

Mechanical Engineering Doctoral Defense

From Data to Predictive Models: Robust Identification and Analysis of the Immune System

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Abstract

In this dissertation, we develop new data-driven techniques to solve three problems related to generating predictive models of the immune system. These problems and their solutions are summarized as follows.

The first problem is that, while cellular characteristics can be measured using flow cytometry, immune system cells are often analyzed only after they are sorted into discrete groups by those characteristics. Instead of analyzing these discrete groups we propose analyzing the cellular characteristics of the cells by generating Probability Density Functions (PDFs) that model the flow cytometry data. To generate a PDF to model the distribution of immune cell characteristics we develop a new class of random variable called Sliced-Distributions (SDs) in Chapter 3 and show that SDs outperform other state-of-the-art methods and can differentiate between immune cells from healthy mice and those with RA.

The second problem is that while immune system cells can be broken into different subpopulations, it is unclear which subpopulations are most significant. We, therefore, formulate a new machine learning algorithm in Chapter 4 to identify subpopulations that are most correlated to disease severity or populations of other immune cells. The proposed machine learning algorithm performs well when compared to other state-of-the-art methods and is applied to an immunological dataset to identify disease-relevant subpopulations of immune cells denoted immune states.

Finally, while immunotherapies have been effectively used to treat cancer, selecting an optimal drug dose and period of treatment administration is still an open problem. In Chapter 5 we propose a method to model positive Lyapunov functions of a system with unknown dynamics. We apply this method to generate a semialgebraic set containing immunotherapy doses and period of treatment that leads to tumor elimination. The problem of selecting an optimal pulsed immunotherapy treatment from this semialgebraic set is formulated as a Global Polynomial Optimization (GPO) problem. In Chapter 6 a new method to solve GPO problems is proposed and optimal pulsed immunotherapy treatments are identified for this system.



September 24, 2021; 2:30 PM;

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