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Diffusional Electrochemical Catalytic (EC') Mechanism Featuring Chemical Reversibility of Regenerative Reaction-Theoretical Analysis in Cyclic Voltammetry

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Abstract: We consider theoretically a specific electrochemical-catalytic mechanism associated with reversible regenerative chemical reaction, under conditions of cyclic staircase voltammetry (CSV). We suppose scenario in which two electrochemically inactive substrates "S" and "Y", together with initial electrochemically active reactant Ox are present in voltammetric cell from the beginning of the experiment. Substrate "S" selectively reacts with initial electroactive reactant Ox and creates electroactive "product" Red (+ Y) in a reversible chemical fashion. The initial chemical equilibrium determines the amounts of Ox and Red available for electrode transformation at the beginning of the electrochemical experiment. Under conditions of applied potential, the electrode reaction Ox(aq) + $ne^- \leftrightharpoons$ Red(aq) occurs, producing flow of electric current. Under such circumstances, the chemical reaction coupled to the electrochemical step causes a regeneration of initial electroactive species during the time-frame of current-measuring segment in CSV. The features of cyclic voltammograms get significantly affected by the kinetics and thermodynamics of reversible regenerative reaction. We elaborate several aspects of this specific electrode mechanism, and we focus on the role of parameters related to chemical step to the features of calculated voltammograms. While we provide a specific set of results of this particular mechanism, we propose methods to get access to relevant kinetic and thermodynamic parameters relevant to regenerative chemical reaction. The results elaborated in this work can be valuable in evaluating kinetics of many drug-drug interactions, but they can be relevant to study interactions of many enzyme-substrate systems, as well.

Keywords: catalytic EC'_{rev} mechanism, catalytic rate constant, drug-drug interactions, cyclic voltammetry, electrode reaction mechanisms.

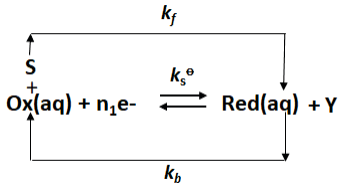
INTRODUCTION

UNDERSTANDING the chemistry of so-called "redox enzymes" can lead to important discoveries related to energy conversion and functioning of many important systems in living cells.[1–3] The search to relate energy conversion in living cells with the enzymes redox chemistry has motivated scientists to look for simple and reliable methods to study complex protein molecules with cheap electrochemical techniques.[1–6] In parallel, significant work has been focused on the development of theoretical electrochemical methods to study the redox chemistry of enzymes, but also of other physiological compounds.[1,2,7–13] Additionally, great efforts have been made in last couple of decades to comprehend the redox chemistry of many drugs, while relevant electrochemical methods were developed to get insight into the chemistry of drug-drug interactions.[3,4,7,14] To achieve these goals, many electrochemists have turned to cyclic voltammetry in order to evaluate relevant kinetics and thermodynamics parameters related to enzyme redox chemistry and the drug-drug interactions.[4,7,9,14] Cyclic voltammetry is recognized as the most valuable voltammetric technique, suitable for studying electrochemical and chemical features of many substances.[1–9,11,14–18] The cyclic voltammetry allows us to get insight into chemical changes that occur during an electrochemical transformation of given "electroactive" substances at working electrode.[7] Due to many efforts focused on the designing of sustainable voltammetric experimental methods for studying redox chemistry of enzymes and drugs, in the past three decades we witness great resurgence in the development of theories of cyclic voltammetry for studying various electrode mechanisms.[1,3,4,7,9–19] The theoretical models in cyclic voltammetry

can be explored to develop relevant methods for the determination of important kinetic and thermodynamic parameters related to the chemistry of many physiologically important substances.[4,7] In the family of electrode mechanisms that are complicated with chemical reactions, the so-called electrochemical-catalytic EC' mechanism is recognized as the most suitable model that provides insight into kinetic parameters relevant to interactions of many drugs, and the enzyme-substrate interactions as well.[3–7] Until recently, theoretical models developed for the EC' mechanisms considered an irreversible chemical reaction involved in the regeneration of initial electroactive reactant.[3,7,9] Only recently, our group[18] and others,[19] assumed a chemical reversibility of the regenerative steps at the EC' mechanism. This scenario brings more complexity in theoretical considerations, since there is one more degree of freedom to be considered in the mathematical models, i.e. the chemical equilibrium constant. By considering EC' mechanism featuring chemical reversibility at the regenerative step, we can get access to catalytic rate constants of chemical reaction, and in addition to the value of chemical equilibrium constant, too. The elaborated mechanism in this work is especially relevant to study the chemistry between hydrophilic systems such as enzyme-substrates, drug-drug and drug-DNA interactions.[3,4,20–25]

Mathematical Model

We consider theoretically a diffusional electrode mechanism: Ox(aq) + ne^- ⇋ Red(aq), with electrode reaction taking place at a stationary planar electrode ("aq" = aqueous). In this mechanism, we assume that both "electroactive" participants of the electrode reaction undergo in the same time a chemical interconversion. We suppose that the initial electroactive compound Ox(aq) reacts chemically with substrate "S" (present in large excess), generating product Red(aq) and substrate "Y" in a chemically reversible manner. Moreover, the product Red(aq) can be also generated electrochemically via electrode transformation of Ox(aq) under applied potential. We additionally assume that electrochemically generated Red(aq) species undergo a chemical regenerative (chemically reversible) reaction with "Y" species (present also in large excess as dissolved species in solution). The chemical reaction between Red(aq) and Y(aq) leads to regeneration of initial electroactive reactant Ox(aq) (and also of substrate "S"). The substrates "Y" and "S" are defined as "electrochemically inactive", since we assume that these compounds do not exhibit electrochemical activity in the region of applied potentials. In addition, we suppose that "S" and "Y" do not react between them, and they are present in large excess in electrochemical cell from the beginning of the experiment (i.e. before the potential is applied). We suppose that both electrochemically active forms of species Ox and Red are dissolved in water solution



Reaction scheme 1. Sequence of chemical and electrochemical steps related to elaborated diffusional catalytic EC_{rev}' mechanism.

("aq") and there is no adsorption taking place in the system. A schematic description of this specific surface electrode mechanism is as presented in Reaction scheme 1.

The molar concentration of "S" and "Y" species in the electrochemical cell is assumed to be much higher than the initial concentration of electroactive species c^*(Ox). Therefore, the both steps of chemical reactions in Scheme 1 are assumed to be of pseudo-first order. With k_s^o we define the rate constant related to electron transfer step, while k_f and k_b are the rate constants of forward and backward steps of the chemical reaction, respectively. If we perform experiments in excess concentration of substrates S and Y, then we can define the chemical rate parameter "ε" as: $\varepsilon = (k_f + k_b)$. The forward and backward chemical rate constants k_f (s^{-1}) and k_b (s^{-1}) are defined as: $k_f = k_f'c(S)$ and $k_b = k_b'c(Y)$. In the last equation, k_f' and k_b' are real chemical rate constant (mol^{-1} cm^3 s^{-1}), while $c(S)$ and $c(Y)$ are molar concentrations ((mol cm^{-3}) of substrates "S" and "Y", respectively. Under conditions of semi-infinite planar diffusion, this mechanism can be described by following equations:

$$\left[\frac{\partial c(\mathrm{Ox})}{dt}\right] = D\left(\frac{\partial^2 c(\mathrm{Ox})}{dx^2}\right) + k_b c(\mathrm{Red}) - k_f c(\mathrm{Ox}) \quad (1)$$

$$\left[\frac{\partial c(\mathrm{Red})}{dt}\right] = D\left(\frac{\partial^2 c(\mathrm{Red})}{dx^2}\right) - k_b c(\mathrm{Red}) + k_f c(\mathrm{Ox}) \quad (2)$$

Differential equations (1) and (2) are solved under following conditions:

(a) $t = 0$; for all x values (x is the distance from the working electrode surface):

(b) $c(\mathrm{Ox}) + c(\mathrm{Red}) = c^*(\mathrm{Ox})$; $[k_f / k_b] = K_{eq}$

(c) $t > 0$; for all x: $c(\mathrm{Ox}) + c(\mathrm{Red}) = c^*(\mathrm{Ox})$; and $[k_f / k_b] = K_{eq}$

However, for $t > 0$, and $x = 0$, and under conditions of applied potential, all changes in concentrations of Ox and Red at $x = 0$ will produce flow of electric current. Under such circumstances, we can apply the Butler-Volmer equation in following form:

(d) $t > 0$; $x = 0$; $I / (nFA) = k_s^o \exp(-\alpha\Phi)\,[c(\mathrm{Ox}) - \exp(\Phi)\,c(\mathrm{Red})]$.

With c^*(Ox) (mol cm^{-3}) we define the initial molar concentration of electroactive compound Ox(aq) in the cell. By Φ we define the dimensionless potential $\Phi = nF(E-E^{o}_{Ox/Red})/(RT)$. In the last equation, E is the applied bias, $E^{o}_{Ox/Red}$ is value of standard redox potential of Ox(aq)/Red(aq) redox couple, R is the gas constant (8.314 J mol^{-1} K^{-1}), and T is the thermodynamic temperature (K). The symbols of A, F, n correspond to: area of working electrode (cm^2), Faraday constant (96485 C mol^{-1}), and number of exchanged electrons, respectively. With "α" we define the coefficient of electron transfer, which was set to equal value of 0.5 both for cathodic and anodic electron transfer step. The solutions of differential equations [1] and [2] were obtained by applying the numerical integration method as described in the Ref [26]. All recurrent formulas needed for calculation of the theoretical cyclic voltammograms are given in the Supplementary Material file. In all simulations, we assumed following parameters to be held at constant values: α = 0.5, T = 298 K, and equal values of diffusion coefficients D of both Ox and Red, $D = 5 \times 10^{-6}$ cm^2 s^{-1}. Cyclic voltammograms were recorded by forward scan starting from positive potentials (+0.40 V) and running the bias towards negative switching potentials. All calculations were performed by commercially available MATHCAD 14 software.

Parameters that Affect the Features of Simulated Cyclic Voltammograms

The dimensionless current of simulated cyclic voltammograms is defined as $\Psi = I\tau^{0.5}/[(D^{0.5}nFAc^*(\mathrm{Ox}))]$. In the last equation, with τ is defined the time of the duration of potential steps in cyclic staircase voltammetry, I is symbol of electric current, while the meaning of other parameters is explained in previous section. The features of simulated cyclic voltammograms of the elaborated EC_{rev}' mechanism are affected by several parameters related to chemical and electrochemical step. The dimensionless electrode kinetic parameter K_{ET} is defined as $K_{ET} = k_s^{o}\tau^{0.5}D^{-0.5}$. The value of K_{ET} reflects the effect of kinetics of electron transfer (via k_s^{o}) relative to the kinetics of mass transfers taking place via diffusion.. In addition, the features of calculated cyclic voltammograms are function of equilibrium constant K_{eq}, and of dimensionless catalytic rate parameter $K_{catalytic}$ ($K_{catalytic} = \varepsilon\tau$). As we explained in previous section, under conditions of excess of molar concentration of species "S" and "Y", k_f and k_b are linked to their bulk concentrations as follows: $k_f = k_f' c(\mathrm{S})$ and $k_b = k_b' c(\mathrm{Y})$. Consequently, in the real experiments, the value of $K_{catalytic}$ can be modified via altering the molar concentrations of substrates S or Y.

In all theoretical calculations, we used following parameters of applied potential: duration of potential steps τ = 0.01 s; step potential dE = 4 mV. We assigned positive values to the forward (reduction) currents, while the backward (oxidation) currents are defined as negative.

RESULTS AND DISCUSSION

Illustrated in Figure 1 is a series of cyclic voltammograms, calculated for K_{ET} = 0.1, K_{eq} = 1000, and for several values of $K_{catalytic}$. Cyclo-voltammetric profiles of considered diffusional EC'rev mechanism under such conditions have features almost identical as of the well-elaborated "simple" electrochemical catalytic EC' mechanism associated with irreversible chemical step.[3,7,9,16] If $K_{catalytic}$ is small relative to time-scale of current measurements, the observed voltammetric patterns appear quasireversible, and peak current ratio between the cathodic and anodic peaks

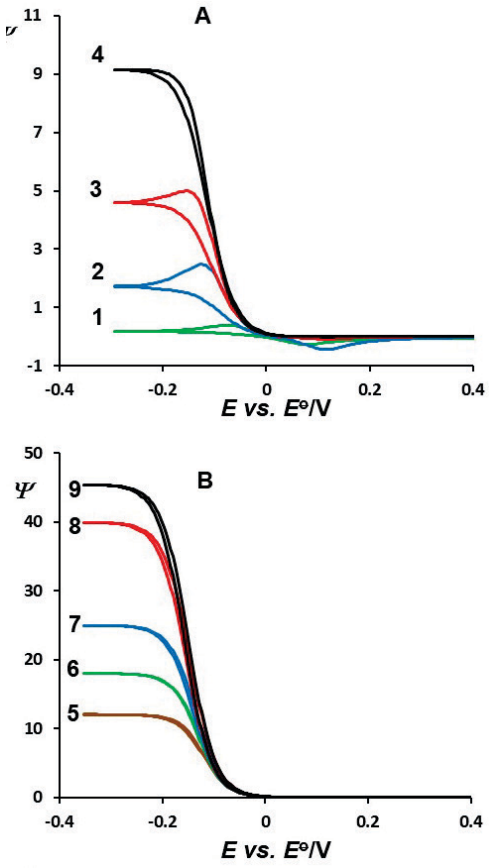


Figure 1. Cyclic voltammograms of catalytic EC'$_{rev}$ mechanism calculated for value of equilibrium constant K_{eq} = 1000, and for several small and moderate values (panel A) and large values (panel B) of catalytic parameter $K_{catalytic}$. The values of $K_{catalytic}$ were set to: 0.001 (1); 0.0316 (2); 0.1 (3) 0.224 (4) for Panel A; and 0.316 (b); 0.562 (6); 1 (7); 4 (8) and 10 (9) for Panel B. The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.1. The other simulation parameters were: step potential dE = 4 mV; duration of potential step τ = 0.01 s; electron transfer coefficient α = 0.5; temperature T = 298 K; diffusion coefficient $D = 5 \times 10^{-6}$ cm^2 s^{-1}.

equals to 1 (voltammogram 1 at figure 1A). An increase of catalytic reaction rate causes increased current of the forward peak and a diminishment of the backward peak current. As the magnitude of $K_{catalytic}$ gets higher values, the amount of Ox that is chemically regenerated during a potential step is increased. This phenomenon affects the shape of corresponding voltammograms that get transition features between diffusion controlled and a steady-state behavior (curves 2–4 in figure 1A). In the same time, we observe also elevating of the "after-peaks" currents recorded at negative potentials. For $K_{catalytic}$ values higher than 0.2, the oxidation current branch is lost, and both current components get a sigmoidal shape as typical for steady-state voltammograms (curves 5–9 in figure 1B). Under such circumstances, the rate of chemical regenerative reaction gets much faster than the rate of the re-oxidation electrode step. This phenomenon leads to multiple occurrence of the Ox + ne$^-$ ⟶ Red electrochemical reaction at all applied potentials. As a consequence, both current branches get sign of reduction currents, and steady-state sigmoidal voltammograms are obtained. For values of $K_{catalytic}$ > 0.2 we also observe a shift of the half-wave potential $E_{1/2}$ in negative direction. As the magnitude of limiting (maximal) current $\Psi_{imiting}$ of the "plateau" of cyclic voltammograms is a linear function of $(K_{catalytic})^{0.5}$, we can use this relationship between the two parameters both for quantitative purposes and to evaluate the kinetics of regenerative step as elaborated in Refs [3,7,9,17,19].

Remarkable feature of this type of catalytic EC' mechanism is seen in the role of equilibrium constant of regenerative chemical step. Since the magnitude of chemical equilibrium constant K_{eq} determines the ratio of Ox and Red species available to undergo electrochemical transformation, K_{eq} should affect all relevant features of cyclic voltammograms. Shown in figure 2 is a series of cyclic voltammograms calculated for $K_{catalytic}$ = 0.0316, K_{ET} of 0.5 and for several K_{eq} values. Obviously, all relevant parameters of the cyclic voltammograms, i.e. the height of the peaks, the peak-to-peak separation (ΔE_p = |(Ep,c–Ep,a)|), as well as the magnitude of currents measured at the negative potentials are affected by Keq. Illustrated in figure 3 is the dependence between the peak-to-peak separation ΔE_p as a function of log(K_{eq}). Curves are simulated for three values of $K_{catalytic}$, and for K_{ET} of 0.5. In general, an increase of K_{eq} causes a decrease of the peak-to-peak separation of cyclic voltammograms. For example, an increase of K_{eq} from 0.001 to 100 (for $K_{catalytic}$ = 0.0178) is followed by a decrease of ΔE_p from 320 mV to 100 mV. Roughly, in the region –1.5 < log(K_{eq}) < 1, there is a linear decrease of ΔE_p by increasing the magnitude of K_{eq}, with slope that is equal of –58 mV / log(K_{eq}), independent on $K_{catalytic}$. For moderate values of $K_{catalytic}$, a sigmoidal dependence is also observed between the ratio of cathodic and anodic peak currents $\Psi_{c,p}/\Psi_{a,p}$ recorded vs. log(K_{eq}) (figure 4). In the region –1.5 < log(K_{eq}) < 0.5 there is a linear decrease of the ratio $\Psi_{c,p}/\Psi_{a,p}$ by increasing of Keq. However, the slopes of linear parts of $\Psi_{c,p}/\Psi_{a,p}$ vs. log(K_{eq}) dependences are function of $K_{catalytic}$. The slopes of linear parts of curves $\Psi_{c,p}/\Psi_{a,p}$ vs. log(K_{eq}) from figure 4 are defined as: –7.26 (for $K_{catalytic}$ =

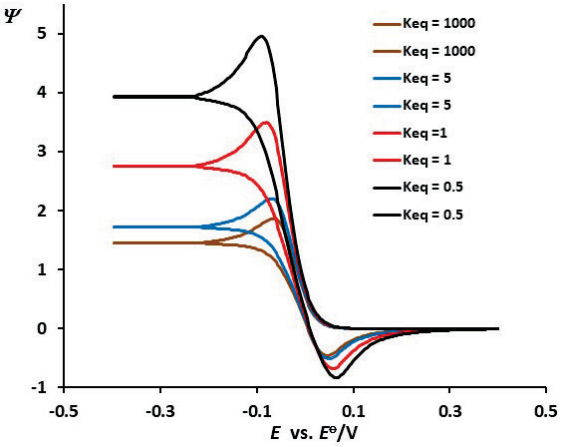


Figure 2. Cyclic voltammograms of diffusional catalytic EC'rev mechanism calculated as a function of equilibrium constant of chemical reaction K_{eq}. Curves are simulated for value of catalytic parameter $K_{catalytic}$ = 0.0316. The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.5. Other simulation conditions were same as those in figure 1.

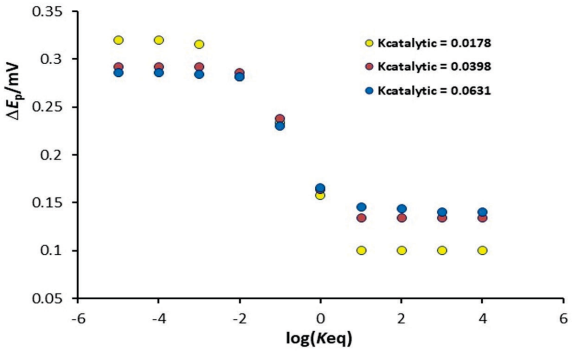


Figure 3. Dependence of the peak-to-peak potential separation (ΔE_p = |($E_{p,c} - E_{p,a}$)|) of cyclic voltammograms as a function of log(K_{eq}). Curves are calculated for three different values of catalytic parameter $K_{catalytic}$ (values of $K_{catalytic}$ are given in the chart). The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.5. Other simulation conditions were same as in figure 1.

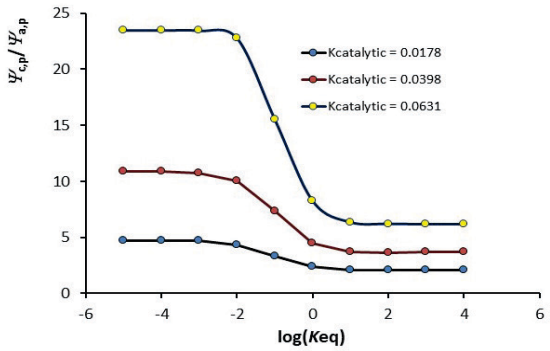


Figure 4. Dependence of the ratio of peak currents of cathodic *vs*. anodic peaks $\Psi_{c,p}/\Psi_{a,p}$ as a function of log(K_{eq}). Curves are calculated for three different values of catalytic parameter $K_{catalytic}$ (values of $K_{catalytic}$ are given in the chart). The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.5. Other simulation conditions were same as in figure 1.

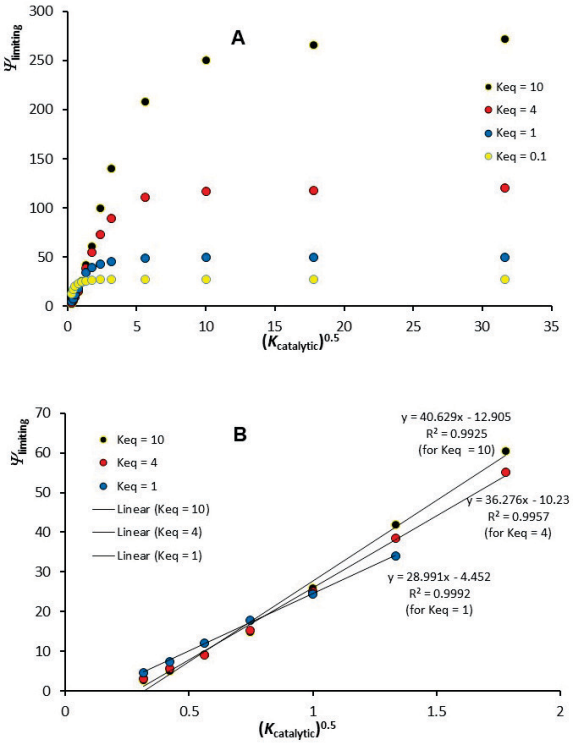


Figure 5. (A) Dependence of the limiting currents $\Psi_{limiting}$ of steady-state cyclic voltammograms on square-root of catalytic parameter $K_{catalytic}$. Curves are simulated for K_{eq} of 0.1; 1; 4 and 10. Panel (B) shows the linear parts of the corresponding curves in panel A, with equations of the linear lines. The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.5. Other simulation conditions were same as in figure 1.

0.0631); –2.781 (for $K_{catalytic}$ = 0.0398); and –0.966 (for $K_{catalytic}$ = 0.0178). Therefore, if the know the value of $K_{catalytic}$, we can use the slopes of $\Psi_{c,p}/\Psi_{a,p}$ vs. log(K_{eq}) for assessing the value of K_{eq}.

When the rate of regenerative chemical reaction is much larger than the rate of re-oxidation electrode step Red(aq) – ne^- → Ox(aq), then we observe steady-state cyclic voltammograms (see voltammograms in figure 1B, for example), whose attributes depend on the parameters related to the chemical regenerative step (K_{eq}, and $K_{catalytic}$). It is important to stress that the magnitude of limiting currents of steady-state voltammograms calculated under such circumstances is function of K_{eq} and $K_{catalytic}$, but it is not affected by the parameters related to electron transfer step of the electrode reaction (k_s^o, α).[7,17,19] As reported elsewhere,[3,7,17–19] the magnitude of "limiting current" ($\Psi_{limiting}$) of steady-state cyclic voltammograms at EC' mechanisms is important parameter that can be explored for quantitative analytical purposes, but also for the kinetic determinations. We analyzed in this work the magnitudes of $\Psi_{limiting}$ as a function of equilibrium constant (measured at various rates of catalytic chemical reaction), and as a function of rate of regenerative chemical reaction (evaluated at several K_{eq} values).

Shown in figure 5A are the dependences between the magnitude of limiting currents $\Psi_{limiting}$ vs. square-root of catalytic rate parameter $(K_{catalytic})^{0.5}$. Curves are calculated for several small and moderate values of equilibrium constant K_{eq}, and for K_{ET} = 0.5. All patterns in figure 5A feature a plateau, developed at large rates of catalytic parameter, and linear parts existing in the region of moderate values of $K_{catalytic}$. The equations of linear

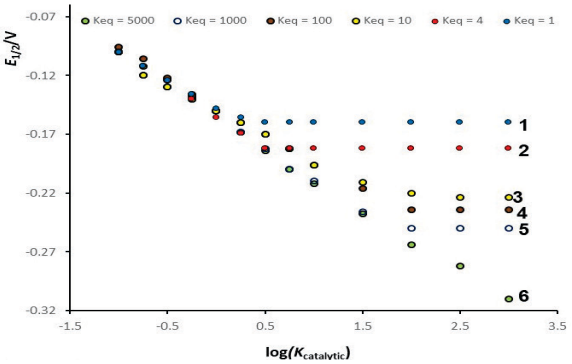


Figure 6. Dependence of the half-wave potentials $E_{1/2}$ of steady-state cyclic voltammograms on logarithm of dimensionless catalytic parameter $K_{catalytic}$. Curves are simulated for several values of equilibrium constant of chemical reaction *K*eq (values of K_{eq} are given in the chart). The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.5. Other simulation conditions were same as in figure 1.

dependences given in figure 5B imply that the relationship between $\Psi_{limiting}$ and $(K_{catalytic})^{0.5}$ can be explored for the determination of rate constant of catalytic reaction in similar manner as explained in the Ref [17]. In figure 6 we present the dependences between the half-wave potentials ($E_{1/2}$) of steady-state cyclic voltammograms as a function of $\log(K_{catalytic})$. Curves are simulated for large, moderate and small values of K_{eq}. All patterns presented in figure 6 feature a linear part with identical slope of –59 mV/$\log(K_{catalytic})$. For small and moderate values of K_{eq} (curves 1–3 in figure 6), the linear part between $E_{1/2}$ and $\log(K_{catalytic})$ exists roughly in the region $-1 < \log(K_{catalytic}) < 0.75$. As the value of K_{eq} becomes bigger, we observe significant enlargement of the region of linearity between $E_{1/2}$ and $\log(K_{catalytic})$. For values of $K_{eq} > 3000$, there is a linear dependence between $E_{1/2}$ and $\log(K_{catalytic})$ existing in a rather wide range of $K_{catalytic}$ values (see linear line 6 in figure 6, and later on the dependences in figure 8). This feature is typical of diffusional EC' mechanism associated with irreversible regenerative step.[4,7–9,17,19] In fact, for $K_{eq} > 3000$, the entire EC'$_{rev}$ mechanism converges to simpler EC' mechanism coupled with irreversible chemical regenerative step, whose features under conditions of cyclic staircase voltammetry are reported in more details elsewhere.[7,17] Briefly, the magnitude of limiting currents of the steady-state cyclic voltammograms of diffusional EC'rev mechanism (for $K_{eq} > 3000$) is a linear function of the square-root of dimensionless catalytic parameter $K_{catalytic}$.[4,7,9,17] Since the catalytic parameter $K_{catalytic}$ is defined as $K_{catalytic} = \varepsilon\tau$, and $\varepsilon = [k_f'c(S) + k_b'c(Y)]$, one can experimentally reconstruct the theoretical linear dependence $\Psi_{limiting}$ vs. $(K_{catalytic})^{0.5}$ by modifying the concentration of catalyzing agent c(Y). By performing experiments at constant concentration of "S" and constant τ, and by plotting the magnitudes of $I_{limiting}$ of experimental cyclic voltammograms as a function of the square-root of the molar concentration of regenerative substance "Y"–$c(Y)^{0.5}$, we should obtain a linear dependence. The slope of that linear dependence of $I_{limiting}$ vs. $[c(Y)]^{0.5}$ is defined as: *slope* = $[(K_{catalytic})^{0.5}[nFAc^*(Ox)\ \tau^{-0.5}D^{0.5}]$. Hence, if the number of electrons exchanged *n,* and the value of the diffusion coefficient D of simple $Ox + ne^- \leftrightharpoons Red$ system are known [for this, see Refs [1–3,18], then we can evaluate the value of $K_{catalytic}$. We should keep constant during the experiments only the τ parameter, and the concentration of substrate "S" as well. As elaborated in Refs [7,17], for these estimations we do not even need to know the values k_s^o and α.

Shown in figure 7 is the effect of equilibrium constant K_{eq} to the features of limiting cyclovoltammetric currents of steady-state voltammograms. Curves are evaluated for values of $K_{catalytic}$ of 10; 31.6 and 100. At all patterns of figure 7 we observe a sigmoidal dependences between $\Psi_{limiting}$ and $\log(K_{eq})$, with slopes having much higher values at bigger $K_{catalytic}$ values. The observed features portrayed in figure 7 are quite specific for this particular regenerative EC' mechanism, since they are commonly observed at electrochemical reactions that are associated with reversible chemical step (i.e. at the EC$_{rev}$ mechanisms).

In our recent paper concerned about new features of EC' mechanism in square-wave voltammetry,[16] we have shown that at very large values of $K_{catalytic}$ (i.e. under steady-state conditions), rate of regenerative reaction affects the kinetics of electron transfer of electrode reaction. In this work we report on similar feature under conditions of cyclic staircase voltammetry. Shown in figure 8 are the dependences between the half-wave potential $E_{1/2}$ of steady-state voltammograms as a function of $\log(K_{catalytic})$. Curves are calculated for several values of K_{ET} and for very large value of K_{eq} = 10000. Regardless of the values of K_{ET} and K_{eq} (if $K_{eq} > 3000$), the slopes of $E_{1/2}$ vs. $\log(K_{catalytic})$ are identical, equal to –59 mV/ $\log(K_{catalytic})$. However, the intercepts of

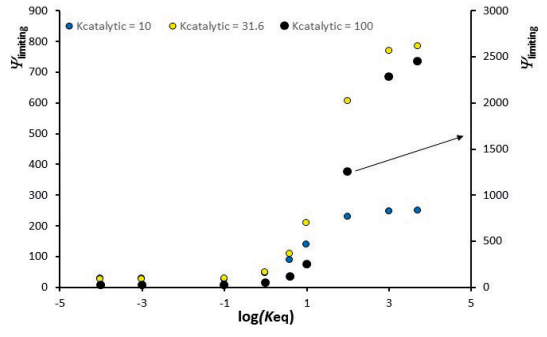


Figure 7. Dependence of the limiting currents $\Psi_{limiting}$ of steady-state cyclic voltammograms on logarithm of equilibrium constant K_{eq}. Curves are simulated for $K_{catalytic}$ of 10; 31.6; and 100. The value of dimensionless kinetic parameter of electrode reaction was set to K_{ET} = 0.5. Other simulation conditions were same as in figure 1.

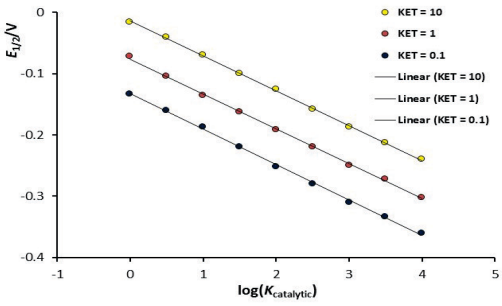


Figure 8. Dependence of the half-wave potentials of steady-state cyclic voltammograms $E_{1/2}$ on logarithm of dimensionless catalytic parameter $\log(K_{catalytic})$. Voltammograms are simulated for K_{eq} = 10000, and for three values of dimensionless kinetic parameter K_{ET} (values of K_{ET} are given in the chart). Other simulation conditions were same as in figure 1.

corresponding dependences are function of K_{ET}. Correspondingly, the equations associated to the linear lines in figure 8 can be explored for evaluating the values of K_{ET}, by exploring equivalent methodology as described in Ref [16].

CONCLUSIONS

Although electrochemical-catalytic EC' mechanism is recognized as a valuable model to mimic chemical interactions of many drug-drug and enzyme-substrate systems, only recently a reversible chemical regenerative reaction has been considered to be coupled to the electron transfer step.[18,19] For the electrode mechanism elaborated in this work, it is important to emphasize one very specific aspect. Since we define to have Ox, Y and S species present in voltammetric cell from the beginning of the experiments, the chemical reaction between Ox and S creates Red species (and Y) even before potential is applied. Therefore, in the time t = 0, we already have some Red species created in the electrochemical cell, whose amount is governed by the value of equilibrium constant K_{eq}. The effect of K_{eq} is clearly visible at the features of cyclic voltammograms in figure 2. However, once we apply a potential between the working and the reference electrode, we also create electrochemically "Red" species in the forward scan of cyclic voltammetry experiments. Under conditions of applied potential, the rate of regenerative reaction between "Red" and "Y" is responsible for the additional re-supply of Ox species. Only in a tinny segment of current measuring interval at potential steps (commonly few milliseconds), we can "feel" the contribution of the rate of regenerative reaction in the measured currents. Indeed, the simultaneous occurrence of the two reactions: (a) Ox(aq) + ne^- ⇋ Red(aq) and (b) Ox(aq) + S ⇋ Red(aq) + Y under conditions of applied potential, is major cause for many of the specific features reported for this mechanism. In the considered EC'$_{rev}$ mechanism, at defined parameters related to the electron transfer step, the features of simulated cyclic voltammograms are affected by the rate of chemical regenerative reaction, and by the magnitude of chemical equilibrium constant. We present in this work valuable set of theoretical results that portray a complex cyclo-voltammetric behavior of this specific electrode mechanism. For K_{eq} > 3000, and at large rates of the chemical regenerative step, the elaborated EC'$_{rev}$ mechanism converges to a simpler EC'$_{irreversible}$. In that scenario, we can use the features of limiting currents as a function of c(Y)$^{0.5}$ to get access to the kinetics of regenerative chemical reaction as elaborated in Refs. [17,19]. Moreover, at very high rates of regenerative reaction, and if K_{eq} > 3000, we can get access to k_s^o from the $E_{1/2}$ vs. log($K_{catalytic}$) dependences as those presented in figure 8.[16] If the value of K_{eq} is known,[18,19] we can use the equations of $\Psi_{limiting}$ vs. ($K_{catalytic}$)$^{0.5}$ dependences as those presented in figure 5B to determine rate parameter of catalytic reaction. For the evaluation of the parameters related to the electron transfer of simple electrode reaction Ox(aq) + ne^- → Red(aq) (i.e. n, k_s^o, α, $E^o_{Ox/Red}$, D), we should perform analysis as those reported in Refs [4,7], but in absence of substrates "S" and "Y". In the end, we should emphasize that time-duration τ of potential steps in CSV affects simultaneously both, the kinetics of electron transfer and the rate chemical reaction. In this respect, in order to avoid additional complications at this mechanism, the experiments should be performed at constant scan rate. To reproduce the dependences vs. the $K_{catalytic}$ parameter elaborated in this work, one should perform experiments in which only concentration of substrate "Y" in the voltammetric cell should be modified.

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