

a) Viral kinetic parameters

Param	Units	Description	Value	Estimation and citation
$p$	1/day $\times \log(\text{cop/ml})$ /10 <sup>9</sup> cells	Lytic viral production rate	2.59	Direct estimate <sup>1</sup>
$\lambda_S$	1/day	Proliferation of epithelial cells	0.74	Fit S2 Fig, data <sup>2</sup>
$S_{max}$	10 <sup>9</sup> cells	Epithelial cells carrying capacity	$S_0$	Direct estimate <sup>3</sup>
$\lambda_{M\Phi}$	$\log(\text{cop/ml})/\text{day}$	Production of alveolar macrophages	5943	Fit S3 Fig, data <sup>4</sup>
$M_{\Phi max}$	10 <sup>9</sup> cells/ml	Alveolar macrophage carrying capacity	$M_{\Phi R,0}$	Fit S3 Fig
$\beta$	1/day $\times$ 1/ $\log(\text{cop/ml})$	SARS-CoV-2 virus infection rate	0.29	Fit Fig 2, data <sup>1</sup>
$\tau_I$	day	Eclipse time	0.17	Direct estimate <sup>5</sup>
$d_I$	1/day	Death rate of infected cells	0.1	Fit Fig 2, data <sup>1</sup>
$\tau_T$	1/day	Delay in CD8 <sup>+</sup> T cell arrival	4.5	Direct estimate <sup>6</sup>

b) Cell production, recruitment, and activation rates

Param	Units	Description	Value	Estimation and citation
$p_{M\Phi I,G}$	1/day	Monocyte to macrophage differentiation by GM-CSF	1.7	Direct estimate <sup>7</sup>
$p_{M\Phi I,L}$	1/day	Monocyte to macrophage differentiation by IL-6	1.7	Direct estimate <sup>7</sup>
$a_{I,M\Phi}$	ml/(10 <sup>9</sup> cells) $\times$ (1/day)	Activation of macs by infected and dead cells	$1.1 \times 10^3$	Direct estimate <sup>8,9</sup>
$p_{M,I}$	1/day	Monocyte recruitment rate by infected cells	0.22	Direct estimate <sup>10</sup>
$p_{T,F}$	1/day	CD8 <sup>+</sup> T cell production rate by IFN	4	Direct estimate <sup>11</sup>
$p_{N,L}$	1/day	Neutrophils recruitment rate by IL-6	0.21	Homeostasis
$p_{T,L}$	1/day	CD8 <sup>+</sup> T cells recruitment rate by IL-6	4	Direct estimate <sup>11</sup>
$p_{T,I}$	1/day	CD8 <sup>+</sup> T cell proliferation rate	1	Direct estimate <sup>12</sup>
$M_{prod}^*$	1/day	Homeostasis reservoir release rate	0.13	Homeostasis
$\psi_M^{max}$	1/day	Maximal reservoir release rate	11.55	Direct estimate <sup>13</sup>
$N_{prod}^*$	1/day	Homeostasis reservoir release rate	0.21	Homeostasis
$\psi_N^{max}$	1/day	Maximal reservoir release rate	4.13	Direct estimate <sup>14</sup>
$C_{BF}^*$	Dimensionless	Homeostasis neutrophil receptor bound fraction	$1.6 \times 10^{-5}$	Direct estimate <sup>14</sup>

c) Cell-related half-effect ( $\epsilon$ ), IC50 ( $IC_{50}$ ), and Hill coefficient ( $h$ ) parameters

Param	Units	Description	Value	Estimation and citation
$\epsilon_{F,I}$	pg/ml	IFN inhibition of viral production	$4.7 \times 10^{-4}$	Direct estimate <sup>15</sup>
$\epsilon_{L,M\Phi}$	pg/ml	IL-6 monocytes to macrophages	0.011	Fit S1 Fig, data <sup>16</sup>
$\epsilon_{G,M\Phi I}$	pg/ml	GM-CSF monocyte to macrophages	0.027	Fit S1 Fig, data <sup>17</sup>
$\epsilon_{G,M}$	pg/ml	GM-CSF recruitment of monocytes	57.2	Fit S1 Fig, data <sup>18</sup>
$\epsilon_{F,T}$	pg/ml	IFN production of CD8 <sup>+</sup> T cells	0.004	Fit S1 Fig, data <sup>19</sup>

$\epsilon_{C,N}$	unitless	G-CSF recruitment of neutrophils	$1.89 \times 10^{-4}$	Fit S1 Fig, data <sup>14</sup>
$\epsilon_{L,N}$	pg/ml	IL-6 recruitment of neutrophils	57.2	Estimated: $\epsilon_{G,M}$
$\epsilon_{I,M}$	$10^9$ cells/ml	Infected cell monocyte recruitment	0.11	Estimated
$\epsilon_{L,T}$	pg/ml	IL-6 production of CD8 <sup>+</sup> T cells	$3 \times 10^{-4}$	Fit S1 Fig, data <sup>20</sup>
$\epsilon_{V,M\Phi}$	log(cop/ml)	Viral load for mac replenishing	2.96	Fit S3 Fig
$\epsilon_{T,I}$	$10^9$ cells/ml	Antigen driven proliferation	$10^{-6}$	Direct estimate <sup>12</sup>
$h_M$	Dimensionless	GM-CSF monocyte recruitment	1.67	Fit S1 Fig, data <sup>18</sup>
$h_{M,M\Phi}$	Dimensionless	GM-CSF monocyte to macrophages	2.03	Fit S1 Fig, data <sup>17</sup>
$h_N$	Dimensionless	Neutrophil induced damage	3.02	Fit S1 Fig, data <sup>21</sup>
$IC_{50,N}$	$10^9$ cells/ml	Neutrophil induced damage	0.047	Fit S1 Fig, data <sup>21</sup>

d) Cell/virus-induced death rates

Param	Units	Description	Value	Estimation and citation
$\delta_{V,M\Phi}$	ml/( $10^9$ cells) × 1/day	Rate of viral clearance by macrophages	768	Fit S2 Fig, data <sup>22</sup>
$\delta_{V,N}$	ml/( $10^9$ cells) × 1/day	Rate of viral clearance by neutrophils	2304	Estimated
$\delta_N$	1/day	Rate of neutrophil inflicted damage	1.68	Fit S2 Fig, data <sup>23</sup>
$\rho$	Dimensionless	Bystander death modulation constant	0.5	Estimated
$\delta_{I,M\Phi}$	ml/( $10^9$ cells) × (1/day)	Rate macrophages phagocytose infected cells	121	Direct estimate <sup>24</sup>
$\delta_{I,T}$	ml/( $10^9$ cells) × (1/day)	Rate CD8 <sup>+</sup> T cells induce apoptosis in infected cells	238	Direct estimate <sup>25</sup>
$\delta_{M\Phi,D}$	ml/( $10^9$ cells) × (1/day)	Rate macrophages die from phagocytosis	6.06	Direct estimate <sup>26,27</sup>
$\delta_{D,M\Phi}$	ml/( $10^9$ cells) × (1/day)	Rate macrophages phagocytose dead cells	8.03	Fit S2 Fig, data <sup>26</sup>

e) Cell death and virus decay rates

Param	Units	Description	Value	Estimation and citation
$d_V$	1/day	Viral decay rate	1.81	Fit Fig 2, data <sup>28</sup>
$d_D$	1/day	Degradation rate of apoptosed cells	8	Direct estimate <sup>29</sup>
$d_{M\Phi R}$	1/day	Alveolar macrophage death rate	0	Direct estimate <sup>30</sup>
$d_{M\Phi I}$	1/day	Inflammatory macrophage death rate	0.3	Direct estimate <sup>31</sup>
$d_M$	1/day	Monocyte death rate	0.76	Direct estimate <sup>32</sup>
$d_N$	1/day	Neutrophil death rate	1.28	Direct estimate <sup>33</sup>
$d_T$	1/day	CD8 <sup>+</sup> T cell death rate	0.4	Direct estimate <sup>34</sup>

f) Cytokine production rates

Param	Units	Description	Value	Estimation and citation
$p_{L,I}$	pg/ml/day	IL-6 production by infected cells	11.89	Fit S4 Fig, data <sup>35</sup>
$p_{L,M\Phi I}$	pg/ml/day	IL-6 production by inflammatory macrophages	1872	Fit S5 Fig, data <sup>36</sup>
$p_{L,M}$	pg/ml/day	IL-6 production by monocytes	72.56	Fit S1 Fig, data <sup>37</sup>

$p_{G,M\Phi I}$	pg/ml/day	GM-CSF production by inflammatory macrophages	2626	Direct estimate <sup>38</sup>
$p_{C,M}$	ng/ml/day	G-CSF production by monocytes	26.26	Estimated: $p_{G,M\Phi I}$
$p_{G,M}$	pg/ml/day	GM-CSF production by monocytes cells	3070	Fit S3 Fig, data <sup>39</sup>
$p_{F,I}$	pg/ml/day	IFN production by infected cells	2.82	Fit S3 Fig, data <sup>40</sup>
$p_{F,M\Phi I}$	pg/ml/day	IFN production by inflammatory macrophages	1.3	Estimated
$p_{F,M}$	pg/ml/day	IFN production by monocytes	3.56	Fit S3 Fig, data <sup>41,42</sup>

*g) Cytokine production half-effect ( $\eta$ ) and Hill coefficient ( $h$ ) parameters*

Param	Units	Description	Value	Estimation and citation
$\eta_{L,I}$	$10^9$ cells/ml	IL-6 production by infected cells	0.7	Fit S4 Fig, data <sup>35</sup>
$\eta_{L,M}$	$10^9$ cells/ml	IL-6 by monocytes	0.0045	Fit S1 Fig, data <sup>37</sup>
$\eta_{L,M\Phi I}$	$10^9$ cells/ml	IL-6 by inflammatory macrophages	$3.6 \times 10^{-5}$	Fit S4 Fig, data <sup>36</sup>
$\eta_{G,M\Phi}$	$10^9$ cells/ml	GM-CSF by macrophages	$3.6 \times 10^{-5}$	Estimated: $\eta_{L,M\Phi}$
$\eta_{G,M}$	$10^9$ cells/ml	GM-CSF by monocytes	0.15	Homeostasis
$\eta_{C,M}$	$10^9$ cells/ml	G-CSF by monocytes	3.05	Homeostasis
$\eta_{F,I}$	$10^9$ cells/ml	IFN by infected cells	0.011	Fit S4 Fig, data <sup>40</sup>
$\eta_{F,M\Phi I}$	$10^9$ cells/ml	IFN by inflammatory macrophages	$1.3 \times 10^{-6}$	Homeostasis
$\eta_{F,M}$	$10^9$ cells/ml	IFN by monocytes	0.54	Fit S3 Fig, data <sup>41,42</sup>

*h) Cytokine linear (renal) clearance and internalization rates*

Param	Units	Description	Value	Estimation and citation
$k_{linL}$	1/day	Rate of IL-6 renal clearance	16.6	Direct estimate <sup>43</sup>
$k_{linG}$	1/day	Rate of GM-CSF renal clearance	11.7	Direct estimate <sup>44</sup>
$k_{linC}$	1/day	Rate of G-CSF renal clearance	0.16	Direct estimate <sup>14</sup>
$k_{linF}$	1/day	Rate of IFN renal clearance	18	Direct estimate <sup>45</sup>
$k_{intL}$	1/day	Internalization rate of IL-6	61.8	Fit S2 Fig, data <sup>46</sup>
$k_{intG}$	1/day	Internalization rate of GM-CSF	73.4	Direct estimate <sup>47</sup>
$k_{intC}$	1/day	Internalization rate of G-CSF	462	Direct estimate <sup>14</sup>
$k_{intF}$	1/day	Internalization rate of IFN	17	Direct estimate <sup>48</sup>

*i) Cytokine binding/unbinding rates and stoichiometric constant*

Param	Units	Description	Value	Estimation and citation
$k_{BL}$	ml/pg/day	IL-6 binding rate	0.0018	Direct estimate <sup>49</sup>
$k_{BG}$	ml/pg/day	GM-CSF binding rate	0.0021	Direct estimate <sup>47</sup>
$k_{BC}$	ml/ng/day	G-CSF binding rate	2.24	Direct estimate <sup>14</sup>
$k_{BF}$	ml/pg/day	IFN binding rate	0.011	Direct estimate <sup>48</sup>
$k_{UL}$	1/day	IL-6 unbinding rate	22.3	Direct estimate <sup>49</sup>
$k_{UG}$	1/day	GM-CSF unbinding rate	522	Direct estimate <sup>47</sup>
$k_{UC}$	1/day	G-CSF unbinding rate	184	Direct estimate <sup>14</sup>

$k_{UF}$	1/day	IFN unbinding rate	6.07	Direct estimate <sup>48</sup>
$POW$	Dimensionless	Stoichiometric constant (G-CSF)	1.4608	Direct estimate <sup>14</sup>
$\hat{p}$	Dimensionless	Stoichiometric constant (IL-6, GM-CSF, IFN)	1	Direct estimate <sup>14</sup>
		Stoichiometry relating constant (G-CSF)	2	
		Stoichiometry relating constant (IL-6, GM-CSF, IFN)	1	

*j) Number of cellular receptors and cytokine molecular weights*

Param	Units	Description	Value	Estimation and citation
$K_{L,N}$	sites/cell	No. IL-6 receptors on neutrophils	720	Direct estimate <sup>50</sup>
$K_{L,T}$	sites/cell	No. IL-6 receptors on T cells	300	Direct estimate <sup>51</sup>
$K_{L,M}$	sites/cell	No. of IL-6 receptors on monocytes	509	Direct estimate <sup>52</sup>
$K_{G,M}$	sites/cell	No. GM-CSF receptors on monocyte	1058	Direct estimate <sup>53</sup>
$K_{C,N}$	sites/cell	No. of G-CSF receptors on neutrophil	600	Direct estimate <sup>54</sup>
$K_{F,T}$	sites/cell	No. of IFN receptors on T cells	1000	Direct estimate <sup>55</sup>
$K_{F,I}$	sites/cell	No. of IFN receptors on infected cells	1300	Direct estimate <sup>56</sup>
$MM_L$	g/mol	Molecular weight of IL-6	21000	Direct estimate <sup>57</sup>
$MM_G$	g/mol	Molecular weight of GM-CSF	14000	Direct estimate <sup>58</sup>
$MM_C$	g/mol	Molecular weight of G-CSF	19600	Direct estimate <sup>14</sup>
$MM_F$	g/mol	Molecular weight of IFN- $\beta$	19000	Direct estimate <sup>59</sup>

*k) Initial conditions*

Param	Units	Description	Value	Estimation and citation
$V_0$	log(copies/ml)	Initial viral load	4.5	Direct estimate <sup>1</sup>
$S_0$	$10^9$ cells/ml	Initial susceptible cells	0.16	Direct estimate <sup>3,60</sup>
$I_0$	$10^9$ cells/ml	Initial infected cells	0	Estimated
$R_0$	$10^9$ cells/ml	Initial resistant cells	0	Estimated
$M_{\Phi R,0}$	$10^9$ cells/ml	Initial resident macrophages	$2.7 \times 10^{-5}$	Direct estimate <sup>3</sup>
$M_{\Phi I,0}$	$10^9$ cells/ml	Initial inflammatory macrophages	$2.9 \times 10^{-7}$	Homeostasis
$M_0$	$10^9$ cells/ml	Initial monocytes	0.0004	Direct estimate <sup>61</sup>
$M_R$	$10^9$ cells/ml	Initial reservoir monocytes	0.0023	Direct estimate <sup>13</sup>
$N_0$	$10^9$ cells/ml	Initial neutrophils	0.0053	Direct estimate <sup>14</sup>
$N_R$	$10^9$ cells/ml	Initial reservoir neutrophils	0.0316	Direct estimate <sup>14</sup>
$T_0$	$10^9$ cells/ml	Initial CD8 <sup>+</sup> T cells	$1.1 \times 10^{-4}$	Direct estimate <sup>62,63</sup>
$L_{U,0}$	pg/ml	Initial unbound IL-6	1.1	Direct estimate <sup>64</sup>
$L_{B,0}$	pg/ml	Initial bound IL-6	$1.4 \times 10^{-6}$	Homeostasis
$G_{U,0}$	pg/ml	Initial unbound GM-CSF	2.43	Direct estimate <sup>65</sup>
$G_{B,0}$	pg/ml	Initial bound GM-CSF	$1.6 \times 10^{-8}$	Homeostasis
$C_{U,0}$	ng/ml	Initial unbound G-CSF	0.025	Direct estimate <sup>14</sup>
$C_{B,0}$	ng/ml	Initial bound G-CSF	$6.5 \times 10^{-10}$	Direct estimate <sup>14</sup>
$F_{U,0}$	pg/ml	Initial unbound IFN	0.015	Direct estimate <sup>66</sup>
$F_{B,0}$	pg/ml	Initial bound IFN	$1.1 \times 10^{-8}$	Homeostasis

*m) List of variables in Eqs. S1-S22*

<b>Variable</b>	<b>Units</b>	<b>Description</b>
$V$	cop/ml	Viral load
$S$	$10^9$ cells/ml	Susceptible cells
$I$	$10^9$ cells/ml	Infected cells
$R$	$10^9$ cells/ml	Resistant cells
$M_{\Phi R}$	$10^9$ cells/ml	Alveolar (resident) macrophages
$M_{\Phi I}$	$10^9$ cells/ml	Inflammatory macrophages
$M$	$10^9$ cells/ml	Monocytes
$M_R$	$10^9$ cells/ml	Bone marrow reservoir monocytes
$N$	$10^9$ cells/ml	Neutrophils
$N_R$	$10^9$ cells/ml	Bone marrow reservoir neutrophils
$T$	$10^9$ cells/ml	CD8 <sup>+</sup> T cells
$L_U$	pg/ml	Unbound IL-6
$L_B$	pg/ml	Bound IL-6
$G_U$	pg/ml	Unbound GM-CSF
$G_B$	pg/ml	Bound GM-CSF
$C_U$	ng/ml	Unbound G-CSF
$C_B$	ng/ml	Bound G-CSF
$C_{BF}$	unitless	Neutrophil G-CSF receptor bound fraction
$F_U$	pg/ml	Unbound IFN
$F_B$	pg/ml	Bound IFN