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Thesis abstract

Fluorescent sensor arrays to monitor heavy metals and therapeutic drugs in biological systems

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Rapid, sensitive and accessible detection of chemical analytes is a widespread challenge, particularly in remote communities that have limited access to technical facilities. Optical sensor arrays are a promising technique to address this challenge, and have demonstrated progress towards the detection of chemical analytes in the environment and in biological fluids. There are many chemical analytes with no suitable on-site detection system, and this thesis outlines the development of a number of new systems to address this gap.

A selection of coumarin sensors was first investigated to determine an optimal candidate for heavy metal ion discrimination. The systems took advantage of the cross-reactivity afforded by modifying the solvent. Of the four sensors investigated, a single thiocoumarin sensor was identified as the optimal candidate, and enabled the sensitive detection and discrimination of seven heavy metal ions.

The effectiveness of platinum chemotherapy is greatly limited by toxic side effects and varied patient tolerance. Therapeutic drug monitoring offers an opportunity to address these challenges, which many clinicians have attributed to ineffective dosing protocols. A six-sensor fluorescent array system was designed and synthesised to monitor various platinum species. The sensor array could distinguish platinum from other biologically relevant metal ions and separately able to discriminate platinum complexes with diverse coordination environments. Following this, the sensor array was utilised to monitor platinum levels in investigations using clinical plasma samples from patients undertaking platinum-based chemotherapy.

Polymers were recognised as promising materials for a potential drug detection sensor array. A strategy of functionalising amino acid mimics on a polymer backbone and a fluorophore on the polymer end-group was proposed. To this end, six polymers were synthesised and one polymer successfully modified with a coumarin fluorophore. The fluorescent polymer was utilised in investigations with a variety of analytes and solution conditions. Upon reaction with a library of antibiotics, the polymer displayed a unique fingerprint fluorescence response to each antibiotic. This result highlights the potential for this strategy to be utilised for future array-based detection of drug analytes.

The systems designed and utilised in this work have contributed significant progress towards the detection of chemical analytes in complex fluids. This thesis outlines the importance of new detection strategies for monitoring chemical analytes and how they can be translated to environmental

and clinical applications in remote areas of Australia.

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