BiophysTO Lunchtime Talks

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Single-cell modeling of the dysfunctional signaling in Chronic Lymphocytic Leukemia

Novel methods in biological physics are becoming critical in clinical application to functionally interpret cancer genomic alterations. For Chronic Lymphocytic Leukemia (CLL), a heterogeneous disease of B-lymphocytes maturing under constitutive B-cell receptor (BCR) stimulation, the functional role of diverse clonal mutations remains largely unknown. We present here a combination of single-cell measurements and computational modeling to demonstrate that alterations in BCR signaling dynamics underlie the progression of B-cells toward malignancy. We apply nonlinear dynamics methods to reveal emergent dynamic features, namely bimodality, hypersensitivity, and hysteresis, in the BCR signaling pathway of primary CLL B-cells. We demonstrate that such signaling abnormalities in CLL quantitatively derive from BCR clustering and constitutive signaling with positive feedback reinforcement, as demonstrated through single-cell analysis of signaling motifs, computational modeling, and superresolution imaging. Such dysregulated signaling segregates CLL patients by disease severity and clinical presentation. Our findings provide a novel quantitative framework and illustrate how approaches borrowed from biological physics help assess complex and heterogeneous cancer pathology.

Host: Dr. Anton Zilman

(Refreshments and pizza will be provided)

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Thursday, February 9, 2017 – 12:00 pm, noon
McLennan Physical Laboratories, Room MP606
(and via streaming to DV3129 at UTM)