

Variable Selection under Logistic Regression for Compositional Functional Data

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- 1 Introduction
- 2 Model setup
- 3 An iterative algorithm
- 4 Theoretical properties
- 5 Simulations
- 6 Real world application



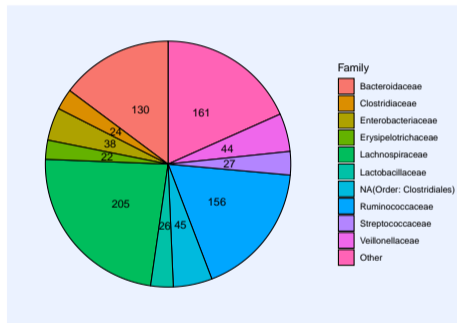
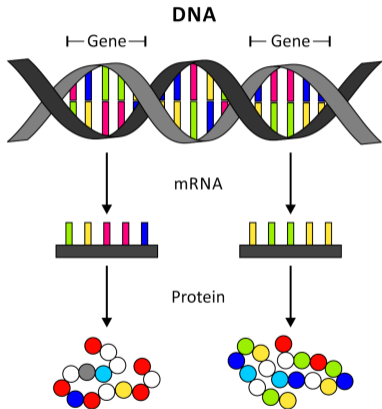


Outline

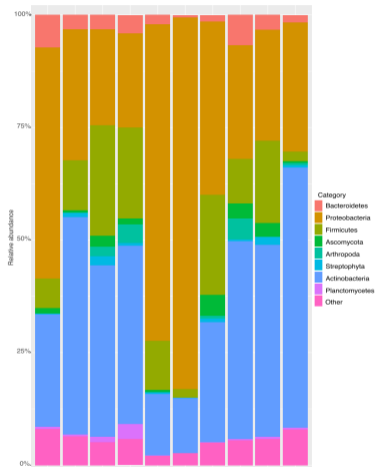
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Background



Background



- Sequencing approaches identify numerous microbes.
- The compositional data is more meaningful than raw counts data when studying microbiome.
- Multiple sampling during the study interval naturally results in the formation of functional curves.



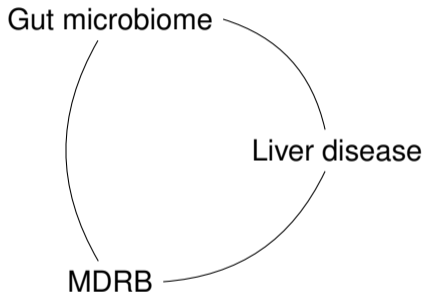
Background

Complexity of the data

- High-dimensional data in needs of variable selection
- Complex formation: functional and compositional



Background



- Intestinal microbiome is related to human health in many ways.
- Infections by Multidrug-resistant bacteria (MDRB) remains a leading cause of morbidity and mortality after liver transplantation.



Related work (compositional functional data analysis)

- Log-contrast model: Aitchison (1984); Lin (2014)
- Variable selection for functional data: Ramsay (2002); Fan (2015)
- Compositional functional data analysis via linear regression: Sun (2020)





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Model setup I

Log-contrast model

For compositional data $z_j \in \mathcal{R}_+, j = 1, \dots, p$ with $\sum_j z_j = 1$, the log-contrast model proposed by (Aitchison, 1984):

$$y = \sum_{j=1}^{p-1} \beta_j \log(z_j/z_p) + \varepsilon.$$

By introducing $\beta_p = -\sum_{j=1}^{p-1} \beta_j$, the model becomes (Lin, 2014):

$$y = \sum_{j=1}^p \beta_j \log z_j + \varepsilon, \quad \text{s.t.} \quad \sum_{j=1}^p \beta_j = 0.$$

Model setup II

Logistic model with compositional functional covariates

For binary response $y_i \in \{0, 1\}$, the logistic model for its conditional probability $\pi_i = P(y_i = 1 | \mathbf{w}_i, X_{ij}(t))$ is

$$\log \left(\frac{\pi_i}{1 - \pi_i} \right) = \alpha_0 + \mathbf{w}_i^T \boldsymbol{\delta}_0 + \sum_{j=1}^p \int X_{ij}(t) \beta_j(t) dt$$
$$\text{s.t. } \sum_{j=1}^p \beta_j(t) = 0, \quad \forall t \in [0, 1],$$

where $X_{ij}(t) = \log Z_{ij}(t)$ is the logarithm of the compositional functional data.



Model setup III

Variable selection for functional covariates

$$\sum_{j=1}^p P_{\lambda} (\|\beta_j(\cdot)\|_2),$$

where $\|\beta_j(\cdot)\|_2 = \sqrt{\int \beta_j^2(t) dt}$ represents L_2 -norm of $\beta_j(\cdot)$.



Model setup IV

Low-rank approximation

Denote $\{b_k(t), k = 1, 2, \dots\}$ a class of orthonormal basis function on $L^2(dt)$. Then we have the representation:

$$X_{ij}(t) = \sum_{k=1}^{\infty} \theta_{ijk} b_k(t), \quad \beta_j(t) = \sum_{k=1}^{\infty} \eta_{jk} b_k(t).$$

Apply low-rank approximation by letting $\theta_{ij} = (\theta_{ij1}, \dots, \theta_{ijk_n})^T$ and $\eta_j = (\eta_{j1}, \dots, \eta_{jk_n})^T$. Then

$$\int X_{ij}(t) \beta_j(t) dt \approx \theta_{ij}^T \eta_j, \quad \text{and} \quad \|\beta_j(t)\|_2 \approx \|\eta_j\|_2,$$

where $\|\eta_j\|_2 = \sqrt{\eta_j^T \eta_j}$ represents the L_2 -norm of a vector.

Low-rank representation of the original model

$$\begin{aligned} \min \mathcal{S}_\lambda^*(\beta) &= -\frac{1}{n}L(\beta) + \sum_{j=1}^p P_\lambda(\|\eta_j\|_2) \\ \text{s.t. } \sum_{j=1}^p \eta_j &= \mathbf{0}_{k_n}, \end{aligned}$$

where $L(\beta)$ is the MLE of the data, $\beta = (\alpha, \delta^T, \eta_1^T, \dots, \eta_p^T)^T$ is the vector of unknown parameters.

Augmented Lagrangian Multiplier(ALM) method

$$S_{\lambda}(\beta) = -\frac{1}{n}L(\beta) + \sum_{j=1}^p P_{\lambda}(\|\eta_j\|_2) + \mu_1^T \sum_{j=1}^p \eta_j + \frac{\mu_2}{2} \left\| \sum_{j=1}^p \eta_j \right\|_2^2,$$

where μ_1 is the multiplier vector and $\mu_2 > 0$ is the parameter for the augmented term.



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An iterative algorithm

Quadratic approximation at β_0

$$-\frac{1}{n}L(\beta) \approx \frac{1}{n} \left(-L(\beta_0) + (\beta - \beta_0)^T \mathbf{X}^T (\boldsymbol{\pi} - \mathbf{Y}) + \frac{1}{2} (\beta - \beta_0)^T \mathbf{X}^T \mathbf{W} \mathbf{X} (\beta - \beta_0) \right),$$

where $\mathbf{W} = \text{diag}(\pi_i(1 - \pi_i)) \leq \frac{1}{4} \mathbf{I}_n$.

Quadratic Majorization

Replace $\mathbf{X}^T \mathbf{W} \mathbf{X}$ with $\mathbf{H} = \frac{1}{4} \mathbf{X}^T \mathbf{X}$.



An iterative algorithm (updating η_{j_0}) I

Apply MM-principle multiple times

$$\begin{aligned}
 S_\lambda(\eta_{j_0}) \leq & \frac{1}{2} \eta_{j_0}^T \left(\frac{d_{j_0, \max}^2}{4n} \mathbf{I}_{k_n} + \mu_2 \mathbf{I}_{k_n} \right) \eta_{j_0} \\
 & - \eta_{j_0}^T \left(\frac{d_{j_0, \max}^2}{4n} \eta_{j_0}^{(m)} - \frac{1}{n} \Theta_{j_0}^T \left(\pi^{(m)} - \mathbf{Y} \right) - \mu_1^{(m)} - \mu_2 \sum_{j \neq j_0} \eta_j^{(m)} \right) \\
 & + P_\lambda(\|\eta_{j_0}\|),
 \end{aligned}$$

where $d_{j_0, \max}^2$ is the maximum eigen value of $\Theta_{j_0}^T \Theta_{j_0}$ and Θ_{j_0} is the low-rank representation of the j_0 th functional covariate.

An iterative algorithm (updating η_{j_0}) II

Local Linear Approximation(LLA)

$$P_\lambda(\|\eta_{j_0}\|) \approx P_\lambda(\|\eta_{j_0}^{(m)}\|) + P'_\lambda(\|\eta_{j_0}^{(m)}\|) (\|\eta_{j_0}\|_2 - \|\eta_{j_0}^{(m)}\|_2).$$

Updating step for η_{j_0}

$$\eta_{j_0}^{(m+1)} = \frac{1}{d_{j_0, \max}^2 / (4n) + \mu_2} \left(1 - \frac{P'_\lambda(\|\eta_{j_0}^{(m)}\|)}{\sqrt{\alpha_{j_0}^{(m)T} \alpha_{j_0}^{(m)}}} \right) \alpha_{j_0}^{(m)},$$

where

$$\alpha_{j_0}^{(m)} = \frac{d_{j_0, \max}^2}{4n} \eta_{j_0}^{(m)} - \frac{1}{n} \Theta_{j_0}^T (\pi^{(m)} - \mathbf{Y}) - \mu_1^{(m)} - \mu_2 \sum_{j \neq j_0} \eta_j^{(m)}.$$



Implementations in R package I

Sample weighting

$$L_v = \sum_{i=1}^n v_i (y_i \pi_i + (1 - y_i) (1 - \pi_i)),$$

where $v_i, i = 1, \dots, n$ is a set of positive weights.



Implementations in R package II

Flexibility and robustness

within-group standardization

multiplier vector

$$S_n = \frac{-1}{a} L_v + \sum_{j=1}^p c_j P_{\lambda_n} (b_j \|\eta\|_2) + \mu_1^T \sum_{j=1}^p \eta_j + \frac{\mu_2}{2} \left\| \sum_{j=1}^p \eta_j \right\|_2^2 + \sum_{j=1}^{h+pk_n} \frac{r_j}{2} \beta_j^2,$$

weights for different modules

robust term

Within-group orthonormalization

$$S_n = \frac{-1}{a} L_v + \sum_{j=1}^P c_j P_{\lambda_n} (b_j \|\tilde{\eta}_j\|_2) + \mu_1^T \sum_{j=1}^P \mathbf{T}_j \tilde{\eta}_j + \frac{\mu_2}{2} \|\mathbf{T}_j \tilde{\eta}_j\|_2^2 + \sum_{j=1}^{h+\sum_k m_k} \frac{r_j}{2} \beta_j^2,$$

where $\tilde{\eta}_j$ is the parameters after within-group orthonormalization. $\mathbf{T}_j = \sqrt{a} \mathbf{V}_j \mathbf{D}_j^{-1}$ is the transforming matrix satisfying $\eta_j = \mathbf{T}_j \tilde{\eta}_j$. Covariates after transforming $\tilde{\Theta}_j = \Theta_j \mathbf{T}_j$ satisfies $\frac{1}{a} \tilde{\Theta}_j^T \tilde{\Theta}_j = \mathbf{I}$.



Implementations in R package IV

FLiRTI (James, 2009) procedure

Pursuit the functional parameters in simple form of curves:

$$S_n = \text{Logistic} + \sum_{j=1}^q \sum_{k=1}^T c_{jk} P_\lambda (b_{jk} \gamma_{(1),jk}) + \mu_1^T \sum_{j=1}^q \gamma_{(1),j} + \frac{\mu_2}{2} \left\| \sum_{j=1}^q \gamma_{(1),j} \right\|_2^2.$$





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Convergence of the algorithm

Checking KKT conditions we know that

Theorem

The objective function coupled with Lasso penalty strictly descends during the iteration. If the current solution $\alpha^{(m+1)}$, $\delta^{(m+1)}$, $\eta_j^{(m+1)}$, $j = 1, \dots, p$ and $\mu_1^{(m+1)}$ stay unchanged after one complete iteration, then the algorithm reaches the minimum point of the objective function.



Consistency of the Lasso estimator I

Theorem (Consistency of the Lasso estimator)

If Assumption 1–3 hold and $pk_n = o(e^n)$, $\lambda \rightarrow 0$. Also there exists constant c such that $\lambda > c\sqrt{k_n \log(pk_n)/n}$. Then with probability approaching to 1, the Lasso estimator $\hat{\xi}^{glasso}$ satisfies

$$\left\| \hat{\xi}^{glasso} - \xi^* \right\|_2 \leq 2(1 + \phi)(2 + \phi) \frac{\sqrt{q_n} \lambda}{\kappa},$$

as $n \rightarrow \infty$, where ϕ is any positive constant and ξ^* is the real underlying parameters.

Consistency of the Lasso estimator II

Corollary

Under the condition that the previous theorem holds, and additionally the minimal signal strength Assumption 4 holds, the with probability approaching to 1,

$$\min_{j \in \{1, \dots, q_n\}} \left\| \hat{\eta}_j^{glasso} \right\|_2 \geq 2(1 + \phi)(2 + \phi) \frac{\sqrt{q_n \lambda}}{\kappa},$$

and

$$\max_{j \in \{q_n + 1, \dots, p\}} \left\| \hat{\eta}_j^{glasso} \right\|_2 \leq 2(1 + \phi)(2 + \phi) \frac{\sqrt{q_n \lambda}}{\kappa}.$$

as $n \rightarrow \infty$.

Necessary assumptions I

- 1 There uniformly exist positive constants K and R , independent of n , such that for $1 \leq i \leq n$, $1 \leq j \leq p$, $1 \leq k \leq k_n$ and $m = 2, 3, \dots$,

$$\mathbb{E} |\theta_{ij,k} (y_i - \pi_i(\xi^*, \Theta))|^m \leq (m!/2) K^{m-2} R^2,$$

where we use $\pi_i(\xi^*, \Theta)$ to emphasize that the computation of π_i relies on underlying parameters ξ^* and data Θ .

- 2 There exists a positive constant κ such that

$$\inf \left\{ \frac{\sqrt{\Delta^T \Theta^T \mathbf{W}(\xi^*, \Theta) \Theta \Delta}}{\sqrt{n} \|\Delta\|_2} : \mathbf{C}^T \Delta = \mathbf{0}, \sum_{j=q_n+1}^p \|\Delta_j\|_2 \leq (1 + \phi) \sum_{j=1}^{q_n} \|\Delta_j\|_2 \right\} = \kappa > 0,$$

where $\Theta = (\Theta_1, \dots, \Theta_p)$ is the $n \times (pk_n)$ low-rank representation of p functional covariates.



Necessary assumptions II

- 3 $E q_3(\xi, \theta) \|\theta\|_{2, \infty}^3$ is bounded in the neighbourhood centered at ξ^* , where $q_3(\xi, \theta)$ represents the 3rd order derivative of the link function of logistic regression.
- 4 The real underlying model parameters satisfy

$$\min_{j \in \{1, \dots, q_n\}} \|\eta_j^*\|_2 \geq 4(1 + \phi)(2 + \phi) \sqrt{q_n} \lambda.$$



Oracle property when applying non-convex penalty

Theorem

If Assumption 1–3, 5–7 hold, and $\lambda = o(n^{-(1-c_2)/2})$, $q_n k_n \sqrt{k_n/n} = o(\lambda)$, $\sqrt{k_n} \log p = o(n\lambda)$ and $n\lambda/\sqrt{k_n} \rightarrow \infty$ are satisfied, then there exists a local minimum $(\hat{\eta}_1^T, \dots, \hat{\eta}_p^T)^T$ of the objective function coupled with SCAD or MCP penalty such that

$$P \left(\left(\hat{\eta}_1^T, \dots, \hat{\eta}_p^T \right)^T = \left(\hat{\eta}_1^{or\ T}, \dots, \hat{\eta}_p^{or\ T} \right)^T \right) \rightarrow 1$$

as $n \rightarrow \infty$, where $(\hat{\eta}_1^{or\ T}, \dots, \hat{\eta}_p^{or\ T})^T$ denotes the oracle estimator.

Necessary assumptions

- 5 There exist two positive constants C_1 and C_2 uniformly for $j \in \{1, \dots, q_n\}$, such that

$$0 < C_1 \leq \lambda_{\min} \left(\frac{1}{n} \Theta_j^T \mathbf{W}(\xi^*, \Theta) \Theta_j \right) \leq \lambda_{\max} \left(\frac{1}{n} \Theta_j^T \mathbf{W}(\xi^*, \Theta) \Theta_j \right) \leq C_2,$$

where $\lambda_{\min}(\cdot)$ and $\lambda_{\max}(\cdot)$ represents the minimum and maximum eigen value of a given matrix. Also it's assumed that $\max_{1 \leq i \leq n} \left\| \left(\theta_{i1}^T, \dots, \theta_{iq_n}^T \right) \right\|_2 = O_p \left(\sqrt{q_n k_n} \right)$ and there exists a constant M_1 such that $\max_{j,k} E |\theta_{jk}| \leq M_1$ for $j \in \{q_n + 1, \dots, p\}$, $k \in \{1, \dots, k_n\}$.

- 6 There exists a positive constant c_1 such that $0 \leq c_1 < \frac{1}{3}$ and $q_n k_n = O(n^{c_1})$.
- 7 There exists a positive constant c_2 such that $2c_1 < c_2 < 1$ and

$$n^{(1-c_2)/2} \min_{1 \leq j \leq q_n} \left\| \eta_j^* \right\|_2 \geq M_2.$$



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Data generation

$$\bar{W}_{ij}(t) = \exp\left(\mathbf{w}_{ij}^T \mathbf{c}(t) + \varepsilon_{ij}(t)\right), \quad i = 1, \dots, n, \quad j = 1, \dots, p,$$

where $\mathbf{c}(t)$ is a set of Fourier basis, $\varepsilon_{ij}(t)$ follows $N(0, 0.5^2)$ at each time points. The functional counting data is acquired by $W_{ij}(t) = \lfloor \bar{W}_{ij}(t) \rfloor$. Hence

$$X_{ij}(t) = \log\left(\frac{W_{ij}(t) + 1}{\sum_{j=1}^p W_{ij}(t) + p}\right), \quad i = 1, \dots, n, \quad j = 1, \dots, p.$$

Simulation settings II

Low-rank approximation

- First q_n terms of $\beta_j(t)$ are generated from $\beta_j = \boldsymbol{\eta}_j^T \mathbf{c}(t)$, where $\boldsymbol{\eta}_j$ is centered so that $\sum_{j=1}^{q_n} \boldsymbol{\eta}_j = \mathbf{0}$. The remaining $\beta_j(t)$, $j = q_n + 1, \dots, p$ are set to constant 0.
- Orthonormalized B-spline Redd (2011) is applied for low-rank approximation.

Magnitude of the simulation

- Sample size $n \in \{75, 100, 150, 250\}$, number of functional covariates $p \in \{50, 500\}$.
- Number of important covariates $q_n \in \{8, 10\}$, number of basis functions $k_n = 6$.



Candidate methods

- Oracle model
- Proposed model, coupled with MCP and Lasso penalty
- GGL (Generalized linear regression with Group Lasso, Yang (2014))
- ZINB (Zero Inflated Negative Binomial model, Zhang (2018))



Simulation results (low-dimensional settings) I

Table 1: $n = 150, p = 50, q = 10$

Model	Criteria	AUC	MSE_{δ}	$ \sum \hat{\eta} _{\infty}$	FP	FN	FDR
Oracle	-	0.947(0.039)	0.711(0.439)	$< 10^{-5}$	0(0)	0(0)	0(0)
MCP	BIC	0.881(0.081)	0.847(0.477)	$< 10^{-5}$	1.010(0.969)	3.860(1.059)	0.138(0.131)
MCP	CV	0.827(0.095)	0.794(0.272)	$< 10^{-5}$	0.150(0.411)	6.420(0.987)	0.035(0.093)
Lasso	BIC	0.870(0.070)	0.803(0.456)	$< 10^{-5}$	1.410(1.156)	3.840(0.801)	0.172(0.130)
Lasso	CV	0.843(0.075)	0.766(0.250)	$< 10^{-5}$	18.030(3.465)	0.790(0.715)	0.657(0.046)
GGL	CV	0.877(0.069)	2.046(1.977)	0.546	12.510(6.522)	1.380(1.277)	0.538(0.172)
ZINB	fdr0.05	0.599(0.092)	1.208(1.255)	0.107	0(0)	9.810(0.465)	0(0)



Simulation results (low-dimensional settings) II

Table 2: $n = 250, p = 50, q = 10$

Model	Criteria	AUC	MSE _δ	$ \sum \hat{\eta} _{\infty}$	FP	FN	FDR
Oracle	-	0.973(0.020)	0.411(0.262)	$< 10^{-5}$	0(0)	0(0)	0(0)
MCP	BIC	0.954(0.030)	0.483(0.204)	$< 10^{-5}$	0.350(0.672)	1.950(0.770)	0.040(0.076)
MCP	CV	0.927(0.052)	0.587(0.225)	$< 10^{-5}$	0.150(0.557)	3.670(1.596)	0.016(0.054)
Lasso	BIC	0.949(0.032)	0.503(0.194)	$< 10^{-5}$	0.700(0.847)	2.230(0.777)	0.074(0.086)
Lasso	CV	0.884(0.053)	0.617(0.167)	$< 10^{-5}$	23.750(3.020)	0.220(0.416)	0.706(0.031)
GGL	CV	0.934(0.037)	1.505(1.330)	0.472	14.850(7.124)	0.590(0.698)	0.571(0.145)
ZINB	fdr0.05	0.573(0.076)	1.111(0.943)	0.078	0.010(0.010)	9.880(0.327)	0.010(0.100)



Simulation results (high-dimensional settings) I

Table 3: $n = 150, p = 500, q = 8$

Model	Criteria	AUC	MSE_{δ}	$ \sum \hat{\eta} _{\infty}$	FP	FN	FDR
Oracle	-	0.947(0.031)	1.093(0.704)	$< 10^{-5}$	0(0)	0(0)	0(0)
MCP	BIC	0.803(0.100)	0.769(0.516)	$< 10^{-5}$	2.920(1.839)	3.200(1.325)	0.362(0.209)
MCP	CV	0.738(0.098)	0.518(0.214)	$< 10^{-5}$	0.580(0.673)	5.280(1.230)	0.150(0.168)
Lasso	BIC	0.804(0.091)	0.587(0.453)	$< 10^{-5}$	3.615(1.670)	2.769(1.231)	0.398(0.157)
Lasso	CV	0.760(0.061)	0.466(0.175)	$< 10^{-5}$	31.173(8.740)	0.981(1.180)	0.804(0.059)
GGL	CV	0.794(0.093)	3.727(4.126)	0.440	26.580(16.519)	1.460(1.854)	0.704(0.225)
ZINB	fdr0.05	0.571(0.061)	0.925(1.330)	0.033	4.260(2.039)	7.900(0.364)	0.966(0.149)

Simulation results (high-dimensional settings) II

Table 4: $n = 250, p = 500, q = 8$

Model	Criteria	AUC	MSE $_{\delta}$	$ \sum \hat{\eta} _{\infty}$	FP	FN	FDR
Oracle	-	0.954(0.023)	1.892(0.947)	$< 10^{-5}$	0(0)	0(0)	0(0)
MCP	BIC	0.951(0.047)	0.233(0.211)	$< 10^{-5}$	0.750(1.065)	0.062(0.250)	0.077(0.101)
MCP	CV	0.929(0.057)	0.185(0.127)	$< 10^{-5}$	0.312(0.602)	0.938(1.482)	0.033(0.063)
Lasso	BIC	0.937(0.036)	0.183(0.127)	$< 10^{-5}$	2.111(2.147)	0.444(0.726)	0.194(0.150)
Lasso	CV	0.840(0.068)	0.314(0.111)	$< 10^{-5}$	39.444(2.963)	0.000(0.000)	0.831(0.011)
GGL	CV	0.921(0.045)	1.442(1.232)	0.322	28.000(19.280)	0.062(0.250)	0.707(0.185)
ZINB	fdr0.05	0.590(0.076)	0.605(0.127)	0.023	5.438(2.449)	7.938(0.250)	0.992(0.031)



Simulation results (settings that mimic real data)

Table 5: $n = 150$, $p = 500$, $q = 8$. Subjects are heterogeneous, mimicing the pattern in real data application.

Model	Criteria	AUC	MSE _δ	$ \sum \hat{\eta} _{\infty}$	FP	FN	FDR
Oracle	-	0.883(0.055)	2.080(2.588)	$< 10^{-5}$	0(0)	0(0)	0(0)
MCP	BIC	0.797(0.081)	0.630(0.837)	$< 10^{-5}$	5.000(1.732)	5.348(0.775)	0.637(0.135)
MCP	CV	0.797(0.085)	0.782(0.551)	$< 10^{-5}$	1.565(2.063)	6.391(1.438)	0.257(0.283)
Lasso	BIC	0.908(0.026)	0.287(0.130)	$< 10^{-5}$	2.000(1.000)	5.200(0.837)	0.410(0.175)
Lasso	CV	0.780(0.047)	1.664(0.742)	$< 10^{-5}$	20.400(9.764)	3.800(1.304)	0.811(0.063)
GGL	CV	0.815(0.070)	1.604(1.306)	0.758	18.913(16.673)	4.565(1.343)	0.737(0.216)
ZINB	fdr0.05	0.773(0.082)	$> 4 \times 10^3$	1.326	0.522(0.790)	6.217(1.043)	0.159(0.259)





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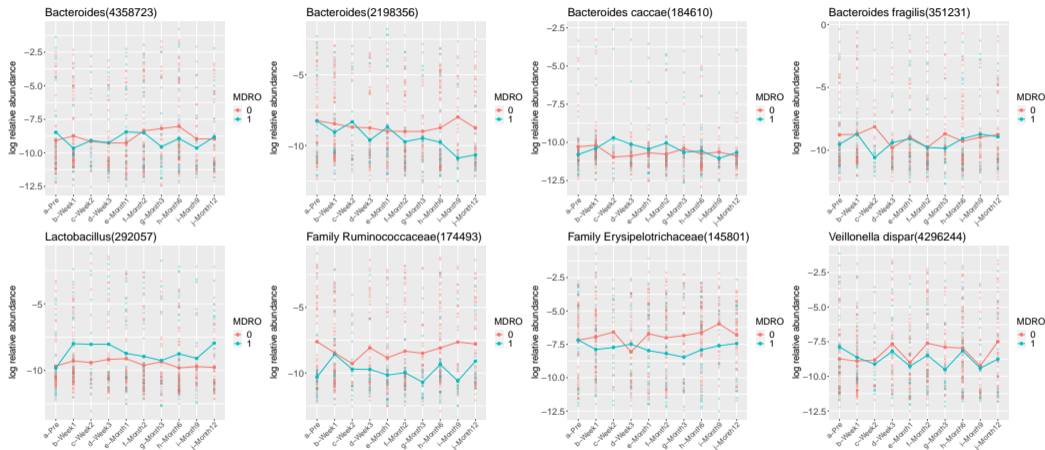


Colonizing MDRB and the intestinal microbiome

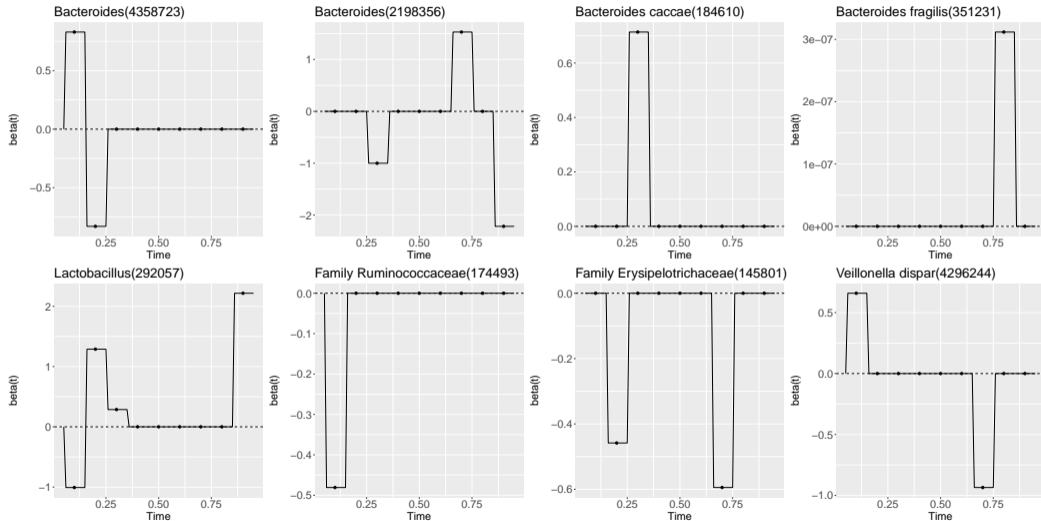
- Infections by Multidrug-resistant bacteria (MDRB) remain a leading cause of morbidity and mortality after liver transplantation(LT).
- Gut dysbiosis characteristic of end-stage liver disease may predispose patients to intestinal MDRB colonization and infection, in turn exacerbating dysbiosis.
- After quality control, data of 131 patients during one year after LT is collected. At Operational Taxonomic Units(OTU) level, 878 different taxons are identified.
- Colonizing status of MDRB for each patients is taken as response.



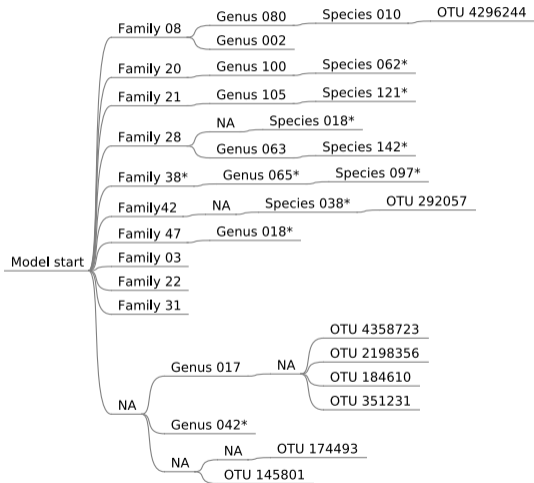
Variable selection



Estimation of functional parameters (after FLiRTI procedure)



Results at different taxonomic levels



Taxonomic levels: Family, Genus and Species.
NA means the corresponding taxon is not included in the model.

Asterisk means the current level is not officially recognized.



Future work

- Deal with confounders such as antibiotic treatment
- From observational study to causal inference
- Post-selection inference





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