Preliminary results on fuzzy analysis of MRI and SPECT data for Alzheimer disease diagnostics

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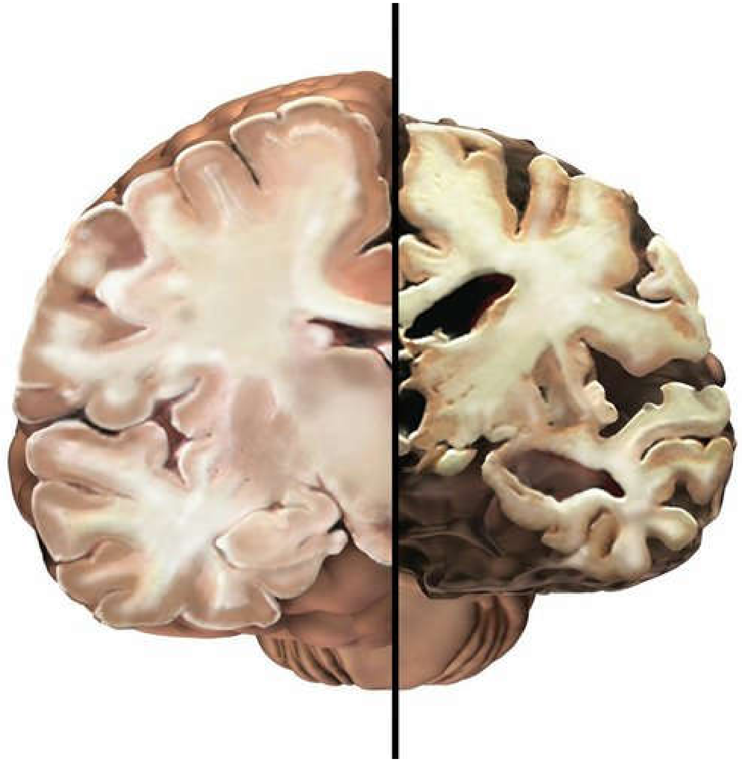
Alzheimer Disease



Alzheimer Disease

Alzheimer disease (AD), is the most common form of dementia. There is no cure for the disease, which worsens as it progresses, and eventually leads to death.

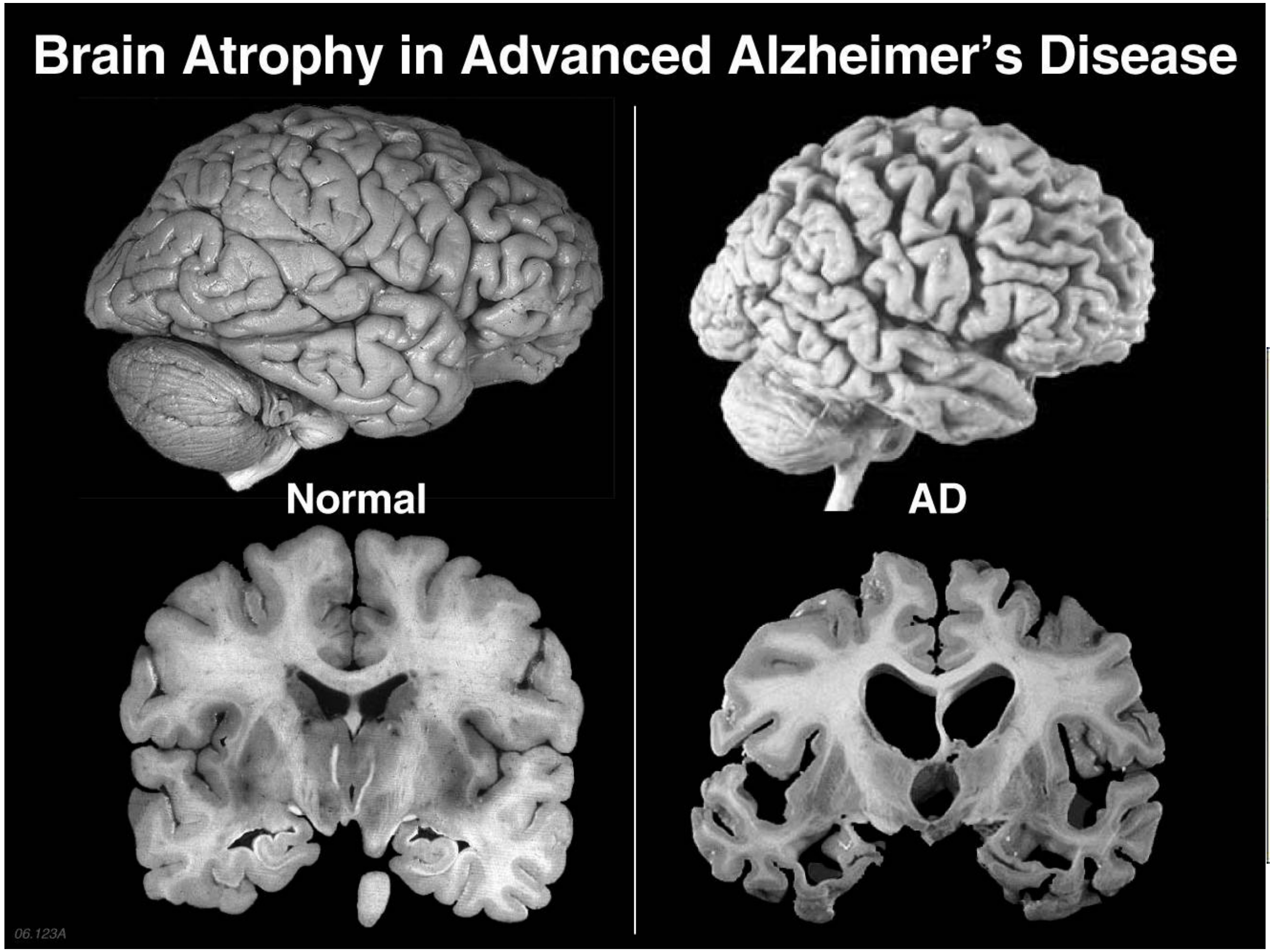
Most common symptoms:
- difficulty in remembering recent events (early stages)
- confusion
- irritability
- aggression
- mood swings
- trouble with language
- long-term memory loss.

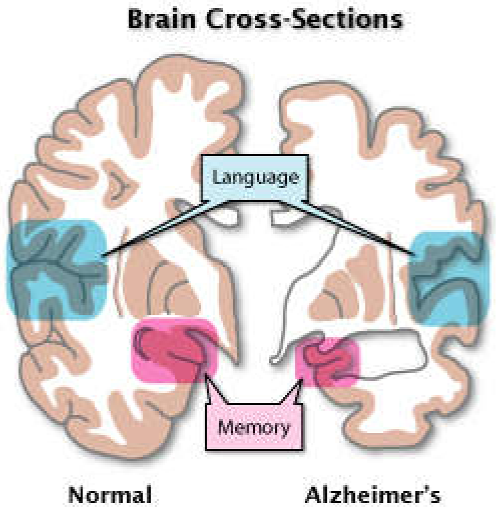
Gradually, bodily functions are lost, ultimately leading to death.

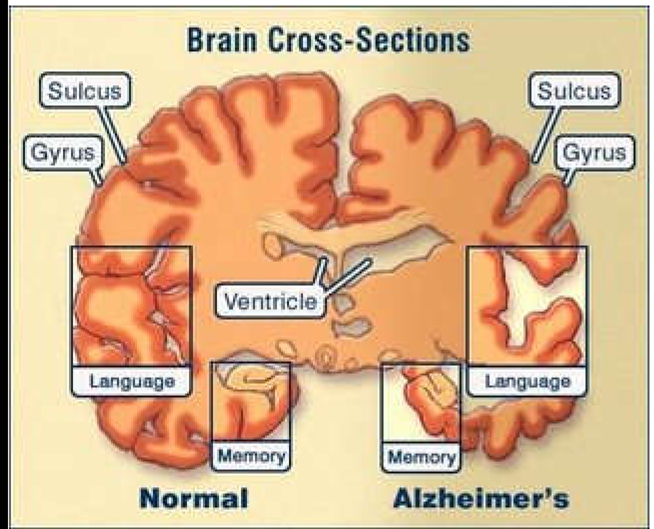
only a post-mortem examination can assure the diagnosis

Cognitive testing

Typically affected brain regions

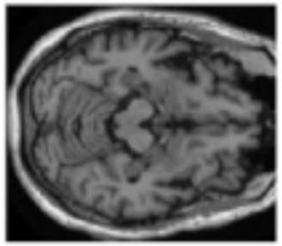
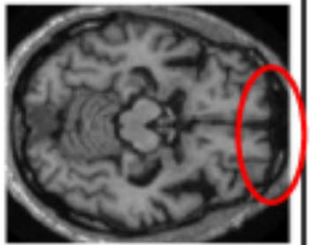
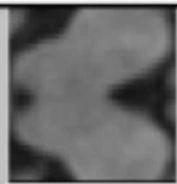
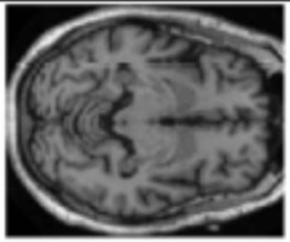
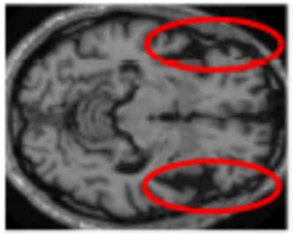
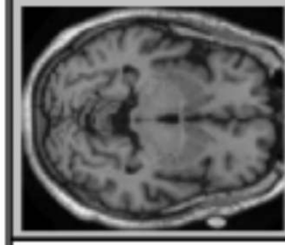
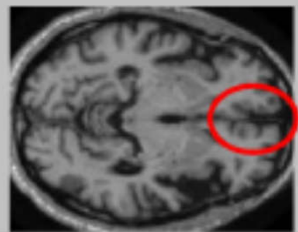
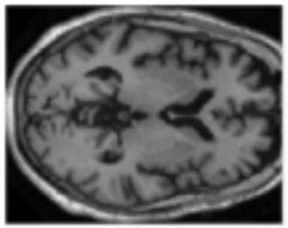
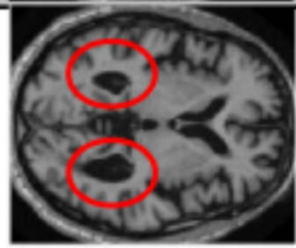




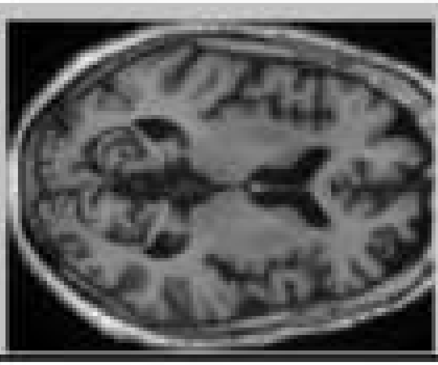
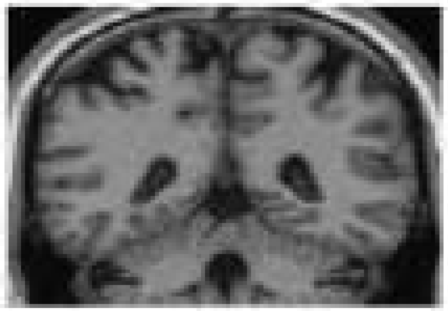
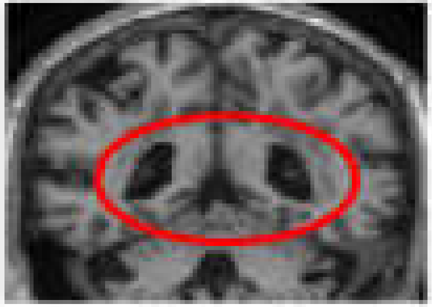
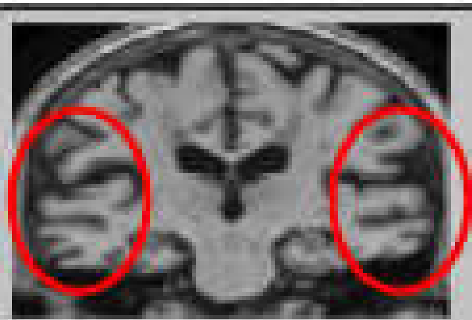


MRI technique for AD diagnostics-1

Differences in brain structure:
- Cortex shrinkage
- Cortex atrophy
- Cortex volume decrease
- Ventricles expansion

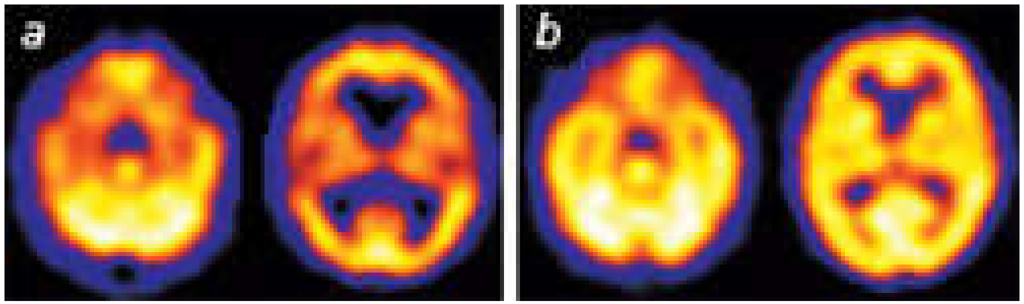
Healthy patient	AD Patient	Comments
		Symmetrical atrophy on the front poles
		Hippocampus atrophy
		Temporal lobe atrophy
		Expanded fissures.
		Ex-vacuo expansion of the Ventricular System.

MRI technique for AD diagnostics-2

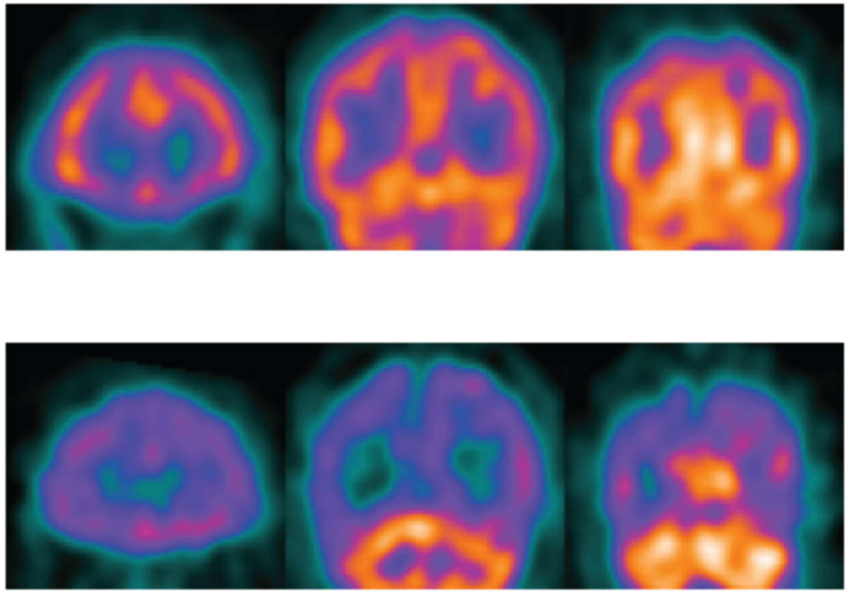
Healthy patient	AD Patient	Comments
		
		Ventricular System expansion
		Cortex volume decrease in temporal lobe region.

Single Photon Emission Computed Tomography (SPECT)

Differences in regional cerebral blood flow



a) Alzheimer's disease, b) control subject.



Top – normal subject, bottom – AD

Regional Cerebral Blood Flow (rCBF) of patien with AD is significantly reduced.

Temporo-parietal region is mostly affected and useful for the early detection of the disease, but is not specific to AD.
Perfusion deficits in **posterior cingulate gyri** and **precunei** are probably more specific and typically affected image by hypo-perfusion in early AD.

suffer from poor resolution and low contrast,
which make it difficult for physicians to put an accurate interpretation for diagnosis

Feature Selection

The aim:
1- to reduce the cost of extracting features,
2-improvement of the classification accuracy, and
3- getting more reliable estimates of performance.

Algorithms for feature selection

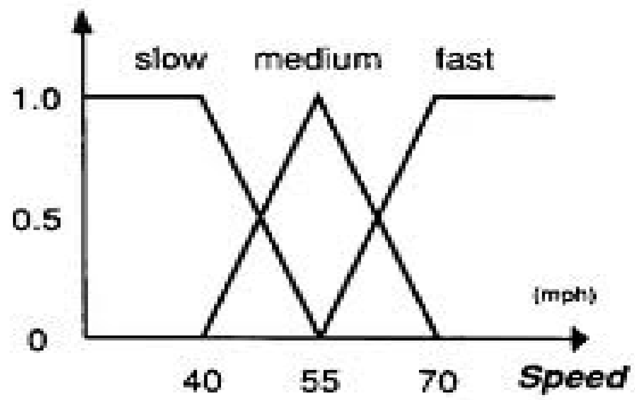
Classifier-specific feature selection (CSFS)
Classifier-independent feature selection (CIFS).

we have to find a feature subset with the largest possible separation between class conditional probability densities.

Types of features

•Raw image slices, voxel (pixel) intensity – Voxels-As-Feature (VAF)
•Mean intensities in regions (averaged over some brain volume)
•Coefficients of wavelet transform, groups of coefficients
•Image with difference between normal and AD subjects, then Gaussian Mixture Model (GMM) parameters
•Manual cortex regionalization, then relative value for the respective region and the cerebellum as region of comparison was calculated (association cortex areas in frontal, temporal, parietal, frontobasal and temporobasal regions in both hemispheres
•similarity measures of the rCBF of each subject and the mean rCBF value associated to normal controls: Normalized Mean Square Error of voxel blocks comparison
•PDF characteristics (mean, STD, skewness, kurtosis) in the sliding block of voxels

Fuzzy Logic



Physical Uncertainty

What is the probability to meet man of
2 m high
in the street?

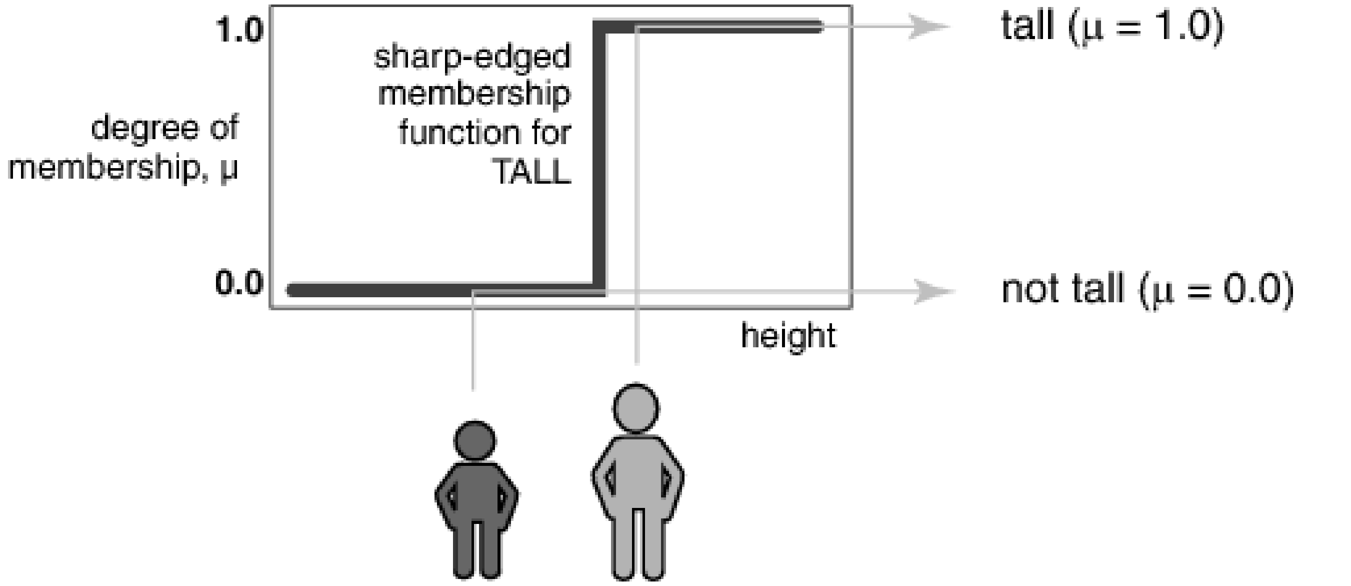
Probability theory:
- PDF of height (localized for particular city)
- PDF of men|women distribution

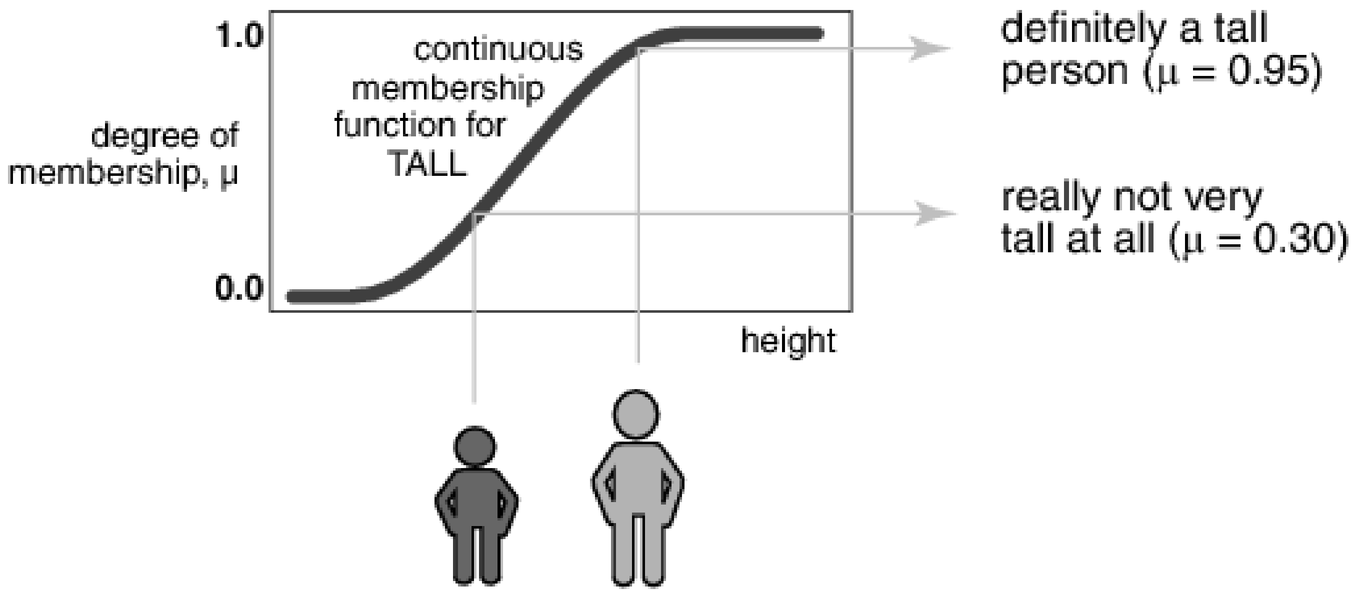
Linguistic Uncertainty

What is the probability to meet
tall
man in the street?

Natural language:

-Sharp pain
-Old man
-High speed
-Too much
-Very funny


1.0
0.0
degree of
membership, μ
sharp-edged
membership
function for
TALL
height
tall (μ = 1.0)
not tall (μ = 0.0)


1.0
0.0
degree of
membership, μ
continuous
membership
function for
TALL
height
definitely a tall
person (μ = 0.95)
really not very
tall at all (μ = 0.30)

Fuzzy Sets

Lotfi A. Zadeh
Professor Emeritus,
EECS, UC Berkeley

Let X be a space of points (objects), with a generic element of X denoted by x. Thus, $X = \{x\}$.

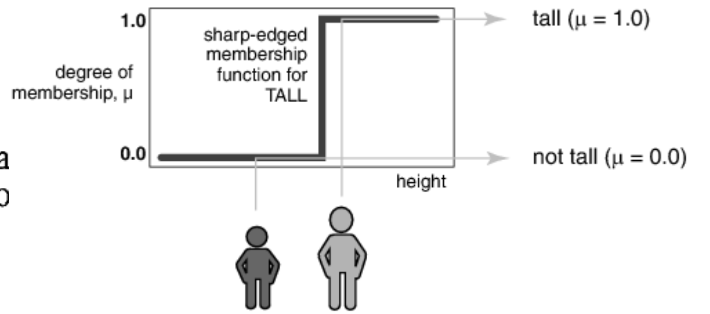
A *fuzzy set* (*class*) A in X is characterized by a *membership* (*characteristic*) *function* $f_A(x)$ which associates with each point[2] in X a real number in the interval $[0, 1]$,[3] with the value of $f_A(x)$ at x representing the "grade of membership" of x in A. Thus, the nearer the value of $f_A(x)$ to unity, the higher the grade of membership of x in A.

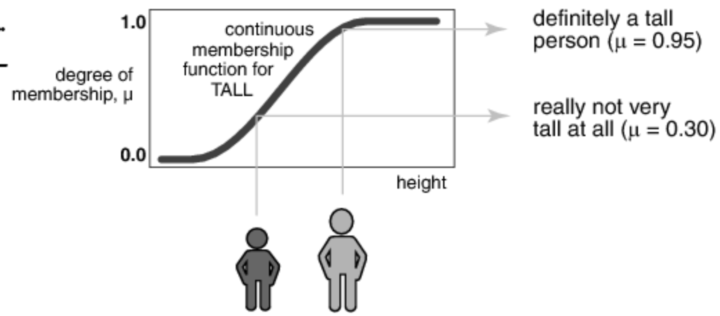
- -Fuzzy set
- -Fuzzy variable
- -Linguistic variable

Пусть **E** — множество, счетное или нет, и x — элемент **E**. Тогда нечеткое подмножество **A** множества **E** определяется как множество упорядоченных пар

$$\{(x, \mu_{\mathbf{A}}(x))\}, \qquad \forall x \in \mathbf{E},$$

где $\mu_{\mathbf{A}}(x)$ — *характеристическая функция принадлежности*, принимающая свои значения во вполне упорядоченном множестве **M**, которая указывает *степень* или *уровень* принадлежности элемента x подмножеству **A**. Множество **M** будет называться *множеством принадлежностей*.





Main Idea

The main idea of “fuzzy” approach to control or classification problem – is to get the results after quantitative representation of all **variables** which are already used for the analysis, in the form of **fuzzy sets**.

Canonical steps:

1. Define inputs and outputs of the system
2. Create or select membership functions
3. Create inference rules
4. Simulate resulting system and run it

The objective – to build the fuzzy system which gives the “degree of AD prominance” based on the input data from MRI or SPECT image.

Fuzzy Inference System

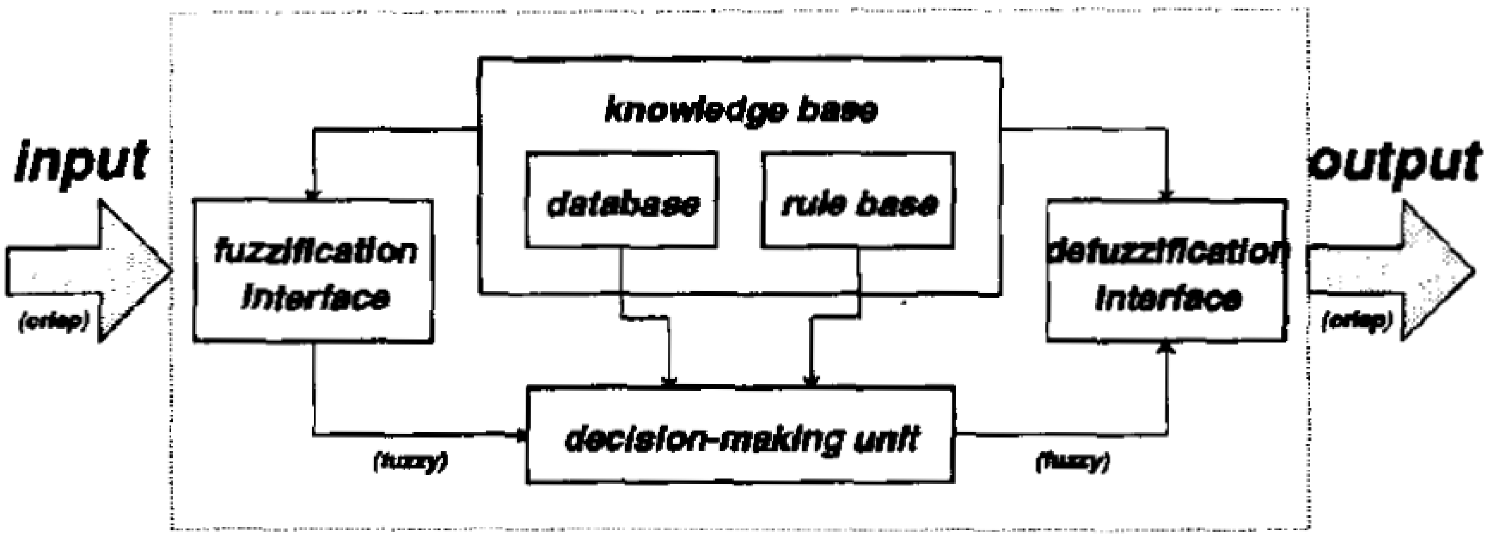
Fuzzy Inference Systems – are used for formalizing the expert's knowledge for obtaining the conclusions about the output variables using fuzzificated input variables and fuzzy rules.

FIS combines all Fuzzy Logic main concepts:

-Membership functions
-Linguistic variables
-Fuzzy logic operations
-Fuzzy implications
-Fuzzy composition

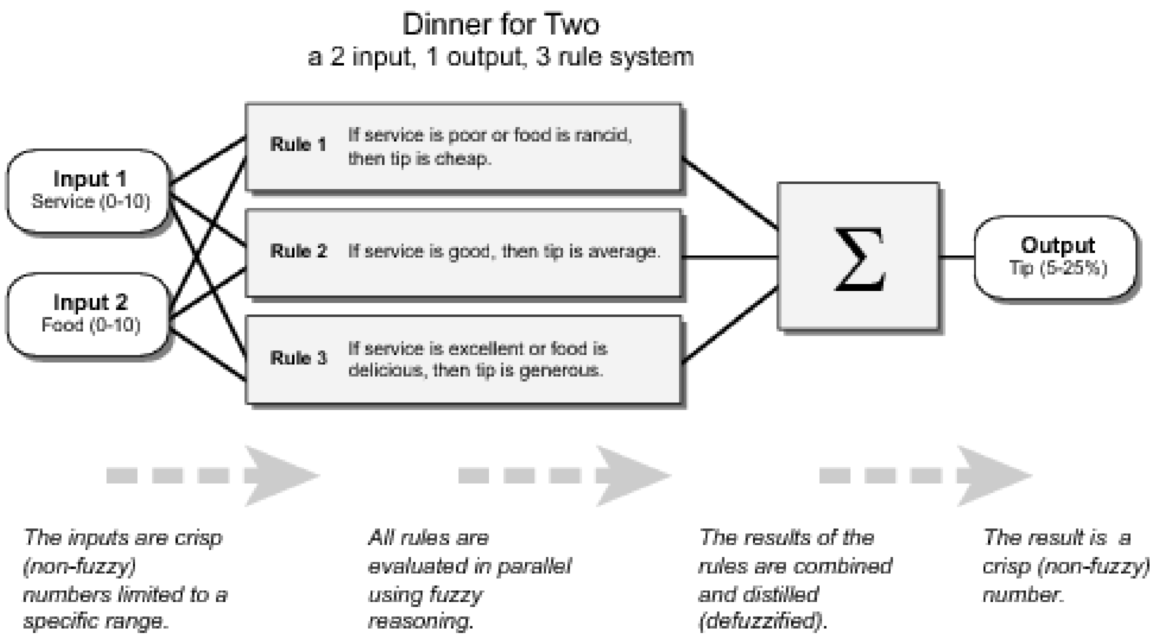
***Applications*:**

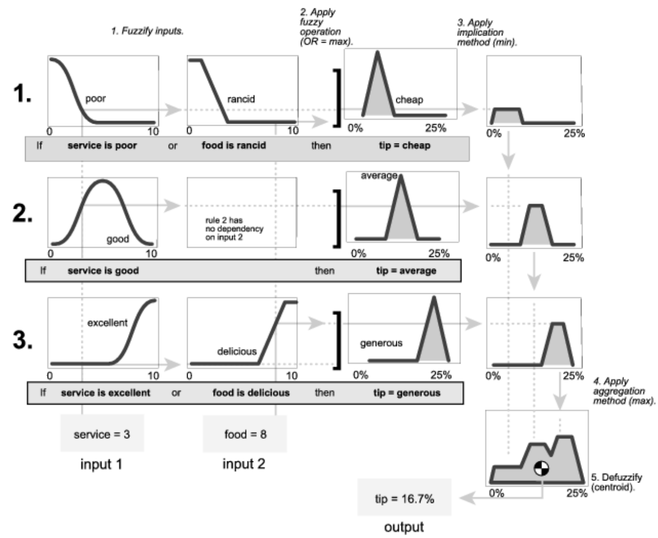
-Control
-Classification
-Pattern recognition
-Decision making
-Machine learning
-etc.



Fuzzy Inference Process

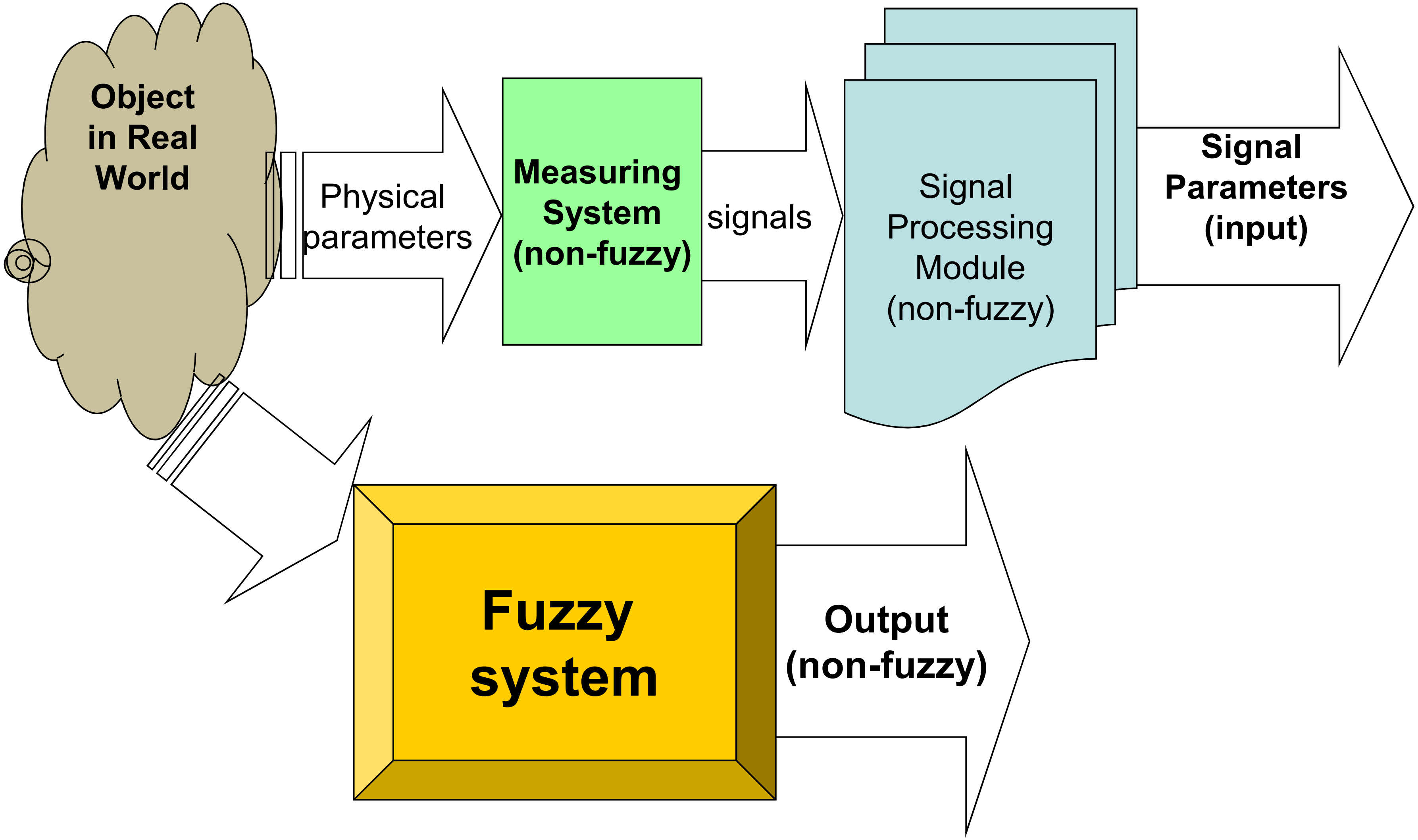
Fuzzy inference is the process of formulating the mapping from a given input to an output using fuzzy logic. The mapping then provides a basis from which decisions can be made, or patterns discerned. The process of fuzzy inference involves all of the pieces that are described in Membership Functions, Logical Operations, and If-Then Rules.





FIS, preliminary part-1

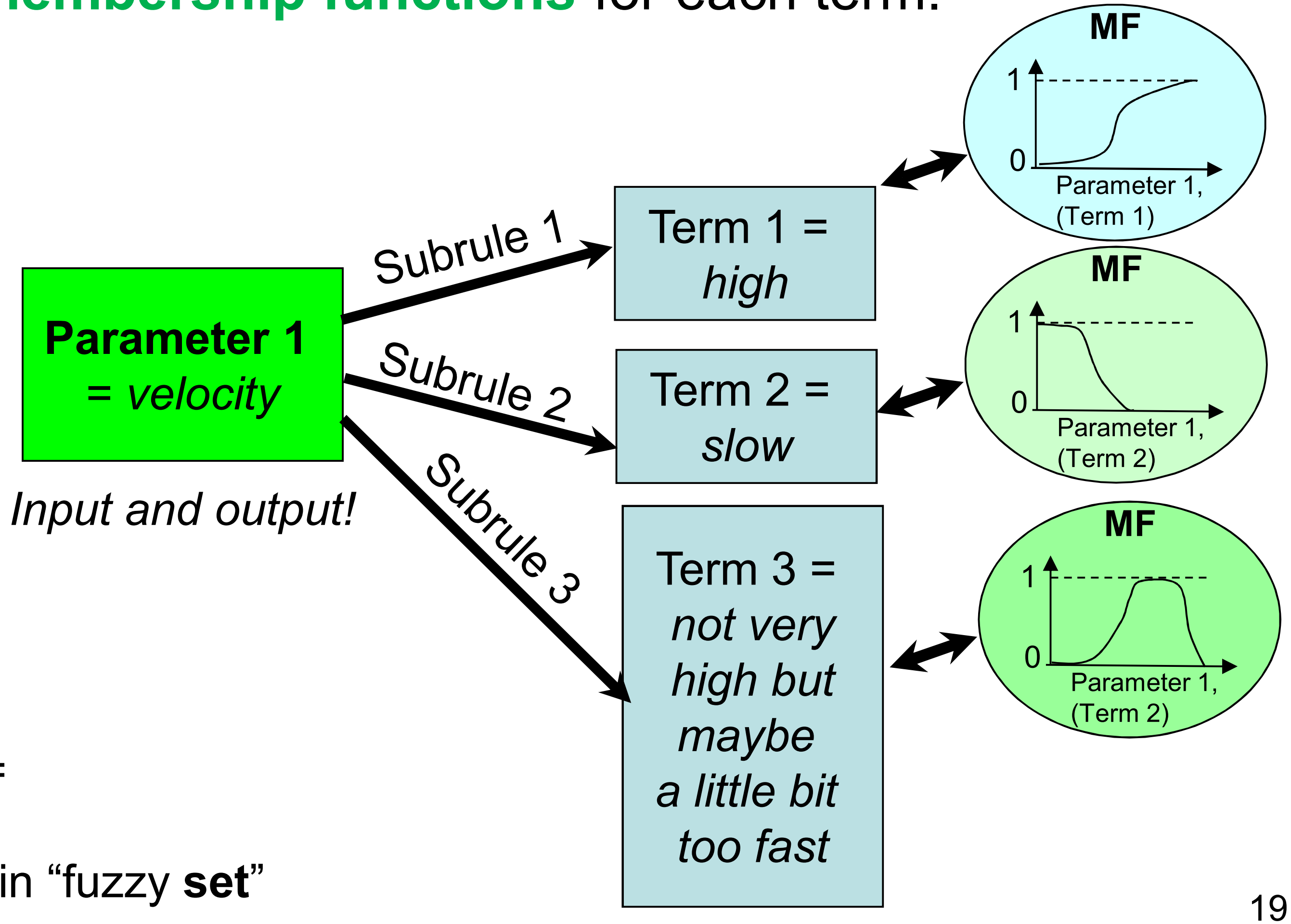
What input and output parameters will we use?



FIS, preliminary part-2

What **fuzzy sets** will correspond to each parameter?

1. Define the linguistic variable (“universum”) for each parameter.
2. Define the terms (“fuzzy”) of each variable.
3. Define the **membership functions** for each term.



Subrule:

A is B =

“parameter” IS “term” =

“linguistic **variable**” IS in “fuzzy **set**”

FIS, preliminary part-3

What **rules** will be applied to **terms**?

1. Combine the values of linguistic variables (terms) according to expert knowledge = *IF-THEN*
2. Use logistic rules (AND, OR, NOT)
3. Combine input terms with output terms

IF
(**Input** parameter 1) **IS** (term 2)
AND
(**Input** parameter 4) **IS** (term 1)
THEN
(***Output*** parameter 3) **IS** (term 4)

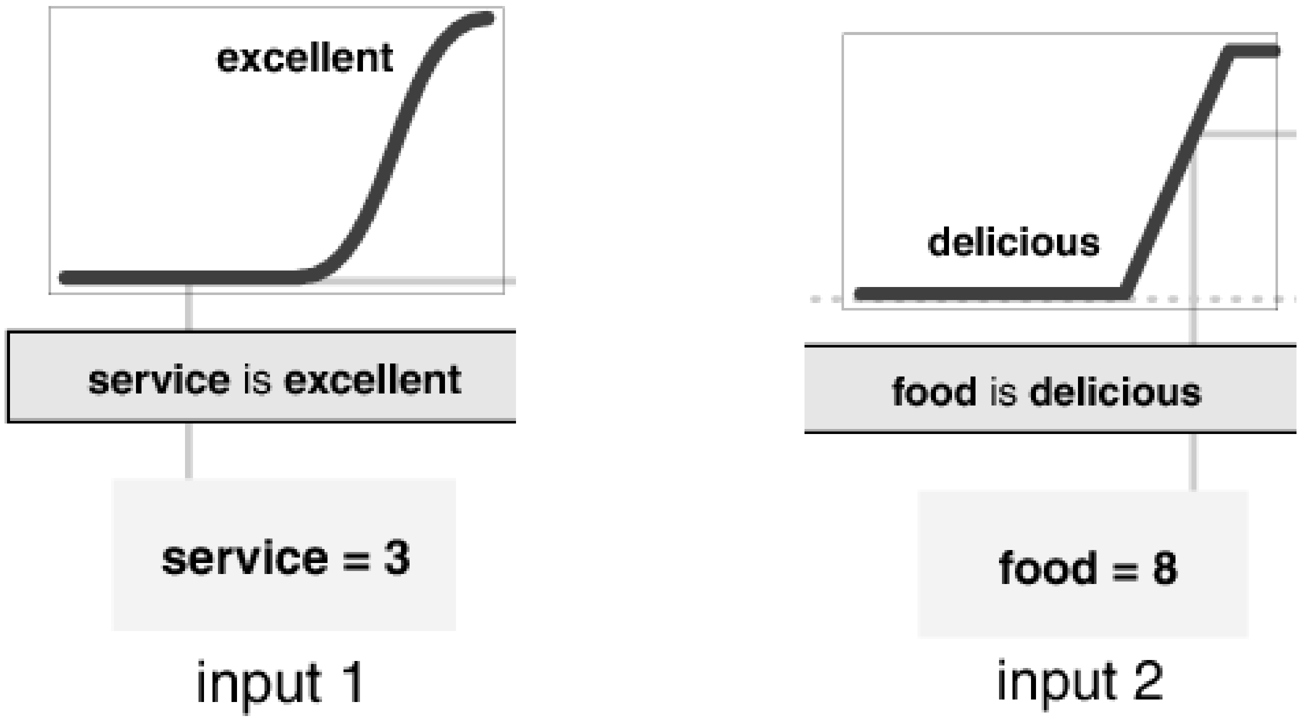
IF
(**Input** parameter 2) **IS** (term 3)
AND
(**Input** parameter 4) **IS** (term 1)
THEN
(***Output*** parameter 3) **IS** (term 4)

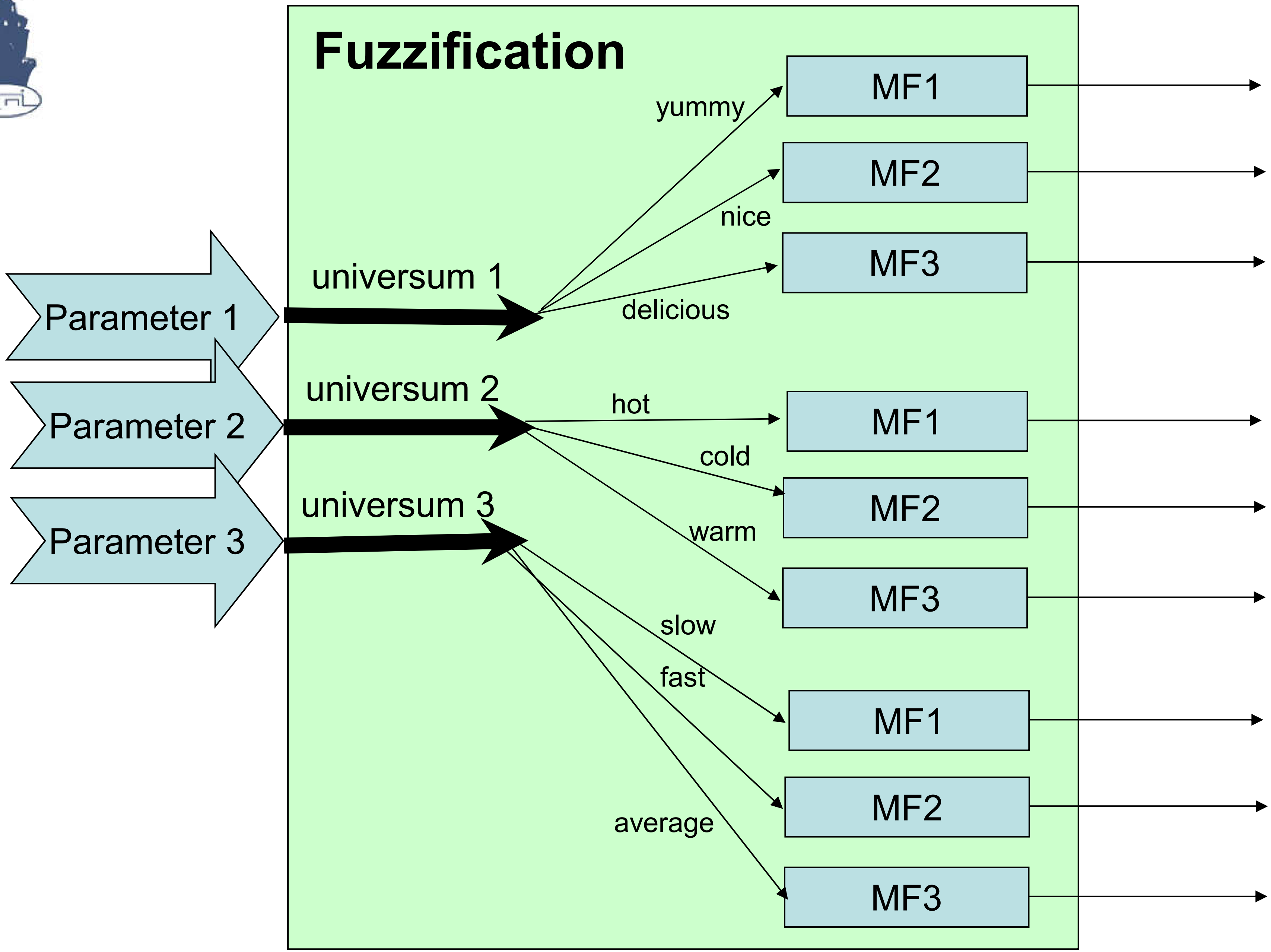
IF
(**Input** parameter 3) **IS** (term 1)
OR
(**Input** parameter 2) **IS** (term 4)
THEN
(***Output*** parameter 1) **IS** (term 2)

1. Fuzzification of input variables

Fuzzification – finding correspondence between the input parameter (value) and the fuzzy set using the *value of membership function*.

Input value – crisp number in some range, eg. [0…10] or [-123..15]
Output – is a fuzzy degree of membership in the fuzzy set (always the interval between 0 and 1).



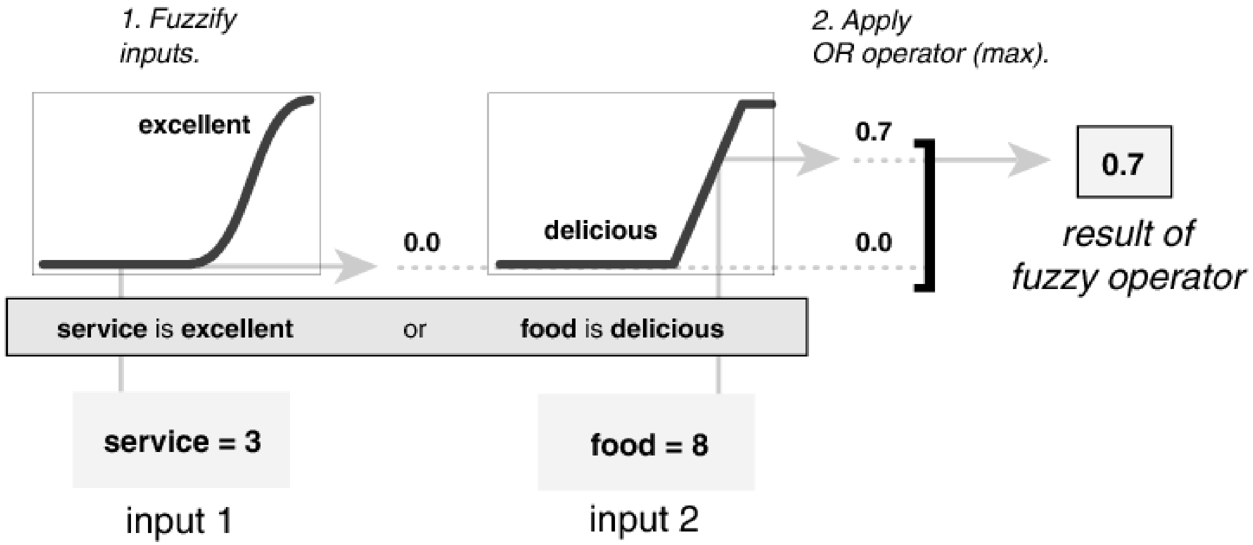

Fuzzification
Parameter 1
Parameter 2
Parameter 3
universum 1
universum 2
universum 3
yummy
nice
delicious
hot
cold
warm
slow
fast
average
MF1
MF2
MF3
MF1
MF2
MF3
MF1
MF2
MF3

2.1 Fuzzy rules (fuzzy operators) -1

Aggregation

Input to the fuzzy rule is two or more values of membership functions (for each input variable (which have been just fuzzified).

Output is a single value in the range [0..1] – membership function for the fuzzy set of rule's results.



IF part

Examples of Fuzzy Rules

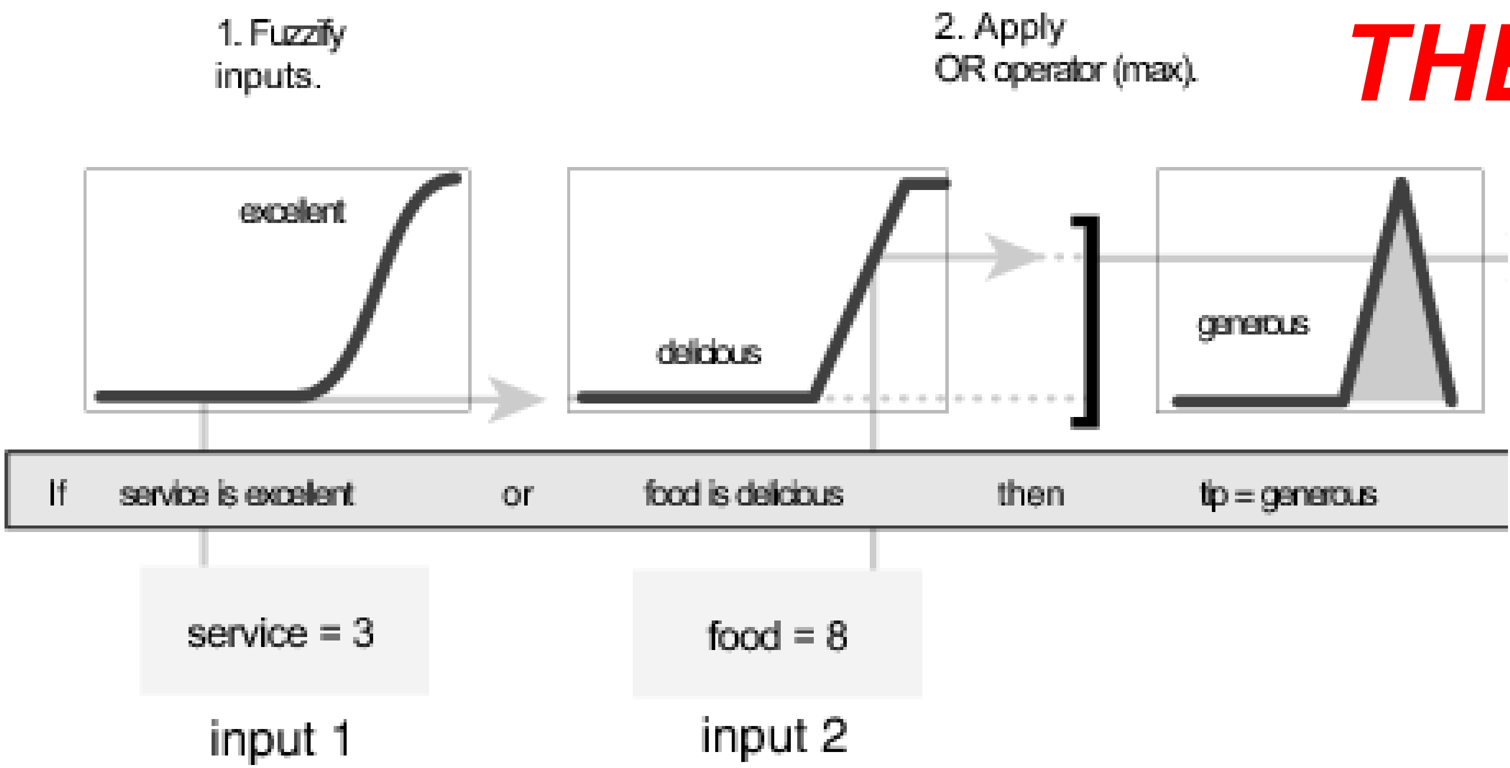
A* AND *B becomes ***min*(*A*,*B*)**.
A* OR *B becomes equivalent to ***max*(*A*,*B*)**.
NOT *A* becomes equivalent to the operation ***1-A***

2.2 Fuzzy rules (fuzzy operators) -2

Inference

Input is the result of ***IF*** part.
It is applied to the membership function of the output set of the rule.

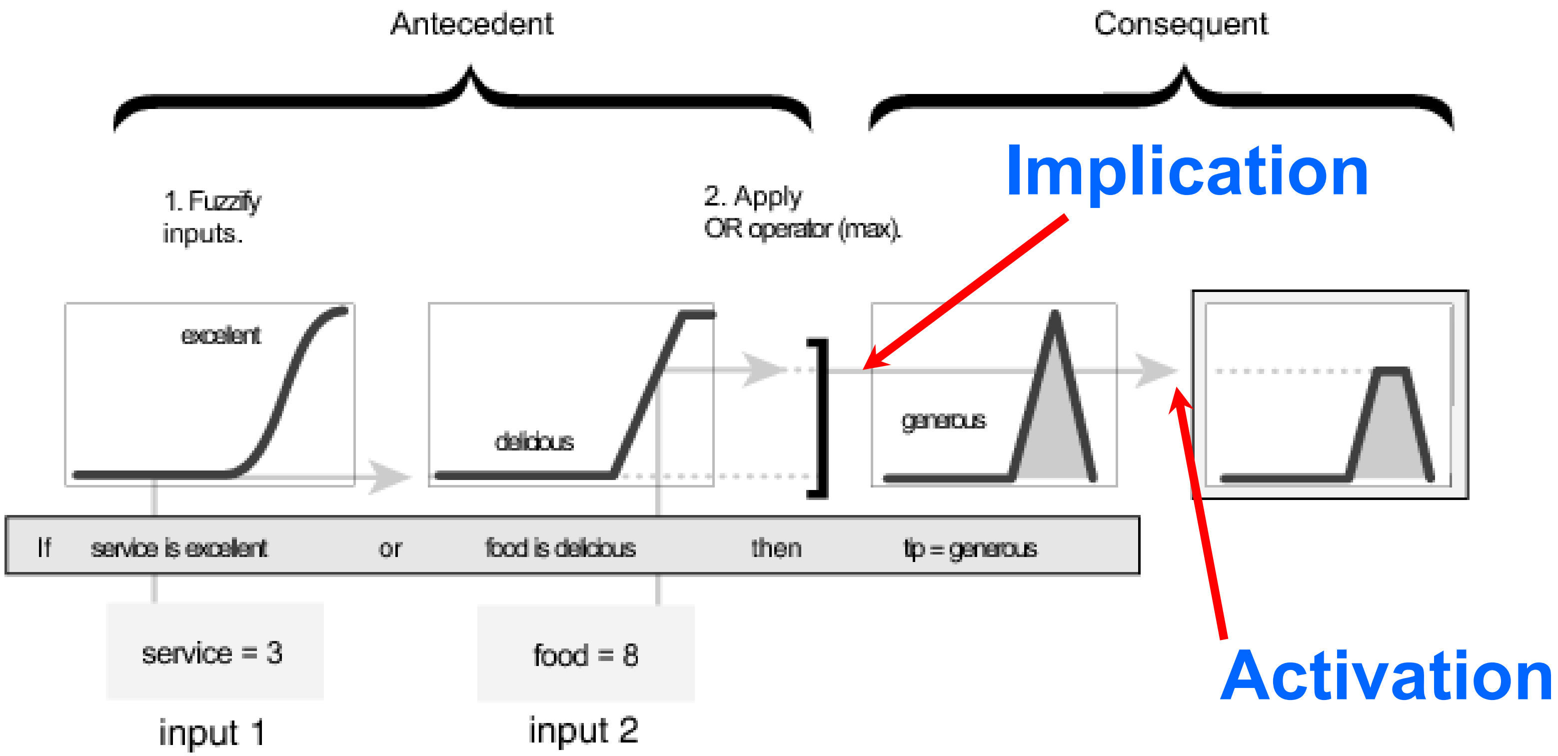
THEN part



Every rule can have a *weight* (a number between 0 and 1), which is applied to the number given by the antecedent.
Generally, this weight is 1 and thus has no effect at all on the implication process.

3. Implication and activation of each rule

Input for the implication process is a single number given by the antecedent (result of fuzzy rule application).
Output is a fuzzy set (membership function) of sub-conclusion

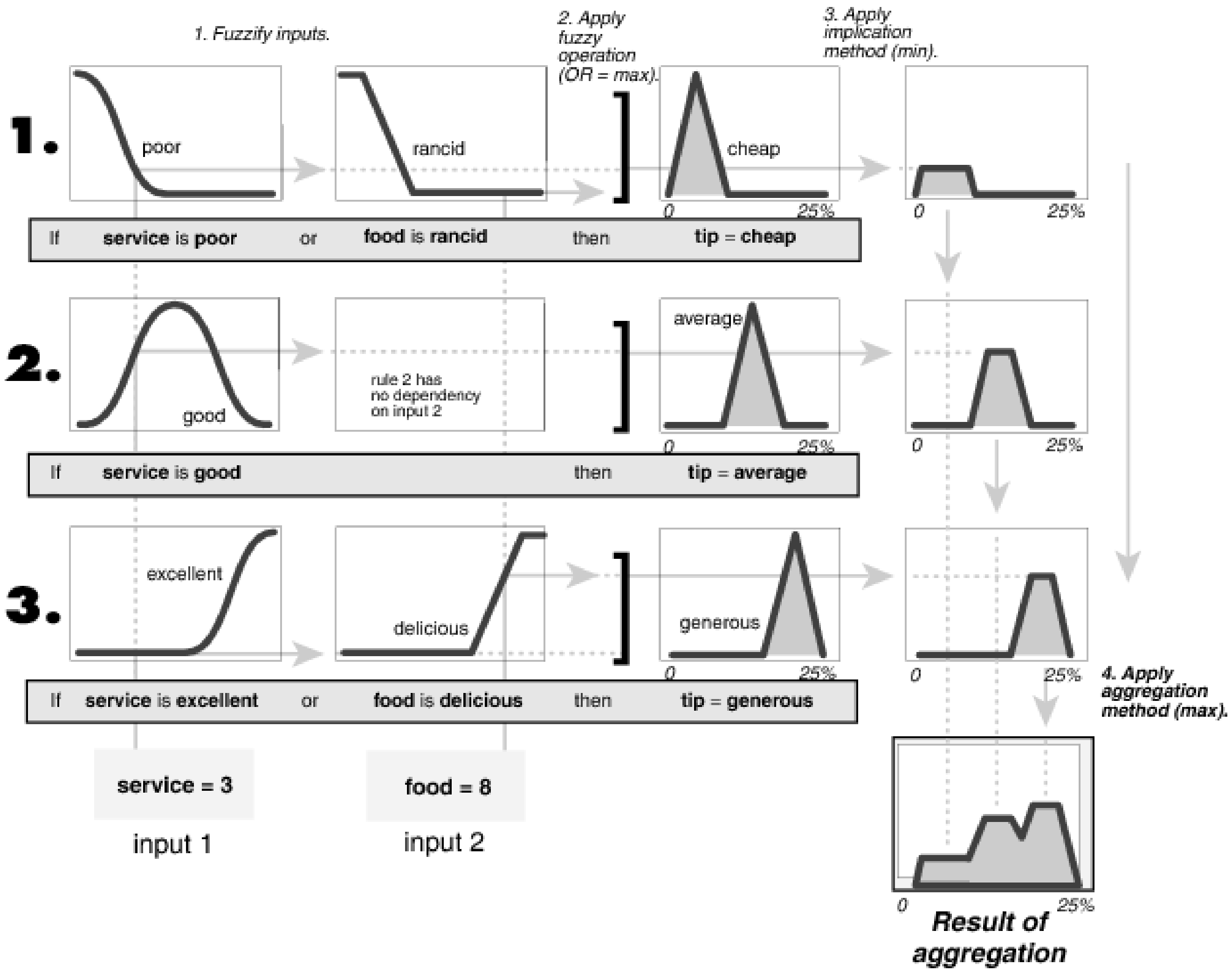


Examples of Activation Rules

MF_act(y)=min(c, MF(y)) -minmum
MF_act(y)= cMF(y) - product
MF_act(y)=0.5 (c + MF(y)) - average

4. Aggregation (accumulation) of all rules

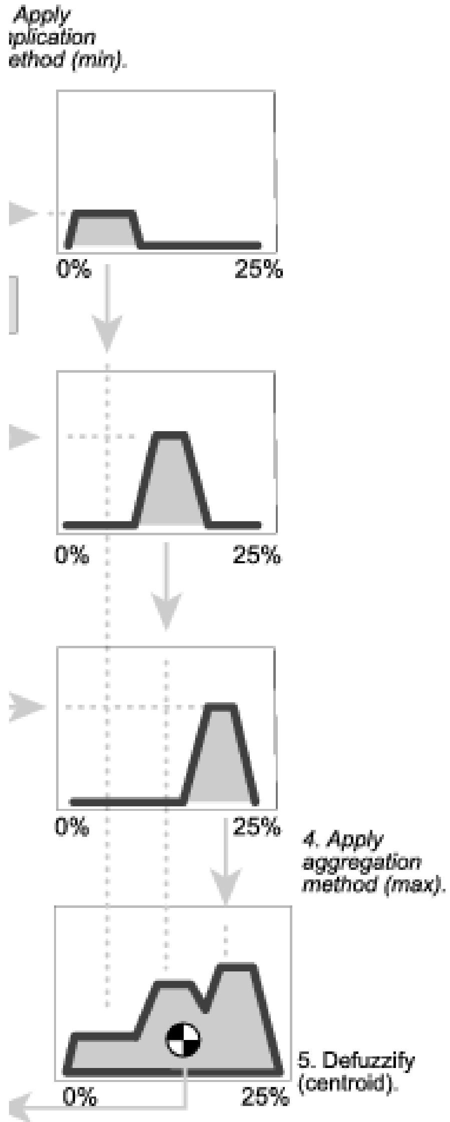
Input is the list of truncated output MF returned by the *implication and activation process*.
Output of the aggregation process is one fuzzy set for *each output* variable.



Aggregation is the process by which the **fuzzy sets** that represent the outputs of each rule are combined into a **single fuzzy set**.

5. Defuzzification

Input is a fuzzy set for each **output value** (the aggregate output fuzzy set)
Output is a **single number** for each output value.

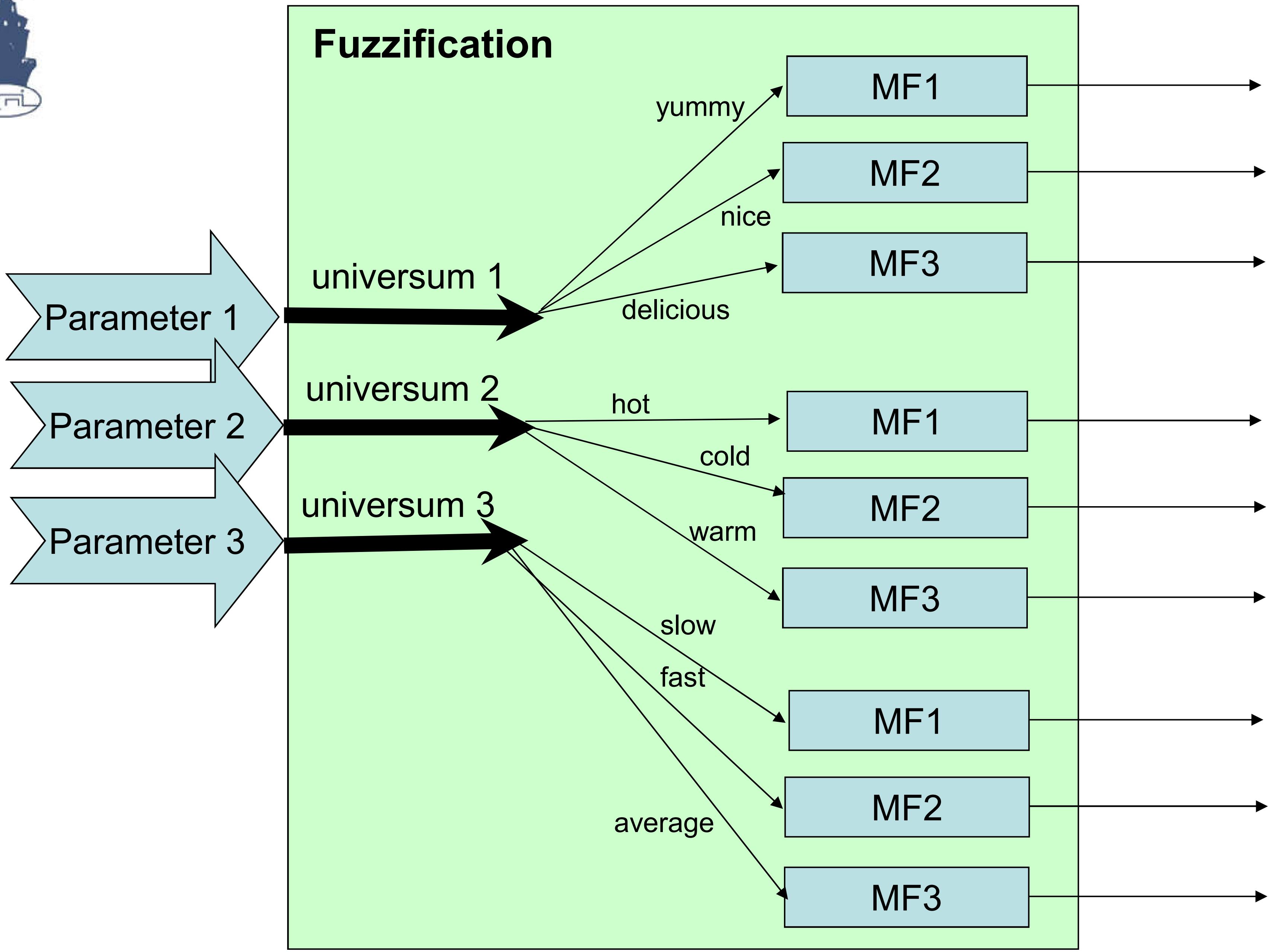


Defuzzification Methods

- Centroid (center of gravity),
- Bisector of area (center of area),
- Left Most Maximum (smallest of maximum),
- Right Most Maximum (largest of maximum)
- Middle of maximum.

The output of each rule is a fuzzy set. The output fuzzy sets for each rule are then aggregated into a single output fuzzy set. Finally the resulting set is defuzzified, or resolved to a single number.

MOST IMPORTANT ISSUE



Membership Functions

Definition of MF

A *membership function* (MF) is a curve that defines how each point in the input space is mapped to a membership value (or degree of membership) between 0 and 1. The input space is sometimes referred to as the *universe of discourse*.

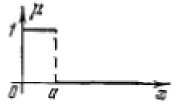
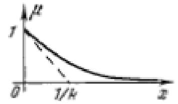
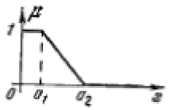
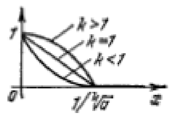
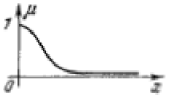
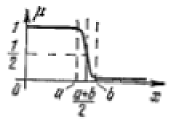
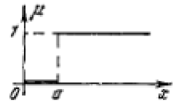
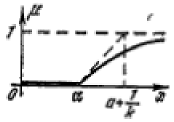
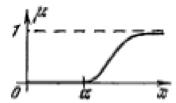
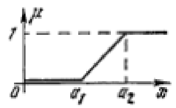
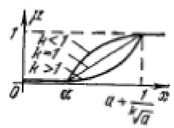
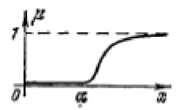
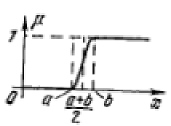
Construction of MF

Direct Methods (*obvious properties* + *scale*):
-Expert assigns the MF value to each element of fuzzy set;
-Expert selects MF for the set.

Indirect Methods (*abstract properties* + *qualitative*):
-Pair-wise comparisons (only finite sets);
-Relative frequency (more then one expert);
-Neural networks;
-Genetic algorithms.

MF types-1

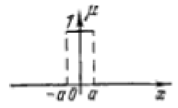
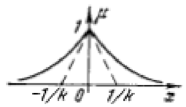
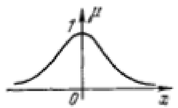
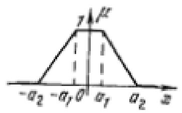
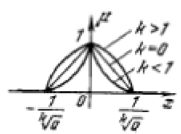
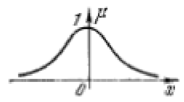
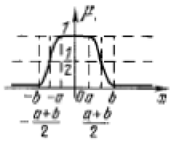
Универсальные множества: R^+, N
Функция принадлежности утверждения «величина x мала»

Область определения	График	Функция	
R^+ N		$\mu(x)=1,\ 0\leqslant x\leqslant a,$ $=0,\ x>a.$	29.1
R^+ N		$\mu(x)=e^{-kx},\ k>0.$	29.2
R^+ N		$\mu(x)=e^{-kx^2},\ k>0.$	29.3
R^+ N		$\mu(x)=1,\ 0\leqslant x\leqslant a_1,$ $=\frac{a_2-x}{a_2-a_1},\ a_1\leqslant x\leqslant a_2,$ $=0,\ a_2\leqslant x.$	29.4
R^+ N		$\mu(x)=1-ax^k,\ 0\leqslant x\leqslant\frac{1}{\sqrt[k]{a}},$ $=0,\ \frac{1}{\sqrt[k]{a}}\leqslant x.$	29.5
R^+ N		$\mu(x)=\frac{1}{1+kx^2},\ k>1.$	29.6
R^+ N		$\mu(x)=1,\ 0\leqslant x\leqslant a,$ $=\frac{1}{2}-\frac{1}{2}\sin\frac{\pi}{b-a}\left(x-\frac{a+b}{2}\right),\ a\leqslant x\leqslant b$ $=0,\ b\leqslant x.$	29.7
R^+ N		$\mu(x)=0,\ 0\leqslant x<a,$ $=1,\ a\leqslant x.$	29.8
R^+ N		$\mu(x)=0,\ 0\leqslant x\leqslant\alpha$ $=1-e^{-k(x-\alpha)},\ \alpha\leqslant x,$ $k>0.$	29.9
R^+ N		$\mu(x)=0,\ 0\leqslant x\leqslant\alpha,$ $=1-e^{-k(x-\alpha)^2},\ \alpha\leqslant x,$ $k>0.$	29.10
R^+ N		$\mu(x)=0,\ 0\leqslant x\leqslant a_1,$ $=\frac{x-a_1}{a_2-a_1},\ a_1\leqslant x\leqslant a_2,$ $=1,\ a_2\leqslant x.$	29.11
R^+ N		$\mu(x)=0,\ 0\leqslant x\leqslant\alpha,$ $=a(x-\alpha)^k,\ \alpha\leqslant x\leqslant\alpha+\frac{1}{\sqrt[k]{a}},$ $=1,\ \alpha+\frac{1}{\sqrt[k]{a}}\leqslant x.$	29.12
R^+ N		$\mu(x)=0,\ 0\leqslant x\leqslant\alpha,$ $=\frac{k(x-\alpha)^2}{1+k(x-\alpha)^2},\ \alpha<x<\infty.$	29.13
R^+ N		$\mu(x)=0,\ 0\leqslant x\leqslant a,$ $=\frac{1}{2}+\frac{1}{2}\sin\frac{\pi}{b-a}\left(x-\frac{a+b}{2}\right),\ a\leqslant x\leqslant b,$ $=1,\ a\leqslant x.$	29.14

MF types-2

Универсальные множества: R, Z

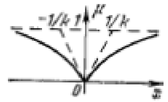
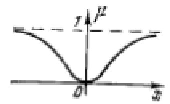
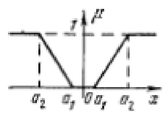
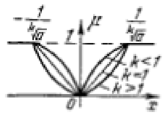
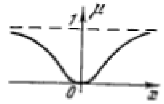
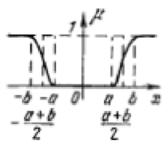
Функция принадлежности утверждения «величина |x| мала»

Область определения	График	Функция	
R Z		$\mu(x)=0, \quad -\infty<x<a,$ $=1, \quad -a\leqslant x\leqslant a,$ $=0, \quad a\leqslant x.$	29.15
R Z		$\mu(x)=e^{kx}, \quad -\infty<x\leqslant 0,$ $=e^{-kx}, \quad 0\leqslant x<\infty,$ $k>1.$	29.16
R Z		$\mu(x)=e^{-kx^2}.$	29.17
R Z		$\mu(x)=0, \quad -\infty<x\leqslant -a_2,$ $=\frac{a_2+x}{a_2-a_1}, \quad -a_2\leqslant x\leqslant -a_1,$ $=1, \quad -a_1\leqslant x\leqslant a_1,$ $=\frac{a_2-x}{a_2-a_1}, \quad a_1\leqslant x\leqslant a_2,$ $=0, \quad a_2\leqslant x<\infty.$	29.18
R Z		$\mu(x)=0, \quad -\infty<x\leqslant -\frac{1}{\sqrt[k]{a}},$ $=1-a(-x)^k, \quad -\frac{1}{\sqrt[k]{a}}\leqslant x\leqslant 0,$ $=1-a(x)^k, \quad 0\leqslant x\leqslant \frac{1}{\sqrt[k]{a}},$ $=0, \quad \frac{1}{\sqrt[k]{a}}\leqslant x<\infty.$	29.19
R Z		$\mu(x)=\frac{1}{1+kx^2}, \quad k>1.$	29.20
R Z		$\mu(x)=0, \quad -\infty<x\leqslant -b,$ $=\frac{1}{2}+\frac{1}{2}\sin\frac{\pi}{b-a}\left(x+\frac{a+b}{2}\right),$ $-b\leqslant x\leqslant -a,$ $=1, \quad -a\leqslant x\leqslant a,$ $=\frac{1}{2}-\frac{1}{2}\sin\frac{\pi}{b-a}\left(x-\frac{a+b}{2}\right),$ $a\leqslant x\leqslant b,$ $=0, \quad b\leqslant x<\infty.$	29.21

MF types-3

Универсальные множества: R, Z

Функция принадлежности утверждения «величина $|x|$ большая»

Область определения	График	Функция	
R Z		$\mu(x)=1, \quad -\infty<x<-a,$ $=0, \quad -a<x<a,$ $=1, \quad a<x<\infty.$	29.22
R Z		$\mu(x)=1-e^{kx}, \quad -\infty<x\leqslant 0,$ $=1-e^{-kx}, \quad 0\leqslant x<\infty,$ $k>1.$	29.23
R Z		$\mu(x)=1-e^{-kx^2}, \quad k>1.$	29.24
R Z		$\mu(x)=1, \quad -\infty<x<-a_2,$ $=-\dfrac{x+a_1}{a_2-a_1}, \quad -a_2\leqslant x\leqslant -a_1,$ $=0, \quad -a_1\leqslant x\leqslant a_1,$ $=\dfrac{x-a_1}{a_2-a_1}, \quad a_1\leqslant x\leqslant a_2,$ $=1, \quad a_2\leqslant x<\infty.$	29.25
R Z		$\mu(x)=1, \quad -\infty<x<-\dfrac{1}{\sqrt[k]{a}},$ $=a(-x)^k, \quad -\dfrac{1}{\sqrt[k]{a}}\leqslant x\leqslant 0,$ $=ax^k, \quad 0\leqslant x\leqslant \dfrac{1}{\sqrt[k]{a}},$ $=1, \quad \dfrac{1}{\sqrt[k]{a}}\leqslant x<\infty.$	29.26
R Z		$\mu(x)=\dfrac{kx^2}{1+kx^2}=\dfrac{1}{1+\dfrac{1}{kx^2}}, \quad k>1.$	29.27
R Z		$\mu(x)=1, \quad -\infty<x\leqslant -b$ $=\dfrac{1}{2}-\dfrac{1}{2}\sin\dfrac{\pi}{b-a}\left(x+\dfrac{a+b}{2}\right), \quad -b\leqslant x\leqslant -a,$ $=0, \quad -a\leqslant x\leqslant a,$ $=\dfrac{1}{2}+\dfrac{1}{2}\sin\dfrac{\pi}{b-a}\left(x-\dfrac{a+b}{2}\right), \quad a\leqslant x\leqslant b,$ $=1, \quad b\leqslant x<\infty.$	29.28

MF fundamental restriction

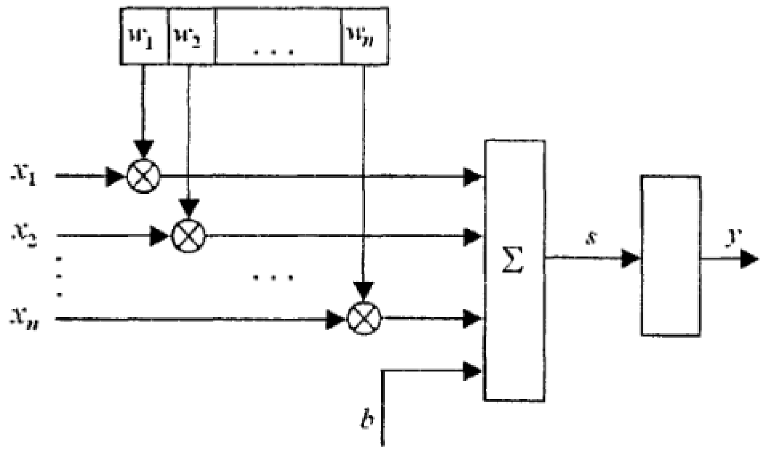
In fuzzy theory, Membership Function has to be set outside of the theory itself. It should be imposed, and its adequacy and applicability **cannot be tested** using the fuzzy theory.

Old-young
Toll-small
Beautiful, tasty, prominent…

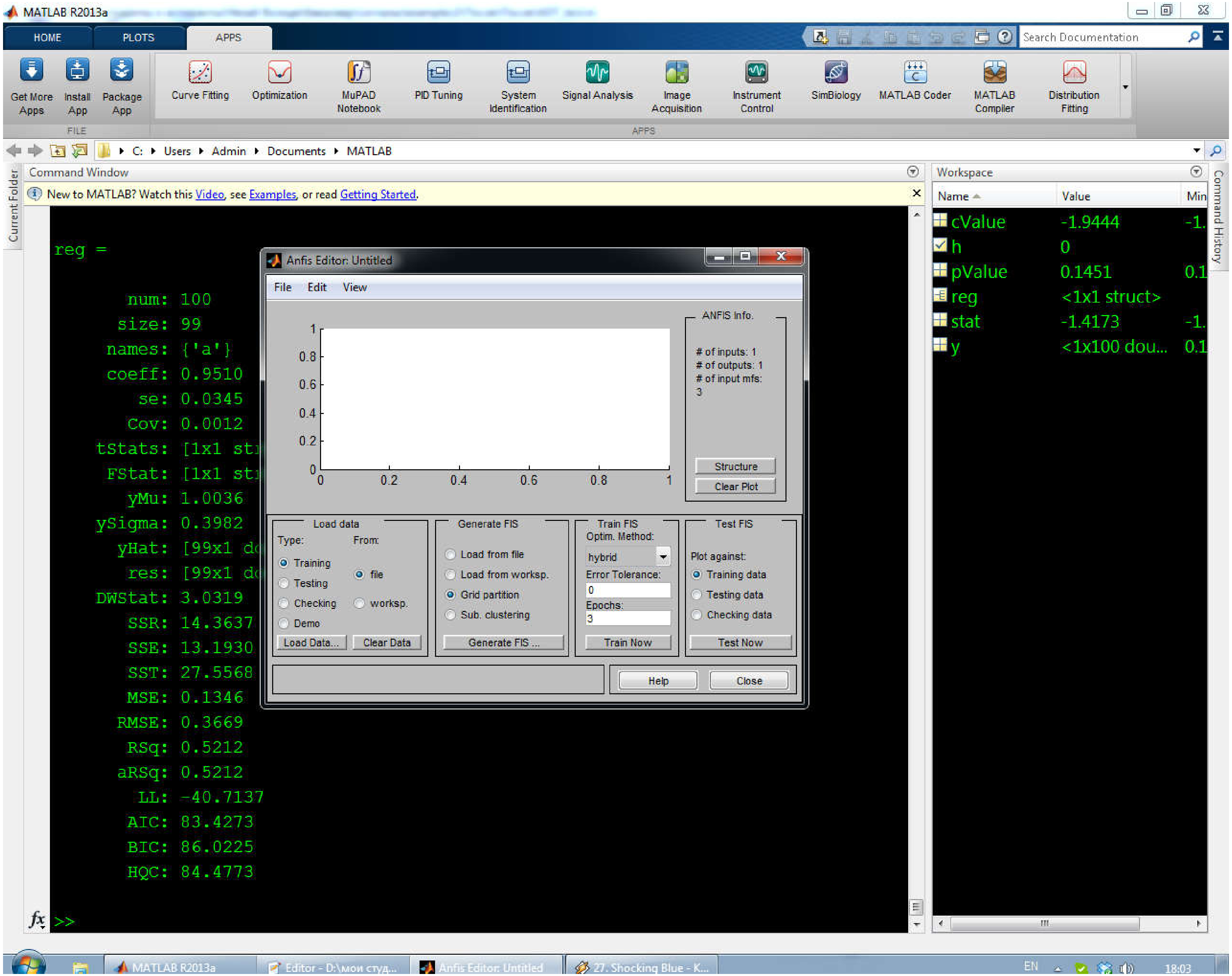
ANFIS for Membership Functions construction

Adaptive Neuro-Fuzzy Inference System (ANFIS)

One can shape membership functions by training them with input/output data rather than specifying them manually.

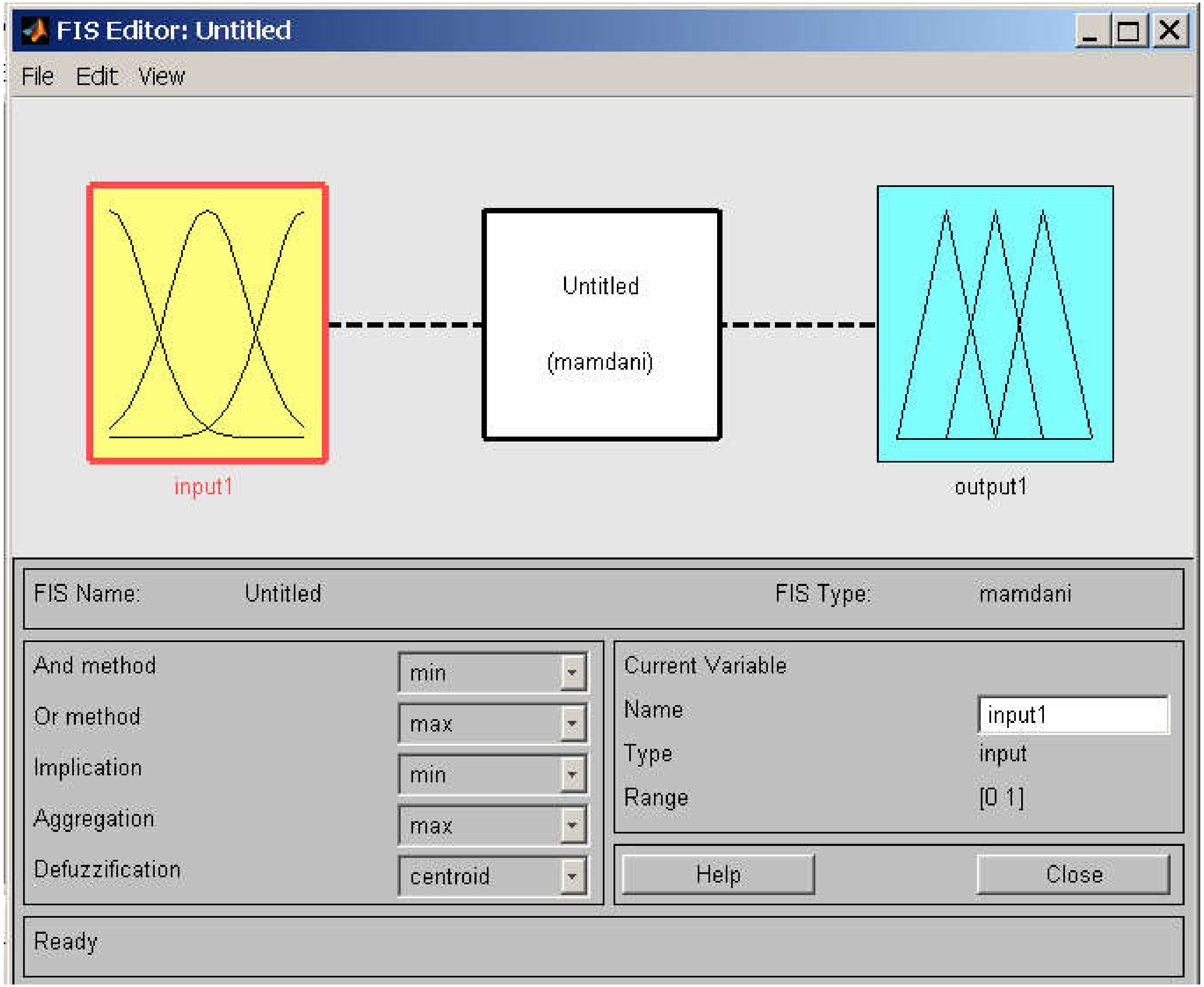


The toolbox uses a back propagation algorithm alone or in combination with a least squares method, enabling your fuzzy systems to learn from the data.

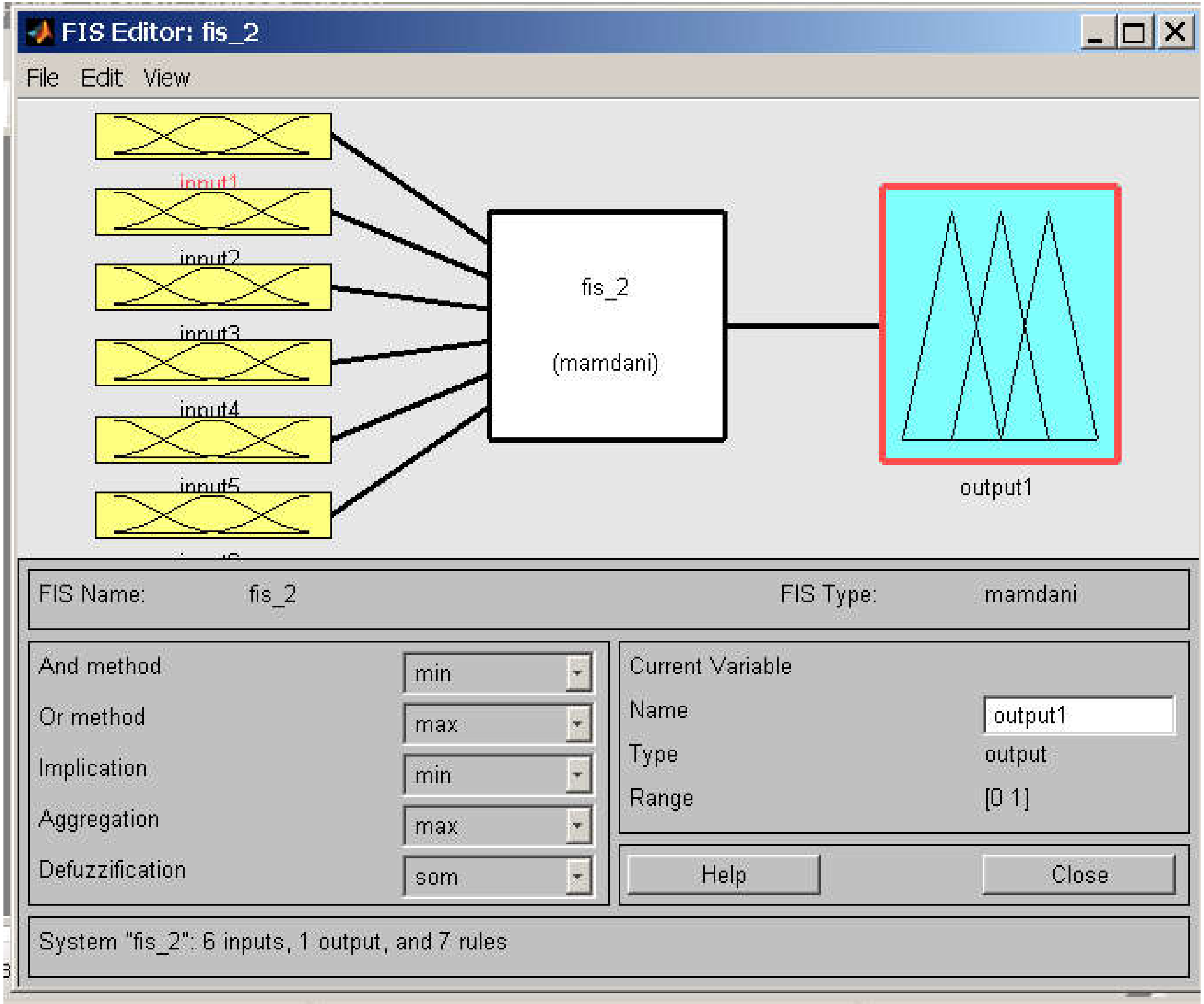

MATLAB R2013a
HOME
PLOTS
APPS
Get More Apps
Install App
Package App
FILE
Curve Fitting
Optimization
MuPAD Notebook
PID Tuning
System Identification
Signal Analysis
Image Acquisition
Instrument Control
SimBiology
MATLAB Coder
MATLAB Compiler
Distribution Fitting
APPS
Search Documentation
C: ▸ Users ▸ Admin ▸ Documents ▸ MATLAB
Command Window
New to MATLAB? Watch this Video, see Examples, or read Getting Started.
reg =
num: 100
size: 99
names: {'a'}
coeff: 0.9510
se: 0.0345
Cov: 0.0012
tStats: [1x1 st
FStat: [1x1 st
yMu: 1.0036
ySigma: 0.3982
yHat: [99x1 d
res: [99x1 d
DWStat: 3.0319
SSR: 14.3637
SSE: 13.1930
SST: 27.5568
MSE: 0.1346
RMSE: 0.3669
RSq: 0.5212
aRSq: 0.5212
LL: -40.7137
AIC: 83.4273
BIC: 86.0225
HQC: 84.4773
fx >>
Anfis Editor: Untitled
File Edit View
ANFIS Info.
# of inputs: 1
# of outputs: 1
# of input mfs:
3
Structure
Clear Plot
Load data
Type: From:
Training
Testing
Checking
Demo
file
worksp.
Load Data...
Clear Data
Generate FIS
Load from file
Load from worksp.
Grid partition
Sub. clustering
Generate FIS ...
Train FIS
Optim. Method:
hybrid
Error Tolerance:
0
Epochs:
3
Train Now
Test FIS
Plot against:
Training data
Testing data
Checking data
Test Now
Help
Close
Workspace
Name Value Min
cValue -1.9444
h 0
pValue 0.1451
reg <1x1 struct>
stat -1.4173
y <1x100 dou...
Current Folder
Command History
MATLAB R2013a
Anfis Editor: Untitled
EN
18:03

FIS constructing and testing

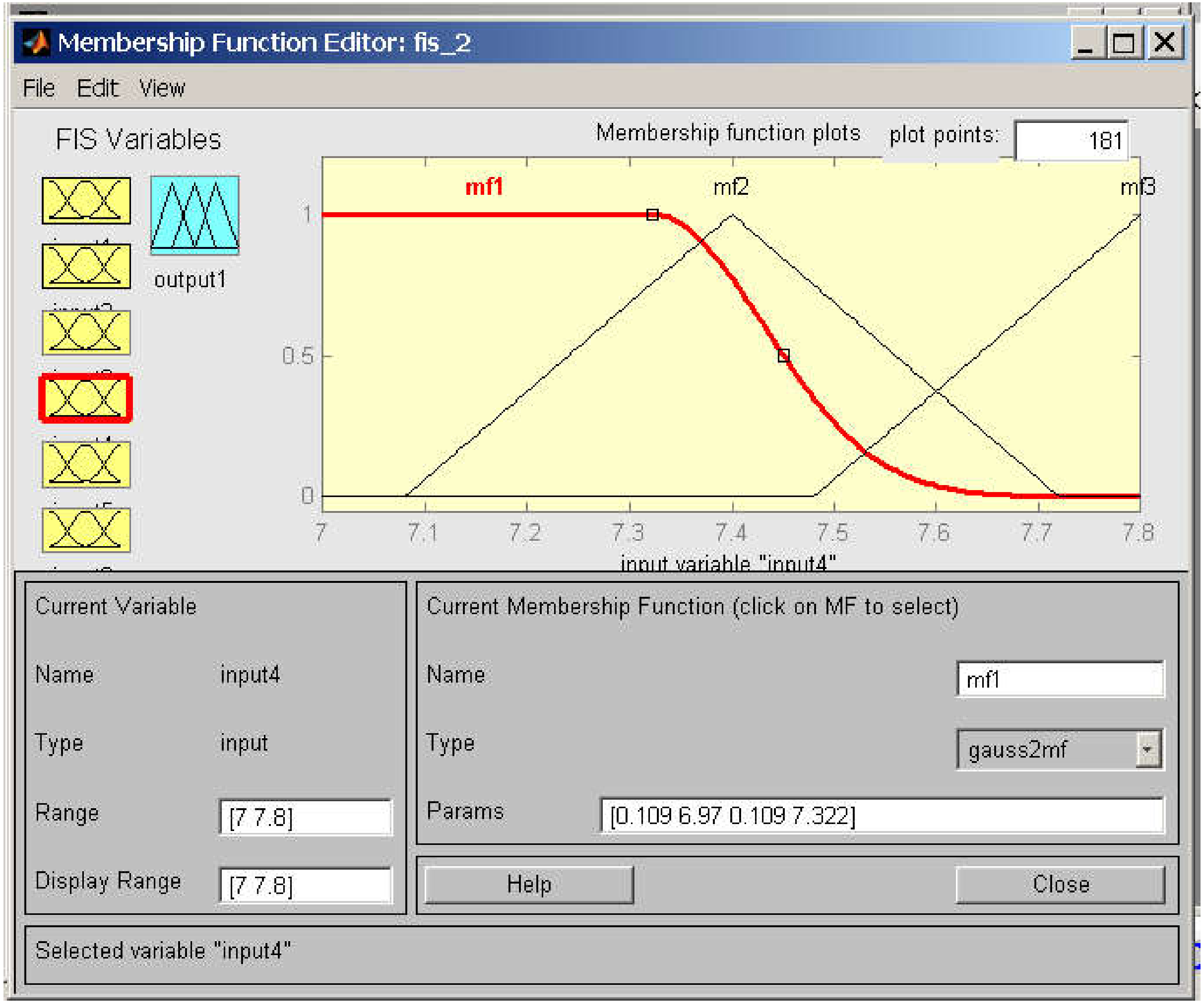
MATLAB FIS GUI



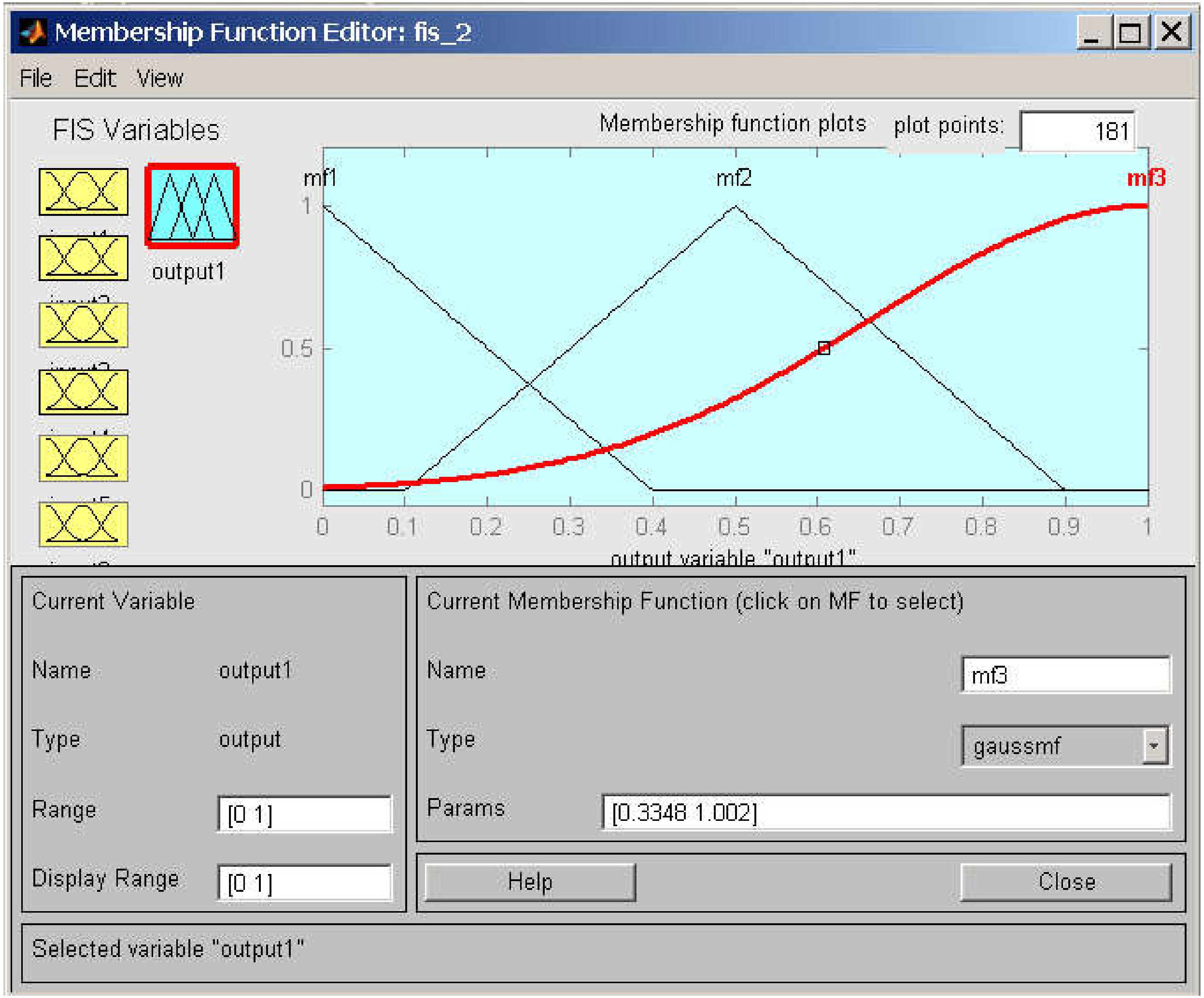
MATLAB FIS GUI



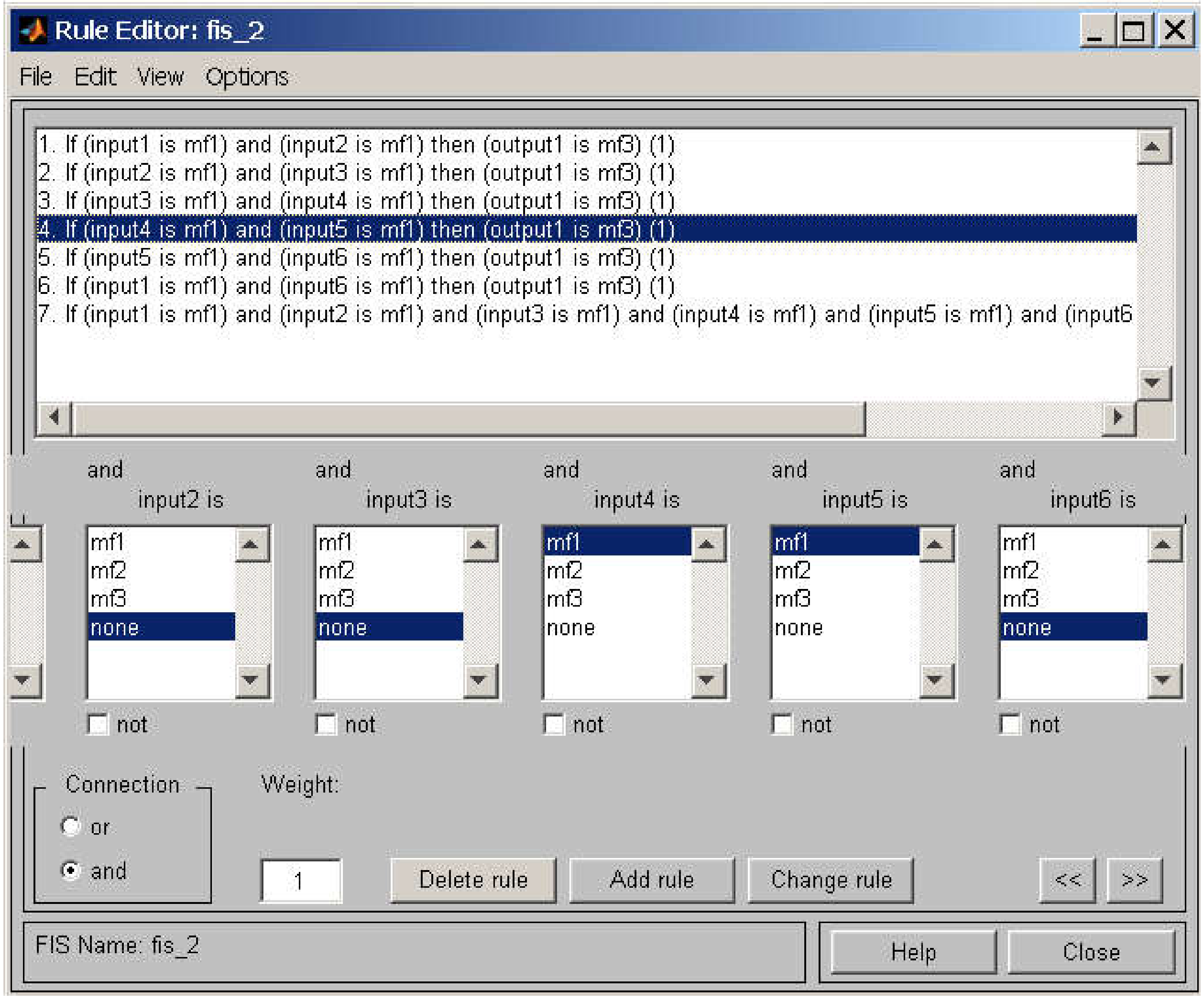
MATLAB FIS GUI



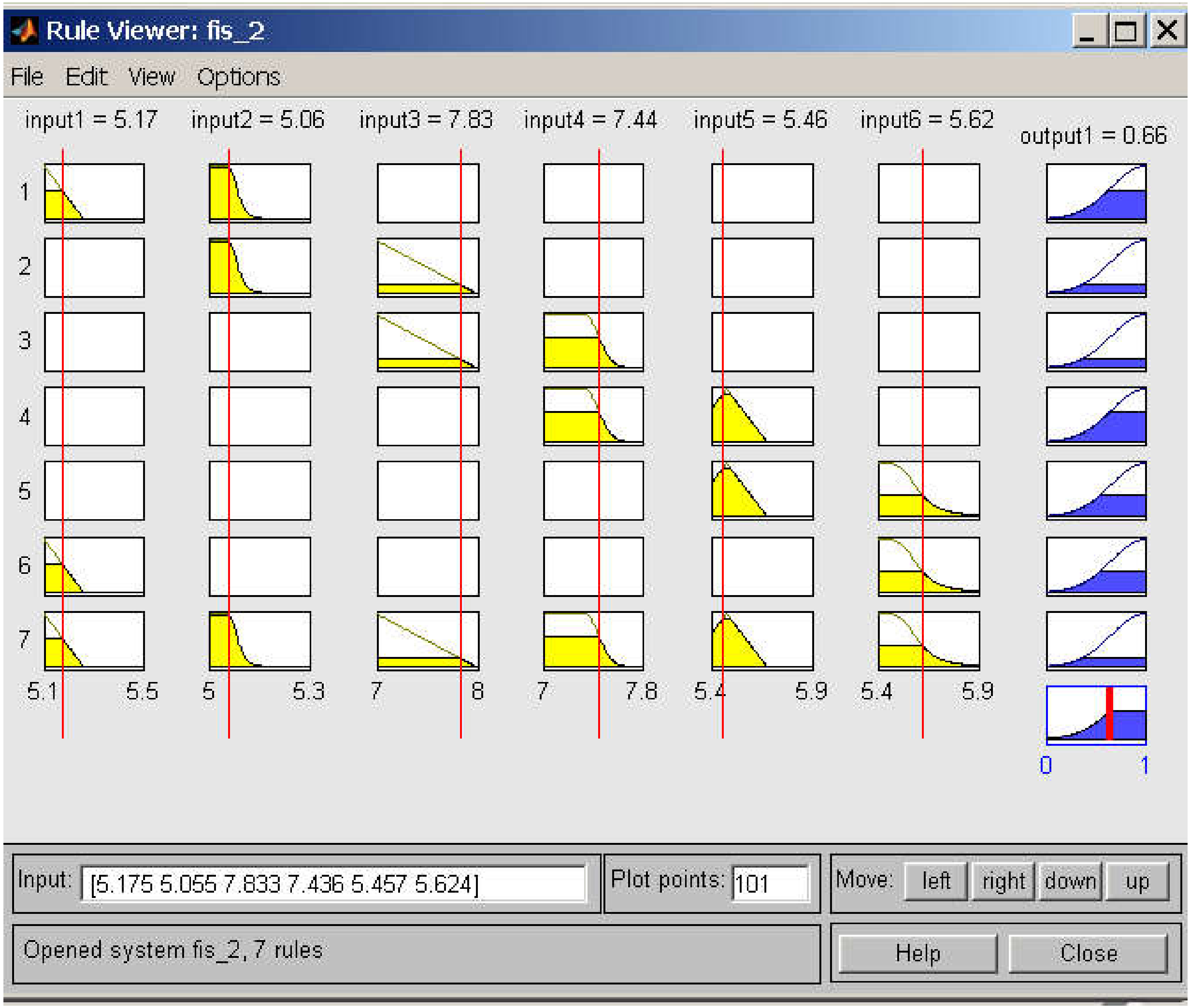
MATLAB FIS GUI



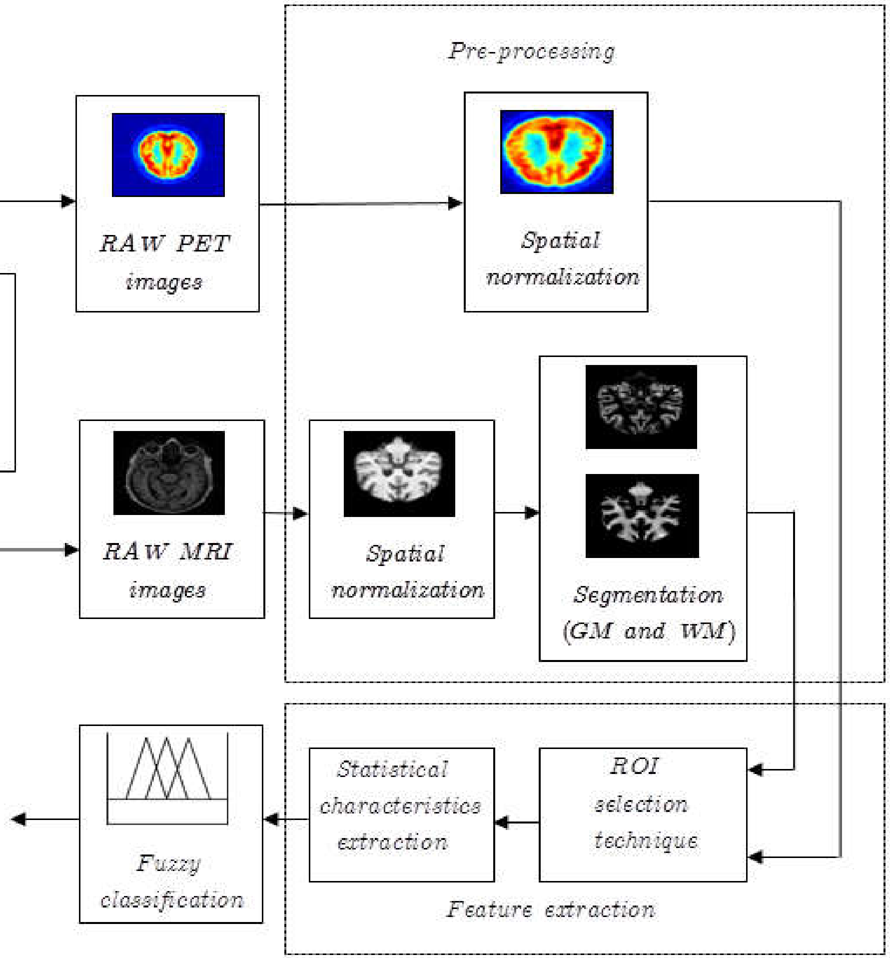
MATLAB FIS GUI



MATLAB FIS GUI

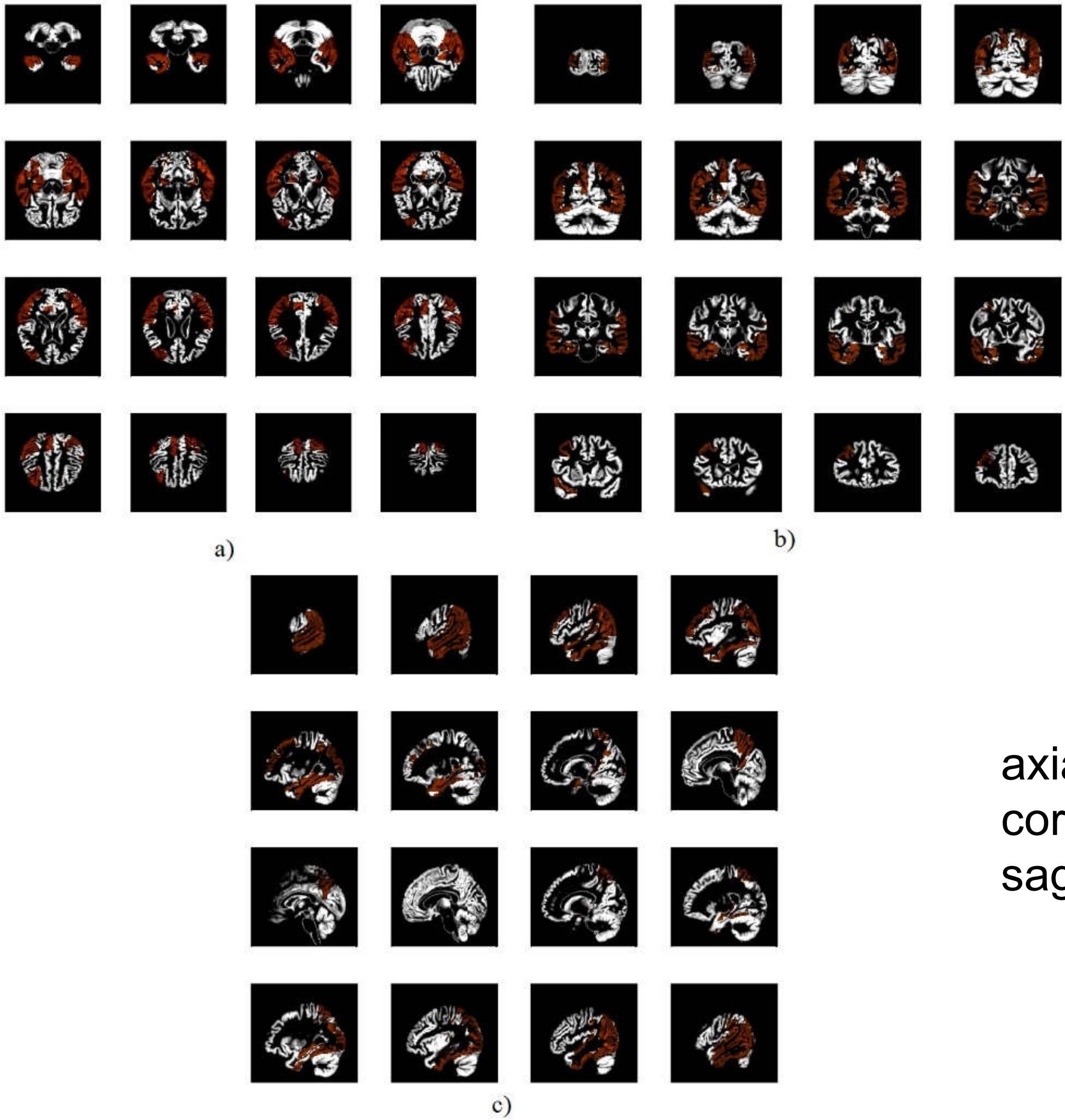


Fuzzy Inference System



	NOR vs. MCI	NOR vs. AD	AD vs. MCI
sens	0.76±0.02	0.93±0.02	0.75±0.01
spec	0.86±0.01	0.92±0.02	0.82±0.01
acc	0.82±0.02	0.90±0.02	0.73±0.01
ppv	0.84±0.02	0.91±0.02	0.80±0.01

Most AD affected regions of human brain



axial (a),
coronal (b)
saggital (c)