

# Bayesian Partition Models for Local Inference in Longitudinal and Survival Data

DISSERTATION DEFENSE

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and Data Sciences**  
*College of Natural Sciences*

# Acknowledgments

Committee members:

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- ▶ Peter Müller<sup>†</sup>
- ▶ Bharath Chandrasekaran<sup>‡</sup>
- ▶ Mingyuan Zhou<sup>§</sup>

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- ▶ Department of Statistics and Data Sciences

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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

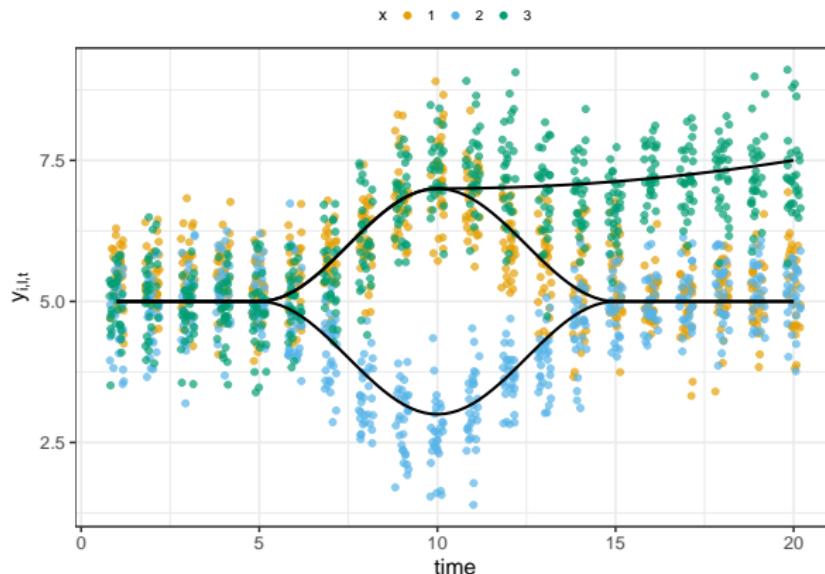
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Paulon, G., Llanos, F., Chandrasekaran, B., & Sarkar, A. (2020). Bayesian semiparametric longitudinal drift-diffusion mixed models for tone learning in adults. *Journal of the American Statistical Association*.

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

# The setting

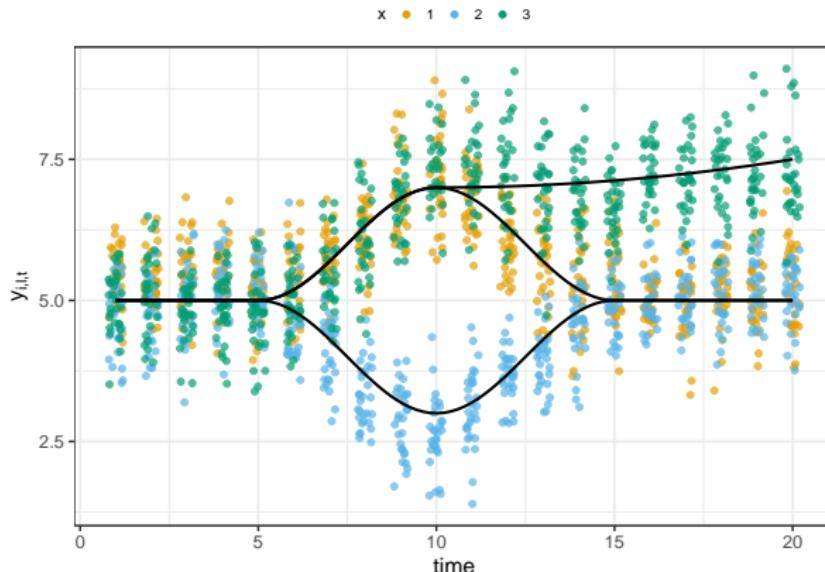
- ▶ Continuous response  $y$  varying smoothly over time
- ▶ Associated categorical predictor  $x$  which may vary with time
- ▶ The levels of  $x$  may affect  $y$  differently in the longitudinal stages



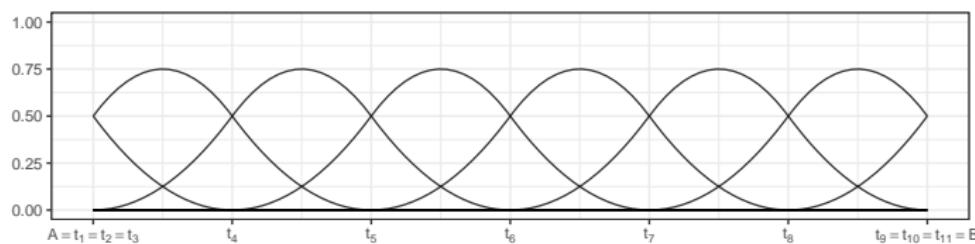
# The setting

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

**Goal:** partition model for the covariate space that evolves dynamically



# Penalized B-splines: fixed effects



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

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

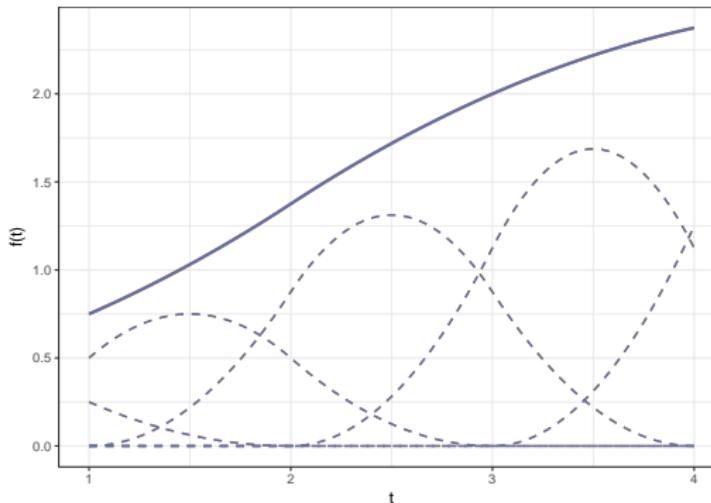
- ▶ Smoothness of curves favored by penalty for ‘roughness’
- ▶ B-splines have local support
- ▶ We can cluster the curves by allowing the spline coefficients to have identical values

# Local clustering: fixed effects

Curves can cluster 'globally'<sup>1</sup>.

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

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



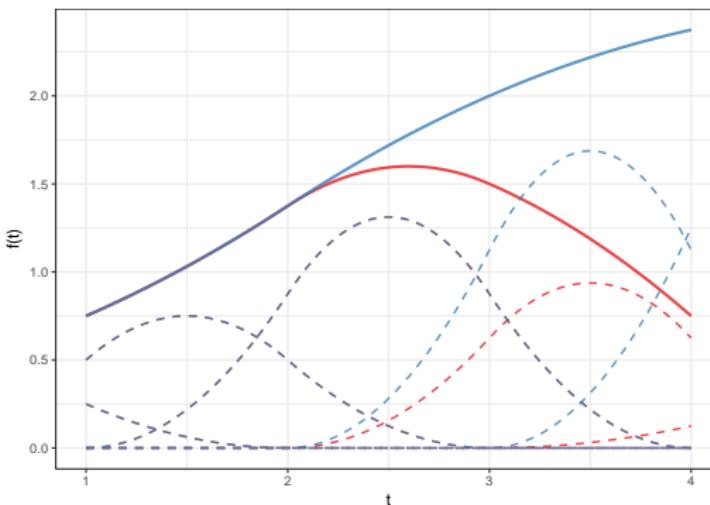
<sup>1</sup>Gelfand, A. E., Kottas, A., & MacEachern, S. N. (2005). Bayesian nonparametric spatial modeling with Dirichlet process mixing. *Journal of the American Statistical Association*, 100, 1021–1035.

# Local clustering: fixed effects

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

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

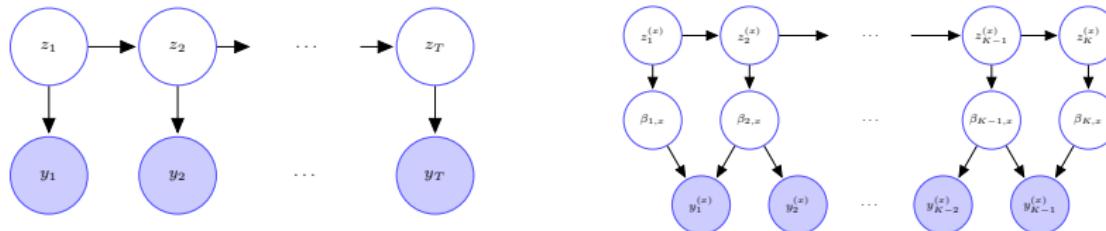
$$\beta_2 = (0.5, 1, 1.75, 1.25, 0.25)^\top$$



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<sup>2</sup>Petrone, 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

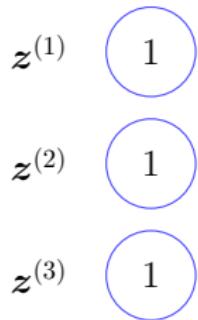
$$y_{i,\ell,t} = f_x(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

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

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

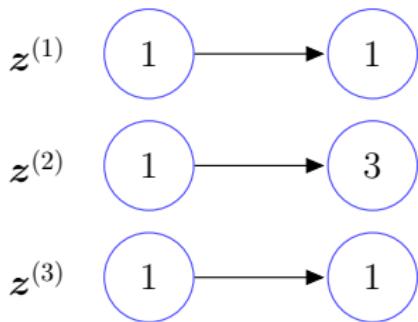
- Dynamic clustering given by time evolving latent variables

# Local clustering: example



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

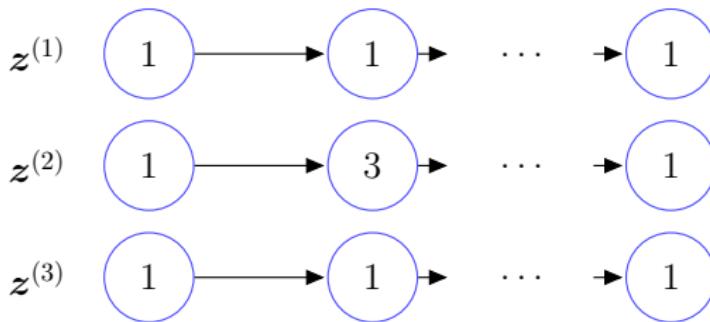
# Local clustering: example



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

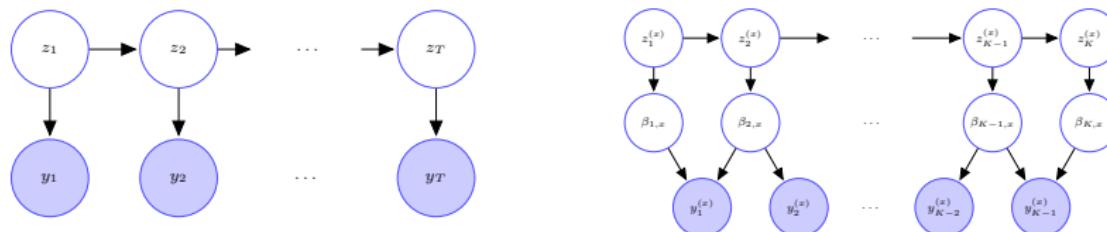
$$\beta_{2,2} = \beta_{1,3}^*$$

# Local clustering: example



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

# Local clustering: fixed effects



Conventional HMM and proposed HMM

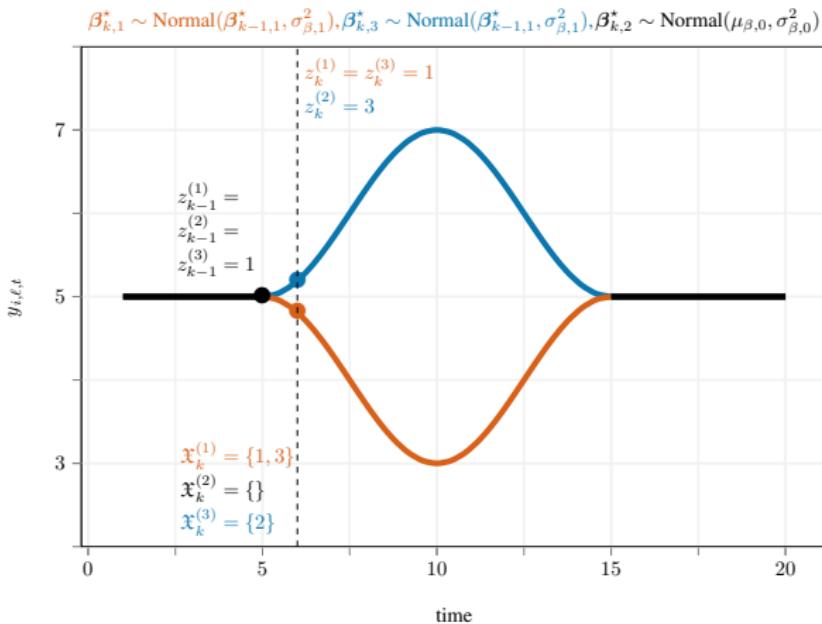
$$y_{i,\ell,t} = f_x(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

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

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

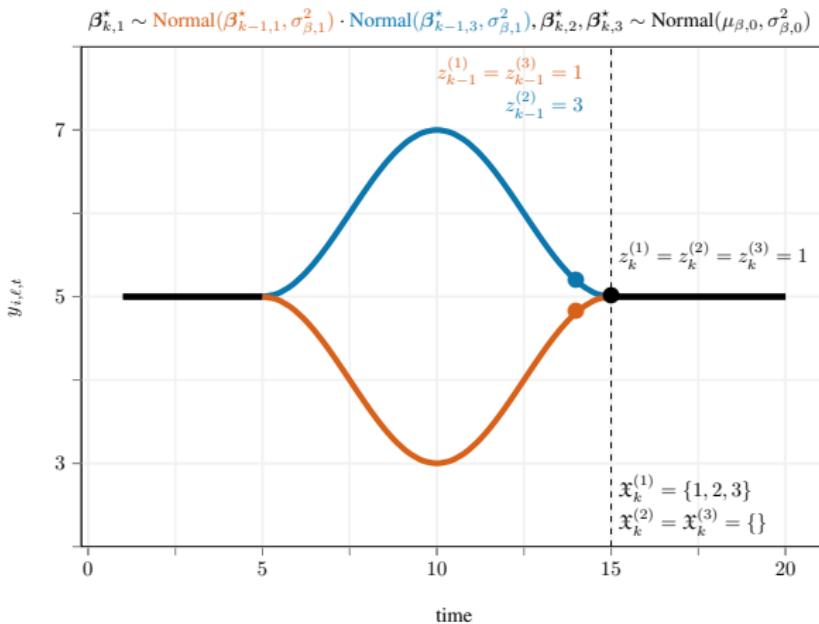
- Each level of the categorical predictor  $x$  is associated to a HMM for the group membership variables

# Smoothing prior: fixed effects



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

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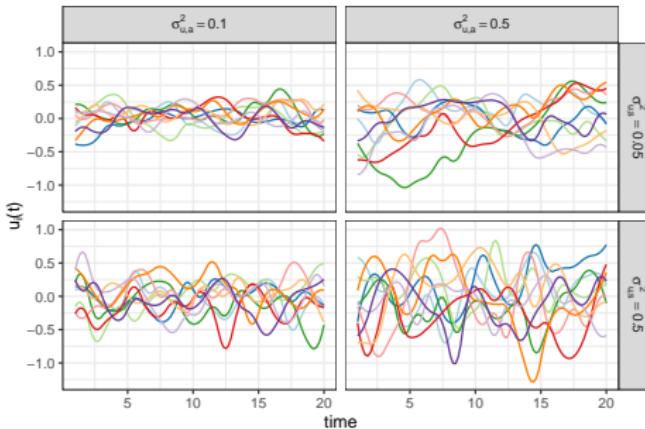
# Random effects

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

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

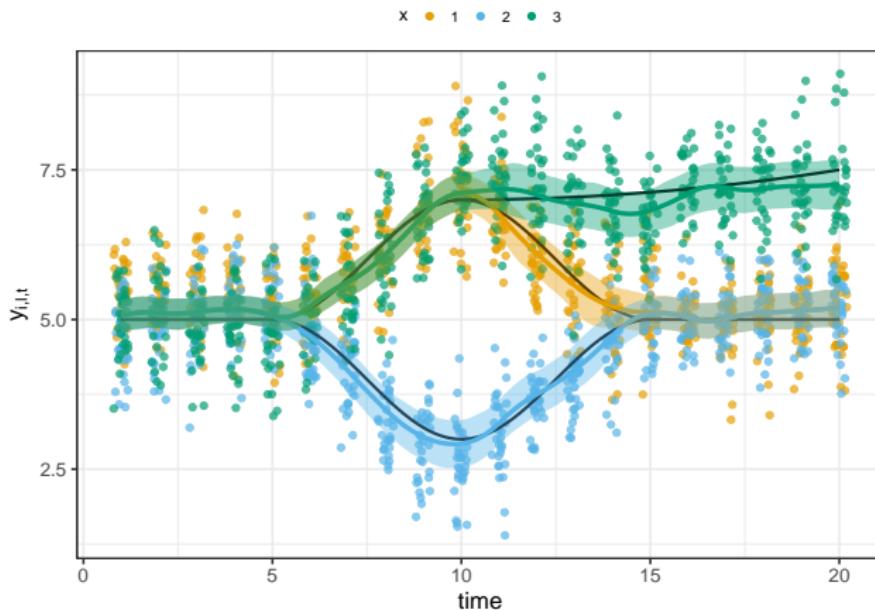
$$\boldsymbol{\beta}_{u,i} \sim \text{MVN}_K \{ \mathbf{0}, (\sigma_{u,a}^{-2} \mathbf{I}_K + \sigma_{u,s}^{-2} \mathbf{P}_u)^{-1} \}$$

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



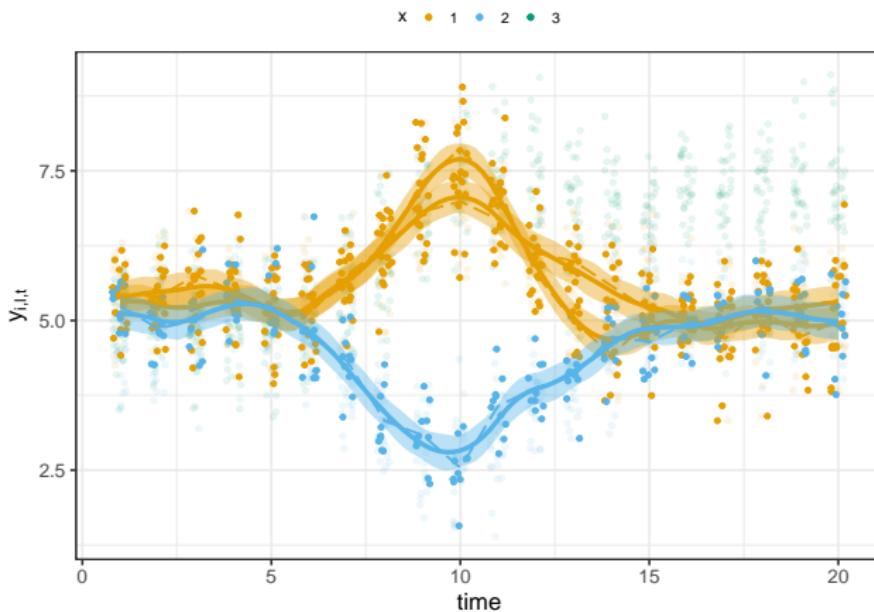
Each panel shows a collection of 10 random draws from the random effects distribution for a combination of  $(\sigma_{u,s}^2, \sigma_{u,a}^2)$

# Results: fixed effects



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

# Results: individual effects



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

# 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

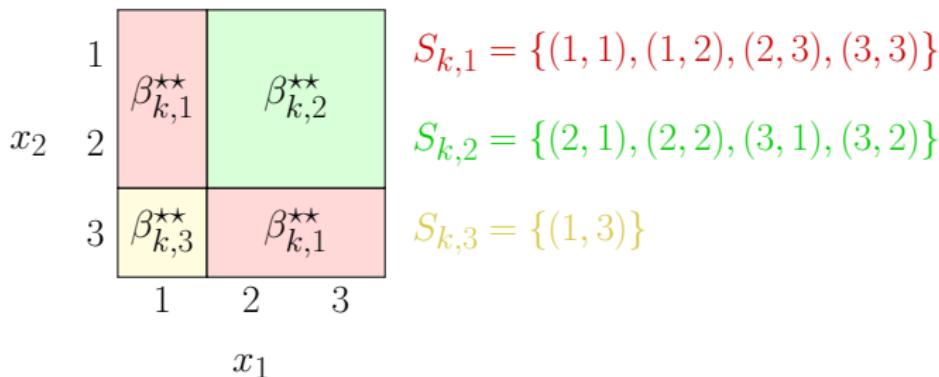
If  $\beta_{x_1, \dots, x_{j-1}, x_j, 1, \dots, x_p} = \beta_{x_1, \dots, x_{j-1}, x_j, 2, \dots, x_p}$  for all combinations of  $(x_1, \dots, x_{j-1}, x_j, x_{j+1}, \dots, x_p)$ , then two levels  $x_{j,1}$  and  $x_{j,2}$  of  $x_j$  have no differential effect on the response.

# 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  $\rho_k$ .

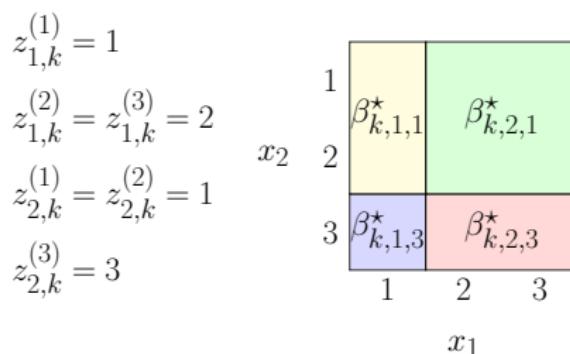
$$\{y_{i,\ell,t} \mid x_{j,i,\ell,t} = x_j, j = 1, \dots, p\} = f_{x_1, \dots, x_p}(t) + u_i(t) + \varepsilon_{i,\ell,t}$$

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



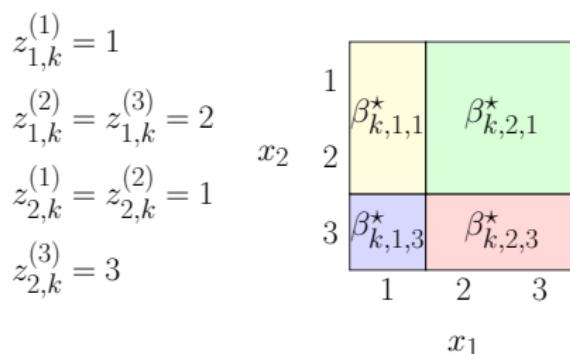
# Local clustering: multiple predictors

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



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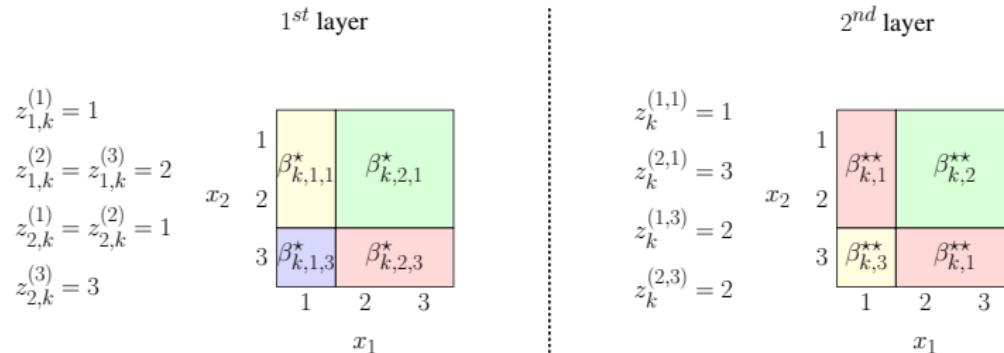


**Limitation:** joint partition is expressed as the product of  $p$  independent marginal partitions.

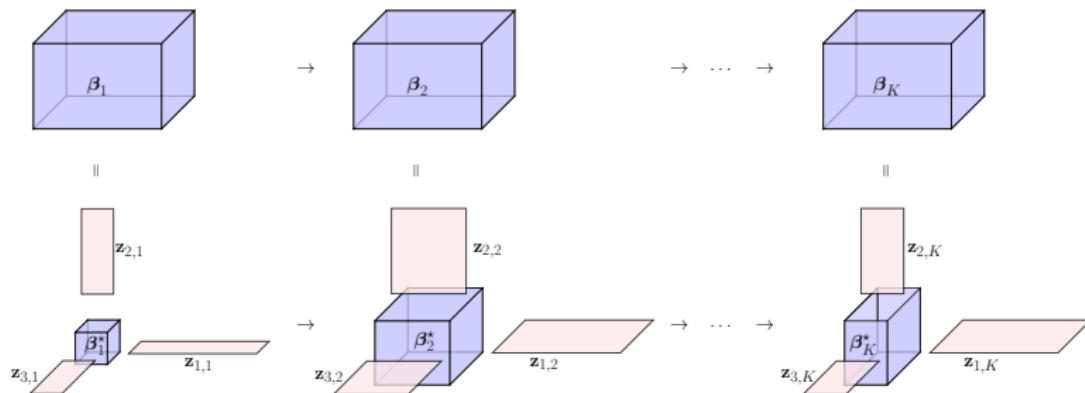
# Dynamic partition model

**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



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

# Theoretical properties

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

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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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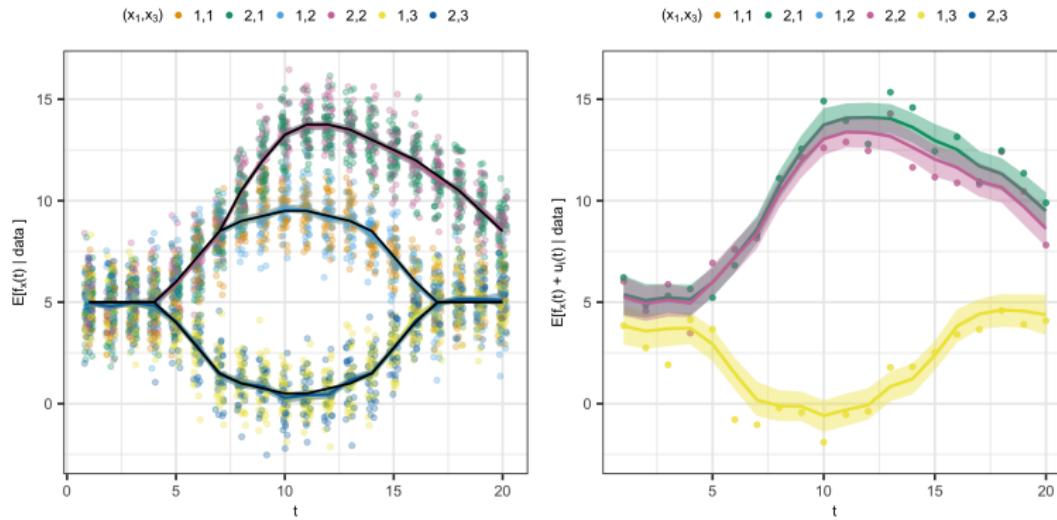
We can also identify the local partitions.

## Local partitions

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

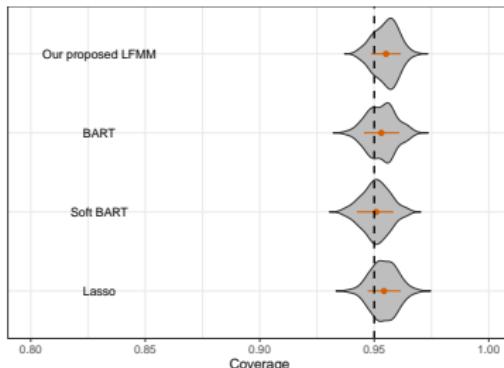
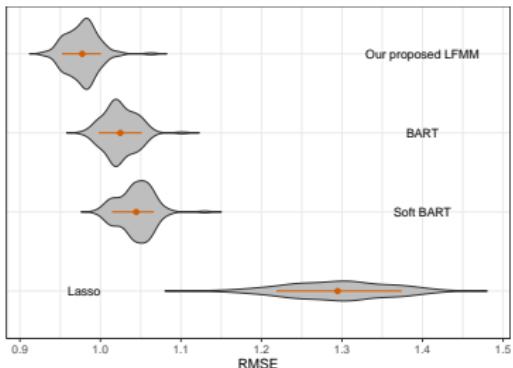
Consistency in recovering the local partitions implies consistency in **local variable selection**.

# 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



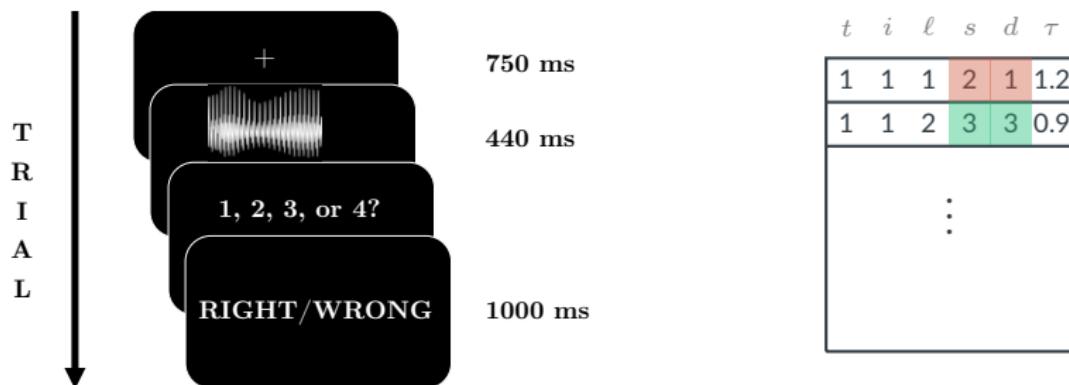
**Goal:** understand learning of novel speech categories in adulthood

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:

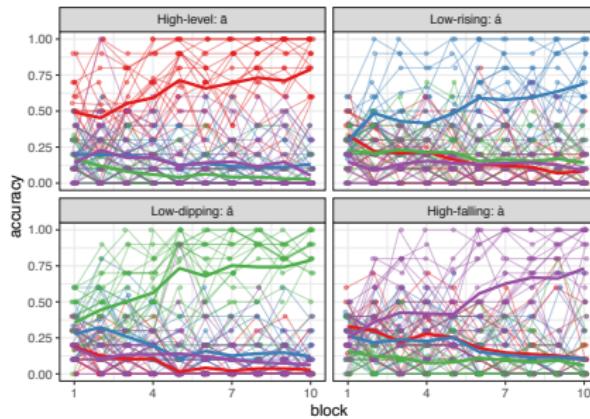
- exposure to perceptually variable tones
  - trial-by-trial corrective feedback



## Improvement of tone categorization within a few hundred trials

# Auditory tone learning experiments

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

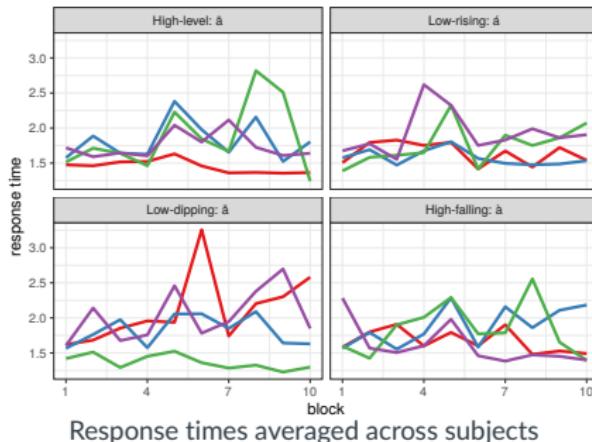


Proportions of times an input tone was classified into different tone categories by different subjects

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

# Auditory tone learning experiments

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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 racing<sup>3</sup> 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

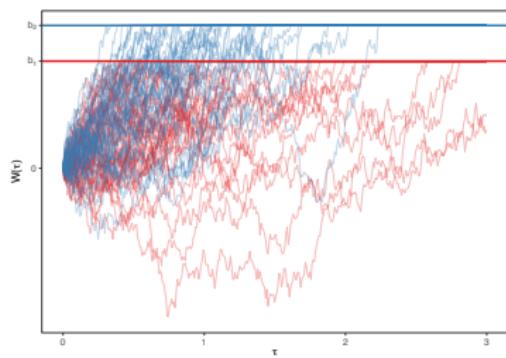
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<sup>3</sup>Usher, M., & McClelland, J. L. (2001). The time course of perceptual choice: The leaky, competing accumulator model. *Psychological review*, 108.

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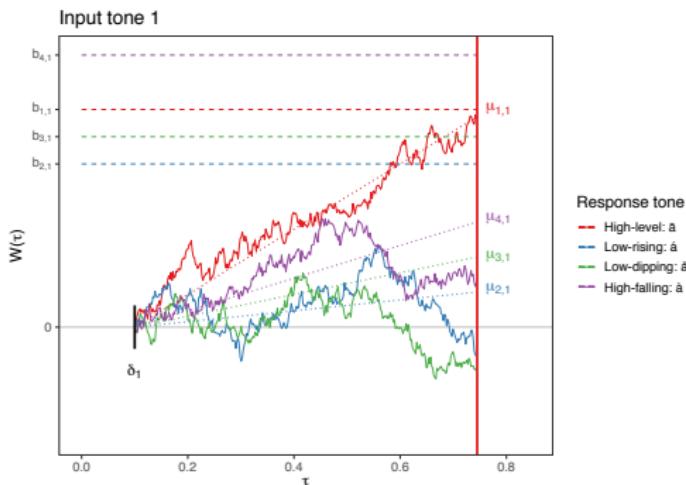
<sup>3</sup> Usher, M., & McClelland, J. L. (2001). The time course of perceptual choice: The leaky, competing accumulators model. *Psychological review*, 108.

# Our proposal

Extend the existing literature to:

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

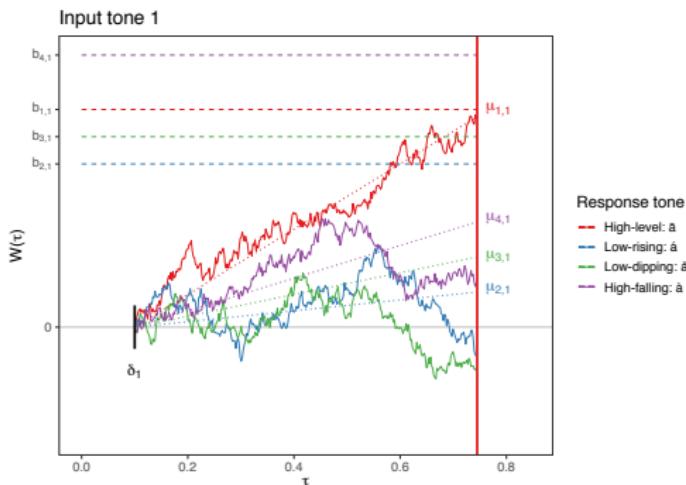
# Drift-diffusion models



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

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

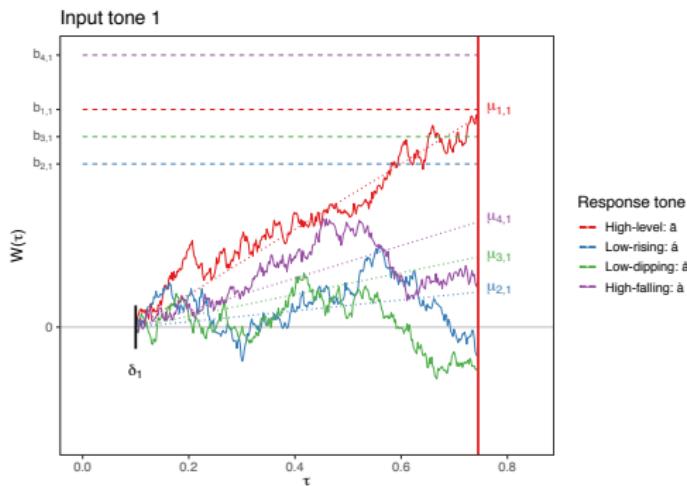
# Drift-diffusion models



- $\delta_s$ : 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,  $s \in \{1, \dots, 4\}$ .

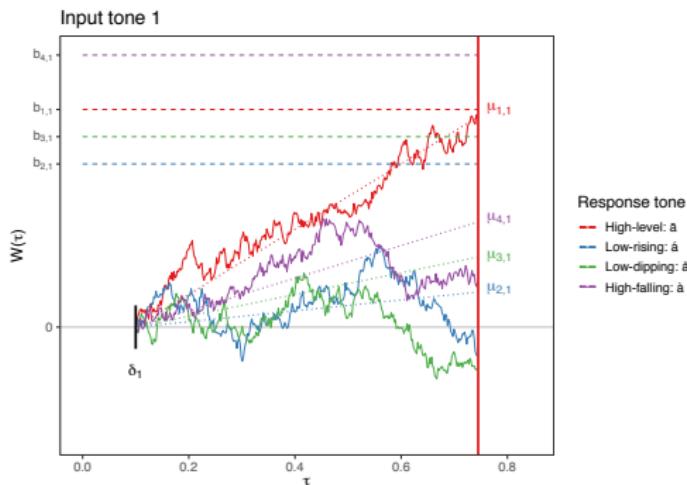
# Drift-diffusion models



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

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

# Drift-diffusion models



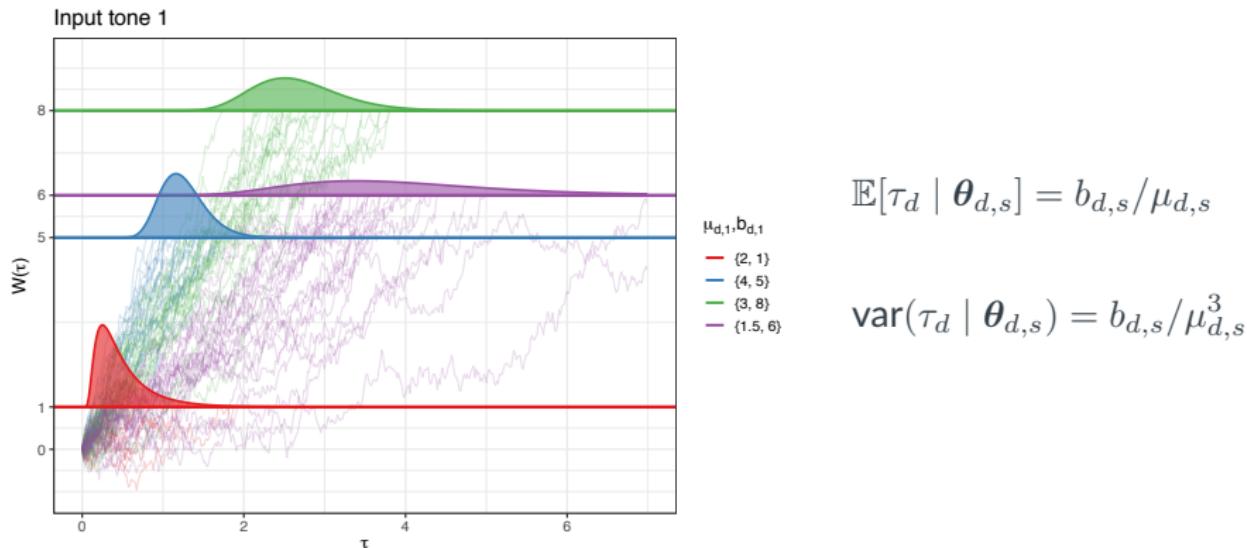
- $b_{d,s}$ : boundary parameter, i.e. amount of evidence needed to decide in favor of  $d$  when the stimulus is  $s$ .

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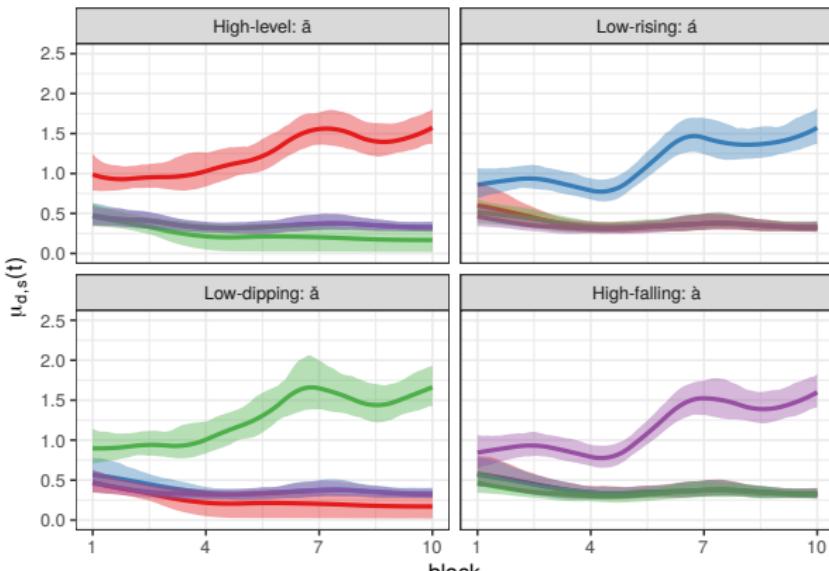
# Drift-diffusion models

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

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

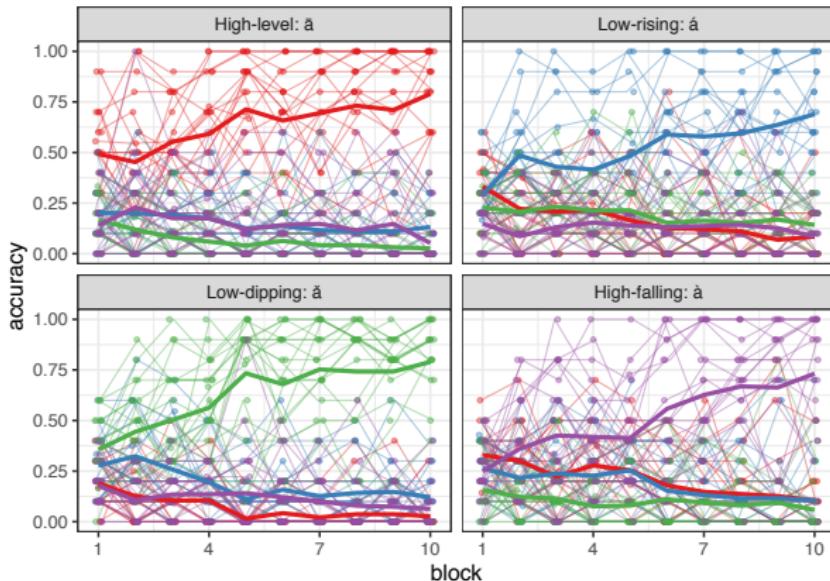


# Results: drift parameters



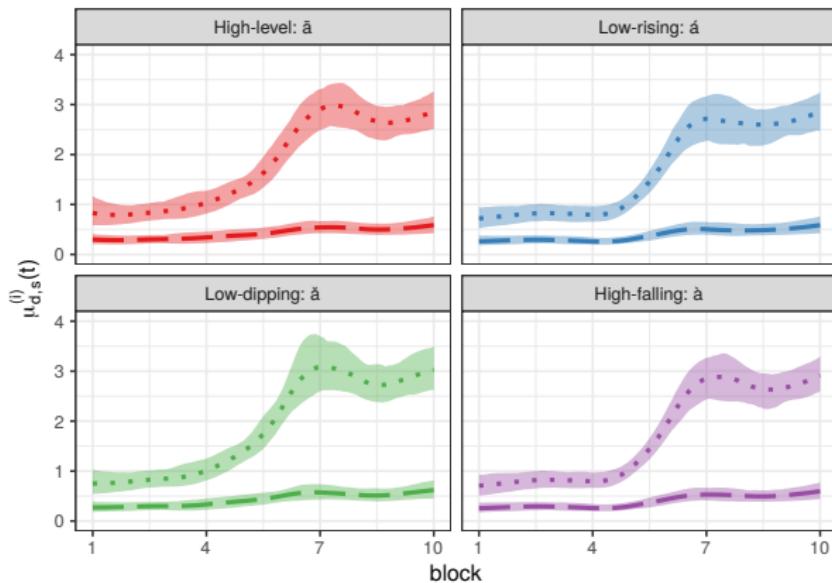
Estimated posterior mean and 95% CI for the population drift parameters  $\mu_{d,s}(t)$

# 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

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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 strategies<sup>4</sup>:

- ▶ **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

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<sup>4</sup> Golden, 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?  $\Delta_{S_i} = \mathbb{1}(S_i < C_i)$

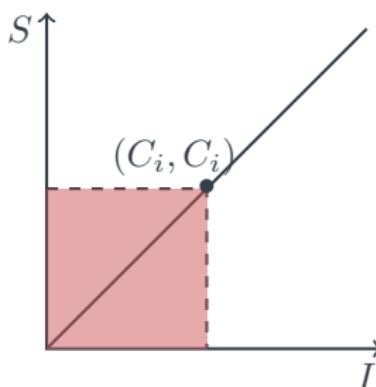
Available information on the outcomes: whether or not they exceed a common monitoring time  $C_i \rightarrow$  bivariate current status data.

This is a very common source of data

# Current status data

Four possible cases:

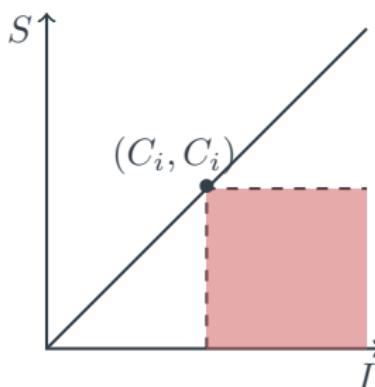
1.  $(\Delta_{I_i}, \Delta_{S_i}) = (1, 1)$ : positive test and presence of symptoms (symptomatic infections)



# 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)

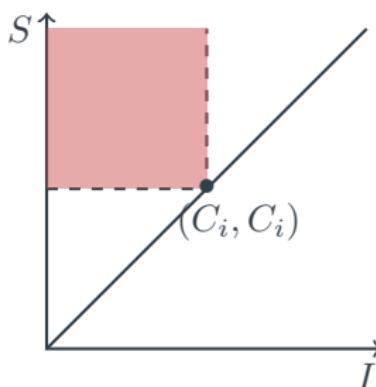


In this case  $I_i > S_i$  and the symptoms must be due to other causes.

# Current status data

Four possible cases:

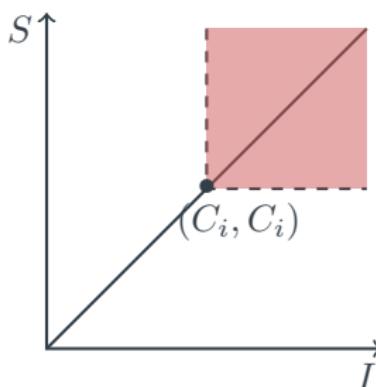
3.  $(\Delta_{I_i}, \Delta_{S_i}) = (1, 0)$ : positive test but absence of symptoms  
(asymptomatic infections)



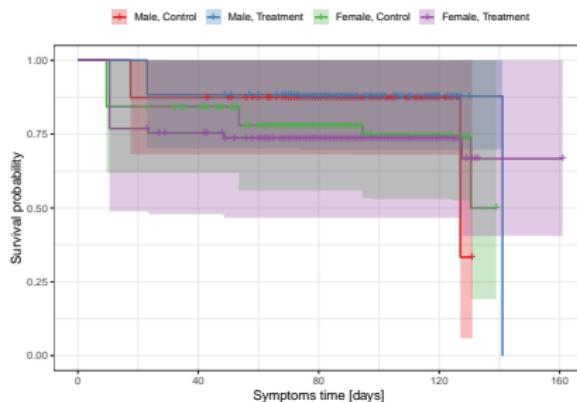
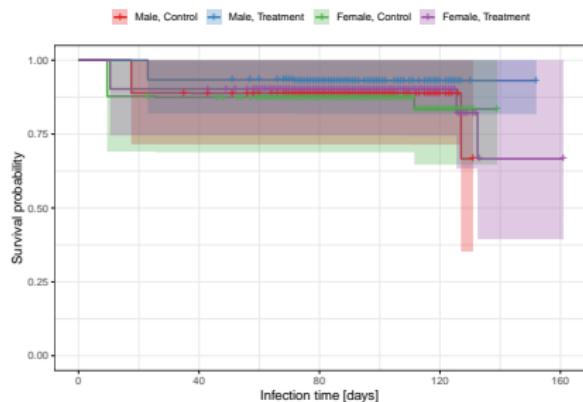
# Current status data

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  $i$
- ▶  $\Delta_{S_i}$ : 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)

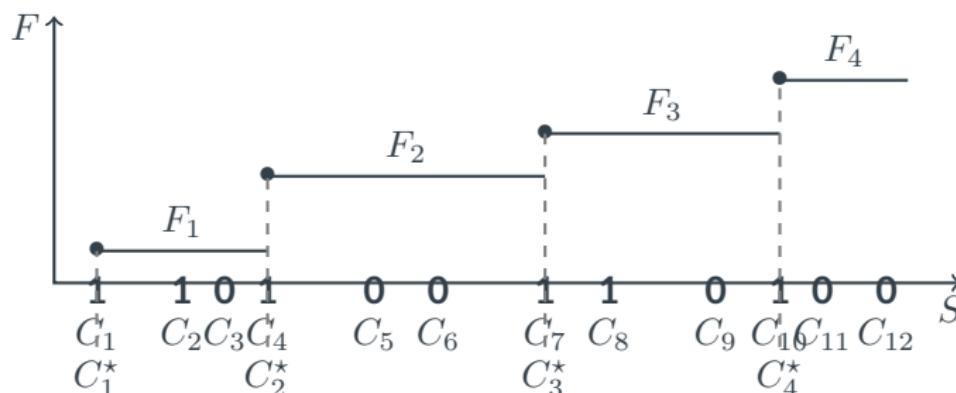
Goal: infer the unknown distribution  $f_S(s)$  based on  $\{(C_i, \Delta_{S_i})\}_{i=1}^n$ ,  
 $i = 1, \dots, n$ .

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.

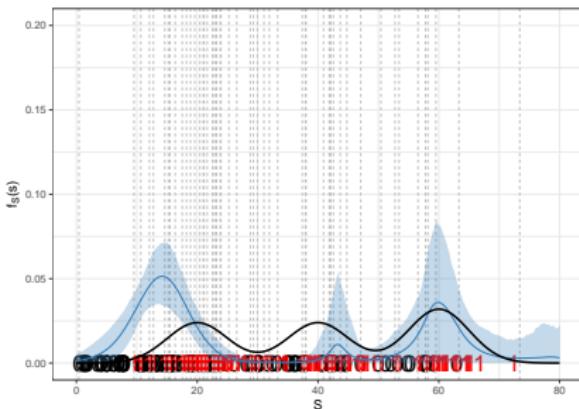
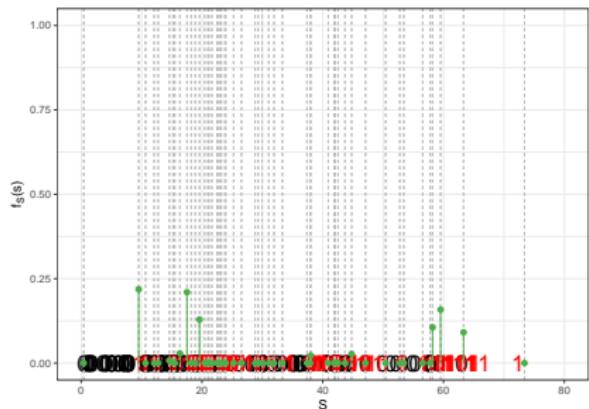
Let  $J = |A|$  and  $\mathbf{C}^* = (C_1^*, \dots, C_J^*) = (C_i, i \in A)$  denote the corresponding censoring times.



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 algorithm<sup>5</sup>.



<sup>5</sup> Groeneboom, 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

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

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

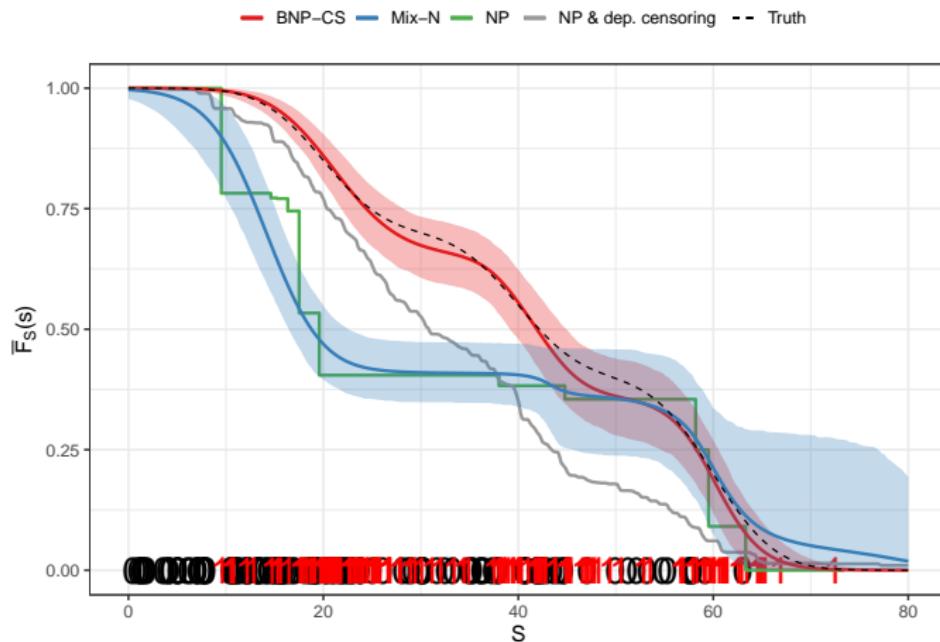
# The setting

Prior shrinkage via BNP model

$$\begin{aligned} S_i \mid H &\sim \int \mathsf{N}(S_i \mid \mu, \sigma^2) dH(\mu, \sigma^2), \quad H \sim \mathsf{DP}(M, H_0) \\ \Rightarrow S_i \mid \{\mu_k, \sigma_k^2, \pi_k\}_{k=1}^{+\infty} &\sim \sum_{k=1}^{+\infty} \pi_k \mathsf{N}(S_i \mid \mu_k, \sigma_k^2) \end{aligned}$$

- ▶ 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  $\Delta_{I_i} = \mathbb{1}\{I_i < C_i\}$ ,  $\Delta_{S_i} = \mathbb{1}\{S_i < C_i\}$ .

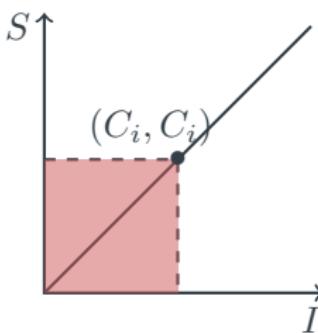
The conditional likelihood only depends on  $F_1(c) = P(I_i \leq c)$ ,  $F_2(c) = P(S_i \leq c)$ ,  $F_3(c) = P(I_i \leq c, S_i \leq c)$ .

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

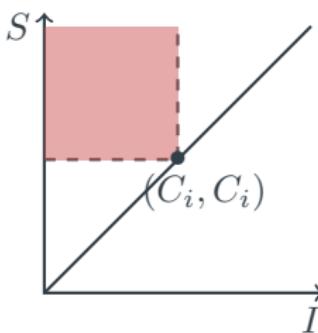


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$$F = \prod_{i=1}^n \{F_3(c_i)\}^{\Delta_{I_i} \Delta_{S_i}} (F_1 - F_3)(c_i)^{\Delta_{I_i}(1-\Delta_{S_i})}$$

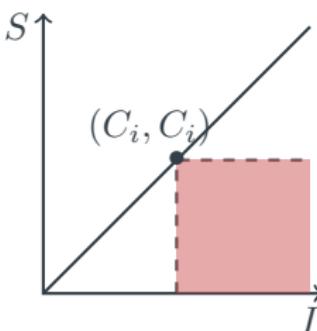


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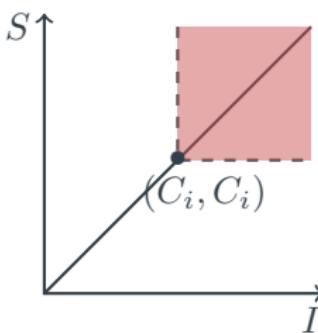


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# Possible solutions

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 structure<sup>6</sup> that reflects the underlying biology

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<sup>6</sup>Wang, 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

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

# A bivariate event time model

Two causes of symptoms:

- ▶ due to other causes → time to infection and time to symptoms are independent
- ▶ due to disease → 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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Positivity constraint on the latency time:

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

# Building dependence structure

Nonparametric priors:

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

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

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Dependent censoring on  $S$  only:

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

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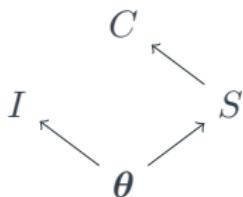
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Dependent censoring on  $S$  only:

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

Censoring regularizes inference on both  $f_I$  and  $f_S$ :



# Building dependence structure

The implied marginal distributions are

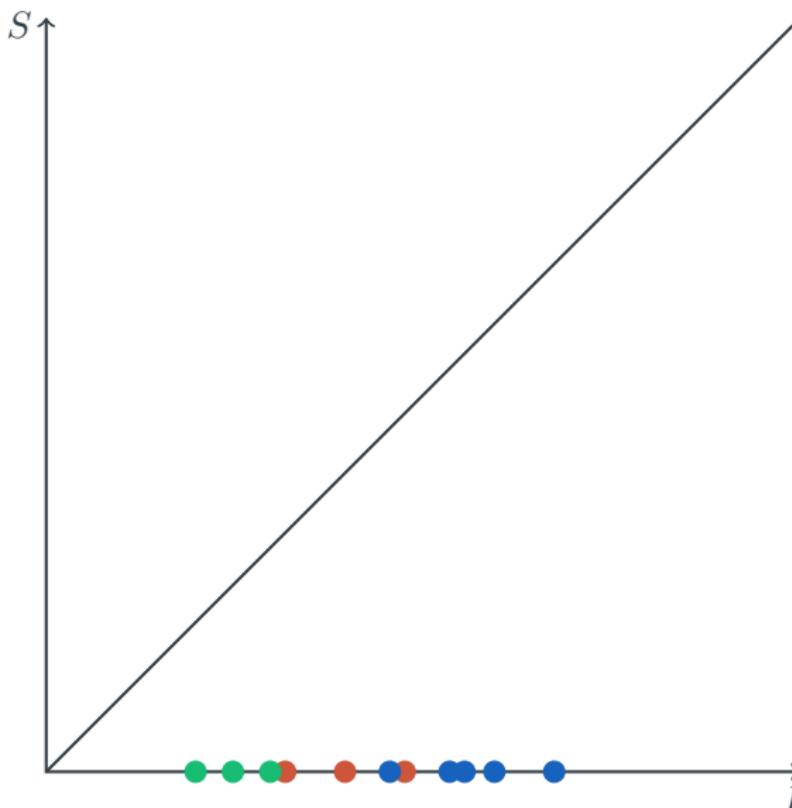
$$\begin{aligned}f_I(I) &= \sum_{k=1}^{+\infty} \pi_k^{(I)} N(I \mid \mu_k^{(I)}, \sigma_k^{(I)2}) \\f_S(S) &= w \sum_{k=1}^{+\infty} \pi_k^{(S)} N(S \mid \mu_k^{(S)}, \sigma_k^{(S)2}) \\&\quad + (1 - w) \sum_{k=1}^{+\infty} \pi_k^{(I)} \text{EMG}(S \mid \mu_k^{(I)}, \sigma_k^{(I)2}, \lambda_L),\end{aligned}$$

where  $\text{EMG}(\mu, \sigma^2, \lambda)$  denotes the exponentially modified Gaussian distribution<sup>7</sup>.

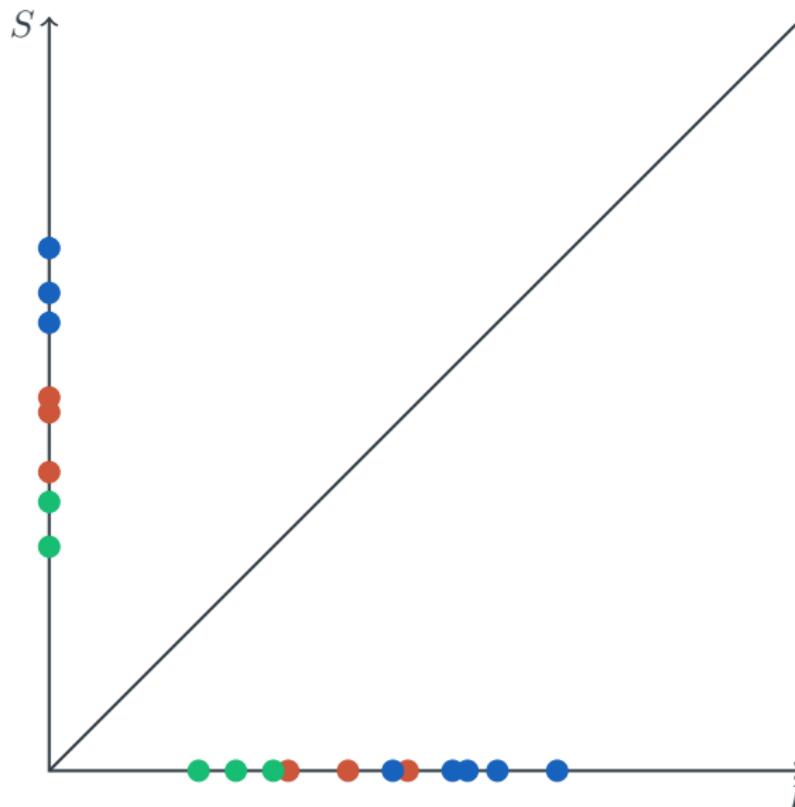
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<sup>7</sup> Grushka, E. (1972). Characterization of exponentially modified Gaussian peaks in chromatography. *Analytical Chemistry*, 44, 1733–1738.

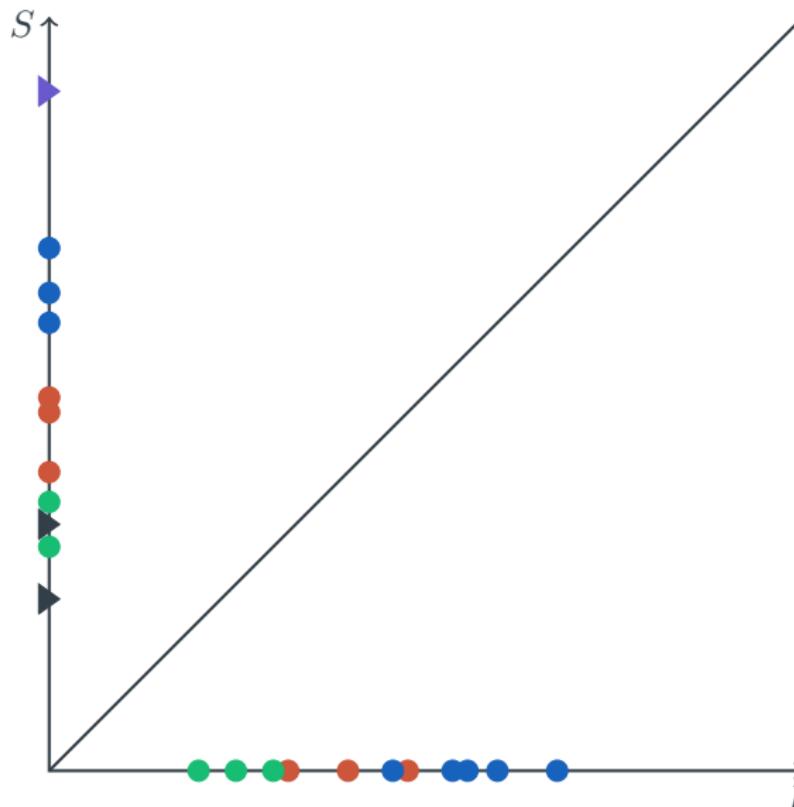
# Dependent partitions



# Dependent partitions



# Dependent partitions



# Regression on covariates

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

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

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

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

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

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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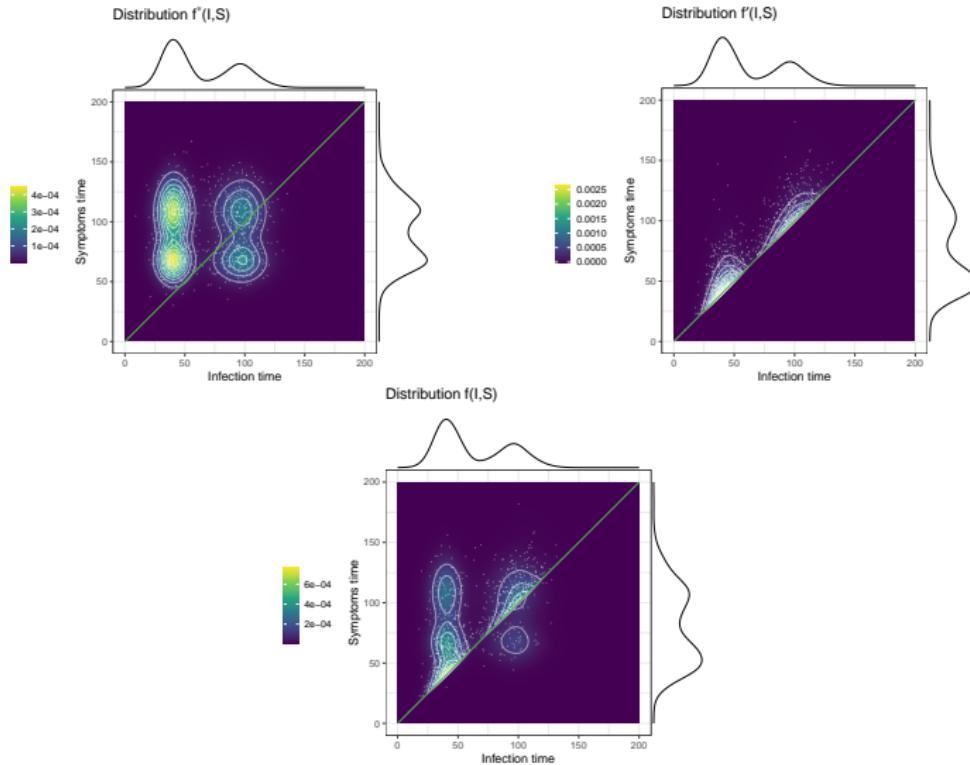
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where

$$d^\top m_k = \delta_k + \alpha_k x_1 + \beta_k x_2 + \gamma_k x_3$$

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

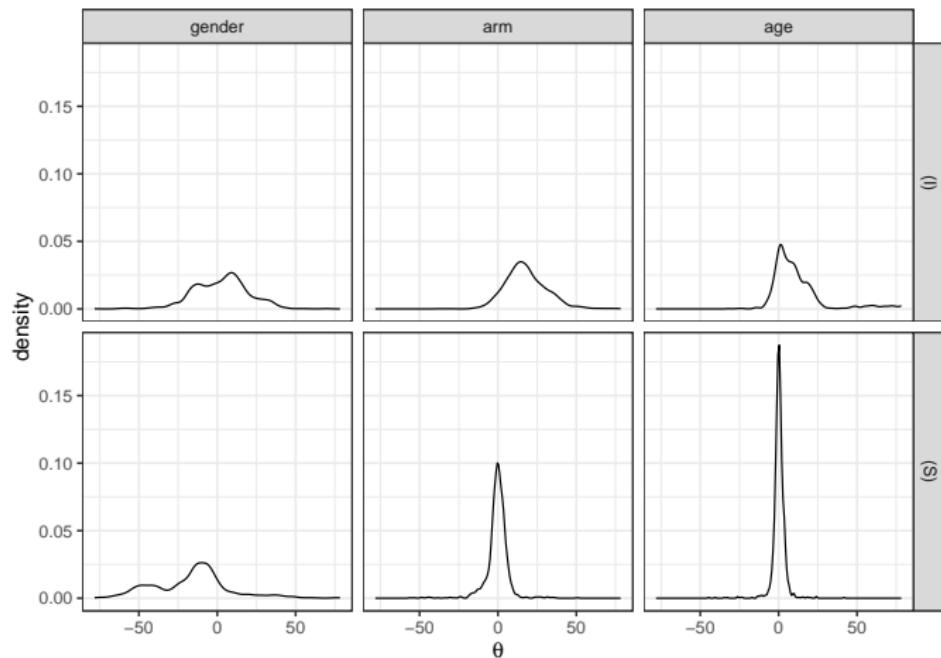
# Results: synthetic data



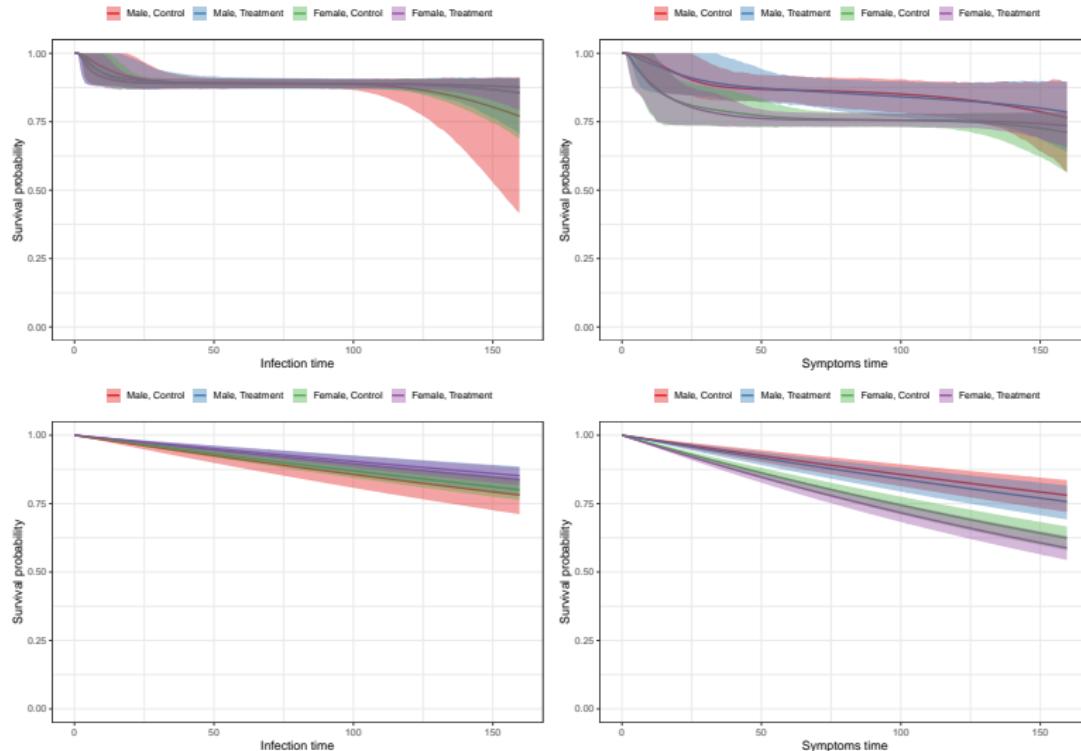
# Results: synthetic data

	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)	<b>0.76</b> (0.22, 2.16)
	$n = 1000$	Inf.	0.80 (0.50, 1.10)	3.12 (3.03, 3.41)	<b>0.19</b> (0.05, 0.50)
		Sym.	8.18 (6.28, 10.32)	10.74 (9.58, 12.49)	<b>0.12</b> (0.02, 0.37)
(III)	$n = 250$	Inf.	4.45 (3.00, 6.30)	4.24 (3.09, 5.79)	<b>0.45</b> (0.08, 1.14)
		Sym.	9.82 (6.70, 13.20)	8.08 (5.72, 12.15)	<b>0.24</b> (0.03, 0.81)
	$n = 1000$	Inf.	4.10 (3.18, 4.96)	3.96 (3.24, 4.81)	<b>0.13</b> (0.01, 0.35)
		Sym.	9.94 (8.44, 11.71)	7.98 (6.31, 10.06)	<b>0.05</b> (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

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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*.

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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

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

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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:

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

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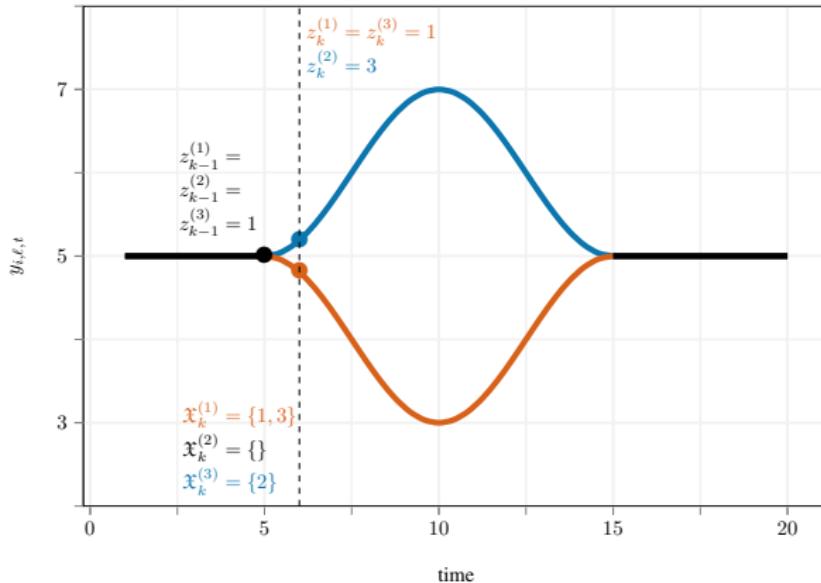
- ▶ Shrinkage priors on the second layer of allocation variables

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

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

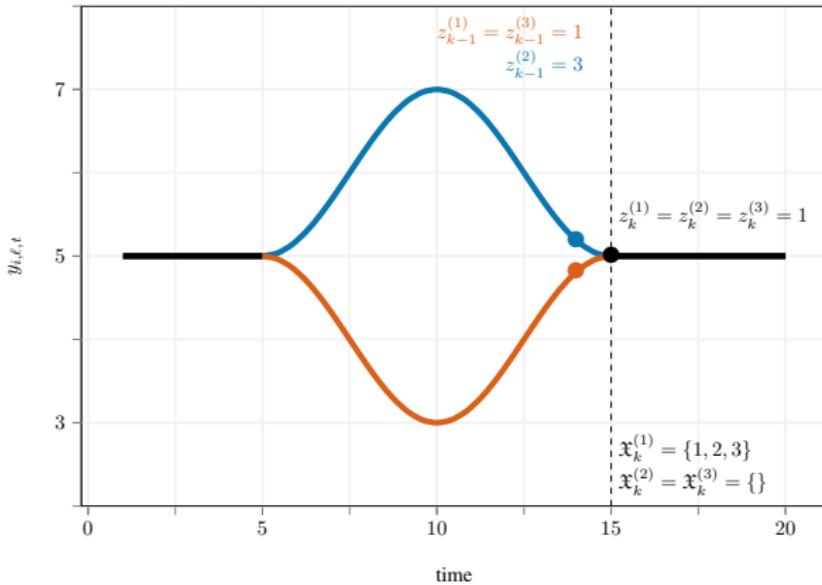
# Smoothing prior: fixed effects

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



# 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  $(\rho_k, \beta_k^{**})$ :

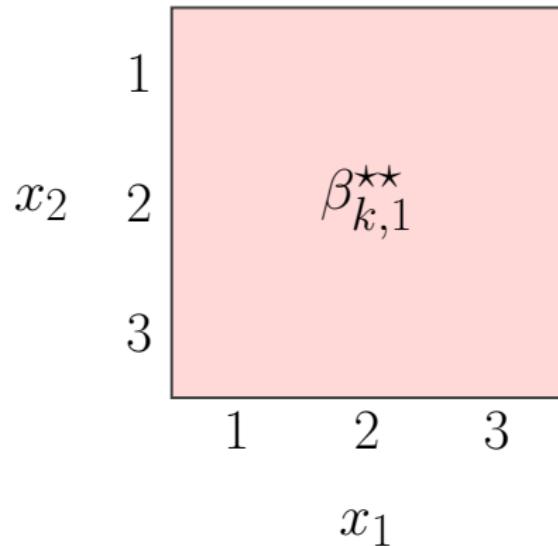
1. propose a change to the partition structure  $\rho_k$
2. conditional on  $\rho_k$ , sample from the posterior of the spline coefficients  $\beta_k^{**} = \{\beta_{k,h}^{**}\}_{h=1}^{M_k}$

**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  $\rho_k$
- (iii) evaluate the acceptance rate, integrating out the curve-specific parameters

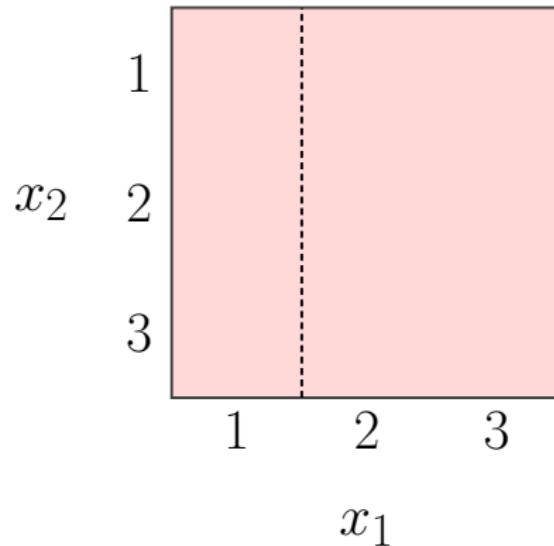
# Posterior inference

Initial configuration



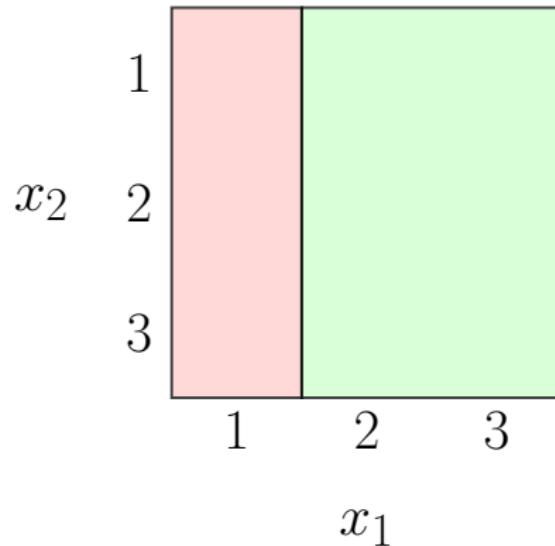
## Posterior inference

Propose marginal partition for  $x_1$ : split



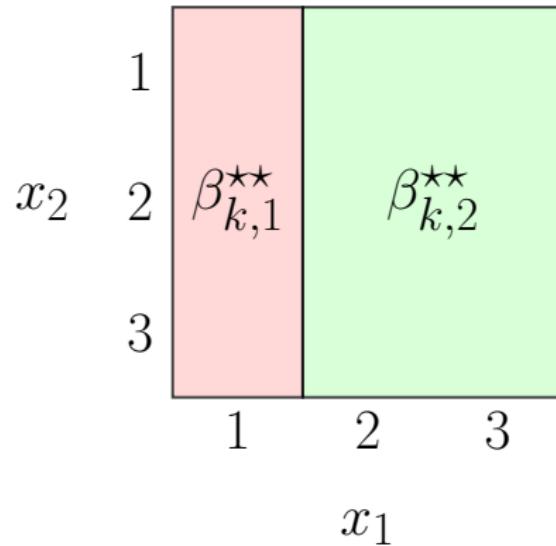
## Posterior inference

Conditional on the marginal partition, propose joint partition



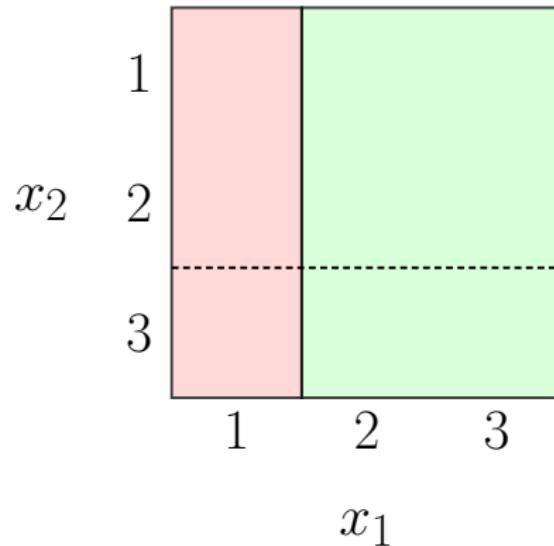
## Posterior inference

If accept, update curve-specific parameters



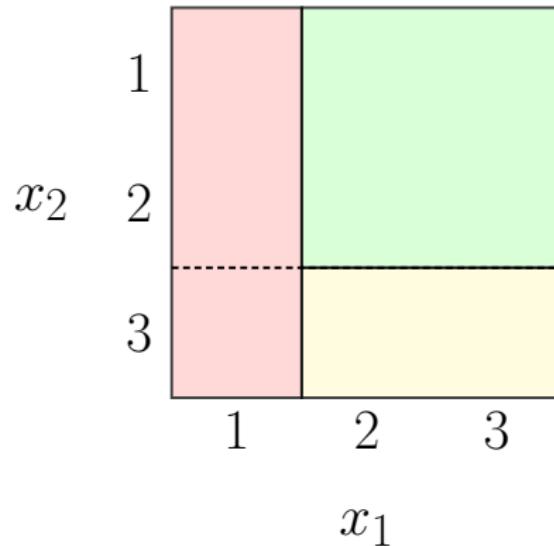
## Posterior inference

Propose marginal partition for  $x_2$ : split



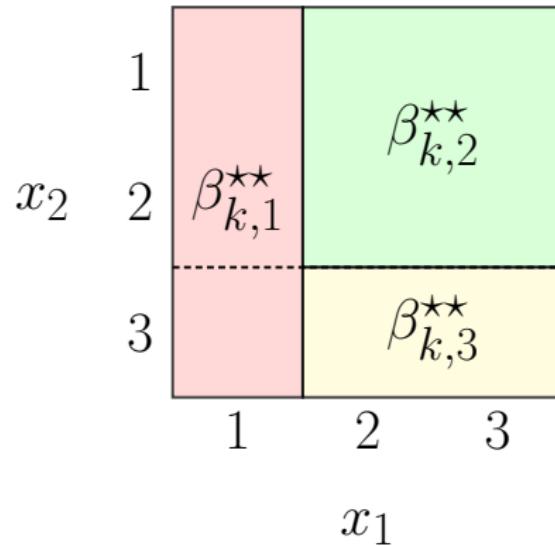
## Posterior inference

Conditional on the marginal partition, propose joint partition



## Posterior inference

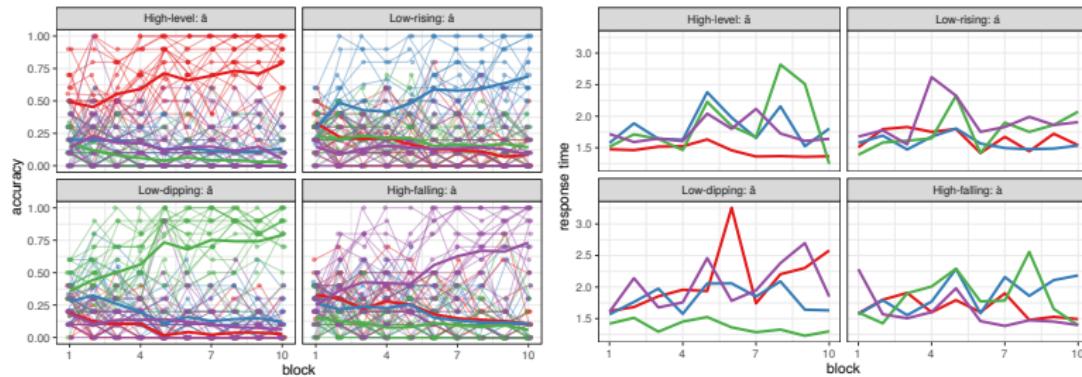
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# Advantages of our approach

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:  $y_{i,\ell,t} = (d_{i,\ell,t}, \tau_{i,\ell,t})$

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

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

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

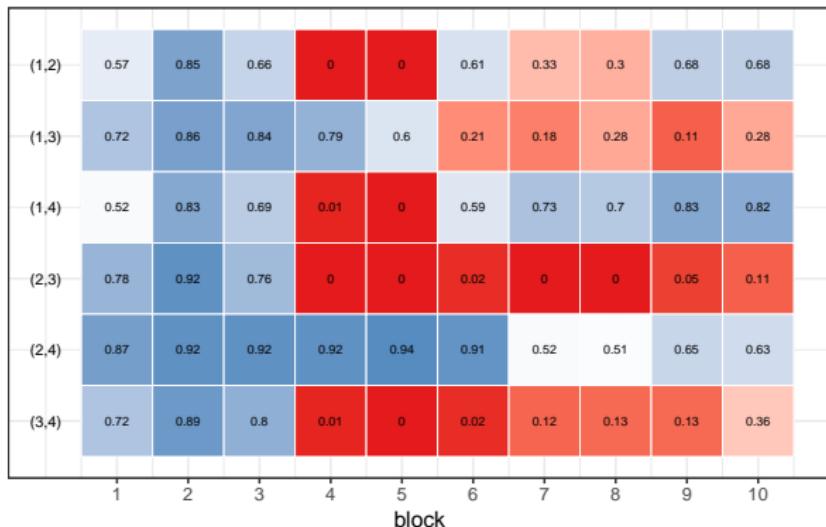
$$\mu_{\boldsymbol{x}}^{(i)}(t) = \exp\{f_{\mu,\boldsymbol{x}}(t) + u_{\mu,\boldsymbol{x}}^{(i)}(t)\}$$

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

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

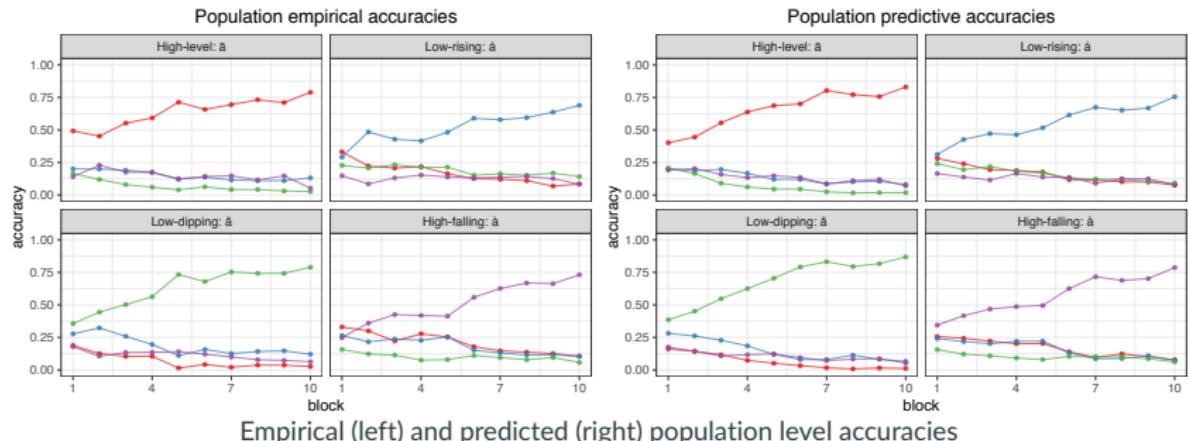
- ▶ Same specification for the boundary parameters  $b_{\boldsymbol{x}}^{(i)}(t)$
- ▶  $\delta_s \sim \text{Unif}(0, \delta_{s,max})$ , where  $\delta_{s,max}$  is the minimum of all response times under stimulus  $s$

# Results: co-clustering probabilities

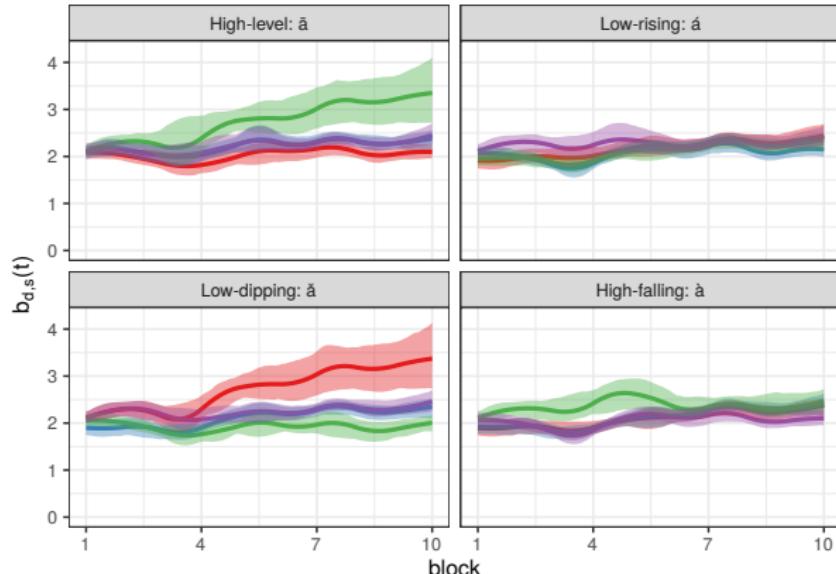


Matrix containing the probabilities of pairwise co-clustering between tones. On the *y*-axis, each pair of success parameters is considered

# Results: predictive check

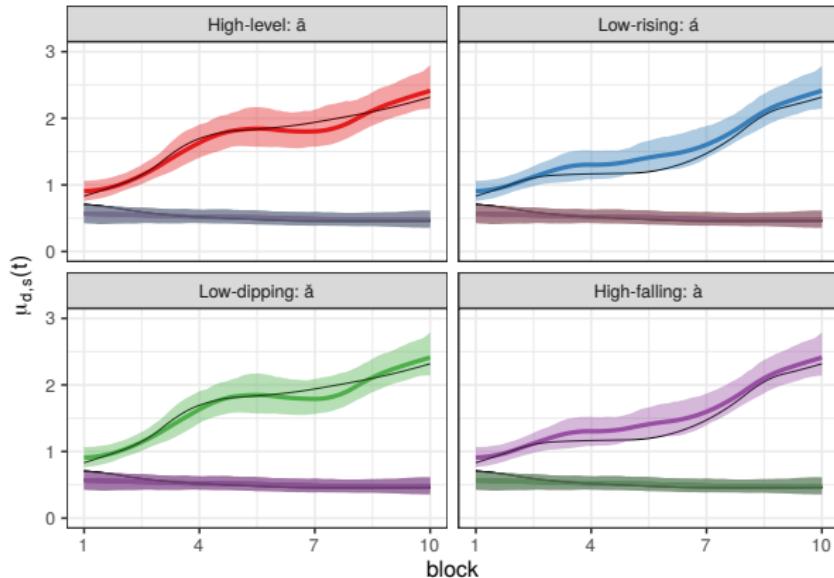


## Results: boundary parameters



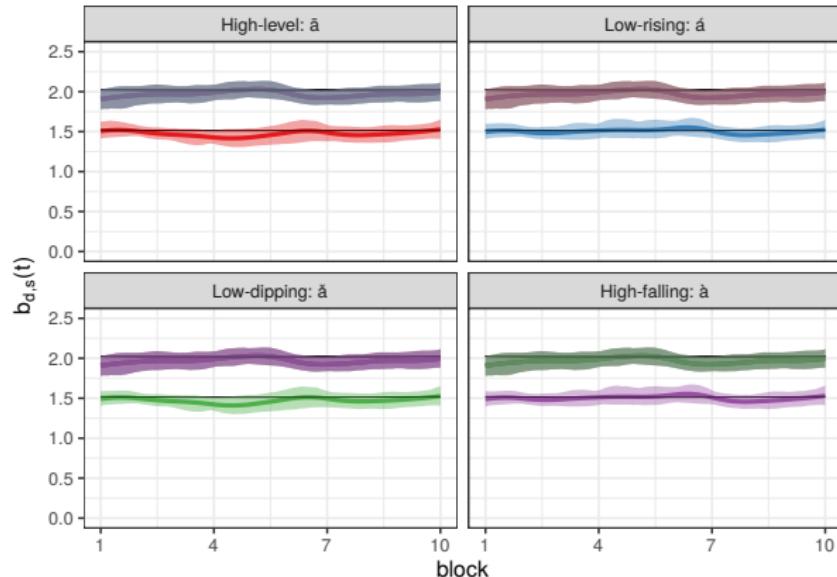
Estimated posterior mean and 95% CI for the population boundaries  $b_{d,s}(t)$

## Synthetic data: population level drifts



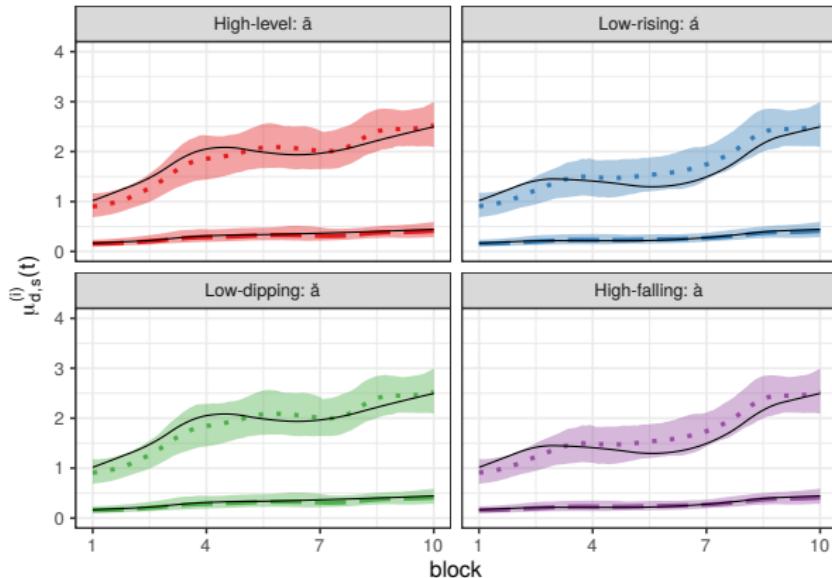
Estimated posterior mean and 95% CI for the population drift parameters  $\mu_{d,s}(t)$

## Synthetic data: population level boundaries



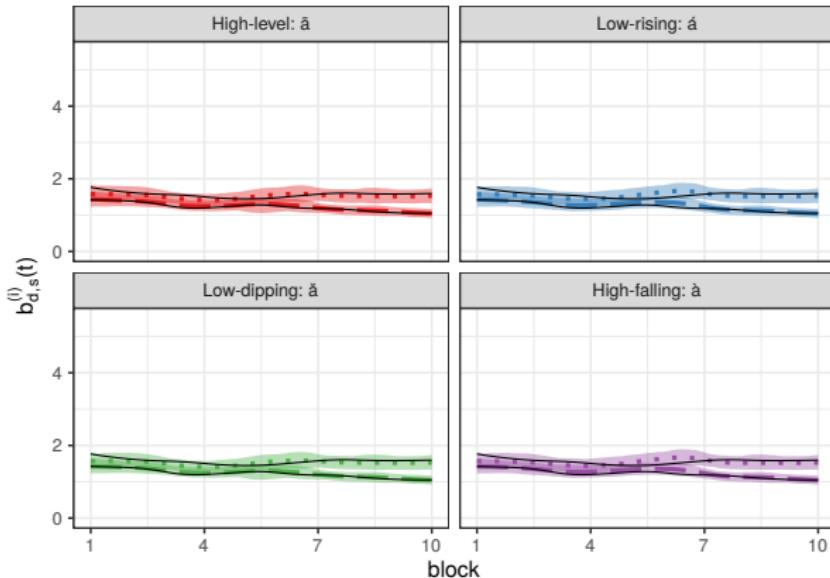
Estimated posterior mean and 95% CI for the population boundary parameters  $b_{d,s}(t)$

## 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  $b_{d,s}^{(i)}(t)$