MICRO AND NANOSTRUCTURED INTERFACES FOR OVERCOMING DRUG DELIVERY BARRIERS

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Efficient drug delivery remains an important challenge in medicine. Continuous release of therapeutic agents over extended time periods and in accordance to a pre-determined temporal profile; local delivery at a constant rate to overcome systemic toxicity; improved ease of administration, and increasing patient compliance are some of the unmet needs of the present drug delivery technology.

Current advancements in the microelectronics industry have led to the creation of new nano- and microstructured materials. These developments have laid the foundation for novel design possibilities that can be used for creating drug delivery devices with a high level of control. In this talk, I will discuss how the ability to combine modular components such as shape, geometry, and size into a single device can be useful for therapeutic delivery. Examples include microfabricated particles to target cells and nanostructured devices for mucosal, transdermal and ocular delivery. By taking advantage of our ability to control topography and chemistry at submicron size scales, we may be able to better control drug permeability and release kinetics and overcome some of the key challenges in drug delivery.

In addition, by creating discreet monodisperse features in the nanoscale regime, one can begin to interact with cell and tissue surfaces in a manner previously unattainable. These subtle interactions can modulate properties such as tight junction morphology and endocytosis, leading to overall changes in drug transport. By gaining a better understanding of how small scale topographies can influence the biological microenvironment, these structures can be harnessed for more efficient drug delivery. In the future, micro and nanostructured materials can add functionality to current drug delivery platforms while becoming an enabling technology leading to new basic discoveries in the pharmaceutical and biological sciences.

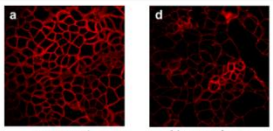
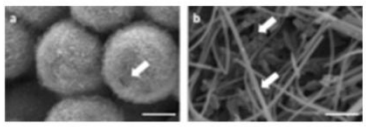
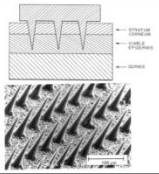
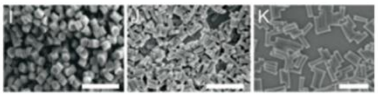
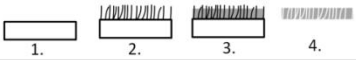
Specific Challenge	Nano or Micro Fabrication Solution	Examples
a. Tight junctions seal epithelial cells together (0.5-2 nm in width)	• Nanowires loosen the tight junctions (ZO-1 and Claudin 1) for paracellular drug delivery	
b. Mucosal Layer & Clearance	• Nanowires enhance adhesion through van der Waals forces • Gecko-inspired wet adhesive materials	
c. Overcoming the stratum corneum barrier for transdermal drug delivery	• Microneedles provide shunts to the dermis, disrupting the dead corneocytes, for topical or systemic drug delivery	
d. Cellular internalization	• Micro or nanoparticle geometry, shape, & surface chemistry influences endocytosis	
e. Achieving zero-order release	• Nanoporous membranes for single-file diffusion	

Table 1. Summary of ways that micro/nanofabrication can be used to address drug delivery challenges. Adapted from Kam et al., J. Mater. Chem. B, 2013, 1, 1878.