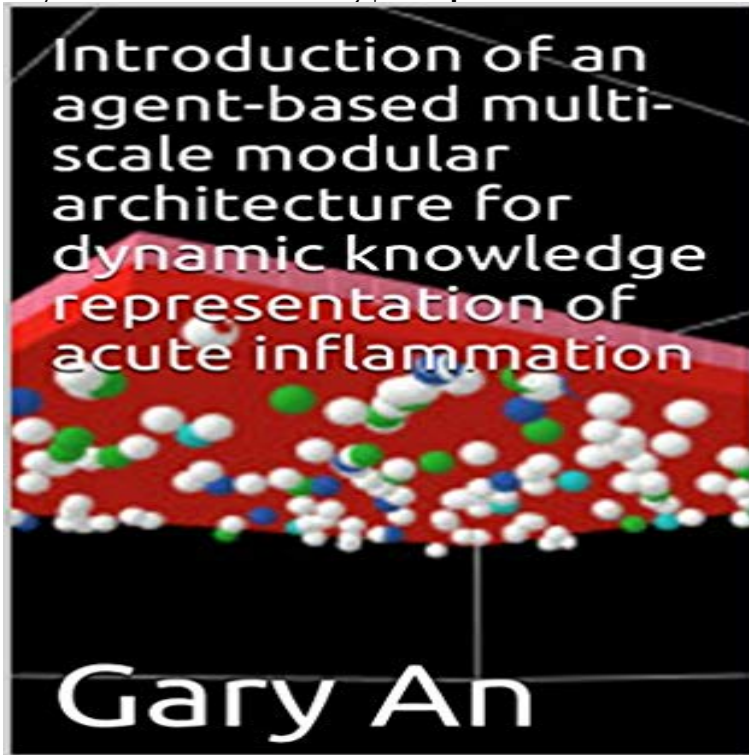


# Introduction of an agent-based multi-scale modular architecture for dynamic knowledge representation of acute inflammation



**Background** One of the greatest challenges facing biomedical research is the integration and sharing of vast amounts of information, not only for individual researchers, but also for the community at large. Agent Based Modeling (ABM) can provide a means of addressing this challenge via a unifying translational architecture for dynamic knowledge representation. This paper presents a series of linked ABMs representing multiple levels of biological organization. They are intended to translate the knowledge derived from in vitro models of acute inflammation to clinically relevant phenomenon such as multiple organ failure. **Results and Discussion** ABM development followed a sequence starting with relatively direct translation from in-vitro derived rules into a cell-as-agent level ABM, leading on to concatenated ABMs into multi-tissue models, eventually resulting in topologically linked aggregate multi-tissue ABMs modeling organ-organ crosstalk. As an underlying design principle organs were considered to be functionally composed of an epithelial surface, which determined organ integrity, and an endothelial/blood interface, representing the reaction surface for the initiation and propagation of inflammation. The development of the epithelial ABM derived from an in-vitro model of gut epithelial permeability is described. Next, the epithelial ABM was concatenated with the endothelial/inflammatory cell ABM to produce an organ model of the gut. This model was validated against in-vivo models of the inflammatory response of the gut to ischemia. Finally, the gut ABM was linked to a similarly constructed pulmonary ABM to simulate the gut-pulmonary axis in the pathogenesis of multiple organ failure. The behavior of this model was validated against in-vivo and clinical observations on the cross-talk between these two organ systems **Conclusion** A series of ABMs are

presented extending from the level of intracellular mechanism to clinically observed behavior in the intensive care setting. The ABMs all utilize cell-level agents that encapsulate specific mechanistic knowledge extracted from in vitro experiments. The execution of the ABMs results in a dynamic representation of the multi-scale conceptual models derived from those experiments. These models represent a qualitative means of integrating basic scientific information on acute inflammation in a multi-scale, modular architecture as a means of conceptual model verification that can potentially be used to concatenate, communicate and advance community-wide knowledge.

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