MITRE Nanotechnology Speaker Series

MITRE Nanosystems Group

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MITRE Nanotechnology Speaker Series

Nose-like Nanosensing Systems

Brigitte Rolfe Nanosystems Group Leader 8 February 2006



Project Goal: Apply Advances in Nanotechnology to Improve Chem/Bio Sensing Systems

- Since the events of the Fall of 2001, developing better sensor systems for early detection of toxic agents has been of great importance to the nation
- In working toward a solution to this problem, the Nanosystems Group is applying lessons learned from
 - the natural nose and artificial noses
 - recent advances in nanometer scale devices
 - ... to further the development of <u>Nanosensing Systems</u> with nose-like sensitivity, accuracy and reliability
- Nose-Like Nanosensing Systems could
 - Perform ubiquitous sensing to secure airports and other public and private spaces
 - Provide ultra-small wearable sensors for soldier protection
 - Identify individuals by their specific chemical (odorant) signature

Why the Olfactory Model?

- Traditional "one-sensor-one-analyte" sensing is not effective for multiple target agents in uncontrolled environments
- Olfaction is a highly sensitive, selective, fast and reliable sensing system that works well in "noisy environments"

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- Some examples of what the nose can do:
 - Human females can detect minute differences in male immunotype by smell
 - A moth can smell a single molecule of the moth pheromone 'bombykol'
 - A bloodhound can pick
 - up a 24 hour-old trail and identify the person
 - Rats need only one sniff (< 200 ms) to accurately discriminate odors*

Facts and dog graphic from the Olfaction website of T.Jacob, University of Cardiff, UK * From N. Uchida & Z. Mainen, Nature Neuroscience, Oct. 19, 2003



MITRE Report Reviews & Proposes Designs for Nose-Like Nanosensors

Report presents:

- A review of natural olfaction
- Survey of artificial noses and their sensing technologies
- Discussion of existing nanosensors
- Designs for integration of nanosensors into sensing <u>systems</u>



Objectives of Presentation

To discuss:

- Goals of Nose-like Sensing R&D
 - Highlights of the Physiology of Olfaction
- Overview of Artificial Noses
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Major Steps in Olfactory Processing

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- Odor molecules make contact with the olfactory receptor (OR) neurons
- The signals from the OR neurons are sent to the olfactory bulb for preprocessing
- From the olfactory bulb, the signals travel to the olfactory cortex and to other regions of the brain



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The Transduction Process

- Odor molecule binds with a G protein-coupled receptor on the surface of the cilium
- Odorant-receptor binding activates the G_{olf} protein inside the cilium
- G_{olf} activates AC
- AC catalyzes conversion of ATP to cAMP
- cAMP travels throughout the cell, opening ion channels in the cell membrane
- Flow of positive ions in and negative ions out reduces the potential across the membrane



• If depolarization reaches threshold, an action potential is generated

AC = adenylyl cyclase, ATP = adenosine triphosphate, CNG= cyclic nucleotide gated AMP = adenine monophosphate, cAMP = cyclic Graphic from T. Jacob website.



Early Processing in the Epithelium



In the Epithelium ...

- Each OR neuron expresses a single receptor type
- Each receptor responds to a range of odorants with similar structures
- Incoming odorants may activate several different types of OR neurons
- All OR neurons of the same type send their axons to the same glomerulus in the olfactory bulb

Source of Graphic: Stuart Firestein, Nature, 413, 9/13/2001



Convergence of Axons to a Glomerulus



<u>A Visualization of</u> <u>Axonal Convergence</u>

P. Mombaerts and his group at Rockefeller U. used gene targeting technology to generate a strain of mice in which expression of a defined OR is coupled to an axonal marker

Photo from: P. Mombaerts, Science, 286, 10/22/99



Signal Flow to the Olfactory Cortex



Trace of Signal Flow from Nose to Brain

Linda Buck's team at Harvard traced signals from two OR types, M5BL (blue) and M50BL (red) from the epithelium to the olfactory cortex

Olfactory Processing

- In the bulb, inputs from different ORs are segregated by type
- Activated glomeruli in the bulb provide a stereotyped map or "code" for the odorant
- In the olfactory cortex, individual cortical neurons may receive input from multiple ORs
- Signals reach multiple areas of the brain, resulting in another map of sensory information

Graphic from: L. Buck et al., Nature, 414, 11/08/2001



Odorant Identification Relies Upon Pattern Recognition and Stored Memories

- The particular combination of neurons that is activated by an odor provides a "code"
- To identify the odor, the code is compared with stored patterns in the brain

This odorant has four qualities:

red, green, square, triangle

qualities are activated

All receptors for any of these



Graphic adapted from: Stuart Firestein, Nature, 413, 9/13/2001



Examples of Combinatorial Receptor Codes

| | S 1 | S3 | S 6 | S18 | S19 | S25 | S41 | S46 | S50 | S51 | S79 | S83 | S85 | S86 | |
|--|------------|----|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Hexanoic Acid | | | | | | | | | | | | | | | rancid, sweaty, sour, goat-like, fatty |
| Hexanol | | | | | | | | | | | | | | | sweet, herbal, woody, Cognac, Scotch whiskey |
| | | | | | | | | | | | | | | | |
| Heptanoic Acid | | | | | | | | | | | | | | | rancid, sweaty, sour, fatty |
| Heptanol | | | | | | | | | | | | | | | violet, sweet, woody, herbal, fresh, fatty |
| | | | | | | | | | | | | | | | |
| Octanoic Acid | | | | | | | | | | | | | | | rancid, sour, repulsive sweaty, fatty |
| Octanol | | | | | | | | | | | | | | | sweet, orange, rose, fatty, fresh, powerful, waxy |
| | | | | | | | | | | | | | | | |
| Nonanoic Acid | | | | | | | | | | | | | | | waxy, cheese, nutlike, fatty |
| Nonanol | | | | | | | | | | | | | | | fresh, rose, oily floral, odor of citronella oil, fatty |
| Receptor Codes for Odorants with Similar Structures but Different Odors | | | | | | | | | | | | | | | |

Table from: B. Malnic, L. Buck, et al., Cell, 96, 5 March 1999



Summary: Key Principles of the Olfactory Model

- Olfaction uses vast numbers of very small, densely spaced, sensing neurons
- Sensing neurons are nonspecific sensors
- The sensing range of an individual neuron overlaps with those of other neurons
- Repetition of the same neuron many thousands of times increases likelihood of odorant binding and amplifies signal
- Odors are identified using a spatio-temporal combinatorial system, along with stored memories

Graphic from: P. Mombaerts, Science, 286, 10/22/99

Glomeruli in the Olfactory Bulb



OR Neurons in the Epithelium

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Artificial Noses Make Use of the Key Principles of Olfaction



The Artificial Nose: An array of non-specific, crossreactive sensors combined with an information processing system

Graphic adapted from: http://www.emsl.pnl.gov:2080/proj/neuron//papers/keller.wcnn96.html



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Pattern Analysis for Artificial-Nose Data

- Signal Preprocessing, e.g. compensation for sensor drift, vector normalization
- Dimensionality Reduction, using Principal Component Analysis (PCA), Fisher's Linear Discriminant Analysis (LDA), etc.
- Classification, e.g. artificial neural networks, parametric methods, partial least squares



Graphs from IBM Zurich Research Center Website

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Taxonomy of Nose-like Sensors



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The KAMINA: A Micro-Scale Tin-Oxide Artificial Nose



The KAMINA detects gases such as ammonia, benzene, carbon monoxide, and formaldehyde



Illustration from: Goschnick et al., "Condition Monitoring for Intelligent Household Appliances," Sensors in Household Applicances, Vol. 5, 2002



An Artificial Nose Using Carbon Black-Polymer Composites

- Sensing elements use carbon black as a conductive filler within a nonconductive organic polymer matrix
- When exposed to an odorant, a composite swells, resulting in a change in conduction
- The sensing properties can be changed easily by changing the carbon black/polymer composition
- Electronic noses using carbon black-polymer composites are in use for diagnosis of bacterial infections, and have been found to successfully detect lung cancer



Image of Cyranose 320 from SpaceDaily, 12 Mar 2002, wysywyg://387/http://www.spacedaily.com/news/future-02a.html



Example of A Silicon Olfactory System using ChemFETs



Graphic adapted from University of Leicester's website at http://www.le.ac.uk/eg/tcp1/avlsi/



A Micromechanical DNA Sensor



Differential deflection of the cantilevers upon ligand binding provides molecular recognition



Microfacricated Silicon Cantilevers

Each cantilever is 1 μ m thick, 500 μ m long, 100 μ m wide, with a pitch of 250 μ m, and spring constant of 0.02 N m⁻¹

Graphics adapted from: J. Fritz et. al., Science Vol. 288, 14 April 2000, pp. 316-318



Artificial Noses Based on High-Density Optical Arrays

- Thousands of microsphere sensors are dispersed across the face of an etched optical imaging fiber
- Interaction of odorant with fluorescent dyes yields a frequency shift in the returned signal
- Each bead is independently addressable through its own light channel
- Fiberoptic artificial noses have been demonstrated to detect land-mines



Graphic adapted from: M. Meusel, of Institut für Chemo- und Biosensorik, presented at Münster Biosensor Symposium Tübingen 2001



A Smart-Chip Chemical Microsensor



Diagram of the Microsystem Architecture

- Incorporates three different transducers, each with sensitive polymeric layers:
 - Mass-sensitive
 - Capacitive
 - Calorimetric
- On-chip control and monitoring of the sensor functions
- Commercial CMOS fab process: chip is 7x7 mm

For truly nose-like sensing, we must integrate nanometer-scale sensors into systems!

Graphic from: O. Brand, H. Baltes, et al., of ETH Zürich, "Smart single-chip gas sensor microsystem," Nature, 15 November 2001



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Selected R&D on Individual Nanosensors

| Туре | Description | Researcher/Institute |
|--------------------|---|--|
| Carbon Nanotube | Semiconducting-SWNT sense NH_3 , NO_2 and H_2 by undergoing a conductance change | Hongjie Dai et al., Stanford University |
| Carbon Nanotube | SWNT show high sensitivity to oxygen or air, changing their electrical properties | A. Zettl et al., UC Berkeley |
| Nanowire | Silicon nanowires in solution sense streptavidin, biotin, etc. with conductance changes | Charles Lieber et al., Harvard University |
| Nanowire | <i>Tin oxide nanowires sense O₂ and CO with conductance changes</i> | Martin Moskovits et al., UC Santa Barbara |
| Nanobelt | Tin oxide nanobelts sense CO, NO ₂ with a change in conductance | Wang/Georgia Tech Sberveglieri/Brescia, Italy |
| Nanobead | 'Almost' nanometer-scale sensing beads used in optical sensors | David Walt, et al., Tufts University |



Single-Walled Carbon Nanotubes (SWNT) as Gas Sensors



Illustration and Graphs from: Hongjie Dai et al., "Nanotube Molecular Wires as Chemical Sensors," Science, 28 Jan 2000



Electronic Properties of Carbon Nanotubes Are Sensitive to the Environment

- Zettl's group at UC Berkeley demonstrated that exposure to oxygen can cause changes in nanotube electrical resistance, thermoelectric power, and local density of states
 - Electrical resistance (R) changed by 10 to 15%
 - Thermoelectric power,
 S= μV/°K, changes both in sign and magnitude
- The electrical properties of carbon nanotubes depend not only on diameter and chirality, but also on their gas exposure history



Graphs from A. Zettl et al., Science, 287, 10 March 2000



Silicon Nanowires (NW) as Chem/Bio Sensors in Solution



Illustration and Graphs from: C. Lieber et al., "Nanowire Nansosensors for Highly Sensitive and Selective Detection of Biological and Chemical Species," Science, 17 Aug 2001



Tin Oxide (SnO₂) Nanowire Gas Sensors

Moskovits' group at UC Santa Barbara tested 60 nm diameter SnO₂ nanowires, at 250° C, as sensors for CO and O₂



Illustrations from M. Moskovits et al., "Detection of CO and O2 Using Tin Oxide Nanowire Sensors," Advanced Materials, 17 June 2003

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Semiconducting Oxide Nanobelts as Gas Sensors



Semiconducting Oxide Nanobelts

- (A) As-synthesized ZnO nanobelts
- (B) A twisted ZnO nanobelt
- (C) Rect. cross-section of broken SnO₂ nanobelt
- (D) Clean & structurally perfect surface of ZnO nanobelt

Wang at Georgia Tech and Sberveglieri at U. Brescia, Italy, demonstrated that single-crystalline SnO_2 nanobelts undergo a change in conductance in the presence of CO, NO_2 , and ethanol

Illustrations from Z. Wang et al., Science, 291, 9 March 2001



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Towards Nanometer-Scale Sensing Beads

- Sensing beads, about 300nm in diameter, are deposited in microwells on the surface of optical fibers
- Binding of a target agent produces a shift in wavelength of returned light
- These sensing systems, developed at Tufts Univ., detect nitroaromatic compounds similar to low-level explosives

2001 Sensitivity Test for TNT

Dog: 1 part per billion (ppb)

Tufts Optical Nose: 10 – 15 ppb

Sensing Beads in Wells



Average Fluorescence Change vs. Time for a set of eighteen sensors



Illustration and Graph from: http://ase.tufts.edu/chemistry/walt/research/projects/Add_apps.htm



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Nose-Like Nanosensing: Where Are We Now?

- Micron-scale sensing elements have been developed and incorporated into small artificial noses
- Nanometer-scale devices demonstrated to function as gas sensors

... However, at this time, no nose-like sensing systems integrated on the nanometer-scale have been developed

- Some of the Challenges Remaining:
 - Complete characterization of sensing behavior of nano-scale devices
 - Precise placement versus random distribution of nanosensors?
 - Nanosensor system/microprocessor integration
 - Useful Next Steps: Development and Integration of
 - Small number of differentially sensitized nanosensors
 - Microprocessor/processing algorithm

into operational nose-like nanometer-scale sensing system

Elements of Nanotechnology for Enabling Novel Sensor Systems



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Building upon Nanomemory Systems for Nose-Like Sensing



- This cross-bar array of nanowires is a nano-sensing system: each junction of 2 crossed nanowires forms a memory bit
- The junctions of the nanowires are decorated with binding agents
- Binding of a target agent at a memory location causes the memory bit to change from "0" to "1"
- The set of memory bits reporting a change in status provide an identifier for the target agent



A Proposal for a Nose-like Nanowire Sensing System

- Core of sensing element is SnO₂ nanowire, as demonstrated by Moskovits*
- Modify by coating the wires with a layer of SiO₂
- As demonstrated by Goschnick**, differential thicknesses of SiO₂ coatings over SnO₂ cause differences in conductivity patterns
- A system of such nanowires, combined with a heating element, should behave as an electronic "nano-nose"



*Moskovits et al., Advanced Materials, 17 June 2003 **Goschnick et al., IEEE Sensors Journal, June 2002



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Summary

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Summary of Study in Nose-Like NanoSensing

- Great advances have been made recently in understanding the olfactory system, our best model for chem-bio sensing
- Artificial noses with relatively small numbers of micron-scale sensors have been developed
- Achieving sensitivity, selectivity and reliability like that of the nose, however, will require systems with large numbers of individual sensing elements
- Only by integrating nanometer-scale sensing elements into sensing systems can we approach nose-like capabilities while maintaining very small form factors

Truly "nose-like" nanosensing systems will increase homeland security, provide personal protection for the soldier, and enhance national intelligence capabilities!



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Workshop on Nanosensors for Nose-Like Sensing

At MITRE McLean: 4 & 5 April 2006

By Invitation Only

Please contact me at brolfe@mitre.org if you wish to be invited



Thank you for your attention!

