M14: Hierarchical Models for Omics Data

Wed. March 8, 8:00 a.m. – 10:24 a.m. PST
Room 206
Sponsoring Units: DBIO
Chair: Mihaela Sardiu, University of Kansas Medical Center
Session Type:

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001 Growing a network via oscillations on nodes
002 Mechanisms of mammalian drug resistance acquired during long-term evolution
003 Specificity, cooperativity, synergy, and mechanisms of splice-modifying drugs
004 Experimental quantification of model identifiability and information loss due to distortions in fluorescence microscopy and image processing
005 Computational agent-based modelling reveals the role of tumour microenvironment on the success of combination chemotherapy/immunotherapy to treat glioblastoma
006 Using the Finite State Projection based Fisher Information Matrix to optimize single-cell experiment designs under different combinations of discrete stochastic models and measurement errors
007 Live imaging of gut-associated innate immune cell motion
008 Identifying the transition genes and state specific gene regulation from single-cell transcriptome data with spliceJAC
009 Analytical model for vaccination protocols that optimally produce broadly neutralizing antibodies
010 A model for how T cell-mediated autoimmunity can be triggered by persistent viral infections
011 Optimal design of cocktail boosters to elicit a polyclonal response against related viral strains
012 Stochastic modeling for studying the effects of BET inhibitors on the modulation of P-TEFb levels

Analytical model for vaccination protocols that optimally produce broadly neutralizing antibodies

Wed. March 8, 9:36 a.m. – 9:48 a.m. PST
Room 206

One way that the adaptive immune system responds to infectious pathogens is by creating antibodies (Ab) that can bind specifically to the associated antigens (Ag). In order to generate such Abs, B cells go through many rounds of Darwinian mutation and selection during the affinity maturation (AM) process. Successful vaccination guides the AM to produce B cells that elicit neutralizing Abs against the pathogen of concern. For highly mutable pathogens such as HIV, however, B cells that respond to the Ags presented during natural infection or vaccination generally neutralize a small number of mutant strains. The desired outcome of vaccination in these cases is to generate optimal amounts of the so-called broadly neutralizing Abs (bnAbs) that protect against various strains of the fast-mutating pathogen. Our goal is to describe the mechanisms via which bnAbs might be elicited by properly designed vaccination procedures. We devise a minimal model of the B cell population dynamics that focuses on their mutations and also the selection forces imposed by the vaccine. Using an analytical approach based on operator formalism, we show that to maximize the bnAb production, the selection forces imposed by sequential vaccination rounds over time need to become more focused on the B cells that have a chance to reach the high breadth state by mutation only. We also investigate how the initial distribution of the B cells may modify the optimal vaccination protocol.

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