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Midwest Mechanics Seminar Series

From Mechanics to Modeling Mechanobiological Regulation of Tissue Structure and Function

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Room 1010 DOW

4:30 p.m.

Midwest Mechanics Zoom Link Passcode 081068

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Abstract

Cells within load-bearing soft tissues sense and respond to diverse stimuli, including mechanobiological and immunobiological. Mechanical homeostasis is a ubiquitous process by which certain mechanical quantities are regulated to remain, within a range, near a preferred value, often called a set point. As an example, both flow-induced wall shear stress and pressure-induced intramural stress tend to be mechano-regulated to remain close to region-specific set-points in vascular mechanics. In some cases, inflammation can support mechanical homeostasis, while in other cases, it can prevent such homeostasis.

In this talk, we will consider two cases wherein it is important to model both the mechanical and the inflammatory signals and responses illustrated here for blood vessels. In the first case, we will consider the in vivo development of a tissue engineered neovessel from an implanted polymeric implant. In the second case, we will consider the growth and remodeling of a native artery in a mouse model of induced hypertension. Although inflammation arises for very different reasons in these two cases, we shall see how a consistent constrained mixture model of growth and remodeling can be used to predict the evolving geometry, composition, and wall properties in both cases. Importantly, computational predictions in the tissue engineered case helped lead to US Food and Drug Administration (FDA) approval of a clinical trial of a promising technology for treating congenital heart defects in children, thus showing translational potential of immuno-mechanical computational models of tissue response. For more information, please find details presented elsewhere [1-4].

References

[1] Szafron J, Khosravi R, Reinhardt J, Best CA, Bersi MR, Yi T, Breuer CK, Humphrey JD (2018) Immuno-driven and mechano-mediated neotissue formation in tissue engineered vascular grafts. *Annl Biomed Engr* 46: 1938-1950.

[2] Latorre M, Bersi MR, Humphrey JD (2019) Computational modeling predicts immuno-mechanical mechanisms of maladaptive aortic remodeling in hypertension. *Int J Engr Sci* 14: 35-46.

[3] Drews J, Pepper VA, Best CA, Szafron JM, …, Humphrey JD, Shinoka T, Breuer CK (2020) Spontaneous reversal of stenosis in tissue-engineered vascular grafts. *Sci Transl Med* 12:eaax6919.

[4] Spronck B, Latorre M, Wang M, Mehta S, Caulk AW, Ren P, Ramachandra AB, Murtada S-I, Rojas A, He C-S, Jiang B, Bersi MR, Tellides G, Humphrey JD (2021) Excessive adventitial stress drives inflammation-mediated fibrosis in hypertensive aortic remodeling in mice. *J R Soc Interface* 18:20210336.

Bio

J.D. Humphrey is John C. Malone Professor of Biomedical Engineering at Yale University. He received a Ph.D. in Engineering Science and Mechanics from The Georgia Institute of Technology and completed a post-doctoral fellowship in Medicine - Cardiovascular at Johns Hopkins University. His research and teaching focuses on vascular mechanics and mechanobiology, with a particular interest in development, hypertension, aneurysms, vascular aging, and tissue engineering. He has authored a graduate textbook (Cardiovascular Solid Mechanics), an undergraduate textbook (An Introduction to Biomechanics), and a handbook (Style and Ethics of Communication in Science and Engineering), and published 350+ archival journal papers. He served for 10 years as founding co-editor for the journal Biomechanics and Modeling in Mechanobiology, for 12 years on the World Council for Biomechanics, including as Chair of the Technical Program of the 2014 World Congress in Biomechanics, and served for two years as Chair of the US National Committee on Biomechanics. He is a Fellow of the American Institute of Medical and Biological Engineering, the International Academy of Medical and Biological Engineering, and the American Society of Mechanical Engineers, from which he received the H.R. Lissner Medal. He lives with his wife Rita of 41 years in Branford, CT.

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