Modeling abnormal TNF Levels and Immunosuppressant Drugs

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Background

Mainly utilized to treat Crohn’s, Ulcerative Colitis, and Arthritis - autoimmune disorders

Reduce the amount of Tumor Necrosis Factor via suppression

Prevents symptoms, varying from acute pain to abscesses and further complications
Goals

Model and Create a control system which includes three main factors: Remicade Levels, Remicade Antibodies, abnormally unhealthy TNF levels (above a normal amount, TNF level of zero equivalent to maximum level of TNF level)

Utilize a Model which utilize various presence of antibodies, and TNF levels
Assumptions and Model

Antibodies begin at zero, peak around two weeks, and decays eventually towards zero - utilized gaussian function to model presence of antibodies

Continuous Remicade Injection - studying the TNF output for a continuous input of Remicade

Remicade does not suppress any healthy levels of TNF
Model - Antibodies
Model - Remicade Levels
Model - TNF Levels
Transfer Function

\[
\frac{1}{10} = \text{average value or the linearize d term}
\]

\[
\begin{align*}
\frac{1}{10} & = \int_{0}^{10} \frac{1}{\sqrt{2\pi x}} e^{-\frac{(x-\frac{1}{2})^2}{2}} \, dx \\
& \approx \frac{1}{10}
\end{align*}
\]

\[
\delta^{-1} \frac{dR}{dt} = -A(t) + \alpha r(t) - cN(t)
\]

\[
\delta^{-1} \frac{dN}{dt} = -\gamma N(t) - r(t)
\]

\[
\delta^{-1} \frac{dA}{dt} = \frac{1}{\sqrt{2\pi x}} e^{-\frac{(x-\frac{1}{2})^2}{2}}
\]

\[
\begin{align*}
R(s) - r(0) &= -\beta A(s) + \alpha R(s) - cN(s) \\
N(s) - n(0) &= -\gamma N(s) - R(s) \\
(\alpha \cdot \text{H}(s)) &= \frac{\alpha}{s^2 + \gamma s + c}
\end{align*}
\]
Bode Plot - Stability Analysis
Advantages

Allows for a variety of inputs, allowing one to model a variety of scenarios for a patient

Create a model for unhealthy levels of TNF relating to Remicade and Remicade Antibodies
Errors

TNF Protein levels are rarely measured specifically - costly both monetarily and time-wise, general protein levels measured typically via blood.

Infusions are periodic, one is not constantly infused with Remicade or similar drugs constantly.

Assuming antibodies reduce over time, antibodies could increase over time => rejection of the drug.

Remicade still decreases amount of TNF (below normal levels).

Simplifications within Sensitivity Analysis.