

Table 6. Learned rules.

Rule 1	IF THEN	Inflammatory (M1) Alveolar Macrophages > 16.289 IL6 = $0.1 \times \text{Inflammatory (M1) Alveolar Macrophages}$ $+ 0.0021 \times \text{Immunosupressed (M2) Alveolar macrophages}$ $- 0.1056$ [763/0.931%]
Rule 2	IF THEN	Inflammatory (M1) Alveolar Macrophages ≤ 1.381 IL6 = $-0.0001 \times \text{Viral Load}$ $+ 0.1025 \times \text{Inflammatory (M1) Alveolar Macrophages}$ $- 0.0101 \times \text{Delayed IL6} - 0.0001 \times \text{T-cell Interferon}$ $+ 0.0019$ [410/1.095%]
Rule 3	IF THEN	Inflammatory (M1) Alveolar Macrophages > 10.592 IL6 = $-0.0002 \times \text{Time (Hour)} - 0.0015 \times \text{Viral Load}$ $+ 0.0833 \times \text{Inflammatory (M1) Alveolar Macrophages}$ $- 0 \times \text{Active Adaptive Immune System}$ $+ 0.0001 \times \text{Resting Alveolar Macrophages}$ $+ 0.1664 \times \text{Delayed IL6}$ $- 0.5716$ [89/0.318%]
Rule 4	IF THEN	Active Adaptive Immune System > 9.922 Inflammatory (M1) Alveolar Macrophages > 6.424 IL6 = $-0.0001 \times \text{Time (Hour)} - 0.0048 \times \text{Viral Load}$ $+ 0.1134 \times \text{Inflammatory (M1) Alveolar Macrophages}$ $- 0.0003 \times \text{Active Adaptive Immune System}$ $- 0.0008 \times \text{Immunosupressed (M2) Alveolar macrophages}$ $+ 0.0011 \times \text{Resting Alveolar Macrophages}$ $- 0.1284 \times \text{Delayed IL6} + 0.0015 \times \text{TcellInterferon}$ $- 5.0631$ [69/0.096%]
Rule 5	IF THEN	TcellInterferon > 0.517 IL6 = $-0.0003 \times \text{Time (Hour)} - 0.0019 \times \text{Viral Load}$ $+ 0.0992 \times \text{Inflammatory (M1) Alveolar Macrophages}$ $+ 0.0001 \times \text{Active Adaptive Immune System}$ $+ 0.1282$ [79/2.143%]
Rule 6	IF THEN	Time (Hour) > 1.5 and Active Adaptive Immune System ≤ 7.841 IL6 = $-0.0003 \times \text{Time (Hour)} - 0.0103 \times \text{Viral Load} + 0.7211$ [11/1.317%]
Rule 7	IF THEN	Viral Load ≤ 0.999 IL6 = $+ 0.9887$ [4/0%]
Rule 8	IF THEN	Time (Hour) > 1 IL6 = $+ 0.9597$ [4/4.369%]
Rule 9	IF THEN	IL6 = $+ 3$ [2]

1 APPENDIX: LEARNING CLASSIFICATION RULES AND RELEVANT ATTRIBUTES

2 APPENDIX: SYSTEM DYNAMICS MODEL: STOCKS, FLOWS AND VARIABLES

Table 7. Stocks.

Stock	Equation	Units
Resting alveolar macrophages	$\frac{d\text{Resting alveolar macrophages}}{dt} = -\text{Activation}(t)$ (1)	macrophages
Inflammatory alveolar macrophages	$\frac{d\text{Inflammatory alveolar macrophages}}{dt} = \text{Activation}(t) - \text{Immunoregulation}(t)$ (2)	macrophages
Immunosuppressed alveolar macrophages	$\frac{d\text{Immunosuppressed alveolar macrophages}}{dt} = \text{Immunoregulation}(t)$ (3)	macrophages
Delayed IL6	$\frac{d\text{Delayed IL6}}{dt} = \text{delayed IL6 net}(t) - \text{delayed IL6 degradation}(t)$ (4)	pg/mL
Viral Load	$\frac{d\text{Viral Load}}{dt} = \text{net new viruses}(t) - \text{Adaptive Immune System Net Effect}(t) - \text{Innate Immune System Net Effect}(t) - \text{virus net deaths}(t)$ (5)	viruses
IL6	$\frac{d\text{IL6}}{dt} = \text{IL6 production}(t) - \text{IL6 degradation}(t)$ (6)	pg/mL
PAMPS	$\frac{d\text{PAMPS}}{dt} = \text{PAMPs and RRS alarm}(t) - \text{Alarm decay}(t)$ (7)	pamps
Active Adaptive Immune System	$\frac{d\text{Active Adaptive Immune System}}{dt} = \text{Response And Activation}(t) - \text{net back off}(t)$ (8)	T-cells
Resting Adaptive Immune System	$\frac{d\text{Resting Adaptive Immune System}}{dt} = -\text{Response And Activation}(t)$ (9)	T-cells
Interferon Strength	$\frac{d\text{Interferon Strength}}{dt} = \text{Interferon Net}(t) - \text{Interferon Decay}(t)$ (10)	Interferon
Uninfected Lung Tissue	$\frac{d\text{Uninfected Lung Tissue}}{dt} = \text{Regeneration Rate}(t) - \text{Infection Rate}(t)$ (11)	lung cells
Infected Lung Tissue	$\frac{d\text{Infected Lung Tissue}}{dt} = \text{Infection Rate}(t) - \text{Destruction Net Rate}(t)$ (12)	lung cells
Destroyed Lung Tissue	$\frac{d\text{Destroyed Lung Tissue}}{dt} = \text{Destruction Net Rate}(t) - \text{Cleaning Rate}(t)$ (13)	lung cells
T-Cell interferon	$\frac{dT\text{-Cell interferon}}{dt} = \text{T-cell Interferon net}(t) - \text{T-cell Interferon Decay}(t)$ (14)	Interferon

Table 8. Flows.

Flow	Equation	Units
Infection Rate	$ \begin{aligned} & (\text{Rate by which a virus infects a lung cell per lung cell present} \\ & \quad \times \text{Viral Load} \times \text{Uninfected Lung Tissue}) \\ & - (\text{success rate infected lung cells alert per interferon hour} \times \\ & \quad \text{Infected Lung Tissue} \times \text{Interferon Strength}) \quad (15) \end{aligned} $	lung cells/Hour
Destruction Net Rate	$ \text{Infected Lung Tissue} \times \text{Infected Lung Tissue} \times \text{Death Proportionality Constant} \quad (16) $	lung cells/Hour
Regeneration Rate	$ \begin{aligned} & \text{regeneration fraction} \times \text{Uninfected Lung Tissue} \\ & + \text{repair rate} \times \text{Immunosuppressed (M2) Alveolar macrophages} \quad (17) \end{aligned} $	lung cells/Hour
Interferon Net	$ \text{Infected Lung Tissue} \times \text{Interferon per hour per cell} \quad (18) $	Interferon/Hour
IL6 production	$ \text{Inflammatory (M1) Alveolar Macrophages} \times \text{IL6 synthesis Rate} \quad (19) $	(pc/mL)/Hour
IL6 degradation	$ \text{IL6} \times \text{IL6 degradation rate} \quad (20) $	(pc/mL)/Hour
delayed IL6 net	$ \text{DELAY FIXED}(\text{IL6 production, IL6 delay time, IL6 production}) \quad (21) $	(pc/mL)/Hour
Delayed IL6 degradation	$ \text{Delayed IL6} \times \text{IL6 degradation rate} \quad (22) $	(pc/mL)/Hour
virus net deaths	$ \text{Viral Load} \times \text{virus death proportionality constant} \quad (23) $	viruses/Hour
net new viruses	$ \text{Infected Lung Tissue} \times \text{new viruses per hour per infected lung cell} \quad (24) $	viruses/Hour
Innate Immune System Net Effect	$ \begin{aligned} & \text{Inflammatory (M1) Alveolar Macrophages} \times \text{rate of macrophages phagocytosis} \\ & \quad \times \text{Viral Load} \quad (25) \end{aligned} $	viruses/Hour
rate of macrophages phagocytosis	$ 0.001/\text{virulence}^3 \quad (26) $	(viruses/Hour) / (viruses \times macrophages)
Interferon Decay	$ 0 \quad (27) $	Interferon/Hour
Alarm Decay	$ \text{Decay rate} \times \text{PAMPs} \quad (28) $	pamps/Hour
PAMPs and RRS alarm	$ \text{sensitivity} \times \text{Viral Load} \quad (29) $	pamps/Hour
Adaptive Immune System Net Effect	$ \begin{aligned} & \text{Active Adaptive Immune System} \\ & \quad \times \text{virus elimination rate by adaptive immune system} \quad (30) \end{aligned} $	viruses/Hour
Activation	$ \text{expected activation} \times \text{Viral Load} \quad (31) $	macrophages/Hour
Immunoregulation	$ \begin{aligned} & \text{Inflammatory (M1) Alveolar Macrophages} \\ & \quad \times \frac{\text{Immunomodulation Rate IL6 modulation factor}}{\text{Delayed IL6} \times \log(\max(3, \text{Delayed IL6}))^3} \quad (32) \end{aligned} $	macrophages/Hour
net back off	$ \text{Active Adaptive Immune System} \times \text{back off rate} \quad (33) $	T-cells/Hour
Response And Activation	$ \text{Inflammatory (M1) Alveolar Macrophages} \times \text{invocation rate} \times \text{PAMPs} \quad (34) $	T-cells/Hour
T-cell Interferon Decay	$ \text{Interferon Decay rate} \times \text{T-cell interferon} \quad (35) $	Interferon/Hour
T-cell interferon net	$ \text{Active Adaptive Immune System} \times \text{T-cell interferon Production by T-cell} \quad (36) $	Interferon/Hour

Table 9. Auxiliary Variables.

Auxiliary variable	Equation	Units
activation rate by which a macrophage is activated per virus present per macrophage	$\min(\text{maximum activation rate}, \text{PAMPs} \times \text{detection factor})$ (37)	macrophages/ (viruses \times Hour)
rate of macrophages phagocytosis	$\frac{0.001}{\text{virulence}^3}$ (38)	(viruses/Hour)/ (viruses \times macrophages)
sensitivity	$0.2 - 0.8(\text{virulende} - 2)$ (39)	pamps/ (viruses \times Hour)
expected activation	$\text{SMOOTH} \left(\begin{array}{l} \text{activation rate by which a} \\ \text{macrophage is activated per, time to diffuse} \\ \text{virus present per macrophage} \end{array} \right)$ (40)	macrophages/ (viruses \times Hour)
success rate infected lung cells alert per interferon hour	IF THEN $\left(\text{Initial Viral Load} > 1, \frac{\text{default rate}}{1000}, \text{default rate} \right)$ ELSE (41)	(1/Hour)/(interferon)

Table 10. Constants.

ID	Parameter	Value	Units
1	back off rate	0.005	1/Hour
2	Cleaning rate per destroyed lung cell	0.2	(lung cells/Hour) / lung cells
3	Decay rate	0.005	(pamps/Hour) / pamps
4	default rate	0.001	1/(Hour \times interferon)
5	detection factor	1e-05	macrophages / (Hour \times viruses \times pamps))
6	feedback rate	0.001	macrophages / (Hour \times interferon))
7	final time	480	Hour
8	IL6 degradation rate	0.8	(pg / (Hour \times mL)) / (pg / mL)
9	IL6 delay time	6	Hour
10	IL6 initial value	3	pg / mL
11	IL6 modulation factor	0.05	pg / mL
12	IL6 synthesis Rate	0.08	pg / (Hour \times mL \times macrophages)
13	Immunomodulation Rate	0.5	macrophages / (Hour \times macrophages)
14	Infected Lung Tissue Death Proportionality Constant	0.5	(lung cells / Hour) / lung cells
15	Initial lung Cells in Thousands	15,000	lung cells
16	Initial time	0	Hour
17	Initial viral load in thousands	1	viruses
18	Interferon decay	0	interferon/Hour
19	Interferon per hour per cell	2	(interferon/Hour)/lung cells
20	Interferon decay rate	0.01	1/Hour
21	invocation rate	0.0001	T-cells/(Hour \times pamps \times macrophages)
22	maximum activation rate	0.07	T-cells/(Hour \times pamps \times macrophages)
23	new viruses per hour per infected lung cell	0.002	(viruses / Hour) / lung cells
24	patient precondition	{0, 1, 2}	Dmnl
25	time step	1	Hour
26	time to diffuse	6	Hour
27	virulence	{1,2}	Dmnl
28	virus death proportionality constant	0.001	(viruses / Hour) / viruses