

Table S4. Uncertain model parameters. “Reaction #s” are the numbers of the reactions governed by the rate parameter, and correspond to the numbering in Tables S2–S3, and Text S1. Allowed parameter ranges (defined by “Min.” and “Max.”) were chosen to encompass the value(s) obtained or calculated from literature, unless otherwise noted. “Optimal” are the parameter values from the optimization yielding the lowest SSR between the predicted and experimentally-measured [NO•] curve for wild-type *E. coli* treated with DPTA under aerobic conditions. Confidence intervals (C.I.) are provided for parameters that were informed by the optimization, and were calculated as the range of optimal parameter values obtained for the top 10% of optimization outcomes (those with the lowest SSR values).

#	Parameter	Parameter description/reaction involved	Reaction #s	Min.	Max.	Optimal	C.I.	Units	Ref.
1	$k_{\text{NO}\cdot\text{[Fe-S]}}$	[Fe-S] nitrosylation by NO•	85,86	1.0×10^4	1.0×10^8	1.40×10^7	--	$\text{M}^{-2}\text{s}^{-1}$	[1]
2	$k_{\text{DNIC-rem}}$	DNIC removal from protein	87,89	1	100	75.8	--	$\text{M}^{-1}\text{s}^{-1}$	[2]
3	$k_{\text{DNIC-bind}}$	DNIC binding to apoprotein	88,90	1	100	84.3	--	$\text{M}^{-1}\text{s}^{-1}$	[2]
4	$k_{\text{DNIC-deg}}$	O ₂ -mediated DNIC degradation	91	0.1	100	52.5	--	$\text{M}^{-1}\text{s}^{-1}$	[3]
5	$k_{\text{IscU-load-Fe}}$	IscA-mediated Fe ²⁺ transfer to IscU	92,93	2.5×10^{-3}	2.5	1.10	--	s^{-1}	[4]
6	$K_{\text{IscU-load-S,Cys}}$	IscS-mediated S transfer from Cys to IscU	151,152	1.0×10^{-6}	1.0×10^{-4}	7.00×10^{-5}	--	M	[5]
7	$K_{\text{IscU-load-S,IscU}}$	IscS-mediated S transfer from Cys to IscU	151,152	1.0×10^{-6}	1.0×10^{-4}	4.39×10^{-5}	--	M	[5,6]
8	$k_{\text{IscU-2Fe2S-insert,cat}}$	IscU-mediated [2Fe-2S] insertion into apoprotein	153,154	1.0×10^{-4}	0.1	0.037	--	s^{-1}	[7]
9	$K_{\text{IscU-2Fe2S-insert,P2Fe2S(apo)}}$	IscU-mediated [2Fe-2S] insertion into apoprotein	153,154	1.0×10^{-6}	1.0×10^{-4}	8.42×10^{-5}	--	M	[7]
10	$k_{\text{IscU-4Fe4S-insert}}$	IscU-mediated [4Fe-4S] insertion into apoprotein	94	1	500	182	--	$\text{M}^{-1}\text{s}^{-1}$	[8]
11	$k_{\text{dN-deam}}$	N ₂ O ₃ -mediated DNA base deamination	95–97	1.0×10^3	1.0×10^6	9.41×10^5	--	$\text{M}^{-1}\text{s}^{-1}$	[9]
12	$K_{\text{dX-excis,DNA(dX)}}$	Excision of xanthine from DNA	155	1.0×10^{-8}	1.0×10^{-6}	2.88×10^{-7}	--	M	[10]
13	$K_{\text{dI-excis,DNA(dI)}}$	Excision of hypoxanthine from DNA	156	1.0×10^{-8}	1.0×10^{-6}	6.68×10^{-7}	--	M	[11]
14	$K_{\text{dU-excis,DNA(dU)}}$	Excision of uracil from DNA	157	1.0×10^{-8}	1.0×10^{-6}	6.60×10^{-7}	--	M	[12]
15	$k_{\text{Hmp,NO}\cdot\text{-on}}$	Hmp detoxification; NO• binding to Hmp-Fe ²⁺	110,113,118	4.0×10^6	2.6×10^7	4.13×10^6	$(4.01\text{--}4.57) \times 10^6$	$\text{M}^{-1}\text{s}^{-1}$	[13]
16	$k_{\text{Hmp,NO}\cdot\text{-ox}}$	Hmp detoxification; NO• binding to Hmp-Fe ²⁺ -O ₂	103,108,125	9.6×10^8	2.4×10^9	1.14×10^9	--	$\text{M}^{-1}\text{s}^{-1}$	[13]
17	$k_{\text{Hmp-exp,max}}$	Hmp expression (maximum rate)	177	2.0×10^{-10}	2.0×10^{-8}	1.93×10^{-8}	$(1.79\text{--}2.00) \times 10^{-8}$	$\text{M}\cdot\text{s}^{-1}$	^a
18	$K_{\text{Hmp-exp,NO}\cdot}$	Hmp expression (regulatory NO• interaction)	177	1.0×10^{-8}	1.0×10^{-5}	3.38×10^{-7}	1.3×10^{-8} – 1.0×10^{-6}	M	^b
19	$k_{\text{NorV-exp,max}}$	NorV expression (maximum rate)	178	2.0×10^{-10}	2.0×10^{-8}	6.81×10^{-9}	--	$\text{M}\cdot\text{s}^{-1}$	^a
20	$K_{\text{NorV-exp,NO}\cdot}$	NorV expression (regulatory NO• interaction)	178	1.0×10^{-8}	1.0×10^{-5}	9.41×10^{-6}	--	M	^b
21	$k_{\text{NorV-O}_2}$	O ₂ -mediated NorV inactivation	146,147	10	1000	549	113–658	$\text{M}^{-1}\text{s}^{-1}$	[14]
22	$k_{\text{NrfA-exp,max}}$	NrfA expression (maximum rate)	179	2.0×10^{-10}	2.0×10^{-8}	7.72×10^{-9}	--	$\text{M}\cdot\text{s}^{-1}$	^a
23	$K_{\text{NrfA-exp,NO}_2^-}$	NrfA expression (regulatory NO ₂ [−] interaction)	179	1.0×10^{-6}	1.0×10^{-3}	9.32×10^{-4}	--	M	^c
24	$K_{\text{NrfA-exp,O}_2}$	NrfA expression (regulatory O ₂ interaction)	179	1.0×10^{-12}	1.0×10^{-10}	3.45×10^{-11}	--	M	^c
25	[Cys] ₀	Initial concentration of cysteine	--	5.0×10^{-5}	2.0×10^{-4}	1.51×10^{-4}	--	M	[15,16]
26	[Trx _{red}] ₀	Initial concentration of reduced thioredoxin	--	5.0×10^{-6}	5.0×10^{-5}	2.89×10^{-5}	--	M	[17,18]
27	[IscU] ₀	Initial concentration of IscU	--	1.0×10^{-8}	1.0×10^{-5}	9.48×10^{-6}	--	M	[5,19]
28	[IscS] ₀	Initial concentration of IscS	--	1.0×10^{-8}	1.0×10^{-5}	4.68×10^{-6}	--	M	[5,19]
29	[P _{2Fe2S} (<i>holo</i>)] ₀	Initial concentration of <i>holo</i> [2Fe-2S] proteins	--	1.0×10^{-6}	1.0×10^{-4}	9.86×10^{-5}	--	M	[20,21]
30	[P _{4Fe4S} (<i>holo</i>)] ₀	Initial concentration of <i>holo</i> [4Fe-4S] proteins	--	5.0×10^{-5}	5.0×10^{-4}	4.27×10^{-4}	--	M	[20,21]
31	[LigA] ₀	Initial concentration of DNA ligase	--	1.0×10^{-8}	1.0×10^{-5}	5.73×10^{-6}	--	M	[22]
32	[PolI] ₀	Initial concentration of DNA polymerase	--	1.0×10^{-8}	1.0×10^{-5}	4.40×10^{-6}	--	M	[22]
33	[DNA(dN)] ₀	Initial concentration of DNA bases (dA,dC,dG)	--	0.001	0.1	0.085	--	M	[21]
34	[Xth] ₀	Initial concentration of DNA exonuclease III	--	1.0×10^{-9}	1.0×10^{-6}	9.07×10^{-7}	--	M	[23]
35	[GS-FDH] ₀	Initial concentration of GSH-dependent FDH	--	1.0×10^{-8}	1.0×10^{-5}	3.94×10^{-6}	--	M	^d
36	[AlkA] ₀	Initial concentration of DNA glycosylase (dX, dI)	--	1.0×10^{-9}	1.0×10^{-6}	9.35×10^{-7}	--	M	[23]
37	[Ung] ₀	Initial concentration of DNA glycosylase (dU)	--	1.0×10^{-9}	1.0×10^{-6}	9.05×10^{-7}	--	M	[23]

38	[Cyo] ₀	Initial concentration of cytochrome <i>bo</i>	--	1.0×10^{-8}	1.0×10^{-5}	3.66×10^{-6}	--	M	[23]
39	[Cyd] ₀	Initial concentration of cytochrome <i>bd</i>	--	1.0×10^{-8}	1.0×10^{-5}	2.99×10^{-6}	--	M	[23]

- a.* The maximum protein expression rates for Hmp, NorV, and NrfA were not found in literature. The allowed parameter range was chosen based on the maximum expression rates reported for a number of enzymes in the work of Kotte *et al* [24]. Values were converted from the reported units of $g_{\text{protein}}/g_{\text{DW}} \cdot s$ to $M \cdot s^{-1}$ assuming a cell density of 448 gDW/L [21], and ranged from approximately 2×10^{-10} (Acs) to $2 \times 10^{-8} M \cdot s^{-1}$ (PfkA).
- b.* The allowed range for the NO• binding constant governing Hmp and NorV expression was chosen based on the reported physiological concentrations of NO• existing in the nM to μM range [25,26].
- c.* The NO₂⁻ binding constant governing NrfA expression was allowed to vary in the μM range, while the O₂ inhibition constant was assumed to be much lower, given that NrfA expression is primarily anaerobic [27,28].
- d.* Concentration was not found in literature, and therefore allowed a wide range, spanning values typically found for other enzymes in the model.

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