Computer-Aided Classification of Impulse Oscillometric Measures of Respiratory Small Airways Function in Children

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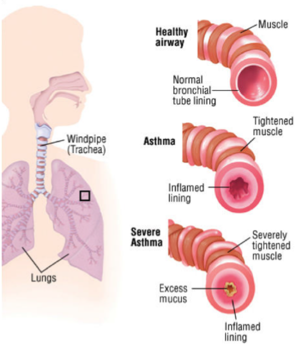
Agenda

- Introduction
- Relevance
- Recognition of a Need
- Objective
- State of the Art
- Data
- Methodology
- Feature Selection
    - Conventional Approach
    - Pre-processing Approach
- Results and Discussion
- Conclusions
- Future Work and Research Interests
- Acknowledgements

Asthma & SAI

- Asthma causes the inflammation and narrowing conditions that importantly affect the lining of the small airways.
  - Small = peripheral = distal airways.
  - They have an inner diameter of about 2 to 0.5 mm.
- Early manifestation prior to asthma could be early Small Airway Impairment (SAI) .
  - SAI: Chronic obstructive bronchitis with narrowing of the bronchioles and small bronchi.
  - If inflammation persists during SAI, asthma could appear.
- An early evaluation and therapy for small airways is often more effective.



Asthma in the World

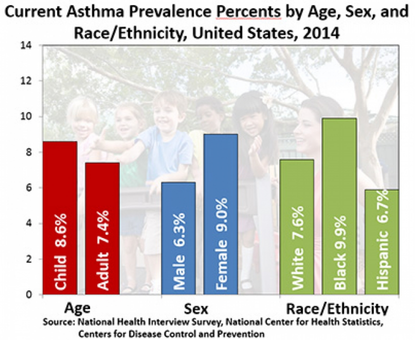
According to the World Health Organization (WHO):

- Asthma is a major chronic disease.
- 235 million people affected in a global scale.
- The most common chronic non-communicable disease among children.

Prevalence of Asthma

The United States National Center for Health Statistics (NCHS) estimated:

- Asthmatic Population: 24 million.
- Asthmatic Children: 6.2 million.
- Prevalence among children > adults.



Prevalence of asthma in children:

- United States: 8.6%.
- México: 4.5% to 12.5%.
- Texas: 9.1% .
- El Paso, TX: 12.3%.
- Juarez, MX: 6.8%.

Both in the United States and México, asthma is a **major cause** of:

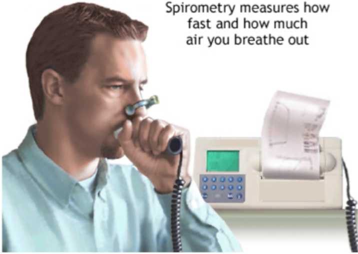
- Missing school.
- Urgent pediatrician consultations.
- Visits to hospital emergency rooms.
- Hospitalization.

Asthma Diagnosis

- The timely diagnosis of asthma is challenging.
  - Its symptoms are similar to other respiratory conditions.
- The diseases affecting the small airways are difficult to detect by traditional diagnostics tests.
- Early childhood is a critical period to assess pulmonary function.
  - Those suffering from asthma usually face the onset of their symptoms during this time.

Spirometry

- Spirometry is a Pulmonary Function Test (PFT).
- It is the most common PFTs used to diagnose Asthma.
- Highly dependent on patient cooperation, since it requires extreme maneuvers.
  - A maximal forced exhalation after a maximum deep inspiration is required.
- Reliable test in adults, but unreliable in children.
  - Pre-school and school-age children have difficulty meeting some of the quality-control criteria required by international guidelines .



Impulse Oscillometry System (IOS)

The IOS could be used as an alternative and objective method for asthma diagnosis and control in children.

- It is a safe-patient-friendly noninvasive-validated technique.
- Only requires patient's passive cooperation.
- It provides fast and reproducible measurements.
- Impulse oscillometric measures correlate well with clinical symptoms and asthma control.

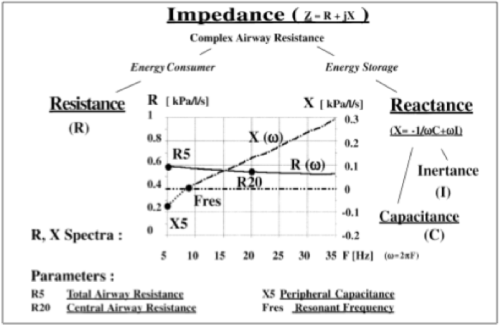
Advantages of IOS vs. Spirometry

- It is a safe-patient-friendly technique.
- Unnoticeable changes in a patient's airway function may be detected earlier .
- IOS provides information in cases in which spirometry cannot be performed .
- In previous studies, IOS was found to be better than spirometry at discriminating between young children with and without asthma.

Impulse Oscillometry System (IOS)

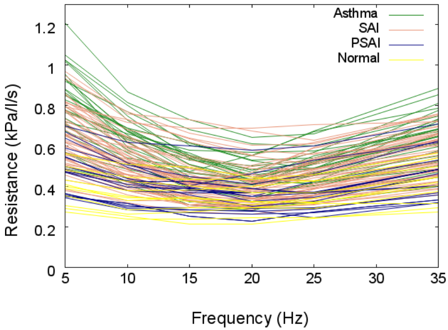
- The IOS uses sound waves to rapidly detect airway changes.

- It measures the respiratory impedance (Z) using short impulses of air pressure.

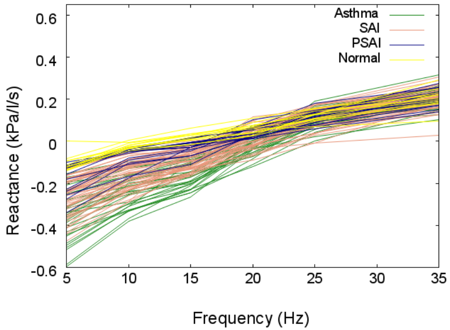


IOS Challenges

- Resulting IOS test values are difficult to understand.
- The high dimensionality and dispersion of the IOS data makes it difficult for the IOS to be broadly accepted and used.



Resistance (R)



Reactance (X)

Recognition of a Need

- There is a need to reliably diagnose and monitor asthma at an early stage, to treat and control the disease and improve the quality of life of asthmatic children.

Therefore, there is a need to improve the diagnostic utility of the IOS to timely diagnose and monitor asthma in children.

Objective

To develop computational classification algorithms with high discriminative capacity (sensitivity, specificity, and accuracy) to distinguish between:

- Asthma.
- Small Airway Impairment.
- Possible Small Airway Impairment.
- Normal lung function.

To facilitate the difficult task of interpreting the IOS data and provide clinicians with a reliable and proven method for accurate classification of children’s lung function.

Methodological Review of IOS Classification Works

The literature review was performed using the following scientific databases and parameters:

1) Scientific Databases:

- “All fields” in PubMed,
- “Full-Text & Metadata” in IEEE Xplore,
- “All Databases” in Web of Knowledge.

2) Words and Logic Operators:
   - "asthma” OR “small airways” OR “peripheral airways” OR “distal airways” AND “classification" AND ``oscillometry".

Results of Methodological Review

A total of 34 articles were found by the search. The title and abstract of these articles were screened and selected based on the following eligibility criteria:

1) Publications that focused on the computer-aided classification of peripheral airway obstruction,
2) Computer-aided classification that included impulse oscillometric features.
3) The bibliography of the selected articles was also screened to find other relevant articles.

Out of the 34 articles identified using scientific web databases, only 7 met the eligibility criteria and an additional article was found through the screening of selected articles' bibliography for a total of 8 articles.

State of the Art

Author	Year	Reference	Conditions Studied	Number of Subjects (N)	N per Gender	Age (Years)	Height (m)	Weight (Kg)
A. Badnjević et al	2016	[24]	Asthma & Healthy	N=1250. Asthma: 728 Healthy: 522	Male: 601 Female: 649	Not reported	Not reported	Not reported
A. Badnjević et al	2016	[25]	Asthma & Healthy	N=1250. Asthma: 728 Healthy: 522	Male: 601 Female: 649	Not reported	Not reported	Not reported
A. Badnjević et al	2015	[26]	Asthma & Healthy	N=289 Asthma: 72 Healthy: 217	Male: 142 Female:147	Asthma : 19.85 +/- SD 8.18 Healthy: 30.03 +/- SD 11.83.	Not reported	Not reported
A. Badnjević et al	2015	[27]	Asthma, COPD & Healthy	N= 455 Asthma: 170 COPD: 248 Healthy: 37	Male: 244 Female: 211	Asthma : 19.85 +/- SD 8.18 COPD: 52.25 +/- SD 7.636 Healthy: 30.03 +/- SD 11.83.	Not reported	Not reported
A. Badnjević et al	2013	[28]	Asthma & Healthy	N=156 Asthma: 72 Healthy: 84	Not reported	Not reported	Not reported	Not reported
Nazila Hafezi et al	2009	[29]	Asthma, SAI, Mild SAI & Healthy	N=112	Not reported	5-17	Not reported	Not reported
Barúa, Miroslava et al	2005	[30]	Asthmatic Constricted & Asthmatic Non-Constricted	N= 361 IOS patterns from 41 subjects. Constricted: 168 Non-constricted: 193	Male: 120 Female: 241	2-8	0.88-1.4	12-32.7
Barúa, Miroslava et al	2004	[31]	Central & Peripheral Diseases	N=131	Male : 64 Female: 67	13-85	1.4 - 1.85	35 - 176

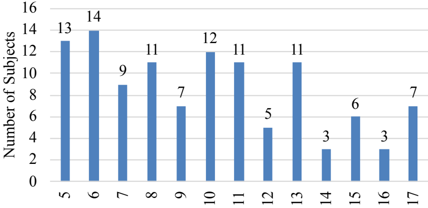
Author	Year	Ref.	Conditions Studied	Diagnostic Techniques Used	Assessment Type	Input Parameters Used	Classification Technique	Accuracy by Condition after Static Assessment			Accuracy by Condition after Static & Dynamic Assessments			Overall Classifier's Accuracy after:	
								Asthma	COPD	Healthy	Asthma	COPD	Healthy	Static Assessment	Static & Dynamic Assessments
A. Badnjević et al	2016	[24]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms** **IOS**: not specified **SPIR:** not specified	ANN	Not reported	Not reported	Not reported	97.11%	N/A	98.85%	Not reported	97.84%
A. Badnjević et al	2016	[25]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms** **IOS:** R5, R20, X5, R5-R20, Fres **SPIR:** FVC, FEV1, FEV1/FVC , PEF	Fuzzy Logic	8.65 % (63/728)	N/A	89.08% (465/522)	91.89%	N/A	95.01%	42.24%	93.20%
A. Badnjević et al	2015	[26]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms and allergy history** **IOS :** R5, R20, R5-R20, X5, Fres **SPIR**: FEV1, FEV1/FVC **Body Plethysmography**	Neuro-fuzzy	11.43% (8/72)	N/A	Not reported	97.22%	N/A	98.61%	Could not be estimated with the information reported	98.20%
A. Badnjević et al	2015	[27]	Asthma, COPD & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms** **IOS :** R5, R20,R5-R20, X5, Fres **SPIR:** FEV1, FVC, FEV1/FVC	Neuro-fuzzy	87.65% (149/170)	85.5% (212/248)	Not reported	99.41%	99.19%	100%	**86.3%	99.34%
A. Badnjević et al	2013	[28]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms, allergies and risk factors** **IOS** : R5, R20,R5-R20, X5, Fres **SPIR**: FEV1, FVC, FEV1/FVC	Neuro-fuzzy	10.70%	N/A	93.67%	90.25%	N/A	94.04%	51.92%	92.30%
Nazila Hafezi et al	2009	[29]	Asthma, SAI, Mild SAI & Healthy	IOS	Static	**IOS:** R5-R15, AX eRIC (R, Rp, I,Cp),	Co-Active Neuro-fuzzy Inference System (CANFIS)	Not reported	N/A	Not reported	N/A	N/A	N/A	*95.54%	N/A
						IOS: R5-R15, AX, aRIC (R, Rp,I, Cp, Ce)		Not reported	N/A	Not reported	N/A	N/A	N/A	*97.32%	N/A
Barúa, Miroslava et al	2005	[30]	Asthmatic Constricted & Asthmatic Non-Constricted	IOS	Static	**IOS :** R5, R10, R15, R20, R25, R35, X5 ,X10, X15, X20, X25, X35 **General:** Age, gender, height, weight.	ANN	Not reported	N/A	Not reported	N/A	N/A	N/A	98.61%	N/A
Barúa, Miroslava et al	2004	[31]	Central & Peripheral Diseases	IOS	Static	**IOS :** R5, R10, R15, R20, R25, R35, X5, X10, X15, X20, X25, X35 **General:** Smoking status, age, gender, height, weight.	ANN	Not reported	N/A	Not reported	N/A	N/A	N/A	61.53%	N/A

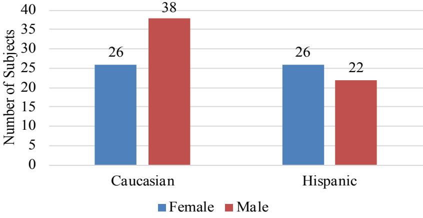
* Accuracy of training data. No validation results available.
** Only taking into consideration the Asthmatic and COPD populations as Healthy results were not reported by the authors

Data

IOS data sets acquired, as part of a NIH-funded study (Asthma on the Border) carried out at the University of Texas at El Paso (UTEP) were deployed for this study.

Height (cm)	Weight (kg)	Age (years)	Ethnicity	Gender	Age (years)	Children Tested
Range: 101.6 - 183.4 Mean ± SD: 139.8 ± 21.31	Range: 14.5 - 93.8 Mean ± SD: 41.02 ± 19.94	Range: 5 - 17 Mean ± SD: 9.88 ± 3.62	Caucasian	Male	5-17	38
				Female	5-17	26
			Hispanic	Male	5-17	22
				Female	5-16	26
					Total	112

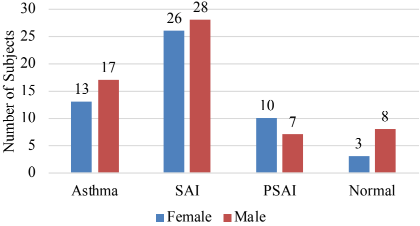


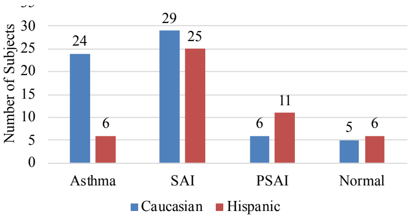


Data

During data collection, three to five tests were recorded for each child; data were carefully reviewed (quality assured) offline by an expert clinician to ensure the lack of artifacts (air leaks, swallowing, breath holding or vocalization).

		Age (years)		
Classification	**Total Datasets**	**Range**	**Mean**	**SD**
Asthma (n=30)	78	5 - 13	8.1	2.5
SAI (n=54)	137	5 - 17	9.3	3.4
PSAI (n=17)	42	5 - 17	12.6	3.8
Normal (n=11)	31	11 - 17	13.4	2.5





Equipment and Collected Data

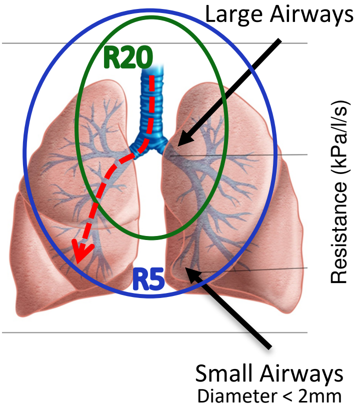
The equipment used for the study was a Jaeger Master Screen IOS.

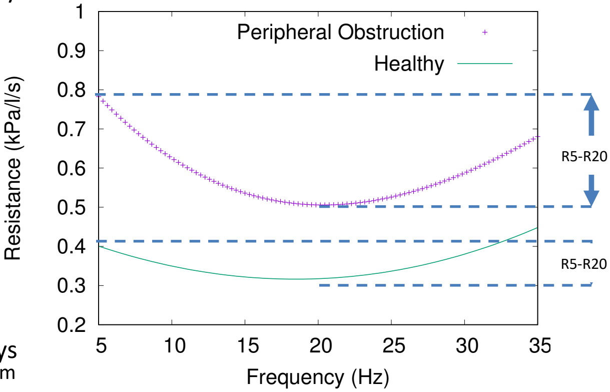
- The collected raw IOS data include:
  - Resistance and reactance measurements at 5, 10, 15, 20, 25 and 35 Hz.
- The estimated IOS parameters:
  - R5-R20, Fres, AX.

In total, 15 IOS derived features for each child were obtained.

Resistance	Reactance	Estimated IOS Parameters
R5	X5	R5-R20 (fdR)
R10	X10	Fres
R15	X15	AX
R20	X20	
R25	X25	
R35	X35	

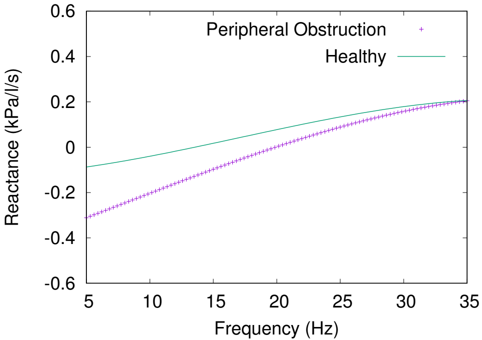
IOS : Resistance (R)

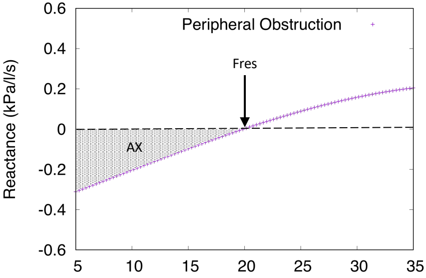


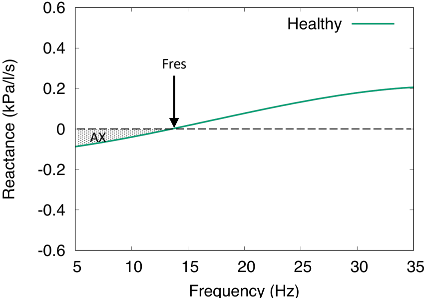


R5, R10, R15, R20. R25, R35, and R5-R20

IOS : Reactance (X)







X5, X10, X15, X20. X25, X35, Fres, and AX.

Methodology

- Feature Selection
  - Conventional Approach : No data pre-processing.
  - Pre-Processing Approach.
- Supervised Classification
  - Training Phase, 75% of the labeled IOS data sets
  - Prediction Phase 25% of the IOS data sets were used as validation data sets.
  - Development of ANN classifiers using input features derived from:
    - Conventional Approach
    - Pre-Processing Approach
    - Combination of Conventional and Pre-Processing Approaches
- ANN Classifiers Performance Evaluation and Selection

Preliminary Classification

Classifier results using all IOS parameters:

Table 1: *Classification Results*

Clinician Classification		Algorithm Classification
Condition	Number of Subjects	RX Classifier
Asthma	30	86.6%
SAD	54	44.4%
Mild SAD	17	35.3%
Normal	11	0.0%

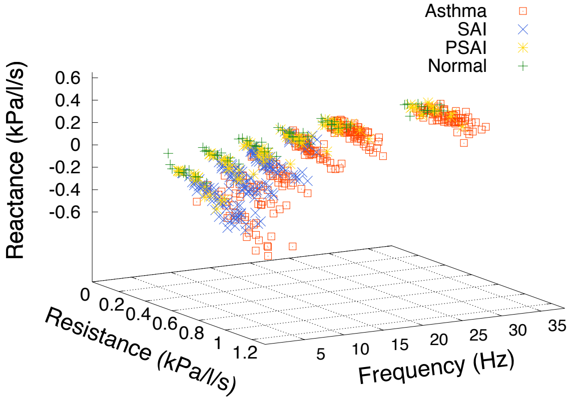
Feature Selection: Conventional Approach

- Identify IOS features that demonstrate statistical significance in the differentiation Asthma (A), Small Airway Impairment (SAI), Possible Small Airway Impairment (PSAI), and Normal (N) respiratory conditions.

Resistance	**Reactance**	**Estimated IOS Parameters**
R5	X5	R5-R20 (fdR)
R10	X10	Fres
R15	X15	AX
R20	X20	
R25	X25	
R35	X35	

Complexity of IOS Data

- The complexity of the data used for this investigation plotted in terms of the respiratory impedance components R and X:



Statistical Analysis

- Statistical analysis (one-way ANOVA) was performed using the MINITAB 18 Statistical Software (Minitab, Inc., State College, USA).

- Each IOS parameter for each class was compared against the same IOS parameter for a different class, until the parameter was compared for all classes.

- The statistical analysis was performed using a confidence level of 95%.

Null Hypothesis H_o :
$\mu_1 = \mu_2$

Alternative Hypothesis H_i :
$\mu_1 \neq \mu_2$

Pvalue $< 0.05 \Rightarrow$ Reject H_o

Pvalue $\geq 0.05 \Rightarrow$ Fail to Reject H_o

Statistical Analysis: Resistance

IOS Parameter	Asthma vs. SAI	Asthma vs. PSAI	Asthma vs. Normal	SAI vs. PSAI	SAI vs. Normal	PSAI vs. Normal
R5	0.000	0.000	0.000	0.000	0.000	0.031
R10	0.000	0.000	0.000	0.001	0.000	0.086
R15	0.002	0.000	0.000	0.055	0.012	0.324
R20	0.027	0.001	0.000	0.073	0.029	0.490
R25	0.018	0.000	0.000	0.005	0.001	0.422
R35	0.000	0.000	0.000	0.004	0.000	0.289

Statistical Analysis : Reactance

IOS Parameter	Asthma vs. SAI	Asthma vs. PSAI	Asthma vs. Normal	SAI vs. PSAI	SAI vs. Normal	PSAI vs. Normal
X5	0.000	0.000	0.000	0.000	0.000	0.015
X10	0.000	0.000	0.000	0.000	0.000	0.002
X15	0.000	0.000	0.000	0.000	0.000	0.001
X20	0.000	0.000	0.000	0.105	0.005	0.003
X25	0.280	0.239	0.149	0.802	0.540	0.627
X35	0.497	0.428	0.687	0.790	0.974	0.821

Statistical Analysis: IOS Derived Parameters

IOS Parameter	Asthma vs. SAI	Asthma vs. PSAI	Asthma vs. Normal	SAI vs. PSAI	SAI vs. Normal	PSAI vs. Normal
R5-R20	0.000	0.000	0.000	0.000	0.000	0.003
Fres	0.002	0.000	0.000	0.000	0.000	0.000
AX	0.000	0.000	0.000	0.000	0.000	0.003

Ranking of IOS Discriminative Parameters

	Coeficient of Variation (%)					
IOS Parameter	Asthma	SAI	PSAI	Normal	CV Avg	Ranking
Fres	8.0	12.6	11.6	18.9	12.8	1
R5	20.2	22.2	23.0	22.8	22.0	2
X5	32.2	34.3	42.7	37.9	36.8	3
AX	32.5	39.5	58.0	32.9	40.7	4
R5-R20	31.3	35.5	48.5	49.8	41.3	5
X10	32.2	42.3	61.5	65.9	50.5	6
X15	35.6	49.7	130.8	128.6	86.2	7

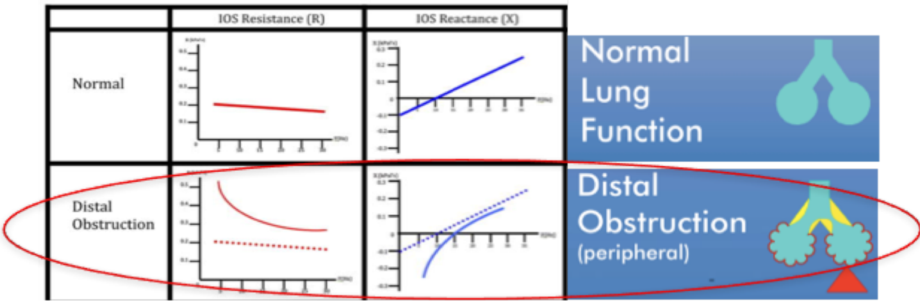
Feature Selection: Conventional Approach

Conclusions:

- Out of the 15 IOS parameters studied, only 7 were found to be sensitive to differentiate between four levels of peripheral lung function in children (Asthma, SAI, PSAI and Normal):
    - Fres, R5, X5, AX, R5-R20, X10, and X15.

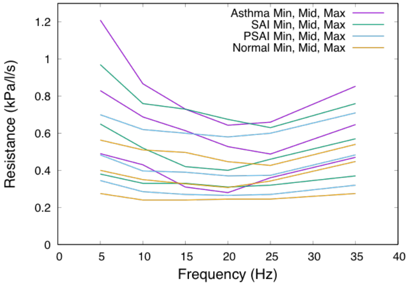
Data Pre-Processing

- IOS graphically displays frequency-dependent curves that are of the utmost importance in the diagnosis of peripheral airways obstruction.

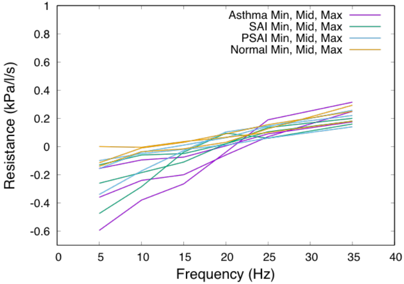


IOS Data Complexity

- Computer-aided classification of multiple classes with different degrees of severity in peripheral obstruction is not an easy task.
- This difficulty could be attributed to the high dimensionality of the IOS parameters and the dispersion of the data generated.



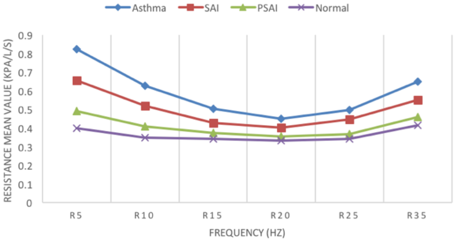
Resistance



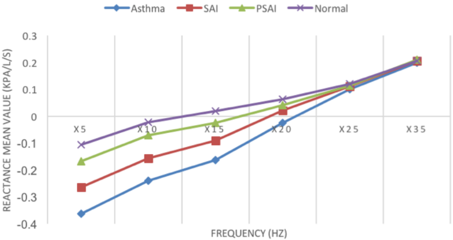
Reactance

Graphical Assessment of the Class Average

- The class average for each of R and X parameters at the different frequencies was calculated (R5, R10, R15, R20, R25, R5, R10, R15, R20, R25, R35, and X5, X10, X15, X20, X25, X35)



Resistance



Reactance

Linear Regressions

- In order to obtain reference deterministic models, quadratic, cubic and quartic order polynomial regressions were performed for Asthma, SAI, PSAI, and Normal datasets

- Polynomial regressions were computed given the general polynomial form:

$$y = a_0 + a_1 x + a_2 x^2 + .. + a_n x^n$$

$$\boldsymbol{y} = \boldsymbol{A} \cdot \boldsymbol{a}$$

$$\begin{pmatrix} \sum_i^n y_i \\ \sum_i^n x y_i \\ \sum_i^n x^2 y_i \\ . \\ . \\ \sum_i^n x^n y_i \end{pmatrix} = \begin{pmatrix} n & \sum_i^n x_i & \dots & \sum_i^n x_i^n \\ \sum_i^n x_i & \sum_i^n x_i^2 & \dots & \sum_i^n x_i^{n+1} \\ \sum_i^n x_i^2 & \sum_i^n x_i^3 & \dots & \sum_i^n x_i^{n+2} \\ . & . & \dots & . \\ . & . & \dots & . \\ \sum_i^n x_i^n & \sum_i^n x_i^{n+1} & \dots & \sum_i^n x_i^{n+n} \end{pmatrix} \cdot \begin{pmatrix} a_0 \\ a_1 \\ a_2 \\ . \\ . \\ a_n \end{pmatrix}$$

$$\boldsymbol{A}^{-1} \cdot \boldsymbol{y} = \boldsymbol{a}$$

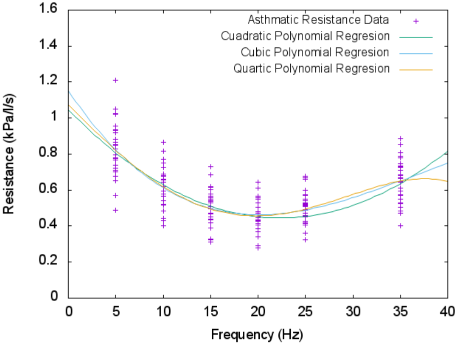
Where,
x= Frequency in Hz,

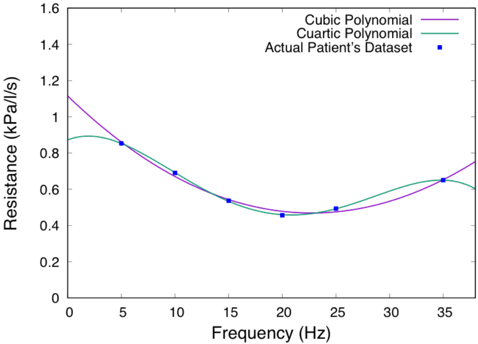
y= R or X in terms of frequency (x) in kPa/l/s,

and coefficients a are calculated by solving the system of equations using the algebraic inverse matrix.

Which Order Polynomials Should We Use?

- A natural idea is to take into account the general monotonicity of IOS curves described in the literature.
- Select the largest degree for which, the resulting best-approximation polynomials follow the same monotonicity pattern.





Class Typical Functions

Resistance

$$R_a(f) = 1.152 - 7.842 \times 10^{-2}x + 2.686 \times 10^{-3}x^2 - 2.443 \times 10^{-5}x^3$$

$$R_s(f) = 8.960 \times 10^{-1} - 5.738 \times 10^{-2}x + 2.067 \times 10^{-3}x^2 - 2.024 \times 10^{-5}x^3$$

$$R_p(f) = 6.076 \times 10^{-1} - 2.717 \times 10^{-2}x + 8.278 \times 10^{-4}x^2 - 4.888 \times 10^{-6}x^3$$

$$R_n(f) = 4.612 \times 10^{-1} - 1.508 \times 10^{-2}x + 4.789 \times 10^{-4}x^2 - 2.424 \times 10^{-6}x^3$$

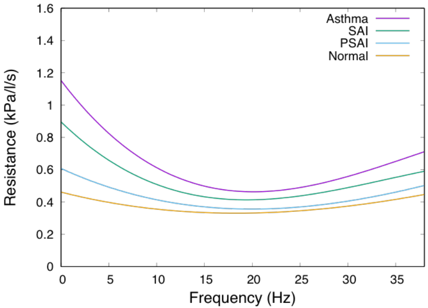
Reactance

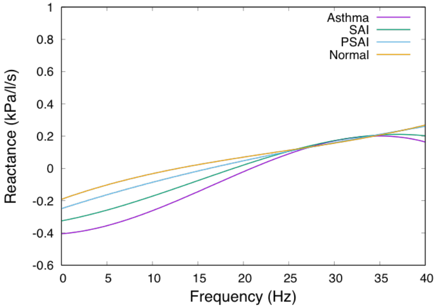
$$X_a(f) = -4.0500 \times 10^{-1} + 4.4909 \times 10^{-3}x + 1.2294 \times 10^{-3}x^2 - 2.4657 \times 10^{-5}x^3$$

$$X_s(f) = -3.2507 \times 10^{-1} + 1.0693 \times 10^{-2}x + 5.9596 \times 10^{-4}x^2 - 1.3338 \times 10^{-5}x^3$$

$$X_p(f) = -2.4920 \times 10^{-1} + 1.8110 \times 10^{-2}x - 1.9477 \times 10^{-4}x^2 + 1.5170 \times 10^{-6}x^3$$

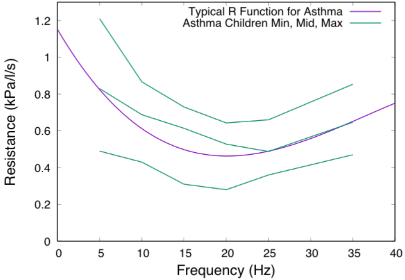
$$X_a(f) = -1.9135 \times 10^{-1} + 2.0045 \times 10^{-2}x - 4.8540 \times 10^{-4}x^2 + 6.7960 \times 10^{-6}x^3$$

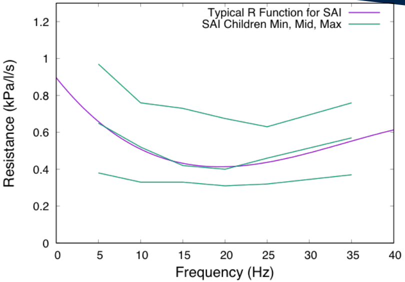


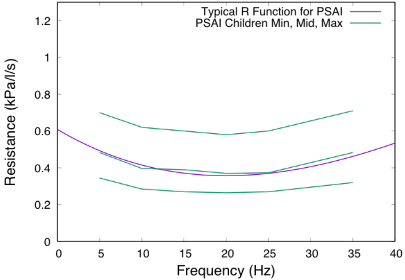


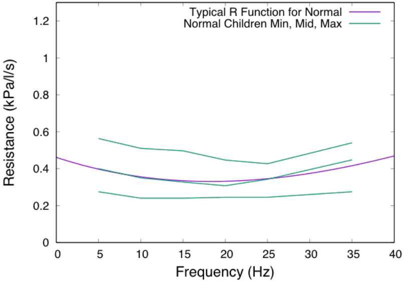
Feature Selection: Pre-Processing Approach

Potential Discriminative Geometrical Features



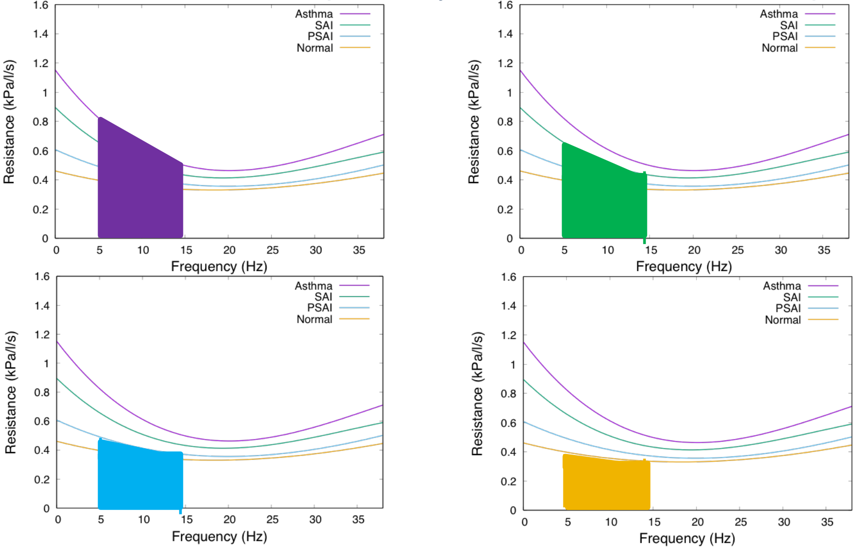






Potential Discriminative Geometrical Features

What other features could be potentially discriminative? Area and Slope



Potential Discriminative Geometrical Features

Area Typical Functions for Resistance and Reactance

Area under the curve (Integral of the class function) :

Resistance:

$$I_{R,a}(f) = \int R_a(f)\,df$$

$$I_{R,s}(f) = \int R_s(f)\,df$$

$$I_{R,p}(f) = \int R_p(f)\,df$$

$$I_{R,n}(f) = \int R_n(f)\,df$$

Reactance:

$$I_{X,a}(f) = \int X_a(f)\,df$$

$$I_{X,s}(f) = \int X_s(f)\,df$$

$$I_{X,p}(f) = \int X_p(f)\,df$$

$$I_{X,n}(f) = \int X_n(f)\,df$$

Potential Discriminative Geometrical Features

Slope Typical Functions for Resistance and Reactance

Slope (derivative of the function) :

Resistance:

$$D_{R_a(f)} = \frac{dR_a(f)}{df}$$

$$D_{R_s(f)} = \frac{dR_s(f)}{df}$$

$$D_{R_p(f)} = \frac{dR_p(f)}{df}$$

$$D_{R_n(f)} = \frac{dR_n(f)}{df}$$

Reactance:

$$D_{X_a(f)} = \frac{dX_a(f)}{df}$$

$$D_{X_s(f)} = \frac{dX_s(f)}{df}$$

$$D_{X_p(f)} = \frac{dX_p(f)}{df}$$

$$D_{X_n(f)} = \frac{dX_n(f)}{df}$$

Potential Discriminative Geometrical Features

In summary, we have 24 functions (12 for R and 12 for X) that describe geometrical patterns of each of the classes studied:

Resistance:

Typical Function	Slope Function	Integral Function
$R_a(f)$	$D_{R_a(f)} = \frac{dR_a(f)}{df}$	$I_{R,a}(f) = \int R_a(f)\,df$
$R_s(f)$	$D_{R_s(f)} = \frac{dR_s(f)}{df}$	$I_{R,s}(f) = \int R_s(f)\,df$
$R_p(f)$	$D_{R_p(f)} = \frac{dR_p(f)}{df}$	$I_{R,p}(f) = \int R_p(f)\,df$
$R_a(f)$	$D_{R_n(f)} = \frac{dR_n(f)}{df}$	$I_{R,n}(f) = \int R_n(f)\,df$

Potential Discriminative Geometrical Features

In summary, we have 24 functions (12 for R and 12 for X) that describe potential geometrical patterns of each of the classes studied:

Reactance:

Typical Function	Slope Function	Integral Function
$X_a(f)$	$D_{X_a(f)} = \frac{dX_a(f)}{df}$	$I_{X,a}(f) = \int X_a(f)\,df$
$X_s(f)$	$D_{X_s(f)} = \frac{dX_s(f)}{df}$	$I_{X,s}(f) = \int X_s(f)\,df$
$X_p(f)$	$D_{X_p(f)} = \frac{dX_p(f)}{df}$	$I_{X,p}(f) = \int X_p(f)\,df$
$X_a(f)$	$D_{X_n(f)} = \frac{dX_n(f)}{df}$	$I_{X,n}(f) = \int X_n(f)\,df$

Similarity/ Dissimilarity Measures

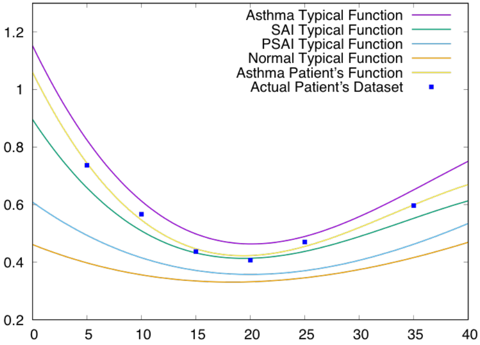
How can we used these 24 functions?

We could compare the typical function for each class against the actual patient's curve.

To do so, we need to be consistent with the approach used for reference models (typical functions), therefore, a cubic polynomial regression was performed for each patient's data set (112 typical functions were obtained, 112 slope functions and 112 area functions). Same methodology as the reference models was done.

Similarity/ Dissimilarity Measures

How can we compare typical class functions versus patient's curves?



Typical Function vs. Patient's Function:

$$S_{R_d} = \int_5^{15} |R_d(f) - (R_i^a(f) + \Delta R_d)|\, df,$$

where $\Delta R_d \stackrel{\text{def}}{=} R_d(10) - R^a(10),$

Typical Area Function vs. Patient's Area Function:

$$S_{I_{R,d}} = \int_5^{15} |I_{R,d}(f) - (I_{R,i}^a(f) + \Delta I_{R,d})|\, df,$$

where $\Delta I_{R,d} \stackrel{\text{def}}{=} I_{R,d}(10) - I_{R,i}^a(10)$

Typical Slope Function vs. Patient's Slope Function:

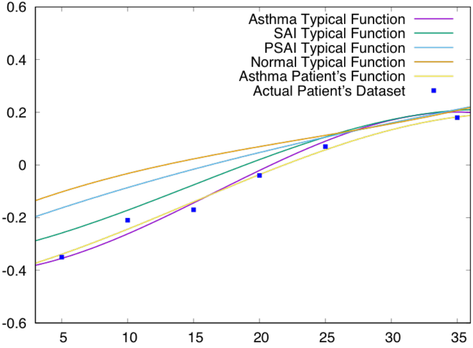
$$S_{D_{R,d}} = \int_5^{15} |D_{R,d}(f) - (D_{R,i}^a(f) + \Delta D_{R,d})|\, df,$$

where $\Delta D_{R,d} \stackrel{\text{def}}{=} D_{R,d}(10) - D_{R,i}^a(10)$

In total we have 12 similarity measures for Resistance for each patient

Similarity/ Dissimilarity Measures

How can we compare typical class functions versus patient's curves?



Typical Function vs. Patient's Function:

$$S_{I_{X,d}} = \int_5^{15} |I_{X,d}(f) - (I^a_{X,i}(f) + \Delta I_{X,d})|\, df,$$

where $\Delta I_{X,d} \stackrel{\text{def}}{=} I_{X,d}(10) - I^a_{X,i}(10)$

Typical Area Function vs. Patient's Area Function:

$$S_{I_{X,d}} = \int_5^{15} |I_{X,d}(f) - (I^a_{X,i}(f) + \Delta I_{X,d})|\, df,$$

where $\Delta I_{X,d} \stackrel{\text{def}}{=} I_{X,d}(10) - I^a_{X,i}(10)$

Typical Slope Function vs. Patient's Slope Function:

$$S_{D_{X,d}} = \int_5^{15} |D_{X,d}(f) - (D^a_{X,i}(f) + \Delta D_{X,d})|\, df,$$

where $\Delta D_{X,d} \stackrel{\text{def}}{=} D_{X,d}(10) - D^a_{X,i}(10)$

In total we have 12 similarity measures for Reactance for each patient

Similarity/Dissimilarity Measures

Similarity Index of Class Typical Functions

Condition	Asthma	SAI	PSAI	Normal
Asthma	0	1.02624	2.49132	3.07514
SAI	1.02624	0	1.46508	2.0489
PSAI	2.49132	1.46508	0	0.583818
Normal	3.07514	2.0489	0.583818	0

Feature Selection

Neural Network classification was performed using similarity/dissimilarity measures:

Type of feature	# Input Features	# Classes	Classes	Training Samples	Validation Samples	Validation Accuracy (%)
Pre-Processed (R)	12	4	Asthma, SAI, PSAI , Normal	214	74	63.7
Pre-Processed (X)	12	4	Asthma, SAI, PSAI , Normal	214	74	68.91
Pre-Processed (R and X combined)	24	4	Asthma, SAD, PSAI , Normal	214	74	71.62

Too many features?

We need to select the most discriminative ones

Feature Selection

Similarity Indices:		Asthma vs. SAI	Asthma vs. PSAI	Asthma vs. Normal	SAI vs. PSAI	SAI vs. Normal	PSAI vs. Normal
Typical Function (R)	S_{Ra}	0.042	0.000	0.000	0.000	0.000	0.000
	S_{Rs}	0.000	0.237	0.014	0.000	0.000	0.000
	S_{Rp}	0.000	0.000	0.000	0.000	0.000	0.801
	S_{Rn}	0.000	0.000	0.000	0.000	0.000	0.000
Area Function (R)	S_{IRa}	0.000	0.000	0.000	0.000	0.000	0.008
	S_{IRs}	0.000	0.000	0.240	0.137	0.000	0.005
	S_{IRp}	0.000	0.000	0.000	0.002	0.006	0.204
	S_{IRn}	0.000	0.000	0.000	0.000	0.000	0.033
Slope Function (R)	S_{DRa}	0.419	0.030	0.000	0.067	0.000	0.010
	S_{DRs}	0.403	0.419	0.818	0.850	0.332	0.091
	S_{DRp}	0.032	0.000	0.000	0.000	0.000	0.101
	S_{DRn}	0.024	0.000	0.000	0.000	0.000	0.019

Feature Selection

Similarity Indices:		Asthma vs. SAI	Asthma vs. PSAI	Asthma vs. Normal	SAI vs. PSAI	SAI vs. Normal	PSAI vs. Normal
Typical Function (X)	S_{Xa}	0.220	0.773	0.507	0.148	0.071	0.611
	S_{Xs}	0.019	0.133	0.027	0.810	0.680	0.456
	S_{Xp}	0.001	0.001	0.000	0.189	0.000	0.002
	S_{Xn}	0.001	0.000	0.000	0.036	0.000	0.002
Area Function (X)	S_{IXa}	0.006	0.000	0.000	0.000	0.000	0.000
	S_{IXs}	0.000	0.071	0.007	0.000	0.000	0.000
	S_{IXp}	0.000	0.000	0.000	0.000	0.001	0.254
	S_{IXn}	0.000	0.000	0.000	0.000	0.000	0.000
Slope Function (X)	S_{DXa}	0.629	0.118	0.002	0.051	0.001	0.135
	S_{DXs}	0.064	0.359	0.581	0.546	0.435	0.786
	S_{DXp}	0.006	0.000	0.000	0.073	0.009	0.209
	S_{DXn}	0.006	0.000	0.000	0.017	0.000	0.072

Feature Selection Summary

In summary, 19 features were selected for further computer-aided classification using Artificial Neural Networks (ANN):

a) 7 features from the Conventional Approach:
   - Fres, R5, X5, AX, R5-R20, X10, and X15

b) 12 features from the Pre-Processing Approach:
   - 8 similarity measures for Resistance Typical and Area Functions
     - S_{Ra}, S_{Rs}, S_{Rp}, S_{Rn}, S_{IRa}, S_{IRs}, S_{IRp}, S_{IRn}
   - 4 similarity measures for Reactance Area functions
     - S_{IXa}, S_{IXs}, S_{IXp}, S_{IXn}

ANN Results – First Stage

Type of Feature	# Features	# Classes	Classes	Training Samples	Validation Samples	Hidden Neurons	Training Error	Validation Accuracy (%)
Conventional (IOS)	7	4	Asthma, SAI, PSAI , Normal	214	74	28	0.035	75.67
Pre-Processed R	12	4	Asthma, SAI, PSAI , Normal	214	74	25	0.035	63.7
Pre-Processed X	12	4	Asthma, SAI, PSAI , Normal	214	74	30	0.045	68.91
Pre-Processed R & X	24	4	Asthma, SAI, PSAI , Normal	214	74	23	0.01	71.62
Conventional (IOS) & Pre-Processed R	19	4	Asthma, SAI, PSAI , Normal	214	74	25	0.02	64.86
Conventional (IOS) & Pre-Processed X	19	4	Asthma, SAI, PSAI , Normal	214	74	28	0.035	63.51
Conventional (IOS) & Pre-Processed R & X	31	4	Asthma, SAI, PSAI , Normal	214	74	25	0.035	71.62

Barúa, Miroslava et al	2004	[31]	Central & Peripheral Diseases	IOS	Static	**IOS :** R5, R10, R15, R20, R25, R35, X5, X10, X15, X20, X25, X35 **General:** Smoking status, age, gender, height, weight.	ANN	Not reported	N/A	Not reported	N/A	N/A	N/A	61.53%	N/A

ANN Results – 2nd Stage

Type of Feature	# Features	# Classes	Classes	Training Samples	Validation Samples	Hidden Neurons	Training Error	Validation Accuracy (%)
Conventional (IOS)	7	2	Asthma, Normal	81	28	10	0.01	100
Pre-Processed R	8	2	Asthma, Normal	81	28	15	0.001	100

A. Badnjević et al	2016	[24]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms** **IOS**: not specified **SPIR:** not specified	ANN	Not reported	Not reported	Not reported	97.11%	N/A	98.85%	Not reported	97.84%
A. Badnjević et al	2016	[25]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms** **IOS:** R5, R20, X5, R5-R20, Fres **SPIR:** FVC, FEV1, FEV1/FVC , PEF	Fuzzy Logic	8.65 % (63/728)	N/A	89.08% (465/522)	91.89%	N/A	95.01%	42.24%	93.20%
A. Badnjević et al	2015	[26]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms and allergy history** **IOS :** R5, R20, R5-R20, X5, Fres **SPIR**: FEV1, FEV1/FVC **Body Plethysmography**	Neuro-fuzzy	11.43% (8/72)	N/A	Not reported	97.22%	N/A	98.61%	Could not be estimated with the information reported	98.20%
A. Badnjević et al	2013	[28]	Asthma & Healthy	IOS, SPIR, BDT, BPT	Static & Dynamic	**Symptoms, allergies and risk factors** **IOS** : R5, R20,R5-R20, X5, Fres **SPIR**: FEV1, FVC, FEV1/FVC	Neuro-fuzzy	10.70%	N/A	93.67%	90.25%	N/A	94.04%	51.92%	92.30%

ANN Results – 3rd Stage

ANN1 – Normal vs. Peripheral Lung Dysfunction

Type of Feature	# Features	# Classes	Classes	Training Samples	Validation Samples	Hidden Neurons	Training Error	Validation Accuracy (%)
Conventional (IOS)	7	2	1: Asthma, SAI, PSAI 2: Normal	214	74	15	0.001	95.94
Pre-Processed R	8	2	1: Asthma, SAI, PSAI 2: Normal	214	74	50	0.001	100
Pre-Processed X	4	2	1: Asthma, SAI, PSAI 2: Normal	214	74	10	0.005	93.24
Pre-Processed R & X	12	2	1: Asthma, SAI, PSAI 2: Normal	214	74	15	0.001	95.94

ANN Results – 3rd Stage

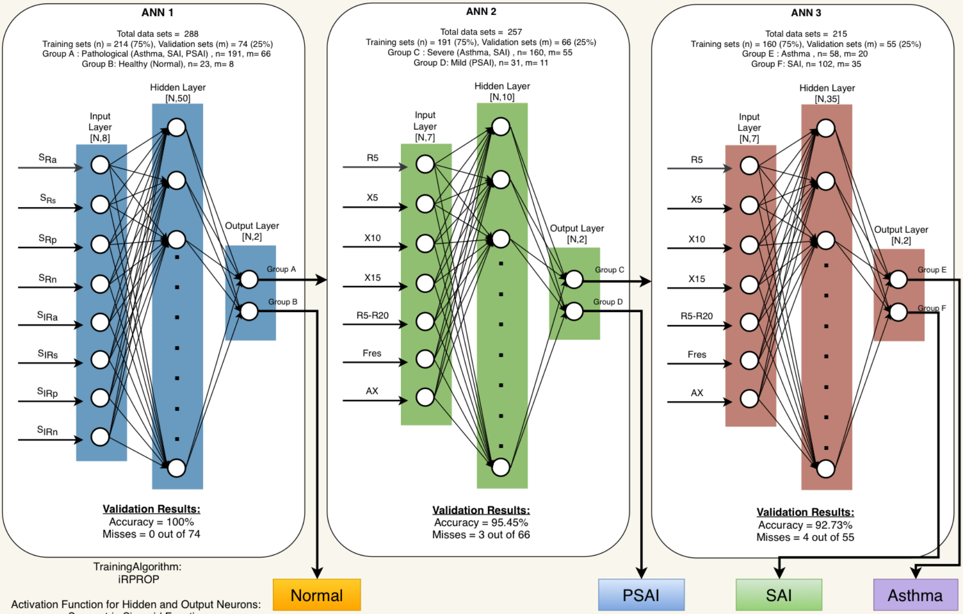
ANN2 – PSAI vs. Severe Peripheral Lung Dysfunction

Type of Feature	# Features	# Classes	Classes	Training Samples	Validation Samples	Hidden Neurons	Training Error	Validation Accuracy (%)
Conventional (IOS)	7	2	1: Asthma, SAD 2: Mild	191	66	10	0.02	95.45
Pre-Processed R	8	2	1: Asthma, SAD 2: Mild	191	66	15	0.005	87.87
Pre-Processed R & X	12	2	1: Asthma, SAD 2: Mild	191	66	20	0.001	89.39
Conventional (IOS) & Pre-Processed R	15	2	1: Asthma, SAD 2: Mild	191	66	15	0.001	89.39
Conventional (IOS) & Pre-Processed R & X	19	2	1: Asthma, SAD 2: Mild	191	66	15	0.01	92.42

ANN3 – SAI vs. Asthma

Type of Feature	# Features	# Classes	Classes	Training Samples	Validation Samples	Hidden Neurons	Training Error	Validation Accuracy (%)
Conventional (IOS)	7	2	Asthma, SAD	160	55	35	0.1	92.73
Pre-Processed R & X	12	2	Asthma, SAD	160	55	15	0.05	81.81

Results and Discussion



TrainingAlgorithm:
iRPROP

Activation Function for Hidden and Output Neurons:
Symmetric Sigmoid Function

Overall ANN Multi-classifier Validation Results: Accuracy = 90.54%, Misses = 7 out of 74

ANN Results

		Actual Condition	
		+	-
Diagnosis	+	TP	FP
	-	FN	TN

Sensitivity = TP/(TP+FN)

Specificity= TN/(TN+FP)

ANN 1

		Actual Condition	
		Healthy	Peripheral Dysfunction
Diagnosis	Healthy	66	0
	Peripheral Dysfuntion	0	8

Sensitivity = 100%

Specificity= 100%

ANN 2

		Actual Condition	
		PSAI	Severe Dysfunction
Diagnosis	PSAI	8	0
	Severe Dysfunction	3	55

Sensitivity = 73%

Specificity= 100%

ANN 3

		Actual Condition	
		SAI	Asthma
Diagnosis	SAI	35	4
	Asthma	0	16

Sensitivity = 100%

Specificity= 80%

		Actual Condition	
		Asthma	SAI
Diagnosis	Asthma	16	0
	SAI	4	35

Sensitivity = 80%

Specificity= 100%

Conclusions

- The best classification performance was achieved when using IOS discriminative features derived from both the Conventional and Pre-Processing approaches.
- 15 IOS derived features that best classify different degrees of respiratory small airway function in children were identified:
  - Resistance and Reactance discriminative IOS direct features (7).
  - Resistance pre-processed features (Typical and Area functions) (8).

  Note: Reactance pre-processed features (Area functions) usually reduced the performance of the ANN.
- The performance of the classification was improved when using multiple bi-class ANNs instead of one multi-class ANN.
- A Diagnostic Support System with high discriminative capacity (sensitivity, specificity, and accuracy) was developed.
- This classification research work is better in performance than any of the classification works performed so far using IOS features.
  - 100% accurate, sensitive and specific to classify Normal function vs. Small Airways Dysfunction.
  - 92%- 95% accurate, 73%-100% sensitive, and 80%-100% specific for classifying a specific type of Small Airways Dysfunction.

Novel Work

Biomedical Novelty:

- First successful algorithm for enhancing diagnostics of Asthma, SAI, PSAI and Normal lung function.

Computational Novelty:

- The use of innovative pre-processing techniques in machine learning: statistical and scale-invariance-based.

- First research work to assess lung function using IOS curve-shape-derived features.

Contribution to Society

- Assist clinicians with a reliable and proven method for accurate classification of children's lung function.
- This improves the clinical utility of the IOS.
- On-time diagnostics of SAI helps in the prevention of asthma and its control.
- Potential reduction of health care expenditures (Annual estimated expenditure is 8 billion dollars).

Future Work

- Test in a greater scale the Diagnostic Support System developed.
    - Collaborate with the National Institute of Respiratory Diseases (INER) in Mexico.
    - Collaborate with National Jewish Health Institute in Denver, CO.
- Increase the scope of current IOS research work by studying other populations and other pulmonary conditions such as Chronic Obstructive Pulmonary Disease (COPD) and pulmonary hypertension.

Publications

Journal Publications:

- *Avila N., Urenda, J., Gordillo, N., Kreinovich V.* ***Scale-Invariance-Based Pre-Processing Drastically Improves Neural Network Learning: Case Study of Diagnosing Lung Dysfunction in Children****. Soft Computing, submitted.*
- *Avila N., Nazeran, H., Gordillo, N., Meraz, E.* ***Computer-aided Classification of Peripheral Pulmonary Airway Obstruction using Impulse Oscillometric Features: A Review****. Biomedical Engineering/Biomedizinische Technik, in review process.*
- *Avila N., Nazeran, H., Meraz, E., Gordillo, N., and Aguilar C.* ***Characterization of Impulse Oscillometric Measures of Respiratory Small Airway Function in Children****. Advances in Electrical and Electronic Engineering. Publication. In press.*
- *Meraz E., Nazeran H., Edelatpour R., Rodriguez C. ,Montano K., Aguilar C. , Avila N., et al.* ***Reference Equations for Impulse Oscillometric and Respiratory System Model Parameters in Anglo and Hispanic Children****. Revista Mexicana de Ingenieria Biomedica. 2016, vol. 37, iss. 1, pp. 49-61. DOI: 10.17488/rmib.37.1.6.*

Conference Publications:

- *Martínez-García E.A, Avila Rodriguez N., Rodriguez R., Mizera-Prietaszko J., Kulandaidaasan J., Mohan R, and Magid E.* ***Non-Linear Fitting Methods for Machine Learning****. In: Xhafa F., Caballé S., Barolli L. (eds) Advances on P2P, Parallel, Grid, Cloud and Internet Computing.. Lecture Notes on Data Engineering and Communications Technologies. 2017, vol 13. Springer, Cham.*

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- ***Impulse Oscillometry Diagnostic Support System for Different Degrees of Peripheral Airways Obstruction*** *(programming code in C++). Received by the U.S.Copyright Office on 1/21/2019, case number 1-7345389751.*

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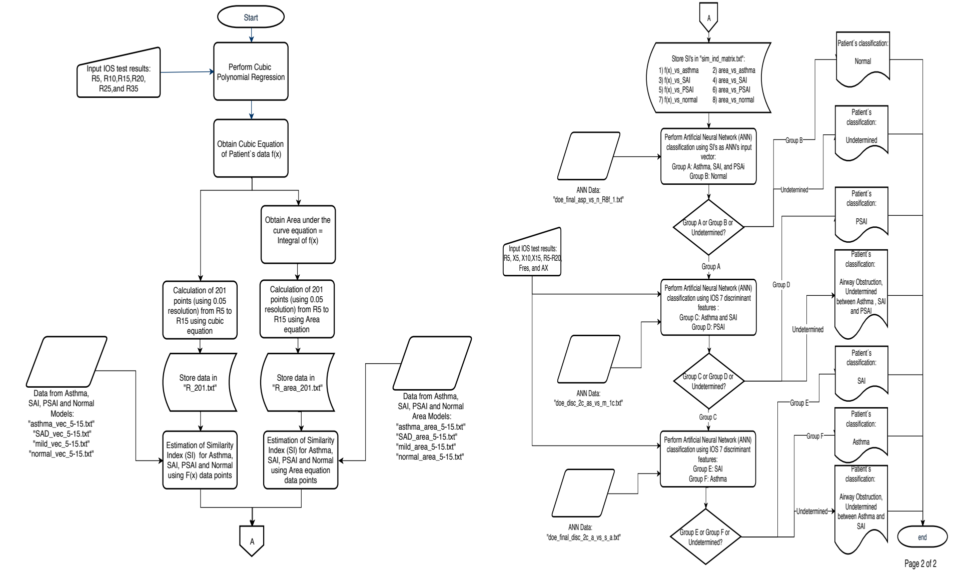
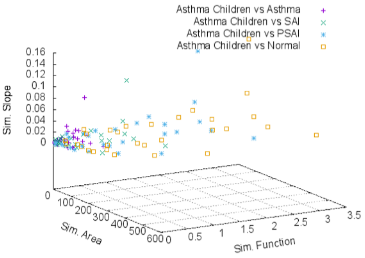
Results and Discussion

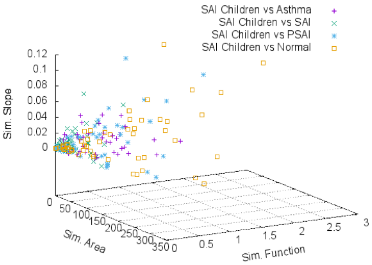
Impulse Oscillometry Diagnostic Support System (C++)

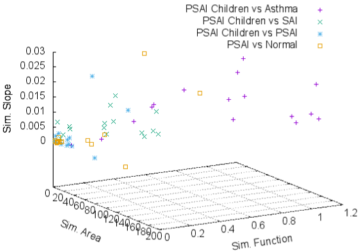


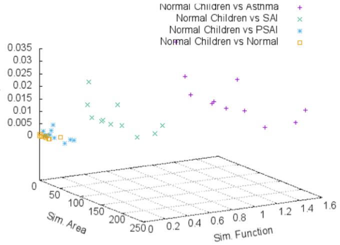
Feature Selection: Pre-Processing Approach

Similarity/Dissimilarity Measures









Feature Selection: Pre-Processing Approach