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LETTER

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Nanochromatography Driven by the Coffee Ring Effect

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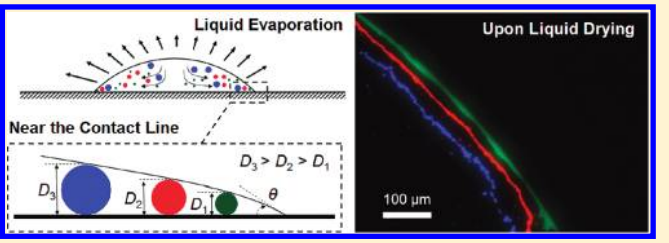
Supporting Information

ABSTRACT: The coffee ring phenomenon has long been known for its ability to concentrate particles at the rim of a dried liquid droplet, yet little is known about its particle separation capability. Here, we elucidate the physics of particle separation during coffee ring formation, which is based on a particle-size selection mechanism near the contact line of an evaporating droplet. On the basis of this mechanism, we demonstrate nanochromatography of three relevant biological entities (proteins, micro-organisms, and mammalian cells) in a liquid droplet, with a separation resolution on the order of ~100 nm and a dynamic range from ~10 nm to a few tens of micrometers. These findings have direct implications for developing low-cost technologies for disease diagnostics in resource-poor environments.



One of the grand challenges in global health is to diagnose disease and health conditions in accurate and economical manners, particularly in underdeveloped countries.[1] Disease diagnostics involve sensitive detection of biomarkers or identification of pathogens associated with diseases. Some of the most infectious diseases, such as human immunodeficiency virus (HIV), malaria, and tuberculosis, are caused by disease pathogens whose length scales are on the order of hundreds of nanometers to a few micrometers.[2,3] Effective isolation and concentration of disease markers from body fluids are therefore fundamental to improve the sensitivity and accuracy of the disease detection.

From the early pioneering development of spot test analysis[4,5] to the latest emerging lab-on-a-chip technologies,[6,7] simple and inexpensive analytical devices are continually sought for sample preparation, especially for disease diagnostics in areas where resources are limited. These directly lead to the need for devices that require minimal use of energy and resources, while at the same time are capable to perform sufficient sample preparation and analytical functions. In this Letter, we explore the concept of particle manipulation within an evaporating droplet, the coffee ring effect, for sample preparation without the use of any external energy devices. Specifically, we show that the coffee ring effect can result in size-dependent nano/microparticle separation near the contact line (CL) region of an evaporating liquid droplet, which enables for a simple chromatography technique for processing biological entities with minimal resource requirements.

The coffee ring effect is a commonly observed occurrence in everyday life, which results when a droplet of colloid evaporates on a solid surface. As the three-phase CL of the droplet is pinned on the surface due to either physical roughness or chemical heterogeneities, the evaporation process induces a capillary flow within the droplet which drives the suspended particles toward the CL and leaves a ring-shaped structure at the rim.[8] While this phenomenon is mostly known for its ability to concentrate particles near the CL of a liquid droplet, little is known about its particle separation capability.[9−12] When a coffee ring begins to form at the rim of an evaporating droplet, there exists a finite empty zone between the leading edge of the particle monolayer and the pinned CL. Interestingly, the radial length of this region remains constant over a broad range of droplet sizes and relative humidity, yet it depends on the particle size and concentration[13] as well as the local contact angle.[14] Since the thickness of the droplet meniscus reduces gradually toward the CL, particles transported by the coffee ring effect may cease at a position where the individual particle size matches the thickness of the local meniscus. Consequently, smaller particles are expected to move closer to the CL as compared to the larger ones, which leads to size-dependent particle separation (Figure 1a).

To verify this mechanism, we prepared a colloid of carboxylate-modified negatively charge-stabilized fluorescent polystyrene spheres of ~40 nm, ~1 μm, and ~2 μm in diameter in deionized water and placed a small drop of the colloid (i.e., ~0.5 μL) on a precleaned cover glass. Upon evaporation under ambient conditions, the suspended particles were transported and concentrated near the CL, forming three well-separated ring structures. The smallest particles formed the outermost ring, whereas the largest particles formed the innermost ring (Figure 1b). Similar observations were observed for amine-modified positively charge-stabilized particles (Figure S-1 in the Supporting Information), as well as for colloids that consist of a mixture of oppositely charged particles under incubation time of less than 30 min (Figures S-2 and S-3 in the Supporting Information). This indicates that the capillary flow

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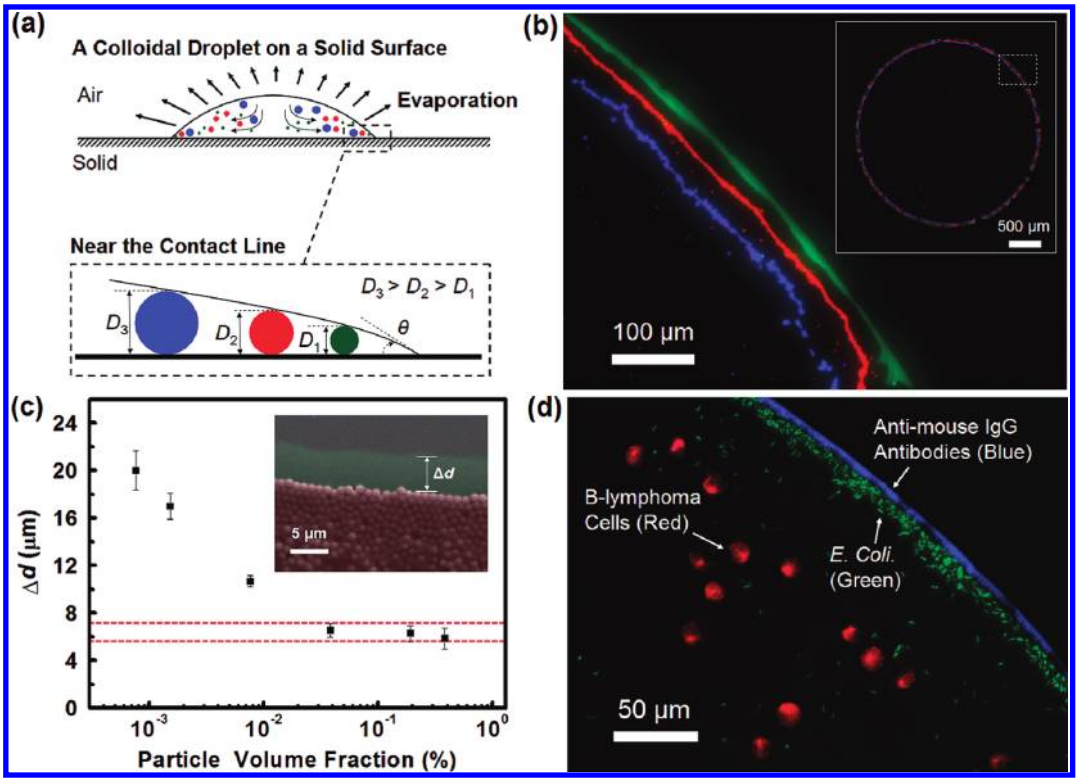

Figure 1. (a) Schematics showing the concept of size-dependent particle separation near the CL of an evaporating colloidal droplet. (b) Optical fluorescence image showing the separation of 40 nm (green), 1 μm (red), and 2 μm (blue) particles after evaporation. (c) A semilog plot showing the dependence of the coffee ring separation distance (edge-to-edge) on particle concentration (see the Supporting Information for details). The upper and lower limits of the separation distance predicted by the initial drop geometries (i.e., $\theta = 9.5° \pm 0.7°$) are indicated by the red dashed lines. The inset shows a false-color electron micrograph of the rim of coffee ring structures formed by ~40 nm (green) and ~1 μm (red) particles. The error bars indicate the standard deviations from 30 individual measurements. (d) Optical fluorescence image showing the separation of antimouse IgG antibodies (blue), *Escherichia coli* (green), and B-lymphoma cells (red) in a dried liquid drop.

driven by the coffee ring effect is more dominant as compared to the electrostatic interactions between the particle-to-particle interface, as well as the particle-to-substrate interface within the specific time scale. In addition, we found that the edge-to-edge separation distance, Δd, between the ring structures is dependent on the particle concentration (Figure 1c). Specifically, with the use of particles of 40 nm and 1 μm in diameter, the separation distance reduces with increasing particle concentration until a critical concentration is reached (i.e., >~0.04% volume fraction for both particles), where the separation distance asymptotically converges to a limiting value Δd_{min}. This value can be estimated from the initial geometry of the meniscus profile, i.e., $\Delta d_{min} = (D_2 - D_1)/2 \tan(\theta/2)$, where D_1 and D_2 are the particle diameters (i.e., $D_2 > D_1$) and θ is the initial contact angle of the droplet, where $\theta < 90°$. On the basis of this relationship, we further investigated the effect of surface wettability (i.e., θ) on Δd_{min} using colloids above the critical particle concentration (i.e., >~0.04% volume fraction, see the Supporting Information). We found that the experimentally measured Δd_{min} can be quantitatively estimated by the proposed geometrical relationship for surfaces with different wettability (Figure S-4 in the Supporting Information), which further supports that the initial curvature of the CL meniscus has a strong influence on the particle separation distance.

Additionally, the dependence of Δd on particle concentration suggested that the particle separation occurs in two different stages. In the first stage of the separation, the particles are transported to the region near the CL, where these particles are separated based on their sizes within the liquid meniscus of the contact angle, θ. This is supported by our observations that smaller particles are consistently transported to the region closer to the CL where the local thickness of the liquid meniscus reduces gradually. Once the initial ring structures are formed, the second stage of the particle separation will be dependent on the liquid evaporation near the CL region[14] as well as the CL pinning/depinning events.[10,15] Particularly, the subsequent motion of the particles is a consequence of the competition between different forces acting on them. These forces include surface tension due to the change of meniscus profile during liquid evaporation,[14] as well as adhesion forces between the particles and the substrate.[10−12] Specifically, the surface tension acting on the particles at the leading edge of the coffee ring structure tend to move the structure away from the CL, whereas the adhesion forces acting within individual particle/substrate interfaces tend to resist such a motion (Figure S-5 in the Supporting Information). At low particle concentrations (i.e., <~0.04% volume fraction), the surface tension dominates over the adhesion forces, thereby resulting in enhanced edge-to-edge particle separation. As the particle concentration increases, more particles are transported to the CL during the early stage of the liquid evaporation. The increased number of particles within the coffee ring structure amplifies the adhesion forces between the particles and the substrate surface, which can further resist the force that tends to carry the particles away from the CL.[12,14] This mechanism is further supported by our theoretical analysis based

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on the studies of Jung et al.[12] and Niida et al.[16] (see the Supporting Information). On the basis of the mechanism, it is evident that Δd_{min} defines the minimum separation resolution that can be achieved by the coffee ring effect. Together, these results reinforce the importance of particle confinement near the CL liquid meniscus for the size-dependent particle separation.

Separation and concentration of molecular/cellular components in biological fluids are important processes for increasing the signal-to-noise ratio to improve the limit-of-detection of diagnostic tests. To this end, the coffee ring-based separation may provide a simple and effective technique for separating specific biological targets from nonrelevant particles and concentrating them into different ring structures based on their physical size. As a proof-of-principle demonstration, we performed separation experiments using a mixture of fluorescently labeled antimouse IgG antibodies (<10 nm), *Escherichia coli* expressing green fluorescent protein (∼order of 500 nm), and fluorescently labeled murine B-lymphoma cells (WEHI-231) (∼order of 5 μm) suspended in deionized water at predetermined concentrations. We observed that the antimouse IgG antibodies were transported to the outermost ring, followed by the *Escherichia coli* which formed the second ring. Both of these rings were well-separated from the B-lymphoma cells (Figure 1d). This result directly shows that the separation mechanism can be used to simultaneously separate and concentrate molecules, micro-organisms, and mammalian cells, with a separation resolution on the order of ∼100 nm and a dynamic range from the order of 10 nm to a few tens of micrometers. Our findings suggest a simple method for on-site separation and concentration of biological markers useful for sample preparation and analysis. When combined with the emerging cellphone-based microscopy[17,18] and suitable bio-detection protocols, nanochromatography technique may present a natural and economical processing tool for low-cost disease diagnostics in resource-limited environments.[19]

■ ASSOCIATED CONTENT

Supporting Information. Preparation of polystyrene particles and biological samples, experimental details for the particle separation experiments, separation of positively charged particles and oppositely charged particles, separation of oppositely charged particles at different incubation time, dependence of particle separation distance on surface wettability, and force balance analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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