A214 · Mathematical Modeling of Macrophage Polarization Dynamics and Molecular Feedback to Predict Immune Modulation Strategies

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In this work, we aim to elucidate the regulatory principles governing the transition from resting (M0-like) to pro-inflammatory (M1-like) macrophages in response to lipopolysaccharide (LPS) and interferon-gamma (IFN-ɣ), through mathematical modeling. We develop a library of model variants that integrate macrophage polarization with key signaling molecules including TNF-α, NOS-2, and IL-10, each capturing a different set of mechanisms. We use Bayesian optimization to fit these models to published time-resolved bulk RNA-sequencing and single-cell trajectories. Three murine studies supply co-stimulation, washout, repolarization, LPS-only, and IFN-ɣ-only time courses; a sequential stimulation study is held out for validation, and four human macrophage datasets serve as further external targets.

The optimized models can then be perturbed to simulate the effects of targeting different mechanisms. Future work will incorporate a tumor module, which can be used to explore immunomodulation strategies for cancer. This approach offers a principled path toward macrophage-reprogramming strategies in cancer and other inflammatory diseases by bridging omic data, mechanistic modeling, and predictive immunomodulation.

Abstract - Veena Naveen - NECB 2026

Mathematical Modeling of Macrophage Polarization Dynamics and Molecular Feedback to Predict Immune Modulation Strategies

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