

# Modelling Natural Killer cell interactions with Tumour cells

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# Natural Killer (NK) cells

- Kill some tumour and virus infected cells
- Identify targets by change in expression levels of proteins normally found in healthy cells
- Have Inhibitory receptors (MHC Class I) and activating receptors (NKG2D and others)
- Unhealthy cells can reduce expression of inhibitory ligands and increase activating ligands
- Receptors and Ligands log normally distributed within population

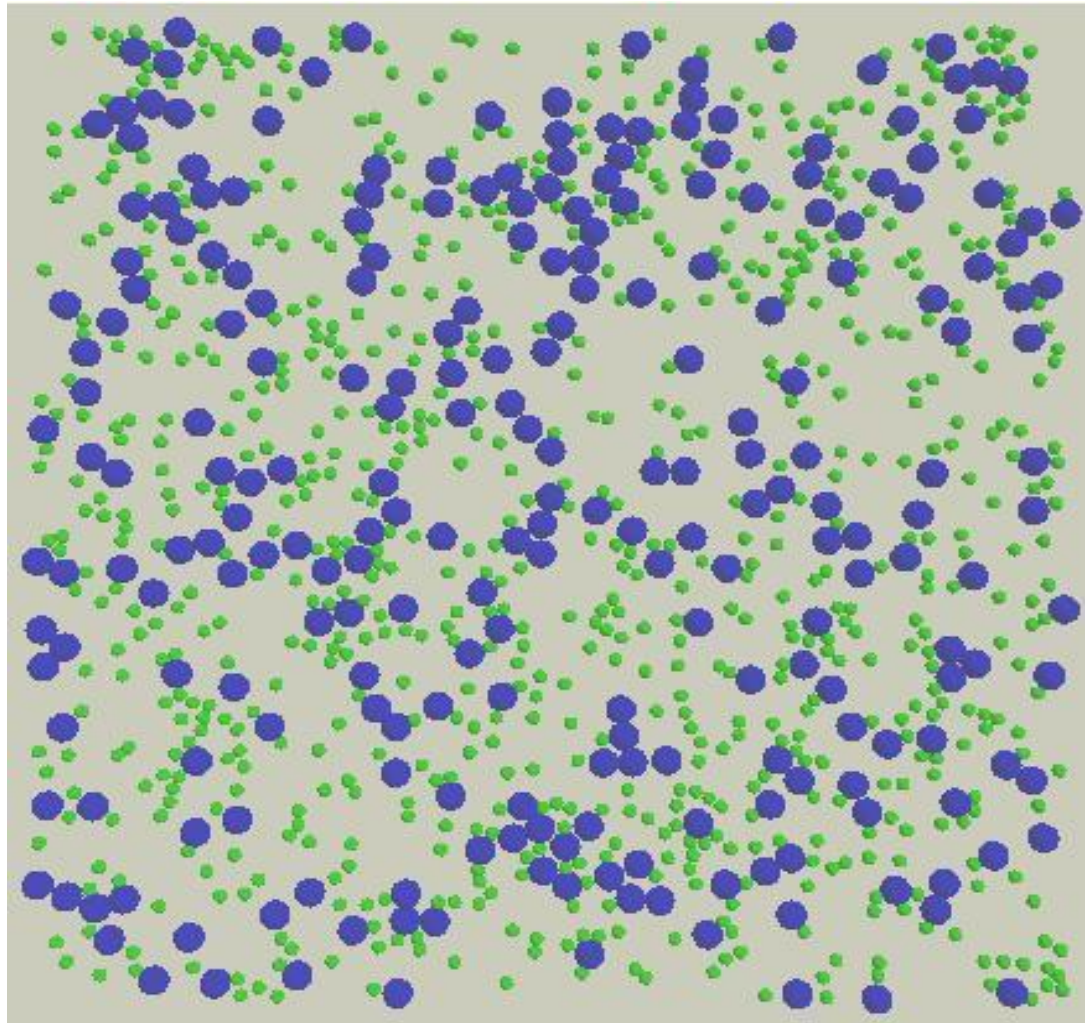
# NK Cells

- Each Receptor type on NK cells is expressed on only a proportion of NK cells
- Each NK cell therefore has a set of receptors each with its own unique level of expression
- Investigate how heterogeneous populations of NK cells can identify and target heterogeneous population of Tumour/Infected cells
- Without killing healthy cells in the process

# Model

- Explore different killing rules to help explain how NK cells determine which cells to kill
- Each agent in model is a cell, either NK or target
- Cells are spread across a 2D environment, mimicking in vitro testing
- Cells move around interacting for 4 virtual hours and number of target cells killed is monitored

# Typical starting layout of 1000 cell model



**250 Tumour cells (blue), 750 NK cells (green)**

# Model.XML

- Very simple model file
- 1 agent type – Cell
- Agent can represent NK cells or target cells based on a 'Type' variable
- Majority of memory is for expression level of the different receptors/ligands
- 1 Message that sends all receptor/ligand data for evaluation in cell:cell interactions

# Functions File

- Also quite simple
- Has functions for movement of cells
- Collision response if cells interact but one is not killed
- Evaluating the killing rule during NK:Target interactions
- Other minor functions such as keeping the cells within the bounds of environment

# 0.XML

- Main complexity of tests
- Every cell has unique receptor/ligand expression
- NK cells have several other variables chosen from distributions
- Testing mainly focuses on creating different starting populations to see how they interact



Agent/Variable	Var Type	Region 1	Region 2
cell			
id	int(SPECIAL)		
type	int	0	1
kill_reserve	double	100000	0
max_reserve	double	normal(10000,2500)	0
active	int	discrete((0.20,0),(0.80,1))	0
fatigue	int	0	0
x	double	rand(0,500)	rand(0,500)
y	double	rand(0,500)	rand(0,500)
z	double	0	0
num_inhib1	double	normal(2.3,0.15)	normal(2.7,0.27)
num_inhib2	double	discrete((0.2,0),(0.8,normal(2.3,0.15)))	discrete((0.2,0),(0.8,normal(2.7,0.27)))
num_inhib3	double	discrete((0.5,0),(0.5,normal(2.2,0.12)))	discrete((0.2,0),(0.8,normal(2.7,0.27)))
num_inhib4	double	discrete((0.5,0),(0.5,normal(2.7,0.18)))	discrete((0.2,0),(0.8,normal(2.7,0.27)))
num_inhib5	double	discrete((0.5,0),(0.5,normal(3,0.15)))	discrete((0.2,0),(0.8,normal(2.7,0.27)))
num_active1	double	normal(2.3,0.15)	normal(2.9,0.25)
num_active2	double	discrete((0.1,0),(0.9,normal(2.3,0.15)))	discrete((0.2,0),(0.8,normal(2.9,0.25)))
num_active3	double	discrete((0.1,0),(0.9,normal(3.2,0.15)))	discrete((0.2,0),(0.8,normal(2.9,0.25)))
num_active4	double	discrete((0.5,0),(0.5,normal(2.8,0.15)))	discrete((0.2,0),(0.8,normal(2.9,0.25)))
num_active5	double	discrete((0.5,0),(0.5,normal(2.6,0.12)))	discrete((0.2,0),(0.8,normal(2.9,0.25)))
dir_x	double	rand(-1,1)	rand(-1,1)
dir_y	double	rand(-1,1)	rand(-1,1)
dir_z	double	0	0