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Mathematical Model of Immune-inflammatory Response in COVID-19 Patients

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Investigating the immune-inflammatory response characteristics in COVID-19 patients can predict disease severity and progression. There is evidence that severity of SARS-CoV-2 infection is linked to the dysregulation of the inflammatory immune response. Previous studies have shown the neutrophil-to-$CD8^+$T cell ratio (N8R) can be used in predicting disease severity in COVID-19 patients. Specifically, N8R increases as COVID-19 disease severity worsens. We developed a mathematical model (system of ordinary differential equations) to describe the inflammatory response to SARS-CoV-2 infection. Specifically, the model incorporates cellular and cytokine populations of neutrophils, macrophages, pro-inflammatory mediators, anti-inflammatory mediators, and $CD8^+$T cells. The model is fit to longitudinal data from COVID-19 patients confirmed to have either mild or severe disease. We identify and classify steady states, and conduct bifurcation analysis to determine parameters required for (1) the resolution of inflammation, (2) the persistence of inflammation (chronic inflammation), and (3) alterations in the neutrophil-to-$CD8^+$T cell ratio (used as a predictor of disease severity). This mathematical model can be used to identify markers for severe COVID-19 and give insight into effective treatment protocols and interventions directed at reducing inflammation and the neutrophil-to-$CD8^+$T cell ratio.