Lesion Segmentation using a Spatially Regularized Mixture Model

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Lesion segmentation

Motivations

- **clinical practice :** diagnosis of stroke, multiple sclerosis.
- **clinical research :** objective assessment of the disease.
  - ▷ gold standard for predictive models, drug evaluation.

Limits of manual segmentation

- time consuming.
- source of inter-observer variability.
- difficult in case of complex 3D structures.

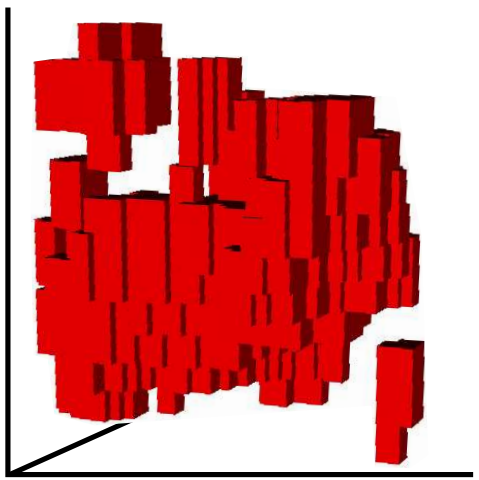

Figure: 3D stroke lesion

State of the art

Current approaches

- level set models

  Osher and Fedkiw, 2003; Weinman et al., 2003; Mouridsen et al., 2013

- supervised learning (glm, machine learning)

  Klëppel et al., 2011; Sweeney et al., 2013

- finite Mixture Models : very popular
  - ▷ unsupervised
  - ▷ few parameters
  - ▷ flexible modelling framework

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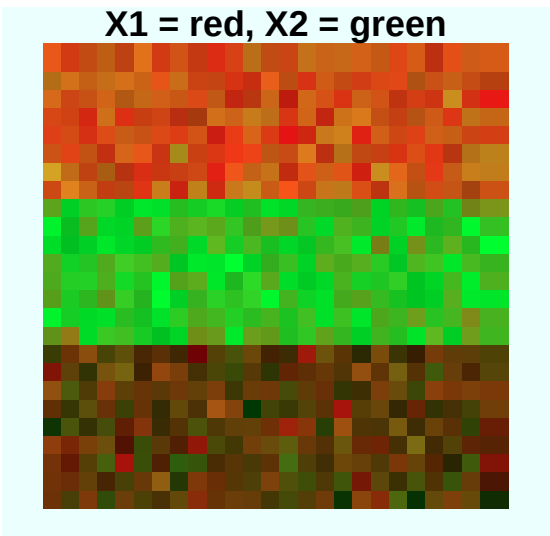
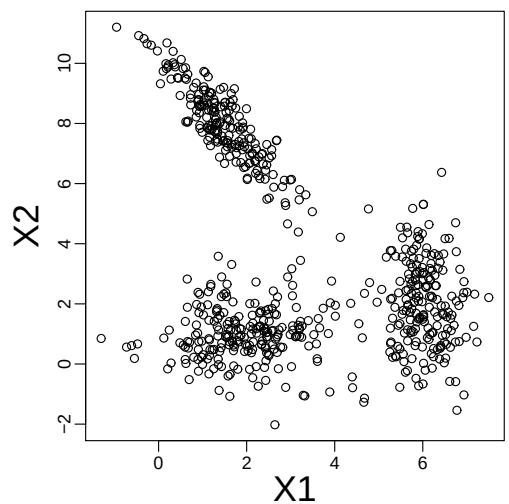


Image



Intensity space

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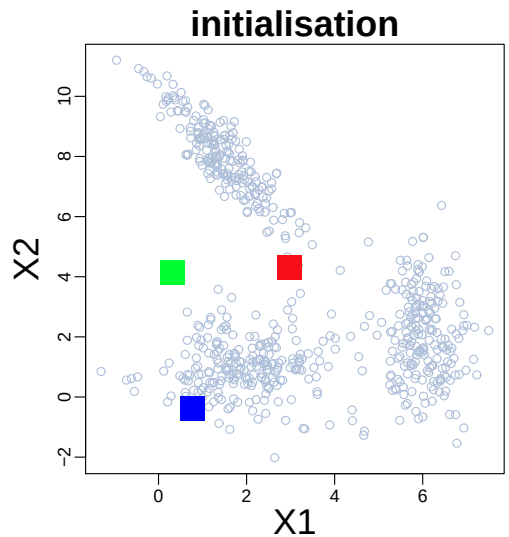

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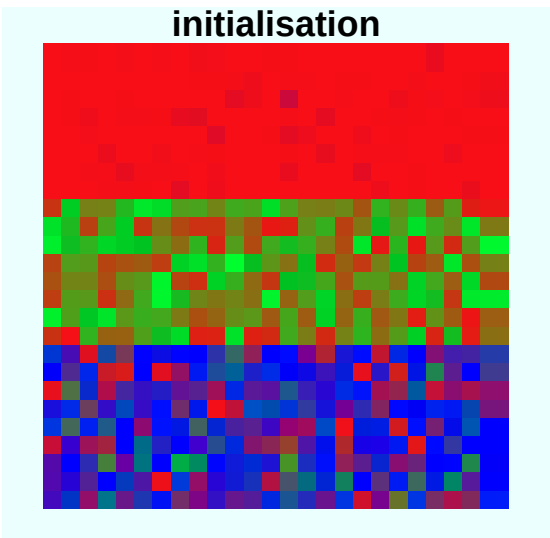

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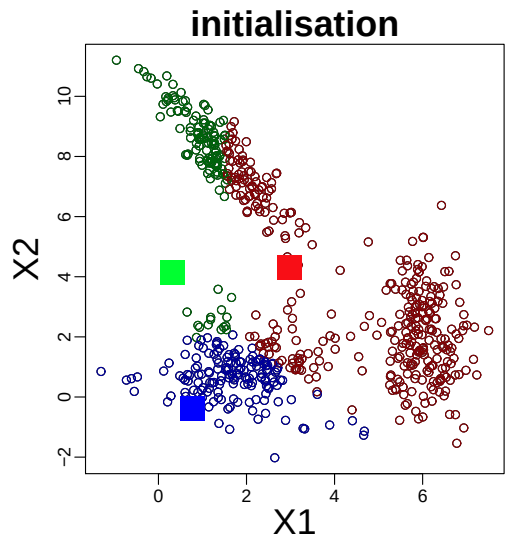

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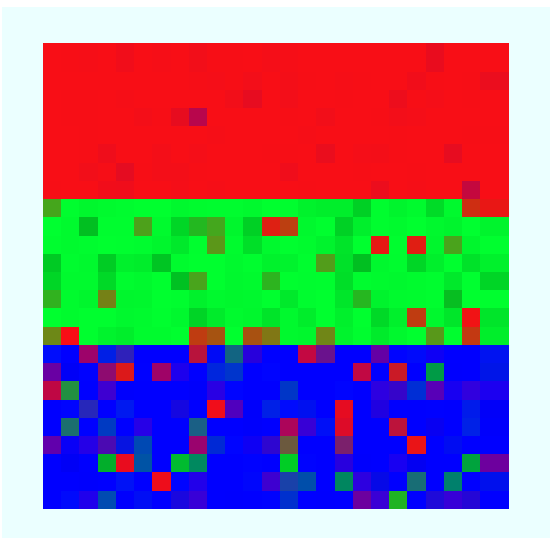

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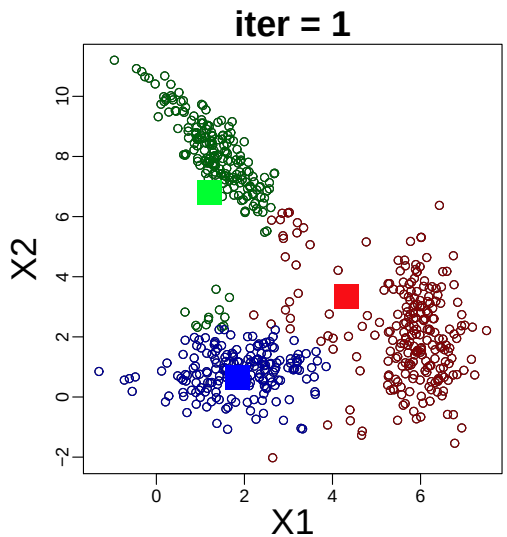

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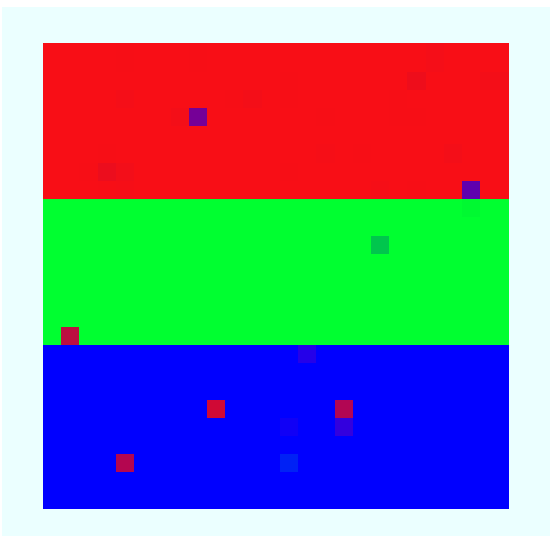

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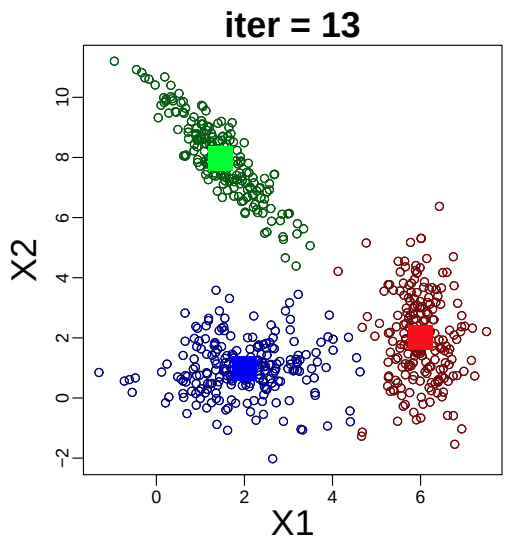


Intensity space

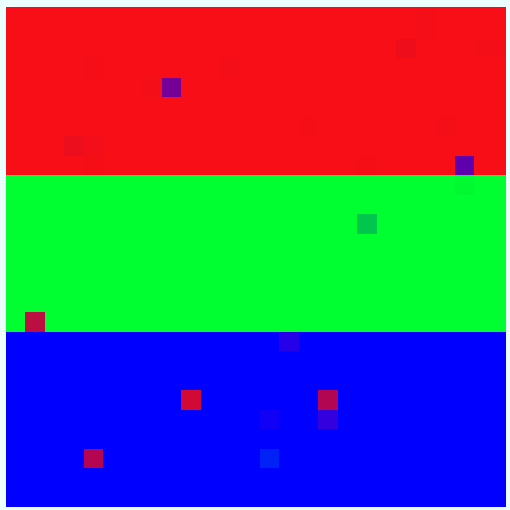
State of the art

Limits

- noise degrades the segmentation
  ▷ *univariate* spatial fMM
  (Woolrich et al., 2005 ; Feng, Tierney, and Magnotta, 2012 ; Zhang et al., 2008)

- white matter disease can be confused with stroke lesion
  ▷ lead to segmentation errors
  ▷ volume over-estimation

⇒ **need for a regional approach**



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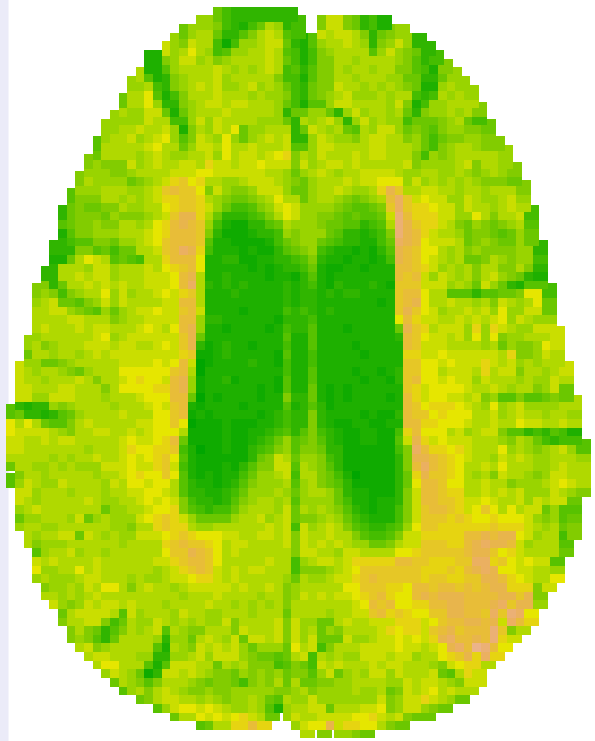

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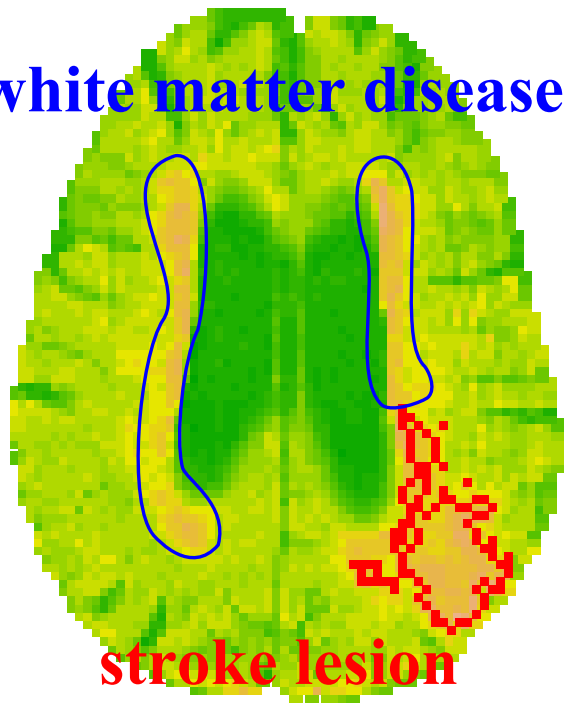
$\Rightarrow$ **need for a regional approach**



Objective

Propose an **unsupervised lesion segmentation algorithm robust** to noise and artefacts :

- allowing multivariate characterization of the lesion
- with a spatial regularization step :
  - ▷ local regularization for noise
  - ▷ regional regularization for artefacts

fMM - General Framework

Markov Random field : n sites where we observe an intensity Y

Mixture assumption : the observed intensity is issued from a mixture of G groups :

$$\mathbb{P}\left[Y_i|\Theta\right] = \sum_{g=1}^{G} \mathbb{P}\left[Y_i|\xi_i = g, \theta_g\right] \mathbb{P}\left[\xi_i = g\right]$$

with

- ξ_i : group membership of observation i
- θ_g : the distribution parameters of group g
- $\mathbb{P}\left[\xi_i = g\right]$: prior group membership of i for group g

Mean Field Approximation (MFA)

$$\mathbb{P}[Y|\Theta] = \prod_{i=1}^{n} ?? \text{ (no more independance)}$$

Mean field approximation : the neighboring group memberships are fixed to their expectation $\overline{\xi_{\mathcal{V}(i)}}$ (Zhang, 1992) :

$$\mathbb{P}^{MFA}[\xi] = \prod_{i=1}^{n} \mathbb{P}\left[\xi_i | \overline{\xi_{\mathcal{V}(i)}}\right] \approx \mathbb{P}[\xi]$$

One can show that the likelihood becomes :

$$\mathbb{P}[Y|\Theta] = \prod_{i=1}^{n} \sum_{g=1}^{G} \mathbb{P}[Y_i|\xi_i = g, \theta_g] \mathbb{P}\left[\xi_i = g | \overline{\xi_{\mathcal{V}(i)}}, \rho\right]$$

Probability distribution on a MRF

Hammersley-Clifford theorem

The join probability of a Markov Random Field (MRF) is a Gibbs distribution :

$$\mathbb{P}[\xi = x] = \frac{1}{Z} \exp[(\rho * U)(x)]$$

- U : spatial potential
- Z : normalizing constant

We define the spatial potential as the sum of :

- a **local potential** U_{loc} with intensity ρ_1
- a **regional potential** U_{reg} with intensity ρ_2

$$\mathbb{P}\left[\xi_i = g|\overline{\xi_{\mathcal{V}(i)}}\right] = \frac{1}{Z_i} \exp\left[\rho_1 U_{loc,g}(\overline{\xi_{\mathcal{V}(i,1)}}) + \rho_2 U_{reg,g}(\overline{\xi_{\mathcal{V}(i,C)}})\right]$$

Standard Potts model

- define the local neighborhood $\mathcal{V}(i,1)$

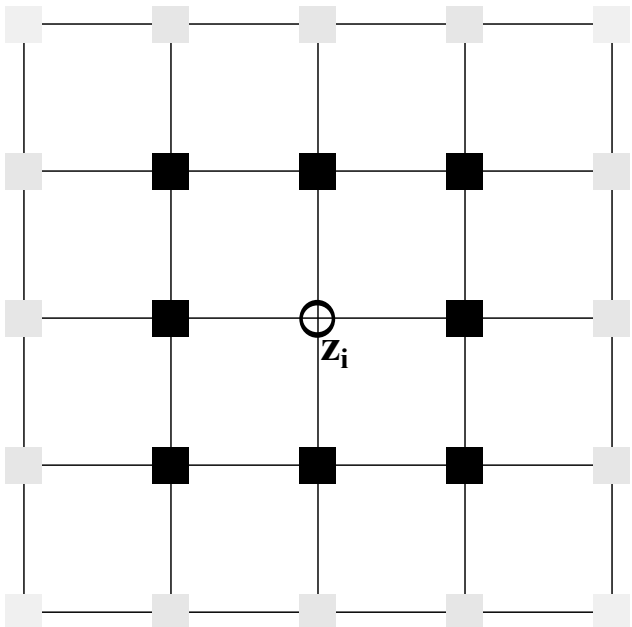


Figure: Queen's neighborhood

- compute the local potential

$$U_{loc,g}(\overline{\xi_{\mathcal{V}(i,1)}}) = \frac{1}{card\mathcal{V}(i,1)} \sum_{j \in \mathcal{V}(i,1)} \mathbb{P}\left[\overline{\xi_j} = g\right]$$

Regional Potts model

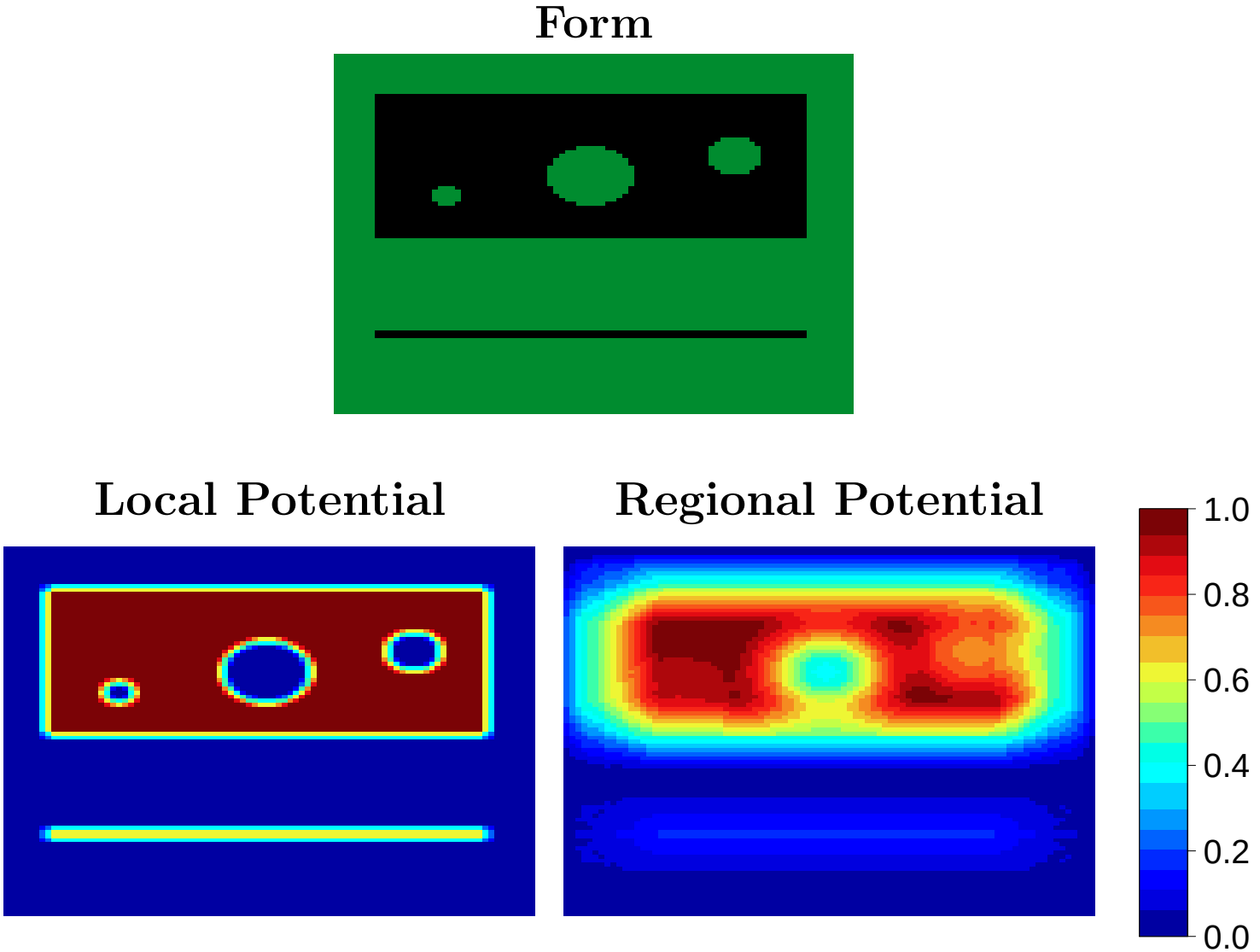
- define a regional neighbourhood as C neighbourhoods with **increasing range** $\mathcal{V}(i,c)$.
- compute the potential for each neighbourhood :

$$U_g^c(\overline{\xi_{\mathcal{V}(i,c)}}) = \frac{1}{card\mathcal{V}(i,c)} \sum_{j \in \mathcal{V}(i,c)} \mathbb{P}\left[\overline{\xi_j} = g\right]$$

- the regional potential is the average of these potentials

$$U_{reg}(\overline{\xi_{\mathcal{V}(i,c)}}) = \frac{1}{C} \sum_{c=1}^{C} U_g^c(\overline{\xi_{\mathcal{V}(i,c)}})$$

Local vs Regional Potential



Estimation - EM algorithm

- *step E* : estimate the group membership $\xi_{i,g}$
  - ▷ initialize the membership probabilities : $\mathbb{P}\left[\xi_i = g | Y_i\right]$
  - ▷ estimate the regularized membership probabilities iteratively over sites : $\mathbb{P}\left[\xi_i = g | \overline{\xi_{\mathcal{V}(i)}}, \rho\right]$

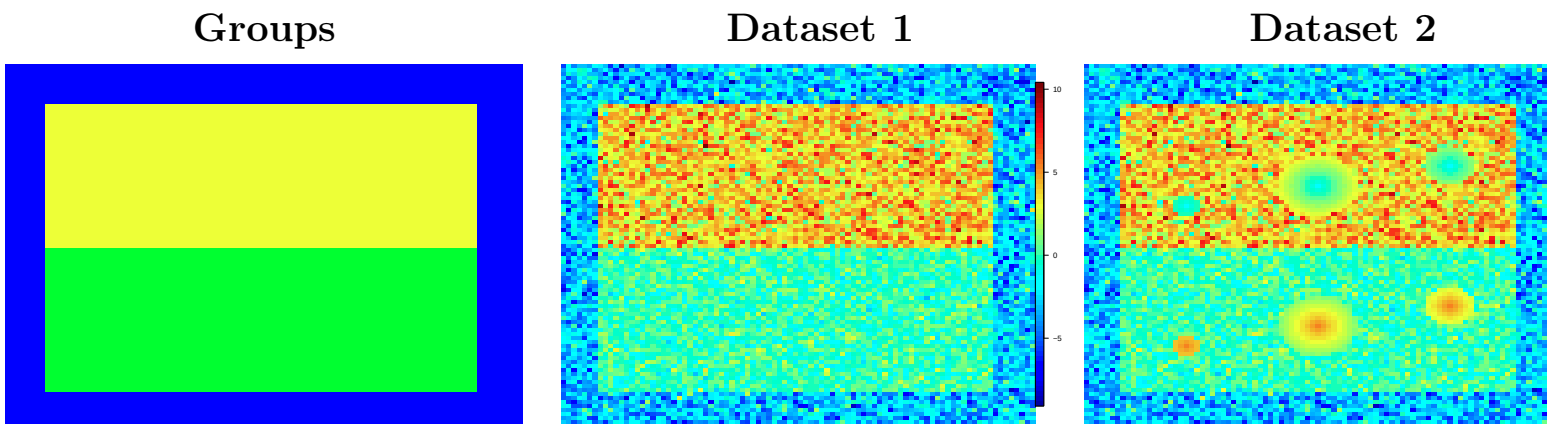
- *step M* : optimize the distribution Θ parameters

Simulation setup

Scenari

- **Dataset 1*** : 3 groups following normal laws with :
  mean : $\mu = (-3, 0, 4)$
  variance : $\sigma^2 = (3, 1, 3)$
- **Dataset 2** : same as scenario 1 with circular artefact

$\Longrightarrow$ The objective is to identify group 3 ('yellow' group)



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Model specification

3 models were compared :

- $\mathcal{M}_0$: $\rho_1 = 0$ and $\rho_2 = 0$
- $\mathcal{M}_{loc}$: $\rho_1 = 6$ and $\rho_2 = 0$
- $\mathcal{M}_{reg}$: $\rho_1 = 0$ and $\rho_2 = 6$

* same simulation as in Woolrich et al., 2005

Simulation results

Non spatial fMM :

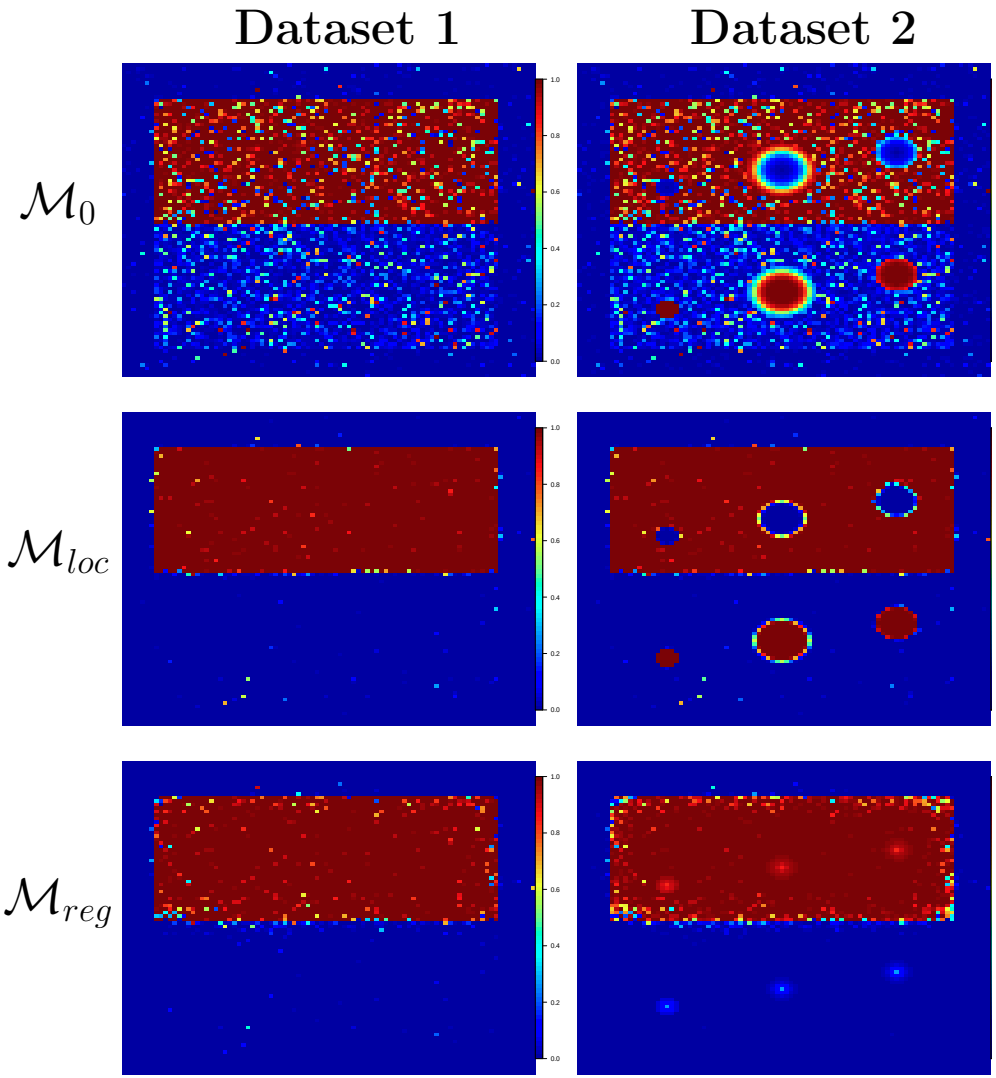
- noise and artefacts.

Local regularisation :

- noise correction.

Regional regularisation :

- artefacts correction.
- noise correction with edge effects.

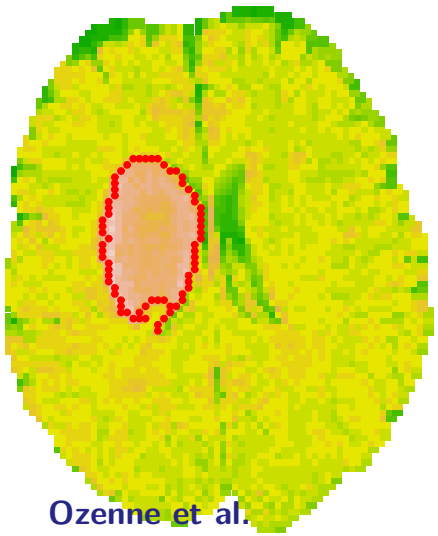


Stroke Segmentation

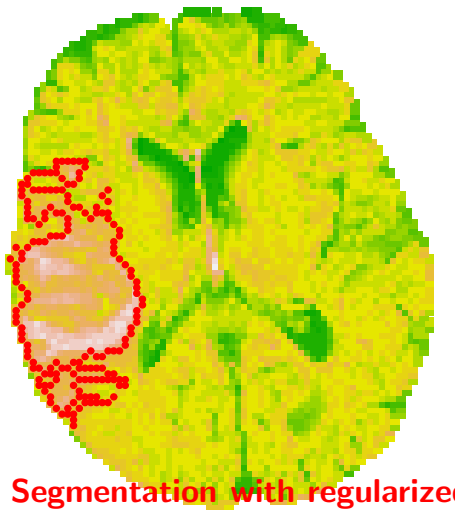
MRI data

- 9 patients with ischemic stroke from the I-know cohort
  - 4 'Typical'
  - 2 with 'Heterogeneity'
  - 3 with 'White Matter Disease'
- T2 FLAIR image at 1-month follow up
- physician segmentation (reference)

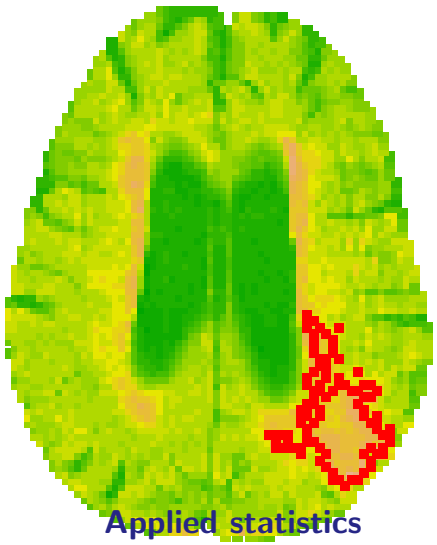
Typical



Heterogeneity



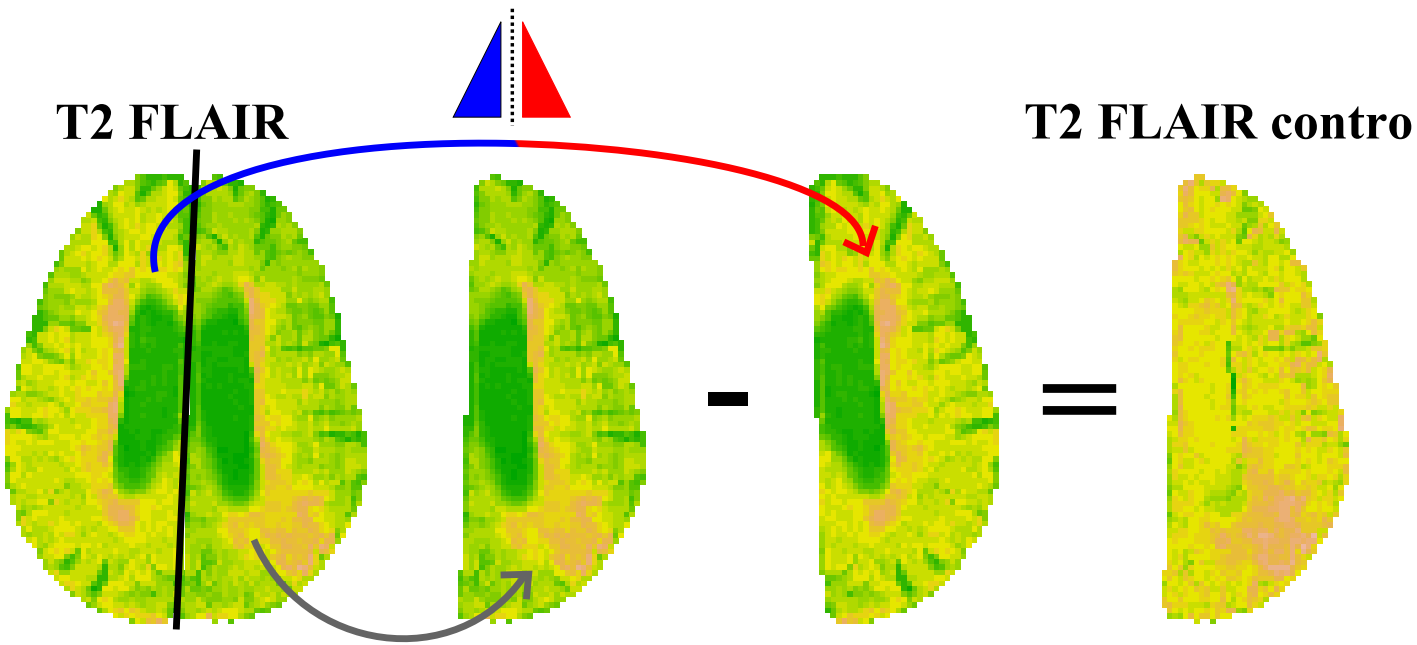
White Matter disease



Stroke Segmentation

main fMM settings

- 4 groups
- 2 parameters : T2 FLAIR and T2 FLAIR contro
- spatial parameters estimated on 'Typical' patients



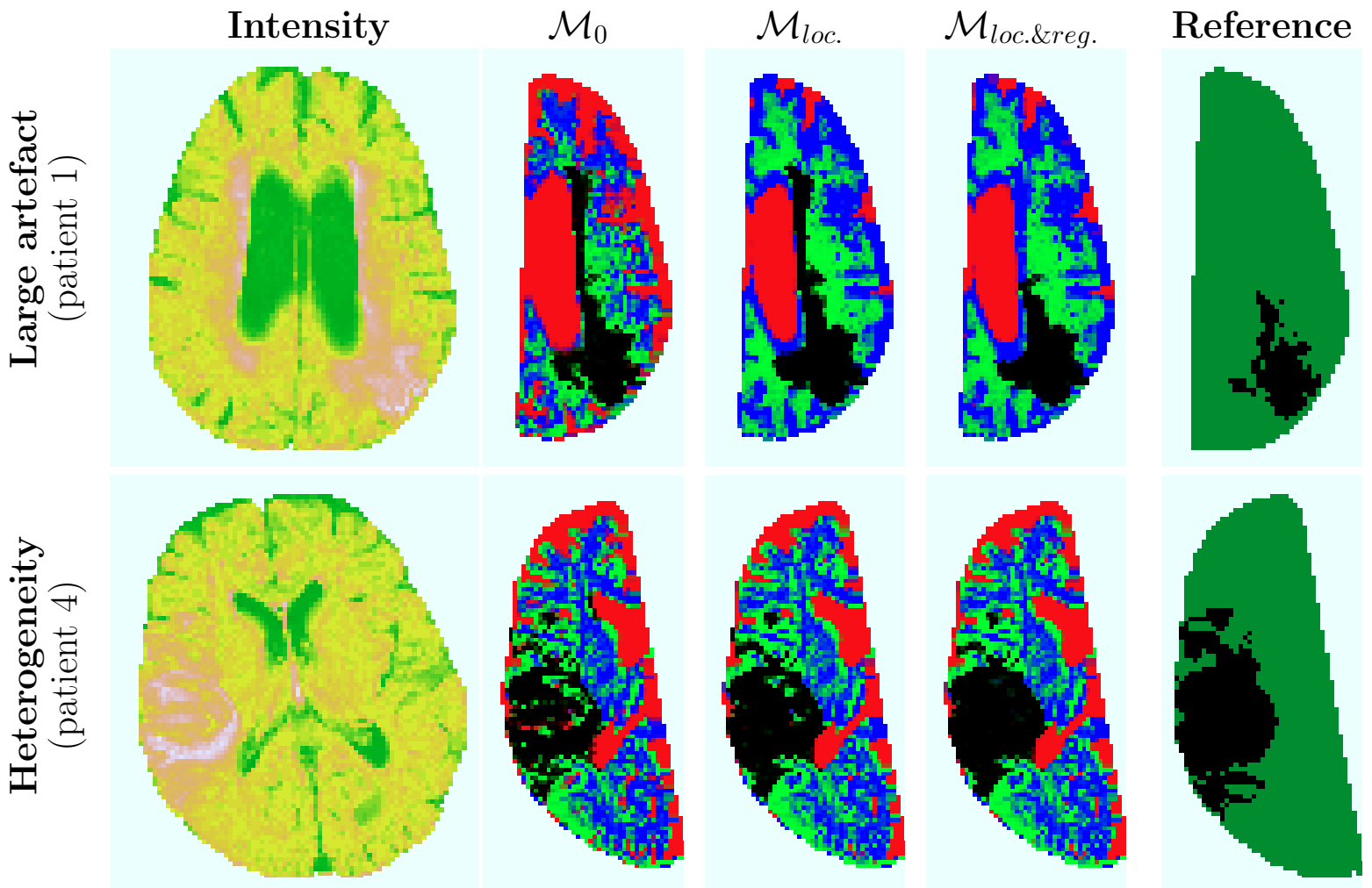
Stroke Segmentation - Results

Quality of the estimated volume (**1 is the optimum**) :

$$Quality = \frac{V_{model}}{V_{reference}}$$

		$\mathcal{M}_0$	$\mathcal{M}_{loc.}$	$\mathcal{M}_{loc.\&reg}$
White Matter disease	patient 1	1.62	1.68	1.17
	patient 2	2.76	1.16	1.10
	patient 3	4.85	1.41	1.29
Heterogeneity	patient 4	0.879	0.933	0.932
	patient 5	0.935	0.975	0.975

Stroke Segmentation - Results



Conclusion

Discussion

- Spatial regularization improves lesion segmentation :
  - ▷ local regularization deals with noise and heterogeneity.
  - ▷ regional regularization corrects artefacts (at least partially).
- A good initialisation is required to find optimal convergence.
  - ▷ k.means or non spatial fMM results.
- Estimation of the spatial parameters is still an issue.
  - ▷ automatic procedure is possible
    but underestimate the regional regularization parameter ρ_2

Perspectives

- Integration of the functions into a  package.
- Validation on a larger sample and with other diseases.

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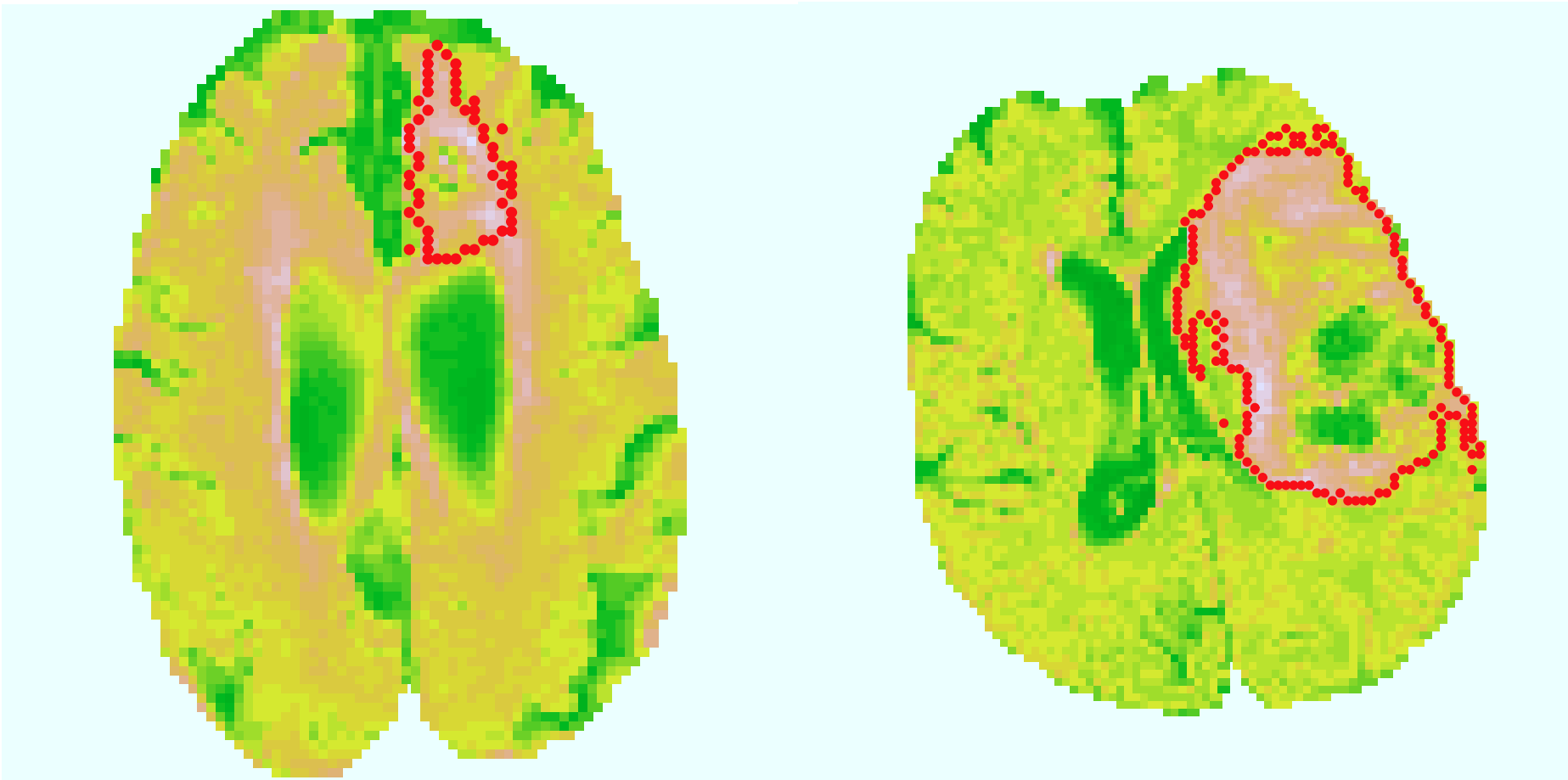
Exemple of excluded patients



Likelihood for spatial fMM

$$
\begin{aligned}
L_v(\Theta|Y,X) &= \mathbb{P}[Y|\Theta,X] \\
&= \sum_{\Gamma=(g_1,\dots g_n)\in[1;G]^n} \mathbb{P}[Y,\xi=\Gamma|\Theta] \\
&\approx \sum_{\Gamma=(g_1,\dots g_n)\in[1;G]^n} \prod_{i=1}^{n} \mathbb{P}\left[Y_i,\xi_i=g_i|\Theta,\overline{\xi_{\mathcal{V}(i)}}\right] \\
&= L_v^{MFA}(\Theta|Y)
\end{aligned}
$$

using mean field approximation

Likelihood for spatial fMM

Then

$$L_v^{MFA}(\Theta|Y,X) = \sum_{\Gamma=(g_1,\dots g_n)\in[1;G]^n} \prod_{i=1}^{n} \mathbb{P}\left[Y_i, \xi_i = g_i | \Theta, \overline{\xi_{\mathcal{V}(i)}}\right]$$

$$= \sum_{\Gamma=(g_1,\dots g_n)\in[1;G]^n} \prod_{i=1}^{n} \mathbb{P}\left[Y_i|\xi_i = g_i, \theta_{g_i}\right] \mathbb{P}\left[\xi_i = g_i | \rho, \overline{\xi_{\mathcal{V}(i)}}\right]$$

$$= \prod_{i=1}^{n}\sum_{g=1}^{G} \mathbb{P}\left[Y_i|\xi_i = g, \theta_g\right] \mathbb{P}\left[\xi_i = g | \rho, \overline{\xi_{\mathcal{V}(i)}}\right]$$

$$= \prod_{i=1}^{n}\sum_{g=1}^{G} \mathbb{P}\left[Y_i|\xi_{i,g} = 1, \theta_g\right]$$

$$\times \frac{1}{Z} \exp\left[\rho_1 U_{loc}(\xi_{\mathcal{V}(i),g}) + \rho_2 U_{reg}(\xi_{\mathcal{V}(i),g})\right]$$

Complete likelihood for spatial fMM

Denoting : $\pi_{i,g}^{posterior} = \mathbb{P}\left[\xi_{i,g} | Y_i, \overline{\xi_{\mathcal{V}(i)}}, \Theta\right]$

$$L_v^c(Y_i|\Theta,\rho) = \prod_{i=1}^{n}\prod_{g=1}^{G}\left(\mathbb{P}\left[Y_i|\xi_{i,g}=1,\theta_g\right]\mathbb{P}\left[\xi_{i,g}=1|\overline{\xi_{\mathcal{V}(i)}},\rho\right]\right)^{\pi_{i,g}^{posterior}}$$

$$l_v^c(Y_i|\Theta,\rho) = \sum_{i=1}^{n}\sum_{g=1}^{G}\pi_{i,g}^{posterior}\log\mathbb{P}\left[Y_i|\xi_{i,g}=1,\theta_g\right] + \pi_{i,g}^{posterior}\log\mathbb{P}\left[\xi_{i,g}=1|\overline{\xi_{\mathcal{V}(i)}},\rho\right]$$

- $\mathcal{M}_{intensity}$: sum of independent weighted glm models
  $\Rightarrow$ IWLS
- $\mathcal{M}_{spatial}$: local and regional Potts model
  $\Rightarrow$ quasi-Newton method (L-BFGS-B)

Estimation of the spatial parameter - Method

$$
\begin{aligned}
& \mathcal{M}_{spatial}(\rho) \\
= & \sum_{i=1}^{n}\sum_{g=1}^{G} \pi_{i,g}^{posterior} \log \frac{1}{Z_i} \exp\left[\rho_1 U_{loc}(\overline{\xi_{\mathcal{V}(i),g}}) + \rho_2 U_{reg}(\overline{\xi_{\mathcal{V}(i),g}})\right] \\
= & \sum_{i=1}^{n}\sum_{g=1}^{G} \pi_{i,g}^{posterior} \left(-\log Z_i + \rho_1 U_{loc}(\overline{\xi_{\mathcal{V}(i),g}}) + \rho_2 U_{reg}(\overline{\xi_{\mathcal{V}(i),g}})\right)
\end{aligned}
$$

with $Z_i = \sum_{g=1}^{G} \exp\left[\rho_1 U_{loc}(\overline{\xi_{\mathcal{V}(i),g}}) + \rho_2 U_{reg}(\overline{\xi_{\mathcal{V}(i),g}})\right]$

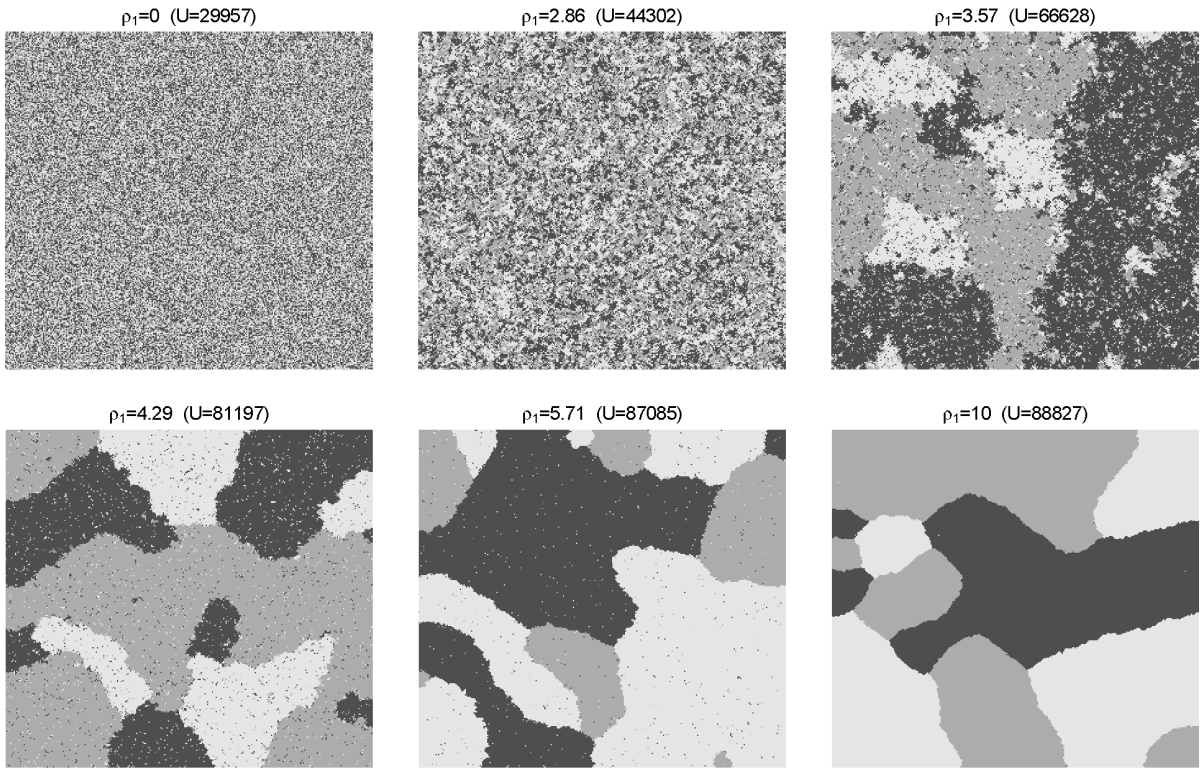
U_{loc} and U_{reg} can be computed for each patient and thus also Z_i.
The function to optimize is a two parameter function that is derivable
$\Rightarrow$ quasi-Newton method.

Estimation of the spatial parameter - Results

type	median estimation	range
local reg. (ρ_1)	4.59	$[4.32 - 5.17]$
local and regional reg. (ρ_1)	3.85	$[3.47 - 4.77]$
local and regional reg. (ρ_2)	2.61	$[0.20 - 4.08]$

Validity of MFA - Simulation

- Potts model simulated by Gibbs sampling (1000 iterations).
- n ranged from 100 to 1000.
- ρ_1 ranged from 0 to 10.
- each scenario was replicated 250 times.



Validity of MFA - Results

- clear decrease in variance when n increases.
- small decrease in bias when n increases.
- MRI data (n $\sim$ 30000) : relative bias $<$5 % for common ρ_1

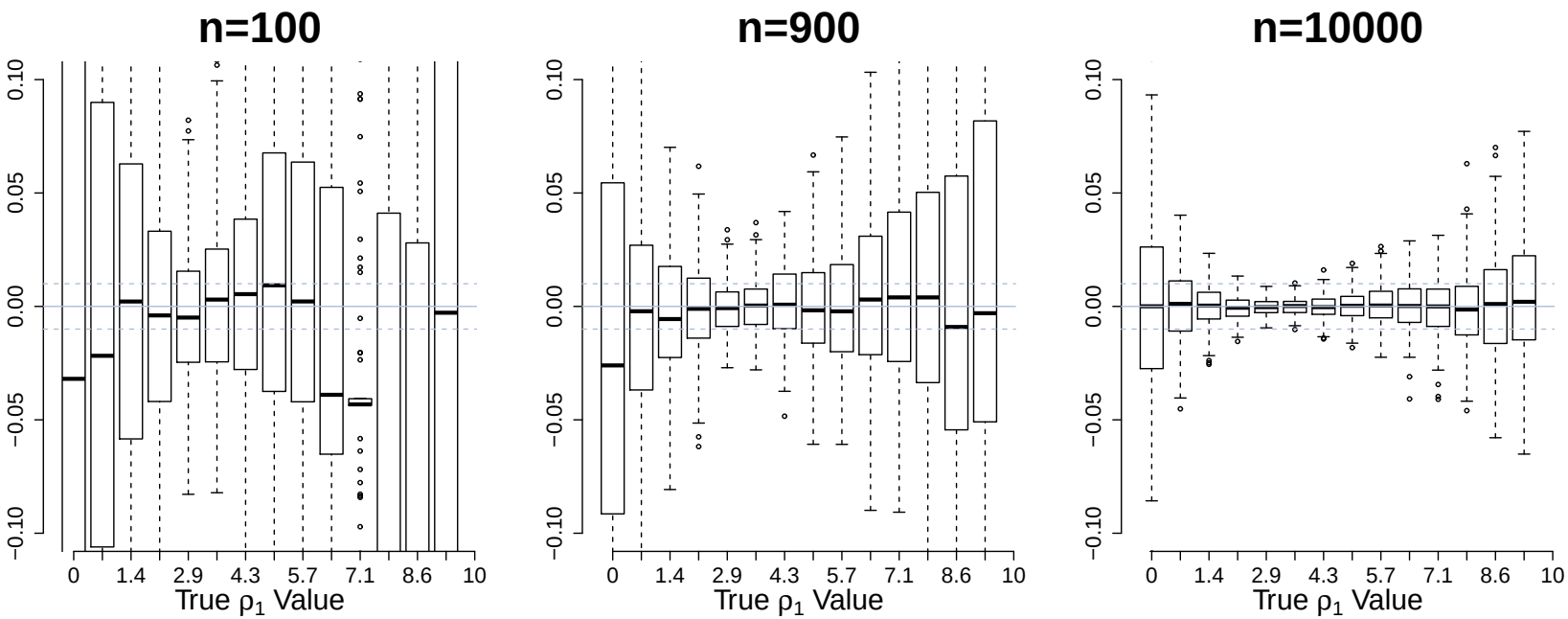


Figure: Relative bias of the ρ_1 estimator

fMMseg - Example

```
> require(fMMseg)
> data(data_test,package="fMMseg")
> str(data_test)

'data.frame': 8100 obs. of  6 variables:
 $ i              : int  1 2 3 4 5 6 7 8 9 10 ...
 $ j              : int  1 1 1 1 1 1 1 1 1 1 ...
 $ group          : num  1 1 1 1 1 1 1 1 1 1 ...
 $ Y              : num  -2.97 -3.32 -5.38 -4.04 -2.49 ...
 $ Y_artlinear    : num  -2.97 -3.32 -5.38 -4.04 -2.49 ...
 $ Y_artspherique: num  -2.97 -3.32 -5.38 -4.04 -2.49 ...
```

fMMseg - Example

```
> res_test <- EM.launcher(G=3,data=data_test,coords=c("i","j"),
+                         distband.SR=sqrt(2),distband.LR=10,
+      var_reg="Y_artlinear",family=gaussian(link="identity"),
+                          test.ICM=T,rho_ICM=c(6,6),
+                          test.ICMregional=T)

* initialisation by k means *
 # initialisation
                groupe 1   groupe 2   groupe 3
intercept 1 :  -3.702351 0.02097692   4.384099
cv criteria :  0.001
*** init. spatial regularization ***
### Iteration FINALE  20  (lv = -15521.41)
                groupe 1   groupe 2   groupe 3
intercept 1 : -3.0083412  0.1448128  3.8479213
sigma 1 :      1.7505830  1.1915927  1.8669002
<prior> :      0.3333333  0.3333333  0.3333333
<posterior> :  0.3330471  0.3308790  0.3360739
ICM parameters :  6 6
*** Convergence ***
*** Export ***
```