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Surface Tension Triggered Wetting and Point of Care Sensor Design

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Graphical abstract

Rapid, simple, and inexpensive point-of-care (POC) medical tests are of significant need around the world. The transition between non-wetting and wetted states is used to create instrument-free surface tension sensors for POC diagnosis, using a layered electrospun mesh with incorporated dye to change color upon wetting.

Keywords

surface tension; point of care; electrospinning; sensor

The wetting of a solid surface by a liquid is a common but intriguingly complex phenomenon.^[1–3] The surface chemistry and topology as well as the pH, ionic strength, and additives in the liquid can affect the degree to which a surface is wetted - with minute

changes often having significant effects. In fact, the wetting of materials with high surface roughness is especially sensitive to the surface tension of liquids with which they are in contact.^[4,5] With the knowledge that changes in the surface tensions of biological fluids are indicators of medical conditions,^[6–8] we hypothesize that a sensor could be designed that switches between wetted and non-wetted states with liquids of a specific surface tension. Specifically, we report a sensor based on a two-layer electrospun polymer mesh composed of a top responsive layer that responds to small changes in liquid surface tension to form a wetted or non-wetted material, and the bottom hydrophilic indicator layer that reveals a color change when wetted to aid visualization, as shown in Figure 1. Electrospun meshes of varying fiber diameters, pore sizes, and polymer compositions were fabricated to alter the surface free energy. If the solid-air and solid-liquid interfacial surface tensions are similar, a small change in liquid surface tension can cause a transition from a high apparent contact angle, heterogeneously wetted state (Cassie-Baxter state) to complete, homogenous wetting (Wenzel state),^[4,5] which is the basis for the sensitivity of our system. Changes in both the liquid-air and liquid-solid interfacial tensions contribute to this effect, and both are lowered as surfactant levels increase. As prototypical examples, two sensors are prepared and evaluated to detect surface tension changes in human breast milk fat (45–48 mN/m) and urinary bile acid levels (50–54 mN/m), of interest for ensuring adequate nutrition to infants and for detecting chronic liver disease, respectively.

Rapid, simple, and inexpensive point-of-care (POC) medical tests are urgently needed in the developing world as well as in home care settings and in walk-in clinics.^[9] POC applications demand portable and inexpensive tests using easily collected bodily fluids that do not require trained medical personnel. Consequently, sensors employing paper microfluidics, colorimetric indicators, mobile phone-based detection,^[10–15] as well as portable electrochemical sensors are actively investigated.^[16–19] Much of this work also utilizes hydrophobic or superhydrophobic materials to transport and support microliter volumes of liquid.^[20,21] Alternatively, surfaces are designed to change hydrophobicity in response to stimuli such as ion exchange^[22–24] or UV exposure.^[25,26] Inspired by the research in these areas, the approach described herein distinguishes itself by focusing on fine-tuning the wetting event to within 2–3 mN/m using electrospun meshes.

The US Surgeon General recommends exclusive breastfeeding infants for the first 6 months of life, yet 83% of mothers do not,^[27] usually out of concern that their breast milk is not providing adequate nutrition and calories compared to formula.^[28] In addition to reassuring mothers, measuring the calorie content of breast milk is crucial in managing low-birth-weight, preterm, and “failure to thrive” infants. For example, in the US low-birth weight babies represent about 8 percent of the 4 million newborns; preterm babies represent about 11 percent; and 5–10% of infants receiving primary care show signs of “failure to thrive”.^[29,30] The most common methods for measuring breast milk fat levels require a centrifuge or HPLC^[31] and therefore are often too expensive and bulky to employ in a home or field setting. Milk lipids are effective surfactants, lowering the surface tension from 47.3 ± 1.2 mN/m for low calorie (skim) milk to 41.9 ± 1.1 mN/m for high calorie (whole) milk.^[32] To create a high specificity sensor, we chose to design meshes that wet at 45.0 mN/m but remain non-wetted at 48.0 mN/m.

Likewise, the surface tension of normal urine (57.1 ± 1.5 mN/m) is determined by the concentration of surfactants such as bile acids,^[33,34] (normally 1.1 ± 0.5 μ M,) which are increased for example to 30.0 ± 20.6 μ M in biliary stenosis,^[35] and to 151 ± 15 μ M in chronic liver disease,^[36] reducing the surface tension of urine below 50 mN/m in both cases. Chronic liver diseases are major causes of morbidity and mortality worldwide, affecting millions.^[37] Additionally, it has been observed as early as Hippocrates that urine is more apt to foam when a patient has proteinuria, making urinary surface tension also a useful indicator of kidney function.^[8] Therefore, we chose to design a high selectivity urine sensor mesh that wets at 50 mN/m but remains non-wetted at 54 mN/m.

Poly(ϵ -caprolactone) (PCL; $M_w = 70\text{--}90$ kDa) is the main polymer component of the meshes, doped with either a hydrophobic poly(glycerol monostearate-co- ϵ -caprolactone) (PGC-C18; 1:20 glycerol carbonate:caprolactone; $M_w = 31.3$ kDa, $M_n = 1.47$) or a hydrophilic poly(glycerol-co- ϵ -caprolactone) (PGC-OH; 1:20 glycerol carbonate:caprolactone; $M_w = 22.9$ kDa, $M_n = 1.32$), prepared following our published procedure^[38] as depicted in Supplementary Figure 1. Non-woven meshes are fabricated from these polymer mixtures using electrospinning, a scalable manufacturing technique that draws out fibers from a polymer solution under high voltage.^[39,40] The indicator layer always includes the same component, 85 or 90% PCL with 5 or 10% PGC-OH (1:4) by weight with 5% bromocresol purple. The milk sensor responsive layer is 7.5% PGC-C18 and 92.5% PCL by weight, and the urine sensor responsive layer is 5% PGC-C18 and 95% PCL. For further details, see the SI. The resulting layered structure is shown in Figure 1e, where the sensor layer is thin enough to observe a rapid color change after wetting.

Contact angle and surface tension measurements are made on a Kruss DSA100 Goniometer at $22.5 \pm 1.5^\circ\text{C}$, using 3 μ L droplets and the Laplace-Young fitting method. Given enough time, all tested mixtures wet to the indicator layer (the energy minimum being a fully wetted hydrophilic layer) so we measure the time until the apparent contact angle θ^* is $<90^\circ$, after which wetting is rapid.^[4,5] Maintaining long-term stability of superhydrophobic surfaces remains challenging,^[41] so we use this measure of apparent contact angle combined with color change to measure the time until transition from Cassie-Baxter to Wenzel states. Mixtures of water with propylene glycol are used to test wetting, due to their low volatility and well-characterized surface tensions.^[42] As shown in Figure 2a, the sensor range can be tuned between 45 and 65 mN/m by altering the polymer composition and fiber diameter. As Figures 2b and 2c show, the meshes tuned to detect surface tensions in the range of milk and urine respectively showed large changes in wetting times, transitioning from immediate wetting to many minutes of non-wetting within just a few mN/m. The distribution of wetting times for the urine sensor mesh with 50, 52, and 53 mN/m solutions is shown in Figure 2d. The lack of overlap between the wetting times using 50 mN/m with those of 52 or 53 mN/m indicates high sensitivity and specificity (Mann-Whitney U-test < 0.001).

As proof of concept, we tested human urine (Innovative Research, Novi, MI) after adding a bile acid (deoxycholic acid, Alfa Aesar) until the surface tension as measured by the pendant drop method was either 54 mN/m (healthy) or 50 mN/m (diseased state). As shown in Figure 3a, normal, healthy urine remained on the surface and did not wet the sensor mesh while the

50 mN/m urine wetted the mesh and turned it purple. More details regarding the timing of color change can be found in the SI.

We next tested the utility of a sensor mesh to distinguish normal from low-fat breast milk. Using normal human breast milk (Innovative Research) compared to breast milk diluted 1:2 with deionized water, Figure 3b shows that the former wetted and became purple whereas the latter remained non-wetted and white. These tests validated that the propylene glycol mixtures modeled urine and milk mixtures well, and that properly tuned sensor meshes can resolve surfactant levels in simulated clinical samples.

As with any diagnostic system, there are limitations to this approach. First, liquid surface tensions vary with temperature (~ 1 mN/m for every 6.5°C for water^[43]) and humidity,^[44] and so these must be accounted for or controlled. Second, in bodily fluids there are many agents that act as surfactants and a measurement of overall surface tension does not distinguish between them. However, surface tension could be used as a first screen prior to more costly tests or procedures, especially given the simple system demonstrated here. Finally, the instructions for use will include a time window as the non-wetted state is a metastable phenomenon, but this is standard for a number of point-of-care sensors such as pregnancy and ovulation tests.

In summary, we report electrospun sensor meshes that visibly switch between non-wetted and completely wetted states within a range of 2–3 mN/m. A pH-indicating dye incorporated into the bottom, hydrophilic layer highlights wetting and aids identification with the naked eye. Two prototype sensor meshes, each tuned to a different surface tension detection range, are designed, evaluated, and tested with human breast milk and urine samples. The sensor mesh system presented here is tunable to a specific surface tension for monitoring different liquids and is inexpensive to fabricate, portable, simple to use, requires no power and only a small sample volume, and therefore may lend itself well to point-of-care diagnosis or self-monitoring at home or in the field.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Diagram of the surface tension sensor mesh. A test droplet either a) remains non-wetted on the upper responsive layer, or b) wets to the hydrophilic dye-containing indicator layer and changes color. c), d) Structure of the polymers used, where $R=H$ for PGC-OH or $R=C(O)C_{17}H_{36}$ for PGC-C18 e) SEM image of an example mesh, demonstrating $1.5 \pm 0.6 \mu\text{m}$ diameter fibers of the responsive layer above the $190 \pm 60 \text{ nm}$ diameter fibers of the indicator layer. Scale bar is $10 \mu\text{m}$.

Figure 2.

Wetting behavior of sensor meshes with 3 μ L droplets of propylene glycol/water mixtures. a) Meshes with varying hydrophobicity of the responsive layer wet or support propylene glycol/water mixtures of different surface tensions. b) The mesh for milk measurement immediately wets with liquid at or below 45 mN/m but has apparent hydrophobicity at 48 mN/m for 4.8 ± 0.3 min. c) The mesh for urine measurement is immediately wets (0.05 ± 0.09 min) at or below 50 mN/m but has apparent hydrophobicity for 8.3 ± 3.6 minutes at 53 mN/m. Error bars represent standard deviations ($n = 5$). d) Histogram demonstrating the distribution of wetting times on the mesh for urine measurement with 53, 52, and 50 mN/m ($n=6$ for 52 mN/m, $n=16$ for 53 and 50 mN/m). The Mann-Whitney U-Test is used to compare 50 mN/m wetting times to those at 52 mN/m ($p = 1.3 \times 10^{-4}$) and 53 mN/m ($p = 3.9 \times 10^{-7}$), and Student's t-test to compare 52 to 53 mN/m ($p = 1.2 \times 10^{-3}$)

Figure 3.

Detection of urinary bile acids and milk fat content. a), the droplet on the left has high bile acids (50 mN/m) and wets quickly, changing color while the lower bile acid droplet on right (54 mN/m) remains unwetted and clear. b) A droplet of human breast milk diluted 1:2 on left compared to normal human breast milk on right, demonstrating wetting and color responses over 2.5 minutes. Scale bars are both 2.0 mm and droplets are 3 μ L.