Lung Cancer Identification by an Electronic Nose based on an Array of MOS Sensors

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SACMI

Outline

- Objective: **Lung Cancer** diagnosis classifying the **Olfactory Signal** acquired by an **Electronic Nose**
- Motivation
- Functioning of the Electronic Nose
- **Classification** of volunteers' breath
- Results and comparison with current diagnostic techniques
- Further directions of research

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- Lung cancer causes more than 160,000 deaths a year in the United States--more than any other cancer
- Once lung cancer is detected the probability of surviving, after 5 years of therapy, is 14%; the survival rate increases to 48% if the cancer is discovered in its earliest stage
- Current diagnostic techniques are invasive, very expensive, have a high risk of complications and a not so good performance
- Efforts at early detection and treatment have been frustrating to date and hence the overall prognosis remains poor

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- **Fundamental Principle of Clinical Chemistry**: "Every pathology changes people chemical composition, modifying the concentration of some chemicals in the human body"
  - In the medical field, clinicians have always considered odor as a fundamental information for the diagnosis of several diseases
- It has been demonstrated (Gordon et al, 1985) that the presence of lung cancer alters the percentage of some **volatile organic compounds (VOCs)** present in **human breath**
  - These VOCs can be considered as **lung cancer markers** and thus used to diagnose it

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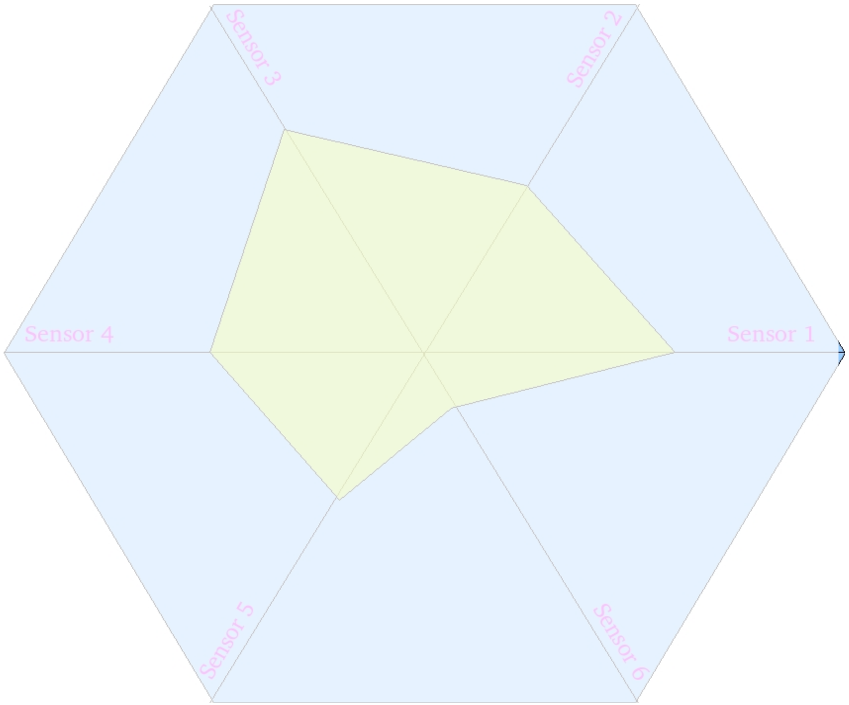
Electronic Nose

- An electronic nose is an instrument able to **acquire, detect and analyse the olfactory signal**
- It is composed of an **array of non specific electronic devices** (sensors) able to **convert a physical or chemical information into an electrical signal**
  - It is non specific because it does not look for particular compounds in the analyzed substance, but for different **patterns**
  - Each sensor reacts in a different way to the analyzed substance providing multidimensional data that can be considered as an **olfactory blueprint** of the substance itself



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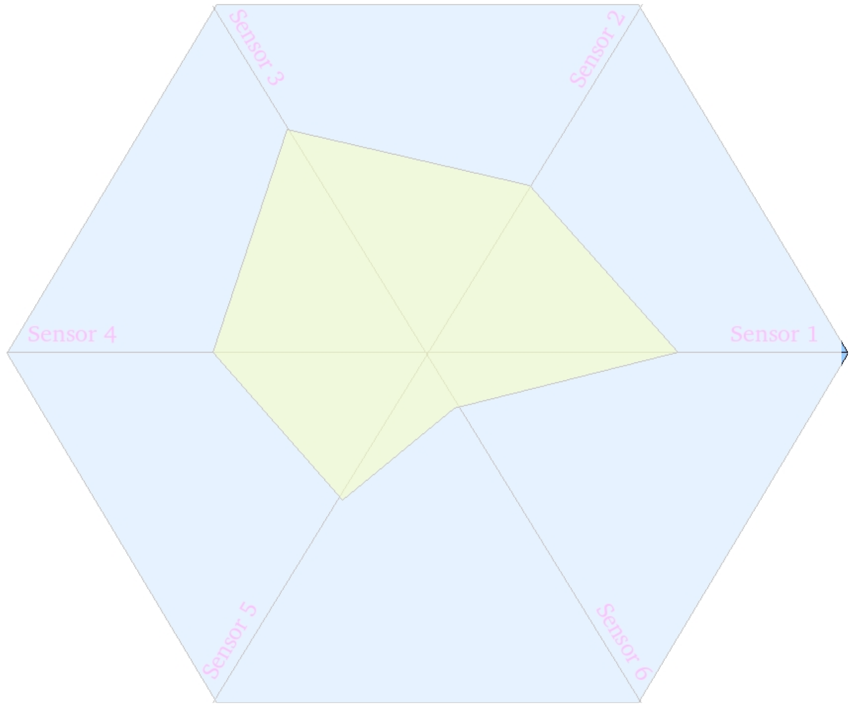

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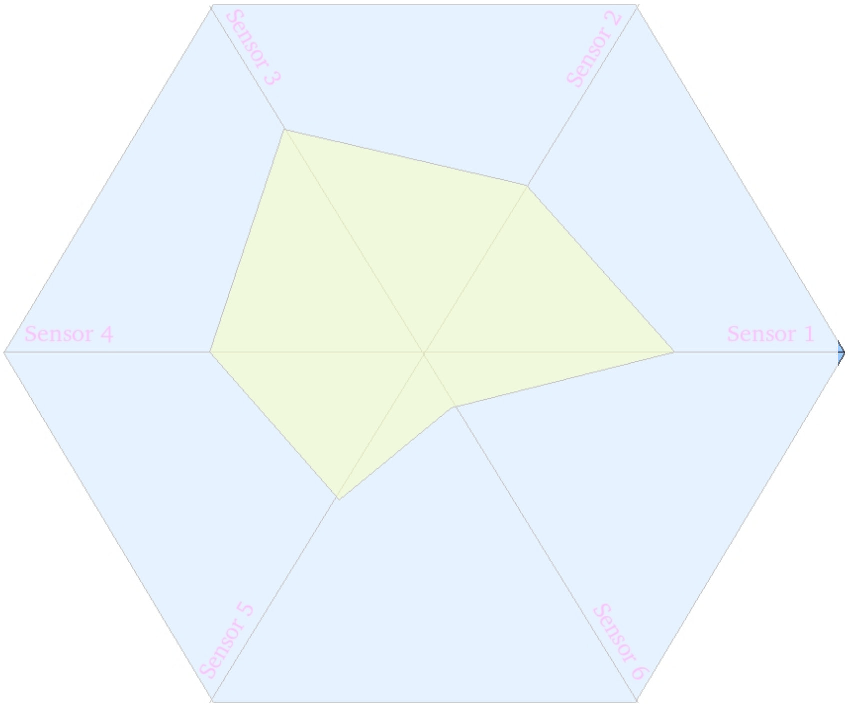

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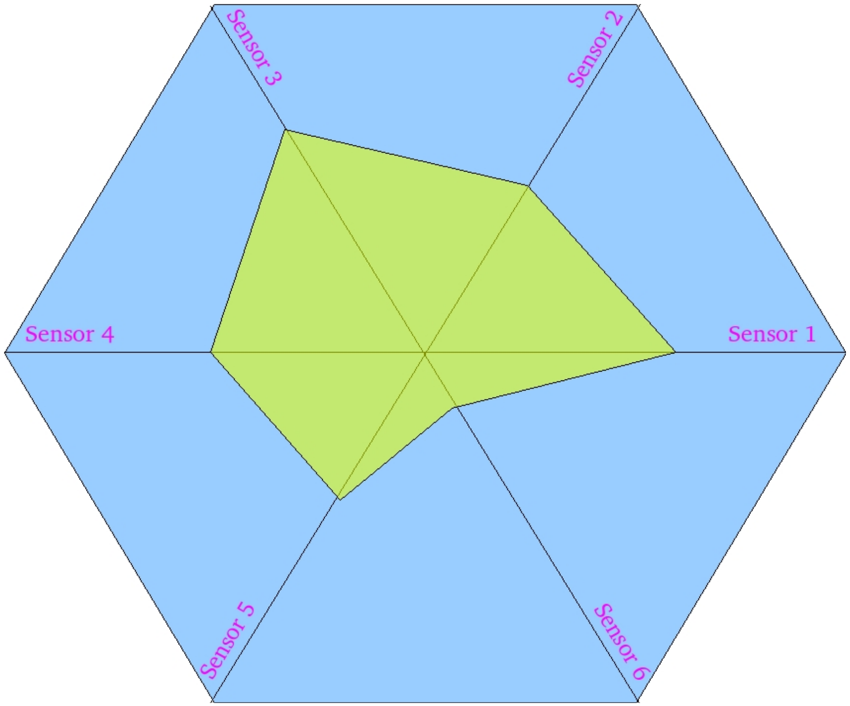

Electronic Nose's Output

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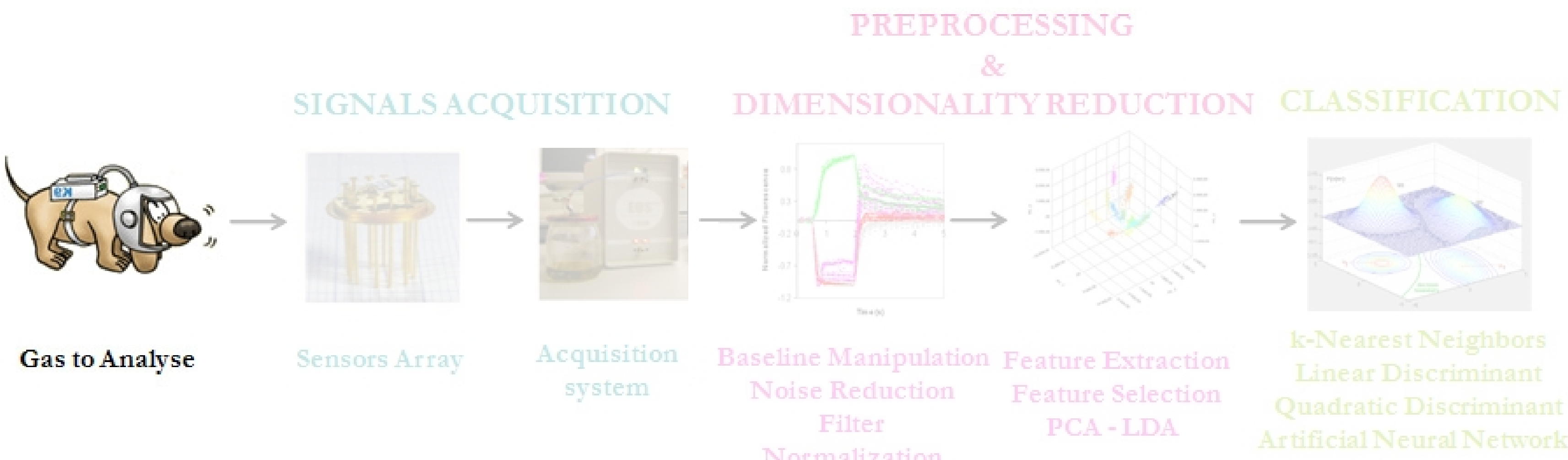
Electronic Nose

1. **Signal Acquisition**
   - Acquisition is done through a sensor array that measures a given physical or chemical quantity and convert it into an electrical signal
2. **Signal Processing**
   - **Preprocessing**: aimed to reduce the impact of noise
   - **Dimensionality Reduction**: reduce the dimensionality of the problem, enhancing classification performance
3. **Classification and Validation**
   - Classification between the two classes “healthy” and “sick”



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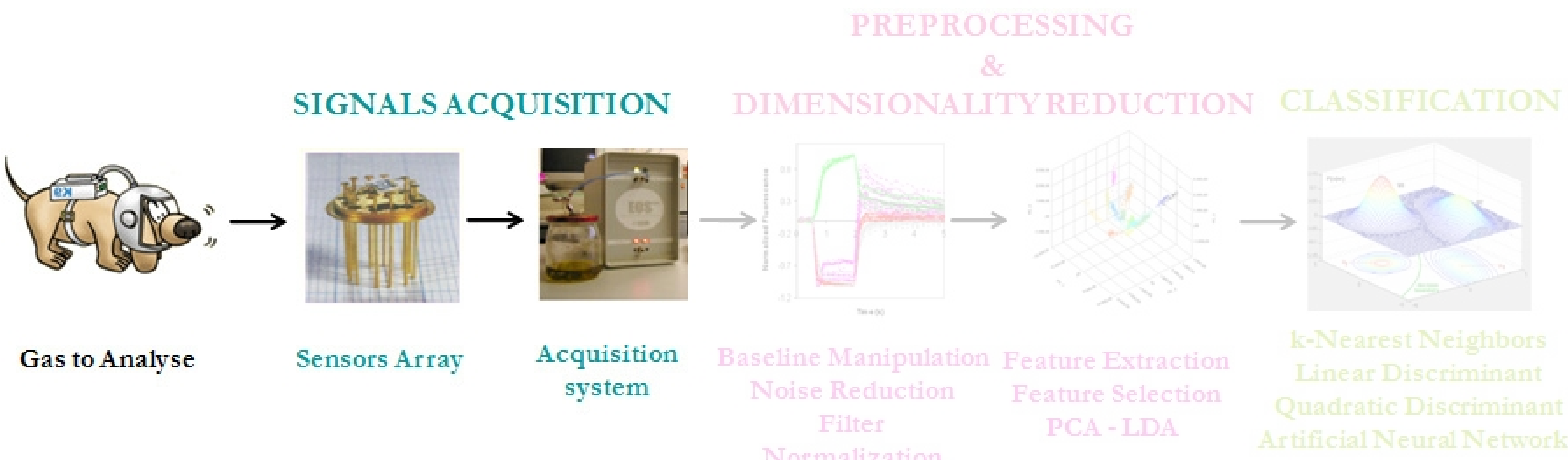

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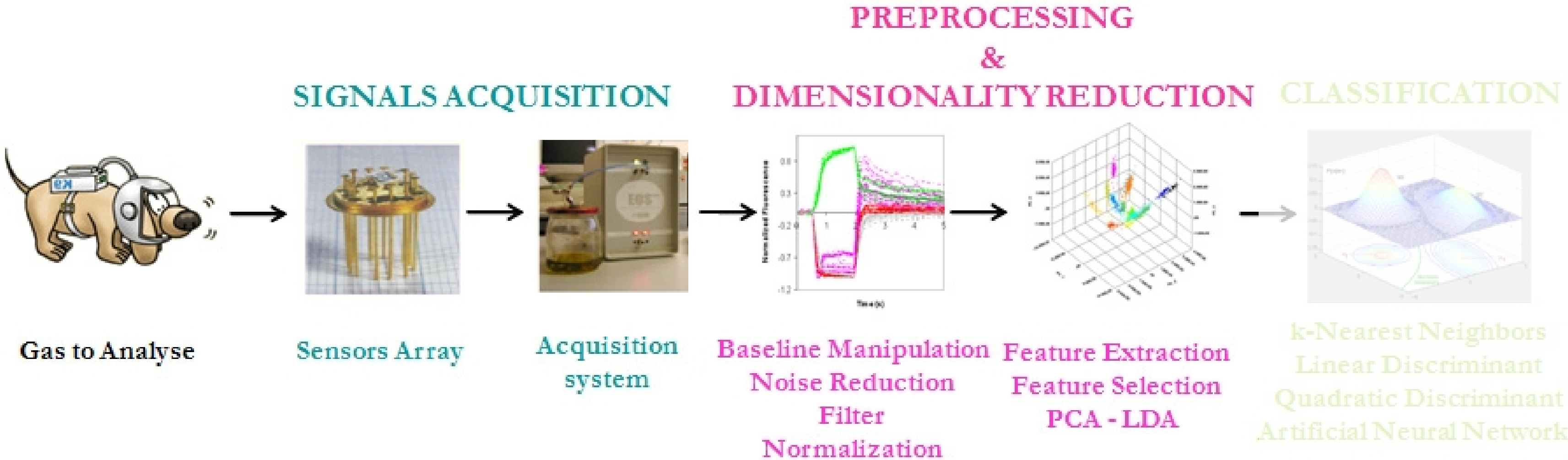

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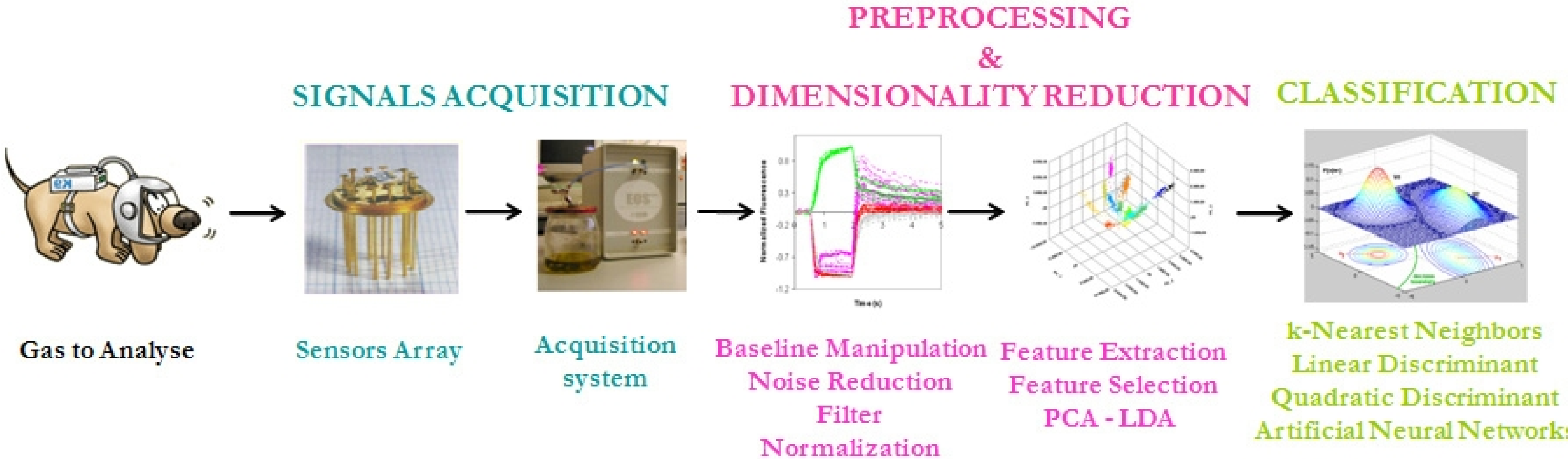

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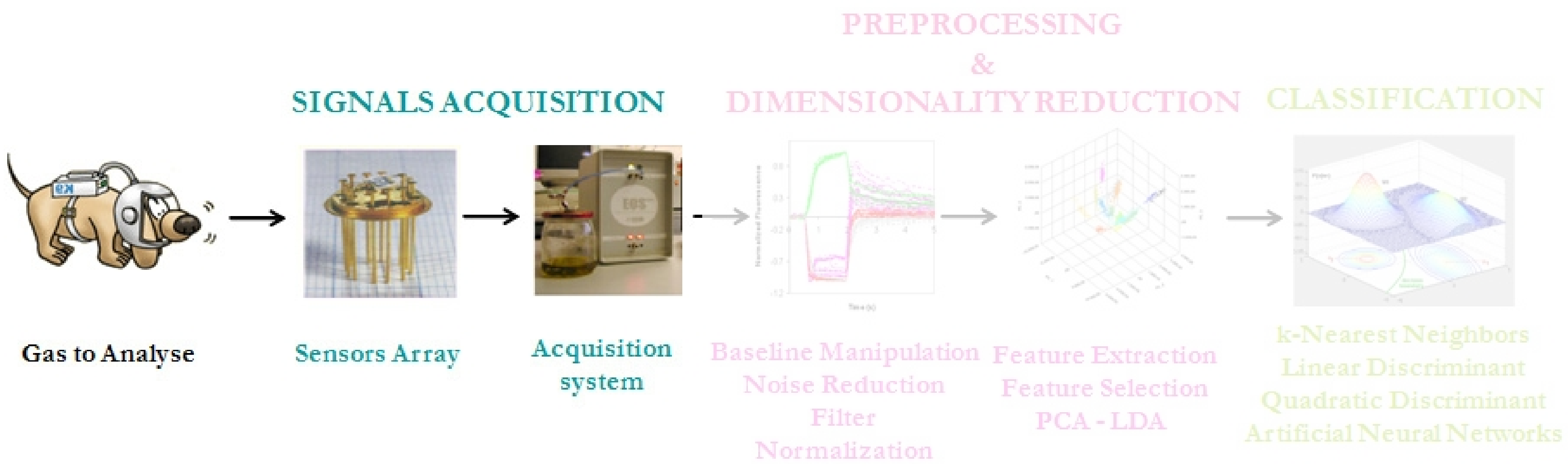

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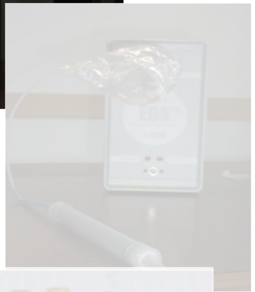
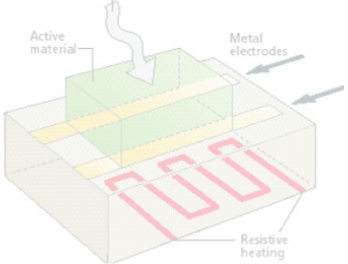
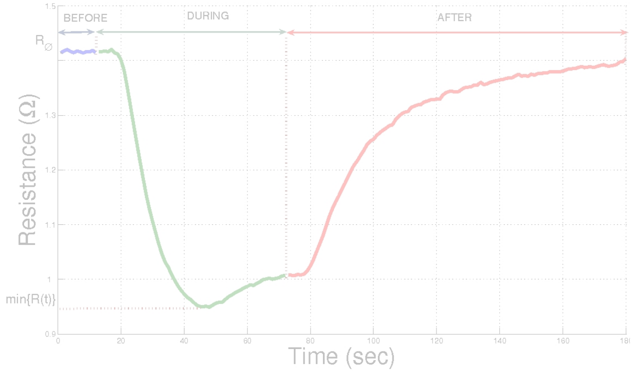


- The breath acquisition has been made inviting all volunteers to blow into a nalophan bag of approximately 400cm^3

- Then, the air contained in the bag was input into the electronic nose



- We used an array of **six MOS sensors** that react to gases with a **variation of resistance**



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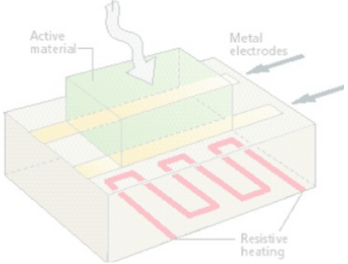

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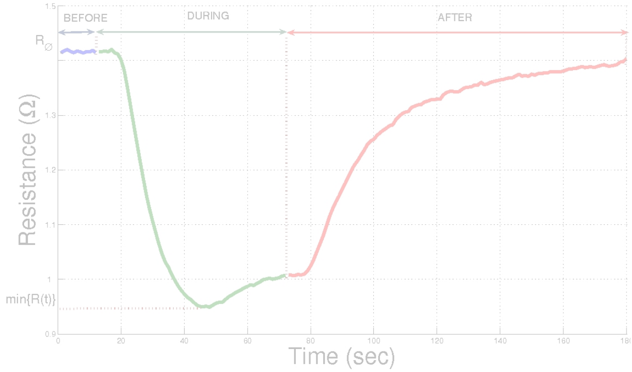

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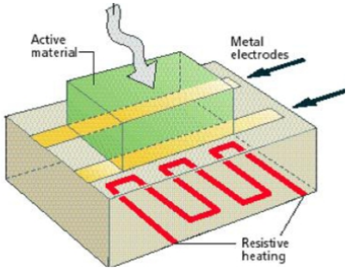

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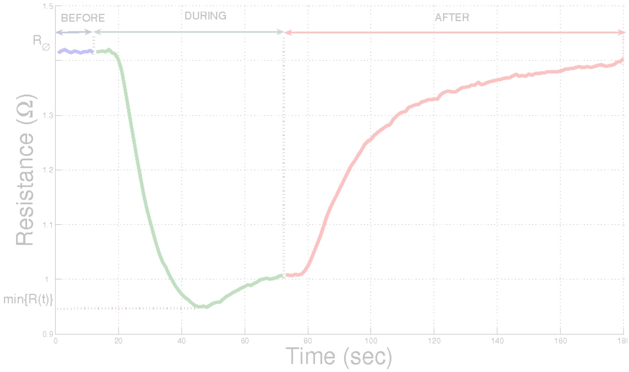

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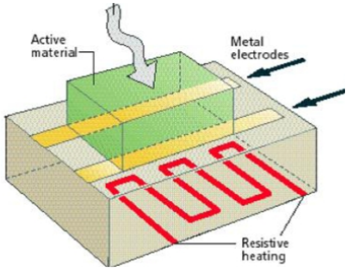

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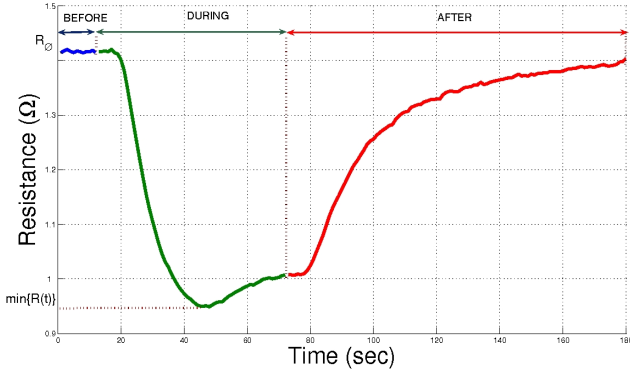

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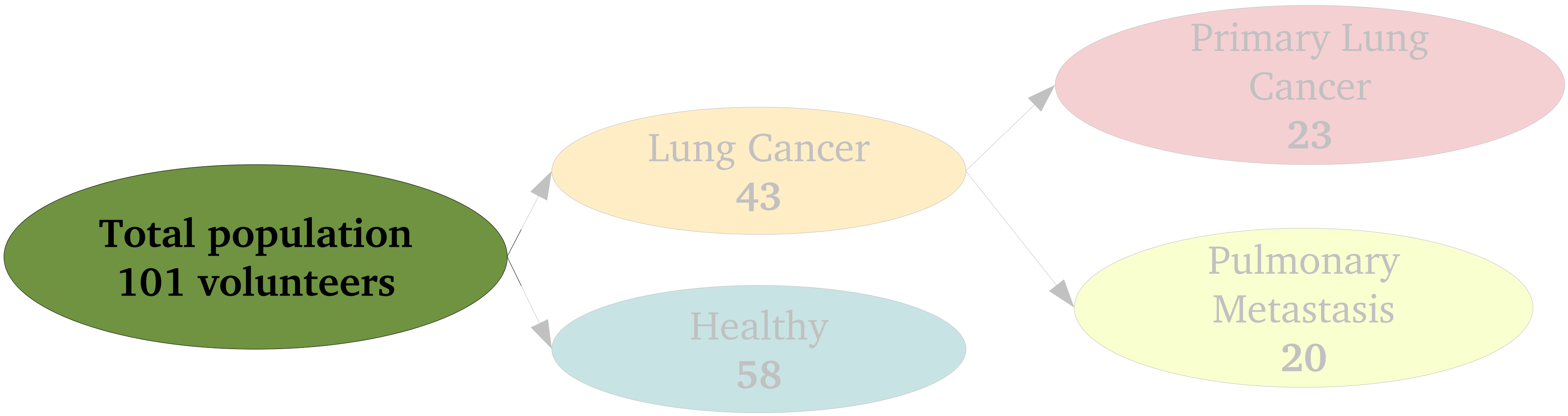
Involved Population

- We analyzed the breath of **101 volunteers**



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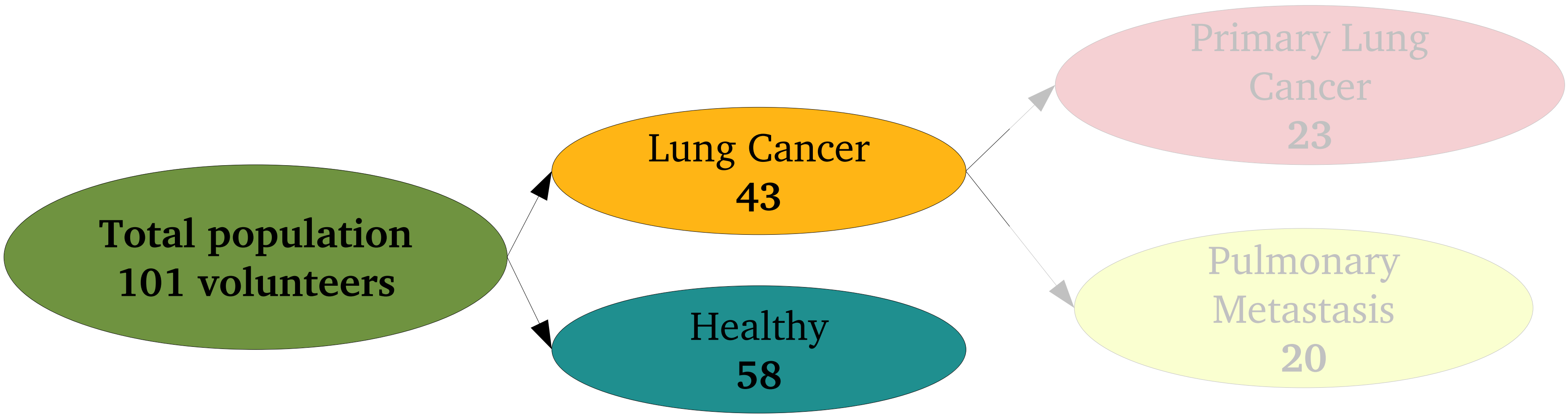

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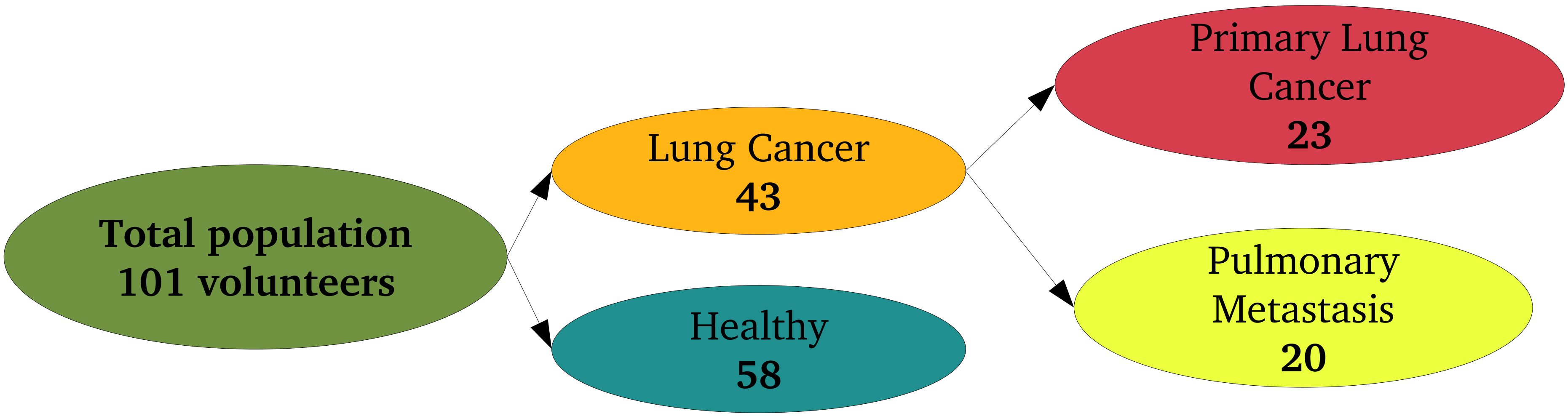

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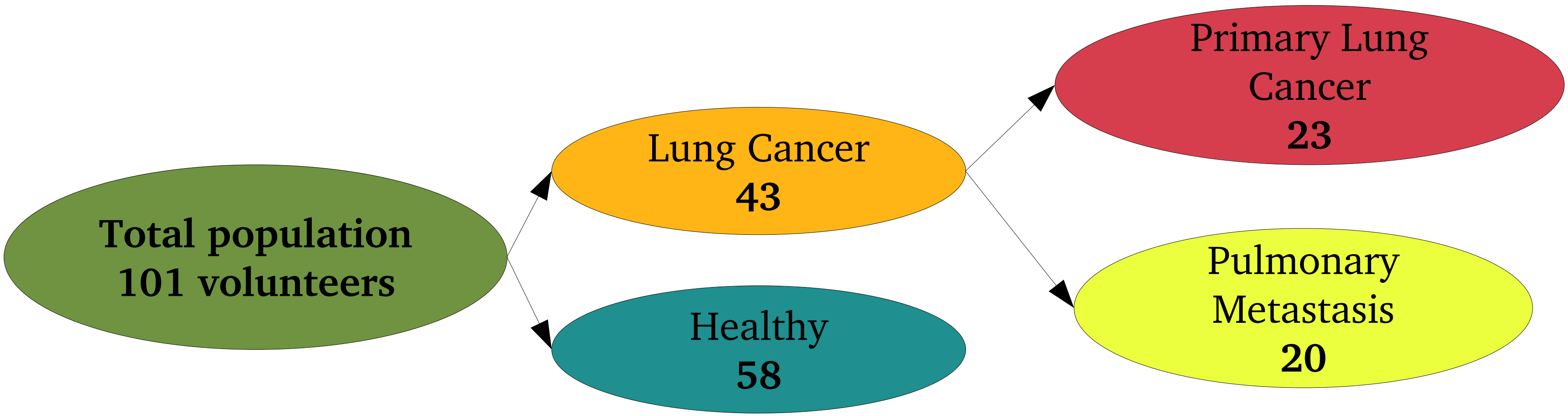

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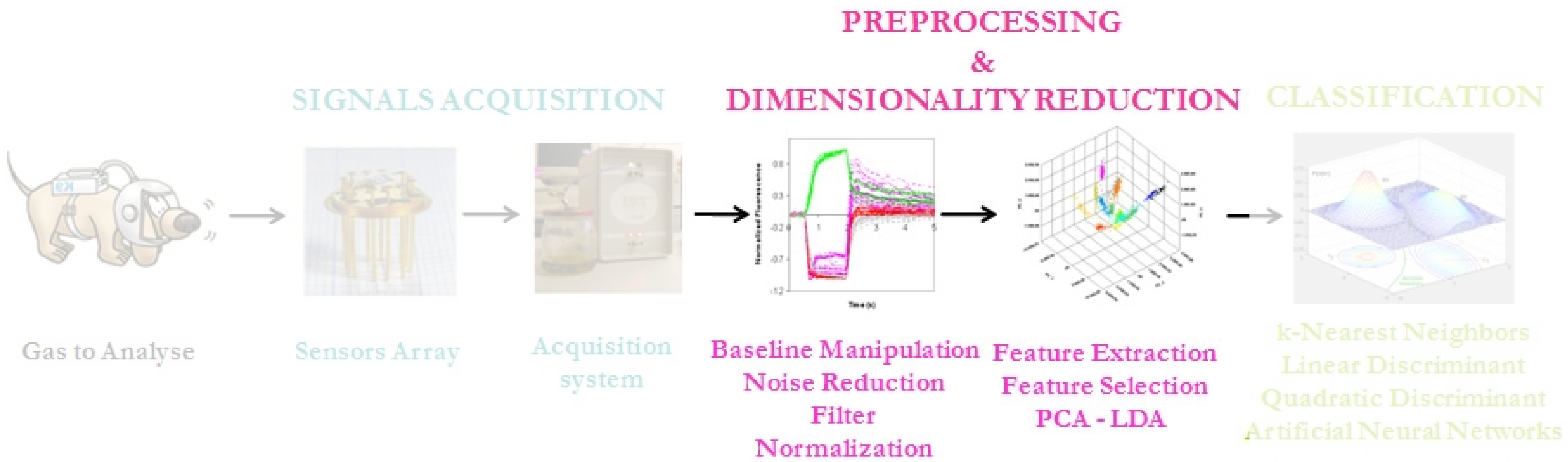
Pre-processing & Dimensionality Reduction



Signal pre-processing

- Manipulation of the **baseline**: transformation of the sensor response w.r.t. its baseline for the purpose of **drift compensation**
- Reduction of **humidity** effects
- **Normalization**: compensation for the scale difference among the six sensors
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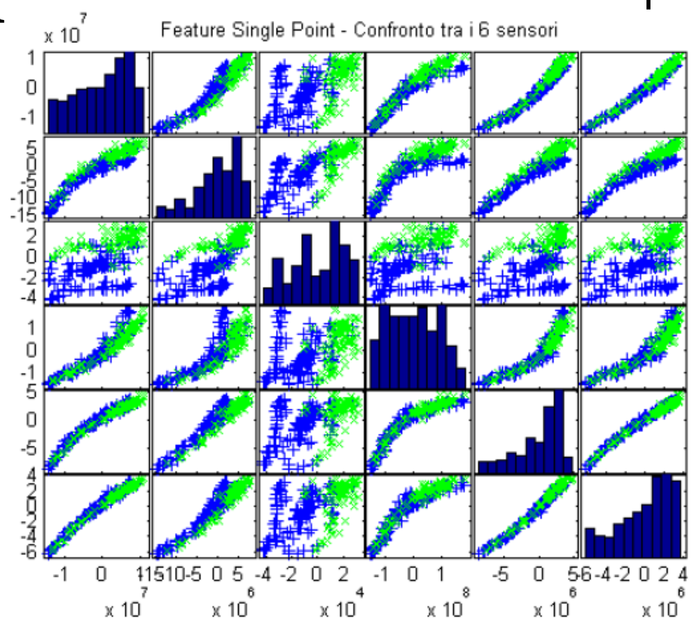
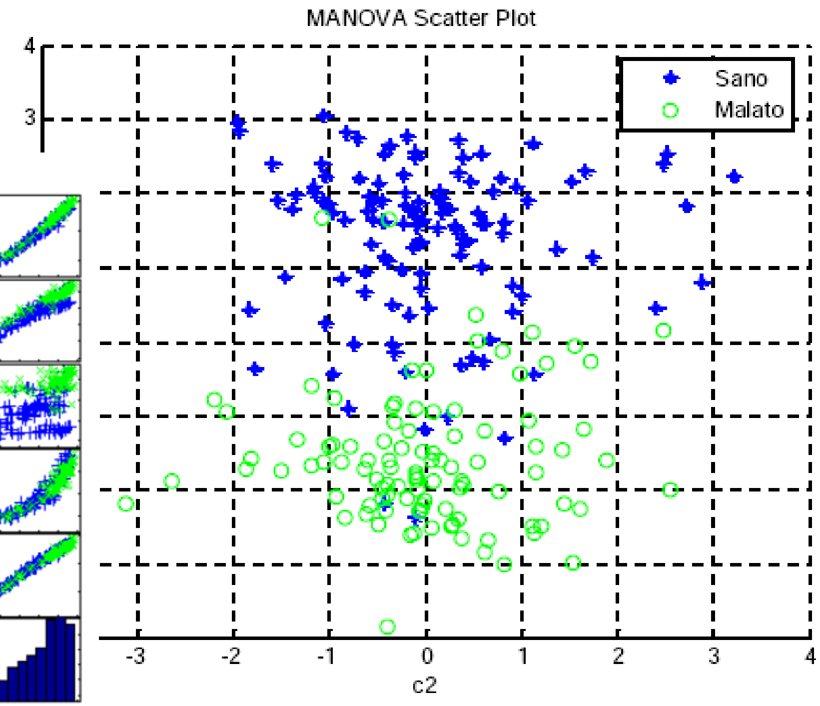
  - Non-parametric test of Mann-Whitney-Wilcoxon
  - Scatter Plot
  - MANOVA





- Feature Extraction

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    - It **removes the unimodal gaussian assumption** by computing the between scatter matrix S_b using the *k*-NN rule
  - Best projection: 1st NPLDA component

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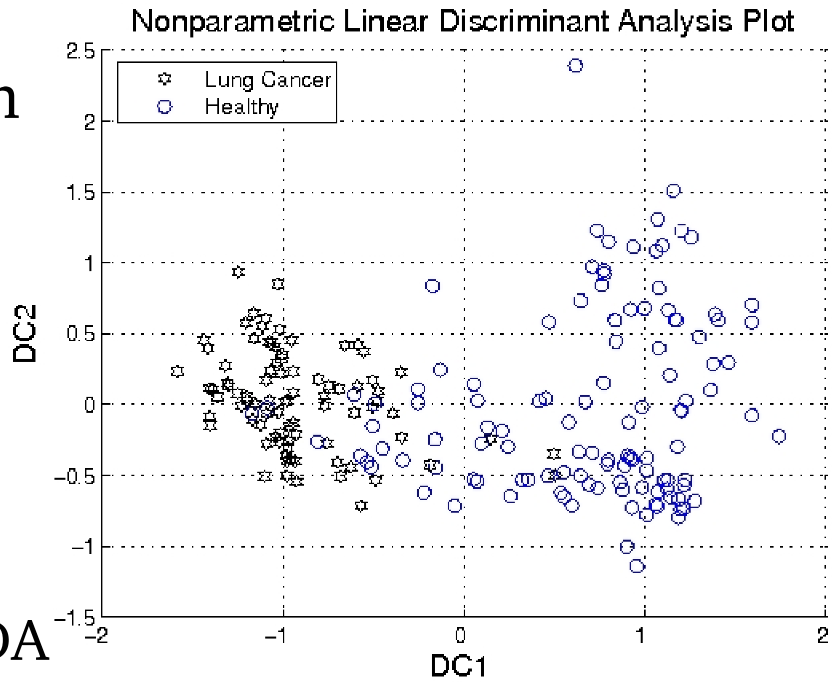

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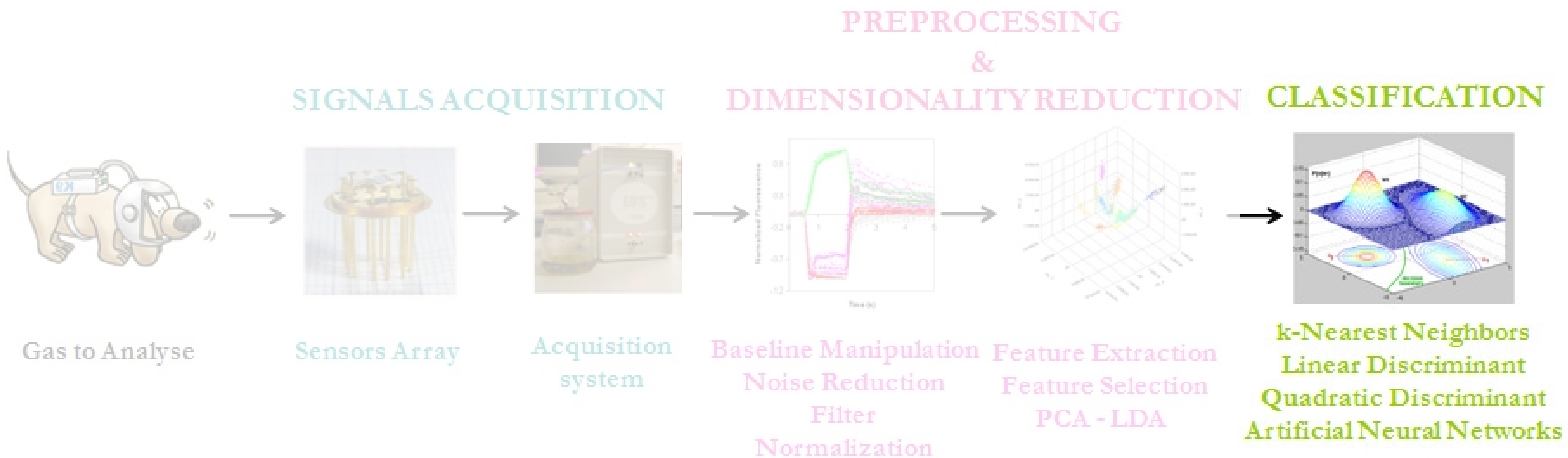

Classification

- Different families of classifiers:
  - **Nearest Neighbor Classifiers (k-NN)**
    - **Classic k-NN**
    - **Modified k-NN** --> k=number of neighbors belonging all to the same class
    - **Fuzzy *k*-Nearest Neighbors** --> assigns a class membership function to each training and test samples
  - **Discriminant Functions** Classifiers
    - Linear
    - Quadratic
  - **Artificial Neural Network**
    - Feedforward Neural Network with one hidden layer

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Results

- Performance has been evaluated through **confusion matrix** and the corresponding **performance indexes** (CI=95%)
- **Cross-validation:** *modified* leave-one-out
- We considered **different values for *k*** (*k*=1,3,5,9,101)

Classifier	NER	TPR	TNR	$PREC_{POS}$	$PREC_{NEG}$
Classic 9-NN	90.1%	89.5%	90.5%	87.5%	92.1%
Confidence Interval	[85.7-94.5]	[85.3-93.8]	[86.0-95.0]	[81.6-93.4]	[86.8-97.4]
Modified 9-NN	91.1%	91.9%	90.5%	87.8%	93.7%
Confidence Interval	[86.8-95.4]	[87.9-95.9]	[86.0-95.0]	[81.9-93.7]	[89.1-98.4]
Fuzzy k-NN	**92.6%**	95.3%	90.5%	88.2%	96.3%
Confidence Interval	[88.5-96.7]	[91.8-98.9]	[86.0-95.0]	[82.3-94.1]	[93.2-99.4]
LD	89.6%	**96.5%**	84.5%	82.2%	**97.0%**
Confidence Interval	[85.0-94.2]	[93.7-99.3]	[79.1-89.9]	[75.2-89.1]	[93.9-100]
QD	**92.6%**	95.3%	90.5%	88.2%	96.3%
Confidence Interval	[88.5-96.7]	[91.8-98.9]	[86.0-95.0]	[82.3-94.1]	[93.2-99.4]
ANN	91.6%	91.9%	**91.3793%**	**88.8%**	93.8%
Confidence Interval	[87.4-95.8]	[87.9-95.9]	[87.0-95.8]	[84.1-93.4]	[88.2-99.4]

Results

- Performance has been evaluated through **confusion matrix** and the corresponding **performance indexes** (CI=95%)
- **Cross-validation:** *modified* leave-one-out
- We considered **different values for *k*** (*k*=1,3,5,9,101)

Classifier	NER	TPR	TNR	$PREC_{POS}$	$PREC_{NEG}$
Classic 9-NN	90.1%	89.5%	90.5%	87.5%	92.1%
Confidence Interval	[85.7-94.5]	[85.3-93.8]	[86.0-95.0]	[81.6-93.4]	[86.8-97.4]
Modified 9-NN	91.1%	91.9%	90.5%	87.8%	93.7%
Confidence Interval	[86.8-95.4]	[87.9-95.9]	[86.0-95.0]	[81.9-93.7]	[89.1-98.4]
Fuzzy k-NN	**92.6%**	95.3%	90.5%	88.2%	96.3%
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LD	89.6%	**96.5%**	84.5%	82.2%	**97.0%**
Confidence Interval	[85.0-94.2]	[93.7-99.3]	[79.1-89.9]	[75.2-89.1]	[93.9-100]
QD	**92.6%**	95.3%	90.5%	88.2%	96.3%
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Results: Confusion Matrix

- Fuzzy k-NN demonstrated to be **robust** to k changes, keeping its results invariant

CONFUSION MATRIX		TRUE LABELS	
		Positive	Negative
ESTIMATED LABELS	Positive	82	11
	Negative	4	105

Indexes	Average Index	Confidence Interval $(CI = 95\%)$
Accuracy	92.6%	[88.5-96.7]
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Classifiers Comparison

- Performing a **student t-test** between all pairs of classifiers, no relevant differences emerged
  - All implemented classifiers result comparable for the considered problem
- The **robustness** showed by Fuzzy k-NN to *k* changes is not verified in the classic and the modified *k*-NN, that leads to different results according to the value of *k*
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Comparison to current diagnostic methods

- The use of an electronic nose as lung cancer diagnostic tool is reasonable if it gives some advantages compared to **current diagnostic techniques**

	Accuracy	Sensitivity	Specificity	$PREC_{POS}$	$PREC_{NEG}$
CAT Confidence Interval	Nd	75% [60-90]	66% [55-77]	Nd	Nd
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Extension and further directions of research

1. Improvement of **Sensors Technology:**
   - Development of longer-lyfe and more stable sensors
   - Development of hybrid systems, able to provide both selective and sensitive abilities
2. Improvement of **Olfactory Signal Analysis techniques and Classification Algorithms**
3. **Exploration of Informations hidden in the Olfactory Signal**
   - Analysis of the **olfactory patterns' changes due to surgery**
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