Integrated Optical Detectors for Point-of-Care Diagnostics

Downsizing of analytical components allows the integration of entire diagnostic processes within credit-card sized devices. However, the realisation of portable diagnostic devices for point-of-care testing has been hampered by the lack of suitable miniaturised optical detection systems. Low-cost solution processable organic semiconductors with tuneable optical properties may provide the answer. To this end, we demonstrate the application of polymer light emitting diodes (pLEDs) and organic photodiodes as integrated detection components. As a step towards the development of disposable, quantitative diagnostic tests, a prototype comprising an analytical microchip, integrated optical detection and support electronics is presented.

Introduction

Over the last decade miniaturisation of analytical instrumentation has been a dominant trend within the chemical and biological sciences. A typical process required for a diagnostic test, comprises a number of distinct analytical operations (such as reagent handling, chemical reactions, product discrimination and target identification). Through miniaturisation, "lab-on-a-chip" or microfluidic technologies may allow successful integration of all the relevant steps on a monolithic chip. Miniaturisation of diagnostic devices not only affords portability and significant cost reductions but also performance gains in terms of speed, analytical efficiency, automation and reproducibility.

A significant challenge encountered in miniaturised diagnostic systems is the ability to efficiently detect analyte molecules. Indeed the small sample volumes and low analyte concentrations typical in microfluidic systems make high sensitivity detection a prerequisite. While in the laboratory these demands are met by sophisticated detection schemes, the realisation of portable diagnostic devices for point-of-care testing necessitates the development of integrated miniaturised detection modules. To date, few if any diagnostic systems with fully integrated optical detectors have been reported. The solution proposed by Molecular Vision is based on recent advances in light-emitting polymers (LEPs). LEPs have been the subject of intense scientific and commercial interest since their discovery in 1990. Until now, commercial interest in LEPs has focused primarily on their potential for display applications. Nevertheless, the use of LEPs in chemical analysis represents a new application of this emerging technology and offers a number of key advantages over competing approaches. As can be seen in Fig. 1, most thin-film LEP devices have simple multilayered structures. For instance a typical polymer light-emitting diode (pLED) comprises one or more layers of polymer sandwiched between two electrodes, of which at least one must be transparent. Under electrical excitation the polymer emits light via radiative combination of injected electrons and holes and therefore may be used as a light source. The same structure can also be used in reverse as a photodetector by illuminating the polymer in order to generate a measurable electrical current. These two components may then be used together as a simple polymer detection system. Owing to the simple layer-by-layer deposition procedures for the polymer components and the planar structure of analytical microchips, integration into existing chip structures occurs at marginal additional cost.

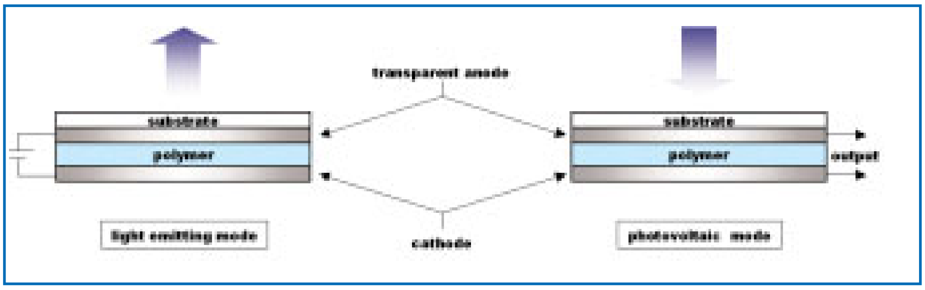

Fig. 1: Schematic representation of an organic semiconductor based LED and photodiode.

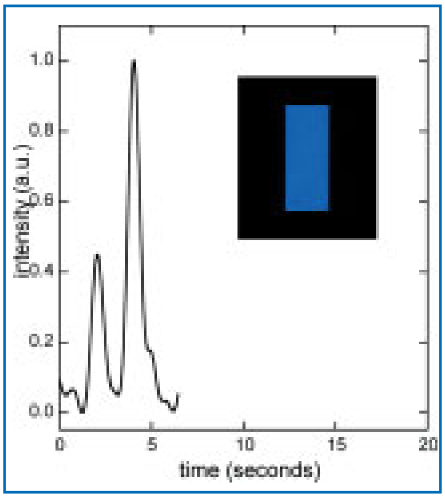

Fig. 2: Electrophoretic separation of fluorescein and 5-carboxyfluorescein within a microfluidic chip. Excitation is provided by an integrated thin-film polyfluorene-based LED. Drive voltage = 6V, lmax = 488 nm.

Fig. 3: Molecular Vision's prototype assay chip incoprorating integrated organic photodiodes. Printed circuit board comprises amplifier and Bluetooth® connector for wireless data transfer to a PDA.

With these advantages in mind we have reported the application of polyfluorene based pLEDs as an integrated excitation source for analysis of microfluidic separations. Similarly we have used organic photodiodes as integrated optical detectors for chemiluminescence (CL) assays. Current work is focussed on creation of a fully-operational prototype diagnostic chip. The device features autonomous sample loading and wireless data transfer to a PDA. The small footprint and low unit cost make this integrated microchip an ideal platform for a new generation of disposable point-of-care tests.

Detector Fabrication

Integrated pLEDs comprise a patterned indium tin oxide (ITO) coated glass substrate onto which poly(3,4-ethylenedioxythiophene)/polystyrene sulphonate and the active polyfluorene layer are deposited. Following thermal evaporation of aluminium electrodes on top, devices are encapsulated using an epoxy resin and glass coverslip. The active pLEDs (40 µm x 1000 µm) are then interfaced to the underside of a planar glass microfluidic chip. Fabrication of the microfluidic devices utilizes well-established lithographic, etching and bonding methods.

Organic photodiodes comprise an ITO coated glass substrate onto which layers of copper phthalocyanine, fullerene and bathocuproine are evaporated. This is followed by deposition of aluminium electrodes through a shadow mask yielding three detection strips of 2000 µm x 8000 µm each. Finally devices are encapsulated using an epoxy resin and glass coverslip. Intrinsic adhesion is used to attach the thin-film photodiodes with elastomeric microdevices.

System Testing

Multi-analyte diagnostic tests typically require the separation of the constituents prior to detection. In case of charged analytes capillary electrophoresis is most frequently used, providing a suitable platform for testing of our pLEDs as integrated excitation sources. To demonstrate integrated optical excitation for electrophoretic analysis, two common fluorescent labels, fluorescein and 5-carboxy-fluorescein, are injected and then separated using standard electrokinetic methods. For fluorescence excitation the blue-emitting pLEDs are driven at 6 V. Using conventional detection, the two components are successfully separated within 4 seconds with good sensitivity (Fig. 2). Importantly, peak intensities for integrated pLED excitation match those achieved using a conventional mercury lamp as an excitation source.

In further experiments organic photodiodes have been used to monitor peroxyoxalate based chemiluminescence reactions. In such experiments, peroxyoxalate reagent, catalyst and hydrogen peroxide are hydrodynamically pumped and mixed within a microchannel, generating blue chemiluminescence. Since hydrogen peroxide is produced by a number of enzymes when in contact with specific analytes and dissolved oxygen (e.g. alcohol, glucose, cholesterol), precise measurement of hydrogen peroxide concentration is an important diagnostic parameter in many biological assays. Preliminary results indicate a linear relationship between photoresponse and hydrogen peroxide concentration in the micromolar to molar range.

Applications & Outlook

While our pLED light sources and organic photodiodes have successfully been applied to integrated microfluidic formats, their suitability as fully-integrated detectors will be defined by the stringent sensitivity requirements imposed by diagnostic tests. Research efforts are ongoing to increase pLED emission intensities, create arrays of tuneable light sources and integrate additional optical components within monolithic substrates. Similarly changes to the composition and architecture of organic photodiode are aimed at enhancing responsivity over a wide wavelength range.

Portability of our miniaturised diagnostic test platforms requires integration of all peripheral equipment. In Molecular Vision's battery driven prototype (Fig. 3) the diagnostic chip is attached to a printed circuit board with amplifier and Bluetooth connection for wireless data transfer to a PDA .The small size, low cost, high-sensitivity and operational flexibility of our diagnostic platform bode well for applications in the point-of-care market. Molecular Vision is currently seeking to co-develop disposable diagnostic tests for point-of-care diagnoses in hospital, surgery or home environments. A key advantage afforded by our polymer detection arrays will be the possibility to group several tests into a diagnostic panel to allow effective monitoring of conditions such as diabetes and heart disease.

References

A list of references can be obtained from the authors.

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