# DNA-wrapped Carbon Nanotubes for Multiplex Sensing and Imagining

**Ming Zheng**

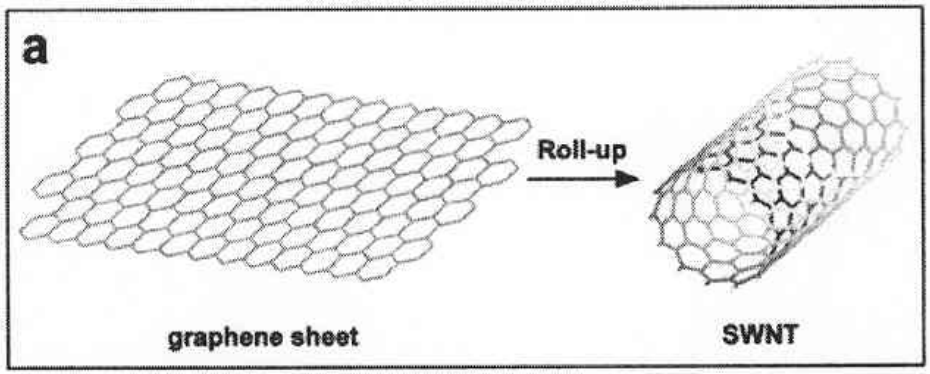
**National Institute of Standards and Technology**

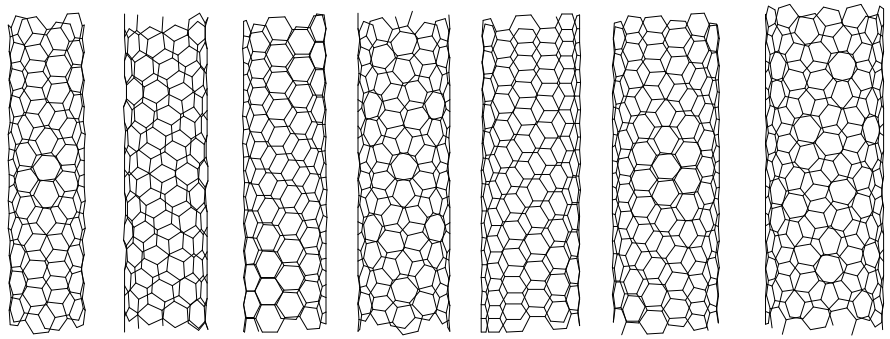
# Collaborators

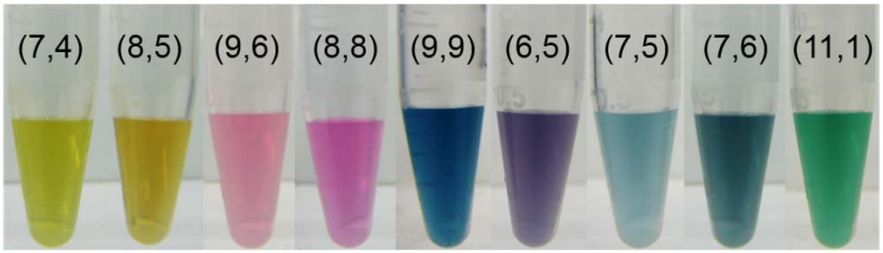
Anand Jagota, Lehigh University

Dan Heller, Memorial Sloan Kettering Cancer Center

# CNTs: Structure Diversity



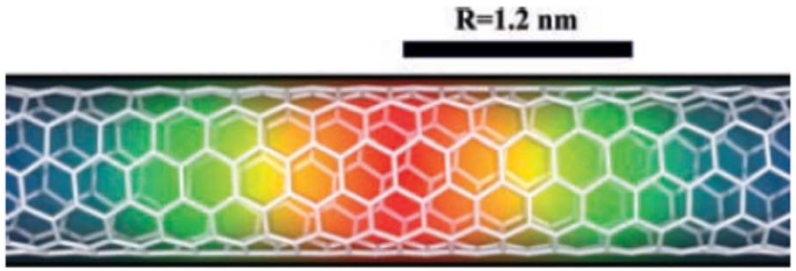



# Excitons

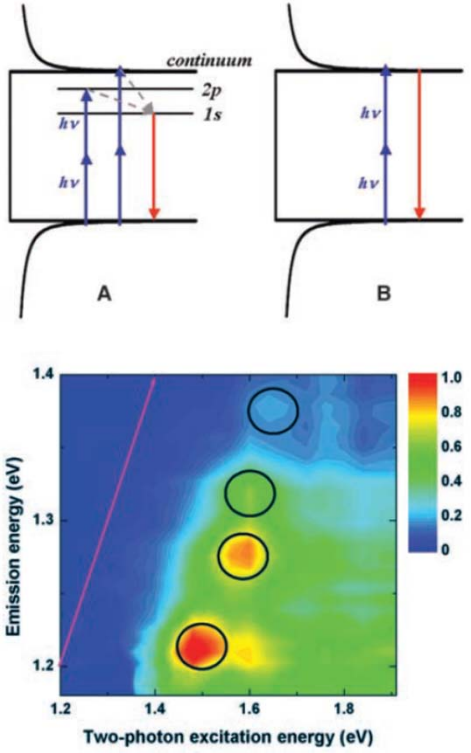
## The Optical Resonances in Carbon Nanotubes Arise from Excitons

Feng Wang,[1*] Gordana Dukovic,[2*] Louis E. Brus,[2] Tony F. Heinz[1†]

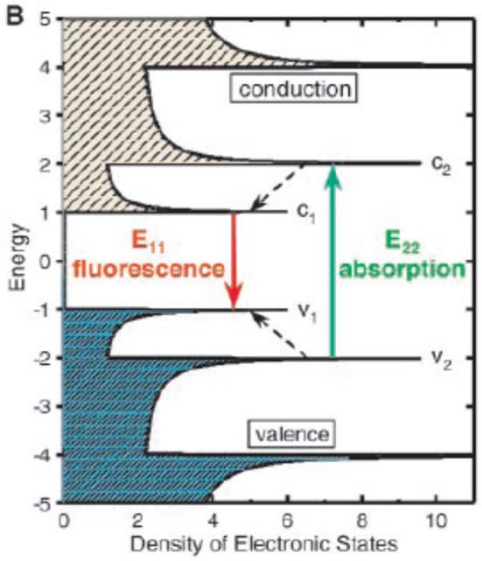
***Science***, vol 308, 838, 2005

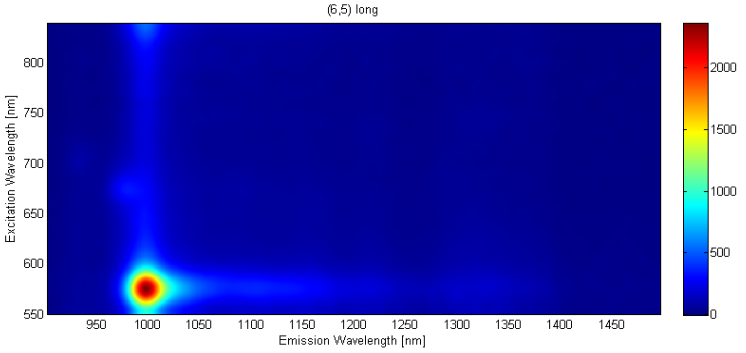


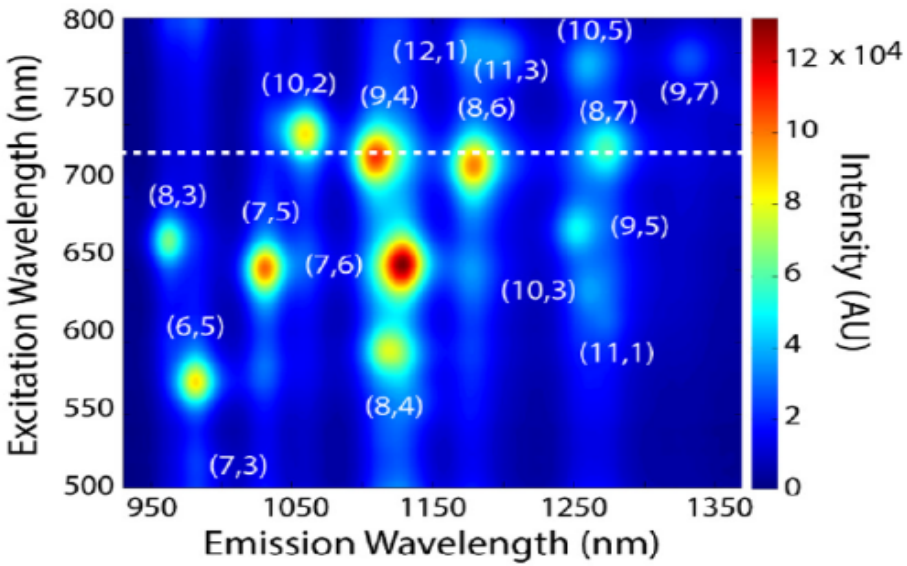

Two-photon excitation spectroscopy



# Light Emission in Near IR



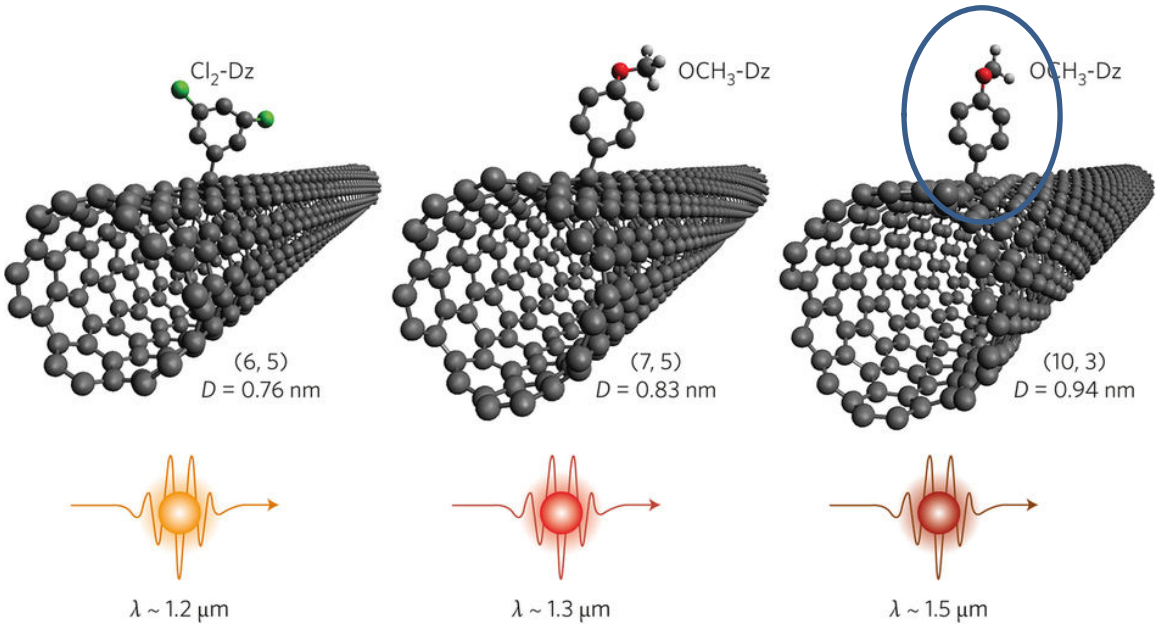




Supercontinuum excitation
and hyperspectral imaging

# Single Photon Emission for Super-Resolution Imaging

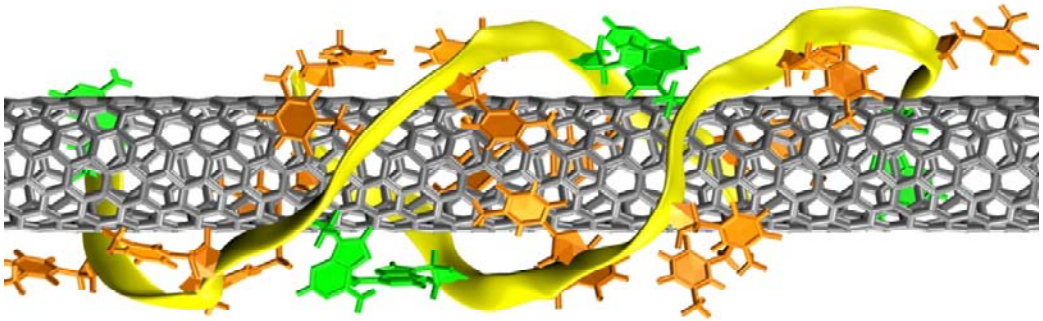
**organic color center**




He *et al*., ***Nature Photonics* 11,** 577, 2017

"News and Views" by Srinivasan and Zheng, ***Nature Photonics* 11**, 535, 2017

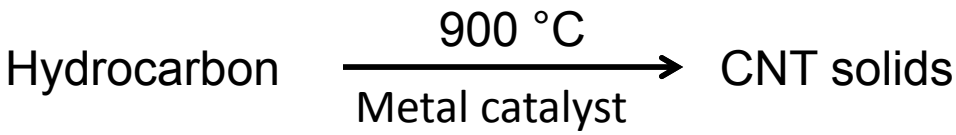
# Interfacing with Biology: Stereo-Regular DNA Coating

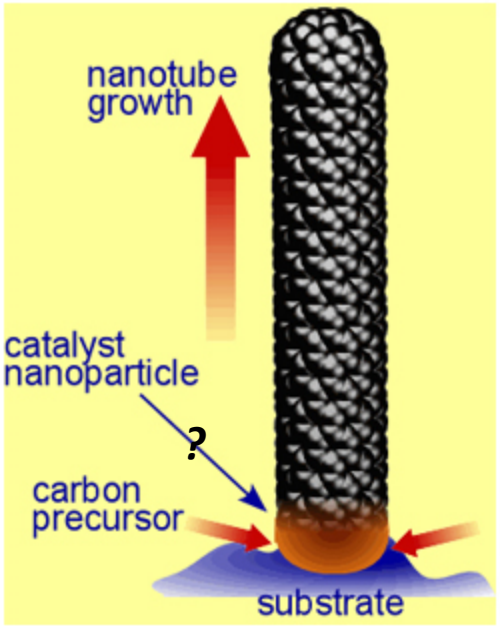


DNA coating controls physical and chemical properties of CNTs and their interactions with other molecules. This enables CNT applications in biology (sensing, imaging, therapeutics).

- Any DNA sequence can wrap around a CNT.
- Some special sequences form stereo-regular structures commensurate with CNTs.
- CNT/DNA sequence pairing rule is emerging!

# CNT Synthesis: Simple but Uncontrollable

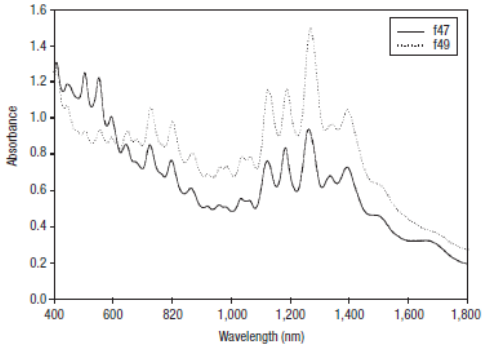



Synthetic products are mixtures of many structure types

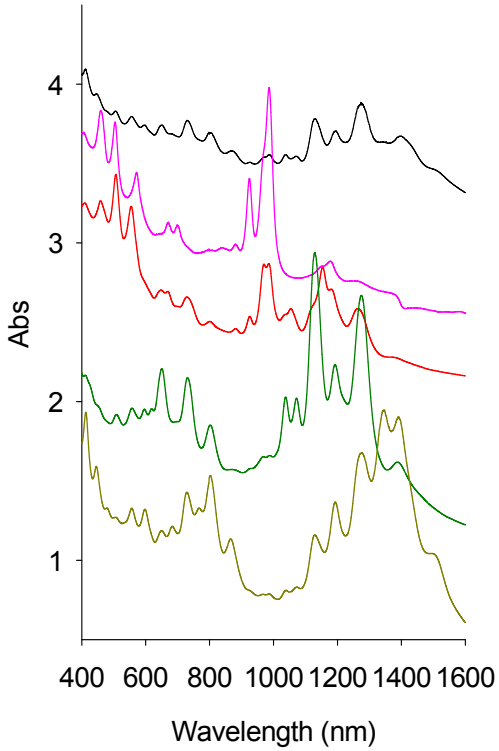
# Past Work: Sorting CNTs by DNA

Poly (C/T)

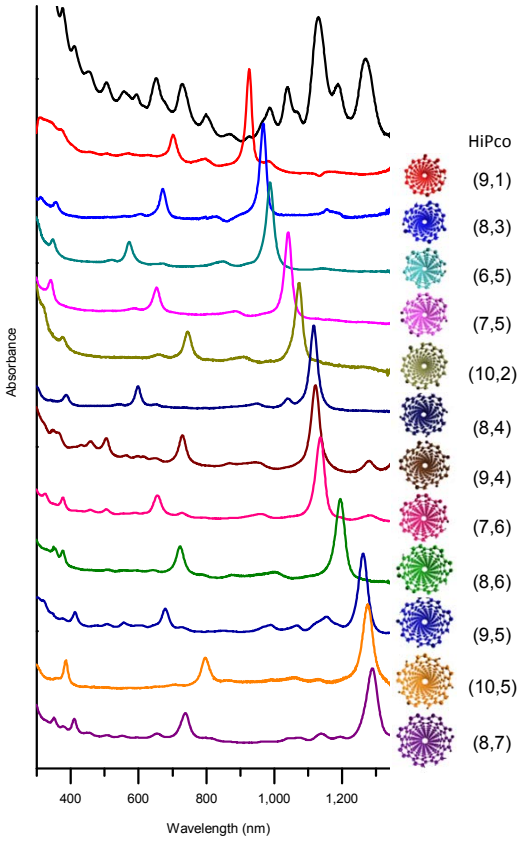



***Nature Materials***
2, 338, 2003

Poly (GT)




***Science***
302, 1547, 2003




***Nature***
460, 250, 2009

# Important Finding: Sequence Dependence

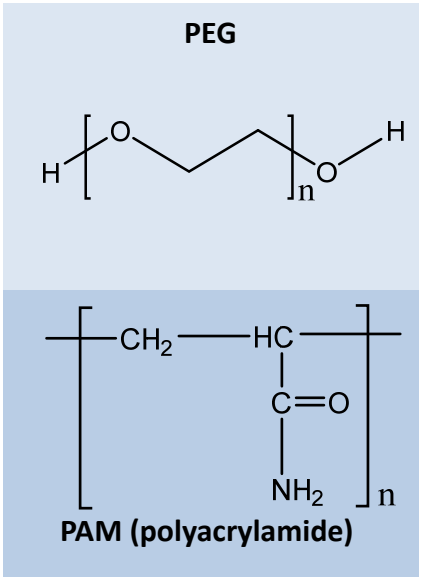
***~ 400 repetitive and short sequences examined!***

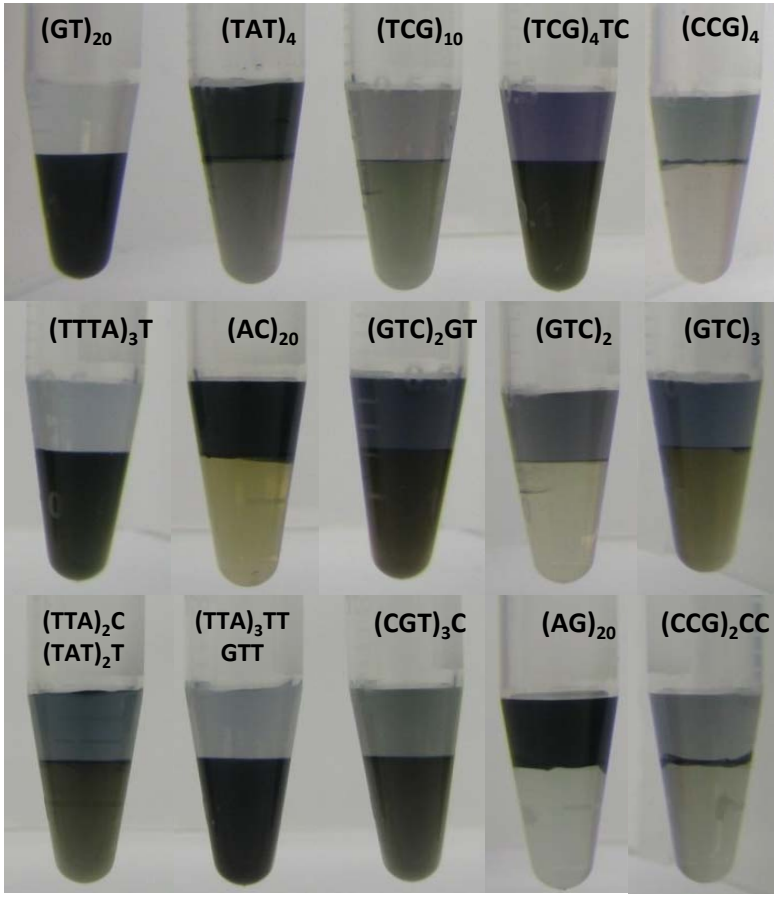
| Chirality (*n*,*m*) | Sequences |
|---|---|
| (9,1) | $(TCC)_{10}$, $(TGA)_{10}$, $(CCA)_{10}$ |
| (8,3) | $(TTA)_4TT$, $(TTA)_3TTGTT$, $(TTA)_5TT$ |
| (6,5) | $(TAT)_4$, $(CGT)_3C$ |
| (7,5) | $(ATT)_4$, $(ATT)_4AT$ |
| (10,2) | $(TATT)_2TAT$ |
| (8,4) | $(ATTT)_3$ |
| (9,4) | $(GTC)_2GT$, $(CCG)_4$ |
| (7,6) | $(GTT)_3G$, $(TGT)_4T$ |
| (8,6) | $(GT)_6$, $(TATT)_3T$, $(TCG)_{10}$, $(GTC)_3$, $(TCG)_2TC$, $(TCG)_4TC$, $(GTC)_2$ |
| (9,5) | $(TGTT)_2TGT$ |
| (10,5) | $(TTTA)_3T$ |
| (8,7) | $(CCG)_2CC$ |

***Nature*** 460, 250, 2009

# Aqueous Two-Phase Extraction: Faster Selection

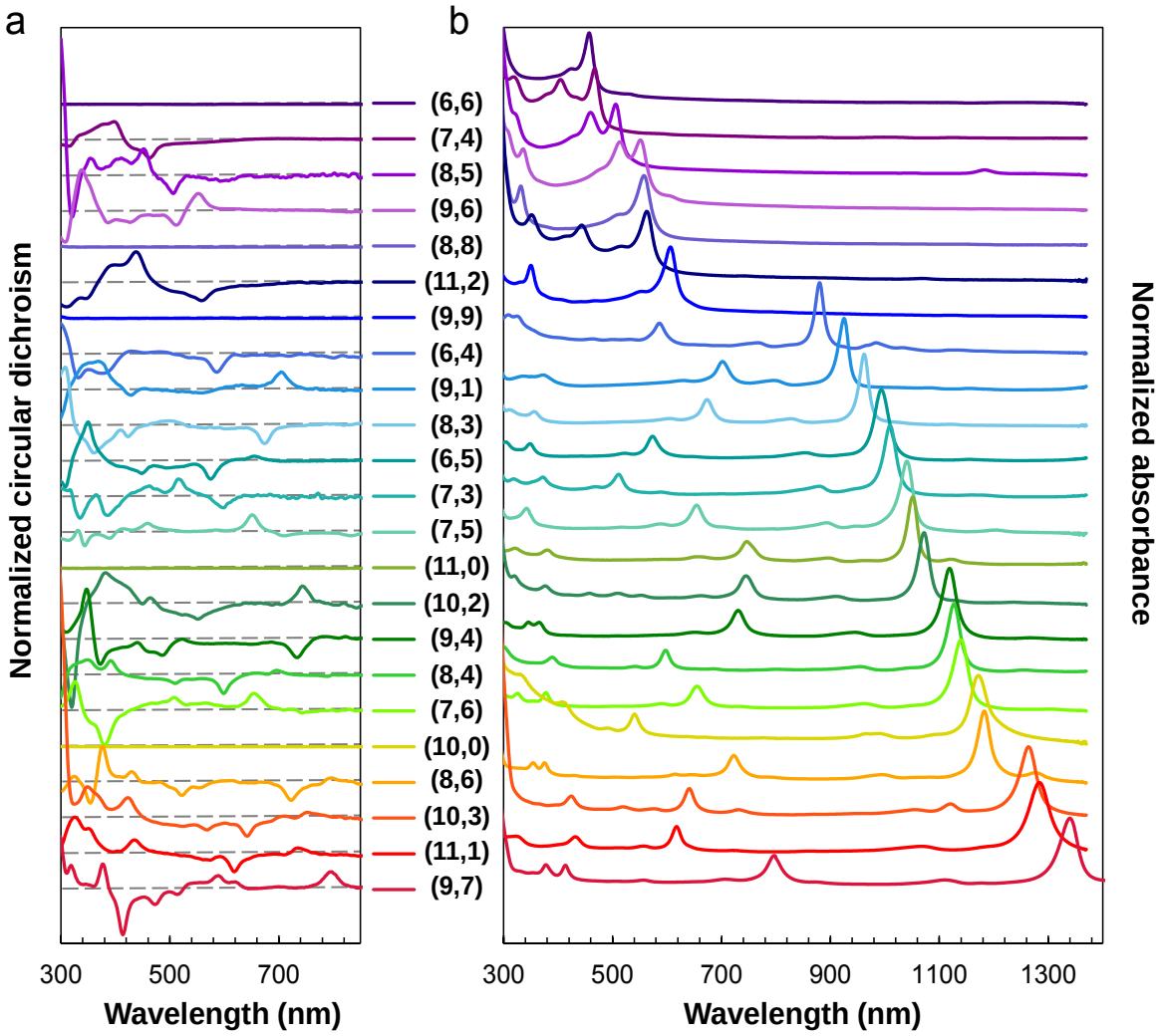
aqueous two-phase system




Ao *et al*., ***JACS*** 136, 10383, 2014

# A Comprehensive Solution




Ao, Streit, *et al*. ***JACS*** 2016, 138, 16677

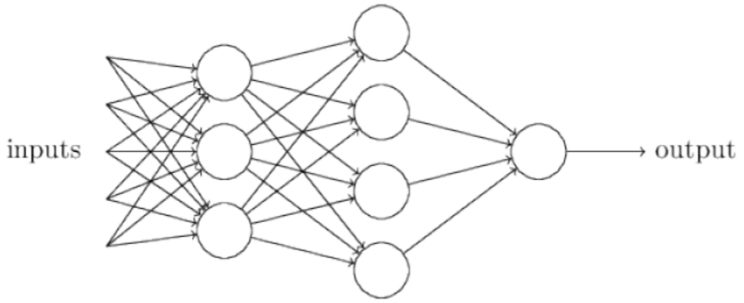
# DNA Selection by Machine Learning

| Helicity | Sequence |
|---|---|
| (9,1) | TCCCTCCTCCCT |
| (9,4) | CTTCCCTTC<br>TTCCCCTT |
| (7,3) | TCTCTCCTCTCT |
| (11,1) | TTTTCCCCTTTT |
| (9,7) | CCCCCTTCCCCC |
| (7,6) | CTCCCTC<br>TTTCCCCCTTT |
| (8,6) | CTTCTTC<br>TCTTCT |
| (8,3) | CTTCCTTC |
| (11,0) | TCCCCCCT<br>CTCCCCCCCCCTC<br>CCCCCCCCCCCC |
| (9,9) | TTTCCCCCCTTT |

Efficient search for recognition sequences is a major challenge.

Physics-based analysis is not effective.

Machine learning approach has shown its potential.




sequence

↓

vector ( $x_1$, $x_2$, $x_3$, …)

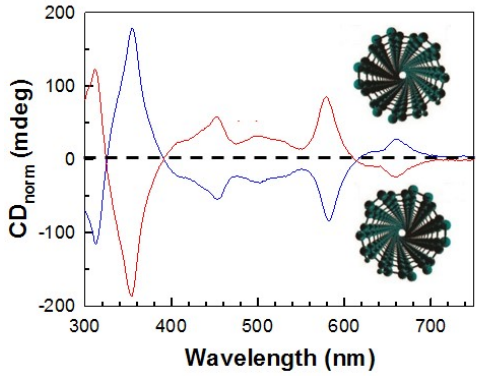
↓

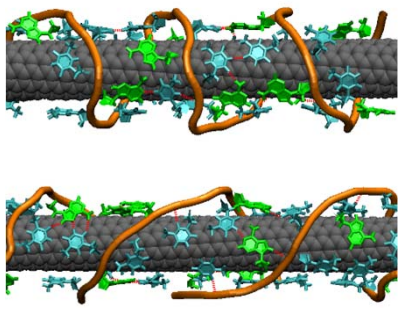
classification

**Sequence selection rule is emerging!**

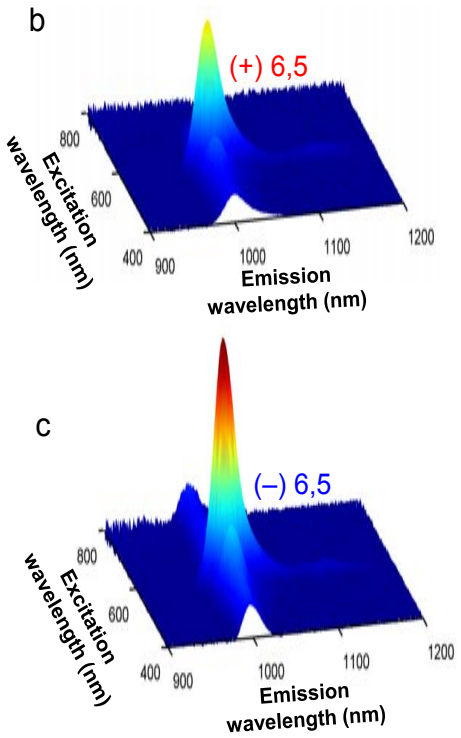
# Coating Structure Controls Chemistry

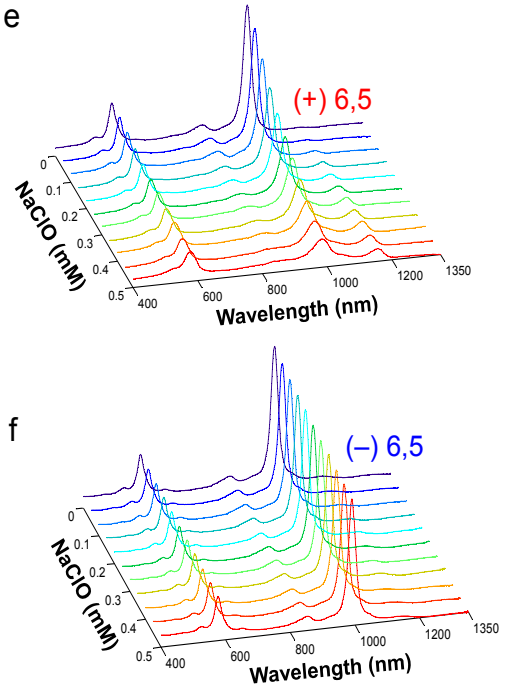
**TTA TAT TAT ATT**



**Oxidation by NaClO**

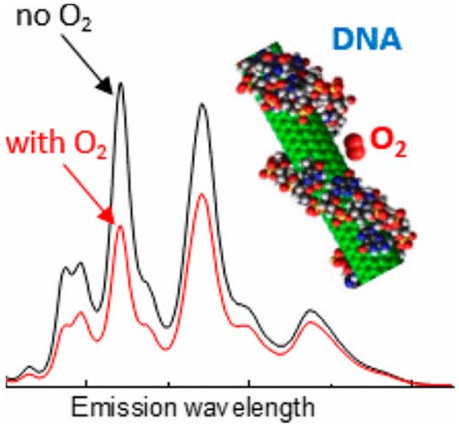



Ao, Streit, *et al*. ***JACS*** 2016, 138, 16677

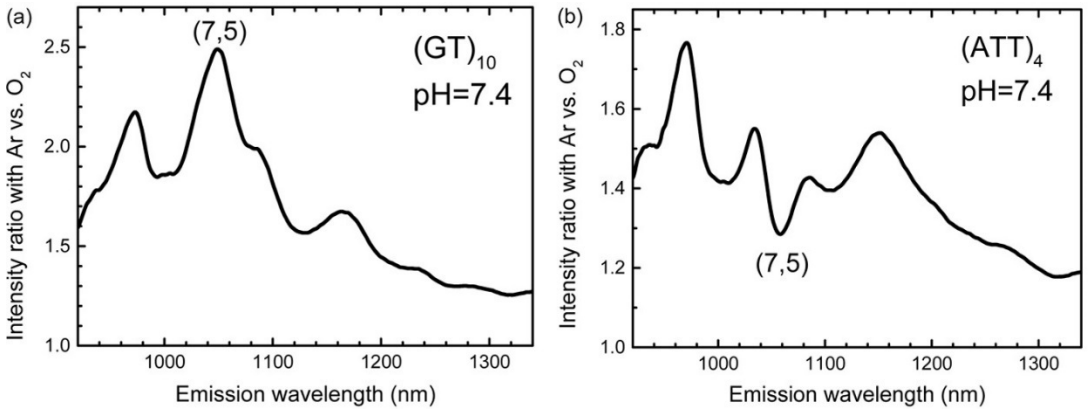
# Sensing Oxygen

Oxygen consumption in brain is related to neural activity



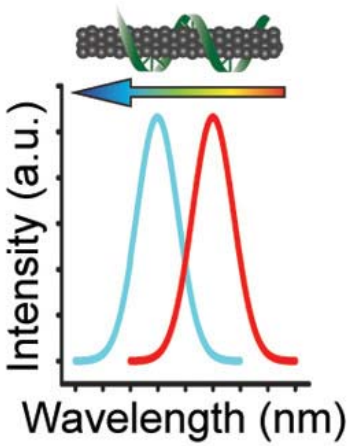

More quenching for (7,5)

less quenching for (7,5)

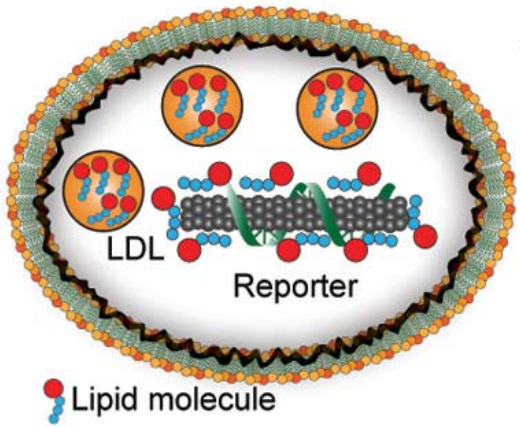



Zheng *et al*. ***JPCL*** 8, 1952, (2017)

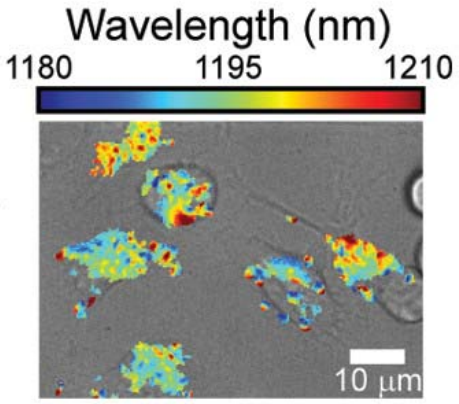
# Sensing Lipids




Increasing lipophilicity




Endolysosomal organelle



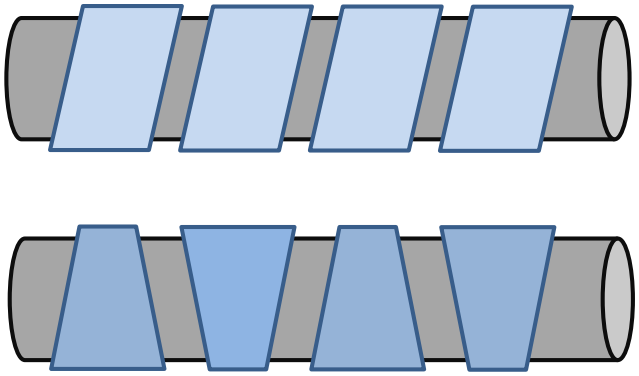

Lipid map in live cells

Jena *et al*., ***ACS Nano***, 2017
**DOI:** 10.1021/acsnano.7b04743

Galassi *et al*., ***Science Translational Medicine,*** under revision

In collaboration with Dan Heller Lab at MSKCC

# DNA-CNT Sensors



Patterning surface by DNA

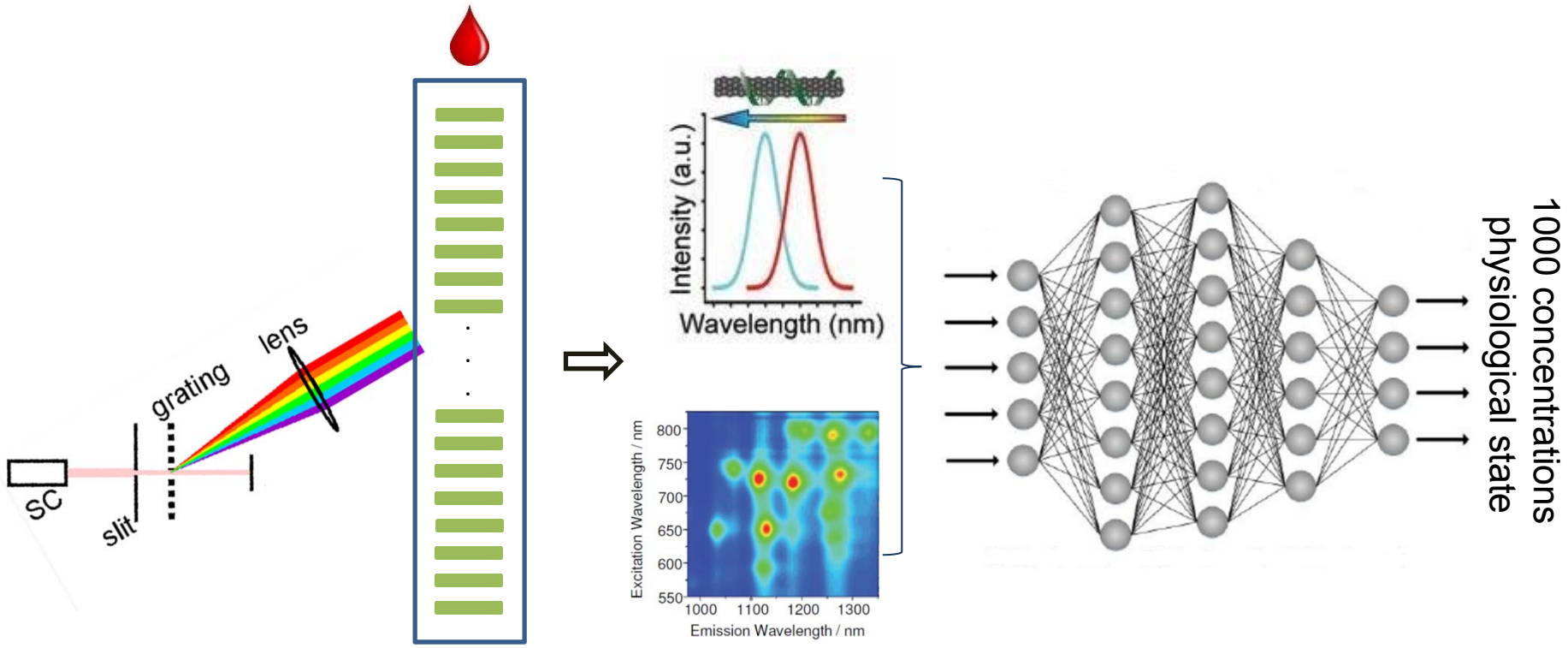
| DNA sequence | analyte | reference |
|---|---|---|
| (GT)6-(8,6) | cholesterol | ***ACS Nano***, 2017<br>**DOI:** 10.1021/acsnano.7b04743 |
| (GT)20 | Tb3+, Eu3+ | *ACS Nano*, **2011**, *5*, 6052–6059 |
| (AT)20 | NO | J. AM. CHEM. SOC. 2011, 133, 567–581 |
| (GT)15 | Hg2+ | *Science*<br>Vol. 311, pp. 508-511 |
| (GT)15-(6,5) and (7,5) | ROS and alkylating agents | *Nature Nanotechnology*, 4, pages114–120 (2009) |
| CTTC3TTC-(9,4) | Cholesterol | Science Translational Medicine (submitted) |
| (GT)15 | Dopamine, L-ascorbic acid, riboflavin | *Nature Nanotechnology* 8 (2013) 959-968. |

Potentially many more sensors can be identified!

# Measuring Metabolome of Biofluids

- Up to $10^3$ molecular species
- Complement genomic and proteomic data
- Traditionally a very important diagnostic tool
- No array-based method for whole metabolome mapping
- Current methods (liquid chromatography + mass spectrometry) focus on identification of individual species

# Molecular Perceptron




supercontinuum excitation

DNA-CNT receptor array

mapping response by hyperspectral imaging

deconvolution by multilayer perceptron

# Technical Summary

Intellectual Merits:

A method to map a metabolome in its entirety is proposed.

The core idea is based on independent sampling of the metabolome by an array of receptors, rather than recognition-based individual analyte detection.

This core idea is justified mathematically by the JL Lemma.

The receptor array is composed of $10^3$ DNA-CNT hybrids, which is estimated to be enough to cover $10^{12}$ distinct metabolome profiles.

The array response is detected via CNT fluorescence.

Collaborators:
Anand Jagota, Lehigh
Dan Heller, Memorial Sloan Kettering Cancer Center
Bruce Weisman, Rice