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University of California, Irvine:

Shrinky-Dinks® All Grown Up

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As a researcher in the area of microfluidics, Khine has long been aware that the challenge of traditional 'top-down' micro- and nano-fabrication of microfluidic chips lies in the difficulties and costs associated with patterning at such high resolution. Indeed, the specialized equipment to make these chips can cost upwards of $100,000. As a new professor starting her first lab, this expensive equipment was not readily obtainable, so she decided to flip the problem upside down to see if she could obtain a more cost-effective solution by patterning at the large scale and subsequently shrinking down to achieve the desired final structures. Incredibly, the inspiration for this innovation was a toy—that perennial childhood favorite: Shrinky Dinks®.

Essentially, just as Shrinky Dinks® start with a large plastic sheet that is shrunk in a hot oven, she has used thermoplastic sheets heated in an oven to create molds for making polymer chips and has even used the etched sheets themselves to create chips directly from the plastic sheets. This method enables her to beat the limit of resolution inherent to traditional 'top-down' manufacturing approaches. Her seminal paper in *Lab on a Chip* introduced 'Shrinky-Dink® Microfluidics' in 2008, and the paper quickly went viral, leading researchers around the world to adopt this approach for a vast range of applications. Importantly, this approach enables researchers to rapidly prototype complete devices within minutes.

Specifically, Khine, using thermoplastic sheets that have been pre-heated and pre-stretched, draws a pattern onto the sheets with ink or etches a pattern on them with a tool and then heats the sheets in an oven. As the inked sheets shrink, the patterns drawn on them shrink and create ridges that can then be used as a mold to create chips with channels for fluid flow. With these tunable shape memory polymers, compatible with roll-to-roll as well as with standard lithographic processing, she can robustly integrate extremely high-resolution, high surface area, and high aspect ratio nanostructures directly into microsystems. When the underlying polymer substrate relaxes and 'shrinks,' a stiffer deposited thin film cannot and therefore buckles. She can control the buckling and therefore create nanostructures of deterministic sizes and patterns. Metallic nanostructures formed due to the stiffness mismatch between the thin metal film deposited on the retracting plastic sheet have demonstrated unprecedented electromagnetic field enhancements. In fact, she has demonstrated single-molecule detection resolution with this approach. To create far-field robust fluorescence enhancements that are not confined to plasmonic 'hot spots', she also developed a concentrating plus optical strategy to achieve >100x increase in the fluorescence signal and significant signal to noise gains. Of particular interest: when the polymer retracts in each dimension by a factor x, it grows in the z direction by a factor x2, allowing the creation of high aspect ratio structures with simple processing approaches.

Khine's ultra-rapid fabrication approach therefore results in field-compatible plastic-based microfluidic systems with integrated nanostructures for robust signal amplification. This design-on-demand approach to create a suite of custom biomedical tools for low cost diagnostics includes sample prep with magnetic nanotraps, embedded on-chip electrodes, microlens arrays, surface enhanced sensing substrates and substrates for stem cell culture and differentiation. She has also developed a manufacturable approach to transfer our extremely rough multiscale patterns into any commodity plastic. Using this, she has demonstrated that she can create low cost, scalable superhydrophobic, antibacterial surfaces that resist not just wetting of water, but also resist bodily fluids including urine, saliva, and blood.

Most recently, she has developed a process to lift off the unique nanostructured patterns from the shrink plastic to transfer them into other materials. This allows her to create truly conformal, high-resolution epidermal electronics that move with the skin. She uses these sensors for various types of physiological monitoring, including fetal movement, respiration, and blood pressure.

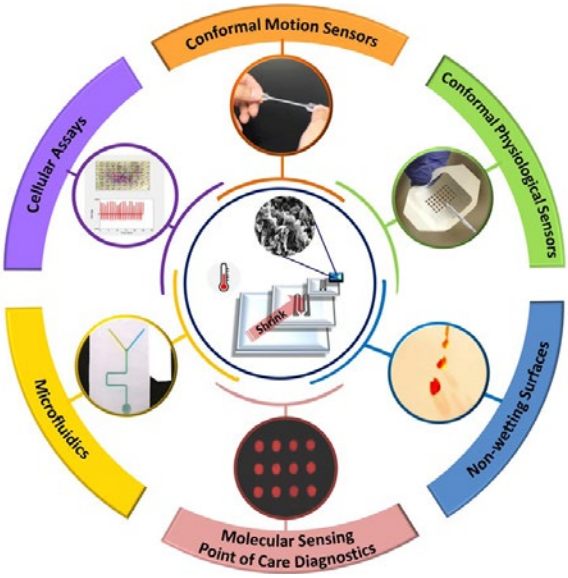

Figure 1. *Overview schematic of our simple shrink platform technology and the various applications we have pursued with it.*