## SUPPLEMENTARY MATERIAL 2 - *HOSTSIM* TECHNICAL DESCRIPTION

This document contains the equations for each compartment in *HostSim*, how they are coupled, parameter ranges, and initial conditions. *HostSim* was originally published by Louis Joslyn, Jennifer Linderman, and Denise Kirschner in the article "A virtual host model of Mycobacterium tuberculosis infection identifies early immune events as predictive of infection outcomes" in 2022 in the Journal of Theoretical Biology.

We have separated this document into sections for readability. In section 1, we detail all of the equations in each granuloma compartment. In section 2, we detail the equations in the lymph node and blood compartments. In section 3, we present the method by which all of our compartments are coupled. In section 4, we describe how we model dissemination - that is, how we represent one granuloma causing another to form. In section 5, we present tables for the parameter ranges and initial condition values for our granuloma (section 5.1), lymph node and blood (subsection 5.2) equations. In each of these sections, we included both a symbolic variable for each variable (e.g., $M_R$ or $\xi_2$) and a corresponding searchable variable (e.g., MR or xi2) for convenience of navigating this document.

## 1. Granuloma equations

Each granuloma will have its own instance of the equations presented in the subsections below. Each host has a "host-scale granuloma parameter base" selected by the LHS sampling scheme using the ranges presented in Section 5.1. To capture intra-host variability, individual granulomas within a host are given parameter values normally distributed around this base host value. Terms indicated by $Pulled\left[\cdot\right]_g$ involve quantities pulled from the lymph node and blood equations, and is described in Section 3. Below is an index of all state variables in granulomas.

| State Variable | Searchable name | Units | Description |
|---|---|---|---|
| $M_R$ | MR | count | Resting macrophages |
| $M_I$ | MI | count | Infected macrophages |
| $M_A$ | MA | count | Activated macrophages |
| $B_I$ | BI | count | Intracellular Mtb |
| $B_E$ | BE | count | Extracellular Mtb |
| $B_N$ | BN | count | Non-replicating Mtb |
| $Ca$ | CA | mass of $M\phi$ | Necrotic tissue mass |
| $T_0^4$ | T40 | count | Mtb-specific Primed CD4$^+$ T-cells |
| $T_1^4$ | Th1 | count | Mtb-specific Th1 CD4$^+$ T-cells |
| $T_2^4$ | Th2 | count | Mtb-specific Th2 CD4$^+$ T-cells |
| $T_{Non}^4$ | CD4Non | count | Nonspecific CD4$^+$ T-cells |
| $T_{EM}^8$ | EMCD4 | count | Mtb-specific CD4$^+$ effector memory T-cells |
| $T_0^8$ | T80 | count | Mtb-specific Primed CD8$^+$ T-cells |
| $T_C$ | TC | count | Mtb-specific Cytotoxic CD8$^+$ T-cells |
| $T^8$ | T8 | count | Mtb-specific Effector CD8$^+$ T-cells |
| $T_{EM}^8$ | EMCD8 | count | Mtb-specific CD8$^+$ effector memory T-cells |
| $T_{Non}^8$ | CD8Non | count | Nonspecific CD8$^+$ T-cells |
| $F_\alpha$ | TNF | pg/mL | TNF-$\alpha$ concentration |
| $I_\gamma$ | IG | pg/mL | IFN-$\gamma$ concentration |
| $I_{12}$ | I12 | pg/mL | Interleukin 12 concentration |
| $I_{10}$ | I10 | pg/mL | Interleukin 10 concentration |
| $I_4$ | I4 | pg/mL | Interleukin 4 concentration |

### 1.1. Macrophage equations.

$M_R$ - MR - Resting Macrophage count

$$\frac{d}{dt}(M_R) = \underbrace{\alpha_{4a}\left(M_A + w_2 M_I\right)}_{\text{Macrophage-driven recruitment}} \underbrace{+ S r_{4b}\left(\frac{F_\alpha}{F_\alpha + f_8 I_{10} + s_{4b}}\right)}_{\text{TNF driven recruitment}} \underbrace{- k_2 M_R\left(\frac{B_E}{B_E + c_9}\right)}_{\text{Infection of } M_R}$$
$$\underbrace{- k_3 M_R\left(\frac{B_E + wB_I + \beta F_\alpha}{B_E + wB_I + \beta F_\alpha + c_8}\right)\left(\frac{I_\gamma}{I_\gamma + f_1 I_4 + f_7 I_{10} + s_1}\right)}_{\text{Activation of macrophages}} - \underbrace{\mu_{M_R} M_R}_{\text{Natural death}}$$

$M_I$ - MI - Infected macrophages

$$\frac{d}{dt}(M_I) = \underbrace{k_2 M_R \left(\frac{B_E}{B_E + c_9}\right)}_{\text{Infection of } M_R} - \underbrace{k_{17} M_I \left(\frac{B_I^2}{B_I^2 + (NM_I)^2}\right)}_{\text{Bursting of } M_I} - \underbrace{k_{14a} M_I \left(\frac{\left(\frac{T_C + w_3 T_1^4}{M_I}\right)}{\left(\frac{T_C + w_3 T_1^4}{M_I}\right) + c_4}\right)}_{\text{T-cell driven apoptosis of } M_I}$$

$$- \underbrace{k_{14b} M_I \left(\frac{F_\alpha}{F_\alpha + f_9 I_{10} + s_{4b}}\right)}_{\text{TNF driven apoptosis of } M_I} - \underbrace{k_{52} M_I \left(\frac{\left(\frac{T_C\left(\frac{T_1^4}{T_1^4 + C_{T_1^4}}\right) + w_1 T_1^4}{M_I}\right)}{\left(\frac{T_C\left(\frac{T_1^4}{T_1^4 + C_{T_1^4}}\right) + w_1 T_1^4}{M_I}\right) + c_{52}}\right)}_{\text{Cytotoxic T-cell driven } M_I \text{ apoptosis}} - \underbrace{\mu_{M_I} M_I}_{\text{Natural death}}$$

$M_A$ - MA - Activated macrophages

$$\frac{d}{dt}(M_A) = \underbrace{k_3 M_R \left(\frac{B_E + wB_I + \beta F_\alpha}{B_E + wB_I + \beta F_\alpha + c_8}\right)\left(\frac{I_\gamma}{I_\gamma + f_1 I_4 + f_7 I_{10} + s_1}\right)}_{\text{Activation of resting macrophages}} - \underbrace{k_4 M_A \left(\frac{I_{10}}{I_{10} + s_8}\right)}_{\text{Deactivation by } I_{10}} - \underbrace{\mu_{M_A} M_A}_{\text{Natural death}}$$

1.2. **Mtb and caseum equations.**

$B_I$ - BI - Intracellular bacterium count

$$\frac{d}{dt}(B_I) = \underbrace{\alpha_{19} \frac{B_I}{M_I} M_I \left(1 - \frac{(B_I/M_I)}{N}\right)}_{\text{Replication}} + \underbrace{k_2 \frac{N}{2} M_R \left(\frac{B_E}{B_E + c_9}\right)}_{\text{Internalization of } B_E} - \underbrace{k_{17} N M_I \left(\frac{B_I^2}{B_I^2 - (NM_I)^2}\right)}_{\text{Bursting of } M_I}$$

$$- \underbrace{k_{14a} \frac{B_I}{M_I} M_I \left(\frac{\left(\frac{T_C + w_3 T_1^4}{M_I}\right)}{\left(\frac{T_C + w_3 T_1^4}{M_I}\right) + c_4}\right)}_{\text{T-cell driven } M_I \text{ apoptosis}} - \underbrace{k_{14b} \frac{B_I}{M_I} M_I \left(\frac{F_\alpha}{F_\alpha + f_9 I_{10} + s_{4b}}\right)}_{\text{TNF driven aptosis}}$$

$$- \underbrace{k_{52} \frac{B_I}{M_I} M_I \left(\frac{\left(\frac{T_C\left(\frac{T_1^4}{T_1^4 + C_{T_1^4}}\right) + w_1 T_1^4}{M_I}\right)}{\left(\frac{T_C\left(\frac{T_1^4}{T_1^4 + C_{T_1^4}}\right) + w_1 T_1^4}{M_I}\right) + c_{52}}\right)}_{\text{Cytotoxic T-celldriven} M_I \text{ apoptosis}} - \underbrace{\mu_{B_I} B_I}_{\text{Natural Death}} - \underbrace{\mu_{M_I} \frac{B_I}{M_I} M_I}_{\text{Natural death of } M_I}$$

$B_E$ - BE - Extacellular Bacterium Count

$$\frac{d}{dt}(B_E) = \underbrace{\alpha_{20} B_E \left(1 - \frac{B_E}{10^6}\right)}_{\text{Replication}} + \underbrace{(1 - C_N)}_{\text{Fraction outside of Caseum}} \left[ \underbrace{k_{17} N M_I \left(\frac{B_I^2}{B_I^2 + (N M_I)^2}\right)}_{\text{Macrophage bursting}} + \underbrace{k_{14a} N_{fracc} \frac{B_I}{M_I} M_I \left(\frac{\left(\frac{T_C + w_3 T_1^4}{M_I}\right)}{\left(\frac{T_C + w_3 T_1^4}{M_I}\right) + c_4}\right)}_{\text{T-cell driven apoptosis}} \right.$$
$$\left. + \underbrace{k_{14b} N_{fraca} \frac{B_I}{M_I} M_I \left(\frac{F_\alpha}{F_\alpha + f_9 I_{10} + s_{4b}}\right)}_{\text{TNF driven apoptosis}} + \underbrace{\mu_{M_I} N_{fracd} \frac{B_I}{M_I} M_I}_{\text{Natural death of } M_I} \right] + \underbrace{k_{Rev} N_{Ca} M_A Ca \cdot B_N}_{\text{Revealing of } B_N}$$
$$- \underbrace{k_2 \frac{N}{2} M_R \left(\frac{B_E}{B_E + c_9}\right)}_{\text{Internalization of } B_E} - \underbrace{k_{15} M_A B_E}_{M_A \text{ killing of } B_E} - \underbrace{k_{18} M_R B_E}_{M_R \text{ killing of } B_E} - \underbrace{\mu_{B_E} B_E}_{\text{Natural death}}$$

$B_N$ - BN - Nonreplicating bacterium count

$$\frac{d}{dt}(B_N) = \underbrace{C_N}_{\text{Fraction inside of Caseum}} \left\{ \underbrace{k_{17} M_I \left(\frac{B_I^2}{B_I^2 + (N M_I)^2}\right)}_{\text{Macrophage bursting}} + \underbrace{k_{14a} N_{fracc} \frac{B_I}{M_I} M_I \left(\frac{\left(\frac{T_C + w_3 T_1^4}{M_I}\right)}{\left(\frac{T_C + w_3 T_1^4}{M_I}\right) + c_4}\right)}_{\text{T-cell driven apoptosis}} \right.$$
$$\left. + \underbrace{k_{14b} N_{fraca} \frac{B_I}{M_I} M_I \left(\frac{F_\alpha}{F_\alpha + f_9 I_{10} + s_{4b}}\right)}_{\text{TNF driven apoptosis}} + \underbrace{\mu_{M_I} N_{fracd} \frac{B_I}{M_I} M_I}_{\text{Natural death of } M_I} \right\}$$
$$- \underbrace{\mu_{B_N} B_N}_{\text{Natural death}} - \underbrace{B_N k_{Rev} N_{Ca} Ca \cdot M_A}_{\text{Revealing of } B_N}$$

$Ca$ - CA - Caseum

$$N_f \frac{d}{dt}(Ca) = \underbrace{k_{17} M_I \left(\frac{B_I^2}{B_I^2 + (N M_I)^2}\right)}_{\text{Bursting of } M_I} + \underbrace{k_{14a} M_I \left(\frac{\left(\frac{T_C + w_3 T_1}{M_I}\right)}{\left(\frac{T_C + w_3 T_1}{M_I}\right) + c_4}\right)}_{\text{T-cell mediated apoptosis of } M_I} + \underbrace{k_{14b} M_I \left(\frac{F_\alpha}{F_\alpha + f_9 I_{10} + s_{4b}}\right)}_{\text{TNF-mediated apoptosis of } M_I}$$
$$+ \underbrace{k_{52} \frac{B_I}{M_I} M_I \left(\frac{\left(\frac{T_C\left(\frac{T_1^4}{T_1^4 + C_{T_1^4}}\right) + w_1 T_1^4}{M_I}\right)}{\left(\frac{T_C\left(\frac{T_1^4}{T_1^4 + C_{T_1^4}}\right) + w_1 T_1^4}{M_I}\right) + c_{52}}\right)}_{\text{Cytotoxic T-cell mediated apoptosis of } M_I} - \underbrace{N_{Ca} Ca M_A}_{\text{Neutrophil-driven caseum clearance}}$$
$$+ \underbrace{\mu_{M_I} M_I + \mu_{M_A} M_A + \mu_{M_R} M_R \left(\frac{F_\alpha}{F_\alpha + f_9 I_{10} + s_{4b}}\right)}_{\text{Natural death of all macrophage populations}}$$

### 1.3. **CD4$^+$ T-cells.**

$T_0^4$ - T40 - Primed CD4$^+$ T-Cell count

$$\frac{d}{dt}\left(T_0^4\right) = Pulled\left[T_0^4\right]_g + \underbrace{\alpha_2 T_0^4\left(\frac{M_A}{M_A+c_{15}}\right)}_{\text{Proliferation}} - \underbrace{k_6 I_{12} T_0^4\left(\frac{I_\gamma}{I_\gamma+f_1 I_4+f_7 I_{10}+s_1}\right)}_{\text{Differentiation to } T_1^4}$$
$$-\underbrace{k_7 T_0^4\left(\frac{I_4}{I_4+f_2 I_\gamma+s_2}\right)}_{\text{Differentiation to } T_2^4} - \underbrace{\mu_{T_0} T_0}_{\text{Natural death}}$$

$T_1^4$ - Th1 - Effector CD4$^+$ T-cell count

$$\frac{d}{dt}\left(T_1^4\right) = \underbrace{k_6 I_{12} T_0^4\left(\frac{I_\gamma}{I_\gamma+f_1 I_4+f_7 I_{10}+s_1}\right)}_{\text{Differentiation from } T_0^4} + \underbrace{k_{31} T_{EM}^4 M_I\left(\frac{M_I}{M_I+3}\right)}_{\text{Differentiation of } T_{EM}^4}$$
$$-\underbrace{\mu_{T_\gamma}\left(\frac{I_\gamma}{I_\gamma+c}\right) T_1^4 M_A}_{\text{IFN}\gamma\text{ apoptosis of } T_0^1} - \underbrace{\mu_{T_1^4} T_1^4}_{\text{Natural death}}$$

$T_2^4$ - Th2 - Effector Th2 CD4$^+$ T-cell count

$$\frac{d}{dt}\left(T_2^4\right) = \underbrace{k_7 T_0^4\left(\frac{I_4}{I_4+f_2 I_\gamma+s_2}\right)}_{\text{Differentiation from } T_0^4} + \underbrace{k_{32} T_{EM}^4 M_A}_{\text{Differentiation from } T_{EM}^4} - \underbrace{\mu_{T_2^4} T_2^4}_{\text{Natural death}}$$

$T_{EM}^4$ - EMCD4 - Effector memory CD4$^+$ T-cell count:

$$\frac{d}{dt}\left(T_{EM}^4\right) = Pulled\left[T_{EM}^4\right]_g - \underbrace{k_{31} T_{EM}^4 M_I\left(\frac{M_I}{M_I+3}\right)}_{\text{Differentiation to } T_1^4} - \underbrace{k_{32} T_{EM}^4 M_A}_{\text{Differentiation to } T_2^4} - \underbrace{\mu_{T_{EM}^4} T_{EM}^4}_{\text{Natural death}}$$

$T_{Non}^4$ - CD4Non - Non-cognate CD4$^+$ T-cell count:

$$\frac{d}{dt}\left(T_{Non}^4\right) = Pulled\left[T_{Non}^4\right]_g - \underbrace{\mu_{T_{Non}^4} T_{Non}^4}_{\text{Natural death}}$$

### 1.4. CD8$^+$ T-cells.

$T_0^8$ - T80 - Primed CD8$^+$ T-cell count:

$$\frac{d}{dt}\left(T_0^8\right) = Pulled\left[T_0^8\right]_g + \underbrace{\alpha_2 T_0^8\left(\frac{M_A}{M_A+c_{15}}\right)}_{\text{Proliferation}}$$
$$-\underbrace{k_6 I_{12} T_0^8\left(\frac{I_\gamma}{I_\gamma+f_1 I_4+f_7 I_{10}+s_1}\right)}_{\text{Differentiation to } T^8 \text{ and } T_C} - \underbrace{\mu_{T_0} T_0^8}_{\text{Natural death}}$$

$T^8$ - T8 - Effector CD8$^+$ T-cell count

$$\frac{d}{dt}\left(T^8\right) = \underbrace{(m) k_6 I_{12} T_0^8\left(\frac{I_\gamma}{I_\gamma+f_1 I_4+f_7 I_{10}+s_1}\right)}_{\text{Differentiation from } T_0^8} + \underbrace{k_{34} T_{EM}^8 M_I\left(\frac{M_I}{M_I+3}\right)}_{\text{Differentiation from } T_{EM}^8} - \underbrace{\mu_{T_{C\gamma}}\left(\frac{I_\gamma}{I_\gamma+c_c}\right) T^8 M_A}_{\text{IFN}\gamma\text{ apoptosis}} - \underbrace{\mu_{T_C} T_8}_{\text{Natural death}}$$

$T_C$ - TC - Cytotoxic CD8$^+$ T-cell count

$$\frac{d}{dt}(T_C) = \underbrace{(1-m)k_6 I_{12} T_0^8 \left(\frac{I_\gamma}{I_\gamma + f_1 I_4 + f_7 I_{10} + s_1}\right)}_{\text{Differentiation from } T_0^8} + \underbrace{k_{33} T_{EM}^8 M_I \left(\frac{M_I}{M_I + 3}\right)}_{\text{Differentiation from } T_{EM}^8} - \underbrace{\mu_{T_{C\gamma}} \left(\frac{I_\gamma}{I_\gamma + c_c}\right) T_C M_A}_{\text{IFN}\gamma \text{ apoptosis}} + \underbrace{\mu_{T_C} T_C}_{\text{Natural death}}$$

$T_{EM}^8$- EMCD8 - Effector Memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(T_{EM}^8\right) = Pulled\left[T_{EM}^8\right]_g - \underbrace{k_{33} T_{EM}^8 M_I \left(\frac{M_I}{M_I + 3}\right)}_{\text{Differentiation to } T_C} - \underbrace{k_{34} T_{EM}^8 M_I \left(\frac{M_I}{M_I + 3}\right)}_{\text{Differentiation to } T^8} - \underbrace{\mu_{T_{EM}^8} T_{EM}^8}_{\text{Natural death}}$$

$T_{Non}^8$ -CD8Non - Non-cognate CD8$^+$ T-cell count

$$\frac{d}{dt}\left(T_{Non}^8\right) = Pulled\left[T_{Non}^8\right]_g - \underbrace{\mu_{T_{Non}^8} T_{Non}^8}_{\text{Natural death}}$$

1.5. **Cytokines.**

$F_\alpha$ - TNF -TNF-$\alpha$ concentration

$$\frac{d}{dt}(F_\alpha) = \underbrace{\alpha_{30} M_I}_{\text{Production by } M_I} + \underbrace{\alpha_{31} M_A \left(\frac{I_\gamma + \beta_2 (B_E + wB_I)}{I_\gamma + \beta_2 (B_E + wB_I) + f_1 I_4 + f_7 I_{10} + s_{10}}\right)}_{\text{IFN-IL mediated production of TNF}\alpha \text{ by } M_A}$$

$$+ \underbrace{\alpha_{32} T_1^4}_{\text{Production by } T_1^4} + \underbrace{\alpha_{33}\left(\frac{T_C + T^8}{2m}\right)}_{\text{Production by CD8}^+ \text{ T-cells}} - \underbrace{\mu_{F_\alpha} F_\alpha}_{\text{Decay}}$$

$I_\gamma$ - IG - Interferon-gamma

$$\frac{d}{dt}(I_\gamma) = \underbrace{s_g \left(\frac{B_E + wB_I}{B_E + wB_I + c_{10}}\right)\left(\frac{I_{12}}{I_{12} + s_7}\right)}_{\text{Other}} + \underbrace{\alpha_{5a} T_1^4 \left(\frac{M_A}{M_A + c_{5a}}\right)}_{\text{Production by } T_1^4} + \underbrace{\alpha_{5b} T^8 \left(\frac{M_A}{M_A + c_{5b}}\right)}_{\text{Production by } T^8} + \underbrace{\alpha_{5c} M_I}_{\text{Production by } M_I}$$

$$+ \underbrace{\alpha_7 T_0^4 \left(\frac{I_{12}}{I_{12} + f_4 I_{10} + s_4}\right) + \alpha_7 T_0^8 \left(\frac{I_{12}}{I_{12} + f_4 I_{10} + s_4}\right)}_{\text{Interleukin-mediated production by primed T-cells}} - \underbrace{\mu_{I_\gamma} I_\gamma}_{\text{Decay}}$$

$I_{12}$ - I12 - Interleukin-12

$$\frac{d}{dt}(I_{12}) = \underbrace{s_{12}\left(\frac{B_E + wB_I}{B_E + wB_I + c_{230}}\right)}_{\text{Other}} + \underbrace{\alpha_{23} M_R \left(\frac{B_E + wB_I}{B_E + wB_I + c_{23}}\right)}_{\text{Production by } M_R} + \underbrace{\alpha_8 M_A \left(\frac{s}{s + I_{10}}\right)}_{\text{Production by } M_A} - \underbrace{\mu_{I_{12}} I_{12}}_{\text{Decay}}$$

$I_{10}$ - I10 - Interleukin-10

$$\frac{d}{dt}(I_{10}) = \underbrace{\delta_7 (M_I + M_A)\left(\frac{s_6}{I_{10} + f_6 I_\gamma + s_6}\right)}_{\text{IFN-IL mediated production by macrophages}} + \underbrace{\alpha_{16} T_1^4 + \alpha_{17} T_2^4}_{\text{Production by CD4}^+ \text{ T-cells}} + \underbrace{\alpha_{18}\left(\frac{T_C + T^8}{2m}\right)}_{\text{Production by CD8}^+ \text{ T-cells}} - \underbrace{\mu_{I_{10}} I_{10}}_{\text{Decay}}$$

$I_4$ - I4 - Interleukin-4

$$\frac{d}{dt}(I_4) = \underbrace{\alpha_{11} T_0^4}_{\text{Production by } T_0^4} + \underbrace{\alpha_{12} T_2^4}_{\text{Production by } T_2^4} - \underbrace{\mu_{I_4} I_4}_{\text{Decay}}$$

## 2. Lymph node and blood equations

The lymph node compartment will clonally expand and differentiate effector cells to be sent to the blood. Cells from the blood can be recruited to granulomas based on their request. We select each parameter in the following equations using the LHS sampling scheme using the ranges presented in Section 5.2. Terms indicated by $Pulled\left[\cdot\right]_g$ involve quantities pulled at each time step by lung granulomas, is described in Section 3. Below is an index of all state variables in the lymph nodes and blood.

| Variable | Searchable name | Unit | Variable description |
|---|---|---|---|
| | **Lymph Node** | | |
| $APC$ | APC | count | Antigen-presenting cells in LN |
| $N_4^{LN}$ | LnN4 | count | Mtb-specific naive CD4$^+$ T-cell count in LN |
| $P_4^{LN}$ | LnP4 | count | Mtb-specific precursor CD4$^+$ T-cell count in LN |
| $E_4^{LN}$ | LnE4 | count | Mtb-specific effector CD4$^+$ T-cell count in LN |
| $CM_4^{LN}$ | LnCM4 | count | Mtb-specific central memory CD4$^+$ T-cell count in LN |
| $EM_4^{LN}$ | LnEM4 | count | Mtb-specific effector memory CD4$^+$ T-cell count in LN |
| $N_{Non,4}^{LN}$ | LnN4Non | count | Nonspecific naive CD4$^+$ T-cell count in LN |
| $CM_{Non,4}^{LN}$ | LnCM4Non | count | Nonspecific central memory CD4$^+$ T-cell count in LN |
| $N_8^{LN}$ | LnN8 | count | Mtb-specific naive CD8$^+$ T-cell count in LN |
| $P_8^{LN}$ | LnP8 | count | Mtb-specific precursor CD8$^+$ T-cell count in LN |
| $E_8^{LN}$ | LnE8 | count | Mtb-specific effector CD8$^+$ T-cell count in LN |
| $CM_8^{LN}$ | LnCM8 | count | Mtb-specific central memory CD8$^+$ T-cell count in LN |
| $EM_8^{LN}$ | LnEM8 | count | Mtb-specific effector memory CD8$^+$ T-cell count in LN |
| $N_{Non,8}^{LN}$ | LnN8Non | count | Nonspecific naive CD8$^+$ T-cell count in LN |
| $CM_{Non,8}^{LN}$ | LnCM8Non | count | Nonspecific central memory CD8$^+$ T-cell count in LN |
| | **Blood** | | |
| $N_4^B$ | BlN4 | pg/mL | Mtb-specific naive CD4$^+$ T-cell count in blood |
| $E_4^B$ | BlE4 | pg/mL | Mtb-specific effector CD4$^+$ T-cell count in blood |
| $CM_4^B$ | BlCM4 | pg/mL | Mtb-specific central memory CD4$^+$ T-cell count in blood |
| $EM_4^B$ | BlEM4 | pg/mL | Mtb-specific effector memory CD4$^+$ T-cell count in blood |
| $N_{Non,4}^B$ | BlN4Non | pg/mL | Nonspecific naive CD4$^+$ T-cell count in blood |
| $E_{Non,4}^B$ | BlE4Non | pg/mL | Nonspecific effector CD4$^+$ T-cell count in blood |
| $CM_{Non,4}^B$ | BlCM4Non | pg/mL | Nonspecific central memory CD4$^+$ T-cell count in blood |
| $EM_{Non,4}^B$ | BlEM4Non | pg/mL | Nonspecific effector memory CD4$^+$ T-cell count in blood |
| $N_8^B$ | BlN8 | pg/mL | Mtb-specific naive CD8$^+$ T-cell count in blood |
| $E_8^B$ | BlE8 | pg/mL | Mtb-specific effector CD8$^+$ T-cell count in blood |
| $CM_8^B$ | BlCM8 | pg/mL | Mtb-specific central memory CD8$^+$ T-cell count in blood |
| $EM_8^B$ | BlEM8 | pg/mL | Mtb-specific effector memory CD8$^+$ T-cell count in blood |
| $N_{Non,8}^B$ | BlN8Non | pg/mL | Nonspecific naive CD8$^+$ T-cell count in blood |
| $E_{Non,8}^B$ | BlE8Non | pg/mL | Nonspecific effector CD8$^+$ T-cell count in blood |
| $CM_{Non,8}^B$ | BlCM8Non | pg/mL | Nonspecific central memory CD8$^+$ T-cell count in blood |
| $EM_{Non,8}^B$ | BlEM8Non | pg/mL | Nonspecific effector memory CD8$^+$ T-cell count in blood |

### 2.1. Antigen Presenting Cells.

$APC$ - APC - Antigen presenting cells. Received APCs are given from granulomas, which is detailed in Section 3.

$$\frac{d}{dt}(APC) = -\mu_5 APC + \sum_{i\in\{\text{Granulomas}\}} \text{Received from Granuloma } i$$

### 2.2. CD4$^+$ T-cells in lymph nodes.

$N_4^{LN}$ - LnN4 - CD4$^+$ Mtb-specific Naive T-cell count (Lymph node)

$$\frac{d}{dt}(N_4^{LN}) = \alpha\left[\underbrace{k_1 N_4^B\left(\frac{APC}{APC+hs_1}\right)}_{\text{Cytokine-driveen recruitment}} + \underbrace{\xi_1 N_4^B}_{\text{LN Influx}}\right] - \underbrace{\xi_2 N_4^{LN}}_{\text{LN Efflux}} - \underbrace{k_2 N_4^{LN} APC}_{\text{Differentiation into } P_4^{LN}}$$

$P_4^{LN}$ - LnP4 - CD4$^+$ Mtb-specific Precursor T-cell count (Lymph node)

$$\begin{aligned}\frac{d}{dt}(P_4^{LN}) = &\underbrace{k_2 N_4^{LN} APC}_{\text{Differentiation from } N_4^{LN}} + \underbrace{k_3 CM_4^{LN} APC}_{\text{Differentiation from } CM_4^{LN}} + \underbrace{k_4 P_4^{LN}\left(1-\frac{P_4^{LN}}{\rho_1}\right)\left(\frac{APC}{APC+hs_4}\right)}_{\text{Proliferation}} \\ &- \underbrace{k_5 P_4^{LN}\left(\frac{APC}{APC+hs_5}\right)}_{\text{Differention into } E_4^{LN}} - \underbrace{k_6 P_4^{LN}\left(1-\frac{APC}{APC+hs_5}\right)}_{\text{Differentiation into } CM_4^{LN}} - \underbrace{\mu_6 P_4^{LN}}_{\text{Natural death}}\end{aligned}$$

$E_4^{LN}$- LnE4 - CD4$^+$ Mtb-specific effector T-cell count (Lymph Node)

$$\frac{d}{dt}(E_4^{LN}) = \underbrace{k_5 P_4^{LN}\left(\frac{APC}{APC+hs_5}\right)}_{\text{Differention from } P_4^{LN}} - \underbrace{\xi_3 E_4^{LN}}_{\text{LN Efflux}} - \underbrace{k_7 E_4^{LN}}_{\text{Differentiation into } EM_4^{LN}}$$

$CM_4^{LN}$- LnCM4 - CD4$^+$ Mtb-specific central memory T-cell count (Lymph Node)

$$\begin{aligned}\frac{d}{dt}(CM_4^{LN}) = &\alpha\left[\underbrace{k_8 CM_4^B\left(\frac{APC}{APC+hs_8}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_4 CM_4^B}_{\text{LN Influx}}\right] + \underbrace{k_6 P_4^{LN}\left(1-\frac{APC}{APC+hs_5}\right)}_{\text{Differentiation from } P_4^{LN}} \\ &- \underbrace{k_3 CM_4^{LN} APC}_{\text{Differentiation to } P_4^{LN}} - \underbrace{\xi_5 CM_4^{LN}}_{\text{LN Efflux}}\end{aligned}$$

$EM_4^{LN}$ - LnEM4 - CD4$^+$ Mtb-specific effector memory T-cell count (Lymph Node)

$$\frac{d}{dt}(EM_4^{LN}) = \underbrace{k_7 E_4^{LN}}_{\text{Differentiation from } E_4^{LN}} - \underbrace{\xi_6 EM_4^{LN}}_{\text{LN Efflux}}$$

$N_{Non,4}^{LN}$ - LnN4Non - Non-cognate naive CD4$^+$ T-cell count

$$\frac{d}{dt}(N_{Non,4}^{LN}) = \alpha\left(\underbrace{k_1 N_{Non,4}^B\left(\frac{APC}{APC+hs_1}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_1 N_{Non,4}^B}_{\text{LN Influx}}\right) - \underbrace{\xi_2 N_{Non,4}^{LN}}_{\text{LN Efflux}}$$

$CM_{Non,4}^{LN}$ - LnCM4Non - Non-cognate central memory CD4$^+$ T-cell count

$$\frac{d}{dt}\left(CM_{Non,4}^{LN}\right) = \alpha\left(\underbrace{k_8 CM_{Non,4}^{B}\left(\frac{APC}{APC+hs_8}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_4 CM_{Non,4}^{B}}_{\text{LN Influx}}\right) - \underbrace{\xi_5 CM_{Non,4}^{LN}}_{\text{LN Efflux}}$$

### 2.3. CD8$^+$ T-cells in lymph nodes.

$N_8^{LN}$ - LnN8 - Mtb-specific naive CD8$^+$ T-cell count

$$\begin{aligned}\frac{d}{dt}\left(N_8^{LN}\right) =&\alpha\left(\underbrace{k_{10}N_8^{B}\left(\frac{APC}{APC+hs_{10}}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_7 N_8^{B}}_{\text{LN Influx}}\right) - \underbrace{\xi_8 N_8^{LN}}_{\text{LN Efflux}}\\ &-\underbrace{k_{11}N_8^{LN}APC\left(\frac{E_4^{LN}+w_{P_4}P_4^{LN}}{E_4^{LN}+w_{P_4}P_4^{LN}+hs_{11}}\right)}_{\text{Priming mediated by CD4-related cytokines}}\end{aligned}$$

$P_8^{LN}$ - LnP8 - Mtb-specific precursor CD8$^+$ T-cell count

$$\begin{aligned}\frac{d}{dt}\left(P_8^{LN}\right) =& \underbrace{k_{11}N_8^{LN}APC\left(\frac{E_4^{LN}+w_{P_4}P_4^{LN}}{E_4^{LN}+w_{P_4}P_4^{LN}+hs_{11}}\right)}_{\text{Priming mediated by CD4-related cytokines}} + \underbrace{k_{12}CM_8^{LN}APC}_{\text{Differentiation from } CM_8^{LN}}\\ &+\underbrace{k_{13}P_8^{LN}\left(1-\frac{P_8^{LN}}{\rho_1}\right)\left(\frac{APC}{APC+hs_{13}}\right)}_{\text{Cytokine-mediated proliferation}} - \underbrace{k_{15}P_8^{LN}\left(1-\left\{\frac{APC}{APC+hs_{14}}\right\}\right)}_{\text{Differentiation to } CM_8^{LN}}\\ &-\underbrace{k_{14}P_8^{LN}\left\{\frac{APC}{APC+hs_{14}}\right\}}_{\text{Differentiation to } E_8^{LN}} - \underbrace{\mu_7 P_8^{LN}}_{\text{Natural death}}\end{aligned}$$

$E_8^{LN}$ - LnE8 - Mtb-specific effector CD8$^+$ T-cell count

$$\frac{d}{dt}\left(E_8^{LN}\right) = \underbrace{k_{14}P_8^{LN}\left\{\frac{APC}{APC+hs_{14}}\right\}}_{\text{Differentiation from } P_8^{LN}} - \underbrace{\xi_9 E_8^{LN}}_{\text{LN Efflux}} - \underbrace{k_{16}E_8^{LN}}_{\text{Differentiation to } EM_8^{LN}}$$

$CM_8^{LN}$ - LnCM8 - Mtb-specific central memory CD8$^+$ T-cell count

$$\begin{aligned}\frac{d}{dt}\left(CM_8^{LN}\right) =&\alpha\left[\underbrace{k_{17}CM_8^{B}\left(\frac{APC}{APC+hs_{17}}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_{10}CM_8^{B}}_{\text{LN Influx}}\right] + \underbrace{k_{15}P_8^{LN}\left(1-\left\{\frac{APC}{APC+hs_{14}}\right\}\right)}_{\text{Differentiation from } P_8^{LN}}\\ &- \underbrace{k_{12}CM_8^{LN}APC}_{\text{Cytokine-mediated differentiation to } P_8^{LN}} - \underbrace{\xi_{11}CM_8^{LN}}_{\text{LN Efflux}}\end{aligned}$$

$EM_8^{LN}$ - LnEM8 - Mtb-specific effector memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(EM_8^{LN}\right) = \underbrace{k_{16}E_8^{LN}}_{\text{Differentiation from } E_8^{LN}} - \underbrace{\xi_{12}EM_8^{LN}}_{\text{LN Efflux}}$$

$N_{Non,8}^{LN}$ - LnN8Non - Non-cognate Naive CD8$^+$ T-cell count

$$\frac{d}{dt}\left(N^{LN}_{Non,8}\right) = \alpha\left[\underbrace{k_{10}N^{B}_{Non,8}\left(\frac{APC}{APC+hs_{10}}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_7 N^{B}_{Non,8}}_{\text{LN Influx}}\right] - \underbrace{\xi_8 N^{LN}_{Non,8}}_{\text{LN Efflux}}$$

$CM^{LN}_{Non,8}$ - LnCM8Non - Non-cognate central memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(C^{LN}_{Non,8}\right) = \alpha\left[\underbrace{k_{17}CM^{B}_{Non,8}\left(\frac{APC}{APC+hs_{17}}\right)}_{\text{Cytokine-mediated recruitment}} + \underbrace{\xi_{10} CM^{B}_{Non,8}}_{\text{LN Influx}}\right] - \underbrace{\xi_{11} CM^{LN}_{Non,8}}_{\text{LN Efflux}}$$

### 2.4. CD4$^+$ T-cells in blood.

$N^B_4$ - BlN4 - Mtb-specific naive CD4$^+$ T-cell count

$$\frac{d}{dt}\left(N^{B}_{4}\right) = \underbrace{\lambda S_{N_4}}_{\text{Source from Thymus}} + \underbrace{\alpha^{-1}\xi_2 N^{LN}_{4}}_{\text{LN Efflux}} - \underbrace{k_1 N^{B}_{4}\left(\frac{APC}{APC+hs_1}\right)}_{\text{Cytokine-mediated recruitment}} - \underbrace{\xi_1 N^{B}_{4}}_{\text{LN Influx}} - \underbrace{\mu_8 N^{B}_{4}}_{\text{Natural dath}}$$

$E^B_4$ - BlE4 - Mtb-specific effector CD4$^+$ T-cell count

$$\frac{d}{dt}\left(E^{B}_{4}\right) = \underbrace{\alpha^{-1}\xi_3 E^{LN}_{4}}_{\text{LN Efflux}} - \underbrace{\mu_1 E^{B}_{4}}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[E^{B}_{4}\right]_g$$

$CM^B_4$ - BlCM4 - Mtb-specific central memory CD4$^+$ T-cell count

$$\frac{d}{dt}\left(CM^{B}_{4}\right) = \underbrace{\alpha^{-1}\xi_5 CM^{LN}_{4}}_{\text{LN Efflux}} - \underbrace{\xi_4 CM^{B}_{4}}_{\text{LN Influx}} - \underbrace{k_8 CM^{B}_{4}\left(\frac{APC}{APC+hs_8}\right)}_{\text{Cytokine-mediated recruitment}}$$

$EM^B_4$ - BlEM4 - Mtb-specific effector memory CD4$^+$ T-cell count

$$\frac{d}{dt}\left(EM^{B}_{4}\right) = \underbrace{\alpha^{-1}\xi_6 EM^{LN}_{4}}_{\text{LN Efflux}} - \underbrace{\mu_2 EM^{B}_{4}}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[EM^{B}_{4}\right]_g$$

$N^B_{Non,4}$ - BlN4Non - Non-cognate naive CD4$^+$ T-cell count

$$\frac{d}{dt}\left(N^{B}_{Non,4}\right) = \underbrace{(1-\lambda)\, s_{N_4}}_{\text{Production in thymus}} + \underbrace{\alpha^{-1}\xi_2 N^{LN}_{Non,4}}_{\text{LN Efflux}} - \underbrace{k_1 N^{B}_{Non,4}\left(\frac{APC}{APC+hs_1}\right)}_{\text{Cytokine-mediated recruitment}} - \underbrace{\xi_1 N^{B}_{Non,4}}_{\text{LN Influx}} - \underbrace{\mu_8 N^{B}_{Non,4}}_{\text{Natural death}}$$

$E^B_{Non,4}$ - BlE4Non - Non-cognate effector CD4$^+$ T-cell count

$$\frac{d}{dt}\left(E^{B}_{Non,4}\right) = \underbrace{s_{E_{Non,4}}}_{\text{Production in thymus}} - \underbrace{\mu_4 E^{B}_{Non,4}}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[E^{B}_{Non,4}\right]_g$$

$CM^B_{Non,4}$ - BlCM4Non - Non-cognate central memory CD4$^+$ T-cell count

$$\frac{d}{dt}\left(CM^{B}_{Non,4}\right) = \underbrace{\alpha^{-1}\xi_5 CM^{LN}_{Non,4}}_{\text{LN Efflux}} - \underbrace{\xi_4 CM^{B}_{Non,4}}_{\text{LN Influx}} - \underbrace{k_8 CM^{B}_{Non,4}\left(\frac{APC}{APC+hs_8}\right)}_{\text{Cytokine-mediated recruitment}}$$

$EM^B_{Non,4}$ - BlEM4Non - Non-cognate effector memory CD4$^+$ T-cell count

$$\frac{d}{dt}\left(EM^{B}_{Non,4}\right) = \underbrace{s_{EM_{Non,4}}}_{\text{Source from thymus}} - \underbrace{\mu_2 EM^{B}_{Non,4}}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[EM^{B}_{Non,4}\right]_g$$

2.5. **CD8$^+$ T-cells in blood.**

$N_8^B$ - BlN8 Mtb-specific naive CD8$^+$ T-cell count

$$\frac{d}{dt}\left(N_8^B\right) = \underbrace{\lambda s_{N_8}}_{\text{Source from thymus}} + \underbrace{\alpha^{-1}\xi_8 N_8^{LN}}_{\text{LN efflux}} - \underbrace{k_{10}N_8^B\left(\frac{APC}{APC+hs_{10}}\right)}_{\text{Cytokine-mediated recruitment}} - \underbrace{\xi_7 N_8^B}_{\text{LN Influx}} - \underbrace{\mu_9 N_8^B}_{\text{Natural death}}$$

$E_8^B$ - BlE8 - Mtb-specific effector CD8$^+$ T-cell count

$$\frac{d}{dt}\left(E_8^B\right) = \underbrace{\alpha^{-1}\xi_9 E_8^{LN}}_{\text{LN Efflux}} - \underbrace{\mu_3 E_8^B}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[E_8^B\right]_g$$

$CM_8^B$ - BlCM8 - Mtb-specific central memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(CM_8^B\right) = \underbrace{\alpha^{-1}\xi_{11} CM_8^{LN}}_{\text{LN Efflux}} - \underbrace{\xi_{10} CM_8^B}_{\text{LN Influx}} - \underbrace{k_{17}CM_8^B\left(\frac{APC}{APC+hs_{17}}\right)}_{\text{Cytokine-mediated recruitment}}$$

$EM_8^B$ - BlEM8 - Mtb-specific Effector memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(EM_8^B\right) = \underbrace{\alpha^{-1}\xi_{12} EM_8^{LN}}_{\text{LN Efflux}} - \underbrace{\mu_4 EM_8^B}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[EM_8^B\right]_g$$

$N_{Non,8}^B$ - BlN8Non - Non-cognate naive CD8$^+$ T-cell count

$$\begin{aligned}\frac{d}{dt}\left(N_{Non,8}^B\right) = & \underbrace{(1-\lambda)\, s_{N_8}}_{\text{Source from thymus}} + \underbrace{\alpha^{-1}\xi_8 N_{Non,8}^{LN}}_{\text{LN Efflux}} \\ & - \underbrace{k_{10}N_{Non,8}^B\left(\frac{APC}{APC+hs_{10}}\right)}_{\text{Cytokine-mediated recruitment}} - \underbrace{\xi_7 N_{Non,8}^B}_{\text{LN Influx}} - \underbrace{\mu_9 N_{Non,8}^B}_{\text{Natural death}}\end{aligned}$$

$E_{Non,8}^B$ - BlE8Non - Non-cognate effector CD8$^+$ T-cell count

$$\frac{d}{dt}\left(E_{Non,8}^B\right) = \underbrace{s_{E_{Non,8}}}_{\text{Source from thymus}} - \underbrace{\mu_3 E_{Non,8}^B}_{\text{Natural death}} \sum_{g\in Granulomas} Pulled\left[E_{Non,8}^B\right]_g$$

$CM_{Non,8}^B$ - BlCM8Non - Non-cognate central memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(CM_{Non,8}^B\right) = \underbrace{\alpha^{-1}\xi_{11} CM_{Non,8}^{LN}}_{\text{LN Efflux}} - \underbrace{\xi_{10} CM_{Non,8}^B}_{\text{LN Influx}} - \underbrace{k_{17}CM_{Non,8}^B\left(\frac{APC}{APC+hs_{17}}\right)}_{\text{Cytokine-mediated recruitment}}$$

$EM_{Non,8}^B$ - BlEM8Non - Non-cognate effector memory CD8$^+$ T-cell count

$$\frac{d}{dt}\left(EM_{Non,8}^B\right) = \underbrace{s_{EM_{Non,8}}}_{\text{Source from thymus}} - \underbrace{\mu_4 EM_{Non,8}^B}_{\text{Natural death}} - \sum_{g\in Granulomas} Pulled\left[EM_{Non,8}^B\right]_g$$

## 3. Coupling granuloma equations to lymph node and blood equations

3.1. **Migration of APCs from granulomas to lymph nodes.** Each granuloma begins to send a portion of its infected macrophages to the lymph node compartment. We use infected macrophages $M_I$ as a proxy for the number of dendritic cells that take Mtb to the lymph node. Each granuloma sends APCs to the lymph nodes after time $\tau_s$ under the assumption that granulomas do not immediately begin to send dendritic cells to the lymphatic system. We compute APCs sent by granuloma $g$ to the lymph node as:

$$APC \text{ Sent by Granuloma } g \text{ at time } t \text{ post-founding} = \begin{cases} 0 & \text{if } t < \tau_s \\ A \cdot M_I & \text{otherwise.} \end{cases}$$

3.2. **Granulomas requests T-cells, and pulls from the blood compartment.** In *HostSim*, a given host begins with 13 granulomas. As infection progresses, each granuloma will begin to attempt to recruit six types of T-cells from the blood compartment: $T_0^4, T_0^8, T_{EM}^4, T_{EM}^8, T_{Non}^4$, and $T_{Non}^8$. At each time step, each granuloma will independently request a number of T-cells given below:

- Requests for $T_0^4$ :

$$\mathit{Requested}\left[T_0^4\right] = \underbrace{\alpha_{1a}\left(w_2 M_I + M_A\right)}_{\text{Macrophage-mediated request}} + \underbrace{Sr_{1b}\left(\frac{F_\alpha}{F_\alpha + f_8 I_{10} + s_{4b2}}\right)}_{\text{TNF-mediated request}}$$

- Requests for $T_0^8$ :

$$\mathit{Requested}\left[T_0^8\right] = \underbrace{\alpha_{1a}\left(M_A + w_2 M_I\right)}_{\text{Macrophage-mediated recruitment}} + \underbrace{Sr_{1b}\left(\frac{F_\alpha}{F_\alpha + f_8 I_{10} + s_{4b2}}\right)}_{\text{TNF mediated recruitment}}$$

- Requests for $T_{EM}^4$:

$$\mathit{Requested}\left[T_{EM}^4\right] = \underbrace{Sr_{4EM}\left(\frac{F_\alpha}{F_\alpha + c_{4EM}}\right)}_{\text{TNF driven recruitment}}$$

- Requests for $T_{EM}^8$:

$$\mathit{Requested}\left[T_{EM}^8\right] = \underbrace{Sr_{8EM}\left(\frac{F_\alpha}{F_\alpha + hs_{8EM}}\right)}_{\text{TNF-mediated recruitment}}$$

- Requests for $T_{Non}^4$:

$$\mathit{Requested}\left[T_{Non}^4\right] = \underbrace{Sr_{4Non}\left(\frac{F_\alpha}{F_\alpha + hs_{4Non}}\right)}_{\text{TNF driven recruitment}}$$

- Requests for $T_{Non}^8$:

$$\mathit{Requested}\left[T_{Non}^8\right] = \underbrace{Sr_{8Non}\left(\frac{F_\alpha}{F_\alpha + hs_{8Non}}\right)}_{\text{TNF driven recruitment}}$$

The blood's response to these requests is to provide lung each granuloma with T-cells. Since we model the T-cell subpopulations in more granularity in the lymph node and blood compartments, we associate the following populations between the terminology of the lymph node and blood equations; and the granuloma equations.

(1) Granuloma requests for $T_0^4$ pull from Lymph/blood concentration $E_4^B$.
(2) Granuloma requests for $T_0^8$ pull from Lymph/blood concentration $E_8^B$.
(3) Granuloma requests for $T_{EM}^4$ pull from Lymph/blood concentration $EM_4^B$.
(4) Granuloma requests for $T_{EM}^8$ pull from Lymph/blood concentration $EM_8^B$.
(5) Granuloma requests for $T_{Non}^4$ pull from both Lymph/blood concentrations $E_{Non,4}^B$ and $EM_{Non,4}^B$.
(6) Granuloma requests for $T_{Non}^8$ pull from both Lymph/blood concentrations $E_{Non,8}^B$ and $EM_{Non,8}^B$.

For $T_0^4, T_0^8, T_{EM}^4$, and $T_{EM}^8$, the amount that is pulled from the blood to provide to granuloma $g$ is given by:

$$\underbrace{\mathit{Pulled}\left[T^*\right]_g}_{T\text{ - Cell count}} = \alpha \cdot \underbrace{\mathit{Pulled}\left[E^*\right]_g}_{E\text{ - Concentration}}$$
$$= \begin{cases} \mathit{Requested}\left[T^*\right]_g & \text{if } \sum_{\text{Granulomas } j} \mathit{Requested}\left[T^*\right]_j < \alpha \cdot E^* \\ \mathit{Relative\ Request}\left[T^*\right]_g & \text{otherwise.} \end{cases}$$

Here, if there are not enough T-cells in the blood to meet the amount requested by the lung granulomas, available T-cells will be divided among the requesting granulomas by using the following relative request. For granuloma $g$, its relative request is

$$\mathit{Relative\ Request}\left[T^*\right]_g = \frac{\alpha \cdot E^*}{\sum_{\text{All granulomas}j} \mathit{Request}\left[T^*\right]_j}.$$

For $T^4_{Non}$ and $T^8_{Non}$, we combine their two associated blood concentrations. For example,

$$\begin{aligned}\mathit{Pulled}\left[T^4_{Non}\right]_g &= \alpha\left(\mathit{Pulled}\left[E^B_{Non,4}\right]_g + \mathit{Pulled}\left[EM^B_{Non,4}\right]_g\right)\\ &= \begin{cases}\mathit{Requested}\left[T^4_{Non}\right]_g & \text{if } \sum_{\text{Granulomas } j} \mathit{Requested}\left[T^4_{Non}\right]_j < \alpha\left(E^B_{Non,4} + EM^B_{Non,4}\right)\\ \mathit{Relative\ Request}\left[T^4_{Non}\right]_g & \text{otherwise}\end{cases}.\end{aligned}$$

If the blood has excess T-cells ($E^B_{Non,4}$ and $EM^B_{Non,4}$ in this case), the weight of their contribution to the granulomas is based on their current relative population:

$$\alpha \cdot \mathit{Pulled}\left[E^B_{Non,4}\right]_g = \mathit{Requested}\left[T^4_{Non}\right]_g \frac{E^B_{Non,4}}{\left(E^B_{Non,4} + EM^B_{Non,4}\right)};$$

$$\alpha \cdot \mathit{Pulled}\left[EM^B_{Non,4}\right]_g = \mathit{Requested}\left[T^4_{Non}\right]_g \frac{EM^B_{Non,4}}{\left(E^B_{Non,4} + EM^B_{Non,4}\right)}.$$

If there are not enough T-cells for the request, the relative requests are calculated similarly and the blood concentration is exhausted:

$$\alpha \cdot \mathit{Pulled}\left[E^B_{Non,4}\right]_g = \frac{\mathit{Requested}\left[T^4_{Non}\right]_g}{\sum_{\text{Granulomas } j} \mathit{Requested}\left[T^4_{Non}\right]_j} \frac{E^B_{Non,4}}{\left(E^B_{Non,4} + EM^B_{Non,4}\right)};$$

$$\alpha \cdot \mathit{Pulled}\left[EM^B_{Non,4}\right]_g = \frac{\mathit{Requested}\left[T^4_{Non}\right]_g}{\sum_{\text{Granulomas } j} \mathit{Requested}\left[T^4_{Non}\right]_j} \frac{EM^B_{Non,4}}{\left(E^B_{Non,4} + EM^B_{Non,4}\right)}.$$

Pulled concentrations for $T^8_{Non}$ are calculated in the same way.

## 4. Dissemination

In *HostSim*, nonsterile granulomas have a chance of disseminating. Each granuloma begins with a local dissemination probability adjustment $L_t$ and nonlocal dissemination probability adjustment $N_t$ when the granuloma is created (either primary at $t = 0$, or at some later time). At each timestep, a dissemination event is determined randomly determining:

$$\{\text{Local dissemination occurs at time } t\} = (L_t + U[0,1]) > 1$$

and

$$\{\text{Nonlocal dissemination occurs at time } t\} = (N_t + U[0,1]) > 1$$

At each time step, the probability adjustment of local dissemination increases:

$$L_t = L_{t-1} + \lambda_{local}\left(\frac{\left[B_I + B_E\right](t)}{\left[B_I + B_E\right](t) + k_{local}}\right).$$

Similarly, nonlocal dissemination probability adjustment builds as

$$N_t = N_{t-1} + \lambda_{nonlocal}\left(\frac{\left[B_I + B_E\right](t)}{\left[B_I + B_E\right](t) + k_{nonlocal}}\right).$$

A new locally-disseminated granuloma is created with its parameters selected to be normally distributed around the parameter values of the primary granuloma that it disseminated from (with $\sigma = 10\%$ of parent value). This is because of the assumption that nearby lung tissue conditions give rise to similar dynamics.

Nonlocally disseminated granlomas are given parameters uniformly sampled out of the ranges presented in Section 5.

Disseminated granulomas begin with one infected macrophage and an average number of intracellular bacteria from its parent ($B_I/M_I$ from the primary granuloma that seeded it).

## 5. Parameter Ranges

**5.1. Granuloma parameter ranges.** Note that the rate constants $k_i$ in the granuloma compartment and LN/blood compartment are different.

| Parameter | Non-symbolic | Units | Description | Minimum Value | Maximum Value |
|---|---|---|---|---|---|
| $s_{rm}$ | Srm | 1/day | $M_R$ recruitment rate | 0 | 0 |
| $\alpha_{4a}$ | alpha4a | 1/day | Macrophage-driven $M_R$ recruitment rate | 0.7246 | 0.9097 |
| $\beta$ | Beta | 1/pg | Scaling factor for $F_\alpha$ for $M_R$ activation | 8652476.9683 | 11390938.3080 |
| $w$ | w | - | Contribution of $B_I$ to $M_R$ recruitment | 0.2601 | 0.3632 |
| $w_2$ | w2 | - | Contribution of $M_I$ to $M_R$ recruitment | 0.9572 | 1.1725 |
| $w_3$ | w3 | - | Contribution of $T_1^4$ to $M_I$ apoptosis | 0.1 | 0.5 |
| $Sr_{4b}$ | Sr4b | 1/day | $F_\alpha$ recruitment rate of $M_R$ | 61.6952 | 947.9850 |
| $f_8$ | f8 | - | Ratio adjustment of $I_{10}/F_\alpha$ on $M_R$ recruitment | 0.02568 | 0.9748 |
| $f_9$ | f9 | - | Ratio adjustment of $I_{10}/F_\alpha$ for apoptosis rates | 0.1 | 1.0 |
| $s_{4b}$ | s4b | pg/mL | Half saturation of $F_\alpha$ on $M_R$ recruitment | 48.02390 | 427.4012 |
| $k_4$ | k4 | 1/day | $M_A$ decativation by $I_{10}$ | 0.08308 | 0.1599 |
| $s_8$ | s8 | pg/mL | Half saturation of $I_{10}$ on $M_A$ deactivation | 118.2688 | 536.2867 |
| $k_2$ | k2 | 1/day | $M_R$ infection rate | 0.1182 | 0.5718 |
| $c_9$ | c9 | count | Half saturation of $B_E$ on $M_R$ infection | 1468.08355 | 9039.5524 |
| $k_3$ | k3 | 1/day | $M_R$ activation rate | 0.1134 | 0.4659 |
| $f_1$ | f1 | - | Ratio adjustment of $I_4/I_\gamma$ on $M_R$ activation | 132.009929 | 477.7016 |
| $s_1$ | s1 | pg/mL | Half saturation of $I_\gamma$ dependent $M_R$ activation | 2.6104 | 97.4874 |
| $c_8$ | c8 | count | Half saturation of $B_E$ and $B_I$ on $M_R$ activation | 3455.3760 | 6811.6706 |
| $\mu_{M_R}$ | muMR | 1/day | $M_R$ death rate | 0.004432 | 0.005695 |
| $k_{17}$ | k17 | 1/day | Maximum rate of $M_I$ bursting | 0.1048 | 0.2273 |
| $N$ | N | count | Carrying capacity of Mtb in one $M_I$ | 6.8186 | 26.3527 |
| $k_{14a}$ | k14a | 1/day | T-cell induced apoptosis rate of $M_I$ | 0.3029 | 0.5 |
| $c_4$ | c4 | count | Half saturation of $T_1^4/M_I$ on T-cell apoptosis | 1805.8568 | 9420.9084 |
| $k_{14b}$ | k14b | 1/day | $F_\alpha$-induced apoptosis rate | 0.2478 | 0.4838 |
| $k_{52}$ | k52 | 1/day | Cytotoxic killing rate of $M_I$ | 0.09547 | 0.3910 |
| $w_1$ | w1 | - | Contribution of $T_1^4$ to cytotoxic killing | 0.2192 | 0.7413 |
| $c_{62}$ | c52 | count | Half-saturation of $T_C$ on cytotoxic $M_I$ killing | 2588.9284 | 8088.5625 |
| $C_{T_1^4}$ | cT1 | count | Half saturation of $T_1^4$ on cytotoxic killing | 22.6446 | 88.4901 |
| $\mu_{M_I}$ | muMI | 1/day | $M_I$ death rate | 0.002965 | 0.003799 |
| $\mu_{M_A}$ | muMA | 1/day | $M_A$ death rate | 0.05 | 0.1 |
| $\alpha_{1a}$ | alpha1a | 1/day | Macrophage request rate of $T_0^4$ | 0.1769 | 0.4336 |

| Parameter | Non-symbolic | Units | Description | Minimum Value | Maximum Value |
|---|---|---|---|---|---|
| $Sr_{1b}$ | Sr1b | 1/day | $F_\alpha$ dependent $T_0^4$ recruitment | 25767.7947 | 53329.7803 |
| $s_{4b2}$ | s4b2 | pg/mL | Half saturation of $F_\alpha$ dependent $T_0^4$ recruitment | 996.03150 | 8822.9850 |
| $\alpha_2$ | alpha2 | 1/day | Maximum growht rate of $T_0^4$ | 0.04446 | 0.9666 |
| $c_{15}$ | c15 | count | Half saturation of $M_A$ proliferation of $T_0^4$ | 531.8574 | 9574.4150 |
| $k_6$ | k6 | 1/day | Maximum $T_0^4$ to $T_1^4$ differentiation rate | 0.003726 | 0.09727 |
| $f_7$ | f7 | - | Effect of $I_{10}$ on $I_\gamma$ induced $T_0^4 \to T_1^4$ differentiation | 6.2748 | 44.6670 |
| $k_7$ | k7 | 1/day | Maximum rate of $T_0^4 \to T_2^4$ differentiation | 0.2437 | 0.6125 |
| $f_2$ | f2 | - | Ratio adjustment of $I_\gamma/I_4$ on $T_0^4 \to T_2^4$ differentiation | 0.1938 | 0.4207 |
| $s_2$ | s2 | pg/mL | Half saturation of $I_4$ for $T_0^4 \to T_2^4$ differentiation | 36.3818 | 964.1090 |
| $\mu_{T_0}$ | muT0 | 1/day | CD3$^+$ primed T-cell death rate | 0.1957 | 0.2474 |
| $m$ | m | - | Fraction of differentiating $T_0^8$ that become $T^8$ (and not $T_C$) | 0.1364 | 0.8643 |
| $\mu_{T_g}$ | muTg | 1/day | $T_C$ death rate | 0.005308 | 0.09570 |
| $c$ | c | pg/mL | Half saturation of $I_\gamma$ on $T_1^4$ apoptosis | 462.9043 | 9539.3955 |
| $\mu_{T_1^4}$ | muT1 | 1/day | $T_1^4$ death rate | 0.2848 | 0.3698 |
| $\mu_{T_2^4}$ | muT2 | 1/day | $T_2^4$ death rate | 0.2913 | 0.3678 |
| $\mu_{T_{C\gamma}}$ | muTCg | 1/day | $I_\gamma$ driven apoptosis rate of $T_C$ and $T^8$ | 0.006021 | 0.09506 |
| $c_c$ | cc | pg/mL | Half saturation of $I_\gamma$ on $T_C$ and $T^8$ apoptosis | 368.2888 | 9634.1767 |
| $\mu_{T_C}$ | muTC | 1/day | $T_C$ death rate | 0.2570 | 0.3325 |
| $\alpha_{30}$ | alpha30 | 1/day | Rate of $F_\alpha$ production by $M_I$ | 0.04474 | 0.09741 |
| $\alpha_{31}$ | alpha31 | 1/day | Rate of $F_\alpha$ production by $M_A$ | 0.05071 | 0.09656 |
| $\beta_2$ | beta2 | 1/pg | Scaling factor of Mtb on $F_\alpha$ production by $M_A$ | 10944.8638 | 13022.3032 |
| $s_{10}$ | s10 | pg/mL | Half saturation of $I_\gamma$ on $F_\alpha$ production by $M_A$ | 102.8084 | 313.4010 |
| $\alpha_{32}$ | alpha32 | pg/(mL*day) | $F_\alpha$ production rate by $T_1^4$ | 0.2048 | 0.3447 |
| $\alpha_{33}$ | alpha33 | pg/(mL*day) | $F_\alpha$ production rate by $T^8$ and $T_C$ | 0.1815 | 0.3330 |
| $\mu_{TNF}$ | muTNF | 1/day | $F_\alpha$ decay rate | 0.9343 | 1.2101 |
| $s_g$ | sg | pg/(mL*day) | $I_\gamma$ production from other sources (e.g. dendritic cells) | 846.3332 | 5484.1532 |
| $c_{10}$ | c10 | count | Half saturation of Mtb production from other sources | 315332.8289 | 536623.8464 |
| $s_7$ | s7 | pg/mL | Half saturation of $I_{12}$ on $I_\gamma$ production from other sources | 591.2493 | 851.7672 |
| $\alpha_{5a}$ | alpha5a | pg/day | Rate of $I_\gamma$ production by $T_1^4$ | 0.5443 | 0.8698 |
| $c_{5a}$ | c5a | count | Half saturation of $M_A$ on $I_\gamma$ production by $T_1^4$ | 303.7365 | 687.08808 |
| $\alpha_{5b}$ | alpha5b | pg/day | $I_\gamma$ production by $T^8$ | 1.1445 | 15.1796 |
| $\alpha_{5c}$ | alpha5c | pg/day | $I_\gamma$ production by $M_I$ | 0.5192 | 0.9184 |
| $c_{5b}$ | c5b | count | Half saturation of $M_A$ on $I_\gamma$ production by $T^8$ | 235.8238 | 846.5511 |
| $\alpha_7$ | alpha7 | pg/day | $I_\gamma$ production by $T_0^4$ | 0.08541 | 0.3098 |
| $f_4$ | f4 | - | Adjustment of $I_{10}/I_{12}$ on $I_\gamma$ production | 1.2966 | 1.6715 |
| $s_4$ | s4 | pg/mL | Half saturation of I12 on $I_\gamma$ | 321.7448 | 865.2110 |
| $\mu_{I_\gamma}$ | muIG | 1/day | $I_\gamma$ decay rate | 5.4475 | 9.6934 |
| $\alpha_{23}$ | alpha23 | pg/day | Rate of $I_{12}$ production by $M_R$ | 0.003485 | 0.004652 |
| $c_{23}$ | c23 | count | Half saturation of Mtb on $I_{12}$ production by $M_R$ | 157.08445 | 525.4198 |

| Parameter | Non-symbolic | Units | Description | Minimum Value | Maximum Value |
|---|---|---|---|---|---|
| $\alpha_8$ | alpha8 | pg/day | Rate of production of $I_{12}$ by $M_A$ | 0.3764 | 0.8612 |
| $s_{12}$ | s12 | pg/day | Rate of production of $I_{12}$ by dendritic cells | 2361.1941 | 4060.7654 |
| $c_{230}$ | c230 | count | Half-saturation of Mtb in $I_{12}$ production by DCs | 365.6847 | 761.7284 |
| $\mu_{I_{12}}$ | muI12 | 1/day | $I_{12}$ decay rate | 0.9319 | 1.2420 |
| $s$ | s | pg/mL | $I_{10}$ effect on $I_{12}$ production by $M_A$ | 191.7181 | 694.3849 |
| $\delta_7$ | delta7 | pg/day | $I_{10}$ production by $M_A$ | 0.1106 | 0.6169 |
| $s_6$ | s6 | pg/mL | Half saturation of $I_{10}$ on self | 587.3834 | 858.9373 |
| $f_6$ | f6 | - | Ratio adjustment of $I_\gamma$ on $I_{10}$ | 0.3011 | 0.3889 |
| $\alpha_{16}$ | alpha16 | pg/day | $I_{10}$ production by $T_1^4$ | 0.4280 | 0.6693 |
| $\alpha_{17}$ | alpha17 | pg/day | $I_{10}$ production by $T_2^4$ | 0.4149 | 0.4786 |
| $\alpha_{18}$ | alpha18 | pg/day | $I_{10}$ production by $T_C$ and $T^8$ | 0.5184 | 0.6648 |
| $\mu_{I_{10}}$ | muI10 | 1/day | $I_{10}$ decay rate | 0.5064 | 4.1388 |
| $\alpha_{11}$ | alpha11 | pg/day | $I_4$ production by $T_0^4$ | 0.02944 | 0.06404 |
| $\alpha_{12}$ | alpha12 | pg/day | $I_4$ production by $T_2^4$ | 0.02110 | 0.06407 |
| $\mu_{I_4}$ | muI4 | 1/day | $I_4$ decay rate | 2.3700 | 3.08806 |
| $\alpha_{19}$ | alpha19 | 1/day | $B_I$ growth rate | 0.8739 | 1.3173 |
| $\alpha_{20}$ | alpha20 | 1/day | $B_E$ growth rate | 0.4190 | 0.5828 |
| $N_{fracc}$ | Nfracc | - | Fraction of surviving $B_I$ released by T-cell $M_I$ apop. | 0.3074 | 0.7893 |
| $N_{fraca}$ | Nfraca | - | Fraction of surviving $B_I$ released by TNF $M_I$ apop. | 0.2680 | 0.5658 |
| $k_{15}$ | k15 | 1/day | $B_E$ killing rate by $M_A$ | 0.03891 | 0.09025 |
| $k_{18}$ | k18 | 1/day | $B_E$ killing rate by $M_R$ | 0.0003264 | 0.0005505 |
| $N_{fracd}$ | Nfracd | - | Fraction of surviving $B_I$ released by $M_I$ natural death. | 0.0008721 | 0.001098 |
| $\mu_{B_I}$ | muBI | 1/day | $B_I$ death rate | 0.00005947 | 0.00009042 |
| $\mu_{B_E}$ | muBE | 1/day | $B_E$ death rate | 0.000000004107 | 0.000000007405 |
| $Sr_{4Non}$ | Sr4Non | 1/day | Rate of TNF-driven $T_{Non}^4$ recruitment | 155.6978 | 504.2867 |
| $hs_{4Non}$ | hs4Non | pg/mL | Half saturation of TNF in $T_{Non}^4$ recruitment | 5.6995 | 50.1242 |
| $\mu_{4Non}$ | mui4Non | 1/day | Death rate of $T_{Non}^4$ | 0.2631 | 0.3579 |
| $Sr_{8Non}$ | Sr8Non | 1/day | Rate of TNF-driven $T_{Non}^8$ recruitment | 153.04868 | 508.8051 |
| $hs_{8Non}$ | hs8Non | pg/day | Half saturation of TNF in $T_{Non}^8$ recruitment | 4.09874 | 40.7487 |
| $\mu_{T_{Non}^8}$ | mui8Non | 1/day | Death rate of $T_{Non}^8$ | 0.2644 | 0.3543 |

| Parameter | Non-symbolic | Units | Description | Minimum Value | Maximum Value |
|---|---|---|---|---|---|
| $Sr_{4EM}$ | Sr4EM | 1/day | Rate of TNF-driven $T^4_{EM}$ recruitment | 49.1138 | 100.03829 |
| $hs_{4EM}$ | hs4EM | pg/mL | Half saturation of TNF in $T^4_{EM}$ recruitment | 0.001 | 0.001 |
| $\mu_{T^4_{EM}}$ | mui4EM | 1/day | Death rate of $T^4_{EM}$ | 0.001368 | 0.002737 |
| $k_{31}$ | k31 | 1/day | Differentiation rate of $T^4_{EM} \to T^4_1$ | 0.005592 | 0.1 |
| $k_{32}$ | k32 | 1/day | Differentiation rate of $T^4_{EM} \to T^4_2$ | 0.0006898 | 0.001086 |
| $Sr_{EM^8}$ | Sr8EM | 1/day | Rate of TNF-driven $T^8_{EM}$ recruitment | 54.7352 | 105.4204 |
| $hs_{EM^8}$ | hs8EM | pg/mL | Half saturation of TNF in $T^8_{EM}$ recruitment | 0.001 | 0.001 |
| $\mu_{T^8_{EM}}$ | mui8EM | 1/day | Death rate of $T^8_{EM}$ | 0.001368 | 0.002737 |
| $k_{33}$ | k33 | 1/day | Differentiation rate of $T^8_{EM} \to T_C$ | 0.006339 | 0.1 |
| $k34$ | k34 | 1/day | Differentiation rate of $T^8_{EM} \to T^8$ | 0.005329 | 0.1 |
| $\tau_s$ | taus | days | Time that granuloma begins sending APCs to LN | 4.02618 | 22.1392 |
| $A$ | APCpercent | - | % of $M_I$ that get sent as APCs | 0.1723 | 0.2893 |
| $k_{local}$ | localDissemCFUHalf | count | Half-saturation of Mtb for local dissemination | 10000.0 | 50000.0 |
| $\lambda_{local}$ | localDissemLambda | 1/day | Maximum rate of local dissemination | 0.005 | 0.025 |
| $k_{nonlocal}$ | nonLocalDissemCFUHalf | count | Half-saturation of Mtb for nonlocal dissemination | 5223.04303 | 10608.01033 |
| $\lambda_{nonlocal}$ | nonLocalDissemLambda | 1/day | Maximum rate of nonlocal dissemination | 0.001 | 0.01 |
| $\mu_{B_N}$ | muBN | 1/day | Death rate of $B_N$ | 0.04032 | 0.06819 |
| $C_N$ | CN | - | Fraction of released $B_I$ that become $B_N$ | 0.1254 | 0.1725 |
| $N_f$ | Nf | M$\phi$/caseum | Macrophage biomass that becomes caseum | 2.09563 | 3.9056 |
| $N_{Ca}$ | Nca | 1/(day*caseum) | Clearance rate of caseum by neutrophils | 0.000001273 | 0.000008516 |

| Initial Condition | Non-Symbolic | Units | Description | Min initial value | Max inial value |
|---|---|---|---|---|---|
| $M_R(0)$ | MR | count | Resting macrophages | 1.0 | 5.0 |
| $M_I(0)$ | MI | count | Infected macrophages | 1.0 | 1.0 |
| $M_A(0)$ | MA | count | Activated macrophages | 1.0 | 1.0 |
| $B_I(0)$ | BI | count | Intracellular Mtb | 1.0 | 1.0 |
| $B_E(0)$ | BE | count | Extracellular Mtb | 0 | 0 |
| $B_N(0)$ | BN | count | Non-replicating Mtb | 0 | 0 |
| $T_0^4(0)$ | T40 | count | Mtb-specific Primed $CD4^+$ T-cells | 0 | 0 |
| $T_1^4(0)$ | Th1 | count | Mtb-specific Th1 $CD4^+$ T-cells | 0 | 0 |
| $T_{Non}^4(0)$ | CD4Non | count | Nonspecific $CD4^+$ T-cells | 0 | 0 |
| $T_2^4(0)$ | Th2 | count | Mtb-specific Th2 $CD4^+$ T-cells | 0 | 0 |
| $T_{EM}^8(0)$ | EMCD4 | count | Mtb-specific $CD4^+$ effector memory T-cells | 0 | 0 |
| $T_0^8(0)$ | T80 | count | Mtb-specific Primed $CD8^+$ T-cells | 0 | 0 |
| $T_C(0)$ | TC | count | Mtb-specific Cytotoxic $CD8^+$ T-cells | 0 | 0 |
| $T^8(0)$ | T8 | count | Mtb-specific Effector $CD8^+$ T-cells | 0 | 0 |
| $T_{EM}^8(0)$ | EMCD8 | count | Mtb-specific $CD8^+$ effector memory T-cells | 0 | 0 |
| $T_{Non}^8(0)$ | CD8Non | count | Nonspecific $CD8^+$ T-cells | 0 | 0 |
| $F_\alpha(0)$ | TNF | pg/mL | TNF-$\alpha$ concentration | 0 | 0 |
| $I_\gamma(0)$ | IG | pg/mL | IFN-$\gamma$ concentration | 0 | 0 |
| $I_{12}(0)$ | I12 | pg/mL | Interleukin 12 concentration | 0 | 0 |
| $I_{10}(0)$ | I10 | pg/mL | Interleukin 10 concentration | 0 | 0 |
| $I_4(0)$ | I4 | pg/mL | Interleukin 4 concentration | 0 | 0 |
| $Ca(0)$ | CA | mass of $M\phi$ | Necrotic tissue mass | 0 | 0 |

5.2. **Lymph Node and Blood parameter ranges.** Note that the rate constants $k_i$ in the granuloma compartment and LN/blood compartment are different.

| Parameter | non-symbolic | Units | Description | Lower range | Upper range |
|---|---|---|---|---|---|
| $\alpha$ | alpha | $\mu$L | Conversion from Blood concentration to LN cell counts | 360000.0 | 360000.0 |
| Host LNs | hostLn | count | Number of involved LNs in host (Used for initial conditions) | 5.0 | 5.0 |
| $\lambda$ | lambda | - | Frequency of Mtb-specific naive cells in the host | 0.0001 | 0.0001 |
| $hs_1$ | hs1 | count | Half saturation of $APC$ in $N_4^B$ recruitment to LN | 13.9295 | 70.7524 |
| $hs_{10}$ | hs10 | count | Half saturation of $APC$ in $N_8^B$ recruitment to LN | 45.5413 | 87.7386 |
| $hs_{11}$ | hs11 | count | Half saturation of CD4$^+$ surrogates in $N_8^{LN}$ priming | 12.9592 | 47.9200 |
| $hs_{13}$ | hs13 | count | Half saturation of $APC$ in $P_8^{LN}$ proliferation | 2684.2696 | 4055.8241 |
| $hs_{14}$ | hs14 | count | HS of $APC$ in $P_8^{LN} \to E_8^{LN}$ and $P_8^{LN} \to CM_8^{LN}$differentiation | 1904.3871 | 4144.4838 |
| $hs_{17}$ | hs17 | count | Half saturation of $APC$ in $CM_8^B$ recruitment to LN | 66.1225 | 403.04107 |
| $hs_4$ | hs4 | count | Half saturation of $APC$ in $P_4^{LN}$ proliferation | 1318.9532 | 4317.6863 |
| $hs_5$ | hs5 | count | HS of $APC$ in $P_4^{LN} \to E_4^{LN}$ and $P_4^{LN} \to CM_4^{LN}$ differentiation | 1257.1402 | 3718.5646 |
| $hs_8$ | hs8 | count | Half saturation of $APC$ in $CM_{Non,4}^B$ recruitment to LN | 40.4710 | 57.04244 |
| $k_1$ | k1 | 1/day | Rate of $N_4^B$ recruitment to LN | 0.1156 | 0.4736 |
| $k_{10}$ | k10 | 1/day | Rate of $N_8^B$ recruitment to LN | 0.7686 | 0.9663 |
| $k_{11}$ | k11 | 1/day | Rate of $N_8^{LN}$ priming | 0.0001043 | 0.0002272 |
| $k_{12}$ | k12 | 1/day | $CM_8^{LN}$ reactivation rate | 0.0001206 | 0.0007482 |
| $k_{13}$ | k13 | 1/day | Rate of $P_8^{LN}$ proliferation | 0.1961 | 0.7954 |
| $k_{14}$ | k14 | 1/day | Rate of $P_8^{LN} \to E_8^{LN}$ differentiation | 0.2548 | 0.7351 |
| $k_{15}$ | k15 | 1/day | Rate of $P_8^{LN} \to CM_8^{LN}$ differentiation | 0.5286 | 0.8602 |
| $k_{16}$ | k16 | 1/day | Rate of $E_8^{LN} \to EM_8^{LN}$ differentiation | 0.1573 | 0.8217 |
| $k_{17}$ | k17 | 1/day | Rate of $CM_8^B$ recruitment to LN | 0.3483 | 0.9012 |
| $k_2$ | k2 | 1/day | Rate of $N_4^{LN} \to P_4^{LN}$ differentiation | 0.3279 | 0.8656 |
| $k_3$ | k3 | 1/day | Rate of $CM_4^{LN} \to P_4^{LN}$ differentiation | 0.02161 | 0.07979 |
| $k_4$ | k4 | 1/day | Rate of $P_4^{LN}$ proliferation | 0.3131 | 1.3564 |
| $k_5$ | k5 | 1/day | Rate of $P_4^{LN} \to E_4^{LN}$ differentiation | 0.2721 | 0.8993 |
| $k_6$ | k6 | 1/day | Rate of $P_4^{LN} \to CM_4^{LN}$ differentiation | 0.3110 | 0.8645 |
| $k_7$ | k7 | 1/day | Rate of $E_4^{LN} \to EM_4^{LN}$ differentiation | 0.1493 | 0.5799 |
| $k_8$ | k8 | 1/day | Rate of $CM_4^B$ recruitment to LN | 0.02620 | 0.06984 |

| Parameter | Non-symbolic | Units | Description | Lower range | Upper range |
|---|---|---|---|---|---|
| $\mu_1$ | mu1 | 1/day | Death rate of $E_4^B$ | 0.2 | 0.2 |
| $\mu_2$ | mu2 | 1/day | Death rate of $EM_4^B$ | 0.001368 | 0.002737 |
| $\mu_3$ | mu3 | 1/day | Death rate of $E_8^B$ | 0.2 | 0.2 |
| $\mu_4$ | mu4 | 1/day | Death rate of $EM_8^B$ | 0.001368 | 0.002737 |
| $\mu_5$ | mu5 | 1/day | Death rate of $APC$ | 0.05 | 0.05 |
| $\mu_6$ | mu6 | 1/day | Death rate of $P_4^{LN}$ | 0.0005 | 0.0005 |
| $\mu_7$ | mu7 | 1/day | Death rate of $P_8^{LN}$ | 0.015 | 0.015 |
| $\mu_8$ | mu8 | 1/day | Death rate of $N_4^B$ | 0.3 | 0.3 |
| $\mu_9$ | mu9 | 1/day | Death rate of $\mu_9^{LN}$ | 0.05 | 0.05 |
| $\rho_1$ | rho1 | count | Precursor cell carrying capacity | 300000000.0 | 300000000.0 |
| $w_{P_4}$ | Wp4 | - | Contribution of $P_4^{LN}$ in $P_8^{LN}$ priming | 0.7355 | 0.7355 |
| $\xi_{11}$ | xi11 | 1/day | $CM_8^{LN} \rightarrow CM_8^B$ LN efflux rate | 0.2750 | 1.2233 |
| $\xi_{12}$ | xi12 | 1/day | $EM_8^{LN} \rightarrow EM_8^B$ LN efflux rate | 0.2190 | 1.5214 |
| $\xi_2$ | xi2 | 1/day | $N_4^{LN} \rightarrow N_4^B$ LN efflux rate | 1.9942 | 4.5066 |
| $\xi_3$ | xi3 | 1/day | $E_4^{LN} \rightarrow E_4^B$ LN efflux rate | 0.9937 | 3.6017 |
| $\xi_5$ | xi5 | 1/day | $CM_4^{LN} \rightarrow CM_4^B$ LN Efflux rate | 1.07179 | 3.9185 |
| $\xi_6$ | xi6 | 1/day | $EM_4^{LN} \rightarrow EM_4^B$ LN Efflux rate | 2.5675 | 3.9231 |
| $\xi_8$ | xi8 | 1/day | $N_8^{LN} \rightarrow N_8^B$ LN Efflux rate | 0.6344 | 2.2140 |
| $\xi_9$ | xi9 | 1/day | $E_8^{LN} \rightarrow E_8^B$ LN Efflux rate | 1.8734 | 4.4935 |
| $\xi_1$ | xi1 | 1/day | $N_4^B \rightarrow N_4^{LN}$ LN Influx rate | 0.3988 | 0.9013 |
| $\xi_4$ | xi4 | 1/day | $CM_4^B \rightarrow CM_4^{LN}$ LN Influx rate | 0.2143 | 0.7837 |
| $\xi_7$ | xi7 | 1/day | $N_8^B \rightarrow N_8^{LN}$ LN Influx rate | 0.1268 | 0.4428 |
| $\xi_{10}$ | xi10 | 1/day | $CM_8^B \rightarrow CM_8^{LN}$ LN Influx rate | 0.05500 | 0.2446 |
| $s_{N_4}$ | Sn4 | 1/day*$\mu L$ | Production rate of naive CD4$^+$ T-cells | 20.1207 | 47.9125 |
| $s_{N_8}$ | Sn8 | 1/day*$\mu L$ | Production rate of naive CD8$^+$ T-cells | 0.3830 | 0.4868 |
| $s_{E_{Non,4}}$ | Senc4 | 1/day*$\mu L$ | Production rate of effector non-specific CD4$^+$ T-cells | 15.3195 | 65.7082 |
| $s_{EM_{Non,4}}$ | Semnc4 | 1/day*$\mu L$ | Production rate of effector memory non-specific CD4$^+$ T-cells | 6.4041 | 17.04971 |
| $s_{E_{Non,8}}$ | Senc8 | 1/day*$\mu L$ | Production rate of effector non-specific CD8$^+$ T-cells | 10.05032 | 69.3024 |
| $s_{EM_{Non,8}}$ | Semnc8 | 1/day*$\mu L$ | Production rate of effector memory non-specific CD8$^+$ T-cells | 2.8856 | 5.5002 |

| Initial condition | Non-Symbolic | Unit | Description | Lower range | Upper range |
|---|---|---|---|---|---|
| $APC(0)$ | APC | count | Antigen-presenting cells in LN | 0 | 0 |
| $N_4^{LN}(0)$ | LnN4 | count | Mtb-specific naive $CD4^+$ T-cell count in LN | 2897.3857 | 6899.4095 |
| $P_4^{LN}(0)$ | LnP4 | count | Mtb-specific precursor $CD4^+$ T-cell count in LN | 0 | 0 |
| $E_4^{LN}(0)$ | LnE4 | count | Mtb-specific effector $CD4^+$ T-cell count in LN | 0 | 0 |
| $CM_4^{LN}(0)$ | LnCM4 | count | Mtb-specific central memory $CD4^+$ T-cell count in LN | 0 | 0 |
| $EM_4^{LN}(0)$ | LnEM4 | count | Mtb-specific effector memory $CD4^+$ T-cell count in LN | 0 | 0 |
| $N_4^{B}(0)$ | BlN4 | pg/mL | Mtb-specific naive $CD4^+$ T-cell count in blood | * | - |
| $E_4^{B}(0)$ | BlE4 | pg/mL | Mtb-specific effector $CD4^+$ T-cell count in blood | * | - |
| $CM_4^{B}(0)$ | BlCM4 | pg/mL | Mtb-specific central memory $CD4^+$ T-cell count in blood | * | - |
| $EM_4^{B}(0)$ | BlEM4 | pg/mL | Mtb-specific effector memory $CD4^+$ T-cell count in blood | * | - |
| $N_8^{LN}(0)$ | LnN8 | count | Mtb-specific naive $CD8^+$ T-cell count in LN | 5515.3085 | 7010.3557 |
| $P_8^{LN}(0)$ | LnP8 | count | Mtb-specific precursor $CD8^+$ T-cell count in LN | 0 | 0 |
| $E_8^{LN}(0)$ | LnE8 | count | Mtb-specific effector $CD8^+$ T-cell count in LN | 0 | 0 |
| $CM_8^{LN}(0)$ | LnCM8 | count | Mtb-specific central memory $CD8^+$ T-cell count in LN | 0 | 0 |
| $EM_8^{LN}(0)$ | LnEM8 | count | Mtb-specific effector memory $CD8^+$ T-cell count in LN | 0 | 0 |
| $N_8^{B}(0)$ | BlN8 | pg/mL | Mtb-specific naive $CD8^+$ T-cell count in blood | * | - |
| $E_8^{B}(0)$ | BlE8 | pg/mL | Mtb-specific effector $CD8^+$ T-cell count in blood | * | - |
| $CM_8^{B}(0)$ | BlCM8 | pg/mL | Mtb-specific central memory $CD8^+$ T-cell count in blood | * | - |
| $EM_8^{B}(0)$ | BlEM8 | pg/mL | Mtb-specific effector memory $CD8^+$ T-cell count in blood | * | - |
| $N_{Non,4}^{LN}(0)$ | LnN4Non | count | Nonspecific naive $CD4^+$ T-cell count in LN | 28970960.05181 | 68987195.6821 |
| $CM_{Non,4}^{LN}(0)$ | LnCM4Non | count | Nonspecific central memory $CD4^+$ T-cell count in LN | 13572957.9382 | 32571421.8047 |
| $N_{Non,4}^{B}(0)$ | BlN4Non | pg/mL | Nonspecific naive $CD4^+$ T-cell count in blood | 402.3744 | 958.1554 |
| $E_{Non,4}^{B}(0)$ | BlE4Non | pg/mL | Nonspecific effector $CD4^+$ T-cell count in blood | 76.5979 | 328.5413 |
| $CM_{Non,4}^{B}(0)$ | BlCM4Non | pg/mL | Nonspecific central memory $CD4^+$ T-cell count in blood | 188.5133 | 452.3808 |
| $EM_{Non,4}^{B}(0)$ | BlEM4Non | pg/mL | Nonspecific effector memory $CD4^+$ T-cell count in blood | 160.1049 | 426.2429 |
| $N_{Non,8}^{LN}(0)$ | LnN8Non | count | Nonspecific naive $CD8^+$ T-cell count in LN | 55147570.5476 | 70096547.5890 |
| $CM_{Non,8}^{LN}(0)$ | LnCM8Non | count | Nonspecific central memory $CD8^+$ T-cell count in LN | 8169880.9373 | 30928893.4342 |
| $N_{Non,8}^{B}(0)$ | BlN8Non | pg/mL | Nonspecific naive $CD8^+$ T-cell count in blood | 765.9384 | 973.5631 |
| $E_{Non,8}^{B}(0)$ | BlE8Non | pg/mL | Nonspecific effector $CD8^+$ T-cell count in blood | 50.2516 | 346.5122 |
| $CM_{Non,8}^{B}(0)$ | BlCM8Non | pg/mL | Nonspecific central memory $CD8^+$ T-cell count in blood | 113.4705 | 429.5679 |
| $EM_{Non,8}^{B}(0)$ | BlEM8Non | pg/mL | Nonspecific effector memory $CD8^+$ T-cell count in blood | 160.3165 | 305.5719 |

*We assume that at $t = 0$, blood and lymph node concentrations are at equilibrium, so blood concentrations are calculated via their lymph-node starting count via the conversion factor $\alpha$ and HostLNs