Magnetic digital microfluidics on a bioinspired surface for point-of-care diagnostics of infectious disease

Kanitthamniyom, Pojchanun; Zhang, Yi

2019

Kanitthamniyom, P., & Zhang, Y. (2019). Magnetic digital microfluidics on a bioinspired surface for point-of-care diagnostics of infectious disease. *ELECTROPHORESIS*, 40(8), 1178–1185. doi:10.1002/elps.201900074

<https://hdl.handle.net/10356/144957>

<https://doi.org/10.1002/elps.201900074>

This is the accepted version of the following article: Kanitthamniyom, P., & Zhang, Y. (2019). Magnetic digital microfluidics on a bioinspired surface for point-of-care diagnostics of infectious disease. *ELECTROPHORESIS*, 40(8), 1178–1185., which has been published in final form at doi:10.1002/elps.201900074. This article may be used for non-commercial purposes in accordance with the Wiley Self-Archiving Policy [<https://authorservices.wiley.com/authorresources/Journal-Authors/licensing/self-archiving.html>].

Downloaded on 26 Apr 2023 21:28:00 SGT

Magnetic Digital Microfluidics on a Bioinspired Surface for Point-of-Care Diagnostics of Infectious Disease

Pojchanun Kanitthamniyom¹ and Yi Zhang^{1*}

¹Singapore 3D Printing Center, School of Mechanical and Aerospace Engineering, Nanyang Technological University, 50 Nanyang Avenue, N3.2-02-52, Singapore

Corresponding authors:

E-mail: yi_zhang@ntu.edu.sg

ORCID ID: 0000-0002-1239-3441.

Abbreviations:

EWOD = electrowetting-on-dielectric

ELISA = enzyme-linked immunosorbent assay

HbsAg = hepatitis B surface antigen

TMB = 3,3',5,5'-Tetramethylbenzidine

HRP = horseradish peroxidase

Keywords: magnetic digital microfluidics, droplet, polydopamine, diagnostics, magnetic particles

Abstract

Magnetic digital microfluidics uses magnetic force to manipulate droplets on a Teflon-coated substrate through the added magnetic particles. To achieve a wide range of droplet manipulation, hydrophilic patterns, known as surface energy traps, are introduced onto the Teflon-coated hydrophobic substrate. However, the Teflon-coated substrate is difficult to modify because it is non-wettable, and existing techniques for patterning surface energy traps have many limitations. Inspired by the mussel adhesion mechanism, we use polydopamine, a bioinspired substance that adheres strongly to almost any materials, to pattern surface energy traps on the Teflon-coated substrate with a great ease. We have optimized the polydopamine coating protocol and characterized the surface properties of the polydopamine surface energy traps. Droplet operations including particle extraction, liquid dispensing, liquid shaping and cross-platform transfer have been demonstrated on the polydopamine surface energy trap-enabled magnetic digital microfluidic platform in both single-plate and two-plate configurations. Furthermore, the detection of hepatitis B surface antigen using enzyme-linked immunosorbent assay (ELISA) has been demonstrated on the new magnetic digital microfluidic platform. This new bioinspired magnetic digital microfluidic platform is easy to fabricate and operate, showing a great potential for point-of-care applications.

1. Introduction

Digital Microfluidics manipulates discrete volume of fluids that spontaneously form droplets on a hydrophobic surface coated with Teflon.[1-4] Based on the droplet actuation mechanism, digital microfluidics can be categorized into several classes including the magnetic,[1, 5-13] the electrowetting-on-dielectric (EWOD),[14-17] and other types.[13, 18-21] On a magnetic digital microfluidic platform, magnetic particles are added into the liquid or the hydrogel[22, 23] droplets as the droplet manipulator. The droplet is usually actuated by the pulling force of the magnet. Occasionally, the hydrogels are manipulated by the pushing force of the magnet due to the diamagnetism.[24] Magnetic digital microfluidics is more well-suited for point-of-care diagnostics in the low-resource environment compared to other microfluidic systems due to its simple fluidic operation and the multifunctionality of the magnetic particles.

In its simplest format, the substrate of the magnetic digital microfluidic platform is a plain surface coated with Teflon AF, which renders the surface hydrophobic to facilitate the droplet movement. In real applications, many additional surface features in the form of physical structures[25-27] or chemical modifications[28, 29] are introduced to the Teflon-coated substrate. For example, chemical modifications have been introduced to create hydrophilic regions on the Teflon-coated surface.[28-30] These hydrophilic regions, known as the surface energy traps, would immobilize the droplet with their high surface tension to facilitate the droplet manipulation. With these chemically modified surface energy traps, the magnetic digital microfluidic platform is able to perform complex heterogeneous and multiplexed bioassays in droplets. However, the chemical modification relies on the traditional microfabrication techniques and has several limitations. First, the throughput for the traditional lithography is low, and it is challenging to achieve a uniform photoresist film on the

Teflon-coated surface because Teflon is non-wettable. Second, the SU8-based shadow mask used in the oxygen plasma etching is brittle and difficult to handle. Third, the hydrophilic effect of oxygen plasma treatment is only temporary, lasting for a couple of days at most.

Because of these aforementioned issues, we realize the need for an easy method of patterning hydrophilic surface energy traps on the Teflon-coated substrate for magnetic digital microfluidics. Inspired by the mussel adhesion mechanism, we have turned our attention to a highly adhesive material known as polydopamine. Polydopamine is one of the natural materials responsible for mussels' strong adhesion to the solid surface.[31-35] In the laboratory settings, polydopamine is synthesized by polymerizing catechol, such as dopamine HCl, in an alkaline environment.[31, 35] Polydopamine adheres to the surfaces made of almost any materials, including Teflon which is non-wettable by the aqueous solution.[36-38] This polydopamine coating is hydrophilic with many hydroxyl, carboxyl and other functional groups.[39-41] Because of its simple coating protocol, great biocompatibility and multifunctionality, polydopamine has been rapidly adopted as a new material for the surface modification and functionalization in many areas.

In this paper, we present a magnetic digital microfluidic platform that manipulates droplets on a bioinspired surface modified with polydopamine for point-of-care diagnostics of infectious diseases. We have developed a technique to pattern the Teflon-coated surface with polydopamine, which creates hydrophilic surface energy traps to facilitate droplet manipulation. We have optimized the polydopamine modification protocol and characterized the wetting property of polydopamine on the Teflon-coated surface by measuring the contact angle. On this new platform, we have demonstrated the diagnostics of hepatitis B by detecting the hepatitis B surface antigen (HBsAg) using the particle-based ELISA. This magnetic digital

microfluidics-based hepatitis B diagnostic platform shows a great potential for point-of-care applications with its simple fluidic operations.

2. Results and Discussion

Chemically modified surface energy trap is a desired feature on the magnetic digital microfluidic platform. Teflon is well-known for its "nonstick" property. Nevertheless, polydopamine could form a hydrophilic thin film that sticks strongly to Teflon. Therefore, polydopamine is an ideal material for modifying the property of the Teflon-coated surface.

2.1 Optimization and Characterization of Polydopamine Thin Film Coating on Teflon

We first optimized the polydopamine coating protocol and characterized the surface property after the polydopamine modification by measuring the contact angle. The polydopamine was deposited *in situ* by polymerizing the dopamine monomer directly on the substrate. Although the Teflon surface was not wetted by the dopamine monomer solution, polydopamine could adhere to the Teflon surface as evidenced by the emergence of a dark brown thin film, a characteristic color of polydopamine.[31] We could selectively pattern specific regions on the Teflon-coated surface with polydopamine by dispensing the dopamine monomer solution as free-standing droplets, which resulted in circular polydopamine regions (**Figure 1a**). Alternatively, we could expose Teflon to the dopamine monomer solution through a stencil, which allowed us to pattern any arbitrary shapes with polydopamine (**Figure 1b**). The liquid would form a droplet with a large contact angle on the Teflon-coated surface (**Figure 1c, left**). But once the Teflon was coated with polydopamine, the liquid would spread and resulted in a small contact angle (**Figure 1c, right**). Droplets could move freely on the Teflon-coated surface. But once the droplets reached the polydopamine surface energy traps, they were anchored (**Figure 1d** and Supplementary Information Video V1). Using the free-standing

droplet method, we could control the size of the circular polydopamine spot by adjusting the volume of the dopamine monomer solution. As shown in **Figure 1e**, the diameter of the polydopamine spot is positively correlated with the volume of the dopamine monomer solution, although the relationship is not linear. Instead, the diameter of the polydopamine spot scales linearly with the cube root of the droplet volume (**Figure 1f**). For droplets with diameters less than the capillary length (2.7 mm for water which corresponds to a droplet of $\sim 10 \mu\text{L}$ in volume),^[42] the shape of the droplet is a spherical cap because the gravitational effect is negligible. As the volume of the droplet increases, the large droplets are no longer spherical in shape, but slightly flattened due to the gravity. Therefore, it comes as a little surprise to see the linear relationship between the diameter of the polydopamine spot and the cube root of the droplet volume up to $50 \mu\text{L}$, which suggests that the contact area between the droplet and the Teflon-coated surface is not strongly influenced by the shape of the droplet.

Figure 1. *In Situ* polydopamine deposition on Teflon-coated surface using a) free-standing droplets and b) silicone stencils. c) Droplets on the Teflon-coated surface and the polydopamine-coated surface. d) The droplet could move freely on the Teflon-coated surface. Once it reaches the polydopamine-coated region, it can no longer move. All frames in panel d) has the same scale bar. e) The diameter of the polydopamine surface energy trap versus the volume of the free-standing dopamine monomer droplet. f) The diameter of the polydopamine surface energy trap versus the cubic root of the free-standing dopamine monomer droplet volume.

We characterized the effect of the polydopamine modification on the Teflon-coated surface by measuring the contact angle. We first optimized the reaction time, i.e. the duration that the dopamine monomer solution was in contact with the Teflon. The Teflon-coated surface was incubated with the dopamine monomer solution for various durations. At time 0, when no polydopamine was formed, the contact angle was above 120° (**Figure 2a**). After a 10-minute incubation, the dopamine monomer solution turned into a light brown color, a characteristic sign of the formation of polydopamine. The polydopamine deposited on Teflon reduced the contact angle to 60°–70°, similar to that of a regular glass coverslip. As we further increased the incubation duration, we did not observe a significant decrease in contact angle up to 24 hours (**Figure 2a**). The contact angles measured at various time point within the 24-hour period all showed similar values ranging roughly between 50–70°. These results suggested that a long incubation period was unnecessary. Protocols reported in the literature usually required incubating the substrate with the dopamine monomer solution for at least several hours to overnight.[31, 35] For the glass substrate, several reports showed that the thickness of the polydopamine coating increased with a longer reaction time, resulting in

decreasing contact angles.[43, 44] However, we did not observe the same trend with the polydopamine coating on the Teflon-coated surface.

Next, we tested the effect of buffer pH and the concentration of the dopamine monomer. Reported protocols usually used 2 mg/mL dopamine monomer solution in a buffer of pH 8-8.5.[31, 35] Using the same concentration of dopamine monomer in the 10 mM Tris buffer at pH 8, a polydopamine thin film was deposited on the Teflon-coated surface with a contact angle of $\sim 70^\circ$, similar to the contact angle of the glass coverslip. As the concentration of the dopamine monomer gradually increased up to 40 mg/mL, we did not observe any significant change in the contact angle (**Figure 2b**). The experiment was repeated under the same condition with the Tris buffer at pH 8.8, and similar results were observed.

Fig. 2 The characterization of polydopamine coating on Teflon by contact angle measurement.

a) The effect of reaction time. b) The effect of buffer pH and dopamine monomer concentration.

The results above suggest that the effect of the polydopamine coating on the Teflon-coated surface is not sensitive to the reaction conditions. The polydopamine thin film of similar wetting properties may be deposited on the Teflon-coated surface using various reaction conditions. On one hand, this phenomenon gives us some leeway to create surface energy traps with a robust and consistent performance using the simple one-step protocol. On the other hand, we are unable to tune the degree of hydrophilicity using polydopamine, which makes this technique less versatile.

Besides the simple protocol, another great advantage of polydopamine is the strong and long-lasting coating. Polydopamine is known for its strong adhesion to the substrate. We notice that the polydopamine-modified surface could retain the wettability for several weeks to months. In comparison, the glass surface modified with the oxygen plasma could only remain hydrophilic for several days at most.

Although this polydopamine-based technique is simpler and more robust compared to the lithography-based approaches, the resolution of the modified pattern is poor in comparison. It is straightforward for lithography to achieve a pitch size in the range of tens of microns. In contrast, the polydopamine-based wet chemistry can hardly achieve a sub-millimeter pitch in practice. Because Teflon is highly non-wettable, it is difficult to dispense a dopamine monomer solution of less than 1 μL onto the surface. 1 μL dopamine monomer solution would result in a surface energy trap of ~ 1 mm in diameter, and it is difficult to create surface energy traps smaller than that. Therefore, the polydopamine-based approach is not suitable for fabricating high-density arrays.

2.2 Droplet Manipulation on the Magnetic Digital Microfluidic Platform with Polydopamine Surface Energy Trap

To control the motion of the droplet on a magnetic digital microfluidic platform, an external magnetic field was applied to drive the magnetic particles. Due to the surface tension of the liquid droplet, the magnetic particle cluster could not break away from the droplet easily. The surface energy trap was introduced to provide an additional force in the direction opposite to the movement to facilitate the particle extraction process. As shown in **Figure 3a**, once the droplet moved over a large polydopamine surface energy trap, the surface energy trap pinned down the droplet while the magnetic particle cluster continued to move, leading to the formation of a necking point between the droplet and the magnetic particle cluster. As the magnetic particle cluster moved further away, the curvature at the necking point was gradually increasing until the Laplacian pressure caused the breakage, resulting in the particle extraction from the droplet. In another scenario, the magnetic particle cluster moved over a small surface energy trap, and a necking point was formed between the droplet and the surface energy trap (**Figure 3b**). Once the necking point broke, a small portion of the droplet was withheld within the surface energy trap while the rest part of the droplet continued moving with the magnetic particles, resulting in the passive liquid dispensing.

In general, as a droplet being dragged over a surface energy trap by a cluster of magnetic particles, two necking points could potentially form (**Figure 3c**), one between the droplet and the surface energy trap (Necking Point 1) and the other between the droplet and the magnetic particle cluster (Necking Point 2). Under certain scenarios, one necking point would break before the other one is fully developed, like the ones shown in **Figure 3a** and **Figure 3b**. When moving at a constant low speed U , the drag force F_{drag} is approximately proportional to U and $V^{1/3}$ where V is the volume of the droplet. The other two external forces are the magnetic

force F_m which is proportional to the total mass M of the magnetic particles and the surface tension F_i which is proportional to the diameter D of the surface energy trap. The necking process causes the droplet deformation and induces the capillary force. The F_{c1} is the capillary force that holds the small droplet within the surface energy trap, and the F_{c2} is the capillary force that holds the magnetic particles within the droplet. F_{c1} is proportional to the length scale of the surface energy trap D , and F_{c2} is proportional to the length scale of the magnetic particle cluster $M^{1/3}$. [42] When the magnetic force F_m is greater than the surface tension F_i and the drag force F_{drag} combined, the capillary force F_{c1} is smaller than the surface tension F_i , and the capillary force F_{c2} is greater than the magnetic force F_m , the necking point 1 would break first, resulting in the liquid dispensing. When the magnetic force is greater than the surface tension F_i and the drag force F_{drag} combined, the capillary force F_{c1} is greater than the surface tension F_i , and the capillary force F_{c2} is smaller than the magnetic force F_m , the necking point 2 would break first, resulting in the particle extraction.

We observed the droplet and magnetic particle's behavior under various conditions by adjusting the amount of the magnetic particles, the size of the surface energy trap, and the droplet volume. The droplet behavior was plotted in a 3D phase diagram (**Figure 3d**) and summarized in the **supplementary Table S1**. This phase diagram would aid the design of polydopamine surface energy traps-enabled magnetic digital microfluidics. For a constant droplet volume (along the xy plane), as the amount of the magnetic particle increases and the size of the surface energy trap decreases, the droplet operation shifts from the particle extraction to the liquid dispensing. For a constant surface energy trap size (along the xz plane), as the amount of the magnetic particles increases and the droplet volume decreases, the droplet operation shifts from the particle extraction to the liquid dispensing.

Figure. 3 The formation of necking points after the droplet moves through a polydopamine surface energy trap of relatively a) big and b) small in size. The necking points are formed at different positions in these two cases. c) The forces on the droplet as it is dragged over a surface energy trap by the magnetic particle cluster. d) 3D phase diagram of the droplet operation. Whether it is the liquid dispensing, or the particle extraction depends on the mass of magnetic particles, the size of the surface energy trap, and the volume of the droplet. e) The volume of the daughter droplets dispensed by the surface energy is approximately proportional to the area of the surface energy trap. The dash lines in all panels indicate the polydopamine surface energy trap. The red arrows indicate the movement direction of the permanent magnet.

The volume of the droplet dispensed using the surface energy trap is proportional to the area of the surface energy trap (**Figure 3e**). The smallest surface energy trap is 1 mm in diameter or 0.78 mm² in area, which allows us to dispense a daughter droplet of ~470 nL in volume. With a surface energy trap of 3.5 mm in diameter or 7.07 mm² in area, we are able to dispense a daughter droplet of 12.5 μL in volume. Surface energy traps greater than 3.5 mm would often lead to particle extraction.

Figure 4. Droplet manipulation on the polydopamine surface energy trap-enabled magnetic digital microfluidic platform in single-plate configuration. a) Particle extraction, b) Liquid dispensing, c) Liquid shaping and d) cross-platform transfer. The dash lines in all panels indicate the polydopamine surface energy trap. The red arrows indicate the movement direction of the permanent magnet.

Using the aforementioned mechanisms, we demonstrated various types of droplet manipulation on the polydopamine surface energy trap-enabled magnetic digital microfluidics (**Figure 4** and supplementary **Figure S1**). In all the subsequent experiments, the circular surface energy traps were fabricated using free-standing droplets, and the surface energy traps of other shapes were fabricated using the silicone stencils. By moving a 10-μL droplet

with 2 μL of magnetic particles ($\sim 0.12\text{mg/mL}$) (MagAttract Suspension G from Qiagen) over a $\sim 3\text{-mm}$ surface energy trap (**Figure 4a** and Supplementary Information Video V2), the entire droplet was immobilized by the surface energy trap, and we could easily extract the magnetic particles from droplet. We were able to dispense multiple aliquots by splitting small daughter droplets from a $10\text{-}\mu\text{L}$ parent droplet using a series of small surface energy traps of $\sim 1.5\text{ mm}$ in diameter (**Figure 4b** and Supplementary Information Video V3). Because the polydopamine surface energy trap was the only wettable region on the Teflon-coated substrate, we could use the polydopamine modification to shape the liquid (**Figure 4c** and Supplementary Information Video V4). We patterned a crescent-shaped region with polydopamine through a silicone stencil. As we dragged a $15\text{-}\mu\text{L}$ droplet over the polydopamine surface energy trap, the fluid wet the entire polydopamine-coated area and was shaped into a crescent. The adhesive force provided by the polydopamine enabled us to selectively transfer droplets from one platform to another. As shown in **Figure 4d** and Supplementary Information Video V5, three green droplets and two orange droplets of $10\text{ }\mu\text{L}$ in volume were placed on a Teflon-coated substrate. On another platform, three polydopamine surface energy traps were created. As the two platforms were brought close, the polydopamine surface energy traps caught the green droplets and lifted them up. As a result, only the green droplets but not the orange droplets were transferred from the first platform to the second. This droplet operation could be used to transfer samples between different magnetic digital microfluidic platforms for multi-stage analysis.

The demonstration in **Figure 4** was performed in a single-plate configuration, which was typical for magnetic digital microfluidics. The EWOD-based digital microfluidics often used a two-plate configuration by sandwiching the droplets between two Teflon-coated glass coverslips. In this study, we also demonstrated the droplet manipulation using polydopamine

surface energy traps in a two-plate configuration on the magnetic digital microfluidic platform (**Supplementary Figure S1**). In this scenario, the droplets were in contact with both coverslips, and the polydopamine surface energy traps were fabricated on the top glass coverslip. As it moved over the surface energy trap, the droplet was pinned to the top glass coverslip whereas the magnetic particles continued moving on the bottom glass coverslip. We demonstrated the particle extraction (**Figure S1a and S1b** and Supplementary Information Video V6 and V7), the liquid dispensing (**Figure S1c and S1d** and Supplementary Information Video V8 and V9) and the liquid shaping (**Figure S1e and S1f** and Supplementary Information Video V10 and V11) using the two-plate configuration with the same operation conditions as the single-plate configuration shown above.

In the single-plate configuration, a minute number of magnetic particles get stuck in the surface energy trap occasionally. This situation is more frequent with large surface energy traps where the magnetic particles need to travel a greater distance over the sticky polydopamine region. In contrast, in the two-plate configuration, the magnetic particles are pulled down to the bottom coverslip by the magnetic force. Consequently, the magnetic particles are not in direct contact with the polydopamine surface energy traps on the top coverslip. As a result, no particle is left behind after passing through the surface energy traps. In spite of this advantage, the two-plate configuration is relatively more complex to implement than the single-plate configuration. Furthermore, the volume of the droplet that could be handled by the two-plate configuration is considerably smaller, which might not be suitable for certain bioassays.

2.3 HBsAg by ELISA on Magnetic Digital Microfluidic Platform with Surface Energy Traps

In the end, we demonstrated the detection of hepatitis B surface antigen (HBsAg) on the polydopamine surface energy trap-enabled magnetic digital microfluidic platform for potential point-of-care diagnostics of hepatitis B. Hepatitis B is a serious infectious disease that affects over 300 million people globally.[45] The HBsAg is a well-recognized early-stage diagnostic marker, and the level of HBsAg in the serum serves as a good indicator of the viral activity. To detect HBsAg, we generated a standard curve using ELISA (**Figure 5**) on our magnetic digital microfluidic platform. First, three washing droplets, one 3,3',5,5'-Tetramethylbenzidine (TMB) droplet and one stopping solution droplet were dispensed onto the platform (**Figure 5a**). All except the stopping solution droplet were dispensed directly on the polydopamine surface energy traps. The polydopamine surface energy traps would pin down these droplets to facilitate the particle extraction and prevent undesired droplet movement during the washing process. To prevent the evaporation during the relatively long incubation period, we incubated all of the samples in a humidity-controlled environment. The stopping solution droplet would be moved to merge with the TMB droplet in the last step, so it was not confined by the surface energy trap. Once primed, the entire assay was performed by moving the magnetic Dynabeads with a permanent magnet. Such a simple operation was well-suited for the point-of-care applications. Next, a twofold serial dilution of the sample containing 15.6 ng/mL to 500 ng/mL of HBsAg was mixed with the capture antibody-conjugated Dynabeads and the horseradish peroxidase (HRP)-labeled detector antibody in the sample droplet that contained 5% bovine serum albumin as the dynamic blocking agent. After a one-hour incubation at the room temperature, the antibodies and the target HBsAg formed a sandwich structure on the Dynabeads surface (**Figure 5b**). Subsequently, the Dynabeads were extracted from the sample droplet with the assistance of

the polydopamine surface energy trap and moved through the three washing buffer droplets in sequence to eliminate any possible carryover contamination. During the washing step, all the washing buffer droplets were anchored to the polydopamine surface energy traps to facilitate the particle extraction. After washing, the Dynabeads with the antibody-antigen sandwich structure on their surface were merged with the TMB droplet and incubated for 15 minutes. During the incubation, the color of the TMB gradually changed from clear to blue (**Figure 5c**). In comparison, the negative control would not cause any color change, and the TMB droplet would remain clear. After the incubation, the Dynabeads were moved out from the TMB droplet and merged with the stopping solution droplet. Lastly, the Dynabeads drove the stopping solution droplet back to merge with the TMB droplet. After the two droplets merged, the enzymatic reaction stopped. The absorbance values were plotted against the HBsAg concentration to generate the standard curve (**Figure 5d**). The limit of detection was calculated to be 67.1 ng/mL based on the linear regression. Studies showed that the hepatitis B patient's serum samples contained more than 1000 IU/mL, or roughly 430-580ng/mL depending on the conversion standard of HBsAg.[46] As a result, we could use the serum samples directly without the need for dilution. We performed the same ELISA assay in the 96-well microplate. The linear range in the microplate was lower with a limit of detection of 3.75 ng/mL (**Supplementary Figure S2**), which was in general agreement with the the limit of detection of ELISA for HBsAg reported in literature (ranging from 0.5 – 1 ng/mL).[47, 48] Although the limit of detection is lower for the conventional ELISA, the input sample volume was 10 times larger than the droplet-based ELISA on the magnetic digital microfluidic platform. Furthermore, the microplate-based ELISA could not use the serum sample directly, sample dilution was required to match the HBsAg concentration with the linear range.

Figure 5 Droplet manipulation on the polydopamine surface energy trap-enabled magnetic digital microfluidic platform in two-plate configuration. a) and b) Side view and top view of article extraction, c) and d) Side view and top view of liquid dispensing, and e) and f) Side view and top view of liquid shaping.

One drawback of polydopamine surface energy trap results from the high reductive capacity of polydopamine. The intrinsic reductive capacity of polydopamine is sufficient to reduce Cu^{2+} to Cu^{1+} , resulting in the false positive in the BCA protein assay (**Supplementary Figure S3**). Polydopamine alone would turn the color of the BCA reagents into dark brown in the absence of any protein. One must take this property into consideration when designing a polydopamine magnetic digital microfluidic platform for diagnostic assays. One potential solution is to covalently conjugate hydrophilic polymers to the polydopamine. The polymer would block the reductive functional groups while maintaining the hydrophilicity in the coated region for surface energy traps.

3. Experimental

Methods and Materials are detailed in the supplementary information.

4. Conclusion

In this work, we have presented a novel method of creating surface energy traps to facilitate droplet manipulations on the magnetic digital microfluidic platform using a mussel-inspired material known as polydopamine. The unique ability of polydopamine to strongly adhere to the otherwise non-wettable Teflon enables us to pattern hydrophilic surface energy traps on the hydrophobic Teflon surface with a great ease. We have optimized the reaction conditions for coating polydopamine on the Teflon surface in terms of dopamine monomer concentration, buffer pH, and reaction time, and characterized the polydopamine coating on the Teflon by measuring the contact angle. The shape and size of the polydopamine surface energy traps are controlled by adjusting the volume of dopamine monomer solution or using a silicone stencil. With the assistance of the polydopamine surface energy traps, we have demonstrated a wide range of droplet operations, including particle extraction, liquid dispensing, liquid shaping and cross-platform transfer on the magnetic digital microfluidic platform. For the first time, we have also shown the surface energy trap-enabled droplet manipulation using the two-plate configuration on the magnetic digital microfluidic platform. In the last part of the work, we have demonstrated the detection of HBsAg using a particle-based ELISA assay on the polydopamine surface energy trap-enabled magnetic digital microfluidic platform for the potential point-of-care diagnostics of hepatitis B infection.

Conflict of Interest

Authors declare no conflict of Interest.

Acknowledgements

Authors would like to thank the Start-Up Grant from the School of Mechanical and Aerospace Engineering at Nanyang Technological University. This work is also supported by Singapore Ministry of Education Tier 1 Grant (RG49/17) and by the Ageing Research Institute for Society and Education (ARISE), Nanyang Technological University, Singapore (ARISE/2017/22).

Uncategorized References

- [1] Zhang, Y., Nguyen, N. T., *Lab Chip* 2017, *17*, 994-1008.
- [2] Choi, K., Ng, A. H. C., Fobel, R., Wheeler, A. R., *Annual Review of Analytical Chemistry* 2012, *5*, 413-440.
- [3] Fair, R. B., *Microfluidics and Nanofluidics* 2007, *3*, 245-281.
- [4] Pollack, M. G., Pamula, V. K., Srinivasan, V., Eckhardt, A. E., *Expert review of molecular diagnostics* 2011, *11*, 393-407.
- [5] Chiou, C. H., Shin, D. J., Zhang, Y., Wang, T. H., *Biosens. Bioelectron.* 2013, *50*, 91-99.
- [6] Lehmann, U., Hadjidj, S., Parashar, V. K., Vandevyver, C., Rida, A., Gijs, M. A. M., *Sens. Actuators B Chem.* 2006, *117*, 457-463.
- [7] Pipper, J., Inoue, M., Ng, L. F. P., Neuzil, P., Zhang, Y., Novak, L., *Nat. Med.* 2007, *13*, 1259-1263.
- [8] Pipper, J., Zhang, Y., Neuzil, P., Hsieh, T. M., *Angew. Chem. Int. Ed.* 2008, *47*, 3900-3904.
- [9] Zhang, Y., Park, S., Liu, K., Tsuan, J., Yang, S., Wang, T. H., *Lab Chip* 2011, *11*, 398-406.
- [10] Zhang, Y., Shin, D. J., Wang, T. H., *Lab Chip* 2013, *13*, 4827-4831.
- [11] Zhang, Y., Wang, T. H., *Adv. Mater.* 2013, *25*, 2903-2908.
- [12] Zhao, Y., Fang, J., Wang, H., Wang, X., Lin, T., *Adv. Mater.* 2010, *22*, 707-710.
- [13] Zhao, Y., Xu, Z., Parhizkar, M., Fang, J., Wang, X., Lin, T., *Microfluid. Nanofluid.* 2012, *13*, 555-564.
- [14] Shamsi, M. H., Choi, K., Ng, A. H. C., Wheeler, A. R., *Lab Chip* 2014, *14*, 547-554.
- [15] Shah, G. J., Ohta, A. T., Chiou, E. P. Y., Wu, M. C., *Lab Chip* 2009, *9*, 1732-1739.
- [16] Miller, E. M., Wheeler, A. R., *Anal. Chem.* 2008, *80*, 1614-1619.
- [17] Abdelgawad, M., Freire, S. L. S., Yang, H., Wheeler, A. R., *Lab Chip* 2008, *8*, 672-677.
- [18] Yeo, L. Y., Friend, J. R., *Annu. Rev. Fluid Mech.* 2014, *46*, 379-406.
- [19] Wang, Z., Zhe, J., *Lab Chip* 2011, *11*, 1280-1285.
- [20] Guttenberg, Z., Müller, H., Habermüller, H., Geisbauer, A., Pipper, J., Felbel, J., Kielpinski, M., Scriba, J., Wixforth, A., *Lab Chip* 2005, *5*, 308-317.
- [21] Ding, X., Li, P., Lin, S. C. S., Stratton, Z. S., Nama, N., Guo, F., Slotcavage, D., Mao, X., Shi, J., Costanzo, F., *Lab Chip* 2013, *13*, 3626-3649.
- [22] Xu, F., Wu, C. A. M., Rengarajan, V., Finley, T. D., Keles, H. O., Sung, Y., Li, B., Gurkan, U. A., Demirci, U., *Adv. Mater.* 2011, *23*, 4254-4260.
- [23] Tasoglu, S., Yu, C., Gungordu, H., Guven, S., Vural, T., Demirci, U., *Nat. Comm.* 2014, *5*, 4702.

- [24] Tasoglu, S., Kavaz, D., Gurkan, U. A., Guven, S., Chen, P., Zheng, R., Demirci, U., *Adv. Mater.* 2013, 25, 1137-1143.
- [25] Zhang, Y., Park, S., Liu, K., Tsuan, J., Yang, S., Wang, T. H., *Lab Chip* 2011, 11, 398-406.
- [26] Mitsuhiro, S., Nobuhiro, N., Rentaro, I., Hiroyuki, H., Mina, O., Hiroshi, I., Kazuo, S., *J. Micromech. Microeng.* 2008, 18, 035034.
- [27] Mitsuhiro, S., Kentaro, T., Hiroyuki, H., Hiroshi, I., Kazuo, S., *J. Micromech. Microeng.* 2006, 16, 1875.
- [28] Zhang, Y., Shin, D. J., Wang, T. H., *Lab Chip* 2013, 13, 4827-4831.
- [29] Zhang, Y., Wang, T. H., *Adv. Mater.* 2013, 25, 2903-2908.
- [30] Ng, A. H., Chamberlain, M. D., Situ, H., Lee, V., Wheeler, A. R., *Nature communications* 2015, 6, 7513.
- [31] Lee, H., Dellatore, S. M., Miller, W. M., Messersmith, P. B., *Science* 2007, 318, 426-430.
- [32] Kim, B. H., Lee, D. H., Kim, J. Y., Shin, D. O., Jeong, H. Y., Hong, S., Yun, J. M., Koo, C. M., Lee, H., Kim, S. O., *Advanced materials* 2011, 23, 5618-5622.
- [33] Lee, B. P., Messersmith, P. B., Israelachvili, J. N., Waite, J. H., *Annu. Rev. Mat. Res.* 2011, 41, 99-132.
- [34] Salazar, P., Martín, M., Mora, J. L. G., *Polym. Sci.* 2016, 385-396.
- [35] Ye, Q., Zhou, F., Liu, W., *Chem. Soc. Rev.* 2011, 40, 4244-4258.
- [36] Kim, B. H., Lee, D. H., Kim, J. Y., Shin, D. O., Jeong, H. Y., Hong, S., Yun, J. M., Koo, C. M., Lee, H., Kim, S. O., *Adv. Mater.* 2011, 23, 5618-5622.
- [37] Shen, B., Xiong, B., Wu, H., *Biomicrofluidics* 2015, 9, 044111.
- [38] You, I., Kang, S. M., Lee, S., Cho, Y. O., Kim, J. B., Lee, S. B., Nam, Y. S., Lee, H., *Angew. Chem. Int. Ed.* 2012, 51, 6126-6130.
- [39] Zhang, W., Yang, F. K., Han, Y., Gaikwad, R., Leonenko, Z., Zhao, B., *Biomacromolecules* 2013, 14, 394-405.
- [40] Kang, S. M., Hwang, N. S., Yeom, J., Park, S. Y., Messersmith, P. B., Choi, I. S., Langer, R., Anderson, D. G., Lee, H., *Adv. Funct. Mater.* 2012, 22, 2949-2955.
- [41] Sundaram, H. S., Han, X., Nowinski, A. K., Ella-Menye, J. R., Wimbish, C., Marek, P., Senecal, K., Jiang, S., *ACS App. Mat. Interfaces* 2014, 6, 6664-6671.
- [42] Long, Z., Shetty, A. M., Solomon, M. J., Larson, R. G., *Lab Chip* 2009, 9, 1567-1575.
- [43] Jiang, J., Zhu, L., Zhu, L., Zhu, B., Xu, Y., *Langmuir* 2011, 27, 14180-14187.
- [44] Yang, H. C., Wu, Q. Y., Wan, L. S., Xu, Z. K., *Chem. Commun.* 2013, 49, 10522-10524.
- [45] Sonneveld, M., Zoutendijk, R., Janssen, H., *J. Viral Hepat.* 2011, 18, 449-457.
- [46] Chan, H. L. Y., Thompson, A., Martinot Peignoux, M., Piratvisuth, T., Cornberg, M., Brunetto, M. R., Tillmann, H. L., Kao, J. H., Jia, J. D., Wedemeyer, H., *J. Hepatol.* 2011, 55, 1121-1131.
- [47] Kim, S., *Immune Netw.* 2017, 17, 451-459.
- [48] Yazdani, Y., Roohi, A., Khoshnoodi, J., Shokri, F., *Avicenna journal of medical biotechnology* 2010, 2, 207-214.