

# Total Nanofluidic Confinement Devices Nanofabricated by Focused Ion Beam Milling

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Characterizing nanomaterials in fluids, including nanoparticles and biomolecules, is an ongoing challenge in nanomanufacturing and nanomedicine. Over the last two decades, microfabricated and nanofabricated fluidic devices have been developed to separate and measure nanomaterials by size, among other relevant nanomaterial characteristics. However, nanofluidic devices have typically implemented a confinement resolution of  $\approx 10$  nm, limiting the application of these emerging methods at the critical, small end of the nanoscale.<sup>1-2</sup>

Here, we present a new approach towards fabricating nanofluidic devices enabling control over nanomaterials by *total nanofluidic confinement*. We define this new concept as a nanofluidic device implementing a confinement resolution of  $\leq 1$  nm over a range of  $\approx 1$  nm to  $\geq 100$  nm. Such nanofluidic devices could potentially widen the nanomaterial characterization bottleneck and facilitate the analysis of small proteins and oligonucleotides for the early diagnosis of disease and quality control of nanoscale therapeutic agents.

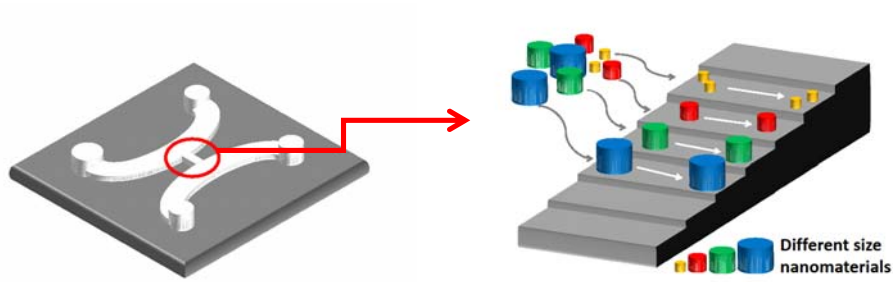
We illustrate our device design in Figure 1. Two microfluidic channels are connected by a nanofluidic channel, which could implement total nanofluidic confinement by, for example, an enclosed staircase or ramp topography nanofabricated by focused ion beam (FIB) milling, as shown in Figure 2 and 3. The schematic in Figure 1 illustrates how the staircase structure could separate nanomaterials by nanofluidic size exclusion. Fabrication results for the staircase and ramp structures, including scanning electron and atomic force micrographs, are shown in Figure 2 and 3, respectively. We have achieved step depths of  $(1.19 \pm 0.32)$  nm (average  $\pm$  standard deviation) and ramp gradients of  $\approx 8.3$  nm/ $\mu$ m to depths  $\approx 45$  nm.

With our current milling process, we could fabricate small analytical devices that could potentially characterize nanomaterials in fluids with  $\approx 1$  nm resolution over a range of  $\approx (1$  to  $50)$  nm. Sub-nanometer resolution and sub-micrometer range are also possibilities by further fine-tuning of our FIB nanofabrication process parameters. Finally, we note that inexpensive replica molding techniques could be used to implement the scalable nanomanufacturing of disposable total nanofluidic confinement devices for nanomaterial characterization.

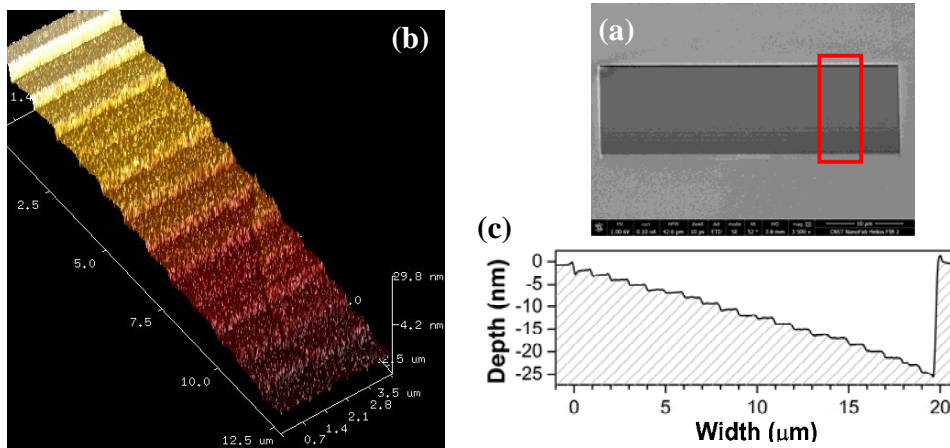
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<sup>1</sup> J. C. T. Eijkel and A. van den Berg, *Microfluid. Nanofluid.*, **1**, 249 (2005).

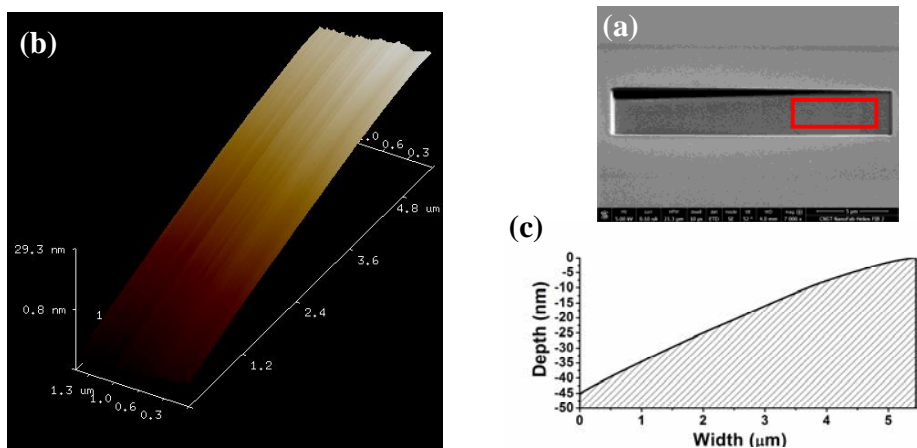
<sup>2</sup> W. Sparreboom, A. van den Berg and J. C. T. Eijkel, *Nat. Nanotechnol.*, **4**, 713 (2009).



**Figure 1: Experimental Concept:** The left schematic shows our overall device design, including sample reservoirs and microfluidic and nanofluidic channels. The right schematic illustrates our goal of nanomaterial size separation and measurement by total nanofluidic confinement and size exclusion.



**Figure 2: Staircase Structure:** (a) A scanning electron micrograph shows a staircase structure fabricated by focused ion beam milling, with an atomic force micrograph zooming in on the red box (b). The staircase profile is shown in (c). The step depth is  $(1.19 \pm 0.32)$  nm (average  $\pm$  standard deviation) over 20 steps.



**Figure 3: Ramp Structure:** As above in Figure 2, SEM and AFM images of a ramp structure are shown in (a) and (b). The slope is  $\approx 8.28$  nm/ $\mu\text{m}$  in (c).