

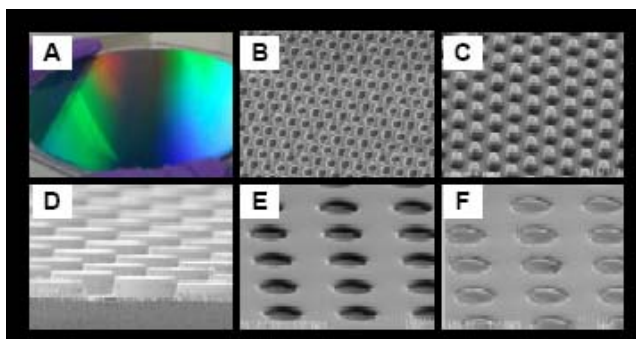
# Using the Fabrication Technologies from the Microelectronics Industry to Address the Unmet Needs in Drug Delivery

Joseph M. DeSimone

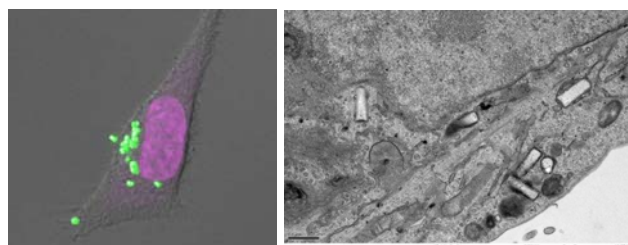
Departments of Chemistry &  
Pharmacology  
University of North Carolina at Chapel Hill

Dept. of Chemical & Biomolecular  
Engineering  
North Carolina State University

To translate promising molecular discoveries into benefits for patients, we are taking a pharmaco-engineering systems approach to develop the next generation of delivery systems with programmable multi-functional capability. Our laboratory has pioneered the development of a technique called **PRINT (Particle Replication in Non-wetting Templates)**. PRINT is a remarkable top-down particle fabrication technique that has its roots in the fabrication techniques used in the microelectronics industry to make transistors. PRINT is a high resolution molding technique that allows the fabrication of precisely defined nano-particles with control over size, shape, deformability and surface chemistry. PRINT allows for the precise control over particle size (20 nm to >100 micron), particle shape (spheres, cylinders, discs, toroidal), particle composition (organic/inorganic, solid/porous), particle cargo (hydrophilic or hydrophobic therapeutics, biologicals, proteins, oligonucleotides, siRNA, imaging agents such as MR contrast agents, positron emitters), particle modulus (stiff, deformable) and particle surface properties (Avidin/biotin complexes, targeting peptides, antibodies, aptamers, cationic/anion charges, Stealth PEG chains).



PRINT Process: A) An 8 inch silicon wafer patterned with approximately 400 billion posts that are 160 nm in diameter and 160 tall; B) A cured PFPE mold of the silicon master template shown in A; C) 160 nm particles made using PRINT and transferred to a medical adhesive for surface functionalization and subsequent harvesting; D) An SEM of an etched silicon wafer template of 3 micron posts having a height of 1.7 microns (to mimic RBCs); E) A cured PFPE mold of the master template shown in D; F) A cured mold containing hydrogel particles.



Internalization of PRINT particles in HeLa Cells. **Left:** Fluorescence micrograph of 2 micron cross-linked particles; **Right:** Transmission micrograph of intracellular PRINT cylindrical particles (d=150 nm, h=450 nm) (Effect of Particle Design on Cellular Internalization Pathways"; Gratton, Ropp, Pohlhaus, Luft, Madden, Napier, DeSimone, *Proceedings of the National Academy of Sciences, Sciences 2008, 105(33)*, 11613.