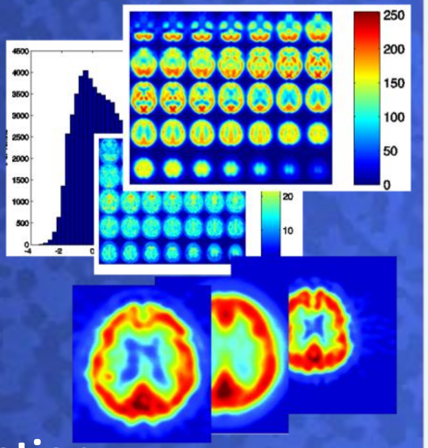
Effective Diagnosis of Alzheimer’s Disease by means of Association Rules



Rosa Chaves (rosach@ugr.es)

J. Ramírez, J.M. Górriz, M. López,

D. Salas-Gonzalez, I. Illán, F. Segovia, P. Padilla

Dpt. Theory of Signal, Networking and Communication

SIPBA Group: Signal Processing and Biomedical Applications

University of Granada, Spain

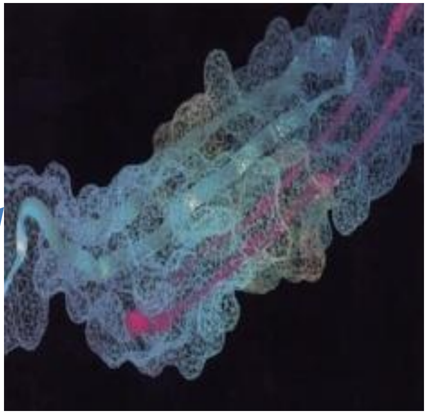
HAIS ’10 5th International Conference on HYBRID ARTIFICIAL INTELLIGENCE SYSTEMS

23rd-25th June, San Sebastián, Spain

Alzheimer's Disease

- AD is the most common cause of dementia in the elderly.
- It affects 30 million individuals worldwide
- A triplication over the next 30 years is expected
- There is no test or biomarker that can predict the development of AD
- the need for early recognition

  has been emphasized.



Sign of AD: tangles and plaques in the brain

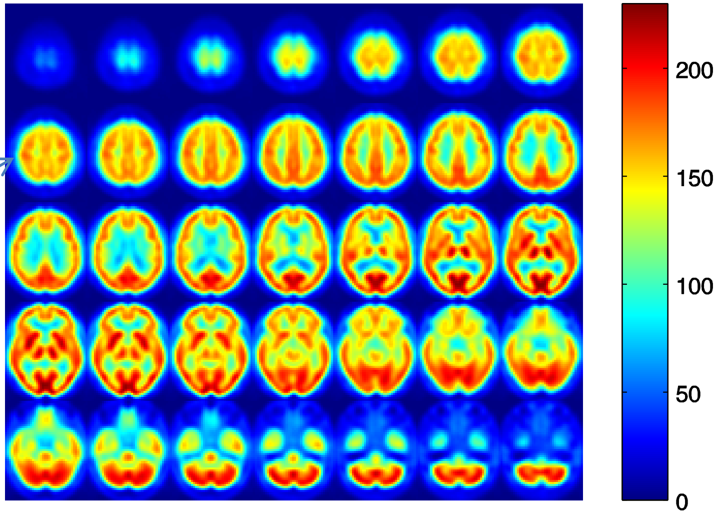
Early Diagnosis for the Alzheimer's Disease (AD)

- Diagnosis of the AD:
  - Based on neuropsychological tests and ***image techniques***
    - It offers difficulty even for a specialist (specially in the initial phase of the disease)
- *Early Diagnosis:*
  - It helps patients and their families to plan the treatment
  - No treatment for stopping the AD, there is medication that can prevent the worsening of some symptoms during a limited time.

Objective → ***Development of a Computed-Aided Diagnosis (CAD) system for the automatic detection of the AD***

Image Techniques: SPECT

- SPECT:
  - study functional properties of the brain
  - Cheaper but longer half-life of tracers than in PET
- SPECT Database:
  - Nuclear Medicine Service, *Virgen de Las Nieves* University Hospital
  - Gamma emiting ^{99m}Tc-ECD radiopharmaceutical.
  - 97 subjects with labelling: 43 normal, 54 AD
  - After normalization: 95x69x79 voxel representation of each subject
  - Activation map displaying the local Intensity of the regional cerebral blood flow (rCBF): Applicable for AD



CAD Systems

- Improve the prediction accuracy in the early stage of AD
- Reproduce the knowledge of medical experts distinguishing AD from controls
- Supervised multivariate approaches:
  - defining feature vectors containing ROIs representing SPECT images: 1 vector by patient
  - Training a classifier with vectors of each patient
  - Advantage: no specific knowledge about the disease is necessary and the method is applicable for different types of brain diseases and brain image techniques

CAD Phases

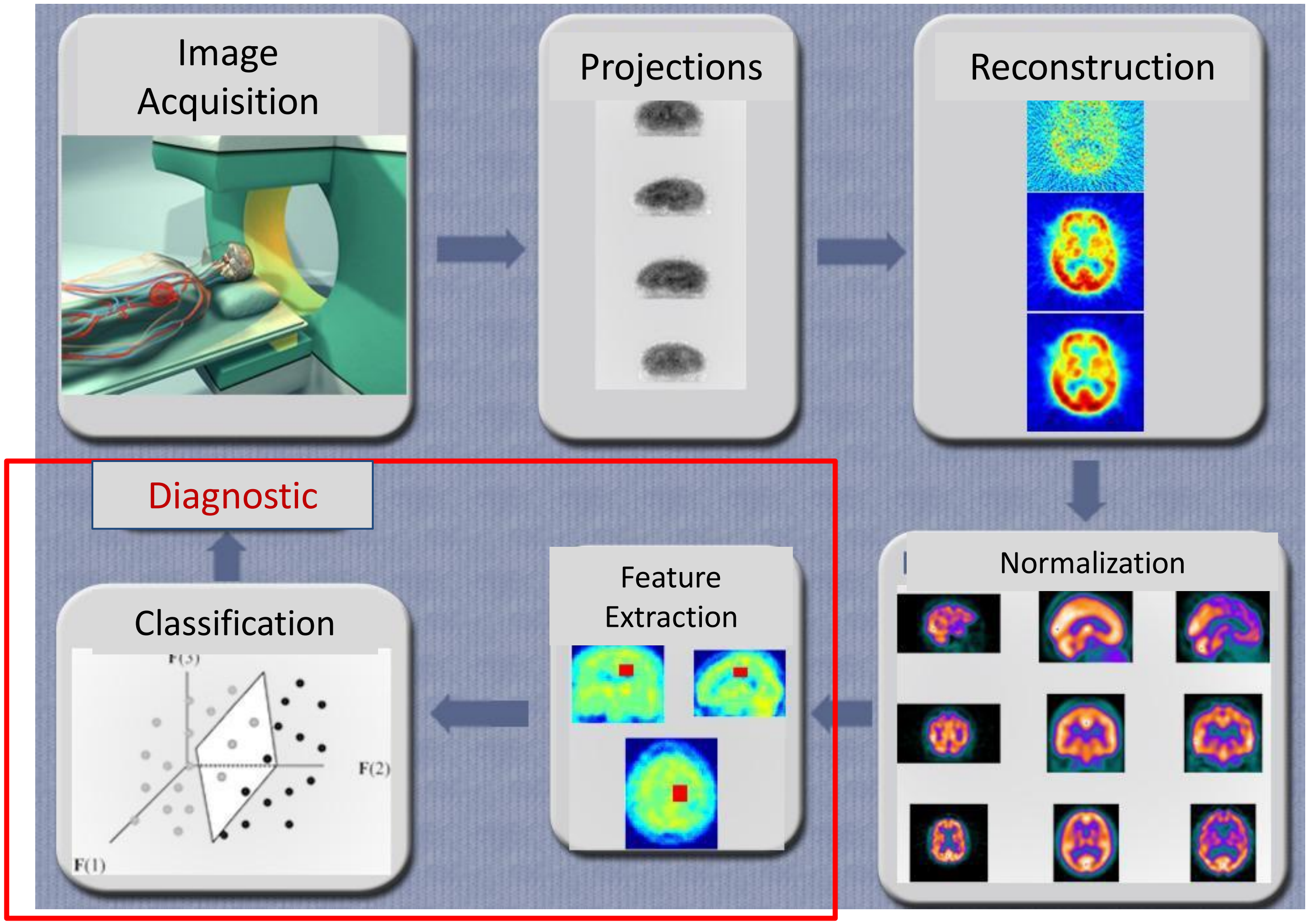


Image Acquisition
Projections
Reconstruction
Normalization
Feature Extraction
Classification
F(3)
F(2)
F(1)
Diagnostic

Feature Extraction

- Combination
  1) VAF (Voxels-As-Features)
  2) AE (Activation Estimation)
- ***VAF:*** Features are all the voxel with intensities

$$I(x_j) \leq \frac{1}{2} \cdot I_{MAX}$$

3D mask: relevant voxels

regional cerebral blood flow

- No inclusion of a priori information about AD

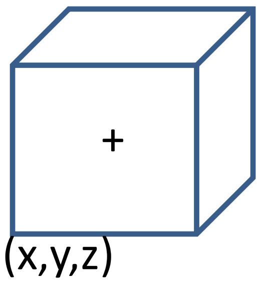
Feature extraction:

- ***AE:*** Only activated regions selected
  - ROIs are 3D blocks with a high concentration of activation coordinates, related to the perfusion level which varies between controls and AD.
  - ROIs of size $(2 \cdot v + 1) \times (2 \cdot v + 1) \times (2 \cdot v + 1)$ at coordinates (x,y,z)

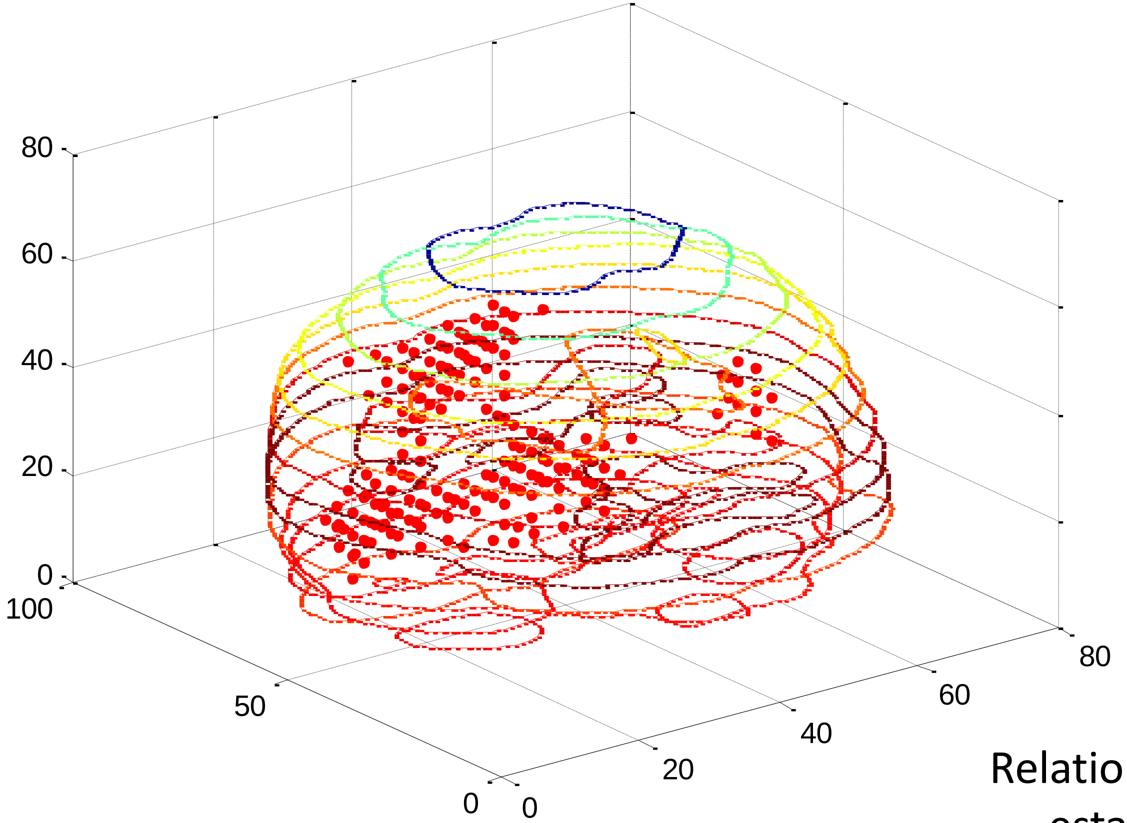
    #voxels activated > Activation Threshold η
  - If η is decreased, more rules are mined

+information to be processed, +computational requirement

Best trade-off: ROI of 9x9x9 has a 90% of voxels activated



Feature Extraction



Tridimensional ROIs
for **CONTROLS**
of size (9x9x9)
centered at red points

↓

INPUT TO AR-MINING ALGORITHM

↓

Relationships between ROIs using ARs are established to efficiently distinguish between AD and controls

Association Rules (ARs)

- Discovery of potentially important relationships between concepts in the **biomedical field**: Attention focussed in **data mining**
- ARs enable to find the associations among input items of any system in large databases and later eliminating some unnecessary inputs. **Strengths:**
  - capability to operate with **large databases**
  - execution time scales almost linearly with the size of the data
- Strengths of ARs are not exploited in this case
  - medicine databases are usually small.
  - But every SPECT image has lots of **attributes** that can be related by ARs, performing excellent results of classification

Association rules (ARs)

- Set of ROIs of controls $\Rightarrow$ $I = i_1, i_2, \ldots, i_m$
- Set of transactions $\Rightarrow$ $T = t_1, t_2, \ldots, t_n$
- AR: $X \Rightarrow Y$ $\begin{cases} X, Y \subseteq ROIs(controls) \\ X \cap Y = \phi \end{cases}$
  - An activation in Area X implies activation in Area Y
  - Parameters
    - **Support** s% transactions in T contain X U Y
    - **Confidence** c% of transactions that contain X, also contain Y

AR mining

- *State of the art:* Apriori Algorithm
  - Works iteratively for finding all frequent sets
  - It is based on the generation of a smaller candidate set using the set of large itemsets found in previous iteration
  - It generates all ARs that have :
    - *Support> Minimum support (user)*
    - *Confidence >Minimum confidence (user)*
    - *If minsup and minconf are increased*

Verified for each AR mined

↓

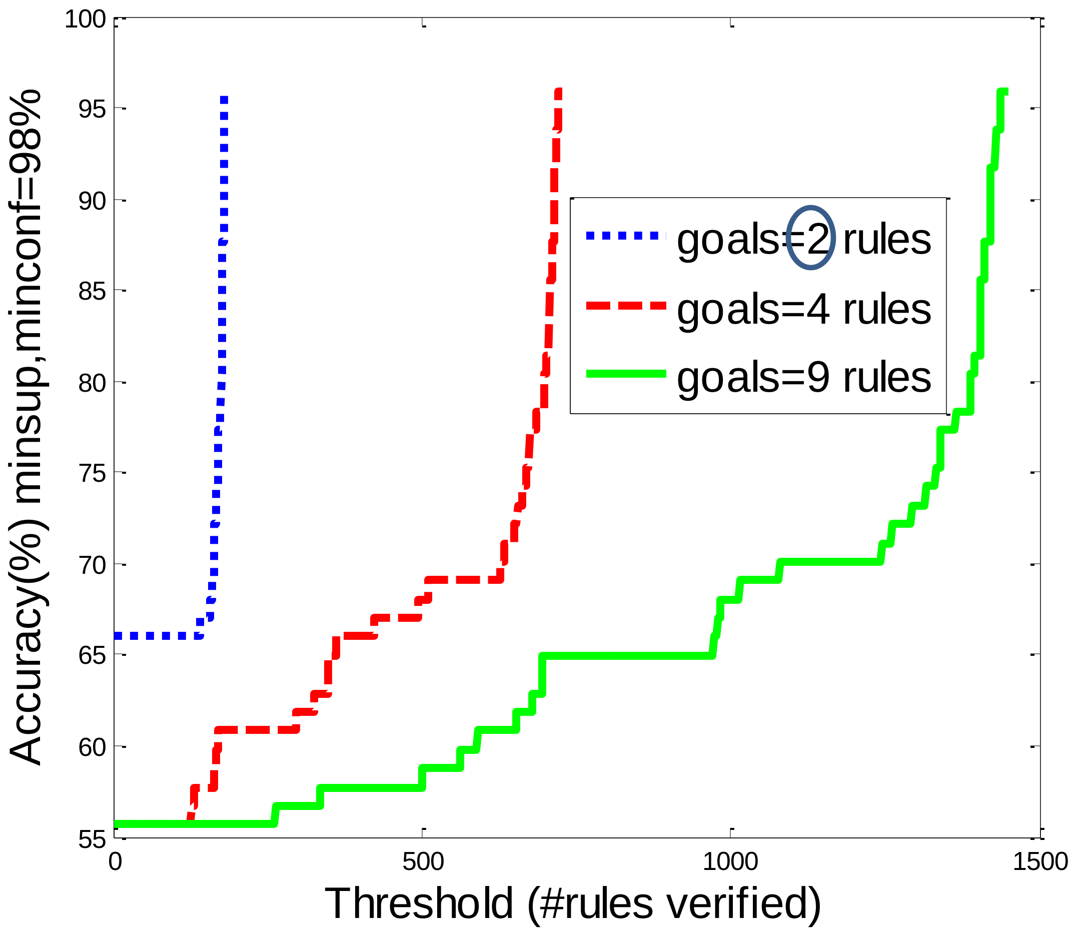
# of rules is lower but the most relevant (Early diagnosis of AD)

AR mining

- *Supervised Mode:*
  - *Distinguished from unsupervised by an apriori knowledge*
  - Integrating discriminant rules in terms of antecedents and consequences as input or prior goals into the mining algorithm
  - Useful in medical databases:
    - More interesting the relationships between the most discriminant ARs for AD Diagnosis
    - It reduces the number of AR mined, accelerating classification process with the same effectiveness

AR mining

- Example of effectiveness of supervised mode:



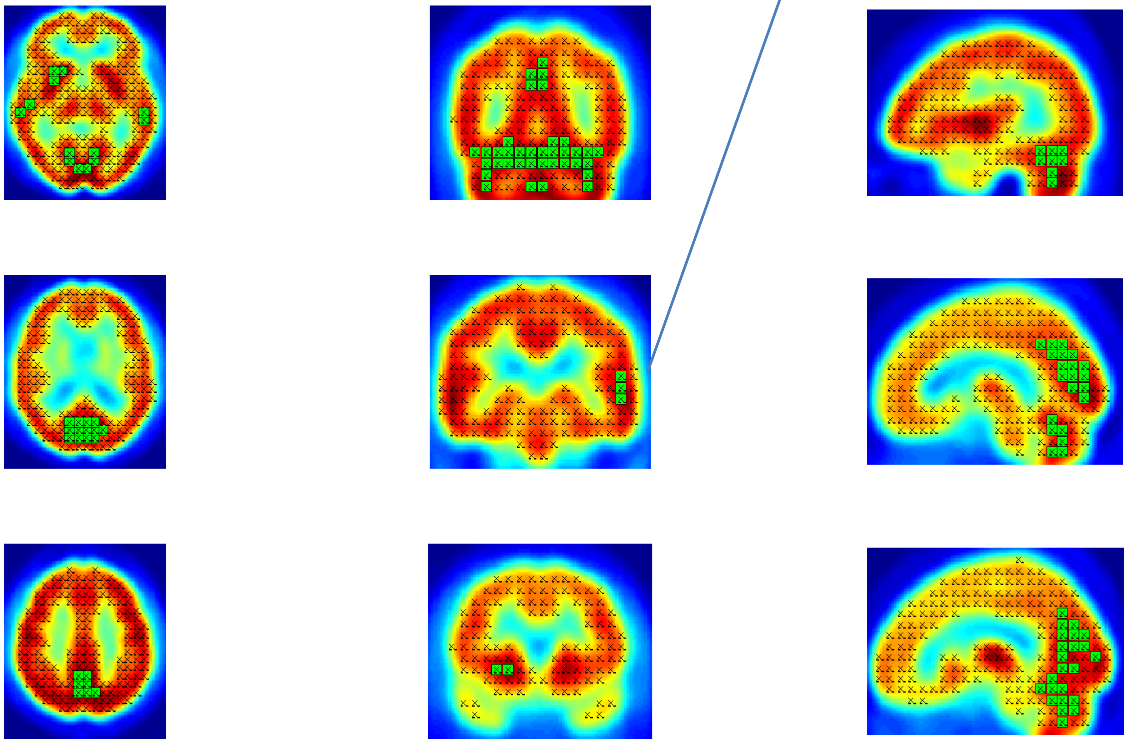
AR mining

Temporoparietal regions: early AD

Axial, sagittal and coronal axis

Rectangles are ROIs involved in ARs (controls)

Supervised mode
Minsup:98%
Minconf:98%



Classifier

- Training phase: ARs are mined only from controls using cross-validation strategy
- Test phase: it is checked the number of ARs that every patient verifies, validating by means of leave-one-out strategy

$$\#ARs(verified_i) \geq class\_threshold \Rightarrow i : NORMAL$$
$$else \Rightarrow i : AD$$

%of sick people identified as having the condition $\longleftarrow$ $$Sensitivity = \frac{TP}{TP + FN}$$

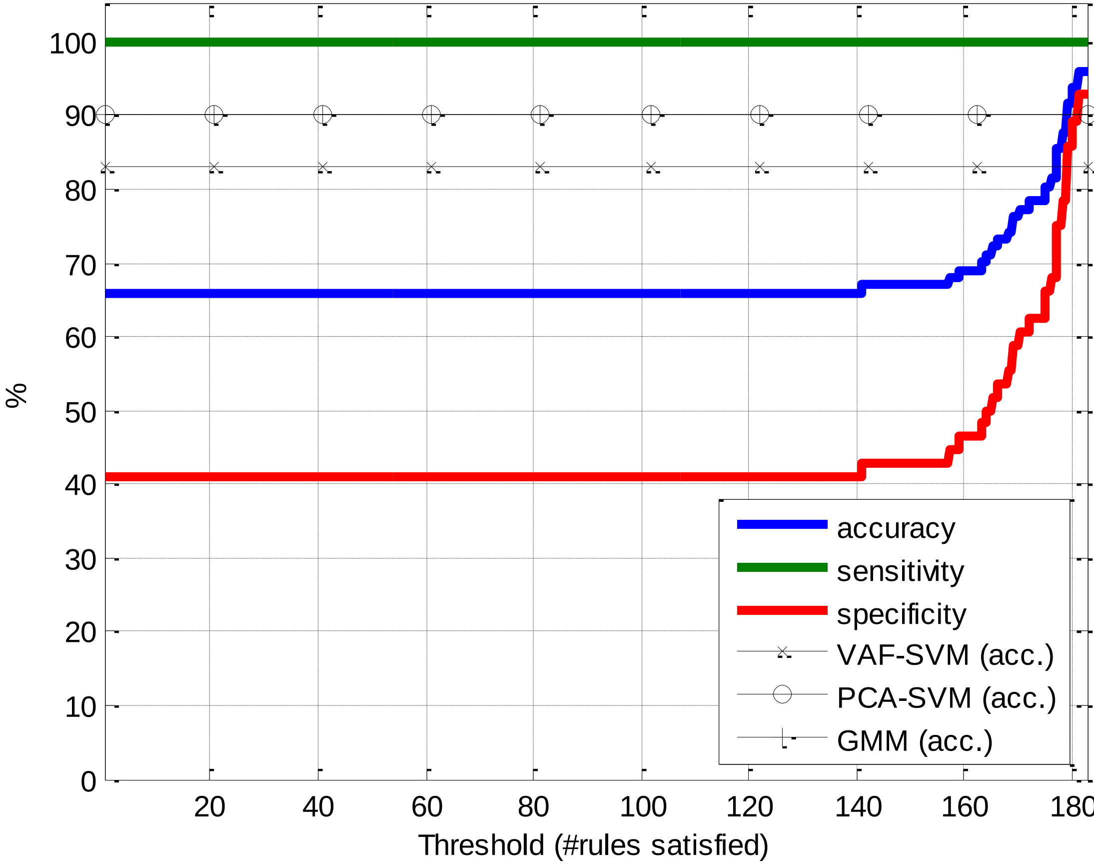
%of healthy people identified as not having the condition $\longleftarrow$ $$Specificity = \frac{TN}{TN + FP}$$

Results

Minsup, minconf	98%	95%	90%	85%	80%
#rules: 2 rules as prior goals (1: Supervised Mode)	183	314	419	506	596
#rules: No prior goals (2: Unsupervised mode)	33646	88347	152790	220660	295040
Aceleration rate (2/1)	183.85	281.35	364.65	436.08	495.033
Accuracy (%)	95.87	90.72	89.69	87.62	86.56

SAME CLASSIFICATION EFFICIENCY BUT FASTER WITH SUPERVISED MODE

Results



Experiments considered increasing threshold and the number of verified ARs by the subject to be classified

$$Acc = 95.87\%$$

$$Sen = 100\%$$

$$Spe = 92.86\%$$

183 rules verified

Conclusions

- ARs were investigated for SPECT images classification for the early AD's diagnosis.
  - results of Acc of 95.87%, Sen of 100% and Spe of 92.86%
- outperforming other recently reported methods including VAF, PCA in combination with a support vector machine (SVM) classifier and the Gaussian mixture modelling (GMM) SVM classifier .

Conclusions

- Accuracy improves when it is increased the threshold of verified rules by the subject.
- These results are in agreement with the expected behavior of the system
  - Controls are assumed to have a common SPECT image pattern and to verify most of the ARs mined.
- Using apriori information on the AR mining is very positive in terms of improving the computational time of the AR extraction and the rest of checkings of the CAD system

Thank you very much for your attention