Sensigent eNose® Sensors

Medical Applications

of

Nanocomposite Sensor Arrays

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Product Platform

Cyranose® 320

- Handheld Chemical Vapor Detector
- Designed for Industrial / Commercial Use
- Evaluated as an exempt Research Tool to determine efficacy of sensor arrays for a variety of medical applications

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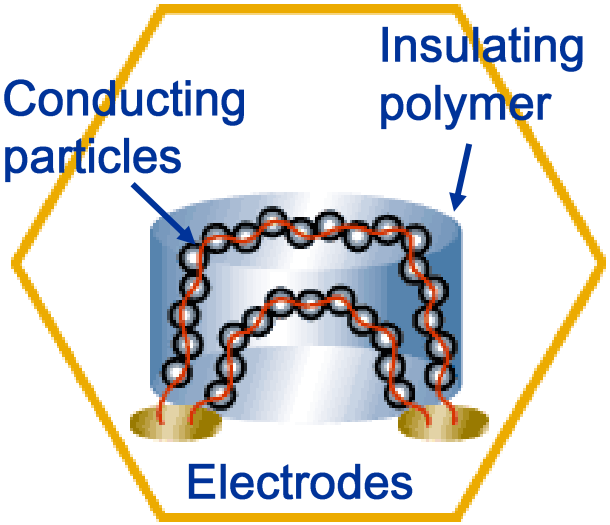
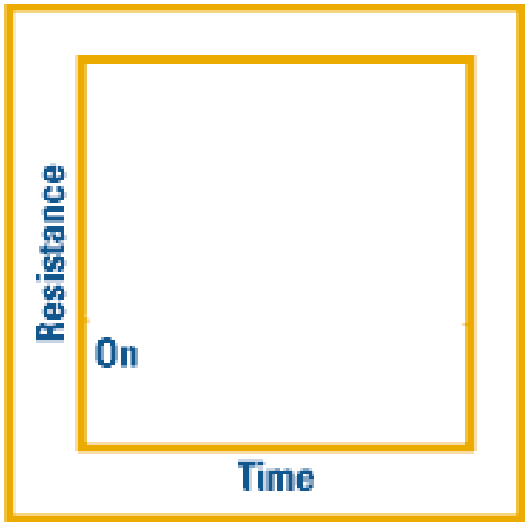
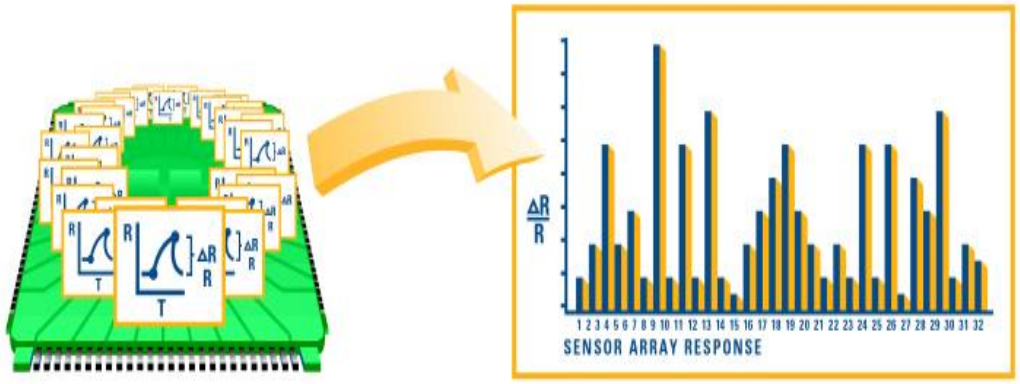
Nanocomposite Sensor Technology





Vapor passes over the polymer matrix and produces a change in dc resistance for each sensor

32 chemical sensors in standard array



Using pattern matching algorithms, the data is converted into a unique response pattern (PCA, CDA, ANN, SVM)

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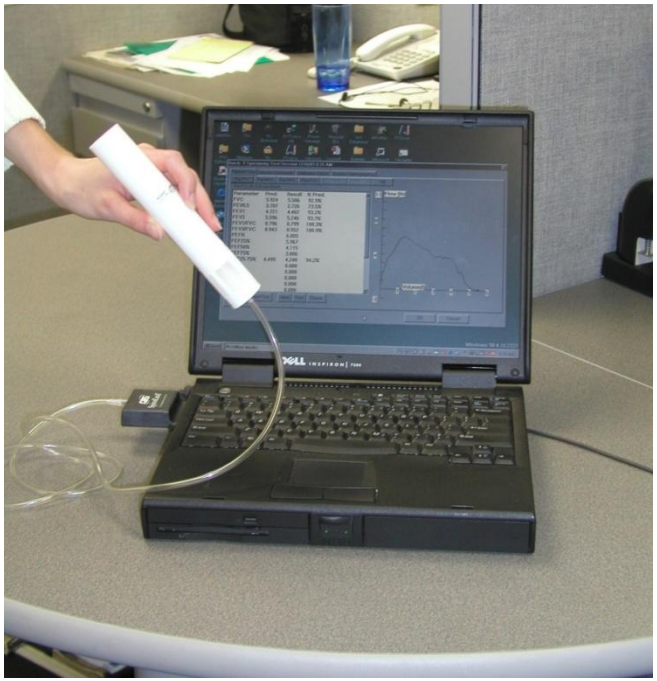
Medical Applications

Premise –
Routine Diagnosis
and
Health Monitoring
through Breath Analysis

product analogy:
spirometer on a PC card



Low cost and low power nanotechnology sensors will enable affordable and reliable devices for home health and point of care products

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History of Breath Analysis

Hippocrates - treatise on breath aroma and disease

Lavoisier and Laplace (1784) - showed that respiration consumes oxygen and eliminates carbon dioxide

Nebelthau (mid 1800s) - showed that diabetics emit breath acetone

Anstie (1874) - isolated ethanol from breath

Pauling (1971) - used GC to detect 250 compounds in breath

Phillips (1999) - used GC/MS to detect 3000 compounds in breath

2000 - present - new advances in breath analysis each year through laser spectroscopy, mass spectrometry **and eNose analysis**

Select Publications of the Handheld eNose 2002 - 2012

University of Pennsylvania uses handheld eNose for pneumonia, CSF and sinusitis research in the ER and outpatient clinic

Lai, S. et al. Identification of upper respiratory bacterial pathogens with the electronic nose. Laryngoscope. 112(6) 975-9 (2002); Aronzon, A. et al. Differentiation between cerebrospinal fluid and serum with electronic nose. Otolaryngol Head Neck Surg 133(1) 9-16 (2005); Thaler, ER, Hanson, CW. Use of an electronic nose to diagnose bacterial sinusitis. American Journal of Rhinology, 20(2) 170-172 (2006)

Cleveland Clinic uses handheld eNose for lung cancer research

Machado, R. et al Detection of Lung Cancer by Sensor Array Analyses of Exhaled Breath. Am. J. Respir. Crit. Care Med. 171(11) 1286-1291 (2005)

University of Amsterdam uses handheld eNose for COPD, asthma and cancer

Dragonieri, S. et al. An electronic nose in the discrimination of patients with asthma and controls. J Allergy Clin Immunol. 120(4): 856-62 (2007); Dragonieri, S. et al. An electronic nose in the discrimination of patients with non-small cell lung cancer and COPD. Lung Cancer 64(2) 166-70 (2009); Lazar, Z. et al. Electronic nose breathprints are independent of acute changes in airway caliber in asthma. Sensors 10(10) 9127-38 (2010); Fens, N. et al. Exhaled air molecular profiling in relation to inflammatory subtype and activity in COPD. Eur Respir. J. 38 1301-1309 (2011).

Research teams around the world use the handheld eNose: *Australia, New Zealand, Germany, Hungary, Italy …*

Dent, A. et al. Electronic nose distinguishes lung cancer from healthy smoking controls. Supplement to Journal of Thoracic Oncology: (2010); Hattesohl AD, et al. Discrimination between COPD patients with and without alpha 1-antitrypsin deficiency using an electronic nose. Respiratory Disease Diagnosis 16(8) 1258-64 (2011); Chapman, EA et al. A breath test for malignant mesothelioma using an electronic nose. Eur Respir J. December 2011. Timms, C. et al. Detection of gastro-oesophageal reflux disease (GORD) in patients with obstructive lung disease using exhaled breath profiling. J Breath Res. January 2012.

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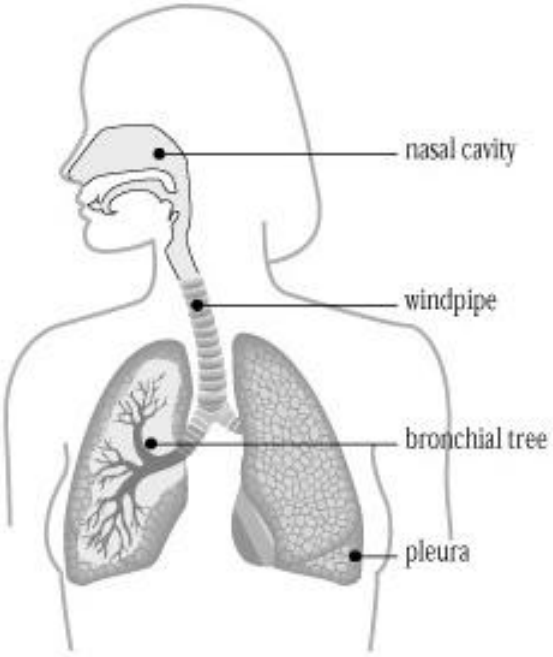
Breath Biomarkers

Disease	Compound as a disease marker	Analysis Instrument
Acute cardiac allograft rejection	Pentane	GC/FID
Myocardial infarction (MI)	Hydrocarbons	GC/FID
Asthma	Nitric Oxide	CL analyzer
COPD / ARDS	NO, CO	CL analyzer
Breast Cancer	Pentane	GC/FID
Diabetes	Acetone	GC/FID
Hemolysis	Carbon monoxide	EC CO analyzer
		GC/TCD
H. pylori infection	$^{13}CO_2$ or $^{14}CO_2$	Isotope Ratio MS
		Isotope Ratio IR
Alcoholic liver disease	Pentane	GC/FID
Liver cirrhosis	Dimethyl sulfide	GC/FPD
	Volatile fatty acid	GC/FID
Weight Reduction	Acetone	GC/FID



VOCs from bacterial infection

acids, alcohols, aldehydes, amines, ketones, hydrocarbons, sulfur compounds

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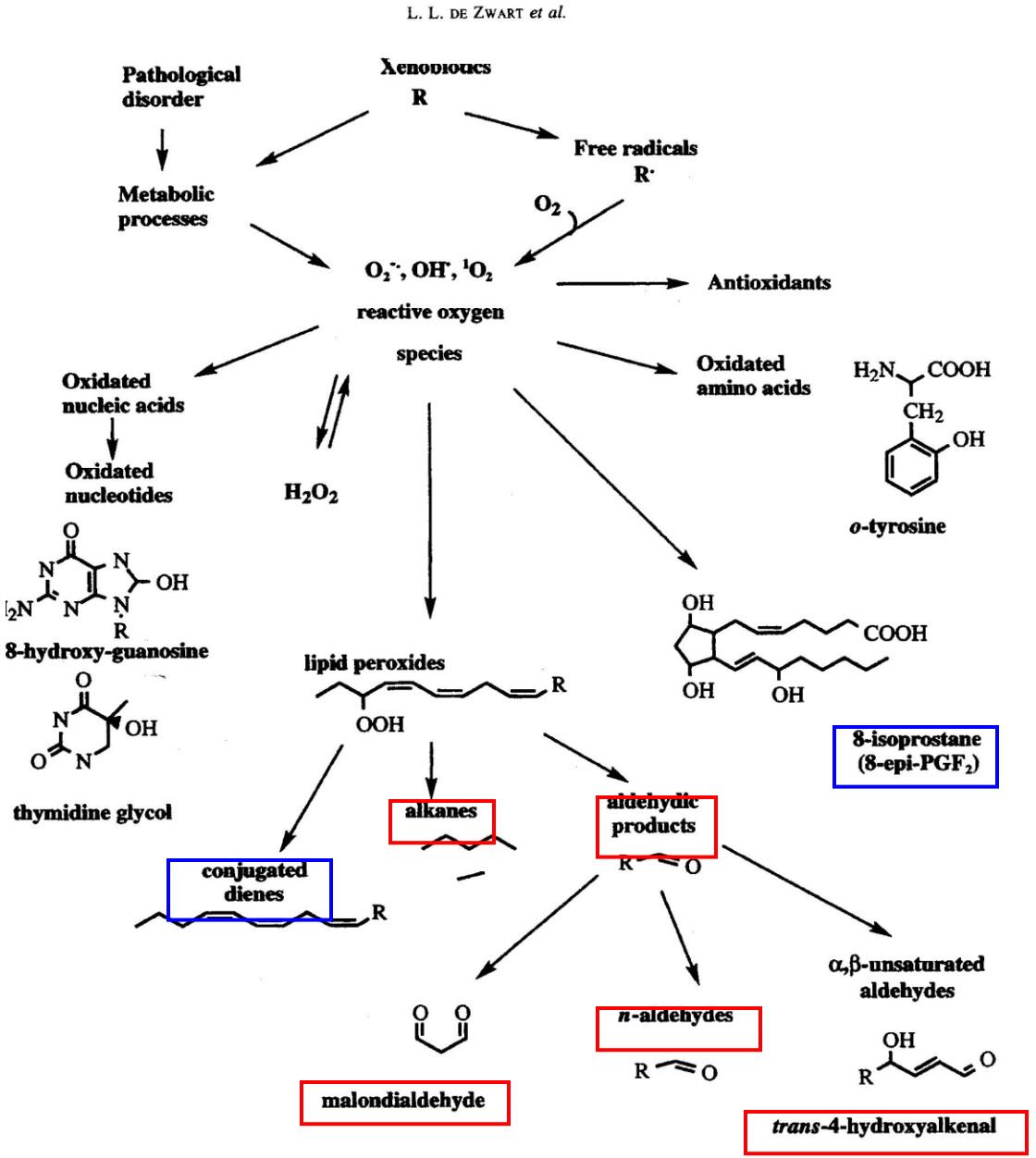
Example:

Free radicals produce measureable volatile products of oxidative stress



semivolatiles in breath condensate

volatiles excreted in breath

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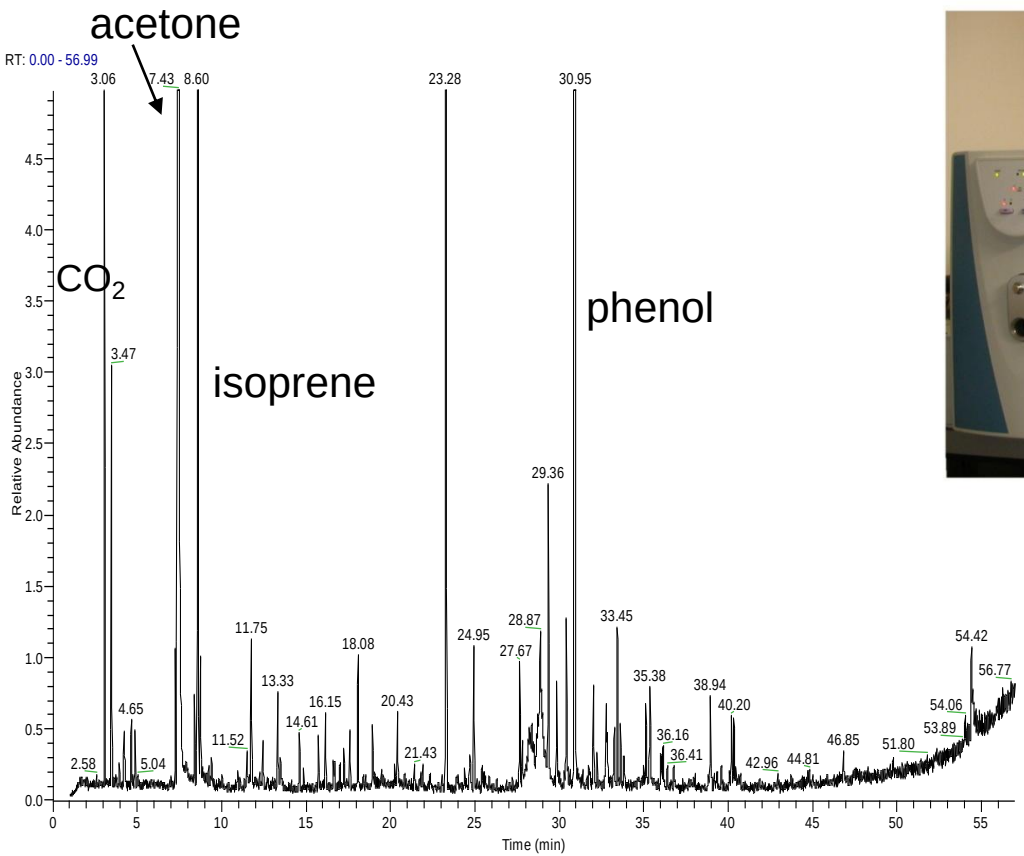
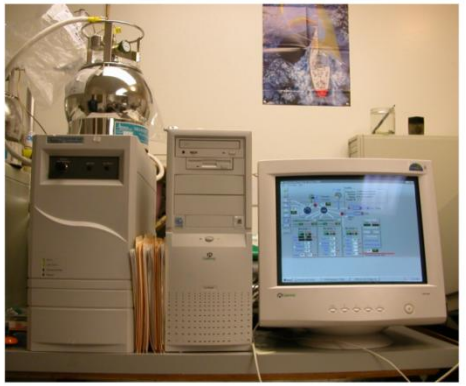
Breath Chemical Analysis





GC/MS can identify many but not all breath constituents

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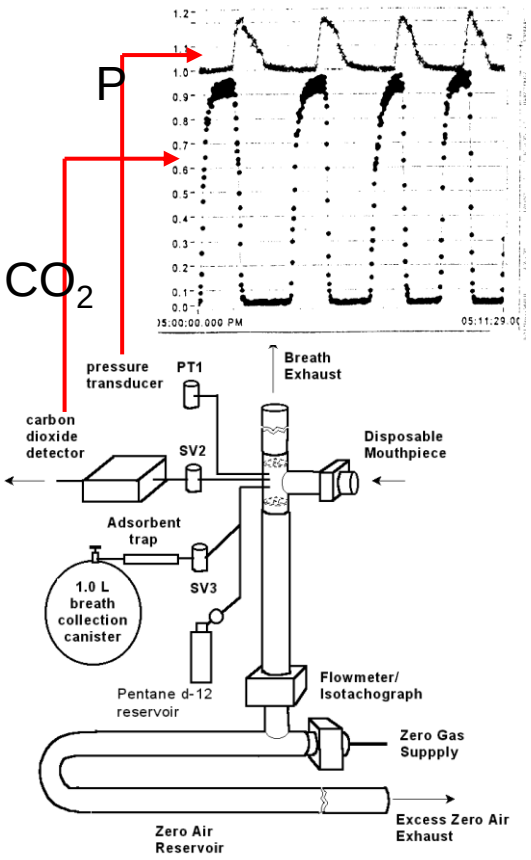
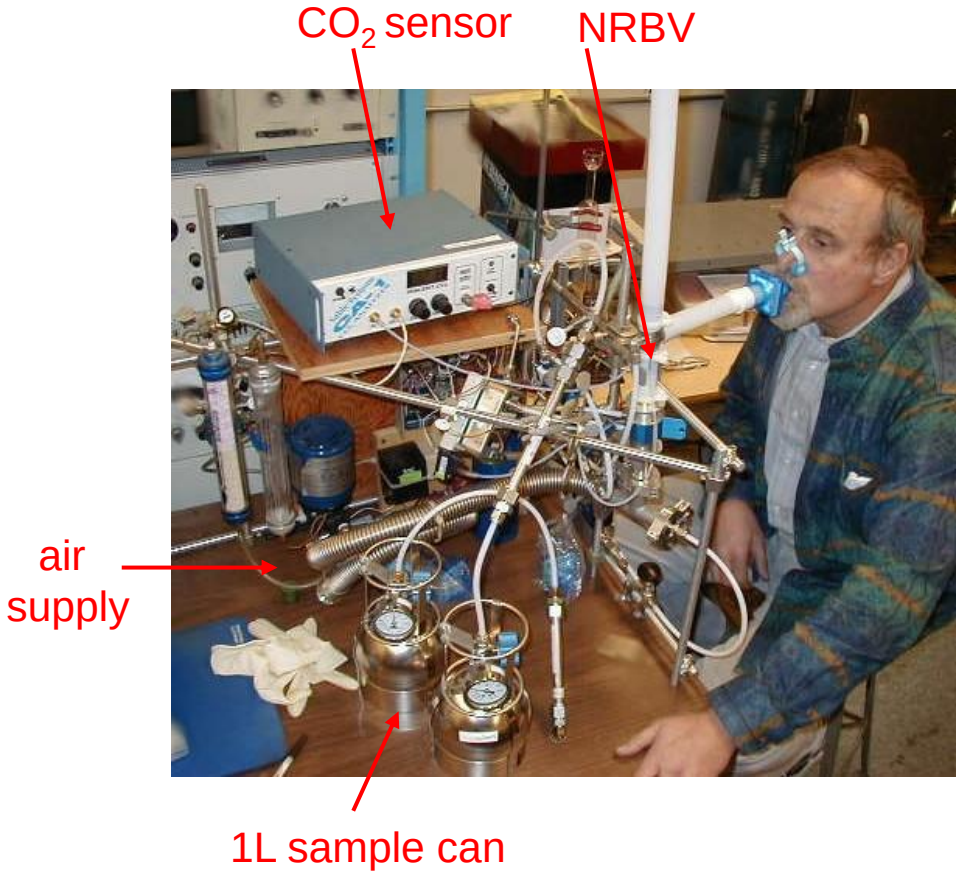
Breath Collection





Elaborate means for collection of breath constituents for analysis

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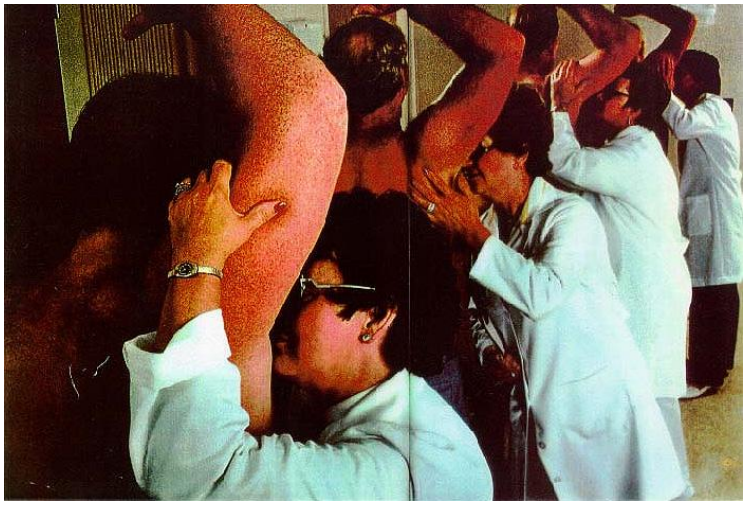
Why use an “Electronic Nose”?



- Measure the entire breath profile
- Simplicity of sample measurement
- An eNose received FDA approval in 2002 for
  - Urinary Tract Infection (UTI)
  - Bacterial Vaginosis (BV)

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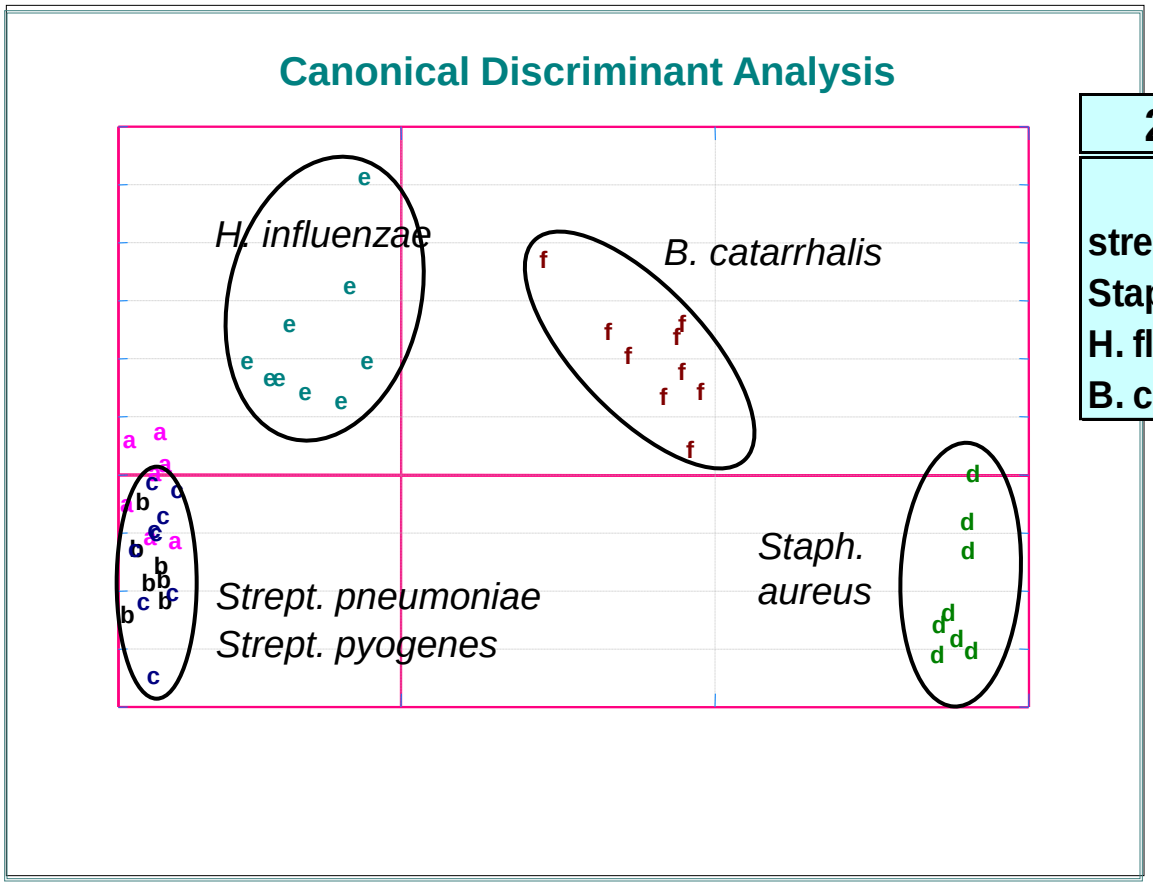
Selected Medical Applications

- Bacteria Identification
  - ENT bacteria, infant Otitis Media, adult Urinary Tract Infection
- Univ. Pennsylvania Hospital (HUP)
  - Ventilator Associated Pneumonia
  - Sinusitis
  - Cerebrospinal fluid in the ER
- Cleveland Clinic Foundation (CCF)
  - Lung Cancer
  - ARDS, COPD, asthma
  - CF, PPH
- Univ. of Amsterdam (AMC)
  - Asthma
  - Small cell cancer and COPD

Identification of ENT Bacteria



2 Week Prediction Success		
	tests	ID
strep A+B	28/28	100%
Staph	13/13	100%
H. flu	15/15	100%
B. catarrh.	15/15	100%

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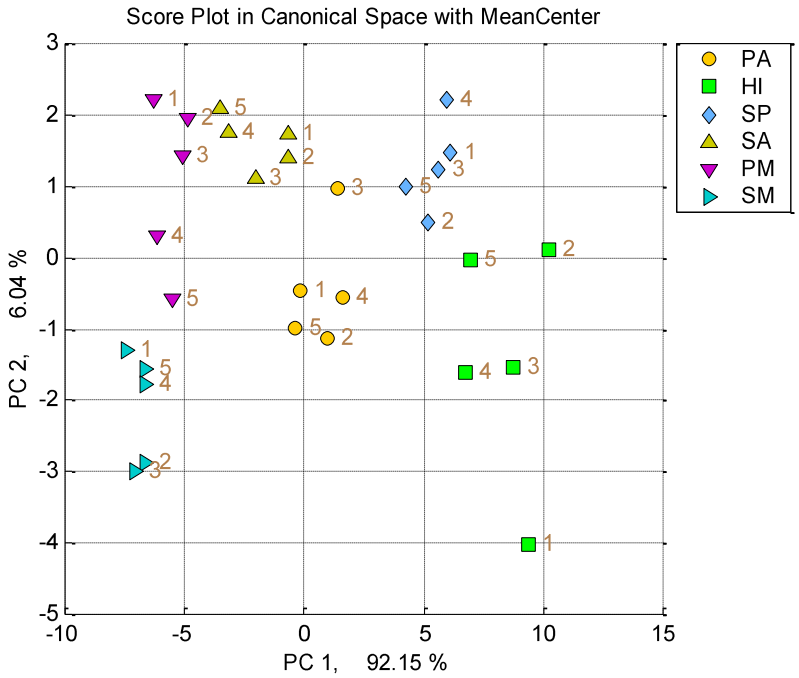
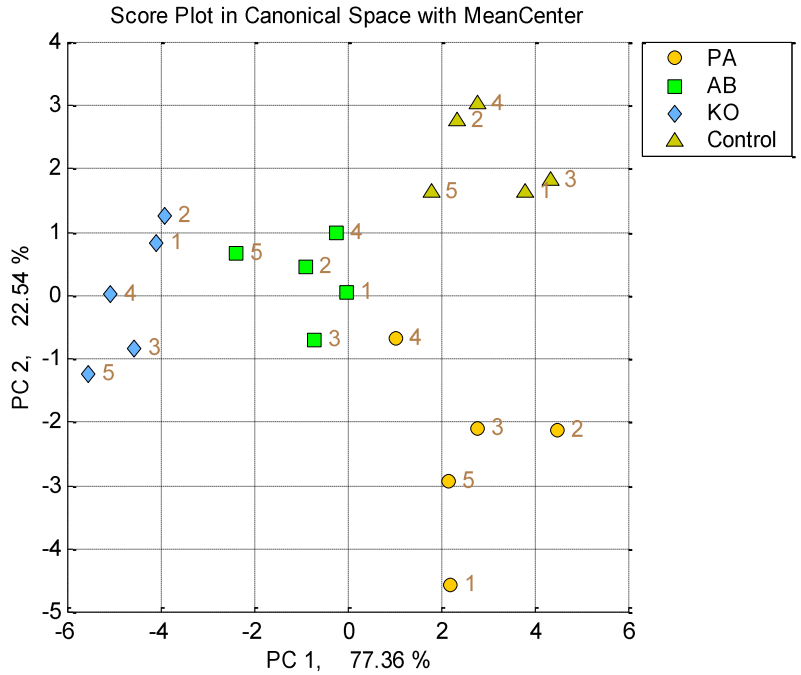
Identification of ENT Bacteria



Lai SY et al, Identification of Upper Respiratory Bacterial Pathogens with the Electronic Nose. *Laryngoscope* 112, 975-9 (2002).



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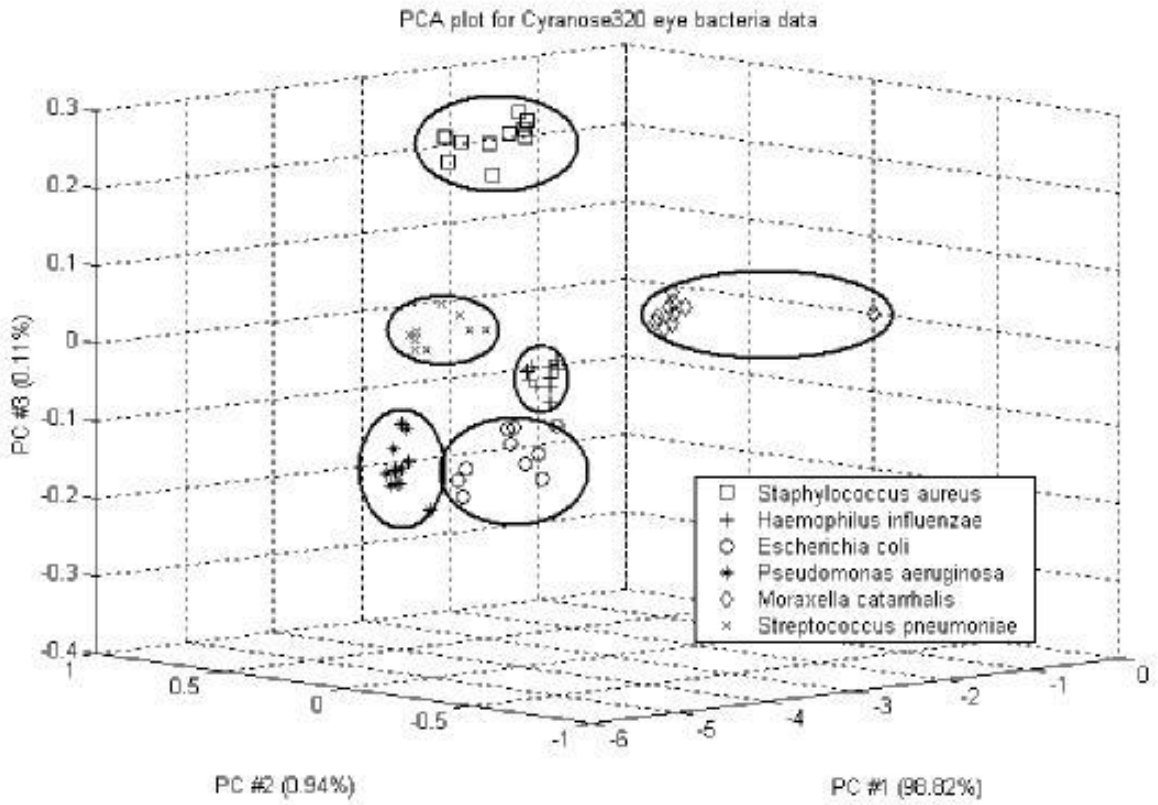
Identification of Eye Bacteria



Bacteria classification using Cyranose 320 electronic nose. Biomed Eng Online. 2002; 1 (1): 4
Ritaban Dutta, [1] Evor L. Hines,[1] Julian W. Gardner,[1] and Pascal Boilot[1]

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Breath Signature of Bacterial Infection

VOCs from bacterial metabolism

alcohols
ketones
aldehydes
organic acids
hydrocarbons
sulfides, thiols
amines

Compounds from immune system response to infection

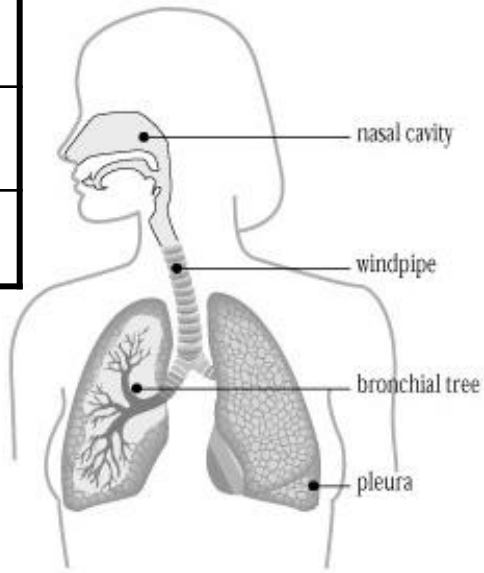
Inflammation: NO_x CO VOCs

Enterotoxin stimulus: VOCs ?

Bacteria	Metabolites
S. aureus	2-methylbutanol 3-methylbutanol
Strept. pneumoniae	2-butanol lactic acid
H. influenzae	acetic acid indole

O_2

amino acids
carbohydrates



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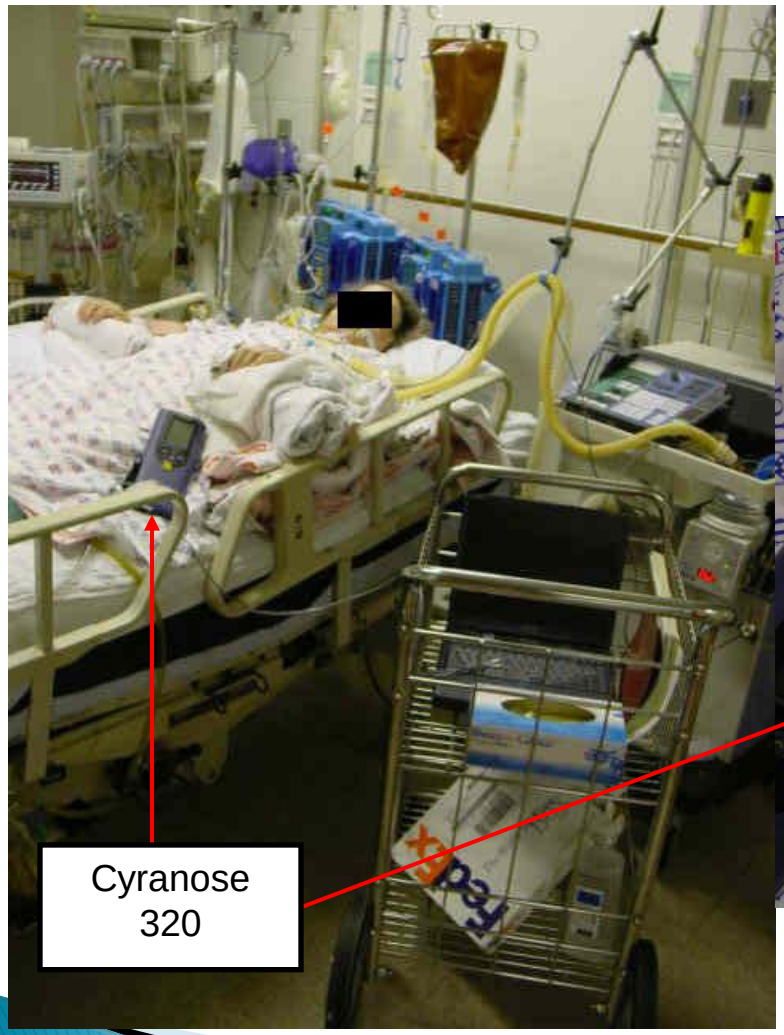
Ventilator Associated Pneumonia (VAP)



Cyranose used to measure exhaled breath in ICU at UPenn Hospital

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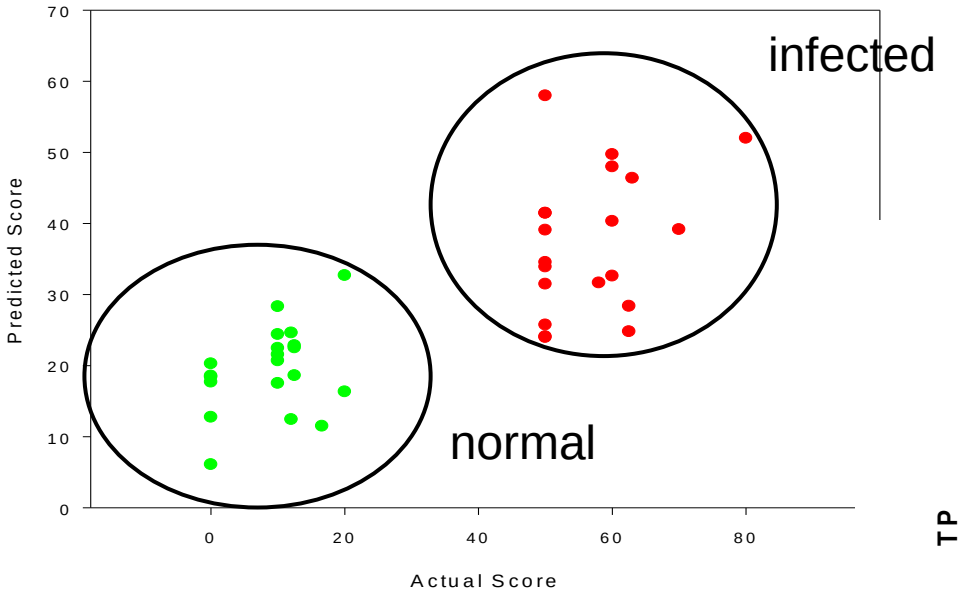
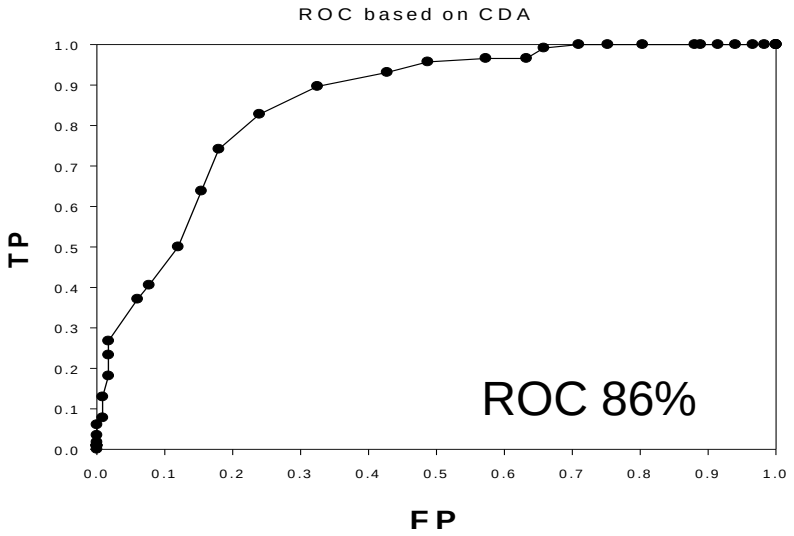
Ventilator Associated Pneumonia



William Hanson, MD
Erica Thaler, MD



eNose measurements on exhaled breath compare favorably to the combined pulmonary infection score (CPIS) used to confirm ventilator associated pneumonia in the ICU

Amer. Thoracic Society 2002

Acute Rhinosinusitis

Model	c=100, w=0.5		c=10, w=5	
	# correct	% correct	# correct	% correct
SVM	123/123	100	118/123	95.9
SVM+PCA(2)	123/123	100	113/123	91.9
SVM+PCA(3)	123/123	100	121/123	98.4

Nasal breathing cup

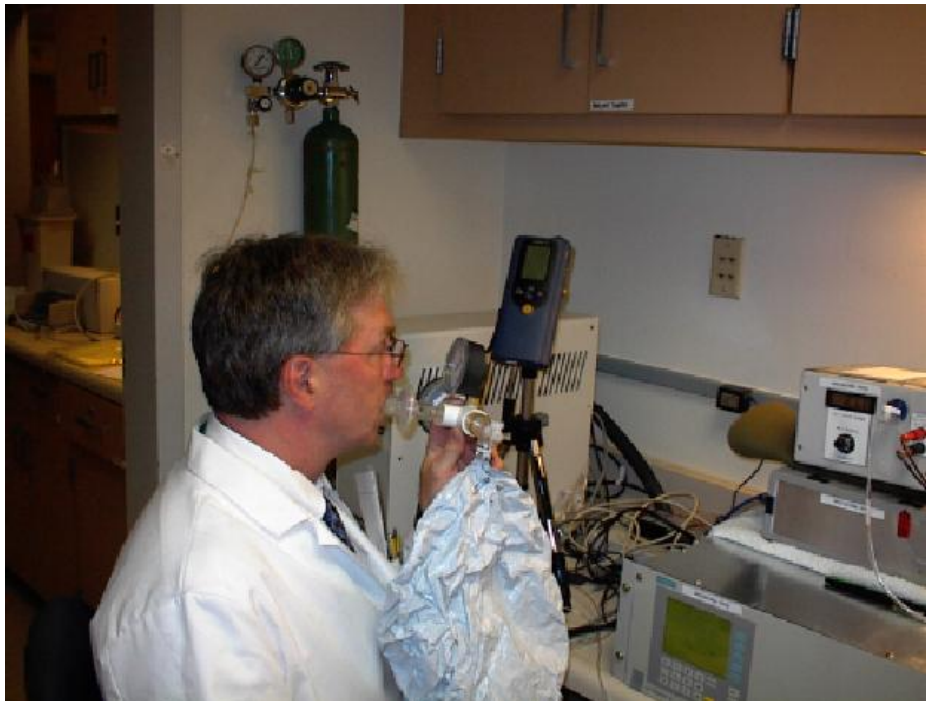
22 subjects
- 11 neg. controls
- 11 positives

4 months

Methods

- Nasal swabs
  - sampling of infection hotspot with calgiswab
- Nasal breathing cup

Respiratory Disease



THE CLEVELAND CLINIC

Cleveland Clinic Foundation

Lung Cancer
Asthma
COPD
ARDS
CF

Serpil Erzurum, MD
Raed Dweik, MD
Roberto Machado, MD

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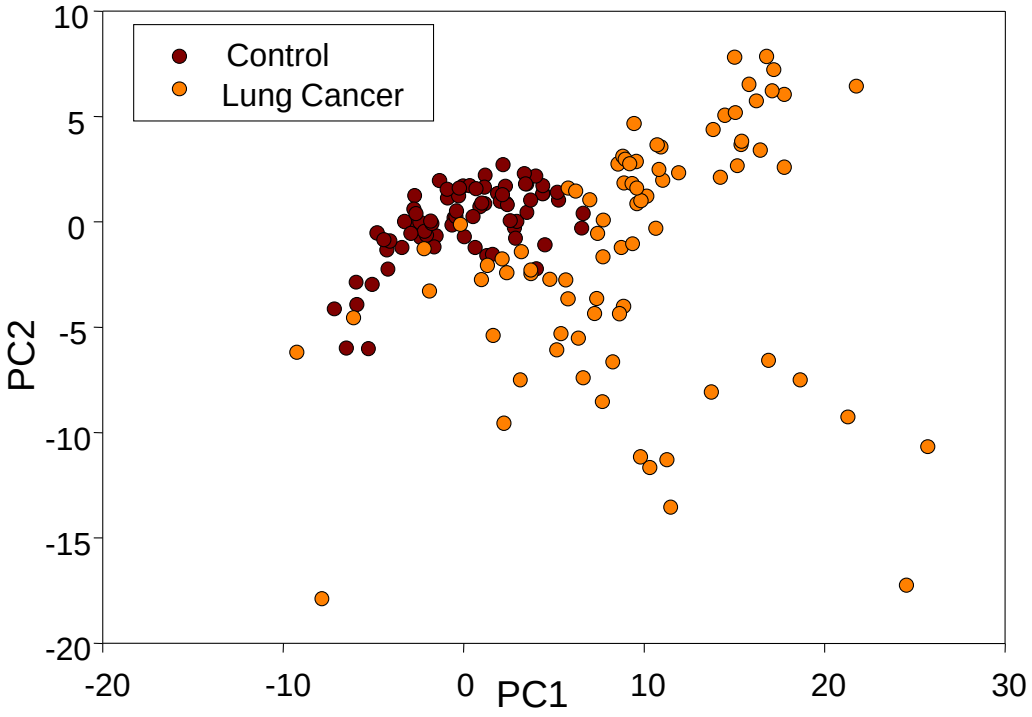
Lung Cancer



- Detection of lung cancer in non-smokers is feasible
- Discrimination from several disease controls: COPD, ARDS, PPH, asthma,a-1, CBE
- Goal: early detection of small tumors

Machado RF et al (CCF) Detection of Lung Cancer by Sensor Array Analyses of Exhaled Breath. *Amer. Jour. Respiratory & Critical Care Medicine v171 1286-1291 (2005).*

DiNatale, et al (Univ Rome) Lung cancer identification by the analysis of breath by means of an array of non-selective gas sensors. *Biosensors & Bioelectronics v18 1209-1218 (2003)*

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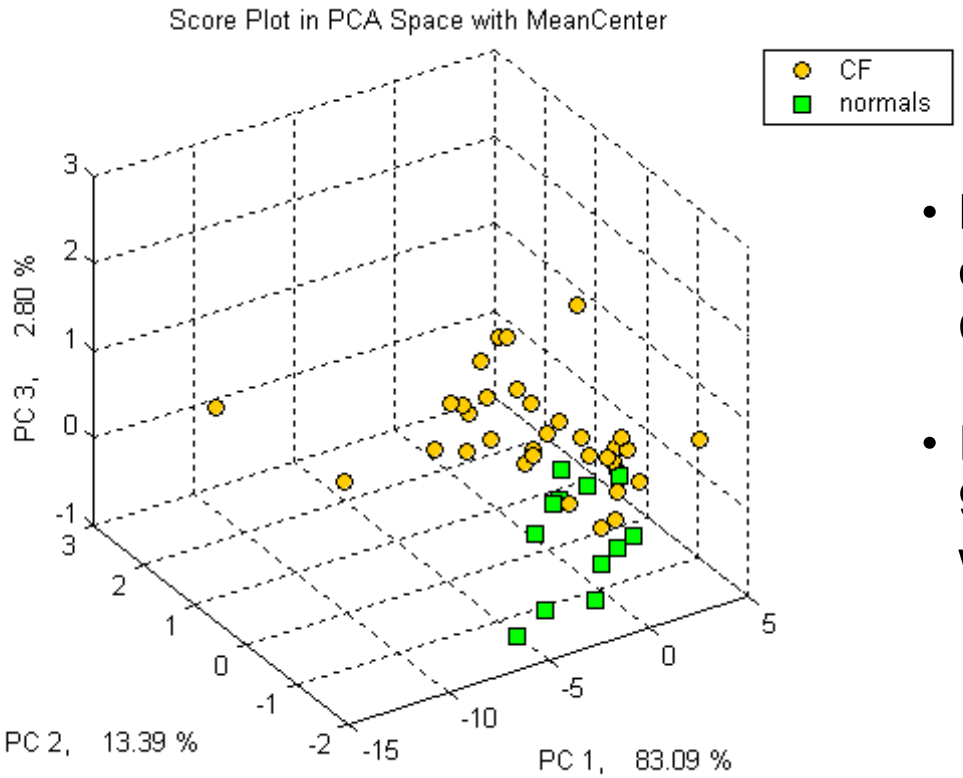
Cystic Fibrosis



- Discrimination of chronically colonized CF subjects is feasible
- In preliminary tests, 93.4% of breath samples were identified correctly

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Conclusions & Hypotheses

- Many diseases produce a measurable pattern of volatile chemicals in breath, urine and blood
- Non-invasive breath measurement will provide rapid diagnosis and treatment monitoring capability for physicians in emergency and point-of-care applications
- Low cost and low power intelligent sensor array devices will enable home health diagnosis and monitoring capability for many individuals

For application or product information, please contact:

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