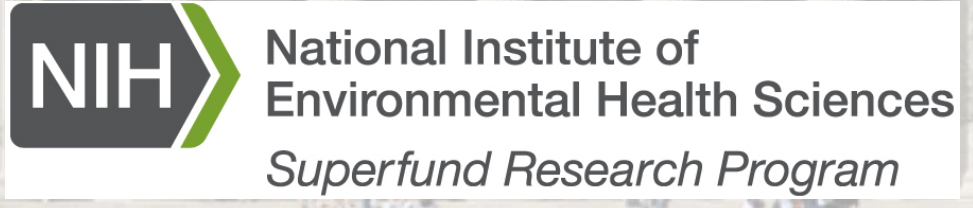
Overview of the MIT Superfund Research Program

Bevin P. Engelward, MIT SRP Program Director

Department of Biological Engineering

John Essigmann, Co-Program Director

Departments of Chemistry and Biological Engineering



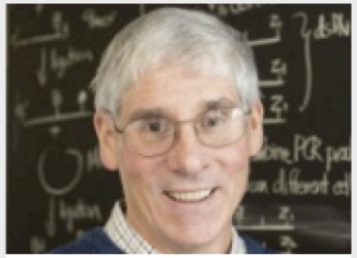
Faculty and Core Leaders

Robert Croy

Bioimaging and Chemical Analysis Facilities Core

Bevin Engelward

Biological Engineering



John Essigmann

Biological Engineering, Chemistry

Harold Hemond

Civil and Environmental Engineering

Jesse Kroll

Civil and Environmental Engineering, Chemical Engineering

Jennifer Kay

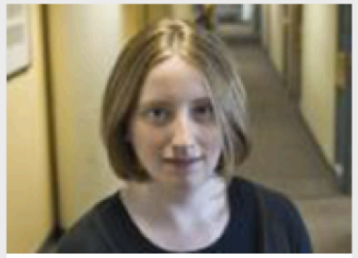
Biological Engineering

Douglas Lauffenburger

Biological Engineering, Chemical Engineering, Biology

Leona Samson

Biological Engineering, Biology



Noelle Selin

Department of Earth, Atmospheric and Planetary Sciences

Timothy Swager

Chemistry

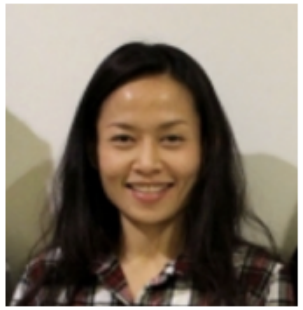
Forest White

Biological Engineering

Kathleen Vandiver

Community Outreach Education and Engagement Core

Trainees


Apple Chawanthayatham

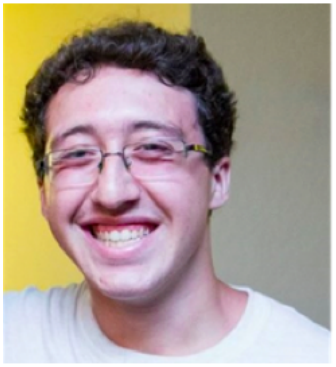

Amanda Armijo


Nora Owiti


Christy Chao


James Rowe


Ishwar Kohale


Josh Moss


Lennon Luo


Maggie He

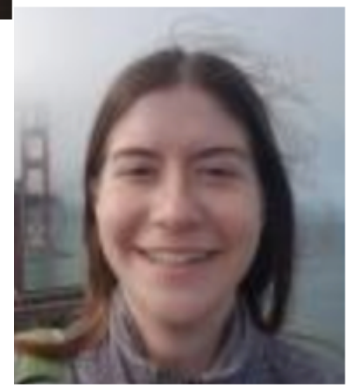

Jenny Kay


Christy Chao


Lizzie Ngo


Irene Hu


Josh Corrigan


Jessica Beard

Nitrosamines in the Mystic River Watershed

PAHs in Native American Territories in Maine

Overview of the Projects

Engagement and Translation Activities

Research Highlight: Tim Swager Projects 1 & 2

Nitrosamines in the Mystic River Watershed

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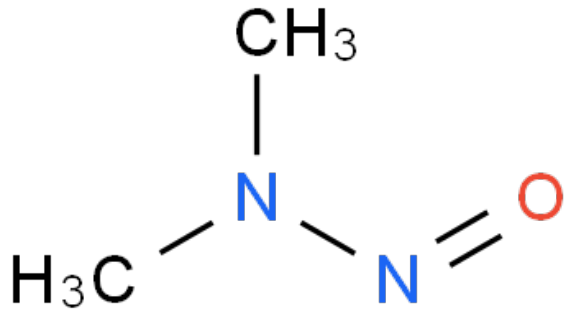
Mystic River Watershed Superfund Sites

Olin Chemical Superfund Site
Wilmington MA

Mystic River Watershed

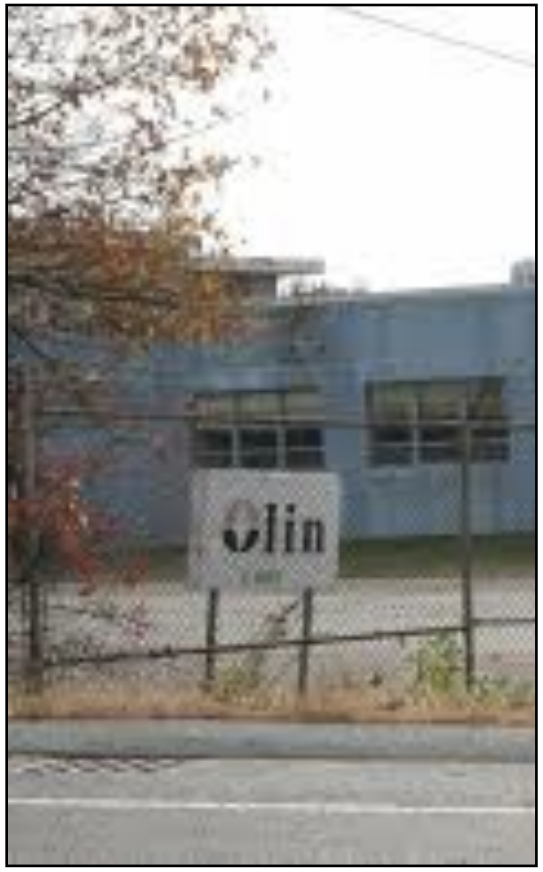
- 21 companies (tanneries, rubber, textiles, paper, insecticides)
- At Olin, from 1953 to 1970 wastes were discharged into lagoons, ponds
- As, Cu, Pb, Zn, Cd, PAHs, NDMA
- NDMA is a key contaminant at the Olin Chemical Superfund Site



N-nitrosodimethylamine (NDMA)
Carcinogenic in animal models

Mystic River Watershed

"They' ve discovered ammonia, chloride, sodium, and sulfate at the site. **But the most important—and the most toxic—is NDMA**"
-Town Crier

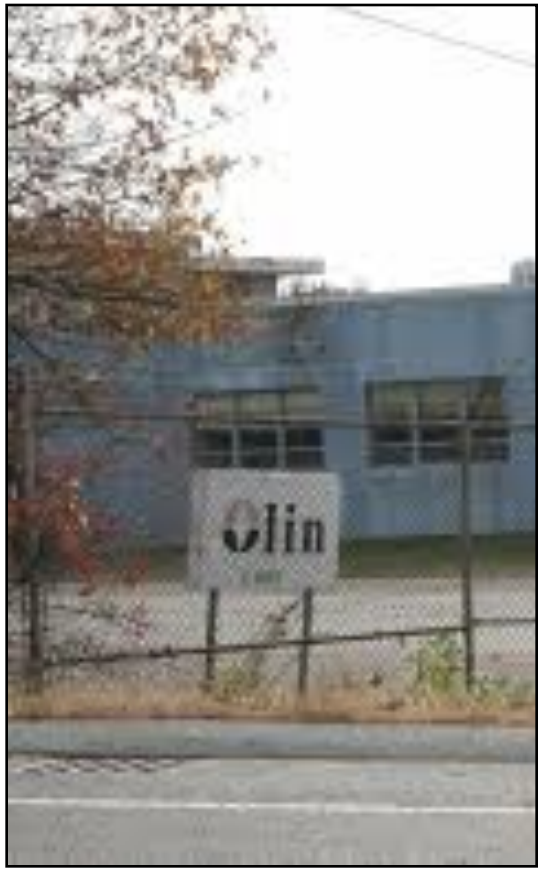


Ms. J. E., former Wilmington resident and cancer survivor:
"I managed to survive childhood cancer, but several others like me in Wilmington who were affected were not so fortunate."

Wilmington Residents ask 'Am I at risk?'

Mystic River Watershed

Malden and Everett are two Environmental Justice Communities



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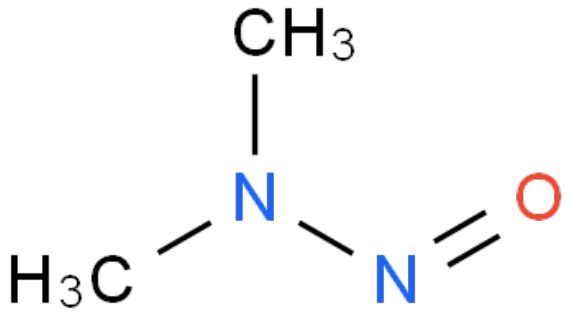
Wilmington Residents ask 'Am I at risk?'

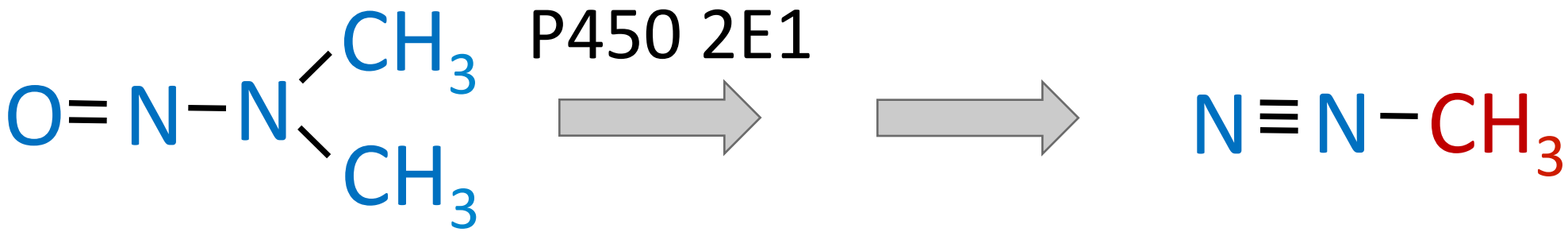
N-Nitrosodimethylamine (NDMA) is Carcinogenic in Animal Models

NDMA



Cancer

N-nitrosodimethylamine (NDMA)

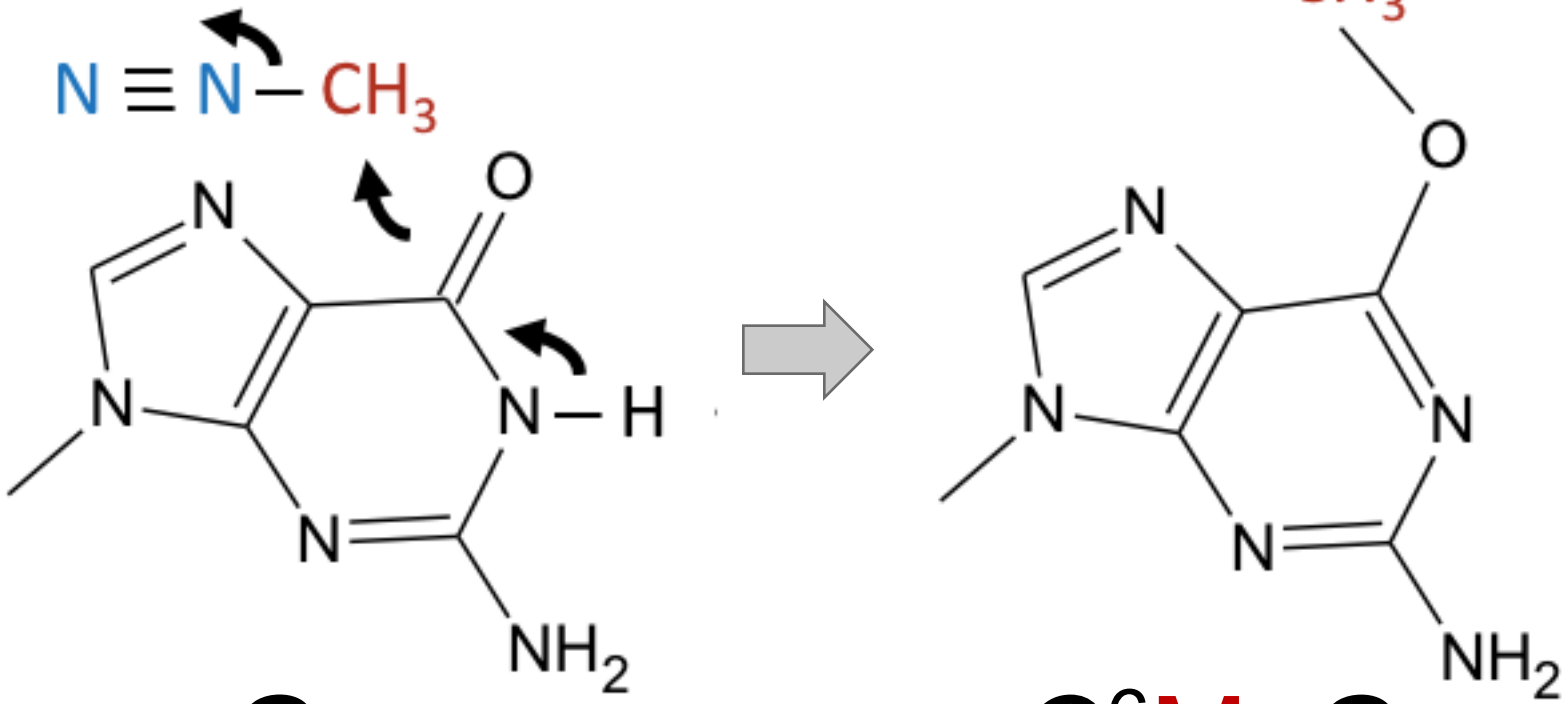


Methyl-diazonium Ion

Adds Methyl Groups to DNA

A methyl lesion matters because…
Structure is Genetic Information.

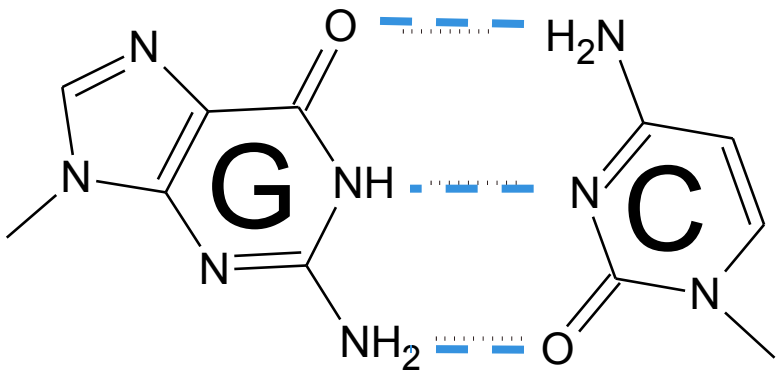
Methyl-diazonium Ion



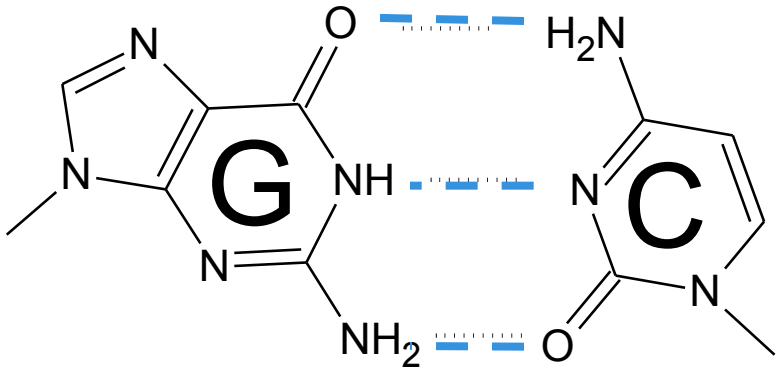
G

O^{6}MeG

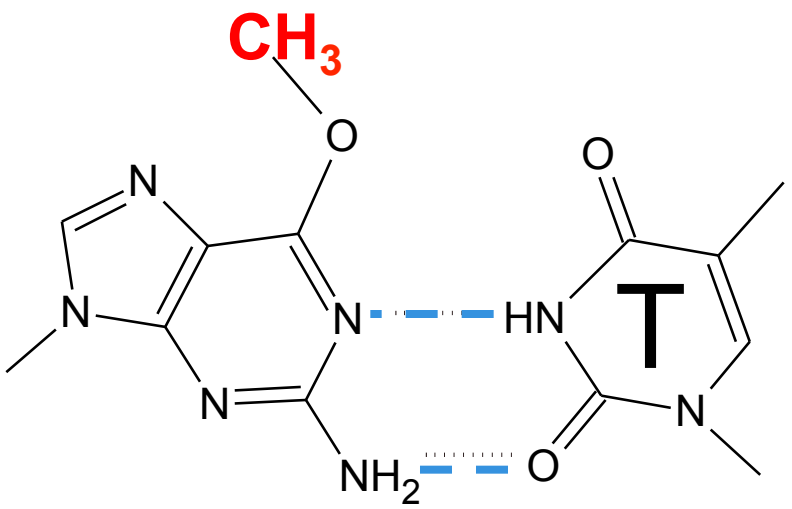
A methyl lesion matters because…
Structure is Genetic Information.



A methyl lesion matters because…
Structure is Genetic Information.

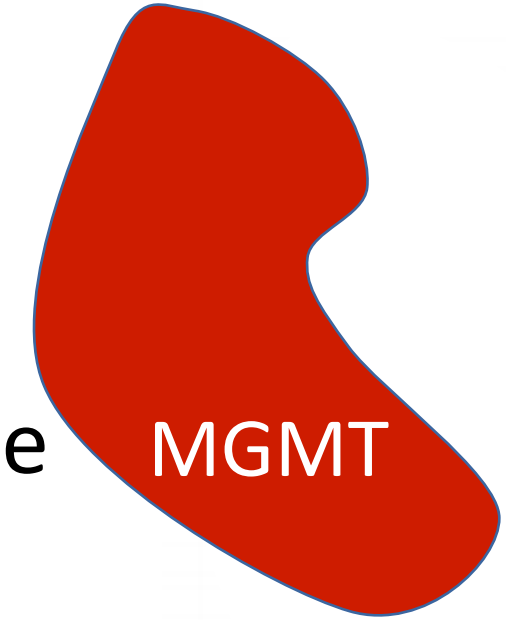


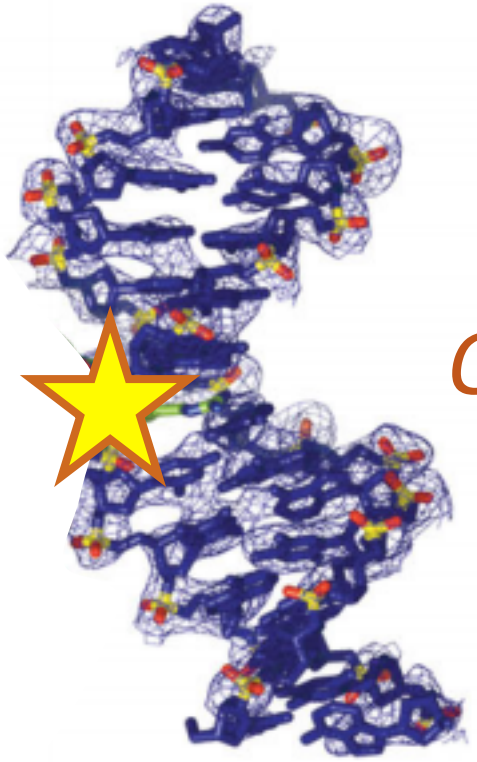
O^6MeG



O^6MeG is Mutagenic: GC to AT

Human
O^6-Methylguanine
DNA Methyltransferase
(MGMT)



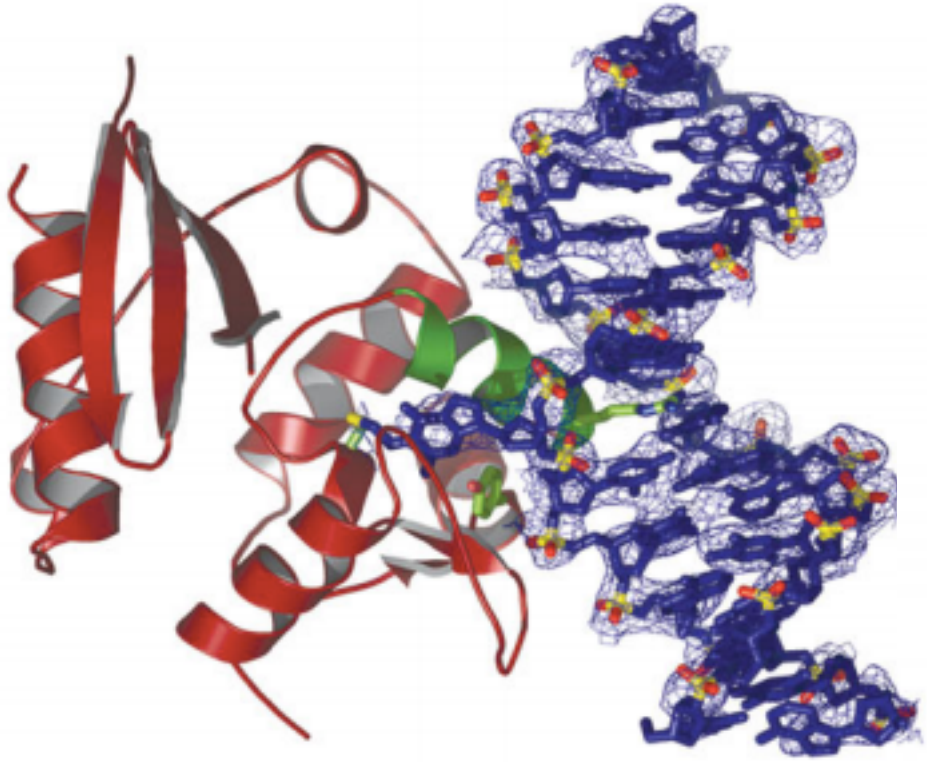


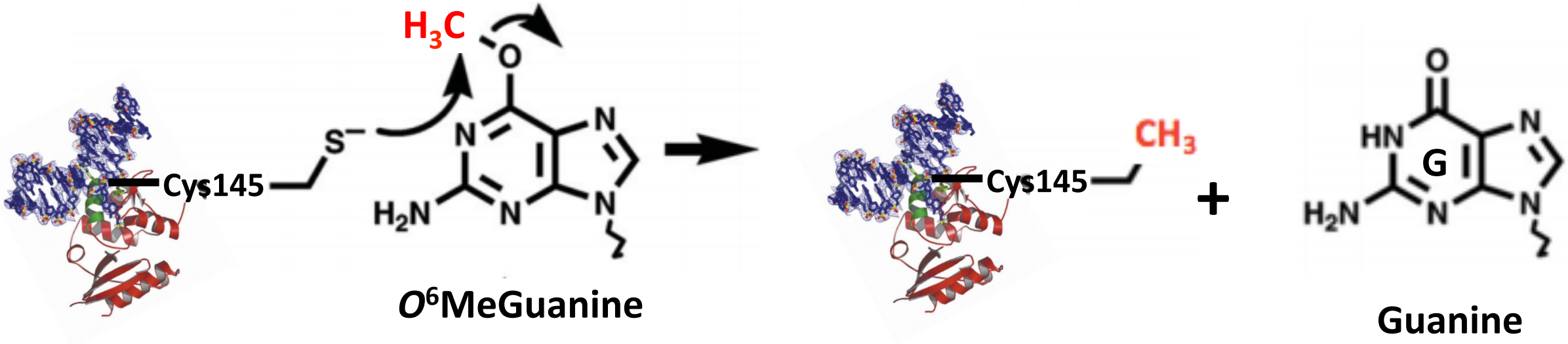
O^6MeG

O^6MeG can be Repaired by MGMT

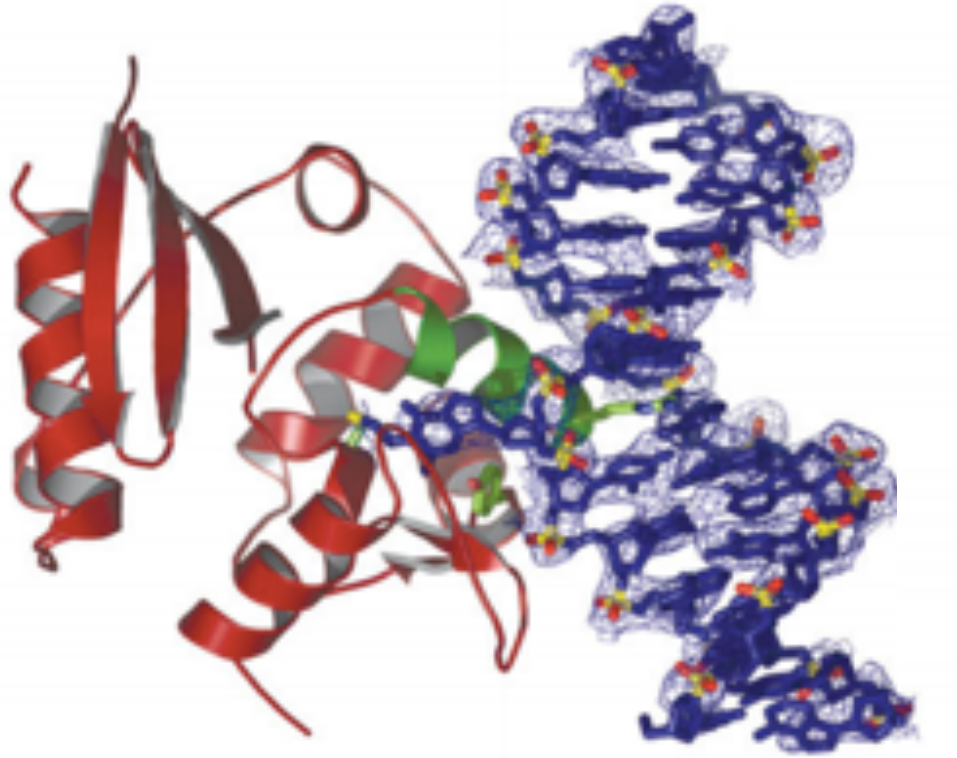
Structure: Daniels…Tainer

Human
O^6-Methylguanine
DNA Methyltransferase
(MGMT)



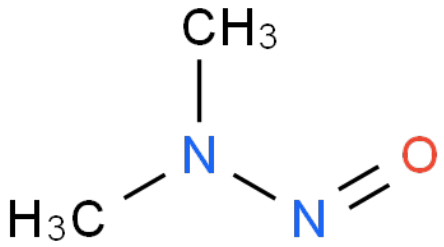


Human
O^6-Methylguanine
DNA Methyltransferase
(MGMT)



Mgmt-/-

NDMA



Sensing & Spatiotemporal Dynamics in the Environment

Cancer
Mutation Spectra
Gene-Env. Interactions
Systems Level Responses

Nitrosamines in the Mystic River Watershed

PAHs in Native American Territories in Maine

Overview of the Projects

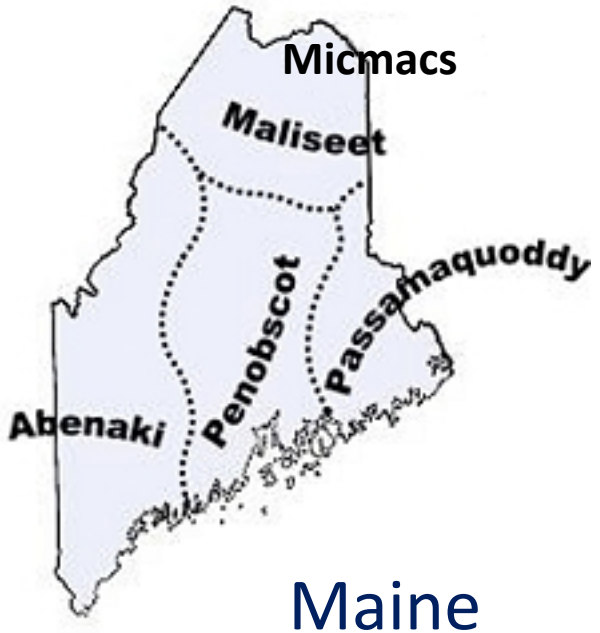
Engagement and Translation Activities

Research Highlight: Tim Swager Projects 1 & 2

One of the groups the MIT SRP aims to serve is the Micmac Tribe

Micmac

The Micmac tribe focuses on conservation of traditional culture.



Maine

Problem to Address: There are Environmental Carcinogens on Micmac Land

The Micmac Tribe acquired the former Loring Air Force Base Superfund Site.

Micmac lands are contaminated with industrial chemicals, including known carcinogens.

Berries and roots may also be contaminated.

The Micmacs have been told by the PRP that they cannot safely use their parts of their land for homes and for natural resources.

The MIT Team is working to help to prevent exposure to carcinogens.

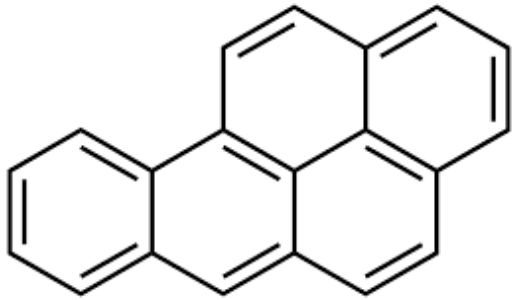
Former Loring Air Force Base Superfund Site: Given to the Micmacs

Landfills: hazardous waste disposal from 1956-1990s.

Contaminants include Polycyclic aromatic hydrocarbons (PAHs)

1,200 people obtain drinking water from wells located within 3 miles of hazardous substances on the base

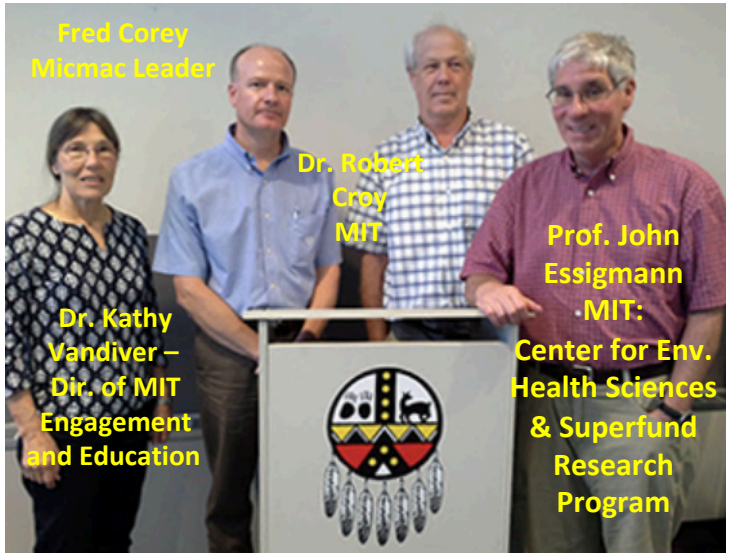
PAHs: Group 1 Carcinogens



Prior to the MIT SRP, CEHS Engaged with the Micmac Tribe

MIT has a long-standing relationship with the Micmac Tribe in Northern Maine.

Prof. John Essigmann and Dr. Kathy Vandiver have been leading the efforts in Maine, with support from Drs. Croy, Selin and others.



MIT Team meets with Director of the Micmac Environment Lab

EPA-Tribal Leaders Summit and Environmental Conference

Prof. Noelle Selin (MIT)

Micmac event at the Summit

Dr. Kathy Vandiver (MIT) and Marvin Cling (Passamaquoddy)

We aim to leverage Research to support the Micmacs

SRP

Superfund.MIT.edu

Through engagement, we have learned about the concerns of the Micmacs.

We have also learned about the perspective of the primary responsible party, the Air Force.

Our goal now is to address the concerns of the Micmacs regarding known contaminants on their land.

Our research is aimed at learning more about contamination, and using what we learn to guide decision making on safe ways to use the land and possible additional clean up efforts.

We will also support the Micmacs through Engagement and Education

SRP

MIT

Superfund.MIT.edu

MIT CEHS

First, we aim to help to bridge the Micmacs with stakeholders who can help.

Second, we aim to provide technical support.

Third, we will continue to provide educational support.

Nitrosamines in the Mystic River Watershed

PAHs in Native American Territories in Maine

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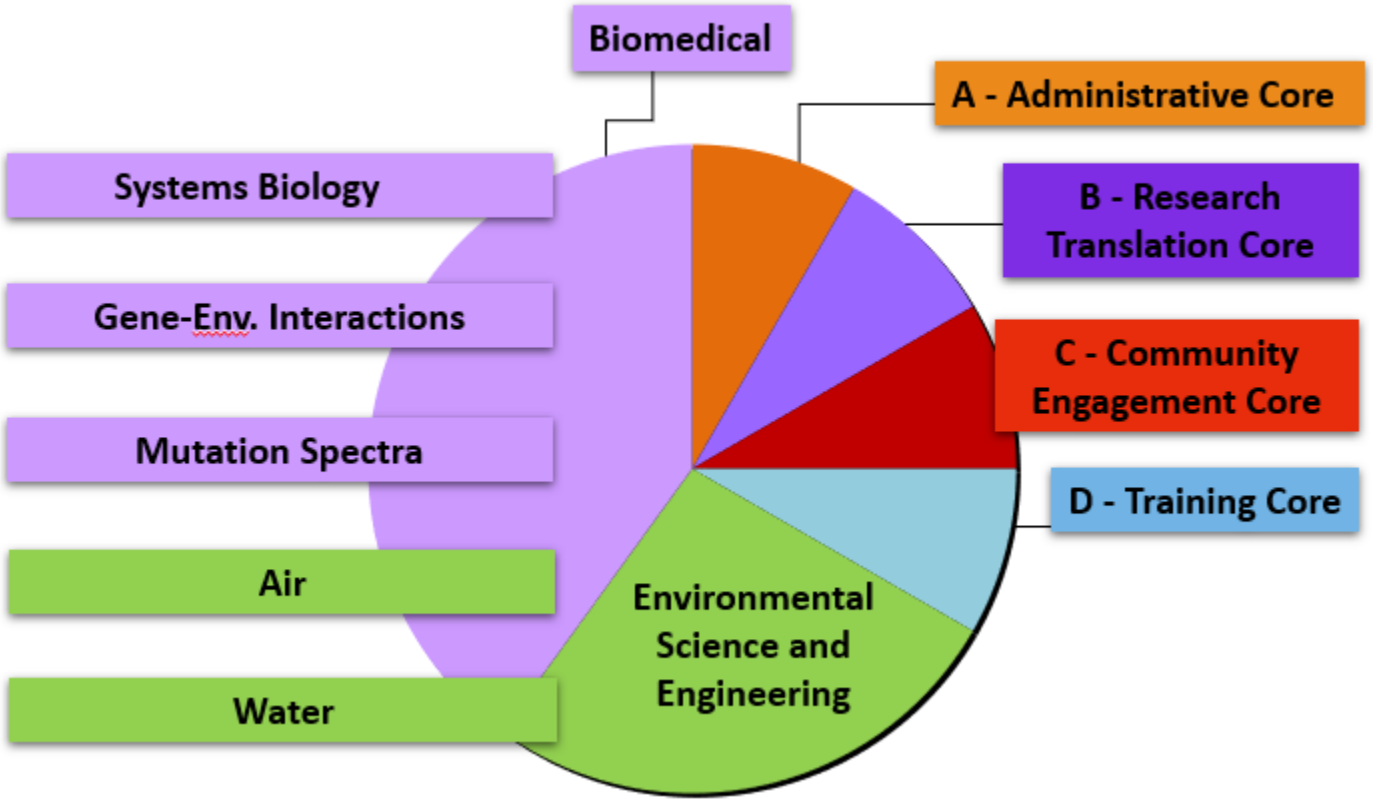
Research Highlight: Tim Swager Projects 1 & 2

MIT P42 Multi-Project Center

All Components Interacting, Addressing Problems



Project 1: Water (Hemond & Swager)

Need to know identity, concentrations, locations, and dynamics of contaminants

Rapid, cost effective portable sensor technologies

Guide environmental remediation

Irene Hu
Deployable Sensor for Sediment Flux

Additional Project 1 Members: Kyle Delwiche, Abigail Harvey, Tchelet Segev, Maggie He, Jessica Beard, Lennon Luo

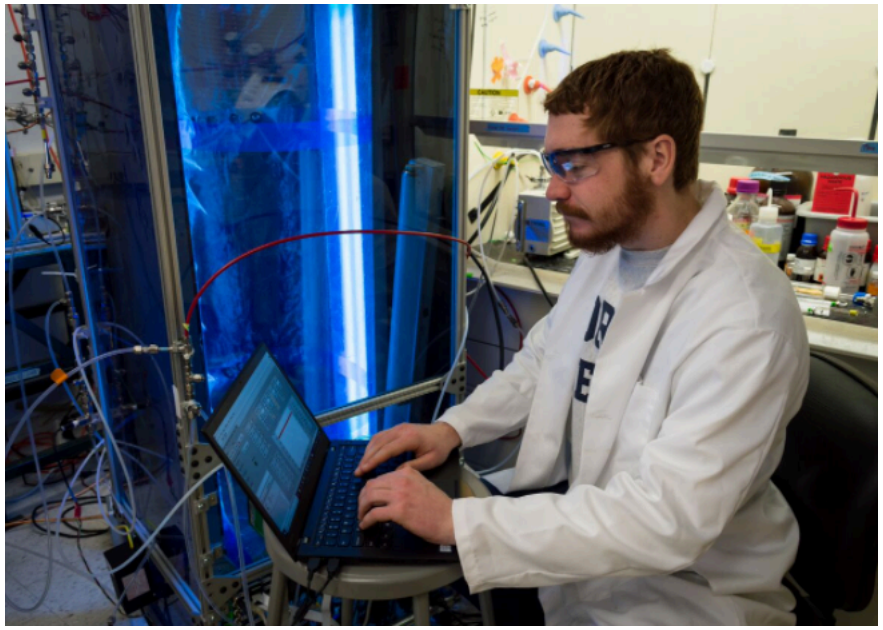
Project 2: Air (Selin, Kroll & Swager)

Sensors

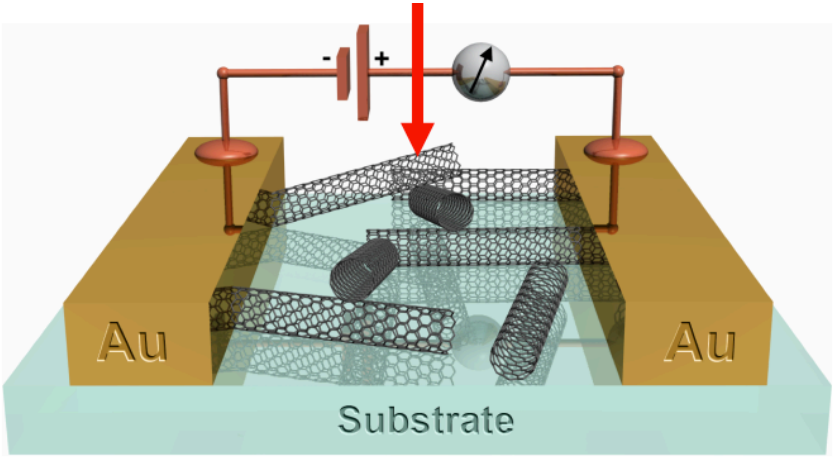
Modeling the spatiotemporal dynamics of air contaminants

Second generation breakdown products

Guide environmental remediation



James Rowe, Laboratory of Jesse Kroll



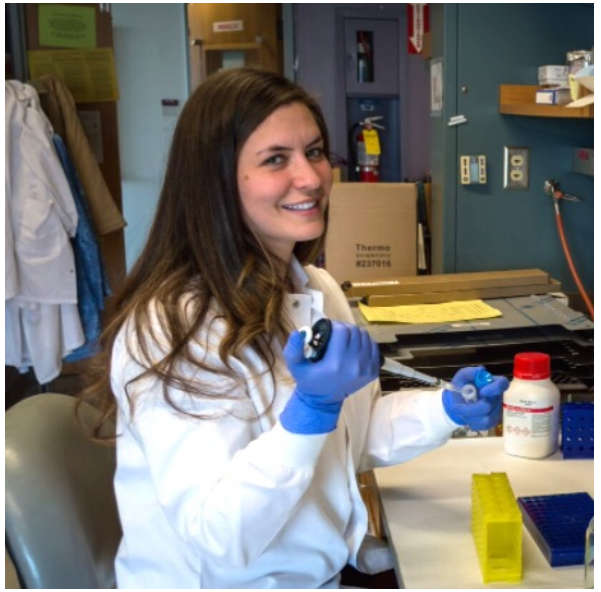
Additional Project 1 Members: Josh Moss, Helene Angot, Nick Hoffman, Maggie He, Jessica Beard, Lennon Luo

Project 3: Mutational Spectra (Essigmann and Croy)

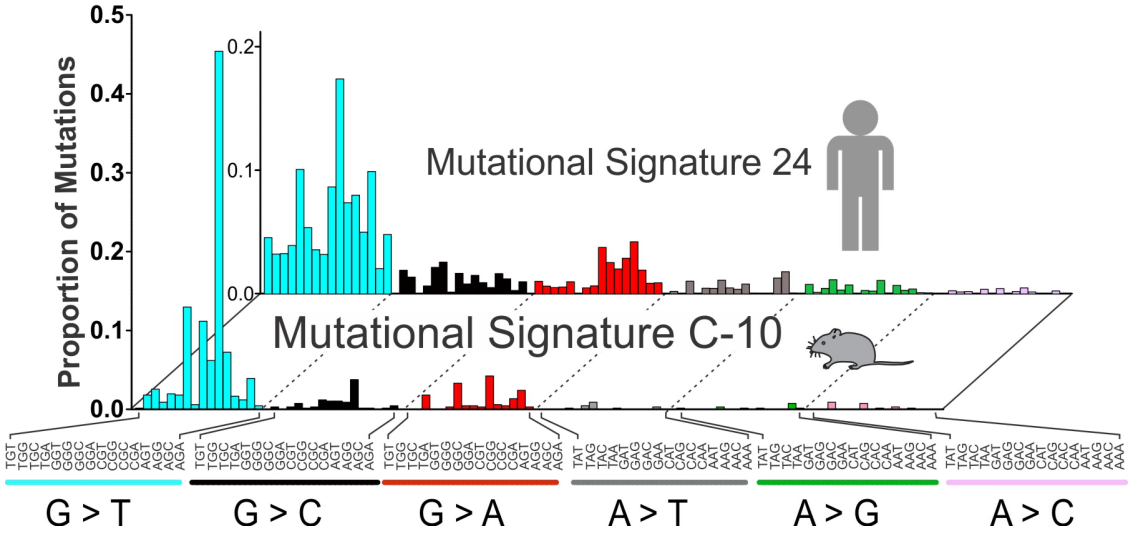
Define distinctive mutational patterns

Signatures of specific exposures

Deduce exposures that cause disease



Amanda Armijo, Laboratory of J. Essigmann



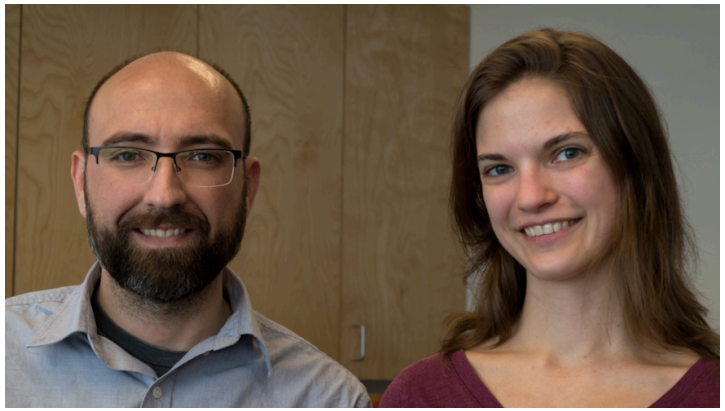
Additional Project 3 Member: Pennapa Thongararam

Project 4: Gene-Environment Interactions (Engelward and Samson)

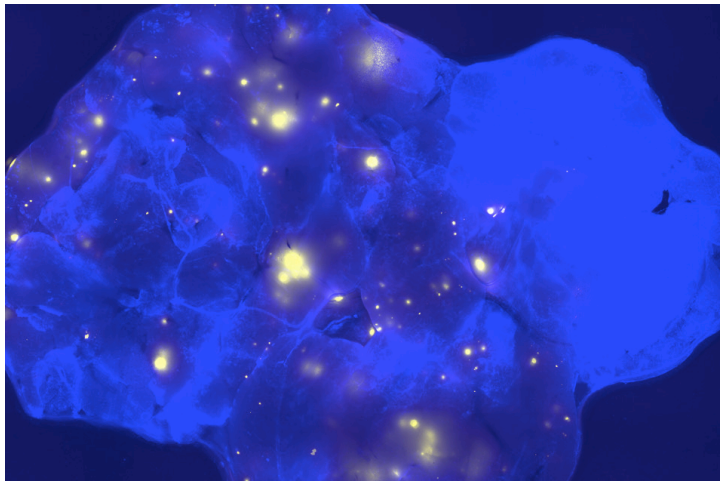
Studying repair of NDMA-induced DNA damage

Gene-environment interactions predict disease susceptibility

Identify susceptible individuals



Joshua Corrigan and Jennifer Kay



Additional Project 4 Members: Lizzie Ngo and Christy Chao

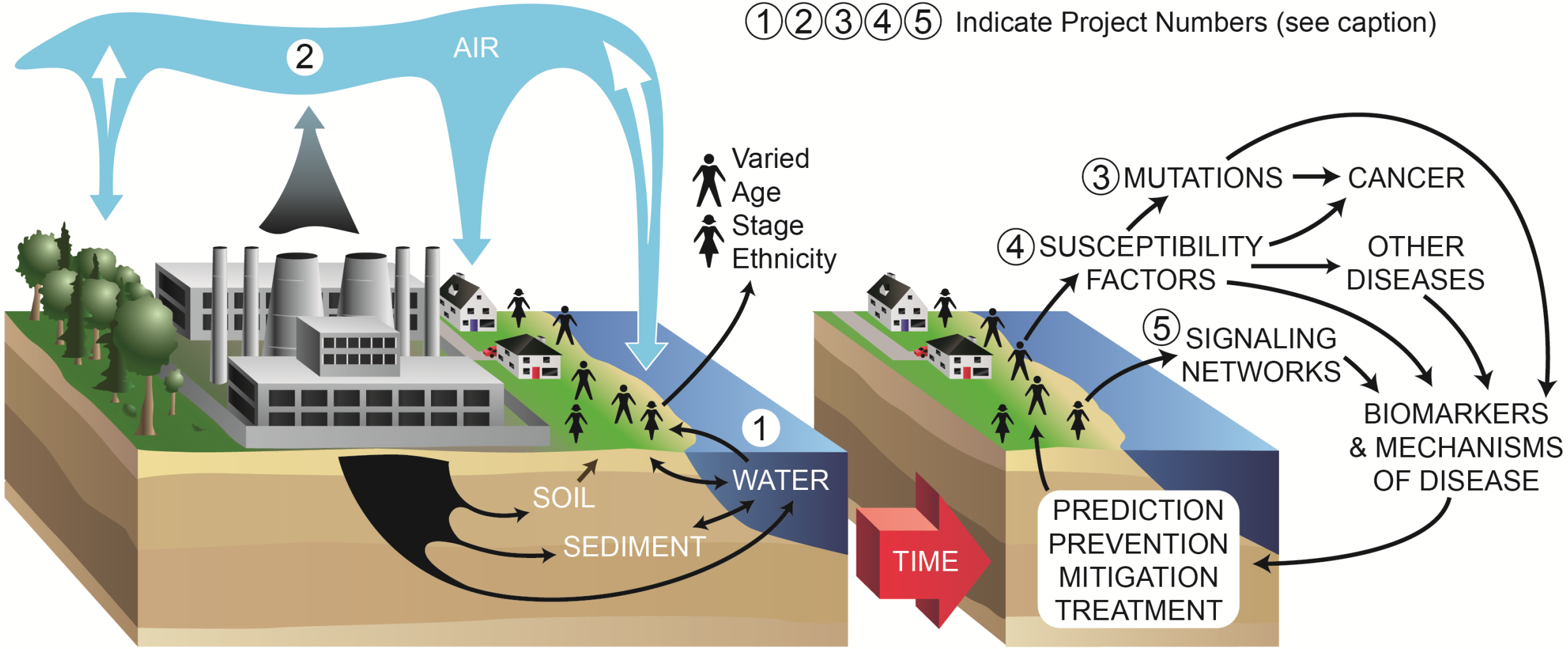
Project 5: Systems Level Responses (White and Lauffenburger)

Systems level responses: Gene Expression & Phosphoproteome

Elucidate mechanism of disease

Develop biomarkers of exposure

Ishwar Kohale, Laboratory of Forest White


①②③④⑤ Indicate Project Numbers (see caption)
2
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Varied
Age
Stage
Ethnicity
1
WATER
SOIL
SEDIMENT
TIME
③ MUTATIONS → CANCER
④ SUSCEPTIBILITY FACTORS
OTHER DISEASES
⑤ SIGNALING NETWORKS
BIOMARKERS & MECHANISMS OF DISEASE
PREDICTION
PREVENTION
MITIGATION
TREATMENT

Jeff Dixon

Nitrosamines in the Mystic River Watershed

PAHs in Native American Territories in Maine

Overview of the Projects

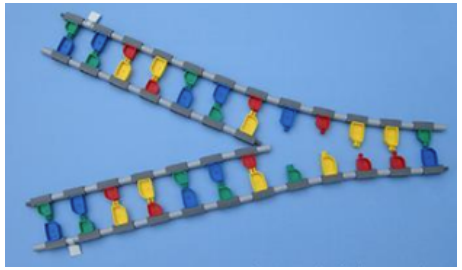
Engagement and Translation Activities

Research Highlight: Tim Swager Projects 1 & 2

Community Engagement & Research Translation Activities

Dr. Kathy Vandiver
CEC Director

Dr. Jennifer Kay
RTC Director



- Citizen Science
- Engagement through Education
- Letter-writing Campaign
- Blog
- Poster Session (April 10th)
- Newsletter (May 1st)

Community Engagement & Research Translation Activities

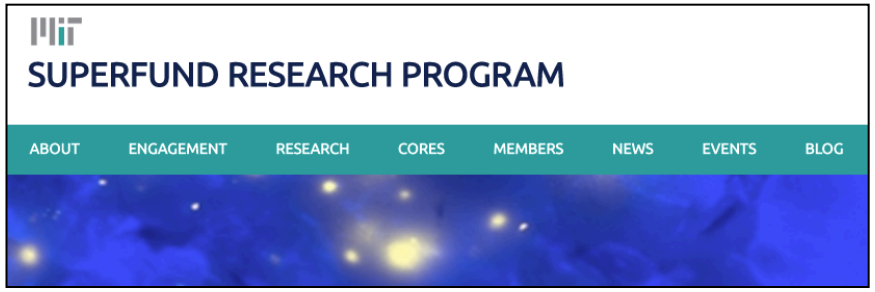
Abby Harvey

Tchelet Segev

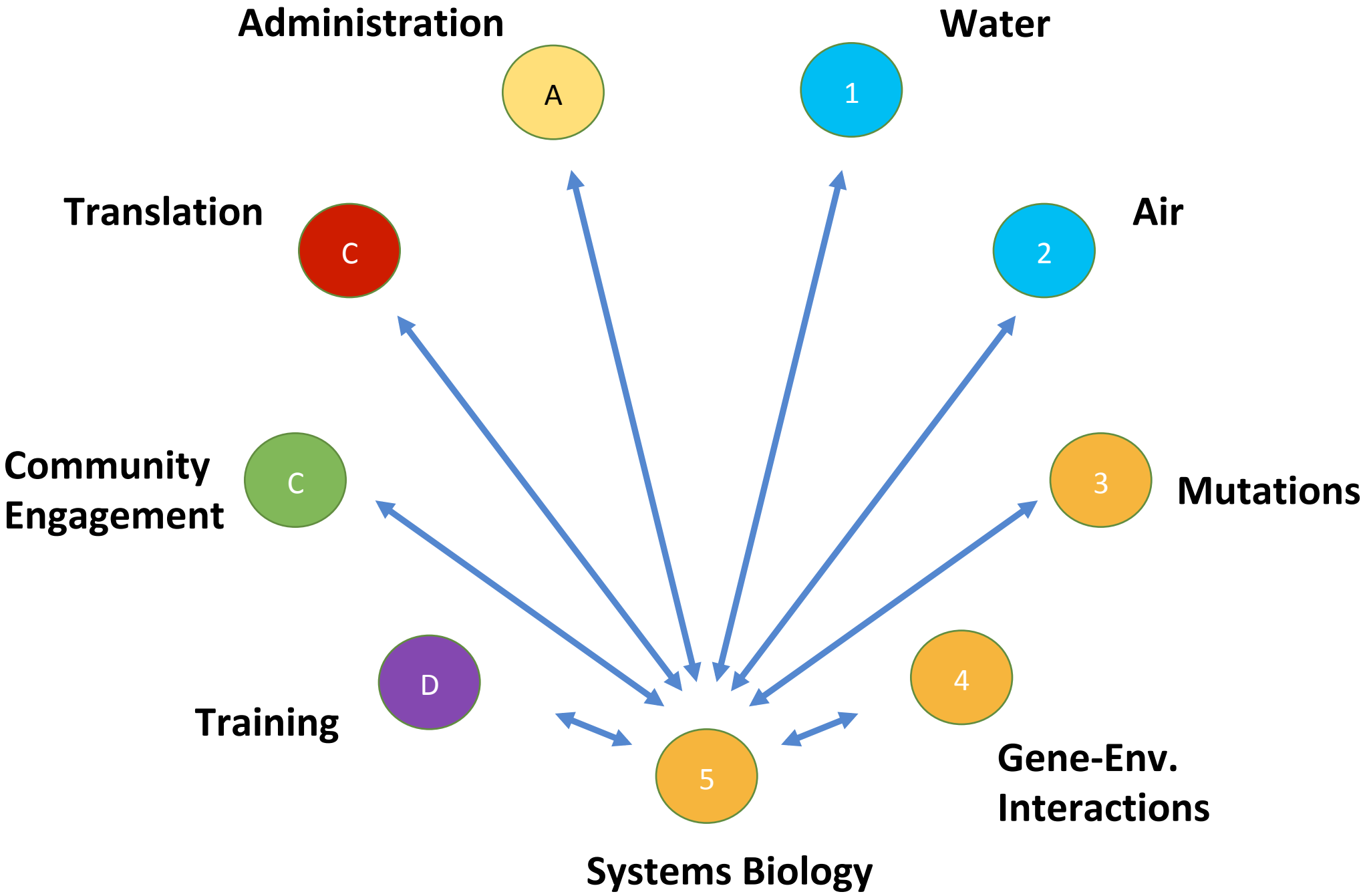
- Abby Harvey and Tchelet Segev; Advised by Harry Hemond, Kathy Vandiver, John Essigmann and Robert Croy
- Citizen science: Passamaquoddy Tribe. High levels of As in some tribe members' well water.
- Water sampling for NDMA contamination in Wilmington is underway!

Please visit and use our websites!

New **MIT Superfund Website** and **Blog**



Portal for Research Protocols


Administration
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Water
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Translation
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Air
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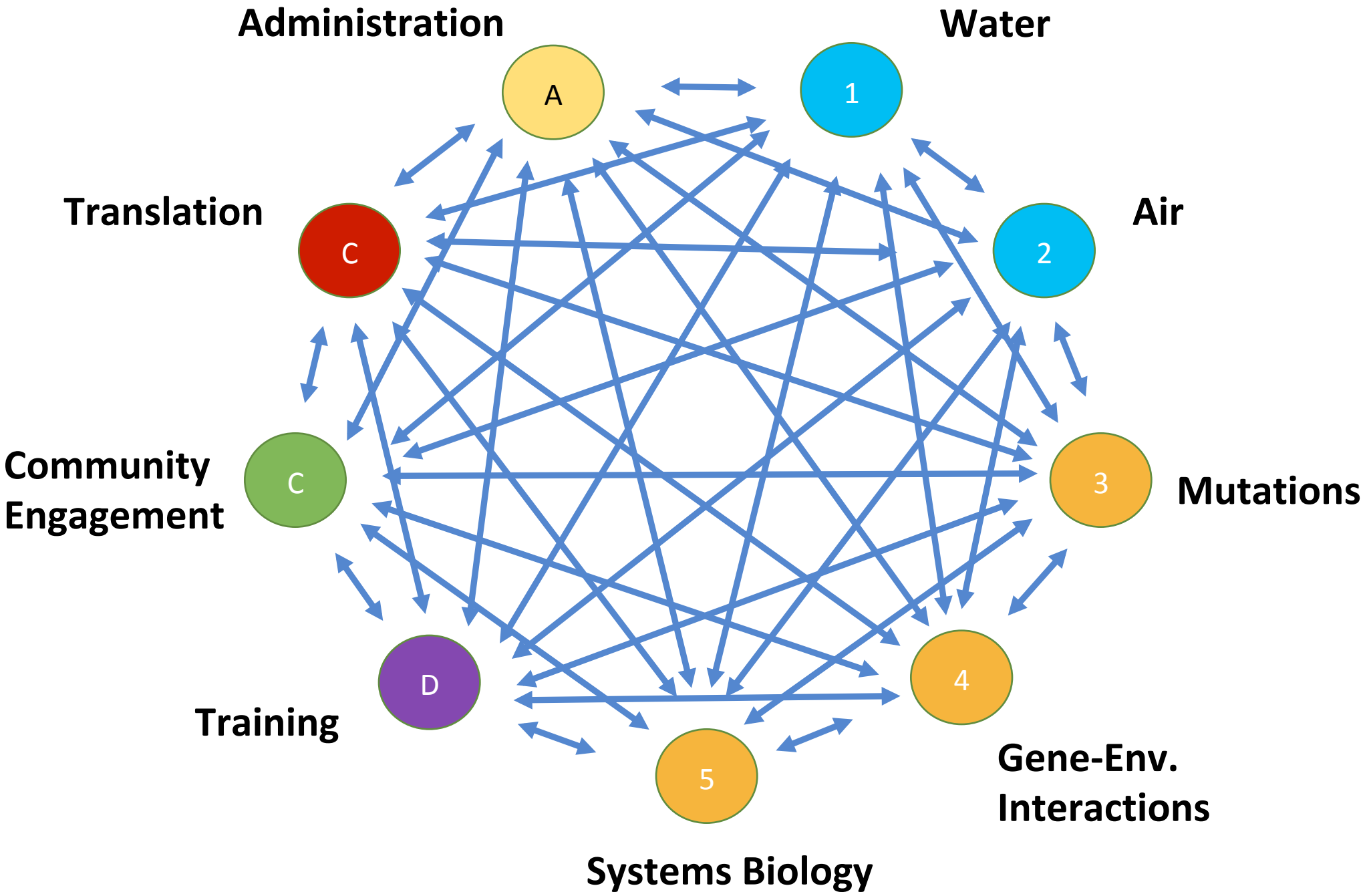
Community Engagement
C
3
Mutations
D
Training
4
5
Gene-Env. Interactions
Systems Biology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Overview of the Projects

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Research Highlight: Tim Swager Projects 1 & 2

Research Story: Dynamic Sensor Development for Spatiotemporal Resolution of Contaminants

Tim Swager

Maggie He

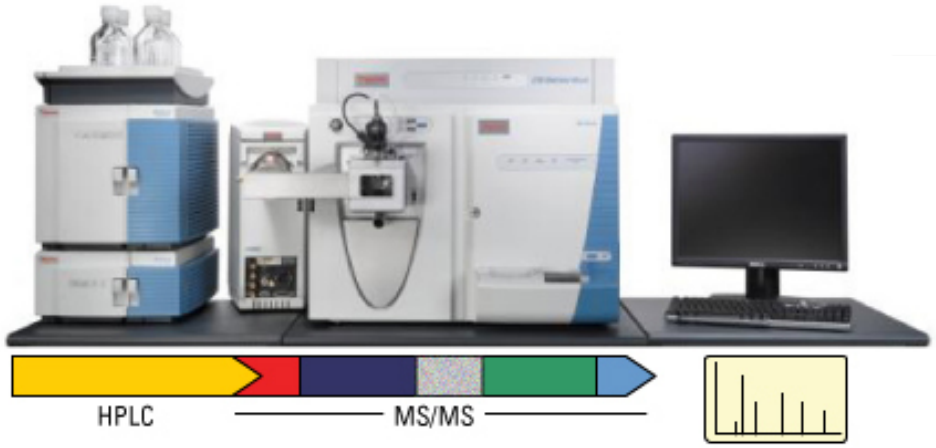
Lennon Luo

Jessica Beard

Current and Desired Detection Methods for NDMA

Current Detection Methods: Need to go to the lab

- Solid phase extraction
- Gas chromatography (GC)
- Liquid chromatography (LC)
- Usually coupled to mass spectrometry (GC-MS, LC-MS)
- Sophisticated instrumentation
- Expensive



Desired Methods for Detection: Portable real-time monitoring

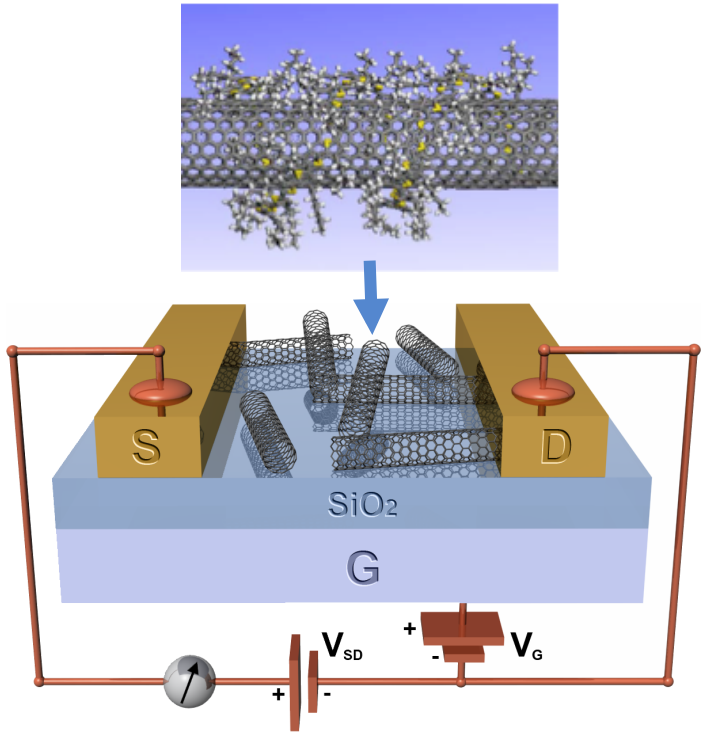
- Low-cost and portable sensors for in-field deployment and mapping of NDMA levels at various sites
- Real-time, continuous online monitoring of contamination levels

Environ. Sci. Technol. **2016**, *50*, 313−320.

Carbon Nanotube Chemiresistors Require High Sensitivity and Selectivity

Intrinsic Advantages of Chemiresistors

- Very Low Power
- Small Footprint
- Wireless Network
- Low Cost



Technical Needs

- High Sensitivity
- **Selectivity**
- No Calibration

Enabling Technology for Creating Large Inexpensive Chemical Sensor Arrays/Networks

Chemical Sense for the Digital World: Internet of “Things”

Food

Home

Industry

Environment

Microphones

Cameras

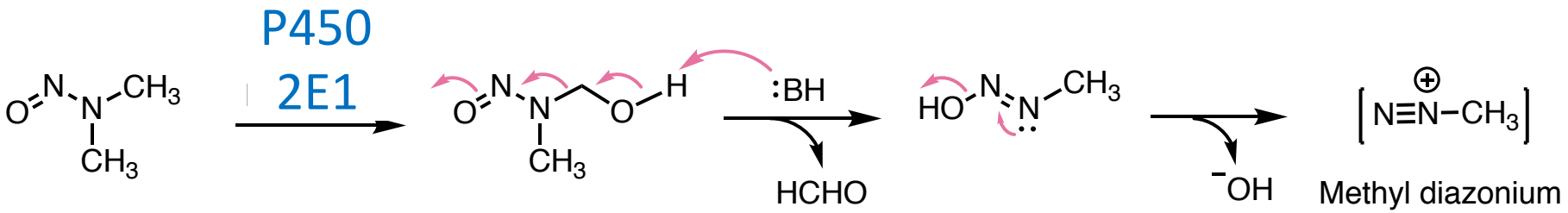
Gas Sensors: Sense of Smell for the Digital World

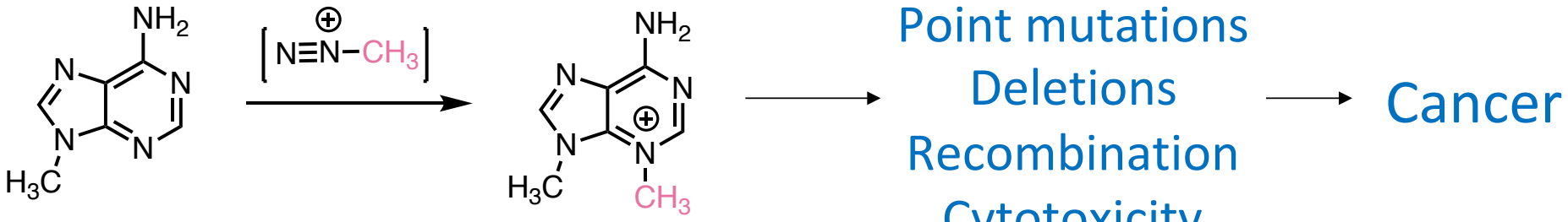
Physical Sensors

Smart Phone Apps
Cloud Services
Big Data
Internet of Things

NDMA and Metalloprophyrins

Nitrosamines require metabolic activation by the heme-containing enzyme cytochrome P450 2E1 in the liver in order to exert their carcinogenic effects



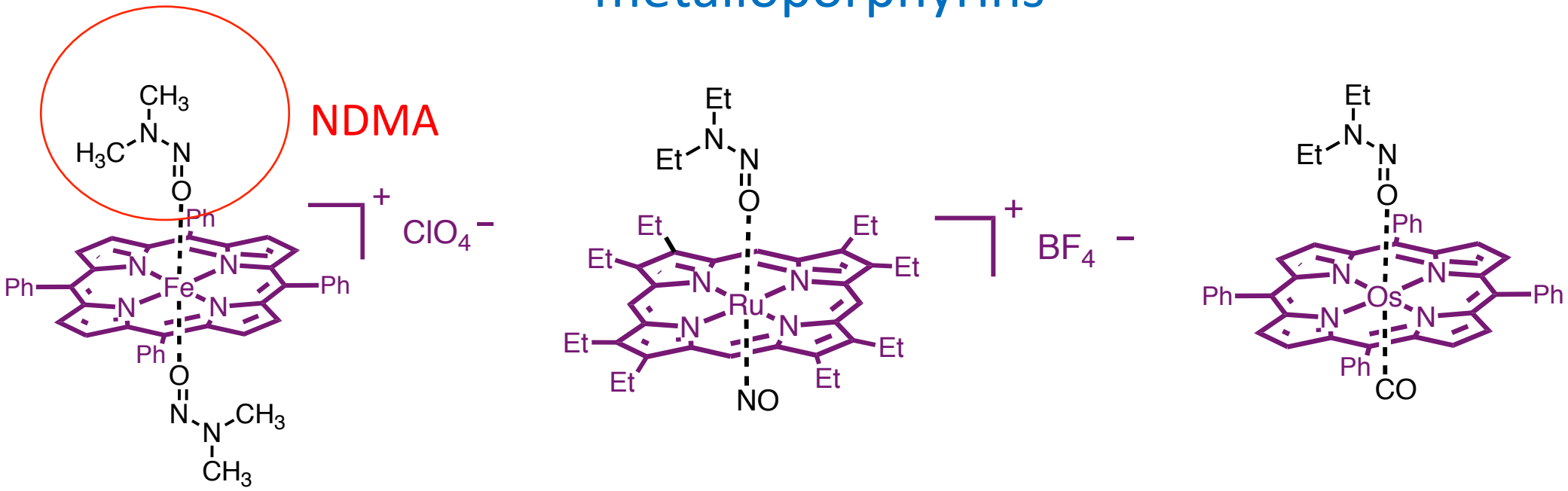


Point mutations
Deletions
Recombination
Cytotoxicity

→ Cancer

NDMA and Metalloprophyrins

N-nitrosodialkylamines form stable complexes with metalloporphyrins

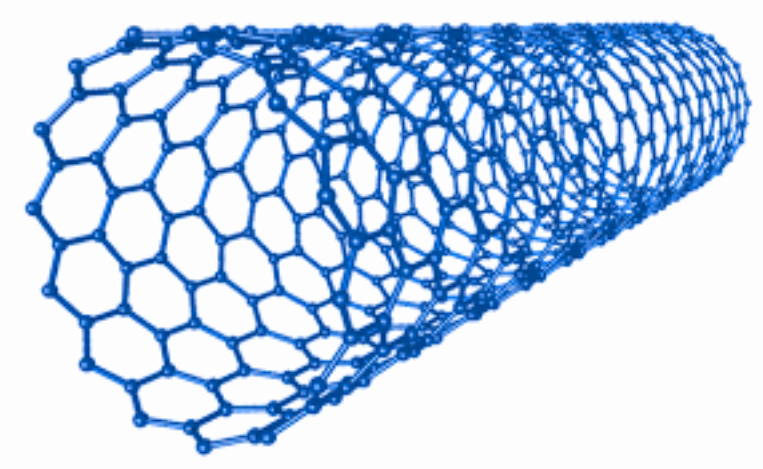


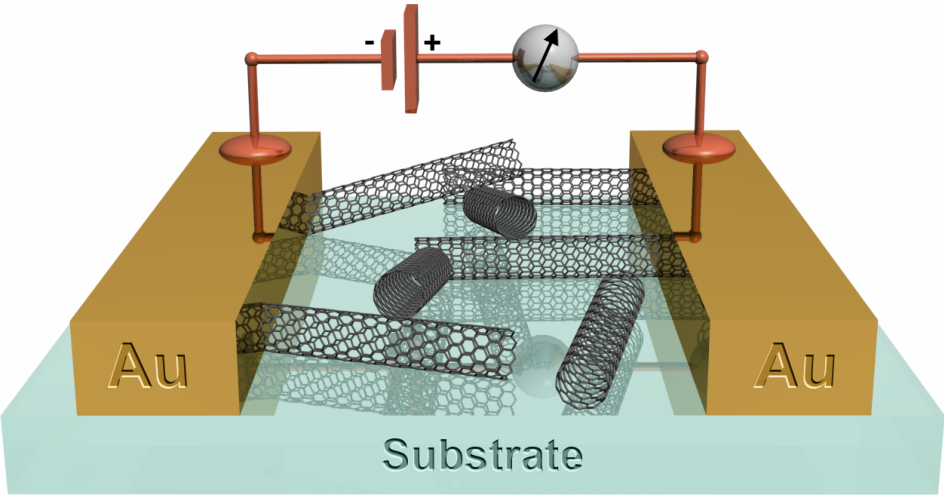
Yamazaki, H.; Inui, Y.; Yun, C.-H.; Guengerich, F P.; Shimada, T. *Carcinogenesis* **1992**, *13*, 1789–1794.

Chen, L.; Yi, G. B.; Wang, L. S.; Dharmawardana, U. R.; Dart, A. C.; Khan, M. A.; Richter-Addo, G. B. *Inorg. Chem.* **1998**, *37*, 4677–4688.

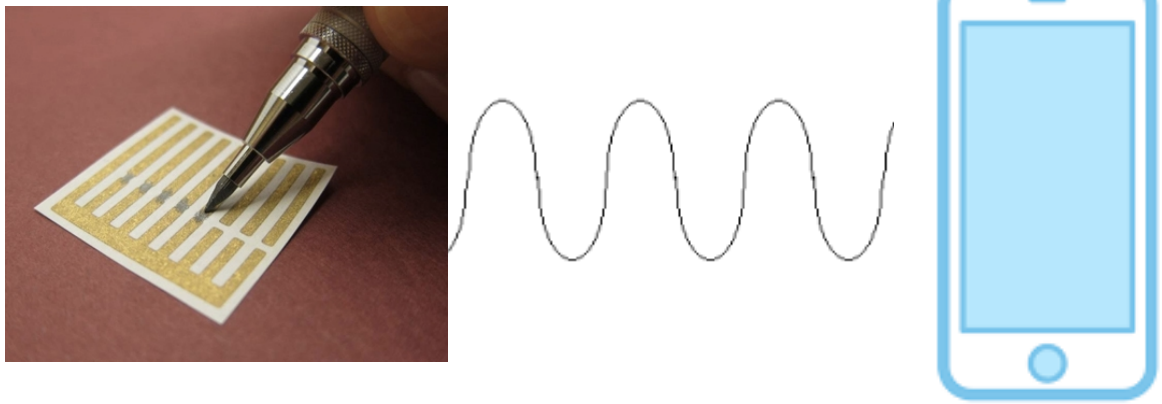
Stefan, M. I.; Bolton, J. R. *Helv. Chim. Acta* **2002**, *85*, 1416–1426.

Sensor Fabrication





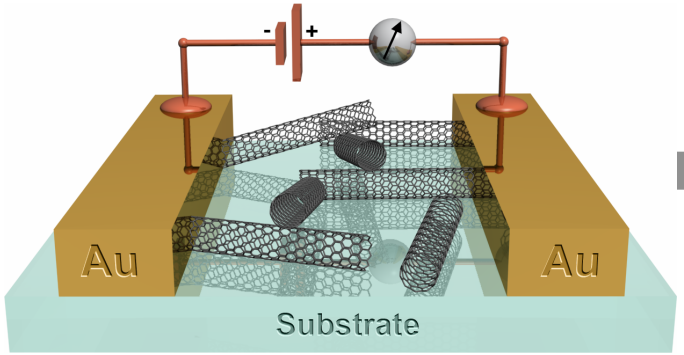
Sensor Fabrication and Response

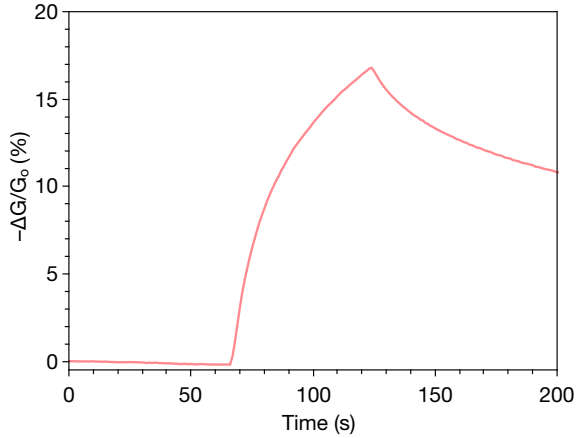


Goal: To create dynamic sensors to communicate with smart phones to convey level of contamination, location and time.

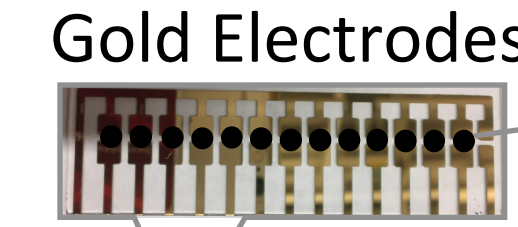
Sensor Fabrication and Gas Sensing

Sensor Fabrication and Response





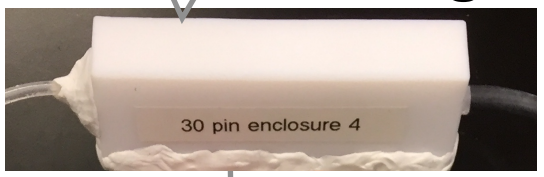
Sensing Apparatus



Gold Electrodes

Sensing Material

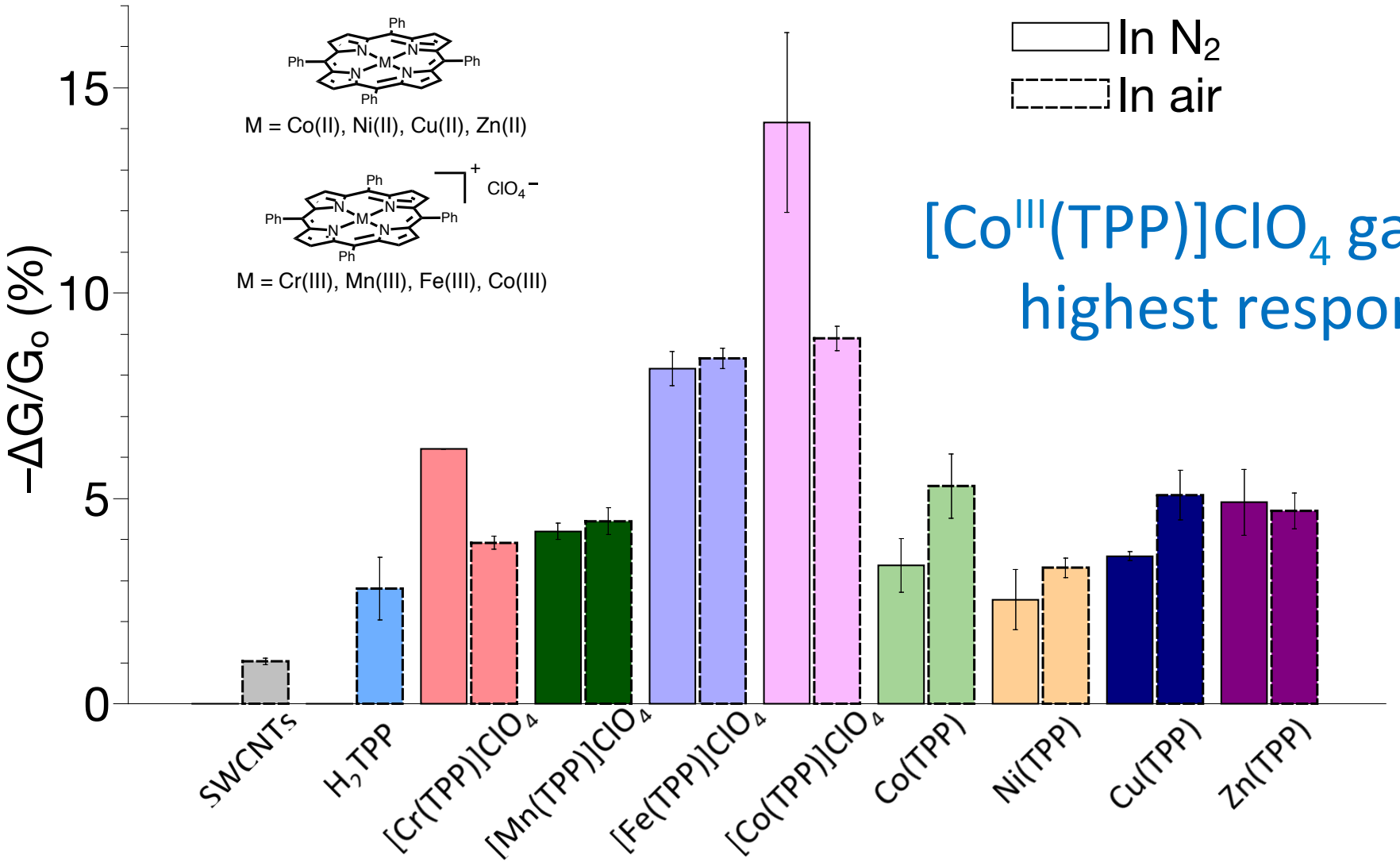
Sensing Enclosure



Destroy NDMA

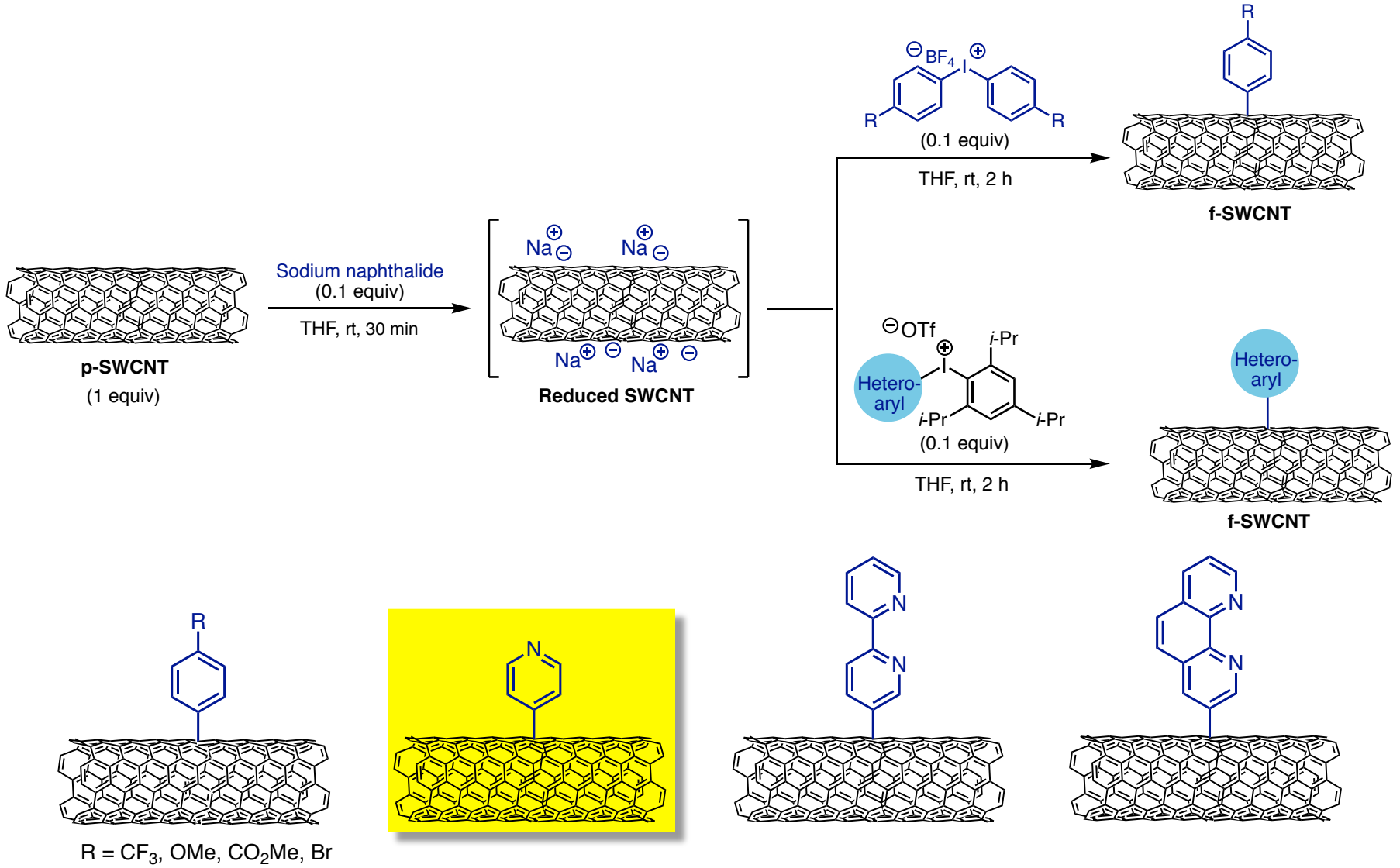
Metalloprophyrin-Chemiresistor Sensitivity

60 s exposure to 100 ppm of NDMA



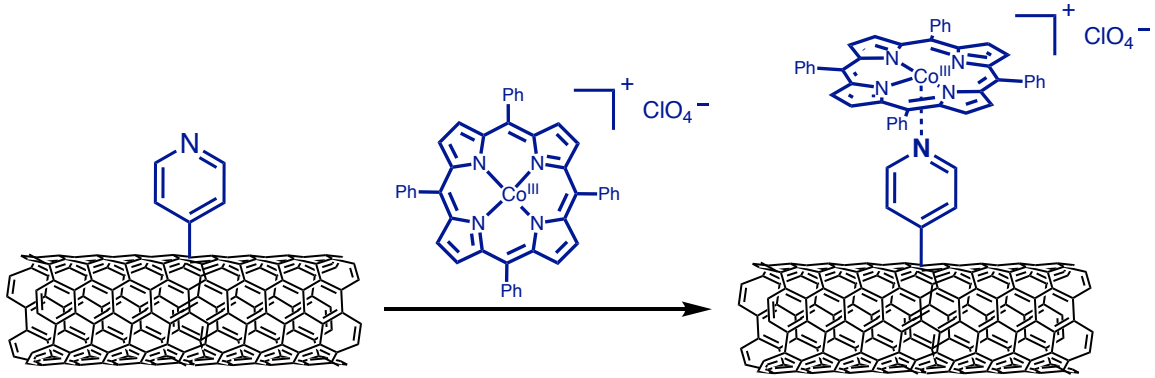
$[Co^{III}(TPP)]ClO_4$ gave the highest response

Covalent Functionalization of Carbon Nanotubes



M. He; T. M. Swager; *Chem. Mater.* **2016**, *28*, 8542–8549.

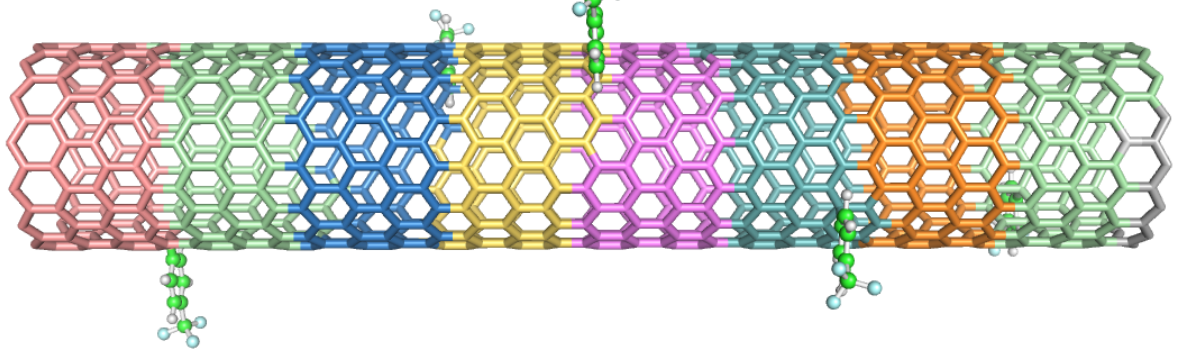
Functionalization Enhances Sensitivity



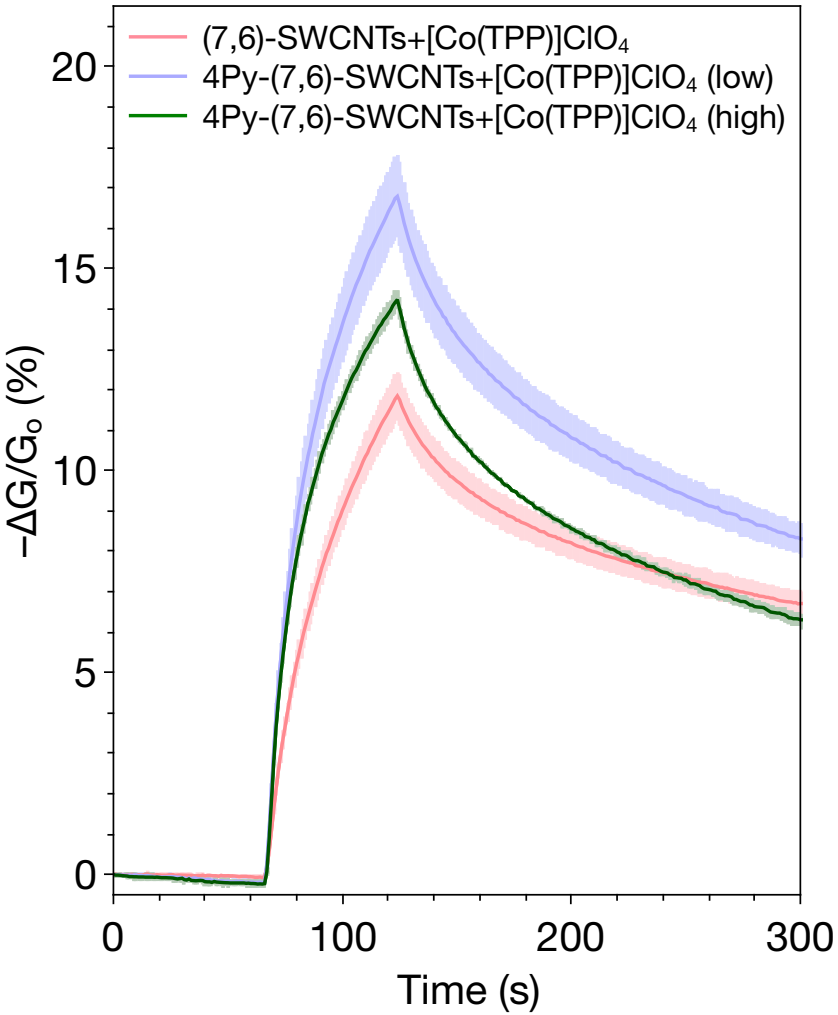
Different degree of functionalization:

f-CNT-1 (low): 1.4 Py groups per 100 carbons

f-CNT-2 (high): 1.9 Py groups per 100 carbons



Response to 100 ppm NDMA

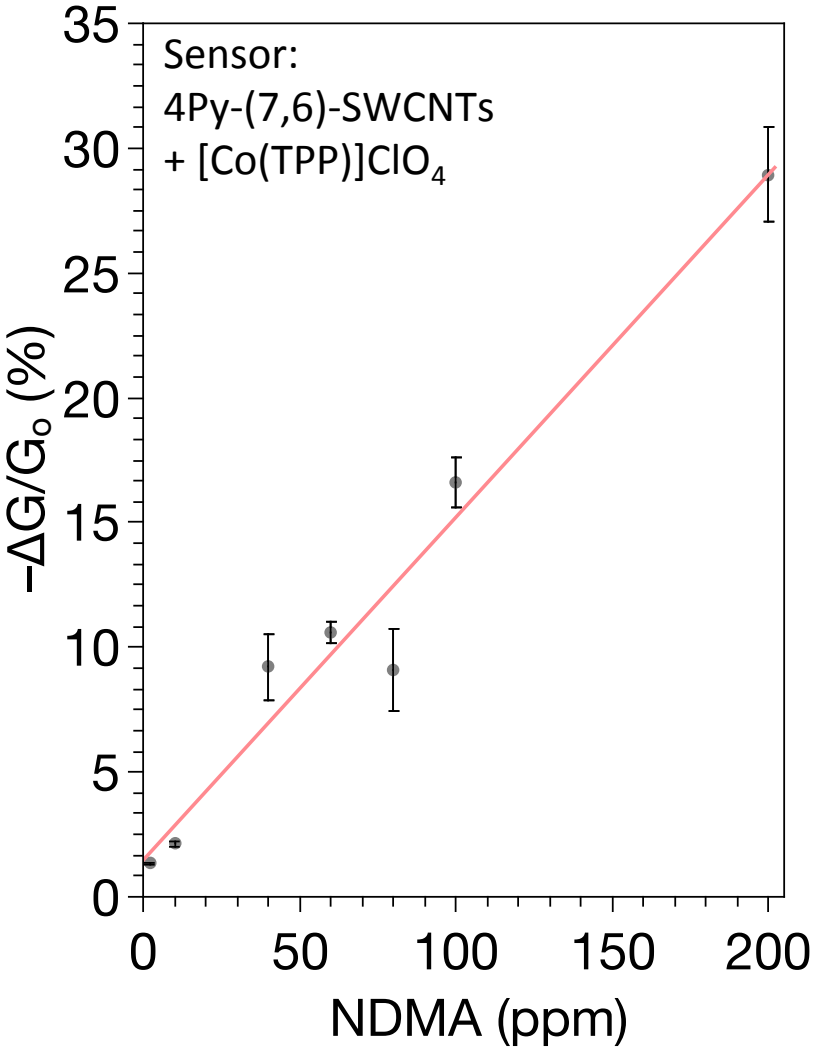


M. He; T. M. Swager; *Chem. Mater.* **2016**, *28*, 8542–8549.

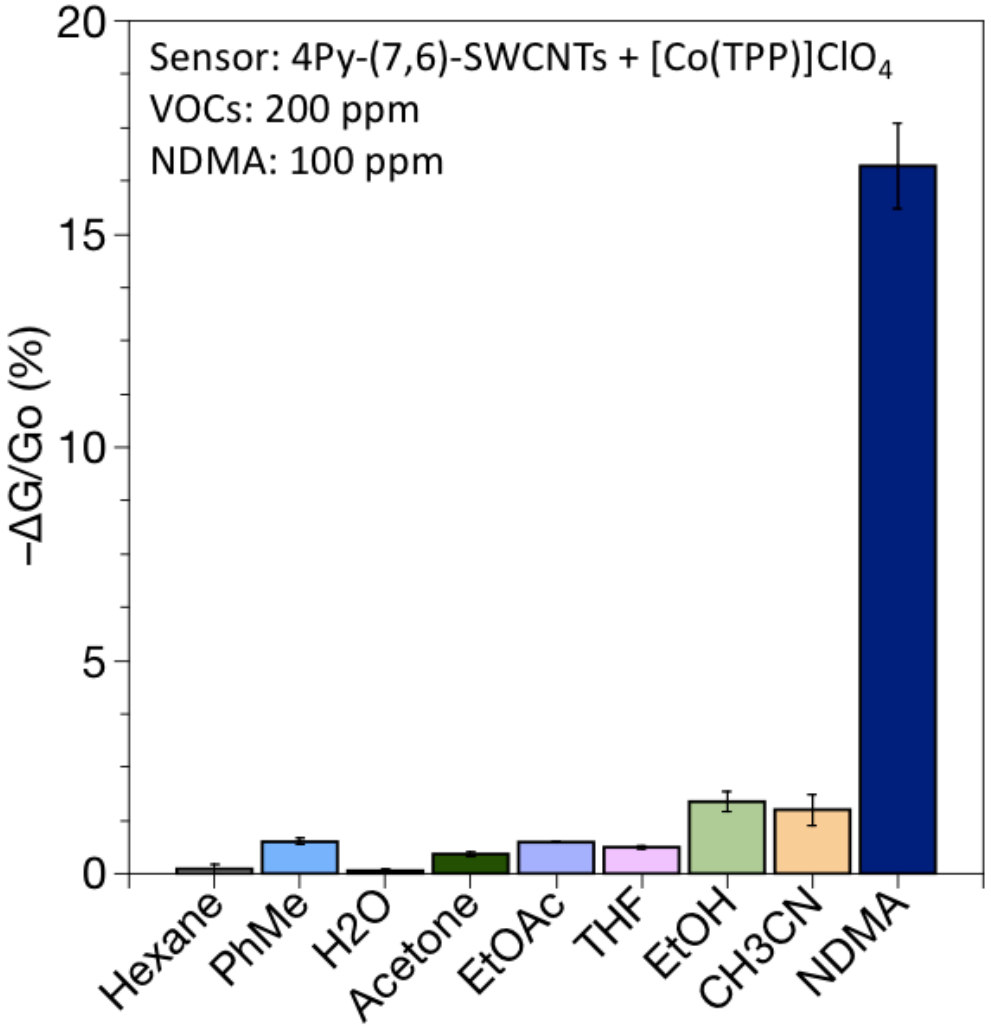
S. Savagatrup; V. Schroeder; X. He; S. Lin; M. He; O. Yassine; K. N. Salama; X.-X. Zhang; T. M. Swager; *Angew. Chem. Int. Ed.* **2017**, 56, 14066–14070.

Sensor Sensitivity and Selectivity

Response to NDMA



Selectivity



Conclusions

- Carbon nanotubes can be functionalized to harbor binding sites for chemical contaminants

- We have created chemical groups on the surface of carbon nanotubes that enable binding to NDMA

- Binding of NDMA to functionalized nanotubes impedes conductance, leading to a detectable signal

- We have demonstrated a dose response profile and chemical specificity

Next Steps: create environmental sensors that communicate to smart phones

Application: collect data on the concentration and location of NDMA

Impact: It will be possible to map the spatiotemporal dynamics of NDMA in the environment, providing valuable information to enable better protection of people from exposure to NDMA.