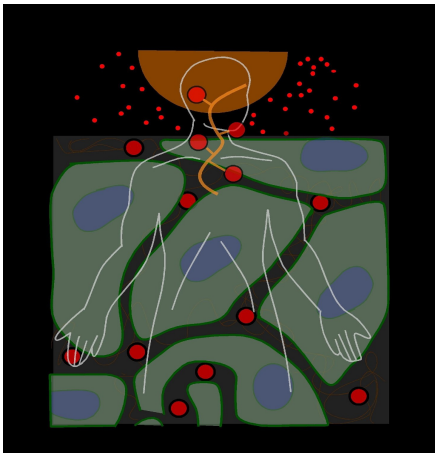

Yale University
Department of Biomedical Engineering ***Special*** *Seminar*

When: ***Thursday, October 13th, 2016***
Place*:* ***Amistad Conference Room 112***
Time: ***4:00PM***

"EPIGENOMIC STOCHASTICITY IN DEVELOPMENT AND DISEASE"

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Abstract: My recent work follows from an idea I had that natural selection will favor the emergence of genetic loci for epigenetic variation that can occur randomly or in response to environmental signals and affect phenotypes in which the environment changes unpredictably but often enough. Of particular interest, although at the genetic level cancer is caused by diverse mutations, epigenetic modifications are characteristic of all cancers, from apparently normal precursor tissue to advanced metastatic disease, and these epigenetic modifications drive tumor cell heterogeneity. We have suggested a unifying model of cancer in which increased epigenetic stochasticity allows rapid selection for tumor cell survival at the expense of the host. Mechanisms involve both genetic mutations and epigenetic modifications that disrupt the function of genes that regulate the epigenome itself. Several exciting recent discoveries also point to a genome-scale disruption of the epigenome that involves large blocks of DNA hypomethylation, mutations of epigenetic modifier genes and alterations of heterochromatin in cancer (including large organized chromatin lysine modifications (LOCKs) and lamin-associated domains (LADs)), all of which increase epigenetic and gene expression plasticity. With my colleague John Goutsias in the School of Engineering, we are developing a novel stochastic mathematical approach to understanding the nature of epigenetic information and its relationship to environmental exposure and biological function. This has led to several new measures, including normalized methylation entropy, which turns out to be surprisingly relevant to understanding some fundamental principles of physical biology.