May 16th, 3:00 PM

Mathematical modeling of energy consumption in the acute inflammatory response

Ivan Ramirez Zuniga
University of Pittsburgh, ivr3@pitt.edu

Mathematical Modeling of the Acute Inflammatory Response and Energy Consumption

Ivan Ramirez-Zuniga, Jonathan E. Rubin, David Swigon, Gilles Clermont

University of Pittsburgh

Abstract

When a pathogen invades the body, an acute inflammatory response is activated to eliminate the invader. In some patients, runaway activation of the immune system may lead to collateral tissue damage and, in the extreme, organ failure and death. Experimental studies have found an association between severe infections and depletion in levels of adenosine triphosphate (ATP), increase in nitric oxide production, and accumulation of lactate, suggesting that tissue energetics is compromised. In this work we present a differential equations model that incorporates the dynamics of ATP, nitric oxide, and lactate accompanying an acute inflammatory response and employ this model to explore their roles in shaping this response. The bifurcation diagram of the model system with respect the pathogen growth rate reveals three equilibrium states characterizing the health, aseptic and septic conditions. We explore the domains of attraction of these states to inform the instantiation of heterogeneous virtual patient populations utilized in a survival analysis. We then apply the model to study alterations in the inflammatory response and survival outcomes in metabolically altered conditions such as hypoglycemia, hyperglycemia, and hypoxia. Finally, we present preliminary results obtained by fitting an extension of our model to animal data.