Multiblock supervised analyses

Should we really normalize blocks?

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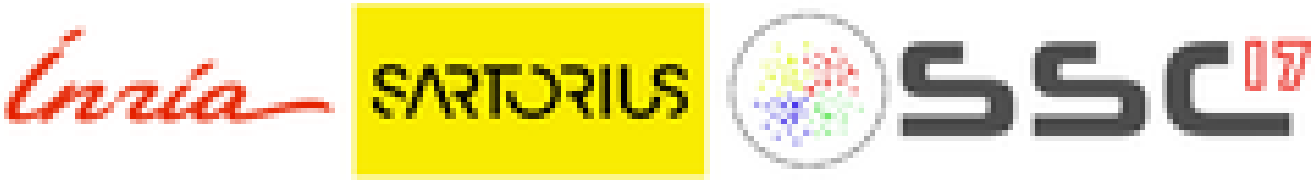
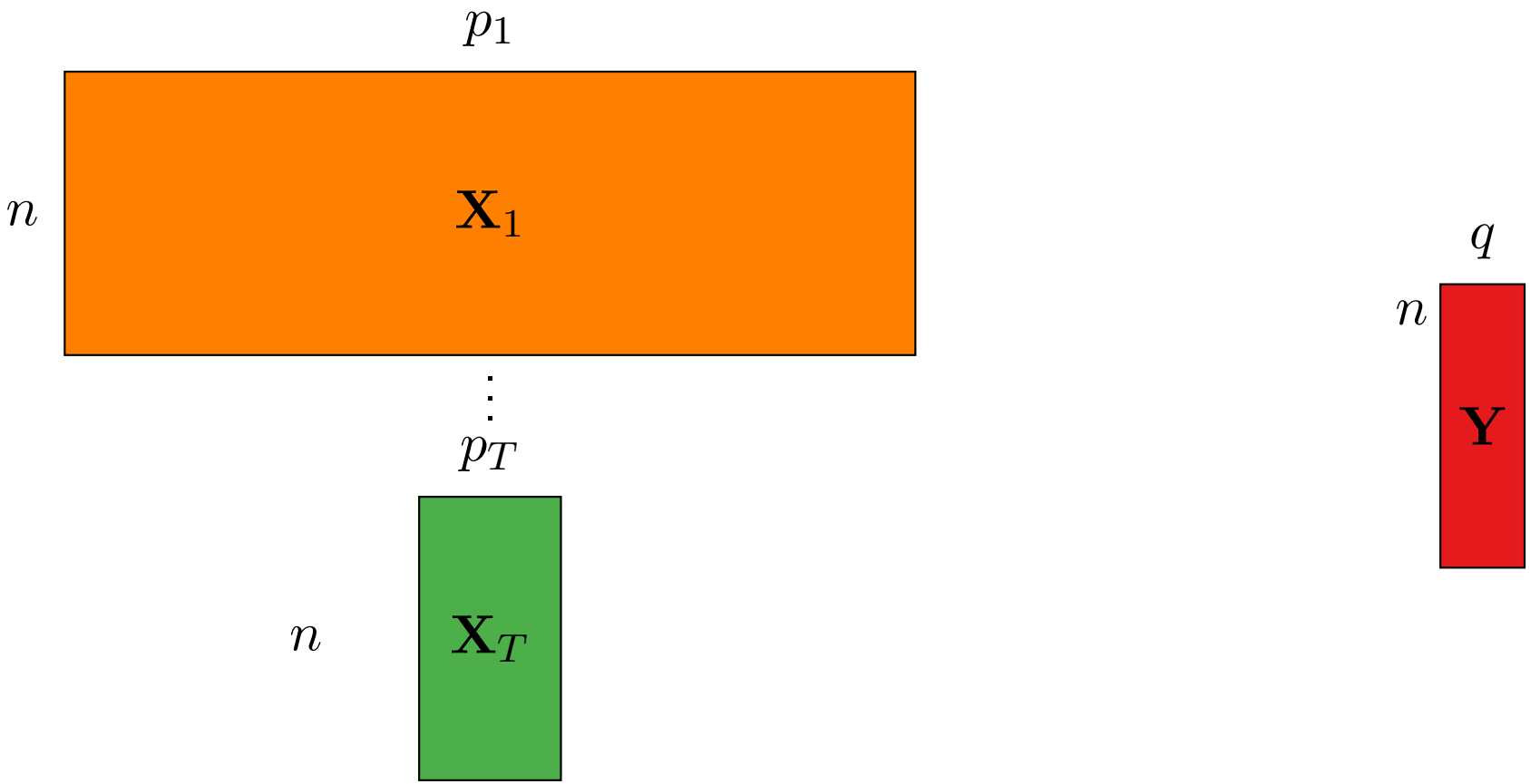


Supervized Multiblock Analyses in linear context



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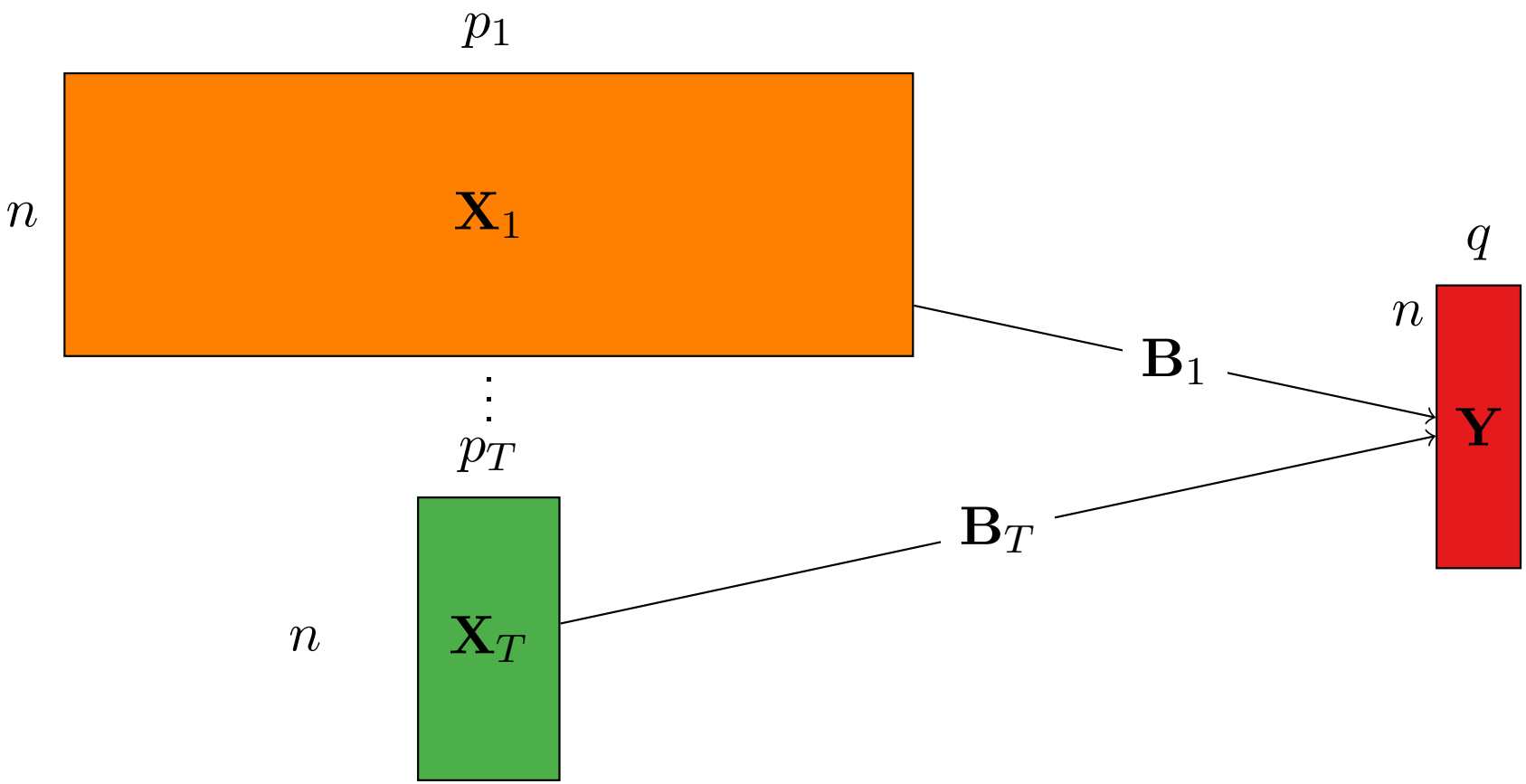

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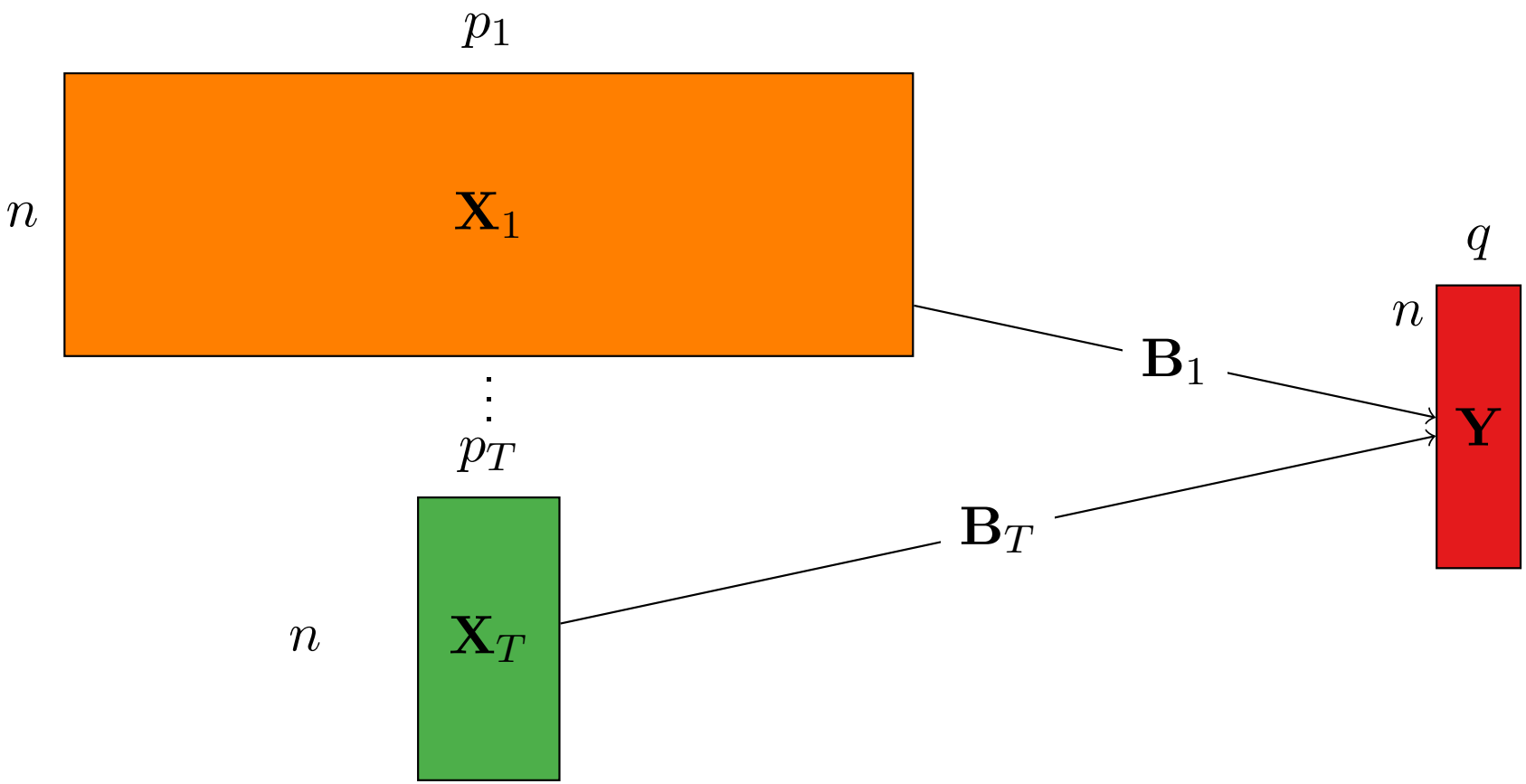

$$\widehat{\mathbf{Y}} = \widehat{\mathbf{B}}_1\mathbf{X}_1 + \cdots + \widehat{\mathbf{B}}_T\mathbf{X}_T$$

Adapt from monoblock supervized analyses

From now on, application to **PLS** Wold (1966) based methodologies.

Adapt classical mono-block analysis such as $\widehat{\mathbf{Y}} = \widehat{\mathbf{B}}\mathbf{X}$.

Different solutions:

- (**V0**) Westerhuis *et al.* (1998): $\mathbf{X} = [\mathbf{X}_1, \ldots, \mathbf{X}_T]$.
- (**V1**) Wold *et al.* (1996): $\mathbf{X} = \left[\mathbf{X}_1/\sqrt{p_1}, \ldots, \mathbf{X}_T/\sqrt{p_T}\right]$.
- (**V2**): $\mathbf{X} = [\mathbf{X}_1/\|\mathbf{X}_1\|, \ldots, \mathbf{X}_T/\|\mathbf{X}_T\|]$.

Remark on the Block Normalization solutions (V1) and (V2)

If variables are standardized, $\forall t = 1 \ldots T,\ \|\mathbf{X}_t\|^2 = np_t$

$$\Longrightarrow \quad \textbf{(V1)}=\textbf{(V2)}$$

Idea and drawbacks of block normalization

The idea

Give the same level of confidence to each block, whatever the size of this block.

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Give the same level of confidence to each block, whatever the size of this block.

The chosen solution

Accept the same proportion of block variance from each block: equivalent SNRs (signal to noise ratios).

Idea and drawbacks of block normalization

A problem for correlated blocks

If the interesting variance proportions from blocks are different:

- $\mathbf{X}_1$ with $p_1 = 20\ 000$ and only 5% of the variance is associated with $\mathbf{Y}$ (Transciptomics, Spectroscopics,...).

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- $\mathbf{X}_2$ with $p_2 = 200$ and 20% of the variance is associated with $\mathbf{Y}$ (Metabolomics for example).

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$$\Longrightarrow \text{ Information from } \mathbf{X}_1 \text{ is hidden by } \mathbf{X}_2, \text{ while } 5\%20\ 000 = 1000 >> 20\%200 = 40.$$

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Additionnal problem in high dimension

For finite n: large p implies over-fitting of models

$$\Longrightarrow \text{ Do regularization.}$$

An unified solution ?

Last observation

Adding useless variables to a block would modify the overall prediction model... a nonsense.

To a new methodology ?

What should it combine ?

- Do not normalize (discard arbitrarily weighting).
- Perform variable selection based on variable marginal correlation with $\mathbf{Y}$: interpretability and regularization.

$$\Longrightarrow \text{ "ddsPLS" .}$$

"ddsPLS" , "PLS" with different covariance matrix estimators

A sparse PLS where sparsity constraints done at covariance estimation step (denoted as $\mathbf{M}^{(r)}$) and not after:

$$\mathbf{S}_\lambda(\mathbf{M}) \quad = \quad \arg\min_{\mathbf{\Sigma}\in\mathbb{R}^{q\times p}} \ \|\mathbf{M}-\mathbf{\Sigma}\|^2 + 2\lambda\,|\mathbf{\Sigma}|, \qquad (1)$$

where λ values are tested along a clever grid and $\mathbf{S}_\lambda$ is the soft-thresholding operator. Interpretation:

- $\lambda = 0$ corresponds to "PLS" model,
- $\lambda = 1$ corresponds to empty model: empirical mean estimation.

"ddsPLS" , the algorithm

The algorithms of "PLS" and "ddsPLS" are close to each other:

"PLS"

$$\begin{cases} \text{(a)} \begin{cases} \mathbf{w}_r = \overrightarrow{\text{RSV}}\left(\mathbf{M}^{(r)}\right), \\ \mathbf{v}_r = \overrightarrow{\text{RSV}}\left(\mathbf{M}^{(r)'}\right), \end{cases} \\ \text{(b)} \quad \mathbf{t}_r = \mathbf{X}^{(r)}\mathbf{w}_r, \\ \text{(c)} \quad \mathbf{p}_r = \mathbf{X}^{(r)'}\mathbf{t}_r/\mathbf{t}_r'\mathbf{t}_r, \\ \text{(d)} \quad \mathbf{c}_r = \mathbf{Y}^{(r)'}\mathbf{t}_r/\mathbf{t}_r'\mathbf{t}_r, \\ \text{(e)} \begin{cases} \mathbf{X}^{(r+1)} = \mathbf{X}^{(r)} - \mathbf{t}_r\mathbf{p}_r', \\ \mathbf{Y}^{(r+1)} = \mathbf{Y}^{(r)} - \mathbf{t}_r\mathbf{c}_r', \end{cases} \end{cases}$$

"ddsPLS"

$$\begin{cases} \text{(a}^\star\text{)} \begin{cases} \mathbf{w}_r = \overrightarrow{\text{RSV}}\left(\mathbf{S}_{\lambda^{(\mathbf{r})}}\left(\mathbf{M}^{(r)}\right)\right), \\ \mathbf{v}_r = \overrightarrow{\text{RSV}}\left(\mathbf{S}_{\lambda^{(\mathbf{r})}}\left(\mathbf{M}^{(r)'}\right)\right), \end{cases} \\ \text{(b)} \quad \mathbf{t}_r = \mathbf{X}^{(r)}\mathbf{w}_r, \\ \text{(c)} \quad \mathbf{p}_r = \mathbf{X}^{(r)'}\mathbf{t}_r/\mathbf{t}_r'\mathbf{t}_r, \\ \text{(d}^\star\text{)} \begin{cases} \mathbf{\Pi}_r = \text{diag}(\delta_{\neq 0}(\mathbf{v}_r)_j) \\ \mathbf{c}_r = \left(\mathbf{Y}^{(r)}\mathbf{\Pi}_r\right)'\mathbf{t}_r/(\mathbf{t}_r'\mathbf{t}_r). \end{cases} \\ \text{(e)} \begin{cases} \mathbf{X}^{(r+1)} = \mathbf{X}^{(r)} - \mathbf{t}_r\mathbf{p}_r', \\ \mathbf{Y}^{(r+1)} = \mathbf{Y}^{(r)} - \mathbf{t}_r\mathbf{c}_r', \end{cases} \end{cases}$$

"ddsPLS" , fix the number of components and the regularization coefficients

Two types of parameters:

- Number R of components,
- regularization parameter per component $(\lambda_r)_{r=1...R}$.

Based on B bootstrap operations for each component:

- Minimize $\bar{R}^2_B - \bar{Q}^2_B$ (minimize over-fitting).
- The $\bar{Q}^2_{B,r}$ must be positive (learn from data).
- The $\bar{Q}^2_B$ is increasing with r (learn something new with the current component).

$\bar{R}^2_B$, $\bar{Q}^2_B$ and $\bar{Q}^2_{B,r}$ are defined in annex but correspond to R^2 and Q^2 at complete model level or component levels in the context of bootstrap considering empirical mean aggregation.

Simulation analysis

Challenge "**ddsPLS**" and "**PLS**" in the high dimensional multiblock context in two cases:

- $\mathbf{X}_t$ blocks are associated with the same sub-space of $\mathbf{Y}$.
- $\mathbf{X}_t$ blocks are associated with different sub-spaces of $\mathbf{Y}$.

Benchmark of 5 approaches

Two blocks are available ($\mathbf{X_1}$ and $\mathbf{X_2}$) with $p_1 >> p_2$. Block $\mathbf{Y}$ such as $q = 1$. Five approaches are compared:

- **(I)**: Predict $\mathbf{Y}$ from $\mathbf{X}_1$ using "**PLS**" ,
- **(II)**: Predict $\mathbf{Y}$ from $\mathbf{X}_2$ using "**PLS**" ,
- **(III)**: Predict $\mathbf{Y}$ from $[\mathbf{X}_1, \mathbf{X}_2]$ using "**PLS**" ,
- **(IV)**: Predict $\mathbf{Y}$ from $[\mathbf{X}_1/\sqrt{p_1}, \mathbf{X}_2/\sqrt{p_2}]$ using "**PLS**" ,
- **(V)**: Predict $\mathbf{Y}$ from $[\mathbf{X}_1, \mathbf{X}_2]$ using "**ddsPLS**" ,

Design 1, Statistical Model

$$
\begin{aligned}
y &= \boldsymbol{\phi_1} + \epsilon \\
\forall j = 1 \dots p_1, \quad x_j^{(1)} &= \begin{cases} \boldsymbol{\phi_1} + \mu_j & \text{if } j = 1 \dots 1\,000, \\ \phi_2 + \mu_j & \text{if } j = 1\,001 \dots 2\,000, \\ \phi_3 + \mu_j & \text{if } j = 2\,002 \dots 3\,000, \\ \mu_j & \text{if } j = 3\,001 \dots 20\,000, \end{cases} \\
\forall j = 1 \dots p_2, \quad x_j^{(2)} &= \begin{cases} \boldsymbol{\phi_1} + \eta_j & \text{if } j = 1 \dots 40, \\ \phi_2 + \eta_j & \text{if } j = 41 \dots 80, \\ \phi_4 + \eta_j & \text{if } j = 81 \dots 120, \\ \eta_j & j = 121 \dots 200, \end{cases}
\end{aligned} \tag{2}
$$

- $\text{var}(y) = \text{var}(x_j^{(1)}) = \text{var}(x_j^{(2)}) = 1$,
- $\text{var}(\phi_1) = \text{var}(\phi_2) = \text{var}(\phi_3) = \text{var}(\phi_4) = \alpha^2 = 0.9$,
- $\text{cov}(\phi_i, \phi_j) = \delta_{i,j}\alpha^2$, $\text{cov}(\phi_i, \epsilon) = \text{cov}(\phi_i, \mu_j) = \text{cov}(\phi_i, \eta_j) = 0$,

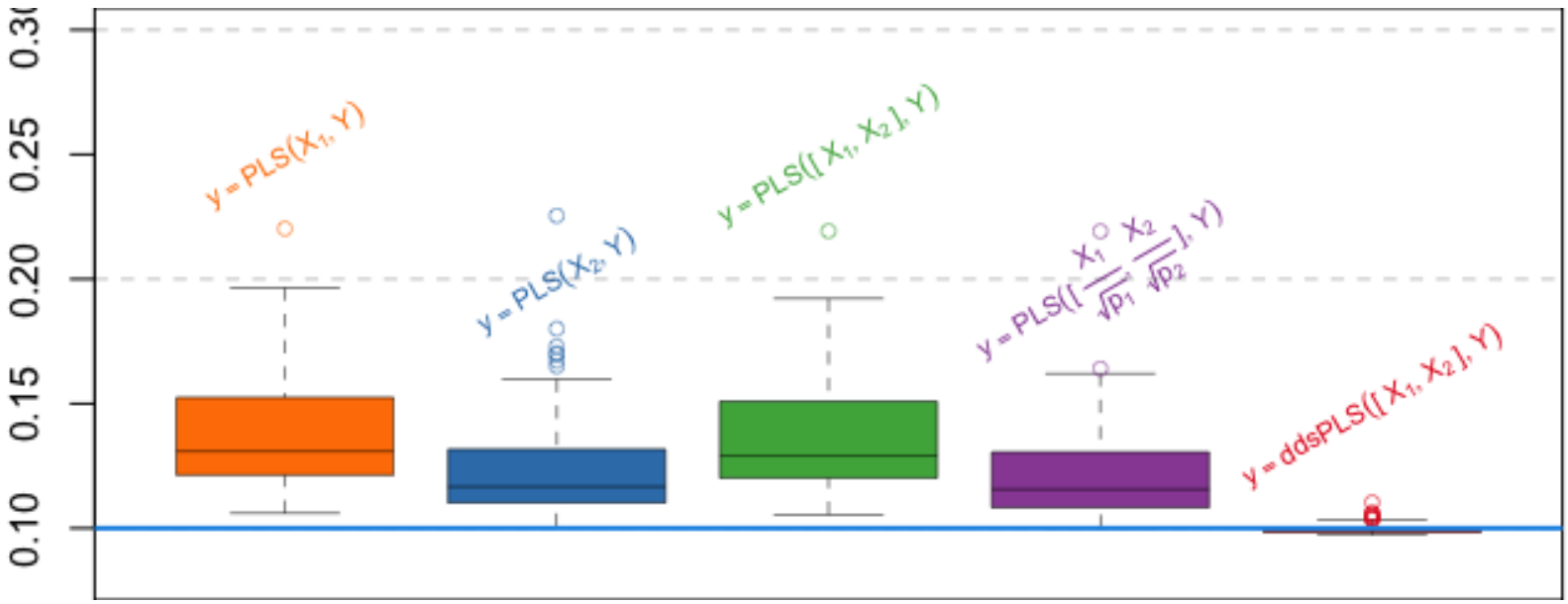
Simulation parameters

- $n = 100$ sampled $N = 100$ times.
- An independent test data-set $n_{test} = 1000$.

Remark

"**ddsPLS**" builds always only 1 component (the objective) and "**PLS**" approaches are constrained to build one component.

MSE on the $n_{test} = 1000$ independent test data set

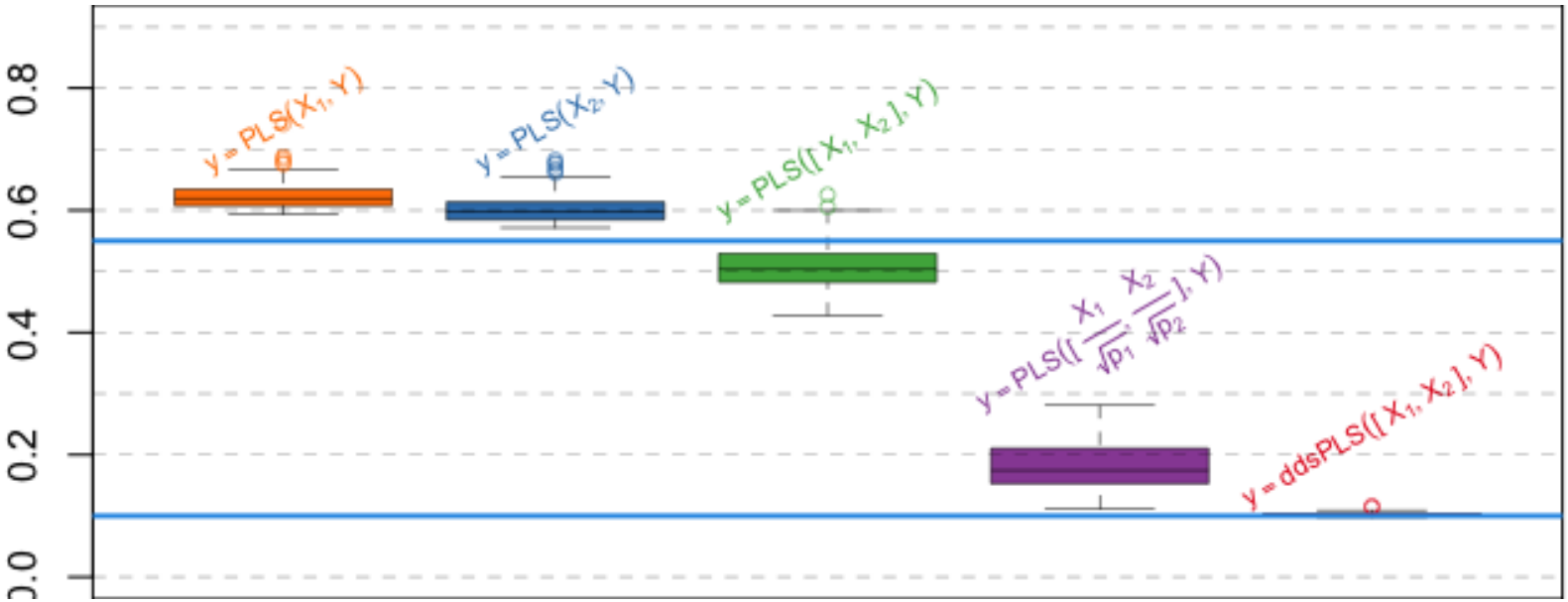


- **(I)** and **(III)** are equivalent: high dimension dominates.
- **(II)** and **(IV)** are equivalent: high SNR dominates.
- "**ddsPLS**" **(V)** deals with high dimension problem with no arbitrary normalization.

Design 2, Statistical Model

$$
\begin{aligned}
y &= (\boldsymbol{\phi_1} + \boldsymbol{\phi_2})/\sqrt{2} + \epsilon \\
\forall j = 1 \dots p_1, \quad x_j^{(1)} &= \begin{cases} \boldsymbol{\phi_1} + \mu_j & \text{if } j = 1 \dots 1\,000, \\ \phi_3 + \mu_j & \text{if } j = 1\,001 \dots 2\,000, \\ \phi_4 + \mu_j & \text{if } j = 2\,002 \dots 3\,000, \\ \mu_j & \text{if } j = 3\,001 \dots 20\,000, \end{cases} \\
\forall j = 1 \dots p_2, \quad x_j^{(2)} &= \begin{cases} \boldsymbol{\phi_2} + \eta_j & \text{if } j = 1 \dots 40, \\ \phi_3 + \eta_j & \text{if } j = 41 \dots 80, \\ \phi_6 + \eta_j & \text{if } j = 81 \dots 120, \\ \eta_j & j = 121 \dots 200, \end{cases}
\end{aligned}
\tag{3}
$$

MSE on the $n_{test} = 1000$ independent test data set



- **(I)** a bit worse than **(II)** due to SNR.
- **(IV)** better than **(III)** hiding $\mathbf{X}_1$ noise due to weighting but cannot properly reconstruct ϕ_1.
- "**ddsPLS**" **(V)** performs better due to regularization and always builds 2 components.

Conclusion over simulations

Performances of traditional normalized multiblock approaches depend on the correlation structure of the data.

It can be wether:

- a relative bad idea (design 1).
- a relative good idea (forgetting high dimensional problem in design 2) but partially hide an important dimension.

In all cases "**ddsPLS**" performs very well in **Prediction**, **Selection** (not shown) and in **Parameter estimation**.

Batch Evolution Modelling

- 5 Chinese Hamster Ovary (CHO) cell cultures performed on univessels.
- Transcriptomics (**Tr**) and Metabolic (**Me**) profiles acquired at 12 time points.

$n = 52$

$p_{\text{Tr}} = 20\ 373$

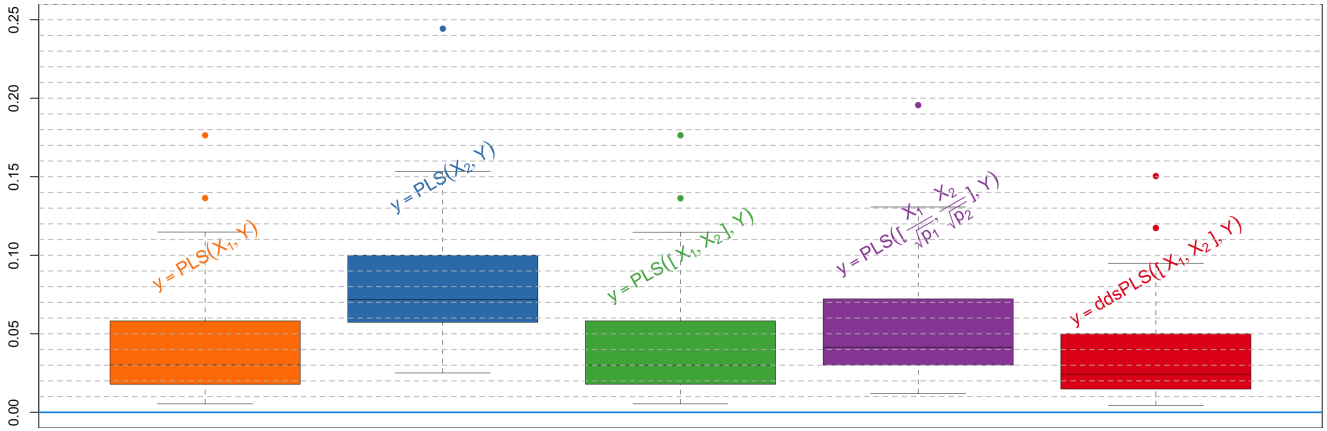
Tr

$p_{\text{Me}} = 58$

Me

Prediction performances (MSE): 50 repetitions (9/10 train, 1/10 test)

Parameter selection (cross-validation): $R_{(I)} = 4$, $R_{(II)} = 2$, $R_{(III)} = 4$, $R_{(IV)} = 4$. And $R_{(V)} = 2$.



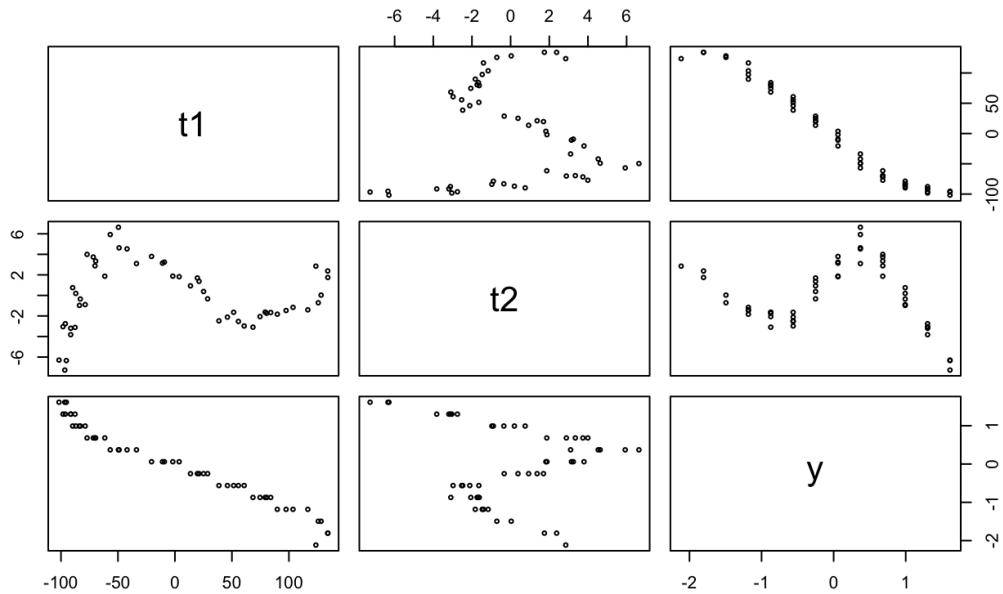
$\mathbf{X}_1$ alone is better than $[\mathbf{X}_1, \mathbf{X}_2]$ or $[\mathbf{X}_1/\sqrt{p_1}, \mathbf{X}_2/\sqrt{p_2}]$: $\mathbf{X}_1$ builds many interesting components through a good SNR.

"**ddsPLS**" **(V)** performs slightly better: regularization effect.

"ddsPLS" performances

Variable selection: **Tr** 48% and **Me** 62%. Two components built:

- Dim 1: 97% variance explained.
- Dim 2: 2% variance explained.



Scores versus y... Non linearities ?

Conclusion

When to use block normalization ?

- Low and equivalent dimensions from one block to another.
- Independent blocks.
- Equivalent "signal to noise ratio" from blocks to blocks.
- . . . so, why using it ?

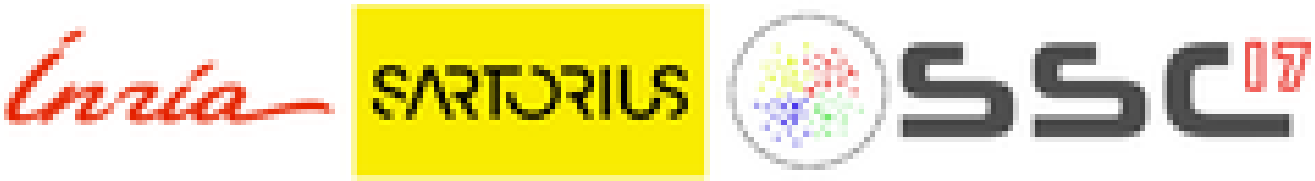
When to **NOT** use block normalization ?

- High dimension.
- Different dimensions in different orders of magnitude.
- Dependent blocks.

"**ddsPLS**" (github.com/hlorenzo/ddsPLS2) selects variables based on their marginal correlations: no need to normalize blocks.

Thanks

INRIA & Sartorius & SSC17 Conference Committee



Quality criteria

$$\bar{R}^2_B = \frac{1}{B}\sum_{b=1}^{B} R^2_b \quad \text{and} \quad \bar{Q}^2_B = \frac{1}{B}\sum_{b=1}^{B} Q^2_b \tag{4}$$

with, for the current bootstrap sample b,

$$\begin{aligned} R^2_b &= 1 - \frac{\sum_{j=1}^{q}\sum_{i\in \mathsf{IN}(b)}\left(y_{i,j} - \hat{y}^b_{i,j}\right)^2}{\sum_{j=1}^{q}\sum_{i\in \mathsf{IN}(b)}\left(y_{i,j} - \bar{y}^b_{j}\right)^2}, \\ Q^2_b &= 1 - \frac{\sum_{j=1}^{q}\sum_{i\in \mathsf{OOB}(b)}\left(y_{i,j} - \hat{y}^b_{i,j}\right)^2}{\sum_{j=1}^{q}\sum_{i\in \mathsf{OOB}(b)}\left(y_{i,j} - \bar{y}^b_{j}\right)^2}, \end{aligned} \tag{5}$$

Quality criteria (2)

In the same way, bootstrapped versions of R^2_r and Q^2_r are given by

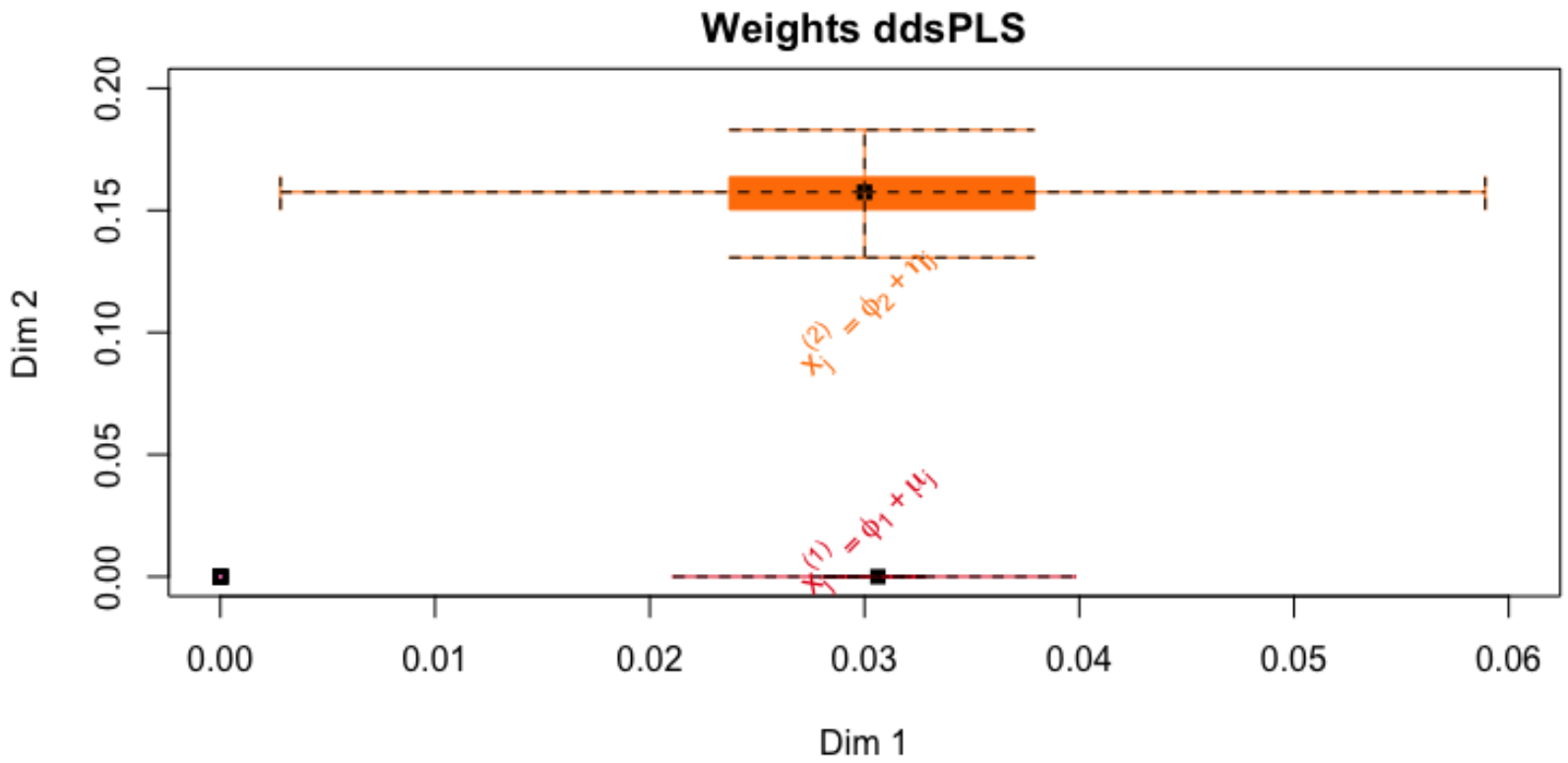
$$\bar{R}^2_{B,r} = \frac{1}{B}\sum_{b=1}^{B} R^2_{b,r} \quad \text{and} \quad \bar{Q}^2_{B,r} = \frac{1}{B}\sum_{b=1}^{B} Q^2_{b,r} \tag{6}$$

where

$$\begin{aligned} R^2_{b,r} &= 1 - \frac{\sum_{j=1}^{q}\sum_{i\in \mathsf{IN}(b)}\left(y_{i,j} - \left(\hat{y}^{b,(r)}_{i,j} - \hat{y}^{b,(r-1)}_{i,j}\right) - \bar{y}^b_j\right)^2}{\sum_{j=1}^{q}\sum_{i\in \mathsf{IN}(b)}\left(y_{i,j} - \bar{y}^b_j\right)^2}, \\ Q^2_{b,r} &= 1 - \frac{\sum_{j=1}^{q}\sum_{i\in \mathsf{OOB}(b)}\left(y_{i,j} - \hat{y}^{b,(r)}_{i,j}\right)^2}{\sum_{j=1}^{q}\sum_{i\in \mathsf{OOB}(b)}\left(y_{i,j} - \hat{y}^{b,(r-1)}_{i,j}\right)^2}. \end{aligned} \tag{7}$$

Variable Selection design 1, "ddsPLS"

Variable Selection design 2, "ddsPLS"



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