

Special issue on mechanics of development

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Developmental biologists have studied morphogenesis and the physical forces that shape embryos for well over a century. At the dawn of the modern era of molecular biology, however, most interest turned toward mapping the signaling pathways that regulate development. This work has provided important insights into the molecular mechanisms of morphogenesis, as well as the causes of human disease and birth defects. In the meantime, however, physical aspects of development received relatively little attention, leading to a fundamental lack of understanding of the connection between molecular mechanisms and the physical processes that actually construct the embryo.

During the 1980s and 1990s, a small group of biophysicists and engineers quietly began to revive interest in the physical mechanisms of development, although much of this work remained relatively obscure to most biologists. During the last decade, however, this situation has evolved as some developmental biologists have begun to recognize the need to relate molecular and physical mechanisms. At the same time, an expanding number of engineers and biophysicists, many of them with training in molecular and developmental biology, have taken up the cause. Nevertheless, the ranks have remained rather thin, especially compared to the number of researchers involved in tissue engineering.

The primary objective of this special issue of *Mechanics and Modeling in Mechanobiology* is to raise awareness of problems in development among researchers in the mechanics community. Many investigators now recognize that regenerative medicine, tissue engineering, synthetic biology, and related fields could benefit enormously by a better understanding of how nature creates tissues and organs. Many of

the problems central to this goal lie at the interface of biomechanics, mechanobiology, and biochemistry. Expanded research in these topics would greatly benefit the health of our society by leading, for example, to new treatments for diseases from embryo to old age.

The papers in this issue include almost an equal number of reviews and original research articles written by leading experts in the field. Several of the authors spoke at a one-day symposium on the Mechanics of Development held on June 21, 2011, immediately prior to the 2011 Summer Bioengineering Conference in Farmington, Pennsylvania. The meeting represented the Third US National Symposium on Frontiers in Biomechanics, which was sponsored by the US National Committee on Biomechanics (USNCB) with funding from the National Institutes of Health and the National Science Foundation.

The first three papers in this special issue deal with fundamental mechanisms of morphogenesis. Joshi and Davidson review epithelial morphogenesis and discuss how tissue engineers may be able to create tissues in vitro using strategies derived from embryos. Mansurov, Stein, and Belousov¹ then present intriguing new results demonstrating how some embryos respond actively to mechanical perturbations. Finally, Brodland and Veldhuis use a cell-level computational model to explore the energy efficiency of various morphogenetic mechanisms in producing equivalent changes in tissue shape. This study may actually raise more questions than it answers.

Biomechanics research in mature organisms has traditionally been dominated by studies of the musculoskeletal and cardiovascular systems. Similarly, cardiovascular

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¹ Professor Belousov, a developmental biologist, is a pioneer in this field, having studied the mechanics of morphogenesis for several decades.

development has been a popular subject for engineers. The next six articles focus on various aspects of this problem. The first two of these papers review blood vessel development. Roman and Pekkan present an overview of the effects of hemodynamics on the mechanotransduction processes involved in the formation of blood vessels in the early embryo. Cheng and Wagenseil focus on artery development at later stages, including the effects of stress on growth and remodeling of the microstructural constituents in the vessel wall.

The next two papers of this group deal with heart development. Goenezen, Rennie, and Rugonyi review the mechanics of pumping in the early embryonic heart tube and the effects of hemodynamic loads on form and function. Next, Buskohl, Jenkins, and Butcher present a computational model to illustrate how growth and remodeling in response to flow-induced stresses can mold mounds of tissue called endocardial cushions into functioning heart valves.

The last two papers of this group review aspects of the development of myocardial cells. First, Majkut and Discher discuss how substrate stiffness affects the development of myofibril organization and contractile function in

cardiomyocytes. Sheehy, Grosberg, and Parker then describe multiscale interactions between myocardial cells and their microenvironment, focusing on mechanotransduction. They suggest that recreating the normal *in vivo* environment is crucial to creating functional myocardial tissue constructs.

The final two papers in this issue focus on other problems in development. Lui, Lee, and Nelson present new evidence that mechanical cues guide differentiation of mammary progenitor cells through the regulation of cytoskeletal contractility. Filas et al. then show how regional regulation of contractility can play a role in creating interspecies differences in shape of the early embryonic brain.

These articles merely scratch the surface of the largely unexplored field of developmental mechanics. Embryos are full of new and exciting (and challenging) problems involving mechanics, many of which are still unknown to most engineers and biophysicists. Solving these problems will require close collaboration between developmental biologists, physicists, and engineers. We hope that this special issue will stimulate new interest in this important area of research.