Non-Nernstian Two-Electron Transfer Reactions for Immobilized Molecules: A Theoretical Study in Cyclic Voltammetry

Joaquin Gonzalez, Manuela Lopez-Tenes, and Angela Molina*

Departamento de Química Física, Facultad de Química, Regional Campus of International Excellence “Campus Mare Nostrum”, Universidad de Murcia, 30100 Murcia, Spain

ABSTRACT: A very simple recurrent theoretical treatment for non-Nernstian two-electron transfer reactions for surface confined molecules is presented and applied to cyclic voltammetry (CV). A systematic kinetic study via the influence on the voltammograms of the variation of the heterogeneous rate constants of both electron transfers (ETs) and the scan rate has been made. The influence of the difference between the formal potentials (ΔE0) and of the rate constants on the degree of cooperativity of the ETs is analyzed. An illustrative zone diagram that enables a direct view of the number of peaks in the voltammogram as a function of ΔE0 and the heterogeneous rate constants as well as methods for determining thermodynamic and kinetic parameters are proposed. This treatment is very useful for any two redox center molecules and is hugely important for modeling noncatalytic voltammetry of redox enzymes attached to the electrode that represent a starting point for understanding more complex situations like coupled catalytic and intramolecular ETs processes.

1. INTRODUCTION

Multielectron transfers processes (i.e., stepwise processes) are related to the redox activity of molecules with different oxidation states and have many current and potential applications in chemistry, biochemistry, environmental chemistry, pharmacy, for example, in energy conversion, bioelectrocatalysis, biosensors, molecular electronics, nanodevices, chemiluminescence, design of new materials, and so on.1–16 A very useful way of characterizing these processes is from the attachment of the molecules at an electrode surface.7

Indeed, electrochemical methods are, in general, very valuable for the study of these systems, and much effort has been devoted to the development of the relevant theory and analysis procedures.1–4,14–16 Among these, cyclic voltammetry (CV) is the electrochemical technique most used in both basic and experimental studies of adsorbed molecules containing multiple redox centers,7–5,13,16–21 and in the specific case of biological molecules, such as oligonucleotides, metalloproteins, enzymes, and so on, the application in recent years of the technique protein film voltammetry (PFV), together with microscopic techniques like in situ scanning tunneling microscopy (STM), has allowed the characterization of the electron transfer (ET) mechanisms for these important molecules.13,21

The characterization of the ET events taking place between the electrode and these confined molecules includes the determination of the thermodynamic and kinetic stability of the different oxidation states in the molecule because the CV response of the system will reflect such stability in the specific conditions of the experiment. (As known, CV or any other electrochemical technique cannot provide information at a molecular level, that is, it cannot differentiate between possible microstates corresponding to a particular oxidation state of the molecule.13) To date, thermodynamic stability has been the main focus of study, through the determination of the relative values of the formal potentials for the different ETs.13–15,22,23 Several terminologies can be found in the literature concerning this question: by taking the example of a two redox center molecule, for a sufficiently negative value of the difference between the formal potentials of the second and first ETs (ΔE0 = E0 2 − E0 1; see scheme I in Theory), we can speak of a “normal” potential difference,14 attractive interactions,15,16,22 or high anticooperativity degree,13,23 between the two centers. In any case, it refers to a stable intermediate redox state of the molecule (I in scheme I in Theory), with two peaks being observed in the reversible response of this system in CV. In contrast, the denominations “inverted” potential difference, repulsive interactions, and cooperativity are used for an unstable intermediate; in such a case, only one peak is obtained in the CV response corresponding to very fast ETs. A rigorous theoretical cyclic voltammetric treatment for adsorbed molecules with several possible oxidation states has been developed for the specific case of very fast ETs, that is, for reversible behavior.19,24,25 However, experimental results for many interesting systems show clear evidence of slow kinetics, which in specific cases have been studied by ad hoc simulation.26–28 So, the modeling of the kinetic data in a rigorous, general and systematic manner is necessary. Indeed, as stated in a review by Léger and Bertrand: “Although of practical interest, no rigorous theoretical treatment has been given for multicenter molecules under non-equilibrium conditions (fast scan rates)”.13

Thus, this article presents the theoretical treatment of surface reactions in which an adsorbed molecule containing two redox
centers reduces in two steps (EE mechanism), considering the kinetic of both interfacial ETs when CV is applied. The solution presented, due to its discrete nature, is applicable to any multipotential step technique (like differential double-pulse voltammetry, reverse-pulse voltammetry, square-wave voltammetry, or staircase voltammetry), by simply changing the potential time waveform, and it also allows us to obtain the continuous limit of CV for which only numerical calculations had been previously used.26–28 Studies for prototype two-center redox molecules are essential to understand the complex behavior of molecules containing more redox centers. This theory is applicable for any strongly adsorbed molecule susceptible to giving two direct ETs between the electrode and the redox centers and is especially interesting for modeling the noncatalytic voltammetry of redox enzymes attached to the electrode, which takes place in several situations, as in the absence of substrate and if the catalysis is either blocked by an inhibitor or outrun by using a sufficiently high scan rate for that the catalytic cycle cannot be completed over the time scale of the voltammetric experiment. In this situation, irreversible ETs are expected, and hence the theory presented in this article needs to be considered. It also represents a first necessary step for the comprehension of more complex situations, such as the catalysis coupled to the charge transfers and intramolecular ETs.3–5,13,17,21,29

From the analysis of the CV signals, it is clear that this mechanism can be completely characterized as a function of the difference between the formal potentials of both steps, of the values of rate constants, and its ratio. So, a systematic study of the interplay between thermodynamics and kinetics driving forces in cyclic voltammograms for the EE mechanism has been carried out.

An interesting result of this general analysis is that there is a singular point in the zero current axis of the voltammograms, \((E^0,0)\), with \(E^0\) being the average formal potential \((E^0_0 + E^0_0)/2\), which acts as a "symmetry center". It will be shown that the degree of symmetry with respect to this point changes with the reversibility of both ETs. Indeed, for reversible reactions, as it is well known, direct and reverse responses in the voltammogram are symmetrical not only with respect to this point but also in relation to the zero current axis (thermodynamic symmetry; see Figure 1). For the general case of slow ETs and different rate constants for the first and second charge transfer steps, the direct and reverse responses in the voltammogram can be very different, but an interesting "symmetry" concerning this point is also found. Thus, we demonstrate here that by exchanging the values of rate constants for both steps, the corresponding voltammogram can be obtained from the original one by rotating \(180^\circ\) around the point \((E^0,0)\;\text{or}\;E^0\); that is, the original cathodic and anodic responses in the CV signal become the anodic and cathodic ones, respectively. (See Figure 1.) This behavior allows us to locate \(E^0\) in any CV response, a fact that provides in a simple way first data for obtaining the formal potentials of both ETs.

It is also demonstrated that the appearance of one or two peaks in the direct and reverse voltammograms depends mainly on the value of \(\Delta E^0\), as under reversible conditions, for equal values of the two dimensionless rate constants, whereas in the general case of different kinetic constants, the appearance of one or two peaks depends on \(\Delta E^0\), the rate constants value, and also the relation of these constants, and so the appearance of two peaks in the cyclic voltammograms is not always due to a thermodynamic anticooperative effect \((\Delta E^0 < 0)\) but to a high anticooperative kinetic one. In these voltammetric studies, the scan rate is a crucial experimental parameter, which can be varied to learn about the kinetics of the process. So, by using a high enough scan rate, even a thermodynamically unstable intermediate (thermodynamic cooperative effect) can be kinetically caught because it does not transform during the time it takes to record the voltammogram. Given the above, this behavior has been explained in terms of stability of the intermediate redox state of the confined molecule (see Scheme I in Theory) by analyzing the evolution of the surfaces coverages with the applied potential.

An illustrative zone diagram showing the number of peaks expected for a specific experiment as a function of \(\Delta E^0\) and dimensionless rate constants is presented. Methods to determine the formal potentials \(E^0_1\) and \(E^0_2\) are also presented, and working curves based on the characteristics of peaks (position, height, and half peak width) are proposed for calculation of rate constants of both steps.

The voltammograms obtained for an EE process have been compared with those for two independent \(E\) processes and for apparent simultaneous two-electron transfer, finding that for not very negative values of \(\Delta E^0\) and/or slow ET reactions (and/or high scan rates) the CV responses are very different.

---

**Figure 1.** Location of the center of symmetry of the cyclic voltammetric responses of an EE mechanism for different kinetics.
2. THEORY

Consider a surface reaction in which molecule O reduces in two steps (EE mechanism). This process can be described by the following scheme corresponding to two interfacial ETs:

\[
\begin{align*}
O + e^{-} & \xrightarrow{k_{o1}} I \quad E_I^0 \\
I + e^{-} & \xrightarrow{k_{o2}} R \quad E_R^0
\end{align*}
\]

(1)
in which O (oxidized), I (intermediate or half-reduced), and R (reduced) refer to the different redox states of adsorbed molecule O, and \(k_{o1}\) and \(k_{o2}\) are the heterogeneous charge-transfer rate constants for the reduction and oxidation processes, respectively, of the step \(i (i = 1, 2)\). \(E_I^0\) and \(E_R^0\) are the formal potentials of the first and second steps, respectively.

We will study the response of the above reaction scheme by using CV, for which we consider the application of a staircase of potential steps \(E_1, E_2, \ldots, E_n\) with a pulse amplitude \(\Delta E\). This potential-time program corresponds to staircase voltammetry, and it is the real perturbation applied by digital instruments.

When the \(\Delta E\) value is very small for a fixed scan rate (i.e., \(\Delta E \leq 0.001\) mV in the practice, see [30,31]), the applied potential waveform (see eq 14) behaves as a ramp (i.e., a continuous function of time) in the way:

\[
\begin{align*}
E(t) = E_{\text{initial}} - vt \quad & \text{for } t \leq \lambda \\
E(t) = E_{\text{initial}} - v(t - \lambda) + v \lambda \quad & \text{for } t > \lambda
\end{align*}
\]

(1)

where \(\lambda\) is the time at which the scan is reversed and \(v\) is the scan rate defined as \(v = dE/dt\).

It will be assumed that the adsorption of molecule O follows the Langmuir isotherm, that heterogeneity of the electroactive monolayer can be ignored and that no desorption takes place in the time scale of the experiment.

Under these conditions, the following is fulfilled for any potential pulse \(E_p^i (p = 1, 2, \ldots, n):

- The maximum surface excess is independent of the potential.
- The total excess \(\Gamma_T^r\) is constant during the whole experiment, so:

\[
\begin{align*}
\Gamma_T^r & = \Gamma_T^r \\
f_J^p + f_{J}^{p-1} + f_J^0 & = 1
\end{align*}
\]

(2)

with the surface coverage of species \(j, f_J^p\), defined as

\[
f_J^p = \Gamma_T^r / \Gamma_T^r \quad \text{for } j = O, I, R
\]

(3)
in which \(\Gamma_T^r\) is the surface excess of species \(j\). In particular, at the beginning of the experiment:

\[
\begin{align*}
f_{O,(i=0)}^0 & = \Gamma_T^r \\
f_{I,(i=0)}^0 & = \Gamma_T^r \\
f_{R,(i=0)}^0 & = \Gamma_T^r
\end{align*}
\]

(4)

The currents corresponding to first, \(I_{p}\) and second, \(I_{p}\) steps in scheme I, for each potential \(E_p^i\), are:

\[
\begin{align*}
\frac{I_{p}}{Q_p} & = -\frac{df_O^i}{dt} \\
\frac{I_{p}}{Q_p} & = \frac{df_R^p}{dt}
\end{align*}
\]

(5)

with

\[
Q_p = F S \Gamma_T^r
\]

(6)

where \(S\) is the electrode area. The current, \(I_{p}^{E(I)}\), for process I is given by

\[
I_{p}^{E(I)} = I_O^p + I_R^p
\]

(7)

From Scheme I and eq 2, the following relationships can be established for the time variation of the surface coverages:

\[
\begin{align*}
-\frac{df_O^p}{dt} & = k_{o1} f_O^p + k_{o2} f_R^p - k_{o2} f_{o1}^0 \\
\frac{df_R^p}{dt} & = -K_RB_O f_O^p - k_{o2} f_{o1}^0 + k_{o1} f_{o2}^0 \\
\frac{df_R^p}{dt} & = - \left( \frac{df_O^p}{dt} + \frac{df_R^p}{dt} \right)
\end{align*}
\]

(8)

with

\[
K_I^p = k_{o1} f_{o1}^0 + k_{o2} f_{o2}^0 \quad i = 1, 2
\]

(9)

To solve the differential equation system given in eq 8, we assume the following solution:

\[
\begin{align*}
f_O^p & = \delta^p (\theta_O^p - 1) + f_{o1}^{p-1} \\
f_R^p & = \gamma^p (\theta_R^p - 1) + f_{o2}^{p-1}
\end{align*}
\]

(10)

with \(\delta^p\) and \(\gamma^p\) being coefficients to be determined and

\[
\theta_O^p = \exp (-K_I^p t^p) \quad i = 1, 2, \quad p = 1, 2, \ldots, n
\]

(11)

where \(t^p\) is the variable time of potential step \(E_p^i\) (with \(0 \leq t^p \leq \tau\)). We will assume that the current of each potential pulse is measured at \(t^p = \tau\).

By introducing the solutions proposed in eq 10 and condition 2 in eq 8, we obtain the following expressions for \(\theta_O^p\) and \(\theta_R^p\) in a recurrent form:

\[
\begin{align*}
\theta_O^p & = (f_{o1}^{p-1} k_{o1} f_{o2}^{p-1} + f_{o1}^{p-1} (k_{o2} f_{o1}^{p-1} + k_{o1} f_{o2}^{p-1})) / (k_{o1} f_{o2}^{p-1} + k_{o1} f_{o2}^{p-1} (\theta_O^p - 1) (\theta_R^p - 1)) \\
\delta^p & = f_{o1}^{p-1} + k_{o1} f_{o2}^{p-1} (\theta_O^p - 1) + \gamma (\theta_R^p - 1)
\end{align*}
\]

(12)

with \(f_{o1}^0 = 1\) and \(f_{o2}^0 = 0\). (See eq 4.)

By taking into account eqs S5, 7, 8, and 10, the current for any potential \(E_p^i\) is given by

\[
\frac{I_{p}^{E(I)}}{Q_p} = \delta^p \theta_O^p - \gamma^p \theta_R^p \quad p = 1, 2, \ldots, n
\]

(13)

Solutions given in eqs 10–13 present the following characteristics:

- They allow us to obtain limiting cases as the reversible and irreversible ones. (See eqs A4–A6 and A7 and A8 of the Appendix.)
- They have a discrete character that makes them applicable to any multipotential step technique (differential double pulse voltammetry, reverse pulse voltammetry, square-wave voltammetry, staircase voltammetry, etc.) by simply changing the potential time waveform. They also allow us to obtain the continuous limit of CV, as stated in this
article, for which only numerical calculations for particular situations had been used.\textsuperscript{26–28} They are independent of the kinetic scheme considered for process I (i.e., they are valid for either Butler–Volmer or Marcus–Hush models). The expressions for coefficients $\delta_p$ and $\gamma_p$ for the particular case of Butler–Volmer kinetics are shown in the Appendix. In the following, this model will be assumed for the interfacial ETs.

3. RESULTS AND DISCUSSION

As has been outlined in the previous section, to calculate the response in CV for the surface reaction described by scheme I, we have used a discrete approach to the continuous potential waveform given in eq 1.\textsuperscript{30,31} Thus, a staircase potential perturbation of the form:

$$
\Delta E_p = - \left( \frac{1}{v \tau} \right) \Delta E_i, \quad p = 1, 2, \ldots, (n/2) + 1
$$

has been considered, which for a given scan rate, $v$, defined as

$$
v = \frac{\Delta E}{\tau}
$$

coincides with that given in eq 1 for $\Delta E \leq 0.001 \text{ mV}$ (i.e., under these conditions, the discrete potential staircase gives rise to the same results than a continuous potential ramp).\textsuperscript{30,31}

For each potential pulse in eq 14, $E_p$, the current $I_{\psi,\text{CV}}$ is calculated from eq 13, with $\delta_p$ and $\gamma_p$ given by eq A3 in the Appendix. Note that dimensionless variables are more appropriate in this case; therefore, the following are used:

$$
\psi_{\psi,\text{CV}} = \frac{I_{\psi,\text{CV}}}{Q_a F}
$$

with

$$
\alpha = \frac{\nu F}{RT}
$$

and $Q_a$ given by eq 6. In the following, the cyclic voltammetric curves $\psi_{\psi,\text{CV}}$ will be discussed.

Figures 2–4 show the cyclic voltammetric curves ($\psi_{\psi,\text{CV}}(E - E^0)$ curves) for an EE mechanism (solid lines), calculated from eqs 13, 14, 16, and A3 for an EE mechanism (solid lines) and from eq 10 in ref 33 for two independent ETs (dashed lines) and an apparent simultaneous two-electron single transfer (dashed-dotted lines). These curves have been calculated for three values of the dimensionless rate constant of the first step, $k_{1,\text{CV}}$, three values of $\Delta E^0 = E^0_2 - E^0_1$ (shown in the curves). ($k_{1,\text{CV}} / k_{2,\text{CV}}$) = 1 for the EE mechanism and the two independent ETs. For the two-electron single transfer it has been assumed that the formal potential coincides with the average potential of the EE mechanism. $\alpha = 0.5$, $T = 298$ K.
Scheme I (eq 17), \((k_{2, CV}^0 / k_{1, CV}^0)\): 1, 0.1, and 0.001 in Figures 2−4, respectively. Each of the three Figures includes the curves calculated for three values of the dimensionless rate constant of the first step, \(k_{1, CV}^0\): 10, 0.1, and 0.01 in panels A, B, and C, respectively, and also for three values of \(\Delta E_0 = (E_2^0 - E_1^0)\) in mV: −200, 0, and 200 in Figures I−III, respectively, by assuming in all cases that \(\alpha = 0.5\) for the two ETs.

The CV curves for two independent ETs (dashed lines) and those corresponding to an apparent simultaneous two-electron ET (dashed-dotted lines) have also been plotted in Figures 2−4 for comparison with those obtained for an EE mechanism with \(\Delta E_0 = -200\) and 0 mV and \(\Delta E_0 = 0\) and 200 mV, respectively. For the two-electron single transfer, it has been assumed that the formal potential coincides with the average potential of the EE mechanism and \(k_{2, CV}^0 = k_{1, CV}^0\). Other conditions as in Figure 2.

These Figures point to a great variety of voltammetric responses, showing one or two peaks on the direct and reverse responses, whose heights and relative positions depend on the values of \(k_{1, CV}^0\), \(\Delta E_0\), and the relation \((k_{2, CV}^0 / k_{1, CV}^0)\), which is equal to (Figure 2) or smaller (Figures 3 and 4) than unity in this set of Figures. Moreover, it is important to highlight that it is not necessary to calculate the CV curves for the inverse case of \(k_{2, CV}^0 > k_{1, CV}^0\). This is because to obtain the responses for the inverse value of \((k_{2, CV}^0 / k_{1, CV}^0)\) (i.e., the curves obtained by exchanging the values of \(k_{2, CV}^0\) and \(k_{1, CV}^0\), as can be easily inferred from eq 8), all that is required is a rotation of 180° with respect to the black dot marked in the Figures; that is, the initial direct (cathodic) and reverse (anodic) responses become the reverse (anodic) and direct (cathodic) ones. Figure 5 shows several examples of this behavior for \(k_{1, CV}^0 \neq k_{2, CV}^0\) for which the direct and reverse responses are different. This singular point is located in coordinates \((E_0 - E_1^0, 0)\), where \(E_0\) corresponds to the average formal potential, defined as:

\[
E_0 = \frac{(E_1^0 + E_2^0)}{2}
\]

Note that this general characteristic of the voltammograms permits us to locate the value of the average formal potential \(E_0\) in any response, with symmetrical (reversible behavior or \(k_{2, CV}^0 = k_{1, CV}^0\), Figure 2) or asymmetrical voltammograms \(k_{2, CV}^0 \neq k_{1, CV}^0\) (Figures 3−5).

In this last case one has to change the sign of current and invert the sense of the potentials in the experimental response, and from comparison of the original and inverted responses, it is immediate to locate the point \((E_0, 0)\).

Other important features of the voltammograms shown in Figures 2−5 are the following:

1. For high values of both heterogeneous rate constants, reversible ET reactions are expected (see eqs A4 and AS). In this
case, the CV responses for the direct and the reverse scans (see Figure 2A) are symmetrical with respect to the zero current line, which acts as an axis of symmetry ("thermodynamic symmetry", see refs 19, 24, 25, and 32). These voltammograms show two peaks centered at the individual formal potentials if $\Delta E^0$ is very negative (Figure 2A-I), which evolve to a single peak centered at the average formal potential $E^\bar{0}$ (eq 19) as $\Delta E^0$ increases. (See Figure 2A-II,A-III.)$^{19,24,25,32}$ As is well known, this behavior responds to the major or minor stability of the species I in scheme I (see Figure 6 below), associated in this case with the fact that the second ET is less or more thermodynamically favored than the first ET (i.e., the degree of thermodynamic cooperativity between the ETs increases with $\Delta E^0$) and is measured by the comproportionation constant value given by: $^{15,16,19}$

$$K = \exp \left( \frac{F \Delta E^0}{RT} \right)$$  \hspace{1cm} (20)

(2) For nonreversible ETs and in the particular case of $k_{2,CV}^0 = k_{2,CV}^0$ (see Figure 2B,C), the stability of the intermediate I in scheme I relies not only on the value of $\Delta E^0$ but also on the kinetics of the process, although the influence of the latter is small, so the appearance of two or one peaks on each scan depends mainly on the value of $\Delta E^0$ in an analogous way to that discussed above for reversible reactions. The decrease in the rate constants manifests in the expected shift of the peaks toward more negative (cathodic scan) or positive (anodic scan) potentials, a broadening of the peaks and a decrease in the peak heights (to maintain the area of the voltammograms).

Under these conditions, the voltammograms show a "kinetic symmetry" (i.e., the CV curves present a center of symmetry located at the point ($E^\bar{0}$,0)).

(3) For the more general case in which the rate constants of the first and second steps are different (i.e., there is kinetic asymmetry), the voltammetric curves corresponding to the direct and reverse scans can become very different (see Figures 3−5), and the number of peaks is fixed not only by the value of $\Delta E^0$ but also by the values of the kinetic constants of steps 1 and 2 in scheme I. Thus, for $k_{2,CV}^0 / k_{1,CV}^0$ = 10$^{-3}$ for the EE mechanism and the two independent ETs. For the two-electron single transfer it has been assumed that the formal potential coincides with the average potential of the EE mechanism and $k_{2,CV}^0 = k_{2,CV}^0$. Other conditions as in Figure 2.

Figure 4. Cyclic voltammetric curves ($\psi_{CV} - (E - E^\bar{0})$ curves), calculated from eqs 13, 14, 16, and A3 for an EE mechanism (solid lines) and from eq 10 in ref 33 for two independent ETs (dashed lines) and an apparent simultaneous two-electron single transfer (dashed-dotted lines). These curves have been calculated for three values of the dimensionless rate constant of the first step, $k_{1,CV}^0$ and three values of $\Delta E^0 = E_2^0 - E_1^0$ (shown in the curves). ($k_{2,CV}^0 / k_{1,CV}^0 = 10^{-3}$ for the EE mechanism and the two independent ETs. For the two-electron single transfer it has been assumed that the formal potential coincides with the average potential of the EE mechanism and $k_{2,CV}^0 = k_{2,CV}^0$. Other conditions as in Figure 2.)

$\Delta E^0=-200$ mV  \hspace{1cm} $\Delta E^0=0$ mV  \hspace{1cm} $\Delta E^0=200$ mV  

A-I  \hspace{1cm} A-II  \hspace{1cm} A-III

B-I  \hspace{1cm} B-II  \hspace{1cm} B-III

C-I  \hspace{1cm} C-II  \hspace{1cm} C-III

\textcopyright 2013 American Chemical Society
This behavior can be easily understood from the evolution of surface coverages of species O (red lines), I (blue lines), and R (green lines) in scheme I (eqs 2 and 10), shown in Figure 6, where the $f_j^a - E$ curves corresponding to the $\psi_{CV} - E$ responses of Figures 2A (reversible behavior) and 4C (irreversible behavior) are plotted. The $f_j^a - E$ curves for the direct and reverse scans appear as solid and dotted lines, respectively.

In Figure 6a,d, the case for $\Delta E^o = -200$ mV is considered. (See also Figures 2A-I and 4C-I, respectively.) In Figure 6a, the reversible surface coverages show superimposed curves for direct and reverse scans, according to the “reversible symmetry” of the CV response in Figure 2A-I, where the peak potentials correspond to the points where the curves of surface coverages intercept, as shown in Figure 6a. The maximum value of surface coverage of intermediate I corresponds to the $E^o$ value, located between both peaks, so the stability of I is clear in this case.

By comparing this behavior with that shown for the surface coverages in Figure 6d, we see the kinetic stabilization (direct scan) and destabilization (reverse scan) of the intermediate I and the shifts of the direct and reverse curves with respect to the reversible behavior (Figure 6a). The scarce appearance of I species at the same range of potentials as O and R gives rise to the appearance of a single peak in the reverse $\psi_{CV} - E$ curve of Figure 4C-I.

In Figure 6b,e, the case for $\Delta E^o = 0$ mV is considered (see Figures 2A-II and 4C-II, respectively), and the kinetic stabilization (direct scan, solid lines) and destabilization (reverse scan, dotted lines) of the intermediate I and the shifts of the curves (Figure 6e) with respect to the reversible behavior (Figure 6b) can also be observed. The stabilization of the intermediate in the direct scan clearly gives rise to the appearance of a second peak in the voltammogram (Figure 4C-II), whereas only one peak remains in the reverse scan. Note that in the reversible case, Figure 6b, the intermediate I is relatively stabilized, but its curve develops in the same range of potentials as those for O and R, and the three curves intercept at $E = E^o = E_{p1} = E_{p2}$, which is the peak potential of the only peak observed in the voltammogram (Figure 2A-II). This intersection corresponds to surface coverages $f_0^a = f_1^a = f_2^a = 1/3$, that is, to a comproportionation constant equal to the unity (eq 20).

Finally, in Figure 6c,f, the case for $\Delta E^o = 200$ mV is considered (see Figures 2A-III and 4C-III, respectively). In this situation, a totally destabilized intermediate I in Figure 6c (reversible behavior) becomes a stabilized one in the direct scan of Figure 6f; therefore, a second peak is registered in the voltammogram. (See Figure 4C-III.) However, at the reverse scan, a totally stabilized intermediate in Figure 6c,f gives rise to a single peak in Figures 2A-III and 4C-III.

(4) The number of peaks in the voltammograms and the variations observed in their positions, heights, and half peak widths can be used to characterize the process and to determine the values of $\Delta E^o$ and the rate constants, as shown below in Section 3.1. Note that as the scan rate $v$ affects the reversibility (see eqs 17 and 18) the feature of the response can be changed simply by varying this parameter.

(5) From the comparison of curves for an EE mechanism with those of two independent E mechanisms and an apparent simultaneous two-electron E mechanism, it can be observed that for $\Delta E^o = -200$ mV the CV curves of EE and two independent ET processes are coincident for reversible and irreversible ETs whenever $k_{1,CV}^i = k_{2,CV}^i$ (Figure 2A-I,B-I,C-I). When $k_{1,CV}^i \neq k_{2,CV}^i$, both responses match less the lower and more different their values are. The CV curve of an EE with $\Delta E^o = 200$ mV only

---

**Figure 5.** Cyclic voltammetric curves ($\psi_{CV} - (E - E^o)$ curves) calculated from eqs 13, 14, 16, and A3 for an EE mechanism. The values of $\Delta E^o$ (in mV) are: (a) $-200$, (b) $0$, and (c) $200$. The values of the dimensionless rate constants of the two steps are: solid lines, $k_{1,CV}^i = 10$, $k_{2,CV}^i = 0.1$; dashed lines, $k_{1,CV}^f = 0.1$, $k_{2,CV}^f = 10$. Other conditions as in Figure 2.

---

thermodynamic anticooperative and cooperative degree of the ETs, respectively. (See also Figure 7.)
coincides with that corresponding to an apparent simultaneous two-electron ET in the reversible case (Figure 2A–III). In the intermediate situation of an EE with $\Delta E_0 = 0$ mV, the CV curve does not match the two independent ETs or an apparent simultaneous two-electron ET. From the above, it is clear that the theory presented in this article is of fundamental importance in the study of an EE mechanism.

To complete and systematize the information obtained from the cyclic voltammograms in Figures 2–5, in Figure 7 a zone diagram has been plotted showing, for different values of $\Delta E_0$, the regions of appearance of one or two peaks in the direct voltammetric scan (indicated with arrows) as a function of $\log(k_{1,CV}^0)$ and $R_k = \log(k_{2,CV}^0/k_{1,CV}^0)$. The same plot can be used for the reverse scan by changing the sign of $R_k$ (i.e., by exchanging the values of $k_{1,CV}^0$ and $k_{2,CV}^0$ in abscissas).

In this Figure, it can be seen that the domains for which one or two peaks are obtained in the direct scan change with $\Delta E_0$. For $\Delta E_0 = -200$ mV, one peak is obtained only for $\log(k_{1,CV}^0) < -1$ and $(k_{2,CV}^0/k_{1,CV}^0) \geq 10$. Under these conditions, the kinetic cooperativity counteracts the high thermodynamic anticooperative degree. With the increase in $\Delta E_0$ (see the curves for $-100$ and $-71.5$ mV), the zone in which one peak appears becomes broader; that is, a peak is also obtained for greater values of $\log(k_{1,CV}^0)$ and smaller values of the ratio $(k_{2,CV}^0/k_{1,CV}^0)$, a fact that is related to an increasingly smaller thermodynamic anticooperative degree.

In contrast with this behavior, for $\Delta E_0 = 0$ mV or positive values (see curve for $\Delta E_0 = 100$ mV), the high thermodynamic cooperativity degree leads to the appearance of one peak in the direct voltammogram, but for small values of the ratio $(k_{2,CV}^0/k_{1,CV}^0)$, the high kinetic anticooperativity degree allows the second peak to be registered.

A singular behavior is observed for $\Delta E_0 \approx -71.2$ mV, for which the transition between one and two peaks in the direct CV...
response is obtained for a fixed value of the ratio ($k_2^{0, \text{CV}}/k_1^{0, \text{CV}}$) = 0.745 independently of the value of $k_1^{0, \text{CV}}$.

Note that as the kinetics of both ET is affected by the variation of the scan rate, two interesting possibilities may arise from Figure 7. A transition two peaks $\rightarrow$ one peak in the direct scan observed as the scan rate increases clearly indicates a value of $\Delta E^0 = -71.5$ mV and $k_2^{0, \text{CV}} = k_1^{0, \text{CV}}$, whereas a one peak $\rightarrow$ two peaks transition observed under the same conditions is characteristic of $\Delta E^0 \geq 0$ mV and $k_2^{0, \text{CV}} < k_1^{0, \text{CV}}$.

3.1. Determination of the Formal Potentials and Rate Constants of the Two Charge Transfer Steps. In this section, we will discuss the main features of the peak parameters of the voltammograms of an EE mechanism to obtain criteria for determining both the formal potentials ($E_1^0$ and $E_2^0$) and the rate constants ($k_1^{0, \text{CV}}$ and $k_2^{0, \text{CV}}$) of the ETs.

Figures 8 and 9 plot the evolution with log($k_1^{0, \text{CV}}$) of the peak parameters: peak potentials (Figures 8a, 9a, and 9d), peak heights (Figures 8b, 9b, and 9e), and half peak widths (Figures 8c, 9c, and 9f) for two values of the ratio of the dimensionless rate constants: ($k_2^{0, \text{CV}}/k_1^{0, \text{CV}}$) = 1 (Figure 8) and ($k_2^{0, \text{CV}}/k_1^{0, \text{CV}}$) = 0.1 (Figure 9). In these figures, three values of $\Delta E^0$ are considered: $-200$ (solid lines), 0 (black circles), and 200 (white circles). $k_1^{0, \text{CV}} = 0.1 k_2^{0, \text{CV}}$. Other conditions as in Figure 2.

Figure 8. Dependence of the cathodic peak potentials relative to $E_1^0$ (a), peak heights (b) and half peak widths (c) of the CV curves with log($k_1^{0, \text{CV}}$) calculated from eqs 13, 14, 16, and A3 for an EE mechanism for three values of $\Delta E^0$ (in mV): $-200$, solid lines; 0, black circles; and 200, white circles. $k_2^{0, \text{CV}} = k_1^{0, \text{CV}}$. Other conditions as in Figure 2.

Figure 9. Dependence of the cathodic and anodic peak potentials relative to $E_1^0$ (a,d), peak heights (b,e), and half peak widths (c,f) of the CV curves with log($k_1^{0, \text{CV}}$), calculated from eqs 13, 14, 16, and A3 for an EE mechanism for three values of $\Delta E^0$ (in mV): $-200$, solid lines; 0, black circles; and 200, white circles. $k_2^{0, \text{CV}} = 0.1 k_1^{0, \text{CV}}$. Other conditions as in Figure 2.
the direct (cathodic, indicated with the subscript “c” in ordinates) voltammogram is considered because the reverse (anodic) one is symmetric, as explained above. (See Figure 2.) In Figure 9, both the direct (cathodic) and the reverse (anodic) scans are considered, indicated with subscripts “c” (Figures 9a–c) and “a” (Figures 9d–f) respectively.

The influence of $\Delta E^0$ in the value of the three peak parameters for reversible behavior has been discussed in detail in ref 19.

Figure 8a shows, according to Figure 7 that for $k_{0}^{2,CV}$ (R ≤ 0) two peaks are obtained for $\Delta E^0 = -200$ mV and only one peak is obtained for $\Delta E^0 = 0$ and 200 mV, as for a reversible process, for any value of $k_{1}^{2,CV}$. (See also Figure 2.) In this Figure it can be seen that for $k_{2,CV}^{1} \geq 1$ the peak potentials for the cathodic scan coincide with the formal potentials of the individual ETs for $\Delta E^0 = -200$ mV or with the average formal potential $E^0$ for $\Delta E^0 = 0$ and 200 mV, a fact that characterizes the reversible behavior. (See also Figure 2.) As $k_{2,CV}^{1}$ decreases, the peak potentials shift toward more negative values, showing a clear linear dependence on $\log(k_{1}^{1,CV})$ for $\log(k_{1}^{1,CV}) \leq -1$, which is typical of an irreversible behavior. 19 For $\Delta E^0 = -200$ mV, the difference between the peaks remains approximately constant ($-200$ mV), even for very irreversible ETs.

Concerning the behavior of the peak heights and half peak widths (Figure 8b,c, respectively), they typically take a constant value in the reversible region ($k_{1}^{1,CV} \geq 1$) (corresponding to that for a mono-electronic ET for $\Delta E^0 = -200$ mV -for each of the two peaks, $\psi_{pc} = \frac{1}{2} \Delta E^0 = 0.25$ and $W^{1/2} = 90$ mV-) and to that for a dielectronic ET for $\Delta E^0 = 200$ mV, $\psi_{pc} = \frac{1}{2} \Delta E^0 = 1.0$, and $W^{1/2} = 45$ mV, taking an intermediate value for $\Delta E^0 = 0$ mV.19 Both the peak heights and half peak widths evolve with $\log(k_{1}^{1,CV})$ until the irreversible constant limit is reached for $\log(k_{1}^{1,CV}) \leq -1$, with the variation being much more pronounced for positive values of $\Delta E^0$.

Now that the characteristics of the peak parameters in this particular situation ($k_{2,CV}^{1} = k_{0,CV}^{1}$) have been shown, the methods for obtaining the thermodynamic and kinetic parameters of the ETs will be analyzed.

The first parameters to be determined are the formal potentials of both charge transfers. Note that it is possible to obtain the average formal potential of the process, $E^0$ (see eq 19), as described above, by determining the location of the point in the zero current line with respect to which a rotation of 180° leads to a symmetrical CV response. Additional data is necessary to obtain the individual formal potentials, and this can be the value of $\Delta E^0$. When two peaks are obtained in the voltammogram, this parameter can be obtained from the peak-to-peak distance, $\Delta E_p$:

$$\Delta E^0 = \Delta E_p \quad \text{if} \quad \Delta E^0 \leq -150 \text{ mV} \quad \text{(21)}$$

for any value of $k_{1,CV}^{0}$, that is, independently of the scan rate.

For low values of the scan rate at which $\Delta E_p$ becomes unaffected by $v$ (reversible limit), $\Delta E^0$ can be obtained as:

$$\Delta E^0 = \Delta E_p \quad \text{if} \quad (-150 < \Delta E^0 \leq -125) \text{ mV}$$

$$\Delta E^0 = 329.97 + 6.91 \Delta E_p \quad \text{if} \quad (-125 < \Delta E^0 \leq -75) \text{ mV} \quad \text{(22)}$$

If only one peak is observed ($\Delta E^0 > -75$ mV), then the half peak width can be used under reversible conditions to determine the value of $\Delta E^0$ as discussed in ref 19.

Once the value of $\Delta E^0$ is known, the rate constants for both ETs can be determined using the curves in Figure 8 (calculated for the particular $\Delta E^0$ value of the system under study) by changing the scan rate and fitting the values of the peak potentials, peak heights, and half peak widths to their corresponding abscissas.

In the case in which $k_{0,CV}^{2} \neq k_{0,CV}^{0}$ (Figure 9), the behavior of peak parameters in the cathodic (Figures 9a–c) and anodic (Figures 9d–f) scans can differ notably, as has been discussed above. (See also Figures 3–5.)

Figure 9a shows, according to Figure 7, that for $k_{0,CV}^{2} = 0.1k_{0,CV}^{1}$ (R = −1) two peaks are obtained in the direct voltammogram for $\Delta E^0 = -200$ mV (solid lines) and one peak is obtained in the case $\Delta E^0 = 200$ mV (white circles) for any value of $k_{0,CV}^{2}$. However, for $\Delta E^0 = 0$ mV, the transition between one peak (high values of $k_{2,CV}^{1}$) and two peaks (low values of $k_{0,CV}^{1}$) is observed for $\log(k_{1,PC}^{1}) \approx -0.5$.

In contrast, in the reverse scan (Figure 9d, see also Figure 7 with $R = 1$ and by changing $k_{0,CV}^{2}$ by $k_{0,CV}^{1}$ in abscissas), only one peak is obtained for $\Delta E^0 = 0$ and 200 mV for any value of $k_{0,CV}^{2}$, and the transition between two and one peaks is observed for $\Delta E^0 = -200$ mV at $\log(k_{1,PC}^{1}) \approx -0.6$ (i.e., $\log(k_{1,PC}^{2}) = -1.6$ in Figure 7).

The peak potentials in Figure 9a,d show a qualitatively similar dependence on $\log(k_{1,PC}^{0})$ to that observed in Figure 8a. The behavior of the peak heights and half peak widths is also similar to that shown in Figure 8a,c, respectively. However, some singular characteristics can be observed. For example, for $\Delta E^0 = 200$ mV, a maximum value of the peak height (Figure 9b) and a minimum of the half peak width (Figure 9c) in the direct response is obtained in the quasi-reversible zone (i.e., the peak is higher and sharper than that for a dielectronic signal).

To obtain the values of the formal potentials of both ETs when the rate constants are different, the reversible limit needs to be used in all cases, and the same conditions as discussed above for $k_{2,CV}^{1} = k_{0,CV}^{1}$ can be applied here to determine $\Delta E^0$ and thus the individual formal potentials $E^0$ and $E^2$.

Once the value of $\Delta E^0$ is known, the rate constants for both ETs can be determined.

When two peaks are observed, the key parameter to be analyzed is the peak-to-peak distance, which changes with the scan rate. Thus, in Figure 10, $\Delta E_{pa} = E_{pa} - E_{pc}$ (solid lines) and $\Delta E_{pa} = E_{pa} - E_{pc}$ (dashed lines), calculated as the differences between the second and first peak potentials of each scan, are plotted versus $\log(k_{1,PC}^{0})$ for $\Delta E^0 = -100$ mV and different values of $R_{p} = \log(k_{1,PC}^{2}/k_{1,PC}^{1})$ with $k_{2,CV}^{1} < k_{0,CV}^{1}$. Note that an identical Figure can be used for the case $k_{2,CV}^{1} = k_{1,PC}^{1}$ by simply changing the sign of $R_{p}$ and $\log(k_{1,PC}^{1})$ for $\log(k_{2,CV}^{1})$ in the abscissas in an analogous way to that discussed above.

From these curves, it can be observed that as the scan rate grows the separation between the cathodic peaks $\Delta E_{pa}$ increases in absolute value more the smaller $R_{p}$ is. Concerning the separation between anodic peaks $\Delta E_{pa}$ this decreases as the scan rate grows, and it tends to zero (only one peak) for lower $v$ values as $R_{p}$ decreases. Thus, the variation of both $\Delta E_{pa}$ and $\Delta E_{pc}$ can be plotted versus $-\log(v)$ to select the $R_{p}$ value that gives rise to the best fittings. Once $R_{p}$ is known, $k_{1,PC}^{1}$ can be obtained from the corresponding abscissa value.

When only one peak appears in both scans, the kinetic constants can be determined by using the plots $\Delta E_{pa} = E_{pa} - E_{pc}$ (difference between the cathodic and anodic peak potentials), and $\psi_{pc}/\psi_{pa}$ (ratio between peak heights) versus $\log(k_{1,PC}^{1})$. (See Figure 11.) These plots allow us to determine the $R_{p}$ and $k_{1,PC}^{1}$ values following a similar procedure to that discussed in Figure 10.
4. CONCLUSIONS

We have carried out a comprehensive study of two-electron transfer (ET) reactions for surface immobilized molecules (EE mechanism) for any value of thermodynamic and kinetic parameters of both ETs in CV. The starting point for this study is the development of easy recurrent theoretical treatment for these molecules, which has been an open question in this field, where only nonsystematic numerical studies have been made. The treatment presented can also be applied to any multipotential step technique (like differential double-pulse voltammetry, reverse pulse voltammetry, square-wave voltammetry, or staircase voltammetry), although we have focused on CV because of its broad use in the study of this mechanism. Moreover, it is independent of the kinetic model of the charge transfers, and it allows us to obtain the current—potential responses corresponding to the limiting cases of totally reversible and irreversible electron transfers from the general solution. We have found that there exists a singular point in the zero current axis of the voltammogram, corresponding to the average potential \( \left( \frac{E_1^0 + E_2^0}{2} \right) \), for which the symmetry properties change with the reversibility of both ETs. Such an important result provides us first data for determining the formal potentials of the charge transfers for any degree of reversibility. It has been also shown that the appearance of one or two peaks in the direct and reverse voltammograms adheres to the association of thermodynamic and kinetic degree of cooperativity of both ETs, and an illustrative zone diagram has been built for the direct assignation of peak number under each specific condition.

Methods to obtain the formal potentials and the heterogeneous rate constants of both charge-transfer steps have been proposed. The spectrum of molecules and situations for which the present treatment is applicable is very wide, for organic and organometallic molecules, and has special interest for biological molecules such as oligonucleotides, metalloproteins, and enzymes. A qualitative comparison between the CV responses obtained for two-redox center molecules and simpler cases of two independent ETs, on the one hand, and an apparent simultaneous two-electron ET, on the other hand, highlights the need for a systematic study of an EE mechanism.

---

**APPENDIX. BUTLER–VOLMER FORMALISM**

The expressions for coefficients \( \theta^* \) and \( \rho^* \) for the particular case of a Butler–Volmer kinetic can be deduced from eq 12 by assuming that the rate constants for reduction and oxidation processes are given by:

\[
k_{\text{red,}\text{CV}}^i = k_0^i \left( I_p^i \right)^{-\alpha} \quad i = 1, 2; \quad p = 1, 2, \ldots n
\]

\[
k_{\text{ox,}\text{CV}}^i = k_0^i \left( I_p^i \right)^{-\alpha} \quad i = 1, 2; \quad p = 1, 2, \ldots n
\]

(A1)

with

\[
I_p^i = \exp \left( \frac{F}{RT} \left( E_p^i - E_0^i \right) \right) \quad i = 1, 2; \quad p = 1, 2, \ldots n
\]

(A2)

\( k_0^i \) and \( E_0^i \) are the heterogeneous rate constant and the formal potential of the redox couple, respectively, for the ET corresponding to step \( i \) (\( i = 1, 2 \)) in scheme I, and \( \alpha \) is the charge-transfer coefficient, assumed to be equal for both ETs.

By taking into account eqs 12, A1, and A2, we obtain:
The Journal of Physical Chemistry C

\[ r_p' = \left( \left( r_p^{-1} - 1 \right) + \left( f_p' \left( \theta_p - 1 \right) + f_o' \left( \theta_o - 1 \right) \right) / \left( 1 + f_p' \left( \theta_p - 1 \right) + f_o' \left( \theta_o - 1 \right) \right) \right) \]

\[ \delta_p' = f_p^{-1} + \frac{f_p'}{1 + f_p'} \left( f_p^{-1} - 1 + \gamma p (\theta_p - 1) \right) \]

(A3)

with \( f_p^0 = 1 \) and \( f_o^0 = 0 \) (see eq 4).

The general expressions for the surface coverages of both species (eq 10) can be simplified in the following limiting situations:

**a. RR Case**

In this case, the \( k_p^0 \) values are very high, so it can be assumed that \( \theta_p' \to 0 \) (\( i = 1, 2 \)) (eqs A1, 9, and 11). By introducing this condition in eq A3, both coefficients are:

\[ r_p' = f_p^0 \quad r_o' = f_o^0 \quad \delta_p' = f_p^0 + f_o^0 \quad \delta_o' = f_o^0 \]

(A4)

The surface coverages of species O and R are given by (eq 10):

\[ f_p^0 = -\delta_o^0 + f_o^0 \quad f_o^0 = -\delta_o^0 + f_o^0 \quad f_o^0 = -\delta_o^0 + f_o^0 \]

(A5)

These expressions are coincident with those previously reported in refs 19 and 24. Note that in this case the surface coverages of species O and R are only potential-dependent in such a way that the current can be obtained as:

\[ I_{EE} = \frac{- df_p^0}{dt} + \frac{df_r^0}{dt} = \pm \left( \frac{df_p^0}{dt} + \frac{df_r^0}{dt} \right) \]

(A6)

with \( K \) being the comproportionation constant given by eq 20.

**b. II Case**

Under irreversible conditions, the \( k_p^0 \) values are very small, so it can be assumed that the exponential terms in eq A3, \( \theta_p' \) (eq 11), can be substituted by a McLauren expansion in the way: \( \theta_p' \simeq 1 - K_p x \) (\( i = 1, 2 \)). By introducing this condition in eq A3, both coefficients are:

\[ r_p' = \left( \left( r_p^{-1} - 1 \right) + \left( f_p' \left( \theta_p - 1 \right) + f_o' \left( \theta_o - 1 \right) \right) / \left( 1 + f_p' \left( \theta_p - 1 \right) + f_o' \left( \theta_o - 1 \right) \right) \right) \]

\[ \delta_p' = f_p^{-1} + \frac{f_p'}{1 + f_p'} \left( f_p^{-1} - 1 + \gamma p (\theta_p - 1) \right) \]

(A7)

Finally, the surface coverages of species O and R in these conditions can be written as:

\[ f_p^0 = -\delta_p^0 K_p x + f_o^0 \quad f_o^0 = -\gamma o^0 K_p x \]

(A8)

**AUTHOR INFORMATION**

**Corresponding Author**

E-mail: amolina@um.es.

**Notes**

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

We greatly appreciate the financial support provided by the Dirección General de Investigación Científica y Técnica (Project Number CTQ2012-35700), and the Fundación SENECA de la Región de Murcia (Project Number 088131/P1/08).

**REFERENCES**


