Glucose Bio-Sensing in Real-Time Using Boronic Acid Derivatives

Danielle Bruen, Larisa Florea* and Dermot Diamond

Insight Centre for Data Analytics, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland

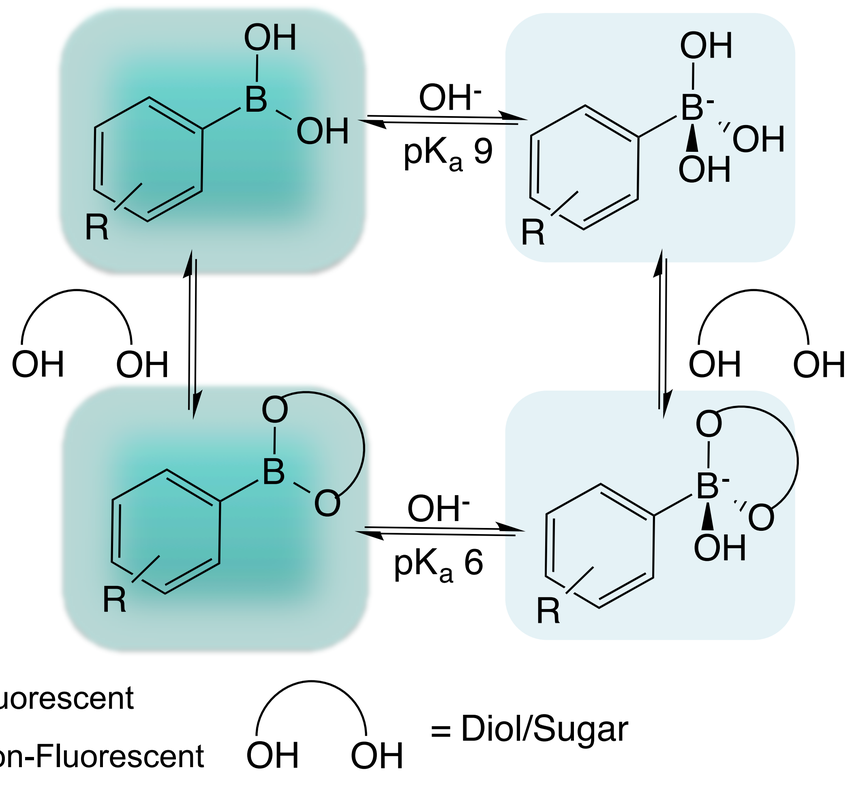
Centre for Data Analytics

Insight

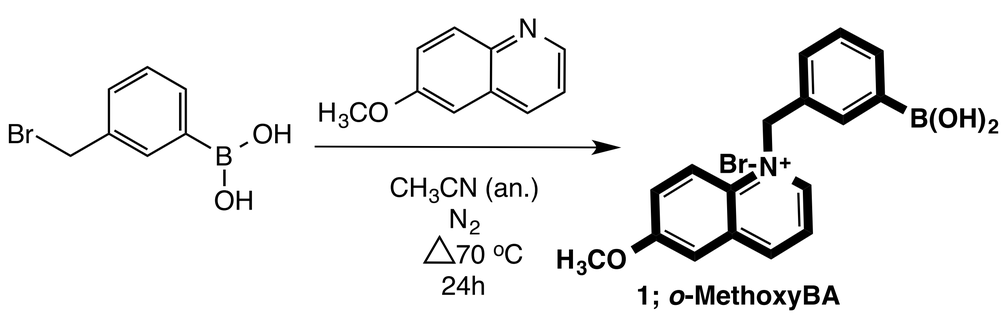
Introduction

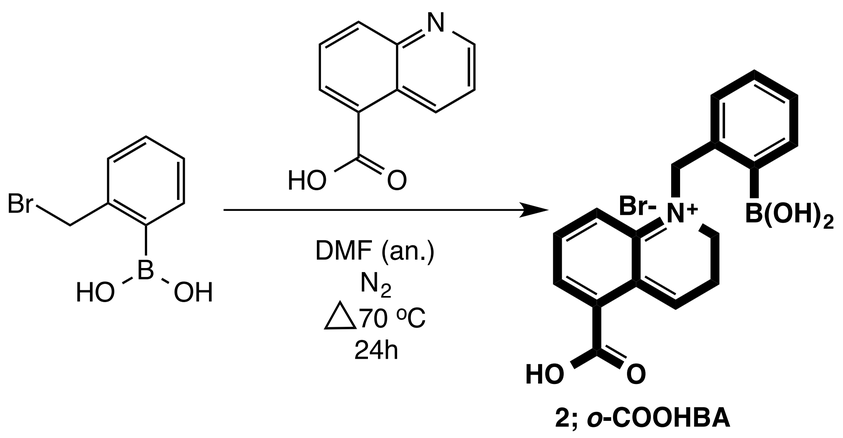
Diabetes is an incurable disease that promotes acute and chronic complications, namely blindness, heart disease or kidney failure. Monitoring the disease marker glucose in blood can prolong life expectancy by allowing diabetics to manage episodes of hypo- or hyperglycaemia. Currently, noninvasive-continuous monitoring systems are not commercially available. The use of boronic acids (BAs) for sensing sugars is well-known, as these Lewis acids have a high affinity for diol-containing compounds. Fluorescent BA derivatives have been investigated for potential use in sensing devices, such as smart contact lenses, as they have shown a decrease in fluorescent intensity on increased glucose concentrations. This novel sensing platform could provide personal management of ocular-glucose levels for diabetics *via* a noninvasive optical sensor, in contrast to the electrochemical approach employed by Google and Novartis.

Sensing Mechanism



Synthesis

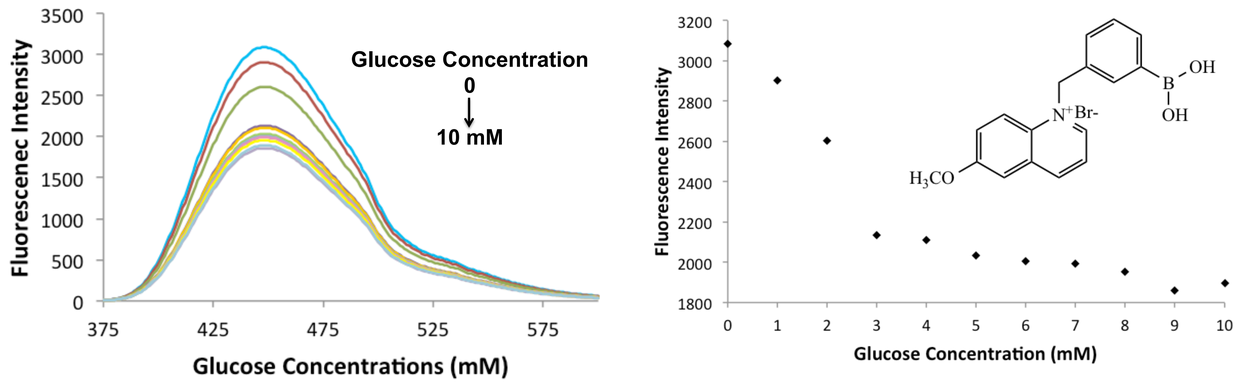




Successful synthesis of novel BA sensor *o*-COOHBA was confirmed by ^{1}H NMR.

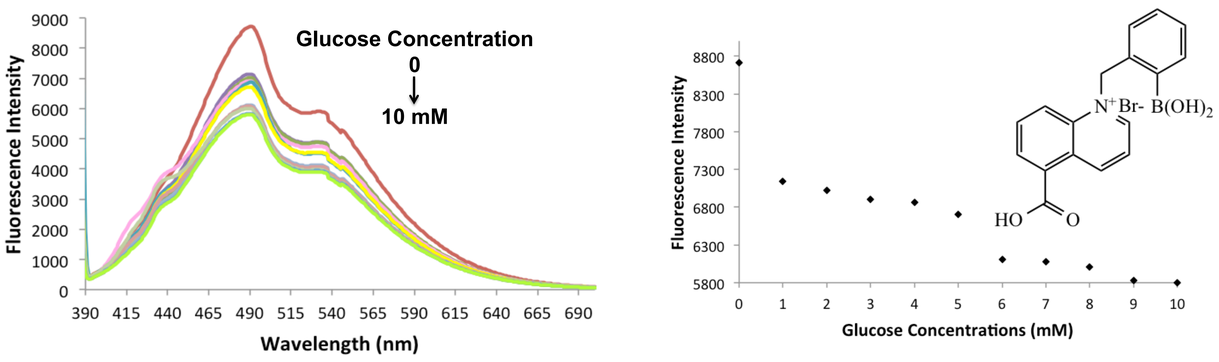
Glucose Sensing

The fluorescence of *o*-COOHBA, a novel BA sensor, has been compared to the fluorescence of *m*-MethoxyBA, a reported BA sensor, when studied in solution at pH 7.4. Both BA sensors were shown to respond to glucose in the dynamic range of 0-10mM, which corresponds to the ocular glucose concentration range in diabetics (~500µM – 5mM).



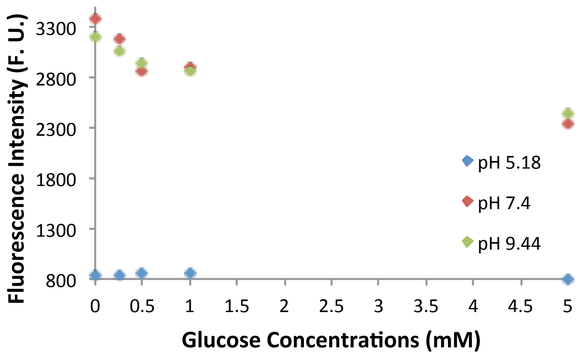
***m*-MethoxyBA**; 0.25 mM in pH 7.4 phosphate buffer and methanol (1:1)

Excitation wavelength: 365 nm; Emission wavelength: 448 nm; Slit width 2.5 nm for excitation and emission, using a high sensitivity.



***o*-COOHBA**; 0.5 mM in pH 7.4 phosphate buffer

Excitation wavelength 380 nm; Emission wavelength: 485 nm; Slit width 5 nm for excitation and emission, using a high sensitivity.



***o*-COOHBA** 0.5 mM was studied in pH buffers 5.18, 7.4 and 9.44 with glucose, correlating to the ocular glucose concentrations. The change in fluorescence intensity was not seen below pH 6, due to the pK_a of 6 for the fluorescent sugar-bound BA form.

Excitation wavelength 380 nm; Emission wavelength: 485 nm; Slit width 5 nm for excitation and 2.5 nm for emission, using a high sensitivity.

Conclusions

Both BA sensors presented here have demonstrated a decrease in fluorescence intensity on increased glucose concentrations. Although *m*-MethoxyBA has shown the highest fluorescence intensity, *o*-COOHBA has demonstrated the ability to sense glucose in the micromolar concentrations correlating to the ocular glucose range in diabetic patients, 0.5-5mM. The higher excitation wavelength of 380 nm is also advantageous, as it lies close towards the visible-region of the electromagnetic spectrum, which allows for the use of cheap, readily available LEDs as excitation sources. Moreover, the carboxylic acid substituent of *m*-COOHBA is desirable for immobilizing the BA sensor on to various polymer substrates.

The authors would like to thank Science Foundation Ireland (SFI) for financial support under the Insight Centre for Data Analytics Initiative, grant number SFI/12/RC/2289.