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Mechanical and electrical interactions between Cardiomyocytes and Cardiac myofibroblasts in a model of fibrotic remodeling

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Following prolonged hypertension or myocardial infarction, cardiac fibroblasts within the heart can convert to myofibroblasts, a larger, contractile phenotype that produces fibrous connective tissue. Cardiac myofibroblasts can interact mechanically and electrically with cardiomyocytes. For example, excess connective tissue from cardiac myofibroblasts stiffens heart muscle, and cardiac myofibroblasts themselves disrupt normal patterns of electrical excitation of the cardiomyoctyes, potentially leading to cardiac failure through any of several pathways. Therapies that control interactions between myofibroblasts and cardiomyocytes would evidently be of value, but little is known about these interactions. We therefore developed a model tissue system (engineered heart tissues, EHTs) in which to study these. We find that limited populations of cardiac myofibroblasts may interact with cardiomyocytes in a way that is beneficial to cardiac function. The twitch force of EHTs increases as cardiac myofibroblast concentration increases, but only up to a critical threshold. We present here these mechanical and electrophysiological experiments, along with coupled mechanical and electrophysiological biophysical simulations that explain these phenomena in terms of mechanical and electrical percolation.

Biography

Guy M. Genin is Associate Professor of Mechanical Engineering and Material Science at Washington University in St. Louis, and a member of Washington University\'s Center for Materials Innovation and Center for Innovation in Neuroscience and Technology Prof. Genin\'s training includes a doctorate in solid mechanics from Harvard University under the guidance of John W. Hutchinson, post-doctoral studies at Cambridge University under the guidance of David Cebon, and further post-doctoral studies at Brown University under the guidance of Allan F. Bower. Prof. Genin also holds bachelor\'s and master\'s degrees from Case Western Reserve University, where he studied under the guidance of Roberto Ballarini.

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