Graduate School in Physics and Astrophysics
XXV cycle

SEGMENTATION of MEDICAL IMAGES with VIRTUAL ANT COLONIES

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OVERVIEW

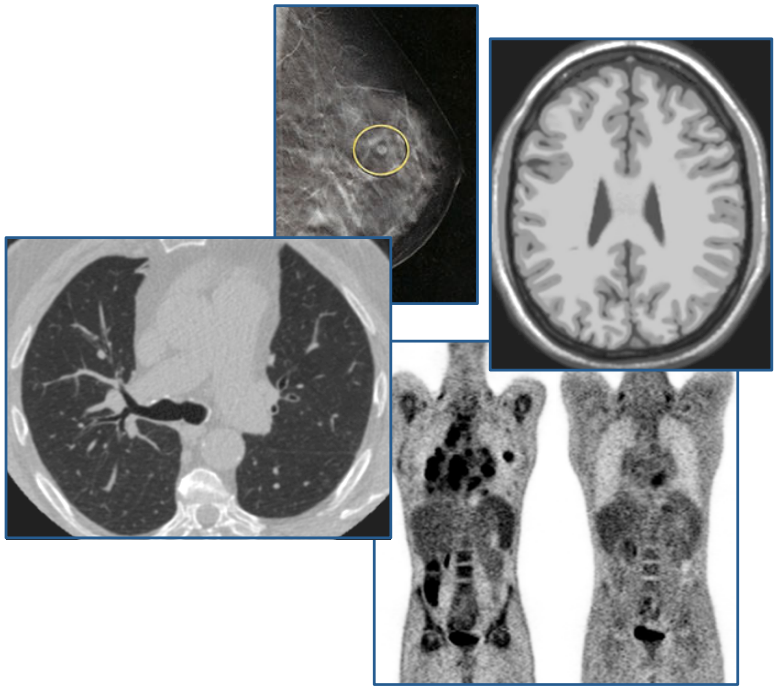
- Introduction
  - Why Medical Imaging requires segmentation tools?
  - Virtual ant colonies
- The Channeler Ant Model
- Segmentation in brain MRI:
  - **White Matter, Grey Matter & CerebroSpinal Fluid segmentations**
  - **Hippocampus segmentation**
- Conclusions & Perspectives

SEGMENTATION IN MEDICAL IMAGING

Segmenting means determining a particular Volume Of Interest in a medical images

mammography,
computed tomography CT,
magnetic resonance imaging MRI,
positron emission tomography PET, …

human tissue,
organs,
cancer,
…



Why automated tools?

- Obtaining a standardized performance
- Analyzing a large amount of information
- Combining information in a non linear way
- Quantifying
- Saving time: e. g. screening programs
- Helping physicians in the diagnosis
- Helping physicians in the therapy and in the treatment planning

VIRTUAL ANT COLONIES (I)

Systems with swarm intelligence (1988 Gerardo Beni, Susan Hackwood and Jing Wan)

- Each agent doesn't know the global state of the system and interacts with the others by modifying the environment

Ant colonies are characterized by:

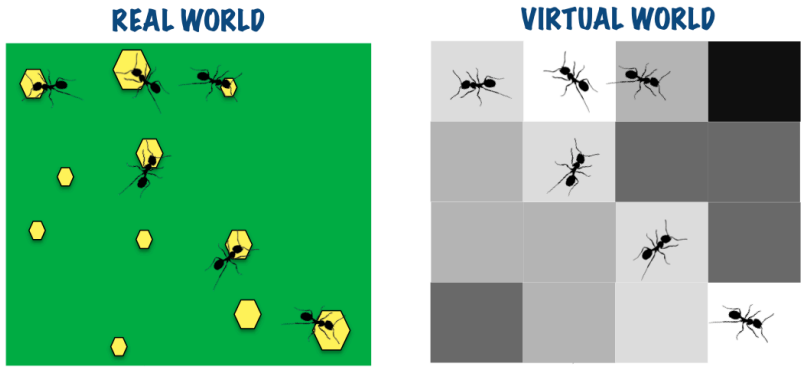
- **Stigmergy & Non-linearity**: there's an indirect way of communication by pheromone, that ants "smell" in a non-linear way
- **Emergence:** the colony behaviour produces the rising of patterns that are unpredictable on the base of the single agent behaviour
- **Self Organization :** the colony organizes itself without external manipulation or control

"ANTS AREN'T SMART. ANT COLONIES ARE."

VIRTUAL ANT COLONIES (II)

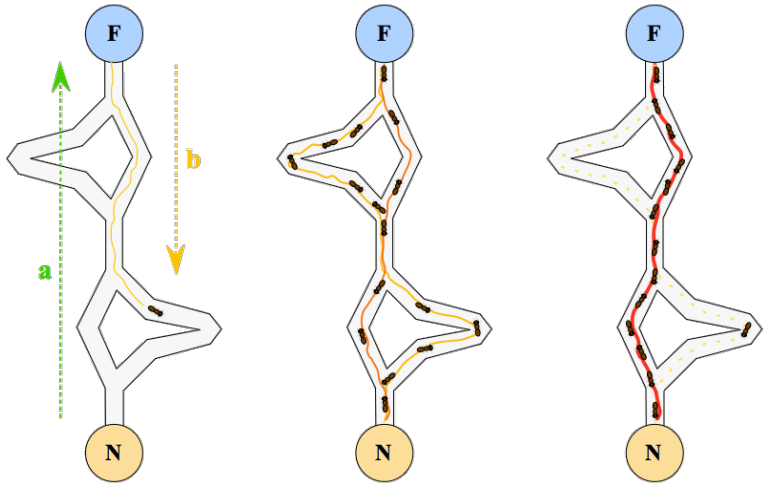
"Food"search: energy source

- For virtual ants, the presence of food is a function of the image features, arbitrarily chosen depending on what you want to segment in the image.

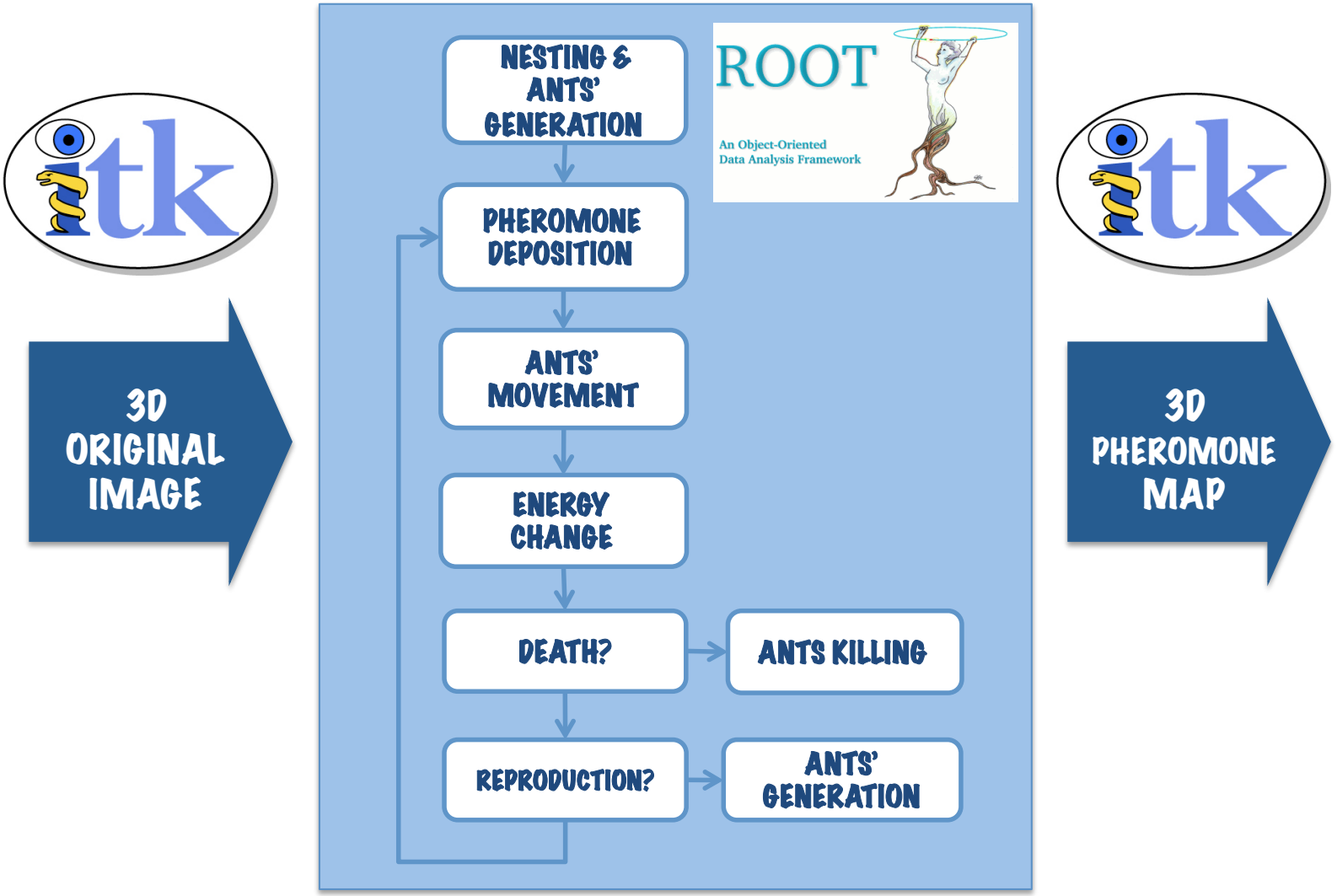


Pheromone Deposition

- For virtual ants, the pheromone deposition depends on the presence of "food"
- Pheromone power is not linear: it is a function of ant's sensory capability and of ant's osmotropotaxis sensitivity.
- In nature, pheromone evaporates.
- **Following pheromone trails real ants can choose the shortest way; following pheromone trails virtual ants make a reprocessing of the image!**



CHANNELER ANT MODEL (CAM)



P. Cerello et al. 3-d object segmentation using ant colonies. Pattern Recognition, 43(4):1476–1490, 2010

MOVING RULE

Probability to choose voxel v_j for an ant that is in v_i :

$$P_{ij}(v_i \rightarrow v_j) = \frac{W(\sigma_j)}{\sum_{n=1}^{26} W(\sigma_n)} \qquad W(\sigma_j) = \left(1 + \frac{\sigma_j / <\sigma>_i}{1 + \delta \cdot \left(\sigma_j / <\sigma>_i\right)}\right)^{\beta}$$

$\beta = 3.5$
$\delta = 0.2$

$W(\sigma_j)$ is a function of the pheromone present in v_j :

σ	quantity of pheromone in the voxel,
$<\sigma>_j$	is the average pheromone (3x3 voxels)
β	determines how strongly pheromone trails attract other ants
$1/\delta$	represents the ants sensitivity in perceiving pheromone

In the beginning, movements are random but, later on, pheromone trails become more and more important for choosing the future destination

Forbidden voxels:

- Occupied
- Outside the volume of Interest ("habitat")
- In which a fixed pheromone threshold is reached

If all 26 nearest voxels are forbidden, an ant cannot move

PHEROMONE DEPOSITION

Each ant releases a quantity of pheromone T:

$$T = \eta + H_{fac} \cdot \Delta_{ph}$$

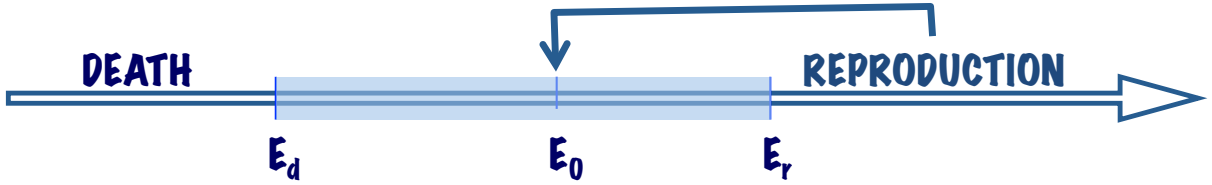
η= 0.05

η	is a minimum quantity of pheromone released anyway
Hfac	is a constant related to the algorithm speed
Δ_{ph}	is the basic link between the image to be segmented and the CAM segmentation, it is a function of some image features

- A pheromone threshold (PhTh) exists: when the pheromone in a voxel reaches the threshold value, the voxel becomes unavailable for any other visit.
- $PhTh/H_{fac}$ is the speed-related free parameter.

The pheromone deposition rule is the key link between the original image and the final segmentation. The pheromone deposition rule defines what has to be segmented.

ENERGY: LIVING PARAMETER



$\alpha = 0.2$
$E_d = 1.0$
$E_r = 1.3$

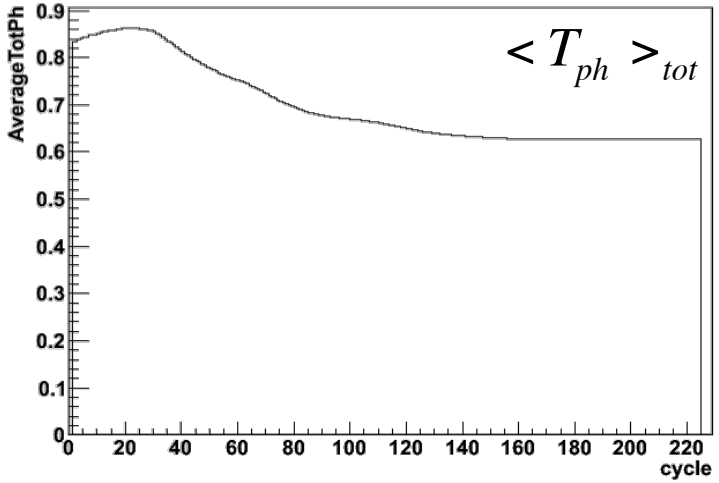
Each ant is born with an energy: $E_0 = 1 + \alpha$

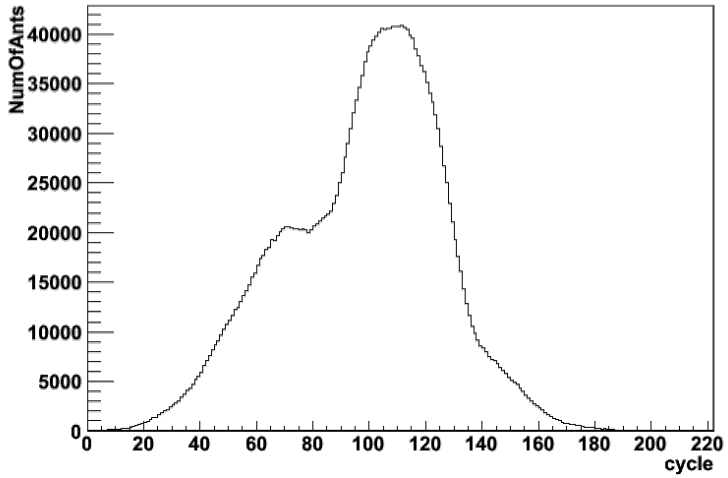
At the cycle i+1 the energy of the ant k is:

$$E_{i+1}^k = E_i^k + \alpha \cdot \left(\frac{T_{ph}^k(i+1)}{< T_{ph} >_{tot}} - 1 \right)$$

$T^k_{ph}(i+1)$ is the pheromone released in the cycle i+1 by ant k

$<T_{ph}>_{tot}$ is the average of all pheromone releases over all the colony life

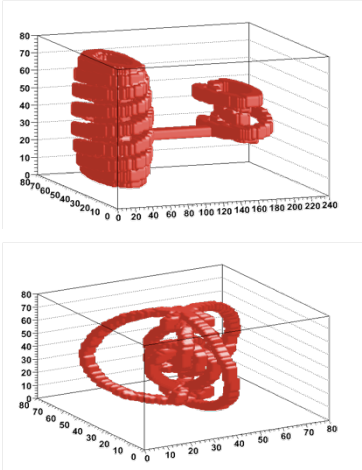




CAM STATE OF THE ART

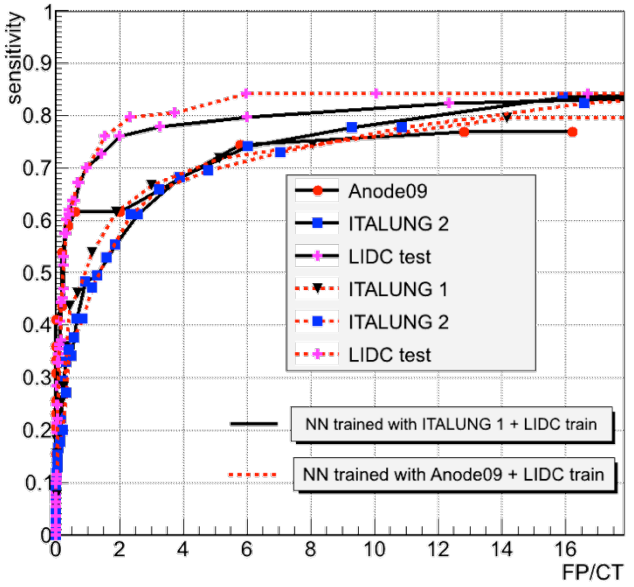
The CAM performance was validated with **3D artificial objects segmentation:**

- The segmentation is independent of the object shape, noise level and intensity range of the image
- The CAM segments in a non linear and probabilistic way and it is more flexible than Region Growing



The CAM was used for the **detection of lung nodules in CT scans**

- The CAM is able to segment effectively both the bronchial and vascular tree and the lung nodules
- The pheromone deposition rule is based on the intensity of the image: the more the intensity of the voxel is, the more the ants deposit pheromone



SEGMENTATION IN BRAIN MRI

White Matter, Grey Matter and Cerebrospinal Fluid segmentations:

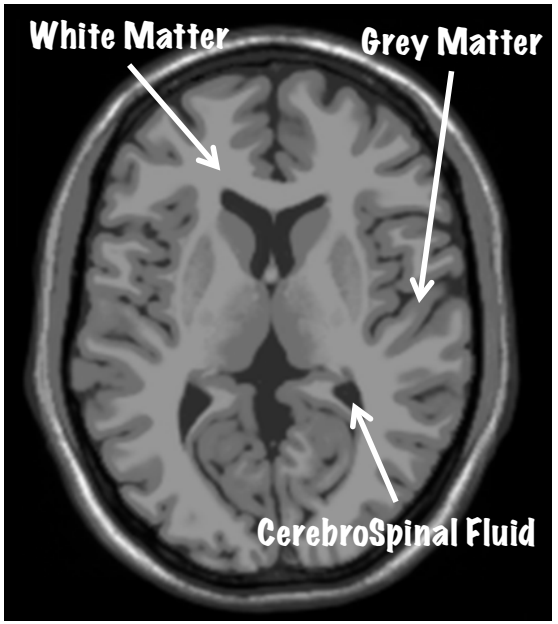
- The **basic step** of several MRI analyses
- **Quantitative** segmentations based on the intensity of structures with very different shapes
- Simulated Brain Database available online: T1 weighted MRI with the Gold Standard segmentations

Hippocampus segmentation:

- **Clinical task:** the evaluation of the hippocampus atrophy and its volume variation in time can improve the diagnosis of the Alzheimer's Disease and other neurological diseases
- Segmentation based both on the intensity and on the **shape**
- Several databases available with the manual hippocampus segmentation given by an expert

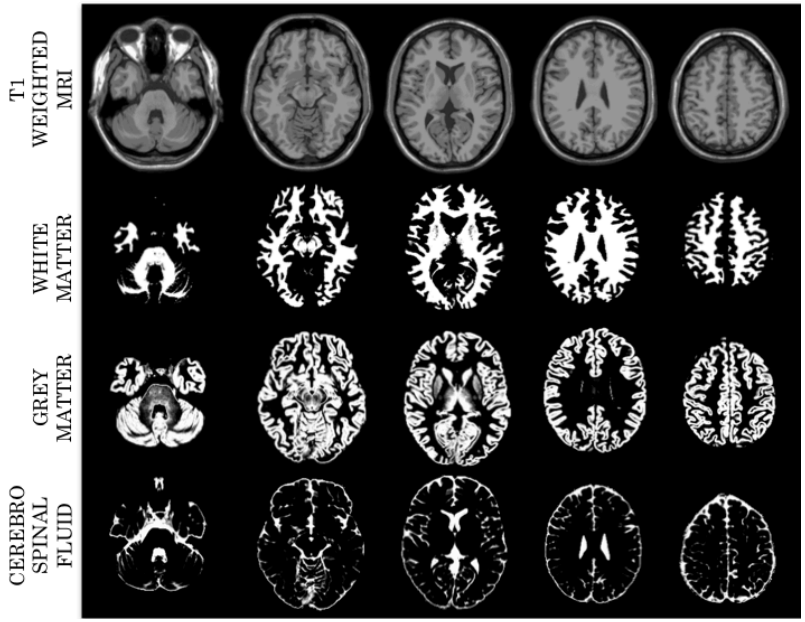
WM, GM & CSF SEGMENTATIONS

- The White Matter (WM), the Grey Matter and the CerebroSpinal Fluid (CSF) are three 3D connected volumes with a different image intensity range, shape and dimension
- "To segment" means to determine the percentage of the different anatomical tissues present in each voxel



- The CAM segments different regions by only changing the pheromone deposition parameters
- The segmentation provides a probabilistic result, not a binary mask

SIMULATED BRAIN DATABASE



http://www.bic.mni.mcgillca/brainweb/

Voxel size: 1x1x1mm, 1x1x5mm

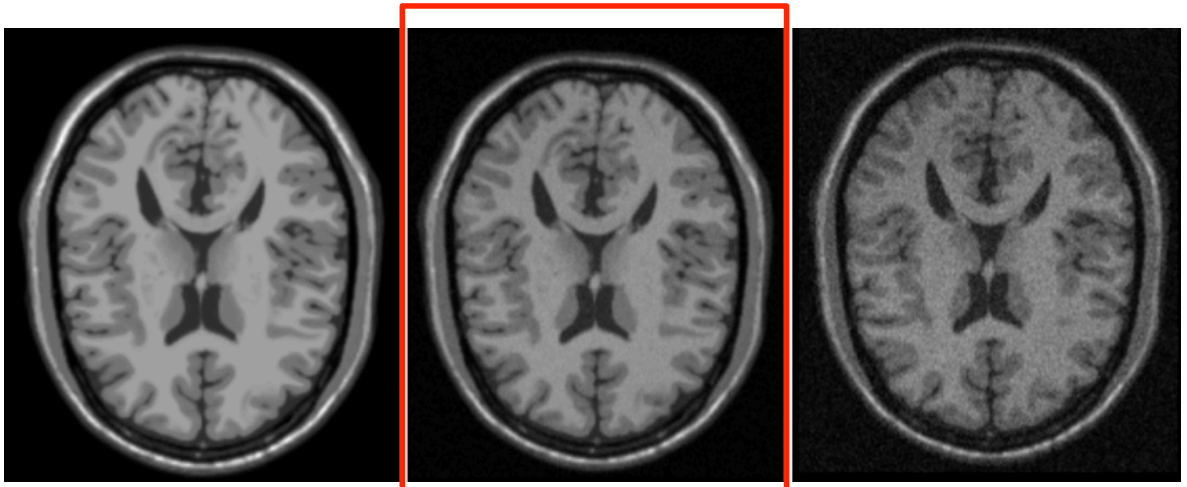
Image volume: 181x217x181mm

Intensity range: 0-255

Noise: 0%, 3%, 5%, 7%, 9%

RF Bias-Field: 0%, 20%,40%

15 slices samples



noise 0% - RF bias 0%

noise 3% - RF bias 20%

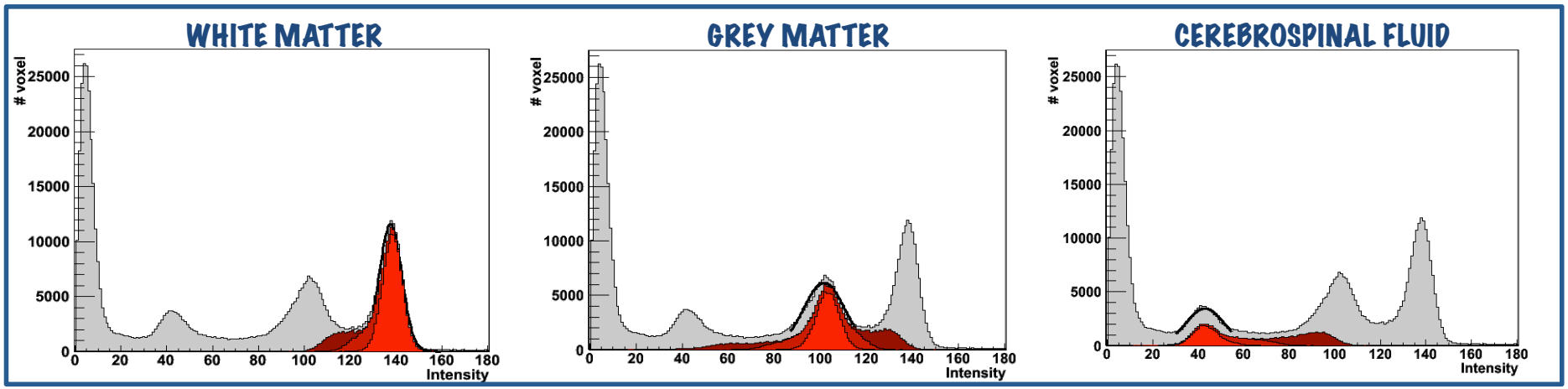
noise 9% - RF bias 40%

PHEROMONE DEPOSITION RULE

Considering the intensity distribution of the images, a gaussian pheromone deposition rule represents a good choice:

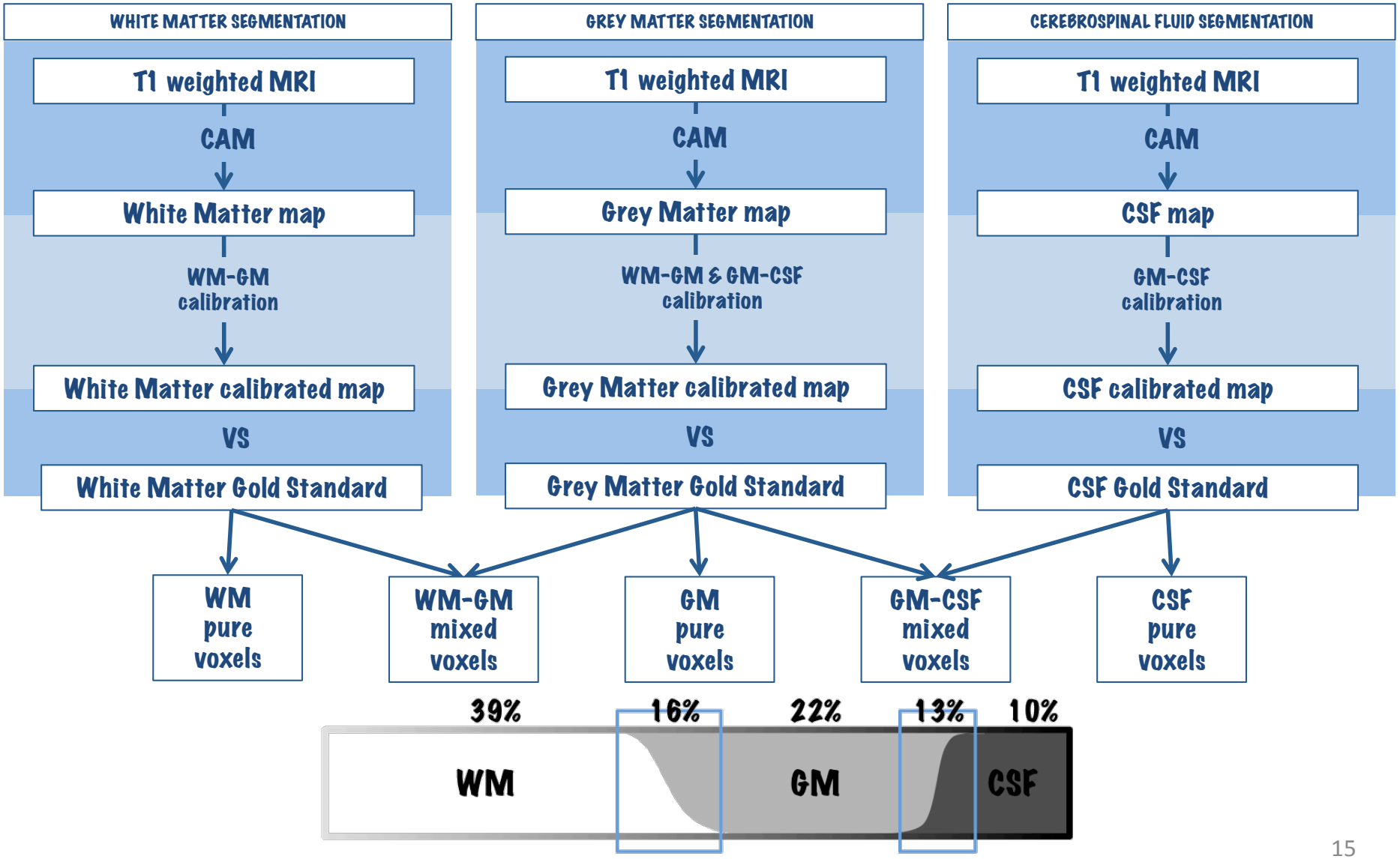
$$\Delta_{ph} = e^{-\frac{(I-<I>)^2}{2*s^2}}$$

Average Intensity: <I>
Intensity Standard Deviation: σ
s = 2σ

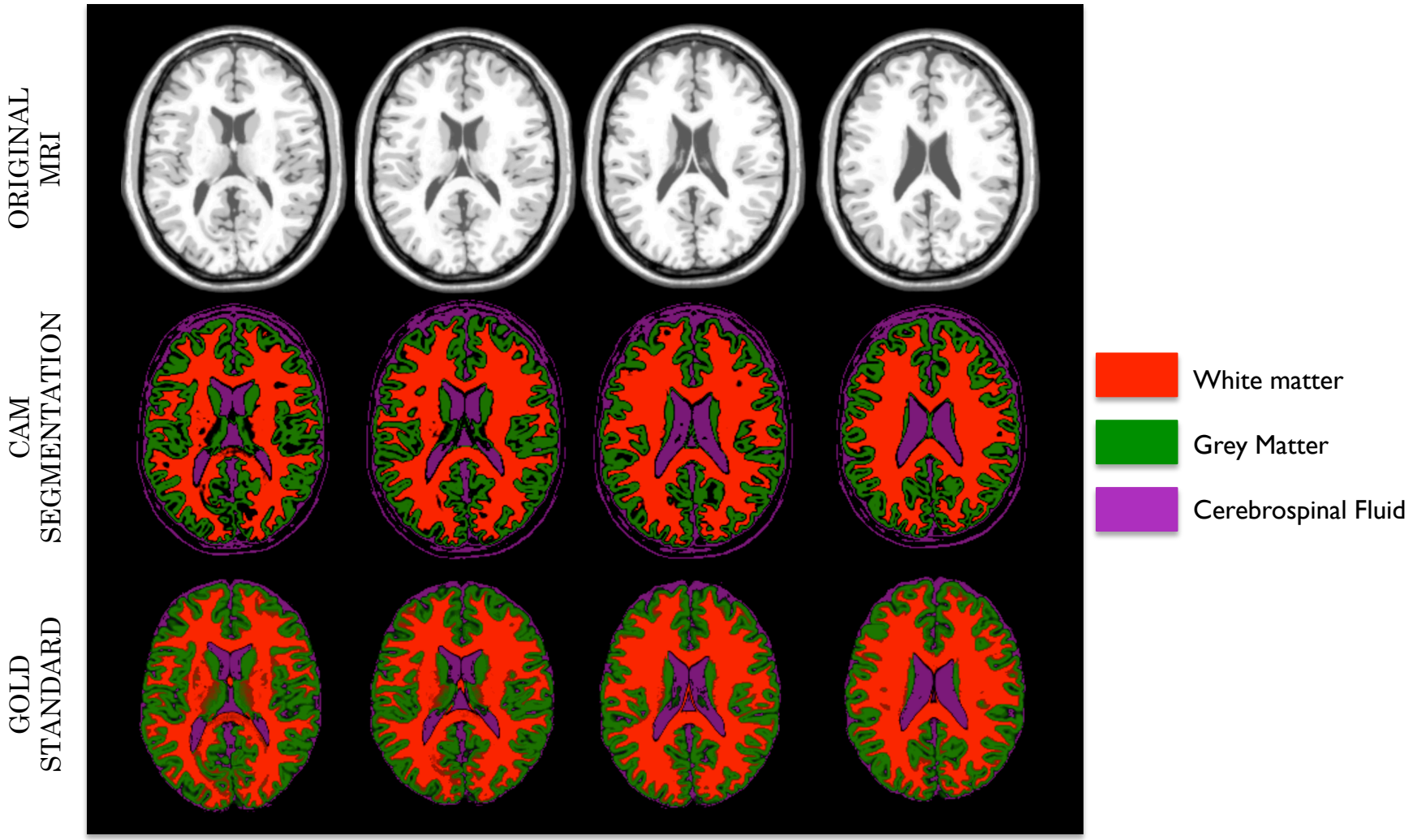


GOLD STANDARD:

SEGMENTATION WORKFLOW

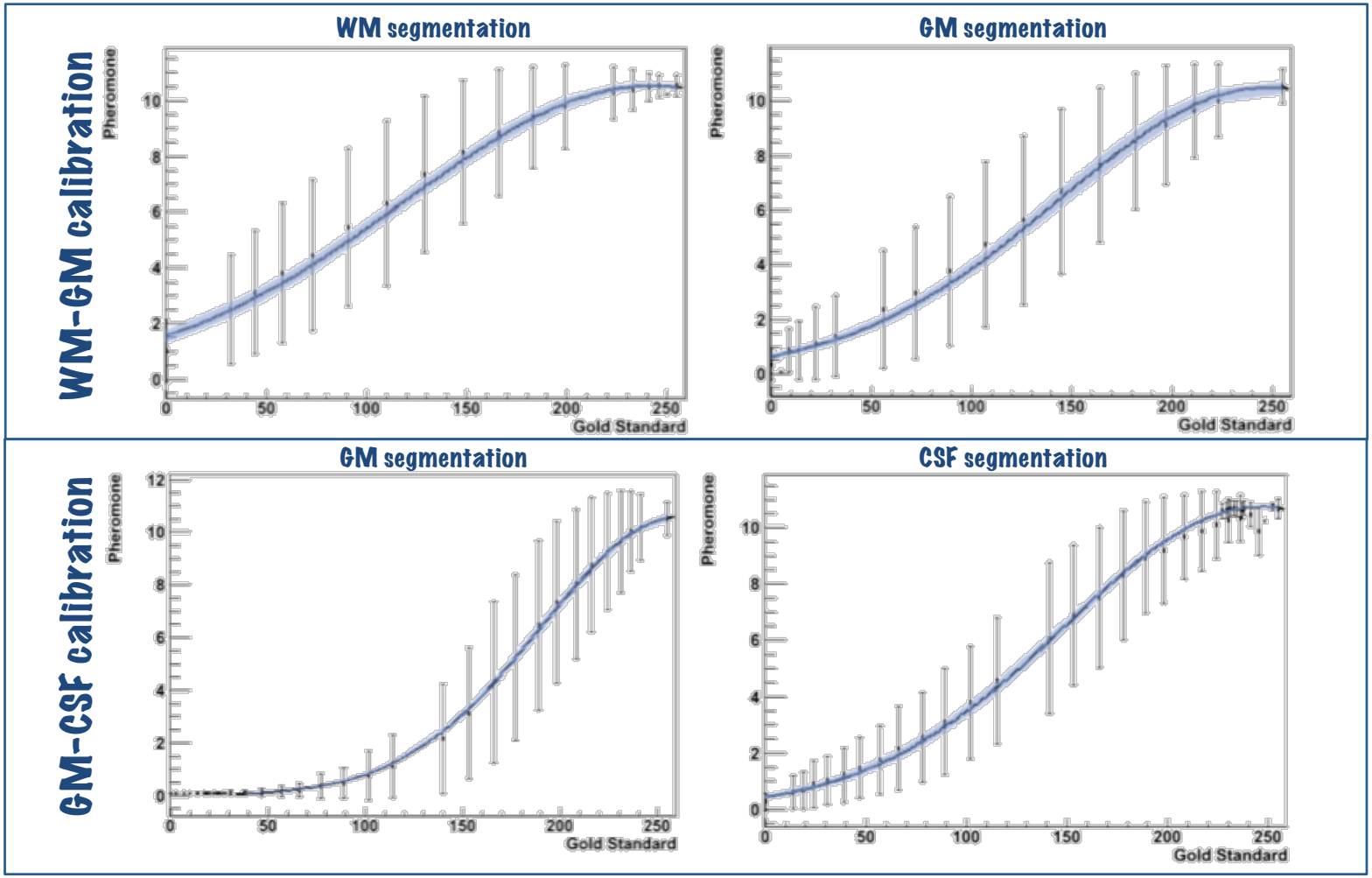


WM, GM & CSF PHEROMONE MAPS



MIXED VOXELS CALIBRATION

There is a correlation between the gold standard value and the average pheromone release: in the graphs the gaussian fits are shown.



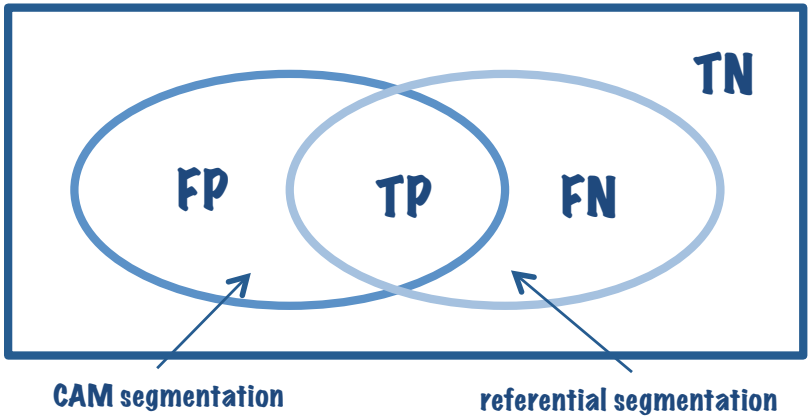
EVALUATION METRICS

True Positive TP

True Negative TN

False Positive FP

False Negative FN



Sensitivity

$$S = \frac{TP}{TP + FN}$$

Specificity

$$s = \frac{TN}{TN + FN}$$

Contamination

$$c = \frac{FP}{TP + FN}$$

Dice Index

$$D = \frac{2TP}{2TP + FP + FN}$$

Jaccard Similarity Index

$$J = \frac{TP}{TP + FP + FN}$$

Relative Absolute Volume Difference

$$RAVD = \frac{FP - FN}{TP + FN}$$

Relative Intensity Difference

$$RID = \frac{I_{CAM} - I_{GS}}{\max(I_{GS})}$$

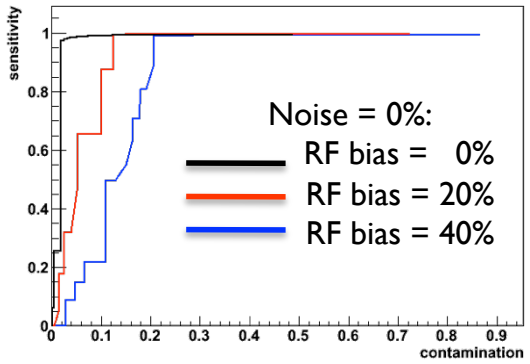
PURE VOXELS ANALYSIS

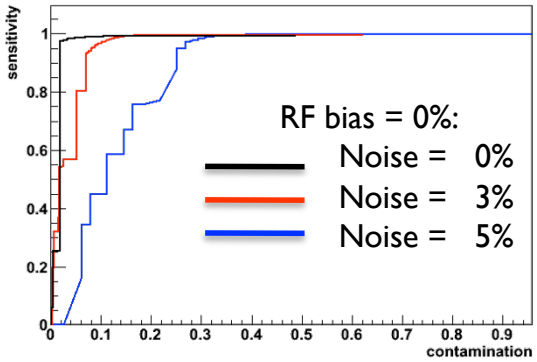
Sensitivity vs Contamination (ROC curves)

The CAM performance depends on the noise level and on the RF bias-field.

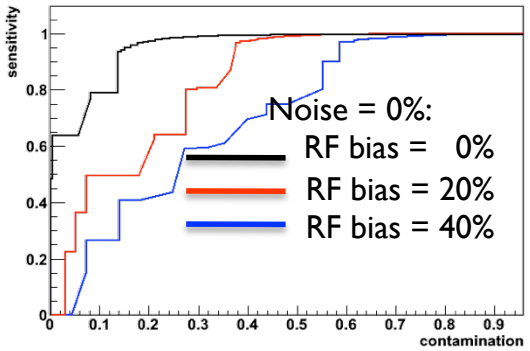
The Grey Matter is the most difficult tissue to segment: the contamination depends on its shape (a lot of waves) and on its intensity features (the Grey Matter peak is in the middle).

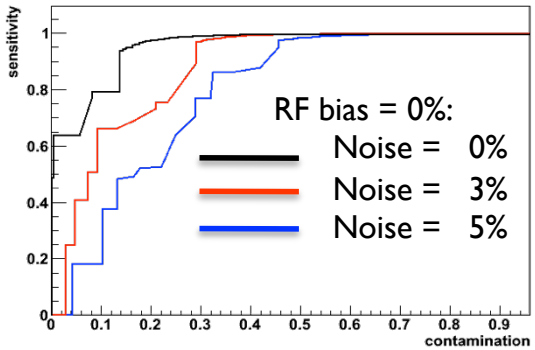
WHITE MATTER



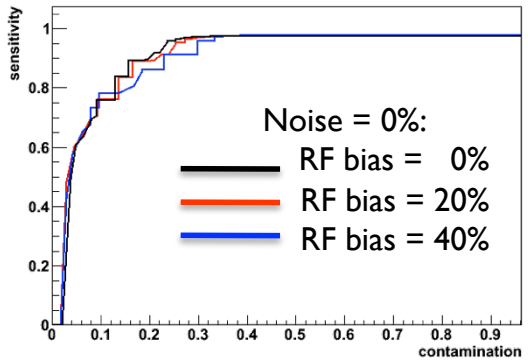


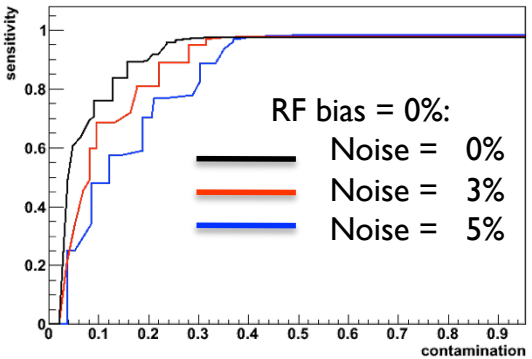
GREY MATTER





CEREBRO SPINAL FLUID

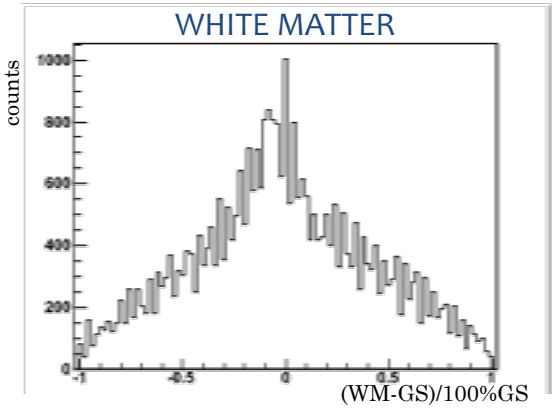


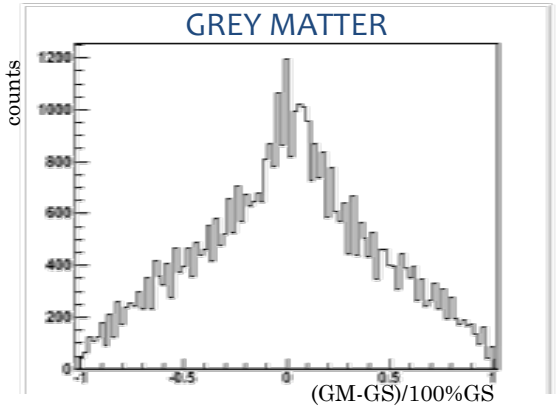


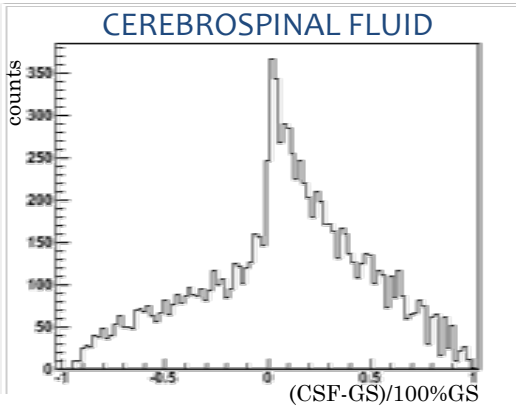
MIXED VOXELS ANALYSIS

Relative Intensity Difference

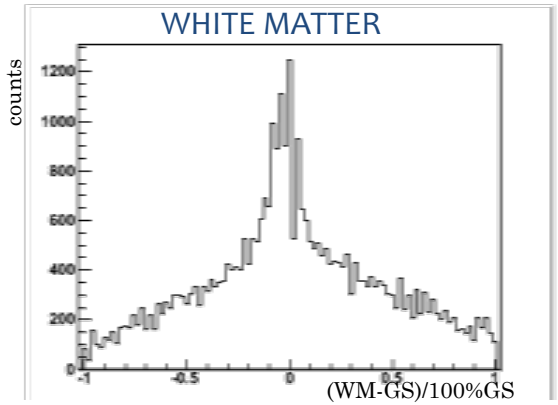
1) Considering only the WM and the CSF segmentations, obtaining the GM through the difference

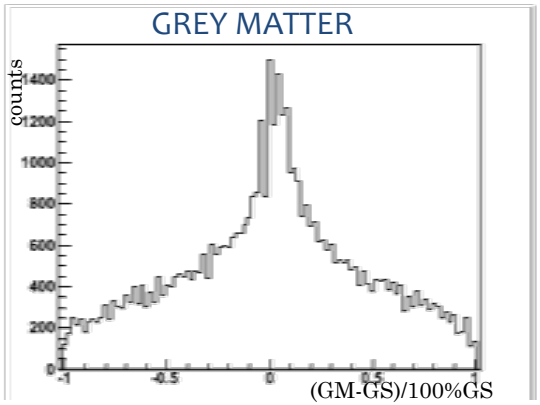


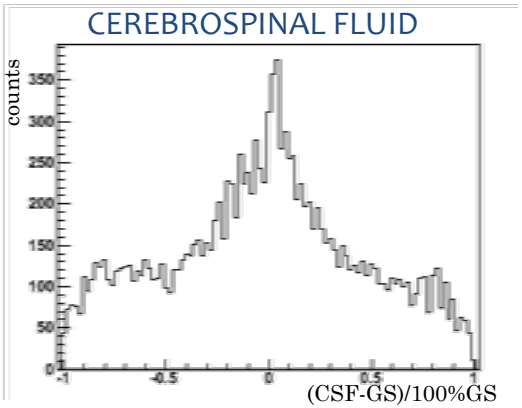




2) Considering the WM, the GM and the CSF segmentations







RESULTS & DISCUSSION (II)

noise	RF bias	WM S	WM C	WM SI	GM S	GM C	GM SI	CSF S	CSF C	CSF SI
0%	0%	0.98	0.02	0.95	0.94	0.14	0.82	0.96	0.25	0.77
0%	20%	0.99	0.12	0.88	0.97	0.29	0.75	0.96	0.27	0.76
0%	40%	0.99	0.21	0.82	0.97	0.45	0.67	0.97	0.33	0.73
3%	0%	0.93	0.07	0.87	0.97	0.38	0.70	0.97	0.31	0.74
3%	20%	0.98	0.20	0.82	0.96	0.40	0.68	0.97	0.33	0.73
3%	40%	0.98	0.22	0.80	0.97	0.61	0.60	0.98	0.39	0.70
5%	0%	0.97	0.27	0.77	0.97	0.59	0.61	0.97	0.37	0.71
5%	20%	0.97	0.25	0.77	0.98	0.70	0.58	0.96	0.35	0.71
5%	40%	0.97	0.27	0.77	0.97	0.80	0.54	0.96	0.37	0.70

noise	RF bias	WM * SI
0%	0%	0.95
0%	20%	0.93
0%	40%	0.92
3%	0%	0.91
3%	20%	0.91
3%	40%	0.88
5%	0%	0.90
5%	20%	0.87
5%	40%	0.86

[P. Huang, H. Cao and S. Luo. An artificial ant colonies approach to medical image segmentation. Computer Methods and Program in Biomedicine 92 (2008) 267-273]

The CAM segmentations for the pure voxels reach a high sensitivity with a contamination that is strongly dependent on the tissue, the noise level and the RF bias-field

* The authors of this article considered only the segmentation of the pure voxels and they did not try to obtain a quantitative segmentation

RESULTS & DISCUSSION (II)

Mixed voxels: RID acceptance level = 0.15

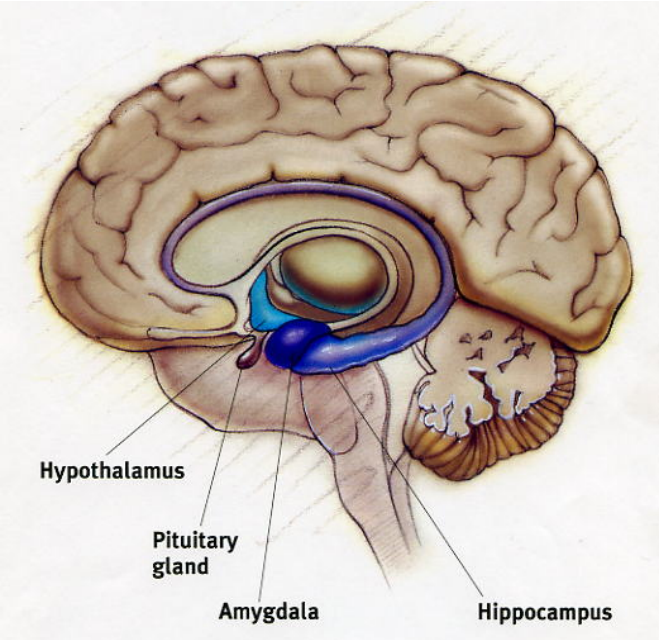
Voxels that are correctly segmented

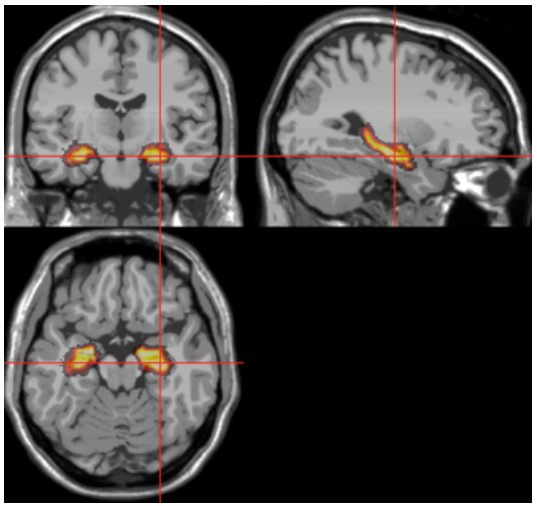
noise	RF bias	WM-CSF	WM-GM-CSF
0%	0%	72%	73%
0%	20%	71%	73%
0%	40%	71%	72%
3%	0%	72%	74%
3%	20%	71%	74%
3%	40%	71%	72%
5%	0%	71%	73%
5%	20%	71%	72%
5%	40%	69%	69%

The voxels that have a Relative Intensity Difference smaller than 0.15 are considered to be correctly segmented.
The CAM performance improves by considering all the three segmentations.

HIPPOCAMPUS SEGMENTATION (I)

- The hippocampus is a paired structure, it belongs to the medial temporal lobe and plays an important role in memory
- **The hippocampus is made almost by grey matter, surrounded and linked to other grey matter structures (e.g.the Amygdala)**
- It is involved in many neurological pathologies and psychiatric disorders, such as the Alzheimer's Disease, schizophrenia, epilepsy and depression.
- Quantifying the atrophy of the hippocampus is important for the diagnosis.
- Studying the hippocampus volume variation in time is helpful for the therapy assessment.
- The hippocampus segmentation can be carried out thanks to the magnetic resonance imaging (MRI), in particular T1 weighted





HIPPOCAMPUS SEGMENTATION (II)

- **The gold standard hippocampus segmentation is the manual segmentation**
- There are several manual segmentation protocols of the hippocampal volume: a volume difference of more than 50% can be reached
- The contours are not always well-contrast defined: e.g. in the hippocampus head some manual protocols adopt arbitrary lines

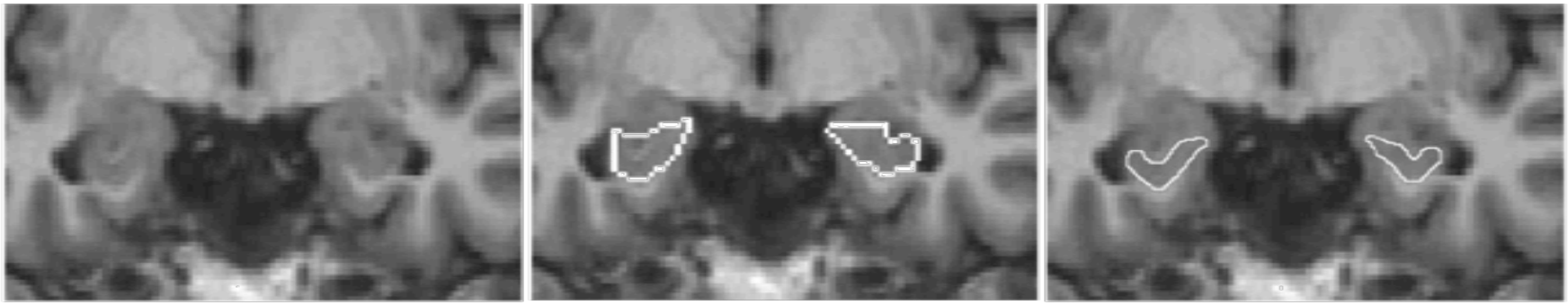


Fig. 3 Coronal section of slice Number 65 of image IBSR_07_ana.img from the IBSR data set. **a** The original image; **b** Manual outlines of the hippocampi provided by the IBSR; **c** Our proposed manual outlines

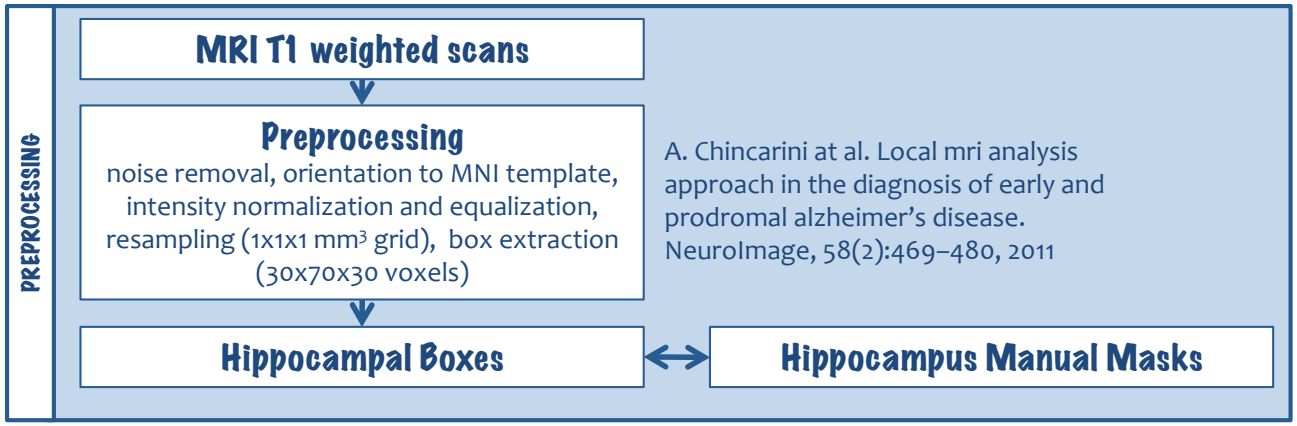
[K. Jafari-Khouzani, K. V. Elisevich, S. Patel, and H. Soltanian-Zadeh. Dataset of magnetic resonance images of nonepileptic subjects and temporal lobe epilepsy patients for validation of hippocampal segmentation techniques. Neuroinformatics, 2011]

HIPPOCAMPUS DATABASES (I)

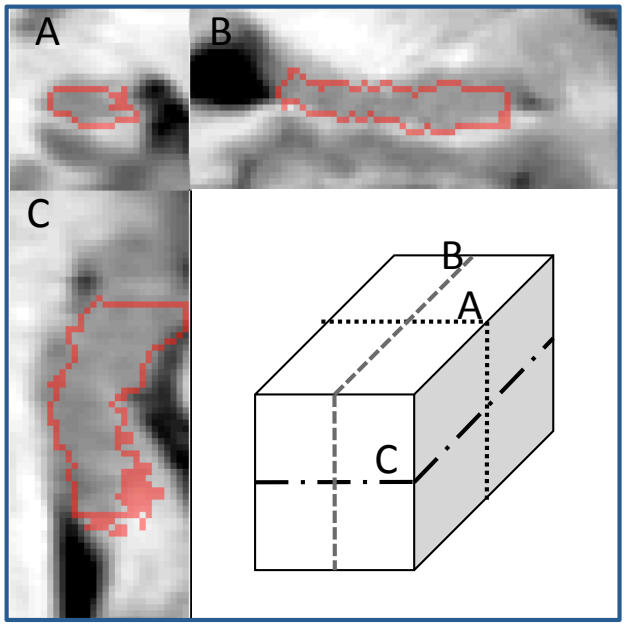
name	num. of images	voxel size [mm^3]	MRI scan type	diagnosis	manual masks
Brescia L	56	1.00 x 1.50 x 1.00	1.5 T	MCI - SMC	x
Brescia R	56	1.00 x 1.50 x 1.00	1.5 T	MCI - SMC	x
HD train L	25	0.78 x 0.78 x 2.00 0.39 x 0.39 x 2.00	1.5 T 3.0 T	Epilepsy - Ctrl	x
HD train R	25	0.78 x 0.78 x 2.00 0.39 x 0.39 x 2.00	1.5 T 3.0 T	Epilepsy - Ctrl	x
HD test L	25	0.78 x 0.78 x 2.00 0.39 x 0.39 x 2.00	1.5 T 3.0 T	Epilepsy - Ctrl	(x)
HD testR	25	0.78 x 0.78 x 2.00 0.39 x 0.39 x 2.00	1.5 T 3.0 T	Epilepsy - Ctrl	(x)
Adni L	380		1.5 T	AD – EMCI – MCI - Ctrl	-
Adni R	380		1.5 T	AD – EMCI – MCI - Ctrl	-

AD – Alzheimer's Disease
MCI – Mild Cognitive Impairment
Ctrl – Healthy Control
EMCI – Early Mild Cognitive Impairment
SMC – Subject Memory Complaints

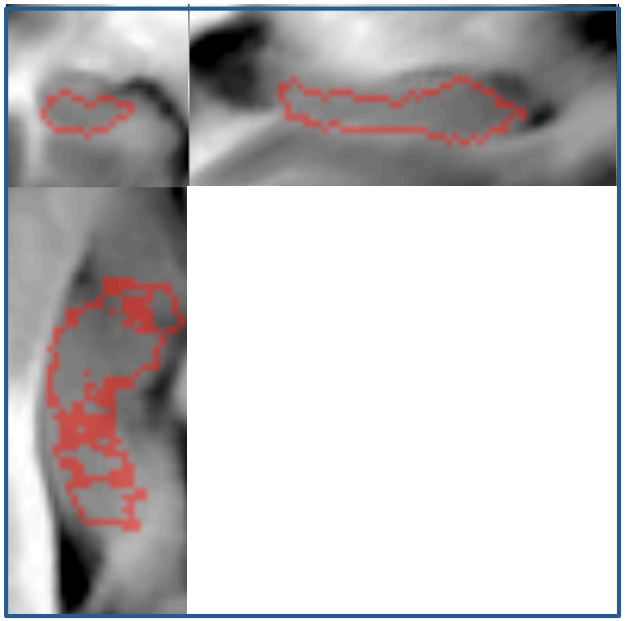
HIPPOCAMPUS DATABASES (II)



Brescia Database



HD train Database



www.radiologyresearch.org/HippocampusSegmentation Database/

PHEROMONE DEPOSITION RULE (I)

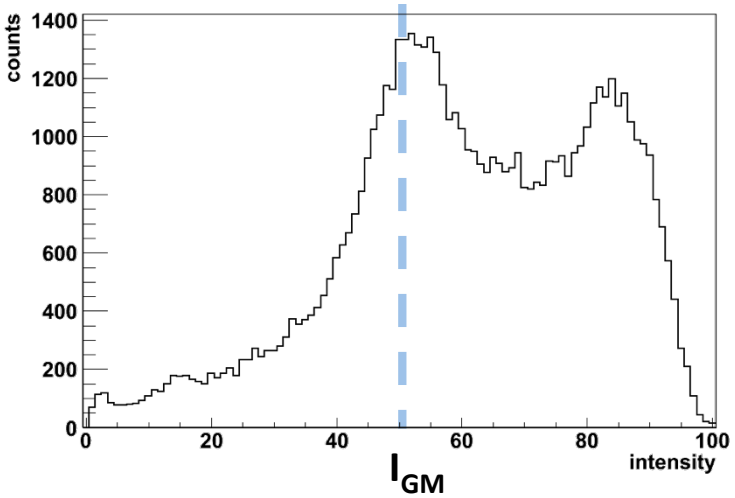
The quantity of pheromone released in the voxel v_i is:

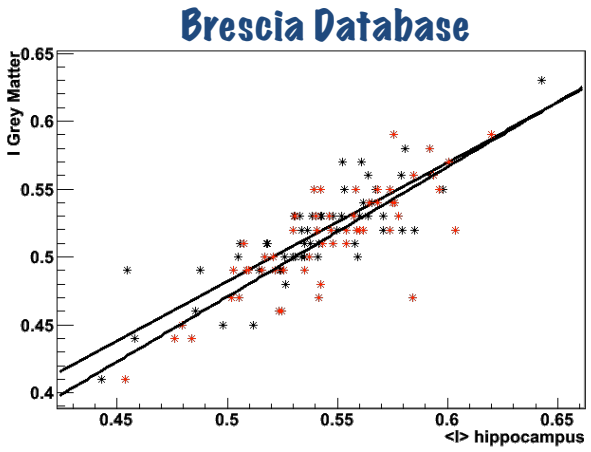
$$\Delta_{ph}(v_i) = k\ \delta_I(v_i) + (1-k)\delta_S(v_i)$$

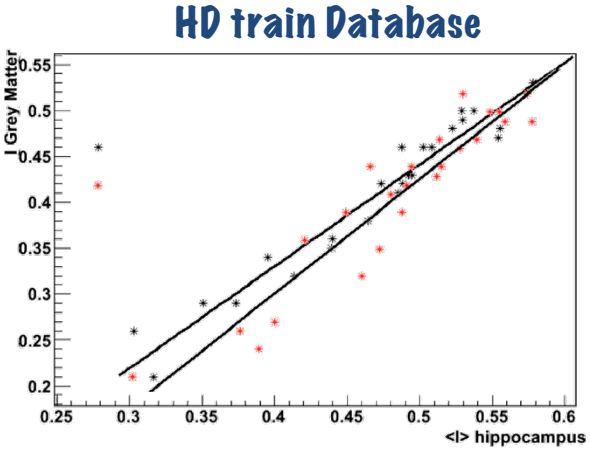
k = 0.5
$0 \le \delta_I \le 1$
$0 \le \delta_S \le 1$

The term $\delta_I(v_i)$ is given by:

$$\delta_I(v_i) = 1 - 2\frac{|I_{GM} - I(v_i)|}{I_{max} - I_{min}}$$





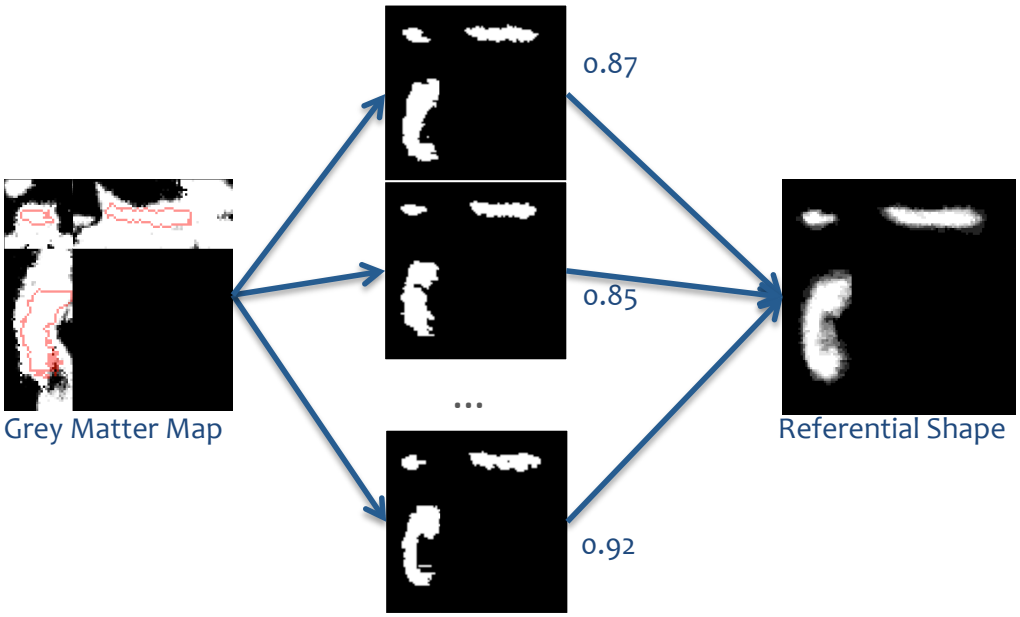


PHEROMONE DEPOSITION RULE (II)

The term $\delta_S(v_i)$ is calculated building a referential shape for the hippocampus.

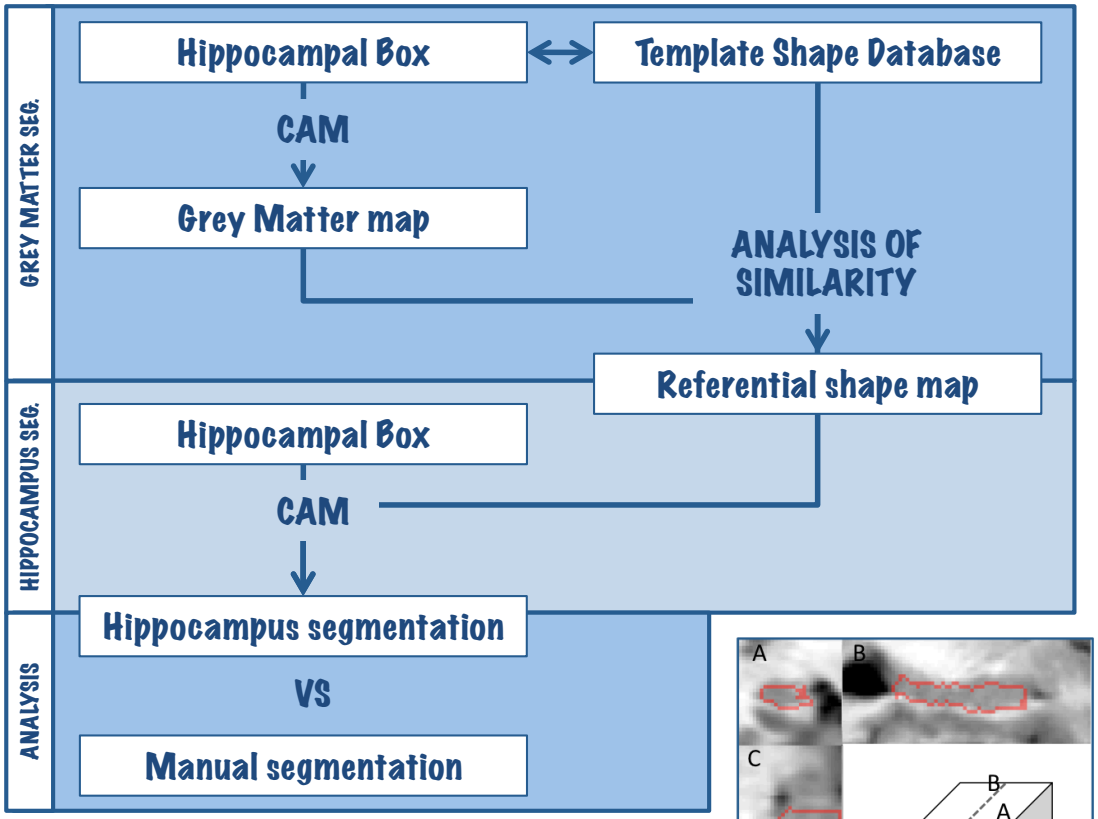
To compare the Grey Matter Map with the masks of the **Template Shape Database** and choose the best N (N=10) shapes, the ε index is used:

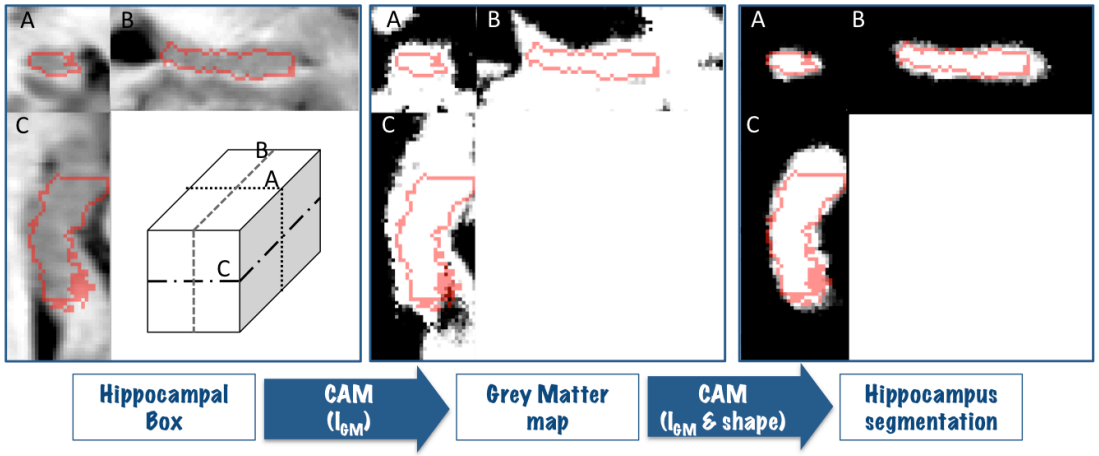
$$\epsilon = 1 - \frac{1}{n_{TP}} \sum_{i=1}^{n_{TP}} |I_{GM}(i) - I_{TP}(i)|$$



Hence, the term $\delta_S(v_i)$ is given by: $\delta_S(v_i) = I_{SH}(v_i)$

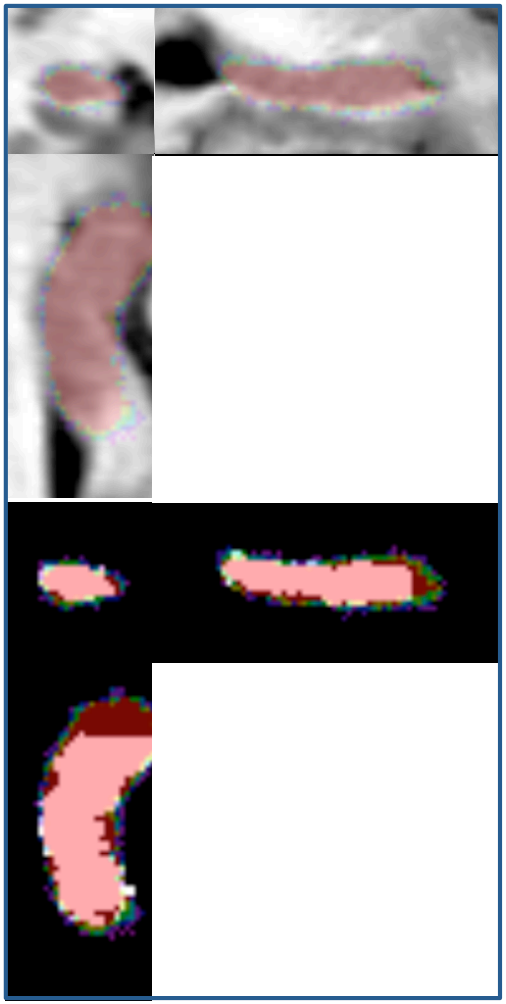
SEGMENTATION WORKFLOW



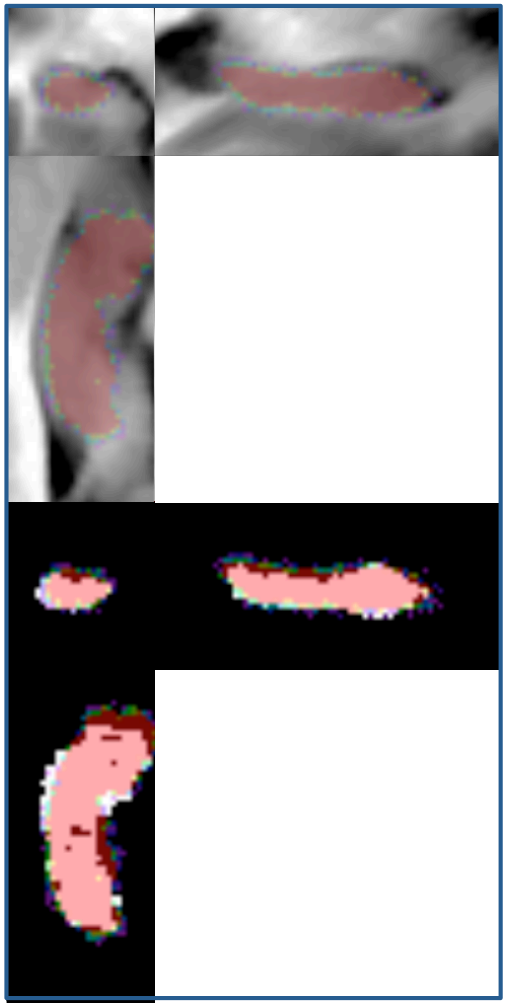


HIPPOCAMPUS PHEROMONE MAPS

Brescia Database



HD train Database



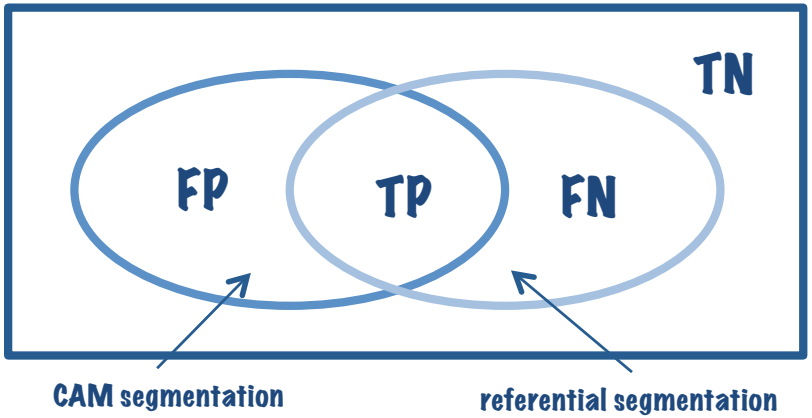
EVALUATION METRICS

True Positive TP

True Negative TN

False Positive FP

False Negative FN



Sensitivity

$$S = \frac{TP}{TP + FN}$$

Specificity

$$s = \frac{TN}{TN + FN}$$

Contamination

$$c = \frac{FP}{TP + FN}$$

Dice Index

$$D = \frac{2TP}{2TP + FP + FN}$$

Jaccard Similarity Index

$$J = \frac{TP}{TP + FP + FN}$$

Relative Absolute Volume Difference

$$RAVD = \frac{FP - FN}{TP + FN}$$

Relative Intensity Difference

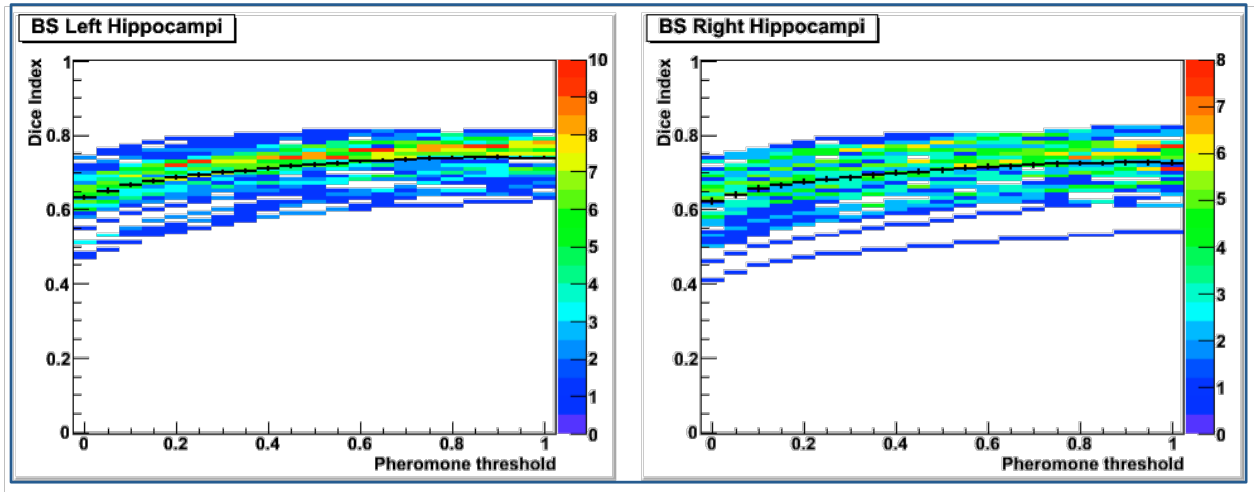
$$RID = \frac{I_{CAM} - I_{GS}}{\max(I_{GS})}$$

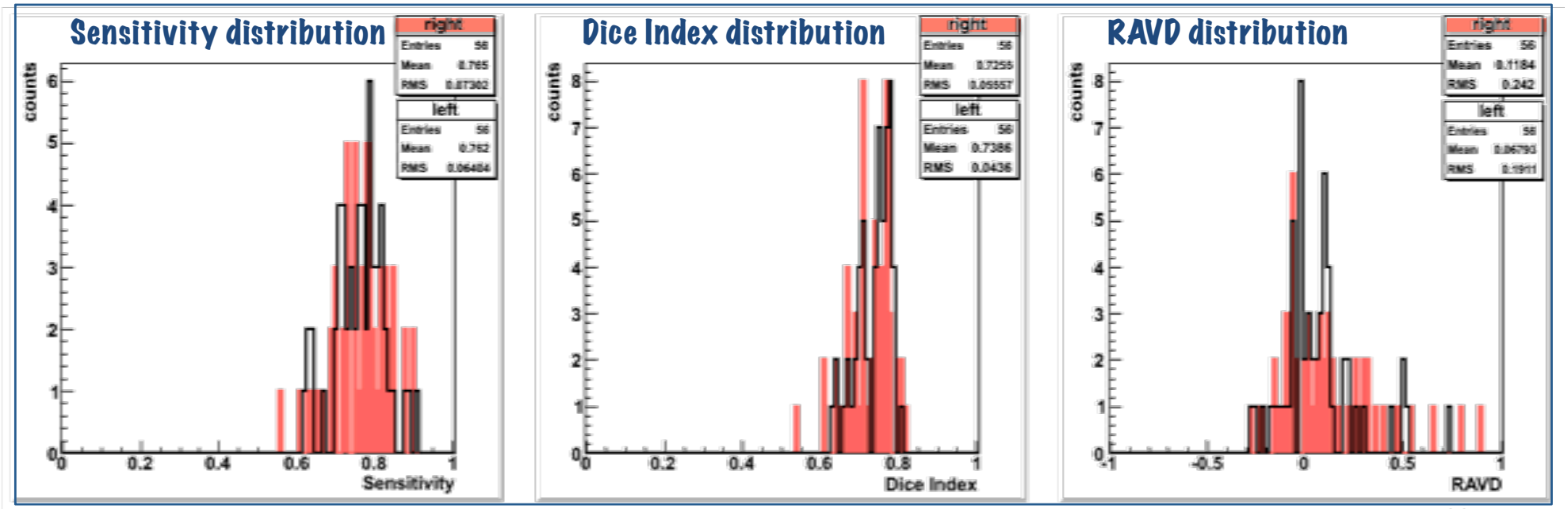
BRESCIA DATABASE ANALYSIS (I)

Dice Index vs pheromone threshold

The maximum <D> is obtained almost at the saturation level, which is selected as the threshold value for further analysis.

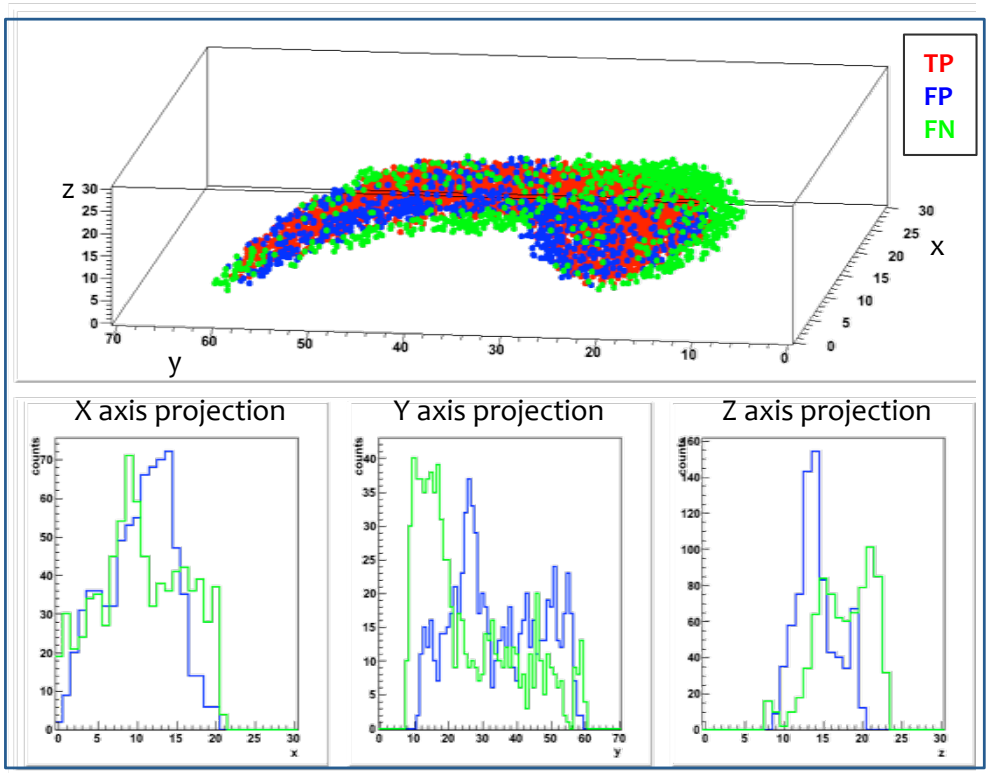
<D>=0.70±0.05(L) 0.67±0.06(R)
<S>=0.71± 0.08(L) 0.70±0.07(R)
<s>=0.983±0.007(L) 0.981±0.006(R)
<RAVD>=0.05±0.25(L) 0.09±0.22(R)

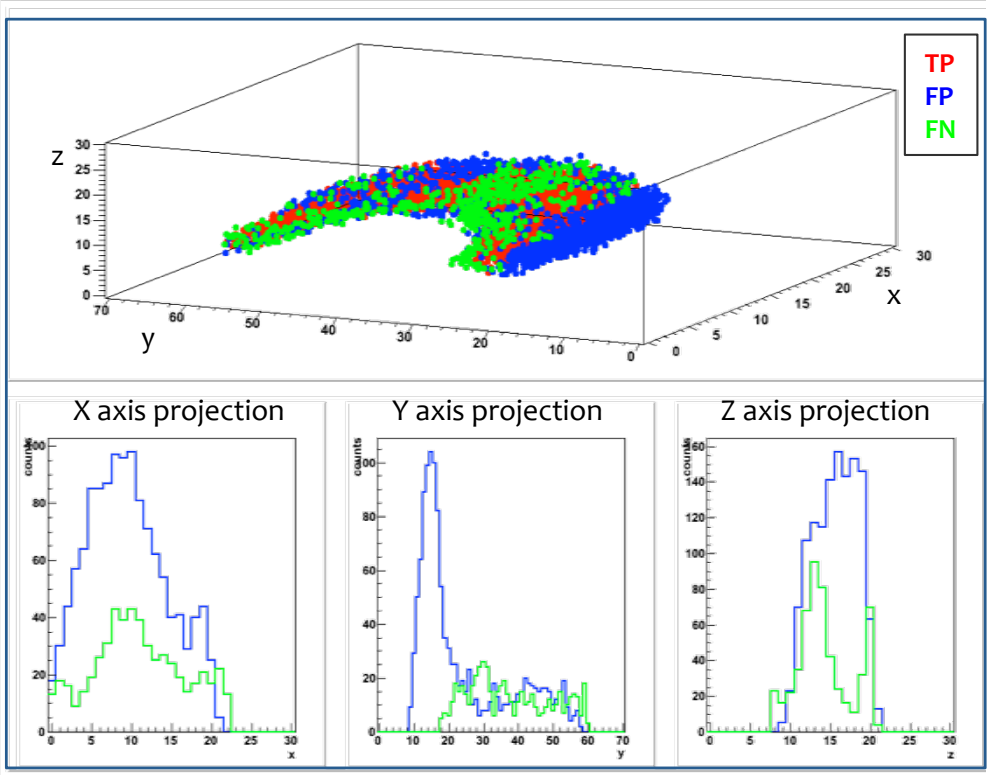




BRESCIA DATABASE ANALYSIS (II)

Examples of the TP, FP and FN 3D distributions





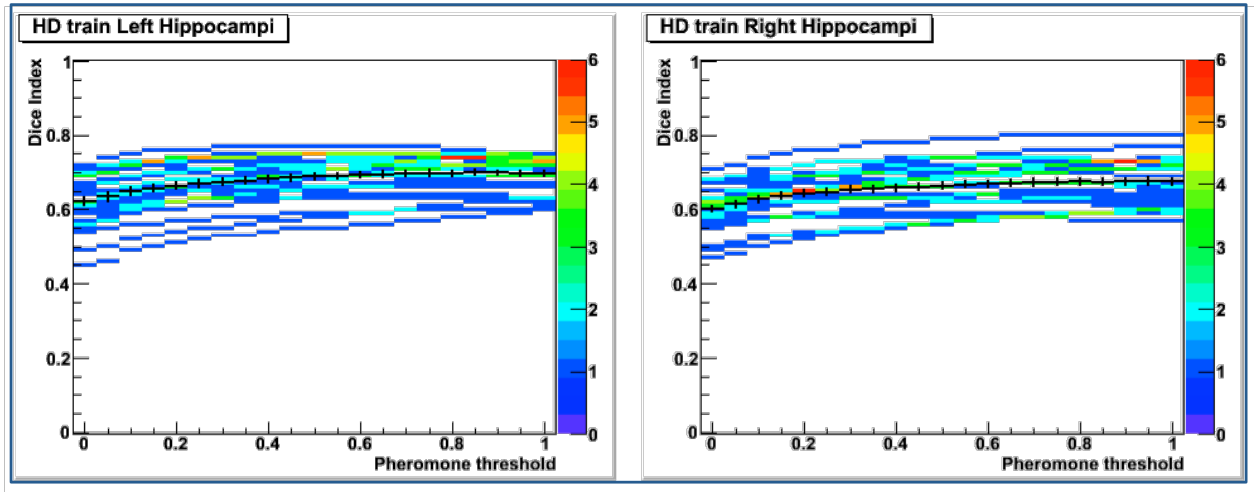
The segmentation reaches a good performance inside the hippocampus.
The head and the tail are the regions more affected by FP and FN while the back is really well segmented because of its anatomical nearness to the cerebrospinal fluid.

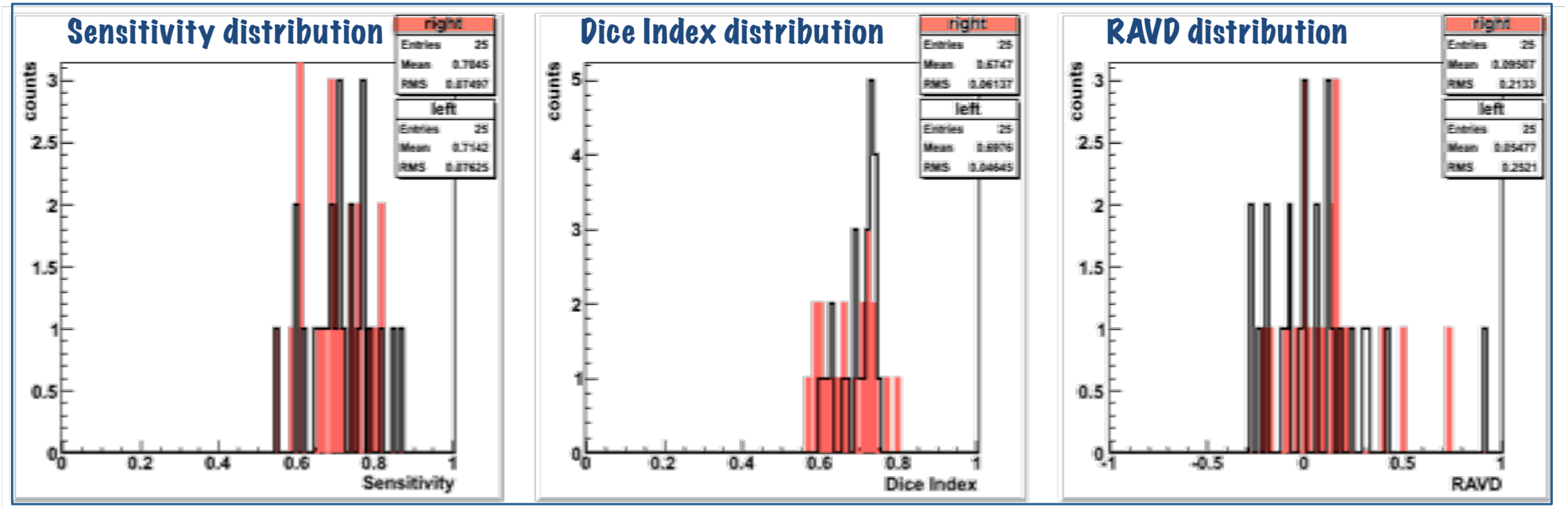
HD TRAIN DATABASE ANALYSIS (I)

Dice Index vs pheromone threshold

The pheromone threshold is set to the pheromone saturation value.

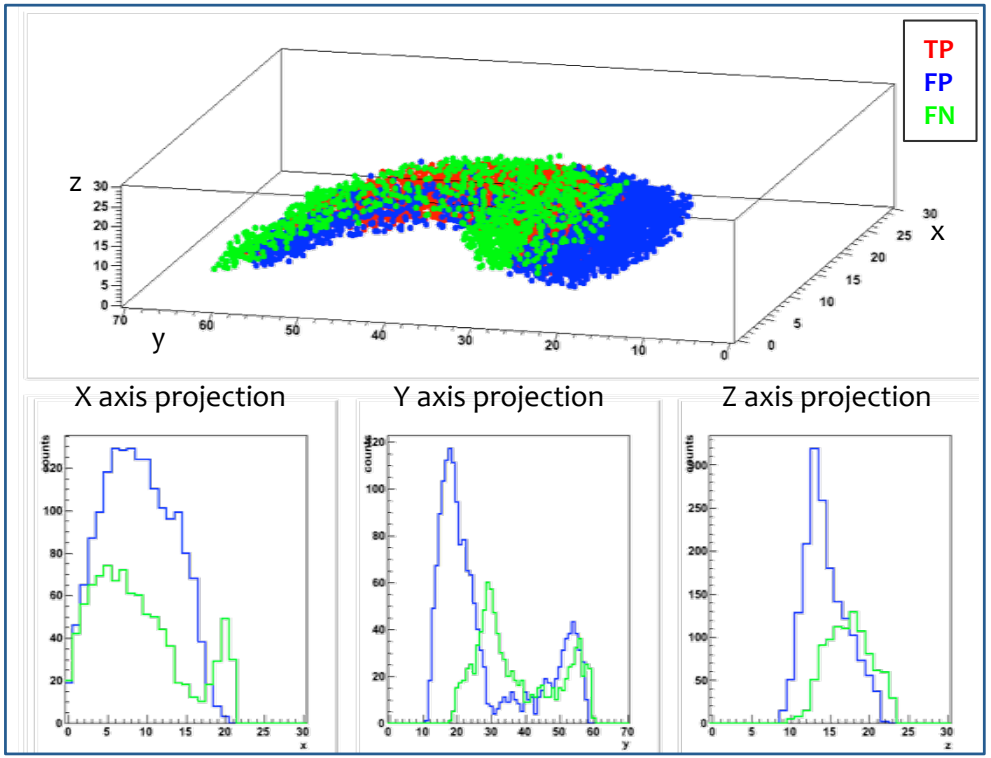
<D>=0.74±0.04(L) 0.72±0.05(R)
<S>=0.76± 0.06(L) 0.76±0.07(R)
<s>=0.986±0.005(L) 0.986±0.006(R)
<RAVD>=0.07±0.19(L) 0.12±0.24(R)

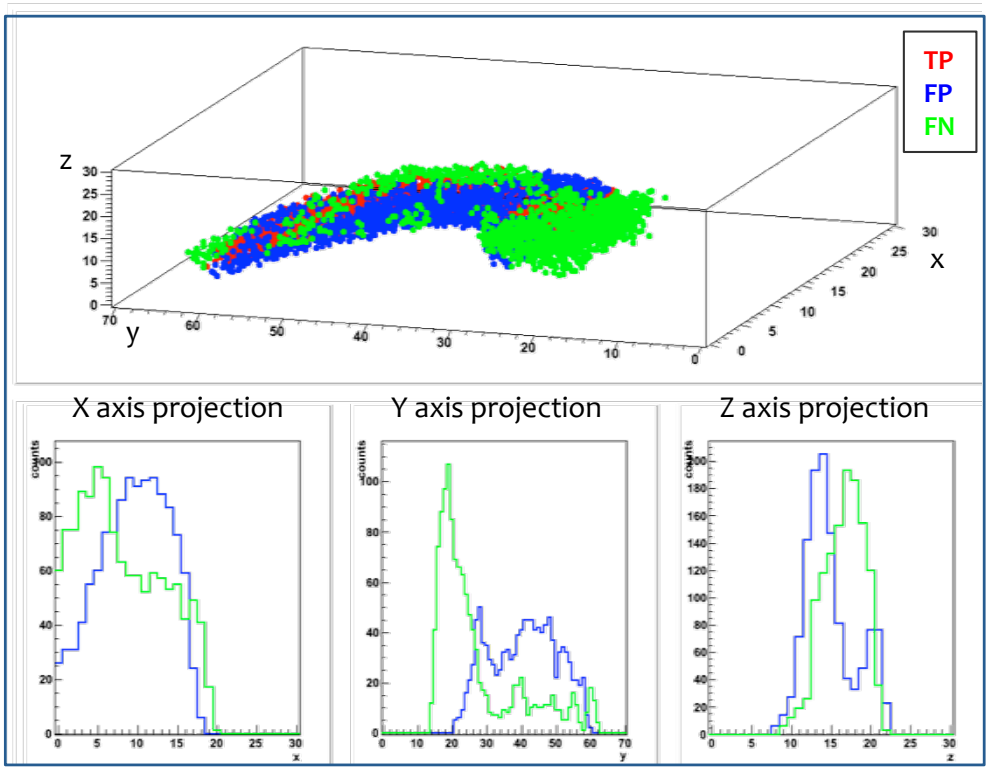




HD TRAIN DATABASE ANALYSIS (II)

Examples of the TP, FP and FN 3D distributions





The fraction of FP and FN is larger than in the previous database: it must be remarked that, for the HD Train segmentation, the leave-one-out technique is not applied.

In fact, in this case, the 56 Brescia manual masks are used as template shapes and the HD Train images are a completely new and unknown dataset.

RESULTS & DISCUSSION

name	<S>	<s>	<RAVD>	<D>
Brescia L	0.76 ± 0.06	0.986 ± 0.005	0.07 ± 0.19	0.74 ± 0.04
Brescia R	0.76 ± 0.07	0.986 ± 0.006	0.12 ± 0.24	0.72 ± 0.05
HD train L	0.71 ± 0.08	0.983 ± 0.007	0.05 ± 0.25	0.70 ± 0.05*
HD train R	0.70 ± 0.07	0.981 ± 0.006	0.09 ± 0.22	0.67 ± 0.06*

article	segmentation tool	database	<D>
[1]	ITK SNAP	10 subjects	0.58 ± 0.06
[1]	Local affine and Demons free-form transformations	10 subjects	0.77 ± 0.06
[2]	SPM5	27 patients with different type of dementia, 9 controls	0.70 ± 0.07 0.69 ± 0.05
[3]	FreeSurfer	25 AD, 23 MCI, 41 controls	0.79 ± 0.10 0.76 ± 0.06
[4]	Brain Parser	HD train & HD test	0.64 ± 0.06*
[4]	Classifier Fusion and Labeling	HD train & HD test	0.75 ± 0.07*

[1] X. Lin, T. Qiu, F. Morain-Nicolier, and S. Ruan. Automatic hippocampus segmentation from brain mri images. International Journal of Computer Information Systems and Indus- trial Management Applications, 2:1–10, 2010

[2] M. J. Firbank, R. Barber, E. J. Burton, and J. T. O'Brien. Validation of a fully automated hippocampal segmentation method on patients with dementia. Human Brain Mapping, 29(12):1442–1449, 2008

[3] G. Sanchez-Benavides, B. Gomez-Anson, A. Sainz, Y. Vives, M. Delfino, and J. Pena-Casanova. Manual validation of freesurfer's automated hippocampal segmentation in normal aging, mild cognitive impairment, and alzheimer's disease subjects. Psychiatry Research, 181(3):219–225, 2010

[4] K. Jafari-Khouzani, K. V. Elisevich, S. Patel, and H. Soltanian-Zadeh. Dataset of magnetic resonance images of nonepileptic subjects and temporal lobe epilepsy patients for validation of hippocampal segmentation techniques. Neuroinformatics, 2011

*The CAM results are calculated over the 30x70x30 boxes instead in [4] the index over the original voxel size image is reported.

CONCLUSIONS

WM, GM and CSF segmentations

- The gaussian pheromone deposition rule is a good choice.
- The CAM is adaptable to images with different values of noise and RF bias-field.
- The CAM parameters are the same used for the artificial objects and for the lung CTs: only the pheromone deposition rule changes.

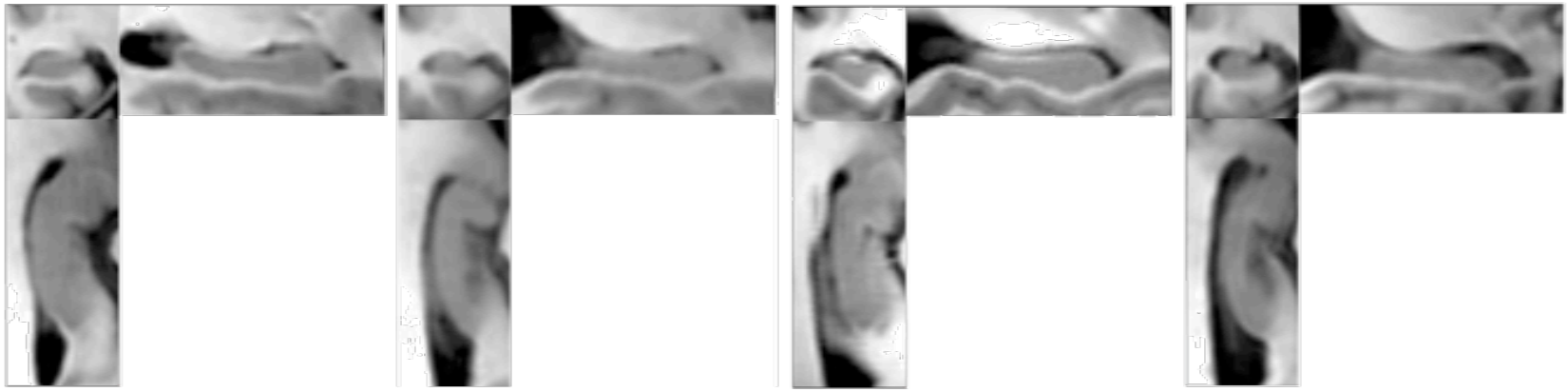
Hippocampus segmentation

- The pheromone deposition rule must be based both on the intensity and on the shape
- The building of the referential shape is a general approach that seems not to be strongly dependent on the manual segmentation protocol in use
- The CAM performance is comparable to others approaches
- The lack of a heavy training procedure (because all the model parameters are fixed) and the speed make this approach very effective
- The HD Train Database results are comparable to the published ones

PROSPECTS (II)

Hippocampus segmentation

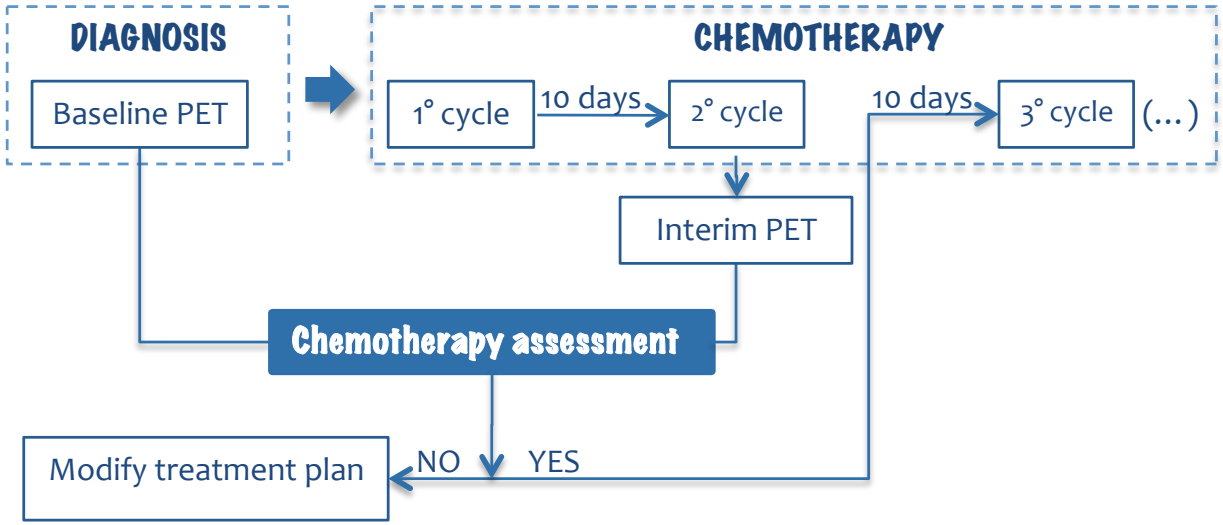
- The **Template Shape Database** can be extended
  - considering more manual masks
  - it will become more general and representative of the hippocampus population
- The procedure to calculate the **referential shape** can be optimized
  - optimizing the number of masks to be considered
  - considering also other features of the images (e. g. the intensity of the voxels)
- The analysis on other databases (**HD test and ADNI**) is ongoing
  - a more detailed comparison to other published results
  - Study of the clinical response (i. e. hippocampus volume analysis)



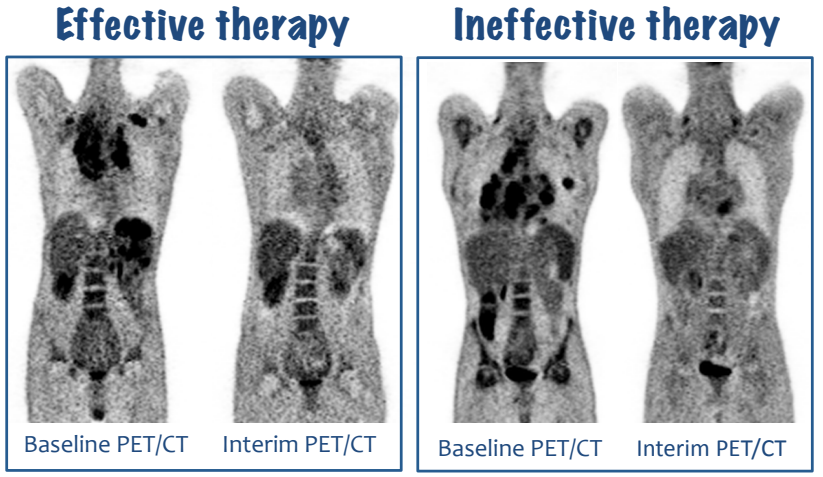
PROSPECTS (II)

Positron Emission Tomography segmentation: Lymphoma chemotherapy assessment

Lymphoma is a cancer that involves the lymphatic cells. It is curable by chemotherapy depending on the histology, type and stage.



Several innovative trials are being promoted to reach a global consensus on the assessment of innovative drugs. The assessment is based on the reduction of the lymphoma volume.



CONFERENCES & PUBLICATIONS

- **IFA 2010**: E. Fiorina, R. Arteche Diaz, P. Bosco, G. Gargano, A. Massafra, R.Megna, C. Oppedisano and S. Valzano. *Channeler Ant Model: 3D segmentation of medical images through ant colonies*. Il Nuovo Cimento della Società Italiana di Fisica 34C (2011) 78–89
- **TMSi 2010**: E. Fiorina. *White matter segmentation in simulated MRI images using the Channeler Ant Model*, Proceedings of 6th TMSi, Technology and Medical Sciences, Taylor &Francis Group, London (2011) 301-304
- **CBMS 2012**: E.Fiorina, R. Bellotti, P. Cerello, A. Chincarini, I. De Mitri and M. E. Fantacci. *Fully automated hippocampus segmentation with virtual ant colonies*. Submitted.

- P. Cerello, S. C. Cheran, S. Bagnasco, R. Bellotti, L. Bolanos, E. Catanzariti, G. D. Nunzio, M. E. Fantacci, E. Fiorina, G. Gargano, G. Gemme, E. Lopez Torres, G. L. Masala, C. Peroni, and M. Santoro. *3-d object segmentation using ant colonies*. Pattern Recognition, 43(4):1476–1490, 2010
- R. Cataldo, A. Agrusti, G. De Nunzio, A. Carlà, I. De Mitri, M. Favetta, M. Quarta, L. Monno, L. Rei, E. Fiorina. *Generating a minimal set of templates for the hippocampal region in MR neuroimages*. Journal of Neuroimaging. In press.
- MeMeA 2011: A. Chincarini, R. Bellotti, G. Gemme, P. Bosco, M. Esposito, L. Rei, L. Monno and E. Fiorina. *Structural and functional brain imaging in the assessment of prodromal Alzheimer's disease.*

Thanks for your attention!