Development of Functional Organic Dyes and Paper-Based Analytical Devices for Chemical and Biochemical Sensing

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(Bio)Chemical sensors are indispensable tools in analytical chemistry allowing to selectively detect target compounds without the need for prior separation even in complex mixtures. This presentation will introduce two major topics related to (bio)chemical sensing: 1) the design and synthesis of functional organic dyes for application to optical chemical sensors and for imaging, and 2) the development of microfluidic paper-based analytical devices (μPADs) for point-of-care testing (POCT) applications.

Functional organic dyes play important roles in optical (bio)chemical sensing by selectively converting chemical information into an optically detectable signal in the form of color (absorbance, reflection), fluorescence or bioluminescence. In addition, they are widely applied for biological imaging. The near-infrared (NIR) spectral range is of particular interest, due to the absence of intrinsically light absorbing and emitting interfering species and deeper penetration of NIR light through biological tissues. We have developed various types of fluorescent dyes such as squaraine and boron dipyrromethene (BODIPY) derivatives. The main feature of these dyes is that they combine strong absorption/fluorescence emission properties with sharp spectra in the NIR region. In particular, fluorescent dyes based on BODIPY show very high molar absorption coefficients and fluorescence quantum yields, narrow spectral widths, and high stability.[1] We are also focusing on the development of NIR bioluminescent substrates. The emission wavelength range of conventional bioluminescence systems has been limited to the visible region. Most previous approaches aimed at extending the wavelength of light emission based on bioluminescence resonance energy transfer (BRET) systems, resulting in a significant decrease in luminescence due to energy loss. We developed NIR emitting luciferins by modifying the molecular structure of the natural luciferin chromophore itself through rational molecular design, and successfully applied it to in vivo imaging.[2]

In recent years, microfluidic paper-based analytical devices (μPADs) have evolved into a very active research field in analytical chemistry.[3] The primary attractiveness of paper lies in its ability to spontaneously transport liquids through capillary forces without external pumping, in addition to low cost and widespread availability. Our group has been among the pioneers in this field, with the goal of creating single-use, low-cost analytical devices of highest user-friendliness applicable for point-of care-testing (POCT) by untrained end-users at any place (e.g. developing countries, home healthcare). We became first to use inkjet printing technology for the fully integrated fabrication (microfluidic patterning and assay reagent deposition) of such devices.[4] Rapid, precise, and reproducible deposition of a broad variety of functional

materials, including analytical assay reagents and biomolecules, has made inkjet printing an effective tool for the fabrication of μPADs.[5] Inkjet printing-based approaches resulted in the highly reproducible fabrication of various types of PADs, as for example demonstrated by the first fully inkjet-printed potentiometric sensor combining an ion-selective electrode with an Ag/AgCl reference electrode on a single-use paper platform.[6]

More recently, we started focusing on the development of μPADs for equipment- and calibration-free semiquantitative clinical assays, demonstrating that μPADs can serve as alternatives to significantly more expensive and time-consuming conventional assays. One example is a μPAD for "distance-based" readout of fluorescence signals, applied to the detection of the tear fluid glycoprotein lactoferrin.[7] μPADs for "distance-based" signaling enable analyte concentration readout by judging the length of a color-changed section of a microfluidic channel on paper, like a classical thermometer. Another example is a μPAD enabling the direct visualization of the urinary albumin (Alb) index (albumin/creatinine ratio) by a graphical method, relying on the simultaneous naked eye detection of Alb and creatinine (Cre) on a single device.[8] For the analysis of a different target in urine (8-hydroxy-2'-deoxyguanosin), a "text-displaying" approach for instrument-free semiquantitative readout of competitive lateral-flow immunoassays with high potential for general applicability was developed.[9] In all these cases, inkjet printing plays an essential role for the successful realization of the devices. Finally, we have demonstrated μPADs as a new platform for antibody detection by making use of bioluminescence resonance energy-transfer (BRET) switching sensor proteins.[10] In contrast to intensity-based bioluminescence signaling, the BRET mechanism enables time-independent color change-based readout of bioluminescence with a digital camera or a smartphone.

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