Optical Micro Analysis in Lab-on-a-chips

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Abstract:
Lab-on-a-chips are microfluidic devices which include biological laboratory functions on a single chip. They offer great advantages in terms of speed of analysis, precision, low sample and reagent consumption and automation of analysis. An efficient detection method in lab-on-a-chips is essential for the detection and quantification of chemical and biological parameters under examination. This review paper focuses on the recent research on optical detection techniques for LOC applications. Furthermore, several emerging detection paradigms which are still being matured are covered in this paper. Also, an analysis of the performance of different optical detection methods is given.

Keywords: Lab-on-a-chips, biosensor, optical detection, limit of detection.

1. INTRODUCTION

In the miniaturised approach of lab-on-a-chip (LOC) microfluidic systems, the detection issue is even more challenging due to the existence of various constraints. The reduced diffusion lengths, planar substrate and confined geometries of these systems highly rely on detection approaches. Due to better robustness, faster separation and higher sensitivity, the optical detection techniques still are the first choice for biochemical analysis. However, the sensitivity of optical detection methods often decreases at lower pathlengths through the sample. In addition, the high cost and bulky size of the optical devices sometimes are incompatible with the concept of LOC. To deal with these dilemmas, researchers are developing ultrasensitive detectors by incorporating optical components such as waveguides, optoelectronic elements and filters. Fig. 1 shows a typical arrangement for optical detection systems for LOC devices. In a LOC device, the sample is first allowed to pass through the microchannel. It is then excited by a suitable optical source (e.g., laser, LED). The presence of bioparticles in the sample emits the fluorescence signal which is focused on to a lens by an optical fiber with very high numerical aperture. In the detection end, some filtering schemes are employed to reduce effect of background signal and auto fluorescence.

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Figure 1. A typical setup for optical detection systems for lab-on-a-chip applications.

The detected optical signal is then converted to the electrical signal which is then further processed to detect the type and presence of foreign particles in the sample passed through the microchannel.

Although optical detection is an emerging platform in LOC applications, only a number of articles have reviewed this topic. Among these, only 1-3 give a more detailed study of the existing methods. However, these papers had been published sometimes ago and thus do not cover the most recent reported work in the field. This paper, however, reviews the recent methods mainly published during 2007-to date. Starting from the discussions on conventional optical phenomena used in detection, the study covers integrated optical components that are nowadays used for on-chip detection. Less common methods for optical detection in microfluidics are also included in this review.

2. FLUORESCENCE BASED DETECTION

Fluorescence is one of the most essential analytical and diagnostic optical methods for biotechnologists, which are frequently used in LOC systems. Nowadays, fluorescence has become the workhorse for analysis in many of today’s LOCs because of its better selectivity and sensitivity. Tremendous progress is growing in DNA sequencing, purification and cloning, and also in computational methods for the analysis of sequences. However, in some cases, auto fluorescence and photobleaching of fluorophores are problems which can occur due to the existence of some species in the sample such as molecules, viruses cells etc. In addition, tagging of non-fluorescent particle is also a great hassle which needs additional sample preparation. But, it allows lower fluorescence background and improves the confidence in the measurement. In addition, microlenses and planar waveguides can also be integrated in microfluidic devices to improve the detection sensitivity.
Based on the excitation source to the fluorophor particle, fluorescence detection is classified as: laser induced fluorescence (LIF) and lamp based fluorescence (LAF). A description of these two approaches is given in the following. Apart from these, to minimize the cost of the designed system, LEDs can be also used as the excitation source for fluorescence signals.

2.1 Laser Induced Fluorescence Detection

LIF is by far the most widely used standard detection method available for on-chip fluorescence detection due to its sensitivity, simplicity and selectivity. Presently, it has become the first choice for the detection despite its limitations. Moreover, device materials and fluorophore adsorption to channel walls also sometimes generate enough background fluorescence which might mislead to the detection of the targeted particle. However, already, Fu et al. 4 developed a solution elucidating the reduction of background signal employing an orthogonal optical arrangement. In general, care should be taken for selection and purity of sample. More frequently, two approaches are extensively taken to resolve this problem. Using high numerical aperture and total internal reflection fluorescence optics for the excitation can eliminate the background fluorescence. In addition, the external optics employed in microfluidic LIF systems is often complex. Nevertheless, more materials and protocols need to be developed to make this technique more reliable and acceptable. In another approach, Poe et al. 5 introduced an in-house built capillary electrophoresis-LIF instrument which is suitable for all sizes of fluorescent microspheres. They obtained an ever better limit of detection (LOD) of $10^{-21}$M.

The concept of integrated on chip fiber free LIF detection systems recently introduced by Chen et al. 6 where they used the fluorescence beads yeast cells and strain white blood cells to demonstrate the performance of their device. After performing a series of experiments, they concluded that the device could be employed for the on chip integration. On the other hand, a dual-wavelength detection approach for simultaneous LIF detection of microparticles using integrated optical fibers and waveguides was presented by Hosseinkhannazer et al. 7. In their designed biochip, an off-chip PMT was used to collect the fluorescence as emitted from the fluorescence polystyrene beads. The modulated laser beams from the PMT were then analyzed with the help of Fourier transform to identify the particular bead type. This technique proved to be a versatile platform in a lab-on-a-chip system for the detection of multiple fluorophores.

The drawbacks of fluorescence detection include: (i) fluorescence labeling and (ii) the need to derivatize most analytes prior to analysis. A versatile technique for label-free fluorescence detection by employing deep-UV fluorescence is recently introduced by Schulze and Belder 8. The main instrumentation setup for their experiment is called the epi-fluorescence design. The native fluorescence is excited by the deep-UV light and the fluorescence of most molecules involved by a radiative transition process. A common problem encountered in deep-UV native fluorescence detection is the high background signal which usually comes from Rayleigh scattering of the excitation light and background fluorescence. However, time-resolved fluorescence detection or cross polarization method of filtering can be applied to overcome this problem which enables the separation of the wanted signal from the background in time domain.

2.2 Lamp Based Fluorescence Detection

The LAF is another widely used method employed with fluorescence microscopy usually to capture the image of biological samples. It is less expensive, easy to use, simpler to construct and more portable comparing with LIF. In addition, it offers variable excitation wavelengths to make it...
suitable for multi-analyte sensing. In terms of LOD, it is poorer than LIF. But, it exhibits the most attainable LOD in microchip capillary electrophoresis (MCE) due to the extremely small sample volume. Therefore, LAF is mainly applicable to some confined areas of MCE, such as detecting trace and ultra-trace components in biological samples.

Kato et al.\(^9\) used LAF for the detection of subsecond chiral separation whereas Natalia et al.\(^10\) used it for the fast separation of amino acids in green tea. With a mercury lamp and photon counter in a MCE system, a highly sensitive fluorescence detection is reported by Yan et al.\(^11\). This approach can be successfully applied for the separation of three amino acids. They showed that it is possible to obtain baseline separation and sensitive detection of FITC-labelled amino acids only in 125 sec with LOD of 9.6 nM (S/N = 3) which ensures the reduction of baseline noise. In their work, it is also investigated that the high background signal will significantly depress the detection limit which can be surmounted by taking the following steps: (i) selecting the optimal detection area, (ii) putting the whole device in a black box, (iii) decreasing the intensity of the Hg-lamp, and so on. On the other hand, Banerjee et al.\(^12\) used a cross-polarization scheme to filter out excitation light from a fluorescent dye emission spectrum. Though they obtained a little bit higher LOD (10 nM) than the previously reported work. They were able to filter out the excitation light from the halide lamp which is a major problem in LAF. Moreover, they projected to potentially improve the LOD which could be possible by incorporating colored-glass filters in combination to the cross-polarization scheme. On the other hand, if a high detection sensitivity is attributed to the photon counting technique to measure the weak light intensity, the detection sensitivity can also be greatly improved. Thus, due to the lower maintenance and cost as compared with LIF, LAF is still increasing its popularity.

However, the most common problem with LAF is the leakage of excitation light into the fluorescence spectrum of the dye used for detection. But, optical long-pass filters, colored-glass filters, or interference filters can be used to filter out excitation light and to ameliorate the signal to noise ratio (SNR). But, it is not easy to fabricate these filters. Moreover, these filters need to be matched to a particular dye and hence cannot be applied for multianalyte detection. However, by improving the filtering mechanism, it is still possible to completely eradicate the background signal and thus to achieve the lower detection limit. All of these inherent facilities integrated in LAF make it simpler.

3. CHEMILUMINESCENCE DETECTION

Chemiluminescence (CL) is an alternative method to the fluorescence and most popular for on-chip detection. In CL, the excitation energy for analytes comes from chemical reactions and reagents and thus the problems of excitation source are completely avoided. Therefore, the background interference is almost eliminated without employing a filter system, resulting in a low detection limit. In recent years, it has created great interests to the researchers because of its low cost, easy operation, selectivity and simpler instrumentation components. Some works\(^13, 14\) have already reported on chemiluminescence detection of analyte separated by a microchannel. However, CL emission suffers from a variety of environmental factors such as temperature, ionic strength, solvent, pH and other sorts present in the system. Moreover, a more complex microchip layout is usually required as the chemiluminescence reagent needs to be mixed with the separated analytes before detection. In addition, strict care has to be always taken during the CL measurements, as CL reaction varies with time and differs from compound to compound.
Recently, Myers and Lee 3 reviewed CL focusing on CMOS active pixel sensor in a smart card form factor for the chemiluminescence detection. Our paper, however, incorporate all recent advances for chemiluminescence detection as follows. A CL based approach to measure the concentration of nitrite in food is successfully implemented by He et al. 15. They used the CL reaction of luminol with ferricyanide to sense the presence of nitrite and claimed the LOD of 4 µgL⁻¹ which was good compared to the results obtained by other researchers. The CL reaction was free from any kind of electrical interference and thus made it simpler and more accurate to manipulate. However, they faced some difficulties when uric acid and vitamin C were present in that sample decreasing the CL intensity sharply. Whereas, Som-Aum et al. 13 developed a work to determine chromium (III) and total chromium using the CL. Instead of using the ferricyanide, they used luminol oxidation with hydrogen peroxide followed by an aqueous solution catalyzed by chromium (III) in their CL reaction. Their method was excellent as it required less than one minute to analysis each sample with a precision of 4.7%. But it was applicable only in the analysis of river water, mineral waters, drinking waters and tap water rather than any other samples. Gao et. al 16 introduced a micro device based gas sensor to realize chlorine gas detection by gas–liquid interface absorption and CL reaction. The performance of this system was also excellent as compared to the previously reported works as the whole sensing cycle from sampling to cleaning required only 30s. Though, they obtained a reasonable LOD, they projected to improve it by curving convex channel or array channels to enlarge gas–liquid contacting area. This microsensor based CL reaction can be successfully applied to determine carbon dioxide. Another potential application is the determination of hydrazine vapor based on luminal CL.

As the time advances, numerous reports have been appearing on the use of CL for the detection of various particles. Recently, Hatakeyama et al. 17 described a novel microfluidic device using a thin film transistor (TFT) photosensor integrating with a microfluidic channel, a photodetector and a DNA chip platform. They used CL based on horse radish peroxidase-conjugated streptavidin for DNA detection. Although, they achieved a lower LOD (0.5nM), the assay took comparatively long time (less than 1 hour) to complete. However, they conceded that the use of CL in DNA-arrayed sensors will be a promising approach for developing a miniaturized, disposable DNA chip with high sensitivity.

4. OPTICAL SPECTROSCOPY DETECTION

Optical spectroscopy is a label free and highly sensitive luminescent bio-analyses and cell imaging technique for biospectroscopy for the investigation of bacteria, eukaryotic cells, or tissues and single molecular detection. However, it suffers from the weak scattered signal and a little has been reported on spectroscopy based detection systems to date. Among these, a number of comprehensive recent review articles on the development of Surface Enhance Raman Spectroscopy (SERS) detection methods for lab-on-a-chip have been already published 18, 19. A SERS based approach in vivo cancer imaging using pegylated gold nanoparticles is recently implemented by Qian et al. 20. In their experimental analysis, they introduced a novel technique named “spectral imaging” which allows chemically identifying the material at each pixel.

A good report about the detection of multiple DNA targets simultaneously on a single array spot was developed by Sun et al. 21. They introduced a non-fluorescent DNA array platform on a gold-coated glass slide for this issue. This approach is treated as a multiple detection tool for comprehensive alternative splicing profiling of any kind of genes relevant to any specific cancers. In another approach, Yakes et al. 22 developed a cancer protein assay platforms based on nano-
particle labels which strongly relies on the construction of gold nano-particle, Raman enhancer and the extrinsic Raman labels (ERLs). Whereas, Huh et al. successfully implemented an on-chip SERS biomolecular detection. Some emerging approaches such as mixing mechanism to boost the reaction rate which virtually reduce the analysis time, and the electrokinetic concentration technique to diminish the limit of detection, were strongly recommended by them. They emphasize particularly on the specificity and sensitivity rather than the other factors such as complexity and flexibility. However, for making the trade-off between these issues, they suggested a number of remedies including the gap distance control between the enhancer and the reporter and eliminating the SERS background signal by blocking of nonspecific binding. Thus, this technology can play a significant role to the ongoing efforts to miniaturize biomolecular analysis for pharmaceuticals testing and the detection of biological warfare agents.

5. ABSORBANCE DETECTION

Absorbance is a popular detection scheme for the microfluidic device as having the high efficiency and high simplicity. In this optical phenomenon, the attenuation of either direct incident UV/visible light is measured as a function of wavelength generally using a spectrophotometer. The linearity, convenience, wide range of samples detected and the lack of chemical derivitizations for fluorescence tagging of absorption technique, has made it well established detection technique in the analytical chemistry as well as in diagnostic laboratory. However, the tiny optical path length inherent in miniaturization of fluidic channels directly impacts on sensitivity and poses a severe problem for sensitive and reliable absorbance measurement, and consequently leads to the difficulty in achieving low LOD. But, several interesting approaches have already addressed this problem, such as thermal lens effect, planar waveguide, multipass configurations, liquid core waveguiding, “slow light” and hollow prisms. However, often, more complex capillary geometries like U-cells, Z-cells, bubble cells or multireflection cells have been implemented to increase the optical pathlength at detection point. A comparatively more interesting way to overcome this problem that has been recently developed by Llobera et al. is by incorporating by “air mirrors”. This takes advantage of refractive index difference between the air and PDMS. In addition, to collimate the light, an integrated biconvex lens was used and conclusion was made that the inclusion of the air mirror significantly reduces the integration time and LOD while increasing SNR and the sensitivity by a factor of up to 2.49 when comparing the single internal reflection configurations with and without air mirrors.

Despite its simplicity and much wider range of sample detection, only a few works have been reported on absorbance based detection systems. To improve the detection sensitivity, Hahn et al. developed an absorbance detection systems having ten times larger optical pathlength, lens structures for collimating light in the detection cells, and slit structures for preventing scattered light from entering detectors. With this components integrated in a lab-on-a-chip device, it is possible to produce a ten times detection sensitivity. Whereas, Steigert and coworkers introduced a completely integrated centrifugal disk (CD/DVD) based microfluidic system for fast colorimetric alcohol detection from human whole blood employing real-time absorption measurement. They used metering, mixing with reagents, and sedimentation of cellular constituents to increase the absorbance values and utilized the total internal reflection scheme to monitor the increase of the absorbance values in real-time. This microfluidic system avoided the error-prone correlation between the alcohol concentration in breath and whole blood. Sometimes, the CD/DVD based microfluidics face difficulties especially when more complex valving is required but still gaining its attraction due to its ubiquity and low cost. It has been already shown that it is possible to
colorimetrically detect the ligand binding by laying the object molecules on to the surface of CDs and observing the data error levels as a CD-ROM reads the disc. However, the optical detection with the CD-ROM integrated microfluidic systems is still on the way to enhance the performance of microfluidic systems.

A comprehensive optical detection unit for the chromatographic applications is recently reported by Van Overmeire et al. 31. To investigate LOD of the absorbance detection system, they infused samples with different concentrations of the coumarin dye dissolved in methanol in the fused silica capillary and then measured the corresponding decrease in PMT voltage with respect to the signal obtained for pure methanol. The measurement of absorbance implied that the measurement of small signal dips in a high signal level means that LOD for absorbance will always be higher than the one for fluorescence. A LOD of the 12 µM was achieved for the absorbance detection which was close to the theoretically obtained value (6 µM) whereas that of the fluorescence detection was 600 pM and was one degree higher than the theoretically obtained value (60 pM). This higher LOD in absorption measurement was due to the higher background noise in the microfabricated systems. Moreover, by using light sources, detectors, and integrated waveguides, and employing more sophisticated detection schemes (e.g., multiplexed detection), absorbance based detection techniques are still establishing themselves as precious competitors and alternatives to the ubiquitous fluorescence based methods.

6. SURFACE PLASMON RESONANCE BASED DETECTION

Surface plasmon resonance (SPR) is a fast and ultrahigh sensitive technique for performing label-free bio-sensing. SPR is an important real-time sensing technique for detection of a small change of analyte concentration and thus is useful for LOC systems. There is substantial potential to reduce the cost and complexity of existing commercial devices by increasing the level of optical integration. This technique relies on a dip plasmon shift in the reflectivity curve. The SPR occurs when any polarized light impinge on a prism covered by a thin (e.g., silver, aluminium, gold etc) metal layer. The free electrons occupying the surface of the biochips then adsorb this incident light and commute them into surface plasmon waves (Fig. 2) following some conditions such as the thickness of the covering layer, wavelength of the impinging light, phase, amplitude, polarization and the incidence angle. After satisfying any of these SPR conditions, a dip in reflectivity of the light is then seen in the reflectivity curve. The interaction between the captured target molecules and probe molecules immobilized on the chip results in the modification of the resonance conditions which shifts the plasmon dip in further in the plot of reflectivity curve.

Figure 2. A schematic representation of the SPR principle showing the prism coupling in the Kretschmann configuration.
Case Study: Investigation of the Role of Coating Materials on the Sensitivity of Biosensors

We have conducted a simulation experiment in which a laser beam is reflected from the base of a prism. The base is covered with the different coating materials (Gold, Silver and Aluminium) and immobilized with the protein layer on its surface. The reflected light which is normal to the surface is then collected as a function of the angle of incidence. The refractive index profile and other properties of the different materials were used in this investigation. The dielectric constant of the prism (glass materials) is treated as 2.11. The thickness of each covered materials was kept the same (50nm). This experimental study was verified using an SPR simulator and the results are shown in Fig. 3. The summary of this investigation is listed in Table I. Our investigation reveals that there is no plasmon dip when the base is not covered with any metal elements (curve 1 in (a)). And there is a plasmon dip for a particular incidence angle when the base of the prism is coated with any of the above mentioned materials. After the immobilization of the captured target molecules

![Graph](image-url)

Figure 3. Reflectivity versus angle of incidence curve for three types of materials to show the shift in SPR angle: (a) Gold coated, (b) Silver coated and (c) Aluminium coated.
(protein in this study), this plasmon dip is shifted from its original position but is different for the different materials. From Table I, it is observed that the shift in the plasmon dip is much better for gold coating while for silver and aluminium is almost similar. Thus gold is much more suitable for the detection of bioparticle to provide a better sensitivity. The other parameters which affect refractive index profile were kept constant for this investigation. Apart from this, the SPR shift is also much affected by the thickness of the immobilized molecules and the wavelength of the incidence wave.

With the technological advancement, SPR sensors are improving in their range of applications and suitability. Chinowsky et al. 32 developed a portable briefcase-style SPR sensor which could simultaneously detect small molecules, viruses, proteins and bacteria. A simple and rather inexpensive multi-channel grating-integrated SPR sensing system is developed by 33 which practically eliminates the expensive and bulky optical components. They were able to successfully detect biomolecules and verified that the detection performance was much better than the earlier reported research outcomes. Another nano-grating disposable SPR sensor chip for the detection of biomolecular concentration was developed by the same group. It has a simple structure and low cost for integrated LOC systems 33. Apart from these SPR sensors, a comprehensive innovation of SPR sensors with more sensitivity and wider application range has been reported recently in 34.

### 7. OTHER METHODS

Apart from the detection methods discussed so far, a number of new approaches and some existing less important methods on microchips were found. Among these, electrochemical (EC) detection is the most prominent and attractive platform for microarray detection because of its high sensitivity, low cost, selectivity and easy operation. As compared to LIF which requires fluorescent tagging and larger dimension for the instrumental setup, EC can be easily micro-fabricated with lesser dimension 36. Mass spectrometry (MS) is another universal label-free method to carry the structural information about the proteomics and biological samples with moderate sensitivity. In conjunction with electrospray ionization interface 37, MS provides relatively better detection information of various polar compounds without cross-contamination. However, it suffers from the inconveniences for real applications. Conversely, interferometric is also another label-free detection technique with relatively high sensitivity than MS.

Although LED-induced fluorescence detection is not as sensitive as the LIF, LEDs are most attractive excitation sources owing to their less consumed power, cheaper cost, and very compact dimensions. However, LED sometimes generates a high level of background signal and usually a special filtering arrangement (e.g., notch filter), are always in need. Ren et al. 35 recently developed a portable fluorescence detection system in which they used a mask to control the emission angle and hence the broader spectrum. A comparison test was also made between the LED and laser in terms of their performance and cost with this setup. The LOD obtained in this system using LED as the excitation source was 0.21µM which was about 3 orders of magnitude higher than that of LIF. But, the equipment normally involves in the LIF setup would cost 3 orders of magnitude more than that of the LED excitation system. We always have to make a trade-off between the performance
<table>
<thead>
<tr>
<th>Investigators</th>
<th>Optical Detection</th>
<th>Filter Scheme</th>
<th>LOD</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Fu et al. 4</td>
<td>LIF</td>
<td>510-nm long-pass filter</td>
<td>1.1 pM</td>
<td>The most sensitive detection scheme as having the lowest LOD among other technique. But, it needs fluorescent tagging except having native fluorescence</td>
</tr>
<tr>
<td>Poe et al. 5</td>
<td>LIF</td>
<td>535DF35 bandpass filter</td>
<td>10⁻²¹ M</td>
<td></td>
</tr>
<tr>
<td>Yan et al. 11</td>
<td>Lamp based fluorescence</td>
<td>Excitation and barrier filters (BP 330–385, 450–480)</td>
<td>1.3 nM</td>
<td>It is cost effective, more portable, and more flexible in terms of the choice of wavelength for multianalyte detection. But, it is not as sensitive as LIF and needs some complex filtering scheme</td>
</tr>
<tr>
<td>Banerjee et al. 12</td>
<td>Lamp based fluorescence</td>
<td>Cross polarization based filtering</td>
<td>10 nM</td>
<td></td>
</tr>
<tr>
<td>Kim et al. 14</td>
<td>CL</td>
<td>None</td>
<td>0.05 fM</td>
<td></td>
</tr>
<tr>
<td>Hatakeyama et al. 17</td>
<td>CL</td>
<td>None</td>
<td>0.5 nM</td>
<td></td>
</tr>
<tr>
<td>Sun et al. 21</td>
<td>SERS</td>
<td>-</td>
<td>1 fM</td>
<td></td>
</tr>
<tr>
<td>Huh et al. 23</td>
<td>SERS</td>
<td>-</td>
<td>30 pM</td>
<td></td>
</tr>
<tr>
<td>Llobera et al. 26</td>
<td>Absorbance</td>
<td>-</td>
<td>41 nM</td>
<td></td>
</tr>
<tr>
<td>Van Overmeire et al. 31</td>
<td>Absorbance</td>
<td>-</td>
<td>12 µM</td>
<td></td>
</tr>
<tr>
<td>Wang et al. 34</td>
<td>SPR</td>
<td>Centrifugal filter device</td>
<td>10⁴ CFU ml⁻¹</td>
<td>These are less common methods as having low LOD but research are still going on to achieve the maximum benefits from these techniques. Among these, SPR and photoacoustic detection methods are gaining its success more enormously and rapidly</td>
</tr>
<tr>
<td>Berti et al. 36</td>
<td>EC</td>
<td>LED induced fluorescence</td>
<td>0.2 nM</td>
<td></td>
</tr>
<tr>
<td>Ren et al. 35</td>
<td>Thermal Lens Detection</td>
<td>0.25 mm thick short-pass interference filter</td>
<td>0.21 µM</td>
<td></td>
</tr>
<tr>
<td>Franko 39</td>
<td>Photoacoustic</td>
<td>-</td>
<td>0.1 nM</td>
<td></td>
</tr>
<tr>
<td>Yang et al. 40</td>
<td>-</td>
<td>-</td>
<td>5 µM</td>
<td></td>
</tr>
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TABLE II
SUMMARY OF THE PERFORMANCE ANALYSIS OF DIFFERENT OPTICAL DETECTION TECHNIQUES IN MICROFLUIDIC APPLICATIONS

and cost. However, a better LOD can still be obtained with the LED excitation by changing the detector (e.g., using PMT detector instead of CCD detector). On top of that, LEDs are still superior to lasers as they are much cheaper than alternative light sources and have a long lifetime and thus can still be employed as a disposable excitation source.

Apart from these, less commonly employed detection strategies, e.g. infrared, nuclear magnetic resonance, thermal lens detection, contactless conductivity detection, photoacoustic, a detection, CMOS luminescence detection and microwave-based detection have recently been introduced elsewhere in 38-40. Among these, research on photoacoustic detection SPR and CMOS luminescence detection are increasing.

8. DISCUSSIONS

After describing the literature on different research works that have been published, we found that fluorescence detection is the more popular and widely used technique. In addition, CL and SERS are also valuable analytical tools for the microfluidic systems but have a limited area of applications. Moreover, other less common methods especially SPR and photoacoustic are also providing impressive results with improvement of device integration. The analytical performances of different micro analysis systems are summarized in Table II.
As can be seen in the table, Poe et al.’s [5] LIF based method and Kim et al.’s [14] CL based approach have produced the lowest LOD which is very desirable for LOC applications.

9. CONCLUSIONS

This paper presented a study of optical detection methods for lab-on-a-chips applications. Despite the fact that the micro-optical detection is an emerging field, only a few articles have reviewed this topic. These articles however do not cover the most recent reported work in this field. This paper reviewed the recent methods mainly published during in and after 2007. It classifies the optical detection approaches into five main groups. It then presents the details of the main published works within each group. In addition, it gives an analysis of the performances of the described work in terms of limit of detection. The best limit of detection reported so far appears to be around $10^{-21} \text{M}$ which is very desirable for lab-on-a-chips applications.

10. REFERENCES


