Validation Strategies for an Agent-based Model of Leukocyte Trafficking

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Leukocyte trafficking is an important process both in normal and pathological physiology. It is key in fighting infection and maintenance of health, while it can also contribute to pathological processes, such as plaque formation in atherosclerosis and intestinal inflammation and scarring in Crohn's disease. The ability to predict leukocyte behavior could be pivotal in developing new treatments for many diseases, as well as suggesting ways in which to control or target leukocytes to specific areas. Because of the complexity of the processes involved in leukocyte rolling, adhesion, and extravasation, prediction of spatial and temporal leukocyte trafficking patterns calls for the use of an agent-based computational model.

Critical in the development of a medically relevant agent-based model is experimental integration – both accurate determination of input parameters / initial conditions and model validation. In order to avoid "programming the proof," experimentally determined initial conditions are at the cellular / molecular level, the model's rule-set connects cellular / molecular interactions to cellular behavior, and experimental validation data is collected at the cellular patterning level.

In this presentation, I will provide an introduction to our ABM of leukocyte trafficking, and discuss the experimental strategies and techniques used to determine input parameters and develop validation data. Flow cytometry is used to determine expression of adhesion proteins on leukocytes, while immunohistochemistry is used to determine expression of binding partners on the vascular wall. Mouse surgical models exposing dermal vasculature and the femoral vessels are used in conjunction with fluorescence intravital video microscopy to view leukocyte trafficking and for validation of model output. I will present some preliminary data determined using these techniques and demonstrate its use in conjunction with the computational model to set up computational runs and validate model results.

In validating ABMs of *in vivo* processes, a number of questions must be addressed, including what level of agreement between experiment and model constitutes acceptable validation, what experimental techniques are best to use, and how can the model be validated while using the fewest animals possible. I will address how we are answering these questions in our research, and am interested in hearing discussion from other researchers about similar issues.