Design of Iron(II) Selective Optical Sensors

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Introduction

Why Iron(II):

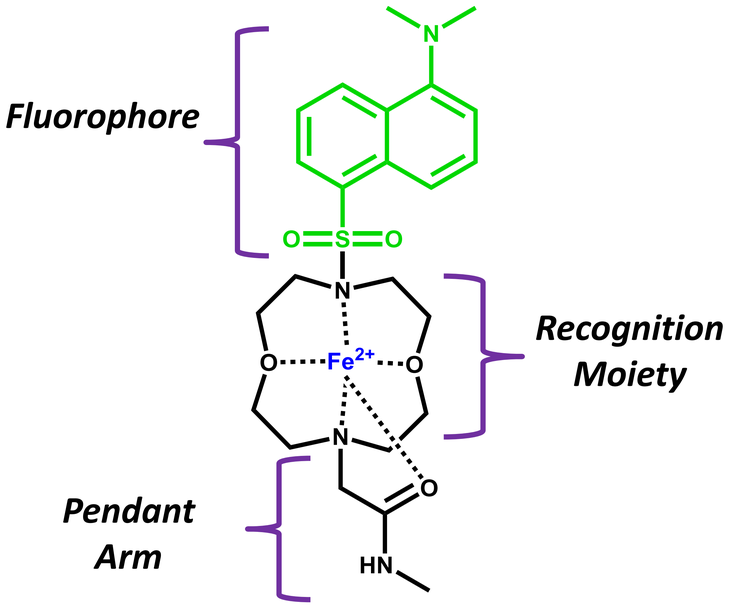
- Most abundant transition metal in the body
- Fe(II) most likely oxidation state in transport
- Ability to monitor Fe(II) in the cell provides better understanding of:
  - ➢ Cellular Concentration of Iron
  - ➢ Iron Transport & Function
- Iron overload linked to neurodegenerative disease states (Alzheimer's & Parkinson's)

Use Fluorescent Optical Sensors!

Sensor Design

Concerns:

- Selectivity
  - ➢ Binding competition with Zinc(II)
- Compatible in Cellular Conditions
- Tightness of Binding
  - ➢ Not too tight as to disrupt function of metal



Fluorophore

- ➢ Turn- off versus Turn-on Fluorescence

Recognition Moiety

- ➢ Donor atoms in chelating ring
- ➢ Size of macrocycle

Pendant Arm

- ➢ Steric effects
- ➢ Additional donor atom

Selectivity

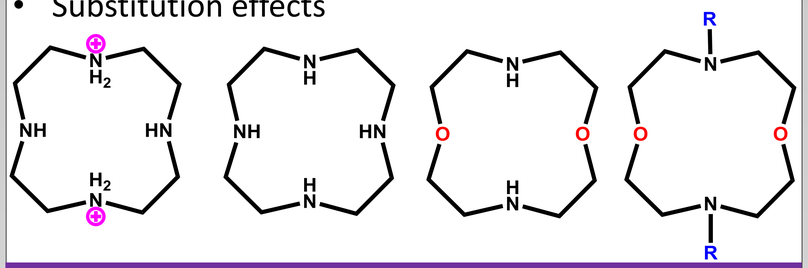
Nitrogen versus Oxygen Donors:

Nitrogen:

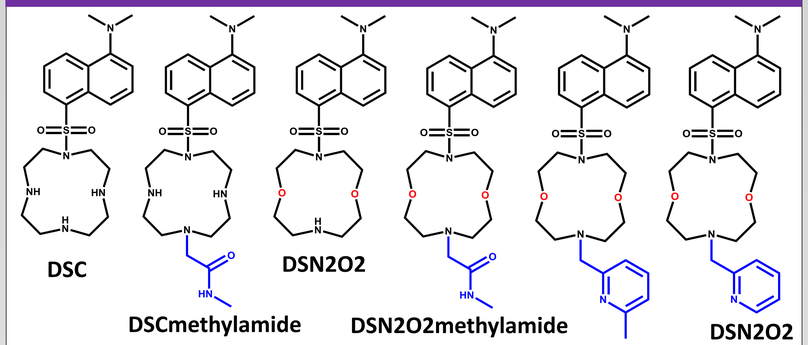
- Binds many metals
- Metal ion binding competes with protonation
- Substitution effects

Oxygen:

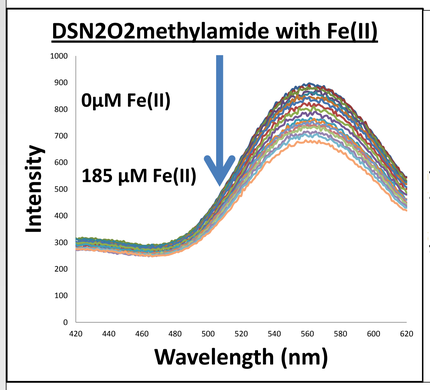
- More selective
- No protonation effects

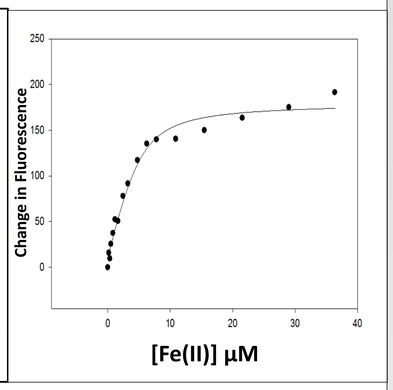


Fluorescence Studies



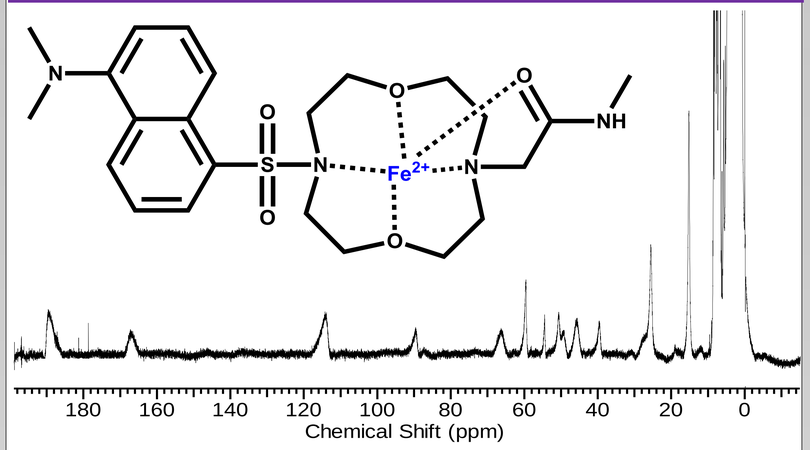
Conditions: 100 mM NaCl, 20mM HEPES, pH 7.0
5.0 µM Ligand
Ex. 335nm. Em. 420-620nm





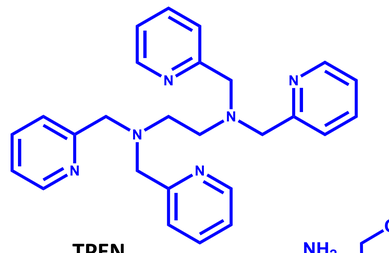
Ligands	K_d (µM)	
	Fe(II)	*Zn(II)*
DSC	Not Observed	< 1.1±.1
DSCmethylamide	< 1.5±.5	20.1±4.0
DSN2O2	< 1.4±.3	< 2.2±1.3
DSN2O2methylamide	< 1.6±.9	< 2.3±1.6
DSN2O2methylpyridine	< 2.1±.5	< 2.2±.8
DSN2O2pyridine	< 3.0±.4	< 3.5±.6

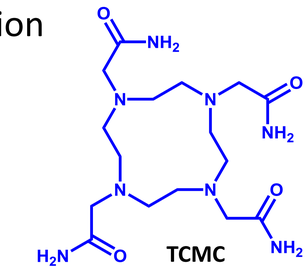
Paramagnetic ^{1}H-NMR

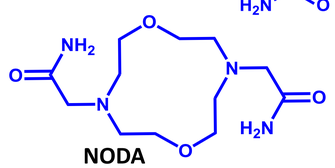


Conclusions & Future Work

- Paramagnetic NMR indicates sensors bind Fe(II) and binding contributes to fluorescence change
- Contrast in binding behavior between DSC and DSCmethylamide indicates that extra donor atom and steric effects of pendant arms favorable for Fe(II) selectivity
- Binding constants for DSN2O2 sensors not markedly different at present conditions
  - ➢ Add competing ligand to weaken apparent binding constant
  - ➢ Allows for differentiation







Acknowledgments

National Institutes of Health
CURCA Center for Undergraduate Research and Creative Activities
NSF