Supporting Information for the Manuscript Entitled

Elucidation of the Interplay between Fe(II), Fe(III) and Dopamine with Relevance to Iron Solubilization and ROS Generation by Catecholamines

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Table S1. Stability constants for Fe(II) and Fe(III) speciations at 25 ℃ and $I = 0$.

No.	species	LogK	Reference
Fe(II) species			
1	$Fe^{2+} + H_2O \rightleftharpoons FeOH^+ + H^+$	-9.51	1
2	$Fe^{2+} + 2H_2O \rightleftharpoons Fe(OH)_2^0 + 2H^+$	-20.6	1
3	$Fe^{2+} + CO_3^{2-} \rightleftharpoons FeCO_3^0$	5.69	2
4	$Fe^{2+} + H^+ + CO_3^{2-} \rightleftharpoons FeHCO_3^+$	11.8	3
5	$Fe^{2+} + 2CO_3^{2-} \rightleftharpoons Fe(CO_3)_2^{2-}$	7.45	2
6	$Fe^{2+} + CO_3^{2-} + H_2O \rightleftharpoons Fe(OH)CO_3^- + H^+$	-4.03	2
7	$Fe^{2+} + Cl^- \rightleftharpoons FeCl^+$	0.3	2
8	$Fe^{2+} + SO_4^{2-} \rightleftharpoons FeSO_4^0$	2.42	2
9	$Fe^{2+} + DA^{2-} \rightleftharpoons FeDA^0$	9.12	4
10	$Fe^{2+} + 2DA^{2-} \rightleftharpoons FeDA_2^{2-}$	14.56	4
Fe(III) species			
11	$Fe^{3+} + H_2O \rightleftharpoons Fe(OH)^{2+} + H^+$	-2.13	5
12	$Fe^{3+} + 2H_2O \rightleftharpoons Fe(OH)_2^+ + 2H^+$	-6.13	5
13	$Fe^{3+} + 3H_2O \rightleftharpoons Fe(OH)_3^0 + 3H^+$	-14.3	5
14	$Fe^{3+} + 4H_2O \rightleftharpoons Fe(OH)_4^- + 4H^+$	-22.2	5
15	$Fe^{3+} + Cl^- \rightleftharpoons FeCl^{2+}$	1.28	5
16	$Fe^{3+} + 2Cl^- \rightleftharpoons FeCl_2^+$	1.16	5
17	$Fe^{3+} + SO_4^{2-} \rightleftharpoons Fe(SO_4)^+$	4.27	5

18	$Fe^{3+} + 2SO_4^{2-} \rightleftharpoons Fe(SO_4)_2^-$	6.11	5
19	$Fe^{3+} + 2CO_3^{2-} \rightleftharpoons Fe(CO_3)_2^-$	19.6	5
20	$Fe^{3+} + DA^{2-} \rightleftharpoons FeDA^+$	21.42	6
21	$Fe^{3+} + 2DA^{2-} \rightleftharpoons FeDA_2^-$	36.46	6
22	$Fe^{3+} + 3DA^{2-} \rightleftharpoons FeDA_3^{3-}$	45.08	6

Aqueous species

23	$H^+ + OH^- \rightleftharpoons H_2O$	14	7
24	$H^+ + CO_3^{2-} \rightleftharpoons HCO_3^-$	10.3	7
25	$2H^+ + CO_3^{2-} \rightleftharpoons H_2CO_3^*$	16.7	7
26	$NH_3 + H^+ \rightleftharpoons NH_4^+$	9.24	8
27	$H^+ + SO_4^{2-} \rightleftharpoons HSO_4^-$	1.99	8
28	$Na^+ + CO_3^{2-} \rightleftharpoons NaCO_3^-$	1.27	2
29	$Na^+ + H^+ + CO_3^{2-} \rightleftharpoons NaHCO_3^0$	10.1	2
30	$Na^+ + SO_4^{2-} \rightleftharpoons NaSO_4^-$	1.06	2
31	$NH_4^+ + SO_4^{2-} \rightleftharpoons NH_4SO_4^-$	1.03	9
32	$H_2DA \rightleftharpoons HDA^- + H^+$	-10.58	10
33	$HDA^- \rightleftharpoons DA^{2-} + H^+$	-12.07	10

(1) Morel and Hering (1993); (2) King (1998); (3) Millero and Hawke (1992); (4) Smith and Martell (1989); (5) Pham *et al.* (2006); (6) Avdeef *et al.* (1978); (7) Millero et al. (1995); (8) Yuan *et al.* (2012); (9) Schecher and McAvoy (1992) and (10) Pham and Waite (2014)
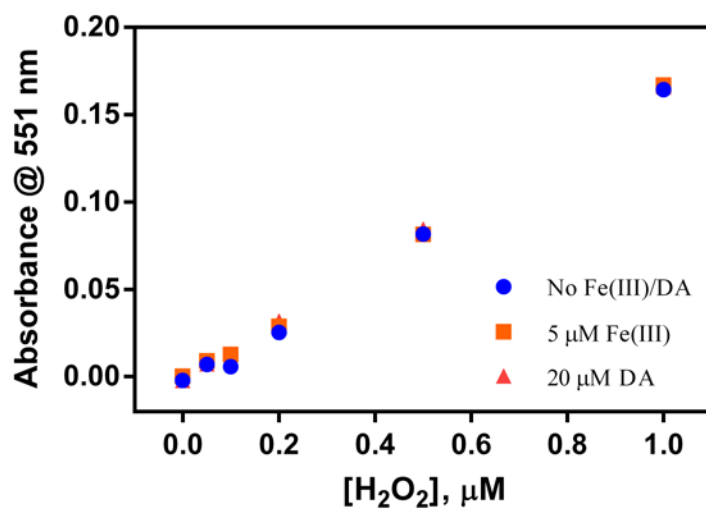
Figure S1. Measured absorbance of H_2O_2 at 551 nm with baseline corrected at 690 nm in 0.1 M NaCl at pH 7.4 in the absence of Fe(III) and DA (●) and in the presence of 5 µM Fe(III) (■) and 20 µM DA (▲). Error bars are standard errors from triplicate measurements.

Figure S1 indicated that the presence of moderate concentrations of Fe(III) (5 µM) and DA (20 µM) has negligible effect on the measurement of H_2O_2 in the presence of 1 mM DTPA, 60 µM DPD and 500 U/L HRP .

(a) 5 μM Fe(III), 10 μM DA

(b) 5 μM Fe(III), 100 μM DA

(c) 5 μM Fe(III), 500 μM DA

(d) 5 μM Fe(II), 1 μM DA

(e) 5 μM Fe(II), 10 μM DA

(f) 5 μM Fe(II), 100 μM DA

Figure S2. Speciation of Fe(III) (a, b and c) and Fe(II) (d, e and f) over the pH range 4.0 - 8.5 in solutions containing varying concentrations of DA with $[Fe(II)]_0 = 5$ µM and $[Fe(III)]_0 = 5$ µM. LogC denotes the log concentration of individual ferrous and ferric species.
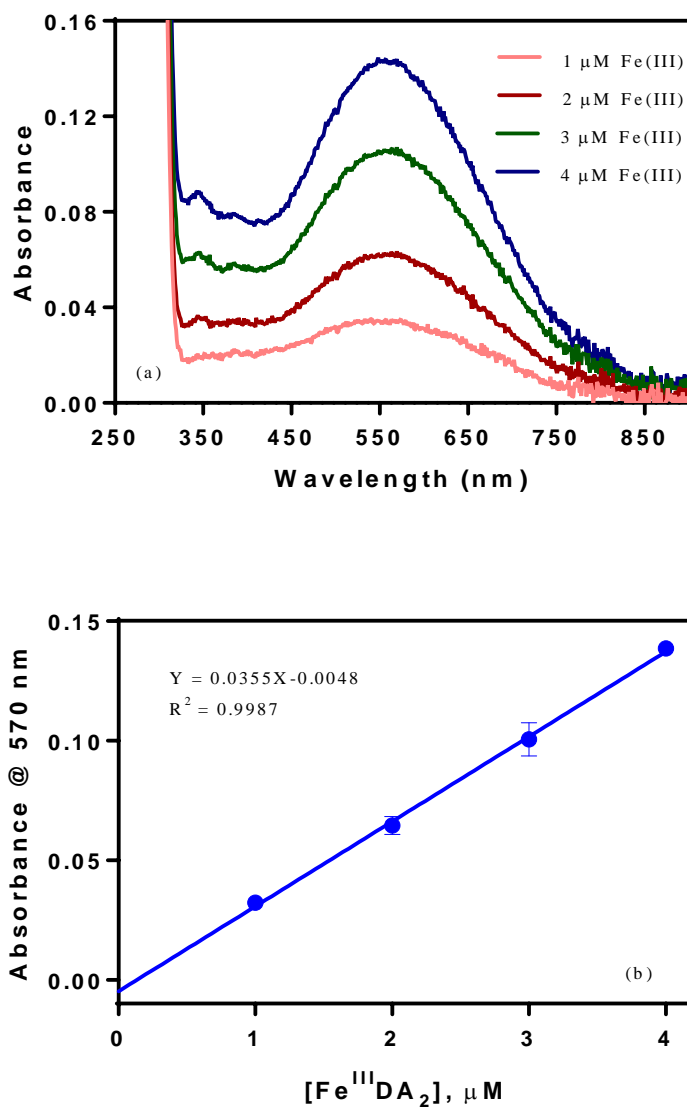
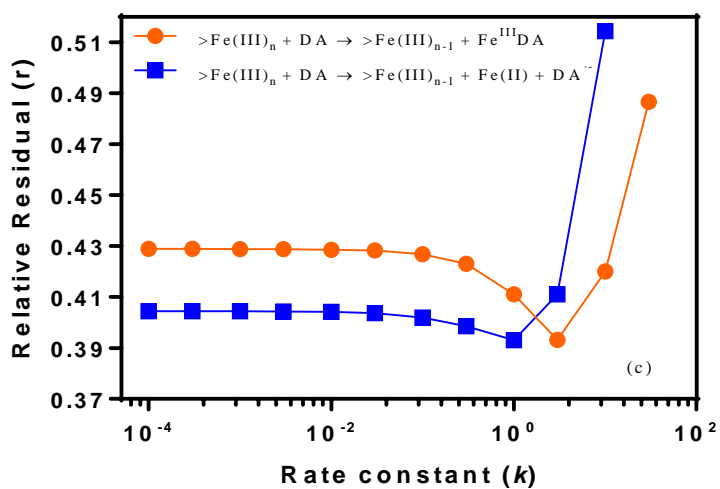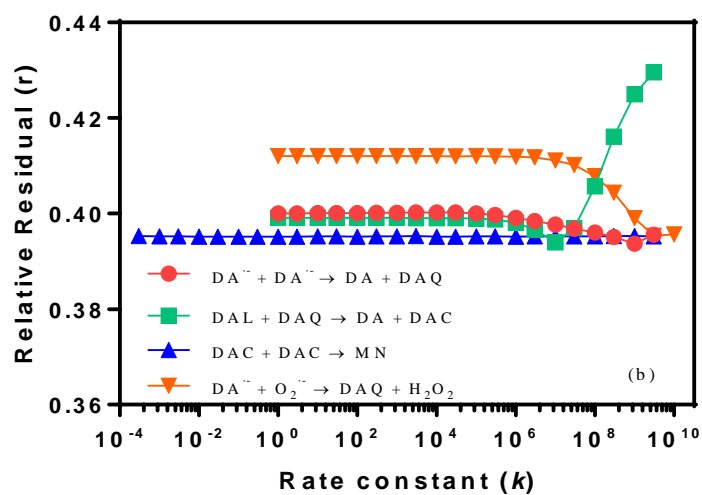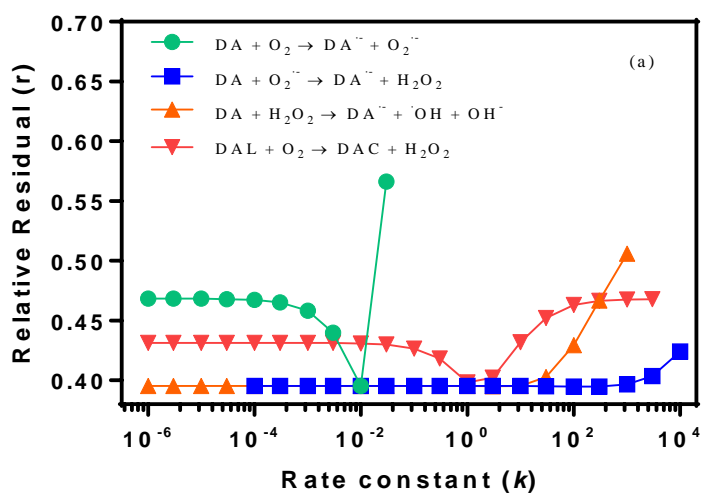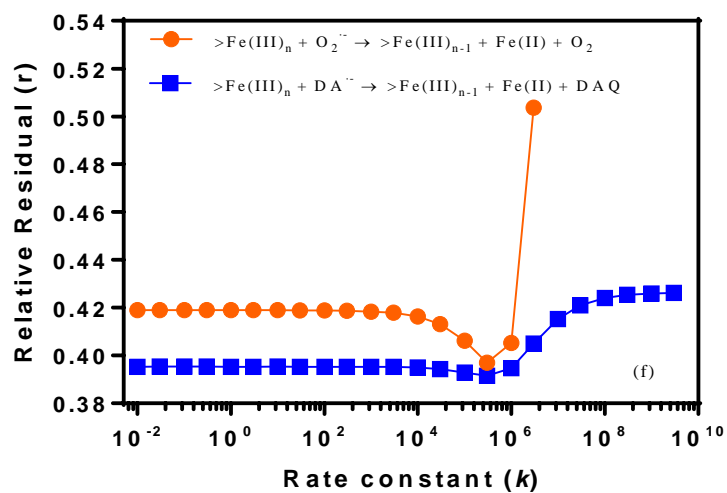Figure S3. Measured absorbance of $Fe^{III}DA_2$ complexes (panel a) and calibration curve for qualification of $Fe^{III}DA_2$ complexes measured at 570 nm with baseline corrected at 850 nm (panel b) in 0.1 M NaCl at pH 7.4 in the presence of 400 µM DA under deoxygenated condition.

Figure S3 indicated that in the presence of moderate concentrations of DA, $Fe^{III}DA_2$ was the dominant complexes and a clear peak can be observed at 570 nm. 400 µM DA was used to ensure that precipitation of Fe(III) is negligible.

(a)

$DA + O_2 \rightarrow DA^{\cdot-} + O_2^{\cdot-}$

$DA + O_2^{\cdot-} \rightarrow DA^{\cdot-} + H_2O_2$

$DA + H_2O_2 \rightarrow DA^{\cdot-} + {}^{\cdot}OH + OH^-$

$DAL + O_2 \rightarrow DAC + H_2O_2$

(b)

$DA^{\cdot-} + DA^{\cdot-} \rightarrow DA + DAQ$

$DAL + DAQ \rightarrow DA + DAC$

$DAC + DAC \rightarrow MN$

$DA^{\cdot-} + O_2^{\cdot-} \rightarrow DAQ + H_2O_2$

(c)

$>Fe(III)_n + DA \rightarrow >Fe(III)_{n-1} + Fe^{III}DA$

$>Fe(III)_n + DA \rightarrow >Fe(III)_{n-1} + Fe(II) + DA^{\cdot-}$

(d)

$Fe^{III}DA_2 \rightarrow Fe(II) + DA + DA^{\cdot\cdot}$

(e)

$Fe(III) + DA \rightarrow Fe^{III}DA$

$Fe^{III}DA + DA \rightarrow Fe^{III}DA_2$

$Fe(II) + DA^{\cdot\cdot} \rightarrow Fe(III) + DA$

$Fe^{II}DA + DA^{\cdot\cdot} \rightarrow Fe^{III}DA + DA$

(f)

$>Fe(III)_n + O_2^{\cdot\cdot} \rightarrow >Fe(III)_{n-1} + Fe(II) + O_2$

$>Fe(III)_n + DA^{\cdot\cdot} \rightarrow >Fe(III)_{n-1} + Fe(II) + DAQ$

(g)

$Fe(II) + DA \rightarrow Fe^{II}DA$

$Fe^{II}DA + H_2O_2 \rightarrow Fe^{III}DA + {}^{\cdot}OH + OH^{-}$

(h)

$Fe^{III}DA + O_2^{\cdot -} \rightarrow Fe^{II}DA + O_2$

$Fe^{II}DA + O_2^{\cdot -} \rightarrow Fe^{III}DA + H_2O_2$

$Fe(III) + DA^{\cdot -} \rightarrow Fe(II) + DAQ$

$Fe^{III}DA + DA^{\cdot -} \rightarrow Fe^{II}DA + DAQ$

(i)

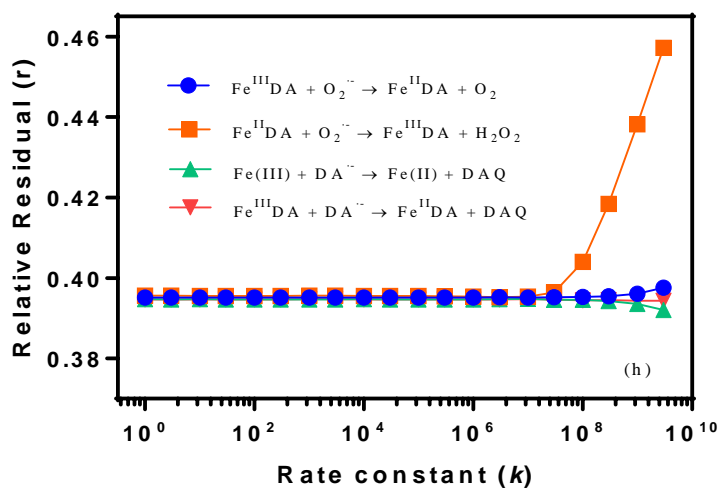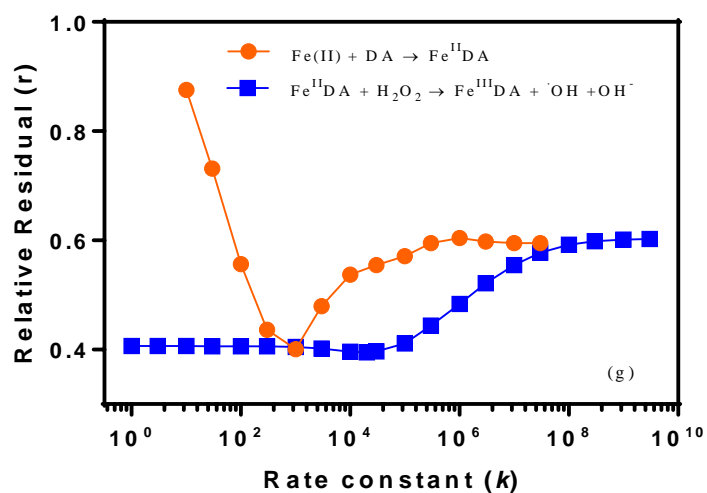$Fe^{II}DA + O_2 \rightarrow Fe^{III}DA + O_2^{\cdot -}$

Figure S4. Sensitivity analysis for different fitting reaction rate constants (Tables 1 - 3, main text) and some other unimportant reactions.
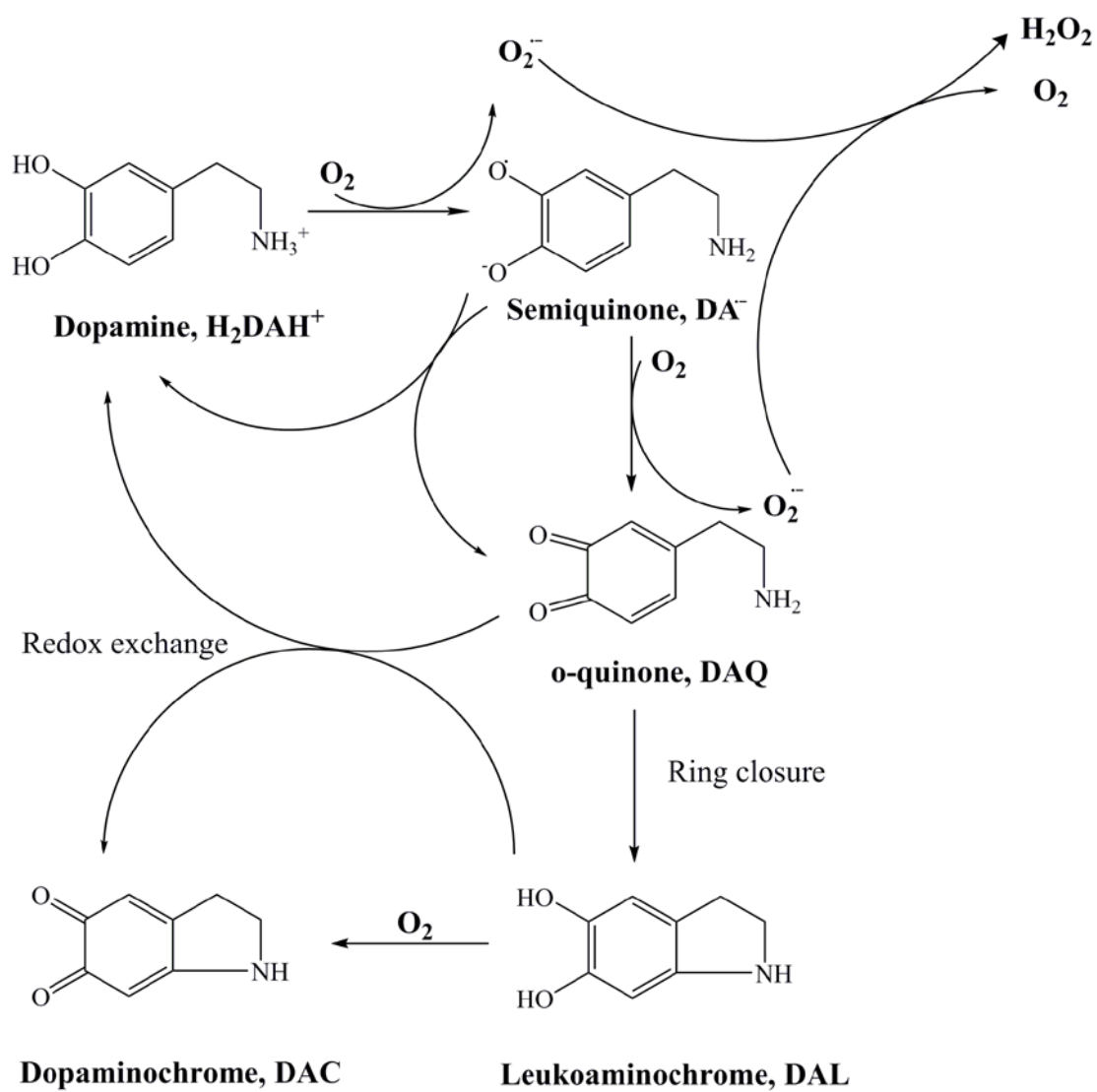
Figure S5. Oxidation pathway of dopamine in the absence of added metals (Pham and Waite 2014)

Text S1

The standard free energy change (ΔG^0) for $Fe^{II}DA$ oxidation to $Fe^{III}DA$ (via one-electron

reduction of O_2 to $O_2^{\cdot-}$) is given by

$$\Delta G^0 = -F(E^0_{O_2 \to O_2^{\cdot-}} - E^0_{Fe^{III}DA \to Fe^{II}DA})$$

Where $E^0_{O_2 \to O_2^{\cdot-}} = -0.18$ V (Koppenol $et\ al.$ 2010), F is the Faraday constant, $E^0_{Fe^{III}DA \to Fe^{II}DA}$

is determined using the Nernst equation (Morel and Hering 1993).

$$E^0_{Fe^{III}DA \to Fe^{II}DA} = E^0_{(Fe^{3+} \to Fe^{2+})} - 0.059 \log_{10}\left(\frac{K_{Fe^{III}DA}}{K_{Fe^{II}DA}}\right)$$

where $E^0_{(Fe^{3+} \to Fe^{2+})} = 0.77$ V (Schumb $et\ al.$ 1937) is the standard reduction potential of Fe^{3+} and Ki

is the stability constant of the complex $Fe^{II}DA$ and $Fe^{III}DA$ shown in Table S1. Thus, the calculated

redox potential of the complexed iron couple should be $E^0_{Fe^{III}DA \to Fe^{II}DA} = 0.044$.

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