Medical Applications of Nanocomposite Sensor Arrays
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
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)
Premise – Routine Diagnosis and Health Monitoring through Breath Analysis

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

Product analogy: spirometer on a PC card
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
University of Pennsylvania uses handheld eNose for pneumonia, CSF and sinusitis research in the ER and outpatient clinic

Cleveland Clinic uses handheld eNose for lung cancer research

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

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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Compound as a disease marker</th>
<th>Analysis Instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute cardiac allograft rejection</td>
<td>Pentane</td>
<td>GC/FID</td>
</tr>
<tr>
<td>Myocardial infarction (MI)</td>
<td>Hydrocarbons</td>
<td>GC/FID</td>
</tr>
<tr>
<td>Asthma</td>
<td>Nitric Oxide</td>
<td>CL analyzer</td>
</tr>
<tr>
<td>COPD / ARDS</td>
<td>NO, CO</td>
<td>CL analyzer</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>Pentane</td>
<td>GC/FID</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Acetone</td>
<td>GC/FID</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>Carbon monoxide</td>
<td>EC CO analyzer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GC/TCD</td>
</tr>
<tr>
<td>H. pylori infection</td>
<td>$^{13}$CO$_2$ or $^{14}$CO$_2$</td>
<td>Isotope Ratio MS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Isotope Ratio IR</td>
</tr>
<tr>
<td>Alcoholic liver disease</td>
<td>Pentane</td>
<td>GC/FID</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>Dimethyl sulfide</td>
<td>GC/FPD</td>
</tr>
<tr>
<td>Weight Reduction</td>
<td>Volatile fatty acid</td>
<td>GC/FID</td>
</tr>
<tr>
<td></td>
<td>Acetone</td>
<td>GC/FID</td>
</tr>
</tbody>
</table>

VOCs from bacterial infection
- acids, alcohols, aldehydes, amines, ketones, hydrocarbons, sulfur compounds
Example: Free radicals produce measureable volatile products of oxidative stress

- semivolatiles in breath condensate
- volatiles excreted in breath
Breath Chemical Analysis

GC/MS can identify many but not all breath constituents
Breath Collection

Elaborate means for collection of breath constituents for analysis
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)
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

Canonical Discriminant Analysis

2 Week Prediction Success

<table>
<thead>
<tr>
<th></th>
<th>tests</th>
<th>ID</th>
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</thead>
<tbody>
<tr>
<td>strep A+B</td>
<td>28/28</td>
<td>100%</td>
</tr>
<tr>
<td>Staph</td>
<td>13/13</td>
<td>100%</td>
</tr>
<tr>
<td>H. flu</td>
<td>15/15</td>
<td>100%</td>
</tr>
<tr>
<td>B. catarrh.</td>
<td>15/15</td>
<td>100%</td>
</tr>
</tbody>
</table>
Identification of ENT Bacteria

Identification of Eye Bacteria

Ritaban Dutta, 1 Evor L. Hines, 1 Julian W. Gardner, 1 and Pascal Boilot 1
Breath Signature of Bacterial Infection

VOCs from bacterial metabolism:
- alcohols
- ketones
- hydrocarbons
- aldehydes
- organic acids
- sulfides, thiols
- amines

Compounds from immune system response to infection:
- Inflammation: \( \text{NO}_x \), CO, VOCs
- Enterotoxin stimulus: VOCs

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Metabolites</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. aureus</em></td>
<td>2-methylbutanol, 3-methylbutanol</td>
</tr>
<tr>
<td><em>Strept. pneumoniae</em></td>
<td>2-butanol, lactic acid</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>acetic acid, indole</td>
</tr>
</tbody>
</table>

\[ O_2 \]

amino acids

carbohydrates
Ventilator Associated Pneumonia (VAP)

Cyranose used to measure exhaled breath in ICU at UPenn Hospital

Sample taken from exhaled gases.

Cyanose 320
Ventilator Associated Pneumonia

eNose® - Medical Applications

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

Nasal breathing cup

22 subjects
11 neg. controls
11 positives
4 months

Methods

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

<table>
<thead>
<tr>
<th>Model</th>
<th># correct</th>
<th>% correct</th>
<th># correct</th>
<th>% correct</th>
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</thead>
<tbody>
<tr>
<td>SVM</td>
<td>123/123</td>
<td>100</td>
<td>118/123</td>
<td>95.9</td>
</tr>
<tr>
<td>SVM + PCA(2)</td>
<td>123/123</td>
<td>100</td>
<td>113/123</td>
<td>91.9</td>
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<tr>
<td>SVM + PCA(3)</td>
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<td>100</td>
<td>121/123</td>
<td>98.4</td>
</tr>
</tbody>
</table>
Respiratory Disease

Cleveland Clinic Foundation

Lung Cancer
Asthma
COPD
ARDS
CF

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


Cystic Fibrosis

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