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Tracking the dynamics of multiple granulomas during infection with Mycobacterium Tuberculosis

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Infection with the bacteria *Mycobacterium tuberculosis* (Mtb) causes a dynamic immune response that spans multiple organs across multiple time scales. The infection may start with just a few Mtb infecting a few macrophages within the lungs, but sites of infection quickly experience local immune responses, and soon after draining lymph nodes become involved to mount an even greater defense. Different mathematical tools are required to simulate this complicated immune response, from the recruitment of the cells from the lymph nodes and their transport through the blood to the sites of infection, to the formation of granulomas, which are the hallmark of Mtb infection and are comprised of immune cells, bacteria, and other molecules. Agent-based modelling has been an effective multiscale approach to simulate the immune response during infection that forms a single granuloma. However, the computational cost of running these simulations begs for a quicker, coarser approach in order to study an infection across multiple granulomas within a single host lung. We propose a novel hybrid agent-based model that uses ordinary differential equations to evolve populations of cells, Mtb, and other molecules within each individual granuloma, that is then simulated as an agent within a whole-lung in silico infection model. The lung compartment can be connected to lymph nodes with granuloma agents spreading between compartments. This will allow for a higher-scale host response simulation to allow us to better address questions at the whole host scale and also be able to calibrate to datasets of whole human hosts.

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