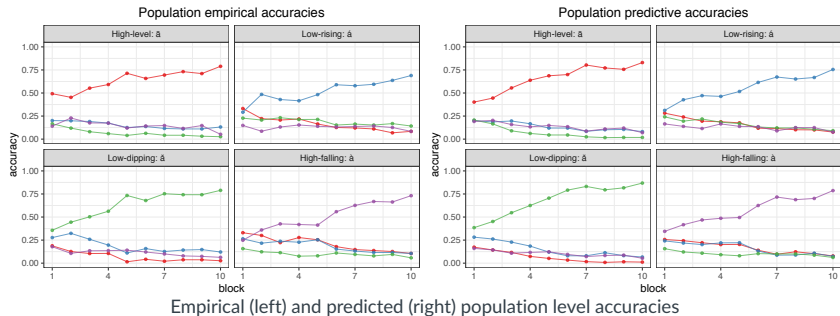
- ▶ Same specification for the boundary parameters $b_{\mathbf{x}}^{(i)}(t)$
- ▶ $\delta_s \sim \text{Unif}(0, \delta_{s, \max})$, where $\delta_{s, \max}$ is the minimum of all response times under stimulus s

Results: co-clustering probabilities

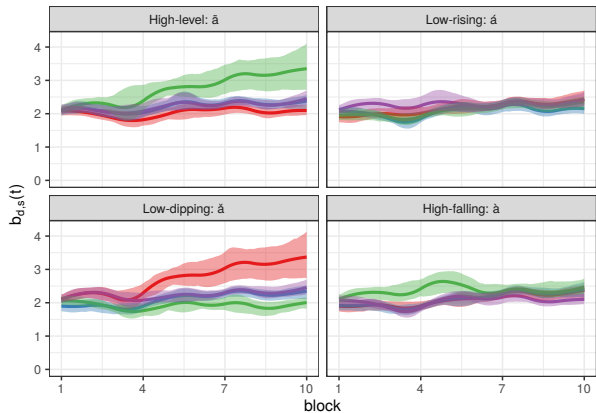


Matrix containing the probabilities of pairwise co-clustering between tones. On the y -axis, each pair of success parameters is considered

Results: predictive check

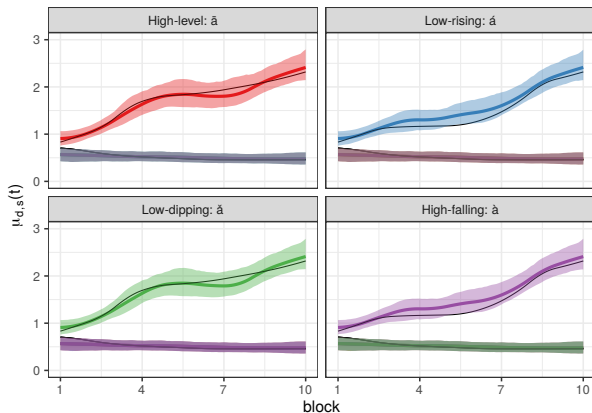


Results: boundary parameters



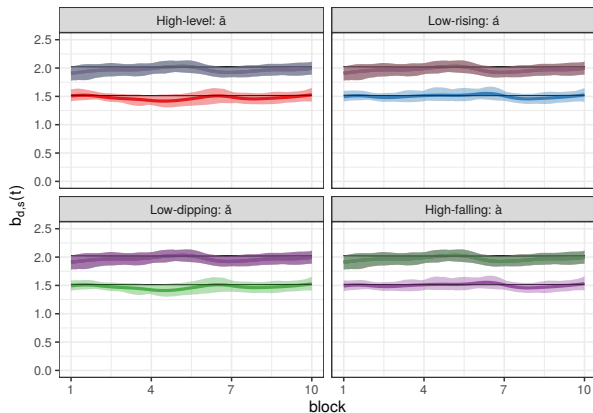
Estimated posterior mean and 95% CI for the population boundaries $b_{d,s}(t)$

Synthetic data: population level drifts



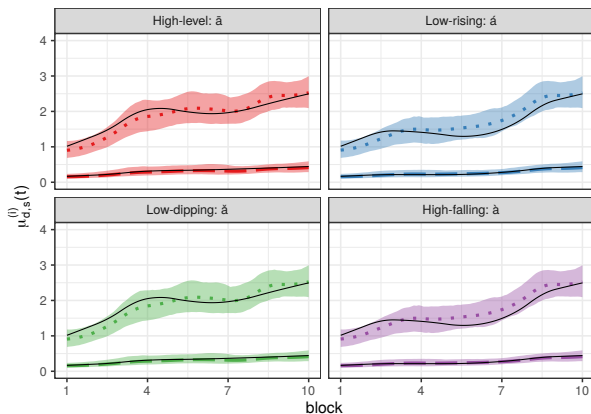
Estimated posterior mean and 95% CI for the population drift parameters $\mu_{d,s}(t)$

Synthetic data: population level boundaries



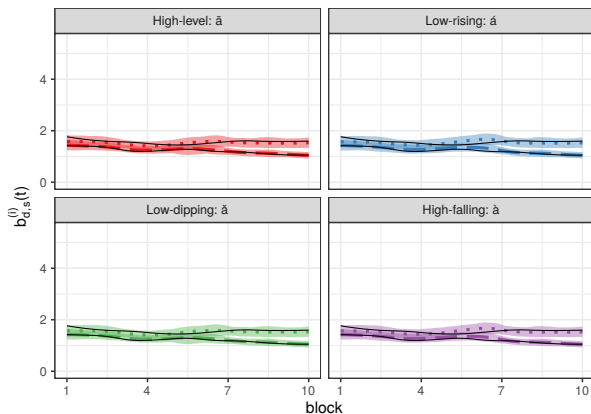
Estimated posterior mean and 95% CI for the population boundary parameters $b_{d,s}(t)$

Synthetic data: individual level drifts



Estimated posterior mean and 95% CI for the individual level drift parameters $\mu_{d,s}^{(i)}(t)$

Synthetic data: individual level boundaries



Estimated posterior mean and 95% CI for the individual level boundary parameters $b_{d,s}^{(i)}(t)$