3-29-2023

Developing Carbon Quantum Dots as Multimodal Contrast Agents

Nicholas Whiting
Rowan University, whitingn@rowan.edu

Developing Carbon Quantum Dots as Multimodal Contrast Agents

Whiting Lab (PI: Nicholas Whiting)

Depts. of Physics & Astronomy and Biological & Biomedical Sciences. Rowan University. Glassboro, NJ 08028 USA

What Are Carbon Dots?

- Small fluorescent nanoparticles (<10 nm diameter) composed primarily of carbon
- Optoelectronic properties allow potential applications that range from photovoltaics and LED lighting to inks and dyes
- Unlike other quantum dots, carbon dots are non-toxic and can be developed as biomedical contrast agents

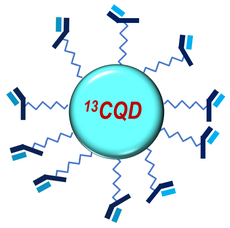


Figure 1: Schematic of ^{13}C-enriched carbon quantum dot (CQD) functionalized with antibodies for targeted molecular imaging.

Multimodal Motivation

- While fluorescent carbon dots provide useful contrast *in vitro* and in mice, the low penetration depth of visible light precludes their utility for deep tissue imaging
- Because the ^{13}C nucleus is detectible by magnetic resonance, carbon dots may also serve as MRI contrast agents

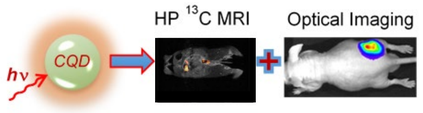


Figure 2: Proposed development of CQDs as dual-mode MRI and optical imaging contrast agents

Carbon Dot Synthesis

- Bottom-up synthesis involves carbonization of water-soluble small-molecule precursors in a hydrothermal autoclave

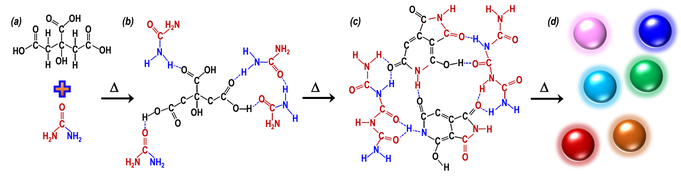


Figure 3: Proposed reaction scheme for synthesizing carbon dots. Small-molecule precursors (e.g., citric acid and urea) are carbonized under heat and pressure to result in fluorescent carbon-based quantum dots.

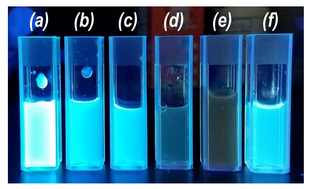


Figure 4: Fluorescent carbon dots synthesized from *(a)* citric acid & urea; *(b)* citric acid; *(c)* urea; *(d)* sodium bicarbonate; *(e)* glucose; and *(f)* maleic acid. Cuvettes illuminated @ 395 nm.

Improving Purification

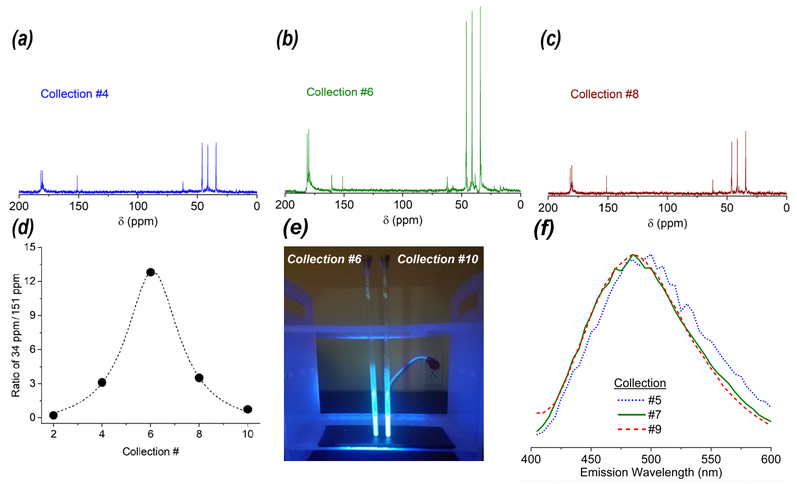


Figure 5: ^{13}C solution-state NMR of carbon dot samples following size exclusion chromatography. ***(a-c)*** example ^{13}C spectra for collections 4, 6, & 8 (vertical axis scaled to 151 ppm peak). ***(d)*** ratio of the 34 ppm vs. 151 ppm peaks for different collections. ***(e)*** photo of collections 6 (*left*) and 10 (*right*) under UV light. ***(f)*** comparison of peak fluorescence for sample collections 5, 7, & 9 showing minimal changes to emission peak despite significant differences in NMR spectra for similar collections.

Hyperpolarization of Nuclear Spins

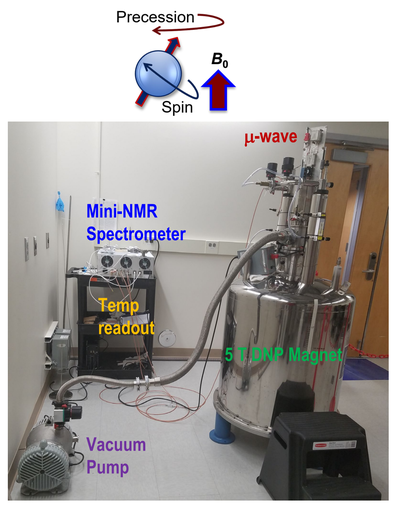


Figure 6: Dynamic nuclear polarizer (DNP) in the PI's lab consists of a 5 T superconducting magnet with integrated cryostat that cools samples to ~2 K. This device is used for both DNP and brute force polarization.

Eq. 1

$$P = \frac{N_{\uparrow} - N_{\downarrow}}{N_{\uparrow} + N_{\downarrow}}$$

Eq. 2

$$P = \frac{\hbar \gamma B_0}{2 k_B T}$$

- Magnetic resonance signals are from small population differences in nuclear spin alignment inside of a strong magnetic field (Eq. 1)
- Because most of these nuclei are oppositely-aligned, their contributions cancel and result in very weak MR signals
- Analogous to detecting 1 in 50,000 nuclei → leads to inherently low sensitivity for MR techniques
- ***Hyperpolarization*** refers to a collection of methods that temporarily re-align the nuclear spins, so they enhance MR signals by orders of magnitude
- One such method—***Brute Force Polarization***—uses low temperatures and high magnetic fields (Eq. 2) to enhance MR signals through improved nuclear spin alignment

Enhanced ^{13}C Dots

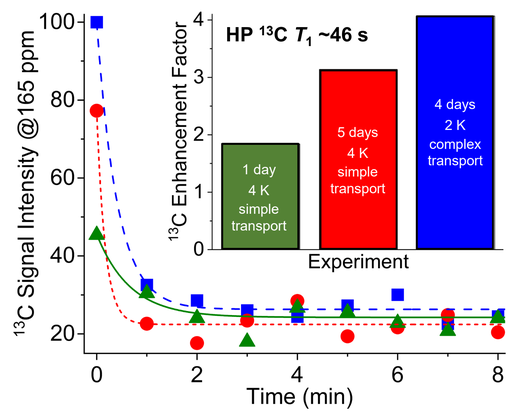
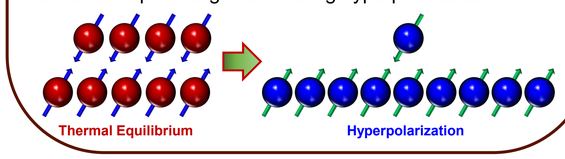


Figure 7: Enhancement of ^{13}C MR signal as a function of time for carbon dots that underwent brute force polarization for different time & temperature values. ***Below:*** schematic of nuclear spin realignment during hyperpolarization.



Carbon Dots in E-Cigs

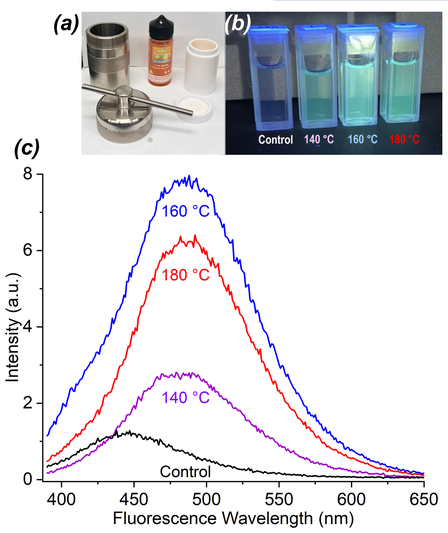


Figure 8: Making carbon dots from e-cig liquids. ***(a)*** e-cig juice bottle with hydrothermal autoclave and Teflon insert. ***(b)*** photo of carbon dots solutions synthesized from e-cig juice. ***(c)*** fluorescence spectra of carbon dots synthesized from e-cig juice at different temps.

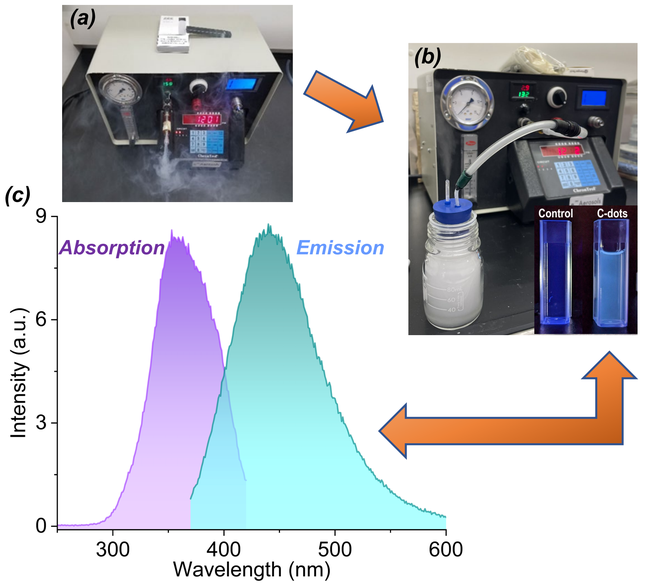


Figure 9: Making carbon dots from e-cig vapor. ***(a)*** e-cig smoking machine. ***(b)*** the resulting vapor is collected; ***inset***: photo of carbon dots from e-cig vapor. ***(c)*** absorption and emission profiles of carbon dots collected from e-cig vapor.

Silicon Carbide

- Introducing a source of silicon (e.g., $SiCl_4$) into the carbon dot synthesis allows for the formation of silicon carbide quantum dots
- ^{29}Si also MR-active → heteronuclear co-polarization

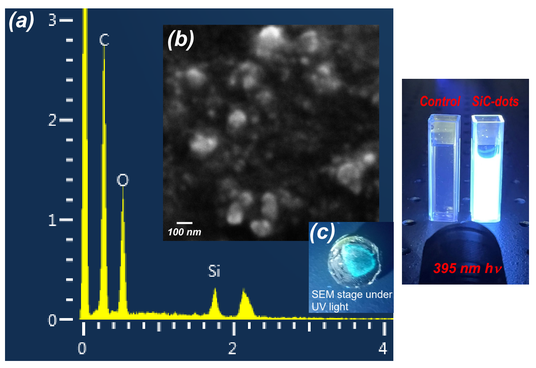


Figure 10: ***(a)*** Electron dispersive X-ray spectroscopy (EDS) of fluorescent silicon carbide nanomaterial. It is expected that SiC quantum dots are present, albeit too small (<10 nm) to be resolved using ***(b)*** SEM imaging. ***(c)*** fluorescent sample on SEM stage.

Acknowledgements

Student researchers that contributed to the carbon dot projects:

Mat. Sci. & Eng. Ph.D. Program

Cody Soper

Undergraduates in the Dept. of Physics & Astronomy

Domenic Marino · **Vincent Ferraro** · **Jimmy Gutierrez** · **Angelita Martinez** · **Maggie Mayfield** · **Paul Mikalic**

We also thank Drs. S. Lofland, N. Nucci, and T. Scabarozi (Dept. of Physics & Astronomy) for helpful conversations and ongoing experimental support

Research Support:

This research project is supported by **NSF CAREER** (2238852). Additional laboratory support from the **American Chemical Society Petroleum Research Fund** (65275-UNI6), the **Eppley Foundation for Research** (1023), and the **New Jersey Health Foundation** (PC 16-18).

ACS PRF

The Eppley Foundation for Research

Support for advanced scientific research

NSF

New Jersey Health Foundation, Inc.