Variational Inference in the Poisson lognormal model

Application to multivariate analysis of count data

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joint work with M. Mariadasou, S. Robin

joint Exposome/LMAP seminaries, Anglet, June, 28 2018

J.C., Mahendra Mariadassou, Stéphane Robin,
Variational inference for probabilistic Poisson PCA
https://arxiv.org/abs/1703.06633 (to appear in the Annals of Applied Statistics)

J.C., Mahendra Mariadassou, Stéphane Robin,
Variational inference for sparse network reconstruction from count data
https://arxiv.org/abs/1806.03120 (submitted)

PLNmodels package, development version on github
`devtools::install_github("jchiquet/PLNmodels", build_vignettes=TRUE)`

Motivations: oak powdery mildew pathobiome

Metabarcoding data from [JFS+16]

- $n = 116$ leaves, $p = 114$ species (66 bacteria, 47 fungies + *E. alphitoides*)

```
counts[1:3, c(1:4, 48:51)]

##       f_1 f_2 f_3 f_4 E_alphitoides b_1045 b_109 b_1093
## A1.02  72   5 131   0             0      0     0      0
## A1.03 516  14 362   0             0      0     0      0
## A1.04 305  24 238   0             0      0     0      0
```

- $d = 8$ covariates (tree susceptibility, distance to trunk, orientation, ...)

```
covariates[1:3, ]

##               tree distTOtrunk distTOground pmInfection orientation
## A1.02 intermediate         202        155.5           1          SW
## A1.03 intermediate         175        144.5           0          SW
## A1.04 intermediate         168        141.5           0          SW
```

- Sampling effort in each sample (bacteria $\neq$ fungi)

```
offsets[1:3, c(1:4, 48:51)]

##       f_1  f_2  f_3  f_4 E_alphitoides b_1045 b_109 b_1093
## [1,] 2488 2488 2488 2488          2488   8315  8315   8315
## [2,] 2054 2054 2054 2054          2054    662   662    662
## [3,] 2122 2122 2122 2122          2122    480   480    480
```

Problematic & Basic formalism

Data tables: $\mathbf{Y} = (Y_{ij}), n \times p$; $\mathbf{X} = (X_{ik}), n \times d$; $\mathbf{O} = (O_{ij}), n \times p$ where

- $Y_{ij} =$ abundance (read counts) of species j in sample i
- $X_{ik} =$ value of covariate k in sample i
- $O_{ij} =$ offset (sampling effort) for species j in sample i

Need for multivariate analysis to help deciphering the pathobiome

- exhibit patterns of diversity
  $\rightsquigarrow$ summarize the information from $\mathbf{Y}$ (PCA, clustering, ...)
- understand between-species interactions
  $\rightsquigarrow$ 'network' inference (variable/covariance selection)
- correct for technical and confounding effects
  $\rightsquigarrow$ account for covariables and sampling effort

$\rightsquigarrow$ need a generic framework to model dependences between count variables

Models for multivariate count data

If we were in a Gaussian world, the general linear model would be appropriate

For each sample $i = 1, \dots, n$, it explains

- the abundances of the p species $(\mathbf{Y}_i)$
- by the values of the d covariates $\mathbf{X}_i$ and the p offsets $\mathbf{O}_i$

$$\mathbf{Y}_i = \underbrace{\mathbf{X}_i\mathbf{B}}_{\text{account for covariates}} + \underbrace{\mathbf{O}_i}_{\text{account for sampling effort}} + \boldsymbol{\varepsilon}_i, \ \boldsymbol{\varepsilon}_i \sim \mathcal{N}(\mathbf{0}_p, \underbrace{\boldsymbol{\Sigma}}_{\text{dependence between species}})$$

$+$ null covariance $\Leftrightarrow$ independence $\rightsquigarrow$ uncorrelated species do not interact

But we are not, and there is no generic model for multivariate counts

- Data transformation $(\log, \sqrt{})$: quick and dirty
- Non-Gaussian multivariate distributions: do not scale to data dimension yet
- Latent variable models: interaction occur in a latent (unobserved) layer

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Poisson-log normal (PLN) distribution

A latent Gaussian model

Originally proposed by Atchisson [AH89]

$$\mathbf{Z}_i \sim \mathcal{N}(\mathbf{0}, \boldsymbol{\Sigma})$$

$$\mathbf{Y}_i \,|\, \mathbf{Z}_i \sim \mathcal{P}(\exp\{\mathbf{O}_i + \mathbf{X}_i^\intercal \mathbf{B} + \mathbf{Z}_i\})$$

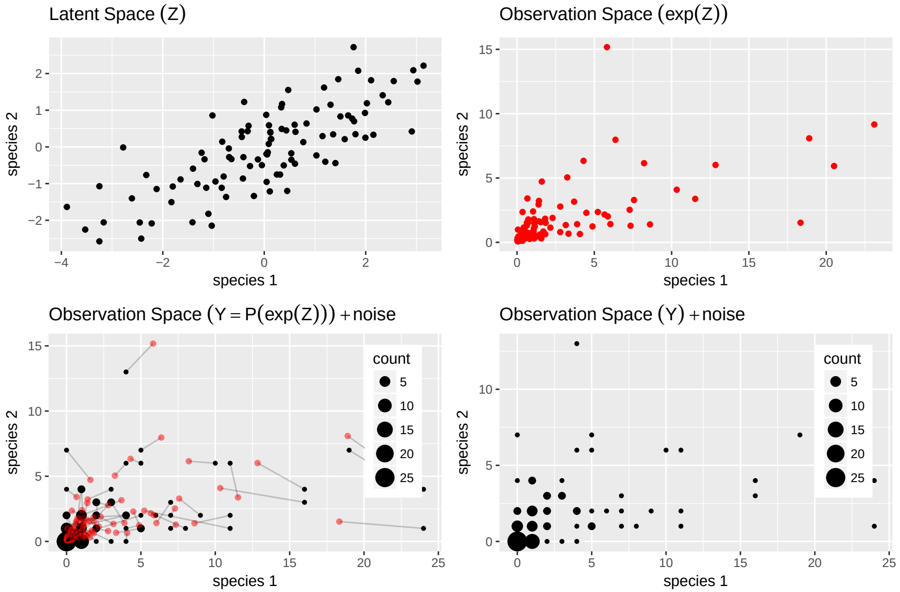
Interpretation

- Dependency structure encoded in the latent space (i.e. in $\boldsymbol{\Sigma}$)
- Additional effects are fixed
- Conditional Poisson distribution = noise model

Properties

+ over-dispersion
+ covariance with arbitrary signs
- maximum likelihood via EM algorithm is limited to a couple of variables

Geometrical view



Outline

Outline

Intractable EM

Aim of the inference:

- estimate $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\Sigma})$
- predict the $\mathbf{Z}_i$

Maximum likelihood

PLN is an incomplete data model: try EM

$$\log p_{\boldsymbol{\theta}}(\mathbf{Y}) = \mathbb{E}[\log p_{\theta}(\mathbf{Y}, \mathbf{Z}) \,|\, \mathbf{Y}] + \mathcal{H}[p_{\boldsymbol{\theta}}(\mathbf{Z} \,|\, \mathbf{Y})]$$

EM requires to evaluate (some moments of)

$$p(\mathbf{Z} \,|\, \mathbf{Y}) = \prod_i p(\mathbf{Z}_i \,|\, \mathbf{Y}_i)$$

but no close form for $p(\mathbf{Z}_i \,|\, \mathbf{Y}_i)$.

- [Kar05] resorts to numerical or Monte-Carlo integration.
- Variational approach [WJ08]: use a proxy of $p(\mathbf{Z} \,|\, \mathbf{Y})$.

Variational EM

Variational approximation: choose a class of distribution $\mathcal{Q}$

$$\mathcal{Q} = \left\{ \tilde{p} : \quad \tilde{p}(\mathbf{Z}) = \prod_i \tilde{p}_i(\mathbf{Z}_i), \quad \tilde{p}_i(\mathbf{Z}_i) = \mathcal{N}(\mathbf{Z}_i; \tilde{\mathbf{m}}_i, \tilde{\mathbf{s}}_i) \right\}$$

and maximize the lower bound ($\tilde{\mathbb{E}}$ = expectation under $\tilde{p}$)

$$J(\theta, \tilde{p}) = \log p_{\boldsymbol{\theta}}(\mathbf{Y}) - KL[\tilde{p}(\mathbf{Z}) \,||\, p_{\boldsymbol{\theta}}(\mathbf{Z} \mid \mathbf{Y})] = \tilde{\mathbb{E}}[\log p_{\boldsymbol{\theta}}(\mathbf{Y}, \mathbf{Z})] + \mathcal{H}[\tilde{p}(\mathbf{Z})]$$

Variational EM.

- VE step: find the optimal $\tilde{p}$:

$$\tilde{p}^h = \arg\max J(\boldsymbol{\theta}^h, \tilde{p}) = \arg\min_{\tilde{p} \in \mathcal{Q}} KL[\tilde{p}(\mathbf{Z}) \,||\, p_{\boldsymbol{\theta}^h}(Z \mid Y)]$$

- M step: update $\hat{\theta}$

$$\hat{\boldsymbol{\theta}}^h = \arg\max J(\boldsymbol{\theta}, \tilde{p}^h) = \arg\max_{\boldsymbol{\theta}} \tilde{\mathbb{E}}[\log p_{\boldsymbol{\theta}}(\mathbf{Y}, \mathbf{Z})]$$

Variational EM

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$$\hat{\boldsymbol{\theta}}^h = \arg\max J(\boldsymbol{\theta}, \tilde{p}^h) = \arg\max_{\boldsymbol{\theta}} \tilde{\mathbb{E}}[\log p_{\boldsymbol{\theta}}(\mathbf{Y}, \mathbf{Z})]$$

Variational EM

Property: The lower $J(\boldsymbol{\theta}, \tilde{p})$ is bi-concave, i.e.

- wrt $\tilde{p} = (\tilde{\mathbf{M}}, \tilde{\mathbf{S}})$ for given $\boldsymbol{\theta}$
- wrt $\boldsymbol{\theta} = (\boldsymbol{\Sigma}, \boldsymbol{\beta})$ for given $\tilde{p}$

but not jointly concave in general.

Optimization: projected gradient ascent for the complete parameter $(\tilde{\mathbf{m}}, \tilde{\mathbf{s}}, \boldsymbol{\theta})$

- algorithm: conservative convex separable approximations [Sva02]
- implementation: `NLopt` nonlinear-optimization package [Joh11]
- initialization: LM after log-trasnformation applied independently on each variables + concatenation of the regression coefficients + Pearson residuals

`PLNmodels` R-package:

`https://github.com/jchiquet/PLNmodels`

Outline

Fit the PLN model

Load the package

```r
library(PLNmodels)
```

Fit the model with offsets

```r
system.time(PLN_offset <- PLN(Y ~ 1 + offset(log(O))))

##
##  Adjusting the standard PLN model.
##    user  system elapsed
##  22.112   0.016   5.844
```

Now the model with offsets and the 'tree' covariate

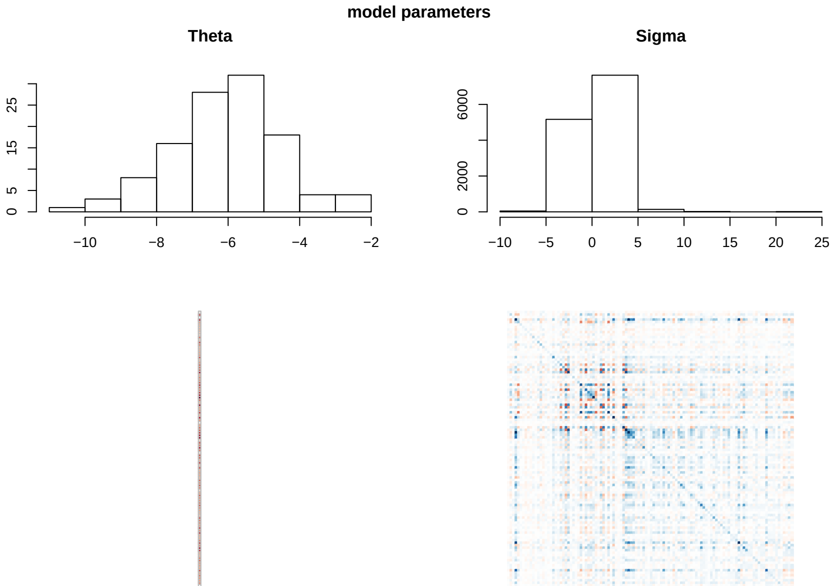
```r
PLN_tree <- PLN(Y ~ 1 + covariates$tree + offset(log(O)))

##
##  Adjusting the standard PLN model.
```

Model with offsets

Plot the model parameters

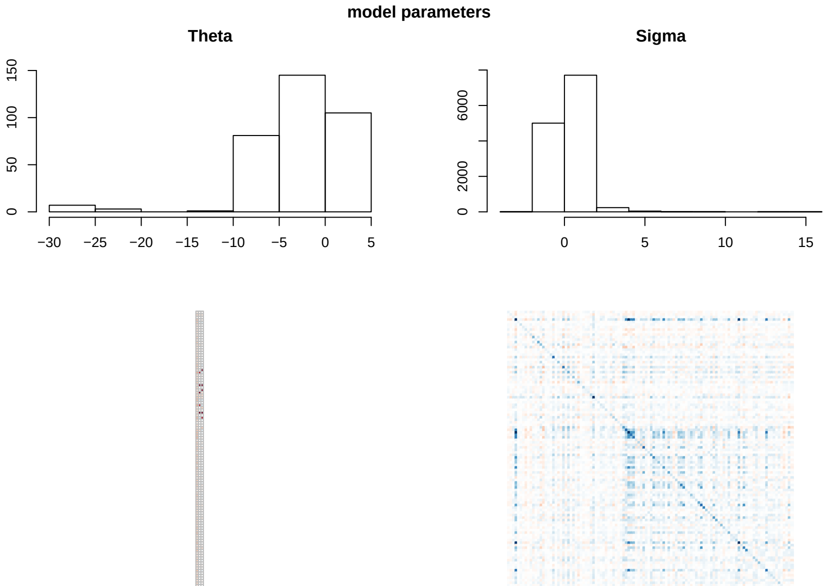
```
PLN_offset$plot(type = "model")
```



Model with offsets and covariates

A large part of the variance is explained by the covariates

```
PLN_tree$plot(type = "model")
```



PLN: natural extensions for multivariate analysis

Idea(s)

Put some additional constraint on the residual variance.

PCA: constraint the rank of $\mathbf{\Sigma}$.

LDA: a 'supervised' version of PCA

Network: put sparsity constraint on $\mathbf{\Omega} = \mathbf{\Sigma}^{-1}$.

Challenges

$\leadsto$ a variant of the variational algorithm is required for each model
$\leadsto$ interpretation is not exactly like in the "usual" Gaussian world

Outline

Variational inference of PLN models

Probabilistic PCA for counts

Illustration: the oak powdery mildew data set

Network inference for count data

Discriminant Analysis

Probabilistic PCA

Dimension reduction. Typical task in multivariate analysis

Model: Probabilistic PCA (pPCA):

$$\begin{aligned} \mathbf{Z}_i \text{ iid} &\sim \mathcal{N}_p(\mathbf{0}_p, \mathbf{\Sigma}), & \text{rank}(\mathbf{\Sigma}) = q \ll p \\ \mathbf{Y}_i \,|\, \mathbf{Z}_i &\sim \mathcal{P}(\exp\{\mathbf{O}_i + \mathbf{X}_i\boldsymbol{\beta} + \mathbf{Z}_i\}) \end{aligned}$$

Recall that: $\text{rank}(\mathbf{\Sigma}) = q \quad \Leftrightarrow \quad \exists \mathbf{B}(p \times q) : \Sigma = \mathbf{B}\mathbf{B}^\intercal$.

pPCA in the PLN model. Variational inference:

$$\text{maximize } J(\boldsymbol{\theta}, \tilde{p})$$

$\rightsquigarrow$ Still bi-concave in $\boldsymbol{\theta} = (\mathbf{B}, \boldsymbol{\beta})$ and $(\tilde{\mathbf{M}}, \tilde{\mathbf{S}})$

Model selection

Number of components q needs to be chosen.

Penalized 'likelihood'.

- $\log p_{\hat{\boldsymbol{\theta}}}(\mathbf{Y})$ intractable: replaced with $J(\hat{\boldsymbol{\theta}}, \tilde{p})$
- BIC $\rightsquigarrow$ $\widetilde{\mathsf{BIC}}_q = J(\hat{\boldsymbol{\theta}}, \tilde{p}) - \frac{1}{2} p(d+q)\log(n)$
- ICL $\rightsquigarrow$ $\widetilde{\mathsf{ICL}}_q = \widetilde{\mathsf{BIC}}_q - \mathcal{H}(\tilde{p})$

Chosen rank:

$$\hat{q} = \arg\max_q \widetilde{\mathsf{BIC}}_q \qquad \text{or} \qquad \hat{q} = \arg\max_q \widetilde{\mathsf{ICL}}_q$$

Visualization

PCA: Optimal subspaces nested when q increases.

PLN-pPCA: Non-nested subspaces.

$\rightsquigarrow$ For the selected dimension dimension $\hat{q}$:

- Compute the estimated latent positions $\mathbb{E}_{\tilde{p}}(\mathbf{Z}_i) = \tilde{\mathbf{M}}\hat{\mathbf{B}}^\top$
- Perform PCA on the $\tilde{\mathbf{M}}\hat{\mathbf{B}}^\top$
- Display result in any dimension $q \leq \hat{q}$

Goodness of fit

pPCA: Cumulated sum of the eigenvalues = % of variance preserved on the first q components.

PLN-pPCA: Deviance based criterion.

- Compute $\tilde{\mathbf{Z}}^{(q)} = \mathbf{O} + \mathbf{X}\hat{\boldsymbol{\beta}}^\top + \tilde{\mathbf{M}}^{(q)} \left(\hat{\mathbf{B}}^{(q)}\right)^\top$
- Take $\lambda_{ij}^{(q)} = \exp\left(\tilde{Z}_{ij}^{(q)}\right)$
- Define $\lambda_{ij}^{\min} = \exp(\tilde{Z}_{ij}^{0})$ and $\lambda_{ij}^{\max} = Y_{ij}$
- Compute the Poisson log-likelihood $\ell_q = \log \mathbb{P}(\mathbf{Y}; \lambda^{(q)})$

Pseudo-R^2:

$$R_q^2 = \frac{\ell_q - \ell_{\min}}{\ell_{\max} - \ell_{\min}}$$

Outline

Fit the PLNPCA models

Fit the model with offsets, and various covariates

```
Qmax = 30; Q <- 1:Qmax;

## Model with offset
PLN_offset <- PLNPCA(Y ~ 1 + offset(log(O)), ranks=Q)

## Models with offset and covariates (tree + orientation)
formula <- Y ~ 1 + covariates$tree + covariates$orientation + offset(log(O))
PLN_tree_orientation <- PLNPCA(formula, ranks=Q)

## model at initialization: log of count + LM
logLM_tree_orientation <-
  PLNPCA(
    formula, ranks=Q,
    control.main=list(inception="LM", maxeval=1),
    control.init=list(inception="LM", maxeval=1)
  )
```

Models selection criteria

```r
PLN_offset$plot()
PLN_tree_orientation$plot()
```

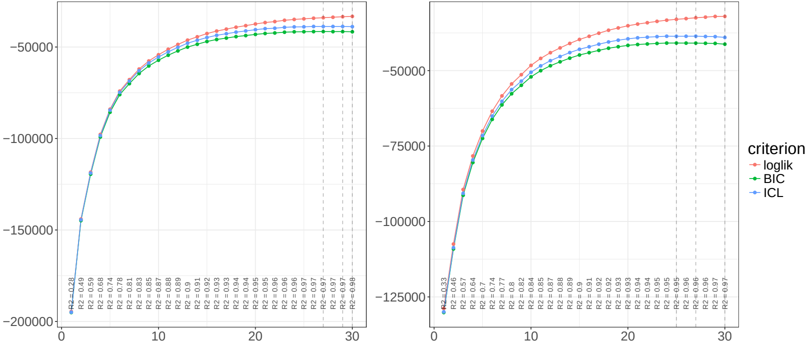


Figure: offset only: $\hat{q} = 24$ offset + covariates: $\hat{q} = 21$

PCA: vizualization I

PLN PCA separates well the kind of tree

```r
myModel_offset <- PLN_offset$getBestModel("ICL")
myModel_offset$plot_individual_map(cols.ind = covariates$tree, axes=c(1,2))

myModel_covariates <- PLN_tree_orientation$getBestModel("ICL")
myModel_covariates$plot_individual_map(cols.ind = covariates$tree, axes=c(1,2))
```

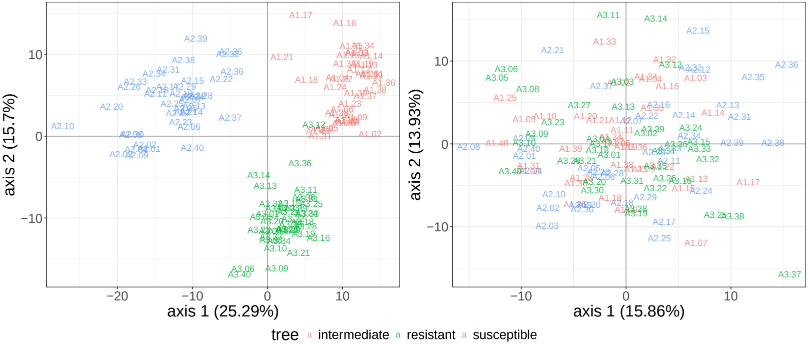


Figure: offset only offset + covariates

PCA: vizualization II

basic transformation + LM fails at exhibiting basic structure in the data

```r
myModel <- logLM_tree_orientation$getBestModel("ICL")
myModel$plot_individual_map(cols.ind = covariates$tree)
```

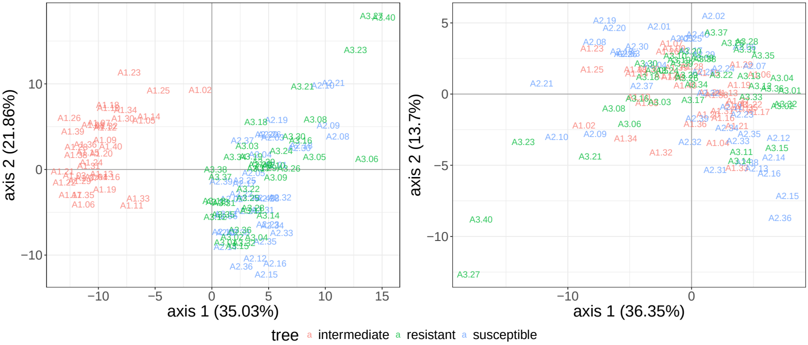


Figure: offset only offset + covariates

PCA: vizualization III

Introduction of covariates unravel hidden patterns

```r
myModel_offset <- models.offset$getBestModel("ICL")
myModel_offset$plot_individual_map(cols.ind = covariates$distoToground, axes=c(1,2))

myModel_covariates <- models.tree.orientation$getBestModel("ICL")
myModel_covariates$plot_individual_map(cols.ind = covariates$distoToground, axes=c(1,2))
```

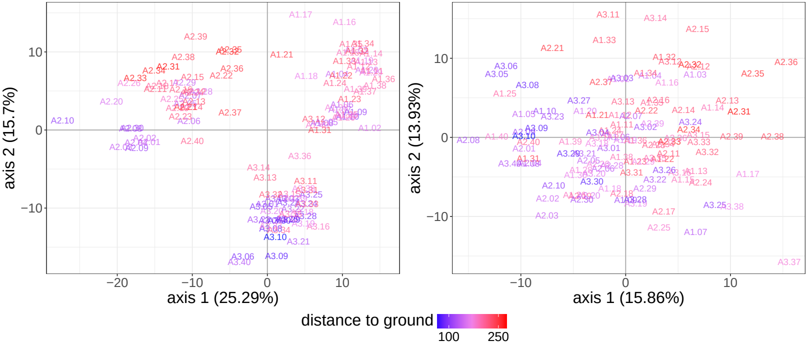


Figure: offset only offset + covariates

PCA: vizualization IV

Introduction of covariates unravel different groups of species

```r
myModel_offset <- models.offset$getBestModel("ICL")
myModel_offset$plot_correlation_circle(cols = out.family, axes=c(1,2))

myModel_covariates <- models.tree.orientation$getBestModel("ICL")
myModel_covariates$plot_correlation_circle(cols = out.family, axes=c(1,2))
```

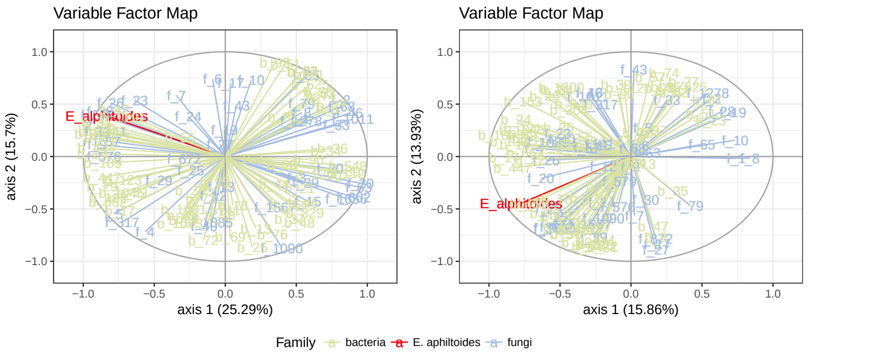


Figure: offset only   offset + covariates

Outline

Background on Gaussian Graphical Models

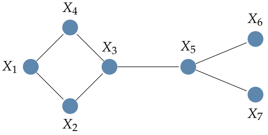
Suppose $\mathbf{Y}_i \sim \mathcal{N}(\mathbf{0}, \mathbf{\Omega}^{-1} = \mathbf{\Sigma})$

Conditional independence structure

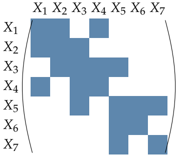
$$(i,j) \notin \mathcal{E} \Leftrightarrow Y_i \perp\!\!\!\perp Y_j \,|\, Y_{\backslash\{i,j\}} \Leftrightarrow \mathbf{\Omega}_{ij} = 0.$$

Graphical interpretation

$\mathcal{G} = (\mathcal{P}, \mathcal{E})$



$\mathbf{\Omega}$



Graphical-Lasso [BDE08,YL08,FHT07]

Network reconstruction is (roughly) a variable selection problem

$$\hat{\mathbf{\Omega}}_\lambda = \arg\max_{\mathbf{\Theta} \in \mathbb{S}_+} \ell(\mathbf{\Omega}; \mathbf{Y}) - \lambda \|\mathbf{\Theta}\|_1$$

PLN network model

Model:

$$\begin{aligned} \mathbf{Z}_i \text{ iid} &\sim \mathcal{N}_p(\mathbf{0}_p, \boldsymbol{\Omega}^{-1}), & \boldsymbol{\Omega} \text{ sparse} \\ \mathbf{Y}_i \mid \mathbf{Z}_i &\sim \mathcal{P}(\exp\{\mathbf{O}_i + \mathbf{X}_i^\top \boldsymbol{\beta} + \mathbf{Z}_i\}) \end{aligned}$$

Interest: Similar to Gaussian graphical model (GGM) inference

Sparsity-inducing regularization: graphical lasso

$$\log p_{\boldsymbol{\theta}}(\mathbf{Y}) - \lambda \left\|\boldsymbol{\Omega}\right\|_{1,\text{off}}$$

Cheat: Use the PLN model and infer the graphical model of Z

Graphical model of $Z \neq$ *Graphical model of* Y

PLN network graphical model: examples I

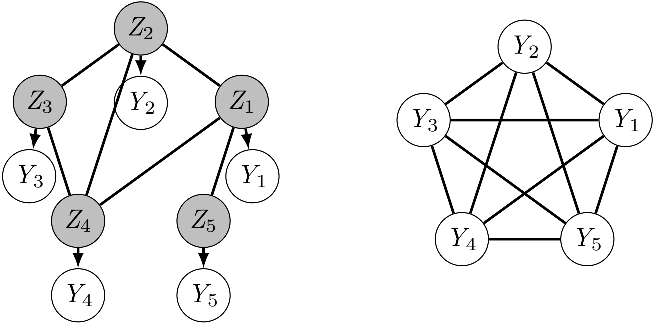


Figure: Left: joint distribution of $p(Z_i, Y_i)$. Right: marginal distribution $p(Y_i)$. The graph on the right is a clique because the graph of the Z_i's on the left is connected.

PLN network graphical model: examples II

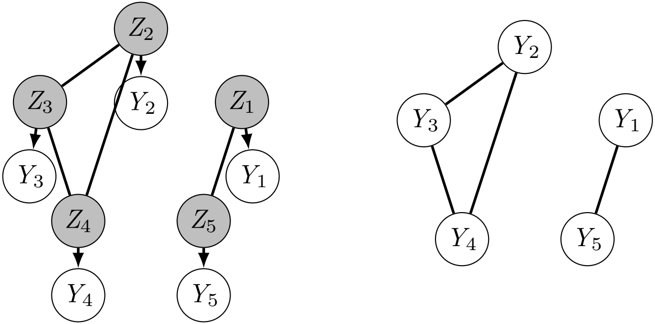


Figure: Left: joint distribution of $p(Z_i, Y_i)$. Right: marginal distribution $p(Y_i)$.

Variational inference

Same problem: $\log p_{\boldsymbol{\theta}}(\mathbf{Y})$ is intractable

Variational approximation: maximize

$$J(\boldsymbol{\theta}, \tilde{p}) - \lambda \left\|\boldsymbol{\Omega}\right\|_{1,\text{off}} = \tilde{\mathbb{E}}[\log p_{\boldsymbol{\theta}}(\mathbf{Y}, \mathbf{Z})] + \mathcal{H}[\tilde{p}(\mathbf{Z})] - \lambda \left\|\boldsymbol{\Omega}\right\|_{1,\text{off}}$$

taking $\tilde{p} \in \mathcal{Q}$.

$\rightsquigarrow$ Still bi-concave in $\boldsymbol{\theta} = (\boldsymbol{\Omega}, \boldsymbol{\beta})$ and $\tilde{p} = (\tilde{\mathbf{M}}, \tilde{\mathbf{S}})$. Ex:

$$\hat{\boldsymbol{\Omega}} = \arg\max_{\boldsymbol{\Omega}} \frac{n}{2} \Big(\log |\boldsymbol{\Omega}| - \mathrm{tr}(\hat{\boldsymbol{\Sigma}}\boldsymbol{\Omega})\Big) - \lambda \|\boldsymbol{\Omega}\|_{1,\text{off}} : \quad \text{gLasso problem}$$

Model selection

Alternative to model selection criteria

Sparsity level λ needs to be chosen.

Stability-based approach for Network by resampling: StARS

1. Infers B networks $\boldsymbol{\Omega}^{(b,\lambda)}$ on subsamples of size m for varying λ.
2. Frequency of inclusion of each edges $e = i \sim j$ is estimated by

$$p_e^\lambda = \#\{b : \Omega_{ij}^{(b,\lambda)} \neq 0\}/B$$

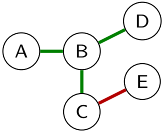
3. Variance of inclusion of edge e is $v_e^\lambda = p_e^\lambda(1 - p_e^\lambda)$.
4. Network stability is $\mathrm{stab}(\lambda) = 1 - 2\bar{v}^\lambda$ where $\bar{v}^\lambda$ is the average of the v_e^λ.

$\rightsquigarrow$ StARS[1] selects the smallest λ (densest network) for which $\mathrm{stab}(\lambda) \geq 1 - 2\beta$

[1] [LRW10] suggest using $2\beta = 0.05$ and $m = \lfloor 10\sqrt{n} \rfloor$ based on theoretical results.

Simulation study

network $\rightsquigarrow$ $\boldsymbol{\Omega}$



abundances $\log \mathbf{a}_i$ $\longrightarrow$ proportions $\boldsymbol{\pi}_i$

$$\begin{pmatrix} 8 \\ 8 \\ 8 \\ 9 \\ 2 \end{pmatrix} \longrightarrow \begin{pmatrix} 0.17 \\ 0.17 \\ 0.17 \\ 0.47 \\ 0.02 \end{pmatrix}$$

$$\begin{pmatrix} 6 \\ 6 \\ 6 \\ 8 \\ 1 \end{pmatrix} \longrightarrow \begin{pmatrix} 0.09 \\ 0.09 \\ 0.09 \\ 0.71 \\ 0.02 \end{pmatrix}$$

$\longrightarrow$ counts

	$i = 1$	$i = 2$
A	3	8
B	3	6
C	5	2
D	8	30
E	1	4
N_i	20	50

Figure: Compositional model used for data generation

i) Draw (unreachable) *abundances* $\mathbf{a}_i$: $\log(\mathbf{a}_i) \sim \mathcal{N}(\mathbf{XB}, \boldsymbol{\Omega}^{-1})$
   - $\mathbf{X}$ accounts for some covariates
   - $\boldsymbol{\Omega}$ is the latent network between species

ii) Transform abundances $\mathbf{a}_i$ to *proportions* $\boldsymbol{\pi}_i$ with logistic-transform

iii) Draw observed *counts* $Y_i \sim \mathcal{M}(N_i, \boldsymbol{\pi}_i)$ with random N_i – the sampling effort

Simulation results
Non-compositional methods fail

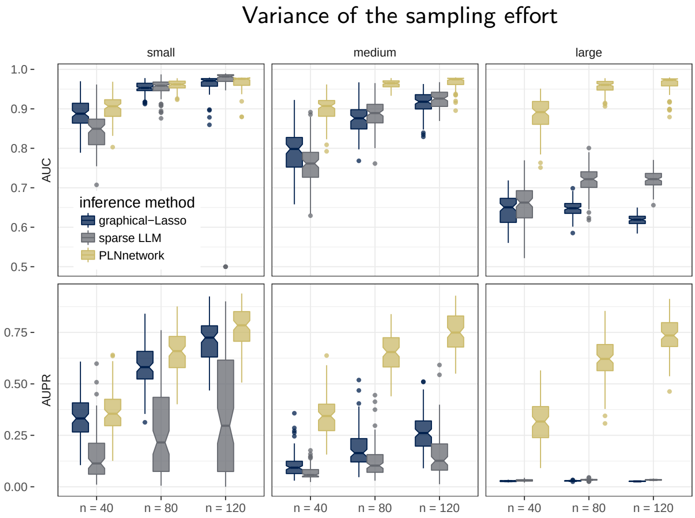


Figure: Effect of the variability of the sampling effort on the quality of the reconstruction of 50-node random networks (100 simulations.)

Simulation results

Accounting for covariates effect does matter

		area under the ROC			area under the PR		
covar.	**method**	$\mathbf{n = p/2}$	$\mathbf{n = p}$	$\mathbf{n = 2p}$	$\mathbf{n = p/2}$	$\mathbf{n = p}$	$\mathbf{n = 2p}$
		scale-free network					
small	`PLNnetwork`	.66 (0.05)	**.78** (0.05)	**.91** (0.03)	**.11** (0.04)	**.25** (0.07)	**.49** (0.08)
	`sparCC`	.66 (0.05)	.73 (0.05)	.79 (0.05)	.09 (0.03)	.16 (0.05)	.24 (0.07)
	`SPiEC-Easi`	**.67** (0.04)	.77 (0.05)	.85 (0.04)	.10 (0.03)	.17 (0.05)	.27 (0.07)
medium	`PLNnetwork`	**.62** (0.05)	**.73** (0.05)	**.85** (0.05)	**.09** (0.03)	**.18** (0.06)	**.34** (0.08)
	`sparCC`	.55 (0.05)	.57 (0.05)	.58 (0.05)	.05 (0.01)	.05 (0.01)	.06 (0.01)
	`SPiEC-Easi`	.61 (0.04)	.66 (0.04)	.71 (0.03)	.06 (0.01)	.06 (0.01)	.07 (0.01)
large	`PLNnetwork`	**.58** (0.05)	**.67** (0.05)	**.78** (0.05)	**.07** (0.03)	**.12** (0.04)	**.23** (0.07)
	`sparCC`	.52 (0.04)	.53 (0.04)	.53 (0.05)	.04 (0.01)	.04 (0.01)	.04 (0.01)
	`SPiEC-Easi`	.57 (0.04)	.60 (0.03)	.65 (0.03)	.05 (0.01)	.05 (0.01)	.05 (0.01)

Table: Areas under the ROC curve and Areas under the Precision-Recall curve of the compositional methods (`PLNnetwork`, `sparCC` and `SPiEC-Easi`) in various settings, averaged over 100 simulations, with standard errors.

Simulation results

Accounting for covariates effect does matter

covar.	method	area under the ROC $\mathbf{n = p/2}$	$\mathbf{n = p}$	$\mathbf{n = 2p}$	area under the PR $\mathbf{n = p/2}$	$\mathbf{n = p}$	$\mathbf{n = 2p}$
				random network			
small	`PLNnetwork`	.77 (0.07)	**.90** (0.04)	**.96** (0.01)	**.14** (0.07)	**.36** (0.11)	**.64** (0.09)
	`sparCC`	.76 (0.06)	.83 (0.06)	.89 (0.04)	.11 (0.05)	.23 (0.09)	.36 (0.11)
	`SPiEC-Easi`	**.78** (0.05)	.87 (0.04)	.92 (0.03)	.11 (0.05)	.23 (0.09)	.36 (0.11)
medium	`PLNnetwork`	**.72** (0.06)	**.85** (0.05)	**.94** (0.02)	**.09** (0.04)	**.24** (0.09)	**.49** (0.10)
	`sparCC`	.59 (0.06)	.61 (0.07)	.62 (0.06)	.03 (0.01)	.04 (0.02)	.04 (0.02)
	`SPiEC-Easi`	.67 (0.05)	.74 (0.05)	.77 (0.03)	.04 (0.01)	.05 (0.02)	.05 (0.01)
large	`PLNnetwork`	**.64** (0.07)	**.78** (0.06)	**.88** (0.04)	**.06** (0.03)	**.14** (0.07)	**.29** (0.09)
	`sparCC`	.54 (0.05)	.53 (0.06)	.54 (0.06)	.02 (0.01)	.02 (0.01)	.03 (0.01)
	`SPiEC-Easi`	.61 (0.05)	.65 (0.04)	.68 (0.03)	.03 (0.00)	.03 (0.00)	.03 (0.01)

Table: Areas under the ROC curve and Areas under the Precision-Recall curve of the compositional methods (`PLNnetwork`, `sparCC` and `SPiEC-Easi`) in various settings, averaged over 100 simulations, with standard errors.

Simulation results

Accounting for covariates effect does matter

		area under the ROC			area under the PR		
covar.	**method**	$\mathbf{n = p/2}$	$\mathbf{n = p}$	$\mathbf{n = 2p}$	$\mathbf{n = p/2}$	$\mathbf{n = p}$	$\mathbf{n = 2p}$
		community network					
small	`PLNnetwork`	.60 (0.04)	.69 (0.04)	**.78** (0.05)	**.17** (0.03)	**.26** (0.04)	**.38** (0.05)
	`sparCC`	**.62** (0.04)	.66 (0.04)	.70 (0.04)	.16 (0.02)	.21 (0.04)	.26 (0.04)
	`SPiEC-Easi`	**.62** (0.04)	**.70** (0.04)	.77 (0.04)	**.17** (0.02)	.24 (0.04)	.31 (0.04)
medium	`PLNnetwork`	.57 (0.03)	**.65** (0.04)	**.73** (0.05)	**.15** (0.02)	**.22** (0.03)	**.31** (0.05)
	`sparCC`	.55 (0.03)	.56 (0.04)	.56 (0.03)	.11 (0.02)	.12 (0.02)	.12 (0.02)
	`SPiEC-Easi`	**.58** (0.03)	.63 (0.03)	.67 (0.03)	.13 (0.02)	.14 (0.02)	.15 (0.02)
large	`PLNnetwork`	**.55** (0.03)	**.60** (0.04)	**.67** (0.04)	**.13** (0.02)	**.17** (0.03)	**.24** (0.04)
	`sparCC`	.52 (0.03)	.52 (0.03)	.52 (0.03)	.10 (0.02)	.10 (0.02)	.10 (0.02)
	`SPiEC-Easi`	**.55** (0.03)	.58 (0.03)	.62 (0.03)	.11 (0.01)	.11 (0.02)	.12 (0.01)

Table: Areas under the ROC curve and Areas under the Precision-Recall curve of the compositional methods (`PLNnetwork`, `sparCC` and `SPiEC-Easi`) in various settings, averaged over 100 simulations, with standard errors.

Outline

PLNnetwork models: consensus or tree-specific networks?

We consider 3 setups

1. resistant samples, with covariates
2. susceptible samples, with covariates
3. both samples samples, with covariates + tree effect and interactions

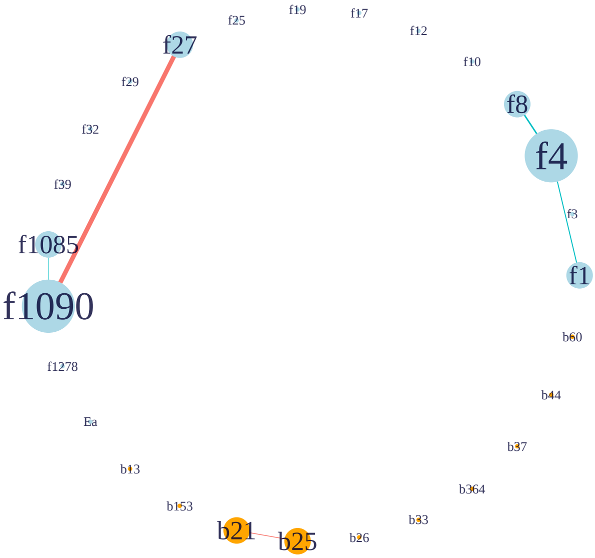
Network inference

`PLNnetwork` + 'StARS' for model selection

- 100 resamplings
- high level of stability (edges frequencies > 0.995)

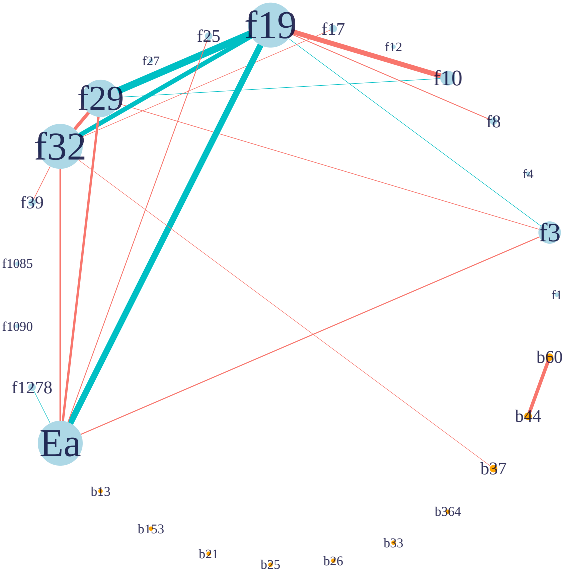
PLNnetwork models: resistant

Trees resistant to mildew (*E. Alphitoïdes*)



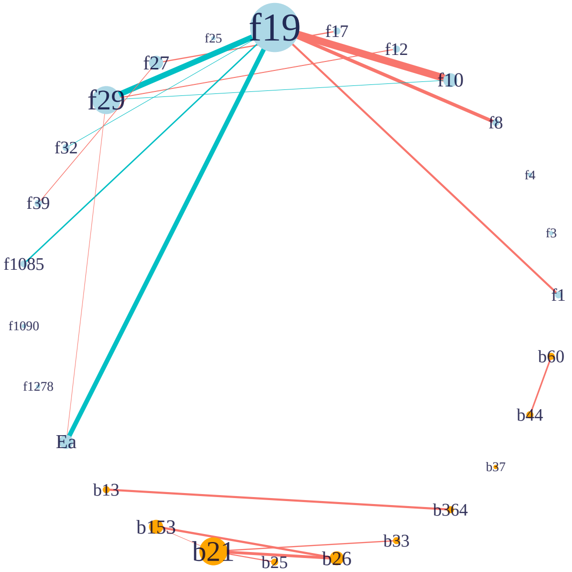
PLNnetwork models: susceptible

Trees susceptibles to mildew (*E. Alphitoïdes*)



PLNnetwork models: consensus

Both Trees



Outline

Background on (Gaussian) LDA

Model

Let $k(i)$ be the ith sample in group k. Suppose $\mathbf{Z}_{k(i)}$ independent with

$$\mathbf{Z}_{k(i)} \sim \mathcal{N}(\boldsymbol{\mu}_k, \boldsymbol{\Sigma}).$$

Let $F^j := F(Z^j)$ be the Fisher statistics for species j:

$$F(Z^j) = \frac{1}{K-1} \sum_k n_k (\mathbf{Z}^j_{k\bullet} - \mathbf{Z}^j_{\bullet\bullet})^2 \Big/ \frac{1}{n-q} \sum_{k,i} (\mathbf{Z}^j_{ki} - \mathbf{Z}^j_{k\bullet})^2$$

Aim of LDA. Find the linear combination $\mathbf{Z}u$ ($u \in \mathbb{R}^p$) maximizing $F(\mathbf{Z}u)$.
Solution. u is the first eigenvector of $\mathbf{W}^{-1}\mathbf{B}$ where

- $\mathbf{W}$ is 'within' variance matrix, i.e. the unbiased estimated of Σ:
- $\mathbf{B}$ is 'between' variance matrix

$\rightsquigarrow$ Further discriminative components are defined based on the second, third, ... eigenvectors of $\mathbf{W}^{-1}\mathbf{B}$.

PLN LDA

Model:

$$\mathbf{Z}_{k(i)} \text{ iid}, \quad \mathbf{Z}_{k(i)} \sim \mathcal{N}(\mathbf{0}_p, \boldsymbol{\Sigma}) \tag{1}$$
$$\mathbf{Y}_{k(i)} \text{ indep.}|\mathbf{Z}, \quad \mathbf{Y}_{k(i)} \sim \mathcal{P}(\exp(\mathbf{O}_{k(i)} + \boldsymbol{\mu}_k + \mathbf{Z}_{k(i)}))$$

Proposed analysis: fit PLN Model (1) then

1. Compute the between variance matrix as

$$\mathbf{B} = \frac{1}{K-1} \sum_k n_k (\hat{\boldsymbol{\mu}}_k - \hat{\boldsymbol{\mu}}_\bullet)(\hat{\boldsymbol{\mu}}_k - \hat{\boldsymbol{\mu}}_\bullet)^\intercal$$

2. Diagonalize $\hat{\boldsymbol{\Sigma}}^{-1}\mathbf{B} = \mathbf{U}^\intercal \Lambda \mathbf{U}$ and get the $K-1$ first eigenvectors.

Graphical representation.

1. Compute the estimated latent position[2] $\tilde{\mathbf{Z}} = G\hat{\boldsymbol{\mu}} + \tilde{\mathbf{M}}$, center
2. Compute the estimated coordinates along the discriminant axes

$$\tilde{\mathbf{Z}}^{LDA} = \tilde{\mathbf{Z}}\mathbf{U}\Lambda^{1/2}$$

[2] G is the design matrix of the grouping

Outline

Variational inference of PLN models

Probabilistic PCA for counts

Network inference for count data

Discriminant Analysis

- Illustration: the oak powdery mildew data set

Fit the PLNLDA models

find the linear combinaison that separates the grouping

Fit the model with offsets, and various covariates

```
myLDA_tree   <- PLNLDA(Y, grouping = treeStatus, O = log(O))
```

```
##
##  Initialization...
##  Adjusting the standard PLN model.
##  Performing Discriminant Analysis...
##  DONE!
```

```
myLDA_branch <- PLNLDA(Y, grouping = covariates$branch, O = log(O))
```

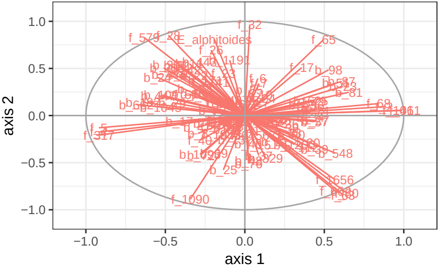
```
##
##  Initialization...
##  Adjusting the standard PLN model.
##  Performing Discriminant Analysis...
##  DONE!
```

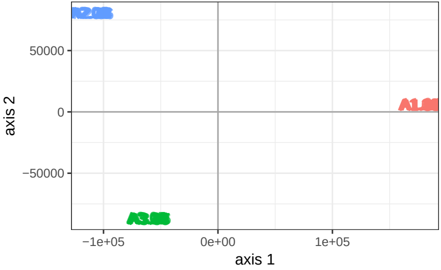
```
myLDA_tree$plot_LDA()
myLDA_branch$plot_LDA()
```

LDA on tree status

Axes contribution

axis 1 : 78.37%
axis 2 : 21.63%



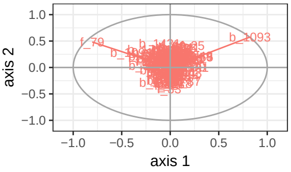


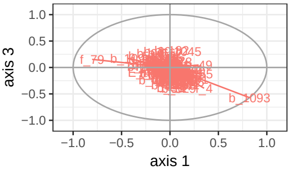
classification
a intermediate
a resistant
a susceptible

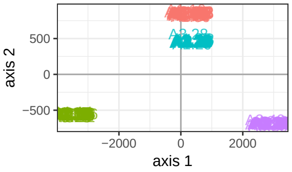
LDA on branch effect

Axes contribution

axis 1 : 81.74%
axis 2 : 16.26%
axis 3 : 2%

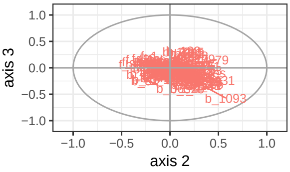


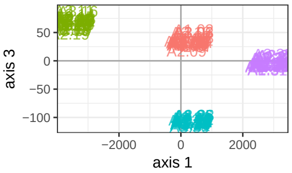


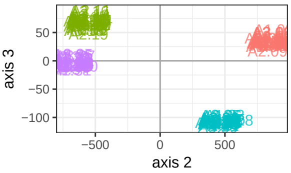


classification

a 1
a 2
a 3
a 4







Model Selection

loglikelihood = NA
BIC = NA
ICL = NA

Discussion

Summary

- PLN = generic model for multivariate count data analysis
- Allows for covariates
- Flexible modeling of the covariance structure
- Efficient VEM algorithm
- `PLNmodels` package: `https://github.com/jchiquet/PLNmodels`

Extensions

- Model selection criterion for network inference
- Other covariance structures (spatial, time series, ...)
- Mixture model in the latent space
- Confidence interval and tests for the regular PLN

Statistical properties of variational estimates

General properties of VEM inference.

- VEM stationary point $\neq$ log-likelihood stationary point
- Some consistency results, typically when $p(Z \mid Y)$ asymptotically belongs to $\mathcal{Q}$ (SBM, Bayesian logistic regression).

Using VEM output as a starting point for regular inference:

- Get maximum-(composite-)likelihood estimates starting from $\tilde{\boldsymbol{\theta}}_{VEM}$ (proposed internship)

$\rightsquigarrow$ Hopefully: few iterations are needed

Thanks to you for your patience and to my co-workers

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