Biomedical Control Strategies for Inflammation in SARS-CoV-2-Induced Complement Activation Supplementary Information

TABLE I: Kinetic constants (KCs) used in the model.

S.no	KCs	Value Adopted
1	k_{on1}	$2.14 \times 10^5 M^{-1}s^{-1}$
2	k_{off1}	$1.70 \times 10^{-2} s^{-1}$
3	k_{on2}	$2.30 \times 10^5 M^{-1}s^{-1}$
4	k_{on3}	$9.50 \times 10^4 M^{-1}s^{-1}$
5	k_{on4}	$6.10 \times 10^5 M^{-1}s^{-1}$
6	k_{off4}	$3.44 \times 10^{-3} s^{-1}$
7	k_{on5}	$8.20 \times 10^5 M^{-1}s^{-1}$
8	k_{off5}	$1.20 \times 10^{-3} s^{-1}$
9	k_{on6}	$4.40 \times 10^3 M^{-1}s^{-1}$
10	k_{1cat}	$5.40 s^{-1}$
11	k_{1m}	$6.10 \times 10^{-6} M$
12	k_{off6}	$5.80 \times 10^{-3} s^{-1}$
13	k_{on7}	$4.30 \times 10^5 M^{-1}s^{-1}$
14	k_{on8}	$2.00 \times 10^5 M^{-1}s^{-1}$
15	k_{off8}	$1.60 \times 10^{-2} s^{-1}$
16	k_{on9}	$2.00 \times 10^5 M^{-1}s^{-1}$
17	k_{off9}	$1.60 \times 10^{-2} s^{-1}$
18	k_{2cat}	$3.17 s^{-1}$
19	k_{2m}	$1.80 \times 10^{-6} M$
20	k_{on10}	$1.50 \times 10^7 M^{-1}s^{-1}$
21	k_{3cat}	$2.00 \times 10^{-2} s^{-1}$
22	k_{3m}	$5.10 \times 10^{-9} M$
23	k_{off10}	$5.00 \times 10^{-3} s^{-1}$
24	k_{on11}	$2.43 \times 10^5 M^{-1}s^{-1}$
25	k_{off11}	$1.40 \times 10^{-3} s^{-1}$
26	k_{4cat}	$5.10 s^{-1}$
27	k_{4m}	$6.10 \times 10^{-6} M$
28	k_{on12}	$1.83 \times 10^4 M^{-1}s^{-1}$
29	k_{off12}	$5.73 \times 10^{-4} s^{-1}$
30	k_{on13}	$9.64 \times 10^4 M^{-1}s^{-1}$
31	k_{off13}	$3.50 \times 10^{-3} s^{-1}$
32	k_{on14}	$4.13 \times 10^3 M^{-1}s^{-1}$
33	k_{off14}	$1.30 \times 10^{-3} s^{-1}$
34	k_{on15}	$1.95 \times 10^5 M^{-1}s^{-1}$
35	k_{off15}	$5.40 \times 10^{-3} s^{-1}$
36	k_{on16}	$1.58 \times 10^4 M^{-1}s^{-1}$
37	k_{5cat}	$5.70 \times 10^{-3} s^{-1}$
38	k_{5m}	$5.73 \times 10^{-4} M$
39	k_{6cat}	$3.46 \times 10^{-2} s^{-1}$
40	k_{6m}	$3.50 \times 10^{-3} M$
41	k_{on17}	$2.60 \times 10^8 M^{-1}s^{-1}$
42	k_{off17}	$0.10 s^{-1}$
43	k_{on18}	$2.20 \times 10^8 M^{-1}s^{-1}$
44	k_{off18}	$0.10 s^{-1}$
45	k_{7cat}	$2.10 \times 10^{-5} s^{-1}$

TABLE I: CONT.

Sources for the kinetic constants
S. nos 1 and 2. The spike (S) protein of SARS-CoV-2 binding to lgG via Fab (ID-1F4) [1], [2]. Wang et al. [1] report that S binds to IgG with an on rate of $2.14 \times 10^5 M^{-1}s^{-1}$, and off rate $1.70 \times 10^{-2} s^{-1}$ for S unbinding S-IgG.
S. no 3. Immunoglobulin G1 (IgG1) subclass antibodies Rituximab (RTX) and Ofatumumab (OFA) bind with C1q [2]. Bondza et al. [3] report association rates of $5.20 \times 10^4 M^{-1}s^{-1}$ and $2.30 \times 10^5 M^{-1}s^{-1}$ for C1q binding to RTX and OFA. lgG is structurally/functionally homologous to lgG1 subclass. An on rate of $2.30 \times 10^5 M^{-1}s^{-1}$ is estimated for the C1q binding to S-IgG.
S. no 4. The inhibition kinetics of C1s, a complement serine protease, by C1INH occur with a binding rate of $9.50 \times 10^4 M^{-1}s^{-1}$ [4], [5].
S. nos 5 and 6. Association and disassociation rates of C1r and C1s were measured with respect to different modules such as x-ray structure of the N-terminal CUB-epidermal growth factor (EGF) marked by different residues. Among the high affinity sites at $C1rCUB_1$–$Y56A$, binding rate $6.10 \times 10^5 M^{-1}s^{-1}$ and unbinding rate $3.44 \times 10^{-3} s^{-1}$ were measured [6].
S. nos 7 and 8. The on and off rates for the C1q to C1r and C1s complex are $8.20 \times 10^5 M^{-1}s^{-1}$ and $1.20 \times 10^{-3} s^{-1}$, respectively [6]–[9].
S. nos 9 and 12. In the binding and unbinding rates for C4b and C2a, under the Quasi steady-state approximation (QSSA), $k_m \approx k_d$, and $k_m \approx \frac{k_{cat}}{k_{on}}$ [10]. $\frac{k_{cat}}{k_m} = 4.4 \times 10^3 M^{-1}s^{-1}$ [11], $k_{off} = 5.8 \times 10^{-3} s^{-1}$ [12].
S. nos 10 and 11. Zewde et al. [9] and Rossi et al. [13] report that C1 can cleave C4 into C4a and C2a with cleavage rate characterized by a k_{cat} of $5.40 s^{-1}$ and a k_m of $6.10 \times 10^{-6} M$.
S. no 13. The binding rate for C1 and C1INH is $4.30 \times 10^5 M^{-1}s^{-1}$ [6]–[9].
S. nos 14-17 The C4BP is associated with C3-convertase (C4b-C2a) and cleaved fragment of C4, known as C4b. The binding rate of $2.0 \times 10^5 M^{-1}s^{-1}$ and the unbinding rate of $1.6 \times 10^{-2} s^{-1}$ for C4BP and C4b are reported in [6]–[9], [12], [14], [15]. The association of C4BP with C4b-C2a is unknown, and the binding and unbinding rates of these entities are estimated based on functional homology.
S. nos 18 and 19. C3-convertase (C4b-C2a) can cleave C3 into C3a and C3b with a cleavage rate following Michaelis–Menten kinetics, having a k_{cat} of $3.17 s^{-1}$ and a k_m of $1.80 \times 10^{-6} M$ [6]–[9], [12].
S. nos 20 and 23. In the binding and unbinding rates for C4b and C2a, under the Quasi steady-state approximation (QSSA), $k_m \approx k_d$, and $k_m \approx \frac{k_{cat}}{k_{on}}$ [10]. $\frac{k_{cat}}{k_m} = 1.5 \times 10^7 M^{-1}s^{-1}$ [11], $k_{off} = 5.0 \times 10^{-3} s^{-1}$ [8].
S. nos 21 and 22. C5-convertase (C4b-C2a-C3b) can cleave C5 into C5a and C5b with a cleavage rate following Michaelis–Menten kinetics, having a k_{cat} of $2.00 \times 10^{-2} s^{-1}$ and a k_m of $5.10 \times 10^{-9} M$ [12].
S. nos 24, 25, and 28-35. Kinetic constants for heparin-complement proteins binding are reported by Yu et al. [16].
S. nos 26 and 27. The complement C1 can cleaves C2 into C2a and C2b with the cleavage rate of k_{cat} is $5.10 s^{-1}$ and a k_m of $6.10 \times 10^{-6} M$, as reported by Zewde et al. [9] and Rossi et al. [13].
S. no 36. Heparin acts as a potentiator of C1INH, and the binding rate for heparin and C1INH is $1.58 \times 10^4 M^{-1}s^{-1}$ [16].

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TABLE I: CONT.

Sources for the kinetic constants
S. nos 37-40 Heparin enzymatically reacts with the cleaved fragments C3b and C4b. The catalytic activity decreases C3b and C4b.
S. nos 41 and 42. For C3a and C3aR1, k_d is found to be $3.85\times10^{-9}M$ [17]. Assume a small value for the off rate of 0.10 s^{-1} and compute the on rate to be $2.60 \times 10^{8}M^{-1}s^{-1}$ using $k_d = \frac{k_{off}}{k_{on}}$.
S. nos 43 and 44. For C5a and C5aR1, k_d is found to be $4.50\times10^{-9}M$ [18]. Using $k_d = \frac{k_{off}}{k_{on}}$, compute the on rate to be $2.20\times10^{8}M^{-1}s^{-1}$. Assume an off rate of 0.10 s^{-1}.
S. no 45. The complex C1q-C1r-C1s can activate C1 with a rate of activation of $2.10 \times 10^{-5}s^{-1}$ [6]–[9].

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