Nanoscale Biosensors Based on Luminescent Quantum Dots

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Objectives
- To develop QD multianalyte biosensors
- Sensors capable of long-term environmental monitoring

Payoffs
- Unexploded Ordnance Detection: Continuous monitoring for underwater detection of explosives
- Biological Screening of Toxins (Force Protection): Sensing systems for monitoring of drugs, toxins, pathogens, and environmental contaminants

Approaches
- Design and implement new syntheses of highly luminescent QDs
- Utilize QDs with bioreceptors to assemble multi-analyte biosensors for long-term environmental monitoring
  - Assembly of biorecognition elements onto luminescent QDs
  - Control FRET between a QD and dye-labeled receptor upon interaction with target analyte

Already constructed and tested: a prototype of a fixed-tether assay
- Assay is based on competition displacement
- Employ reverse quenching as the transduction signal

Design of QD nanoscale TNT sensor based on Fluorescence Resonance Energy Transfer (FRET)

1. FRET concept
- FRET involves the exchange of excitation energy
- Transfer efficiency varies at ~10^{-7}
- FRET occurs in a 2 Å range
- It is a powerful sensing tool for detection of binding events
- Requires spectral overlap or energy transfer

2. Advantages of QDs in FRET
- Tunable photon emission
  - Size
  - Choice of group II or VI elements
  - Maintain the same composition but vary the size across the range of accessible wavelengths

3. Illustration of energy transfer: Time-resolved fluorescence
- Photoluminescence domain varies for a fixed QD size
- Homogeneous core formation
- Tunable photon emission
  - % composition
  - Choice of group II or VI elements
  - Size
  - Maintain uniform size across wide wavelength domain

4. FRET-based sensor concept
- Digital cytochrome C
- Analog-labeled quencher
- QD
- No analyte
- No QD emission
- Analyte in recognition site
- QD emits
- Properties:
  - Robust, real-time
  - Able to regenerate
  - Resistant to fouling with buffer

5. TNT monitoring system
- Recognition element: withstand nonstandard matrices (seawater)
- Robust reporters: photo-chemically stable QDs
- Easily identifiable: 'On' or 'Off' luminescence

Key research milestones
- Design and develop new QDs with broad emission wavelengths
- Develop QD-surface ligands for water-compatibility and cell-conjugation
- Optimization of QD-acceptor FRET spectral overlap and separation distances
- Sensor optimization by linker and donor-acceptor pairs
- Design and optimization of multireceptor QD-bioconjugates
- Develop sensors that target analytes of interest to the Navy

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Publications
- 14 refereed publications, 1 patent, 9 proceedings, and 3 book chapters

Work highlighted in Science, Nature Biotechnology, and Small Time magazine

Seminars:
- 8 Tutorials, 7 talk, 5 workshops, and 4 book chapters