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A low-cost and rapid microfluidic paper-based analytical devices fabrication method: Flash Foam Stamp Lithography

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Abstract: A novel and facile fabrication method of microfluidic paper-based analytical devices (μPADs) with flash foam stamp lithography (FFSL) is presented in this paper. First, a flash foam (also called photosensitive seal) stamp with desired patterns is made by flash exposing. Next, the stamp is immersed in a hydrophobic solvent such as polydimethylsiloxane (PDMS) to absorb the ink. Finally, the hydrophobic solvent is stamped on filter paper to form hydrophobic barriers. After the hydrophobic solvent cures, the μPAD is complete. Compared to common fabrication methods such as wax printing, inkjet printing, or direct writing, this paper will demonstrate that the FFSL method is convenient, quick, and cheap.

Keywords: Flash foam stamp lithography (FFSL); microfluidic paper-based analytical devices (μPADs); Photosensitive seal.

1 Introduction

μPADs, first proposed by Martinez et al [1], have received plenty of attention from researchers due to their favorable potential application in disease diagnosis and biochemical analysis [2,3], as they possess many attractive features including usability, low cost, low consumption of reagents and samples, pumpless driving, portability, and disposability. Several methods have been used to fabricate μPADs, including photolithography [1, 4, 5], wax printing [6-8], inkjet printing [9-11], screen-printing [12, 13], direct writing of PDMS [14], paper cutting [15,16], and others.

At first, Martinez et al used SU-8 photoresist to make a hydrophobic port on papers [1]. Haller et al [4] used a method of solventless initiated chemical vapor deposition to sedimentate photochromics on filter paper for UV lithography, then washed unreacted material to create μPADs. He et al [5] exposed the pre-hydrophobic filter paper to an octadecyltrichlorosilane (OTS) solution, then used UV mask photolithography to cause the irradiated areas to turn highly hydrophilic. μPADs fabricated by photolithography can acquire high resolution, however many materials used in photolithography isn’t environmentally friendly.

Lu et al [6, 7] and Carrilho et al [8] proposed a μPAD fabrication method based on wax printing. After using a spray wax printer to print the pattern of the hydrophobic region, they heated the paper until that wax could permeate it, creating μPADs with interphase hydrophilic and hydrophobic channels. Now this method is widely used in μPADs fabrication due to convenience and low cost. The wax might be attacked by organic solvents and the μPAD would be easily damaged due to bending and folding of paper [5].

Fabricating μPADs with inkjet printing is another low cost method. Abe et al [9, 10] soaked filter paper into a toluene solution with polystyrene. After the toluene volatilized, the filter paper became hydrophobic. They used inkjet printing to spray toluene solution onto the hydrophilic areas, then the toluene dissolved the polystyrene, creating μPADs. Li et al [11] printed AKD solution on filter paper, then dried the AKD solution to form hydrophobic areas, creating μPADs. The disadvantages of this method include the number of printing iterations required to dissolve the polystyrene, and the requirement of a modified printer. Its major advantage, conversely, is that it can sedimentate different chemical markers in different areas by printing many times.

Dungchai et al [12, 13] used a screen-printing method to fabricate μPADs. In 2009, they reported the use of screen-printing to make the electrodes of μPADs, where they used traditional photolithography to make channels. In 2011, the team developed a wax screen-printing method. They sprayed wax onto a screen which was used as a mask, then dried it to create a wax barrier. The end result was a functional μPAD. The main disadvantage of this method is its low accuracy. The minimum widths of the hydrophilic channel and hydrophobic barrier are 600μm and 1300 μm, respectively.

Bruzewicz et al [14] fabricated μPADs by using a direct writing method. They used a modified pen to extrude PDMS, then manipulated the pen in a two-dimensional motion to construct hydrophobic areas by plotting instrument. This method is very convenient but it is difficult to control the fabrication resolution.

Laser treatment and knife cutting are also reported to fabricate μPADs. Chitnis et al [15] processed hydrophilic channels on hydrophobic filter paper by laser. They sedimentated silica nanoparticles into the channels to realize the capillary drives of the hydrophilic channels. Fenton et al [16] deposited a regent on chromatography paper, then cut the filter paper to form hydrophilic channels by computer-controlled knife plotter. They then cut liquid inlets into cover tape to create μPADs. The main disadvantages of these methods are the high number of calibrations required, and its relatively low accuracy.

Various micro contact printing methods have been widely used to pattern polymers [17], biomolecules [18], and bacteria [19] et al on a variety of substrate. Although these methods could also be applied in producing μPADs, they are often expensive, and their resolutions are greater than that required for paper-based devices [20]. Now some developments of fabricating μPADs with stamping have been reported as alternative methods in comparison to conventional techniques [20-22]. Cheng et al [20] assembled a stamp with paper and tape, which can be used to pattern biochemical in paper. A PDMS high-relief stamp was used for replicate μPADs in chromatographic paper within 10s by Curto et al [21]. Zhang et al [22] reported how to fabricate an iron stamp and how to transfer wax to the paper surface with the stamp. As the above stamps are all not handheld, a lightweight stainless steel stamp was used to create paraffin barriers by Garcia et al [23]. The above stamps reported were almost the hard stamp, so wax was commonly used as the hydrophobic barriers and this method may have the same shortage with wax printing. On the other hand, all the above stamps have low resolution, which means these fabrication methods are better suited for qualitative than quantitative work. Fabrication of μPADs with stamping is easy to operate, but different patterns of μPADs need different stamps, so finding low cost stamp is also necessary.

Flash foam stamp (FFS,) is also called flash pre-inked stamp, or photosensitive seal stamp. When flash foam material is exposed to an intense burst of light, its micro-porous surface is sealed. If a masked area atop the flash foam is exposed, the pattern of the mask will be transferred to the flash foam, creating an FFS. Ink can then be stamped onto paper through the unsealed surface area of the FFS. Currently, FFS is commonly used to create personal stamps. It is favorable for this because it avoids the use of an inkpad, as the ink is stored in the micro-porous foam. Because FFS is already widely used in the fabrication of personal stamps, the process is quite cheap, and convenient.

In this paper, we propose a low-cost method of fabricating μPADs using FFS, called FFSL. With FFSL, only two steps are needed: the fabrication of the FFS, and stamping. A PDMS solvent was used as stamp ink, stamped on the filter paper to form hydrophobic barriers. After the solvent solidified, hydrophilic channels were formed between the hydrophobic barriers, and creating μPADs. All the materials used in FFSL are nontoxic, and the only specialized device required is a flash stamp machine. In addition, μPADs are easily bended and folded without damage as the hydrophobic barriers are formed by soft PDMS.

2. Materials and methods

2. 1 Fabrication of FFS

The FFS and flash stamp machine were purchased from Liaocheng Beike Electronic Information Materials Co., Ltd. (Liaocheng, China,) shown in Fig.1a. The negative patterns of the μPADs were designed on the CorelDraw X4 (Corel Co., Ltd. Canada) then printed on tracing paper with an HP inkjet printer (600DPI) as the mask, shown in Fig.1b. The flash foam, combined with the mask, is exposed in a flash stamp machine with Xenon tubes, which delivers the intense burst of light that seals the non-printing area, or hydrophilic channels. A fine example of FFS is shown in Fig.1c, where the dark area are the sealed micro holes, and the gray unsealed area is where stamp ink is stored for transfer to the paper during stamping.

Flash foam is a kind of ultra-micro bubble material, typically made by polyethylene, and the size of the microporous is very small and the average diameter is less than 30 microns, as shown in Fig.2a &2b. Due to microporous structures inside, the material itself has the characteristic of oil storage and permeation. Under strong light radiation, flash foam can absorb the light energy and transform it to heat energy. At the light exposure area, the surface of the flash foam instantly absorbs a great deal of energy and the temperature of flash foam quickly rises up to melting point. After the exposure, the temperature falls rapidly and the exposure area of flash foam forms a film, which has the function of porous sealing and isolation from the ink. This is the reason why FFS also called photosensitive seal stamp. As shown in Fig.2c &2d, the microporous are shrunk to close after exposition, from unsealed size of 20-30μm to sealed size of 2-3μm, so the ink could not passed through this area.

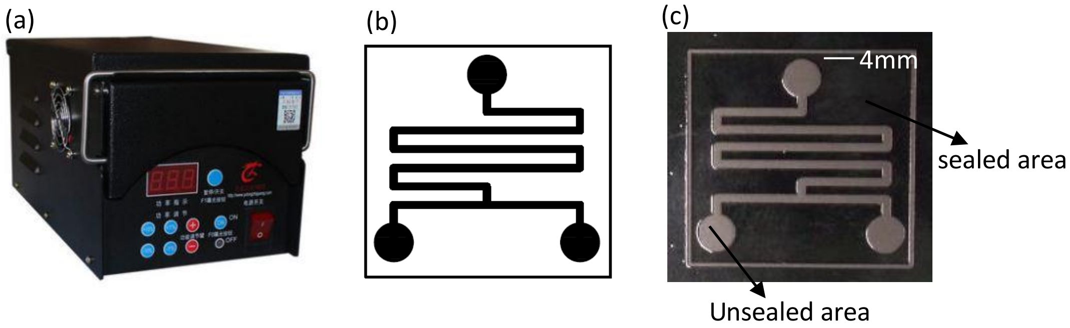

Fig.1 Schema of fabrication of FFS (a) Flash stamp machine; (b) Mask pattern; (c) Flash foam after exposed with mask.

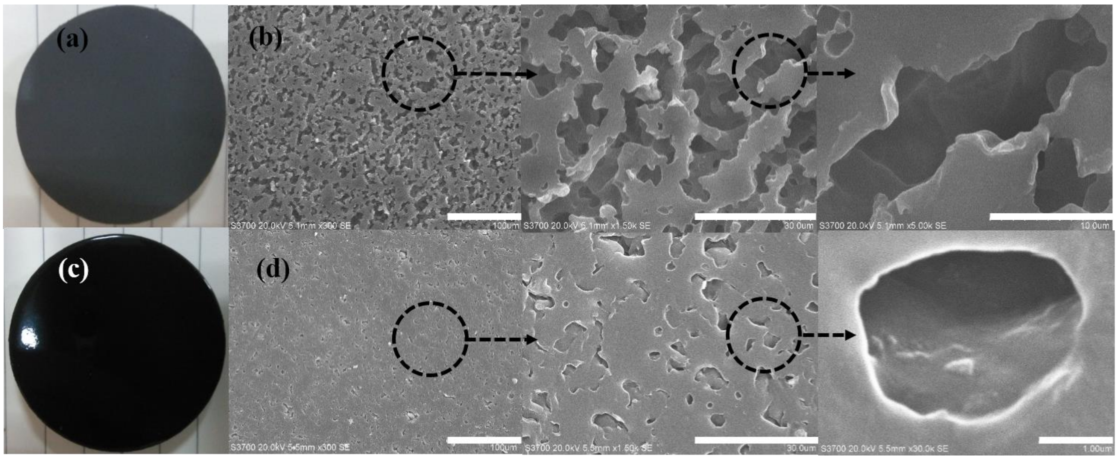

Fig.2 Micro structure of flash foam before and after exposure, before exposure (a) & (b), after exposure (c) & (d).

2. 2 FFSL Process

A typical FFSL process is shown in Fig.3. First, an FFS with designed channels is fabricated, then immersed in hydrophobic solvent, in order to absorb ink, for about fifteen minutes. When the FFS is stamped onto the paper, the hydrophobic solvent transfers to the paper. μPADs with hydrophobic barriers are obtained after the hydrophobic solvent has solidified in a vacuum oven for about fifteen minutes in a temperature of 60 °C, or for an hour or so at room temperature.

PDMS was chosen as the hydrophobic solvent, also used in the fabrication of μPADs with direct writing [14]. PDMS part A and part B (Sylgard 184, Dow Corning,) was mixed in a 10:1 (weight:weight) ratio and stirred for two minutes. The PDMS was then placed in vacuum desiccators for 10-13 minutes for degassing.

A μPAD fabricated by the FFSL method is shown in Fig.4. When the PDMS solidified, the hydrophobic barrier area became semitransparent, as demonstrated in Fig.4a. The contact angle of the hydrophobic barriers is about 120°, proving its favorable hydrophobic effect (Fig.4b). Red ink can be absorbed and permeated from inlet to outlet at the hydrophilic area (Fig.4c), demonstrating that the hydrophilic channel is interconnected well.

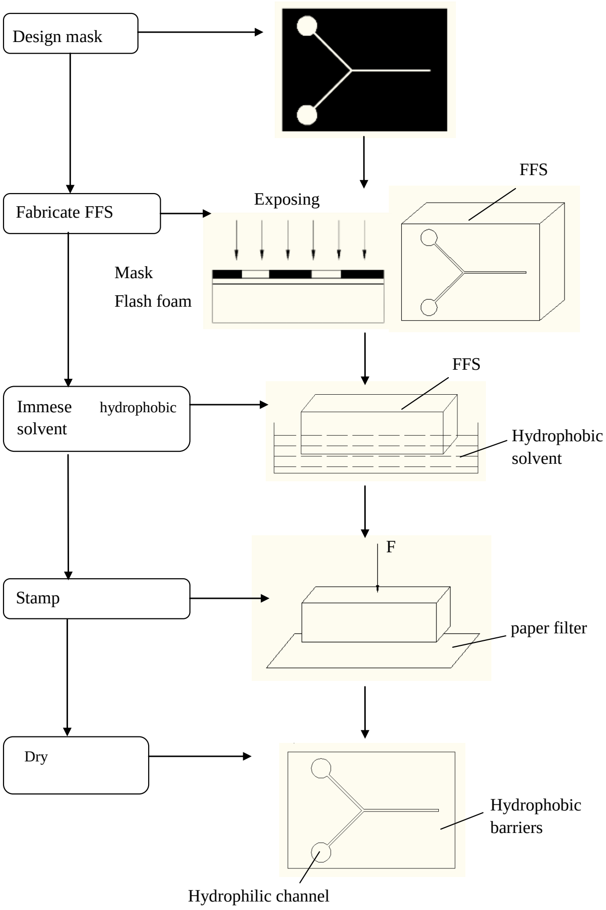

Fig. 3 Typical process of FFSL.

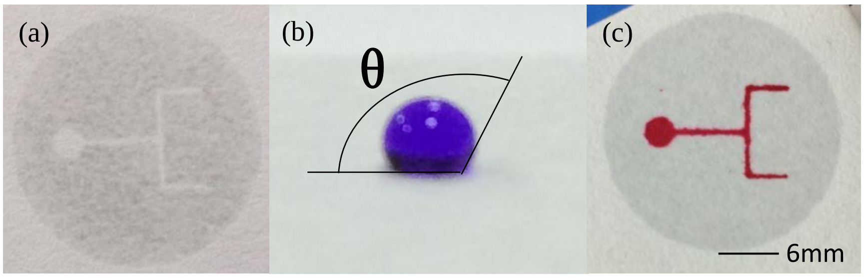

Fig.4 μPAD fabricated by FFSL method (a) After PDMS solidified; (b) Ink in hydrophobic area with contact angle about 120˚; (c) Red ink absorbed by capillary action.

The resolution of μPADs fabricated by FFSL were assessed by testing how the minimal width of the hydrophilic channel and hydrophobic barrier are preserved when the μPAD is immersed in dye. The minimal width of the hydrophilic channel with complete submersion is defined as the resolution of the hydrophilic channel. Conversely, the minimal width of the hydrophobic barrier without submersion is defined as the resolution of the hydrophobic barrier. To determine the resolution of the FFSL method, the final widths of the hydrophobic barrier and hydrophilic channel were studied in the range of 50-1300μm, with a design width of 50μm, 100μm, 200μm, 300μm…1300μm. Each barrier/channel in the FFS was repeated three times in the mask. After fabrication, the μPAD was immersed in red food dye for five seconds in order to visualize the hydrophobic and hydrophilic properties.

Quantitative analysis of NO_2- was used to evaluate the performance of FFSL in performance analysis as a case study. Now this case has become a standard way to evaluate a new μPAD fabrication method. There are several reports about the NO_2- analysis with μPADs [5, 18-20]. The detailed pattern and analysis method used in our case study can be found in ref 5.

3. Results and discussion

3.1 Resolution of FFSL method

As shown in Fig.5a, the hydrophilic channels between Group 1 and Group 5 weren't completely saturated by the dye, so the average width of the hydrophilic channels in Group 6 was the resolution for hydrophilic channels, with a measured width of 428 ± 21μm, shown in Fig.5a. The hydrophobic barriers in Group 1 and Group 2 were partly saturated, so the average width of the hydrophobic barriers in

Group 3 was the resolution for hydrophobic barriers, with a measured width of 357 ± 28μm, as shown in Fig.5b.

The resolution for hydrophilic channels of the μPADs fabricated by plotter printing was about 1000μm, and the hydrophobic barriers was about 1000μm [8] as well. The resolution for hydrophilic channels of the μPADs fabricated by screen-printing was 650μm, and the hydrophobic barriers was 1300μm [12]. Compared to these two methods, the resolution of FFSL is more favorable.

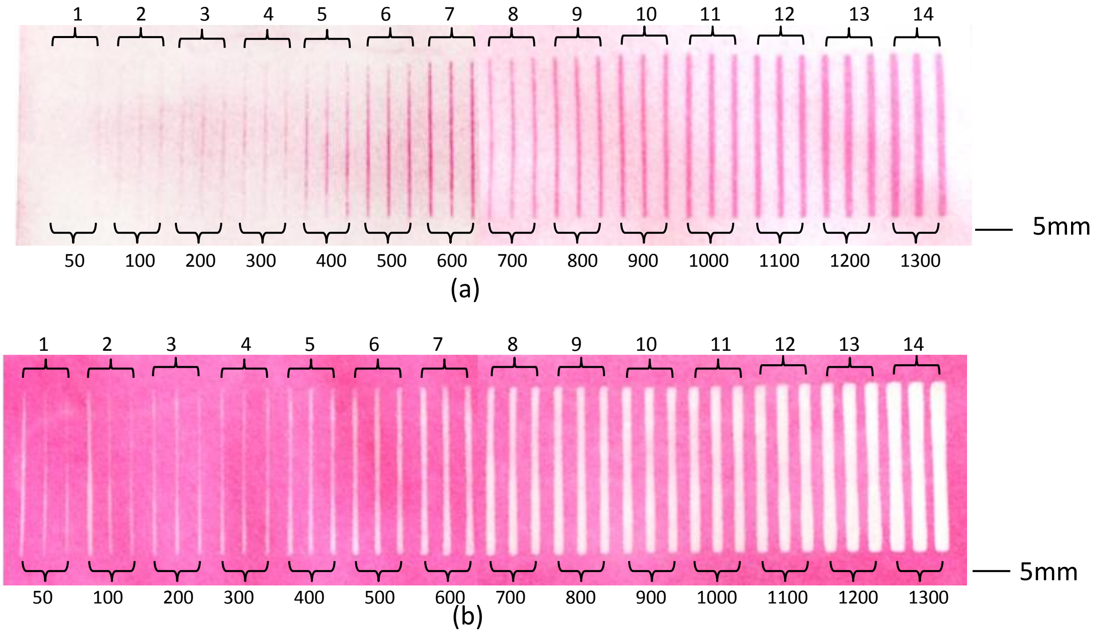

Fig.5 Static resolution testing (a) Hydrophilic channel testing; (b) Hydrophobic barrier testing.

3.2 FFSL Cost & Resolution Analysis

The primary advantages of FFSL are its low cost and simplicity of operation. All the materials and instruments required are of low cost. The most expensive investment in FFSL manufacturing is the flash stamp machine, which is widely used to manufacture personal stamps and still only costs about $100. This machine is very compact, with a size of 320mm×170mm×170mm, and conveniently portable, for when immediate fabrication of μPADs may be needed for an in-line field test. The other materials needed are listed in Tab. 1. The total cost of fabricating a piece of μPAD for the first time is only about fifteen cents (¥0.91/$0.15). As the FFS can be re-used to stamp several μPADs, the cost is much lower for subsequent μPADs.

The resolution of different μPADs fabrication methods of are listed in Tab.2, although fabrication with photolithgrayphy and UV degradation & self-assembling layer have the highest resolution, the cost and the toxic material during the fabrication will restrict their wide use. The method of wax printing now is very popular and has a good resolution. The main instrument of wax printing is the wax printer, which is designed for replacement of inkjet and laser printer at the beginning. However, wax printer is completely defeated by inkjet printer and laser printer, and is seldom found in the office. If the wax printer is canceled by the manufacturer, how to fabricating μPADs with wax printing maybe a problem. FFSL can acquire almost the same resolution comparing with by inkjet printing, and don’t need to customize any devices. Another low cost fabrication methods such as plotter printing of PDMS, wax screen-printing and knife cutting have low resolution, however FFSL can get a balance between cost and resolution.

Tab. 1 Cost of FFSL

Item	Amount	Cost
Filter Paper	40×40mm²	¥0.15
Flash foam	40×40mm²	¥0.09
Tracing Paper	40×40mm²	¥0.001
PDMS	0.5g	¥0.4
Electric charge	≈0.1kW·h	¥0.05

Mask	1 piece of paper	¥0.01
Total		¥0.91/$0.15

Tab.2 Comparison of µPADs fabrication methods

Method	Channel(µm)	Barrier(µm)	Advantages	Disadvantages
Photolithgrayphy [1]	186±13	248±13	High resolution	Expensive device; Complex fabrication;
UV degradation & self-assembling layer [5]	233±30	137±21	High resolution; Easy to fabricated	Hydrophilic channels exposed to polymers or solvents
Wax printing [8]	561±45	850±50	Simple; Suitable for mass-produce	The design of the patterns must account for the spreading of the wax
Inkjet printing [11]	590	302	High resolution; Rapid; Low cost	Requires a customized inkjet printer
Wax screen-printing [12]	650±71	1300±104	Easy to fabricated	Low resolution
Plotter printing of PDMS [14]	～1000	～1000	Hydrophilic channels not exposed to polymers or solvents	Low resolution; Requires a customized plotter
Knife Cutting[25]	2000	——	Low cost; Rapid, Can fabricate 3D µPADs	Low resolution
FFSL	632± 27	306± 20	Low cost; Rapid; Flexible; Environmentally friendly	

3.3 Complicated pattern fabrication

Some µPADs with more complicated channel patterns are fabricated to demonstrate the capability of FFSL method. Included examples are a Chinese map, Fig.6a, logo of Zhejiang University, Fig.6b, and dot array widely used in spotting, Fig.6c, all successfully fabricated. The hydrophilic channels are well-preserved by hydrophobic barriers, allowing dye to diffuse to all hydrophilic channels. As shown here, the FFSL method performs well in the fabrication of many types of μPADs.

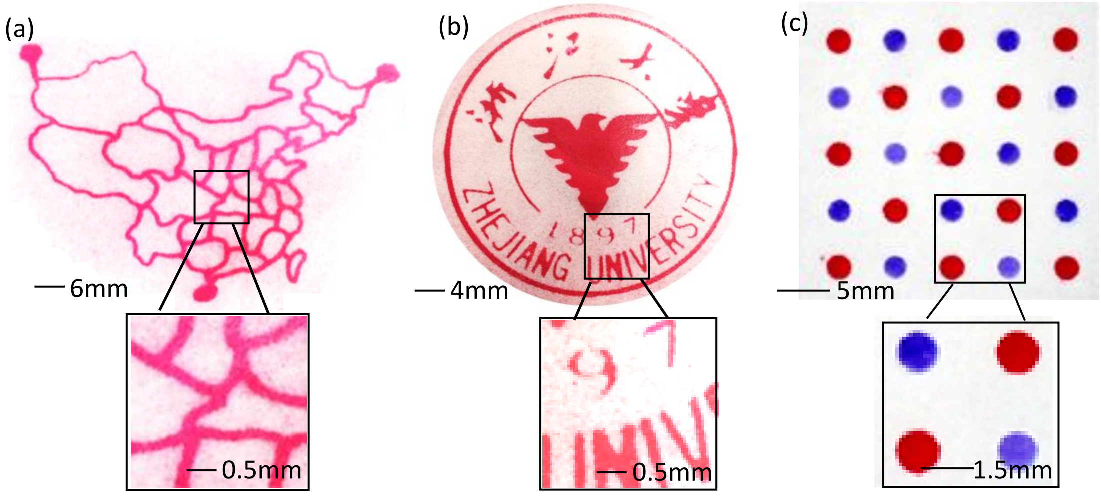

Fig.6 μPADs with complicated patterns, (a) Chinese map; (b) Logo of Zhejiang University; (c) Dot array.

3.4 Case study

To replicate this process, measure a concentration of NO_2^- for the sample according to the method described above. As shown in Fig.7a, the concentrations of structural solution of NO_2^- in sample testing areas No. 1-7 are 0.3 $mg\cdot L^{-1}$, 0.5$mg\cdot L^{-1}$, 1 $mg\cdot L^{-1}$, 2 $mg\cdot L^{-1}$, 3 $mg\cdot L^{-1}$, 4 $mg\cdot L^{-1}$, 5$mg\cdot L^{-1}$ in proper order, with a sample solution at a concentration of 1.8 $mg\cdot L^{-1}$ in sample testing area No. 8. Transform Fig.7a to grayscale by Adobe Photoshop, and draw a structure curve of the grayscale. The result of this is shown in Fig.7b. The grayscale is proportional to the concentration, the regression equation of which is y=5.9104x+67.659 (where x represents the concentration of NO_2^- with a unit of $mg \cdot L^{-1}$, and y represents the grayscale, which is dimensionless.) According to the regression equation and the grayscale of the sample, we can calculate the concentration of NO_2^- in the sample solution,1.75 $mg \cdot L^{-1}$. The result agrees with the actual concentration of the sample, 1.8 $mg \cdot L^{-1}$.

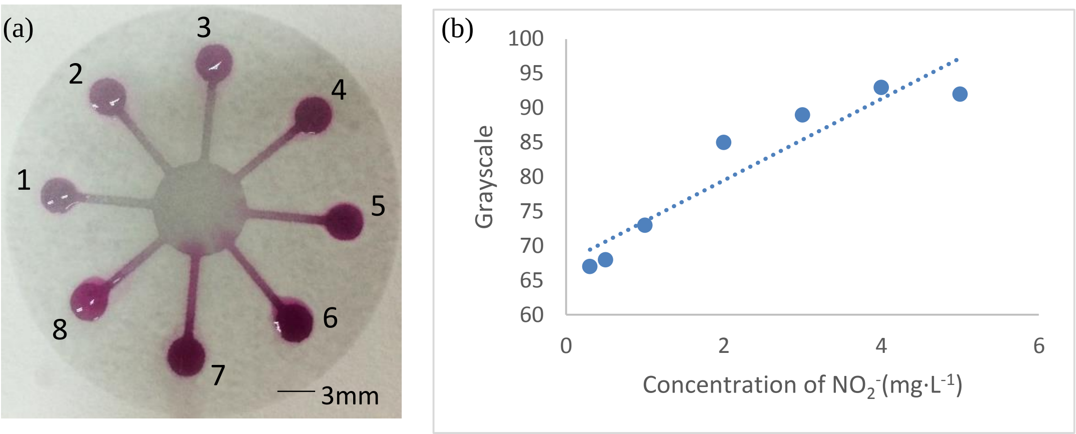

Fig.7 Quantitative analysis of NO_2^- (a) The analysis result of the concentration of NO_2^-; (b) The linear relationship between the grayscale and the concentration of NO_2^-.

3.5 Discussion

FFSL can be seen as a lightweight μPAD fabrication method with a middle resolution and a low cost, especially easy implementation. In this report, we just chose PDMS as the ink to stamp hydrophobic barriers, as this material is widely used in the analytical field. However, as a stamp method, various inks can be used to fabricate μPADs. Theoretically, any ink which will be solidified after stamp and keeps hydrophobic can used to form hydrophobic barriers, for example each type of ultraviolet (UV) resin. Compared with widely used μPAD fabrication method, such as wax printing and inkjet printing, FFSL provides an ability that researchers can design and choose suitable materials to form hydrophobic barriers according to different analytical environment.

4. Conclusion

A novel μPAD fabrication method, FFSL, was proposed. FFS, a method already widely used in the fabrication of personal stamps, is introduced for stamping μPADs. μPAD fabrication is simplified to two steps: FFS fabricating, and μPAD stamping. The process is incredibly simple to learn, and it is possible to fabricate flexible μPADs within 30 minutes, as the fabrication itself is very simple. Fabrication of FFS requires no toxic substances, which avoids the pollution of the environment, unlike photolithography. Furthermore, the only specialized instrument required is the flash stamp machine, which only costs about $100 and is lightweight and portable. Using FFSL, any lab can fabricate μPADs immediately and successfully in a cost-effective manner.

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