Two-Component Fluorescence Sensing of Saccharides

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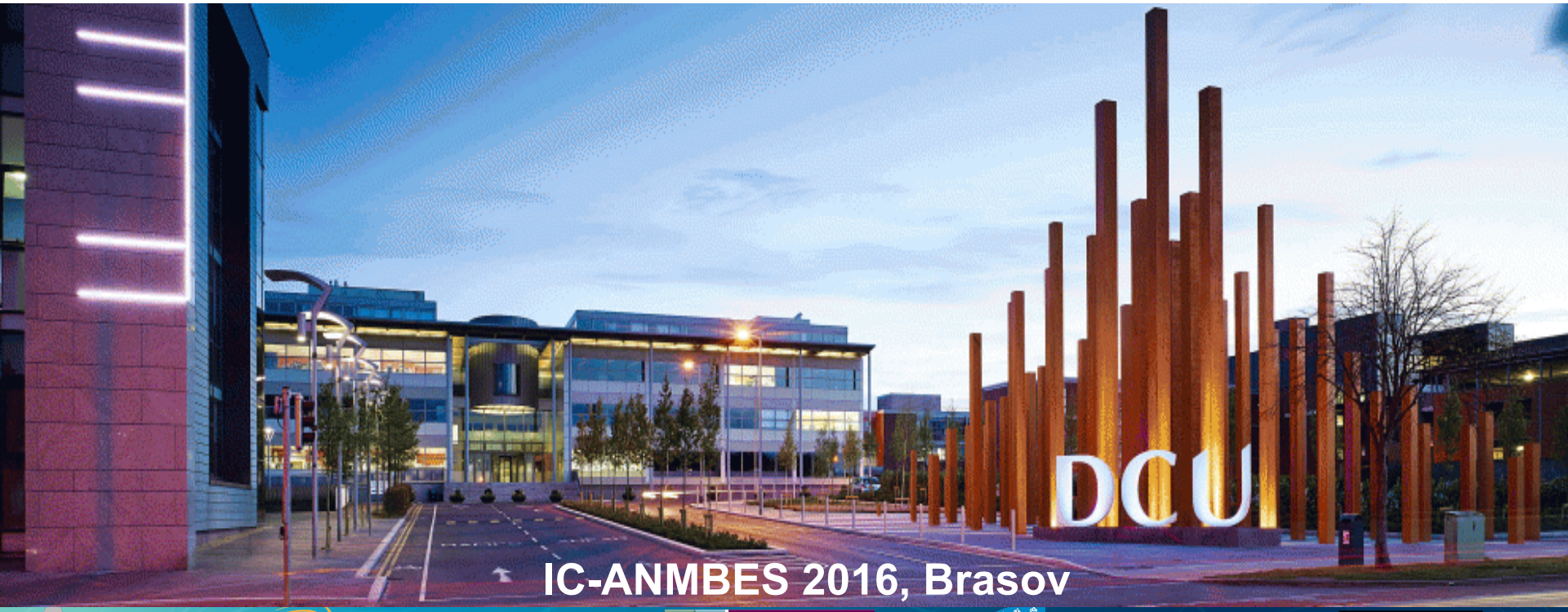


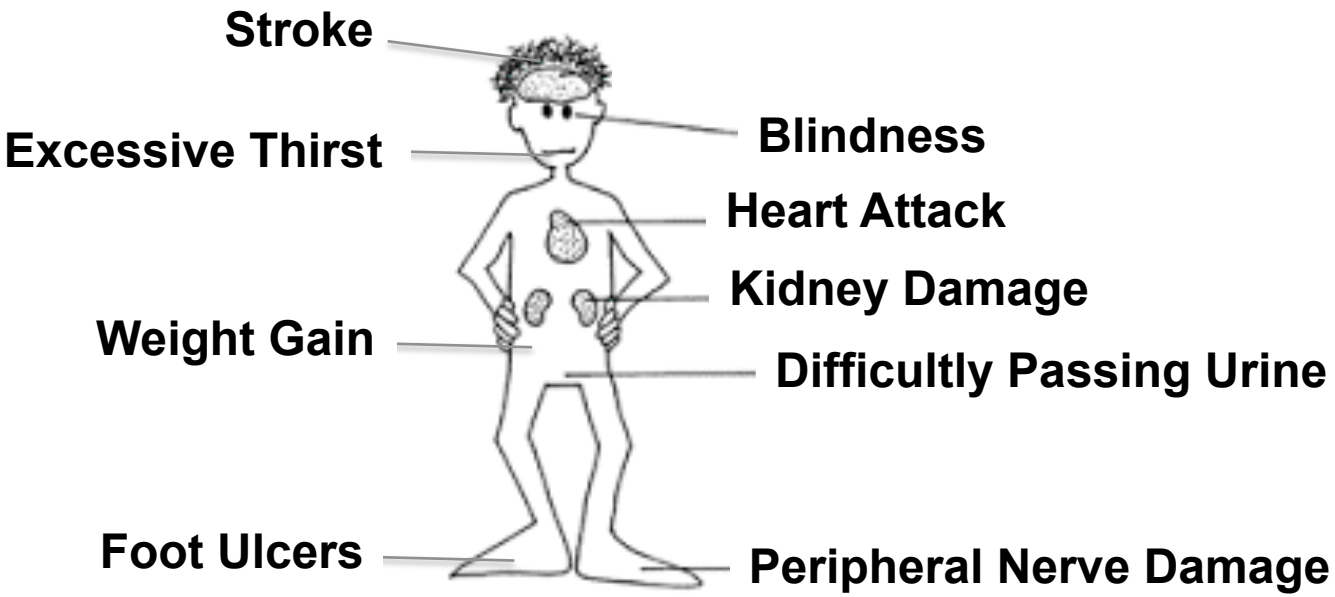
IC-ANMBES 2016, Brasov

Overview

- Background
  - Diabetes – Side Effects
  - Monitoring Devices
- Project Goal
- Boronic Acids (BAs) for Sugar Recognition
- Direct Sensing
- Indirect Sensng
- Conclusions
- Future Work

Importance of Saccharide Sensing

- Disease: Diabetes and the consequential side effects



- Monitoring glucose levels to prolong life expectancy
- Currently no noninvasive, continuous monitoring systems available
- Demonstrates a need for real-time, non-invasive monitoring

Current Monitoring Methods

Implanted Wearable Devices

Roche

ACCU-CHEK®

Advantages:

- Real-time monitoring
- Continuous
- Coupled to insulin pump
- Elimates injections *via* syringe

Disadvantages:

- Invasive

Finger Pricking Method

Advantages:

- Minimally Invasive

Disadvantages

- Not continuous
- Insulin injections required
- Miss episodes of hyper- and hypoglycaemia

https://www.accu-chek.co.uk/gb/products/

Contact Lenses – The Answer!

Electrochemical sensor in a wearable platform

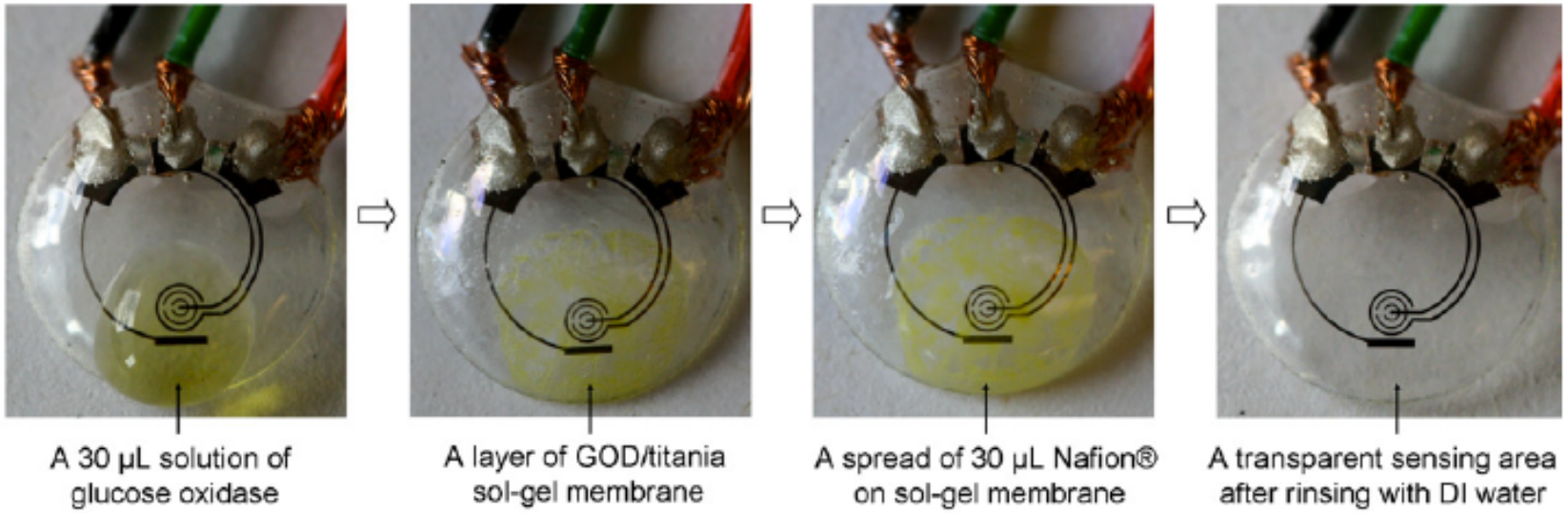
- Battery Powered ✗
- Interference from Electroactive Species in Ocular fluid ✗
- Use of Enzymes ✗

Google

NOVARTIS

H. Yao, et al, *Biosensors and Bioelectronics*, **2011**, *26*, 3290-3296
B.E. Watt, et al, *Toxicol. Rev.*, **2004**, *23(1)*, 51-57

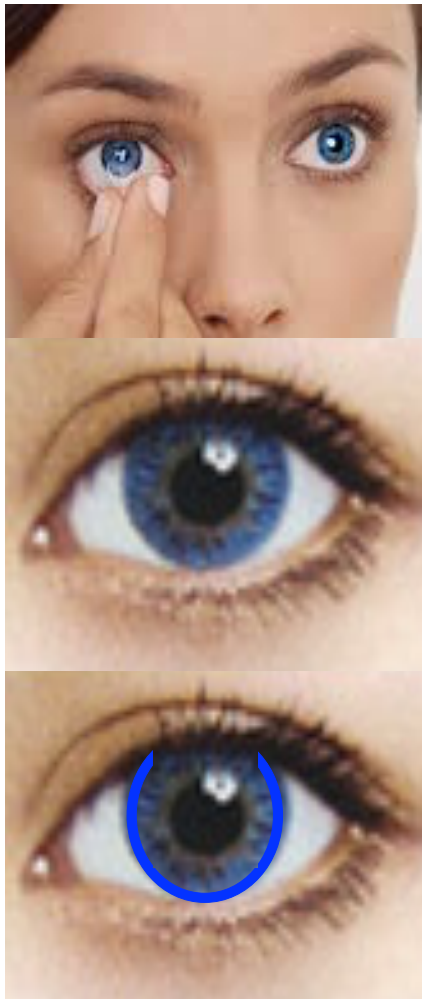
Realistically....Not a Real Working Device

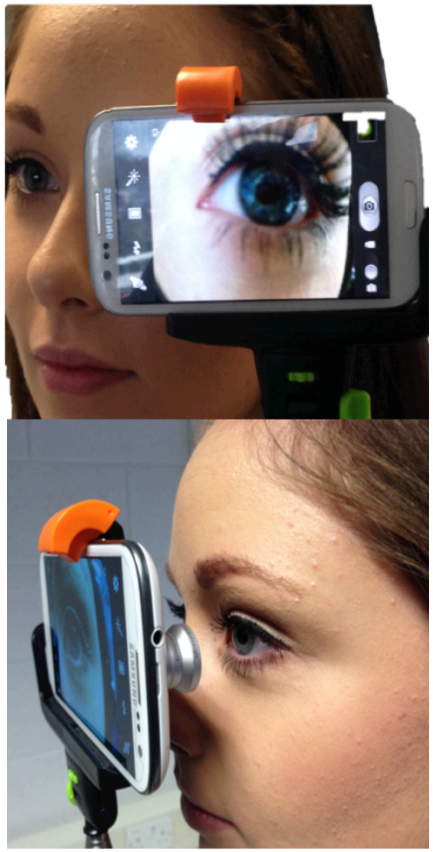


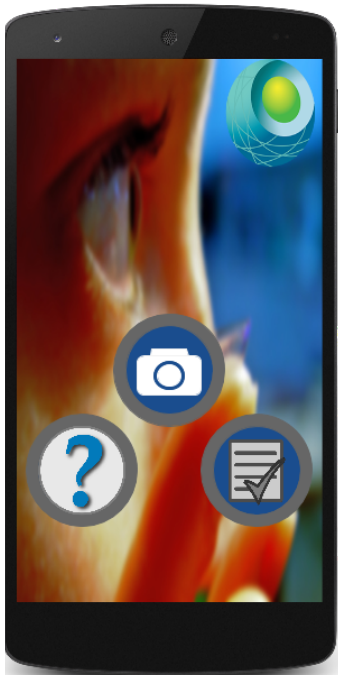
- Attached to a BASi Epsilon- EC Potentiostat +400 mV
- Sensing platform proposes glucose monitoring between 0.5-50 mM
- Ocular glucose range is 0.05-0.5 mM and up to 5 mM in diabetics
- Major shortcomings to meet immediate expectations

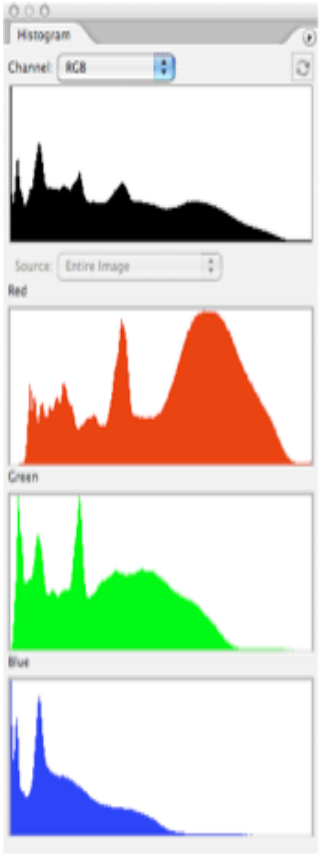
H. Yao, et al, *Biosensors and Bioelectronics*, **2011**, *26*, 3290-3296

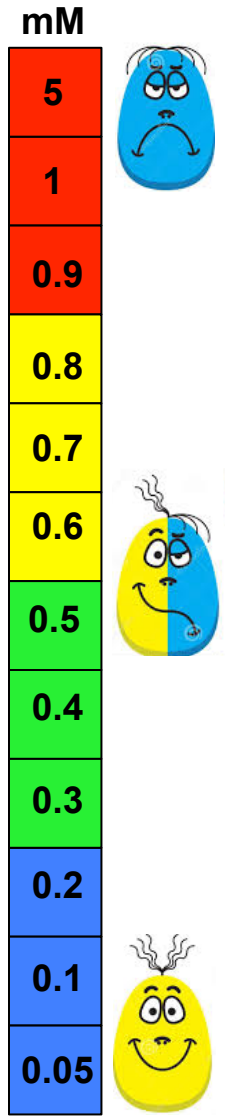
The Solution!



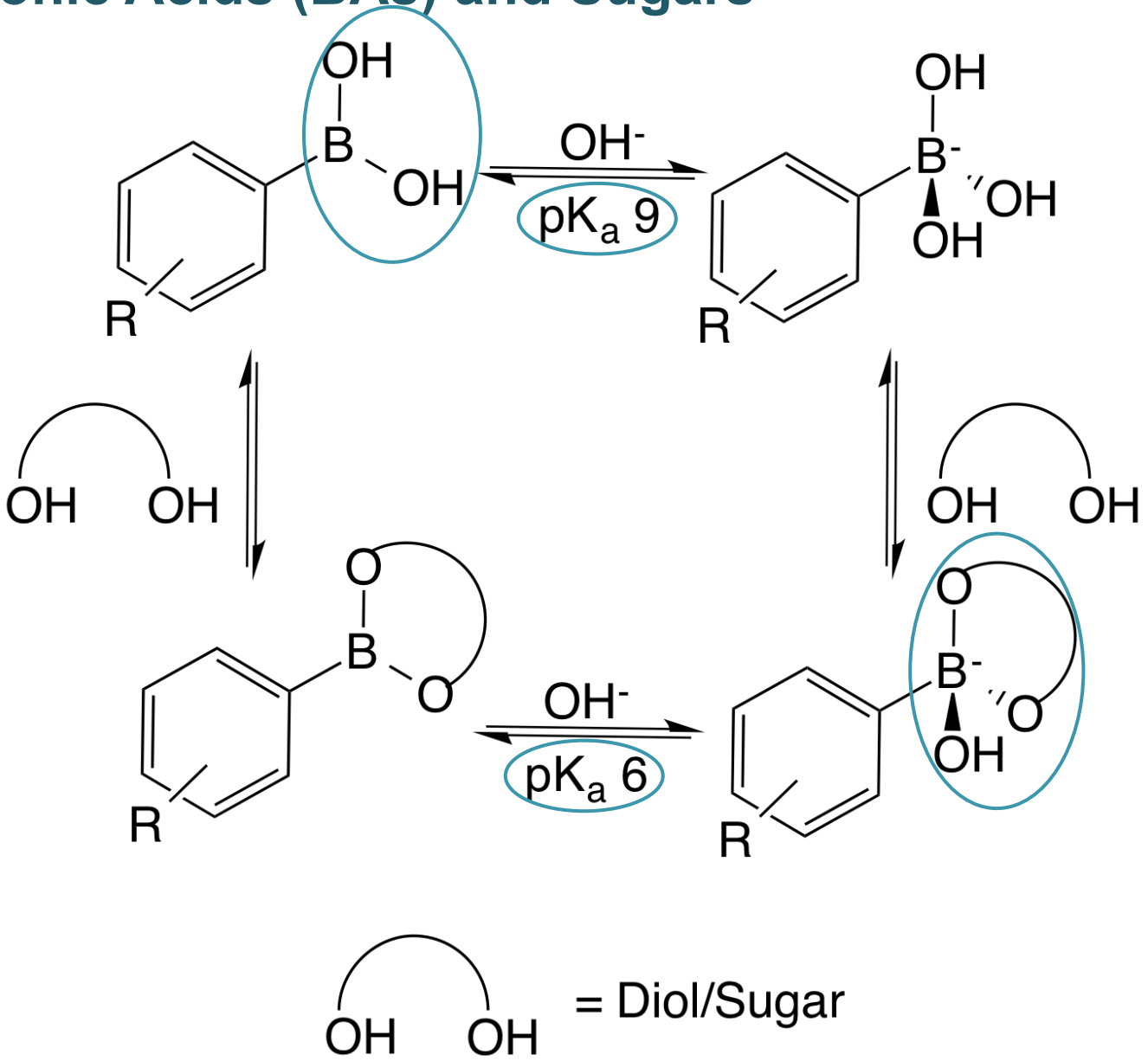






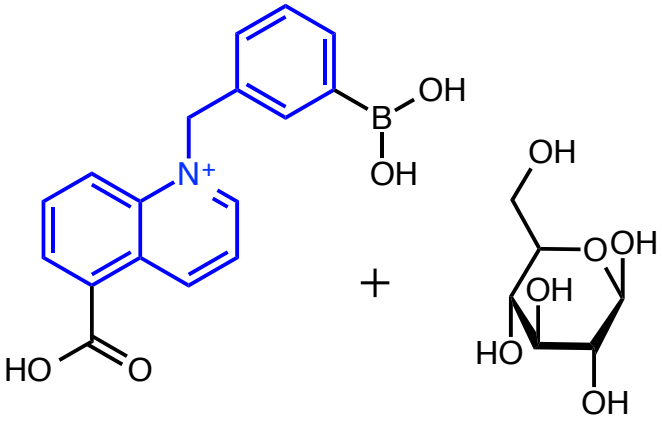


Boronic Acids (BAs) and Sugars



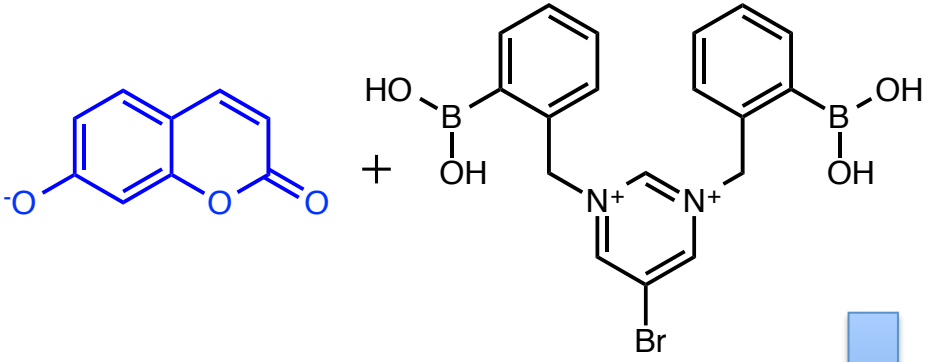
Direct vs. Indirect Sensing

Direct Sensing

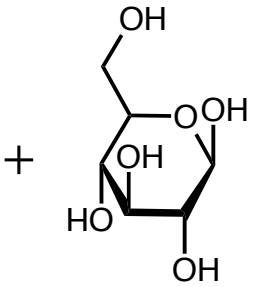


Fluorescence Decrease

Indirect Sensing



Fluorescence Decrease

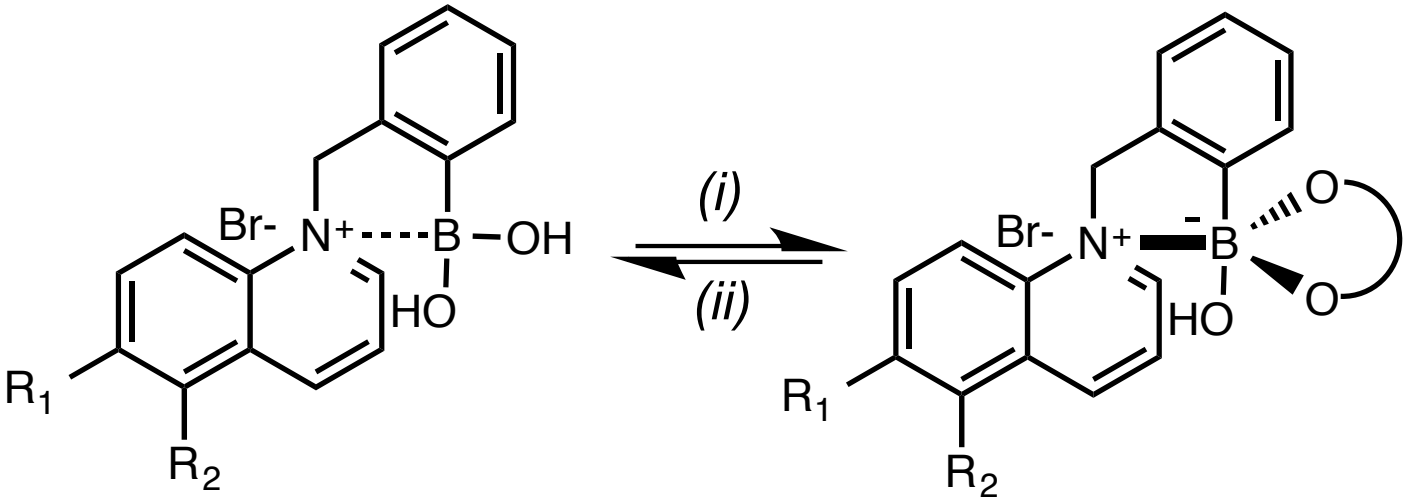


Fluorescence Increase

Fluorophore

Direct Sensing

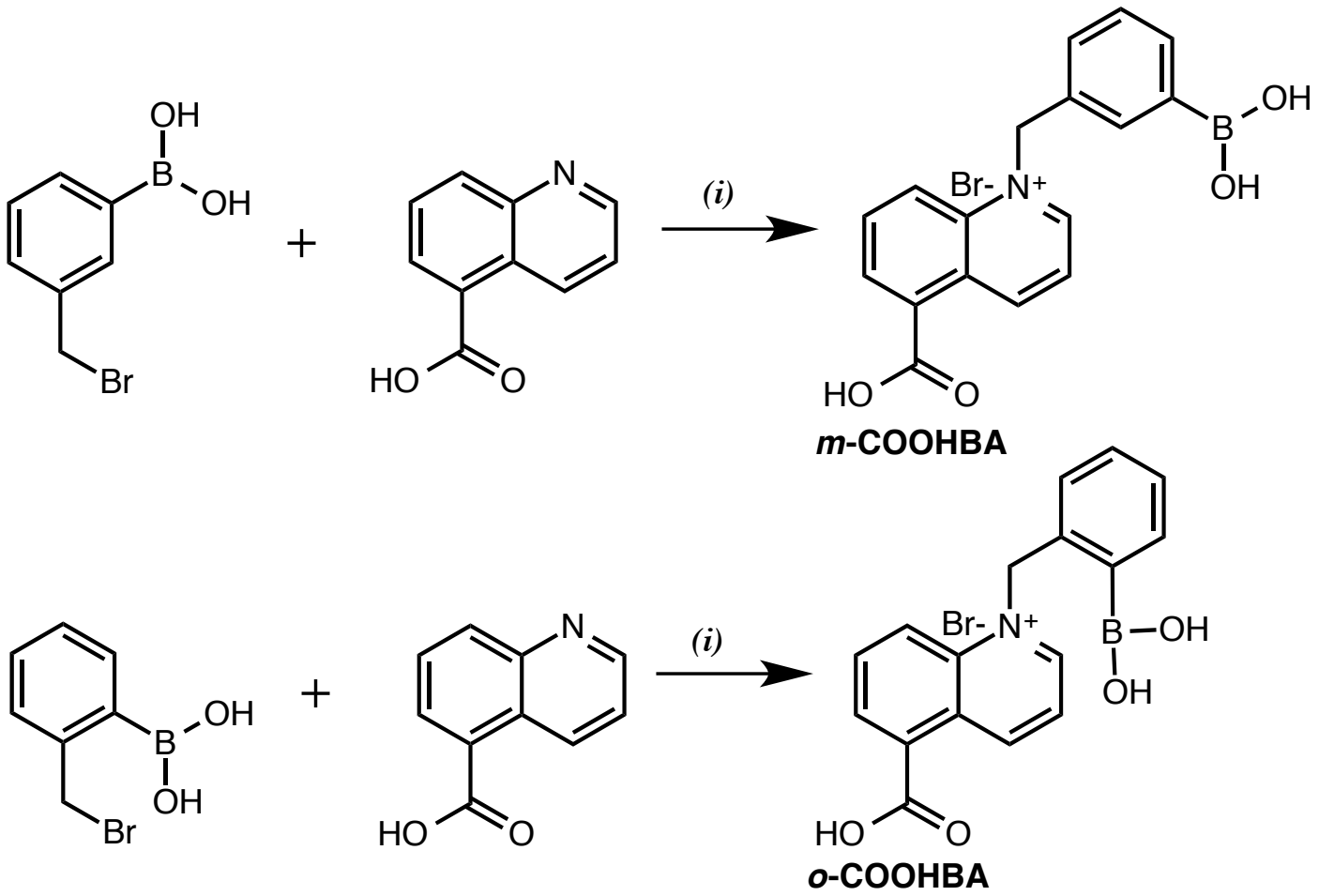
Direct Sensing



Fluorescent **Non-Fluorescent**

(i) Addition of OH^- ions/glucose
(ii) Addition of water/removal of glucose

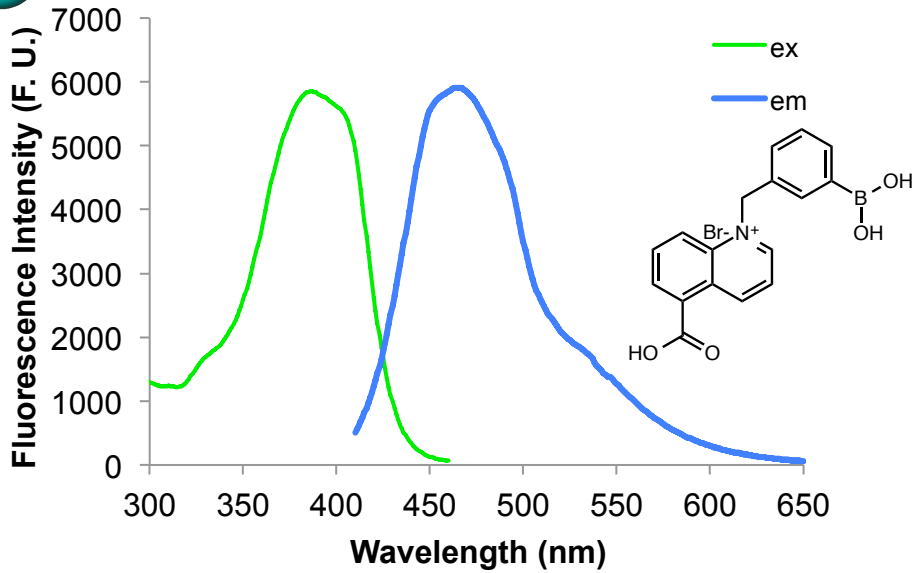
Synthesis of COOHBA Sensors

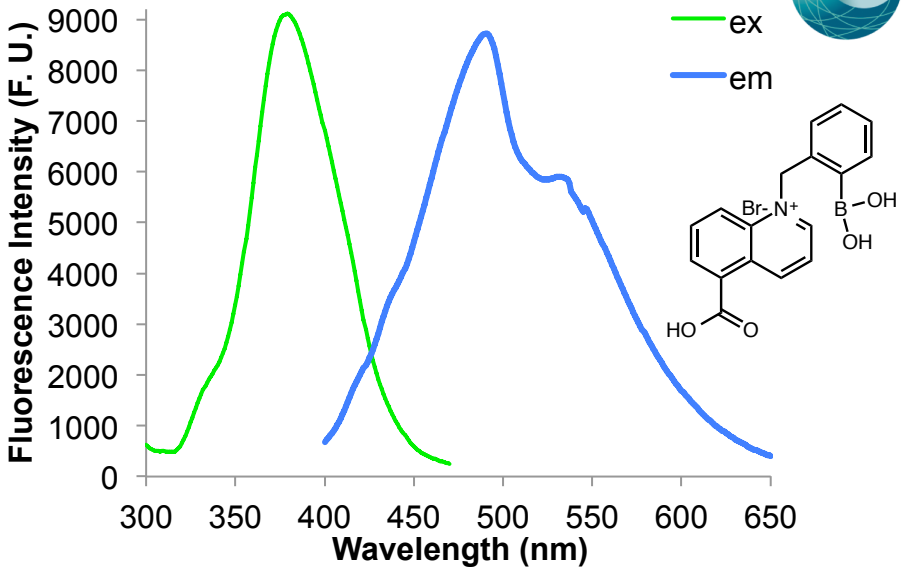


(i) Anhydrous dimethylformamide, N_2, 80 ^{0}C for 48h.

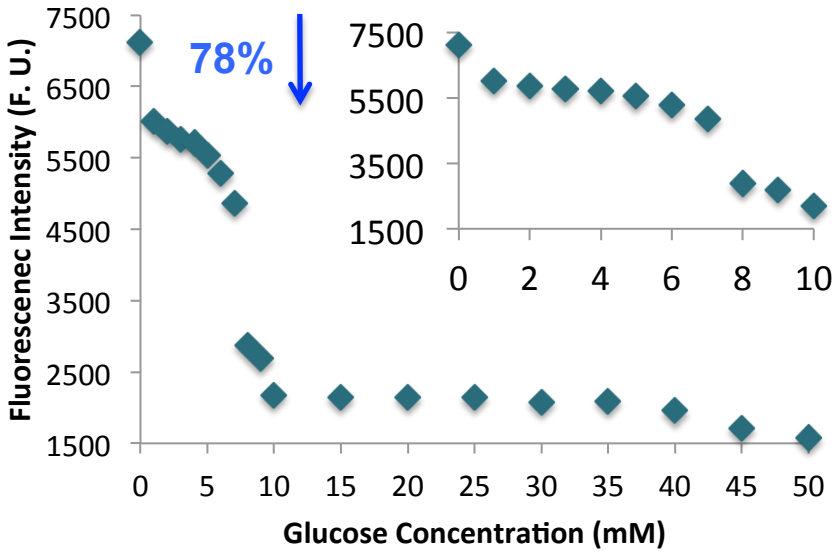
Successful synthesis of novel BA sensors were confirmed by NMR.

Fluorescence Results

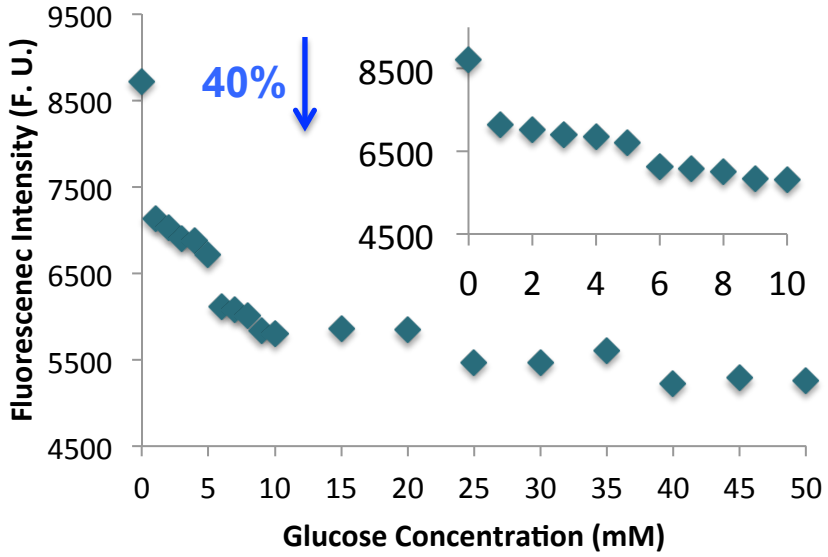




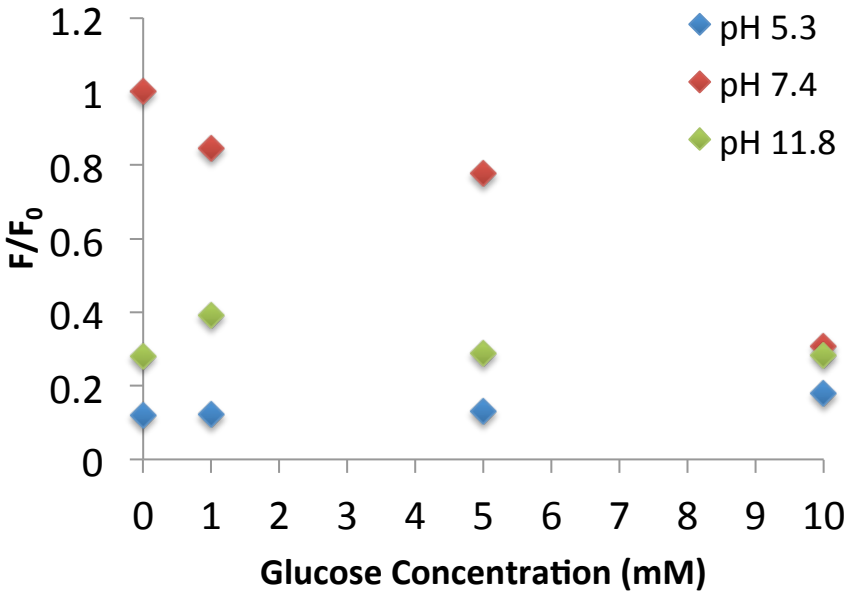
m-COOHBA *0.5 mM in pH 7.4 phosphate buffer; Excitation 390 nm; Emission 465 nm*

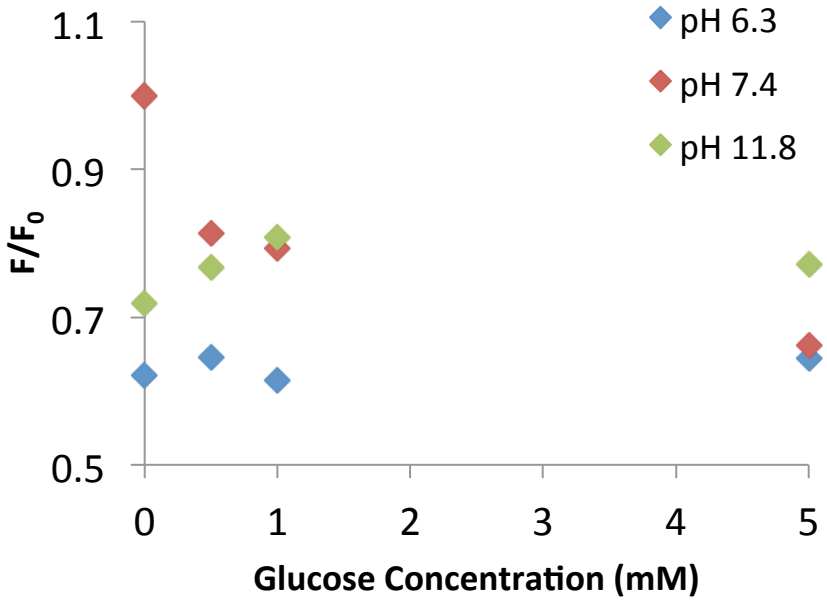


o-COOHBA *0.5 mM in pH 7.4 phosphate buffer; Excitation 380 nm; Emission 485 nm*

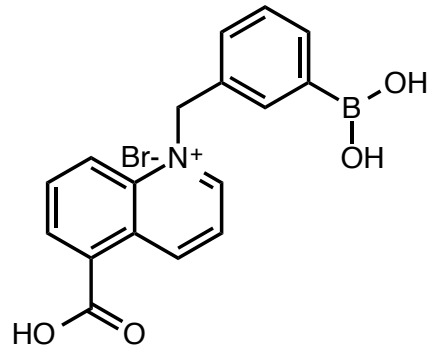


pK_a Investigation – Glucose Sensing pH Range

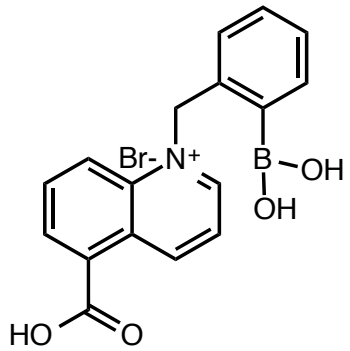




Glucose response for m-COOHBA and o-COOHBA (0.5 mM) in different pH buffer solutions ranging from pH 5-11.



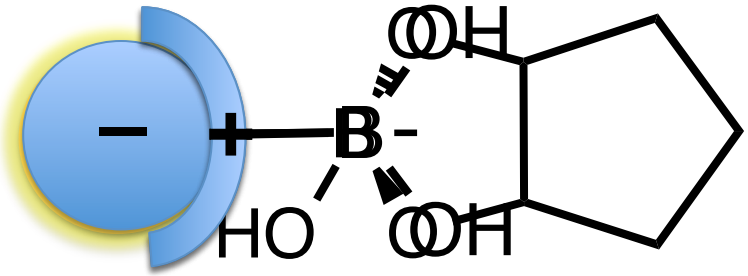
***m*-COOHBA**



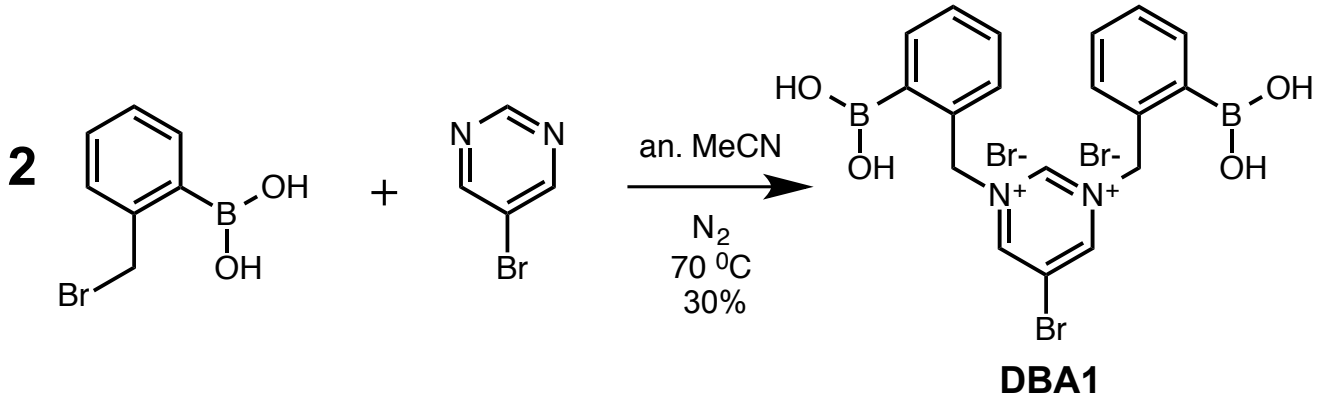
***o*-COOHBA**

Indirect Sensing

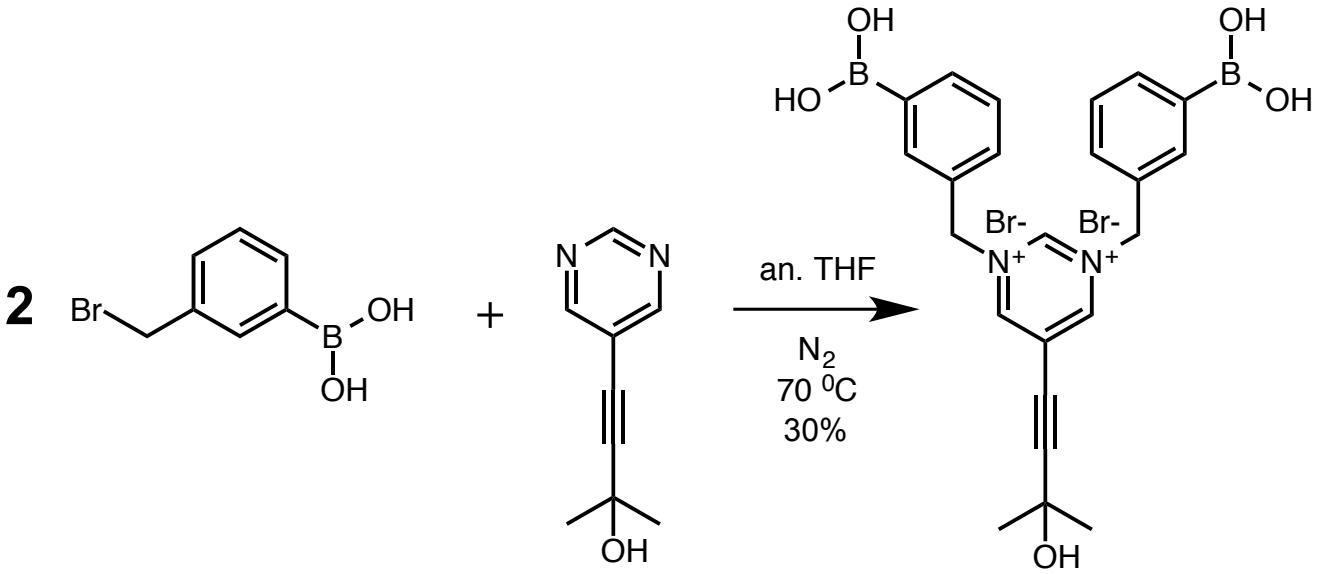
Two-Component Sensing



Indirect Sensing – Sensor Synthesis

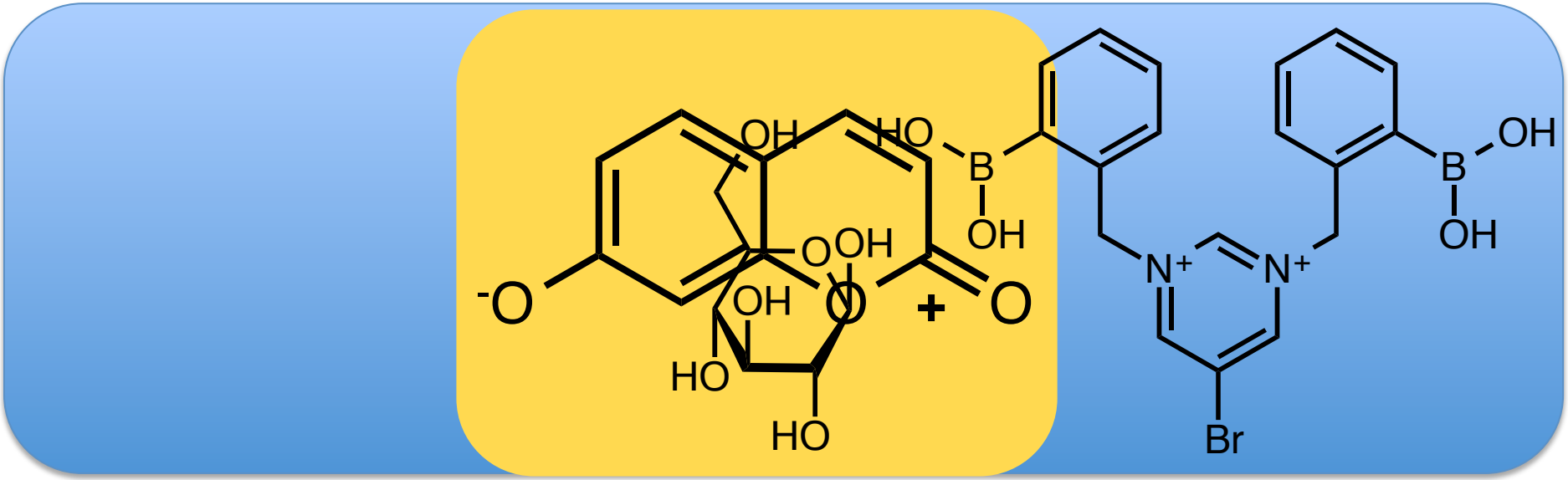


DBA1



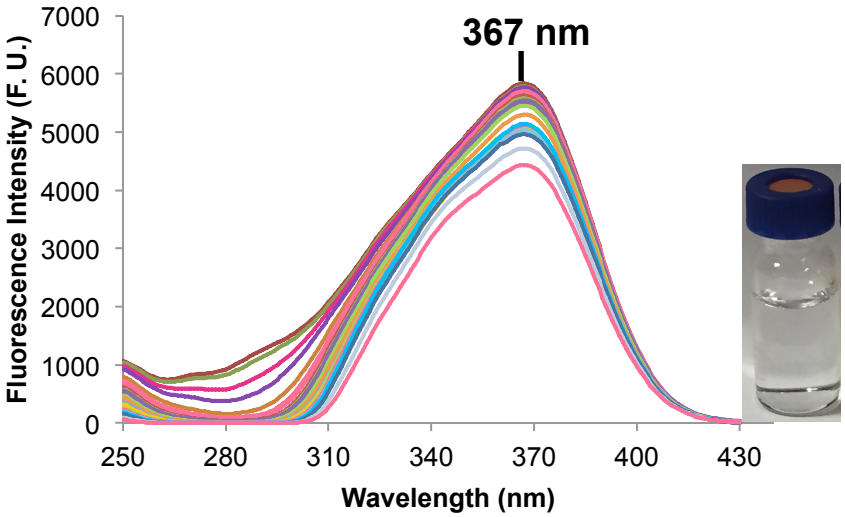
DBA2

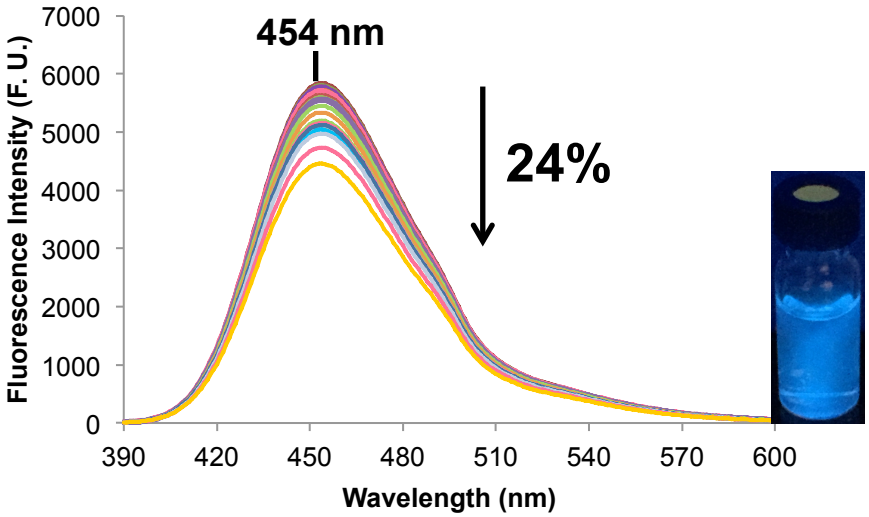
Two-Component Sensing



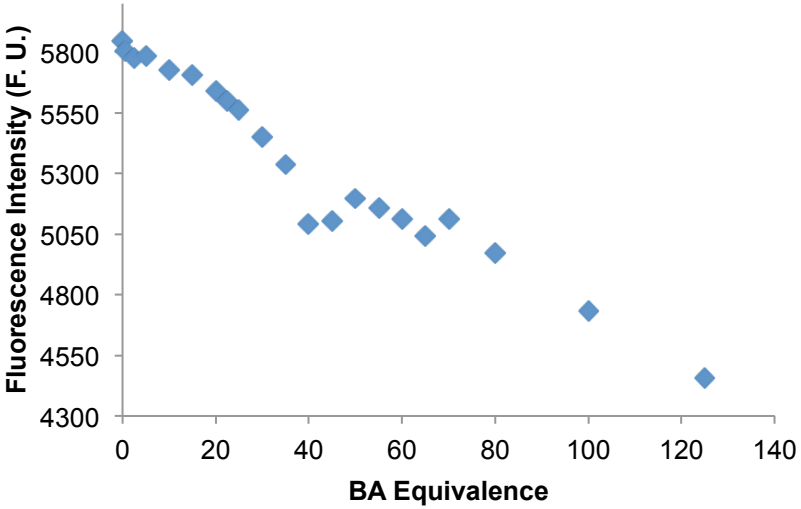
Non-Fluorescent Fluorescent

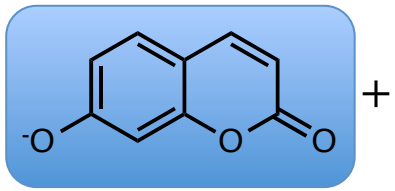
Two-Component Sensing – Fluorescence Quenching





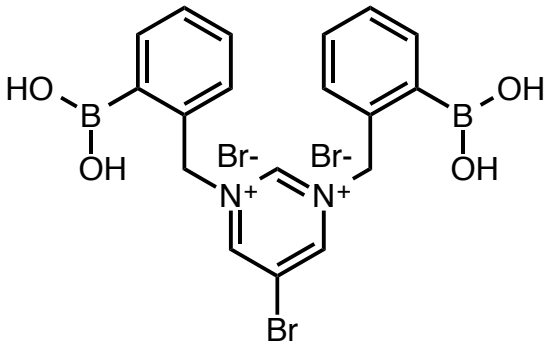
Excitation and emission spectra of 4 μM 7HC in pH 8.12 buffer solution with increasing DBA1 concentrations up to 0.5 mM (125 eq.); Medium sensitivity; 2.5 nm bandwidth





7HC

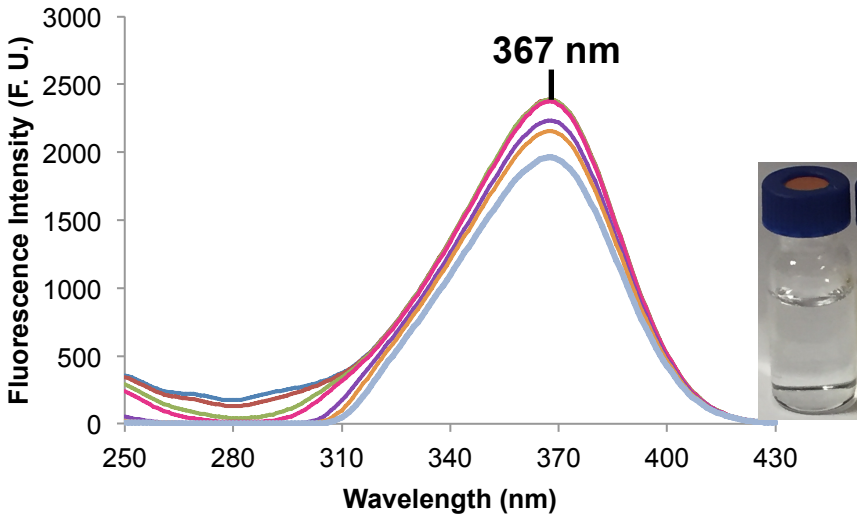
+

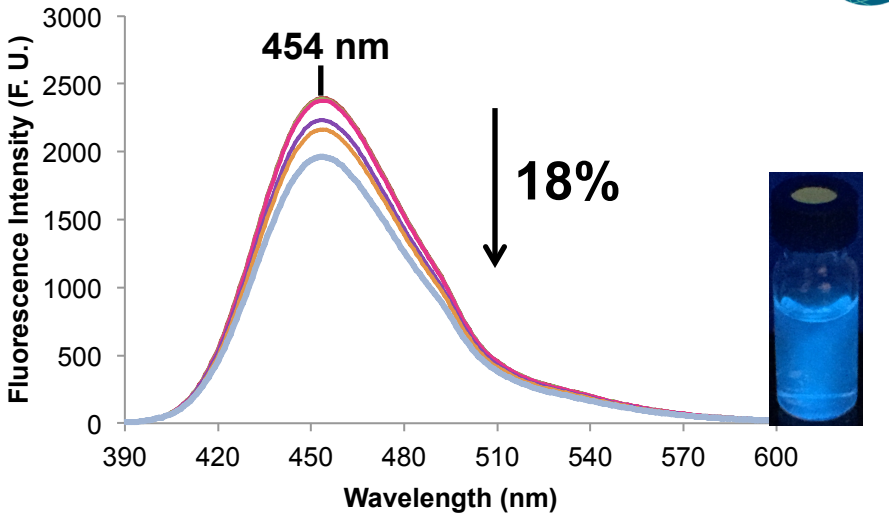


DBA1

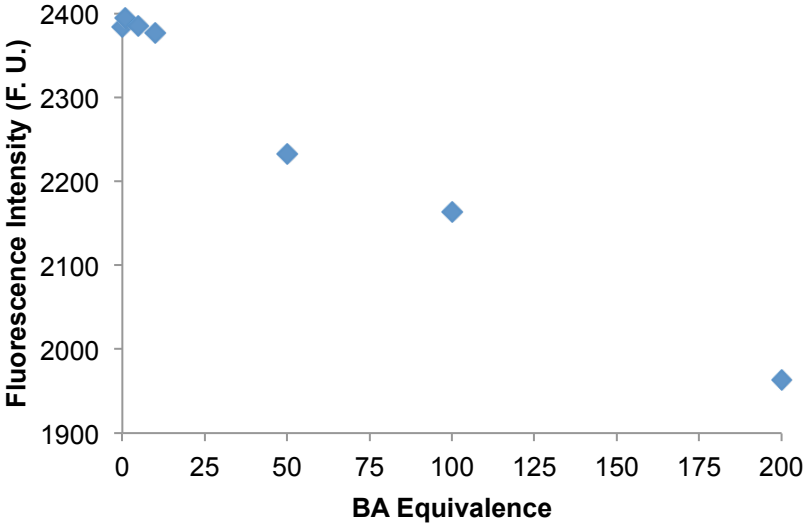
Fluorescence OFF

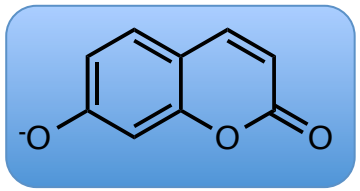
Two-Component Sensing – Fluorescence Quenching





Excitation and emission spectra of 4 μM 7HC in pH 8.88 buffer solution with increasing DBA1 concentrations up to 0.8 mM (200 eq.); Medium sensitivity; 2.5 nm bandwidth





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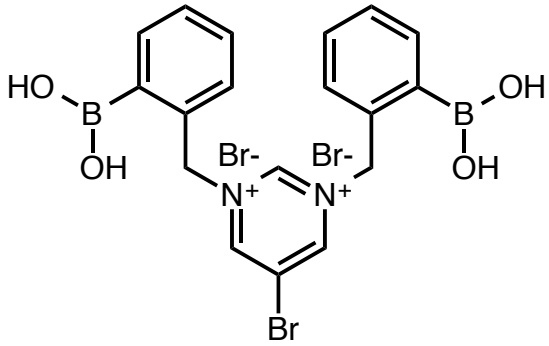
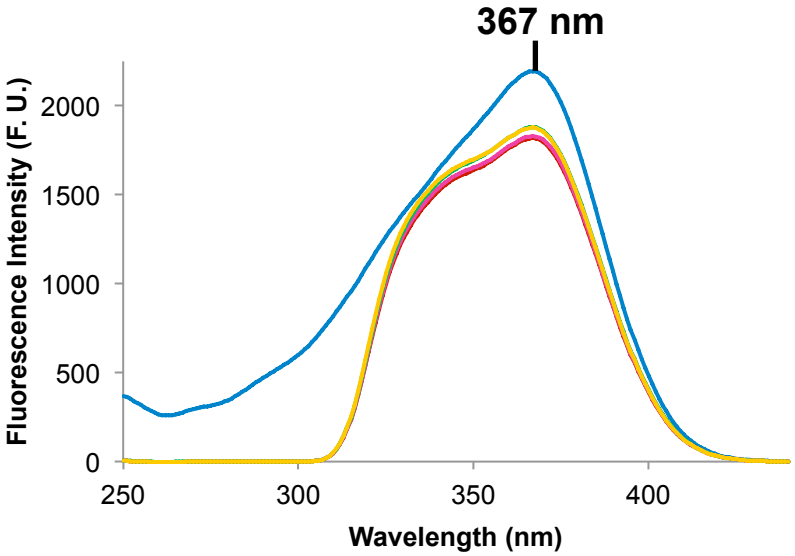
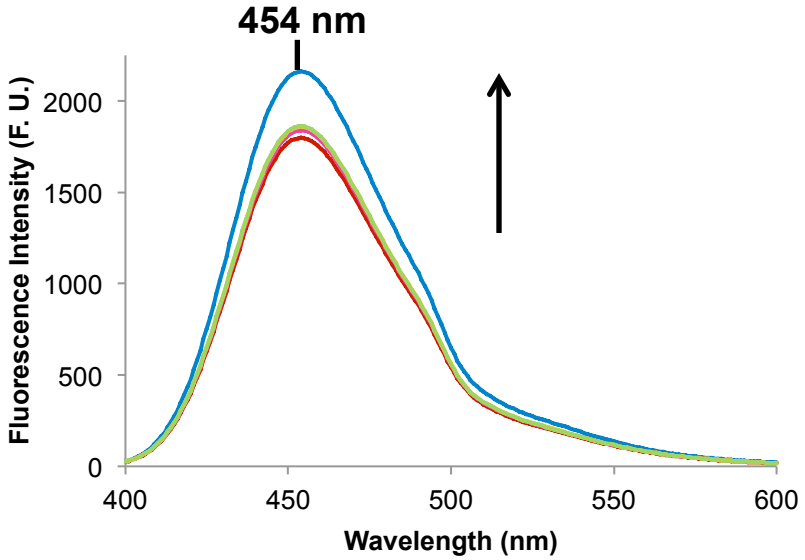


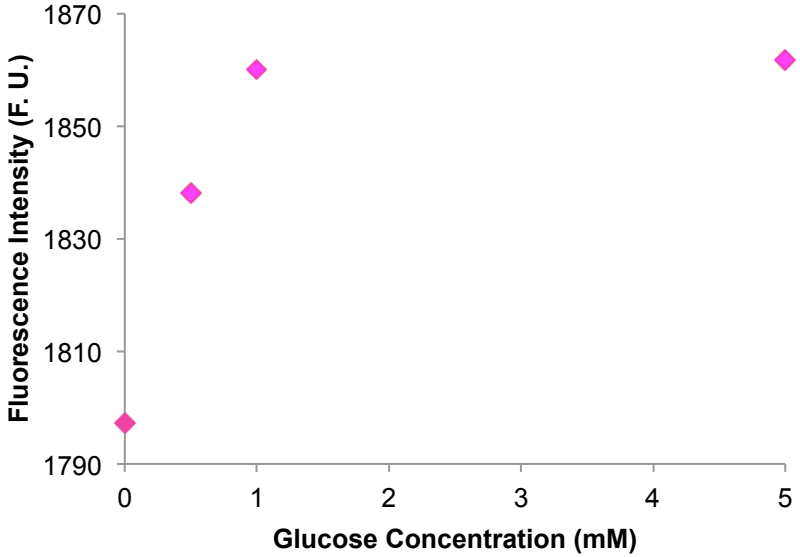
Fluorescence OFF

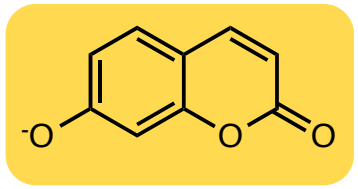
Two-Component Sensing – Fluorescence Recovery





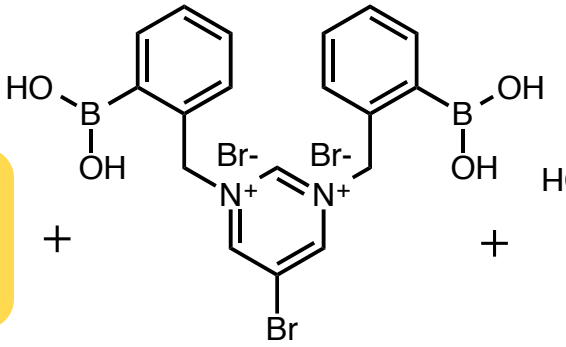
Excitation and emission spectra of 7HC (4 μM) and DBA2 (700 μM) (1:175 eq.) in pH 8.12 buffer solution with increasing concentrations of glucose up to 5 mM; Medium sensitivity; 2.5 nm bandwidth





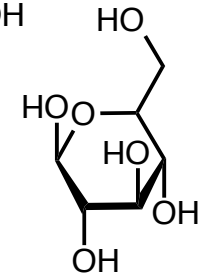
7HC

+



DBA1

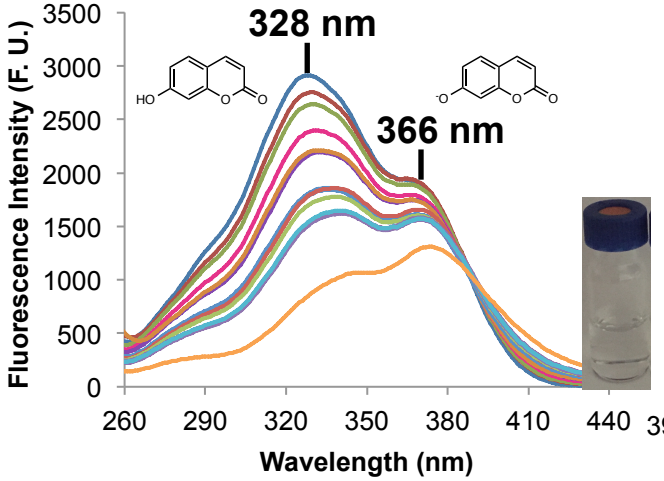
+

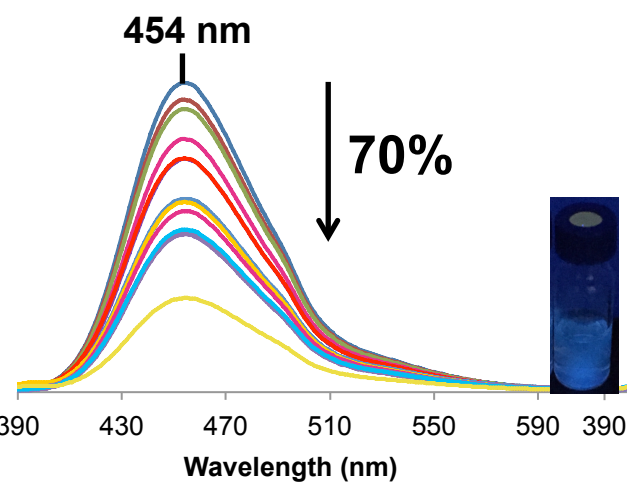


Glucose

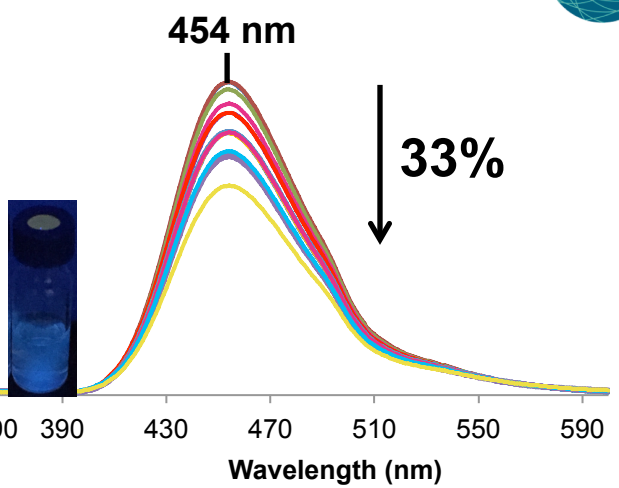
Fluorescence ON

Two-Component Sensing – Fluorescence Quenching



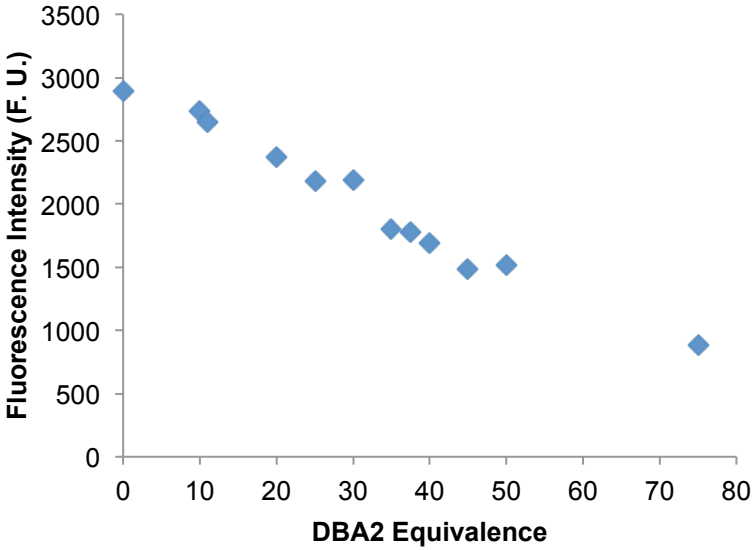


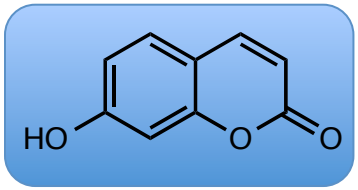
λ_{ex} = 328 nm



λ_{ex} = 366 nm

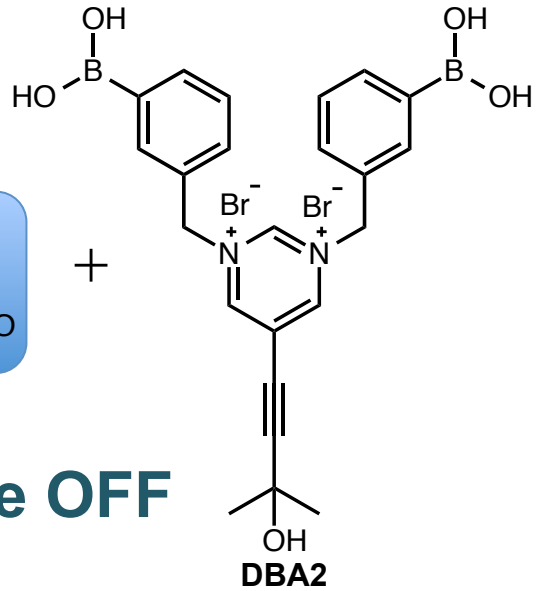
Excitation and emission spectra of 4 μM 7HC in pH 7.4 with minimal MeOH (40 μL) with increasing DBA2 concentrations up to 0.3 mM (75 eq.); Medium sensitivity; 2.5 nm bandwidth





7HC

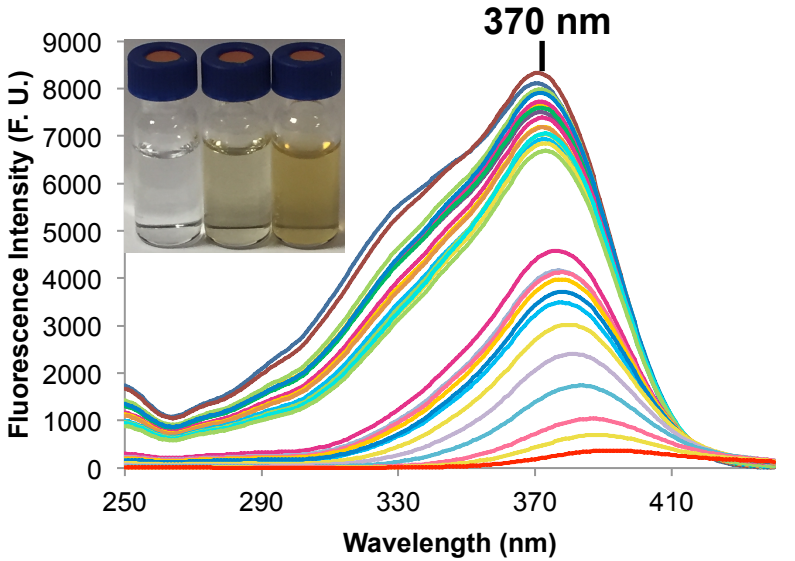
+

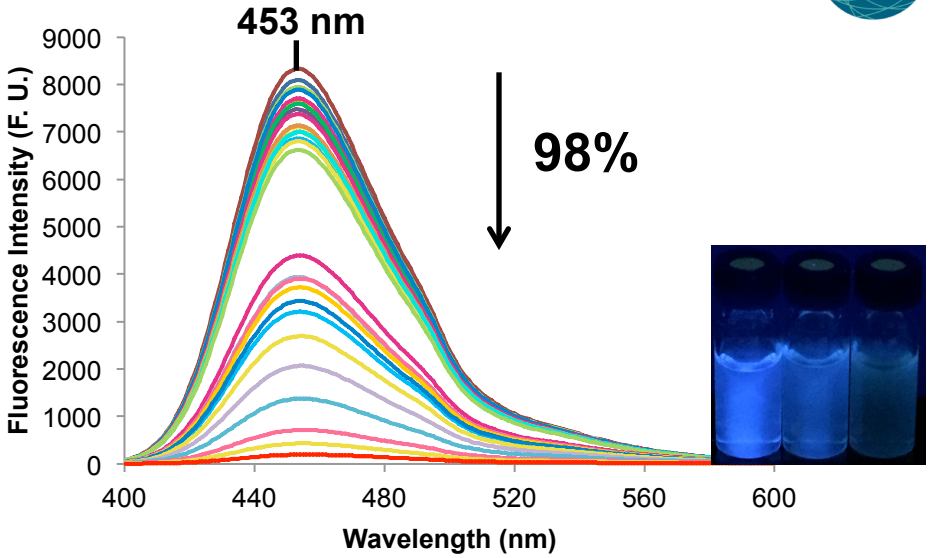


DBA2

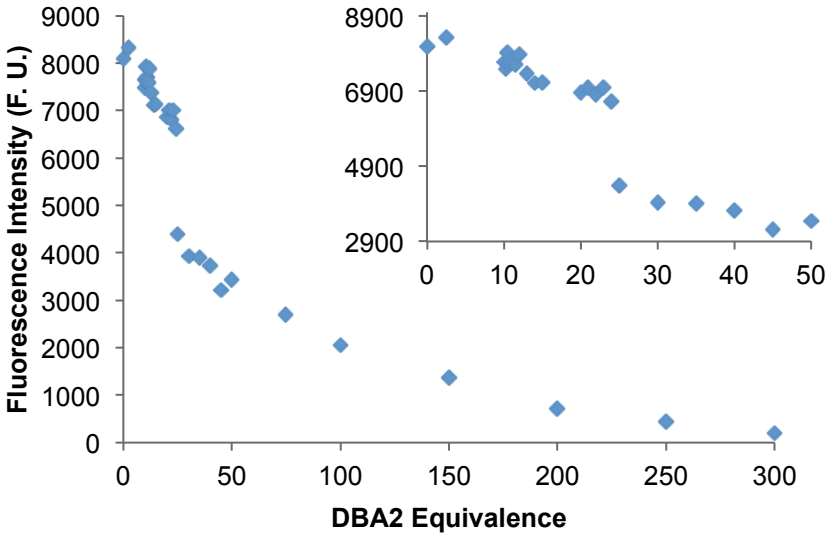
Fluorescence OFF

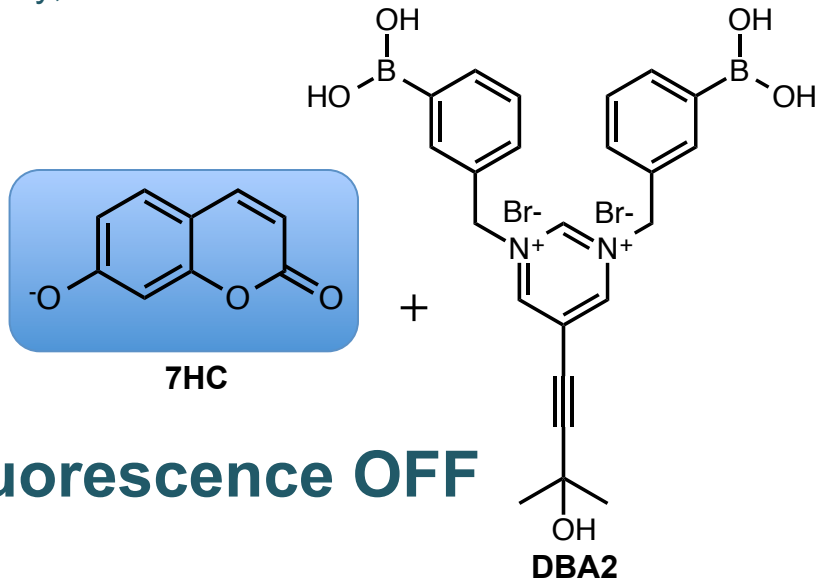
Two-Component Sensing – Fluorescence Quenching





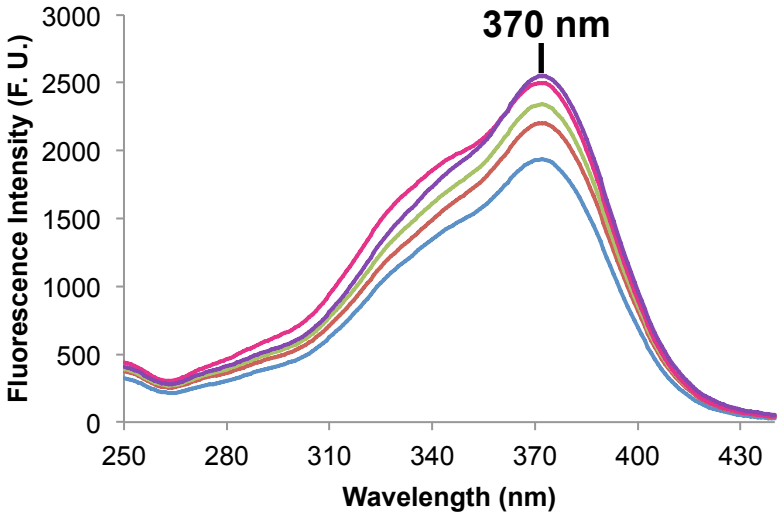
Excitation and emission spectra of 4 μM 7HC in pH 7.4:MeOH (1:1) (pH 8.6) with increasing DBA2 concentrations up to 1.2 mM (300 eq.); Medium sensitivity; 2.5 nm bandwidth

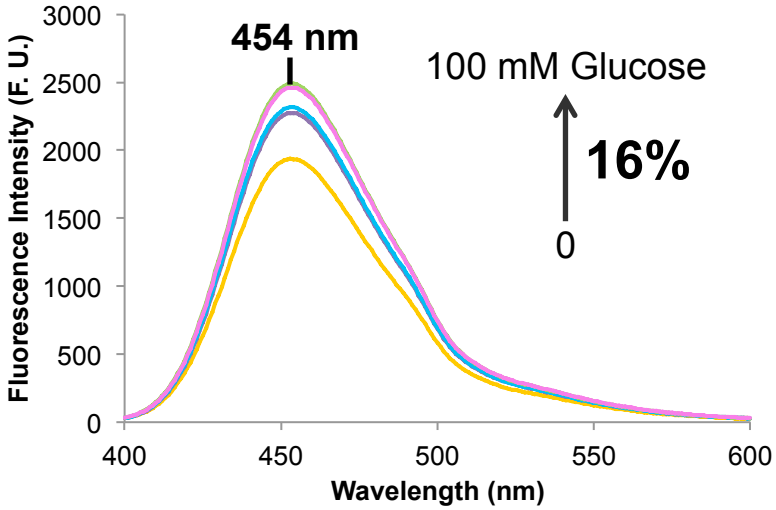




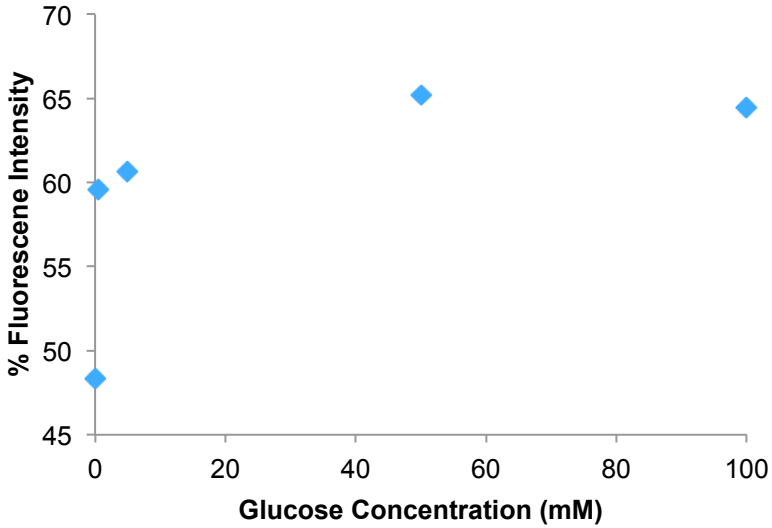
Fluorescence OFF

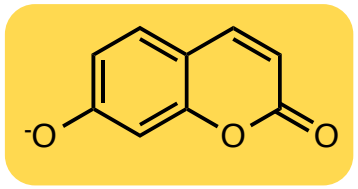
Two-Component Sensing – Fluorescence Recovery





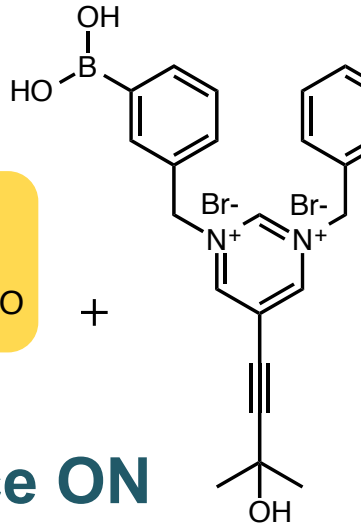
Excitation and emission spectra of 7HC (4 μM) and DBA2 (80 μM) (1:20 eq.) in pH 7.4:MeOH (1:1) (pH 8.6) with increasing concentrations of glucose up to 100 mM; Medium sensitivity; 2.5 nm bandwidth





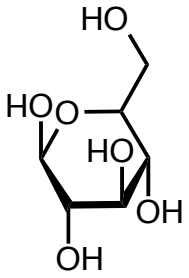
7HC

+



DBA2

+



Glucose

Fluorescence ON

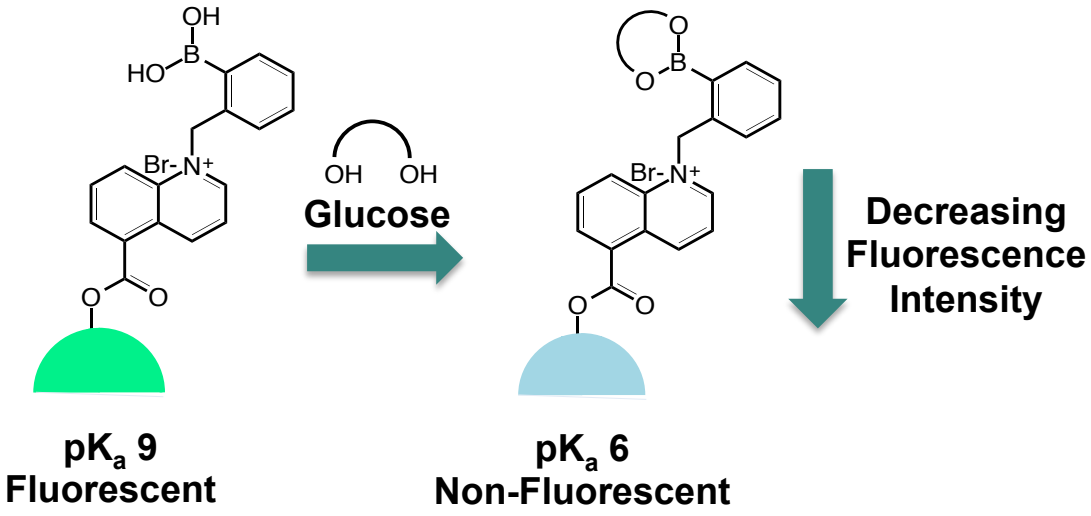
Conclusions and Future Work

Conclusions

- Novel BAs are capable of direct and indirect glucose sensing
- -COOH substituent for desired anchoring possibilities
- Two-Component Sensing depends on the pK_a of the fluorophore and hence, the pH of the buffer solution

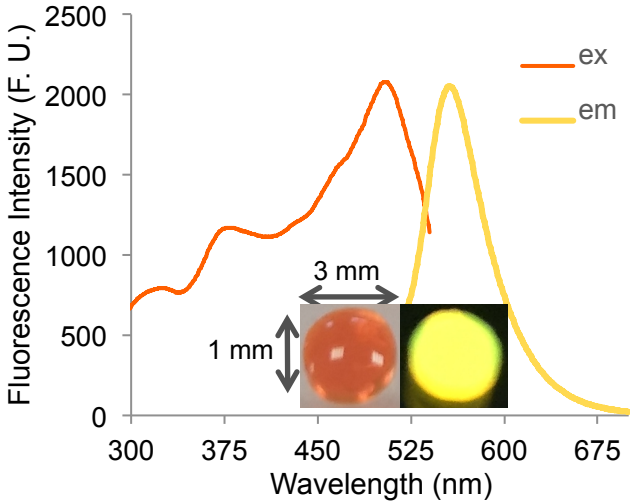
Future Work

- Immobilisation of the sensors on to a lens-like platform
- The incorporation of the two component sensing system in to ionogels



pK_a 9
Fluorescent

pK_a 6
Non-Fluorescent



Thanks to…..

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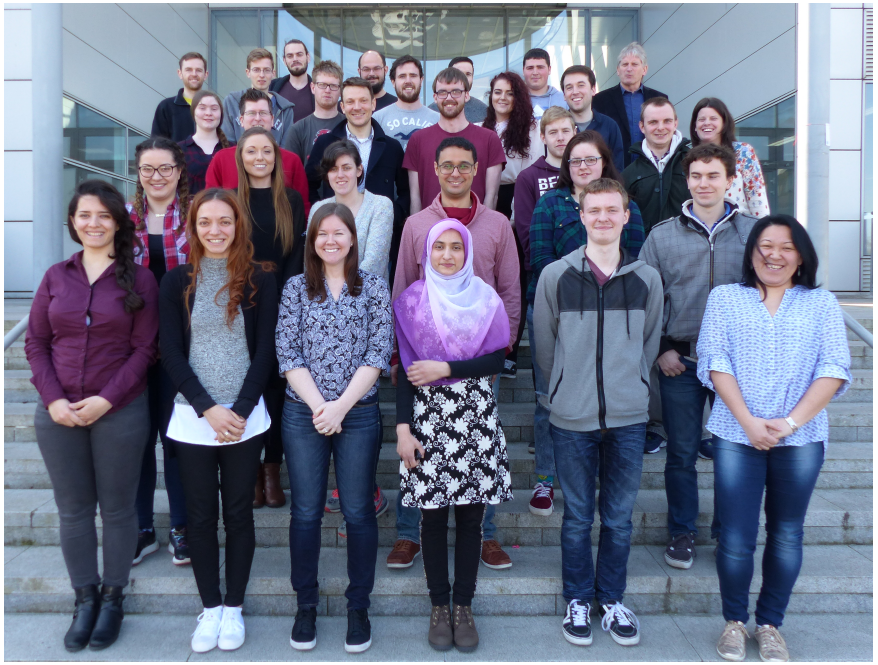
- Science Foundation Ireland & INSIGHT Centre (SFI/12/RC/2289)



Thank You for Your Attention!

SEVENTH FRAMEWORK PROGRAMME
MARIE CURIE ACTIONS
MASK
Project no: 269302
Materials and Advanced Sensor Knowledge Exchange
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ORGANIC BIOELECTRONICS
NAPES
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COMMON SENSE
MARINE SENSORS - MARINE MONITORING
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