Cancers behave like complex systems and are comprised of multiple distinct cell populations and structural and chemical signaling components. These elements of tumor microenvironments are not uniform across the tumor but instead vary in both space and time to sustain and promote disease as well as provide resistance to therapeutic interventions. Over the past decade, engineering and mathematics have begun to make critical contributions to our understanding of the physical and molecular mechanisms by which tumor microenvironments, and in particular the extracellular matrix, vasculature, and immune cell populations, influence disease progression. Thus, efforts to develop faithful quantitative approaches, mathematical models, and cutting edge technologies, which are critically needed to define elusive disease processes or address unmet clinical needs, has already begun. Indeed, from these contributions new technologies and therapeutic strategies have emerged. Yet, there remain critical gaps in our understanding of how heterogeneous tumor microenvironments drive disease and how we can successfully manipulate tumor microenvironments to bring novel therapeutic strategies.

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