Tensor multiblock logistic regression to classify liver tumors from MRI images

SELVESTREL Alexandre

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Université Paris-Saclay, CNRS, CentraleSupélec, Laboratoire des signaux et systèmes

Supervisors : Arthur Tenenhaus, Laurent Lebrusquet

Medical partner : Henri Mondor hospital, radiologist: Sébastien Mulé

Liver tumors classification

6$^{\text{th}}$ most widespread cancer and 4$^{\text{th}}$ mortality cause by cancer

Classification:

- Hepatocellular Carcinoma (HCC): 75% of cases, resection often possible
- CCK = Cholangiocarcinoma (CCK): 6% of cases, resection difficult (possible in 30% of cases)
- Others: benign (18% of cases) or Hepatoblastoma (1% of cases)

Difficulties for classification

- No perfect method using MRI images (contrast, shape, size, location): disagreement between radiologists
- High levels of alpha-fetoprotein indicate HCC, but not always.
- Biopsy: invasive and potentially lethal (0.02% of patients)

But a lot of clues even without biopsy $\rightarrow$ Machine Learning

Available data

- MRI images in 3D of liver tumors (arterial, portal, late)
- gender (63 men, 27 women)
- age at disease (average: 63 years old)

From Henri Mondor hospital: Sébastien Mulé

Same variables extracted from each MRI image at 3 times $\rightarrow$ specific structure

Need to adapt existing machine learning methods to this structure

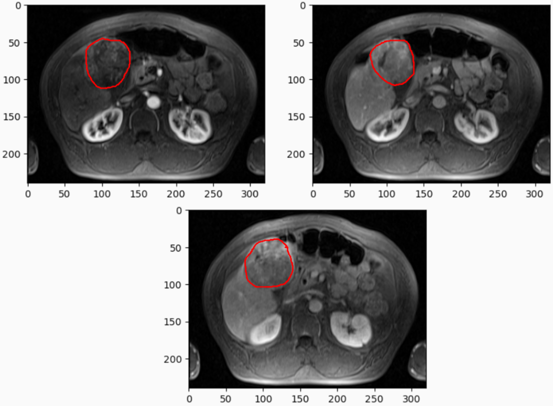

Figure 1: Example of MRI images of a HCC tumor (arterial, portal, late). More contrast in arterial

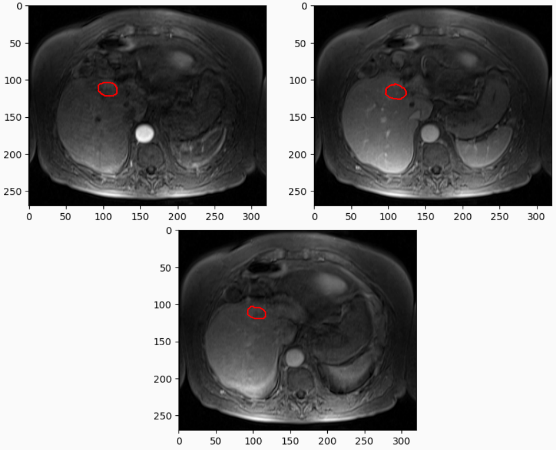

Figure 2: Example of MRI images of a CCK tumor (arterial, portal, late)

Correlation matrix of features about texture (GLDM)

Strong correlations between imaging times for a given variable

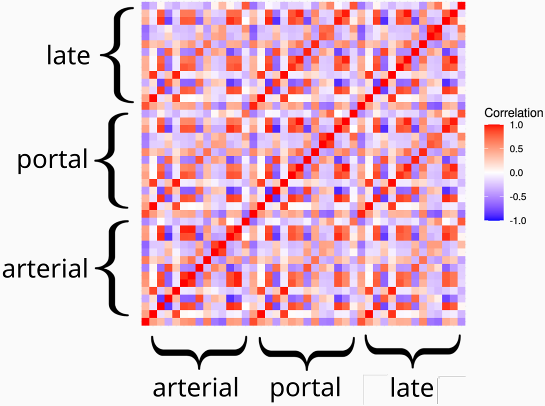

Figure 3: Correlation matrix of the features relative to the Gray Level Dependence Matrix (GLDM)

Tensor data

Finding the best algorithm considering the structure of the data.

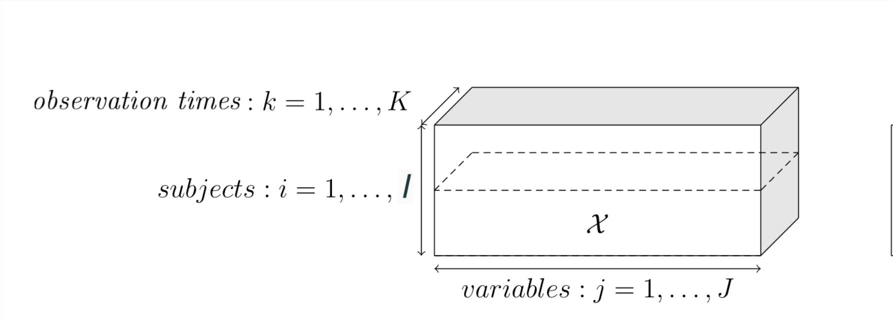

Figure 4: Type of data: tensorial

Multiblock data

Features about pixel/voxel intensities, shape and texture: different natures

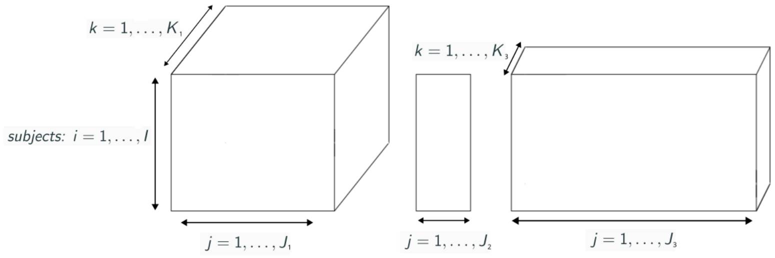

Figure 5: Type of data: multiblock

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Machine learning models

Logistic regression

Classical machine learning (works with few data and explainable)

$$P(Y=1|x) = \frac{\exp(\beta_0 + \boldsymbol{x}^T\boldsymbol{\beta})}{1+\exp(\beta_0 + \boldsymbol{x}^T\boldsymbol{\beta})}$$

Defines a likelihood function $\mathcal{L}(\boldsymbol{\beta}) = \prod_{i=1}^{I} P(Y_i = y_i|x_i)$

To many features (vs I) $\rightarrow$ need to limit variance of prediction.
Penalization proportionnal to $\|\boldsymbol{\beta}\|_1$: lasso

Function to minimize : $-\log(\mathcal{L}(\boldsymbol{\beta})) +$ penalization

Naive approach: unfolding

$$\boldsymbol{\beta} = (\beta_{j,k})_{j \in [\![1,J]\!], k \in [\![1,K]\!]} \text{ so } JK \text{ parameters to determine}$$

$$x^T \boldsymbol{\beta} \rightsquigarrow \sum_k \sum_j \beta_{j,k} x_{j,k} \quad \text{and} \quad \|\boldsymbol{\beta}\|_1 = \sum_k \sum_j |\beta_{j,k}|$$

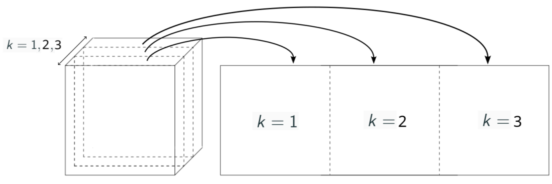


Figure 6: Unfolding a tensor

Limitation of lasso: Elimination of features without specific consideration for the same feature at other times/ other features at the same time

Group lasso

Common solution: grouping regression coefficients together in the penalization

$$\sum_{j,k} |\beta_{j,k}| \rightsquigarrow \sum_{g=1}^{G} \|\boldsymbol{\beta}^g\|_2$$

Tendency to set regression coefficients to zero by entire blocks.

But: grouping either by mode or by variable, not both
→ Adapting the model to the structure of the data: aim of the internship

Tensor regression models

Idea: each variable and mode has its own influence on the prediction (i.e. on β) [2].

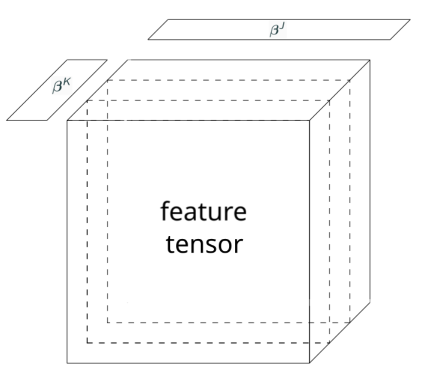


Figure 7: Tensor structure of β

Tensor regression models

Idea: each variable and mode has its own influence on the prediction (i.e. on $\boldsymbol{\beta}$) [2].

For J variables observed on K modalities (e.g. times)

$$\beta_{j,k} = \beta_j^J \beta_k^K$$

β_j : impact of variable j

β_k : impact of modality k

Only $J + K$ parameters to determine (instead of JK)

Limits of rank 1

$\beta_{j,k} = \beta^J_j \beta^K_k$ implies that $\boldsymbol{\beta}$ looks like:

Figure 8: Example of rank 1 pictogram (only 0 and 1)

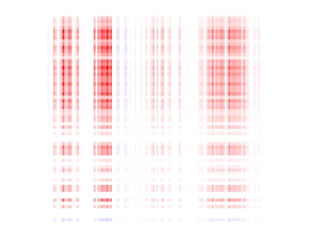
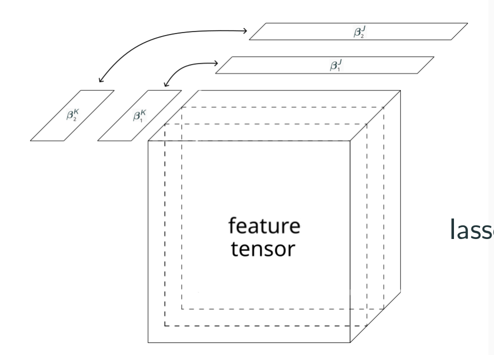


Figure 9: Example of rank 1 matrix (all values allowed)

This can be too simplistic

Rank R tensor logistic regression [1]

$$\text{Summing rank 1 together : } \beta_{j,k} = \sum_{r=1}^{R} \beta^J_{j,r} \beta^K_{k,r}$$



$$\text{lasso} \rightsquigarrow \sum_{r=1}^{R} \left(\|\boldsymbol{\beta}^J_{(1,r)}\|_1 \|\boldsymbol{\beta}^K_{(1,r)}\|_1 \right)$$

Figure 10: Tensor structure of $\boldsymbol{\beta}$

Blocks of variables

Problem: Several groups of variables of different natures (first order, shape, texture). But β_r^K and β_r^J common to all groups. $K_1 = K_2 = K_3$ needed or else:

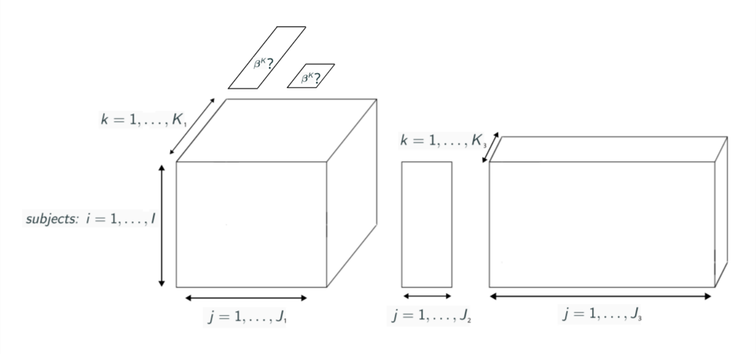


Figure 11: Problem if blocks have different orders or dimensions

Tensor multiblock logistic regression

Solution: giving each block its own β^J and β^K

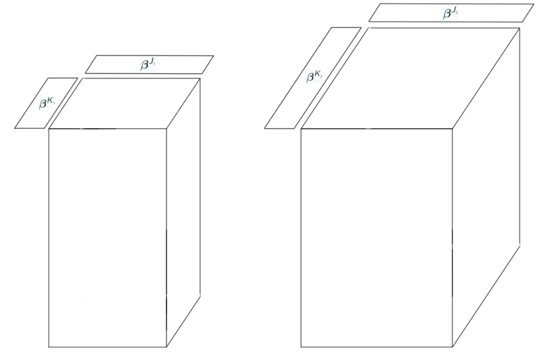


Figure 12: Tensor multiblock model for rank 1

Tensor multiblock logistic regression

Mathematically, this gives :

$$\mathbf{x}^T \boldsymbol{\beta} \rightsquigarrow = \sum_{l=1}^{L} \sum_{j,k} x_{j,k}^l \beta_{j,k}^l$$

With, for rank 1: $\beta_{j,k}^l = \beta_j^{J_l} \beta_k^{K_l}$

But each $\boldsymbol{\beta}^l$ can have a different rank R_l, which gives:

$$\beta_{j,k}^l = \sum_{r=1}^{R_l} (\beta_r^{J_l})_j \, (\beta_r^{K_l})_k$$

Simulations

Parameters to control:

- Difficulty of the classification (overlap between classes, distance between means of classes etc ...)
- Balance between classes
- Structure of the regression parameter $\boldsymbol{\beta}$ (several blocks)
- Quality of the classification (Area Under the ROC Curve : AUC)
- Quality of the reconstruction of $\boldsymbol{\beta}$

Illustration in 2D

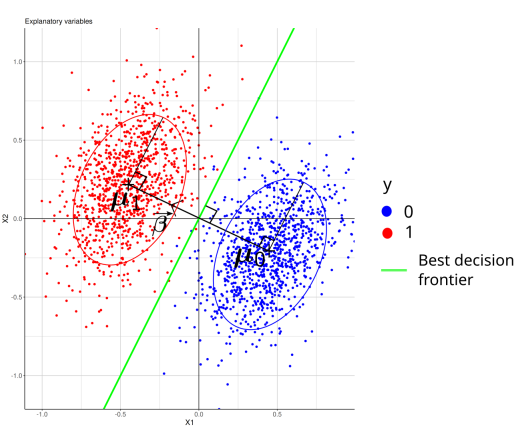


Figure 13: Example of explanatory variables for $\beta = (-2, 1)$

Data generation

Choose the $\boldsymbol{\beta}$ to be reconstructed (pictograms)

Generate the $(\mathbf{x}_i)_{i \in [\![1,I]\!]}$ with 2 multivariate normal laws of means $\boldsymbol{\mu}_0$ and $\boldsymbol{\mu}_1$ and common covariance matrix $\boldsymbol{\Sigma}$ such that:

- $\boldsymbol{\mu}_1 - \boldsymbol{\mu}_0$ colinear to $\boldsymbol{\beta}$
- One of the principal axis of $\boldsymbol{\Sigma}$ colinear to $\boldsymbol{\beta}$

Separation of classes linked with eigenvalues of $\boldsymbol{\Sigma}$ (to be compared with $\|\boldsymbol{\mu}_1 - \boldsymbol{\mu}_0\|$)

AUC simulated data

Table 1: Cross validated AUC for each model on simulated data for 3000 individuals

$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}})$	lasso	g.l. (blocks)	g.l. (mode)	g.l. (var)	tensor	tensor blocks
(0.1,0.5)	0.83	0.86	0.94	0.94	0.99	0.99
(0.1,0.8)	0.63	0.64	0.68	0.68	0.93	0.99

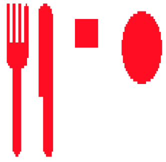
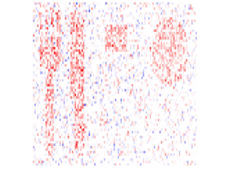
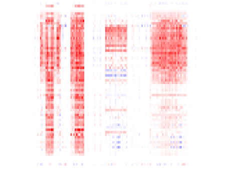


Figure 14: Pictogram of shape 66×117

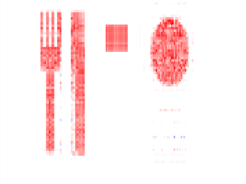
Reconstructed β



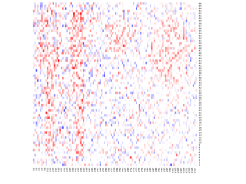
(a) lasso
$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}}) = (0.1, 0.5)$



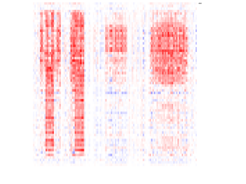
(b) tensor $R : 10$
$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}}) = (0.1, 0.5)$



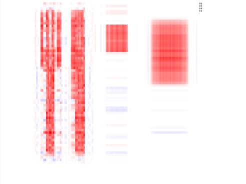
(c) T.M. $R : (12, 1, 10)$
$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}}) = (0.1, 0.5)$



(d) lasso
$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}}) = (0.1, 0.8)$



(e) tensor $R : 10$
$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}}) = (0.1, 0.8)$



(f) T.M. $R : (6, 1, 1)$
$(\sigma_{\boldsymbol{\beta}}, \sigma_{\text{noise}}) = (0.1, 0.8)$

Liver tumor data

Feature extraction with pyradiomics [3]

Extraction of $\simeq$ 100 features (about intensities, shape, texture) for each 2D or 3D image.

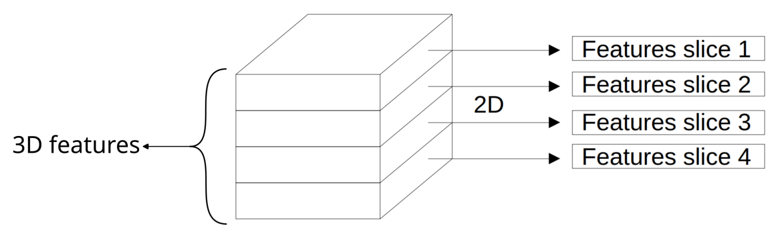


Figure 16: Feature extraction with pyradiomics for an MRI image composed of 4 slices

Feature extraction in 3D

Each radio $\rightarrow$ 1 particular spacing along (x, y, z)

But : Calculations of pyradiomics only use voxels ($=$ 3D pixels).

Not always meaningful if the scale changes at each radio (e.g. for Gray Level Run Length Matrix, based on number alignments of voxels of same intensity)

Solution: Standardize the spacing along (x, y, z). Allowed by resampling (interpolation) of the image.

Feature extraction in 2D

Slices along z axis $\rightarrow$ same spacing along (x, y)

Difficulty Tumors are of variable locations, sizes and shapes in the frontal plane (front - back plane)

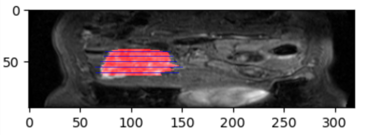


Figure 17: Extracting 5 slices in a big tumor

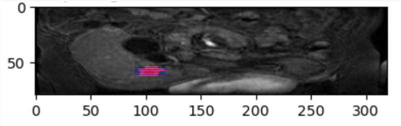


Figure 18: Extracting 5 slices in a small tumor

Feature extraction in 2D

Every slice not equally informative:

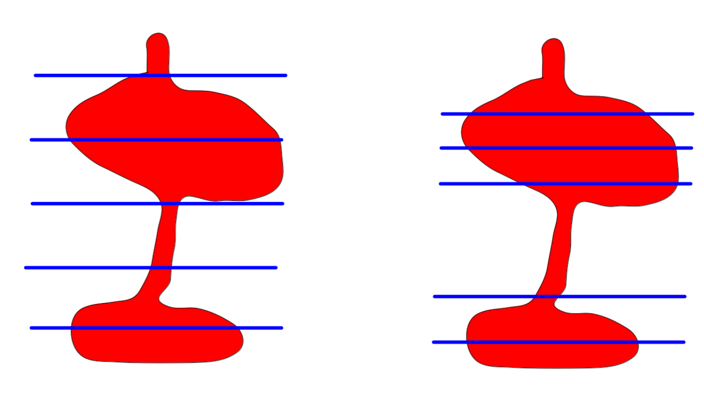


Figure 19: Slicing relative to the depth vs. relative to the volume travelled in the tumor

Results

Type of data	lasso	g.l. (block)	g.l. (time)	g.l. (var)	tensor	tensor blocks
3D	0.74 ± 0.04	0.78 ± 0.03	0.76 ± 0.03	0.73 ± 0.03	0.77 ± 0.03	0.77 ± 0.03

Cross validated AUC on 3D real data

Type of data	lasso	g.l. (block)	g.l. (slice)	g.l. (time)	g.l. (var)	tensor	tensor blocks
2D	0.73± 0.03	0.71± 0.03	0.70± 0.04	0.71± 0.03	0.71± 0.03	0.66± 0.04	0.71± 0.03

Cross validated AUC on 2D real data

Latest data

12 binary features determined by radiologists (late enhancement, non peripheral washout etc...) + sex and existence of chronical disease

With lasso model:

- AUC: 0.97 ± 0.02
- balanced accuracy: 0.88 ± 0.05

Would be interesting to test other models...

Feature importance

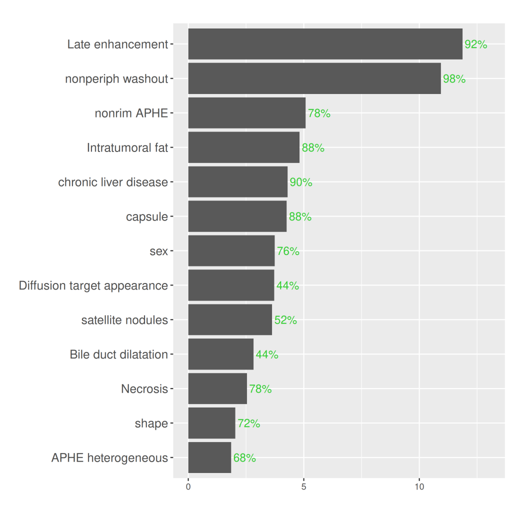


Figure 20: Feature importance with lasso (in green percentage of runs with non null coefficient)

Possible extensions

Testing other penalizations (group lasso, elastic net)

Extending the multiblock approach to other classical machine learning algorithms (other GLMs, SVM etc...). Comparing it to CNN.

Testing other models on the latest data (in order to obtain a model that can be deployed in the hospital).

Getting the same results as those obtained with the features created by the radiologists, but from the raw MRI images (to obtain a clinical routine)

Retrospective Analysis

Personal learnings

Direct impact: continuing in thesis (increase in motivation for research activities)

Soft skills in machine learning: becoming more critical vs results, searching for other data whenever possible

Being part of a team in a scientific context (not only 1 supervisor): importance of communication and reporting (even when no written documents)

Research in machine learning: an accessible world

Conclusion

A promising framework for the diagnosis of liver tumors

The simulation part of an article on the multiblock tensor model

Ethically positive impact (controllable deployment, a precise need, no replacement of human beings...)

On a personal level:

A good representation of a research work (and its challenges)

Supportive, available and calm supervision (even as deadlines approach)

Looking forward to continuing in this direction

Bibliography

Fabien Girka, Pierrick Chevaillier, Arnaud Gloaguen, Giulia Gennari, Ghislaine Dehaene-Lambertz, Laurent Le Brusquet, and Arthur Tenenhaus.
Rank-R Multiway Logistic Regression.
In *52èmes Journées de Statistique*, Nice, France, 2021.
les 52èmes journées de Statistique 2020 sont reportées ! Elles auront lieu du 7 au 11 Juin 2021.

Laurent Le Brusquet, Gisela Lechuga, and Arthur Tenenhaus.
Régression Logistique Multivoie.
In *JdS 2014*, page 6 pages, Rennes, France, June 2014.

Joost J.M. van Griethuysen, Andriy Fedorov, Chintan Parmar, Ahmed Hosny, Nicole Aucoin, Vivek Narayan, Regina G.H. Beets-Tan, Jean-Christophe Fillion-Robin, Steve Pieper, and Hugo J.W.L. Aerts.
Computational Radiomics System to Decode the Radiographic Phenotype.
Cancer Research, 77(21):e104–e107, 10 2017.

Hua Zhou, Lexin Li, and Hongtu Zhu.
Tensor regression with applications in neuroimaging data analysis.
Journal of the American Statistical Association, 108:540–552, 06 2013.