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Micro patterned quantum dots excitation and imaging for cellular microarray screening

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ABSTRACT

We developed a colloidal quantum dot (QD)-based multicolor excitation light source array designed for compact lab-on-a-chip cell screening and imaging. We have demonstrated multicolor *ex vivo* transmission mode microscopy to evaluate the nucleus–cytoplasm ratios of cancer cells. We have also performed immunofluorescence excitation of two types of cancer cells (MDA-MB 435 and SKBR3) that are cultured in a microwell array to quantify the disease specific protein expression. Printed array of color filters and microwells were used to perform fluorescence excitation and measurement of the biomarkers. Our method provides patterned multicolor light sources at low-cost that are suitable for high-throughput microarray cellular screening.

1. Introduction

Colloidal quantum dots (QDs) are 5–10 nm-sized semiconductor nanocrystals where electrons and holes are confined in the three dimensions. Due to this quantum confinement, the energy levels of a single QD are discrete and the band gap is highly related to the size and the shape [1]. QDs have demonstrated potential as fluorescent markers for bioimaging [2–4]. The tunable band gap of QDs has also been utilized for optoelectronic devices such as light emitting diodes [5] and solar cells [6]. The benefits of QDs for such applications include the emission and absorption wavelengths can be easily tailored through proper choice of materials and sizes; they are much more stable and slow to photobleaching compared to commonly used organic fluorescent dyes.

The compatibility with the advanced microfabrication techniques is another important advantage of integrating QDs on microsystems. In previous studies, we have shown micropatterning of colloidal QDs on silicon substrates [7–9]. The feature size of patterned QDs can be arbitrary chosen from millimeter scale to single molecular order [7]. The patterned QDs were also electrically excited to compose light emitting diodes (LEDs) that were used for nanoscale fluorescence excitation [10].

The unique characteristics of quantum dots as an integrated on-chip excitation source include (1) capability of multicolor emission from visible to IR wavelengths, (2) various available methods for photo/electrical excitation, and (3) compatibility with silicon fabrication and micropatterning which make QDs an ideal material to be used in an arrayed format. One example of QD arrays is high definition displays, where red, green, and blue QD pixels are patterned in a dense array to allow creation of full color images [11]. In this paper, we propose a colloidal QD-based multicolor excitation light source which is designed for arrayed lab-on-a-chip systems for cell culture, analysis and imaging. It is made on a glass slide and adds the functions of absorption and fluorescence imaging to a standard microscope.

We utilized printing-based techniques to construct the miniature array of QD light sources, chambers, and optical filters. Such integrated microscopic systems enable novel microarrays for cell culture and screening, where cells are investigated while grown in several hundreds of microwells under precisely controlled environments [12]. Another important potential application is microchip based detection of tumor cells [13], where integrated immunofluorescence imaging is much needed. Imaging of multiple biomarkers enables precise identification and quantification of cells [14]. In order to demonstrate the efficacy of our light source, we perform *ex vivo* transmission mode microscopy and fluorescence imaging of

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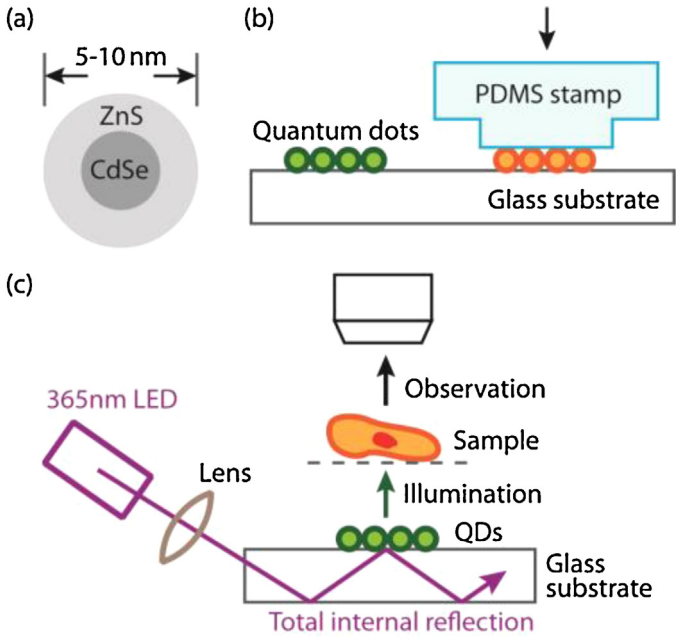

Fig. 1. Schematics of the quantum dots nanocrystal, the device and the system. (a) The core shell structure of the CdSe–ZnS quantum dots. (b) Fabrication procedure and (c) experimental setup of the arrayed multicolor light source for cellular imaging.

cancer cells with the micropatterned QD based light source. When excited by a high power UVLED, the QDs work as an illumination source suitable for high-throughput cellular screening.

2. Fabrication and characterization of QD light source

QDs we used in this study are CdSe/ZnS core–shell quantum dots, which have a core shell structure where the core is composed

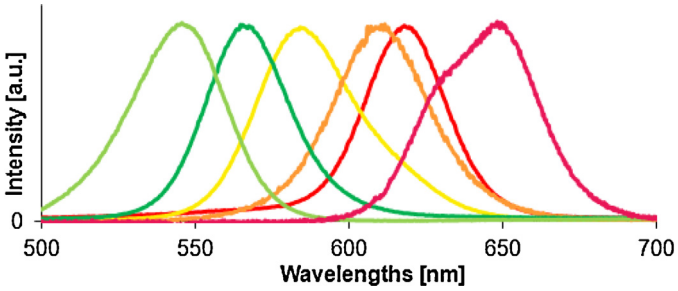

Fig. 3. Emission spectra of the QDs. Emission peaks ranging from 540 nm to 620 nm were used in the measurement.

of one material and is coated by a shell of another material with a larger band gap. The shell increases the stability of the QDs against environmental changes, and more importantly, improves quantum yield by passivating the surface trap states. Fig. 1(a) shows the structure of the core–shell QDs.

Fig. 1(b) and (c) illustrates the fabrication procedure and the working principle of the arrayed QD light source. QDs are patterned onto a glass slide using the micro contact printing technique, where PDMS stamps formed by a SU-8 mold are utilized. Details of the stamping technique are reported in [8,9]. An UV light with the emission wavelength peaked at 365 nm from a high-power LED (200 mW) is focused and introduced inside a glass slide. The total internal reflection of the transmitted UV light induces an evanescent field on the glass slide surface to excite the QD films.

Fig. 2 shows photographs of the QD fluorescence and the experimental setup built on a standard fluorescence microscope (Olympus BX51). Since the UV evanescent field on the glass slide decays quickly in the near-field and does not transmit energy in the far-field, the UV light intensity observed with the microscope is negligible compared to that of the excited QDs. Fig. 3 shows the emission spectra of the QD array. Peak emission wavelengths can be

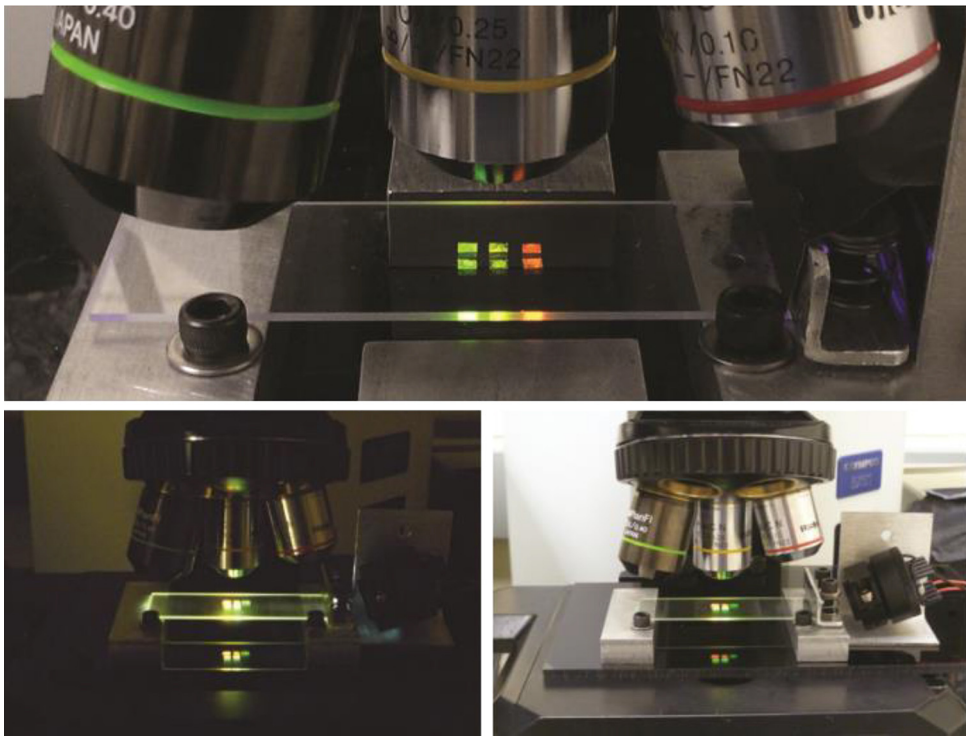

Fig. 2. Emission from the QD array and experimental setup with a standard fluorescence microscope.