Effect of pH and Oxidant on the First Steps of Polydopamine Formation : A Thermodynamic Approach

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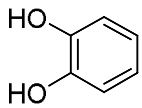
SUPPORTING INFORMATION

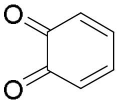
Compilation of relevant spectral data in literature

Catechol



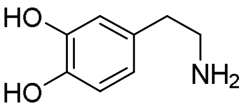
$\lambda_{\max} = 275\,nm$, shifts to 292 upon metal binding/deprotonation.[1]

o-quinone



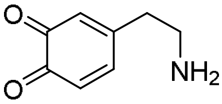
$\lambda_{\max} = 389\ nm$, other transitions seen as shoulders at 310 nm and 245 nm.[2]

Dopamine



$\lambda_{\max} = 220\,nm,\ 280\,nm$ [3,4]

Dopaminequinone (DQ)



$\lambda_{\max} = 395\,nm$ [4] (see above for o-quinone)

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[1] Sever, M. J.; Wilker, J. J.; Visible absorption spectra of metal-catecholate and metal-tironate complexes, *Dalton Trans*. **2004**, 1061-1072.

[2] Albarran, G.; Boggess, W.; Rassolov, V.; Schuler, R. H.; Absorption Spectrum, Mass Spectrometric Properties, and Electronic Structure of 1,2-Benzoquinone, *J. Phys. Chem. A* **2010**, *114*, 7470-7478.

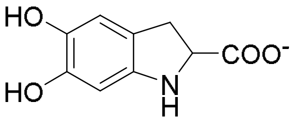
[3] Bernsmann, F.; Ersen, O.; Voegel, J.; Jan, E.; Kotov, N. A.; Ball, V.; Melanin-Containing Films: Growth from Dopamine Solutions versus Layer-by-Layer Deposition, *ChemPhysChem* **2010**, *11*, 3299-3305.

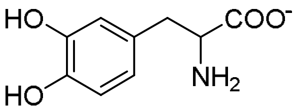
[4] Bisaglia, M.; Mammi, S.; Bubacco, L., *J. Biol. Chem*. **2007**, *282*, 15597-15605.

Dopasemiquinone

$\lambda_{\max} = 305\,nm$, $\varepsilon =$ 12000 M^{-1} cm^{-1}.[5]

Leucodopa (cyclodopa) and dopa





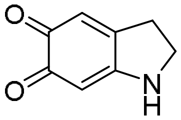
Leucodopa (acidic solution) $\lambda_{\max} = 285nm$, higher ε that with dopa.[6,7] The cyclodopa absorption tails over 300 nm but that of dopa does not.

Dopa $\lambda_{\max} = 279nm$ (acidic solution).[6]

Cyclodopasemiquinone

$\lambda_{\max} = 480nm$[7]

Dopaminechrome (aminochrome, AC)



$\lambda_{\max} = 300\,nm,\ 475\,nm$[4]

$\varepsilon(480\,\text{nm}) = 3280\,\text{M}^{-1}\,\text{cm}^{-1}$.[8]

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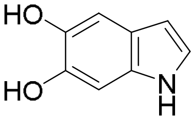
[5] Thompson, A.; Land, E. J.; Chedekel, M. R.; Subbarao, K. V.; Truscott, T. G.; A pulse radiolysis investigation of the oxidation of the melanin precursors 3,4-dihydroxyphenylanine (dopa) and the cysteinyldopas. *Biochem. Biophys. Acta – General Subjects* **1985**, *843*, 49-57.

[6] Wyler, H.; Chiovini, J.; Die Synthese von Cyclodopa (Leukodopachrom). *Helvetica Chim. Acta* **1968**, *51*, 1476-1494.

[7] Land, E. J.; Ito, S.; Wakamatsu, K.; Riley, P. A.; Rate Constants for the First Two Chemical Steps of Eumelanogenesis. *Pigm. Cell.; Melanoma Research* **2003**, *16*, 487-493.

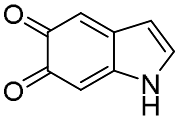
[8] Pham, A. N.; Waite, T. D.; Cu(II)-catalyzed oxidation of dopamine in aqueous solutions: Mechanism and kinetics. *J. Inorg. Biochem.* **1993**, *21*, 392-410.

5,6-dihydroxyindole (DHI)



$\lambda_{\max} = 276\,nm,\ 298\,nm$ (296 nm)[9]

Indoloquinone



$\lambda_{\max} = 620\,nm$ [101]

Fe-catecholate complexes Fe(cat)$_n$ [1]

1:1 complex $\lambda_{\max} = 429\,nm\ (\varepsilon = 880),\ 700\,nm\ (\varepsilon = 1000)$

1:2complex $\lambda_{\max} = 374\,nm(\varepsilon = 1950), 576\,nm\ (\varepsilon = 2900)$

1:3 complex $\lambda_{\max} = 483\,nm\ (\varepsilon = 3700)$

Cu-catecholate complexes [1]

1:1 complex $\lambda_{\max} = 449\,nm(\varepsilon = 53),\ 743\,nm\ (\varepsilon = 36)$

1:2 complex $\lambda_{\max} = 401\,nm(\varepsilon = 220),\ 655\,nm\ (\varepsilon = 28)$

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[9] Zhang, F.; Dryhurst, G.; *Bioorg. Chem.* **1993**, *21*, 392-410.

[10] Salomäki, M.; Tupala, M.; Parviainen, T.; Leiro, J.; Karonen, M.; Lukkari, J., Preparation of Thin Melanin-Type Films by Surface-Controlled Oxidation, *Langmuir* **2015**, *32*, 4103-4112.

Dopamine autoxidation at pH 8.5

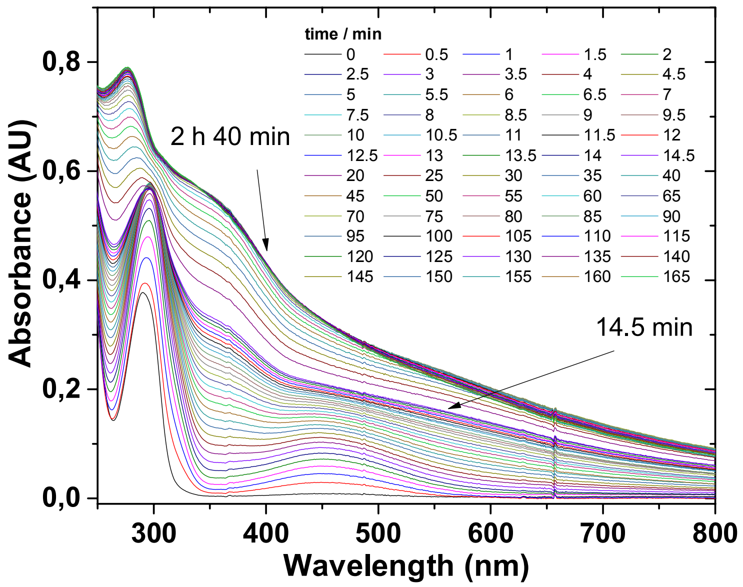


Fig. S1. Evolution of spectra during autoxidation of 0.1 mM dopamine by dissolved oxygen at pH 8.5 Tris buffer and 50 °C.

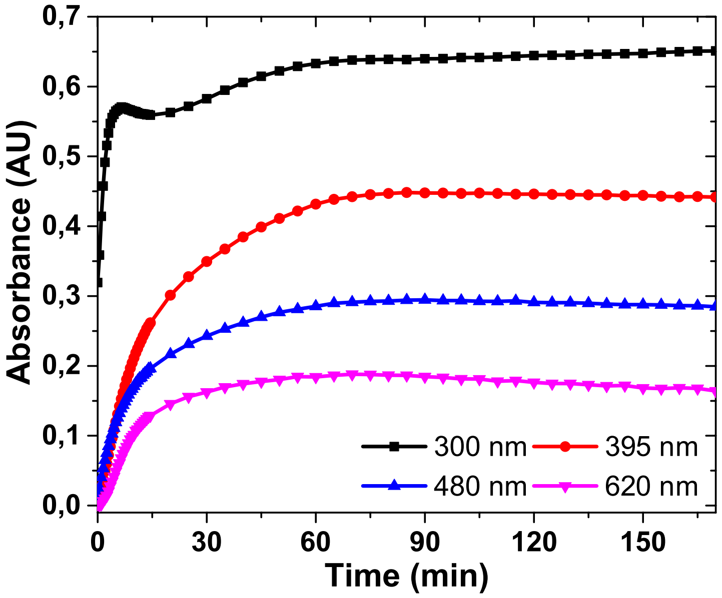


Fig. S2. Evolution of absorbance at different wavelengths in fig.S1. The wavelengths correspond to the maximum absorbances as follows: Black line (300 nm), mainly leucodopaminechrome; red line (395 nm), dopaminequinone; blue line (480 nm), dopaminechrome; magenta line (620 nm), indolequinone.

Spectra as a function pH during the titration of 0.1 mM dopamine with 0.5 M NaOH in the presence of dissolved oxygen and metal ions

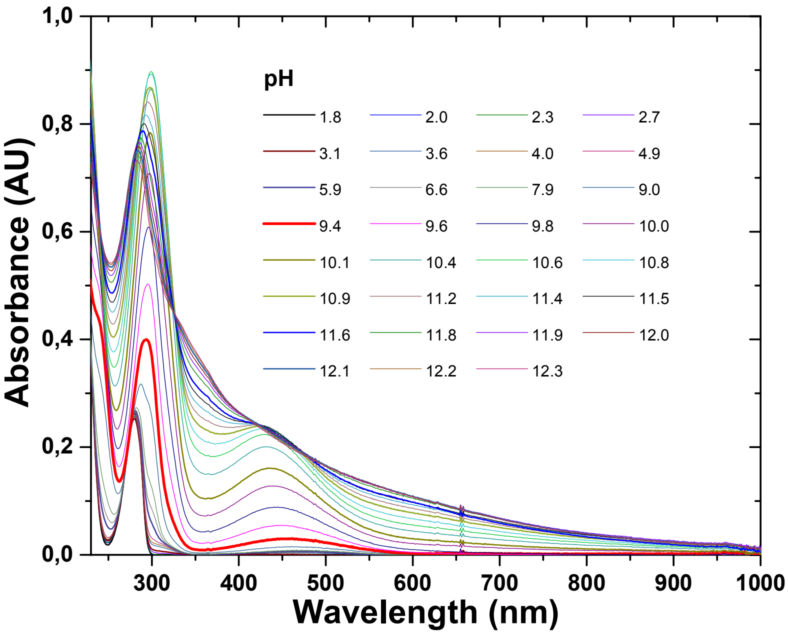


Figure S3. Spectra taken during the titration of 0.1 mM dopamine with 0.5 M NaOH in the presence of dissolved oxygen only.

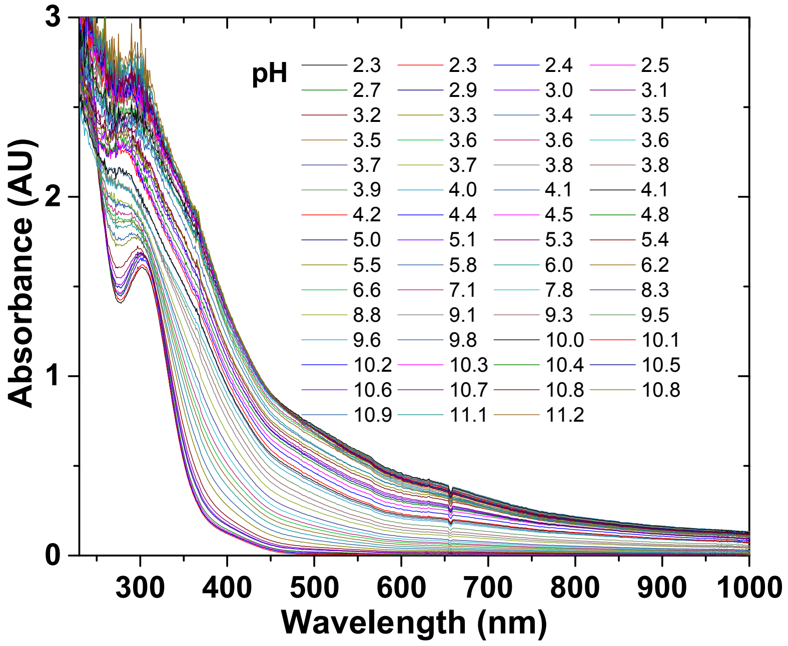


Figure S4. Spectra taken during the titration of 0.1 mM dopamine with 0.5 M NaOH in the presence of dissolved oxygen and 1 mM Fe(III).

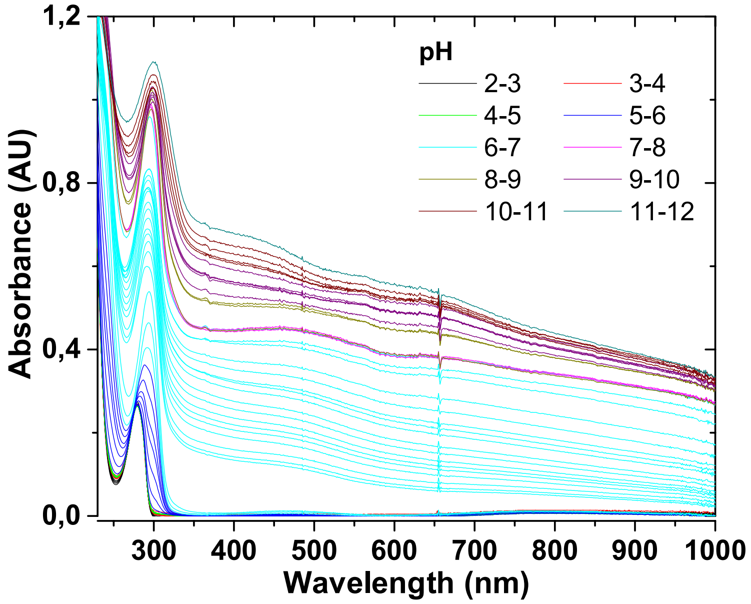


Figure S5. Spectra taken during the titration of 0.1 mM dopamine with 0.5 M NaOH in the presence of dissolved oxygen and 1 mM Cu(II).

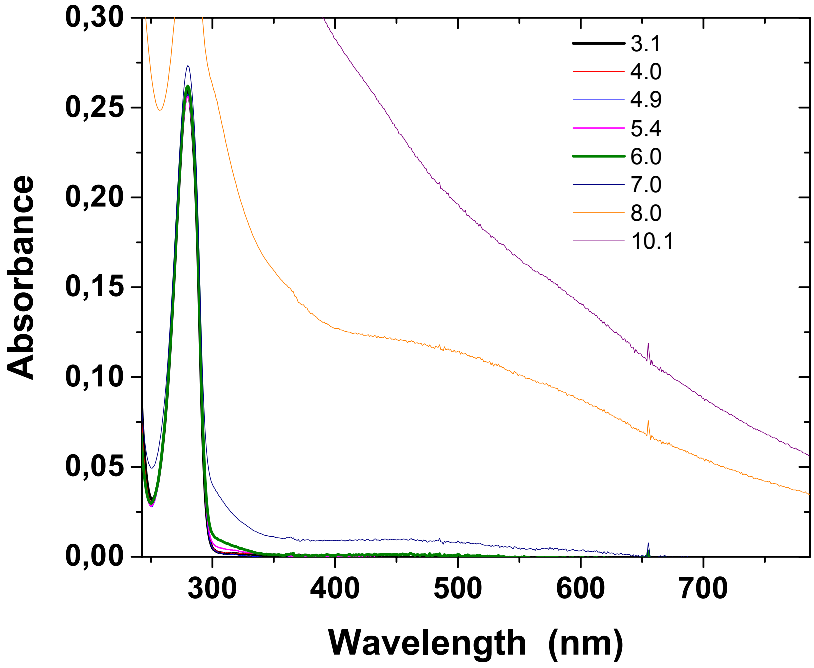


Figure S6. Spectra of 0.1 M dopamine solution in an open vessel after 20 h reaction time at pH indicated (10 mM phosphate citrate buffer, adjusted with NaOH).

Effect of transition metal ions on catechol oxidation : UV-Vis spectra

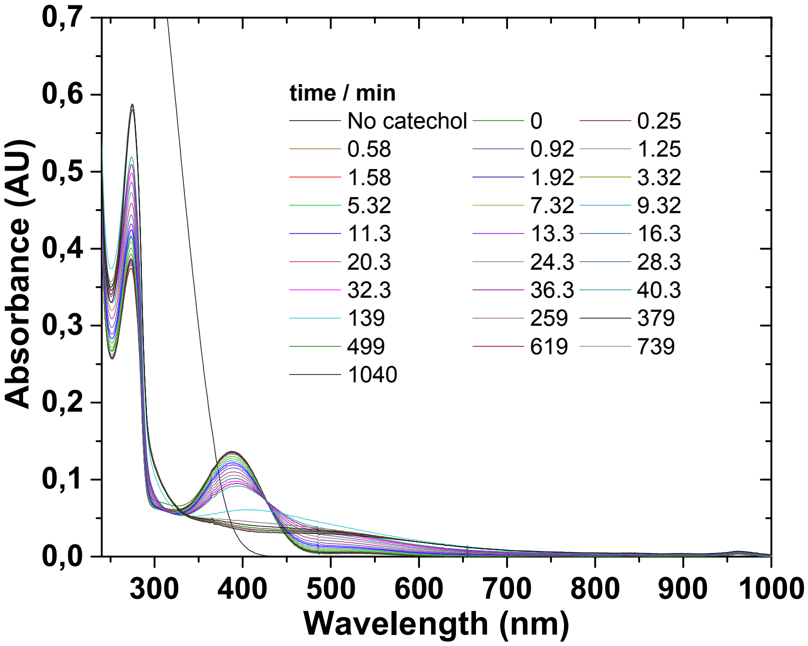


Figure S7. Reaction of catechol (0.2 mM) with Ce(IV) (0.2 mM) at pH 4.5 (0.1 M acetate buffer) in the absence of O_2. Times in minutes.

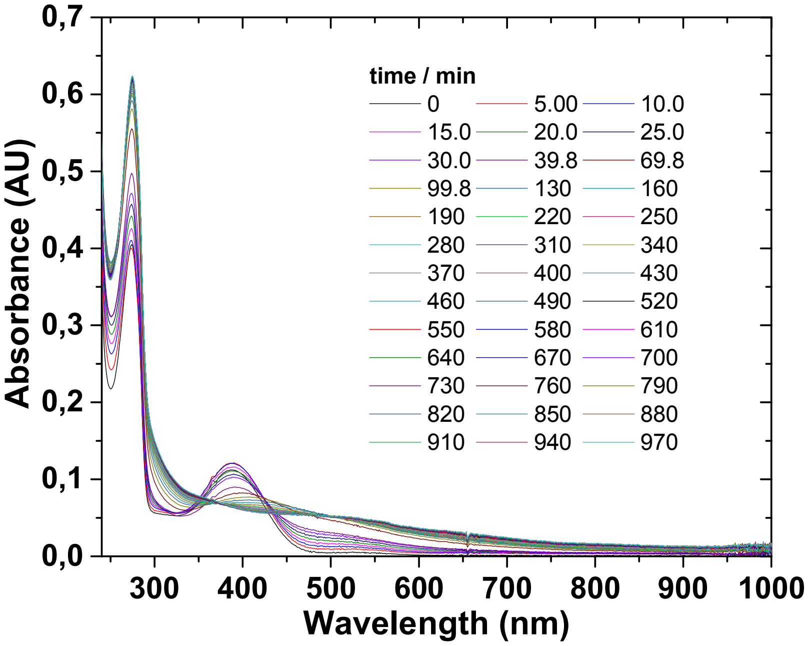


Figure S8. Reaction of catechol (0.2 mM) with Ce(IV) (0.2 mM) at pH 4.5 (0.1 M acetate buffer) in the presence of dissolved O_2. Times in minutes.

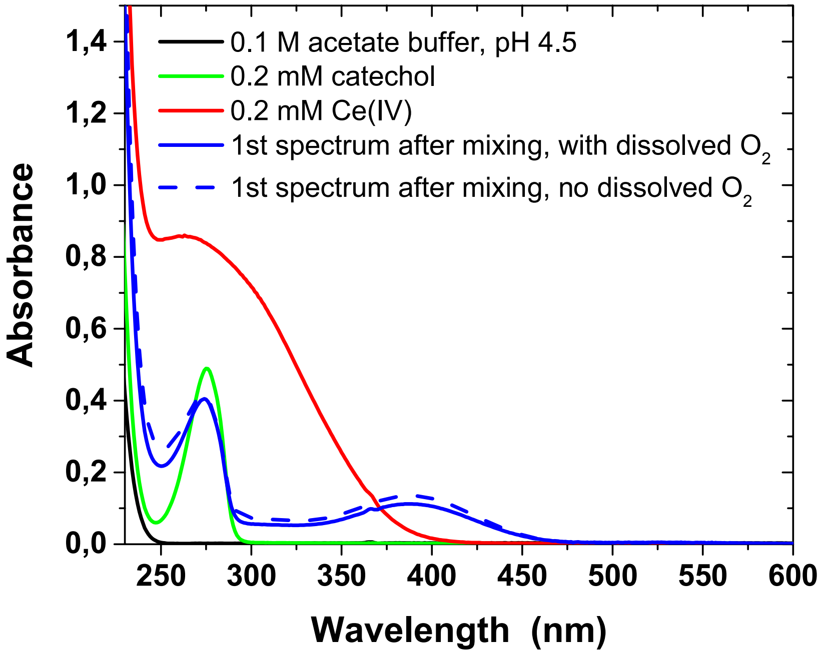


Figure S9. Comparison of the reactant spectra and the first measured spectrum in the reaction between catechol and Ce(IV) at pH 4.5 with/without dissolved O_2.

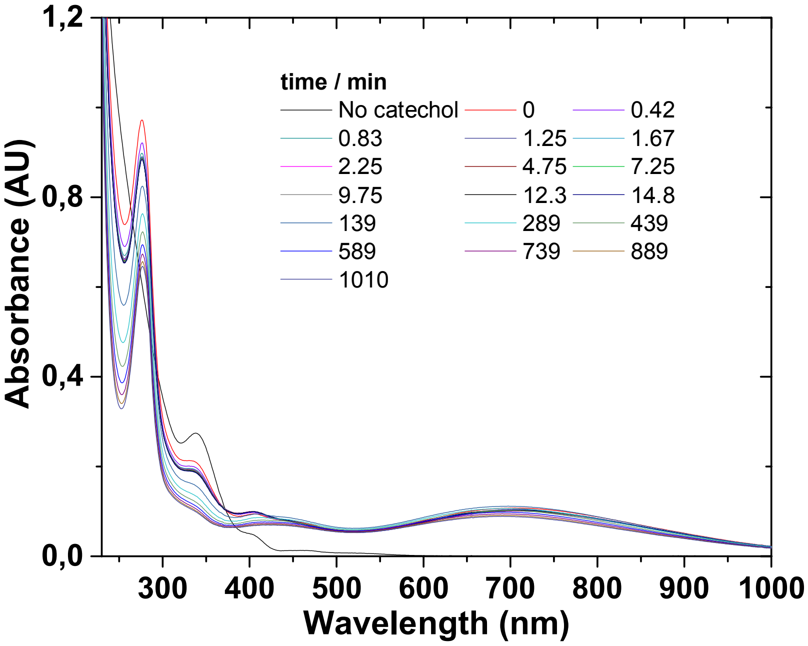


Figure S10. Reaction of catechol (0.2 mM) with Fe(III) (0.2 mM) at pH 4.5 (0.1 M acetate buffer) in the absence of O_2. Times in minutes. Bands at 440 nm and 700 nm due to the 1:1 Fe-catechol complex.

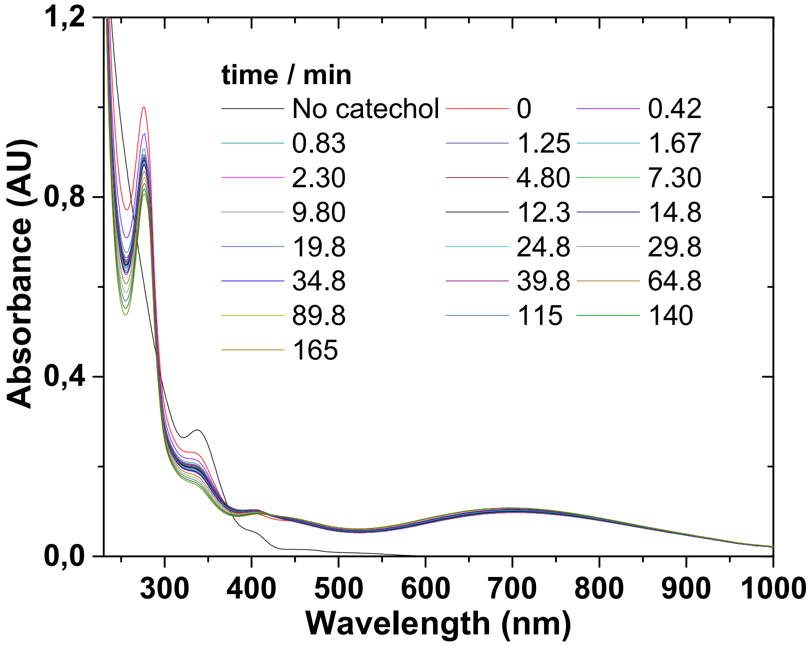


Figure S11. Reaction of catechol (0.2 mM) with Fe(III) (0.2 mM) at pH 4.5 (0.1 M acetate buffer) in the presence of dissolved O_2. Times in minutes. Bands at 440 nm and 700 nm due to the 1:1 Fe-catechol complex.

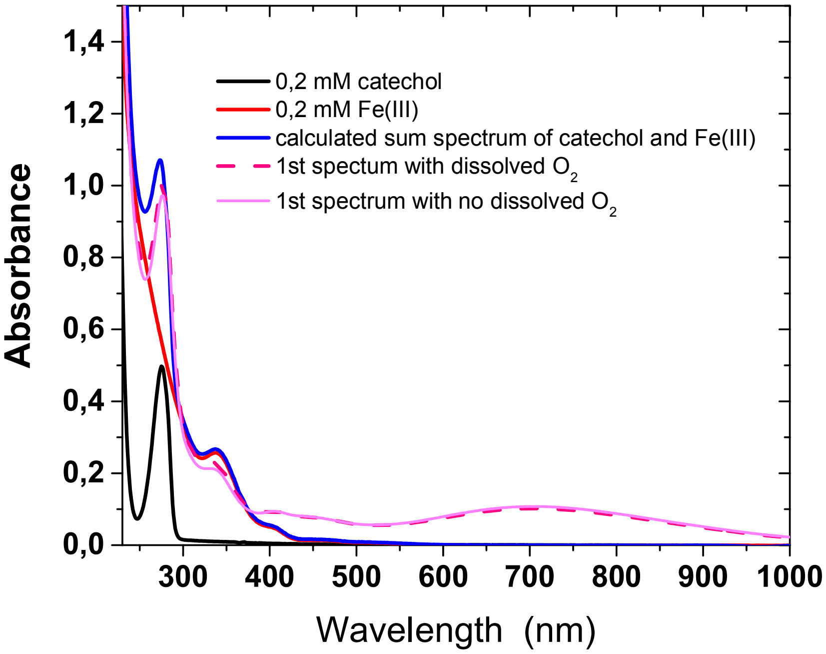


Figure S12. Comparison of the reactant spectra, their calculated sum, and the first measured spectrum in the reaction between catechol and Fe(III) at pH 4.5 with/without dissolved O_2.

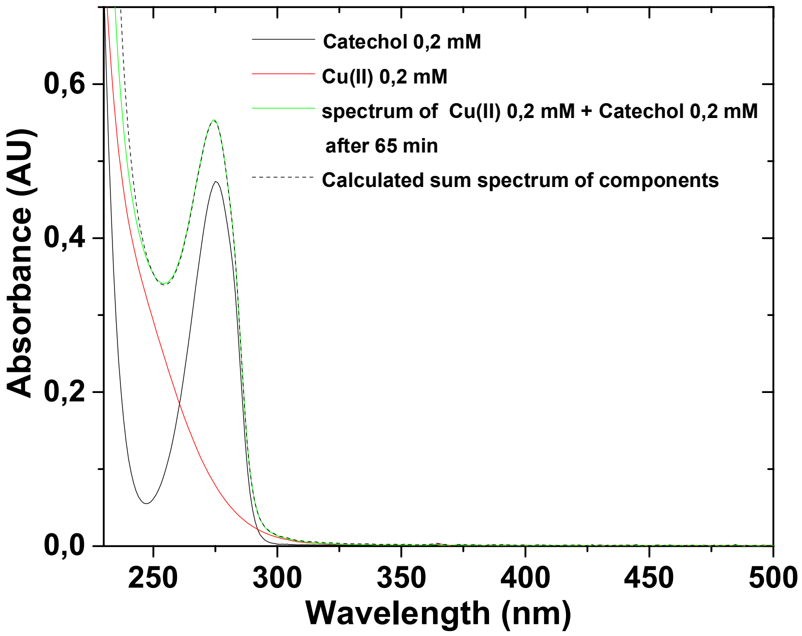


Figure S13. Comparison of the reactant spectra, their calculated sum, and the measured spectrum at time t = 65 min in the reaction between catechol and Cu(II) at pH 4.5 without chloride in the presence of dissolved O_2.

Effect of transition metal ions on dopamine oxidation and cyclization : UV-Vis spectra

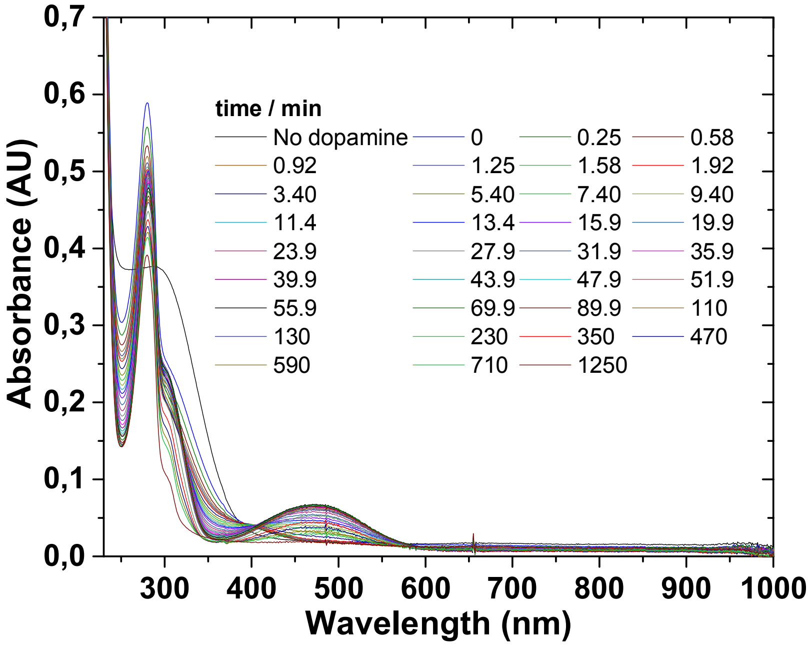


Figure S14. Reaction of dopamine (0.1 mM) with Ce(IV) (0.1 mM) at pH 4.5 (10 mM acetate buffer) in the absence of dissolved O_2. Times in minutes.

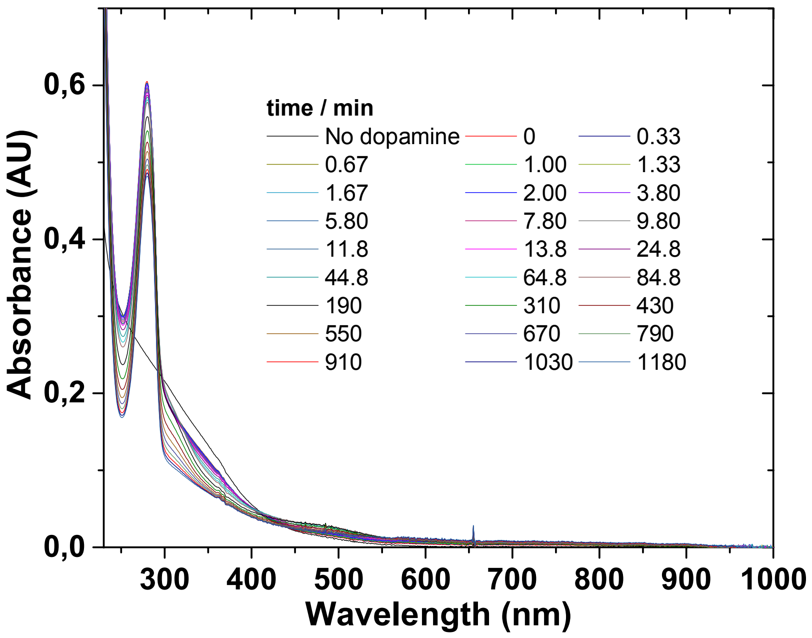


Figure S15. Reaction of dopamine (0.1 mM) with Fe(III) (0.1 mM) at pH 4.5 (10 mM acetate buffer) in the absence of dissolved O_2. Times in minutes.

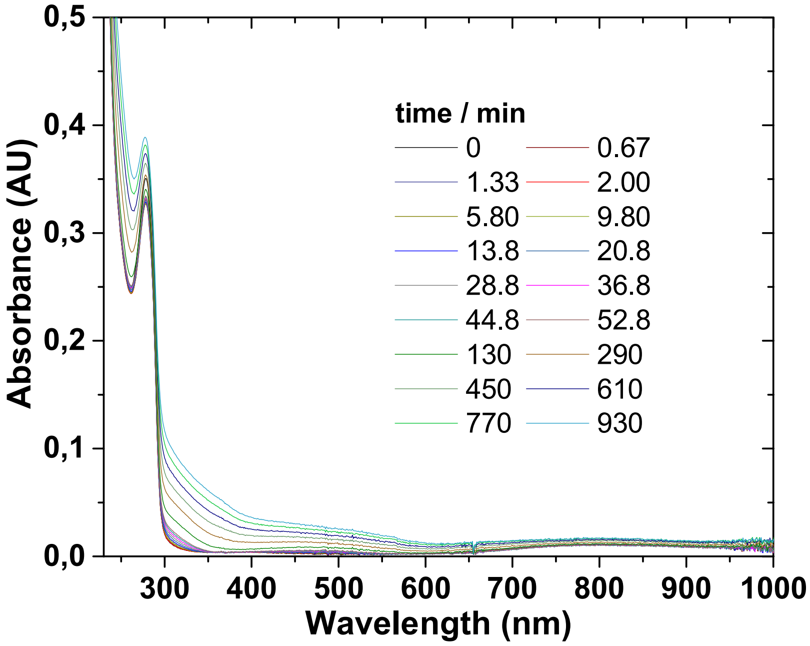


Figure S16. Reaction of dopamine (0.1 mM) with Cu(II) (0.6 mM) and 0.1 M NaCl at pH 4.5 (10 mM acetate buffer) in the presence of dissolved O_2. Times in minutes. Band at 800 due to Cu.

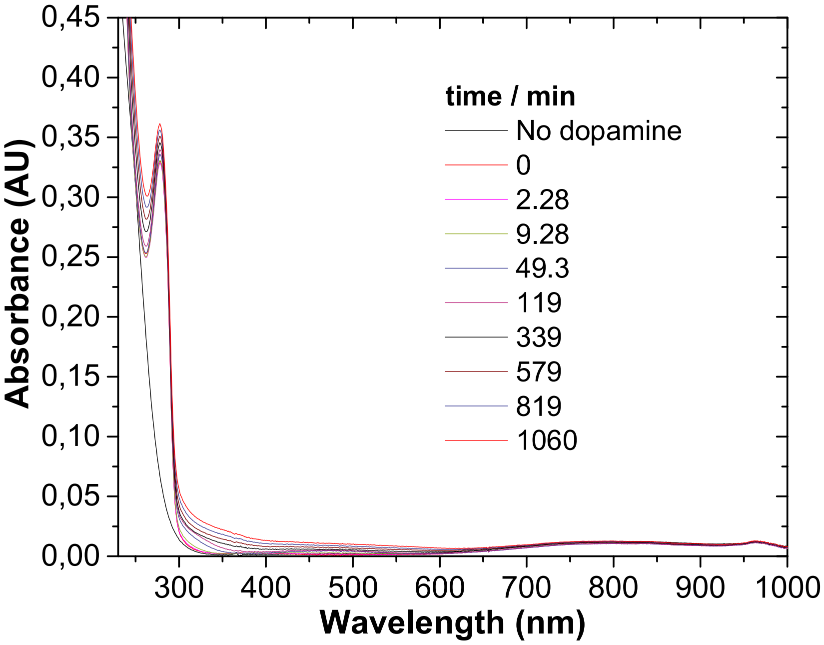


Figure S17. Reaction of dopamine (0.1 mM) with Cu(II) (0.6 mM) and 0.1 M NaCl at pH 4.5 (10 mM acetate buffer) in the absence of dissolved O_2. Times in minutes. Band at 800 nm due Cu.

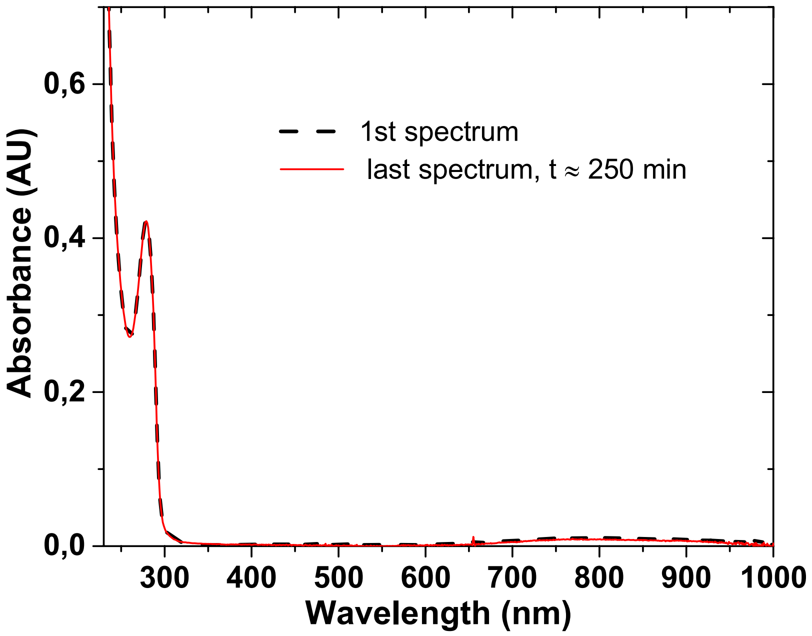


Figure S18. Reaction of dopamine (0.1 mM) with Cu(II) (0.6 mM) at pH 4.5 (10 mM acetate buffer) in the absence of chloride and O_2. Times in minutes. Band at ca. 800 nm due to Cu.

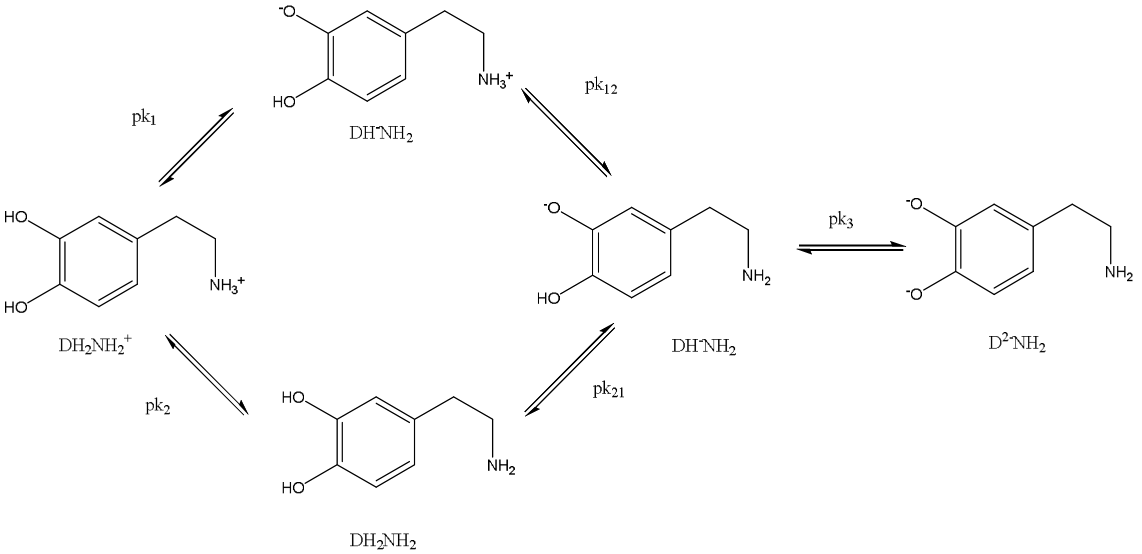
Dopamine protonation equilibria

The macroscopic pK-values of catechol and dopamine have been determined

	pK_1	pK_2	pK_3
catechol[11]	9.22	13.00	
dopamine	8.87, 8.89	10.63, 10.41	13.1

These macroscopic acidity constants are superpositions of the microscopic ones, which relate the different internal protonation states of the molecules. In case of dopamine, we can differentiate the following microscopic protonation/deprotonation equilibria :

Scheme S1



The effective pH range of the first and second macroscopic acidity constants of dopamine overlap and, therefore, they represent a sum effect of the microscopic equilibria. The microscopic deprotonation constants have been determined for dopamine, too.[11,12]

pk_1	pk_2	pk_{12}	pk_{21}
8.87, 8.90	9.95, 10.06	10.36, 10.60	9.39, 9.44

The fractional concentrations of all four species can be calculated from the equations:

$$f_{DH_2NH_3} = \left(1 + \frac{k_1}{\left[H^+\right]} + \frac{k_2}{\left[H^+\right]} + \frac{k_2 k_{12}}{\left[H^+\right]^2} + \frac{k_2 k_{21} k_3}{\left[H^+\right]^3}\right)^{-1}$$

$$f_{DHNH_3} = \left(\frac{\left[H^+\right]}{k_1} + \frac{k_{12}}{\left[H^+\right]} + \frac{k_{12}}{k_{21}} + 1 + \frac{k_{12} k_3}{\left[H^+\right]^2}\right)^{-1}$$

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[11] Martin, R. B., Zwitterion Formation upon Deprotonation in L-3,4-Dihydroxyphenylalanine and Other Phenolic Amines, *J. Phys. Chem.* **1971**, *75*, 2657-2661.

[12] Kiss, T.; Gergely, A.; Complexes of 3,4-Dihydroxyphenyl Derivatives, III. Equilibrium Study of Parent and some Mixed Ligand Complexes of Dopamine, Alanine and Pyrocatechol with Ni(II), Copper(II) and Zinc(II) Ions. *Inorg. Chim. Acta* **1979**, *36*, 31-36.

$$f_{DH_2NH_2}=\left(\frac{\left[H^+\right]}{k_2}+\frac{k_{21}}{k_{12}}+\frac{k_{21}}{\left[H^+\right]}+1+\frac{k_{21}k_3}{\left[H^+\right]^2}\right)^{-1}$$

$$f_{DHNH_2}=\left(\frac{\left[H^+\right]^2}{k_1k_{12}}+\frac{\left[H^+\right]^2}{k_2k_{21}}+\frac{\left[H^+\right]}{k_{21}}+1+\frac{k_3}{\left[H^+\right]}\right)^{-1}$$

$$f_{DNH_2}=\left(\frac{\left[H^+\right]^3}{k_1k_{12}k_3}+\frac{\left[H^+\right]^2}{k_3k_{12}}+\frac{\left[H^+\right]^2}{k_3k_{21}}+\frac{\left[H^+\right]}{k_3}+1\right)^{-1}\equiv\left(\frac{\left[H^+\right]^3}{k_2k_{21}k_3}+\frac{\left[H^+\right]^2}{k_3k_{12}}+\frac{\left[H^+\right]^2}{k_3k_{21}}+\frac{\left[H^+\right]}{k_3}+1\right)^{-1}$$

The distributions corresponding the two sets of data above are shown below (solid and dashed lines) together with the macroscopic protonation constants from the same sources. The first macroscopic value, pK_1, can clearly be attributed to the deprotonation of the first phenolic hydroxyl group. However, the second macroscopic constant pK_2 can not be connected to the amino group deprotonation. On the other hand, the last macroscopic constant can be attributed to the formation of the dopamine dianion with unprotonated aminogroup.

In dopaminequinone, the only group involved in protonation/deprotonation reactions is the amino group. There is no literature data for the pK_a of the $-NH_3^+$ group in dopaquinone but 4-(2-aminoethyl)phenol has pK = 9.77 and phenylethylamine pK = 9.83. The acidity calculator of the University of Kentacky (https://epoch.uky.edu/ace/public/pKa.jsp) allows to estimate the pK value of the amino group in dopaminequinone as 9.8. The measured value for dimethoxydopaminequinone is pK = 9.58, which is adopted in this work.

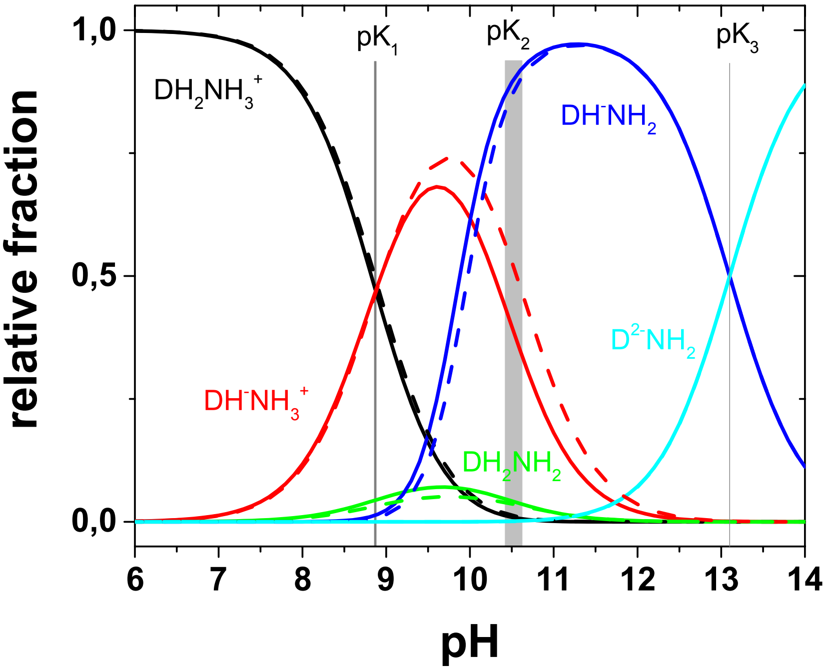

Figure S19. Protonation states of dopamine as a function pH. Solid and dashed curves refer to data sets in references 2 and 3, respectively, and the width of the pK bars to the range of the reported macroscopic values.

Possible Coulombic effect on the pK of the amino group

The protonation equilibrium of the amino group is given by

$$-\mathrm{NH_3}^+ \rightleftharpoons -\mathrm{NH_2} + \mathrm{H}^+$$

The thermodynamic condition for an equilibrium can be expressed using chemical potentials of the species involved

$$\mu^{\ominus}_{NH_3^+} + kT\ln a_{NH_3^+} = \mu^{\ominus}_{NH_2} + kT\ln a_{NH_2} + \mu^{\ominus}_{H^+} + kT\ln a_{H^+}$$

where all terms are expressed as per molecule (not per mole). Rearrangement yields

$$\ln\left(\frac{a_{NH_2}a_{H^+}}{a_{NH_3^+}}\right)_{eq} = \ln K = \frac{\mu^{\ominus}_{NH_3^+} - \mu^{\ominus}_{NH_2} - \mu^{\ominus}_{H^+}}{kT}$$

However, if there is a charged metal ion complexed with the catechol moiety it adds a local Coulombic potential, which can be sensed by the protonated amino group. This modifies the thermodynamics accordingly

$$(\delta) - \mathrm{NH_3}^+ \rightleftharpoons (\delta) - \mathrm{NH_2} + \mathrm{H}^+$$

where δ represents the effective charge in catechol. This means that equilibrium must be expressed using the electrochemical potentials. If we denote the molecular interaction pair potential between the metal-induced positive charge and the protonated amino group by $V(\langle r\rangle)$, where $\langle r\rangle$ = the average distance between the metal-induced positive charge and the protonated amino group, we have for the electrochemical potentials in equilibrium

$$\mu^{\ominus}_{NH_3^+} + kT\ln a_{NH_3^+} + V(\langle r\rangle) = \mu^{\ominus}_{NH_2} + kT\ln a_{NH_2} + \mu^{\ominus}_{H^+} + kT\ln a_{H^+}$$

Deprotonated amino group does not have any (Coulombic) interaction and, in equilibrium, the proton is assumed to be so far away (actually, infinitely far away) that this potential does not have any effect. In this case, rearrangement gives

$$\ln\left(\frac{a_{NH_2}a_{H^+}}{a_{NH_3^+}}\right)_{eq} = \ln K^* = \frac{\mu^{\ominus}_{NH_3^+} - \mu^{\ominus}_{NH_2} - \mu^{\ominus}_{H^+}}{kT} + \frac{V(\langle r\rangle)}{kT} = \ln K + \frac{V(\langle r\rangle)}{kT}$$

which yields for the modified acidity constant K^*

$$pK^* = pK - \frac{V(\langle r\rangle)}{2.303kT}$$

If we assume the interaction potential to be a simple Coulombic one between two point charges (in aqueous solution, a screened potential should be used; however, we assume that the charges are so close to each other that screening ions in solution do not have significant effect in the small space between them) we have

$$V\left(\langle r\rangle\right)=\frac{e^2\delta}{4\pi\varepsilon_0\varepsilon_r\langle r\rangle}$$

The two unknown parameters in this equation are δ and $\langle r\rangle$. At 298 K, the equation is (in water, using $\varepsilon_r=78$)

$$pK^*=pK-3.12\cdot10^{-10}\frac{\delta}{\langle r\rangle}$$

Molecular mechanics calculations suggest that $\langle r\rangle\sim7\,\text{Å}$. Therefore, the unscreened potential would predict a negative shift of $\Delta pK\sim-0.45$ per one effective positive charge. This is well in accordance with the difference between the microscopic pk_2 and pk_{12} values.

Dopamine cyclization kinetics

In the cyclization process

$$\mathrm{DQNH_3}^+ + \mathrm{OH}^- + \underset{k_p}{\overset{k_d}{\rightleftharpoons}} \mathrm{DQNH_2} + \mathrm{H_2O} \xrightarrow{k_c^0} \mathrm{DAL}$$

where

$\mathrm{DQNH_3}^+$ = dopaminequinone with protonated amino group

$\mathrm{DQNH_2}$ = dopaminequinone with deprotonated amino group

DAL = cyclized leucodopaminechrome

and for ethylamine we have[13]

$k_d = 3.2 \cdot 10^{10}\ \mathrm{M^{-1}\,s^{-1}}$ and $k_p = 1.4 \cdot 10^7\ \mathrm{s^{-1}}$,

which can be used for the aminogroup in dopaminequinone, too (in general, for aliphatic amines the protonation and deprotonation rates are almost constant although steric hindrance decreases the protonation rate k_p). Now, because the reaction between hydronium and hydroxide ions is diffusion controlled, the equilibrium constant for the reaction above is given by

$$K' = \frac{\left[\mathrm{DQNH_2}\right]}{\left[\mathrm{DQNH_3}^+\right]\left[\mathrm{OH}^-\right]} = \frac{k_d}{k_p} = \frac{\left[\mathrm{DQNH_2}\right]\left[\mathrm{H}^+\right]}{\left[\mathrm{DQNH_3}^+\right]K_w} = \frac{K_{NH_3}}{K_w}$$

The value $K_{NH_3} = 10^{-9.58}$ has been estimated for the acidity constant of the amino group in dopaminequinone.[14]

Application of the steady-state assumption to the deprotonated form yields

$$\left[\mathrm{DQNH_2}\right] = \frac{k_d\left[\mathrm{OH}^-\right]}{k_p + k_c^0}\left[\mathrm{DQNH_3}^+\right]$$

The total concentration of the uncyclized form is

$$C_{\mathrm{DQ}} = \left[\mathrm{DQNH_2}\right] + \left[\mathrm{DQNH_3}^+\right] = \frac{k_p + k_c^0 + k_d\left[\mathrm{OH}^-\right]}{k_d\left[\mathrm{OH}^-\right]}\left[\mathrm{DQNH_2}\right]$$

As $K_{NH_3} = K_w K' = K_w \dfrac{k_d}{k_p}$ we obtain

$$\frac{d\left[\mathrm{DAL}\right]}{dt} = k_c^0\left[\mathrm{DQNH_2}\right] = \frac{k_c^0 k_d\left[\mathrm{OH}^-\right]}{k_d\left[\mathrm{OH}^-\right] + k_c^0 + k_p} C_{\mathrm{DQ}} = \frac{k_c^0 K_{NH_3}}{K_{NH_3} + \left[\mathrm{H}^+\right]\left(1 + \dfrac{k_c^0}{k_p}\right)} C_{\mathrm{DQ}} \approx \frac{k_c^0 K_{NH_3}}{K_{NH_3} + \left[\mathrm{H}^+\right]} C_{\mathrm{DQ}}$$

because generally $k_p >> k_c^0$.

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[13] Eigen, M.; Maass, G.; Schwartz, G., *Z. Phys. Chem.* **1971**, *74*, 319-330.

[14] Young, T. E.; Babbitt, B. W., *J. Org. Chem.* **1983**, *48*, 562-566.

Formal redox potentials

The general step-by-step procedure to obtain the formal one-electron redox potentials can be given as follows:

1) Identify all possible protonation and redox states of the components of the redox system. This allows draw the square scheme (electron transfer horizontal, proton transfer vertical).
2) Find standard redox potentials between different redox states. Note that all horizontal potentials in the square scheme are pH independent.
3) Find all acidity constants of the redox species involved.
4) If the protonation/deprotonation fall outside of the pH range considered it can be neglected.
5) Assuming the proton transfer reactions to be in equilibrium calculate the total amount of oxidized and reduced species as a function of $\left[\mathrm{H}^{+}\right]$.
6) The formal one-electron redox potential can be calculated from
$$E^{\ominus,f}_{\mathrm{Ox/Red}} + \frac{RT}{F}\ln\frac{[\mathrm{Ox}]_{tot}}{[\mathrm{Red}]_{tot}} = E^{\ominus}_{m/n} + \frac{RT}{F}\ln\frac{\left[\mathrm{Ox}^{(m)}\right]}{\left[\mathrm{Red}^{(n)}\right]}$$
where $E^{\ominus}_{m/n}$ = the standard redox potential between chosen protonation forms $\mathrm{Ox}^{(m)}$ and $\mathrm{Red}^{(n)}$.
7) Change to common (Briggs) logarithm in order to express the result as a function of pH

Oxygen

Several reports on spontaneous oxidation of dopamine by dioxygen confirm the formation of hydrogen peroxide. The appropriate redox reaction is[15]

$$O_2 + 2H^{+} + 2e^{-} \rightleftharpoons H_2O_2 \qquad E^{\ominus}_{O_2/H_2O_2} = 0.67\ \mathrm{V}\ \text{vs NHE}$$

For the 2-electron redox process we have at 25 °C

$$E = E^{\ominus}_{O_2/H_2O_2} + \frac{RT}{2F}\ln\frac{[O_2]\left[H^{+}\right]^2}{[H_2O_2]} = E^{\ominus}_{O_2/H_2O_2} + \frac{2.303RT}{F}\lg\left[H^{+}\right] + \frac{RT}{2F}\ln\frac{[O_2]}{[H_2O_2]}$$

and

$$E^{\ominus f}_{O_2/H_2O_2} = E^{\ominus}_{O_2/H_2O_2} - 0.059\mathrm{V}\cdot pH = 0.67\,\mathrm{V} - 0.059\mathrm{V}\cdot pH$$

This is, however, based on the standard state of $O_2(g)$ at 1 bar. For reactions in solutions, a better standard state is dissolved oxygen $O_2(aq)$ at 1 m or 1 M.

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[15] Sánchez-Sánchez, C. M.; Bard, A. J., *Anal. Chem.* **2009**, *81*, 8094-8100.

In the following the standard potentials are thermodynamic potentials (pH 0) and the standard state is dissolved oxygen $O_2(aq)$, not $O_2(g)$ at 1 bar. Literature values are corrected accordingly.

Dioxygen O_2 is a triplet and it is slow to oxidize organic compounds, which are usually singlets. The first 1-electron redox potential[16]

$O_2 + e^- \rightleftharpoons O_2^{\bullet -}$ $\quad E^{\ominus}_{O_2/O_2^{\bullet -}} = -0.18\ \mathrm{V}$ at pH 7 (biochemical standard state, but is pH independent)

is low, which makes molecular oxygen a poor oxidant.

The superoxide anion is a strong oxidant

$$O_2^{\bullet -} + 2H^+ + e^- \rightleftharpoons H_2O_2 \qquad E^{\ominus}_{O_2^{\bullet -}/H_2O_2} = +0.91\ \mathrm{V}$$

Superoxide radical can be protonated[17]

$$O_2^{\bullet -} + H^+ \rightleftharpoons HO_2^{\bullet} \qquad K_{O_2H^{\bullet}} = \frac{\left[H^+\right]\left[O_2^{\bullet -}\right]}{\left[HO_2^{\bullet}\right]} = 10^{-4.8}$$

and the protonated form is a still better oxidant

$HO_2^{\bullet} + H^+ + e^- \rightleftharpoons H_2O_2$ $\quad E^{\ominus f}_{H_2O_2/HO_2^{\bullet -}}(pH7) = 1.05\ \mathrm{V}$ at pH 7 (biochemical standard state)

For the thermodynamic standard state

$$E^{\ominus}_{H_2O_2/HO_2^{\bullet -}} \equiv E^{\ominus f}_{H_2O_2/HO_2^{\bullet -}}(pH0) = 1.46(3)\ \mathrm{V}$$

because

$$E^{\ominus f}_{H_2O_2/HO_2^{\bullet -}} = E^{\ominus}_{H_2O_2/HO_2^{\bullet -}} - 0.059\mathrm{V} \cdot pH$$

The superoxide radical anion and perhydroxyl radical are much stronger oxidants, as shown by the thermodynamic standard potentials (vs NHE) of the reactions [16]

$$\mathrm{O_2^{\bullet -}} + 2\mathrm{H}^+ + e^- \rightleftharpoons \mathrm{H_2O_2} \qquad E^{\ominus}_{\mathrm{O_2^{\bullet -}/H_2O_2}} = +1.74\ \mathrm{V}$$

$$\mathrm{HO_2^{\bullet}} + \mathrm{H}^+ + e^- \rightleftharpoons \mathrm{H_2O_2} \qquad E^{\ominus}_{\mathrm{H_2O_2/HO_2^{\bullet}}} = +1.47\ \mathrm{V}$$

Hydrogen peroxide is a weak acid

$$H_2O_2 \rightleftharpoons H^+ + HO_2^- \qquad K_{H_2O_2} = \frac{\left[H^+\right]\left[HO_2^-\right]}{\left[H_2O_2\right]} = 10^{-11.62}$$

The dioxygen/superoxide/hydrogen peroxide redox system can be described by an incomplete 3x3 square scheme

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[16] Koppenol, W.H.; Stanbury, D.M.; Bounds, P. L., *Free Rad. Biol. Med.* **2010**, *49*, 317-322.

[17] Buettner, *Arch. Biochem. Biophys.* **1993**, *300*, 535.

Scheme S2

$$\begin{array}{lll}
O_2 \xrightleftharpoons{E^{\ominus}_{O_2/O_2^{\bullet-}}} O_2^{\bullet-} & & \\
\quad pK_{HO_2^{\bullet}} = 4.8 \updownarrow & & \\
 & HO_2^{\bullet} \xrightleftharpoons{E^{\ominus}_{HO_2^{\bullet}/HO_2^{-}}} HO_2^{-} & \\
 & \quad pK_{H_2O_2} = 11.62 \updownarrow & \\
 & & H_2O_2
\end{array}$$

This can be formally presented as two 1-electron redox processes

$$O_2 \xrightarrow{E_1^{\ominus}} SO \xrightarrow{E_2^{\ominus}} HP$$

where SO = superoxide and HP = hydrogen peroxide (all protonation forms).

Now

$$[SO] = \left[O_2^{\bullet-}\right] + \left[HO_2^{\bullet}\right] = \left[O_2^{\bullet-}\right]\left(1 + \frac{\left[H^+\right]}{K_{HO_2^{\bullet}}}\right) = \alpha_{O_2^{\bullet-},H}\left[O_2^{\bullet-}\right] = \left[HO_2^{\bullet}\right]\left(1 + \frac{K_{HO_2^{\bullet}}}{\left[H^+\right]}\right) = \alpha_{HO_2^{\bullet},H}\left[HO_2^{\bullet}\right]$$

where the side reaction coefficients of the superoxide species with respect to protonation are given by

$$\alpha_{O_2^{\bullet-},H} = 1 + \frac{\left[H^+\right]}{K_{HO_2^{\bullet}}} \qquad \text{and} \qquad \alpha_{HO_2^{\bullet},H} = \left(1 + \frac{K_{HO_2^{\bullet}}}{\left[H^+\right]}\right)$$

For the first step we can write

$$E = E_1^{\ominus} + \frac{RT}{F}\ln\frac{[O_2]}{[SO]} = E_1^{\ominus} - \frac{RT}{F}\ln\alpha_{O_2^{\bullet-},H} + \frac{RT}{F}\ln\frac{[O_2]}{\left[O_2^{\bullet-}\right]} = E_1^{\ominus} - \frac{RT}{F}\ln\alpha_{O_2^{\bullet-},H} + E - E^{\ominus}_{O_2/O_2^{\bullet-}}$$

From which we obtain

$$\boxed{E_1^{\ominus} = E^{\ominus}_{O_2/O_2^{\bullet-}} + \frac{RT}{F}\ln\alpha_{O_2^{\bullet-},H} = -0.18\,\mathrm{V} + \frac{RT}{F}\ln\left(1 + \frac{\left[H^+\right]}{K_{HO_2^{\bullet}}}\right) = -0.18\,\mathrm{V} + 0.059\,\mathrm{V}\lg\left(1 + \frac{\left[H^+\right]}{K_{HO_2^{\bullet}}}\right)}$$

Similarly,

$$[HP] = \left[HO_2^{-}\right] + \left[H_2O_2\right] = \left[H_2O_2\right]\left(1 + \frac{K_{H_2O_2}}{\left[H^+\right]}\right) = \alpha_{H_2O_2,H}\left[H_2O_2\right]$$

where

$$\alpha_{H_2O_2,H} = \left(1 + \frac{K_{H_2O_2}}{\left[H^+\right]}\right)$$

and we can write for the second step

$$E = E_2^{\ominus} + \frac{RT}{F}\ln\frac{[SO]}{[HP]} = E_2^{\ominus} + \frac{RT}{F}\ln\frac{\alpha_{HO_2^{\bullet},H}}{\alpha_{H_2O_2,H}} + \frac{RT}{F}\ln\frac{\left[HO_2^{\bullet}\right]}{\left[H_2O_2\right]}$$

We know the standard potential of the redox cross reaction

$$HO_2^{\bullet} + H^+ + e^- \rightleftharpoons H_2O_2 \qquad E = E^{\ominus}_{H_2O_2/HO_2^{\bullet}} + \frac{RT}{F}\ln\frac{\left[HO_2^{\bullet}\right]\left[H^+\right]}{\left[H_2O_2\right]}$$

Therefore, combining these two equations

$$E = E_2^{\ominus} + \frac{RT}{F}\ln\frac{\alpha_{HO_2^{\bullet},H}}{\alpha_{H_2O_2,H}} + \frac{RT}{F}\ln\frac{\left[HO_2^{\bullet}\right]}{\left[H_2O_2\right]} = E_2^{\ominus} + \frac{RT}{F}\ln\frac{\alpha_{HO_2^{\bullet},H}}{\alpha_{H_2O_2,H}} + E - E^{\ominus}_{H_2O_2/HO_2^{\bullet}} - \frac{RT}{F}\ln\left[H^+\right]$$

and we obtain for the second 1-electron standard potential

$$E_2^{\ominus} = E^{\ominus}_{H_2O_2/HO_2^{\bullet}} + \frac{RT}{F}\ln\left[H^+\right] - \frac{RT}{F}\ln\frac{\alpha_{HO_2^{\bullet},H}}{\alpha_{H_2O_2,H}} = E^{\ominus}_{H_2O_2/HO_2^{\bullet}} + \frac{RT}{F}\ln\frac{\alpha_{H_2O_2,H}\left[H^+\right]}{\alpha_{HO_2^{\bullet},H}}$$

Finally,

$$\boxed{E_2^{\ominus} = E^{\ominus}_{H_2O_2/HO_2^{\bullet}} + \frac{RT}{F}\ln\frac{\left[H^+\right]\left(\left[H^+\right] + K_{H_2O_2}\right)}{\left(\left[H^+\right] + K_{HO_2^{\bullet}}\right)} = 1.47\,\mathrm{V} - 0.059\,\mathrm{V}\cdot pH + 0.059\,\mathrm{V}\cdot \lg\frac{\left[H^+\right] + K_{H_2O_2}}{\left[H^+\right] + K_{HO_2^{\bullet}}}}$$

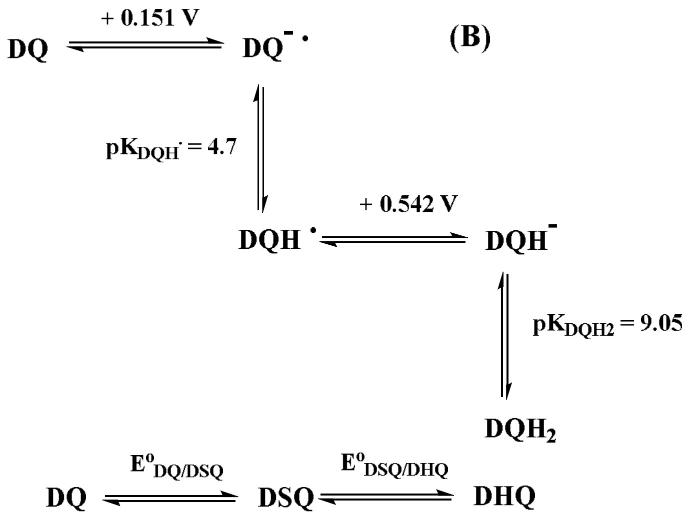
These two expressions have been used to draw the one-electron redox potentials as a function pH for the oxygen/superoxide/peroxide system.

Dopamine

There are only a few reports on the one electron redox potentials of dopamine and the properties of dopamine semiquinone. The following discussion is based on data given Waite *et al* and Sanchez-Rivera *et al.*[18,19] In addition, it is assumed that the protonation state of the amino group does not affect the redox processes of the catechol system. In fact, the deprotonation degree of this group is low in the pH range studied.

The 2-electron redox process of dopamine is described by an incomplete 3x3 square scheme below pH 10, in which range only the first deprotonation of the catechol moiety has to be taken into account. In addition, the protonation of the *o*-quinone moiety can be neglected.

Scheme S3



The following one-electron standard redox potentials (vs NHE) are known

$$\mathrm{DQ} + e^- \rightarrow \mathrm{DQ}^{-\bullet} \qquad E^{\circ}_{\mathrm{DQ/DQ^{-\bullet}}} = 0.151\ \mathrm{V}$$

$$\mathrm{DQ}^{-\bullet} + 2\mathrm{H}^+ + e^- \rightarrow \mathrm{DQH_2} \qquad E^{\circ}_{\mathrm{DQ^{-\bullet}/DQH_2}} = 1.353\ \mathrm{V}$$

$$\mathrm{DQH}^{\bullet} + \mathrm{H}^+ + e^- \rightarrow \mathrm{DQH_2} \qquad E^{\circ}_{\mathrm{DQ^{\bullet}/DQH_2}} = 1.076\ \mathrm{V}$$

together with the 2-electron standard potential

$$\mathrm{DQ} + 2\mathrm{H}^+ + 2e^- \rightarrow \mathrm{DQH_2} \qquad E^{\circ}_{\mathrm{DQ/DQH_2}} = 0.752\ \mathrm{V}$$

The square scheme can be formally represented as two successive one-electron redox processes

$$DQ \xrightarrow{E^{\circ}_{\mathrm{DQ/DSQ}}} \mathrm{DSQ} \xrightarrow{E^{\circ}_{\mathrm{DSQ/DHQ}}} \mathrm{DHQ}$$

where the abbreviations DQ, DSQ and DHQ represent generally the dopaquinone, dopasemiquinone and dopahydroquinone species, respectively.

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[18] Pham, A, N,; Waite, T. D. *J. Inorg. Biochem*. **2014**, *137*, 74-84.

[19] Sánchez-Rivera, A. E.; Corona-Avendaño, S.; Alarcón-Angles, G.; Rojas-Hernández, A.; Ramírez-Silva, M. T.; Romero-Romo, M. A. *Spectrochim. Acta A* **2003**, *59*, 3193-3203.

Now

$$\left[\mathrm{DSQ}\right]=\left[\mathrm{DQ}^{-\bullet}\right]+\left[\mathrm{DQH}^{\bullet}\right]=\left[\mathrm{DQ}^{-\bullet}\right]\left(1+\frac{\left[\mathrm{H}^{+}\right]}{K_{\mathrm{DQH}^{\bullet}}}\right)=\left[\mathrm{DQH}^{\bullet}\right]\left(1+\frac{K_{\mathrm{DQH}^{\bullet}}}{\left[\mathrm{H}^{+}\right]}\right)$$

$$\left[\mathrm{DHQ}\right]=\left[\mathrm{DQH}^{-}\right]+\left[\mathrm{DQH}_{2}\right]=\left[\mathrm{DQH}^{-}\right]\left(1+\frac{\left[\mathrm{H}^{+}\right]}{K_{\mathrm{DQH}_{2}}}\right)=\left[\mathrm{DQH}_{2}\right]\left(1+\frac{K_{\mathrm{DQH}_{2}}}{\left[\mathrm{H}^{+}\right]}\right)$$

and

$$\begin{aligned}E&=E^{\ominus}_{\mathrm{DQ/DSQ}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DQ}\right]}{\left[\mathrm{DSQ}\right]}=E^{\ominus}_{\mathrm{DQ/DSQ}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DQ}\right]}{\left[\mathrm{DQ}^{-\bullet}\right]}-\frac{RT}{F}\ln\left(1+\frac{\left[\mathrm{H}^{+}\right]}{K_{\mathrm{DQH}^{\bullet}}}\right)=\\&=E^{\ominus}_{\mathrm{DQ/DQ}^{-\bullet}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DQ}\right]}{\left[\mathrm{DQ}^{-\bullet}\right]}\end{aligned}$$

This yields for the first formal one-electron standard potential (DQ/DSQ couple)

$$\boxed{\begin{aligned}E^{\ominus}_{\mathrm{DQ/DSQ}}&=E^{\ominus}_{\mathrm{DQ/DQ}^{-\bullet}}+\frac{RT}{F}\ln\left(1+\frac{\left[\mathrm{H}^{+}\right]}{K_{\mathrm{DQH}^{\bullet}}}\right)=E^{\ominus}_{\mathrm{DQ/DQ}^{-\bullet}}+0.059\,\mathrm{V}\cdot\lg\left(1+\frac{\left[\mathrm{H}^{+}\right]}{K_{\mathrm{DQH}^{\bullet}}}\right)=\\&=0.151\,\mathrm{V}+0.059\,\mathrm{V}\cdot\lg\left(1+10^{4.7}\left[\mathrm{H}^{+}\right]\right)\end{aligned}}$$

On the other hand,

$$\begin{aligned}E&=E^{\ominus}_{\mathrm{DSQ/DHQ}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DSQ}\right]}{\left[\mathrm{DHQ}\right]}=E^{\ominus}_{\mathrm{DSQ/DHQ}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DQH}^{\bullet}\right]}{\left[\mathrm{DQH}_{2}\right]}+\frac{RT}{F}\ln\frac{\left(1+\frac{K_{\mathrm{DQH}^{\bullet}}}{\left[\mathrm{H}^{+}\right]}\right)}{\left(1+\frac{K_{\mathrm{DQH}_{2}}}{\left[\mathrm{H}^{+}\right]}\right)}=\\&=E^{\ominus}_{\mathrm{DSQ/DHQ}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DQH}^{\bullet}\right]}{\left[\mathrm{DQH}_{2}\right]}+\frac{RT}{F}\ln\frac{\left[\mathrm{H}^{+}\right]+K_{\mathrm{DQH}^{\bullet}}}{\left[\mathrm{H}^{+}\right]+K_{\mathrm{DQH}_{2}}}=\\&=E^{\ominus}_{\mathrm{DQ}^{\bullet}/\mathrm{DQH}_{2}}+\frac{RT}{F}\ln\frac{\left[\mathrm{DQH}^{\bullet}\right]\left[\mathrm{H}^{+}\right]}{\left[\mathrm{DQH}_{2}\right]}\end{aligned}$$

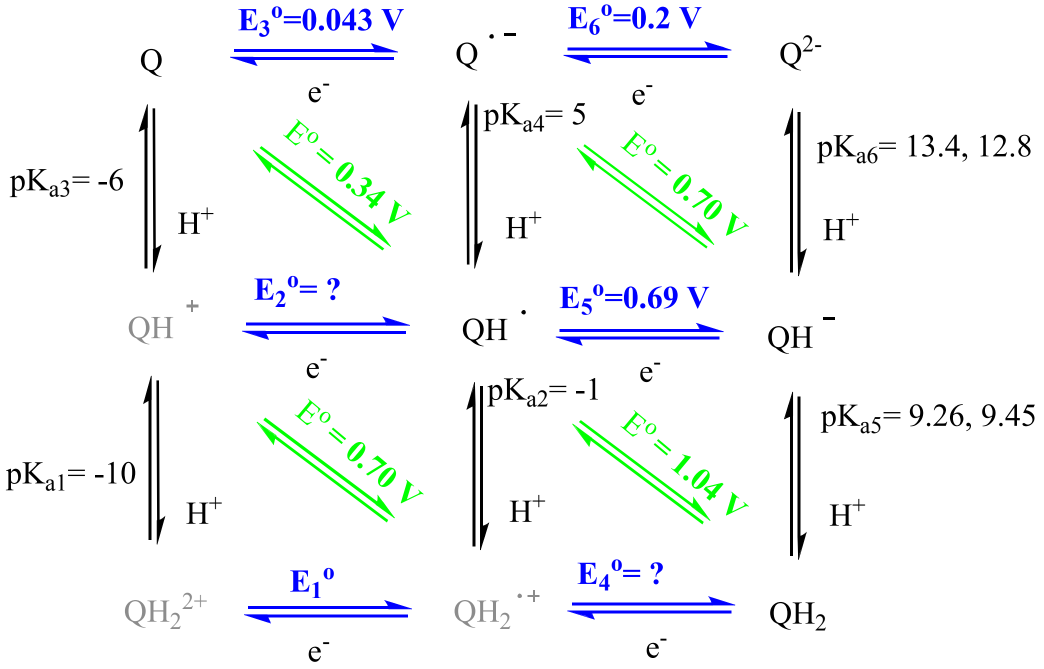
which gives for the second formal one-electron standard potential (DSQ/DHQ couple)

$$\boxed{\begin{aligned}E^{\ominus}_{\mathrm{DSQ/DHQ}}&=E^{\ominus}_{\mathrm{DQ}^{\bullet}/\mathrm{DQH}_{2}}+\frac{RT}{F}\ln\frac{\left[\mathrm{H}^{+}\right]\left(\left[\mathrm{H}^{+}\right]+K_{\mathrm{DQH}_{2}}\right)}{\left[\mathrm{H}^{+}\right]+K_{\mathrm{DQH}^{\bullet}}}=E^{\ominus}_{\mathrm{DQ}^{\bullet}/\mathrm{DQH}_{2}}+0.059\,\mathrm{V}\cdot\lg\frac{\left[\mathrm{H}^{+}\right]+K_{\mathrm{DQH}_{2}}}{1+\frac{K_{\mathrm{DQH}^{\bullet}}}{\left[\mathrm{H}^{+}\right]}}=\\&=1.076\,\mathrm{V}+0.059\,\mathrm{V}\cdot\lg\frac{\left[\mathrm{H}^{+}\right]+10^{-9.05}}{1+\frac{10^{-4.7}}{\left[\mathrm{H}^{+}\right]}}\end{aligned}}$$

Catechol

The analysis of the *o*-quinone/catechol pair is done using the 9-member scheme below. Potentials between horizontal lines (in blue) are pH independent whereas "cross potentials" (in green) depend on pH.[20,21] The lower left triangle can be neglected at normal pH.

Scheme S4



Lower left corner potential; $E_2{}^o$, is obtained as

$$E_2{}^o = E^o_{QH^+/QH_2{}^{\bullet+}} - \frac{RT}{F}\ln K_{a2} = 0.70V - 0.059V \cdot \ln 0.1 = 0.836V \approx 0.84V$$

The apparent one electron redox reactions

$$Q_{ox} + e^- \rightleftharpoons Q_{sem} \qquad E = E^\circ_{r1} + \frac{RT}{F}\ln\frac{[Q_{ox}]}{[Q_{sem}]}$$

and

$$Q_{sem} + e^- \rightleftharpoons Q_{red} \quad E = E^\circ_{r2} + \frac{RT}{F}\ln\frac{[Q_{sem}]}{[Q_{red}]}$$

The apparent standard potential E°_{r1} of the first step is obtained in terms of the standard potentials and pK's in the 9-membered scheme as follows

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[20] Warren, J.J.; Tronic, T. A.; Mayer, J. M., Thermochemistry of Proton-Coupled Electron Transfer Reagents and Its Implications, *Chem. Rev*. **2010**, *110*, 6961-7001.

[21] Lin, Q.; Li, Q.; Batchelor-McAuley, C.; Compton, R.G., *J. Phys. Chem. C* **2015**, *119*, 1489-1495.

$$\boxed{E^\circ_{r1} = E^\circ_2 + \frac{RT}{F}\ln\left(\frac{\frac{K_{a4}}{\left[H^+\right]}+1+\frac{\left[H^+\right]}{K_{a2}}}{\frac{K_{a3}}{\left[H^+\right]}+1+\frac{\left[H^+\right]}{K_{a1}}}\right) = E^\circ_2 + \frac{RT}{F}\ln\left(\frac{K_{a4}+\left[H^+\right]+\frac{\left[H^+\right]^2}{K_{a2}}}{K_{a3}+\left[H^+\right]+\frac{\left[H^+\right]^2}{K_{a1}}}\right)}$$

or, alternatively, from

$$\boxed{E^\circ_{r1} = E^\circ_3 + \frac{RT}{F}\ln\left(\frac{1+\frac{\left[H^+\right]}{K_{a4}}+\frac{\left[H^+\right]^2}{K_{a2}K_{a4}}}{1+\frac{\left[H^+\right]}{K_{a3}}+\frac{\left[H^+\right]^2}{K_{a1}K_{a3}}}\right) = E^\circ_3 + \frac{RT}{F}\ln\left(\frac{K_{a4}+\left[H^+\right]+\frac{\left[H^+\right]^2}{K_{a2}}}{K_{a1}+\left[H^+\right]+\frac{\left[H^+\right]^2}{K_{a3}}}\right)}$$

Now, with the catechol/o-quinone system we have $K_{a1}, K_{a3} >> 1$, which leads to

$$E^\circ_{r1} = E^\circ_3 + \frac{RT}{F}\ln\left(\frac{1+\frac{\left[H^+\right]}{K_{a4}}+\frac{\left[H^+\right]^2}{K_{a2}K_{a4}}}{1+\frac{\left[H^+\right]}{K_{a3}}+\frac{\left[H^+\right]^2}{K_{a1}K_{a3}}}\right) \approx E^\circ_3 + \frac{RT}{F}\ln\left(1+\frac{\left[H^+\right]}{K_{a4}}+\frac{\left[H^+\right]^2}{K_{a2}K_{a4}}\right)$$

Similarly, for the apparent one-electron redox process between the semiquinone and hydroquinone forms, we have

$$\boxed{E^\circ_{r2} = E^\circ_5 + \frac{RT}{F}\ln\left(\frac{\frac{K_{a6}}{\left[H^+\right]}+1+\frac{\left[H^+\right]}{K_{a5}}}{\frac{K_{a4}}{\left[H^+\right]}+1+\frac{\left[H^+\right]}{K_{a2}}}\right) = E^\circ_5 + \frac{RT}{F}\ln\left(\frac{K_{a6}+\left[H^+\right]+\frac{\left[H^+\right]^2}{K_{a5}}}{K_{a4}+\left[H^+\right]+\frac{\left[H^+\right]^2}{K_{a2}}}\right)}$$

Here, all acidity constants are known for the catechol/o-quinone system
Based on the expressions above the following Pourbaix diagram can be calculated for all relevant redox pairs.

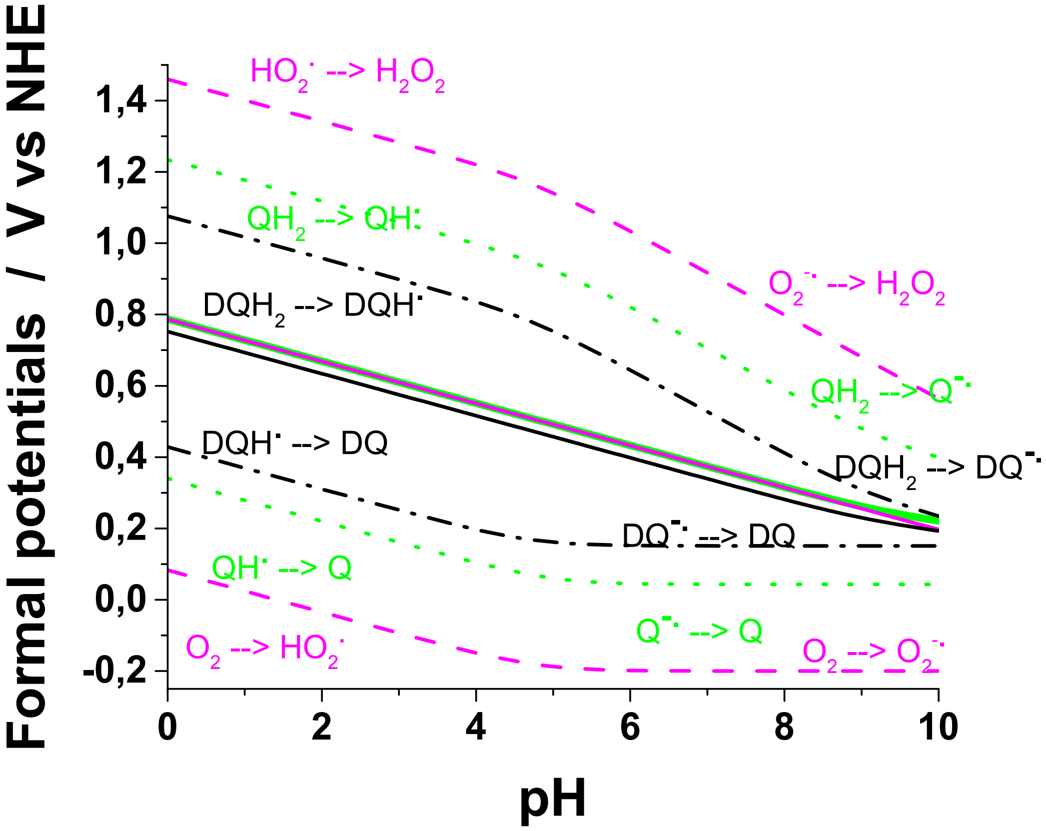

Figure S20. Formal redox potentials for dopamine/dopaminesemiquinone/dopaminequinone (DQ, black lines), catechol/catechol semiquinone/o-quinone (Q, green lines)) and oxygen/superoxide/hydrogen peroxide (magenta lines) redox systems. Solid lines give the 2-electron potentials, dashed and dotted lines the 1-electron potentials. Relevant protonation states of redox species shown.

Oxidizing power of metals

All three transition metals used in this work form sparingly soluble hydroxides, which often turn to corresponding oxides, in their both oxidation states. The redox properties are controlled by the solubility of these compounds, and the Pourbaix diagrams have to be calculated for each total metal concentration separately. The following results have been calculated with total metal concentration of 0.1 mM. It should be pointed out that the discussion is somewhat semiquantitative because of the large uncertainties in the relevant constants found in literature. In addition, no activity effects are taken into account. The diagrams here are modified from those found in literature.[22]

The treatment here assumes that the complexation reactions of all components are reversible and all ligands are non-innocent. This is most probably true for Fe and Cu but, for simplicity, it is assumed also for Ce. Thermodynamically electron transfer reactions within a complex and between free metal ion and dopamine (catechol) are identical in this case.

Complexation stabilizes the oxidation state in question and either decreases (oxidized metal complexed) or increases (reduced metal complexed) the oxidation power. Dopamine (and catechols in general) strongly complex transition metals but, now, the ligand itself is the redox active component. The higher the charge of the metal ion the higher the stability of the complex; therefore, oxidized metal ions Ce(IV), Fe(III), or Cu(II) form stronger complexes than the reduced ones(Ce(III), Fe(II), or Cu(I). However, form the thermodynamic point of view, the effect of complexation is different if the (innocent) ligand is itself redox-active.

In case of redox-inactive ligand (L), the redox process is described by the reactions (e.g., for Fe; for simplicity, only 1:1 complexes considered; protonation states ignored for simplicity, too):

$$Fe(III) + L \rightleftharpoons Fe(III)L \qquad \times(-1)$$

$$Fe(III) + HQ \rightleftharpoons Fe(II) + SQ$$

$$Fe(II) + L \rightleftharpoons Fe(II)L$$

net reaction $$Fe(III)L + HQ \rightleftharpoons Fe(II)L + SQ$$

Therefore, the formation of a strong Fe(III)-L complex (referred to the Fe(II)-L complex) shifts the equilibrium to the left, thereby decreasing the oxidizing power of Fe(III). This can be taken into account by the side reaction coefficients.

If the ligand itself is redox active, the process involves intraligand charge transfer:

$$Fe(III) + HQ \rightleftharpoons Fe(III)(HQ)$$

$$Fe(III)(HQ) \rightleftharpoons Fe(II)(SQ)$$

$$Fe(II)(SQ) \rightleftharpoons Fe(II) + SQ$$

net reaction $$Fe(III) + HQ \rightleftharpoons Fe(II) + SQ$$

This net reaction is identical to the case, in which HQ or SQ is not supposed to form a complex (corresponding half reaction written here; similar half reaction could be written for all redox processes above, too) :

$$Fe(III) + e^{-} \rightleftharpoons Fe(II)$$

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[22] Schweitzer, G. K.; Pesterfield, L. L., *The Aqueous Chemistry of the Elements*, Oxford University Press, Oxford, **2010**.

$$HQ \rightleftharpoons SQ + e^-$$

net reaction $$Fe(III) + HQ \rightleftharpoons Fe(II) + SQ$$

Both latter cases are thermodynamically identical and, therefore, complexation of dopamine (catechol) does not affect the oxidizing power of the metal.

The results below describe the pH dependence of the oxidizing power of metal solutions with total metal concentrations $C_{M_{ox}} = C_{M_{red}} = 0.1\,\mathrm{mM}$ but allow the calculation using any concentration.

This treatment utilizes the side reaction coefficient approach to solution equilibria.[23] Generally, for a redox pair

$\mathrm{Ox} + ze^- \rightarrow \mathrm{Red}$ $E^{\ominus}_{Ox/\mathrm{Red}}$ = standard redox potential

in which one or both forms take part in other reactions (side reactions), too, and all products are soluble, the formal standard redox potential is given by

$$E^{\ominus,f}_{\mathrm{Ox/Red}} = E^{\ominus}_{\mathrm{Ox/Red}} - \frac{RT}{zF}\ln\frac{\alpha_{\mathrm{Ox}}}{\alpha_{\mathrm{Red}}}$$

where α_{Ox} and α_{Red} are the side reaction coefficients of the oxidized and reduced form, respectively. In case of solid components the treatment is slightly different.

The general step-by-step procedure is as follows:

1) Identify all possible side reactions (acid-base, complex formation, precipitation etc.) possible for the species involved.

2) Find the corresponding equilibrium constants

3) Form expressions for the side reaction coefficients. They are defined as

$$\sum_{\substack{\text{all possible}\\ \text{forms } j \text{ of}\\ \text{species M}}} \left[\mathrm{M}_j\right] = [\mathrm{M}]' = \alpha_{\mathrm{M}}\left[\mathrm{M}_{free}\right]$$

4) Calculate possible formal solubility products and, using them, estimate the pH (or pC) ranges where solid species can be formed.

5) For a redox pair Ox/Red (Ox + ze$^-$ → Red), assume that $[\mathrm{Ox}]' = [\mathrm{Red}]'$, and calculate the formal redox potential $E^{\ominus,f}_{\mathrm{Ox/Red}}$ from

$$E^{\ominus,f}_{\mathrm{Ox/Red}} = E^{\ominus,f}_{\mathrm{Ox/Red}} + \frac{RT}{zF}\ln\frac{[\mathrm{Ox}]'}{[\mathrm{Red}]'} = E^{\ominus}_{\mathrm{Ox/Red}} + \frac{RT}{zF}\ln\frac{\alpha_{\mathrm{Red}}}{\alpha_{\mathrm{Ox}}}$$

for all different pH (or pC) ranges. Remember that in case of precipitate the solubility **equilibrium totally determines the concentration of involved species in solution.**

6) Change to common (Briggs) logarithm in order to express the result in terms of pH (or pC).

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[23] Sucha, L.; Kotrlý, S., *Solution Equilibria in Analytical Chemistry*, van Nostrand Reinhold, New York, 1972

In the following figure, all calculated redox potentials are shown as a function of pH. Detailed calculations can be found below.

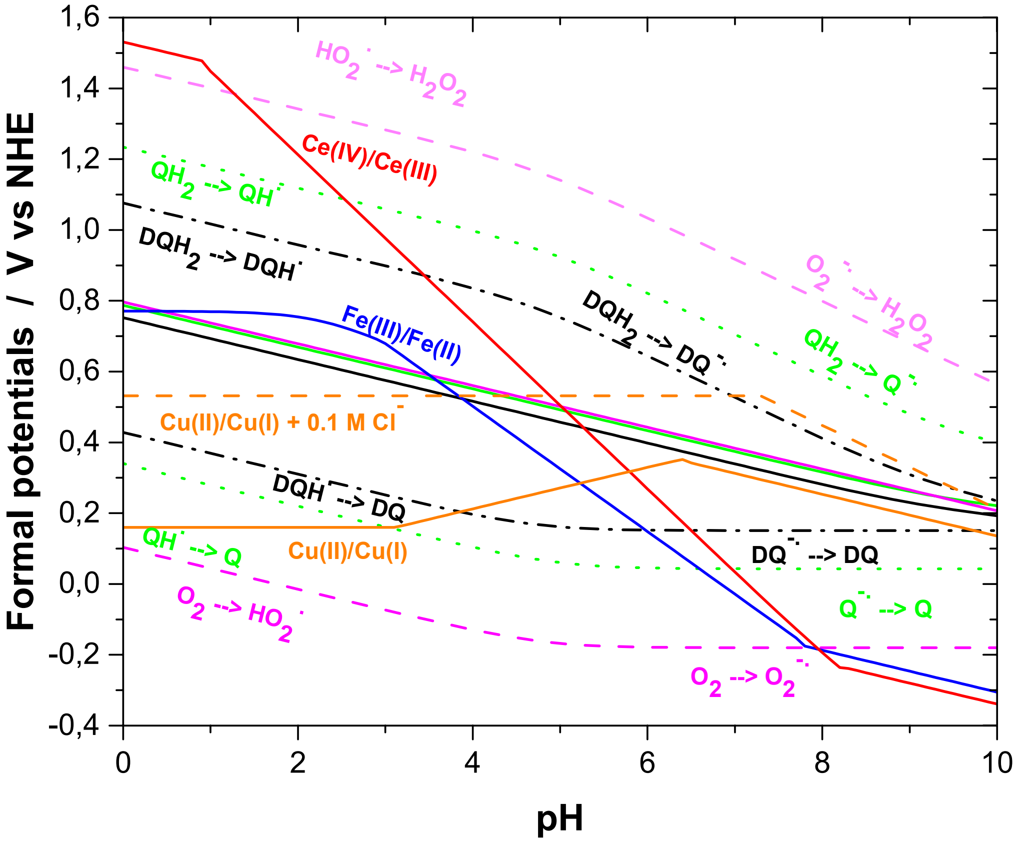

Figure S21. The formal potentials of redox systems formed by dopamine (black lines; solid line is the formal 2-electron redox potential), catechol (green lines, solid line as with dopamine), oxygen (magenta lines, solid line as with dopamine) species, and for the oxidized metal (0.1 mM) / reduced metal (0.1 mM) systems of Ce(IV)/Ce(III) pair (red line), Fe(III)/Fe(II) pair (blue line), and Cu(II)/Cu(I) without (solid orange line) and with 0.1 M NaCl (dashed orange line). No activity effects considered.

Fe(III)/Fe(II)

The following the stability constants of the soluble hydroxyl complexes formed by Fe(III) and Fe(II) have been reported.[24] Slightly different values can be found elsewhere in literature.[25] For $E^{\ominus'}_{Fe^{2+}/Fe^{3+}} = 0.771\text{V}$ vs NHE.[26]

Fe(II):

$$Fe^{2+} + H_2O \rightleftharpoons FeOH^+ + H^+ \qquad \beta_{1,II} = \frac{\left[FeOH^+\right]\left[H^+\right]}{\left[Fe^{2+}\right]} = 10^{-9.397}$$

$$Fe^{2+} + 2H_2O \rightleftharpoons Fe(OH)_2 + 2H^+ \qquad \beta_{2,II} = \frac{\left[Fe(OH)_2\right]\left[H^+\right]^2}{\left[Fe^{2+}\right]} = 10^{-20.494}$$

Fe(III):

$$Fe^{3+} + H_2O \rightleftharpoons FeOH^{2+} + H^+ \qquad \beta_{1,III} = \frac{\left[FeOH^{2+}\right]\left[H^+\right]}{\left[Fe^{3+}\right]} = 10^{-2.187}$$

$$Fe^{3+} + 2H_2O \rightleftharpoons Fe(OH)_2^{\ +} + 2H^+ \qquad \beta_{2,III} = \frac{\left[Fe(OH)_2^{\ +}\right]\left[H^+\right]^2}{\left[Fe^{3+}\right]} = 10^{-4.594}$$

$$Fe^{3+} + 3H_2O \rightleftharpoons Fe(OH)_3 + 3H^+ \qquad \beta_{3,III} = \frac{\left[Fe(OH)_3\right]\left[H^+\right]^3}{\left[Fe^{3+}\right]} = 10^{-13.60}$$

$$Fe^{3+} + 4H_2O \rightleftharpoons Fe(OH)_4^{\ -} + 4H^+ \qquad \beta_{4,III} = \frac{\left[Fe(OH)_4^{\ -}\right]\left[H^+\right]^4}{\left[Fe^{3+}\right]} = 10^{-21.588}$$

Using the stability constant defined in this way, we can write the side reaction coefficients of Fe(II) and Fe(III) with respect to H$^+$-ion as

$$\left[Fe(II)\right]' = \left[Fe^{2+}\right] + \left[FeOH^+\right] + \left[Fe(OH)_2\right] = \left[Fe^{2+}\right]\left(1 + \frac{\beta_{1,II}}{\left[H^+\right]} + \frac{\beta_{2,II}}{\left[H^+\right]^2}\right) = \alpha_{Fe(II),H}\left[Fe^{2+}\right]$$

$$\left[Fe(III)\right]' = \left[Fe^{3+}\right] + \left[FeOH^{2+}\right] + \left[Fe(OH)_2^{\ +}\right] + \left[Fe(OH)_3\right] + \left[Fe(OH)_4^{\ -}\right] =$$

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[24] Uchimiya, M.; Stone, A. T., Redox reactions between iron and quinones: Thermodynamic constraints, *Geochim. Geophys. Acta* **2006**, *70*, 1388-1401. Data originally from Martell, A. E.; Smith, R. M., Motekaitis, R. J., *Critically Selected Stability Constants of Metal Complexes Database*, U.S. Dept. of Commerce, National Institute of Standards and Technology (NIST), **2004**.

[25] Sun, Y.; Pham, A. N.; Waite, T. D., Elucidation of the interplay between Fe(II), Fe(III), and dopamine with relevance to iron solubilization and reactive oxygen species generation by catecholamines, *J. Neurochem.* **2016**, *137*, 955-968.

[26] Bard, A.J., Faulkner, L. F., *Electrochemical Methods. Fundamentals and Applications*, 2nd ed.,

$$=\left[Fe^{3+}\right]\left(1+\frac{\beta_{1,III}}{\left[H^+\right]}+\frac{\beta_{2,III}}{\left[H^+\right]^2}+\frac{\beta_{3,III}}{\left[H^+\right]^3}+\frac{\beta_{4,III}}{\left[H^+\right]^4}\right)=\alpha_{Fe(III),H}\left[Fe^{3+}\right]$$

On the other hand, the solubility products are[27]

$$Fe^{2+}+2OH^- \rightleftharpoons Fe(OH)_2(s) \qquad K_{s,Fe(OH)_2}=\left[Fe^{2+}\right]\left[OH^-\right]^2=\frac{K_w{}^2\left[Fe^{2+}\right]}{\left[H^+\right]^2}=4.87\cdot10^{-17}$$

$$Fe^{3+}+3OH^- \rightleftharpoons Fe(OH)_3(s) \qquad K_{s,Fe(OH)_3}=\left[Fe^{3+}\right]\left[OH^-\right]^3=\frac{K_w{}^3\left[Fe^{3+}\right]}{\left[H^+\right]^3}=2.79\cdot10^{-39}$$

Let the total concentrations be equal, $C_{Fe(III)}=C_{Fe(II)}=1.0\cdot10^{-4}\,\mathrm{M}$. If no precipitation takes place $\left[Fe(III)\right]'=\left[Fe(II)\right]'=1.0\cdot10^{-4}$ and the redox potential of the Fe(III)/Fe(II) pair is given by

$$E=E^{\ominus'}_{Fe^{2+}/Fe^{3+}}+\frac{RT}{F}\ln\frac{\left[Fe^{3+}\right]}{\left[Fe^{2+}\right]}=E^{\ominus'}_{Fe^{2+}/Fe^{3+}}+\frac{RT}{F}\ln\frac{\alpha_{Fe(II),H}}{\alpha_{Fe(III),H}}\frac{\left[Fe(III)\right]'}{\left[Fe(II)\right]'}=$$

$$=E^{\ominus'}_{Fe^{2+}/Fe^{3+}}-\frac{RT}{nF}\ln\frac{\alpha_{Fe(III),H}}{\alpha_{Fe(II),H}}=0.771\,\mathrm{V}-0.059\,\mathrm{V}\cdot\lg\frac{\alpha_{Fe(III),H}}{\alpha_{Fe(II),H}}$$

As pH increases hydroxides start to precipitate. The same side reaction coefficients above also describe the effect of complex reactions on the solubility equilibria

The conditional solubility product for Fe(OH)2 is given by

$$K'_{s,Fe(OH)_2}=\left[Fe^{2+}\right]'\left[OH^-\right]^2=\alpha_{Fe(II),H}K_{s,Fe(OH)_2}$$

and for Fe(OH)3 by

$$K'_{s,Fe(OH)_3}=\left[Fe^{3+}\right]'\left[OH^-\right]^3=\alpha_{Fe(III),H}K_{s,Fe(OH)_3}$$

These allow calculate the pH at which precipitation occurs in the presence of complexation reactions. The first leads to a second-order equation but the second is of the 4th order, and they are both best solved numerically.
Before precipitation, we take $\left[Fe^{3+}\right]'=\left[Fe^{3+}\right]'=1.0\cdot10^{-4}\,\mathrm{M}$ as all metal is in a soluble form.

Precipitation occurs when

$\left[Fe^{2+}\right]'\left[OH^-\right]^2>K'_{s,Fe(OH)_2}$ or $\left[Fe^{3+}\right]'\left[OH^-\right]^3>K'_{s,Fe(OH)_3}$

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[27] David R. Lide, ed., *CRC Handbook of Chemistry and Physics, Internet Ed. 2005,* CRC Press, Boca Raton, FL, U.S.A., **2005**.

Therefore,

- below ca. pH 2 only soluble complexes form and the effective redox potential is given by

$$E^{\ominus,f}_{Fe^{II}/Fe^{III}} = E^{\ominus'}_{Fe^{2+}/Fe^{3+}} - \frac{RT}{nF}\ln\frac{\alpha_{Fe(III),H}}{\alpha_{Fe(II),H}} = 0.771\,\mathrm{V} - 0.059\,\mathrm{V}\cdot\lg\frac{\alpha_{Fe(III),H}}{\alpha_{Fe(II),H}}$$

- between ca. 2 < pH < 8 Fe(III) forms insoluble $Fe(OH)_3(s)$, which determines the Fe(III) concentration in solution. Fe(II) forms soluble complexes only and $\left[Fe(II)\right]' = 1.0\cdot 10^{-4}$. We consider a case with

$$\alpha_{Fe(II),H} = 1 + \frac{\beta_{1,II}}{\left[H^+\right]} + \frac{\beta_{2,II}}{\left[H^+\right]^2}$$

Now

$$E = E^{\ominus'}_{Fe^{2+}/Fe^{3+}} - \frac{3RT}{F}\ln\left[OH^-\right] + \frac{RT}{F}\ln K_{s,Fe(OH)_3} + \frac{RT}{F}\ln\alpha_{Fe(II),H} - \frac{RT}{F}\ln\left[Fe^{2+}\right]' =$$
$$= E^{\ominus'}_{Fe^{2+}/Fe^{3+}} + 0.177\,\mathrm{V}\cdot\left(14 - pH\right) + 0.059\,\mathrm{V}\cdot\lg K_{s,Fe(OH)_3} + 0.059\,\mathrm{V}\cdot\lg\alpha_{Fe(II),H} - 0.059\,\mathrm{V}\cdot\lg\left[Fe(II)\right]' =$$
$$= 1.210\,\mathrm{V} - 0.177\,\mathrm{V}\cdot pH + 0.059\,\mathrm{V}\cdot\lg\alpha_{Fe(II),H}$$

Without side reactions the potential depends only on the free Fe^{2+} concentration. With the side reactions taken into account it depends only on concentration Fe(II)’ (all soluble Fe(II) species).

- above ca. pH > 8 both Fe(III) and Fe(II) form insoluble hydroxides and the solubility constants determine the concentration of free ions

$$E = E^{\ominus'}_{Fe^{2+}/Fe^{3+}} + \frac{RT}{F}\ln\frac{\left[Fe^{3+}\right]}{\left[Fe^{2+}\right]} = E^{\ominus'}_{Fe^{2+}/Fe^{3+}} + \frac{RT}{F}\ln\frac{K_{s,Fe(OH)_3}}{\left[OH^-\right]^3}\frac{\left[OH^-\right]^2}{K_{s,Fe(OH)_2}} =$$
$$= E^{\ominus'}_{Fe^{2+}/Fe^{3+}} - \frac{RT}{F}\ln\left[OH^-\right] + \frac{RT}{F}\ln\frac{K_{s,Fe(OH)_3}}{K_{s,Fe(OH)_2}} = E^{\ominus'}_{Fe^{2+}/Fe^{3+}} + 0.059\,\mathrm{V}\cdot\left(14 - pH\right) + 0.059\,\mathrm{V}\cdot\lg\frac{K_{s,Fe(OH)_3}}{K_{s,Fe(OH)_2}} =$$
$$= 0.285\,\mathrm{V} - 0.059\,\mathrm{V}\cdot pH$$

The boundary pH values between these domains cannot reliably be calculated because of uncertainties in the constants involved. However, the potential of the Fe(III)/Fe(II) pair must be a continuous function of pH. Therefore, the boundaries are here assumed to be the intersection pH values of the successive E vs pH functions given above.

Redox pair Ce(IV)/Ce(III)

Stability and solubility values for the cerium ions are much harder to find in literature than those of iron or copper. The following ones have been selected to be used in this work; if the same constants have been found elsewhere in literature they are usually rather similar. For $E^{\ominus'}_{Ce^{4+}/Ce^{3+}} = 1.72\ \mathrm{V}$ vs NHE.[26]

Stability constants for the soluble hydroxyl complexes.[28]

Ce(III)

$$CeOH^{2+} \rightleftharpoons Ce^{3+} + OH^- \qquad K_{1,III} = \frac{\left[Ce^{3+}\right]\left[OH^-\right]}{\left[CeOH^{2+}\right]} = 10^{-5.65}$$

$$Ce(OH)_2{}^+ \rightleftharpoons Ce^{3+} + 2OH^- \qquad K_{2,III} = \frac{\left[Ce^{3+}\right]\left[OH^-\right]^2}{\left[Ce(OH)_2{}^+\right]} = 10^{-10.4}$$

$$Ce(OH)_3 \rightleftharpoons Ce^{3+} + 3OH^- \qquad K_{2,III} = \frac{\left[Ce^{3+}\right]\left[OH^-\right]^3}{\left[Ce(OH)_3\right]} = 10^{-14.8}$$

$\beta_{1,III} = 10^{-5.65}$, $\beta_{2,III} = 10^{-16.05}$, $\beta_{3,III} = 10^{-30.85}$

The formation of polynuclear complexes [$Ce_3(OH)_5{}^{4+}$] is neglected (lgK=-36.5).

Ce(IV)

$$CeOH^{3+} \rightleftharpoons Ce^{4+} + OH^- \qquad K_{1,IV} = \frac{\left[Ce^{4+}\right]\left[OH^-\right]}{\left[CeOH^{3+}\right]} = 10^{-17.2}$$

$$Ce(OH)_2{}^{2+} \rightleftharpoons Ce^{4+} + 2OH^- \qquad K_{2,IV} = \frac{\left[Ce^{4+}\right]\left[OH^-\right]^2}{\left[Ce(OH)_2{}^{2+}\right]} = 10^{-30.0}$$

The formation of polynuclear complexes [$Ce_2(OH)_2{}^{6+}$] is neglected (lgK=-31.0).

Division of $K_w = 1.0 \cdot 10^{-14}$,$K_w{}^2$ and $K_w{}^3$ (water autoprotolysis constant) by $K_{1,III}$, $K_{2,III}$ and $K_{3,III}$, respectively, transfers the stability constants to the form analogous to that given in case of Fe. Therefore, the side reaction coefficient of Ce(III) with respect to OH-complex formation is given analogously as

$$\alpha_{Ce(III),H} = 1 + \beta_{1,III}\left[OH^-\right] + \beta_{2,III}\left[OH^-\right]^2 + \beta_{3,III}\left[OH^-\right]^3 = 1 + \frac{\beta_{1,III}'}{\left[H^+\right]} + \frac{\beta_{2,III}'}{\left[H^+\right]^2} + \frac{\beta_{3,III}'}{\left[H^+\right]^3}$$

where

$\beta_{1,III}' = 10^{-8.35}$ $\beta_{2,III}' = 10^{-17.6}$ $\beta_{3,III}' = 10^{-27.2}$

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[28] Spahiu, K.; Bruno, J., *A selected thermodynamic database for REE to be used in HLNW performance assessment excercises*, Technical Report 95-35, Swedish Nuclear Fuel and Waste Management Co (SKB), **1995**; http://www.iaea.org/inis/collection/NCLCollectionStore/_Public/28/019/28019633.pdf

Similarly for Ce(IV), division of K_w and $K_w^{\ 2}$ (water autoprotolysis constant) by $K_{1,IV}$ and $K_{2,IV}$, respectively, transfers the stability constants to the form analogous to that given in case of Fe. The side reaction coefficient of Ce(IV) with respect to OH-complex formation is given analogously as

$$\alpha_{Ce(IV),H} = 1 + \frac{\beta_{1,IV}'}{\left[H^+\right]} + \frac{\beta_{2,IV}'}{\left[H^+\right]^2}$$

where

$$\beta_{1,IV}' = 10^{3.2} \quad \text{and} \quad \beta_{2,IV}' = 10^{2.0}$$

In acidic solutions both oxidation states form soluble species only, and the potential of a redox system with $C_{Ce(IV)} = C_{Ce(III)} = 1.0 \cdot 10^{-4}\,\mathrm{M}$ is given by

$$E = E^{\ominus\prime}_{Ce^{4+}/Ce^{3+}} - \frac{RT}{nF}\ln\frac{\alpha_{Ce(IV),H}}{\alpha_{Ce(III),H}} = 1.72\,\mathrm{V} - 0.059\,\mathrm{V}\cdot\lg\frac{\alpha_{Ce(IV),H}}{\alpha_{Ce(III),H}}$$

Both oxidation states form sparingly soluble hydroxides. The stable form of the solid hydroxide Ce(OH)$_4$ is the oxide CeO$_2$. Using the data in literature (standard free energies of formation)[22] the equilibrium constants (solubility products) for the following reactions are as follows:

For the reaction

$$Ce(OH)_3(s) + 3H^+ \rightleftharpoons Ce^{3+} + 3H_2O$$

$$K_{Ce(OH)_3,H} = 10^{20.3} = \frac{\left[Ce^{3+}\right]}{\left[H^+\right]^3} \Rightarrow K_{Ce(OH)_3,H}K_w^{\ 3} = \left[Ce^{3+}\right]\left[OH^-\right]^3 = K_{s,Ce(OH)_3} = 10^{-21.7}$$

Now the pH at which Ce(OH)$_3$ starts to precipitate when $C_{Ce(III)} = 10^{-4}$ can be estimated either from the $K_{Ce(OH)_3,H}$ or the solubility product $K_{s,Ce(OH)_3} = \left[Ce^{3+}\right]\left[OH^-\right]^3 = K_{Ce(OH)_3,H}K_w^{\ 3} = 10^{-21.7}$.

The side reaction coefficient for Ce(III) is given by

$$\alpha_{Ce(III),H} = 1 + \beta_{1,III}\left[OH^-\right] + \beta_{2,III}\left[OH^-\right]^2 + \beta_{3,III}\left[OH^-\right]^3 = 1 + \frac{\beta_{1,III}'}{\left[H^+\right]} + \frac{\beta_{2,III}'}{\left[H^+\right]^2} + \frac{\beta_{3,III}'}{\left[H^+\right]^3}$$

and Ce(OH)$_3$ precipitates when

$$\left[Ce^{3+}\right]'\left[OH^-\right]^3 > K'_{s,Ce(OH)_3} = \alpha_{Ce(III),H}K_{s,Ce(OH)_3}$$

For the reaction

$$CeO_2(s) + 2H^+ \rightleftharpoons Ce(OH)_2^{\ 2+}$$

we have

$$K_{CeO_2,H} = 10^{-2.6}$$

In the presence of solid CeO$_2$ this last equilibrium always holds. Precipitation of solid CeO$_2$ occurs when

$$\frac{\left[Ce(OH)_2{}^{2+}\right]}{\left[H^+\right]^2} > K_{CeO_2,H}$$

Using the constants given above we see that the pH range can be divided into three domains:

- Below ca. pH < 1 only soluble species

$$E = E^{\ominus'}_{Ce^{4+}/Ce^{3+}} - \frac{RT}{nF}\ln\frac{\alpha_{Ce(IV),H}}{\alpha_{Ce(III),H}} = 1.72\,\mathrm{V} - 0.059\,\mathrm{V}\cdot\lg\frac{\alpha_{Ce(IV),H}}{\alpha_{Ce(III),H}}$$

- Between ca. 1 < pH < 8, only CeO_2 precipitates. The solubility product $K_{s.CeO_2}$ determines the concentration of $Ce(OH)_2{}^{2+}$(aq) in solution. $\left[Ce(III)\right]' = 1.0\cdot 10^{-4}$.

$$E = E^{\ominus'}_{Ce^{4+}/Ce^{3+}} + \frac{RT}{F}\ln\frac{\left[Ce^{4+}\right]}{\left[Ce^{3+}\right]} = E^{\ominus'}_{Ce^{4+}/Ce^{3+}} + \frac{RT}{F}\ln\frac{\alpha_{Ce(III),H}}{\left[Ce^{3+}\right]'}\frac{K_{2,IV}\left[H^+\right]^2\left[Ce\left(OH\right)_2{}^{2+}\right]}{K_w{}^2} =$$

$$= 1.685\,\mathrm{V} - 0.236\,\mathrm{V}\cdot pH + 0.059\,\mathrm{V}\cdot\lg\alpha_{Ce(III),H}$$

- above pH > ca. 8, both $Ce(OH_4)$ and $Ce(OH)_3$ precipitate and the concentration of Ce^{4+}(aq) and Ce^{3+}(aq) both are determined by the appropriate solubility constant. $\left[Ce(III)\right]' = \left[Ce(IV)\right]' = 1.0\cdot 10^{-4}$

$$E = E^{\ominus'}_{Ce^{4+}/Ce^{3+}} + \frac{RT}{F}\ln\frac{\left[Ce^{4+}\right]}{\left[Ce^{3+}\right]} = E^{\ominus'}_{Ce^{4+}/Ce^{3+}} + \frac{RT}{F}\ln\frac{\alpha_{Ce(III),H}\left[Ce^{4+}\right]}{\left[Ce^{3+}\right]'} =$$

$$= E^{\ominus'}_{Ce^{4+}/Ce^{3+}} + \frac{RT}{F}\ln\frac{\alpha_{Ce(III),H}\left[OH^-\right]^3}{K'_{s,Ce(OH)_3}}\frac{K_{2,IV}\left[H^+\right]^4 K_{CeO_2,H}}{K_w{}^2} =$$

$$= 0.251\,\mathrm{V} - 0.059\,\mathrm{V}\cdot pH$$

Redox pair Cu(II)/Cu(I)

The behaviour of this redox pair can be affected by OH⁻ions (hydroxide and hydroxo complex formation) and, e.g., Cl⁻ ions (chloro complex and precipitate formation). For the Cu(II)/Cu(I) pair, $E^{\circ}_{Cu(II)/Cu(I)} = 0.159\ \mathrm{V}$ vs NHE,[26] and the following equilibrium constants have been reported in literature.[29,30]

Effect of Cl⁻

Cu(I)

$$Cu^{+} + Cl^{-} \rightleftharpoons CuCl(aq) \qquad \beta_{1Cl,I} = \frac{\left[CuCl(aq)\right]}{\left[Cu^{+}\right]\left[Cl^{-}\right]} = 10^{3.10}$$

$$Cu^{+} + 2Cl^{-} \rightleftharpoons CuCl_2^{-}(aq) \qquad \beta_{2Cl,I} = \frac{\left[CuCl_2^{-}(aq)\right]}{\left[Cu^{+}\right]\left[Cl^{-}\right]^2} = 10^{5.68}$$

$$Cu^{+} + 3Cl^{-} \rightleftharpoons CuCl_3^{2-}(aq) \qquad \beta_{3Cl,I} = \frac{\left[CuCl_3^{2-}(aq)\right]}{\left[Cu^{+}\right]\left[Cl^{-}\right]^3} = 10^{5.02}$$

$$Cu^{+} + Cl^{-} \rightleftharpoons CuCl(s) \qquad K_{s,CuCl} = \left[Cu^{+}\right]\left[Cl^{-}\right] = 10^{-6.82}$$ CuCl solubility product

Cu(II)

$$Cu^{2+} + Cl^{-} \rightleftharpoons CuCl^{+}(aq) \qquad \beta_{1Cl,II} = \frac{\left[CuCl^{+}(aq)\right]}{\left[Cu^{2+}\right]\left[Cl^{-}\right]} = 10^{0.2}$$

$$Cu^{2+} + 2Cl^{-} \rightleftharpoons CuCl_2(aq) \qquad \beta_{2Cl,II} = \frac{\left[CuCl_2(aq)\right]}{\left[Cu^{2+}\right]\left[Cl^{-}\right]^2} = 10^{-0.26}$$

$$Cu^{2+} + 3Cl^{-} \rightleftharpoons CuCl_3^{-}(aq) \qquad \beta_{3Cl,II} = \frac{\left[CuCl_3^{-}(aq)\right]}{\left[Cu^{2+}\right]\left[Cl^{-}\right]^3} = 10^{-2.29}$$

$$Cu^{2+} + 4Cl^{-} \rightleftharpoons CuCl_4^{2-}(aq) \qquad \beta_{4Cl,II} = \frac{\left[CuCl_4^{2-}(aq)\right]}{\left[Cu^{2+}\right]\left[Cl^{-}\right]^4} = 10^{-4.59}$$

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[29] Pham, A. N.; Waite, T. D., Cu(II)-catalyzed oxidation of dopamine in aqueous solutions: Mechanism and kinetics, *J. Inorg. Biochem.* **2014**, *137*, 74-84.

[30] Wang, M.; Zhang, Y.; Muhammed, M., Critical evaluation of thermodynamics of complex formation of metals in aqueous solutions III. The system Cu(I,II) - Cl⁻ - e at 298.15 K, *Hydrometallurgy*, **1997**, *45*, 53-72.

Effect of OH⁻

$$Cu^{2+}+H_2O \rightleftharpoons CuOH^+(aq)+H^+ \qquad \beta_{1OH,II}=\frac{\left[CuOH^+(aq)\right]\left[H^+\right]}{\left[Cu^{2+}\right]}=10^{-7.50}$$

$$Cu^{2+}+2H_2O \rightleftharpoons Cu(OH)_2(aq)+2H^+ \qquad \beta_{2OH,II}=\frac{\left[Cu(OH)_2(aq)\right]\left[H^+\right]^2}{\left[Cu^{2+}\right]}=10^{-16.2}$$

$$Cu^{2+}+3H_2O \rightleftharpoons Cu(OH)_3^-(aq)+3H^+ \qquad \beta_{3OH,II}=\frac{\left[Cu(OH)_3^-(aq)\right]\left[H^+\right]^3}{\left[Cu^{2+}\right]}=10^{-26.9}$$

$$Cu^{2+}+4H_2O \rightleftharpoons Cu(OH)_4^{2-}(aq)+4H^+ \qquad \beta_{4OH,II}=\frac{\left[Cu(OH)_4^{2-}(aq)\right]\left[H^+\right]^4}{\left[Cu^{2+}\right]}=10^{-40}$$

In the absence of chloride the speciation is determined by the formation of hydroxyl complexes (assuming that copper concentration is so slow that precipitation can be neglected).

In this case

$$[Cu(II)]'=\left[Cu^{2+}\right]+\left[CuOH^+\right]+\left[Cu(OH)_2\right]+\left[Cu(OH)_3^-\right]+\left[Cu(OH)_4^{2-}\right]=$$

$$=\left[Cu^{2+}\right]\left(1+\frac{\beta_{1OH,II}}{\left[H^+\right]}+\frac{\beta_{2OH,II}}{\left[H^+\right]^2}+\frac{\beta_{3OH,II}}{\left[H^+\right]^3}+\frac{\beta_{4OH,II}}{\left[H^+\right]^4}\right)=\alpha_{Cu(II),H}\left[Cu^{2+}\right]$$

and

$$E^{\ominus,f}_{Cu(II)/Cu(I)}=E^{\ominus'}_{Cu^{2+}/Cu^+}-\frac{RT}{F}\ln\alpha_{Cu(II),H}=0.159\,\mathrm{V}-0.059\,\mathrm{V}\cdot\lg\alpha_{Cu(II),OH}$$

The solubility of Cu(II) and Cu(I) hydroxides is low and they form already at low pH. Therefore, the solubility constants effectively determine the concentrations of free $Cu^{2+}(aq)$ and $Cu^+(aq)$ in solution.

The stable form of CuOH is the oxide Cu_2O. For the reaction[22]

$$Cu_2O(s)+H^+ \rightleftharpoons 2Cu^+ +OH^-$$

$$K_{Cu_2O,H}=\frac{\left[Cu^+\right]^2\left[OH^-\right]}{\left[H^+\right]}=\frac{K_w\left[Cu^+\right]^2}{\left[H^+\right]^2}$$

and

$$\lg K_{Cu_2O,H}=-15.77$$

Similarly, for $Cu(OH)_2(s)$

$$Cu(OH)_2(s)+2H^+ \rightleftharpoons Cu^{2+}+2H_2O$$

$$K_{Cu(OH)_2,H}=\frac{\left[Cu^{2+}\right]}{\left[H^+\right]^2}$$

and

$$\lg K_{Cu(OH)_2,H} = 10^{8.7}$$

On the other hand,

$$K_{s,Cu(OH)_2} = \left[Cu^{2+}\right]\left[OH^-\right]^2 = K_w{}^2 \frac{\left[Cu^{2+}\right]}{\left[H^+\right]^2} = K_w{}^2 K_{Cu(OH)_2,H} = 10^{-19.3}$$

which is practically the same value as given, e.g., by Schott ($\lg K_{s,Cu(OH)_2} = -19.5$).[31]

<u>No chloride in solution</u>

Formation of $Cu(OH)_2(s)$ and $Cu_2O(s)$.

The conditional solubility constant for $Cu(OH)_2$ is given by

$$K'_{s,Cu(OH)_2} = \alpha_{Cu(II),H} K_{s,Cu(OH)_2} = \left[Cu^{2+}\right]'\left[OH^-\right]^2$$

Because $\left[Cu^{2+}\right]' = 10^{-4}$ precipitation of $Cu(OH)_2$ takes place when

$$\left[Cu^{2+}\right]'\left[OH^-\right]^2 > K'_{s,Cu(OH)_2} = \alpha_{Cu(II),H} K_{s,Cu(OH)_2} = \left(1 + \frac{\beta_{1OH,II}}{\left[H^+\right]} + \frac{\beta_{2OH,II}}{\left[H^+\right]^2} + \frac{\beta_{3OH,II}}{\left[H^+\right]^3} + \frac{\beta_{4OH,II}}{\left[H^+\right]^4}\right) K_{s,Cu(OH)_2}$$

On the other hand, because Cu(I) does not form soluble hydroxides, solid Cu_2O forms if

$$\frac{K_w\left[Cu^+\right]^2}{\left[H^+\right]^2} > K_{Cu_2O,H}$$

where $\left[Cu^+\right] = 10^{-4}$ before precipitate formation.

There are three domains

- below approximately pH < 3 only soluble species exist, and potential can be calculated from (because $\alpha_{Cu(I),OH} = 1$)

$$E^{\ominus,f}_{Cu(II)/Cu(I)} = E^{\ominus'}_{Cu^{2+}/Cu^+} - \frac{RT}{F}\ln\frac{\alpha_{Cu(II),OH}}{\alpha_{Cu(I),OH}} = 0.159\,\mathrm{V} - 0.059\,\mathrm{V}\cdot\lg\alpha_{Cu(II),OH}$$

- between ca. 3 < pH < 6 solid Cu_2O forms but all Cu(II) species are soluble. Concentration of Cu(I) is determined by equilibrium

$$\frac{K_w\left[Cu^+\right]^2}{\left[H^+\right]^2} = K_{Cu_2O,H}$$ and

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[31] Schott, H., Relationship between Zero Point of Charge and Solubility Product for Hydroxides of Polyvalent Cations, *J. Pharm. Sci.* **1977**, *66*, 1548-1550.

$$E = E^{\ominus'}_{Cu^{2+}/Cu^{+}} + \frac{RT}{F}\ln\frac{\left[Cu^{2+}\right]}{\left[Cu^{+}\right]} = E^{\ominus'}_{Cu^{2+}/Cu^{+}} + \frac{RT}{F}\ln\left\{\frac{\left[Cu^{2+}\right]'}{\alpha_{Cu(II),H}\left[H^{+}\right]}\left(\frac{K_w}{K_{Cu_2O,H}}\right)^{1/2}\right\} =$$

$$= -0.025\,\mathrm{V} + 0.059\,\mathrm{V}\cdot pH - 0.059\,\mathrm{V}\cdot \lg\alpha_{Cu(II),H}$$

- above ca. pH > 6, solid $Cu(OH)_2$ starts to precipitate,too, and we have the concentration of Cu^{2+} is determined by the equilibrium

$$K_{s,Cu(OH)_2} = \left[Cu^{2+}\right]\left[OH^{-}\right]^2 = K_w{}^2\frac{\left[Cu^{2+}\right]}{\left[H^{+}\right]^2} = 10^{-19.3}$$

$$E = E^{\ominus'}_{Cu^{2+}/Cu^{+}} + \frac{RT}{F}\ln\frac{\left[Cu^{2+}\right]}{\left[Cu^{+}\right]} = E^{\ominus'}_{Cu^{2+}/Cu^{+}} + \frac{RT}{F}\ln\left\{\left[H^{+}\right]\frac{K_{s,Cu(OH)_2}}{K_w{}^2}\left(\frac{K_w}{K_{Cu_2O,H}}\right)^{1/2}\right\} =$$

$$= 0.724\,\mathrm{V} - 0.059\,\mathrm{V}\cdot pH$$

At chloride concentration 0.1 M

If we assume that $\left[Cl^{-}\right] \gg \left[Cu\right]_{total}$ the chloride concentration remains constant, i.e., negligible amount of chloride is bound in complexes. This is the case when $\left[Cl^{-}\right] = 0.1\,\mathrm{M}$ and $C_{Cu(I)} = C_{Cu(II)} = 0.1\ \mathrm{mM}$.

Now

$$\alpha_{Cu(II),Cl} = 1 + \frac{\beta_{1Cl,II}}{\left[Cl^{-}\right]} + \frac{\beta_{2Cl,II}}{\left[Cl^{-}\right]^2} + \frac{\beta_{3Cl,II}}{\left[Cl^{-}\right]^3} + \frac{\beta_{4Cl,II}}{\left[Cl^{-}\right]^4}$$

and

$$\alpha_{Cu(I),Cl} = 1 + \frac{\beta_{1Cl,I}}{\left[Cl^{-}\right]} + \frac{\beta_{2Cl,I}}{\left[Cl^{-}\right]^2} + \frac{\beta_{3Cl,I}}{\left[Cl^{-}\right]^3}$$

Cu(II) can also form hydroxo complexes, and we have for the total side reaction coefficients

$$\alpha_{Cu(II);H,Cl} = \alpha_{Cu(II),H} + \alpha_{Cu(II),Cl} - 1$$

The conditional solubility constant for CuCl is given by

$$K'_{s,CuCl} = \left[Cu^{+}\right]'\left[Cl^{-}\right] = \alpha_{Cu(I),Cl}K_{s,CuCl}$$

Under these conditions the conditional ionic product $\left[Cu^{+}\right]'\left[Cl^{-}\right] = 10^{-5}$ and the conditional solubility constant

$$\left(1+\frac{\beta_{1Cl,I}}{\left[Cl^-\right]}+\frac{\beta_{2Cl,I}}{\left[Cl^-\right]^2}+\frac{\beta_{3Cl,I}}{\left[Cl^-\right]^3}\right)K_{s,CuCl}=\left(1+10^{4.10}+10^{7.68}+10^{8.02}\right)10^{-6.82}=1.526\cdot10^{8}\cdot10^{-6.82}>10^{-5}$$

Therefore, CuCl does not precipitate under these conditions but Cu(I) forms stable chloride complexes. Possible Cu_2O formation would further inhibit CuCl(s) formation.

The conditional constant for Cu_2O(s) formation is

$$K'_{Cu_2O,H}=\frac{\left[Cu^+\right]'^2\left[OH^-\right]}{\left[H^+\right]}=\frac{K_w\left[Cu^+\right]'^2}{\left[H^+\right]^2}=\frac{K_w\alpha^2{}_{Cu(I),Cl}\left[Cu^+\right]^2}{\left[H^+\right]^2}=\alpha^2{}_{Cu(I),Cl}K_{Cu_2O,H}=3.954$$

Therefore, under these conditions Cu_2O can form only when $\left[H^+\right]<5.0\cdot10^{-12}\;\Rightarrow\;pH>11.3$ which is outside the pH range studied here. Therefore, in the pH range considered, we can set the total side reaction coefficient for Cu(I) as

$$\alpha_{Cu(I);H,Cl}\equiv\alpha_{Cu(I),Cl}$$

Therefore, Cu(I) forms only soluble species in the studied pH range.

For Cu(II), the conditional solubility constant of $Cu(OH)_2$ is given by

$$K'_{s,Cu(OH)_2}=\left[Cu^{2+}\right]'\left[OH^-\right]^2=\frac{K_w{}^2\left[Cu^{2+}\right]'}{\left[H^+\right]^2}=\alpha_{Cu(II);H,Cl}K_{s,Cu(OH)_2}=$$

$$=\left(77.189+\frac{\beta_{1OH,II}}{\left[H^+\right]}+\frac{\beta_{2OH,II}}{\left[H^+\right]^2}+\frac{\beta_{3OH,II}}{\left[H^+\right]^3}+\frac{\beta_{4OH,II}}{\left[H^+\right]^4}\right)\cdot10^{-19.3}$$

Precipitation of $Cu(OH)_2$ takes place if $\left[Cu^{2+}\right]'\left[OH^-\right]^2>K'_{s,Cu(OH)_2}$

There are two pH ranges;

- approximately pH < 7 only soluble species present and we have

$$E=E^{\ominus'}_{Cu^{2+}/Cu^+}+\frac{RT}{F}\ln\frac{\left[Cu^{2+}\right]}{\left[Cu^+\right]}=E^{\ominus'}_{Cu^{2+}/Cu^+}+\frac{RT}{F}\ln\left(\frac{\alpha_{Cu(I),Cl}}{\alpha_{Cu(II);H,Cl}}\frac{\left[Cu^{2+}\right]'}{\left[Cu^+\right]'}\right)=$$

$$=0.159\,\mathrm{V}+0.059\,\mathrm{V}\cdot\lg\frac{\alpha_{Cu(I),Cl}}{\alpha_{Cu(II);H,Cl}}$$

- approximately above pH > 7 solid $Cu(OH)_2$ forms and its solubility determines the concentration of Cu^{2+} in solution

$$E=E^{\ominus'}_{Cu^{2+}/Cu^+}+\frac{RT}{F}\ln\frac{\left[Cu^{2+}\right]}{\left[Cu^+\right]}=E^{\ominus'}_{Cu^{2+}/Cu^+}+\frac{RT}{F}\ln\left(\frac{K_{s,Cu(OH)_2}\left[H^+\right]^2}{K_w{}^2}\frac{\alpha_{Cu(I),Cl}}{\left[Cu^+\right]'}\right)=$$

$$=0.909\,\mathrm{V}-0.118\,\mathrm{V}\cdot pH+0.059\,\mathrm{V}\cdot\lg\alpha_{Cu(I),Cl}$$

The effect of chloride concentration

Formation of solid CuCl(s) takes place (below pH ca 11) if

$$\left[Cu^+\right]'\left[Cl^-\right] > K'_{s,CuCl} = \alpha_{Cu(I),Cl}K_{s,CuCl} = \left(1+\frac{\beta_{1Cl,I}}{\left[Cl^-\right]}+\frac{\beta_{2Cl,I}}{\left[Cl^-\right]^2}+\frac{\beta_{3Cl,I}}{\left[Cl^-\right]^3}\right)K_{s,CuCl}$$

In this case, $\left[Cu^+\right]' = 10^{-4}\,\mathrm{M}$, and the threshold chloride concentration (pH independent) is given by

$$\left[Cl^-\right]^4 - \left(\left[Cl^-\right]^3 + \beta_{1Cl,I}\left[Cl^-\right]^2 + \beta_{2Cl,I}\left[Cl^-\right] + \beta_{3Cl,I}\right)\frac{K_{s,CuCl}}{\left[Cu^+\right]'} > 0$$

This would require $\left[Cl^-\right] > 9.1\,\mathrm{M}$; therefore, CuCl(s) formation does not affect the formal potential. The effect of chloride concentration can be calculated from equations given above

$$E = 0.159\,\mathrm{V} + 0.059\,\mathrm{V}\cdot\lg\frac{\alpha_{Cu(I),Cl}}{\alpha_{Cu(II);H,Cl}} \qquad \text{below ca. pH 7}$$

$$E = 0.909\,\mathrm{V} - 0.118\,\mathrm{V}\cdot pH + 0.059\,\mathrm{V}\cdot\lg\alpha_{Cu(I),Cl} \qquad \text{above ca. pH 7}$$

The result is shown below in Fig. S22.

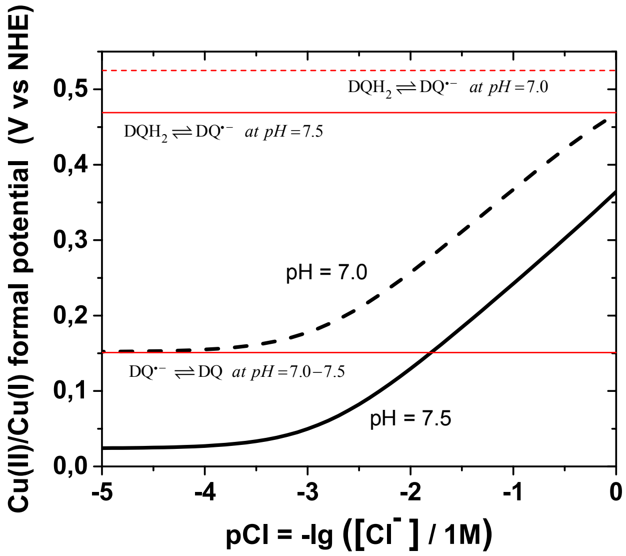

Figure S22. The effect of chloride concentration on the formal potential of the Cu(II)/Cu(I) pair around pH 7. Horizontal lines show the formal redox potentials of the dopamine/dopaminesemiquinone and dopaminesemiquinone/dopaminequinone redox pairs at the same pH. The potential of the $O_2^{\bullet-}/H_2O_2$ pair (0.92 V or 0.86 V at pH 7 or 7.5, respectively) and the $O_2(aq)/O_2^{\bullet-}$ pair (-0.18 V) are outside the scale of the potential axis.

A general model of dopamine oxidation and cyclization kinetics

We analyze the following reaction scheme, which should be the major pathway in the initial phases of the reaction, when other reactions between the intermediates and products can be neglected

$$\mathrm{DHQ}+\mathrm{O_2}(aq)\underset{k_{1b}}{\overset{k_{1f}}{\rightleftharpoons}}\mathrm{DSQ}+\mathrm{SO}\underset{k_{2b}}{\overset{k_{2f}}{\rightleftharpoons}}\mathrm{HP}+\mathrm{DQ}\xrightarrow{k_c}\mathrm{DAL}\underset{k_{3b}}{\overset{k_{3f}}{\rightleftharpoons}}\mathrm{DAC}$$

Here
DHQ = dopamine (hydroquinone form)
DSQ = dopamine semiquinone
DQ = dopaminequinone
SO = superoxide radical
HP = hydrogen peroxide
DAL = leucodopaminechrome
DAC = dopaminechrome
in the appropriate protonation form. In addition, there are the bimolecular rate constants $k_{1f}, k_{1b}, k_{2f}, k_{2b}, k_{3f}, k_{3b}$, and the unimolecular constant k_c .

Classical Marcus theory allows express the electron transfer rate constants as

$$k_{1,2;f}^{(app)} = k_{app;1,2}^{0} \exp\left[-\frac{\left(\Delta G_{1,2}^{\ominus'} + \lambda\right)^2}{4\lambda RT}\right] = k_{app;1,2}^{0} \exp\left[-\frac{\left(-F\Delta E_{1,2}^{\ominus'} + \lambda\right)^2}{4\lambda RT}\right]$$

where $\Delta G_{1,2}^{\ominus'}$ and $\Delta E_{1,2}^{\ominus'}$ are the pH dependent conditional Gibbs free energy change and the formal potential difference for the redox steps 1 or 2, respectively, $\lambda = \lambda_{is} + \lambda_{os}$ is the reorganization energy, given as the sum of inner and outer sphere energies, and k_{app}^{0} = maximum apparent rate constant (at $-\Delta G_{1,2}^{\ominus'} = \lambda$), which also includes the equilibrium constant for the encounter complex formation. The backward electron transfer rates are calculated using the conditional equilibrium constants for the steps as

$$k_{1,2;b}^{(app)} = \frac{K_{1,2}}{k_{1,2;f}^{(app)}}$$

The inner and outer reorganization energies are not available for all species involved but we can use the values reported for self-exchange reactions of the $\mathrm{O_2}^{\bullet-}/\mathrm{O_2}$ ($\lambda_{is} \sim 70\,\mathrm{kJ\,mol^{-1}}$, $\lambda_{os} \sim 120\,\mathrm{kJ\,mol^{-1}}$) and the *p*-benzoquinone species ($\lambda_{is} \sim 40\,\mathrm{kJ\,mol^{-1}}$, $\lambda_{os} \sim 80\,\mathrm{kJ\,mol^{-1}}$) as rough approximations.[32,33] These values lead to an estimate of

$$\lambda = \left(\lambda_{\mathrm{O_2/SO}}^{(self\,exch)} + \lambda_{\mathrm{HQ/SQ}}^{(self\,exch)}\right)\Big/2 \sim 150\ \mathrm{kJ\,mol^{-1}}\quad (1.5\ \mathrm{eV}).$$ [26]

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[32] German, E. D.; Kuznetsov, A. M.; Efremenko, I.; Sheintuch, M. Theory of the Self-Exchange Electron Transfer in the Dioxygen/Superoxide System in Water. *J. Phys. Chem. A* **1999**, *103*, 10699–10707.

[33] Stack, A. G.; Rosso, K. M.; Smith, D. M. A.; Eggleston, C. M. Reaction of hydroquinone with hematite II. Calculated electron-transfer rates and comparison to the reductive dissolution rate. *J. Colloid Interface Sci.* **2004**, *274*, 442–450.

This is a crude estimate because the reorganization energies should also be pH dependent as they refer to different species at different pH. However, it turns out that the value of λ does not have marked influence on the shape and position of the pH profiles calculated for the reactions.

In spite of the seemingly simple mechanism the scheme above is rather difficult to treat analytically. The cyclization reaction is irreversible, and we can initially forget the oxidation of the leuco form. The concentrations of semiquinone (DSQ) and superoxide (SO) species can be assumed to be low and allow the use of the steady-state approximation. On the other hand, the proper analysis should take into consideration that the reactants DHQ and O2(aq) are consumed in the reaction as DQ, HP and DAL are formed. If the DAL formation is neglected we can approximate $[\mathrm{DHQ}]=C_Q-[\mathrm{DQ}]$, $[\mathrm{O}_2(aq)]=C_{O_2}-[\mathrm{DQ}]$, and $[\mathrm{HP}]=[\mathrm{DQ}]$. This case can still be solved analytically by the same procedure as discussed below. However, if DAL formation is included we would have $[\mathrm{DHQ}]=C_Q-[\mathrm{DQ}]-[\mathrm{DAL}]$, $[\mathrm{O}_2(aq)]=C_{O_2}-[\mathrm{DQ}]-[\mathrm{DAL}]$, and $[\mathrm{HP}]=[\mathrm{DQ}]+[\mathrm{DAL}]$, which no longer allows an analytical solution and should be numerically treated.

In general, we can make a simplifying assumption that the dissolved oxygen concentration remains constant if the reaction is carried out in an open vessel, i.e., $[\mathrm{O}_2(aq)]=C_{O_2}$ ($\approx 0.25\,\mathrm{mM}$ at 25 °C in contact with air). In addition, if we are interested only on the pH dependence of the reaction we can assume that the initial dopamine concentration is also so high that its changes can be neglected in the early stages of the reaction, i.e., that $C_Q \gg [\mathrm{DQ}]+[\mathrm{DAL}]$ always. Therefore, in the following, we discuss the pH dependence of the reaction path above assuming that $[\mathrm{O}_2(aq)]=C_{O_2}$ and $[\mathrm{DHQ}]=C_Q$. The results obtained under these assumptions refer to the initial stages of the reaction. These triggering steps determine the relative probability of the process at the pH considered.

We apply the steady-state approximation to the concentration of the semiquinone form

$$\frac{d[\mathrm{DSQ}]}{dt}=k_{1f}[\mathrm{DHQ}][\mathrm{O}_2(aq)]-(k_{1b}+k_{2f})[\mathrm{DSQ}][\mathrm{SO}]+k_{2b}[\mathrm{HP}][\mathrm{DQ}]=0 \quad \Rightarrow$$

$$[\mathrm{DSQ}][\mathrm{SO}]=\frac{k_{1f}[\mathrm{DHQ}][\mathrm{O}_2(aq)]+k_{2b}[\mathrm{HP}][\mathrm{DQ}]}{k_{1b}+k_{2f}} \overset{\text{assumption}}{=} \frac{k_{1f}C_QC_{O_2}+k_{2b}[\mathrm{HP}][\mathrm{DQ}]}{k_{1b}+k_{2f}}$$

For the quinone form we can write the differential equation and insert the expression above to yield

$$\frac{d[\mathrm{DQ}]}{dt}=k_{2f}[\mathrm{DSQ}][\mathrm{SO}]-k_{2b}[\mathrm{HP}][\mathrm{DQ}]-k_c[\mathrm{DQ}]=$$

$$=-\frac{k_{1b}k_{2b}}{k_{1b}+k_{2f}}[\mathrm{HP}][\mathrm{DQ}]-k_c[\mathrm{DQ}]+\frac{k_{1f}k_{2f}}{k_{1b}+k_{2f}}C_QC_{O_2}$$

Because $k_{1b}=k_{1f}/K_1$ and $k_{2b}=k_{2f}/K_2$ we have

$$-\frac{K_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f}k_{2f}}\frac{d[\mathrm{DQ}]}{dt}=[\mathrm{HP}][\mathrm{DQ}]+\frac{k_cK_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f}k_{2f}}[\mathrm{DQ}]-K_1K_2C_QC_{O_2}$$

Assuming that, in the beginning at least, $[\mathrm{HP}]=[\mathrm{DQ}]$, we have a non-linear differential equation

$$-\frac{K_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f}k_{2f}}\frac{d[\mathrm{DQ}]}{dt}=[\mathrm{DQ}]^2+\frac{k_cK_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f}k_{2f}}[\mathrm{DQ}]-K_1K_2C_QC_{O_2}$$

This is of a general form

$$a\frac{dy}{dt}=y^2+by+c$$

which is separable and can be integrated. General integral tables yield for this

$$a\int\frac{dy}{y^2+by+c}=\frac{a}{\sqrt{b^2-4c}}\ln\frac{2y+b-\sqrt{b^2-4c}}{2y+b+\sqrt{b^2-4c}}+const=t$$

The initial condition $[\mathrm{DQ}]_{t=0}\equiv y(0)=0$ yields

$$\frac{2y+b-\sqrt{b^2-4c}}{2y+b+\sqrt{b^2-4c}}=\frac{b-\sqrt{b^2-4c}}{b+\sqrt{b^2-4c}}\exp\left(\frac{\sqrt{b^2-4c}}{a}t\right)$$

In the present case

$$a=-\frac{K_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f}k_{2f}}$$

$$b=\frac{k_cK_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f}k_{2f}}=-ak_c$$

$$c=-K_1K_2C_QC_{O_2}$$

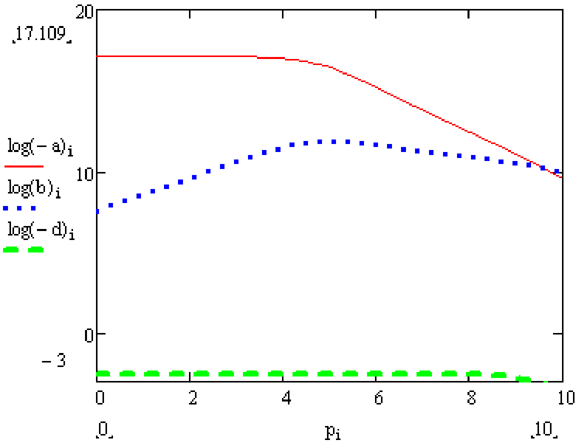

Figure S23. The coefficients of the differential equation a function of pH

Therefore,

$$\sqrt{b^2-4c}=\frac{K_2\left(k_{1f}+k_{2f}K_1\right)}{k_{1f1}k_{2f2}}\gamma=-a\gamma$$

where we use the notation

$$\gamma = \left\{ k_c^2 + \frac{4k_{1f}^2 k_{2f}^2 K_1}{K_2\left(k_{1f}+k_{2f}K_1\right)^2} C_Q C_{O_2} \right\}^{1/2}$$

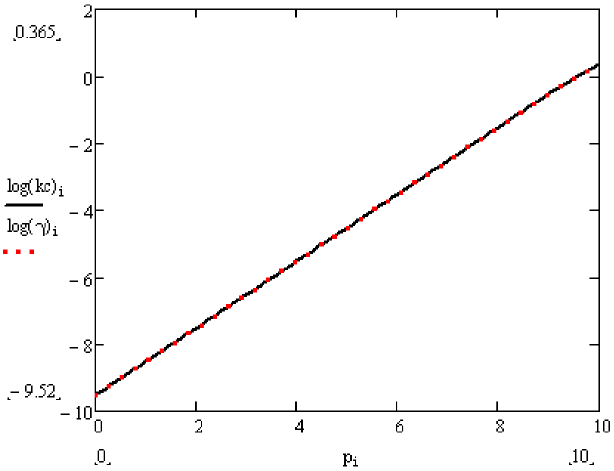

Figure S24. Factors γ and k_c compared as a function of pH.

However, numerical calculations (see figure above) show that $\gamma \approx k_c$. We can use the series expansion $\sqrt{\alpha+x} = \sqrt{\alpha} + \frac{x}{2\sqrt{\alpha}} - \frac{x^2}{8\alpha^{3/2}} + O\left(x^3\right)$ at $x=0$, which converges when $|x|<|\alpha|$ (this assumption is valid here), for γ. This yields

$$\gamma = \left\{ k_c^2 + \frac{4k_{1f}^2 k_{2f}^2 K_1}{K_2\left(k_{1f}+k_{2f}K_1\right)^2} C_Q C_{O_2} \right\}^{1/2} = k_c + \frac{2k_{1f}^2 k_{2f}^2 K_1}{k_c K_2\left(k_{1f}+k_{2f}K_1\right)^2} C_Q C_{O_2} + - \cdots$$

On the other hand, we have

$$\frac{\sqrt{b^2-4c}}{a} = -\gamma$$

$$\frac{b}{\sqrt{b^2-4c}} = -\frac{b}{a\gamma} = \frac{k_c}{\gamma}$$

$$\frac{b-\sqrt{b^2-4c}}{b+\sqrt{b^2-4c}} = \frac{k_c-\gamma}{k_c+\gamma}$$

The solution of the differential equation can now be written as

$$\frac{(k_c+\gamma)\left[2y-a(k_c-\gamma)\right]}{(k_c-\gamma)\left[2y-a(k_c+\gamma)\right]} = \exp(-\gamma t)$$

yielding

$$y = [\mathrm{DQ}] = \frac{a(k_c - \gamma)[1 - \exp(-\gamma t)]}{2\left[1 - \dfrac{k_c - \gamma}{k_c + \gamma}\exp(-\gamma t)\right]}$$

which is the exact solution.

It is noteworthy that the solution predicts that $[\mathrm{DQ}] \sim 0$ always because $k_c \sim \gamma$. We can approximate the exact solution in different ways (which all yield the same approximate result). Using $k_c \sim \gamma$ and taking only the first-order term in the series expansion of γ yields

$$y = [\mathrm{DQ}] = \frac{a(k_{cyc} - \gamma)[1 - \exp(-\gamma t)]}{2\left[1 - \dfrac{k_{cyc} - \gamma}{k_{cyc} + \gamma}\exp(-\gamma t)\right]} \approx -\frac{a\dfrac{2k_{1f}^2 k_{2f}^2 K_1}{k_c K_2 \left(k_{1f} + k_{2f} K_1\right)^2} C_Q C_{O_2}\left[1 - \exp(-k_c t)\right]}{2\left[1 - \dfrac{k_{1f}^2 k_{2f}^2 K_1}{k_c{}^2 K_2 \left(k_{1f} + k_{2f} K_1\right)^2} C_Q C_{O_2} \exp(-k_c t)\right]}$$

The factor in the denominator

$$\frac{k_{1f}^2 k_{2f}^2 K_1}{k_c{}^2 K_2 \left(k_{1f} + k_{2f} K_1\right)^2} C_Q C_{O_2} \exp(-k_c t) < \frac{k_{1f}^2 k_{2f}^2 K_1}{k_c{}^2 K_2 \left(k_{1f} + k_{2f} K_1\right)^2} C_Q C_{O_2} \equiv \delta$$

Numerical calculation shows that $\delta \ll 1$ always (the fig. S25 calculated for $\lambda = 1.5\,\mathrm{eV}$ but the same conclusion is obtained in the range of reorganization energies used in the text).

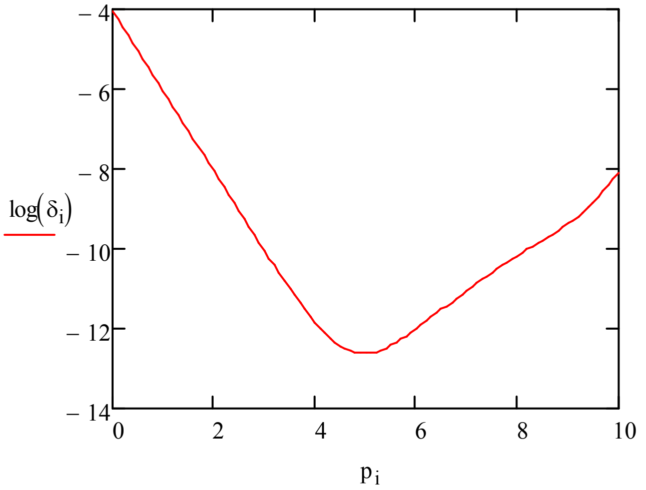

Figure S25. Factor δ for $\lambda = 1.5\,\mathrm{eV}$ as a function of pH.

Therefore, the expression can be simplified to

$$[\mathrm{DQ}] = \frac{k_{1f} k_{2f} K_1}{k_c\left(k_{1f} + k_{2f} K_1\right)} C_Q C_{O_2}\left[1 - \exp(-k_c t)\right] \approx \frac{k_{1f} k_{2f} K_1}{\left(k_{1f} + k_{2f} K_1\right)} C_Q C_{O_2} t$$

where the last expression is valid only for $t \ll 1/k_c$. The amount of DQ slowly increases with time from zero ($t = 0$) to $\frac{k_{1f}k_{2f}K_1}{k_c\left(k_{1f}+k_{2f}K_1\right)}C_QC_{O_2}$ ($t \to \infty$). After the pH dependent characteristic time $t = 1/k_c$ the concentration is given by

$$[\mathrm{DQ}] = \frac{0.632k_{1f}k_{2f}K_1}{k_c\left(k_{1f}+k_{2f}K_1\right)}C_QC_{O_2}$$

From the expression for the DQ concentration we obtain

$$\frac{d[\mathrm{DQ}]}{dt} = \frac{k_{1f}k_{2f}K_1}{\left(k_{1f}+k_{2f}K_1\right)}C_QC_{O_2}\exp\left(-k_ct\right)$$

which has the maximum in the beginning (initial rate) and decreases exponentially with the time constant $\tau = 1/k_c$. The time constant is large and practically constant when pH < 8. The same result is obtained by differentiating the exact solution and applying the condition $k_c \sim \gamma$.

Using the same approximation the leucodopaminechrome formation rate is given by

$$\frac{d[\mathrm{DAL}]}{dt} = k_c[\mathrm{DQ}] = \frac{k_{1f}k_{2f}K_1}{\left(k_{1f}+k_{2f}K_1\right)}C_QC_{O_2}\left[1-\exp\left(-k_ct\right)\right] \approx \frac{k_ck_{1f}k_{2f}K_1}{\left(k_{1f}+k_{2f}K_1\right)}C_QC_{O_2}t$$

where the last expression is valid during the initial stages of the reaction ($t \ll 1/k_c$; the rate of DAC formation increases with time because the DQ concentration grows).

Any comparison of the DQ and DAL formation kinetics has to refer to the same phase of the reaction. The discussion here focuses the early stages of the process, and the initial DQ formation rate is chosen to represent the pH dependence of the oxidation process. The DAL formation rate is zero at $t = 0$, therefore, the term

$$\xi_{DAL} = \frac{k_ck_{1f}k_{2f}K_1}{\left(k_{1f}+k_{2f}K_1\right)}C_QC_{O_2}$$

describes the pH dependence of the cyclization reaction during the early stages.

Author contributions

MS and JL planned and supervised the work, LM performed most of the experimental work and participated in data analysis and writing, TO participated in the experimental work, JL performed most of data analysis and interpretation, HK participated in data analysis and interpretation. JL is the main author, all authors have commented on the manuscript.