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Method Article

Numerical tools for the simulation of enzymatic bio porous-electrodes operating in DET mode ☆

Tien Dung Le [a], Didier Lasseux [b,*]

[a] CNRS, LEMTA, University of Lorraine, Nancy F-5400, France
[b] I2M, UMR 5295, CNRS, University Bordeaux, 351, Cours de la Libération, Talence, CEDEX 33405, France

A B S T R A C T

Modeling of diffusion/enzymatic reaction in porous electrodes operating in direct electron transfer mode is developed. The solution at the pore-scale is extremely cumbersome due to the complex geometry of the porous material. The upscaled model is much easier to solve, while keeping the essential of the physico-chemical behavior. The method to carry out the solution can be described as follows

- The effective diffusion coefficient involved in the macroscopic equations is accurately computed by solving a closure problem in a representative elementary volume.
- Electrochemical parameters are identified by a direct resolution of the macroscopic model solved with a COMSOL Multiphysics code coupled to a curve fit procedure carried out on voltammetry experimental results using a Matlab code. Electrodes with different thicknesses may be considered in the fitting procedure to improve accuracy. An alternative use of the COMSOL Multiphysics code is to predict the electrode behavior and further optimize its design, if all the electrochemical parameters are identified.
- To validate the upscaled model, the pore scale model may be solved with direct numerical simulations carried out in a 3D microstructure using another COMSOL Multiphysics code to compare with the solution of the upscaled model in the 1D-reduced geometry.

A R T I C L E I N F O

Method name: Novel numerical tool to identify experimental parameters in enzymatic porous bio-electrode and predict the electrode behavior
Keywords: Enzymatic porous electrode, Direct electron transfer, Upscaled model, Parameters identification
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* Corresponding author.
E-mail address: didier.lasseux@u-bordeaux.fr (D. Lasseux).

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Specifications table

Subject Area;	
More specific subject area;	*Multiscale modeling, enzymatic porous-electrode*
Method name;	*Novel numerical tool to identify experimental parameters in enzymatic porous bio-electrode and predict the electrode behavior*
Name and reference of original method;	*N/A*
Resource availability;	https://www.researchgate.net/publication/356,907,533_Codes_dedicated_to_MethodsX_paper

Method details

A new macroscopic model, based on a rigorous upscaling procedure was derived for diffusion and electrochemical enzymatic reaction involved in a porous electrode operating in direct elctron transfer (DET) mode [1]. This model does not make any specific assumption on the macroscopic shape of the electrode, nor on its microstructure. In the following, the numerical procedure is illustrated on a cylindrical electrode. The porous active part of the electrode is deposited onto a cylindrical bare wire and, once immersed in the reactive fluid, a diffusion layer develops around the electrode that must be considered in modeling. A section of the electrode and diffusion layer is sketched in Fig. 1 (top right). Upon assuming that the microstructure of the material is pseudo-periodic, a representative elementary volume is identified, that can be restricted to a unit cell of the periodic pattern forming the porous structure. Typically, for real materials as those considered in [1] (see also [2,3]), a face-centered cubic (FCC) structure can be used (see Fig. 1 for more details on the geometry). The effective diffusivity tensor present in the macroscopic model is obtained from the solution of a closure problem in the representative elementary volume of the electrode material. Alternatively, a real 3D structure, extracted from image analysis can be employed [4]. Such a methodology provides an insight into the macroscopic laws at the electrode scale taking into account the microstructure of the medium. It yields an operational model of interest for designers and end-users as it can be used for comparison with experimental data, to identify parameters and/or predict the current delivered by the electrode. A validation of the proposed model is made through a comparison between direct numerical simulations of the pore-scale model in the three-dimensional structure and numerical results of the macroscopic model carried out in the 1D corresponding reduced-domain. The objective of the article is to describe the procedure to solve the macroscopic model, identify unknown electro-chemical parameters if necessary, and, additionally, indicate how direct numerical

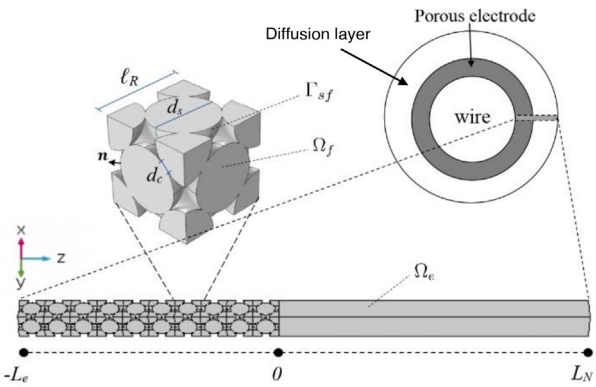

Fig. 1. 3D domain for the direct numerical simulation. In the porous electrode, the fluid occupies the domain Ω_f colored in gray. The solid phase corresponds to the transparent region with the solid/fluid interface Γ_{sf}. FCC unit cell (top left). Computational domain including the electrode part saturated by the fluid ($-L_e \le z \le 0$) and the diffusion layer ($0 \le z \le L_N$) (bottom). Section of the electrode, normal to the bare wire axis (top right).

simulation of the original 3D pore-scale problem, when required, can be carried out. Nevertheless, the latter is not supposed to be performed routinely and does not constitute the core of the method reported here. Indeed, this method leads to a powerful numerical tool for predicting the behavior of bio porous-electrode with a considerable speed-up compared to direct numerical simulations [1], and for the electrode's design in the sense of [3,4]. Voltammetry experiments, carried with several gold porous-electrodes with different thicknesses, functionalized with a bilirubin oxidase reported in [1], serve as illustrative data for the modeling procedure. The macroscopic equations solved with COMSOL Multiphysics are directly coupled with a parameter identification procedure, carried out in Matlab, in order to determine the unknown electrochemical parameters involved in the experiments. To summarize, the method reported here involves three main steps, i.e., (i) solution of the closure problem on a representative unit cell of the electrode material (solved with a COMSOL Multiphysics code). This step provides a more accurate solution for estimating the effective coefficients, in comparison to predictive correlations for the effective diffusivity (see for instance [5,6]); (ii) solution of the macroscale problem in the reduced 1D corresponding domain (COMSOL Multiphysics code); (iii) use of this solution together with a fitting procedure (Matlab code) to identify missing electrochemical parameters, if required, and/or predict the behavior of the current produced by the electrode. In addition, direct numerical simulation (DNS) of the 3D pore-scale model, providing the pore-scale concentration fields, can be performed with another COMSOL Multiphysics code to compute the current delivered by the electrode. This solution, once averaged, may be compared to that of the macroscale problem to validate the upscaled model, as reported in [1].

Without any restriction, the physico-chemical process is illustrated in the following by considering the reduction of O_2 at the cathode in which bilirubin oxidase (BOD) has been adsorbed at the pore surface. Current production results, at the cathode, from diffusion of O_2 within the open pores of the porous medium and reduction within the BOD catalytic layer, the electron transfer to the pore surface occurring in DET mode. The same modeling can be generalized to any other catalyzed reaction for which electron transfer occurs in DET mode.

Direct numerical simulation of the pore-scale model

At the pore-scale, the process is governed by the microscopic model summarized below (see [1] for details).

- Microscopic model

The BOD enzyme deposited onto the solid surface of the porous skeleton to reduce the oxygen contains type 1 copper at T_1 sites and types 2 and 3 copper at *TNC* sites. The oxidized enzyme *Ox* accepts n_1 electrons from the solid to form the reduced enzyme *Re* ata T_1 site. They are transferred from the T_1 site toa *TNC* site where reduction of oxygen takes place. The catalytic reactions in this DET mode can be written in the following form

$$Ox + n_1 e^- \underset{k_{1a}}{\overset{k_{1c}}{\rightleftharpoons}} Re \text{ at } T_1 \text{ site} \tag{1}$$

$$\frac{4}{n_1} Re + O_2 + 4H^+ \underset{k_{2a}}{\overset{k_{2c}}{\rightleftharpoons}} \frac{4}{n_1} Ox + 2H_2O \text{ at TNC site} \tag{2}$$

where k_{1a} and k_{1c} are the electron transfer rate constants, whereas k_{2a} and k_{2c} are the catalytic rate constants.

The diffusion equation of oxygen at the pore-scale level is given by

$$\frac{\partial c_{O_2}}{\partial t} = \nabla \cdot \left(D_{O_2} \nabla c_{O_2} \right) \quad in\ \Omega_f \tag{3}$$

with the interface condition given by

$$-\boldsymbol{n} \cdot D_{O_2} \nabla c_{O_2} = k_{2c} c_{Re} c_{O_2} - k_{2a} (c_E^t - c_{Re}) \quad at\ \Gamma_{sf} \tag{4}$$

together with the outer boundary conditions (at the macroscopic boundaries of the computational domain; see Fig. 1) and initial conditions. The mass balance of the reduced enzyme at the solid/fluid interface is written as

$$\frac{\partial c_{Re}}{\partial t} = (k_{1c} + k_{2a})c_E^t - \left(k_{1c} + k_{1a} + k_{2a} + k_{2c}c_{O_2}\right)c_{Re} \quad at\ \Gamma_{sf} \tag{5}$$

supplemented by the initial condition.

In the above equations, c_{O_2} and D_{O_2} are the oxygen bulk molar concentration and diffusion coefficient in the fluid saturating the electrode, whereas c_{Re} and c_E^t are the reduced and total surface enzyme concentrations. Note that c_E^t is constant. Moreover, Ω_f and Γ_{sf} denote the fluid domain and the solid-fluid interface, which unit normal directed from the fluid to the solid is $\boldsymbol{n}$.

The total current produced by the electrode is given by

$$I = \int_{\Gamma_{sf}} F\left(k_{1a}c_{Re} - k_{2c}\left(c_E^t - c_{Re}\right)\right)dS \tag{6}$$

Here, F is Faraday's constant.

- Direct numerical simulation

The direct numerical simulation of the microscopic model can be performed in a 3D geometry using the software COMSOL Multiphysics. The porous electrode is made of periodic FCC unit cells in the z-direction and periodic conditions are imposed in the x and y-directions (see Fig. 1), that are equivalent to a zero-flux conditionin a symmetric structure. This structure is chosen as it realistically represents the actual structure as discussed in [4]. In addition, to allow oxygen diffusion through the porous medium, a connection window between two spherical adjacent pores is considered. This window corresponds to an open disk of diameter d_c (see Fig. 1, top right). In the vicinity of the electrode, a diffusion layer of thickness L_N is considered as part of the computational domain where diffusion of oxygen takes place.

The microscopic Eqs. (3)–(5), subject to the outer boundary and initial conditions can be solved with COMSOL Multiphysics 5.4 (or more recent versions) by using the *Transport of Diluted Species* for the diffusion/reaction problem of oxygen and *ODE interfaces* for the mass balance equation of enzyme. Typically, a zero oxygen flux is considered at $z = -L_e$ and a constant concentration $c_{O_2} = c_{O_2}^0$ at $z = L_N$, while at $t = 0$, $c_{O_2} = c_{O_2}^0$ in the whole fluid domain inside the porous medium and in the diffusion layer, and $c_{Re} = 0$ at Γ_{sf}.

The COMSOL Multiphysics program *3D-DNS_comparison.mph* that solves this model can be downloaded at the following link https://www.researchgate.net/publication/356,907,533_Codes_dedicated_to_MethodsX_paper

It should be noted that the direct numerical simulation does not constitute the essential element of the method described in this article. Nevertheless, it is provided here for completeness as it may be used in some circumstances for validation purposes. The solution of the macroscopic model is to be preferred and is described in the following paragraphs.

Simulation of the macroscopic model and validation

- Macroscopic equations

The macroscopic mass transport and balance equations for the oxygen and enzyme are obtained by upscaling the above pore-scale problem. They are given by

$$\varepsilon_f \frac{\partial \langle c_{O_2}\rangle^f}{\partial t} = \nabla \cdot \left(\varepsilon_f \boldsymbol{D}_{eff} \cdot \nabla \langle c_{O_2}\rangle^f\right) - k_{2c}a_v\langle c_{O_2}\rangle^f\langle c_{Re}\rangle_{sf} - k_{2a}a_v\left(\langle c_{Re}\rangle_{sf} - c_E^t\right) \qquad in\ \Omega \tag{7}$$

and

$$\frac{\partial \langle c_{Re}\rangle_{sf}}{\partial t} = -(k_{1c} + k_{1a} + k_{2a})\langle c_{Re}\rangle_{sf} - k_{2c}\langle c_{Re}\rangle_{sf}\langle c_{O_2}\rangle^f + (k_{1c} + k_{2a})c_E^t \qquad in\ \Omega \tag{8}$$

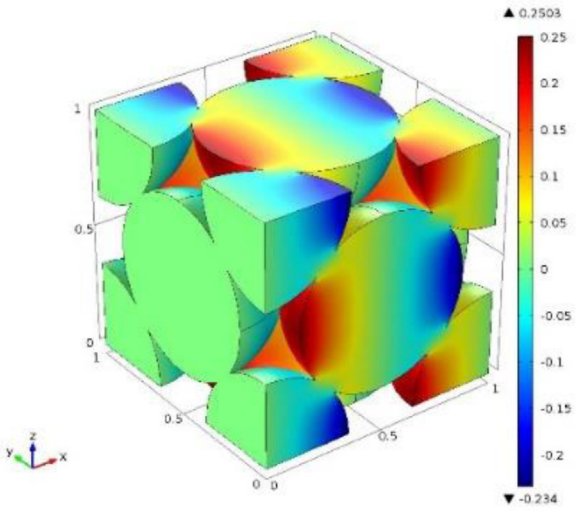

Fig. 2. Numerical result on the x-component of $\boldsymbol{b}$ in a FCC structure. $\varepsilon_f = 0.763$.

where $\langle c_{O_2}\rangle^f$ and $\langle c_{Re}\rangle_{sf}$ denote the volume and surface averaged concentrations of oxygen and reduced enzyme respectively. In addition, ε_f is the porosity and a_v the specific area, i.e., the fluid-solid interfacial area per unit volume of the porous structure. The effective diffusivity tensor $\boldsymbol{D}_{eff}$ depends on the microstructure of the medium. It is obtained from the following expression

$$\boldsymbol{D}_{eff} = D_{O_2}\left(\boldsymbol{I} + \frac{1}{V_f}\int_{A_{sf}} \boldsymbol{nb}\,dA\right) \tag{9}$$

in which $\boldsymbol{I}$ is the identity tensor, whereas V_f and A_{sf} respectively represent the volume of the fluid domain and the fluid-solid interface contained in the porous unit cell. Moreover, $\boldsymbol{nb}$ is the outer product between vectors $\boldsymbol{n}$ and $\boldsymbol{b}$, the latter being solution of the following closure problem defined in the unit cell (cube of edge size ℓ_R) of the porous material (see top left of Fig. 1)

$$\begin{aligned} &\nabla^2\boldsymbol{b} = 0 \quad in\ \mathrm{V}_f \\ &\boldsymbol{n}\cdot\nabla\boldsymbol{b} = -\boldsymbol{n} \quad at\ A_{sf} \\ &\langle\boldsymbol{b}\rangle^f = 0 \end{aligned} \tag{10}$$

supplemented by periodic boundary conditions at the edges of the unit cell in the three directions.

The total current is given by

$$I = n_1 a_v \int_{\Omega} F\left(k_{1a}\langle c_{Re}\rangle_{sf} - k_{1c}\left(c_E^t - \langle c_{Re}\rangle_{sf}\right)\right)dV \tag{11}$$

In the above equations, Ω represents the entire electrode domain.

- Computation of the effective coefficient

The closure problem Eq. (10) can be solved in a representative elementary volume in order to compute the vector b and then the effective diffusivity tensor from Eq. (9). In Fig. 2, the field of the x-component of vector b is represented in the case of a FCC structure with $\varepsilon_f = 0.763$. Since the FCC structure is isotropic, all the other diagonal components are the same and $\boldsymbol{D}_{eff}$ is a spherical tensor.

The program *Effective_coefficient.mph* that solves the closure problem is available at the following link https://www.researchgate.net/publication/356,907,533_Codes_dedicated_to_MethodsX_paper

It should be emphasized that the numerical simulation of the closure problem is not restricted to an ideal structure, but can be generalized to any geometry, like a real structure reported in [4].

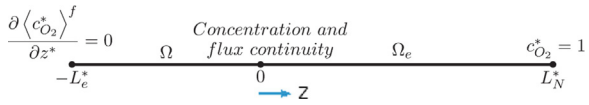

Fig. 3. 1D configuration of the macroscopic domain for the simulation of the upscaled model.

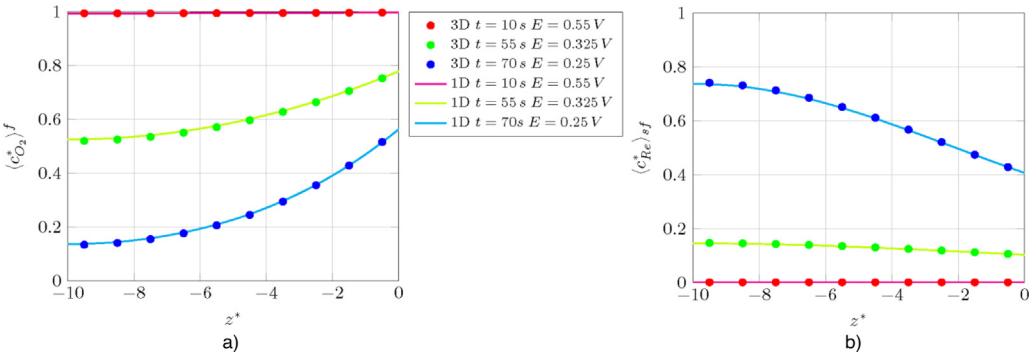

Fig. 4. Comparison of the oxygen (a) and reduced enzyme (b) average concentration profiles at three different times obtained from 3D DNS and predicted from the 1D macroscopic model.

- Simulation of the macroscopic model in the reduced domain and validation

The macroscopic domain to be considered at this level is now 1D, as schematized in Fig. 3 Eqs. (7) and (8) are to be solved in the electrode domain, Ω, whereas, in the fluid domain corresponding to the diffusion layer, Ω_e, Eq. (3) is to be considered as only diffusion of O_2 occurs. The macroscopic boundary conditions correspond to those employed for the pore-scale model, namely, a zero-oxygen flux at $z = -L_e$, continuity of the average oxygen concentration and flux at $z = 0$ and the Dirichlet condition $c_{O_2} = c^0_{O_2}$ at $z = L_N$. Accordingly, the initial conditions are $\langle c_{O_2} \rangle^f = c^0_{O_2}$, $\langle c_{Re} \rangle_{sf} = 0$ in Ω and $c_{O_2} = c^0_{O_2}$ in Ω_e. The equations are rewritten in a dimensionless form using ℓ_R, $\frac{\ell_R^2}{D_{O_2}}$, $c^0_{O_2}$ and c^t_E as the reference length, time, oxygen and enzyme surface concentrations, respectively, with the dimensionless variables denoted with the superscript * (see [1] for the details).

The COMSOL program *1D_DET_comparison.mph* to solve the macroscopic problem can be found here https://www.researchgate.net/publication/356,907,533_Codes_dedicated_to_MethodsX_paper

The reduced enzyme and oxygen average concentration profiles along the electrode can be obtained versus time and compared with DNS results, once numerically averaged using a moving averaging domain having the size of a unit cell, for validation purposes. A comparison is illustrated in Fig. 4 (see [1] for details on the parameters used for the simulations), showing excellent agreement.

In addition, the current density dependence upon the potential predicted from the macroscopic model (Eq. (11)) can be compared to that obtained from DNS of the microscopic model (Eq. (6)). An example of the comparison between the current obtained from the two approaches is represented in Fig. 5, further proving the relevance and accuracy of the 1D upscaled model as already reported in the original article [1].

Advantageously, the latter is much faster to simulate than the pore-scale model (speedup of roughly 1300). Due to its relevance and performance, the 1D model can hence be routinely used in different ways that are shortly detailed in the following section.

Parameters identification and prediction of the electrode behavior

- Parameters identification

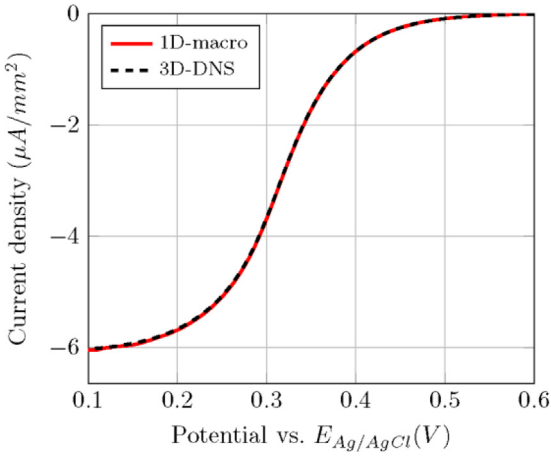

Fig. 5. Current versus potential obtained from a 3D DNS and predicted from the solution of the 1D upscaled model. See [1] for details on the parameters used for the simulations.

The 1D macroscopic model can be first used as a tool to identify electrochemical parameters characteristic of an electrode/reagents system operating in DET mode. To do so, a COMSOL Multiphysics program to solve the macroscopic equations with given parameter values was implemented in a cylindrical system of coordinates, namely *1D_model_Livelink.mph*. The output of the program is the total current according to the scanning potential, E, applied to the electrode, whereas the input refers to the reaction rates k_0, k_{2c}, the electron transfer coefficient α, the standard potential of the redox center E^0, the total enzyme concentration c_E^t, and the diffusion layer thickness L_N. Note that, due the quasi irreversible character of the oxygen reduction, k_{2a} can be reasonably taken equal to zero. The parameters α and E^0 are involved in the electron transfer rate coefficients that can be expressed as $k_{1a} = k_0 Exp(\frac{n_1(1-\alpha)F(E-E^0)}{RT})$ and $k_{1c} = k_0 Exp(-\frac{n_1\alpha F(E-E^0)}{RT})$, R being the ideal gas constant, T the temperature and n_1 the number of exchanged electrons that is known a priori. A Matlab function, namely *Comsol_fun_NO_bubbling.m*, is used to manage the input and output of the COMSOL Multiphysics program. This function is used in the main Matlab program. This program, named *Optimization_NO_bubbling.m*, allows the above-mentioned parameters identification by fitting experimental data.

As an example, experimental data stored in a text file (see *Exp_result_NO_bubbling.txt* at https://www.researchgate.net/publication/356907533_Codes_dedicated_to_MethodsX_paper) can be read in the program to provide experimental voltammetry curves for four electrodes with different thicknesses. The electrode thickness is denoted by the number of half layers (HL) of beads (pores) deposited on the bare-wire, namely 3HL, 7HL, 11HL, 19HL. To fit the experimental curves, the function *lsqcurvefit* is employed with controllable options, such as the function and optimality tolerances. To proceed with the parameter identification, the 11HL data set is first fitted, yielding k_0, k_{2c}, α, E^0, c_E^t and L_N for this particular electrode. Because, k_0, k_{2c}, α and E^0 can be considered as characteristic of the system under study and independent of the electrode thickness, they are kept unchanged for the three other electrodes. However, c_E^t and L_N are thickness-dependent parameters and, in the absence of any other information to predict them, they are fitted with a similar procedure for the other electrodes.

As shown in Fig. 6, a satisfactory fitting is achieved for the four electrodes, proving that the procedure is consistent and that the parameters involved in the experiments under concern are well identified. Again, this highlights that the essential of the physics involved at the microscale is captured by the upscaled 1D model.

- The 1D model as a predictive tool

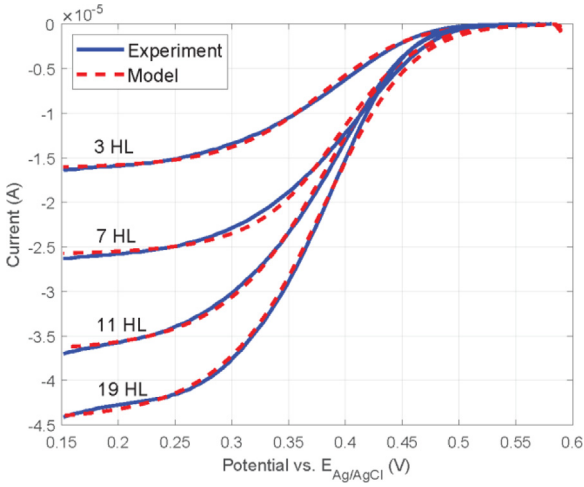

Fig. 6. Examples of current versus potential for four electrodes of different thicknesses obtained experimentally and from the 1D model after parameters identification. See [1] for details.

An alternative use of the numerical tool that solves the 1D upscaled model is to predict the behavior of a given electrode. Indeed, should all the electrochemical parameters be known (they may be identified with alternative means), the program *1D_DET_comparison.mph* can be employed as a predictive tool, providing the electrode behavior (current versus potential characteristics and concentration profiles inside the electrode). It can be further used to optimize the design of an electrode.

It must be emphasized that the macroscopic model does not make any special assumption on both the macroscopic shape of the electrode and on the microstructure (pore-shape). Although in the present article, the numerical procedures were illustrated on a cylindrical electrode deposited on a cylindrical substrate, they can be readily applied to a plane geometry, for instance, with little straightforward modifications in the numerical tools provided as supplementary materials. In particular, the codes *Effective_coefficient.mph* that solves the closure problem and *1D_DET_comparison.mph* can be used for a plane electrode.

As a final remark, it should be noted that the use of the macroscopic model is subject to constraints that can be summarized as follows. First, a scale hierarchy is expected to hold between the pore size, the size of the representative elementary volume and the macroscopic size of the electrode. Second, the observation time of the process should be such that $t \gg O(\frac{\ell_p^2}{D_{O_2}},\ \frac{1}{k_{1c}+k_{1a}+k_{2a}+k_{2c}\langle c_{O_2}\rangle^f})$, ℓ_p denoting the pore size (in the case illustrated in this paper, $\ell_p \equiv d_s$, see Fig. 1). Finally, the kinetic number, Ki, of the process should satisfy $Ki = \frac{k_{2c}\ \ell_p c_E^t}{D_{O_2}} \ll 1$. These constraints are, most of the time overly severe and the model usually remains accurate far beyond these limits. Nevertheless, in case they are not satisfied, one may carry out a direct numerical simulation to check the validity of the solution.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.mex.2022.101655.

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