Designing an Agent-Based Model for Pericyte-to-Myofibroblast Transition in Lung Injury
(Technical Report)

Analyzing the Impact of the Lung Allocation Score on Lung Disease Treatment Using Care Ethics
(STS Research Paper)

An Undergraduate Thesis Portfolio

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Socio-Technical Synthesis: Agent-Based Modeling and Lung Allocation

Idiopathic pulmonary fibrosis (IPF) is a fatal disease characterized by the progressive stiffening of lung tissue in the absence of any known provocation. Due to a limited understanding of the disease's progression, existing therapeutics remain largely ineffective in treating IPF. Thus, my technical and STS research projects both aim to improve the understanding and treatment of IPF, such that the mortality of the disease is decreased. However, my two works differ in their approach to improving care for IPF. My technical project aims to improve understanding of IPF through a computational model to accelerate development of novel treatments for IPF. Meanwhile, my STS research aims to improve care of IPF patients by highlighting the inadequacies of the lung allocation system currently used for lung transplants – the only existing cure for IPF. While both of my works seek to improve standards of care for IPF, my technical work aims to improve understanding of IPF to aid development of future IPF treatments, while my STS work intends to improve the current care available to IPF patients.

My technical project integrates the novel pericyte-to-myofibroblast transition, which was recently implicated in the progression of renal fibrosis, into an agent-based model (ABM) of IPF to understand the influence of this pathway on disease progression. Pericytes are support cells critical to vascular integrity, while myofibroblasts are cells responsible for the aberrant tissue stiffening characteristic of fibrosis. ABMs utilize a logic-based ruleset to control agent behavior and enable the discovery of emergent phenomena. My ABM, implemented in NetLogo, strives to recapitulate the following attributes of native pulmonary tissue: architecture of the microvasculature; cytokine signaling pathways; known pericyte behaviors such as proliferation, migration, and apoptosis; and mechanotransduction. Sensitivity analysis of the optimized model enabled inquiry into how four major cytokines: VEGF, PDGF, TGF-$\beta$and Thy-1 influenced the

pericyte-to-myofibroblast transition and ECM stiffness. The goal of this project was to provide a cost-effective and time-efficient platform to test hypotheses related to the pericyte-myofibroblast transition in IPF progression as a means of promoting new effective treatments.

My STS research project also explores treatment of IPF, but as it relates to an existing cure – lung transplants. The lung allocation score (LAS) was implemented in 2005 with the intention of reducing the use of waitlist time as an allocation criterion, reducing waitlist mortality, prioritizing candidates based on urgency, and maximizing benefits to transplant recipients. While the LAS system was largely effective in providing equitable access to lung transplants, the goal of my project was to use care ethics to provide a new lens through which to identify the inadequacies of the LAS algorithm. I focused on three facets of care ethics – attentiveness, competence, and responsiveness – to argue that the current iteration of the LAS system fails to improve clinical outcomes of lung transplants relative to the pre-LAS era, and thus does not improve the quality of care available to patients. Ultimately, my goal was to highlight how further work must be done on the LAS system if it aims to meet its original goals.

Through working on these two projects simultaneously, I learned that assumptions implemented in algorithms/models can affect their findings and downstream implications. Specifically, my STS research project on the lung allocation system educated me on how deficiencies in the LAS algorithm created by assumptions of the patient populations and provider systems led to poor clinical outcomes for lung disease patients. Thus, when designing my own model, I was careful to document all the assumptions I made and leverage them to explain findings of my model that were contrary to research published from *in vivo* experimentation. Overall, the simultaneous execution of my technical and STS research projects ensured that my designed ABM can serve as an adaptable platform for future research on IPF treatments.

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