Guest Editorial
Advancing Mechanobiology by Micro/Nanosystems

THE capabilities of living cells to sense and respond to biomechanical cues in the native microenvironment play critical roles in various physiological and pathological processes. A century ago, the observations of cell shape changes and tissue deformation during embryo development allured developmental biologists to believe that mechanical forces dictate morphogenesis, while these thoughts were then masked by the huge success of genetics. The recent two decades witness the resurgence of mechanobiology research, thanks to the close collaborations between biologists, material scientists, and bioengineers. A range of micro/nanoengineered biomaterials and devices that precisely quantify and control matrix stiffness, topography, external forces, and delivery of small molecules have been developed and deployed to various biological systems [items 1) and 2) in the Appendix]. Coupled with advanced molecular and cell biology techniques, we now have a much deeper mechanistic understanding of the mechanosensing machineries in cells and tissues. In addition, advanced computational modeling tools have been utilized to integrate findings at different scales to construct a comprehensive framework for mechanobiology.

This Special Issue is a collection of eight recent exciting contributions to the mechanobiology field; efforts spanning a broad range of domains including cellular responses to bionanomaterials, and computational modeling of cell behaviors. A focused area is the effect of nanotopography on cells (see the review by Kim *et al.* in this issue [item 3) in the Appendix]). Specifically, using unique single and binary colloidal assemblies, Wang *et al.* studied how different topographies can modulate the pluripotency and differentiation of human embryonic stem cells [item 4) in the Appendix] and morphology of fibroblasts [item 5) in the Appendix]. Uto *et al.* developed a free-standing nanopatterned poly(ε-caprolactone) (PCL) thin film [item 6) in the Appendix]. Since nanogrooves can facilitate cell alignment, such functionalized, free-standing substrates may have great potential in tissue engineering as scaffolds. Biomaterial-cell interactions are investigated in another two studies. Using a 3D microfluidic system to quantitatively characterize angiogenesis, Ahn *et al.* discovered that high-density lipoproteins, or HDL, -mimetic nanoparticles exhibited a bi-phasic effect on angiogenic sprout growth and inhibited TNF-α stimulated angiogenesis [item 7) in the Appendix]. In another work, Hu *et al.* developed a novel approach to utilize quantum dots to measure the cytoskeletal pore size. As cytoskeleton can be modeled as porous materials, quantification the pore size of cytoskeleton is important for not only characterizing intracellular transportation, but also validating biomechanical models of cells [item 8) in the Appendix]. In this issue, two computational models are reported to study the effect of substrate stiffness (Fang *et al.* [item 9) in the Appendix]), and shear flow (Ye *et al.* [item 10) in the Appendix]) on cell adhesion. These new models provide insights into the changes of cell adhesion behaviors when exposed to different mechanical stimuli observed in experiments. Together, new material systems and computational tools reported in this issue have the potential to be broadly applied to future mechanobiology research.

While significant progresses have been made in fundamental mechanobiology studies, leveraging the obtained knowledge to transform current clinical practices and develop next-generation diagnostic and therapeutic approaches are of utmost importance. We are excited to see that several technologies reported in this issue have great potentials for translational applications. For example, functionalized, nanopatterned PCL thin films may be used in wearable devices to guide local tissue regeneration [item 6) in the Appendix]; computational models for cell adhesion can aid the design of vehicles for drug or therapeutic cell delivery [item 10) in the Appendix]; and the angiogenesis-on-a-chip device facilitates the drug screening process *in vitro* [item 7) in the Appendix]. With the joint effort from different disciplines, we envision that mechanobiology will continue to be one of the most attractive fields in years to come.

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Y. Sun, *Guest Editor*
Department of Mechanical and Industrial Engineering
University of Massachusetts Amherst
Amherst, MA 01003 USA
e-mail: ybsun@umass.edu

D.-H. Kim, *Guest Editor*
Department of Bioengineering
University of Washington
Seattle, WA 98195 USA
e-mail: deokho@uw.edu

P. K. Wong, *Guest Editor*
Department of Biomedical Engineering
Pennsylvania State University
State College, PA 16802 USA
e-mail: pak@engr.psu.edu

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APPENDIX
RELATED WORK

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