Mathematical Model beyond Surface EC_{rev} Mechanism in Protein-Film Voltammetry Considered by Butler-Volmer Kinetics

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Protein-film voltammetry is an elegant electrochemical methodology based on the direct electrochemical conversion of redox-active species immobilized at the electrode surface. In this case, the reacting molecules do not diffuse from the bulk solution toward the electrode. Instead, the entire electrochemical response is controlled by the amount of adsorbed material, the rate of heterogeneous electron transfer, and possible coupled chemical transformations inside the surface-confined film.

The surface mechanism considered here is a reversible one-electron transformation between the adsorbed reduced and oxidized forms of a protein, followed by a reversible chemical conversion of the oxidized form into another adsorbed state:

$$\mathrm{Red(ads)} \rightleftharpoons \mathrm{Ox(ads)} + e^-$$

$$\mathrm{Ox(ads)} \rightleftharpoons \mathrm{Y(ads)}$$

The first reaction is the electrode reaction. It is characterized by the standard heterogeneous electron-transfer rate constant, k_s, and the electron-transfer coefficient, α. The second reaction is a surface-confined reversible chemical reaction, described by the forward rate constant k_f, the backward rate constant k_b, and the equilibrium constant K_{eq} equal to $K_{eq} = k_f/k_b$.

The total surface concentration of all adsorbed forms is conserved:

$$\Gamma_T = \Gamma_{Red} + \Gamma_{Ox} + \Gamma_Y$$

In last equation, Γ_T is the total surface coverage, while Γ_{Red}, Γ_{Ox}, and Γ_Y are the surface concentrations of the reduced, oxidized, and chemically transformed adsorbed species. This condition is essential for surface-confined protein-film voltammetry, because no mass transport from the solution is involved. All changes in the voltammetric signal originate from redistribution of the fixed surface population among the three adsorbed states.

As mentioned earlier, the reversible chemical step is defined by:

$$K_{eq} = \frac{k_f}{k_b}$$

When the chemical step is sufficiently fast compared with the time scale of the voltammetric experiment, the chemical equilibrium condition can be written as:

$$\Gamma_Y = K_{eq}\Gamma_{Ox}$$

By substituting this relation into the total surface conservation equation, one obtains:

$$\Gamma_T = \Gamma_{Red} + \Gamma_{Ox} + K_{eq}\Gamma_{Ox}$$

or:

$$\Gamma_T = \Gamma_{Red} + (1 + K_{eq})\Gamma_{Ox}$$

From this expression, the surface concentration of the oxidized form can be evaluated as:

$$\Gamma_{Ox} = \frac{\Gamma_T - \Gamma_{Red}}{1 + K_{eq}}$$

Similarly, the surface concentration of the reduced form can be expressed as:

$$\Gamma_{Red} = \Gamma_T - (1 + K_{eq})\Gamma_{Ox}$$

These equations show that the reversible chemical conversion of Ox(ads) into Y(ads) decreases the amount of electrochemically active Ox(ads) available for the backward electron-transfer reaction. When K_{eq} is high, a larger fraction of the oxidized state is converted into Y(ads), and therefore the concentration of free Ox(ads) becomes smaller. As a result, the cathodic component of the voltammetric response can be suppressed even when the electron-transfer reaction itself is not slow.

The electron-transfer kinetics are described by the Butler-Volmer formalism. The potential-dependent oxidation rate constant is:

$$k_{ox} = k_s \exp\left[\frac{\alpha F(E - E^0)}{RT}\right]$$

The potential-dependent reduction rate constant is:

$$k_{red} = k_s \exp\left[-\frac{(1 - \alpha)F(E - E^0)}{RT}\right]$$

In these equations, E is the applied electrode potential, E^0 is the formal potential of the surface redox couple, F is the Faraday constant, R is the gas constant, and T is the absolute temperature. The parameter k_s determines how fast the adsorbed protein exchanges electrons with the electrode at the formal potential. A large k_s produces nearly reversible voltammetric behavior, whereas a small k_s leads to quasireversible or irreversible features, such as peak broadening, peak displacement, and decrease of the backward component.

The parameter α describes the symmetry of the activation barrier. When $\alpha = 0.5$, the effect of the applied potential on oxidation and reduction is symmetric. If α differs from 0.5, the oxidation and reduction branches respond differently to the same potential perturbation, which can lead to asymmetric voltammetric peaks.

For a surface-confined system, the faradaic current is proportional to the net rate of electron transfer between the electrode and the adsorbed film:

$$I = nFA(k_{ox}\Gamma_{Red} - k_{red}\Gamma_{Ox})$$

where n is the number of transferred electrons and A is the electrode area. The first term, $k_{ox}\Gamma_{Red}$, represents the anodic oxidation flux of Red(ads) into Ox(ads). The second term, $k_{red}\Gamma_{Ox}$, represents

the cathodic reduction flux of Ox(ads) back to Red(ads). Therefore, the measured current is the difference between the forward and backward electron-transfer rates.

Using the equilibrium expression for the chemically coupled step, the current can be written only in terms of Γ_{Red} and the total surface coverage:

$$I = nFA\left[k_{ox}\Gamma_{Red} - k_{red}\left(\frac{\Gamma_T - \Gamma_{Red}}{1 + K_{eq}}\right)\right]$$

This form is useful because it explicitly shows how the chemical equilibrium modifies the Butler-Volmer current. If K_{eq} increases, the denominator $(1 + K_{eq})$ increases, and the effective concentration of Ox(ads) available for reduction decreases. Consequently, the backward current becomes smaller. This effect can make the voltammogram appear more irreversible, even if the heterogeneous electron transfer is relatively fast.

Alternatively, the current can be written in terms of Γ_{Ox}:

$$I = nFA\left[k_{ox}\left(\Gamma_T - (1 + K_{eq})\Gamma_{Ox}\right) - k_{red}\Gamma_{Ox}\right]$$

This expression emphasizes the opposite viewpoint: formation of Ox(ads) during oxidation is immediately influenced by its chemical conversion to Y(ads). The larger the value of K_{eq}, the more strongly the total surface population is shifted away from Ox(ads), which changes both the peak current and the shape of the voltammetric response.

If the chemical reaction is not sufficiently fast to maintain equilibrium, the full kinetic model must be used. The time evolution of the surface concentrations is then described by the following differential equations:

$$\frac{d\Gamma_{Red}}{dt} = -k_{ox}\Gamma_{Red} + k_{red}\Gamma_{Ox}$$

$$\frac{d\Gamma_{Ox}}{dt} = k_{ox}\Gamma_{Red} - k_{red}\Gamma_{Ox} - k_f\Gamma_{Ox} + k_b\Gamma_Y$$

$$\frac{d\Gamma_Y}{dt} = k_f\Gamma_{Ox} - k_b\Gamma_Y$$

The first equation describes the loss of Red(ads) by oxidation and its regeneration by reduction of Ox(ads). The second equation describes the formation and consumption of Ox(ads) through both the electron-transfer step and the reversible chemical step. The third equation describes the accumulation of Y(ads) from Ox(ads) and the regeneration of Ox(ads) through the reverse chemical reaction.

For numerical simulations, these equations can be solved step by step. At each time increment, the surface concentrations are updated according to:

$$\Gamma_{Red}^{j+1} = \Gamma_{Red}^{j} + \Delta t\left(-k_{ox}^{j}\Gamma_{Red}^{j} + k_{red}^{j}\Gamma_{Ox}^{j}\right)$$

$$\Gamma_{Ox}^{j+1} = \Gamma_{Ox}^{j} + \Delta t\left(k_{ox}^{j}\Gamma_{Red}^{j} - k_{red}^{j}\Gamma_{Ox}^{j} - k_f\Gamma_{Ox}^{j} + k_b\Gamma_Y^{j}\right)$$

$$\Gamma_Y^{j+1} = \Gamma_Y^{j} + \Delta t\left(k_f\Gamma_{Ox}^{j} - k_b\Gamma_Y^{j}\right)$$

Here, j denotes the current time step, $j + 1$ denotes the next time step, and Δt is the time increment. After each update, the current is calculated from the Butler-Volmer expression:

$$I^j = nFA\left(k_{ox}^j \Gamma_{Red}^j - k_{red}^j \Gamma_{Ox}^j\right)$$

This procedure is particularly important for square-wave voltammetry, cyclic staircase voltammetry, or any other dynamic voltammetric technique in which the potential changes with time. Since k_{ox} and k_{red} depend on the applied potential, they must be recalculated at every potential step.

At the beginning of the experiment, the initial condition is often selected so that the protein film is fully reduced:

$$\Gamma_{Red}(t = 0) = \Gamma_T$$

$$\Gamma_{Ox}(t = 0) = 0$$

$$\Gamma_Y(t = 0) = 0$$

These initial conditions are appropriate when the starting potential is sufficiently negative to keep the surface-confined redox protein in its reduced state. If the experiment starts from a more positive potential, different initial surface distributions may be required.

Several limiting cases can be obtained from the same model. If the chemical reaction is absent, then:

$$k_f = 0 \quad \text{and} \quad k_b = 0$$

and the mechanism reduces to a simple surface-confined electron-transfer reaction:

$$\text{Red(ads)} \rightleftharpoons \text{Ox(ads)} + e^-$$

Under this condition, the voltammetric response is controlled only by k_s, α, and the total surface coverage. This is the simplest protein-film voltammetric model.

If the chemical step is irreversible, then:

$$k_f > 0 \quad \text{and} \quad k_b = 0$$

In this case, Ox(ads) is continuously consumed to form Y(ads). The backward current decreases because less Ox(ads) is available for electrochemical reduction. This limiting case corresponds to a surface EC mechanism with irreversible chemical follow-up reaction.

If both chemical rate constants are nonzero:

$$k_f > 0 \quad \text{and} \quad k_b > 0$$

then the chemical step is reversible. The degree to which the chemical equilibrium influences the voltammetric response depends on the values of k_f, k_b, and K_{eq} relative to the experimental time scale. Fast chemical kinetics produce an equilibrium-controlled response, whereas slow chemical kinetics produce a kinetically controlled response.

When k_s is very large, the electron transfer is fast and the surface concentrations of Red(ads) and Ox(ads) tend to follow the applied potential almost reversibly. In this case, the chemical reaction becomes the dominant factor shaping the voltammogram. When k_s is small, electron transfer itself becomes the limiting process, and the chemical reaction may have a weaker observable effect because Ox(ads) is generated slowly.

Thus, the surface EC mechanism treated with Butler-Volmer kinetics provides a flexible theoretical framework for protein-film voltammetry. It allows the simultaneous evaluation of electron-transfer kinetics, surface concentration redistribution, and chemically coupled conformational or ligand-binding processes. The most important feature of this formalism is that the experimentally measured current is directly linked to the dynamic surface concentrations of Red(ads) and Ox(ads), which are themselves controlled by both the electrode potential and the coupled chemical equilibrium.

Entire MATHCAD simulation protocols for simulating square-wave and cyclic voltammograms of this mechanism is given in Repository of Goce Delcev University, Stip, for free.

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