www.vbripress.com/aamc, DOI: 10.5185/aamc.2016 Published online by the VBRI Press in 2016

Florescence Sensing for Non-Invasive and Continuous Glucose Detection

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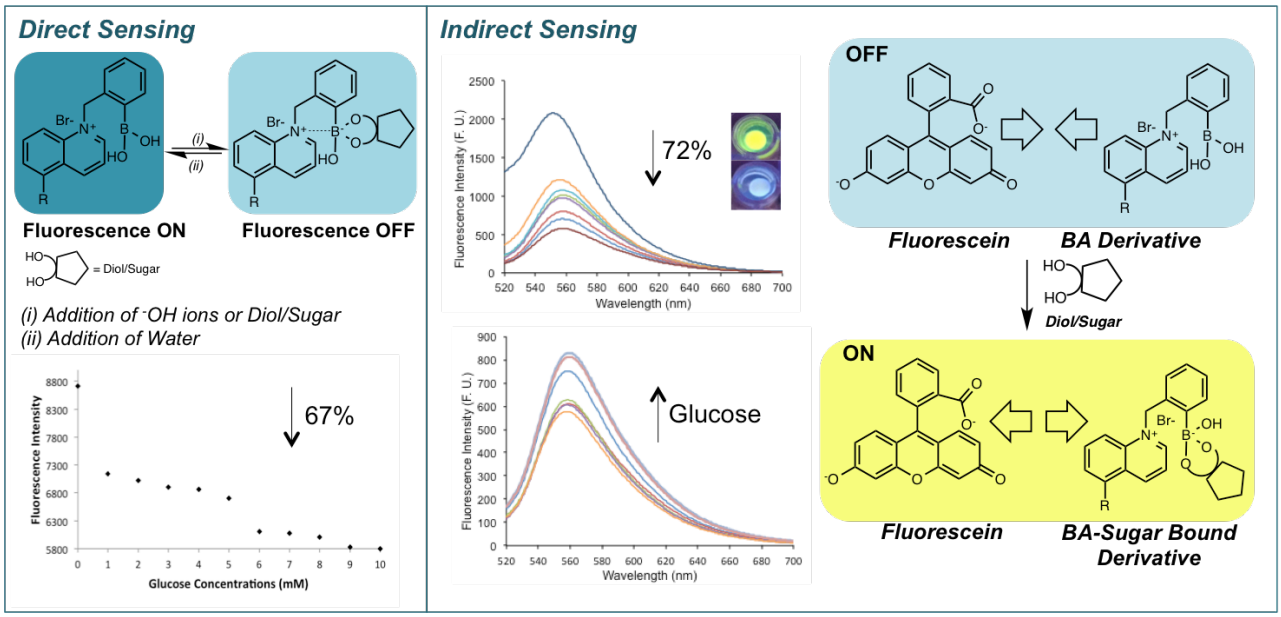
Table of contents



Direct and indirect glucose sensing using fluorescent BA derivatives

ABSTRACT

One of the most life-threatening diseases currently known worldwide is diabetes[1]. From progressive side effects such as heart disease or renal failure, this condition has had a global impact, particularly in the developing world[1]. The disease is expected to proliferate from 422 million in 2016 to 700 million by 2030 and as the numbers suffering from this disease continue to rise, so too will the economic costs[1]. Monitoring this disease has proven to prolong life expectancy for diabetics, although current monitoring systems are either invasive or non-continuous[2]. This highlights the consumer demand for a real-time, affordable, continuous and non-invasive glucose-monitoring device. Over recent years, many fluorescent boronic acid (BA) derivatives have been explored for their glucose sensing properties[3]. Boronic acids (BAs) are Lewis acidic, meaning they are electron deficient, allowing for strong but reversible interactions with diol-containing compounds such as saccharides[3]. By combining BAs and fluorophores, BA-sugar interactions can be monitored by changes in fluorescence. A conformational change in the BA group, from sp^2 to sp^3 hybridisation is induced upon interaction with glucose, resulting in the anionic boronate-diester form. In the

case of direct sensing, this negatively-charged BA species is capable of interacting with the positively charged N present in the structure, known as a charge neutralisation-stabilisation interaction, which leads to an overall quenched state of fluorescence[3]. Conversely, indirect sensing using BA derivatives has also been explored in which the BA derivative is paired with a fluorophore molecule. In this case, fluorescence of the fluorophore is quenched due to electrostatic interactions with the BA. On sequential additions of glucose to this system, the BA derivative preferentially binds to the sugar, restoring the fluorescence intensity by releasing the fluorophore[4]. In this work, BA-sensors containing a positively charged N atom have been synthesised and investigated for direct sensing in solution and indirect sensing using a fluorescein ionogel. Fluorescein was chosen as it is biocompatible and has been extensively studied for its potential use in biosensing[5]. In the case of direct glucose sensing, the BA sensor proposed showed extensive quenching of up to 67% on glucose addition (10 mM) in solution. Similarly, a fluorescence decrease of 72% of the fluorescein ionogel was observed with incremental BA additions and with increased glucose concentrations, the fluorescence recovery reached almost 40%. Both of these sensing approaches have the potential to act as recognition tools for determination of glucose levels in the body. The direct-sensing approach shows enhanced glucose responses corresponding to the ocular-glucose ranges in diabetic patients (between 0-5 mM) and the indirect-sensing approach offers sensing in the range correlating to diabetic blood-glucose levels (2-40 mM). Our aim is to fabricate an affordable, continuous and minimally invasive glucose-monitoring device, which offers diabetics personal control over monitoring their glucose levels, to aid the prevention of the acute and chronic side effects associated with the disease.

Keywords: Glucose; Biosensors; Direct Sensing; Indirect Sensing; Fluorescence

Acknowledgements
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.

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Reviewers: Lourdes Basade-Desmonts; Thorfinnur Gunnlaugsson; A. P. de Silva

