Engineering Quantum Biosensors with Nanodiamonds

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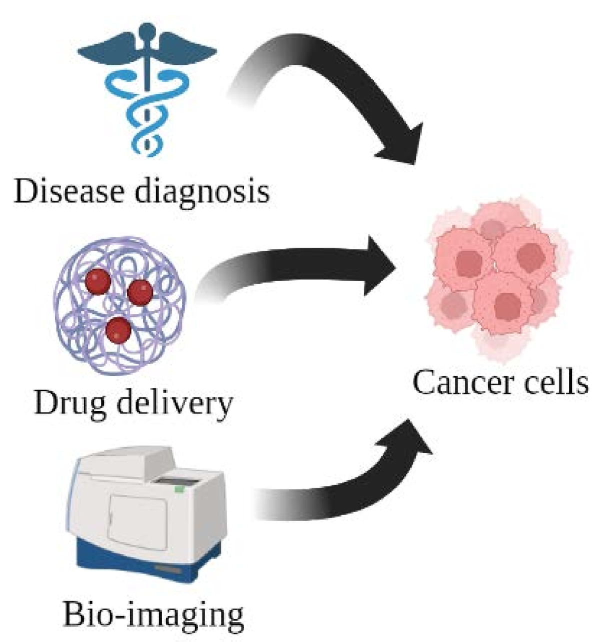
Introduction

Because of their size, colloidal stability, room temperature quantum properties and exceptional biocompatibility, nanodiamonds (ND) containing nitrogen-vacancy (NV) centers have many promising applications in quantum sensing, biolabeling, and nanomedicine. By conjugating nanodiamonds to various biomolecules, such as antibodies, therapeutics and reporter particles, we can create a nano-sensing platform with simultaneous detection, diagnostic, and treatment capabilities. However, current methods of conjugating biomolecules to the nanodiamond surface have low yield and a high tendency of forming agglomerates. Here, we investigate ways to prevent nanodiamond agglomeration and increase conjugation yield by nanodiamond emulsions to increase the number of potential conjugations sites by a factor of 4x.

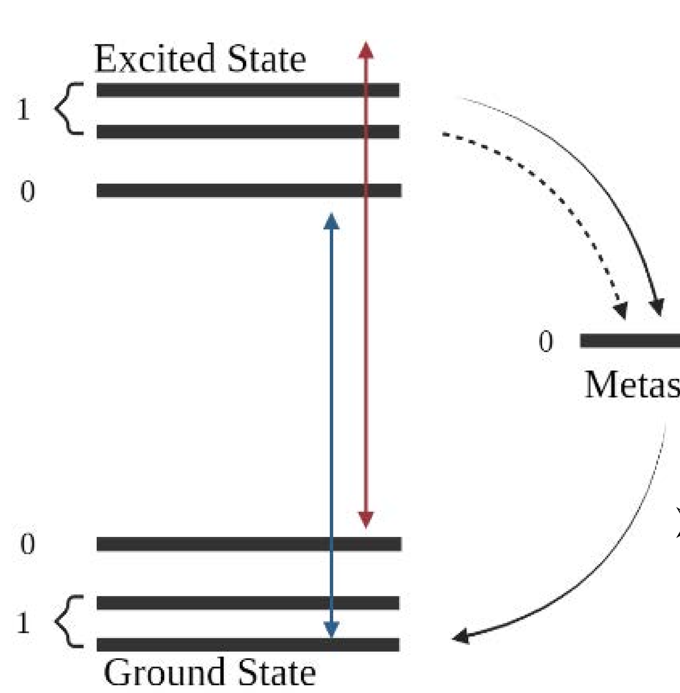
Applications for NV-Center Nanodiamonds (NDs)



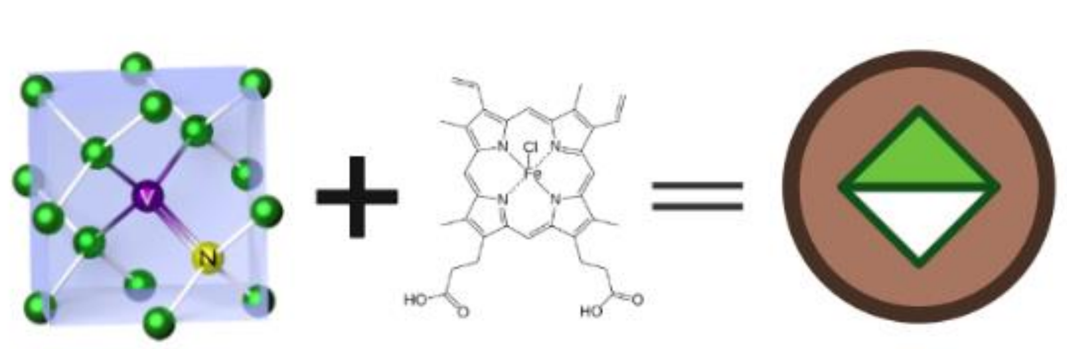
Benefits of NV-center NDs:

- Nanoscale sensitivity
  - Including Magnetic,
  - Electronic,
  - Temperature, and pH sensitivity
- Biocompatibility
- Long-term optical stability
- Optically addressable spin state

NV-Center ND Spin States for Relaxometry



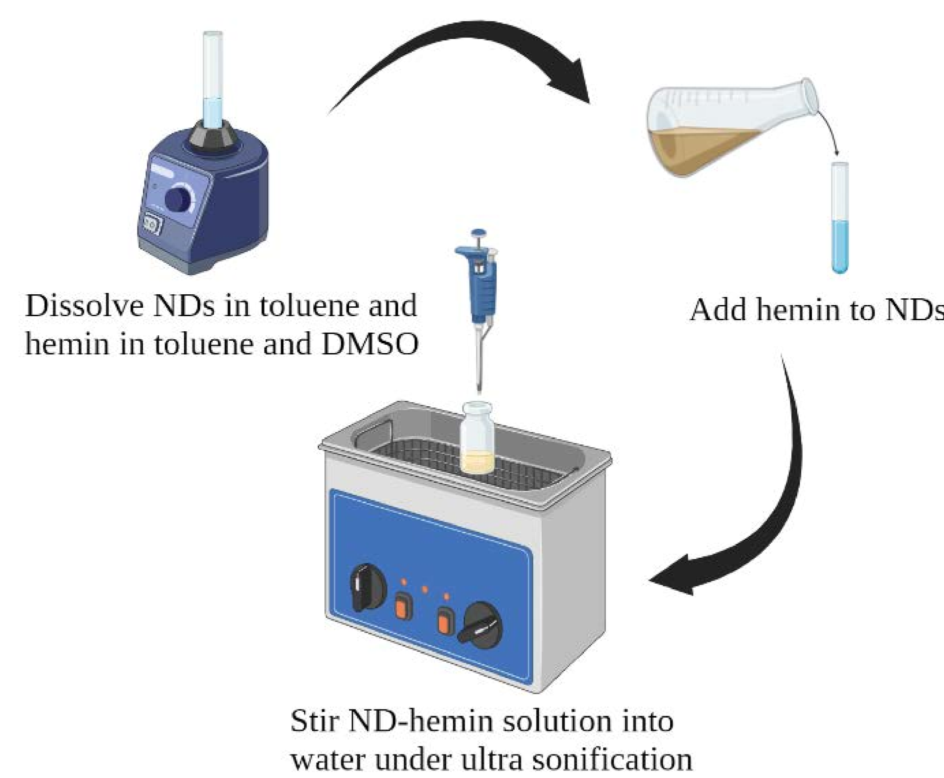
- Nonradiative intersystem crossing allows us to optically detect the NV center's spin state



- Creating an emulsion with NDs and Hemin exposes more reactive surface carboxyl groups on the nanodiamonds
- We can then form covalent bonds between carboxyl groups of hemin and amine groups of conjugates—biomolecules, therapeutics, and markers—for in vivo/in vitro fluorescence imaging and drug delivery

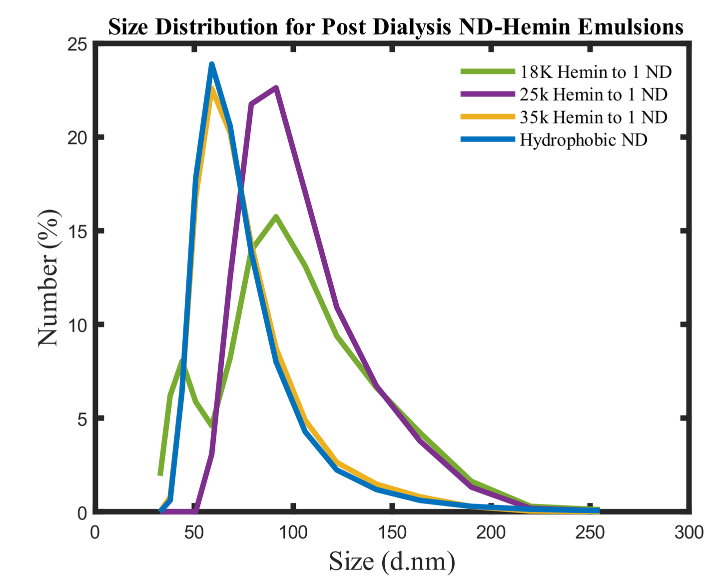
Nanodiamond-Hemin Emulsions

Nanodiamond-Hemin Emulsions

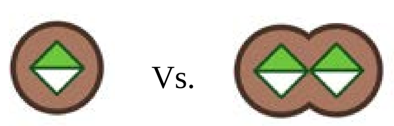


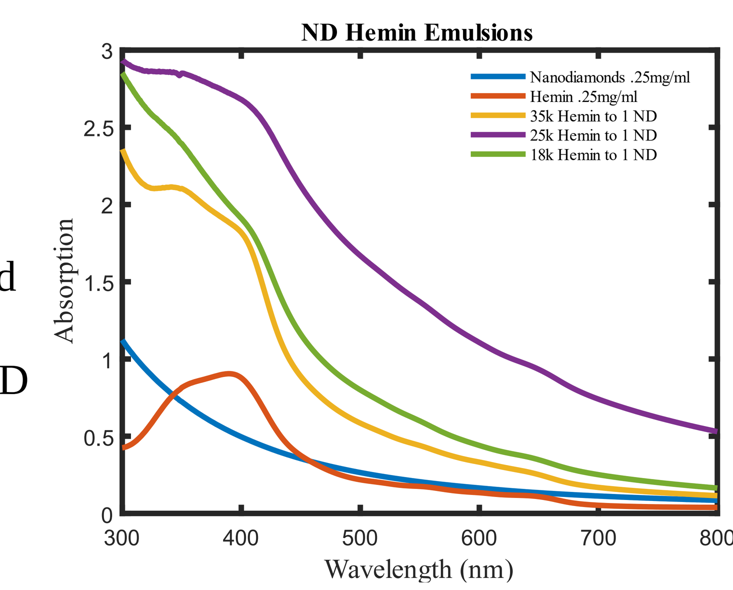
- Prepare emulsions with 1:35k (10:1), 1:25k (15:1), and 1:18k (20:1) mole (mass) ratios of ND to hemin
- A 1:1 mass ratio of ND to hemin ~360K hemin to 1 ND
- Emulsifying hydrophobic nanodiamonds with hydrophilic hemin improves colloidal suspension and prevent agglomeration while increasing carboxyl coverage

Post Dialysis Analysis



- Dynamic light scattering to determine emulsion size
- More hemin typically leads to single nanodiamond emulsions
- Too few hemin particles or inadequate mixing can lead to multi-nanodiamond emulsions

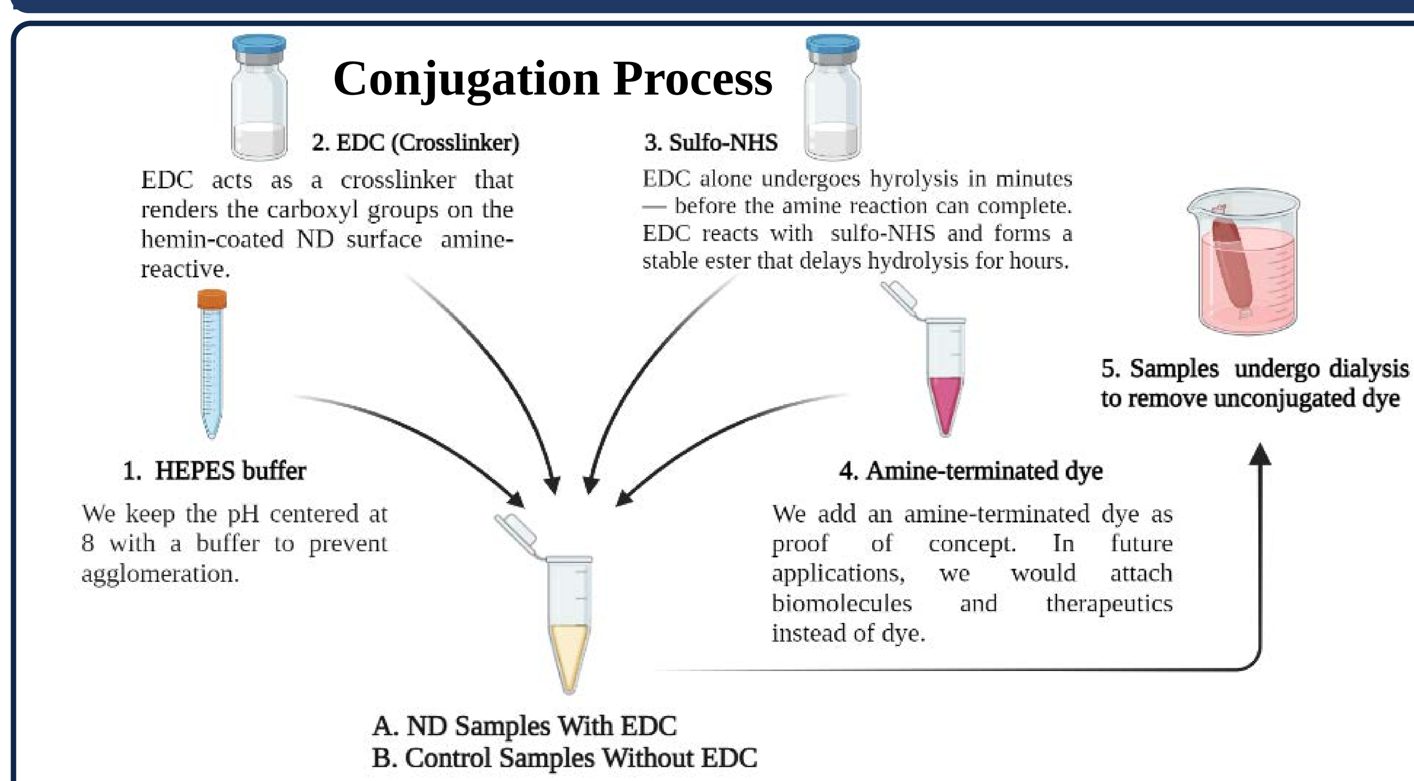


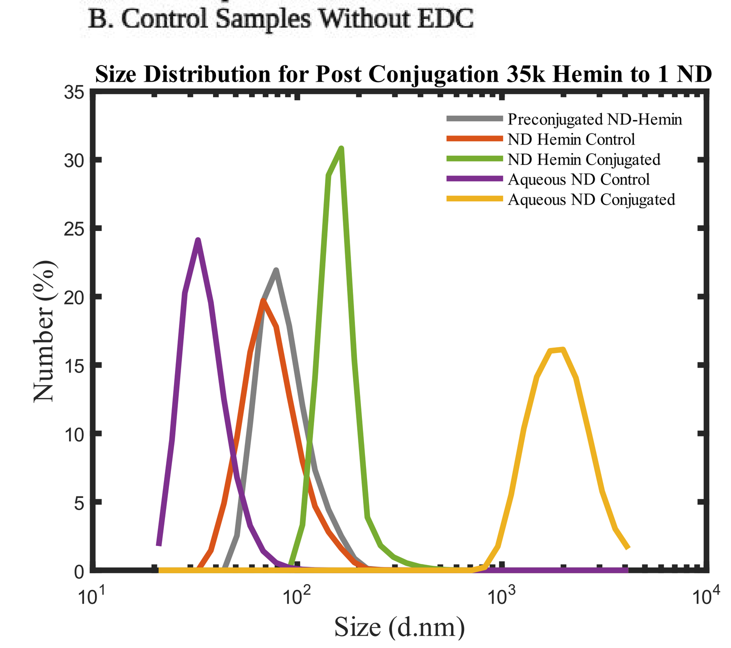


- Scattering and absorption characteristics of nanodiamonds (Blue), hemin molecule (Red) and ND-Hemin emulsions (Yellow, Purple, Green).
- Nanoparticle scattering takes the form of ~ $1/\lambda^4$
- Changes in magnitude or shape of these curves indicate agglomeration (increased scattering) or additional materials

Conjugating Dye to Nanodiamonds

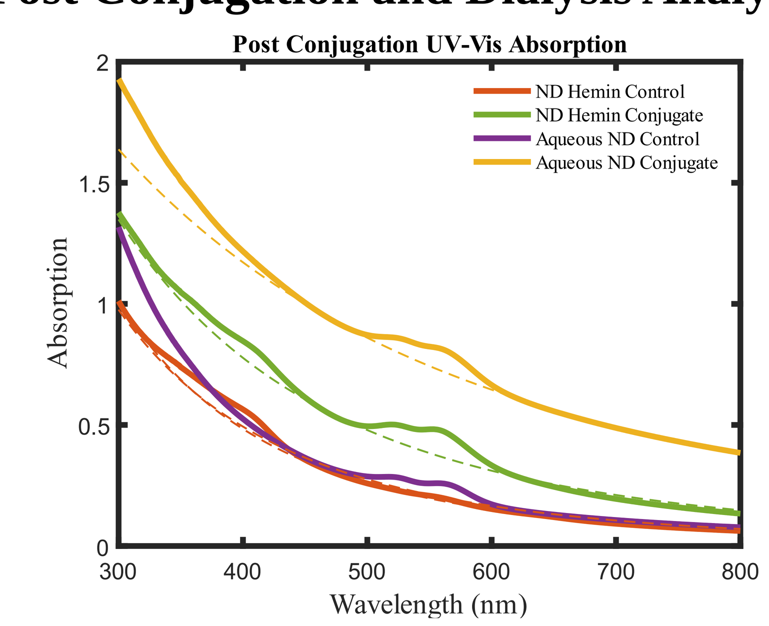
Conjugation Process



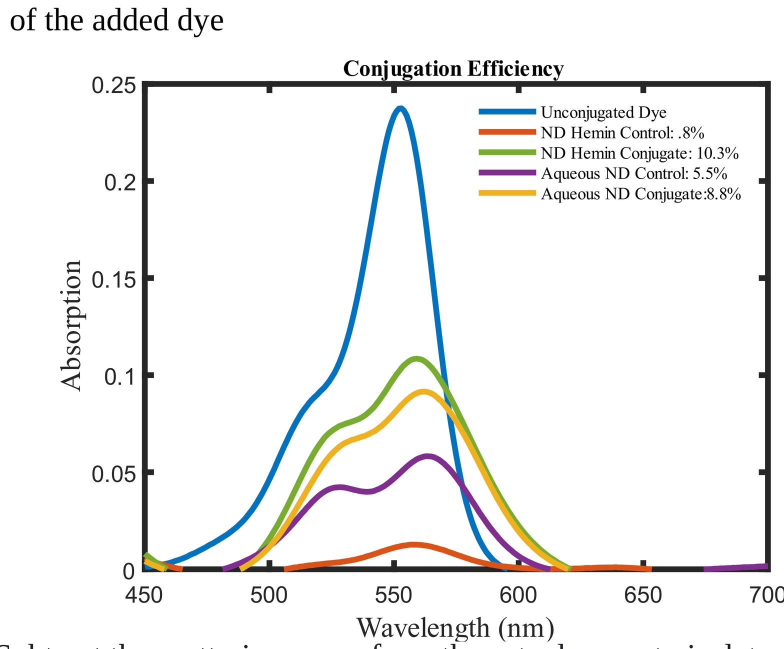


- Uncoated aqueous NDs agglomerated significantly during conjugation
- Some agglomeration expected due to instability of dye molecules

Post Conjugation and Dialysis Analysis



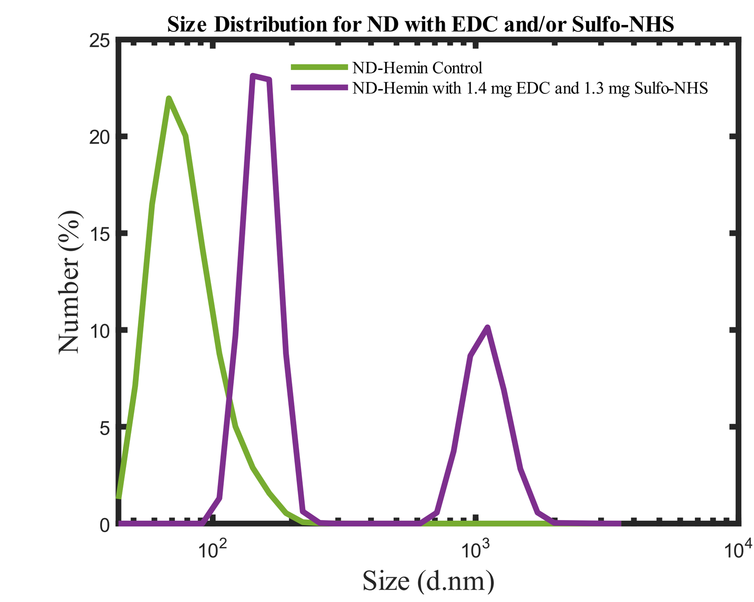
- Deviation from the scattering curves (dotted) indicate the presence of the added dye



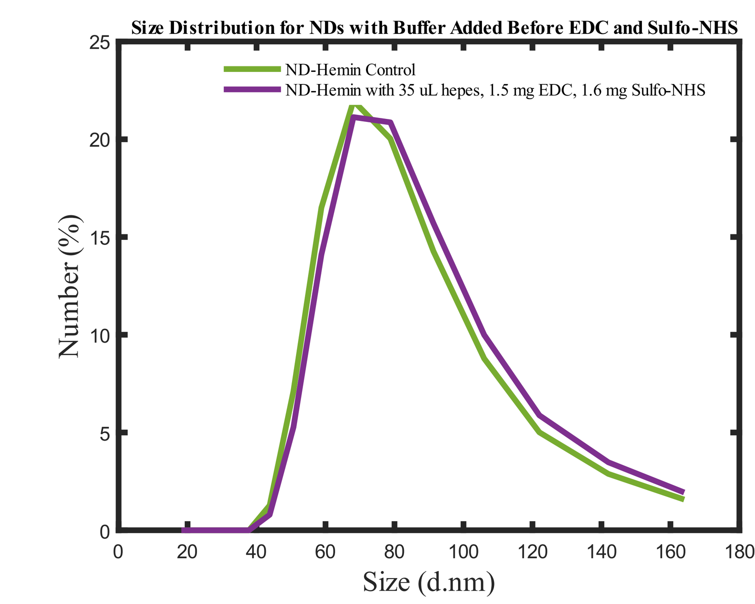
- Subtract the scattering curve from the actual curve to isolate dye signal
- By comparing to unconjugated dye, we can determine the efficiency of our process (Remaining Dye/Added Dye)
- Dye remaining in control samples indicates absorption to the ND surface

What's Next?

The Persistence of Agglomeration



- EDC and Sulfo-NHS drastically reduce pH and lead to irreversible particle agglomeration



- Adding buffer before EDC and Sulfo-NHS keeps the pH at 8 throughout the conjugation process, which prevents some agglomeration

Further Factors that may contribute to agglomeration:

- Loss of coating material during dialysis
- Dye less stable than water

Further Possible Solutions:

- Increase or modify emulsion material
- Utilize more stable conjugate materials

Further Studies

- More analysis: analyzing Fourier-transform spectroscopy to confirm covalent bond formation between ND-hemin and conjugates
- Emulsify nanodiamonds with other materials: oleic acid, other porphyrin materials
- Conjugate to biological materials (antibodies, proteins, and oligos)
- Conjugate to charge or spin labels for enhanced sensing
- Preform *in vivo* and *in vitro* sensing experiments

Acknowledgements

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