Multi-paradigm Simulation of Cellular Pathways

Aslam Ahmed
Background

• Overview
  Past and current work

• Interests
  Immune system, Computer modelling

• Software
  BASIC, C, C++, .NET

• Research
  TRAPS, Inflammation
TRAPS

• TRAPS (TNF receptor-associated periodic syndrome)

• A dominantly inherited disease which is a result of missense mutations occurring in TNFR1 (TNF Receptor 1) gene.

• As a result of these mutations, patients suffer from inflammation and bouts of fever.

• TNF is released by macrophages when they encounter infectious material. Initiate inflammation. Coined the ‘master regulator’ of inflammation.

• Mutation of TNF receptor increases levels of Apoptosis.
The Role of TNF

- Antigen
- Macrophage
- TNF
- TNF
- TNF
- TNF
- TNF
- TNF
- Inflammation
- Apoptosis

The University of Nottingham
Why Model TRAPS?

• Understand the processes involved
  Cells and messages

• Determine the scope of simulation
  Limits, strengths and weaknesses

• Provide a useful tool
  Pre-laboratory analysis
  Starting point for further investigation
TRAPS components

- Extracellular layer
- Receptor layer
- Intracellular layer

Cells/Signals of the immune system

Binding of TNF to the receptor

Internal Pathways

The University of Nottingham
Extracellular components

- Dendritic Cells
  - Surveillance, Antigen Presentation
- Macrophages
  - Scavenge, Antigen Presentation
- T Cells
  - Cell mediation
- Natural Killer Cells
  - Kill stressed cells
- B Cells
  - Generate antibodies
Receptor/Intracellular components

- **TNFR1**
  - Binding activates pathway

- **NF-KB**
  - Controls cFLIP production

- **Inflammation**
  - Kill stressed cells

- **Apoptosis**
  - Caspase-8

- **cFLIP**
  - Apoptosis inhibitor

The University of Nottingham
Cell Simulation

- AnyLogic
- Agent Based
- Evaluation
- Results
- Parameters
- Logging

The University of Nottingham
Questions

Aslam Ahmed