A Mathematical Model to Explain the Differential Clinical Effects of TNF-α

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• Background

• An important question

• The model and the reasons it was used

• Meaning of the model’s behavior

• Take home message
Neutralization of TNF-α
Therapeutic Use of Neutralization

- Rheumatoid Arthritis
  - Chronic inflammation
  - Binding active TNF-α improves condition

- Systemic Inflammatory Response Syndrome (SIRS)
  - Uncontrolled inflammatory response
  - No response to neutralization in clinical trials
Why the different effects?
Mathematical Modeling: Good for Dynamic Systems

- Interactions between receptor, ligand, and inhibitor
- Nonlinear differential equation model
- Used published kinetic parameters for two inhibitors:
  - Infliximab
  - Etanercept
Model for Equilibrium Behavior

(Rheumatoid arthritis model)
Total TNF- α Over Time

Inhibition leads to an increase in total TNF- α
Model for Non-Equilibrium Behavior

(SIRS model)
Comparing Total TNF-α Over Time

(Rheumatoid arthritis model) (SIRS model)
Take Home Message

• SIRS is a non-equilibrium condition
  – Over time inhibitors act as slow release reservoirs of TNF-α

• Rheumatoid arthritis is an equilibrium condition
  – anti-TNF therapies are a success

• Success or failure of therapeutic agents is dependent on dynamic interactions
Thank you for coming!