M5. Dimensionality module

M5.1 Slot, options and selection

Summary. GranSim builds for a two-dimensional or a three-dimensional lattice; the two-dimensional build is the default. Dimensionality is fixed when the executable is built and changes no process, order or timestep. It changes the geometry every block reads: grid shape, neighbourhood sizes and traversal orders, normalising constants, the diffusion solver and the observation formulae.

What the slot controls

M5 specifies how the dimensionality is selected and every point at which the program behaves differently between the builds. The spine and the S# documents are normative for the two-dimensional build, and nothing here revises a two-dimensional rule. Two-dimensional facts appear only beside their three-dimensional counterparts.

Dimensionality is not a process. It adds or removes no block of the cellular timestep, and it changes neither the order of operations nor the timestep values. The schedule (spine 3.2) and the synchronisation constraints (M1.2) are the same in both builds. What it determines is the geometry each block reads:

- the shape and indexing of the grid;
- the size and traversal order of every neighbourhood;
- the normalising constants derived from neighbourhood size;
- the implementation of the diffusion solver;
- the observation formulae that convert compartment counts into radii, diameters and scaling factors.

Every quantity specified here is fixed when the executable is built or when the program starts. Nothing here is written during a simulation.

Options

Option	Summary	Selected by default
Two-dimensional	A square lattice of n^2 compartments. The spine and the S# documents specify it as written.	Yes
Three-dimensional	A cubic lattice of n^3 compartments with 27-compartment radius-1 and 125-compartment radius-2 neighbourhoods. Rules are the same source text, applied over the larger neighbourhoods, except where M5.2 to M5.12 state otherwise. The Crank–Nicolson ADI solver is absent.	No

Where dimensionality enters the cellular timestep

Block (spine 3.2)	Dimension-dependent part	See
Initialisation	Grid shape, source stratification, random placement, density-to-count conversion	M5.2, M5.6
Diffusion block	Solver implementation, propagation coefficient, normalisation, stencil, accuracy limit	M5.10
Split half-step, vascular sources	Exchange area, density gate	M5.7, M5.11
Split half-step, smoother	Stencil and stability limit	M5.10
Movement	Neighbourhood size, iteration order, ordinal decoding	M5.3, M5.4
Recruitment	Source list built at initialisation; admission predicates	M5.6
Next-state computation	Contact and sensing neighbourhoods; daughter placement	M5.6, M5.9
Extracellular-bacteria sweep	Entrapment neighbourhood, growth-count neighbourhood, sweep order	M5.8
Statistics block	Cell density, extents, area and volume statistics, centre of mass	M5.2, M5.5, M5.7, M5.12
Connected-region construction	Region growth, diameters, bounding test	M5.12
Ring scaling	Whether scaling is applied	M5.12

Reads and writes

Reads:

- the compile-time macro `DIMENSION`, value 2 or 3;
- the command-line options `--dim`, a single integer n, and `--diffusion`;
- the `row`, `col`, `slice`, `pos` and `offset` attributes of the parameter-file Init section.

Writes, all fixed for the run:

- the grid extent, n^2 or n^3 compartments;
- the initial positions of deterministically placed entities;
- the diffusion solver and the set of valid method numbers;
- the neighbourhood constants: the radius-1 Moore count M_N (9 or 27) and the dimension count D (2 or 3);
- the geometry functions (equivalent radius, scaling factor, neighbourhood size, compartment measure)

and the neighbourhood iterators with their traversal orders.

The build macro

Dimensionality is selected at compile time by the macro `DIMENSION`, which must be 2 or 3; the build sets it. No option, parameter or loaded state can change it, so the two builds are separate executables. Any other value fails compilation.

Shared model code is written against build-bound type aliases, not against dimension-specific types. Most rules are therefore the same source text in both builds and take their dimension-dependent behaviour from the bound types: a periodic radius-1 loop visits 9 compartments in one build and 27 in the other. A rule that looks dimension-independent can still differ between builds, through its iterator's size and traversal order (M5.3).

Code that is not dimension-agnostic through the aliases takes one of these forms:

- **Preprocessor branches in shared files.** These are the CCL5 and CXCL9 ratio assignment, which has a two-coordinate and a three-coordinate loop; the Crank–Nicolson ADI header and its case in the method selection; and the help text and method switch for `--diffusion`.
- **Whole-file substitutes.** The spectral and explicit solvers each have a three-dimensional source file defining the same class. The build selects source files as well as setting the macro.
- **A run-time test on the dimension count.** Both branches are compiled into both builds, and the outcome is fixed by the build. The instance is ring scaling (M5.12).

Grid shape

The extent comes from `--dim` (default 300), which sets every coordinate to the same value. The grid is therefore always square or cubic:

$$N_{\text{grid}} = n^D, \qquad D \in \{2, 3\}.$$

There is no option for unequal extents. The default, n = 300, gives 9×10^4 compartments in two dimensions; the same value in a three-dimensional build gives 2.7×10^7. That size exceeds the stack limit of M5.6 and the memory limit of M5.10.

The extent is passed to the parameter store when it is created, before parameters are resolved, because computed parameters depend on it (spine 7.0, "Computed parameters").

Provenance

The build dimension is recorded at start-up on standard output (a line `DIM: 2` or `DIM: 3`) and in a string embedded in the model executable. Run output gives no other indication. Statistics files have the same column names in both builds, even where a column's meaning changes (M5.5, M5.12), so a consumer must check the recorded dimension before reading area, diameter or scaled-count columns.

M5.2 Positions, indexing and storage order

Position types

A position holds two or three integer coordinates x, y and z (row, column, slice); the same types hold grid extents.

Positions are ordered lexicographically by x, then y, then z. Multiplying a position by a real rounds each coordinate to the nearest integer. Its only model use places the M8 reinfecting macrophage; in three dimensions that point lies on the cube's main diagonal, at the fraction `Core_reinfectionLocation` of the way from the origin.

Positions read from the parameter file

The Init-section rules are those of spine 5.4, with the build's arity:

1. A `pos` attribute is either `center` or a parenthesised, comma-separated list of signed integers, with optional whitespace. It must have exactly two components in the two-dimensional build and three in the three-dimensional build. `pos` together with any of `row`, `col` or `slice` is fatal.
2. Otherwise `row` and `col` are required in both builds, and `slice` in the three-dimensional build. An absent required attribute is fatal.
3. Every coordinate must then lie on the grid; this range check is applied before any offset. If an `offset` attribute is present, it is parsed with the build's arity and added, and the range check is applied again (spine 5.4).

The builds read the same attribute names but enforce different arities, so a parameter file is not in general valid for the other build:

Init entry written as	Two-dimensional build	Three-dimensional build
`pos="center"`	Accepted	Accepted
`row` and `col` only	Accepted	Fatal: `slice` absent
`row`, `col` and `slice`	Accepted; `slice` ignored, and no warning is issued	Accepted
Two-component `pos` or `offset`	Accepted	Fatal
Three-component `pos` or `offset`	Fatal	Accepted

The default file has a single entry, `pos="center"`, which either build accepts. In the row with `slice` ignored, a three-dimensional file read by a two-dimensional executable places every entity in the plane given by its row and column, and no warning is issued.

Storage order

Fields, agent slots and bacterial containers are stored with the last coordinate fastest in both builds. The entire-grid iterator visits positions in this storage order: y fastest in two dimensions; z, then y, then x in three. Every whole-grid sweep therefore runs in storage order. The sweeps whose order affects the result are given in M5.8.

Wrapping and distances

The wrap function is that of spine 2.1, applied per axis. In three dimensions periodic wrapping makes the domain a three-torus: every compartment, including those on a face, edge or corner, has a full periodic neighbourhood of 27, or 125 at radius 2.

The Euclidean and Moore distances extend to three coordinates:

$$d_E(p,q) = \sqrt{\sum_i (p_i - q_i)^2}, \qquad d_M(p,q) = \max_i |p_i - q_i|.$$

The periodic iterator's radius is computed from the unwrapped position, as in two dimensions (spine 2.1). The largest Moore radius about a position whose shell still holds an on-grid compartment bounds the connected-region sweep (S9.6).

Centre of mass

The centre of mass is the per-axis mean, with one accumulator per axis, returned as a double-valued position. It serves the connected region and ring scaling (M5.12).

The statistics block reports it twice, through two accessors that differ in the z component:

Statistic	Source of the z value	Two-dimensional value	Three-dimensional value
`CenterOfMassX`, `Y`	Double-valued mean	Mean	Mean
`CenterOfMassZ`	z accessor of the double-valued position, which returns an integer	Constant 1	Mean z, truncated toward zero
`GranulomaCenterOfMassX`, `Y`	Double-valued mean	Mean	Mean
`GranulomaCenterOfMassZ`	z accessor of the accumulator, which returns a double	Constant 0.0	Mean z

The x and y columns of the two pairs are identical in both builds. In two dimensions the z columns hold different constants, neither a coordinate (S9.7). In three dimensions they differ by the fractional part of the mean, so `CenterOfMassZ` is below `GranulomaCenterOfMassZ` by less than one compartment.

M5.3 Neighbourhoods

Moore ordinals and neighbourhood constants

Ordinals

Spine 2.1 gives the two-dimensional convention: nine ordinals 0 to 8, centre 4. The three-dimensional convention numbers the 27 compartments 0 to 26, slice by slice, with the centre at 13:

$$\begin{array}{ccc|ccc|ccc} 24 & 25 & 26 & 15 & 16 & 17 & 6 & 7 & 8 \\ 21 & 22 & 23 & 12 & 13 & 14 & 3 & 4 & 5 \\ 18 & 19 & 20 & 9 & 10 & 11 & 0 & 1 & 2 \end{array}$$

From left to right, the panels are the slice above the centre (δ_slice = +1), the centre's own slice (0) and the slice below (-1). Within each panel, rows increase upward in the first coordinate and columns rightward in the second, as in spine 2.1. Ordinal 4 lies directly below the centre and ordinal 22 directly above it.

The displacement for ordinal k, applied to the first, second and third coordinates, is

$$\delta_{\mathrm{row}} = (\lfloor k/3 \rfloor \bmod 3) - 1, \qquad \delta_{\mathrm{col}} = (k \bmod 3) - 1, \qquad \delta_{\mathrm{slice}} = \lfloor k/9 \rfloor - 1,$$

or equivalently k = 9(δ*slice + 1) + 3(*δrow + 1) + (δ*col + 1). The second coordinate varies fastest with k, then the first, then the third. For k < 9 the first two displacements reduce to those of spine 2.1, so the two-dimensional convention is the bottom panel without* δslice, and the same function body serves both builds.

Rules that select a neighbour by ordinal use the wrapping conversion (spine 2.1). The correspondence between ordinals and iterator order holds in two dimensions and fails in three (Moore neighbourhood iteration order; M5.4).

Neighbourhood constants

Constant	Two-dimensional	Three-dimensional	Meaning
M_N	9	27	Compartments in a radius-1 Moore neighbourhood, centre included; the number of ordinals. Also held as a double, for use as a denominator
D	2	3	Number of spatial dimensions

The number of compartments in a Moore neighbourhood of radius r is (2r + 1)^D: 9, 25 and 49 for r = 1, 2 and 3 in two dimensions, and 27, 125 and 343 in three. This count serves where a radius other than 1 is needed: the per-agent caseation statistic and the computed growth thresholds (M5.8, M5.13). Radius-1 sizes use M_N. The uptake-in-caseum statistic divides by M_N while summing over a neighbourhood of configurable radius, in both builds (S9.13).

Random movement

Without chemotactic signal, the destination is drawn uniformly over the M_N ordinals, centre included (S1.3). A random attempt therefore stays put with probability $1/9 \approx 0.111$ in two dimensions and $1/27 \approx 0.037$ in three. Every other destination has the same probability; 4 of 8 share a face with the centre in two dimensions, and 6 of 26 in three. The movement admission predicates (S1.4) apply identically in both builds.

Moore neighbourhood iteration order

Why the order matters

The iterators guarantee which compartments are visited, in a fixed order that differs between builds. Order has no effect on a rule that only sums, counts or tests for existence. It changes outcomes for a rule that pairs a traversal position with an ordinal, of which there is one (M5.4). For a rule that makes one draw per visited compartment, or builds a list in traversal order and selects from it by a draw, the order fixes only which draw goes with which compartment.

Moore regular and periodic iterators

Both range over the box $[c - r, c + r]^D$ lexicographically, last coordinate fastest:

Build	Fastest	Middle	Slowest
Two-dimensional	y		x
Three-dimensional	z	y	x

The regular iterator skips off-grid positions and the periodic one wraps them (spine 2.2). The periodic iterator therefore visits 27 positions at radius 1 and 125 at radius 2 in three dimensions.

Every whole-grid sweep uses the entire-grid iterator, in storage order (M5.2). These sweeps include the statistics sweep, the extracellular-bacteria sweep, secretion from caseated compartments and the sorted position list for ring scaling.

Relation to the ordinals at radius 1

In two dimensions the ordinal order is the iterator order, so the i-th compartment of a radius-1 periodic traversal has ordinal i (spine 2.1).

In three dimensions the orders differ. Ordinals have the second coordinate fastest, then the first, then the third; the iterator has the third fastest, then the second, then the first. With offset (δx, δy, δz), the traversal index i and the ordinal k are

$$i = 9(\delta_x + 1) + 3(\delta_y + 1) + (\delta_z + 1), \qquad k = 9(\delta_z + 1) + 3(\delta_x + 1) + (\delta_y + 1),$$

related by

$$k = 9\,(i \bmod 3) + \lfloor i/3 \rfloor, \qquad i = 3\,(k \bmod 9) + \lfloor k/9 \rfloor.$$

Index and ordinal coincide only for i = 0, 13 and 26: the centre and the two ends of the main body diagonal. These are the solutions of 3δx + δy = 4δz with every offset in $\{-1, 0, +1\}$.

The ordinal convention exists only at radius 1. At radius 2 the traversal still has z fastest, and no rule converts a radius-2 traversal position to an ordinal.

Moore shell iterator

The shell iterator is regular: its box is clipped to the grid on every axis first, and the shell is the boundary of the clipped box (S9.6). It serves the connected-region sweep and region growth. The two-dimensional traversal runs counter-clockwise round the clipped box (S9.6).

In three dimensions the clipped box is traversed slice by slice, from z_min to z_max:

1. The bottom slice, z = z_min, is visited in full, y fastest, then x.
2. Each middle slice is visited as a ring, by the two-dimensional rule, starting from (x_min, y_min, z).
3. The top slice, z = z_max, is visited in full, y fastest, then x.

The bottom and top slices are visited in full because their interiors belong to the shell. An unclipped shell of radius $r \geq 1$ has $24r^2 + 2 = (2r+1)^3 - (2r-1)^3$ positions, each visited once: 26 at r = 1 and 98 at r = 2, against 8 and 16 in two dimensions. At radius 0 the shell is the centre alone in both builds. A clipped box two positions deep along z has no middle slices, and both slices are visited in full.

Von Neumann neighbourhood

Construction

Neither build has a dedicated Von Neumann geometry. Both step through Moore ordinals, skipping the centre. In two dimensions the step gives the four face neighbours, N_4 (spine 2.1).

In three dimensions the step is +2 from ordinal 1, with one extra increment on reaching 9 or 18. It visits

$$1, 3, 5, 7,\ 10, 12, 14, 16,\ 19, 21, 23, 25,$$

and ordinal 27 ends it: twelve compartments.

Ordinals	**Offsets (δx, δy, δz)**	**Relation to the centre**
10, 12, 14, 16	$(-1,0,0)$, $(0,-1,0)$, (0,+1,0), (+1,0,0)	Face neighbours in the centre's slice
1, 3, 5, 7	$(-1,0,-1)$, $(0,-1,-1)$, $(0,+1,-1)$, $(+1,0,-1)$	Edge neighbours in the slice below
19, 21, 23, 25	$(-1,0,+1)$, $(0,-1,+1)$, (0,+1,+1), (+1,0,+1)	Edge neighbours in the slice above
4, 22 (not visited)	$(0,0,-1)$, (0,0,+1)	Face neighbours directly below and above

The set therefore holds four of the six face neighbours and eight of the twelve edge neighbours. It differs both from N_6 and from N_6 with the edge neighbours (eighteen members). The regular and periodic Von Neumann iterators follow the same sequence; the regular one skips off-grid positions and the periodic one wraps them.

Consumers

The only consumer is the local-concentration average at a vascular source, under the M6 and M7 fluxes (M6, M7). It uses the regular iterator, sums the field over the positions visited, divides by their number and then by the molecular weight. In an interior compartment the divisor is 4 in two dimensions and 12 in three. Randomly placed sources avoid a border one compartment wide (M5.6), so their divisor is always 4 or 12; a source placed deterministically on the domain edge would have fewer. Oxygen exchange reads the source's own compartment, not this average (M5.11).

In a three-dimensional build with M6 or M7, the average includes eight positions at distance $\sqrt{2}$ as well as four at distance 1, and omits the two positions directly above and below the source. A gradient along the third axis is sampled only through edge neighbours, so the local concentration entering the flux weights the third axis differently from the other two. With M6 and M7 disabled and the two-dimensional build selected, the set has no effect.

M5.4 Chemotaxis axis permutation

Mechanism

The chemotactic weighting rule is that of S1.3. Its weight array has M_N entries. A radius-1 periodic iterator and a counter k advance together from zero, and weight k receives the signal sensed at the k-th compartment of the traversal. The selected index is then decoded as a Moore ordinal with the wrapping conversion (S1.3).

Weight k is therefore sensed at the k-th traversal compartment, but the agent goes to the compartment whose ordinal is k. In two dimensions these coincide for every k (M5.3). In three dimensions they coincide only for k = 0, 13 and 26.

The weighting code is compiled unchanged into the three-dimensional build, so the mapping holds in every three-dimensional run. Let the iterator visit offset (a, b, c). Its traversal index is i = 9(a + 1) + 3(b + 1) + (c + 1). Decoding i as an ordinal gives δ*slice* = *a,* δrow = b and δ_col = c, so the destination offset is

$$\sigma(a, b, c) = (b, c, a).$$

σ is a cyclic permutation of the axes. The move to offset (x, y, z) takes the weight sensed at $\sigma^{-1}(x, y, z) = (z, x, y)$. The fixed points of σ are the offsets with a = b = c: the centre and the two ends of the main body diagonal.

Consequence for the direction of movement

A signal concentrated on one axis sends the agent along another:

Highest weight sensed at	Agent moves to	Effective direction
(+1, 0, 0)	(0, 0, +1)	+x becomes +z
(0, +1, 0)	(+1, 0, 0)	+y becomes +x
(0, 0, +1)	(0, +1, 0)	+z becomes +y
(+1, +1, +1)	(+1, +1, +1)	Unchanged

In the three-dimensional build, under a linear field the mean step is the gradient rotated 120° about the body diagonal; its component along the gradient lies in $[-1/2, 1]$, with mean zero over gradient directions. The axis permutation holds exactly for any field. Because the source stays where it is, an agent displaced along an axis other than the gradient's senses the same gradient next time and is displaced the same way again.

These parts of the rule are unaffected:

- the concentration window, read at the agent's own compartment;
- the probability of no displacement, since index 13 and ordinal 13 are both the centre;
- the uniform fallback when no weight is positive, which draws an ordinal directly.

The first-maximum tie-break follows traversal order. With `Core_Mac_movementBonusFactor` and `Core_Tcell_movementBonusFactor` at their default of 1.0, the bonus has no effect and neither does the tie-break; above 1 the permuted destination receives it. The admission predicates and the blocked-by-large-agent statistic are evaluated at the permuted destination.

S1.3 specifies one weighting rule for macrophages, Tgam, Tcyt and Treg, so the permutation applies to all four.

Rules that are unaffected

A rule that enumerates ordinals and decodes the same ordinals, or that builds a list with an iterator and indexes that list, is unaffected. Only conversion of a traversal index through the ordinal conversion is affected.

Rule	Form	Effect of three-dimensional order
Random movement	Uniform draw over ordinals, decoded as an ordinal	None
Daughter placement (S3.5)	Loops over ordinals; candidate list in ordinal order	None
Caseous-neighbour count by ordinal	Loops over ordinals	None
Intracellular drug dispersal (M6)	Loops over ordinals	None
Bacterial dispersal (S4.13)	Shuffled ordinals, decoded as ordinals	None
Macrophage exposure test (S2.10)	Regular iterator; first match ends the search	None on the outcome
NF-κB bacterial sum, cell density, entrapment and growth counts	Iterator sums and counts	None

Rule	Form	Effect of three-dimensional order
Activated-macrophage caseum sweep (S2.8)	Periodic iterator; one shared healing draw, then one draw per caseous neighbour holding bacteria	Distribution unaffected; draw assignment follows the order

M5.5 Compartment geometry and physical constants

Lengths, areas and volumes

The compartment dimensions are declared once and shared by both builds. The values are the same; which a rule reads differs.

Quantity	Value	Read by
Length δx	2×10^{-3} cm (20 μm)	Spectral propagation coefficient; accuracy factor ℓ; ring scaling and diameter conversion (in μm)
Face area	4×10^{-6} cm^2 (400 μm^2)	Explicit solver and smoother, as δx^2; compartment measure in two dimensions
Two-dimensional lateral area, four faces	1.6×10^{-5} cm^2	Vascular flux in both builds (M5.11); drug-permeability check (M5.10)
Three-dimensional surface area, six faces	Declared integer; initialiser 6 $\times$ face area, stored as 0	Read by no rule
Two-dimensional and three-dimensional areas in μm^2	1600 and 2400 μm^2	Read by no rule
Volume in μm^3	8000 μm^3	Compartment measure in three dimensions
μm to mm	10^{-3}	Diameter conversion

The three-dimensional surface area in square centimetres is stored as an integer, and its value is 0. No rule reads it. The vascular flux reads the two-dimensional constant in both builds, so three-dimensional exchange is not zero (M5.11).

Compartment volume

The compartment volume $V = 8 \times 10^{-12}$ L $= (20\ \mu\mathrm{m})^3$ is the same in both builds, as are the macrophage and bacterial volumes and Avogadro's number (spine 2.1), and the molecular weights (S9 for the cytokines, S7.2 for oxygen).

In the two-dimensional build V is the volume of a cube of side δx. A two-dimensional compartment is therefore a cube, and the grid a slab one compartment thick with no exchange across its two faces. The same thickness δ x appears in the ring scale factor (S9.9).

Every conversion that uses V is identical in both builds: the occupancy proxy (S6.2), the IL-10 conversion that gates chemokine secretion, the oxygen half-saturation and the vascular flux. The same molecule count is the same molar concentration in either build. The unit conversions and decay lengths of S6 therefore do not depend on dimension, and the S9 scaling corrects no field quantity.

Lesion concentrations

The volume-normalised concentrations divide a whole-grid field total by the lesion volume, formed from the compartment count of the cell-density extent (S9.11). They are not comparable between builds: that count is taken against a density threshold whose integer requirement changes, 5 of 9 against 14 of 27 (M5.7), so the two builds count different sets of compartments as lesion.

Compartment measure

The compartment measure is 400 μm^2 in two dimensions and 8000 μm^3 in three. A statistic formed as a compartment count times this measure therefore reports μm^2 in one build and μm^3 in the other, under the same column name (M5.12).

The constant pi

The program's pi, 3.141592653 (spine 2.1), enters the spectral eigenvalues of both builds (M1.3, "The propagator and incorporation of decay"), the equivalent radii and the compact diameter (M5.12). It does not enter the ring scale factor.

M5.6 Occupancy and initial placement

Occupancy, slots and random positions

Slots

Occupancy does not depend on dimension. The two slots per compartment and the size classes are those of spine 2.3, and each route's admission predicates read only the target compartment (S1.4, S3.5, S8.9, M9.3, spine Element 5). What changes is how many compartments are examined: a Moore neighbourhood of 27 compartments holds up to 54 agents (M5.9), and the cell density is taken over 27 (M5.7).

Daughter placement

Daughter placement enumerates ordinals 0 to $M_N - 1$ (S3.5). In three dimensions the candidate list holds up to 27 compartments in ordinal order. The parent's own compartment, ordinal 13, is a candidate whenever it has a free slot, as ordinal 4 is in two dimensions. The rule is unaffected by the axis permutation of M5.4.

Random grid positions

A random grid position takes one uniform integer per axis: two draws in two dimensions and three in three. It serves every rejection-sampled placement at initialisation (spine 5.3, 5.4): background macrophages, initial cognate Tgam, dendritic cells, fibroblasts and neutrophils (M9.3), and the remainder of the vascular sources (Stratified placement of vascular sources).

Failed attempts consume draws, and both the draws per attempt and the acceptance rates depend on the build. The random-number streams therefore diverge from the first placement, and two runs with the same seed and parameter file in different builds share no trajectory, even before any model rule differs.

The initial macrophage count is bounded by the grid size n^D; a larger computed count fails initialisation (spine 5.3).

Entity counts and source placement

Order of placement

The order of initial placement is the same in both builds (spine 5.1). What depends on dimension is the stratification of sources, the draws per placement and the counts derived from densities.

Entity counts from densities

A density read from the parameter file is converted to a count as $n = \lfloor \rho N_{\text{grid}} \rfloor$, with $N_{\text{grid}} = n^D$ (spine 7.0, "Computed parameters"). A density is therefore a fraction of compartments in either build: per area in two dimensions, per volume in three. Counts grow as n^3 in the three-dimensional build.

Quantity	Two-dimensional, n = 300	Three-dimensional, n = 200	Three-dimensional, n = 300
N_grid	9×10^4	8×10^6	2.7×10^7
Vascular sources, `Core_sourceDensity` = 0.08762770113823116 (spine 5.2)	7886	701 021	2 365 947
Initial resting macrophages, `Core_Mac_initDensity` uniform on [0.00479863597111917, 0.0102617209270614]	431 to 923	38 389 to 82 093	129 563 to 277 066

At about 0.088 sources per compartment, a radius-1 neighbourhood holds about 0.79 sources in two dimensions and 2.37 in three. The initial macrophage count is also the recruitment floor (S8.7), which scales the same way.

Stratified placement of vascular sources

The algorithm, its capacity check, retry limit and remainder are those of spine 5.2, with an axis added. Write n_rand = `Core_nrSources` and b = `Core_sourceBorderSize`. In three dimensions:

- the border-adjusted region, of side $a = n - 2b$, is divided into m^3 subgrids of side $s = a/m$, with m

$= \lfloor n_{\mathrm{rand}}^{1/3} \rfloor$ in place of $\lfloor \sqrt{n_{\mathrm{rand}}} \rfloor$; roots, s and subgrid bounds are computed in single precision;

- subgrids are visited z fastest, then y, then x, and each selection takes one real draw per axis;
- the retry limit is $2\lfloor s^3 \rfloor$ attempts, and $n_{\mathrm{rand}} - m^3$ sources remain for rejection sampling;
- the capacity at n = 300 and b = 1 is 298^3 = 26 463 592 compartments.

The capacity check guarantees a free position for the remainder, so its rejection sampling terminates with probability one.

With b = 1 no randomly placed source lies on a face of the cube, as none lies on an edge of the square in two dimensions; M5.3 relies on this for the Von Neumann divisor.

Stack allocation of the occupancy record

The record of which compartments hold a source is a variable-length array of n^D bytes on the stack: 90 000 bytes in two dimensions at n = 300, 8 000 000 bytes (7.6 MiB) in three at n = 200, and 27 000 000 bytes (25.7 MiB) at n = 300. Against a common 8 MiB stack limit, n = 200 leaves under 0.4 MiB for everything else, and n = 300 exceeds it; the program then terminates at initialisation, without the capacity check's diagnostic. The limit is a property of the platform and shell environment, so the largest usable three-dimensional extent is not fixed by the program. This is a limitation of three-dimensional studies, independent of the memory limit of M5.10.

The grid centre

The grid centre (spine 5.4) resolves `center`, seeds the connected-region sweep and gives `DistanceFromCenter`. In three dimensions it is a point of the cube, so infection is seeded at the centre of a volume.

M5.7 Neighbourhood fractions and vascular gating

Fractions

Both neighbourhood fractions use the same functions in both builds and divide by M_N (S9.3). The cell density δ counts occupied compartments of the periodic radius-1 neighbourhood over 9 or 27. The occupied-cells fraction δ_cells counts cell-occupied compartments of the clipped radius-1 neighbourhood over the same constant.

Thresholds as integer counts

Each threshold is an integer requirement, which changes with the denominator:

Threshold	Where used	Two-dimensional	Three-dimensional
$\delta \geq 0.5$, `--area-cell-density-threshold`	Threshold granuloma, the in-granuloma flag, cell-density extent, lesion volume	At least 5 of 9 (0.556)	At least 14 of 27 (0.519)
$\delta_{\mathrm{cells}} \geq 0.66$, `occupiedNeighborFraction`	Connected-region eligibility	At least 6 of 9 (0.667)	At least 18 of 27 (0.667)

Threshold	Where used	Two-dimensional	Three-dimensional
δ < 0.8, fixed	Vascular delivery of oxygen, and of drugs and immunomodulators under M6 and M7	At most 7 of 9 (0.778)	At most 21 of 27 (0.778)

The region threshold and the gate fall at the same fraction in both builds, because the smallest count meeting 0.66 (18 of 27) and the largest count passing 0.8 (21 of 27) are both multiples of 3. The threshold granuloma does not: 14 of 27 is below the two-dimensional minimum of 5/9. It is the threshold that does not transfer between builds. No threshold lies within rounding error of an attainable fraction.

Boundary caps on the occupied-cells fraction

A boundary compartment's maximum δ_cells is its on-grid count divided by the full count:

Position	Two-dimensional count and cap	Three-dimensional count and cap	Eligible at 0.66
Interior	9, cap 1	27, cap 1	Yes
On a face of the cube	Not applicable	18, cap 0.667	Only if all 18 hold cells
On an edge	6, cap 0.667	12, cap 0.444	Two-dimensional: only if all 6 hold cells. Three-dimensional: never
At a corner	4, cap 0.444	8, cap 0.296	Never

The square's edge plays the role of the cube's face. Compartments on the cube's twelve edges and eight corners can never join a connected region.

Vascular gating

The gate rule is that of S7.4. In three dimensions it reads the periodic δ over 27 compartments. A source is suppressed when 8 or more of its 9 compartments are occupied in two dimensions, and 22 or more of 27 in three.

M5.8 Caseation, entrapment and the growth count

The caseation cascade, partial caseation and healing are per-compartment rules, the same in both builds (S5.3, S5.7, S5.8). What depends on dimension is the entrapment test and the growth count, which one routine computes over two different neighbourhoods. The routine walks the periodic radius-2 neighbourhood, centre included: 25 compartments in two dimensions and 125 in three. Radius 2 is a fixed constant.

Entrapment

A compartment is trapped if every compartment of its radius-1 shell is caseated: all 8 in two dimensions, all 26 in three (S5.4). Entrapment uses radius 1 in both builds; the radius-2 walk serves only the growth count. The entrapment re-kill is specified in S5.4.

In three dimensions enclosure needs all 26 neighbours, including the 9 in each adjacent slice. A compartment whose 8 in-plane neighbours are caseous is trapped in two dimensions, but in three only if the 18 above and below are caseous too. Fenestrated caseous regions therefore fill in by entrapment less readily in three dimensions.

The growth count

The growth count G is the number of caseated compartments plus the number holding a chronically infected macrophage, over the periodic radius-2 neighbourhood including the centre (S5.5). G is at most 25, or 125 in three dimensions, except transiently where a senescing chronically infected macrophage remains in a newly caseous compartment (S5.5); the formal ceiling is 50, or 250.

G is compared with two computed thresholds, $\theta = \lfloor \phi(2r+1)^D \rfloor$ with r = `Mtb_Agents_noGrowthExtMtbCaseatedRadius` (S4.6). The dimension count reaches the derivation from the build. At r = 2 and the default fractions:

Threshold	Fraction ϕ	Two-dimensional	Three-dimensional
Growth reduction	0.23	$\lfloor 5.75 \rfloor = 5$ of 25, fraction 0.200	$\lfloor 28.75 \rfloor = 28$ of 125, fraction 0.224
Growth arrest	0.56	$\lfloor 14.0 \rfloor = 14$ of 25, fraction 0.560	$\lfloor 70.0 \rfloor = 70$ of 125, fraction 0.560

Truncation puts the reduction threshold at a different fraction in each build. The arrest threshold falls at the same fraction because 0.56×25 and 0.56×125 are integers; their floating-point floor is checked at S4.16.

The radius parameter does not set the neighbourhood

The radius parameter (range 1 to 3) enters only the threshold derivation; the counted neighbourhood is always radius 2. They agree only at r = 2, the default value (S5.5):

r	Two-dimensional thresholds	Reachable against 25	Three-dimensional thresholds	Reachable against 125
1	2 and 5	Both	6 and 15	Both
2	5 and 14	Both	28 and 70	Both
3	11 and 27	Reduction only	78 and 192	Reduction only

At r = 3 arrest is unreachable in either build. At r = 1 arrest needs 5 of the 25 compartments counted (20 %), with the arrest fraction at 56 %; in three dimensions, 15 of 125 (12 %). The arrest-above-reduction constraint holds at every radius, and the program does not check that r = 2 (S4.16).

Sweep order

The extracellular-bacteria sweep runs in storage order, and entrapment flags and killing counts are updated in place (S5.5). Entrapment and healing therefore propagate forward within one sweep, in the direction of increasing index: increasing z, then y, then x in three dimensions, against y then x in two.

M5.9 Agent sensing and contact neighbourhoods

Principle

Every sensing and contact rule reads a Moore neighbourhood of radius 1 or 2, with no dimension branch. In three dimensions each therefore reads 27 compartments at radius 1 and 125 at radius 2. Probabilities and rates are unchanged; only the number of candidate compartments and partners changes.

Rules that read only the agent's own compartment are identical in both builds. These are TNF-induced apoptosis, NF-κB activation by TNF, STAT3 activation by IL-10, the IL-10 modulation of TNF and chemokine secretion, oxygen consumption, uptake and killing by resting and infected macrophages, the activated macrophage's own-compartment kill, and recruitment admission at a source. S6 reads no neighbourhood, so its rules are unchanged; its neighbourhood consumers appear in the neighbourhood-size table.

Neighbourhood sizes by rule

Rule	Radius and boundary	Two-dimensional	Three-dimensional	Specified in
Chemotactic weighting and random movement	1, periodic	9	27	S1.3, M5.4
Daughter placement	1, periodic, by ordinal	9	27	S3.5, M5.6
Macrophage exposure memory	1, clipped	9	27	S2.10
NF-κB activation by extracellular bacteria	1, periodic	9	27	S2.4
Activated-macrophage caseum sweep	1, periodic	9	27	S2.8, S5.8
Cell density, threshold granuloma, vascular gate	1, periodic	9	27	M5.7
Entrapment	1, periodic, centre excluded	8	26	S5.4, M5.8
Growth count for extracellular bacteria	2, periodic	25	125	S5.5, M5.8
Proliferation readiness of cognate T cells	1, periodic	9	27	S3.5
Fas-mediated and cytotoxic target selection	1, periodic	9	27	S3.8, S3.9
Treg contact suppression	1, periodic	9	27	S3.10
Coarse-grained IFN-γ action	2, periodic	25	125	S3.7

Rule	Radius and boundary	Two-dimensional	Three-dimensional	Specified in
T cell interaction counting	2, periodic	25	125	S3.6
Bacterial dispersal on cell death	1, periodic, by ordinal	up to 9	up to 27	S4.13
Per-agent caseation statistic	`Core_caseationStatRadius`, clipped	9	27	S9.13
Uptake-in-caseum statistic	`Core_caseationStatMooreRadius`, clipped	9	27	S9.13
Reinfection fallback	1, clipped	9	27	M8

Consequences rule by rule

NF-κB activation by extracellular bacteria. `Core_Mac_nrExtMtbNFkB` is a total over the radius-1 neighbourhood, not a density (S2.12). In three dimensions the same total is reached at a third of the mean bacterial density per compartment, so a file carrying the two-dimensional range makes bacterial NF-κB activation easier.

Exposure memory. Exposure is an existence test over 27 compartments in three dimensions, so a given scatter of bacteria flags more macrophages. Exposure licenses T cell proliferation and delays reversion to the resting state (S2.10), so both are more widespread for the same bacterial distribution.

Activated-macrophage caseum sweep. One healing draw is shared by every caseous compartment of the neighbourhood (S2.8): up to 26 in three dimensions, against 8. The per-compartment healing rate is unchanged. Each caseous neighbour that holds live bacteria and is not being healed gets its own kill draw against the fixed probability 0.1, so the expected kill by one activated macrophage at a caseum margin scales with the number of caseous neighbours.

Target selection. A Tgam or Tcyt draws one target uniformly from the macrophage-holding compartments of its neighbourhood and attacks only an infected or chronically infected one (S3.8, S3.9). The attack probability per attempt is a local composition, independent of dimension. Three times as many candidates are expected in three dimensions, but each attempt still selects one.

Treg suppression. An active Treg draws once per eligible agent in its neighbourhood (S3.10). The neighbourhood holds at most 18 agents in two dimensions and 54 in three, the Treg included. Tregs cannot be suppressed, so one Treg can suppress at most 17 or 53 agents per timestep. With the per-target probability unchanged, expected suppressions per Treg scale with eligible neighbours, up to threefold.

Coarse-grained IFN-γ action. A producing Tgam acts with certainty at Moore distance at most 1 and with probability `Core_Tcell_Tgam_probIFNMooreExtend` = 0.25 at distance exactly 2 (S3.7):

Zone	Two-dimensional	Three-dimensional
Distance at most 1, certain	9	27
Distance exactly 2, probabilistic	16	98
Expected compartments reached	13	51.5

T cell interaction counting. Every macrophage in the radius-2 neighbourhood increments the counters: up to 25 increments per T cell per timestep in two dimensions and 125 in three. The counters feed M8 exhaustion, disabled by default by its sentinel threshold.

Bacterial dispersal. Dispersed bacteria are divided over up to M_N compartments by ordinal (S4.13), so a given number is spread over up to 27 in three dimensions, about a third as many each. The truncation rule does not depend on dimension.

Caseation statistics. The per-agent statistic divides its clipped count by (2r + 1)^D (S9.13). With r = 1 and `Core_caseationStatFraction` = 0.11, one caseous compartment of 9 meets it in two dimensions; three of 27 are needed in three, since 2/27 = 0.074 and 3/27 = 0.111. Neither caseation statistic affects dynamics.

A parameter set calibrated in one build therefore does not reproduce the balance of contact effects in the other.

M5.10 Diffusion

Spectral solver

Transforms and plans

The three-dimensional spectral solver is a whole-file substitute (M5.1). The plan-type selection and the derived-field assignment are shared. It builds the same four in-place real-to-real plans as the two-dimensional solver (M1.3, "Boundary conditions"), over three axes: a type-II sine forward and type-III sine reverse transform for the zero-boundary fields, and the corresponding cosine pair for the no-flux fields of M6 and M7. Each field's boundary condition is the same in both builds. Method 5 is the spectral (FFT) option, the default, and method 6 the spectral option with estimate planning (M1.3, "Planning strategy and determinism").

Propagation coefficient

Every propagation matrix is computed once, at construction (M1.3, "The propagator and incorporation of decay"). For mode (i, j, ℓ), the solver multiplies the transformed coefficient by $\Pi = \exp(-P\,\delta t_d)$, where for the zero-boundary fields

$$P_{ij\ell} = \frac{2D}{\Delta x^2}\left(3 + \frac{k\,\Delta x^2}{2D} - \left[\cos\frac{\pi(i+1)}{n_x+1} + \cos\frac{\pi(j+1)}{n_y+1} + \cos\frac{\pi(\ell+1)}{n_z+1}\right]\right),$$

and for the no-flux fields

$$P_{ij\ell} = \frac{2D}{\Delta x^2}\left(3 + \frac{k\,\Delta x^2}{2D} - \left[\cos\frac{\pi i}{n_x-1} + \cos\frac{\pi j}{n_y-1} + \cos\frac{\pi \ell}{n_z-1}\right]\right).$$

The two-dimensional form has the constant 2 and no third cosine (M1.3, "The propagator and incorporation of decay"). The three-dimensional solver repeats the type-I eigenvalue arguments on its third axis, and the zero-diffusivity case holds in both builds; both are specified in M1.3, "The propagator and incorporation of decay".

Normalisation

The solver scales each transformed coefficient, in the loop that applies Π, by 1/(4 n_x n_y) in two dimensions and 1/(8 n_x n_y n_z) in three. Each is the reciprocal of its build's transform round-trip factor and serves the sine and cosine pairs alike. In three dimensions, assembly, disassembly and both matrix constructions use the storage index (M5.2), which matches the transform library's array layout on any extent.

Per-field sequence

The per-field sequence, the derived-field assignment and the cutoff are those of M1.3, "Derived assignment of CCL5 and CXCL9", "Normalisation and the cutoff" and "Non-transformed fields and grid buffering", in the same order in both builds. In three dimensions the derived-field assignment loops over three coordinates, z innermost. Neither solver advances nor copies oxygen, so only the surviving buffer's history counts, at every smoother exchange too (M1.3, "Non-transformed fields and grid buffering"; S7.6). The Etanercept binding sign differs between solvers, in both builds (M7).

Copy-constructed solver

A copied spectral solver rebuilds its plans and matrices (M1.3, "Construction"). In two dimensions the rebuilt plans equal the originals. In three dimensions the rebuilt no-flux plans differ on the third axis:

Plan	Primary constructor, axes x, y, z	Copy constructor, axes x, y, z
No-flux forward	Cosine II, cosine II, cosine II	Cosine II, cosine II, sine II
No-flux reverse	Cosine III, cosine III, cosine III	Cosine III, cosine III, sine III

A copied three-dimensional solver therefore applies a sine transform along z to the no-flux fields, with the cosine-mode propagation matrix; this affects only the M6 and M7 fields, and only in a run that advances a copied simulation.

Smoother

The smoother is that of M1.3, "The smoother"; at zero iterations it does nothing. Its three-dimensional step is a seven-point stencil,

$$C'_{ij\ell} = C_{ij\ell} + Fo\,(C_{i\pm1} + C_{j\pm1} + C_{\ell\pm1} - 6\,C_{ij\ell})\,, \qquad Fo = D\,\Delta t_s/\Delta x^2,$$

against five points with $-4C$ in two dimensions. Zero-boundary fields read the zero halo and no-flux fields reflect; there is no degradation or cutoff, so values can go negative. The step is stable only for $\mathrm{Fo} \le 1/4$ in two dimensions and 1/6 in three. At δt_s = 1.2 s the largest stable diffusivity is 8.33×10^{-7} cm^2/s in two dimensions and 5.56×10^{-7} cm^2/s in three. TNF and the chemokines (Fo = 0.0156) and IL-10, uniform on [4×10^{-8}, 6×10^{-8}] cm^2/s (Fo at most about 0.018), are stable in both builds. No start-up check tests smoother stability.

Storage

Padded field storage grows as $(n+2)^3$ in three dimensions. At n = 300 the three-dimensional build needs about 15 GB for field storage and propagation matrices with the nine fields of the default configuration, and 23 GB with all fifteen. Together with the stack limit of M5.6, this bounds the practical three-dimensional extent well below the default two-dimensional extent of 300.

Explicit and ADI alternatives and the timestep checks

Solver availability by build

Method	Solver	Two-dimensional	Three-dimensional
4	Alternating-direction explicit	Available	Available, substitute file
5	Spectral (FFT)	Default	Default
6	Spectral, estimate plan	Available	Available
7	Crank–Nicolson ADI	Available	Absent

In a three-dimensional build `--diffusion 7` is rejected as an invalid method, and the program stops before the simulation is built. The Crank–Nicolson timestep parameters are still read at startup by both builds (Appendix B). Every run constructs the explicit solver first, so its 60 s ceiling is enforced in both builds (M1.1, M1.4).

The three-dimensional explicit scheme

The explicit solver of M1.4 gains one axis. With δt = `Diffusion_ADE_timestepDiffusion`, the same δx^2 on every axis, and diffusivity D,

$$\lambda = \frac{3D\Delta t}{\Delta x^2}, \qquad a = \frac{1-\lambda}{1+\lambda}, \qquad b = c = d = \frac{D\Delta t/\Delta x^2}{1+\lambda},$$

against $\lambda = 2D\delta t/\delta x^2$ and coefficients a, b, c in two dimensions. The coefficients b, c and d multiply the neighbour pairs along the first, second and third axes.

1. **The u sweep** visits compartments in increasing order on every axis, z innermost:

$$u'_{ij\ell} = a\,u_{ij\ell} + b\,(u'_{i-1} + u_{i+1}) + c\,(u'_{j-1} + u_{j+1}) + d\,(u'_{\ell-1} + u_{\ell+1}),$$

where primed lower-side values have been updated in this sweep and unprimed upper-side values have not.

2. **The v sweep** visits compartments in decreasing order on every axis, z innermost, with updated values on the upper side and old values on the lower side.

Cutoff, averaging, degradation, field order and no-flux handling follow M1.4 in both builds.

Timestep checks

The checks of M1.2 are the same code in both builds. Dimension enters through the accuracy factor $\ell = 2/\delta x^2 = 5 \times 10^5$ cm^{-2} in two dimensions and $3/\delta x^2 = 7.5 \times 10^5$ cm^{-2} in three. The accuracy limit $\kappa/(D_{\mathrm{TNF}}\ell)$, with $\kappa = 2$ for the explicit solver and 10^4 otherwise, is therefore two thirds of its two-dimensional value:

Solver	Two-dimensional limit	Three-dimensional limit	Diffusion timestep	Passes
Spectral	3.85×10^5 s	2.56×10^5 s	60 s	Both builds
Explicit	76.9 s	51.3 s	30 s	Both builds
Crank–Nicolson ADI	3.85×10^5 s	Not available	60 s	Two-dimensional

Only the TNF diffusivity is checked (M1.2).

The drug-permeability check uses the two-dimensional lateral area in both builds, as the vascular flux does (M1.2, M5.11).

M5.11 Vascular exchange

Both vascular flux functions take a source's exchange area to be the four-face lateral area, 1.6×10^{-5} cm^2, in both builds. Neither reads the three-dimensional area constant. One serves oxygen and the M6 antibiotics, the other the M7 immunomodulators. The flux rule and its guard are those of S7.5. With the same area into the same V, the per-source flux for a given deficit is independent of dimension, and κ is the same in both builds: 0.768 with the spectral solver and 0.384 with the explicit one.

The guard fails exactly when $\kappa > 1$ with a non-zero deficit (S7.5). With the six-face area of 2.4×10^{-5} cm^2, the spectral κ would be 1.152, failing the guard at the first source with any deficit. The explicit solver, at $\kappa = 0.576$ for six faces, would tolerate it. The four-face area is therefore the only one of the two declared areas that passes the guard at δt_d = 60 s and this permeability.

Under M6 and M7, the local concentration at each source is the Von Neumann average, over twelve compartments in three dimensions (M5.3); both fluxes use the four-face area. Total supply differs between builds only through the number and arrangement of sources (M5.6) and the density gate (M5.7).

M5.12 Observation

Granuloma definitions, connected region and extents

Threshold definition and eligibility

The threshold granuloma uses the same code in both builds (S9.4). At 0.5 it needs 14 of 27 occupied compartments in three dimensions (M5.7). The flag, the per-type in-granuloma counts and the cell-density extent are therefore volumes in the three-dimensional build, under the same statistic names.

Connected-region eligibility needs at least one immune cell and $\delta_{\text{cells}} \geq$ `occupiedNeighborFraction`: at 0.66, 18 of 27 compartments of the clipped neighbourhood in three dimensions. It is never possible on a cube edge or corner, and on a face only if all 18 on-grid neighbours hold cells (M5.7).

Connected region

The construction is that of S9.6, the same source text in both builds. In three dimensions the radius-1 shell has 26 compartments, so regions are 26-connected. The outward sweep covers volumes, so the number of positions it can examine grows with n^3.

The maximum diameter is twice the largest Euclidean distance from the centre of mass to a member, with three components in three dimensions (S9.7). The compact diameter, `MinGranulomaDiameterMM`, is $2\sqrt{n/\pi}$ in both builds: the diameter of a disc of n compartments. Its computation does not use the equivalent-radius function, so the three-dimensional build also uses the disc formula.

Members n	$2\sqrt{n/\pi}$**, as computed**	$2(3n/4\pi)^{1/3}$**, equivalent sphere**	**Ratio**
100	11.3	5.8	1.96
1000	35.7	12.4	2.88
10000	112.8	26.7	4.22

The ratio grows as n^{1/6}. For three-dimensional regions of more than a few tens of compartments, the reported compact diameter exceeds the maximum diameter. Dynamics are unaffected.

The bounding test

The bounding test treats a position as inside if it lies within half the maximum diameter of the centre of mass (S9.8): a bounding disc in two dimensions and a bounding sphere in three. The region's member set is not retained. Neutrophil injection and ring scaling read the current timestep's region; the macrophage release test and the neutrophil outside-granuloma routine (M9.2) read one a timestep old (S9.8), in both builds. Its readers are the release statistics (S9.8), M8 neutrophil injection (M8.9) and a neutrophil routine (M9.2).

Extents

The extents use the same predicates in both builds (S9.5). Only the conversion from compartment count to radius, diameter and scaling factor differs:

Quantity	**Two-dimensional**	**Three-dimensional**
Equivalent radius r, in compartments	$\sqrt{n/\pi}$, a disc	$(3n/4\pi)^{1/3}$, a sphere
Diameter	2rδx	2rδx
Scaling factor	max(4r/3, 1)	1

In three dimensions the extent diameters are sphere diameters while the compact diameter is a disc diameter. A statistic formed as a count times the compartment measure reports $\mu\mathrm{m}^2$ in two dimensions and $\mu\mathrm{m}^3$ in three (M5.5).

Two-dimensional to three-dimensional scaling

Ring scaling runs once per timestep after the connected-region construction and branches on the dimension count, fixed by the build. The positions counted and the shell loop are those of S9.9, in both builds. With no connected region it writes nothing; the scaled statistics then hold zero (S9.9, S9.10). Its shells are annuli in two dimensions and spherical shells in three.

In the three-dimensional branch the shells are counted but not scaled:

- the ring-scaled statistics are set equal to the unscaled statistics;
- each realised ring factor is the ratio of unscaled to unscaled by a guarded division that returns 0 for a zero denominator, so it is 1 where the count is non-zero and 0 where it is zero;
- the extent-scaled statistics are the unscaled counts multiplied by the extent scaling factors, which are 1 (Extents).

The scaled counts therefore equal the unscaled counts, but the realised factors are 0, not 1, wherever a count is zero. The bacterial stopping thresholds, where enabled, apply to these unscaled three-dimensional counts, which are typically larger than the two-dimensional ones (S9.20).

M5.13 Parameters

Scope

One parameter table serves both builds. No parameter has a build-specific default, and both builds read, range-check and validate the same entries with the same cross-parameter constraints. A parameter file therefore loads in either build, apart from the Init-section arity (M5.2).

This section lists the parameters whose effective meaning changes: those compared against a quantity counted or summed over a neighbourhood, those that set a neighbourhood size, and densities. A file calibrated in two dimensions and run in three applies them to neighbourhoods three times larger at radius 1 and five times larger at radius 2.

Neighbourhood fractions

These fractions are integer requirements that depend on the build:

Identifier	Value or range	Units	Meaning
`occupiedNeighborFraction`	0.66	fraction	Connected-region eligibility: at least 6 of 9, or 18 of 27. Affects dynamics only through neutrophils: injection's use of the bounding test (M8) and a neutrophil routine (M9); the release statistics and ring scaling are observation
`Core_caseationStatFraction`	0.11	fraction	Per-agent caseation statistic: at least 1 of 9, or 3 of 27. No effect on dynamics
`Core_caseationStatMoorKillingFraction`	0.65	fraction	Uptake-in-caseum statistic: at least 70.2 to 105.3 killings for a caseation threshold of 12 to 18, or 210.6 to 315.9. No effect on dynamics
`Mtb_Agents_growthRateExtMtbCaseatedFrac`, `Mtb_Agents_noGrowthExtMtbCaseatedFrac`	0.23, 0.56	fraction	Converted at load to the thresholds 5 and 14, or 28 and 70 (M5.8)

To require one caseous compartment in three dimensions, as the default value does in two, `Core_caseationStatFraction` must lie in (0, 1/27], for example 0.037.

The growth fractions are fractions of the same radius-2 neighbourhood in both builds; truncation makes the reduction threshold a slightly larger fraction in three dimensions, and the radius agrees with the counted neighbourhood only at 2 (M5.8). The parameter file supplies 0 for both integer thresholds, which are overwritten in either build (S4.16).

Parameters applied over a neighbourhood

These keep their meaning per compartment or per target but act on a neighbourhood sum or on every member of a neighbourhood (M5.9); ranges are owned by S2 and S3:

Identifier	Applied to	Two-dimensional	Three-dimensional
`Core_Mac_nrExtMtbNFkB`	Live extracellular bacteria summed over radius 1	Mean of 16.1 to 28.4 per compartment	Mean of 5.37 to 9.47 per compartment
`Core_Tcell_Treg_probTregDeactivate` / `Core_Tcell_Treg_factorDeactIL10`	Every eligible agent of radius 1	At most 17 targets	At most 53 targets
`Core_Tcell_Tgam_probIFNMooreExtend`	Every susceptible macrophage at distance 2	16 compartments	98 compartments

Identifier	Applied to	Two-dimensional	Three-dimensional
`Core_Mac_probHealCaseation`	One draw shared by the caseous compartments of radius 1	Up to 8 per draw	Up to 26 per draw
`Core_Mac_nrExtMtbUptakeAct`	Own compartment, and each caseous neighbour holding bacteria with probability 0.1	Up to 8 neighbours	Up to 26 neighbours

Single-target probabilities, such as `Core_Tcell_Tgam_probApoptosisFasFasL` and `Core_Tcell_Tcyt_probKillMac`, apply once per attempt to one target and need no adjustment. `Mtb_growthExtMtbBound` (one container), and `Core_Mac_nrIntMtbCInf` and `Core_Mac_nrIntMtbBurstCInf` (one macrophage), are unaffected.

Densities and the source border

`Core_sourceDensity` and `Core_Mac_initDensity` are fractions of compartments in either build (M5.6). The neutrophil and fibroblast densities, 0 by default, convert alike (spine 5.3). `Core_sourceBorderSize` = 1 excludes a border one compartment wide on every face: 298^2 positions in two dimensions at n = 300, and 298^3 or 198^3 in three at n = 300 or 200.

Command-line inputs

Option	Program default	Default configuration	Two-dimensional effect	Three-dimensional effect
`--dim`	300	300	n^2 compartments	n^3 compartments; extents much above 200 are limited by stack and memory (M5.6, M5.10)
`--diffusion`	5	5	Methods 4 to 7	Methods 4 to 6; 7 is fatal (M5.10)
`--area-cell-density-threshold`	0.5	0.5	At least 5 of 9	At least 14 of 27
`--area-tnf-threshold`	0.5	0.5	Compartments reaching the threshold counted	Same per-compartment test; the count is over a volume
`--days`, `--timesteps`	200 days	154 days	Unchanged	Unchanged
`--seed`	Time-based	Supplied	Sets the stream	A different stream for the same seed (M5.6)

Both area thresholds are validated to [0, 1] in both builds (S9). Every other command-line option has the same meaning in both builds.

Fixed structural constants

Fixed in the source and the same in both builds; their three-dimensional effect is as stated:

- vascular density gate, cell density below 0.8: at most 21 of 27 (M5.7);
- growth-count radius 2: 125 compartments (M5.8);
- entrapment shell, Moore distance 1: all 26 neighbours caseous (M5.8);
- caseum kill probability 0.1 per caseous neighbour holding bacteria: up to 26 neighbours (M5.9);
- caseum chemokine secretion at 0.25 of the macrophage rates, two slots per compartment, V, the four-face exchange area, the 10^{-12} cutoff, the 30 s molecular ceiling and the 60 s explicit ceiling: unchanged;
- accuracy factors $\kappa = 2$ (explicit) and 10^4 (otherwise), combined with $\ell = 3/\delta x^2$: each limit two thirds of its two-dimensional value (M5.10).

Constraints not checked at start-up

Smoother stability and the IL-10 explicit accuracy limit are not checked at start-up in either build (M1.2; M1.3, "The smoother"). The sampled IL-10 range satisfies both in both builds (M5.10).

Stopping thresholds

The stopping criteria are disabled (S9.20). The area criteria compare the cell-density extent's compartment count. In three dimensions the count can reach n^3, so at n = 300 (2.7×10^7) `areaCellDensityStoppingThreshold` (1.8×10^7) no longer exceeds the grid; `areaCellDensityStoppingThreshold2` (3×10^8) still does.

M5.14 Interfaces

Every dependency is a hook fixed at build time (Grimm et al. 2020, ¶5.5): a module or submodel reads a neighbourhood, constant, iterator or solver that the build has bound. Every dependency runs from M5 to the other document, and no document alters a quantity specified here.

With	Provides or receives	See
Spine module-slot table	The M5 summary	M5.1
Spine 2.1	Ordinal convention, wrap, distances, Von Neumann N_4 and constants for the two-dimensional build; M5 gives the three-dimensional counterparts	M5.2, M5.3, M5.5
Spine 2.2, 2.3	Iterator boundary behaviour; slots and size classes, the same in both builds	M5.3, M5.6
Spine 3.2	The schedule, the same in both builds	M5.1

With	Provides or receives	See
Spine 5.1–5.4, 7.0	Placement order, source placement, Init-section rules, grid centre and density conversion; M5 adds the axis and arity	M5.2, M5.6
S1	Destination neighbourhood of 27; the three-dimensional axis permutation of chemotactic weights; probability of no displacement	M5.3, M5.4
S2	Exposure, NF-κB bacterial sum and caseum sweep over 27	M5.9
S3	Target selection, suppression, IFN-γ zones and interaction counting over 27 and 125; daughter placement over 27 ordinals	M5.6, M5.9
S4	Computed thresholds 28 and 70; dispersal over up to 27	M5.8, M5.9
S5	Entrapment over 26; growth count over 125 (formal 250); sweep direction; re-kill, radius and sweep-order items specified in S5.4 and S5.5	M5.8
S6	No direct effect: S6 reads no neighbourhood, and its unit conversions and decay lengths are dimension-independent; its neighbourhood consumers are listed in M5.9	M5.5, M5.9
S7	Four-face exchange area in both builds; density gate over 27; source count and arrangement; S7 links M5.5 and M5.11	M5.6, M5.7, M5.11
S8	Source list and recruitment floor built by M5; the rule is unchanged	M5.6
S9	Two-dimensional shell traversal (S9.6), with its three-dimensional counterpart; densities, extents, connected region, compact diameter, bounding sphere, ring scaling, centre-of-mass statistics, area statistics as volumes	M5.2, M5.3, M5.5, M5.7, M5.12
M1	Solver set (method 7 two-dimensional only), transform axes, propagation constant, normalisation, stencils and ℓ; eigenvalue form, zero diffusivity and oxygen buffering specified in M1 for both builds	M5.10
M2	Source count and arrangement for the probabilistic option (M2.8); the per-timestep source shuffle consumes draws in proportion to the list, so the stream depends on the build	M5.6
M3	MHC class II activation radius `Molecular_MHCII_tcellActivationRadius` and input neighbourhoods of 27, 98 and 27 compartments (9, 16 and 9 in two dimensions); the conversion factors multiply counts over larger neighbourhoods; own-compartment equations unchanged; distance statistics in three coordinates (M3.6)	M5.9

With	Provides or receives	See
M4	TGF-β fields diffused or copied whatever the selection; fibroblast placement takes three draws; the Tgam-triggered secretion reduction tests 27 compartments; the freeze of the in-granuloma flag applies to 27-compartment densities	M5.6, M5.10, M5.12
M6	Twelve-compartment Von Neumann average; intracellular drug dispersed by ordinal over 27, one twenty-seventh each; four-face permeability check; lesion partition by the threshold granuloma over 27; the copied solver's no-flux plans	M5.3, M5.10, M5.11
M7	Twelve-compartment Von Neumann average; six no-flux fields and the copied solver's plans; binding-sign difference specified in M7	M5.3, M5.10, M5.11
M8	Reinfection on the main diagonal, rounded, with a fallback over up to 27 candidates; neutrophil injection inside the bounding sphere (M8.9); exhaustion counts over 125 per T cell per timestep, reaching the threshold sooner; depletion and growth-rate randomisation read no neighbourhood	M5.2, M5.9, M5.12
M9	Sets M_N = 27 in the neutrophil saturation denominators and destination neighbourhood (M9.4, M9.5); neutrophil placement takes three draws per attempt (M9.3)	M5.3, M5.6
Appendix B	Indexes `DIMENSION`, the selector headers and substitute files, the run-time dimension test, `--dim` (300), the build-dependent `--diffusion` values, `--area-cell-density-threshold` and the Crank–Nicolson timestep parameters read in both builds	M5.1, M5.10, M5.13