

The background features abstract, overlapping green geometric shapes in various shades, creating a modern and dynamic visual effect. The shapes are primarily triangles and polygons, some with thin white outlines, set against a white background.

A novel model of TB progression using CompuCell3D

James Doran

Outline

- ▶ Introduction
- ▶ Model
- ▶ Results
- ▶ Discussion

Introduction

- ▶ TB is caused by airborne *Mycobacterium tuberculosis* (*Mtb*) transmission
 - ▶ 1.6 million died from TB in 2021
 - ▶ TB is treated with antibiotics (~6 months)
- ▶ Bowness et al. (2018)
 - ▶ Distance to nearest blood vessel is important
 - ▶ Dormant bacteria tend to remain after treatment
- ▶ CompuCell3D (CC3D) models biological cellular processes
- ▶ I'm developing a within-host TB model using CC3D

Model

- ▶ Conceptual model
- ▶ CompuCell3D

Conceptual model

▶ Cells:

- ▶ Macrophages
- ▶ T cells
- ▶ *Mtb* bacteria
- ▶ Blood vessels
- ▶ Caseum

▶ Chemical fields:

- ▶ Oxygen
- ▶ Chemokine
- ▶ Macrophage activating cytokine

Macrophages



T cells

► Either



► Or



Mtb bacteria

▶ Slow-growing
extracellular



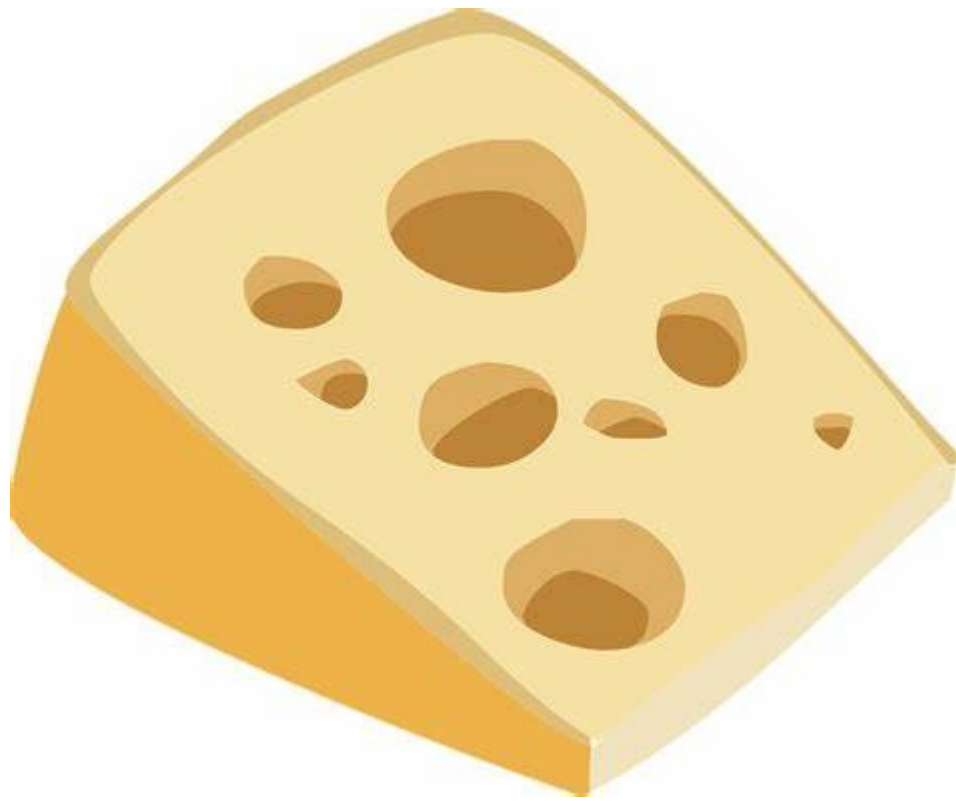
▶ Fast-growing
extracellular



▶ Intracellular



Caseum



Fields

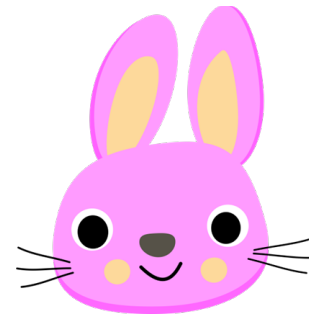
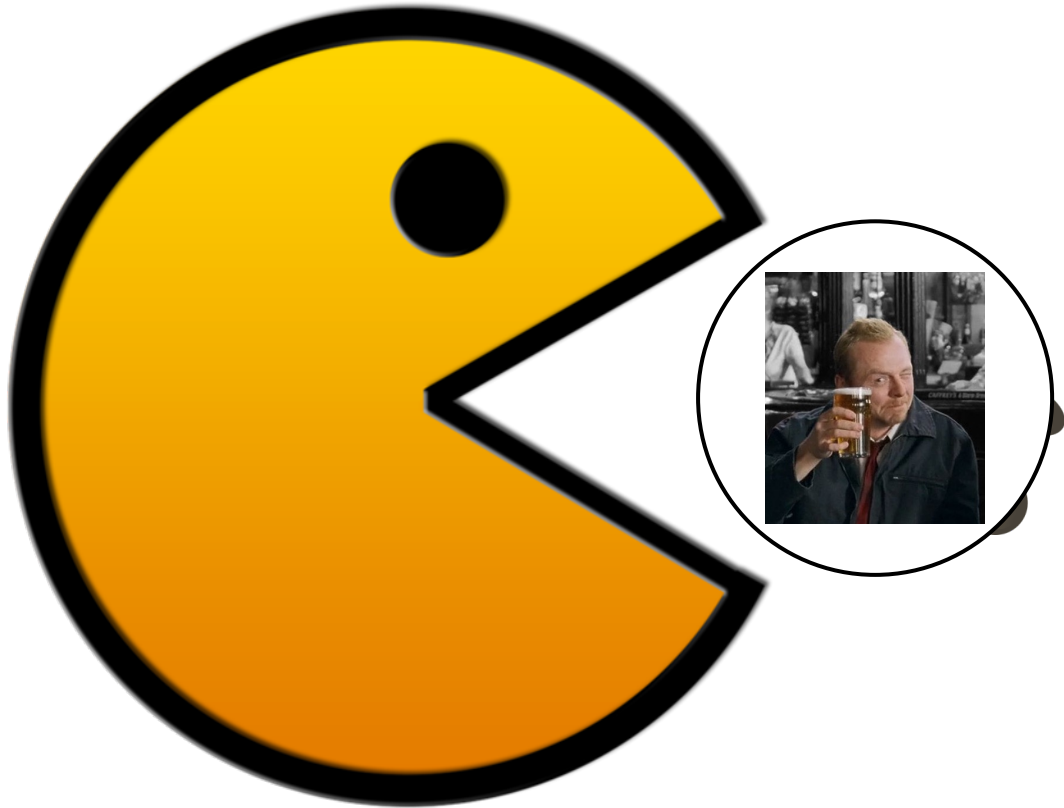
- ▶ Oxygen
 - ▶ Turns pandas into rabbits
- ▶ Chemokine
 - ▶ **HELP**
- ▶ Macrophage activating cytokine
 - ▶ Shia LaBeouf's voice

Biological processes

- ▶ Phagocytosis
- ▶ Immune cell recruitment
- ▶ *Mtb* bacteria state transition
- ▶ Chemotaxis
- ▶ Macrophage activation
- ▶ Killing of (chronically) infected macrophages
- ▶ Bursting of chronically infected macrophages
- ▶ Replication

Phagocytosis

HELP



Immune cell recruitment



Oxygen Oxygen Oxygen **HELP** Oxygen Oxygen



HELP



Mtb bacteria state transition

Oxygen

Oxygen

Oxygen

Oxygen

Oxygen

Oxygen

Oxygen

Oxygen



Chemotaxis

HELP

HELP HELP

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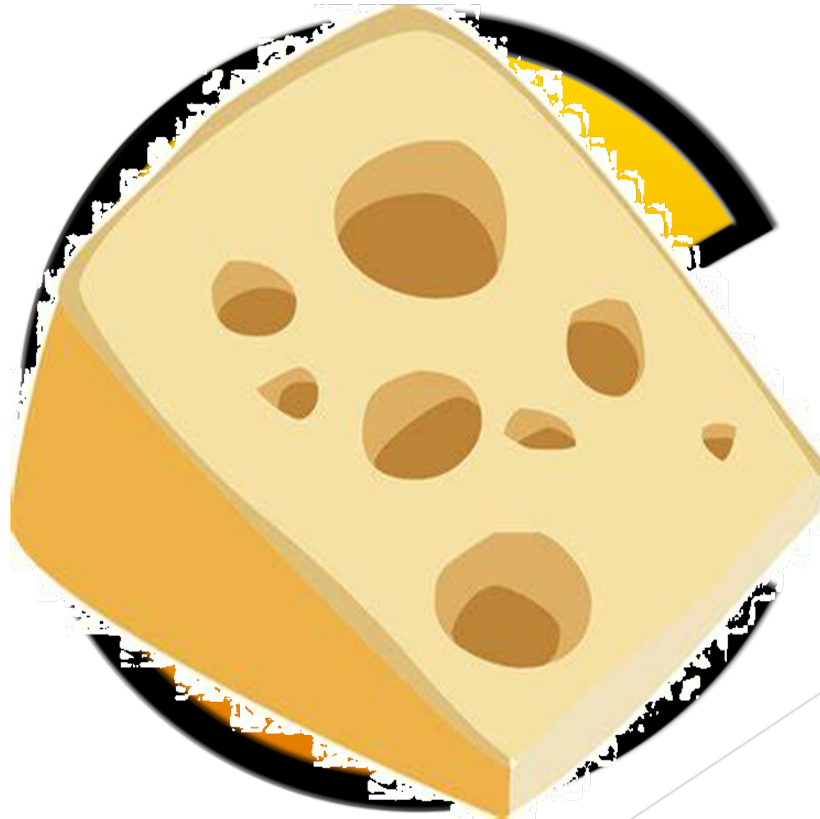
HEL P HEL P HE

T cells activate resting macrophages

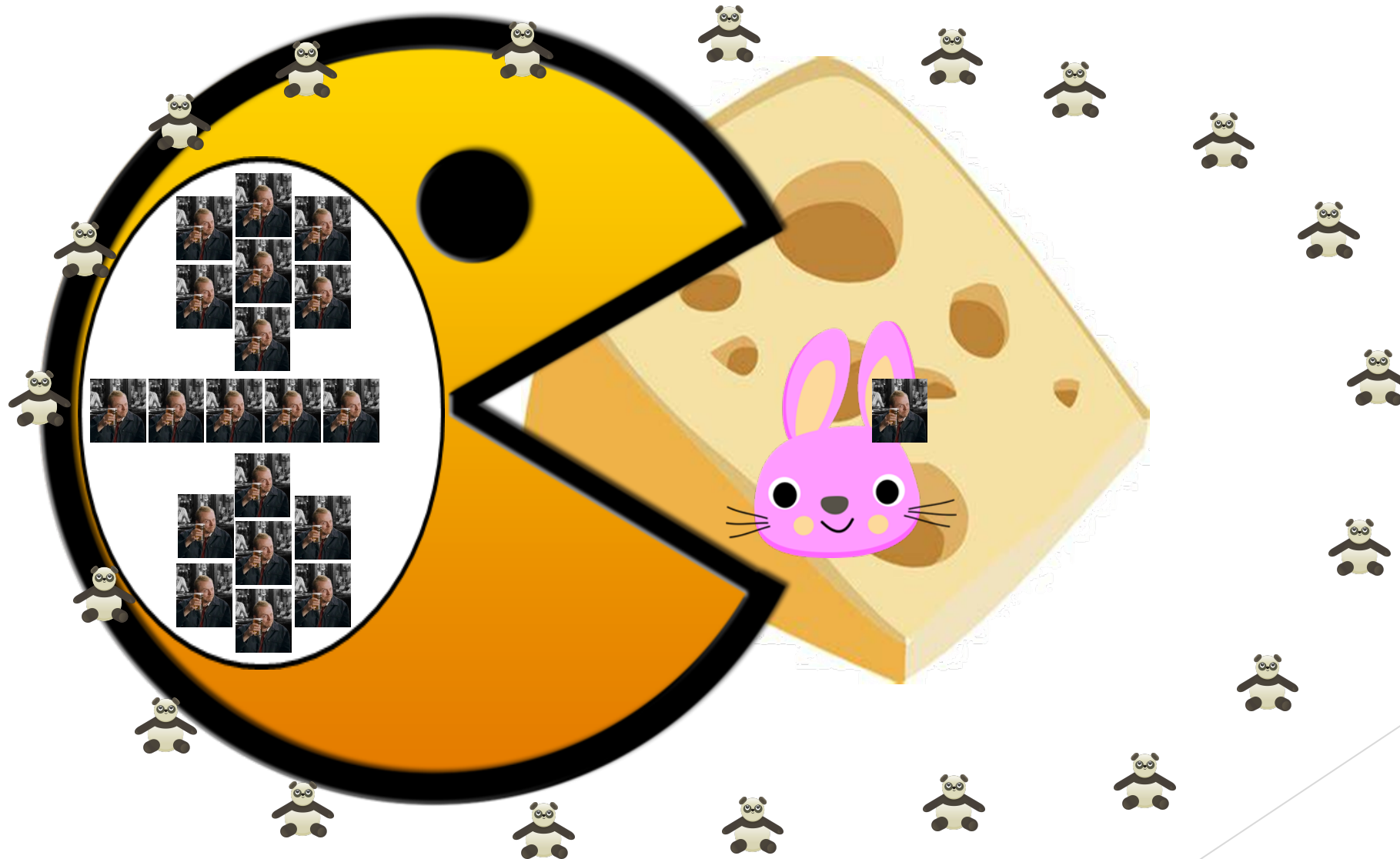


ZZZ

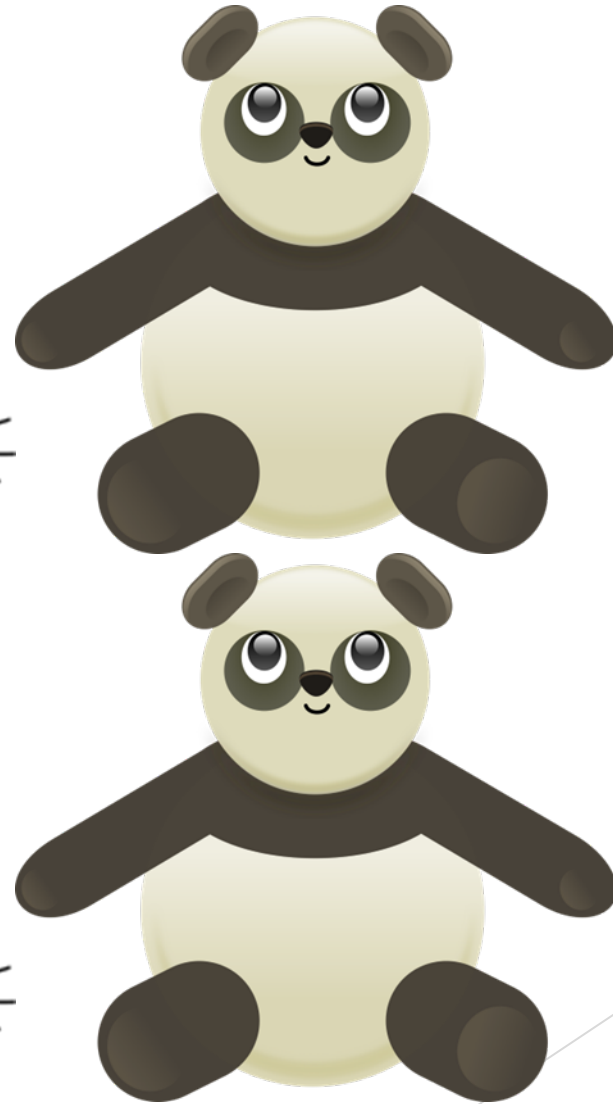
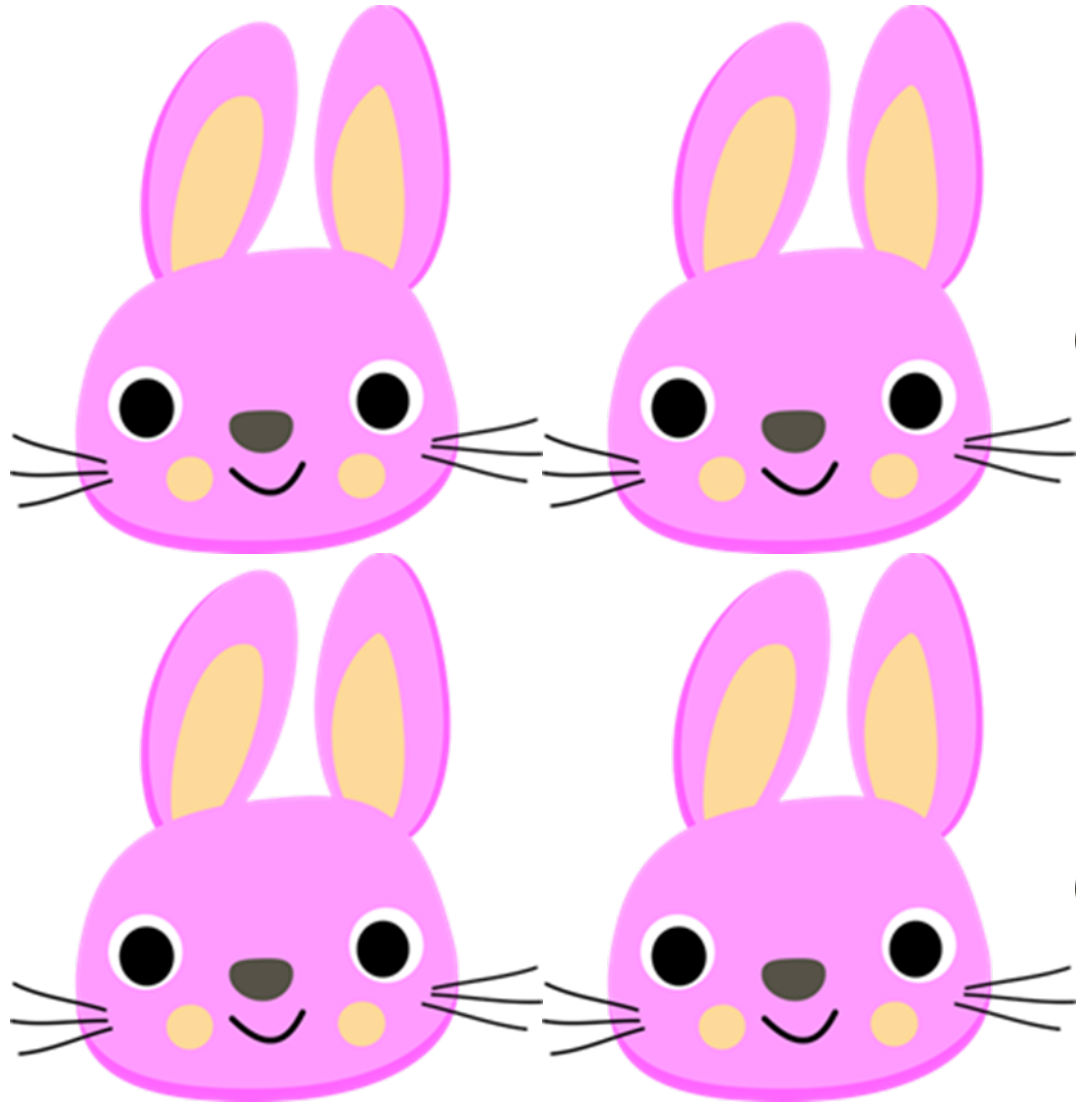
T cells kill (chronically) infected macrophages



Chronically infected macrophages burst



Replication



Outcomes

► Either:



► Or



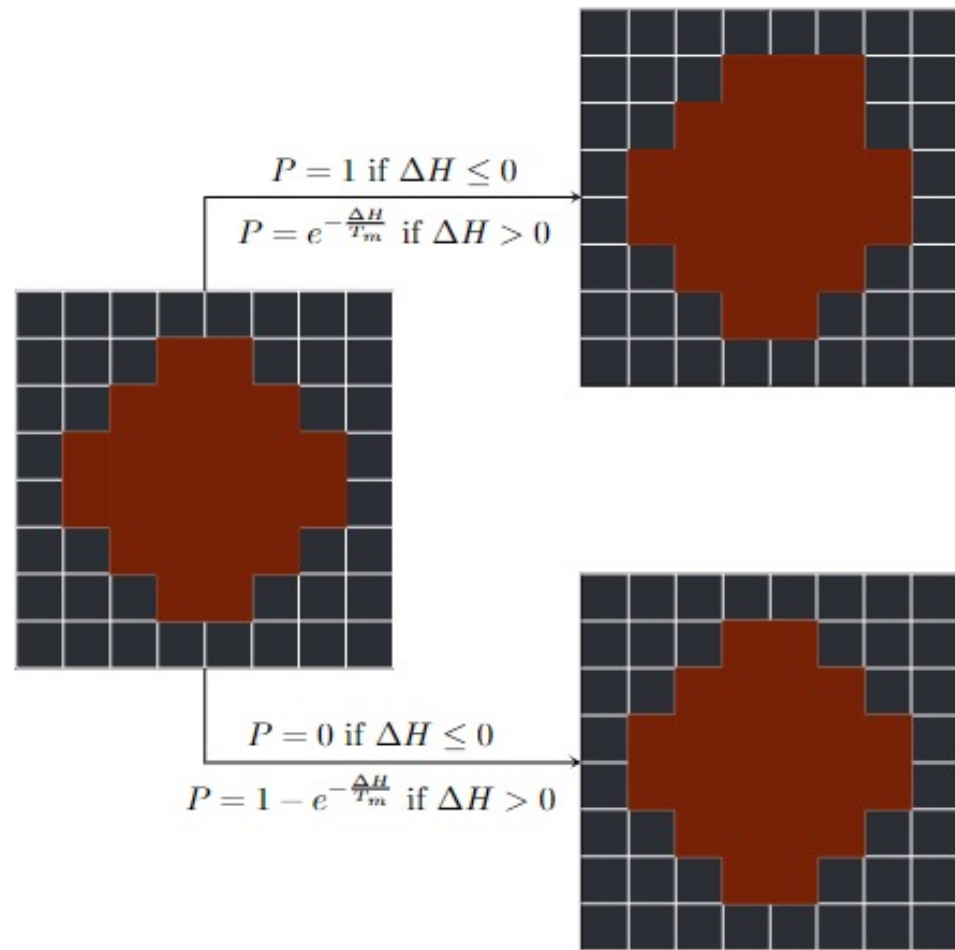
CompuCell3D

- ▶ Mixture of XML script and Python
- ▶ Cells:
 - ▶ live on a lattice
 - ▶ are assigned attributes
 - ▶ can interact with chemical fields

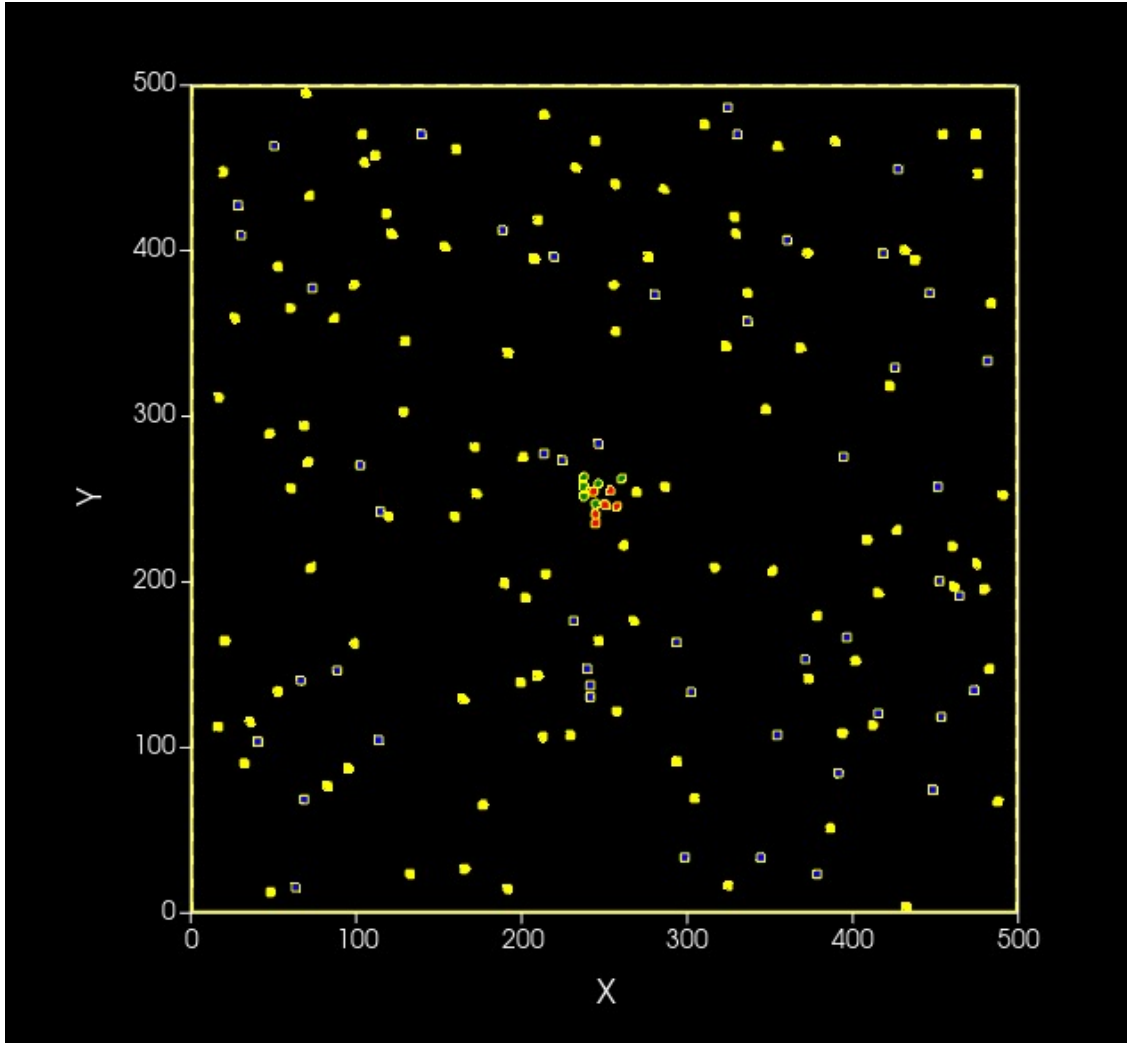
CompuCell3D

- ▶ Proposed cell configurations are accepted/rejected as follows:
 1. Choose a random lattice site
 2. Choose a neighbouring site to copy to
 3. Calculate the proposed change in energy (ΔH)
 - a. If $\Delta H \leq 0$, accept the new configuration
 - b. If $\Delta H > 0$, accept with probability $e^{-\frac{\Delta H}{T_m}}$

CompuCell3D



Initial conditions



Slow-growing
extracellular bacteria
(6)

Fast-growing
extracellular bacteria
(6)

Resting macrophage
(105)

Blood vessel (49)

Wall (1)



Results

- ▶ TBC!
- ▶ Expected results:
 - ▶ Containment in about 90% of simulations
 - ▶ Exponential growth in about 10% of simulations
 - ▶ Longer average distance to initial cluster
 - ▶ Predominantly slow-growing extracellular bacteria left

Discussion

- ▶ Easy to understand
- ▶ Can update states/parameters over time
- ▶ Allows for stochasticity and complex dynamics
- ▶ Open source, modular and easy to share
- ▶ Not analytically tractable
- ▶ Lots of parameters!
- ▶ Need to average over many (slow) simulations



Future work

- ▶ Finish parameterisation
 - ▶ Sensitivity and uncertainty analysis
- ▶ Test all model components in full
- ▶ Run 100 simulations and compare to original model
- ▶ Incorporate into a multi-scale TB model

Summary

- ▶ First within-host TB model made using CC3D
- ▶ Cellular Potts approach plus cell-field interactions
- ▶ Results should validate Bowness et al. (2018)

Acknowledgements

- ▶ My supervisors (Ruth and Kit)
- ▶ 2022 CompuCell3D workshop instructors
- ▶ My Hackathon teammates
- ▶ Aminat and Chris



UNIVERSITY OF
BATH



Thank you

► Any questions?




Macrophages



T cells

► Either  ► Or 

Mtb bacteria


► Slow-growing extracellular  ► Fast-growing extracellular  ► Intracellular 

Fields

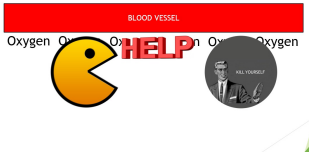
- Oxygen
- Turns pandas into rabbits
- Chemokine
- **HELP**
- Macrophage activating cytokine
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Phagocytosis

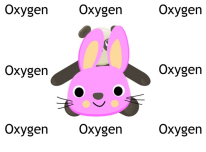
HELP



Immune cell recruitment



Mtb bacteria state transition



Chemotaxis

HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP HELP

T cells activate resting macrophages



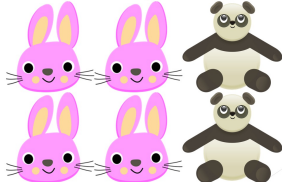
T cells kill (chronically) infected macrophages



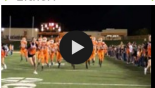
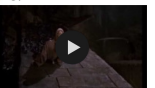
Chronically infected macrophages burst



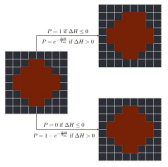
Mitosis (replication)



Outcomes

► Either:  ► Or 

CompuCell3D



Initial conditions

