Lability of a Mixture of Metal Complexes under Steady-State Planar Diffusion in a Finite Domain

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The rigorous analytical solution for the fluxes from a mixture of 1:1 metal complexes toward an active surface under steady-state planar diffusion in a finite domain and excess ligand conditions allows for the computation of the global degree of lability of the system as well as particular degrees of lability of each complex in the mixture. This kind of system is found in a variety of fields ranging from electrochemical techniques (such as stripping chronopotentiometry at scanned deposition potential, SSCP) to analytical devices (such as diffusion gradients in thin-film gels, DGT). Among the specific effects arising from the presence of a mixture of ligands competing for the metal we highlight the following: (i) The degree of lability of a complex in the mixture differs from its degree of lability in an unmixed system with the same ligand concentration, and (ii) the degree of lability of one complex depends on (i.e., can be modified with) the concentrations of the ligands in the mixture. The impact of these characteristics on the metal flux crossing the active surface reaches the highest value when both complexes are partially labile. The complex contribution to the metal flux goes through a maximum when the thickness of the diffusion domain is varied. Thus, the thickness of the diffusion domain can be chosen to enhance the contribution of one particular complex. Lability criteria for each complex of the mixture within the reaction layer approximation are also reported. In particular, the reaction layer formulation for a complex is discussed in detail for two limiting cases: the rest of complexes are all nonlabile or the rest of complexes are all labile.

Introduction

The availability of metal species to an analytical sensor or an accumulating organism in an aquatic ecosystem is generally influenced by the metal interactions with ligands or surfaces present in the medium and by the kinetics of interconversion of metal species, transport and internalization phenomena.[1−5] Lability criteria have been developed to predict which process controls the metal flux when a ligand is present in the system:[4−6] either the dissociation process (in which case the system is called partially labile or nonlabile), or the transport process to the surface (in which case the system is called labile). Recently, a quantitative parameter called the degree of lability has been introduced to measure the percentage of the complex contribution to the uptake flux with respect to its maximum contribution obtained when the kinetics of the complexation processes were fast enough to reach equilibrium conditions at any time and relevant spatial position.[2,4,5,7−9] Among others, lability is influenced by the kinetics of the complexation processes, the transport phenomena present in the system, the size of the sensor, and the processes at the surface leading to the internalization.

A broad range of situations have been properly analyzed in the literature of the subject[4,5,7,8,10,11] including planar or spherical sensing surfaces, 1:1, 1:2, and a general 1:n stoichiometric relationship between metal and ligand, transient or steady state situations, etc. Despite that mixtures of ligands generally occur in aquatic natural media, very few papers have considered the effect of the interactions of the complexes in the mixture, which can play relevant roles by modifying the availability of each complex species.

Moreover, the interest for the dynamic interactions in solution on the resulting flux across surfaces is not only restricted to the environmental field, since these interactions mediate a wide variety of processes. In a biochemical context, substrate-receptor interactions play a key role in immune, neurological, and cell growth processes,[12−14] and industrial processes of gas separation, chromatography, and colloid and polymer science in general are also impacted by interactions between soluble ligand species and surfaces.[15,16]

In this paper, a rigorous mathematical framework is used to obtain the limiting metal flux in a system which contains a mixture of ligands, each leading to a 1:1 complex species with the metal ion. Steady-state conditions in finite planar diffusion are considered with zero metal concentration at the active surface (conditions of maximum flux). These are not unusual conditions in analytical techniques such as permeation liquid membrane (PLM),[17] diffusion gradients in thin films gels (DGT),[18,19] or voltammetric techniques,[20] which are used "in situ" or in the lab for the measurement of the availability of the metals. An analogous natural situation arises in many microorganisms or in assemblies or aggregates of unicellular organisms or biofilms, so that we also expect that results here developed can be relevant for these systems.

Results and Discussion

1. Mathematical Formulation. Let us consider in solution a mixture of h independent ligands ^1L, ^2L, ..., ^hL, which can bind a metal ion M according to the scheme

$$M + {}^iL \underset{k_{d,i}}{\overset{k_{a,i}}{\rightleftharpoons}} M\,{}^iL \qquad i = 1, 2, ..., h \qquad (1)$$
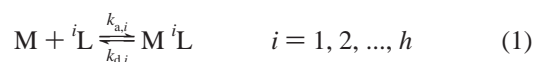
where K_i, $k_{a,i}$ and $k_{d,i}$ are, respectively, the equilibrium and the

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association and dissociation kinetic constants of the complexation process to the ligand ^{i}L. Let us also assume that each ligand is present in the system in a great excess with respect to the metal so that $c_{i_L} = c_{i_L}^*$ (superscript * indicates bulk values) is constant at any spatial point. The corresponding equilibrium conditions read

$$K_i' \equiv K_i c_{i_L}^* = \frac{k_{a,i} c_{i_L}^*}{k_{d,i}} = \frac{k_{a,i}'}{k_{d,i}} = \frac{c_{M^iL}^*}{c_M^*} \qquad (2)$$

where $K_i' = K_i c_{i_L}^*$, $k_{a,i}' = k_{a,i} c_{i_L}^*$.

When diffusion toward a stationary planar surface, situated at $x = 0$ and acting as a perfect sink, is the only relevant transport mechanism, for steady-state conditions we can write

$$D_M \frac{d^2 c_M}{dx^2} + \sum_{i=1}^{h} k_{d,i} c_{M^iL} - (\sum_{i=1}^{h} k_{a,i}') c_M = 0 \qquad (3)$$

$$D_{M^iL} \frac{d^2 c_{M^iL}}{dx^2} - k_{d,i} c_{M^iL} + k_{a,i}' c_M = 0 \qquad i = 1, 2, ..., h \quad (4)$$

with boundary conditions,

$$x = 0 \qquad c_M = 0;$$

$$\left(\frac{dc_{M^1L}}{dx}\right)_{x=0} = \left(\frac{dc_{M^2L}}{dx}\right)_{x=0} = ... = \left(\frac{dc_{M^hL}}{dx}\right)_{x=0} = 0 \quad (5)$$

$$x = g \qquad c_M = c_M^*; \quad c_{M^1L} = c_{M^1L}^*; \quad ...; \quad c_{M^hL} = c_{M^hL}^* \quad (6)$$

where g indicates the thickness of the diffusion domain of the system. Notice that in ligand excess conditions, the kinetics of interconversion between M and M^iL are pseudo first order and the system (3)−(4) is linear.

A procedure for the rigorous solution of the system (3)−(4) is outlined in Appendix A (see Supporting Information). It is based on uncoupling the system using as unknowns the linear combinations of the concentrations that diagonalize the matrix of coefficients that appears when (3)−(4) is written in a matricial form.[5,7,21,22] Rewriting the solution in terms of the original concentrations we obtain the concentration profile of all the species and the metal flux, given by

$$J_M = D_M \left(\frac{dc_M}{dx}\right)_{x=0} \qquad (7)$$

2. Degree of Lability. The degree of lability, ξ, was introduced to quantify the contribution of the complexes to the metal flux.[2,4,5,7−9] It measures the fraction of the current contribution of the complexes to the metal flux with respect to the maximum complex contribution that would arise when the system was fully labile, that is, when equilibrium conditions between metal and each ligand are reached at any relevant spatial position and time of the experiment:

$$\xi \equiv \frac{J_M - J_{free}}{J_{labile} - J_{free}} \qquad (8)$$

where J_{free} is the metal flux arising in the system if all the complexes were inert and J_{labile} is the metal flux arising in the system if all the complexes were labile. Thus, we have ξ close to 1 for a labile system and ξ close to 0 for a nonlabile or inert one.

Let us obtain a quantitative expression of this fraction in terms of the relevant parameters of the specific system studied here. Adding all the diffusion equations (3)−(4), and solving, the metal flux can be rewritten as

$$J_M = D_M \frac{c_M^*}{g} + \sum_{i=1}^{h} \left[D_{M^iL} \frac{c_{M^iL}^*}{g} \left(1 - \frac{c_{M^iL}^0}{c_{M^iL}^*}\right) \right] \qquad (9)$$

where $c_{M^iL}^0$ indicates the concentration of the complex M^iL at the active surface $x = 0$ (e.g., the electrode surface or bioactive surface).

In the first term of the right hand side of eq 9, we recognize J_{free} for this system. The second term indicates the increase of the metal flux due to the presence of the complexes in the system, which has been labeled $J_{complex}$,[4,5]

$$J_{complex} = \sum_{i=1}^{h} \left[D_{M^iL} \frac{c_{M^iL}^*}{g} \left(1 - \frac{c_{M^iL}^0}{c_{M^iL}^*}\right) \right] = \sum_{i=1}^{h} J_{complex,i} \quad (10)$$

As $0 < (1 - c_{M^iL}^0/c_{M^iL}^*) < 1$, eq 9 evidences that in steady state conditions the following applies: (i) The maximum kinetic contribution that a given complex can achieve is just the maximum purely diffusive flux of M^iL (reached when $c_{M^iL}^0 = 0$), $J_{dif,i} = D_{M^iL} c_{M^iL}^*/g$. The particular degree of lability of the complex M^iL, ξ_i, is then given by[7]

$$\xi_i \equiv \frac{J_{complex,i}}{J_{dif,i}} = \left(1 - \frac{c_{M^iL}^0}{c_{M^iL}^*}\right) \qquad (11)$$

(ii) The maximum contribution of the complexes to the metal flux is just the addition of the purely diffusive flux of all the complexes, and (iii) the global degree of lability of the system becomes

$$\xi = \frac{J_M - J_{free}}{J_{labile} - J_{free}} = \frac{J_M - D_M c_M^*/g}{\sum_{i=1}^{n} D_{M^iL} c_{M^iL}^*/g} = \frac{\sum_{i=1}^{h} \epsilon_i K_i' \xi_i}{\sum_{i=1}^{h} \epsilon_i K_i'} = \sum_{i=1}^{h} \frac{J_{dif,i}}{\sum_{j=1}^{h} J_{dif,j}} \xi_i$$
$$\qquad (12)$$

where ϵ_i stands for the ratio of diffusion coefficients $\epsilon_i = D_{M^iL}/D_M$.

Thus, the global lability degree is a weighted average of the particular degrees of lability of the different complexes present in the mixture with weighting factors dependent on the particular diffusion coefficients and on the respective abundances in the bulk solution, that is, on the fraction of the maximum diffusive flux of M^iL, $J_{dif,i}$, over the total maximum diffusive flux of all the complexes.

As a reference we recall here the particular system with only one ligand, $h = 1$. The methodology outlined in Appendix A (Supporting Information) leads to an expression for the concentration profiles and metal flux converging to those previously published.[4] The degree of lability reads

$$\xi = \left(1 - \frac{c_{ML}^0}{c_{ML}^*}\right) = \frac{g - \sqrt{\frac{D_M}{n}} \tanh\left[g\sqrt{\frac{n}{D_M}}\right]}{g + \epsilon K' \sqrt{\frac{D_M}{n}} \tanh\left[g\sqrt{\frac{n}{D_M}}\right]} \qquad (13)$$

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with

$$n = \frac{k_d}{\epsilon} + k_a' = \frac{k_d(1 + \epsilon K')}{\epsilon} \tag{14}$$

As we are mainly interested in cases where the contribution of the complex is large, we can assume that $\epsilon K' \gg 1$, which leads to $n \approx k_a'$. Additionally, in most configurations g is larger than μ^∞ (μ^∞ is the effective reaction layer thickness for planar semi-infinite diffusion, $\mu^\infty = (D_M/k_a')^{1/2}$. Then, eq 13 reduces to

$$\xi \approx \frac{g}{g + \epsilon K' \mu^\infty} = \frac{g}{g + \epsilon K \sqrt{D_M/k_a} c_L^{*1/2}} \tag{15}$$

The general methodology outlined in the Supporting Information allows the derivation of explicit analytical expressions for both the metal flux and the concentration profiles of all the species when two ligands are present in the system. These expressions are reported in Appendix B (Supporting Information).

3. The Reaction Layer Approximation and the Lability Criteria in a Mixture of Ligands. *3.1. Definition of the Terms.* In the preceding section we have developed a rigorous solution to quantify, by means of the degree of lability, the contribution of the complex species to the metal flux in a system that contains a mixture of ligands. Here, we additionally develop for this system lability criteria, which predict whether the metal flux to a sink is limited by the kinetics of the complexation processes or by the transport processes.[4,23−26] Lability criteria are written as analytical inequalities and are especially useful in the cases where the degree of lability as defined in the preceding section cannot be straightforwardly obtained. When the dissociation is the rate limiting step, we say that the system is partially labile, while, if the flux is limited by the transport process, we say that the system is labile and equilibrium conditions can be applied to any relevant spatial and time positions. A classical way to obtain these criteria is the use of the reaction layer approximation to assess the hypothetical maximum metal flux in the absence of diffusion limitations, usually denoted as J_{kin}.

The reaction layer was introduced by Brdicka and Wiesner[27,28] as a way to evaluate the limiting current in systems with kinetic complexes by means of approximate analytical expressions. The simplest case, $h = 1$, in a finite domain has recently been revised by comparing the approximate analytical results with the rigorous solution.[4]

Mathematically, the reaction layer approximation is based on uncoupling the metal diffusion equation from the complex concentration by assuming a constant complex concentration at least at some region close to the active surface. The existence of this approximately constant concentration reflects the limitation of the kinetics of the dissociation process in maintaining the equilibrium conditions with the depleted metal concentration profile. Obviously, the limitation and concentration will be complex dependent.

The maximum hypothetical metal flux in absence of diffusion limitation is computed by assuming the maximum value for the constant complex concentration, that is, the bulk complex concentration (J_{kin}). In the classical case of only one complex and semi-infinite diffusion, the "inert" component (J_{free}) becomes 0 and $J_M = J_{kin} = D_M (c_M^*/\mu^\infty) = k_d c_{ML}^* \mu^\infty$, where μ^∞ is called the reaction layer thickness. When $J_{free} \neq 0$, the equality $J_M = J_{kin}$ is no longer valid. We adhere from now on to an operational definition of the reaction layer thickness (different for different scenarios) on the basis of using[4,5]

$$J_{kin} = k_d c_{ML}^* \mu \tag{16}$$

The straightforward extension of the standard procedure to the case of a mixture would consist in writing the kinetic component as the summation of the dissociation fluxes of each complex along its own reaction layer (μ_j):

$$J_M = J_{free} + J_{kin} = J_{free} + \left(\sum_{j=1}^{h} k_{d,j} c_{M^jL}^* \mu_j \right) \tag{17}$$

If we want to assess the lability of $j = 1$, we need to compute μ_1. The standard procedure to find μ_1 would be to solve a case of eq 3 with no kinetic limitation for the dissociation of M^1L. But, to obtain the value of μ_1, we have to previously assume in (3) some value (or extra relationship) for the other c_{M^jL} values. This fact indicates that the rest of the complexes modify the lability of a given complex, as another instance of mixture effect.[29] As these extra concentrations (or conditions) cannot be known a priori, we cannot state a general lability criteria. However we will discuss, next, two different limiting cases which will provide the needed additional hypotheses to determine a given μ_j.

3.2. Lability Criteria When All Other Complexes Are Non-labile. We turn now to study the lability of complex M^iL when all other complexes are nonlabile. Under these conditions, to evaluate $J_{kin,i}$, we assume $c_{M^iL} \cong c_{M^iL}^*$ at any spatial point for any i (there is no diffusion limitation). Equation 3 can then be approximated as

$$\frac{d^2 c_M}{dx^2} = \frac{c_M - c_M^*}{(\mu_c^\infty)^2} \tag{18}$$

where

$$\frac{1}{(\mu_c^\infty)^2} \equiv \sum_{j=1}^{h} \frac{k_{a,j}'}{D_M} = \sum_{j=1}^{h} \frac{1}{(\mu_j^\infty)^2} \tag{19}$$

In the rightmost term, we have used the reaction layer thickness for planar semi-infinite diffusion for a particular complex j (i.e., when there was no other complex in the solution)[30]

$$\mu_j^\infty \equiv \sqrt{\frac{D_M}{k_{a,j}'}} \tag{20}$$

The reason for labeling the denominator in eq 18 as $(\mu_c^\infty)^2$ will appear below, when eq 24 is derived.

The integration of the preceding eq 18 in conditions of maximum metal flux, $c_M(x = 0) = 0$, and finite diffusion leads to

$$\left(\frac{dc_M}{dx} \right)_{x=0} = \frac{c_M^*}{\mu_c^\infty} \coth\left[\frac{g}{\mu_c^\infty} \right] \tag{21}$$

The metal flux can be written as a term accounting for the diffusion of the free metal, J_{free}, plus another one which will consider the hypothetical maximum contribution of the complexes, J_{kin} (see eq 17). We write this hypothetical contribution J_{kin}, as $(\sum_{j=1}^{h} k_{d,j} c_{M^jL}^*) \mu_c$. The subscript "c" in μ_c highlights the fact that in eq 17 we are taking a common reaction layer thickness for all the complexes present in the solution:

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$$D_M\left(\frac{dc_M}{dx}\right)_{x=0} = J_{\text{free}} + J_{\text{kin}} = D_M\frac{c_M^*}{g} + (\sum_{j=1}^{h}k_{d,j}c_{M^jL}^*)\mu_c \quad (22)$$

Notice that the metal transport, given in eq 18, only depends on the parameter $\sum_{j=1}^{h}k_{d,j}c_{M^jL}^* = \sum_{j=1}^{h}k_{a,j}c_{jL}^*$ so that J_M can only be dependent on this parameter (and on the boundary values). This justifies the form of (22) and the use of a common μ_c which at the same turn can only be dependent on these parameters. If not all the complexes are nonlabile, the region where c_{M^jL} is constant depends on j and we have particular μ values for each complex.

Isolating μ_c from (21) and (22), we obtain the expression for the common reaction layer thickness in planar geometry and finite domain:

$$\mu_c = \mu_c^\infty\left[\coth\left(\frac{g}{\mu_c^\infty}\right) - \frac{\mu_c^\infty}{g}\right] \quad (23)$$

Notice that μ_c is less than μ_c^∞ in agreement with the fact that equilibrium conditions are closer to the active surface in a finite diffusion domain than in semi-infinite diffusion conditions. Moreover, the limit

$$\lim_{g\to\infty}\mu_c = \mu_c^\infty \quad (24)$$

indicates that μ_c^∞ is the common reaction layer thickness under semi-infinite planar diffusion.

On the other limit,

$$\lim_{g\to 0}\frac{\mu_c}{g} = \frac{1}{3} \quad (25)$$

indicates that, when the diffusion domain shrinks, μ_c also shrinks.

We stress that (i) we are using a common reaction layer thickness, μ_c, according to the parametric dependence of the metal transport equation. Thus, we have now one equation, eq 22, to determine only one unknown: the common reaction layer thickness μ_c. The accuracy of (23) will be examined below. (ii) The reaction layer thickness of each complex considered as the only complex in the system is not, in general, a good estimation of the reaction layer thickness in the mixture. Indeed, the presence of several other complexes in the system will supply free metal (along its profile) and there will be, thus, less need for the studied complex to dissociate (i.e., the other complexes are buffering the metal concentration profile), leading to a smaller reaction layer thickness, that is, $\mu_c < \mu_c^\infty < \mu_j^\infty$ $\forall j$ as can be seen from (19) and (23).

Once we have an expression for the reaction layer thickness, we move to derive the corresponding lability criterion following the concepts explained in section 3.1. Assume that we focus on a given complex i. The hypothetical maximum metal flux coming from the complex M^iL, $J_{\text{kin},i}$ is then

$$J_{\text{kin},i} = k_{d,i}c_{M^iL}^*\mu_c \quad (26)$$

while the hypothetical maximum metal flux under diffusion and steady-state conditions is given by

$$J_{\text{dif},i} = D_{M^iL}\frac{c_{M^iL}^*}{g} \quad (27)$$

so that the lability parameter for M^iL reads

$$L_i = \frac{J_{\text{kin},i}}{J_{\text{dif},i}} = \frac{k_{d,i}\mu_c g}{D_{M^iL}} = \frac{k_{d,i}g\mu_c^\infty}{D_{M^iL}}\left(\coth\left(\frac{g}{\mu_c^\infty}\right) - \frac{\mu_c^\infty}{g}\right) \quad (28)$$

and the lability criterion is

$$L_i \gg 1 \quad (29)$$

One can see that

$$\lim_{g\to 0}L_i = 0 \quad (30)$$

indicating that the complexes tend to be inert with decreasing diffusion domain thickness, while they become fully labile when g tends to infinity.

When $g \gg \mu_c^\infty$,

$$L_i \approx \frac{k_{d,i}g\mu_c^\infty}{D_{M^iL}} = \frac{k_{d,i}g}{D_{M^iL}}\frac{1}{\sqrt{\sum_{j=1}^{h}(\mu_j^\infty)^{-2}}} \quad (31)$$

3.3. Lability Criteria for M^hL When the Rest of Complexes Are Labile. We now move to another limiting case where we can determine the reaction layer thickness of one complex: when all other complexes are fully labile. For the sake of simplicity in the presentation, and without any loss of generality, we label M^hL the partially labile or non labile complex ($c_{M^hL} \cong c_{M^hL}^*$) whose reaction layer thickness we are looking for.

The different concentrations of labile M^jL complexes in eq 3 can be expressed in terms of c_M via $c_{M^jL} = K_j'c_M$. Then, adding eq 3 and eq 4 up to $j = h - 1$, we have

$$(D_M + \sum_{j=1}^{h-1}D_{M^jL}K_j')\frac{d^2c_M}{dx^2} + k_{d,h}c_{M^hL}^* - k_{a,h}'c_M = 0 \quad (32)$$

which can be expressed as

$$\frac{d^2c_M}{dx^2} = \frac{c_M - c_M^*}{D_M(1 + \sum_{j=1}^{h-1}\epsilon_jK_j')/k_{a,h}'} = \frac{c_M - c_M^*}{(\mu_{\text{lab},h}^\infty)^2} \quad (33)$$
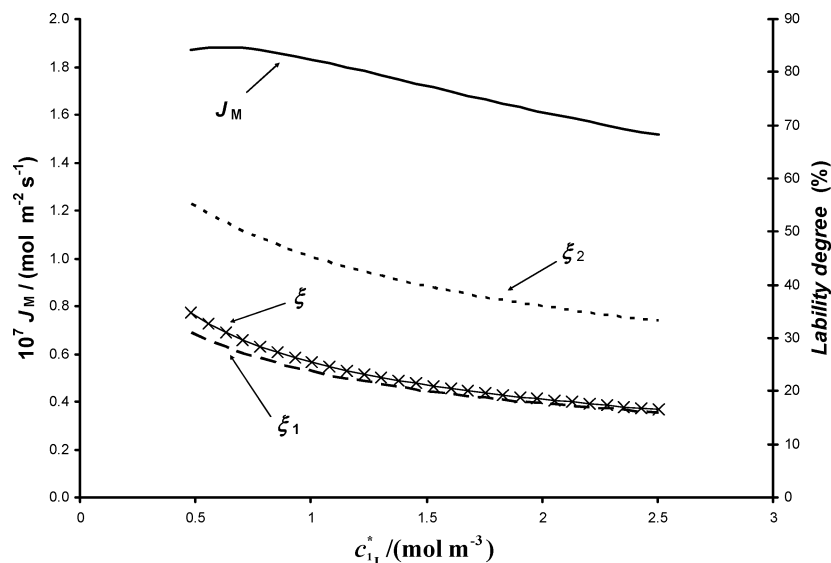
just by defining

$$\mu_{\text{lab},h}^\infty \equiv \sqrt{\frac{D_M}{k_{a,h}'}(1 + \sum_{j=1}^{h-1}\epsilon_jK_j')} = \mu_h^\infty\sqrt{1 + \sum_{j=1}^{h-1}\epsilon_jK_j'} \quad (34)$$

As eq 33 is equivalent to previous eq 18, analogous expressions to (21), (23), and (24) can be stated for this case by just replacing μ_c^∞ with $\mu_{\text{lab},h}^\infty$ and μ_c with $\mu_{\text{lab},h}$:

$$\mu_{\text{lab},h} = \mu_{\text{lab},h}^\infty\left(\coth\left(\frac{g}{\mu_{\text{lab},h}^\infty}\right) - \frac{\mu_{\text{lab},h}^\infty}{g}\right) \quad (35)$$

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Figure 1. Metal flux at the active surface $x = 0$, labeled as J_M (continuous line) and referred to the left ordinate axis and the global degree of lability of the system, (ξ, continuous line with marker $\times$), the degree of lability of complex M^1L , (ξ_1, long dashed line), and the degree of lability of complex M^2L, (ξ_2, short dashed line) in the mixture, referred to the right ordinate axis as functions of the bulk concentration of ligand ^1L. The parameters are $c^*_{T,M} = 0.1$ mol m^{-3}, $c^*_{2L} = 1.5$ mol m^{-3}, $K_1 = 100$ m^3 mol^{-1}, $K_2 = 50$ m^3 mol^{-1}, $k_{a,1} = k_{a,2} = 100$ m^3 mol^{-1} s^{-1}, $D_M = 10^{-9}$ m^2 s^{-1}, $\epsilon_1 = 0.9$, $\epsilon_2 = 0.1$, and $g = 8 \times 10^{-5}$ m. The change of the concentration of ligand ^1L in the figure leads to a change in the fraction of M^1L with respect to the total metal bound from $c^*_{M^1L}/(c^*_{M^1L} + c^*_{M^2L}) = 0.35$ in the leftmost part of the plot to $c^*_{M^1L}/(c^*_{M^1L} + c^*_{M^2L}) = 0.80$ at the rightmost part of the figure.

As we are interested in $J_{kin,h}$, we can write this contribution in a separate term so that

$$D_M\left(1 + \sum_{j=1}^{h-1} \epsilon_j K_j'\right)\left(\frac{dc_M}{dx}\right)_{x=0} =$$

$$k_{d,h} c^*_{M^hL} \mu_{lab,h} + D_M\left(1 + \sum_{j=1}^{h-1} \epsilon_j K_j'\right)\frac{c^*_M}{g} \quad (36)$$

where the second term of the right hand side of (36) contains the contribution to the metal flux of all the labile complexes.

Similar reasonings to the ones in the previous subsection lead to the corresponding lability parameter for this case of other complexes being fully labile:

$$L_h = \frac{J_{kin,h}}{J_{dif,h}} = \frac{k_{d,h}\mu_{lab,h}g}{D_{M^hL}} = \frac{k_{d,h}g\mu^\infty_{lab,h}}{D_{M^hL}}\left(\coth\left(\frac{g}{\mu^\infty_{lab,h}}\right) - \frac{\mu^\infty_{lab,h}}{g}\right) \approx$$

$$\frac{k_{d,h}g\mu^\infty_{lab,h}}{D_{M^hL}} \quad (37)$$

The lability criterion, then, reads $L_h \gg 1$.

3.4. Guidelines for the General Case. For a general case, it might happen that one does not know a priori whether other complexes are labile or not, and the number of combinations of labile and non labile complexes increases rapidly with the number of ligands in the mixture. So, we aim here at just giving some guidelines on the lability of a certain complex. Combining (19) and (34) we have

$$\mu^\infty_c < \mu^\infty_h < \mu^\infty_h\sqrt{1 + \sum_{j=1}^{h-1} \epsilon_j K_j'} = \mu^\infty_{lab,h} \quad (38)$$

And, as the function $f(x) = x(\coth(x^{-1}) - x)$ increases monotonically with x, we can conclude that the lability parameter value computed with (28) is always less than the one

given by (37). Thus, if the inequality in (29) holds, then inequality below (37) also holds, and we can state that the complex under analysis is labile, independently of the degree of lability of the other complexes present in the mixture. Likewise, if the inequality below (37) does not hold, the complex is nonlabile independently of the degree of lability of the rest of complexes.

4. Effect of the Mixture on the Degree of Lability. Let us analyze a mixture of two ligands. Figure 1 plots the metal flux J_M computed using eq 9, together with the degree of lability of the system ξ using (12) and the individual degrees of lability of both complexes ξ_1 and ξ_2 using (11), against c^*_{1L}.

When the composition of the mixture is changed, bulk complex concentrations change according to the equilibrium conditions assumed in (2) and (6). New values of J_M then arise depending both on the set of mobility values and the respective degrees of lability of the complexes. Thus, increasing c^*_{1L} in Figure 1, there is a shift of the equilibria toward the formation of M^1L, which leads to an initial increase in J_M, as we see in the leftmost part of the figure, because of the higher mobility of M^1L with respect to M^2L. The metal flux decreases along the rest of the figure. In this range of c^*_{1L}, the lower degree of lability of M^1L with respect to M^2L (i.e., $\xi_1 < \xi_2$) and the decrease of ξ_1 as c^*_{1L} increases are the dominant effects. Accordingly, we can find systems exhibiting a variety of behaviors for J_M (e.g., flux always increasing, flux always decreasing, flux going through a maximum or a minimum, etc.) when the concentration of one of the ligands is changed in the mixture. Obviously, this behavior depends on the respective mobilities and labilities of the complexes present in the mixture.

Figure 1 also shows that when c^*_{1L} increases, then the lability of both complexes ξ_1 and ξ_2 as well as the global ξ decreases, with ξ progressively approaching ξ_1 as the weight of complex M^1L increases. The decrease of ξ_1 is expected from the behavior of a system with only one ligand (the ligand concentration increases more markedly than the complex concentration whenever we are under excess of ligand conditions, and the
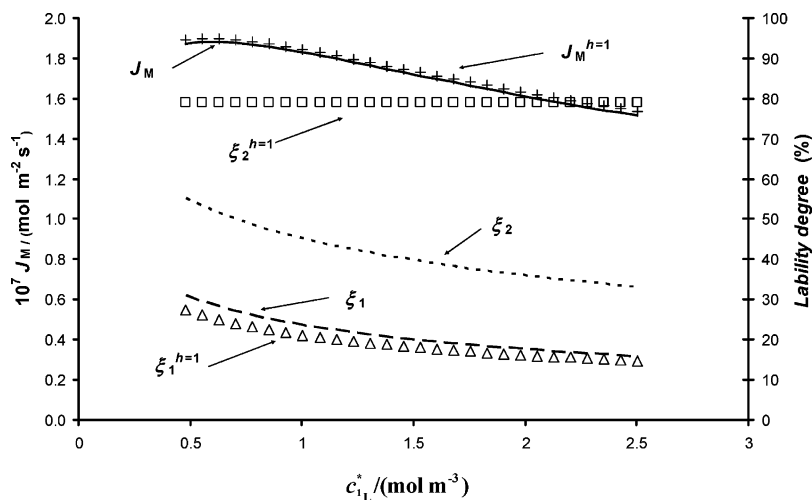
Figure 2. Apart from the rigorous metal flux J_M (continuous line) and degrees of lability of the two complexes, M^1L (ξ_1, long dashed line) and M^2L (ξ_2, short dashed line), already depicted in Figure 1, this figure includes the approximated degrees of lability $\xi_1^{h=1}$ ($\triangle$) and $\xi_2^{h=1}$ ($\square$) obtained from (13), i.e., corresponding to the systems with only M^1L or only M^2L being present. The figure also depicts the approximated metal flux $J_M^{h=1}$ (+) expected in the mixture system when the degrees of lability of both complexes were $\xi_1^{h=1}$ and $\xi_2^{h=1}$. The parameters are $c_{T,M}^* = 0.1$ mol m^{-3}, $c_{2L}^* = 1.5$ mol m^{-3}, $K_1 = 100$ m^3 mol^{-1}, $K_2 = 50$ m^3 mol^{-1}, $k_{a,1} = k_{a,2} = 100$ m^3 mol^{-1} s^{-1}, $D_M = 10^{-9}$ m^2 s^{-1}, $\epsilon_1 = 0.9$, $\epsilon_2 = 0.1$, and $g = 8 \times 10^{-5}$ m.
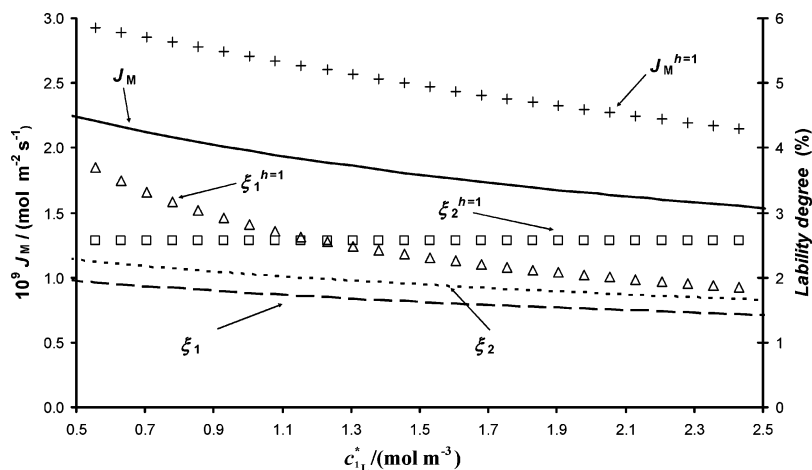

Figure 3. Degree of lability of complex M^1L (ξ_1, long dashed line), and degree of lability of complex M^2L (ξ_2, short dashed line), together with $\xi_1^{h=1}$ ($\triangle$) and $\xi_2^{h=1}$ ($\square$) obtained by means of (13) for the single M^1L and M^2L systems, referred to the right ordinate axis as functions of the bulk concentration of ligand ^1L. Metal flux, J_M (continuous line) and $J_M^{h=1}$ (+) referred to the left ordinate axis expected in the mixture system when the degree of lability of both complexes was $\xi_1^{h=1}$ and $\xi_2^{h=1}$. The parameters are $K_1 = K_2 = 10^3$ m^3 mol^{-1}, $k_{a,1} = 0.9$ m^3 mol^{-1} s^{-1}, $k_{a,2} = 1.1$ m^3 mol^{-1} s^{-1}, $\epsilon_1 = \epsilon_2 = 1$ and $g = 10^{-3}$ m. The rest of parameters are as in Figure 1.

increase of the association rate is then dominant in keeping $c_{M^1L}^0$ closer to $c_{M^1L}^*$) and, although not seen in the figure, the decrease of ξ_1 shows a good linearity with $(c_{1L}^*)^{-1/2}$. [4,31] This is the dependence expected from the reaction layer approximation which is a good approximation to the behavior of this system because of the low ξ_1 value (see eq 15).

The effect of c_{1L}^* on ξ_2 is due to the coupling of both complexes (both ligands compete in the metal binding). When c_{1L}^* increases, $c_{M^1L}^*$ increases from 40% to 80% of the metal bound in the plot, and $c_{M^2L}^*$ decreases. There is no increase in c_{2L}^* since we are in excess ligand conditions and a constant c_{2L}^* has been used along all range of c_{1L}^* considered in the plot. The decrease of $c_{M^2L}^*$ reduces the dissociation rate of this complex leading to a new steady-state situation with lower degree of lability for M^2L. In all the cases studied we have seen a decrease of ξ_1 and ξ_2 with c_{1L}^*. Moreover, given that ξ tends to ξ_1 when c_{1L}^* increases, the behavior of ξ depends, in principle, on the relative values of ξ_1 and ξ_2.

In addition to the ξ_1 and ξ_2 values seen in Figure 1, Figure 2 also depicts, in discontinuous line, the degree of lability, $\xi_1^{h=1}$ and $\xi_2^{h=1}$, of M^1L and M^2L corresponding to single ligand systems with the same bulk free ligand concentration than in the mixture. Thus, $\xi_1^{h=1}$ and $\xi_2^{h=1}$ are obtained by using eq 13. There is a large effect of the mixture on the degree of lability of M^2L since we see a large difference between $\xi_2^{h=1}$ and the actual ξ_2 value in the mixture: $\xi_2^{h=1} \approx 80\%$ versus $\xi_2 \approx 30\%$ under concentrations given at the end of the rightmost part of the plot. The impact of this effect on ξ_1 is not so noticeable. In general, the most labile complex tends to show a lower degree of lability in the mixture than in the unmixed system, while the less labile tends to increase its degree of lability in the mixture. However, we have obtained some sets of parameters where this trend is not fulfilled, both complexes being more labile in the mixture than in the separate systems, as is the case of Figure 3.

To assess for the "mixture effect" [29] we can compute as a reference value the hypothetical metal flux which results from

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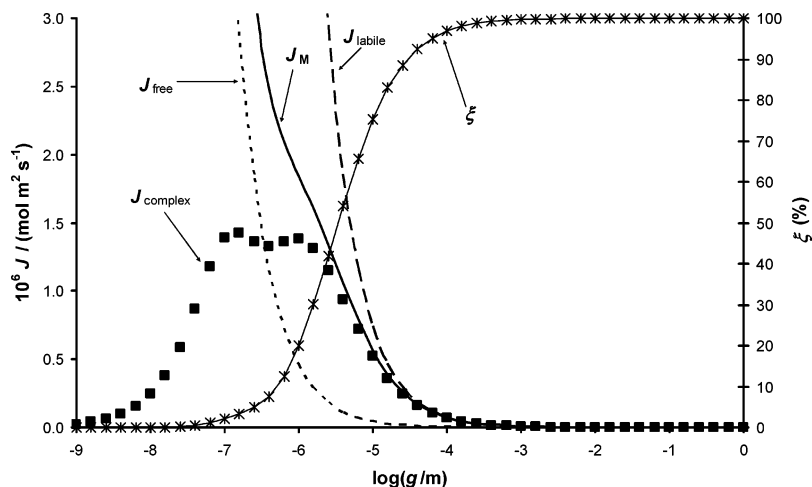
Figure 4. Metal flux at the active surface J_M (continuous line), the complex contribution to the metal flux $J_{complex}$ (■), J_{labile} (long dashed line) and J_{free} (short dashed line), referred to the left ordinate axis and the global degree of lability of the system, ξ (marker ∗, in %), referred to the right ordinate axis as functions of $\log(g/m)$. The parameters are $k_{a,1} = 10^4$ m^3 mol^{-1} s^{-1}, $k_{a,2} = 10^5$ m^3 mol^{-1} s^{-1} and $\epsilon_1 = 0.1$, $\epsilon_2 = 0.01$. The rest of parameters are as in Figure 1.
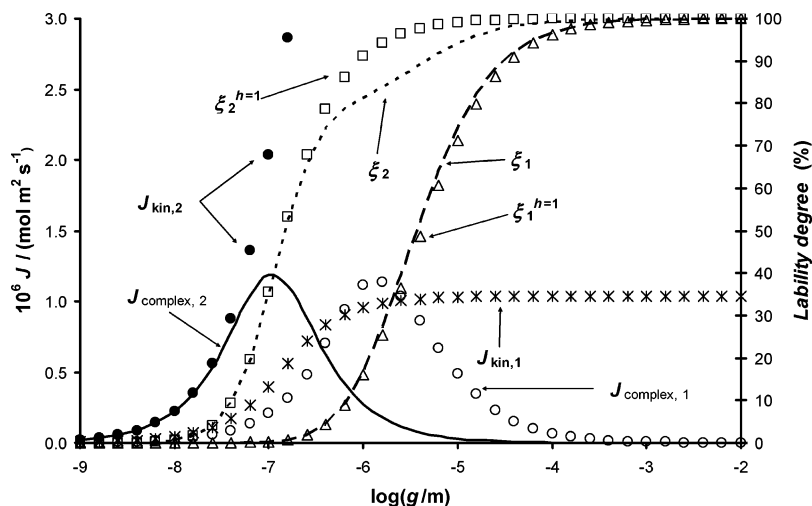
Figure 5. Degree of lability of complex M^{1}L (ξ_1, long dashed line), degree of lability of complex M^{2}L (ξ_2, short dashed line), both obtained from (11), together with $\xi_1^{h=1}$ (△) and $\xi_2^{h=1}$ (□) corresponding to the single M^{1}L and M^{2}L systems (obtained by means of eq 13), all referred to the right ordinate axis as functions of $\log(g/m)$. $J_{complex,1}$ (○), $J_{complex,2}$ (continuous line), and $J_{kin,1}$ (∗) and $J_{kin,2}$ (●) obtained using (26) referred to the left ordinate axis. All parameters as in Figure 4.

considering the individual degrees of lability of each complex as if each ligand was the only one (with the same c_{iL}^* and $c_{M^iL}^*$ existing in the real mixture):

$$J_M^{h=1} = J_{free} + D_{M^1L}\frac{c_{M^1L}^*}{g}\xi_1^{h=1} + D_{M^2L}\frac{c_{M^2L}^*}{g}\xi_2^{h=1} \quad (39)$$

In Figure 2 we see that the impact of the mixture effect on the metal flux is small: the discrepancies between the complex contributions to the metal flux in the unmixed and the mixed systems tend to cancel and the final effect in the difference between J_M and $J_M^{h=1}$ is reduced. However, other sets of parameters can yield important differences. The example reported in Figure 3 leads to a difference of the order of 40% in J_M when J_M in the mixture is compared with $J_M^{h=1}$ computed using the degrees of lability of both complexes in the unmixed systems. While for this particular mixture $J_M < J_M^{h=1}$, other sets of parameters give rise to an increase in the expected metal flux due to the mixture effect.

Aiming at a global overview of the mixture effects, we now analyze the influence of the thickness of the diffusion layer,

which allows us to move from a labile system for a large enough diffusion layer to an inert system when this thickness is decreased.

Figure 4 plots the metal flux J_M, using eq 9, together with $J_{complex}$ (computed as $J_{complex} = J_M - J_{free}$) and the degree of lability ξ given in (12) versus $\log(g)$ for a system with two ligands. In the figure we can see the decrease of ξ as the diffusion domain decreases, while, coincident with this decrease, J_M diverges from J_{labile} to approach J_{free}. The complex contribution, $J_{complex}$, shows then a double peaked behavior, and the system tends to be inert as the diffusion layer (or the time to reach steady state) decreases. Figure 5 analyses the complex contribution for data of Figure 4 by identifying the individual contribution of each complex species:

$$J_{complex,i} = D_{M^iL}\frac{c_{M^iL}^*}{g}\xi_i \quad (40)$$

where ξ_i is obtained from (11) after the rigorous calculation of the concentration profiles.

The decrease of ξ_1 as g decreases indicates that M^{1}L is the first complex to become inert. Accordingly, the concentration
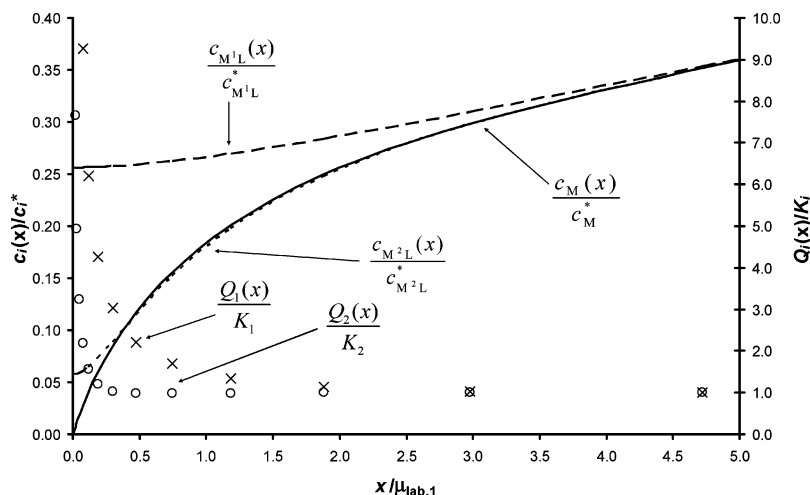
Figure 6. Normalized concentration profiles c_i/c_i^* of M (continuous line), M^1L (long dashed lines), and M^2L (short dashed line) referred to the left ordinate axis and the quotients $Q_1/K_1 \equiv \{c_{M^1L}(x)/[c_M(x)c_{1L}^*(x)]\}\{(c_M^* c_{1L}^*)/c_{M^1L}^*\}$ (marker x) and $Q_2/K_2 \equiv \{c_{M^2L}(x)/[c_M(x)c_{2L}^*(x)]\}\{(c_M^* c_{2L}^*)/c_{M^2L}^*\}$ (○) referred to the right ordinate axis for a diffusion domain of thickness $g = 10^{-5}$ m and the rest of parameters as in Figures 4 and 5.

profiles for $g = 10^{-5}$ m depicted in Figure 6 show that c_{M^1L} is poorly depleted in a large vicinity of the active surface (say at $x = \mu_{lab,1}$) while c_{M^2L}, in the same region, is depleted so as to keep the equilibrium with M (see how the normalized concentration profiles of M and M^2L still collapse around $x = \mu_{lab,1}/2$) in agreement with the labile behavior of the M^2L complex. We can also highlight the accuracy of the reaction layer thickness $\mu_{lab,1}$ given in (35) for one complex (M^1L in the present case) when the rest are labile (M^2L in the present case). The constancy of c_{M^1L} down to $x = \mu_{lab,1}$ indicates that (35) is a good approximation in this case. Coincident with this constancy, we see the rapid increase in

$$Q_1/K_1 \equiv \frac{c_{M^1L}(x)}{c_M(x)c_{1L}(x)} \frac{c_M^* c_{1L}^*}{c_{M^1L}^*}$$

Finally, for very small values of g in Figure 5, we see that $J_{complex,2}$ becomes very small because now both complexes are nonlabile.

The values of $J_{kin,1}$ and $J_{kin,2}$ (calculated using μ_c as (26) indicates) are also depicted in Figure 5. These values show a good agreement with the respective $J_{complex,i}$ from the leftmost part of the plot up to the transition from nonlabile to the labile regimes (e.g., log $g = -7.5$ for M^2L and log $g = -6$ for M^1L), this indicating the accuracy of the reaction layer approximation in reproducing the contribution of each complex at low degrees of lability and the usefulness of the corresponding lability criteria obtained.

Figure 5 also depicts the degrees of lability ($\xi_1^{h=1}$ and $\xi_2^{h=1}$ computed from eq 13) of each complex in a solution with only this complex being present. In the regimes of fully labile or nonlabile behavior (rightmost or leftmost parts of the figure), these degrees of lability yield results quite close to the ones for the system with both complexes being present, indicating the absence of noticeable mixture effects. However, when both complexes are partially labile, there is an impact of the dissociation of one complex on the other so that the behavior of the mixture is different from that expected in the unmixed systems. Notice that, for the case of the figure, the most labile complex (M^2L) becomes less labile in the mixture than it would in the unmixed system, while the less labile complex exhibits an opposite behavior: M^1L is slightly more labile in the mixture than in the unmixed system.

The mixture effects become negligible when the transition from the labile to the nonlabile behavior takes place for each complex at a well separated range of g values (data not shown), whereas it becomes relevant when the peaks of the respective $J_{complex}$ appear closer to each other. From a qualitative point of view, we can say that the overlapping of $J_{complex,i}$ (as in Figure 4 or 5) increases when the difference between the kinetic constants of both complexes decreases and when the width of the peaks increases. We can have some quantitative information on the position, g_{peak}, and on the half width of the peak of the complex flux, $\Delta g_{1/2}$, by using the analytical expressions obtained for a system with only one complex being present. In this case, the position of the peak and the width at $J_{complex,max}/2$ become

$$g_{peak} \approx \sqrt{D_{ML}} \frac{1 + \sqrt{1 + \epsilon_i K_i'}}{\sqrt{k_{d,i}}\sqrt{1 + \epsilon_i K_i'}} \tag{41}$$

and

$$\Delta g_{1/2} \approx$$
$$\sqrt{D_M}\sqrt{\frac{\epsilon_i\{16(1 + \sqrt{1 + \epsilon_i K_i'}) + \epsilon_i K_i'[\epsilon_i K_i' + 8(2 + \sqrt{1 + \epsilon_i K_i'})]\}}{k_{d,i}(1 + \epsilon_i K_i')}} \tag{42}$$

These expressions indicate that the position of the peak is mainly dependent on the kinetic dissociation constant ($k_{d,i}$). On the other hand, the width increases as $K_i'\epsilon_i$ increases, but it decreases as the kinetic dissociation constant ($k_{d,i}$) of the M^iL increases.

A complete quantitative prediction of the degree of lability of a complex can be obtained with the methodology here developed. This analysis could be then used to select the thickness of the sensor for a given percentage of the contribution of each complex to the metal flux. With the results of the present work, a systematic evaluation of the mixture effects for the typical composition of natural waters of different environments seems to be of high interest in order to evaluate the availability of metal species in natural media.

Conclusions

A methodology to determine the effect of a ligand mixture on the contribution of the complexes to the metal flux in systems

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under diffusion-limited conditions in a planar finite domain for any value of the association/dissociation rate constants has been developed.

The degree of lability of each complex in the mixture as well as the degree of lability of the whole system can be computed within this framework. On the basis of the reaction layer approximation, lability criteria for a given complex species in the mixture have also been suggested, these criteria being dependent on the kinetic behavior of the rest of complexes.

Among the mixture effects, we have observed that (i) the increase of the concentration of one type of ligand decreases both degrees of lability (its own as well as the one of the other complex species) and that (ii) the degree of lability of a complex differs from the degree of lability of the same complex under the same conditions in an unmixed system. In general, the mixture effect can lead to an increase or decrease of the degree of lability of a complex in a mixture and can have an important impact on the metal flux, especially under conditions that render both complexes partially labile. In the rest of cases this effect is negligible, and the degree of lability of one complex in a mixture can be accurately approximated with the expressions obtained for unmixed systems.

The behavior of the mixture with respect to the thickness of the diffusion domain indicates that the complex contributions of the species M^1L and M^2L show a peaked behavior when plotting $J_{\text{complex},i}$ versus $\log g$, and that the mixture effect (difference between the degree of lability of a complex in an unmixed system with respect to the degree of lability in the mixture) is especially noticeable when both peaks overlap, that is, under conditions where both complex species are partially labile.

The methodology developed can be used to determine the thickness of the diffusion domain that yields a given contribution of a complex in the metal flux.

Supporting Information Available: Details of the general analytical solution in Appendix A and derived equations for the case of two ligands ($h = 2$) in Appendix B in pdf format. This material is available free of charge via the Internet at http://pubs.acs.org.

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