Bayesian Distributed Lag Interaction Models to Identify Perinatal Windows of Vulnerability in Child Health

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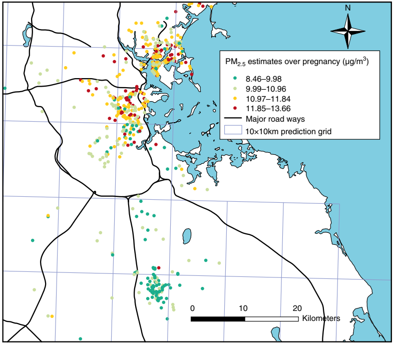
ACCESS Prospective Birth Cohort

Study participants (i):
997 Boston-area births between 8/2002 and 1/2007

Exposure (X_{it}): $PM_{2.5}$ at maternal residence for each week (t) of pregnancy

Outcome (Y_i): child asthma



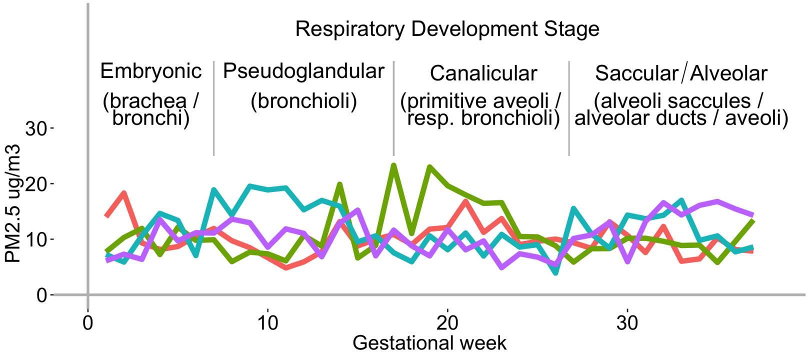
Baseline covariates ($\mathbf{Z}_i$): child sex, maternal pre-pregnancy BMI, age, education, race/ethnicity, atopy, self reported smoking during pregnancy, stress index, neighborhood disadvantage index

[figure source: Hsu et al. *Am. J. Respir. Crit. Care Med.* 2015]

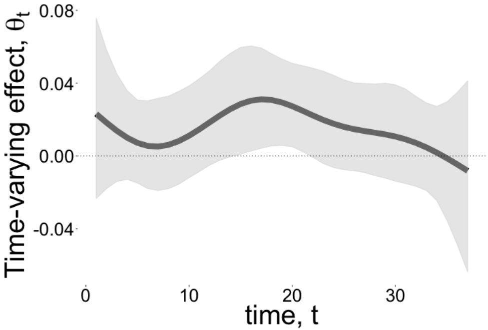
Critical Windows of Vulnerability

Definition

A period in time during which there is an increased association between exposure and a future health outcome.



Asthma Example with DLM



Estimated association between $PM_{2.5}$ and childhood asthma among 283 boys

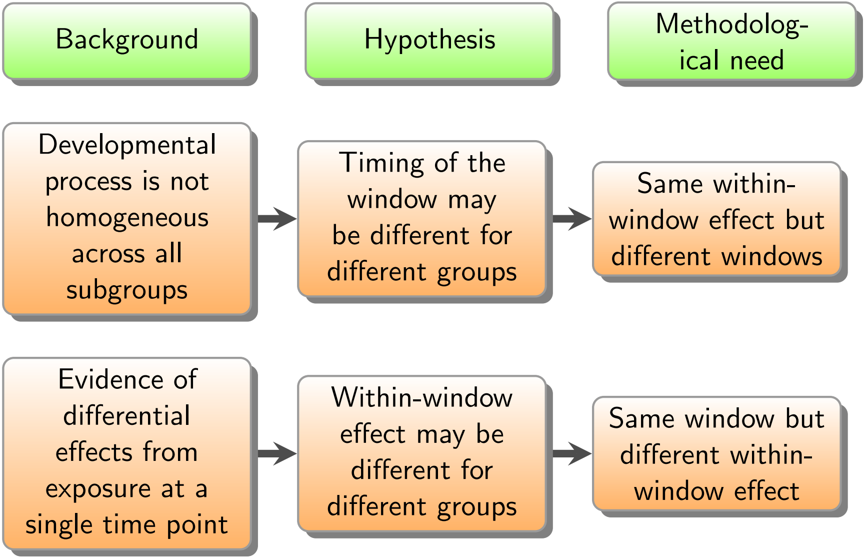
$$g\left(\mu_i\right) = \alpha + \sum_{t=1}^{T} \theta_t X_{it} + \mathbf{Z}_i^T \gamma$$

- $E(Y_i) = \mu_i$ and $g(\cdot)$ is a link function

Patterns of Heterogeneity

Background	Hypothesis	Methodolog-ical need
Developmental process is not homogeneous across all subgroups →	Timing of the window may be different for different groups →	Same within-window effect but different windows

Patterns of Heterogeneity

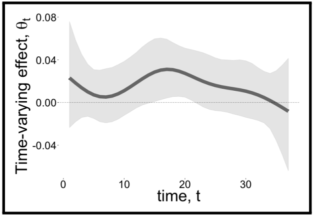


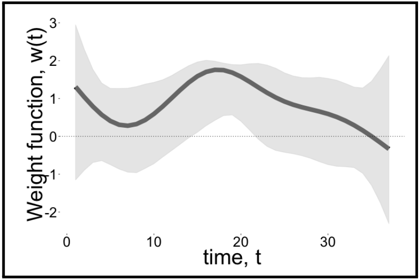
Patterns of Heterogeneity

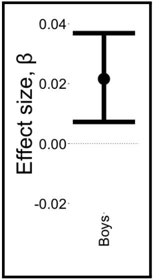
window		within-window effect: same	within-window effect: different
	same	DLM	methods gap
	different	methods gap	stratified DLM

Separating Windows and Effects

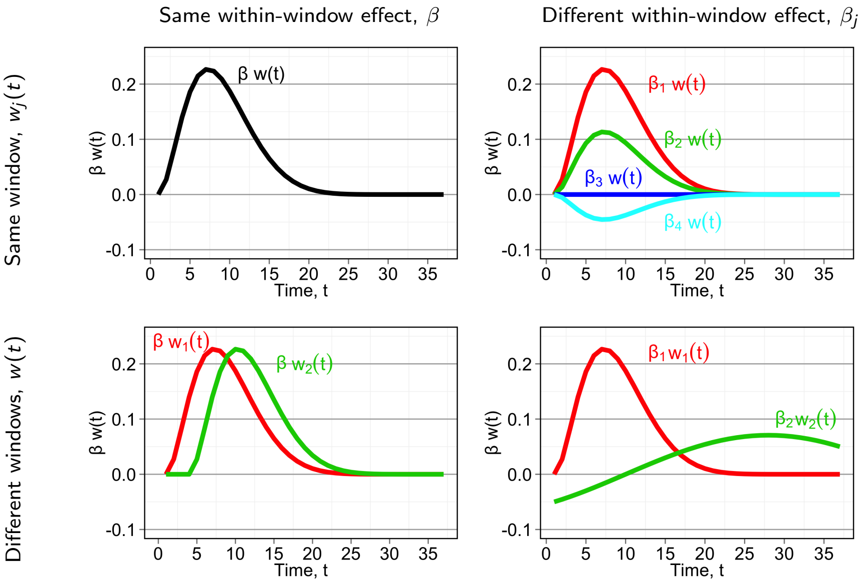
$$\theta_t = \beta w(t)$$







Separating Windows and Effects w/ Heterogeneity



Bayesian Distributed Lag Interaction Model

- With no effect heterogeneity (BDLIM-n) the model is:

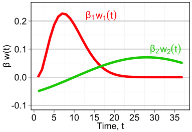
$$g\left(\mu_i\right) = \alpha + \beta \int X_i(t) w(t) dt + \mathbf{Z}_i^T \boldsymbol{\gamma}$$

- $w(t)$ identifies critical windows of vulnerability
- β is the within-window effect
- Identifiability constraints:
  - $\int \{w(t)\}^2 dt = 1$
  - $\int w(t) dt \geq 0$

BDLIM with Effect Modification

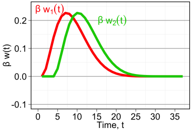
- BDLIM-bw

$$g\left(\mu_i\right) = \alpha_{j_i} + \beta_{j_i} \int X_i(t) w_{j_i}(t) dt + \mathbf{Z}_i^T \gamma$$



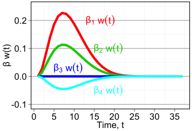
- BDLIM-w

$$g\left(\mu_i\right) = \alpha_{j_i} + \beta \int X_i(t) w_{j_i}(t) dt + \mathbf{Z}_i^T \gamma$$



- BDLIM-b

$$g\left(\mu_i\right) = \alpha_{j_i} + \beta_{j_i} \int X_i(t) w(t) dt + \mathbf{Z}_i^T \gamma$$



- Subject i is in group j_i

Parameterization of the Functional Components

- Use eigenfunction basis $\{\psi_k(t)\}_{k=1}^{K}$ of smoothed $\widehat{\Sigma}^X(\cdot,\cdot)$

$$X_i(t) = \sum_{k=1}^{K} \xi_{ik}\psi_k(t) \qquad \& \qquad w(t) = \sum_{k=1}^{K} \theta_k\psi_k(t)$$

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- Now a mixed model ($\mathbf{X}_i^* = \widehat{\mathbf{X}}_i\mathbf{\Psi}^T$)

$$g(\mu_i) = \alpha + \beta\mathbf{X}_i^{*T}\boldsymbol{\theta} + \mathbf{Z}_i^T\boldsymbol{\gamma}$$

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$$g(\mu_i) = \alpha + \beta \mathbf{X}_i^{*T} \boldsymbol{\theta} + \mathbf{Z}_i^T \boldsymbol{\gamma}$$

$$\|\boldsymbol{\theta}\| = 1 \quad \Longleftrightarrow \quad \int \{w(t)\}^2 dt = 1$$

$$\mathbf{1}^T \boldsymbol{\Psi} \boldsymbol{\theta} \geq 0 \quad \Longleftrightarrow \quad \int w(t) dt \geq 0$$

$K = 3$

Prior Specification & Computation

Priors

$$\begin{aligned} \boldsymbol{\theta} &\sim \text{Unif}\left\{\boldsymbol{\theta} : \|\boldsymbol{\theta}\| = 1 \ \& \ \mathbf{1}^T \boldsymbol{\Psi}\boldsymbol{\theta} \geq 0\right\} \\ \beta &\sim \text{N}(0, \tau^2) \end{aligned}$$

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Computation 1: Reparameterization and Gibbs

- Reparameterize BDLIM-n and BDLIM-bw: $\beta\boldsymbol{\theta} = \boldsymbol{\theta}^* \sim \text{N}(0, \kappa\tau^2\mathbf{I})$
- Estimate as mixed model

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Computation 2: Slice Sampler

- Sample directly from constrained space

Simulation

Sim A: Compares BDLIM-n and DLM with no heterogeneity

- BDLIM-n and DLM are near identical

Simulation

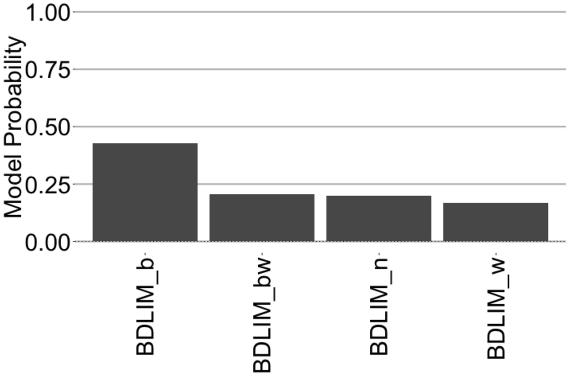
Sim A: Compares BDLIM-n and DLM with no heterogeneity

- BDLIM-n and DLM are near identical

Sim B: Tests BDLIM with effect heterogeneity

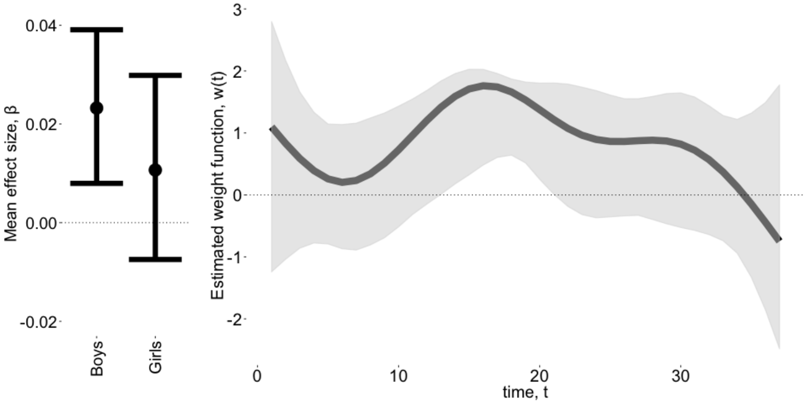
- Correctly identifies patterns of heterogeneity
- Improves estimation (RMSE, bias) relative to BDLIM-bw
- Maintains 95% interval coverage of β and $w(t)$

Asthma Results



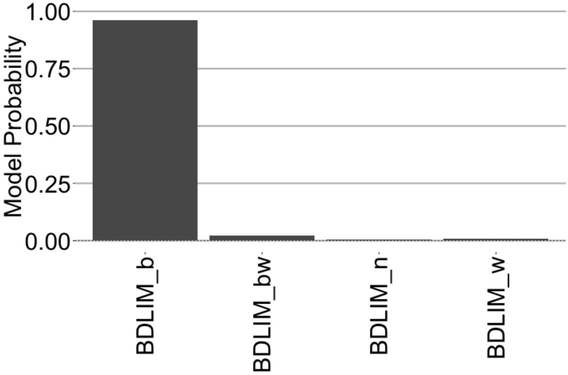
	n
female baby	261
male baby	283
total	544

Asthma Results



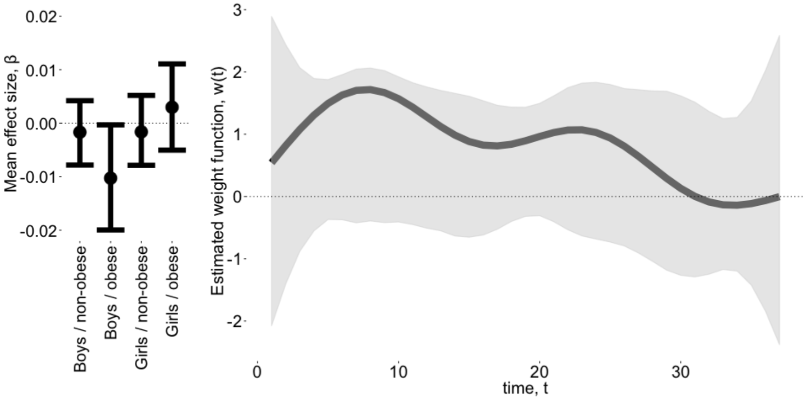
note: 10% smaller posterior standard deviation for $\widehat{\beta}_j$ than with BDLIM-bw

BWGA *z*-score Results



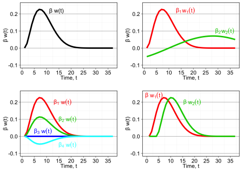
	non-obsese mother	obsese mother	total
female baby	155	84	239
male baby	182	85	267
total	337	169	506

BWGA z-score Results

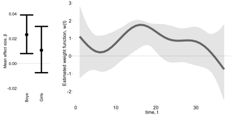


note: 14% smaller posterior standard deviation for $\widehat{\beta}_j$ than with BDLIM-bw

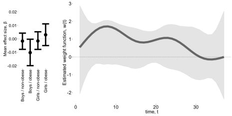
Summary



Proposed BDLIM to estimate under 4 hypothesized models of heterogeneity



Identified window where $PM_{2.5}$ exposures were associated with increased asthma incidence in boys



Evidence of a negative association between $PM_{2.5}$ and BWGA*z* among boys born to obese mothers

Software available in `regimes` R package
anderwilson.github.io/regimes/bdlim.html

Collaborators

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- Hsiao-Hsien Leon Hsu
- Robert O. Wright
- Rosalind J. Wright

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This presentation contents are solely the responsibility of the grantee and do not necessarily represent the official views of the US EPA.

Computation 1: Reparameterization and Gibbs

- Reparameterize BDLIM-n and BDLIM-bw
  - $\kappa = \beta^2\tau^{-2}$
  - $\boldsymbol{\theta}^* = \beta\boldsymbol{\theta}$
- Reparameterized priors are
  - $\kappa \sim \chi_1^2$
  - $\boldsymbol{\theta}^* \sim \mathrm{N}(0, \kappa\tau^2\mathbf{I})$
- Estimate as mixed model
  - $g(\mu_i) = \alpha + \mathbf{X}_i^{*T}\boldsymbol{\theta}^* + \mathbf{Z}_i^T\boldsymbol{\gamma}$
  - $\kappa|\text{rest} \sim$ generalized inverse-Gaussian
- Still identifiable
  - $\beta = \|\boldsymbol{\theta}^*\| \times \text{sign}\{\mathbf{1}^T\boldsymbol{\Psi}\boldsymbol{\theta}^*\}$
  - $\boldsymbol{\theta} = \boldsymbol{\theta}^*\beta^{-1}$

Computation 2: Slice Sampler

- For BDLIM-b, BDLIM-w, and all GLMs sample directly from constrained space

- Adapt elliptical slice sampling approach
  - Neal (2003) *Ann. Stat. 2003*
  - Murray et al. (2012) *J. Mach. Learn. Res. W&CP*

- Reduce problem to sampling on 1-dimensional paths through the constrained K-dimensional parameter space

Simulation

Sim A: Compares BDLIM-n and DLM with no heterogeneity

- BDLIM-n and DLM are near identical

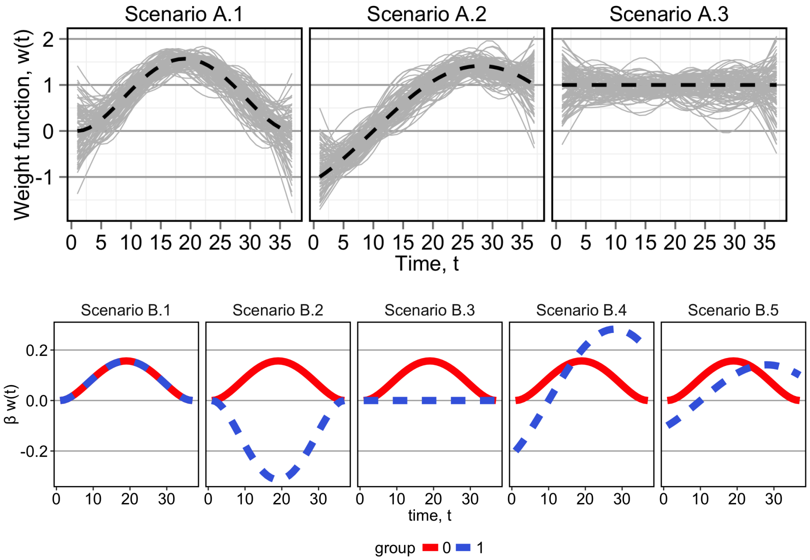
Sim B: Tests BDLIM with effect heterogeneity

- Correctly identifies patterns of heterogeneity
- Improves estimation of shared parameters

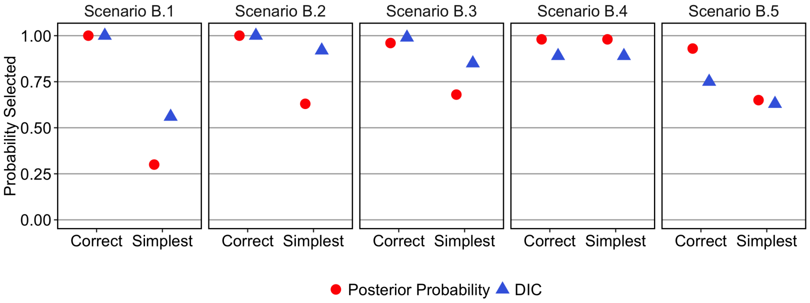
Details

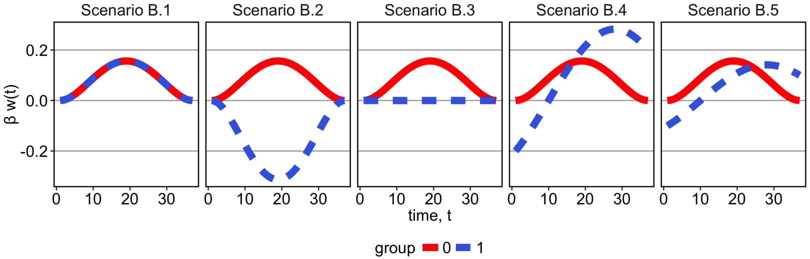
- $n = 506$, 239 girls ($j = 0$) and 267 boys ($j = 1$)
- 13 covariates (3 continuous and 10 binary)
- 1000 simulated datasets

Simulation $w(t)$

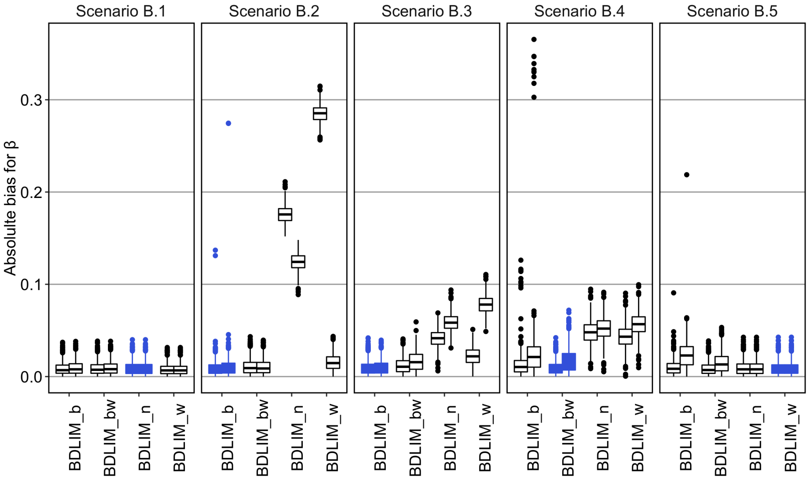


Simulation Results: Posterior Model Probability



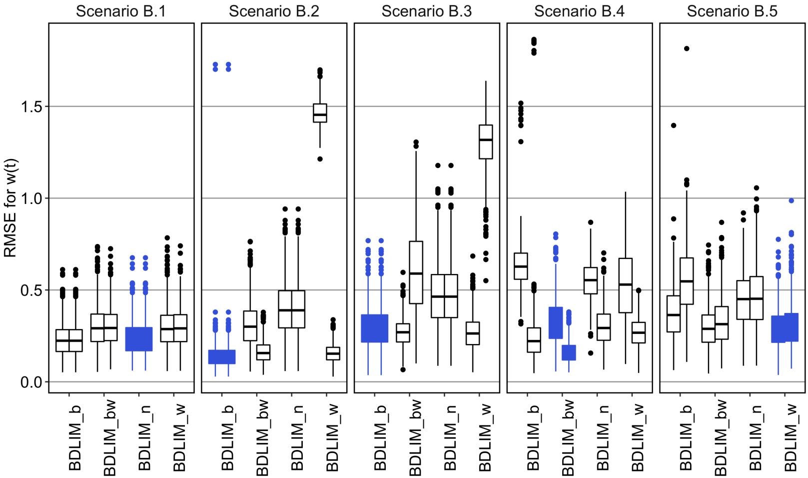


Simulation Results: Absolute Bias for β



Blue is model corresponding to the true data generating patterns

Simulation Results: RMSE for $w(t)$



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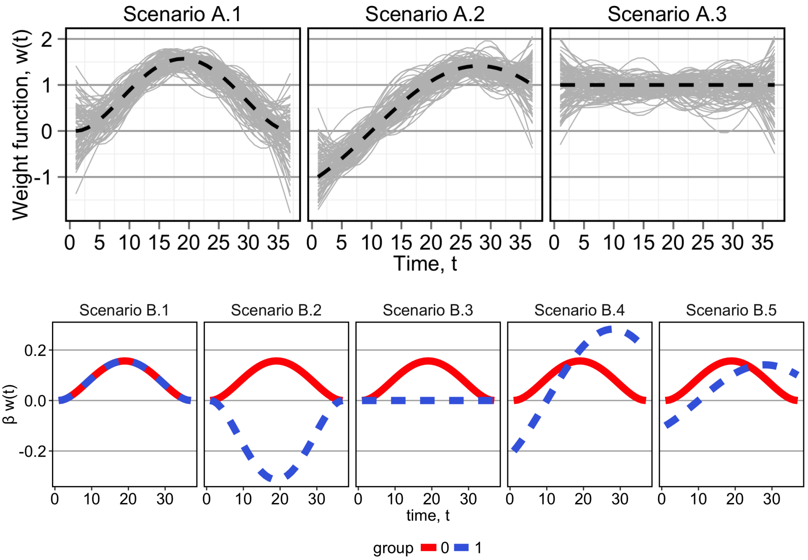
Simulation $w(t)$



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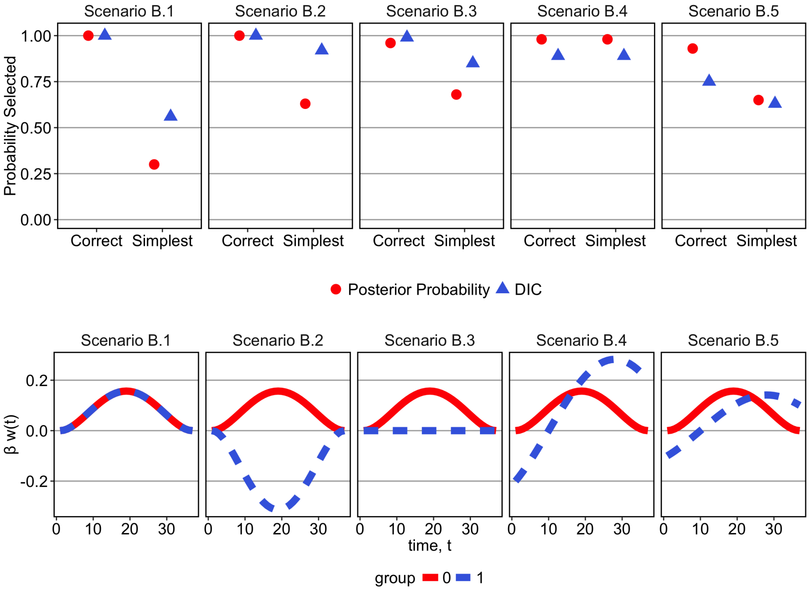

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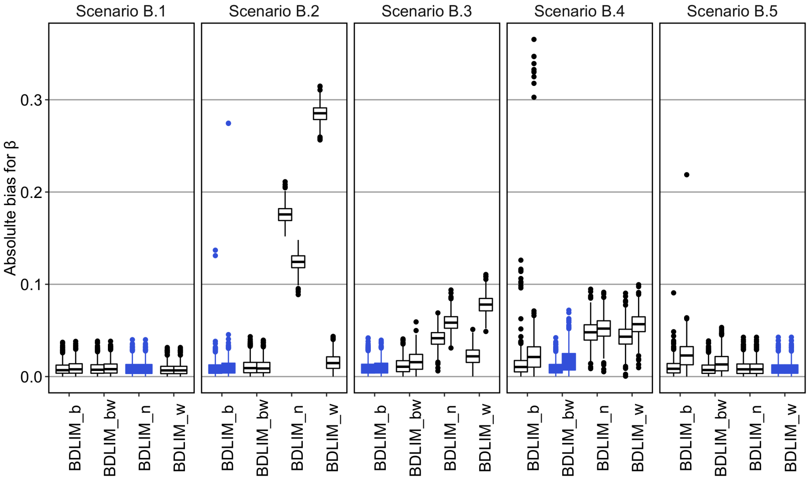

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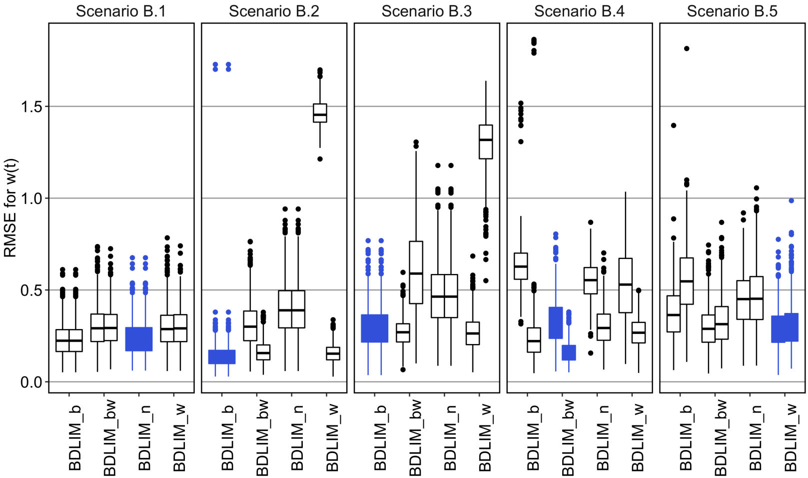
Simulation Results: RMSE for $w(t)$



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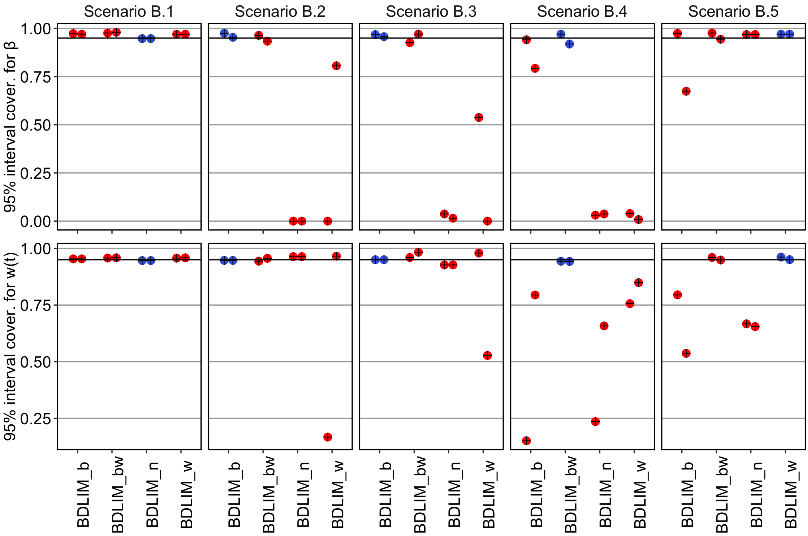
Simulation Results: Coverage



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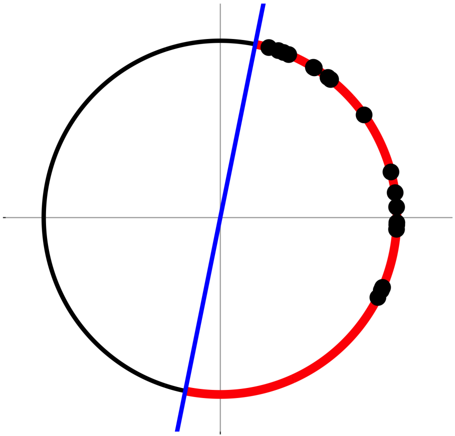
Summarizing the Posterior of $w(t)$



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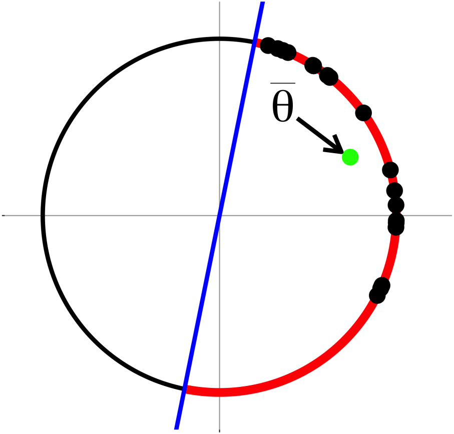

- Posterior mean $\bar{\theta}$

$$\Rightarrow \int \bar{w}(t)^2 dt \neq 1$$

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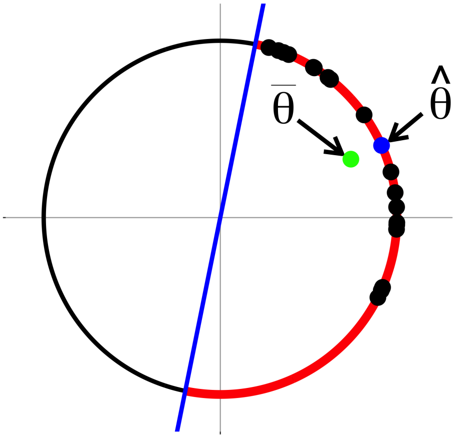

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$$\Rightarrow \int \bar{w}(t)^2 dt \neq 1$$

- Bayes estimate w.r.t.

$$L(\boldsymbol{\theta}, \widehat{\boldsymbol{\theta}}) = \frac{\|\boldsymbol{\theta} - \widehat{\boldsymbol{\theta}}\|^2}{\mathbb{1}\{\|\widehat{\boldsymbol{\theta}}\| = 1\}}$$

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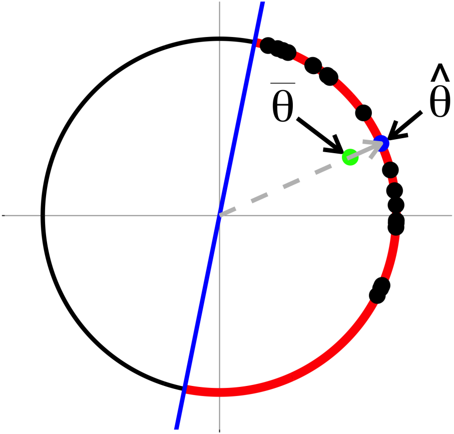

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- Equivalently

$$\widehat{\boldsymbol{\theta}} = \bar{\boldsymbol{\theta}} \|\bar{\boldsymbol{\theta}}\|^{-1}$$