Q1: In both papers you define a "velocity" at which a particular cell type moves, e.g. 1 um/sec, and then map this to a frequency of hops on the lattice to a random (possibly biased) neighbor, e.g. 1 hop every hour. Since a random walk mimics diffusive movement, I would think mapping the hop frequency to a diffusion coefficient was more natural, which would be in units like um^2/sec. Can you explain the rationale for using cell velocities?

A1: The ABM building process underwent several stages. Since its inception, macrophages have been the key players/cells/agents to track during TB infection. We did not have data on cell (macrophage) displacement in the lung (even less so on diffusion) by then, so we decided to map what was known on macrophage speed to a hop frequency. We used the size of a macrophage (20μm) as our reference for microcompartment size, and adjust the hop frequency accordingly. This has been applied to T cell movement as well.

We use a discrete grid instead of a continuous grid because it is simpler and more efficient. Using a continuous grid would require detecting physical overlaps between cells and resolving those conflicts when they occur. This would be complex to implement and computationally expensive. Using a discrete grid avoids this issue entirely – when a cell want to move to another compartment we can easily tell from our crowding rules whether or not that is allowed.

Q2: I'm unclear on how you convert a cell velocity into a hop frequency. In the 2004 paper (sec 3.2) you list Tcell velocity = 11 um/min in mice, and say you are using a value 10x smaller. However Table 1 lists Tcell speed as 10 um/min. You also say this maps to a hop frequency of once every 10 minutes for Tcells. This is for a grid cell size of 20 um. If you are using Tcell speed = ~1 um/sec (despite the table), wouldn't this be one hop every 20 minutes?

Similarly, for resting vs infected machophages you list speeds of 1 and 0.0007 um/min in sec 3.2 of the 2004 paper. I think this is the same in the 2009 paper. However in the 2009 supplementary materials (IIb, p 7), you list movement of Mr (resting) on a 20 minute interval and Mi (infected) on a 24-hour interval. 20 min for Mr seems consistent with moving thru a 20 um grid cell at a speed of 1 um/min (although the next page says Tcells are moving at a 10-minute interval, and they are also 1 um/min?). However Mi is moving 1/0.0007 = 1430x slower, but the hop interval is only 72x smaller?

Since these hop frequencies seem like they will be important for reproducing the qualitative results of the model (clearance vs dissemination, etc), we'd like to get this right.

A2: You are correct in pointing out some discrepancies in the values given in the text. Since your goal is to "get it right", the hop frequency used for T cells maps to an average speed of 2 μm/min. The statement "using a value 10x smaller" has been applied in a semi-quantitative way, thus leading to the hop frequency of 2 μm/min, rather then 1 μm/min for T cell. The 0.0007 μm/min for Mi is simply an erroneous calculation, resulting from dividing 1 μm by 1440 (minutes in 1 day). In fact 1/1440 μm/min is equivalent to 0.0007 μm/min. It should be 20/1440 μm/min (0.01389 μm/min). The important thing is that the correct values have been used in the code.

Q3: One detail of the biased move rule, described in the 2009 supplement (IIIc, p 9), is not clear to me. For each of the 8 neighbor cells, you use its chemokine concentration to form a probability distribution which you then sample from to pick one of the 8 cells. You only do this if the concentration is between threshold and saturation limits. My question is, if one (or more) neighbor cell's concentration is not between those limits, does it still contribute to the distribution, and is a candidate for the move? If so, how much does it contribute to the distribution?

Also, this biased move rule is the same as what was used in the 2004 paper?

A3: We apologize if the rule wasn't clearly explained in the 2009 supplement (IIIc, p 9). So, the biased move rule is as follow:

i) Check if the concentration of chemokines in the microcompartment where the cell resides are within min and max thresholds (only the chemokines affecting movement of the specific cell are checked)
ii) If all the chemokines affecting movement of the cell are outside the ranges, then the movement is random
iii) If one (or more) of the chemokines affecting movement of the cell are within the ranges, then all the 9 microcompartments' concentrations (Moore neighborhood + the microcompartment where the cell resides) are used to generate the probability distribution

The biased move in the 2004 and 2009 papers did not use either chemokine threshold or saturation to affect whether or not a chemokine was included in the the probability calculation. All chemokine values in the Moore neighborhood were used unconditionally.