

A biomathematical model of SARS-CoV-2 in Syrian hamsters - supplement material

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Parameters and initial values

Table S1. Parameter estimates.

parameter	meaning	value	95% confidence intervals	
k_{EU}	regeneration rate of unaffected cells	1.291E+01	[7.822E+00 , 1.844E+01]	fitted
k_{EU_V}	infection rate of susceptible cells	3.510E-03	[3.265E-03 , 3.801E-03]	fitted
d_{EI}	removal rate of infected cells	4.508E+01	[4.199E+01 , 4.897E+01]	fitted
k_{EA_CD8+}	removal rate of affected cells by CD8 ⁺ T cells	4.874E-04	[2.435E-04 , 9.871E-04]	fitted
k_{EA_NK}	removal rate of affected cells by NK cells	4.081E-02	[1.860E-02 , 9.027E-02]	fitted
d_{IM}	influx rate of activated macrophages	2.177E-01	[1.400E-01 , 2.978E-01]	fitted
k_{IM_V}	increased influx of IM due to virus presence	1.156E-03	[9.047E-04 , 1.949E-03]	fitted
k_V	virus replication rate	1.905E+03	[1.764E+03 , 2.050E+03]	fitted
k_{V_AB}	depletion of virus by neutralizing antibodies	1.589E-01	[1.463E-01 , 1.721E-01]	fitted
k_{V_IgM}	depletion of virus by IgM type antibodies	1.025E-02	[6.876E-03 , 1.504E-02]	fitted
d_V	virus decay	9.876E+00	[9.504E+00 , 1.280E+01]	fitted
k_V^{Delay}	delay of cell reaction due to virus presence	6.332E-01	[4.234E-01 , 9.198E-01]	fitted
k_{CD8+_CXCL10}	attraction of CD8 ⁺ T cells by CXCL10	3.283E-02	[2.256E-02 , 4.911E-02]	fitted
k_{CD8+_CCL8}	attraction of CD8 ⁺ T cells by CCL8	4.614E-01	[3.047E-01 , 6.431E-01]	fitted
k_{CD8+_V}	activation of CD8 ⁺ T cells by virus	3.910E-02	[2.525E-02 , 6.078E-02]	fitted
k_{CD4+_CXCL10}	attraction of CD4 ⁺ T cells by CXCL10	1.073E-02	[7.330E-03 , 1.587E-02]	fitted
k_{CD4+_CCL8}	attraction of CD4 ⁺ T cells by CCL8	5.148E-01	[3.547E-01 , 7.573E-01]	fitted
k_{CD4+_V}	activation of CD4 ⁺ T cells by virus	5.695E-03	[3.739E-03 , 8.415E-03]	fitted
k_{B_CXCL10}	attraction of B cells by CXCL10	5.113E-02	[3.368E-02 , 7.609E-02]	fitted
k_{CXCL10_IM}	production of CXCL10 by IM	2.507E+00	[9.636E-01 , 4.394E+00]	fitted
$k_{CXCL10_IM_V}$	additional CXCL10 production by IM due to virus presence	3.479E-02	[1.875E-02 , 8.178E-02]	fitted
k_{CXCL10}^{Delay}	delay of additional CXCL10 production by IM	3.537E-01	[2.179E-01 , 6.004E-01]	fitted

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Table S1 – continued from previous page

parameter	meaning	value	95% confidence intervals	
	due to virus presence			
$k_{\text{CCL8_EA}}$	CCL8 production by EA	2.147E+01	[1.118E+01 , 3.763E+01]	fitted
$k_{\text{CCL8_EI.V}}$	CCL8 production by EI	1.359E+02	[7.882E+01 , 2.852E+02]	fitted
$k_{\text{CCL8}}^{\text{Delay}}$	delay of CCL8 production by EI	2.716E-01	[1.895E-01 , 3.987E-01]	fitted
k_{IgM}	IgM antibody production	1.388E+00	[9.369E-01 , 2.133E+00]	fitted
$k_{\text{IgM.V}}$	additional IgM antibody production	7.496E-01	[5.040E-01 , 1.111E+00]	fitted
	due to virus presence	0.000E+00		
$Z_{\text{IgM}}^{\text{max}}$	maximum of IgM production	2.269E+00	[1.083E+00 , 4.992E+00]	fitted
$Z_{\text{IgM}}^{\text{nor}}$	IgM production in steady-state	1.161E-01	[4.832E-02 , 2.233E-01]	fitted
$Z_{\text{IgM}}^{\text{b}}$	sensitivity of IgM production regarding virus presence	9.043E-02	[3.907E-02 , 1.942E-01]	fitted
$Z_{\text{IgM}}^{\text{min}}$	minimum of IgM production	0.000E+00		set
$k_{\text{B.PC}}$	maturation rate of antibody affinity	1.740E-03	[1.002E-03 , 2.152E-03]	fitted
d_{PC}	decay of plasma cells	6.001E-01	[4.034E-01 , 8.696E-01]	fitted
$k_{\text{AB}}^{\text{Delay}}$	delay of plasma cell maturation	8.003E+01	[3.649E+01 , 1.725E+02]	fitted
$k_{\text{NK_CCL8}}$	NK recruitment by CCL8	7.073E-01	[4.610E-01 , 1.151E+00]	fitted
$k_{\text{NK_CXCL10}}$	NK recruitment by CXCL10	2.883E-03	[1.934E-03 , 4.204E-03]	fitted
$k_{\text{NK.V}}$	NK recruitment due to virus presence	3.031E-05	[1.976E-05 , 4.635E-05]	fitted
$Z_{\text{AB}}^{\text{max}}$	maximum AB production by plasma cells	6.443E+01	[4.378E+01 , 9.272E+01]	fitted
$Z_{\text{AB}}^{\text{nor}}$	AB production by plasma cells in steady-state	3.869E-01	[2.608E-01 , 5.430E-01]	fitted
Z_{AB}^{b}	steepness of increase in AB production by plasma cells	5.818E+00	[3.515E+00 , 7.666E+00]	fitted
$Z_{\text{AB}}^{\text{min}}$	minimum AB production by plasma cells	0.000E+00		set
d_{AB}	waning of neutralizing antibodies	1.000E-02	[2.137E-03 , 3.935E-02]	set
d_{NK}	decrease of NK	7.102E-01		set
d_{CD4^+}	decrease of CD4 ⁺ T cells	5.255E-01		set
d_{CD8^+}	decrease of CD8 ⁺ T cells	4.942E-01		set
d_{CXCL10}	decrease of CXCL10	2.507E+00		set
d_{B}	decrease of B cells	5.113E-02		set
d_{CCL8}	decrease of CCL8	2.147E+01		set
d_{IgM}	decrease of IgM	1.195E-01		set
d_{EA}	decrease of EA	1.278E+03		set
P_{EU}	production of EU	1.282E+03		set

Table S2. Initial values and normal values. Initial parameters of model state parameters are typically set. Steady-state values are derived from the data and are multiplied with the modeled state parameter to allow comparisons with the data.

EU_0	initial percentage of unaffected epithelial cells [%]	9.900E+01
EI_0	initial percentage of infected epithelial cells [%]	0.000E+00
EA_0	initial percentage of activated epithelial cells [%]	1.000E+00
V_0	initial virus load (virus titers in lung homogenates per g lung)	0.000E+00
AB_0	initial concentration of neutralizing antibodies	0.000E+00
$CD8_{A0}^+$	initial value of $CD8^+$ T cells (set)	1.000E+00
$CD8_{A_{nor}}^+$	$CD8^+$ steady-state value of T cells [cells per lung lobe] from data	1.812E+04
$CD4_{A0}^+$	initial value $CD4^+$ T cells (set)	1.000E+00
$CD4_{A_{nor}}^+$	$CD4^+$ steady-state value of T cells value [cells per lung lobe] from data	4.095E+04
B_0	initial value of B cells (set)	1.000E+00
B_{nor}	steady-state value of B cells [cells per lung lobe] from data	1.083E+06
NK_{A0}	initial value of NK cells (set)	1.000E+00
$NK_{A_{nor}}$	steady-state value of NK cells [cells per lung lobe] from data	2.252E+05
IgM_0	initial value of IgM type antibodies (set)	1.000E+00
IgM_{nor}	steady-state value IgM type antibodies from data	9.134E+00
IM_0	initial value of inflammatory macrophages (set)	1.000E+00
IM_{nor}	steady-state value of inflammatory macrophages [cells per lung lobe] from data	1.816E+06
$CXCL10_0$	initial value of CXC chemokine ligand 10 (set)	1.000E+00
$CCL8_0$	initial value of chemokine CCL8 (set)	1.000E+00
PC_0	initial value of plasma cells (set)	0.000E+00

Sensitivity analysis

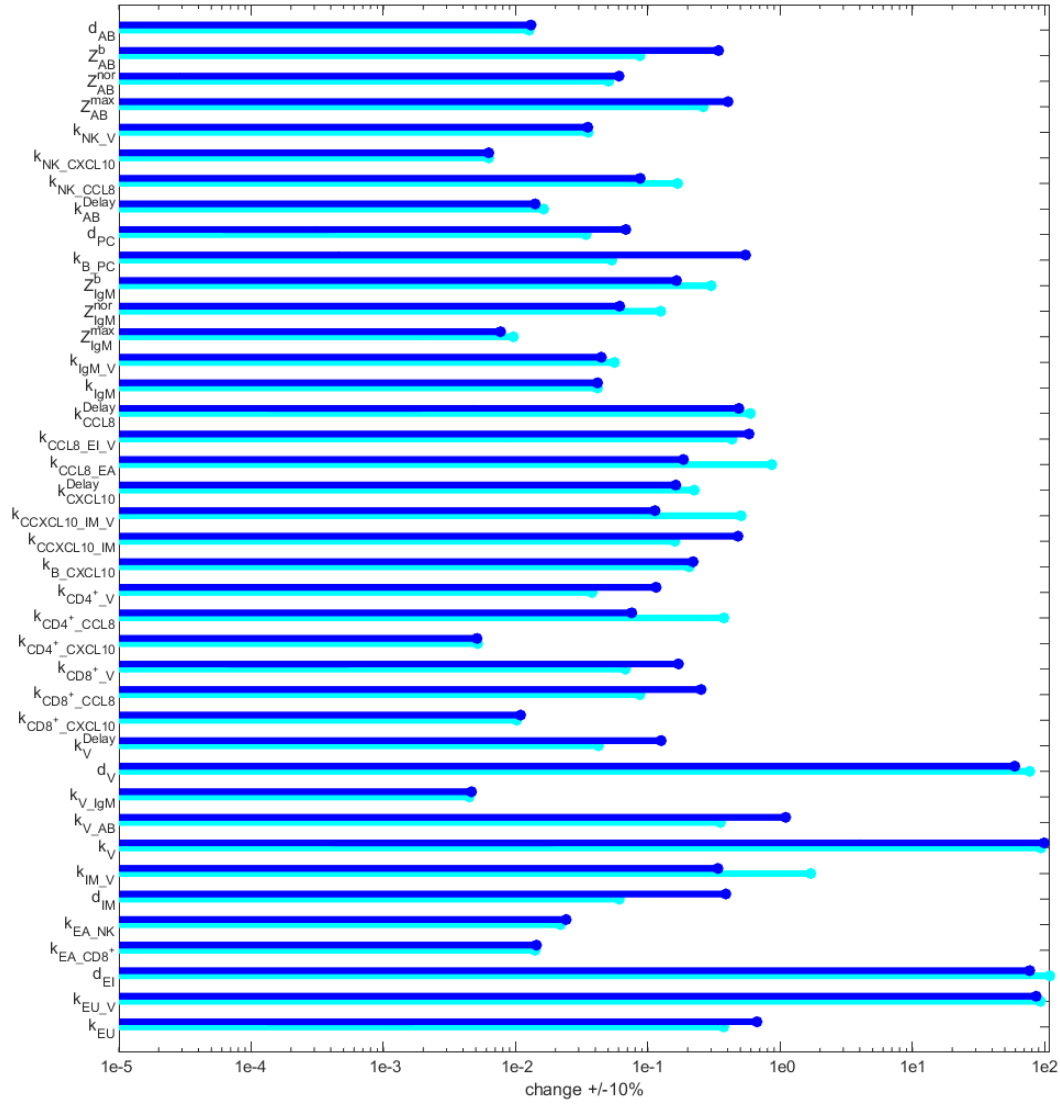


Fig S1. Parameter sensitivity when changing a single parameter. The horizontal bars show the deterioration of the objective function (in %) when the parameter value is multiplied by the factor 0.9 (cyan) or 1.1 (blue).

Table S3. Quantification of model fitness. We present values of the fitness function (residual sum of squares) for the different compartments with available data. We compare the fitness of the model with infection at day zero with that of a null model without infections. BIC and AIC denote Bayesian information criterion respectively Akaike information criterion. The Bayes factor between our model and the constant model is decisive

variable	infection model	constant model
V	9.41E-01	5.85E+01
EI	2.93E+00	4.85E+01
IgM	9.42E-01	1.07E+01
AB	3.47E+00	1.65E+02
NK cells	3.88E+01	2.24E+02
IM cells	1.60E+01	7.09E+01
CD8 cells	5.67E+00	1.25E+02
CD4 cells	6.44E+00	1.12E+02
B cells	2.31E+00	6.85E+00
CXCL10IMprod	3.81E+01	3.15E+02
CCL8prod	1.81E+01	1.31E+02
sum of fitness functions	1.34E+02	1.25E+03
BIC	1.29E+02	3.04E+02
AIC	5.45E+01	2.29E+02

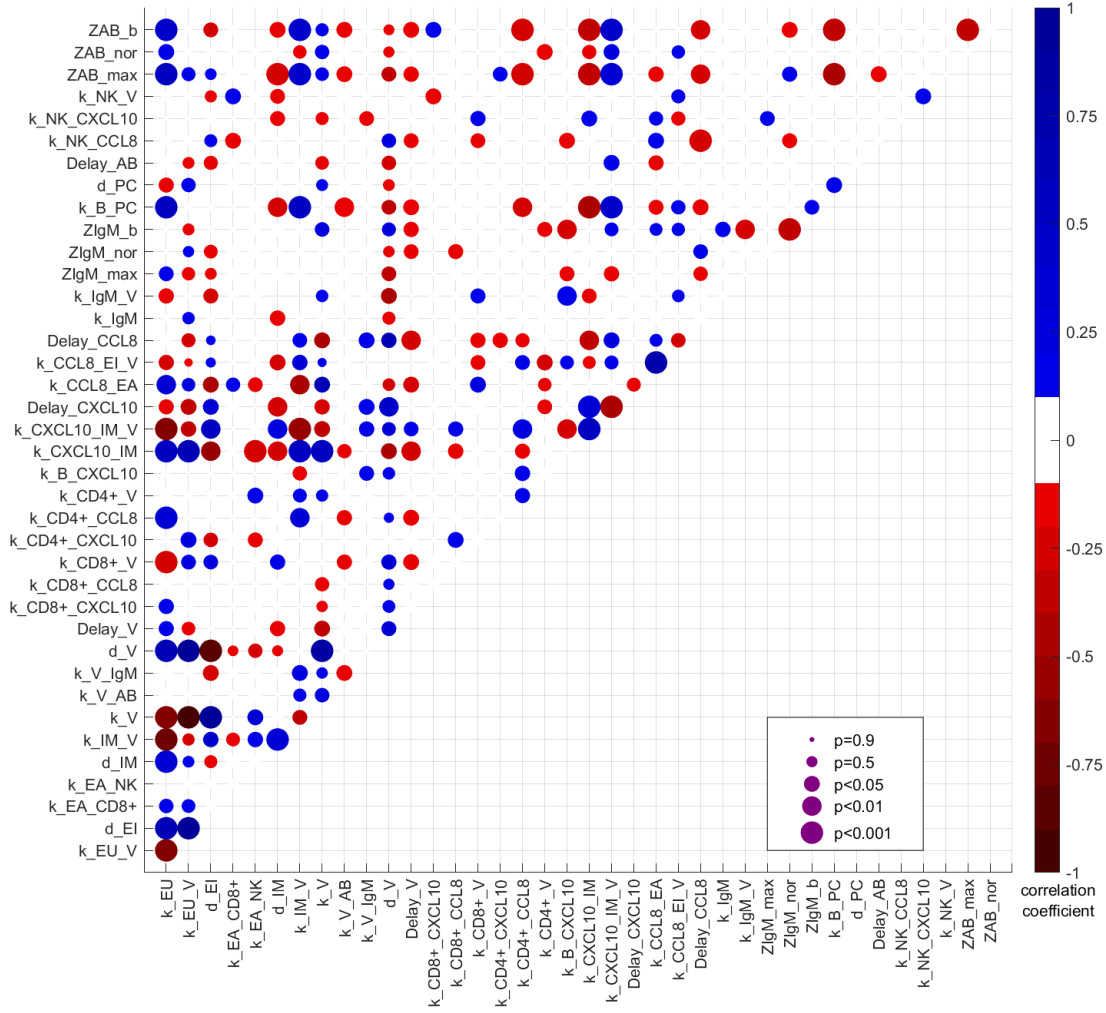


Fig S2. Correlation of parameter estimates. We present the results of our correlation analysis of parameter estimates. Estimated Pearson correlations between two parameter estimates are color-coded (red=negative correlations, blue=positive correlations).