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Modeling the Proliferation and Regulation of CD4+ T Cells During an Immune Response

Most mathematical models for immune responses incorporating CD4+ T cell dynamics, such as HIV models, overly simplify this proliferation as an exponential growth with a rate less than the death rate of CD4+ T cells. Yet the autocrine reaction of IL-2 and CD4+ T cells suggests a much faster response, and the clearance of activated CD4+ T cells after the infection depends on induced regulatory T cells (Tregs). We prove mathematically that the interaction of IL-2, CD4+ T cells, and Tregs allows two modes of proliferation: the first mode is solely driven by the activation of naive CD4+ T cells, and the second mode is an excitable response in which the Treg population rapidly but briefly increases to a high level. These two modes are characterized by whether the proliferation rate is dominated by the CD4+ T cell death rate. We extend our model to include more realistic regulation terms and fit the models to CD4+ count data. The best-fit model parameters show that the immune system operates in the excitable mode.