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From normal mammary gland development to breast tumor growth: step-by-step development of a multiscale modeling approach

The normal homeostatic processes used for formation and maintenance of a given tissue can be altered to lead to progressive changes in cellular behavior and tissue architecture, which can ultimately lead to the formation of a tumor. In 1998, an elite group of breast biologists and breast tumor researchers stated: Our limited understanding of the biology and developmental genetics of the normal mammary gland is a barrier to progress. The importance of understanding the connection between normal development and tumor growth is obvious when one considers just the currently unanswered question: What cell types within the normal mammary gland are capable of being the cells of origin for human breast tumors?

In this talk, I will present a data-driven modeling approach for the normal development of mammary gland based on cell-lineage and cell transport in the constraint geometry of the terminal end bud (TEB). I will show how we plan to extend this approach to investigate 1) spatial organization of the various cell types within the TEB and along the duct and 2) carcinogenesis and the early stages of breast cancer development.

At later times of the development, modeling breast tumor growth requires the description of billons of cancer cells resulting from the early development of the disease. Thusly, I will present a theoretical multiscale framework inspired from physical sciences to bridge the gap between the descriptions of a few thousand cells in a normal end bud, and billions of cells involved in a growing macroscopic breast tumor that would result from dysregulation of the homeostatic processes within the mammary gland.