Lability of metal complexes at spherical sensors. Dynamic voltammetric measurements

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The diffusive-kinetic steady-state (dkss) approximation is applied to the case of a metal ion reaching a transforming/consuming spherical surface (sensor) when the ion is involved in a complexation reaction in solution. Simple time-dependent expressions for the surface metal flux, the lability degree and the half-wave potential are presented, valid for any value of the ratio of concentrations at the surface and the sensor radius. The solution presented is compared with other theoretical approaches, such as the kinetic steady state (kss) and the total steady state (tss), pointing out that the easy dkss approach is much more accurate than the tss one to study the metal flux and the lability degree for any value of the radius, from ultramicro to planar sensors.

1. Introduction

The availability of metal species in natural media and the corresponding nutritive or toxic properties towards microorganisms, biofilms, algae and plants are determined by a set of chain events which involve transport and chemical reaction in solution with ligands, particles, etc. and internalization at the membrane of the biosensor.1 When all the processes in the solution are much faster than the internalization, homogeneous concentration profiles arise and the internalization flux is just dependent on the free metal concentration. This is the typical situation in which the Free Ion Activity Model (FIAM) or Biotic Ligand Model (BLM) apply.2,3 However, when the internalization or transformation process is faster than the solution ones, the uptake flux depends on the kinetic and mobility parameters and a dynamic situation arises. Some effort has been devoted in recent years to develop dynamic speciation techniques to be used in risk assessment. These measurements, based on metal flux, correlate with the uptake or toxicity data.

In the interpretation of dynamic measurements, lability criteria allow the prediction of the limiting step that determines the received metal flux.4–8 If diffusion is the limiting step, the system is called labile and, if it is the kinetics of association/dissociation processes which limit the metal flux, then the system is called partially labile or inert. These criteria can be stated in terms of the lability parameter, L, which compares the flux in both cases.

In a further step, a quantitative evaluation of the lability of complexes has been studied by defining the so-called lability degree.7 This parameter measures the actual contribution of the complexes to the metal flux with respect to the maximum contribution reached if the system was labile. Analytical expressions for the lability degree have been reported for some simple cases, which include one or more ligands and steady state conditions in spherical or planar geometry with a finite diffusion domain.9–15 Actually, the availability problem is formally analogous to the chronoamperometric CE electrochemical problem16 once differences at the electrode surface are properly considered. Thus, analytical approximations based on the reaction layer approximation, developed by Koryta and Koutecký17–19 for the kinetic currents have been applied to the availability prediction.

Recently, it has been shown that the time scale and size of the sensor (electrode) to reach steady state conditions in a CE chronoamperometric experiment could be quite restrictive.20 For a fast chemical reaction, the chronoamperometric measurement can be approached by using the kinetic steady state approximation (kss) early introduced by Koutecký for planar diffusion,21 and later extended to spherical diffusion in references.22–24 A simplification of the kss was introduced by Molina et al.23,24 and called the diffusive-kinetic steady state (dkss) which allowed one to obtain simple analytical expressions for a size and time-dependent linear diffusion layer and a size and kinetics dependent linear reaction layer thicknesses of the CE voltammetric experiment for a broad range of sizes ranging from ultramicro to planar electrodes. From this last approach, a time-independent solution (total steady state, tss) is derived, which is applicable when the particle radius is much smaller than the planar linear diffusion layer thickness. From the tss solution, approximate expressions for the lability degree have also been previously deduced in the literature7,13 for systems that include mixture of ligands in seminfinite14 or finite diffusion domains.15

Taking advantage of the similarity between the availability and electrochemical processes we proceed to consider more general electrochemical conditions with respect to the applied potential. In this way we can overcome the restriction of limiting conditions usually considered in the availability studies and we can discuss the availability behaviour in more general conditions where the internalization process establishes a given ratio of concentrations at the surface of the species with a non-null volumic concentration at the limiting
surface. This is the case of the electrochemical sensors when the redox process is electrochemically reversible, but it is also the case of sensors using a resin layer to which species in solution get attached up to equilibrium conditions.

The organization of the paper is as follows: in Section 1 the mathematical formulation of the potential dependent expressions for the metal flux in a chronopotentiometric CE experiment under spherical diffusion is reviewed. Section 2 is devoted to developing expressions for the lability degree. A comparison of the kss, dkss and tss flux is reported in section 3 which also analyses the influence of the system parameters. As a conclusion, the dkss seems to be very accurate and simple in reproducing the metal flux in the approach of the system to steady state for most of the voltammetric typical conditions while severe limitations are shown for the true steady-state expressions.

2. Theory

Let us consider the complexation of a metal ion M with a ligand L to give, in solution, a complex ML

\[ M + L \xrightarrow{\text{k}_a} ML \]

where \( k_a \) and \( k_d \) are the rate constants for complex association and dissociation, respectively. In case of a large excess of ligand, the effective stability constant of the complex is given by the quotient:

\[ K' = K_{ML} = \frac{k_a c_M^l}{k_d} = \frac{k_a c_M^l}{k_d} = \frac{c_{ML}}{c_M^l} \]

being \( c_M^l \) (\( i \equiv \text{M, ML, L} \)) the bulk concentrations of the different species.

Only the free metal ion is consumed/transformed at an active surface (analytical sensor, (micro)organism, electrode) in contact with the solution (we adhere to the electrochemical notation although the problem is more general as pointed out above):

\[ M + ne^- \rightarrow \text{M(Re)d} \]

If we consider spherical diffusion of all species and that the homogeneous chemical reaction is fast enough (\( i.e., \kappa \gg 1 \), \( \kappa = k_a + k_d \)), the kinetic steady-state approximation (kss) can be used. The only approximation behind kss consists in assuming that the perturbation of the chemical equilibrium, \( \phi(r,t) = c_{ML}(r,t) - Kc_M(r,t) \), is independent of time. Under this condition, the solution of function \( \phi \), which is null at the bulk of the solution \( \phi(r \rightarrow \infty) = 0 \), is given by:

\[ \phi(r) = \frac{r_0}{r} \phi(r_0) e^{-\sqrt{r_0^2 + Dr(r_r_0)}} \Rightarrow \left( \frac{\partial \phi}{\partial r} \right)_{r=r_0} = -\frac{\phi(r_0)}{\delta_r} \]

where

\[ \delta_r = \left( \frac{1}{r_0^2} + \frac{1}{D} \right)^{-1} \]

and \( D \) is the common diffusion coefficient of all the species. Notice that eqn (5) is the expression, within the dkss approximation, for the linear reaction layer thickness, \( i.e., \) the effective linear thickness of the disequilibration layer (\( \phi \neq 0 \)).

The diffusive-kinetic steady state approximation (dkss) also assumes that the total metal concentration profile, \( \zeta(r,t) = c_M(r,t) + c_{ML}(r,t) \), has the form of a species only suffering diffusion, then

\[ \zeta(r,t) = \frac{r_0}{r} \left( \zeta(r_0) - \zeta(r_0) \right) \text{erfc} \left( \frac{r - r_0}{2\sqrt{Dt}} \right) \]

\[ \Rightarrow \left( \frac{\partial \zeta}{\partial r} \right)_{r=r_0} = \frac{\zeta - \zeta(r_0)}{\delta_d} \]

and:

\[ c_{M(Re)d}(r,t) = \frac{c_M(r_0)}{\delta_d} \left( \frac{c_M(r,t) - c_M(r_0)}{\delta_d} \right) \text{erfc} \left( \frac{r - r_0}{2\sqrt{Dt}} \right) \]

\[ \Rightarrow \left( \frac{\partial c_{M(Re)d}}{\partial r} \right)_{r=r_0} = \frac{c_M(r_0) - c_M(r_0)}{\delta_d} \]

being \( \delta_d \) the linear diffusion layer thickness in spherical geometry measured from the surface electrode, given under the dkss approximation, by:

\[ \delta_d = \left( \frac{1}{r_0} + \frac{1}{\sqrt{D}r_0} \right)^{-1} \]

As eqn (6) or (7) indicate, \( \delta_d \) is the linear thickness of the total metal or the reduced metal concentration profile.

Note that both linear layers, \( \delta_d \) and \( \delta_r \), are independent of the ratio of concentrations at the surface (applied potential in case of electrochemical sensors). When the transforming surface is planar (\( i.e., \) \( r_0 \rightarrow \infty \)), \( \delta^\text{plane} = \sqrt{D}r_0 \) and \( \delta^\text{plane} = \sqrt{D}/\kappa \), respectively, whereas for very small radii (\( r_0 \rightarrow 0 \)), both layers take the same value: \( \delta^\text{micro} = \delta^\text{micro} = r_0 \).

As the surface process is not limiting the metal flux received at the surface of the sensor, concentrations of the free and reduced metal at the electrode surface are considered to fulfill an equilibrium condition (here referred as ratio of concentrations at the surface and being represented by \( \theta \))

\[ c_M(r_0)/c_{M(Re)d}(r_0) = \theta \]

where \( \theta \) for a reversible electron transfer reaction is given by the Nernst condition, \( \theta = \exp[\frac{\alpha}{2F}(E - E^\theta)] \). Then, the general expression for the metal flux at the active surface is given by

\[ J_M = D \left( \frac{\partial c_M}{\partial r} \right)_{r=r_0} = D \left( \frac{\zeta - \zeta(r_0,t)}{\delta_d} \right) \]

\[ = \frac{D \phi(r_0,t)}{K' \delta_r} \left( \frac{\phi(r_0,t)}{\delta_r} \right) \]

\[ = \frac{D \phi(r_0,t)}{K' \delta_r} \left( 1 + (1 + K') \theta \right) \]

which, using dimensionless parameters (see notation appendix) and \( c_M^{lim}(r_0) = 0 \) can be written as

\[ J_M^{lim \text{ plane}} = \frac{\alpha + \sqrt{\omega}}{\alpha \sqrt{\omega} + 1} \left( \frac{\alpha + \sqrt{\omega} + 1}{\alpha + \sqrt{\omega}} \right) \]

\[ = \frac{\alpha + \sqrt{\omega} + 1}{\alpha + \sqrt{\omega}} \left( \frac{\alpha + \sqrt{\omega} + 1}{\alpha + \sqrt{\omega}} \right) \]

\[ = \frac{\alpha + \sqrt{\omega} + 1}{\alpha + \sqrt{\omega} + 1} \]
where \( J_{\text{labile, plane}}^{\text{lim}} = \frac{Dc^*}{\sqrt{\pi D t}} \omega = \frac{2\sqrt{D}}{\gamma_0^*} \) (dimensionless sphericity parameter) and \( \gamma = \kappa t \) (dimensionless kinetic parameter).

The above time-dependent expressions hold for any sensor radius and equilibrium constant of the complex whenever \( \kappa \gg 1 \).

Eqn (9) is also applied in chemical sensors using resins, but the electrochemical experiment has the advantage of allowing the tuning of this equilibrium constant by changing the applied potential.

Two important limits of eqn (10) are

\[
J_{\text{labile}}^{\text{lim}} = J_M(\theta \to 0) = \frac{Dc^*}{K\delta_d + \delta_d}
\]

and

\[
J_{\text{labile}}^{\text{lim}} = J_M(\theta \to \infty) = \frac{Dc^*_M}{\delta_d}
\]

Eqn (12) and (13) are very simple time-dependent expressions that give the metal (M) and reduced metal (M_{Red}) surface fluxes under limit conditions (c_M(r_0) = 0 and c_{M_{Red}}(r_0) = 0, respectively). Eqn (13) indicates that the limit flux of species M_{Red} is only different from zero when an initial reduced metal concentration, \( c_{M_{Red}} \), is present in the system.

From eqn (10)–(13) and for the case of electrochemical sensors, a simple \( E-J \) response can be deduced formally identical to that corresponding to a simple charge transfer process:

\[
E-E_{1/2} = \frac{RT}{nF} \ln \left( \frac{J_{\text{labile}}^{\text{lim}} - J_M}{J_{\text{labile}}^{\text{lim}} + J_M} \right)
\]

but the half-wave potential is now given by eqn (24) (see below).

2.1 Limiting cases

(i) \textbf{Labile complexes}. When the system is labile, the metal flux can be obtained from eqn (10) together with the specific conditions (\( \kappa \gg 1, \delta_t \ll \delta_d, c_M(r,t) = K^*c_M(r,t) \)), so that

\[
J_{\text{labile}} = \frac{Dc^*(1 + (1 + K^*) \theta c_M(r_0)/c^*)}{\delta_d(1 + (1 + K^*) \theta)} = D(K^* + 1)(c^*_M - c_M(r_0,t))/\delta_d
\]

Additionally, under the limit conditions \( \theta \to 0 \) (c_M(r_0,t) = 0) the metal flux for a fully labile system reduces to,

\[
J_{\text{labile}}^{\text{lim}} = Dc^*\frac{\gamma_0^*}{\delta_d}
\]

an expression equivalent to the response of a simple transformation process at surface without any coupled complexation reaction where the concentration of the target species is \( c_M + c_{M_{ML}} \). Notice, however, that for non-limit conditions \( (c_M(r_0) \neq 0) \), the response differs from that corresponding to a simple transformation process and depends on the \( K^* \) value, as was discussed in a previous paper.²⁶

(ii) \textbf{Inert complexes}. In this case the complexation equilibrium is frozen and the surface metal flux is obtained by taking \( \delta_t \to \delta_d \) in eqn (10):

\[
J_{\text{free}} = Dc^*_M(1 - \theta c_{M_{Red}}/c^*_M) = D\left(\frac{c^*_M - c_M(r_0,t)}{\delta_d} \right)
\]

indicating that the flux is only due to the diffusion of the free metal ion.

(iii) \textbf{Total steady state approximation (tss)}. The general expression (10) for \( J_M \) together with the values for limit conditions and for labile or inert complexes are valid for the total steady state approximation whenever \( \delta_d \) given in (8) is replaced with \( r_0 \). Under these conditions, a time-independent response is obtained.

3. \textbf{Lability degree}

The lability degree, \( \xi \), was introduced to quantify the contribution of the complexes to the metal flux.²⁹,²¹ It measures the fraction of the current contribution of the complex to the metal flux with respect to the maximum complex contribution that would arise when the system was fully labile, i.e., when equilibrium conditions between metal and ligand are reached at any relevant spatial position and time of the experiment. Thus,

\[
\xi = \frac{J_M - J_{\text{free}}}{J_{\text{labile}} - J_{\text{free}}}
\]

and it is close to 1 for a labile system while it approaches 0 for a non-labile or inert one.

From the \( dkss \) solution (eqn (10), (15), and (17)) an expression of the lability degree for any value of the ratio of concentrations at the surface can be easily obtained:

\[
\xi_{dkss} = \frac{J_{M,dkss} - J_{\text{free}}}{J_{\text{labile}} - J_{\text{free}}} = \left(\frac{\delta_d}{\delta_x} - 1\right)(1 + (1 + K^*) \theta) / K^* + \frac{\delta_d}{\delta_x}(1 + (1 + K^*) \theta)
\]

From eqn (11), (15), and (17) we deduce that the lability degree can also be expressed as a function of the surface concentrations in the way

\[
\xi_{dkss} = \frac{1 - c_M(r_0,t)/c^*_M}{1 - c_M(r_0,t)/c^*_M}
\]

this result is a direct consequence of eqn (6) and (7), obtained within the diffusive-kinetic steady state (\( dkss \)) approximation, and it is formally identical to that previously obtained within total steady state (\( tss \)) conditions.²⁶,²⁷

Eqn (19) is a time-dependent expression that indicates that the lability degree is a monotonous function of the ratio of concentrations at the surface \( \theta \), decreasing as \( \theta \) diminishes. Under the limit condition \( \theta \to 0 \) \( (c_M(r_0) = 0) \) the degree of lability reduces to:

\[
\xi_{\text{lim}} = \frac{\delta_d - \delta_t}{K^* \delta_d + \delta_d}
\]

Eqn (21) is also valid for the planar case by just using the linear diffusion and reaction layer thickness of the planar case \( (r_0 \to \infty) \) in eqn (5) and (8) becoming

\[
\xi_{\text{lim}} = \frac{\sqrt{\pi K^* \gamma_0^*} - 1}{K^* + \sqrt{\pi K^*}}
\]
For microelectrodes with $\sqrt{D/k} < r_0 < \sqrt{\pi Dt}$, the total steady state is reached. So, by using $\delta_d = r_0$, we deduce

\[ \frac{d_{\text{lim}}}{d_{\text{tss}}} = \frac{r_0 \sqrt{c}}{1 + K' + r_0 \sqrt{c}} \]  

(23)

In the limiting case of labile complexes, $\delta_d \gg \delta_p$, eqn (19) reduces, as expected, to $d_{\text{tss}}(d_0) \approx d_0$, while in the limit case corresponding to non-labile complexes $d_{\text{tss}} \approx 0$ as can be deduced by making $\delta_d \rightarrow \delta_d$ in eqn (19).

**Total steady state (tss):**

Eqn (19)–(21) are still valid for the total steady state approximation whenever $\delta_d = r_0$.

### 4. Results and discussion

Fig. 1 depicts the metal flux at $r = r_0$ and $\theta \rightarrow 0$ (limit conditions) with respect to determining parameters: $\sqrt{j_r/K'}$ (Fig. 1a) and $r_0$ (Fig. 1b).

It is shown (see Fig. 1a), that the metal flux increases with $\sqrt{j_r/K'}$ due to the higher contribution of the complex species, until reaching a constant value corresponding to the labile limit. Note that the parameter $\sqrt{j_r/K'}$ reduces to the well-known Davison lability criterion $k_a b^{1/2}/k_d^{1/2}$ for planar geometry when we take $k_a > k_d$. Regarding the sensor radius, the flux decreases as $r_0$ increases (Fig. 1b) due to the increase of the effective diffusion domain. The different curve types of line refer to the different approximate solutions: diffusive-kinetic steady state ($dkss$, solid curves, eqn (11)), kinetic steady state ($kss$, dotted curves obtained as indicated in ref. 22–24) and total steady state ($tss$, dashed curves obtained from eqn (10) taking $\delta_d = r_0$). For any $\sqrt{j_r/K'}$ value, the metal flux obtained from the $dkss$ solution is smaller than that corresponding to the $kss$ solution, both being somewhat greater than the time-independent solution ($tss$). This agrees with the decreasing behaviour of the transient flux as time increases and with the fact that the $dkss$ solution can be deduced from the long time behaviour of the $kss$ one while the $tss$ still refers to longer times.

As can be seen, the $dkss$ solution compares well with the more accurate $kss$ solution. The difference between them decreases when $\sqrt{j_r/K'}$ increases and/or $r_0$ decreases. So, the smaller the radius and the faster the kinetics, the better the behaviour of the $dkss$ solution is. Notice that decreasing the electrode radius, the time scale of the experiment is shortened and the steady state is reached sooner. Thus, for a given time, the $dkss$ results converge to the $kss$ ones as the sensor radius diminishes.

For planar surfaces, the relative difference between $dkss$ and $kss$ solutions is lower than 5% for $\sqrt{j_r/K'} > 10$. For spherical surfaces, the $dkss$ solution is more accurate, being the relative error between both solutions lower than 5% for $\sqrt{j_r/K'} > 10$ when $\omega = 0.5$ (which corresponds to a spherical surface with $r_0 \approx 120 \mu m$ under standard conditions of $t = 1$ s and $D = 10^{-5} \text{cm}^2 \text{s}^{-1}$), and for $\sqrt{j_r/K'} > 3$ when $\omega = 1$ (corresponding to $r_0 \approx 60 \mu m$ under standard conditions). Note that the validity range of the $dkss$ solution with microelectrodes covers the common range of values of metal complexes studied with voltammetric techniques. For instance, considering nickel acetate and lead acetate as examples of inert and labile complexes in voltammetric sensors, most of the metal complexes are located in the range $0.5 < \sqrt{j_r/K'} < 10^5$ (for $c_*^M = 10^{-4} \text{M}$ and $t = 1$ s).

The $tss$ solution considerably diverges from the $kss$ and $dkss$ solutions for any $\sqrt{j_r/K'}$ value under the conditions probed in Fig. 1a, large sphericity values ($\omega > 13$, $r_0 < 5 \mu m$) being required to ensure errors smaller than 5%. This is shown in Fig. 1b so that very small radii are needed so that the $tss$ solution converges without significant errors to the $kss$ and $dkss$ solutions.

In Fig. 2, the variation of the metal flux at a spherical surface with the ratio of concentrations at the surface ($\theta$) is plotted for various values of the chemical rate constants (Fig. 2a) and the equilibrium constant (Fig. 2b) by using the three approximate solutions. The curve corresponding to a simple transformation process of a metal ion with the same total concentration $c^M + c^M_*$ but without any coupled complexation reaction is also plotted (grey line). For a given $\theta$ value, the metal flux of a kinetic system is lower than that of a simple transformation process at surface with the same total

\[ \frac{d_{\text{lim}}}{d_{\text{tss}}} = \frac{r_0 \sqrt{c}}{1 + K' + r_0 \sqrt{c}} \]  

(23)

In the limiting case of labile complexes, $\delta_d \gg \delta_p$, eqn (19) reduces, as expected, to $d_{\text{tss}}(d_0) \approx d_0$, while in the limit case corresponding to non-labile complexes $d_{\text{tss}} \approx 0$ as can be deduced by making $\delta_d \rightarrow \delta_d$ in eqn (19).

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\[ \frac{d_{\text{lim}}}{d_{\text{tss}}} = \frac{r_0 \sqrt{c}}{1 + K' + r_0 \sqrt{c}} \]  

(23)
metal concentration (Fig. 2a). Increasing \( \chi = \kappa \cdot \iota \), both fluxes approach and tend to coincide in the limit \( \theta \to 0 \) when the system becomes labile (see eqn (16)). Actually, in the labile regime the limit flux is only dependent on the diffusion process and when the metal and complex share a common diffusion coefficient the ability of the diffusion to bring metal at the sensor surface is not influenced by the speciation. Furthermore, the kinetic wave is shifted towards smaller values of \( \theta \) in comparison to the simple transformation process due to the stabilization of the metal through the complex formation. The shift can be predicted in a general kinetic case by eqn (27) and by eqn (28) for the labile case (see below).

With respect to the equilibrium constant (Fig. 2b), there is a noticeable influence on the position of the voltammogram, so that the greater \( K' \), the more negative the \( E_{1/2} \) value. In addition, there is a decrease of the metal flux as \( K' \) increases due to the shift of the chemical equilibrium towards the electroinactive species.

Regarding the \( kss \) and \( dkss \) solutions, the difference between them decreases going towards larger values of \( \theta \), where the distortion of the concentration profiles from the equilibrium values is less noticeable. So, the above discussion about the accuracy of the \( dkss \) solution fully applies here.

**Half-wave potential, \( E_{1/2} \)**

In the particular case of an electrochemical sensor \( (\theta \) is given by the Nernst condition), from the \( dkss \) solution a simple expression for the half-wave potential \( E_{1/2} \) (which is the potential corresponding to the half-value of the metal limit flux) is easily obtained:

\[
E_{1/2} = E^0 + \frac{RT}{nF} \ln \left( \frac{1 + K' \delta_t / \delta_d}{1 + K'} \right)
\]  

(24)

so that \( E_{1/2} \) depends on the radius, the ligand concentration (through \( K' \) and \( \kappa \)) and the time (through \( \delta_d \)).

In the case of labile complexes \( (\kappa \gg 1, \delta_t \ll \delta_d) \), eqn (24) becomes:

\[
E_{1/2}^{labile} = E^0 + \frac{RT}{nF} \ln \left( \frac{1}{1 + K'} \right)
\]  

(25)

which indicates that \( E_{1/2}^{labile} \) is time independent and it does not depend on kinetic or geometrical parameters, but only depends on the equilibrium constant.

In the other limit situation, for non-labile systems \( (\delta_t \to \delta_d) \) or when the ligand concentration is null \( (c_L^0 = 0) \), the half-wave potential is also time independent and it equals the formal metal potential, since the response is identical to that of a surface transformation process with no coupled homogeneous reaction:

\[
E_{1/2}^{free} = E_{1/2}^{labile}(c_L^0 = 0) = E^0
\]  

(26)

If we define \( \Delta E_{1/2} = E_{1/2}(c_L^0 \neq 0) - E_{1/2}(c_L^0 = 0) \), the shift of the half wave potential with the ligand concentration for a general kinetic case can be written as

\[
\Delta E_{1/2} = \frac{RT}{nF} \ln \left( \frac{1 + \delta_t K'}{1 + K'} \right)
\]  

(27)

which for a labile system reduces to

\[
\Delta E_{1/2}^{labile} = \frac{RT}{nF} \ln (1 + K')
\]  

(28)

and coincides with the well-known DeFord–Hume equation deduced for planar diffusion. 30 This equation can be used to determine the stability constant in labile systems independently of the sensor radius by plotting \( F_0 = \exp \left( \frac{RT}{nF} \Delta E_{1/2}^{labile} \right) \) vs. the ligand concentration \( c_L^0 \).

In Fig. 3 we have plotted the variation of \( \Delta E_{1/2} \) with different parameters when \( dkss \) (solid lines) and \( tss \) (dashed line) are used.

Fig. 3a shows the time dependence of \( \Delta E_{1/2} \). The half-wave potential takes more negative values as time increases when \( dkss \) solution is used, this variation being more noticeable as the kinetic constants \( (\kappa) \) decrease. Within the \( tss \) approximation, \( \Delta E_{1/2} \) is time independent reaching the limit of the \( dkss \) solutions at very long times. The inset of Fig. 3a plots
exp(\(\frac{\Delta E_{1/2}}{RT}\)) versus \(1/\sqrt{t}\) for the curves depicted in the Figure. This representation is linear and the values of the slope and the intercept (see the equation imbedded in the Figure) can be used to characterize the coupled reaction by determining \(\kappa\) and \(K'\) values. This way of studying the preceding chemical reaction can be very useful since it can be easier than working with solutions of different ligand concentrations.

Fig. 3b shows that within both approximations (\(dkss\) and \(tss\)), the absolute value of \(\Delta E_{1/2}\) increases with the radius up to a constant limiting value reached at large \(r_0\) values (planar surfaces) which in the case of \(dkss\) solution is given by:

\[
\Delta E_{1/2} = \frac{RT}{nF} \ln \left( \frac{\sqrt{\kappa K' (1 + K')} + \sqrt{\kappa K' (1 + K')}}{\sqrt{\kappa K' (1 + K')}} \right)
\]

The limit of \(tss\) approximation for large radius has no physical meaning since this is only applicable to very small electrodes.

The influence of the radius diminishes when the chemical kinetic constants increase (compare curves with \(\kappa = 10^3 \text{s}^{-1}\) and \(\kappa = 10^5 \text{s}^{-1}\) in Fig. 3b). When \(\kappa = 10^5 \text{s}^{-1}\), the labile limit behaviour is almost reached and \(\Delta E_{1/2}\) almost coincides with the value given by eqn (28).

In Fig. 3c, we study the dependence of \(\Delta E_{1/2}\) with the ligand concentration. As stated above, the increase of \(c'_l\) shifts \(\Delta E_{1/2}\) towards more negative values. This behaviour is observed with both approximate solutions although the \(tss\) solution only coincides with the \(dkss\) one for very fast chemical kinetics.

Note that, for values of the ligand concentration smaller than tens of millimolar, \(c'_l\) must be considerably changed to obtain a variation of \(\Delta E_{1/2}\) of 10 mV. However, for small \(\kappa\) values this shift can be easily reached by simply varying the pulse duration tenths of second, as shown in Fig. 3a. For large \(\kappa\) values, varying \(c'_l\) is more convenient since the time variation of \(\Delta E_{1/2}\) may not be high enough. So, both methodologies are complementary in the characterization of the complexation process.

**Lability degree**

In Fig. 4 and 5 the lability degree from \(kss\) (dotted lines), \(dkss\) (solid lines) and \(tss\) (discontinuous lines) solutions are plotted for different values of the ratio of concentrations at the surface \((\theta)\), chemical rate constants \((\gamma)\), equilibrium constant \((K')\) and sensor sphericity \((\omega)\).

As can be seen in both Figures, the higher \(\gamma\) and the smaller \(\omega\), the greater the lability degree, a result that is predicted by eqn (19) which refers to the \(dkss\) approximation and that can also be understood recalling that when increasing the kinetic constants, the relative contribution of the kinetic dissociation increases while a decrease of the sensor radius tends to enhance the diffusion and freeze the kinetics.

Fig. 4 shows the decrease of the lability degree as the stability constant increases. As the different curves correspond to a fixed value of \(\gamma\), an increase of log \(K'\) implies a decrease of \(k_d\) which justifies the decrease of the lability degree. Keeping a fixed log \(K'\) value, the different curves depict decreasing lability degrees as the sensor radius decreases, as indicated above.

Concerning the influence of the ratio of concentrations at the surface on the lability degree, Fig. 5 shows that the lability degree decreases as the ratio \(c_{M(R0)}/c_{M(Resd)}/R_0\) decreases. Thus, as the metal concentration at the surface is lowered, the depletion of the metal concentration profile is deeper and the dissociation needs to be faster to reach equilibrium, i.e., for a labile behaviour of the system.

Noticeable differences between the lability degree obtained with the different approximations can be reported. The total steady state approximation overestimates the lability degree while this is underestimated by the \(dkss\) approximation.
However, $dkss$ and $kss$ results tend to converge rapidly as the sensor sphericity or $K'$ increase. The $tss$ solution involves smaller errors in the calculation of the lability degree than those obtained with the metal flux, although its applicability is also restricted to very small sensors and high stability constants. On the contrary, the $dkss$ approach is much more accurate for the study of the metal flux and the lability degree for any $r_0$ value, from ultramicro to planar sensors.

Fig. 4 Variation of the lability degree under limit conditions ($\theta \to 0$) with the equilibrium constant of the complex ($K'$) at spherical sensors of different sphericities (indicated on the curves). The different traces refer to the different theoretical approaches (types of lines as in Fig. 1). $\chi = 10$ (Fig. 4a), $\chi = 10^2$ (Fig. 4b) and $\chi = 10^3$ (Fig. 4c).

Fig. 5 Variation of the lability degree with the ratio of concentrations at the surface ($\theta$) at sensors of different sphericities (indicated on the curves). The different traces refer to the different theoretical approaches (types of lines as in Fig. 1). $\chi = 10$ (Fig. 5a), $\chi = 10^3$ (Fig. 5b) and $\chi = 10^5$ (Fig. 5c).

5. Conclusions

A system made up by a metal that interacts with a ligand giving rise to an (electro)inactive complex which dissociates at a kinetic regime due to the metal consumption at a spherical surface of any size is studied. Under the diffusive-kinetic steady state approximation, a general expression for the metal flux in terms of the ratio of concentrations at the surface ($\theta$) is reported. Limiting cases corresponding to $\theta \to 0$ and $\theta \to \infty$, as well as fast and slow kinetics and micro–macro-planar sensors are considered. The analytical expression reported is
time-dependent and yields very simple expressions for the linear reaction and diffusion layer thicknesses.

In case of electrochemical sensors, the shift of the half-wave potential, defined as $\Delta E_{1/2} = E_{1/2}(c^*_{\infty} \neq 0) - E_{1/2}(c^*_{\infty} = 0)$, and here calculated with the $dkss$ approximation, shows to be time-dependent. This feature leads to an alternative method to determine the kinetic and equilibrium constants, which has some advantages with respect to the variation of $\Delta E_{1/2}$ with the ligand concentration when the kinetics of the coupled chemical reaction is not too fast.

The expression for the flux is also used to obtain the lability degree, a key parameter to understand the ecotoxic properties of a metal in natural media. It is shown that the lability degree decreases when the equilibration of the heterogeneous transformation process shifts towards the transformed metal and when the sensor radius, the time of the experiment or the kinetic constant decrease.

While the total steady state approximation ($tss$) overestimates the lability degree with respect to kinetic steady state approximation ($kss$), it is underestimated by the diffusive kinetic steady state approximation ($dkss$). The error, in this last case, is lower than 5% when $K' > 10$ and $\chi > 4$ for micro and conventional electrodes. The applicability of the total steady state approximation requires the use of ultramicroelectrodes (electrode radius in the range of microns), which limits the use of this approximation in the assessment of the lability degree with voltammetric sensors.

**Notation and definitions**

- $r_0$ Radius of the particle/sensor/organism/electrode
- $c^*_j$ Bulk concentration of species $i$ ($\equiv M, ML, M_{\text{Red}}$)
- $c_j(r,t)$ Concentration of species $i$ ($\equiv M, ML, M_{\text{Red}}$) at a distance $r$ from the centre of the particle/sensor/organism at time $t$
- $D$ Common diffusion coefficient of all the species ($D_M = D_{ML} = D_{M_{\text{Red}}}$)
- $k'_a$ Effective association rate constant of the complex ML
- $k_d$ Dissociation rate constant of the complex ML
- $K$ Stability constant
- $K'$ Effective stability constant ($= K \cdot c^*_L = c_{ML}/c_M = k'_a/k_d$)
- $K = \sum$ Sum of the rate constants ($= k'_a + k_d$)
- $\chi = K \cdot t$ Dimensionless parameter related to the kinetics of complexation
- $\omega = 2\sqrt{D \cdot r_0}$ Dimensionless parameter related to the particle/sensor/organism sphericity
- $\phi(r,t) = c_{ML}(r,t)$ Perturbation of the chemical equilibrium
- $- K' c_M(r,t)$ Perturbation of the chemical equilibrium
- $\bar{c}(r,t) = c_M(r,t)$ Total metal concentration

**Continued**

- $\zeta^* = c^*_M + c^*_{ML}$, $\varphi^* = 0$ Bulk values of $\zeta$ and $\varphi$ variables
- $\delta_d = \left(\frac{1}{r_0} + \frac{1}{\sqrt{D_d}}\right)^{-1}$ Linear diffusion layer thickness for spherical particle/sensor/organism of any size

**Kinetic steady-state ($kss$)**

Approximation based on assuming that $\varphi$ is independent of time. For details, see ref. 21–24

**Diffusive-kinetic steady-state ($dkss$)**

Approximation based on assuming that $\varphi$ is independent of time and the profile of the total metal concentration, $c(r,t)$, is identical to that of a species only suffering diffusion

**Total steady-state ($tss$)**

Approximation based on assuming time independent concentrations for all the species

- $\delta_d^{\text{plane}} = \delta_d(r_0) > \sqrt{\pi D t}$ Linear diffusion layer thickness for planar particle/sensor/organism
- $\delta_d^{\text{micro}} = \delta_d(r_0) < \sqrt{\pi D t}$ Linear diffusion layer thickness for very small particle/sensor/organism
- $\delta_t = \left(\frac{r_0}{\sqrt{D} + \sqrt{\pi}}\right)^{-1}$ Linear reaction layer thickness for spherical particle/sensor/organism of any size
- $\delta_t^{\text{plane}} = \delta_t(r_0) > \sqrt{D/k}$ Linear reaction layer thickness for very small particle/sensor/organism
- $\delta_t^{\text{micro}} = \delta_t(r_0) < \sqrt{D/k}$ Linear reaction layer thickness for very small particle/sensor/organism

**Ratio of concentrations at the surface**

- $J_{M}$, $J_{M_{\text{Red}}}$ Surface flux of species $M$ and $M_{\text{Red}}$, respectively
- $J_{\text{labile}}$, $J_{\text{labile}}^{\lim}$ Surface flux of species $M$ if the complex was labile
- $J_{\text{free}}$ Surface flux of species $M$ if the complex was inert

**Applied potential in case of an electrochemical sensor**

- $E_{1/2}$ Half-wave potential
- $L_{\text{labile}}$, $L_{\text{labile}}^{\lim}$ Lability degree
- $L_{\text{free}}$ Lability degree under $dkss$ approximation
- $L_{\text{lim}}$, $L_{\text{lim}}^{\lim}$ Lability degree under $dkss$ approximation and limit conditions ($c_M(r_0) = 0$)
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