S5. Caseation and entrapment

S5.1 Scope and schedule

S5 specifies tissue damage and necrosis: the per-compartment killing count and the deaths that increment it; the two routes by which a compartment becomes caseous, by threshold and by entrapment; the cascade that kills a compartment's occupants when it caseates; the radius-2 sweep that performs the entrapment test and returns the count consumed by extracellular growth; the consequences of caseation that no other document owns; partial caseation; and healing.

Caseation is compartment state

No agent owns the mechanism. Its state is three per-compartment integers held by the grid (spine 2.6): the killing count K(p), the entrapment flag E(p) and the healing clock H(p). Caseation status is not stored. It is a predicate evaluated on demand from the count and the flag (S5.3).

Caseation has no block of its own. Agents increment the killing count during their own next-state rules; the entrapment flag and the healing clock are evaluated in the extracellular pass; consumers read the predicate when their own rules run. No point in the timestep computes caseation for the whole grid.

The caseation threshold is cached. The grid constructor copies `Core_nrKillingsCaseation` into a grid member θ, which is serialized with the grid. The caseation predicate and the fractional quantity read θ, never the parameter. The partial-caseation predicate, by contrast, reads `Core_partialCaseationFraction` live on every evaluation. Within a run the distinction is immaterial. After a saved state is reloaded with an altered parameter file, the threshold is the saved one and the partial-caseation fraction the new one.

Schedule

Block	Caseation activity	Role
Split half-step, twice per diffusion step	Every caseous compartment secretes CCL2, CCL5 and CXCL9 at one quarter of the macrophage rates (S5.6)	Consumes
Movement	No motile agent other than a neutrophil enters a caseous compartment (S1; M9.3)	Consumes
Recruitment	A caseous source recruits nothing and is counted as blocked (S8)	Consumes
Next-state	Every damaging death increments the killing count at the dying agent's compartment, and may trigger the cascade (S5.2, S5.3)	Produces
Next-state, activated macrophages only	The healing clock of a caseous neighbour is stamped, under one shared draw per macrophage (S2.8, S5.8)	Produces
Extracellular pass, per compartment in row-major order	Entrapment test; extracellular processing; healing completion; decay (S5.4, S5.5, S5.8)	Produces and consumes

Block	Caseation activity	Role
Daughter commitment	A daughter promised to a compartment that has since become caseous is discarded and the count incremented (S5.2; S3.5)	Produces
Statistics	Caseous and partially caseous counts, the fractional sum, per-type caseous-surroundings counts, the cell-density extent and ring scaling (S9)	Consumes

At each compartment the extracellular pass runs, in this order: the entrapment test; if live extracellular bacteria are present, growth consuming the test's return value, re-designation of the container and, if the compartment is caseous, density-dependent death (S4); then healing completion; then bacterial decay.

These features of the placement change outcomes:

- **One traversal serves two purposes.** The entrapment test evaluates enclosure, with its occupant kill, and returns the radius-2 count that growth consumes at once (S5.4, S5.5). The two are not separable.
- **Healing follows growth within a visit.** A halving relieves growth suppression only from the next timestep.
- **The flag is not latched.** It is recomputed at every visit, in row-major order, so a compartment's entrapment can depend on how far the pass has progressed (S5.4).

Reads and writes

Reads: the killing count, entrapment flag and healing clock; the caseation status of compartments within radius 2, and any chronically infected macrophage there; the agent slots of the compartment and each occupant's current and pending state; θ, `Core_partialCaseationFraction`, `Core_caseationHealingTime` and the current timestep; the macrophage chemokine secretion rates.

Writes: the killing count, incremented once per damaging death, once per occupant killed by the cascade or by entrapment, and once per discarded daughter, and halved on healing; the entrapment flag, at every evaluation; the healing clock, stamped and cleared; the current and pending state of every agent killed by the cascade or by entrapment; the intracellular containers of macrophages so killed, dispersed at fraction 1.0, and the extracellular containers of up to nine compartments that receive them; the caseum bacterial-kill statistic and the caseation statistics (S9); the CCL2, CCL5 and CXCL9 fields at caseous compartments.

Caseation reads no diffusing field and no oxygen value. Oxygen does not affect caseation. Caseation affects oxygen only by suppressing delivery at caseous sources (S7).

S5.2 The killing count

What the count represents

Each compartment carries an integer killing count K(p), set to zero at grid construction (spine Element 5). It is only ever incremented, except that healing halves it (S5.8). It is not reset at the start of a timestep, on caseation or on vacancy, and it is serialized with the grid.

The count represents accumulated local tissue damage, not a count of deaths. A death is damaging if and only if its route calls the incrementing routine; no property of the compartment or of the dying cell is evaluated at the time. A separate per-compartment death counter is incremented once for every dead agent removed (spine 2.6). The two counters are not equal.

The count is the only state through which cell death drives necrosis. The entrapment flag is the only other input to the caseation predicate, and it derives from the caseation of neighbouring compartments.

The incrementing routines

The position-only form increments the count at a compartment and then evaluates the cascade (S5.3). It kills nothing on its own behalf.

The agent-naming form first kills the named agent, writing its current and its pending state, and then calls the position-only form. Every counted death is therefore immediately visible to agents processed later in the pass. The coincidence of immediacy and killing-count contribution specified in S2.2 follows from this routine.

Both forms return whether the compartment is caseous after the increment. Cytotoxic killing reads the value (S3.9); every other caller discards it.

The compartment incremented is always the dying agent's own. For T cell killing it is the target's compartment, not the actor's.

Increment sites

Route	Agent killed	Form	Owner
Senescence of an activated macrophage	Self	Agent-naming	S2.3
TNF-induced apoptosis of a macrophage	Self	Agent-naming	S2.3
Bursting of a chronically infected macrophage	Self	Agent-naming	S2.7
TNF-induced apoptosis of a T cell, any type	Self	Agent-naming	S3.4
Fas-mediated killing	Target macrophage	Agent-naming, after dispersal	S3.8
Cytotoxic killing, clean outcome	Target macrophage	Agent-naming; the clean-kill routine has already written both states	S3.9
Cytotoxic killing, dispersing outcome	Target macrophage	Agent-naming	S3.9
Threshold cascade	Each remaining occupant	Inline in the position-only form	S5.3

Route	Agent killed	Form	Owner
Entrapment	Each remaining occupant	Inline in the entrapment test	S5.4
Discard of a daughter promised to a compartment that has since become caseous	None; the daughter is never placed	Position-only	S3.5

The daughter discard is the only increment with no agent on the grid. The daughter is a proliferation-list entry, deleted rather than killed, so no state is written and no bacteria are involved. The rationale is that the daughter is treated as though it had been present when the compartment caseated.

Non-cognate T cells take part fully. Their early return in dispatch follows both death tests (S3.4), so they die by TNF-induced apoptosis and increment the count like cognate cells.

Deaths that do not increment the count

- Senescence of a resting, infected or chronically infected macrophage: the increment is conditional on the activated state (S2.3).
- Senescence of a T cell of any type: no T cell senescence path calls the routine (S3.4).
- Death of a myofibroblast by its apoptosis proxy, under M4: it writes only the pending state (M4).
- Bacterial death by any route: bacteria are not grid occupants (S4).
- Removal of a dead agent, which increments only the death counter.

The exclusion of the senescence routes is the defining property of the count. Entrapment can nevertheless charge, on the same timestep, a death that senescence withheld (S5.4).

Position of the increment within a death

In every self-inflicted death and in Fas-mediated killing, the increment follows the dying cell's bacterial release or dispersal.

Bacteria released or dispersed before the increment are already in their destination containers. If the increment triggers the cascade, the cascade kills the compartment's remaining occupants but does not reach those bacteria (S5.3), and dispersed bacteria in neighbouring compartments are beyond its scope.

Bound on the count

In the absence of neutrophils the count is bounded by $\theta + 1$:

- At the start of a next-state block a habitable compartment has a count of at most $\theta - 1$, since at θ it is caseous and holds nothing.
- Over the rest of the timestep it can be charged at most N_slots times. The chargeable entities are the agents in its slots, live or awaiting removal, and the daughters promised to it; a promise needs a free slot in the reservation map (S3.5).
- Each slot is charged at most once, because every charging route kills its agent outright or, for entrapment, skips an agent already dead. The increment that crosses θ is one of these charges.

Hence $K(p) \le \theta - 1 + N_{\text{slots}} = \theta + 1$, with N_slots = 2. Once caseous, a compartment holds no agent and admits none other than a neutrophil, and no new daughter can be promised to it. A daughter promised before the crossing may still be discarded there, but it is one of the N_slots charges already counted. The cascade finds no live occupant, and the entrapment kill requires one. After healing the count re-accumulates to the same bound. The bound is reached only if a second entity was chargeable at the crossing; otherwise the count rests at exactly θ. The fractional quantity of S5.7 therefore exceeds 1 by at most $1/\theta$: about 8 per cent at $\theta = 12$ and 6 per cent at $\theta = 18$.

Neutrophils may stand in caseum, and each neutrophil death charged there adds one with no cap (M9.8).

Other agent types

Neutrophils contribute probabilistically on senescence, are killed by the cascade and are exempt from the entrapment kill (M9.8). Fibroblasts and myofibroblasts under M4 are killed through the agent interface by the cascade and by entrapment, each charging one increment. Myofibroblast death by its apoptosis proxy does not increment the count; entrapment on the same timestep re-kills the cell and charges one increment, as for the senescence routes (S5.4; M4). Dendritic cells, a macrophage subclass, would contribute exactly as macrophages.

The only random draw in this submodel is the shared healing draw of an activated macrophage (S2.8). The incrementing routines, the cascade and the entrapment test make none.

S5.3 Threshold caseation and the occupant cascade

The caseation predicate

$$\text{caseated}(p) \iff K(p) \ge \theta \ \text{ or } \ E(p) = 1,$$

where θ is the cached threshold of S5.1, sampled per simulation (S5.9).

The comparison is non-strict: a compartment becomes caseous on the increment that brings its count to θ. There is no "just became caseous" state; every consumer reads the predicate. The flag term is the entrapment route (S5.4).

The incrementing routines

```
increment, agent-naming form (p, a):
    kill a                                  // writes current and pending state
    return increment, position-only form (p)

increment, position-only form (p):
    K(p) <- K(p) + 1
    if caseated(p):                         // evaluated after the increment
        for each slot of p, in slot order:
            b <- occupant of the slot
            if b present and not dead and not dead-next:
                if b is a macrophage:
```

```
                n <- macrophage kill of b, dispersal fraction 1.0
                caseum bacterial-kill statistic <- statistic + n
            else:
                agent-interface kill of b
            K(p) <- K(p) + 1            // once per occupant killed
        return true
    return false
```

Every counted death uses the agent-naming form except the daughter discard, the sole caller of the position-only form. All three cytotoxic branches use the agent-naming form, although the clean-kill routine has already written both of the target's states. The second write is idempotent, and the cascade's guard then skips the target as already dead.

The cascade tests status, not the crossing

The cascade tests caseation status after the increment, not whether this increment crossed θ. An increment at an already-caseous compartment therefore also enters the loop.

In the absence of neutrophils only the daughter discard can increment an already-caseous compartment, and the loop then finds nothing: admission excludes caseum, and the occupants present at the crossing were killed by it. A reimplementation that tested for the crossing would differ wherever an agent can occupy caseum, as neutrophils can (M9.8).

The occupant guard

The loop runs over the compartment's two slots in slot order. An occupant is killed only if it is present, not dead and not dead-next, so the cascade cannot kill an agent twice or charge twice for one death. The guard applies to every occupant type, neutrophils included (M9.8).

Testing the pending state distinguishes this guard from the entrapment guard (S5.4). An agent that senesced this timestep, a macrophage not activated or a T cell of any type, is dead-next but live-current. The cascade skips it; entrapment does not.

Per-type treatment

Occupant	Kill	Bacteria
Macrophage in any live state; dendritic cell	Macrophage kill routine, dispersal fraction 1.0	Whole container dispersed over the Moore neighbourhood; none destroyed
T cell of any type; fibroblast or myofibroblast under M4	Agent interface	None held
Neutrophil	Agent interface (M9.8)	Not dispersed; destroyed at removal (M9.6)

Each occupant killed increments the count once.

Fraction 1.0 is the largest the dispersal mechanism allows and destroys nothing (S4): the live and dead lists go to up to nine compartments, the caseating one included. A macrophage caught by the cascade therefore releases its full bacterial burden, the same outcome as bursting.

Roughly one ninth of the dispersed bacteria land in the caseating compartment's own extracellular container. The cascade does not kill them. Later in the same timestep, in the extracellular pass, their container is designated non-replicating and they are subject to density-dependent death (S4).

The cascade does not reach bacteria

Extracellular bacteria present when a compartment becomes caseous are untouched: they are not killed, removed or counted. They are held in a container, not a slot (spine 2.3), and their kill member is a no-operation (S4). The only bacteria affected by a caseation event are those inside macrophages the cascade kills, and these are dispersed, not destroyed.

The macrophage branch adds the kill routine's return value, the number of bacteria dying in dispersal, to the caseum bacterial-kill statistic. At fraction 1.0 this value is always zero. The statistic is non-zero only through density-dependent death in caseum (S4; S9).

Timing within the caseating timestep

The cascade is synchronous with the increment that triggers it, at whatever point of the next-state pass the death occurred.

- A compartment that caseates during the macrophage pass is caseous for the T cell passes. A Tgam or Tcyt finds its target dead and abandons the attempt (S3.8); a Treg's suppression sweep skips it.
- An agent that moved into the compartment earlier in the timestep is killed without having acted there.
- A cell recruited into the compartment this timestep is killed on the same timestep, possibly before it has computed a next state.

S5.4 Entrapment

The sweep

The entrapment test runs once per compartment per cellular timestep, in the extracellular pass, in row-major order. It is unconditional: it precedes the pass's early return for compartments without bacteria, so every compartment of the grid is tested.

```
entrapment test at p:
    caseous <- 0        // whole periodic radius-2 neighbourhood, centre included
    ring <- 0           // radius-1 ring only
    chronic <- 0        // whole periodic radius-2 neighbourhood, centre included
    for each q in the periodic neighbourhood of p of radius 2:   // literal radius
        if caseated(q):
            caseous <- caseous + 1
            if q != p and Chebyshev distance of q from p <= 1:
                ring <- ring + 1
        if q holds a chronically infected macrophage:
            chronic <- chronic + 1          // at most one per compartment
    if ring == Moore-neighbourhood size - 1: // 9 - 1 = 8 in two dimensions
        E(p) <- 1
        for each slot of p, in slot order:
            b <- occupant of the slot
            if b present and not dead:      // pending state not tested
```

```
                if b is a neutrophil:
                    continue                // exempt (M9.8)
                if b is a macrophage:
                    n <- macrophage kill of b, dispersal fraction 1.0
                    caseum bacterial-kill statistic <- statistic + n
                else:
                    agent-interface kill of b
                K(p) <- K(p) + 1
    else:
        E(p) <- 0
    return caseous + chronic
```

The return value is consumed at once by growth at the same compartment (S5.5).

The ring test

The ring is the compartments of the radius-2 neighbourhood other than the centre and at Chebyshev distance at most 1 from it: eight compartments in two dimensions. Enclosure is equality against the Moore-neighbourhood size minus 1, that is $9 - 1 = 8$. Because the set has exactly eight members, equality and $\geq$ are interchangeable. Distance is the unwrapped displacement reported by the neighbourhood iterator, as in the IFN-γ sweep of S3.7, so the ring geometry holds across the periodic wrap.

The centre's own caseation is excluded from the ring count and included in the caseous count. A compartment already caseous by threshold is still tested, and may have its flag set too, with no further effect.

The flag is recomputed, not latched

The flag is written at every evaluation: to 1 if enclosed and to 0 otherwise. It is never set and left.

Entrapment therefore reverses without healing. If a ring neighbour stops being caseous, by its own count being halved (S5.8) or by its own flag clearing, the enclosed compartment's flag clears on the same timestep if that neighbour was halved or cleared earlier in the pass, and on the next timestep otherwise. The compartment is then habitable if its own count is below θ, which for a compartment caseous purely by entrapment it may well be.

Flag clearing is the only way caseation ends other than halving of the compartment's own count. It needs no delay, no draw and no macrophage.

Entrapment without damage

A compartment can be caseous with a count of zero, since the ring test ignores the compartment's own count. Such a compartment is caseous for every purpose: it excludes agents other than neutrophils, secretes chemokines, suppresses delivery and recruitment at a source, and its container is designated non-replicating. Its fractional quantity (S5.7) is zero, and the per-agent caseous-surroundings statistic, which reads the count, does not count it (S9).

Propagation within a timestep

Each neighbour's caseation reads its count and its flag. A neighbour visited earlier this timestep shows its new flag; one not yet visited shows the flag of the last timestep.

Entrapment can therefore propagate across several compartments in one timestep, but only in the direction of travel. An enclosed row fills from its lower-indexed end within one pass, while its mirror image fills one compartment per timestep. This dependence on traversal order is part of the specification: computing all flags from the previous timestep, or traversing in another order, changes trajectories. The growth count also depends on sweep order (S5.5).

The occupant kill and its guard

The kill applies to the enclosed compartment's own occupants only, in slot order, as in the cascade: macrophages at fraction 1.0, other types through the agent interface, one increment per occupant killed, and zero credited to the caseum bacterial-kill statistic. It differs from the cascade in its guard and in exempting neutrophils (M9.8).

The entrapment guard tests only the current state. Because the pass runs after the whole next-state block, every agent that decided its own death this timestep without calling the incrementing routine is dead-next and live-current when the pass arrives.

Death this timestep	Current state at the pass	Killed again by entrapment
Senescence of a macrophage not activated	Live	Yes
Senescence of a T cell, any type	Live	Yes
Myofibroblast apoptosis proxy, under M4	Live	Yes
Senescence of an activated macrophage; TNF-induced apoptosis; bursting; Fas-mediated or cytotoxic killing; an earlier cascade	Dead	No

The exposed set is exactly the deaths that write only the pending state and do not increment the count. A compartment enclosed on the timestep such a death occurred there gains one increment per such occupant, which the death route withheld. There is no bacteriological consequence: a macrophage that senesced without activation has already released its container locally, and T cells and myofibroblasts hold no bacteria. The exposure window is the whole pass on every timestep. The re-kill requires the compartment to become enclosed on the same timestep, an occupant being present only while the compartment is habitable. S2.9, S3.3, S3.4 and M4 refer to this rule.

The chronic count

The chronic accumulator counts compartments, not macrophages: a compartment holding any chronically infected macrophage adds one. The two coincide by default, since a compartment holds at most one macrophage; they would not in a configuration allowing more than one large agent per compartment.

S5.5 The growth-modulation count

Definition

$$c(p) = |\{q \in N(p,2) : \text{caseated}(q)\}| + |\{q \in N(p,2) : q \text{ holds a chronically infected macrophage}\}|,$$

where N(p, 2) is the periodic radius-2 neighbourhood of 25 compartments, the centre included in both terms.

c(p) is passed straight to growth at the same compartment and is read nowhere else. Growth compares it with two thresholds to choose among three regimes (S4).

The two terms are summed before growth sees them, so growth cannot tell necrosis from live infected tissue.

Bound. c(p) is at most 25, except transiently where a senescing chronically infected macrophage remains in a newly caseous compartment; the formal ceiling is 50. The exception arises because the cascade skips that macrophage as dead-next (S5.3), so it still shows its chronic state when the pass arrives and its compartment counts in both terms. A chronically infected macrophage almost always bursts long before it senesces (S2.7).

The centre counts on its own behalf. A centre holding a chronically infected macrophage adds one to its own count. A caseous centre adds one too, but growth returns zero there before using the count (S4).

Sweep order. Entrapment at a compartment sets its flag and kills its occupants at once, so compartments swept later in the same pass see one more caseous compartment and one fewer chronically infected macrophage than compartments swept earlier. The growth count c(p) therefore depends on grid sweep order within a timestep. Likewise a compartment decaseated by halving earlier in the pass counts as not caseous for compartments swept after it.

The thresholds

S4 owns the two thresholds, computed at load from fraction parameters and the radius `Mtb_Agents_noGrowthExtMtbCaseatedRadius`; by default they are 5 (onset of reduction) and 14 (arrest). The thresholds govern the combined count (S4.6). At the reduction threshold of 5, five compartments holding chronically infected macrophages, with no caseum, already reduce growth.

The sweep radius is the literal 2, while the threshold radius is the parameter `Mtb_Agents_noGrowthExtMtbCaseatedRadius`, declared on [1, 3] and set to 2. With the parameter at 1 the thresholds are 2 and 5 against a 25-compartment count; at 3 they are 11 and 27, and the arrest threshold exceeds the count's practical maximum of 25.

No coupling to oxygen

c(p) is computed from compartment and agent state only. It reads no oxygen, and oxygen does not read it. A bacterium in a hypoxic compartment with c(p) < 5 grows at its full rate.

The sweep must run everywhere

A reimplementation may skip the two counts at compartments holding no bacteria, but must run the ring test and its occupant kill at every compartment. The flag and the occupant kill are the traversal's persistent effects; skipping a compartment would leave a stale flag and spare an occupant.

S5.6 Consequences of a caseous compartment

Inventory

Consequence	Owner
Every agent except a neutrophil is refused admission and movement	S5.6; S1; M9.3
Occupants present at caseation are killed	S5.3, S5.4
A daughter promised to the compartment is discarded and the count charged	S5.2; S3.5
CCL2, CCL5 and CXCL9 are secreted at one quarter of the macrophage rates	S5.6
Vascular oxygen delivery is suppressed	S7
Recruitment is suppressed and the source counted as blocked	S8
Extracellular growth is arrested by the growth modulator's early return	S4
The bacterial container is re-designated non-replicating	S4
Extracellular bacteria are subject to density-dependent death, gated on the fluoroquinolone test	S4; M6
An adjacent activated macrophage may kill extracellular bacteria there, at a literal probability of 0.1	S2.8
The healing clock may be stamped	S5.8
The compartment counts as occupied for cell density, and so toward the threshold granuloma and the cell-density extent	S9
The compartment contributes to the entrapment of its neighbours	S5.4
Under M6, drug binds to caseum, at a caseum level computed from the killing count	M6.7

Exclusion of agents

Caseation is the first test in the movement predicates for macrophages, T cells and fibroblasts, which return false before examining occupancy. The admission predicates wrap the movement predicates, so admission and movement treat caseation identically (S1). Agent addition applies its own caseation test too, for every type except the neutrophil.

Neutrophils are the one agent type permitted to occupy caseum (M9.3).

Exclusion applies to agents, not to bacteria: the transfer and dispersal routines have no caseation test (S4), so bacteria move freely into caseum, including by the cascade's own dispersal. Exclusion does not touch vascular sources, which are positions in a list; they are neither destroyed nor moved when their compartment caseates (S7). Exclusion is evaluated at the attempt, so an agent already present when its compartment caseates is removed by the cascade, not by exclusion.

Chemokine secretion from caseum

Caseum secretion sweeps the grid once per split half-step: twice per diffusion step and 20 times per cellular timestep. At every caseous compartment it adds

$$\Delta C_m = \tfrac{1}{4}\, d_m \,\mathrm{d}t$$

of each of the three chemokines, where d_m is the macrophage rate parameter (`Core_Mac_dCCL2`, `Core_Mac_dCCL5` or `Core_Mac_dCXCL9`; S6) and $dt = \Delta t_d/2 = 30$ s. Per cellular timestep a caseous compartment adds 900, 900 and 1800 molecules of CCL2, CCL5 and CXCL9, against 3600, 3600 and 7200 for a macrophage secreting at its full state factor.

- **Caseum has no secretion parameters of its own.** It reads the macrophage rates, so changing them changes caseum output in the same proportion. The quarter is a literal at the call site.
- **Caseum escapes IL-10 inhibition.** The term is a direct field increment that bypasses the shared secretion helper, so it escapes the step reduction above `Core_IC50ChemokineIL10` (S6). It also increments no per-compartment secretion counter (S9).
- **Caseum writes the three chemokines only,** no TNF and no IL-10.
- **Secretion is unconditional on bacterial load** and continues after sterilization.

CCL5 and CXCL9 are derived from CCL2 after each diffusion solve. The writes of the final secretion half-step of the diffusion loop, caseum's included, survive into the values agents read (S6.14).

Chemotactic weights read no caseation (S1). A caseous compartment is therefore a candidate destination with a raised weight, being itself a source; an agent that draws it is refused and does not move, with no retry and no second draw (S1).

What caseation does not do

- **Oxygen at the compartment.** Delivery is suppressed at a caseous source, but no oxygen is removed and none consumed, no macrophage being present.
- **TNF and IL-10 fields.** Caseum neither secretes nor absorbs them; the receptor sink is an agent operation.
- **Diffusion.** The solver has no caseation term, so a caseous compartment transports every diffusing species normally.

S5.7 Partial caseation

The fractional quantity

$$f(p) = \begin{cases} 0 & \theta \leq 0 \\ K(p)/\theta & \text{otherwise} \end{cases}$$

computed in single precision against the cached threshold θ.

The guard is reachable only if `Core_nrKillingsCaseation` ≤ 0, which no validity range prevents (S5.9). Every compartment would then be caseous from the first timestep, the predicate comparison being non-strict, while f reads zero everywhere. The guard protects against division by zero; the default parameter file does not exercise it.

The quantity is a ratio, not a percentage. In the absence of neutrophils it is bounded by $(\theta + 1)/\theta$, not by 1 (S5.2), an overshoot of at most 8 per cent. It reads as accumulated damage in units of θ.

The partial-caseation predicate

$$\text{partiallyCaseated}(p) \iff f(p) \geq \texttt{Core_partialCaseationFraction},$$

with the parameter at 0.5, read live. In killings, a compartment is partially caseous once its count reaches $\lceil \theta/2 \rceil$, which is 6 to 9 over the sampled range [12, 18].

The two measures are not nested

The caseation predicate reads the count or the flag; the partial predicate reads the count alone, so neither set contains the other. A compartment with count at or above θ is both caseous and partially caseous; one with count at least $\theta/2$ but below θ is partially caseous only; and an entrapped compartment with count below $\theta/2$, zero included, is caseous only. Entrapped low-count compartments are routine inside caseous regions, not edge cases. The caseous and partially caseous counts can therefore cross (S9).

Healing and the parity of the threshold

Healing halves the count by integer division (S5.8), leaving $\lfloor n/2 \rfloor$ and a ratio of $\lfloor n/2 \rfloor/\theta$.

- For $n = \theta$, an even θ gives exactly 0.5 and the compartment counts as partially caseous; an odd θ falls just below.
- For $n = \theta + 1$, the halved ratio is at least 0.5 for every sampled θ, so the compartment is partially caseous whatever the parity.

In the absence of neutrophils no other count is attainable at healing: a caseous compartment accrues nothing more, so the count at healing is the count at caseation. One healing restores habitability but leaves the compartment at or near the partial boundary, so healed tissue is reported as damaged.

In the absence of neutrophils, since $\theta + 1 < 2\theta$ for every sampled θ, one healing always decaseates. A second healing needs re-damage to θ and fresh caseation, since stamping requires a caseous compartment (S5.8).

Consumers

Neither quantity is read by any rule that affects dynamics in the default configuration. The fractional quantity feeds the grid-wide sum and ring scaling, and the partial predicate the partially caseous count (S9). Under M6 the drug statistics also sum concentrations over partially caseous compartments (M6.15).

S5.8 Healing

Two stages

Healing has two stages. In the next-state block, an activated macrophage stamps the healing clock of an adjacent caseous compartment with the current timestep. In the extracellular pass, every compartment's clock is examined every timestep; once the delay has elapsed the count is halved and the clock cleared. The stages are 9.63 to 11.44 days apart, so the initiating macrophage has almost always died before the halving.

Initiation

S2.8 owns the activated-macrophage sweep and its shared draw. A compartment is stamped when it lies in the periodic Moore neighbourhood of an activated macrophage, is caseous, and its clock reads 0. One draw against `Core_Mac_probHealCaseation` decides all nine compartments at once.

- **Initiations are clustered.** Because the draw is shared, a macrophage with k eligible neighbours stamps all k or none. The mean rate is unchanged; the variance and the spatial pattern are not.
- **A compartment is stamped at most once per cycle.** A stamped clock is not 0, so a second macrophage cannot reset it and postpone the halving. The first macrophage in list order wins.
- **A macrophage's own compartment is never stamped,** since it holds a live macrophage and so is not caseous.

At `Core_Mac_probHealCaseation` in [0.003898, 0.006992], an activated macrophage with a continuously available eligible neighbour initiates healing on average once per 143 to 257 timesteps, about once a day to once every two days, and between six and ten times over its ten-day activated life.

Neutrophils initiate no healing (M9.8).

The clock

The healing clock H(p) is a per-compartment integer, initially 0, stamped with the initiating timestep, cleared on halving and serialized with the grid. The value 0 means no healing in progress.

The sentinel is unambiguous in practice: the timestep is incremented before any agent acts, so the earliest stamp is 1, and nothing is caseous at the start of a run. Every other timer in the model uses -1 as its sentinel. A reimplementation using -1 throughout must change the completion test.

Completion

```
healing completion at p, timestep t:
    if H(p) == 0:
        return
    if t - H(p) > Core_caseationHealingTime:
        K(p) <- floor(K(p) / 2)            // integer division
        H(p) <- 0
```

Completion runs at every compartment on every timestep, in the extracellular pass, unconditionally and after the bacterial processing there (S5.1).

- **The delay test is strict,** so the realized delay is the parameter plus one: [1387, 1648] timesteps, 9.63 to 11.44 days.
- **The action is a halving, not a clearing.** Nothing in the model clears a count to zero.
- **Completion reads only the clock.** It tests neither caseation, nor the count, nor occupants.

One healing suffices

In the absence of neutrophils a stamped compartment's count lies in $[\theta, \theta + 1]$ (S5.2), so halving leaves at most $\lfloor (\theta + 1)/2 \rfloor$, between 6 and 9 by default. In general one halving decaseates exactly when

$$\lfloor n/2 \rfloor < \theta \iff n < 2\theta,$$

which always holds, since $\theta + 1 < 2\theta$. A compartment is never left caseous by its own healing, and its clock is not re-stamped without a return to habitability. Each repeat cycle needs at least the realized delay plus about half a threshold of new damaging deaths. With neutrophils the count can exceed 2θ, and a still-caseous compartment can be healed again (M9.8).

Entrapment and healing

In practice a compartment caseous only by entrapment cannot be stamped. Enclosure needs all eight ring members caseous, and stamping needs an activated macrophage in one of them, which a caseous compartment cannot hold. Entrapped compartments revert only by flag clearing (S5.4).

In practice, therefore, every compartment healing acts on has a count of at least θ, so healing never halves a zero count. Likewise, although completion reads only its clock, in practice it does not act on a stale clock: a stamped compartment is caseous by count, only completion lowers a count, and so the clock does not become stale.

The exclusion is practical, not an invariant. The entrapment flag is written in the extracellular pass and read by the macrophage sweep on the next timestep, so a flag can be one timestep stale when a ring neighbour is healed later in the same pass that set it. During that next timestep a macrophage could occupy the healed neighbour and stamp the entrapped compartment, leaving a stale clock on a compartment with an arbitrary count.

What healing restores

If the halving takes the count below θ, these are restored: admission, and extracellular growth, from the next timestep; the end of chemokine secretion from the compartment, from the next timestep's first half-step; vascular delivery and recruitment, if the compartment holds a source; the replicating designation of its container, from the next timestep; its contribution to neighbours' growth counts; and possibly the clearing of neighbours' entrapment flags.

Healing restores none of: the occupants killed at caseation, the bacteria dispersed from them, the chemokine already secreted, the damage history (the count is halved, not cleared), or any statistic.

Healing initiations are counted at initiation, not at completion (S9).

S5.9 Parameters

Identifier	Value or range	Range	Units	Meaning
`Core_nrKillingsCaseation`	Sampled	[12, 18]	integer, killings (none declared)	Caseation threshold θ, cached at grid construction (S5.1, S5.3)[1] [2]
`Core_caseationHealingTime`	Sampled	[1386, 1647]	integer, timesteps	Healing delay; the realized delay is one greater (S5.8)[3]
`Core_partialCaseationFraction`	0.5	—	none declared	Partial-caseation fraction, read live (S5.7). [0, 1], checked

Both sampled parameters are integer-valued and sampled uniformly over inclusive integer bounds.

Growth arrest and density-dependent death in caseum (S4) consult caseation through the caseation predicate. The sampled threshold spans a factor of 1.5 across the library, so the rate at which those mechanisms engage varies with it, although no bacterial parameter does.

[1] Startup fails unless `Core_maxNrKillingsCaseation` $\geq$ `Core_nrKillingsCaseation`. The constraint keeps the uptake histogram index in bounds as well as fixing output width (S5.10, Observation; S9).

[2] Declared with a minimum of 0 and no maximum, which builds no range (spine 7.0, "Validity ranges"). Zero and negative values therefore pass validation, and either would make every compartment caseous from the first timestep while the fractional quantity reads zero (S5.7).

[3] No declared bounds. Stamping precedes completion within a timestep, so with a negative value the strict test holds at once (0 > `Core_caseationHealingTime`) and a stamped count is halved on the timestep of initiation. With a value of 0 it is halved on the next timestep.

The cross-parameter constraints are the only guards on these parameters beyond the declared [0, 1] ranges of the fraction and probability parameters and the [1, 3] radius range: the histogram bound, `Core_maxNrKillingsCaseation` $\geq$ `Core_nrKillingsCaseation`, and the two growth-threshold constraints, on the fractions and on the computed integers, held by S4.

Fixed structural constants: entrapment sweep radius 2; enclosure target, the Moore-neighbourhood size minus 1, which is 8 and dimension-correct without modification; caseum secretion fraction 0.25; dispersal fraction 1.0 on both occupant kills; healing divisor 2; healing clock sentinel 0; agent slots per compartment 2 (spine 2.3). None can be varied without recompiling.

Read but without effect by default: the neutrophil caseation parameters (M9.10.1) and the per-drug caseum parameters `caseumUnboundFraction` and `caseumBindingRateConst` of M6 (Appendix B).

S5.10 Interfaces

With	Provides or receives	See
Spine 2.3	Receives the agent slots per compartment and the hybrid update	Spine 2.3
Spine 2.6	Receives the field inventory holding the killing count, entrapment flag, healing clock and death counter	Spine 2.6
Spine Element 3	Places caseation activity in the cellular timestep	S5.1
Spine Element 7	S5 expands the caseation and entrapment submodel listed there	Spine Element 7
S1	Movement and admission predicates test caseation first; chemotactic weights read none	S1
S2	Provides the increment for activated senescence, apoptosis and bursting; receives the healing sweep, its shared draw and `Core_Mac_probHealCaseation`, and the 0.1 caseum kill; the entrapment re-kill of senesced macrophages is held at S5.4	S2.3, S2.7, S2.8, S5.4
S3	Provides the increment for T cell apoptosis and Fas and cytotoxic killing; cytotoxic killing reads the return value, "caseous after the increment"; daughter discard; the entrapment re-kill of senesced T cells is held at S5.4	S3.4, S3.5, S3.8, S3.9, S5.4
S4	Provides c(p); S4 owns the thresholds, their fractions, radius and constraints, the naming of the fraction parameters, dispersal, re-designation and density-dependent death	S4
S6	Receives `Core_Mac_dCCL2`, `Core_Mac_dCCL5` and `Core_Mac_dCXCL9` for caseum secretion; the derived-field relation and final-half-step survival; the IL-10 step caseum escapes	S6, S6.14
S7	Provides caseation of sources, which suppresses oxygen delivery	S7
S8	Provides caseation of sources, which suppresses recruitment and counts the source as blocked	S8
S9	Provides the predicates, fractional quantity, killing count, healing initiation and zero crediting of the caseum bacterial-kill statistic	S9

With	Provides or receives	See
M1	The caseum increment is linear in the interval, so the amount per cellular timestep is solver-independent; the boundary condition affects edge contributions; final-half-step survival holds under every option. Default: spectral solver	M1
M2	Under either option a caseous source recruits nothing; the blocked-source statistic differs	M2, S8
M3	Caseum secretion is a direct increment, unaffected by M3's restructuring of macrophage secretion. Under the fine-grained option with transcription factors a macrophage writes no chemokine increment, the quarter relation lapses and caseum is the only direct writer. Default: coarse-grained	M3
M4	Fibroblasts and myofibroblasts are killed by the cascade and by entrapment; their admission tests caseation; myofibroblast proxy death is re-killed by entrapment; fibrosis remodels the same compartments, and the threshold-granuloma freeze interacts with caseation. Default: none	M4
M5	In three dimensions the ring has 26 members, the swept neighbourhood 125, c(p) is at most 125 (formal ceiling 250), the thresholds are 28 and 70: the growth fractions are fractions of the same radius-2 neighbourhood in both builds, the computed thresholds differ, and truncation shifts the reduction threshold; dispersal reaches 27 compartments and one healing draw covers 27; the in-sweep propagation direction differs. Default: two-dimensional	M5
M6	Caseum binding from a caseum level computed from the killing count; drug statistics over caseous and partially caseous compartments; density-dependent death in caseum disabled while a fluoroquinolone is dosed	M6.7, M6.14, M6.15
M7	Anti-TNF would reduce TNF-induced apoptosis, an increment route; the effect is indirect. Default: off	M7
M8	Reinfection adds a further focus; TNF depletion reduces TNF-induced apoptosis. Default: all off	M8
M9	Neutrophils may occupy caseum, contribute probabilistically on senescence, are killed by the cascade and exempt from entrapment, have a lifespan shortened by the killing count, and charge it without cap; they initiate no healing	M9.3, M9.8
Appendix B	Indexes the inert parameters of disabled modules	Appendix B

Observation

S9 owns the caseation statistics, their reset codes, the observation parameters and the uptake-in-caseum histogram. S5 supplies the quantities they read: the caseation and partial-caseation predicates, the fractional quantity, the killing count, and the healing initiation event.

The cascade and the entrapment kill each credit zero to the caseum bacterial-kill statistic (S5.3).

The caseation measures differ for compartments caseous by entrapment alone. The whole-grid count and ring scaling use the caseation predicate and include them. The per-agent caseous-surroundings statistic compares the killing count with `Core_nrKillingsCaseation` and excludes them.

The uptake histogram is indexed by the killing count at a living macrophage's compartment, which is at most $\theta - 1$. The startup constraint $\theta \leq$ `Core_maxNrKillingsCaseation` therefore keeps the index in bounds (S5.9; S9).