

Electrochemical Impedance Spectroscopy in carbonate buffered media for biosensing applications

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Abstract

We present the development of a COMSOL model aimed at optimizing and pre-validating the design of a micro-electrode based Electrochemical Impedance Spectroscopy (EIS) sensor. These electrodes are intended for measuring the EIS response in carbonate-buffered media typically used for biological cell perfusion in organ-on-chip applications. Using a 1D EIS model of a two-electrode system, we simulated the electrode-electrolyte interaction, including the bulk reaction of the buffer solution, with sinusoidal voltage excitation at the electrode. We evaluate impedance plots for two different electrode spacings, providing valuable insights into the optimal electrode design for such electrolyte media.

Keywords: Impedance spectroscopy, carbonate buffered media, electrode design

Introduction

Electrochemical Impedance Spectroscopy (EIS) is a technique commonly used to investigate the properties of the electrode surface and the bulk electrolyte in an electrochemical cell [1]. An AC excitation signal is applied with a frequency range, typically from 0.1 Hz to 1 MHz, and the resulting impedance response, consisting of magnitude of impedance $|Z|$ and phase shift, is evaluated. In an electrolyte, the impedance response at low frequencies (typically below 100 Hz) provides information about the characteristics of the electrode surface, i.e., double layer capacitance, whereas, at higher frequencies (typically in the kHz range), the impedance is primarily governed by the bulk electrolyte resistance [1]. In biosensing applications, EIS technique can be used to detect biomarkers by monitoring the electrode-electrolyte interactions as well as the bulk electrolyte properties [2].

To design an EIS electrode for a specific frequency range, it is crucial to have a thorough understanding of the electrode-electrolyte interface and the bulk electrolyte properties. While simplified estimations can be made for electrode geometries such as a parallel plate capacitors and inert electrolytes (those with no bulk or electrode surface reactions) using a simple Randles's circuit, the calculations become cumbersome and inaccurate when dealing with the complex electrode geometries such as planar interdigitated electrodes. Moreover, the bulk reactions in the electrolyte add further complexity. In such cases, numerical simulation offers a more effective solution.

Theory

Impedance spectroscopy

In impedance spectroscopy a periodic excitation, such as sinusoidal voltage signal, is applied between two electrodes and the resulting current response is

measured. Depending on the applied frequency of excitation voltage, the current response has a phase shift. The expression for such an excitation signal, E , and the resulting current response, I , is given in equation (1) and (2).

$$E = E_0 \sin(\omega t) \quad (1)$$

$$I = I_0 \sin(\omega t + \varphi) \quad (2)$$

Here, E_0 and I_0 are the amplitude of the voltage and current, φ is the phase shift of the current response and ω is the angular frequency, which is equal to $2\pi f$, where f is the excitation frequency in hertz.

The impedance is then evaluated using the Ohm's law. The impedance spectroscopy data can be presented as a Bode plot [1]. In Bode plot, the magnitude of the impedance and the phase shifts are plotted against the applied excitation frequencies. The phase shift, φ , is then extracted by comparing the phase of the current response to the applied voltage. The magnitude of impedance, $|Z|$, is evaluated as shown in equation (3).

$$|Z| = E_0 / I_0 \quad (3)$$

Impedance of an electrode in an electrolyte can be understood from a simple Randle's circuit, as shown in Figure 1 [1]. This circuit corresponds to an ideally polarizable electrode. The electrode-electrolyte interface is expressed as a double layer capacitance, C_{dl} and the electrolyte resistance is expressed as simple resistor, R_s . A typical impedance spectroscopy response of such a system using micro-electrodes (electrode dimension in the order of 10 μm) is shown in Figure 2.

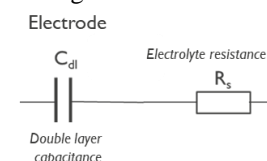


Figure 1: Simple Randle's circuit

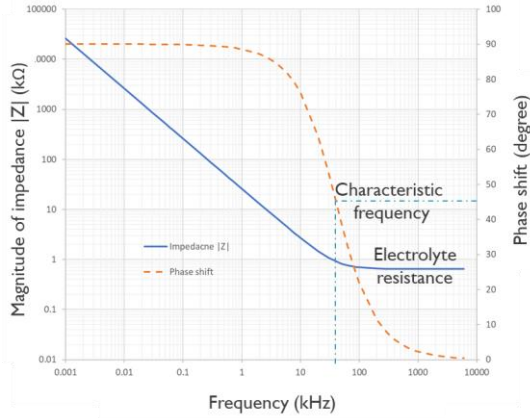
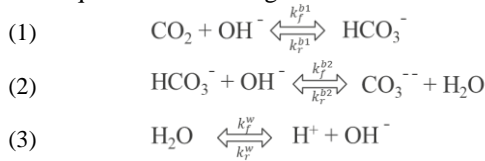


Figure 2: A typical impedance spectroscopy response of an electrochemical cell based on the simple Randle's circuit

Figure 2 is the bode plot representation of the impedance. The frequency at which the phase shift is 45° is called the characteristic frequency and is equal to $1/R_s C_{dl}$. The phase-shift changes from 90° at low frequencies to 0° at high frequencies. The magnitude of the impedance, $|Z|$, decreases with the increase in excitation frequency and at higher frequencies ($>$ characteristic frequency) it reaches plateau. The values of $|Z|$ at the plateau gives the resistance of the electrolyte R_s .

Electrolyte

The electrolyte for this model is a carbonate buffered solution composed of 100 mM potassium bicarbonate (KHCO_3). Carbonate buffered solutions are one of the most relevant media for biomedical applications to maintain pH while mimicking the human physiology conditions [3]. In total there are five ionic species in the electrolyte: K^+ , OH^- , HCO_3^- , CO_3^{2-} and H^+ ions. The buffer reactions of this salt in the aqueous media are given as follows.



All the ions and molecules in these reactions are denoted with their standard chemical symbol and charge numbers. Here, k_f^{b1} and k_r^{b1} are forward and reverse rate constant of reaction (1), k_f^{b2} and k_r^{b2} are forward and reverse rate constant of reaction (2) and k_f^w and k_r^w are forward and reverse rate constant for water dissociation, reaction (3). The reaction rate values for each reaction are taken from literature [4] and will be used in the model to define the electrolyte media.

Governing equations

In this model we need to solve the ion concentrations and the resulting potential drop in the electrolyte to evaluate the impedance. Two main equations will be used to solve these parameters: Poisson and Nernst-Planck equations. The electrostatic behavior of the ion species is defined by the Poisson equation as:

$$\nabla^2 \phi + \frac{F \sum_i z_i c_i}{\epsilon_0 \epsilon_r} = 0 \quad (4)$$

The transport of ions, i.e., the flux, J_i , of each species is given by the Nernst-Planck equation as:

$$J_i = -D_i \nabla c_i - \frac{D_i z_i F c_i \nabla \phi}{RT} \quad (5)$$

These equations will be solved in a time-dependent simulation, by determining the rate of change of the concentration, which is then given by the continuity equation:

$$\frac{\partial c_i}{\partial t} = -\nabla \cdot J_i + R_i \quad (6)$$

By incorporating equation (5), this rate of the change of concentration for ion species, i , is given by:

$$\frac{\partial c_i}{\partial t} = D_i \nabla^2 c_i + \frac{D_i z_i F \nabla (c_i \nabla \phi)}{RT} + R_i \quad (7)$$

In these equations (4) – (7), ϕ is the potential profile, F is the faraday constant, $\epsilon_0 \epsilon_r$ is the permittivity of water, z_i is the charge number, D_i is the diffusion coefficient, R_i is the reaction rate constant and c_i is the concentration of the species i . R is the general gas constant and T is the absolute temperature. The model will use these equations to determine concentration of each species and the potential profile in the electrolyte in time and space.

Use of COMSOL Multiphysics

The equations defined to solve the model are implemented in the COMSOL Multiphysics 6.1 platform, using the ACDC and electrochemical modules with the underlying physics of Electrostatics (es) and Transport of dilute species (tds), respectively. The details of each important step in the modelling are described in the following sections.

Variables

The first step is to define the variable involved in the model. The model will solve for the potential profile in the electrolyte and the concentration of five ionic species in the electrolyte. The details of the variable are mentioned in Table 1. Moreover, the table of parameters used in this model is given in appendix table A.

Table 1: Variables details

Symbol	Details	Unit
ϕ	Electrolytic potential	V
c_H	H^+ concentration	mol/m^3
c_K	K^+ concentration	mol/m^3
c_{OH}	OH^- concentration	mol/m^3
c_{CO_3}	CO_3^{2-} concentration	mol/m^3
c_{HCO_3}	HCO_3^{-1} concentration	mol/m^3

Geometry

1D geometry for two electrodes as two points with the distance between electrode as L . For L , $20 \mu\text{m}$ is used. The electrode at which the voltage signal is

applied is at distance $x = 0$ and the second electrode which is at ground is at distance $x = L$.

Boundary conditions

When solving for the potential profile near the electrode surface, the stern layer thickness, λ_s (ca. 0.5 nm), also needs to be considered. The stern layer results in a potential drop between electrode and electrolyte. This means that at both the electrode boundaries, the sum of stern layer drop, and the electrolyte potential is equal to the applied external potential at the electrode, so boundary conditions at:

- 1- $x = 0$ (boundary 1); $\lambda_s(n \cdot \nabla\phi) + \phi = \phi_M$
- 2- $x = L$ (boundary 2); $\lambda_s(n \cdot \nabla\phi) + \phi = 0$

Here, ϕ_M is the applied voltage at electrode 1 ($x=0$). The applied potential at electrode 2 ($x=L$) is zero since it is at ground. The surface normal vector n is oriented outwards away from the bulk electrolyte. Moreover, there are no-flux conditions at both the boundaries, so:

- 3- $x = 0$ (boundary 1); $n \cdot J_i = 0$
- 4- $x = L$ (boundary 2); $n \cdot J_i = 0$

Initial conditions

Initially, there is no applied potential, and the electrolyte is charge neutral, meaning there is no potential drop in the electrolyte, so electrolyte potential, $\phi = 0$. Moreover, the initial concentration of each ion species is equal to their bulk electrolyte concentration, i.e., $c_i = c_{i_bulk}$.

Bulk electrolyte reaction

Since there are five ionic species as variables, which the model will solve the concentration profiles for, the reaction for each species is defined. The reaction rates for each species are given in equation (8) to (12). These reaction rates are used to determine the rate of change of concentration for each species in equation (7).

$$R_{OH} = -k_r^w c_H c_{OH} - k_f^{b2} c_{OH} c_{HCO_3} - k_f^{b1} c_{CO_2} c_{OH} + k_f^w + k_r^{b2} c_{CO_3} + k_r^{b1} c_{HCO_3} \quad (8)$$

$$R_{HCO_3} = -k_f^{b2} c_{OH} c_{HCO_3} - k_r^{b1} c_{HCO_3} + k_f^{b1} c_{CO_2} c_{OH} + k_r^{b2} c_{CO_3} \quad (9)$$

$$R_{CO_3} = -k_r^{b2} c_{CO_3} + k_f^{b2} c_{OH} c_{HCO_3} \quad (10)$$

$$R_H = -k_r^w c_H c_{OH} + k_f^w \quad (11)$$

$$R_k = 0 \quad (12)$$

Study: Time dependent

A time dependent study is used to evaluate the change of concentration and the corresponding electrolyte potential over time.

Post processing

The current density, I_t , at the electrode boundary can be estimated from the rate of change of the electric field, E . The electric field is given by the gradient of the electric potential, $-\nabla\phi$. The electric current density is then estimated by the Gauss law in integral form at the electrode surface, and given by:

$$I_t = \epsilon_0 \epsilon_r \frac{dE}{dt} \quad (13)$$

Once the current response is determined from the sinusoidal voltage excitation, the impedance can be represented by the magnitude, $|Z|$ and the phase shift, ϕ , from equation (1) to (3). For the impedance spectroscopy, multiple voltage excitation frequencies are applied, i.e., 0.1, 1, 10, 100, 1k, 5k, 10k, 50k, 100k, 1M and 10M Hz, and the corresponding magnitude of impedance and phase shift are determined and displayed as a bode plot.

Simulation Results and Discussions

Step voltage response

For the validation of the model, a step voltage is applied at the electrode 1. The applied step voltage and the corresponding current response is shown in Figure 3.

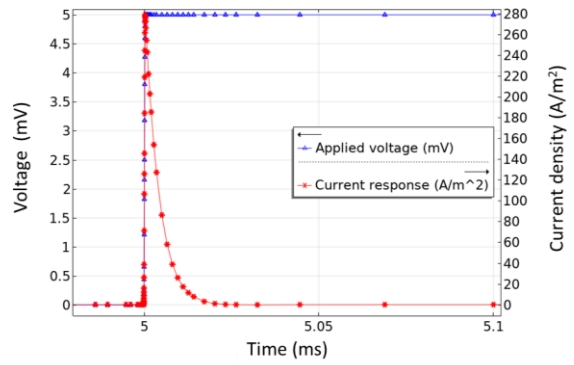


Figure 3: Step function response

The voltage step of 5 mV with a rise time of 0.5 μ s is applied at 5 ms and the corresponding current response is measured from equation (13). So, voltage at the electrode is zero just before 5 ms and after 5 ms the voltage at the electrode rises to 5 mV. The electrolyte with ions is considered as charge neutral, meaning the potential drop in the electrolyte is zero before any potential is applied at the electrode surface. The potential profile across the electrolyte between two electrodes at different time instance close to 5 ms when the voltage step is applied is shown in Figure 4 and Figure 5.

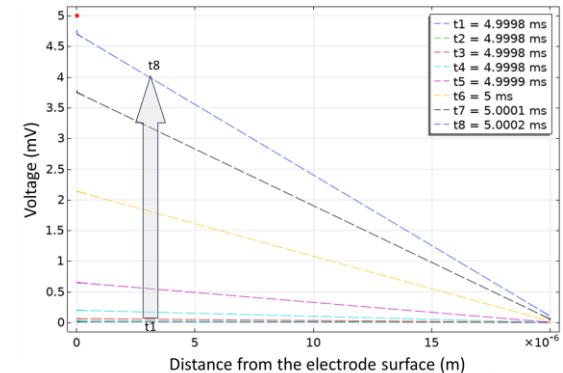


Figure 4: Potential profile over time just before the applied potential step

In Figure 4, the instance from t1 when the voltage started to rise to time t8 when the voltage step reaches 5 mV step are plotted. At t1, the voltage drop is zero, this is just before the voltage step is applied. From t2 to t8, the applied voltage rises over time, giving the linear voltage drop across the electrolyte. After the applied voltage reaches step of 5 mV at t8 (5.0002 ms), the linear voltage drop in the electrolyte starts dropping, as shown in Figure 5 from t8 to t15. The voltage drop transition is from linear to an exponential decay of at the electrode surface. Moreover, there is also a potential drop at the electrode surface from the stern layer thickness. The voltage drops in the electrolyte over time and the voltage drop due to stern layer are expected behavior.

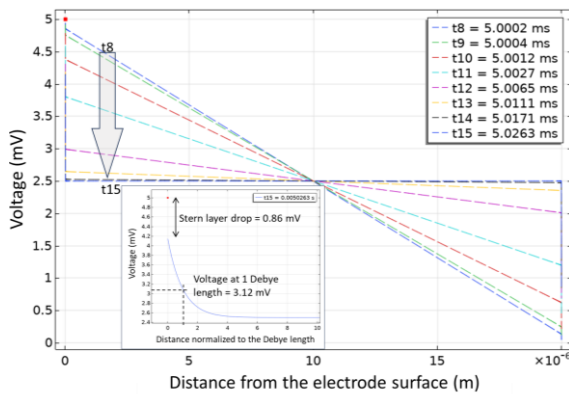


Figure 5: Potential profile in the electrolyte over time after the potential step

To illustrate the voltage-drop across the Stern layer and the voltage drop at the Debye length, λ_D , a zoomed-in view of the voltage at the electrode surface at time t15 is presented as an inset in Figure 5. The Debye length is calculated to be 0.9618 nm using equation (14).

$$\lambda_D = \sqrt{\frac{\epsilon_0 \epsilon_r RT}{F^2 \sum_i z_i^2 c_{i_bulk}}} \quad (14)$$

The voltage decreases from 5 mV to 4.14 mV (0.86 mV drop) at the electrode surface due to the Stern layer. Beyond the Stern layer, the voltage exhibits an exponential decline, decreasing from 4.14 mV to 3.12 mV (1.02 mV drop) over the Debye length.

Sinusoidal excitation response

For impedance measurement a sinusoidal excitation voltage is usually applied, and the resulting current response is measured as discussed before. Depending on the applied frequency the amplitude and phase shift of the current response changes. The sinusoidal excitation voltage of 1 kHz and its corresponding current response are shown in Figure 6. In this case the current response has a phase of 90° as compared to the applied voltage signal. The magnitude of impedance can be estimated from the amplitude of voltage and current, from equation (3), and is found to be $6.68 \cdot 10^{-4} \Omega m^2$. It is also observed

that the current response needs some cycles to stabilize, in this case 3 cycles. Therefore, for impedance calculations we use the last cycle of the current response.

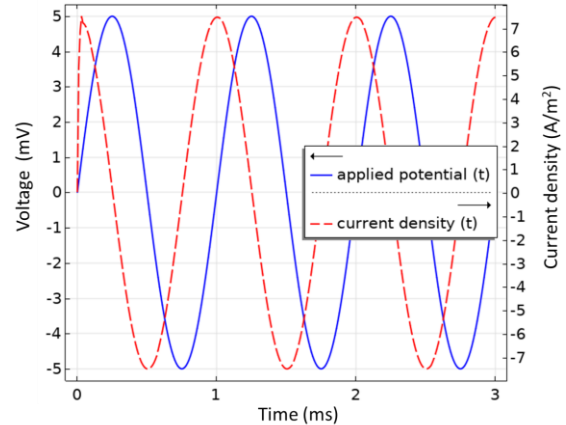


Figure 6: Applied sinusoidal voltage of 1 kHz and the corresponding current response

To observe the influence of excitation frequency on the impedance, an excitation frequency of 1 MHz is applied. The applied voltage and current response are shown in Figure 7. As expected from an electrode in an electrolyte, the phase shift will decrease with the increase in frequency. The phase shift reaches zero and the voltage and current as in-phase. In this case the magnitude of impedance is $1.73 \cdot 10^{-5} \Omega m^2$. For the impedance spectroscopy plot, the magnitude and phase shift are measured and plotted at different frequencies, 0.1 Hz to 10 MHz.

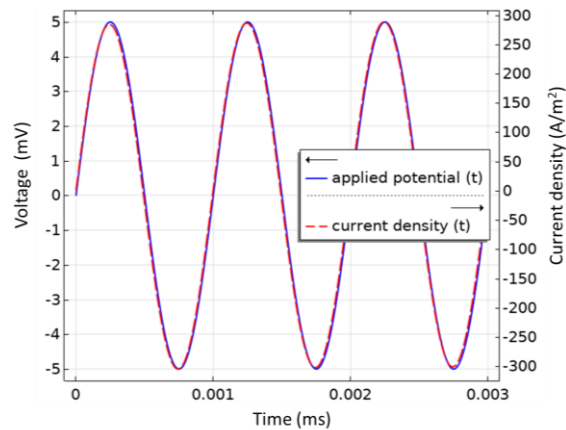


Figure 7: Applied sinusoidal voltage of 1 MHz and the corresponding current response

Impedance spectroscopy: Effect of changing distance between electrodes

The spacing between the electrode is an important design parameter for the sensors based on impedance spectroscopy. Since the absolute electrolyte resistance will change proportionally to the spacing between the electrodes [5]. To evaluate the effect of spacing between the electrodes, the spacing is varied 10 times from 20 μm to 200 μm . The impedance spectroscopy plot comparing two electrodes spacings, 20 μm and 200 μm is shown in Figure 8.

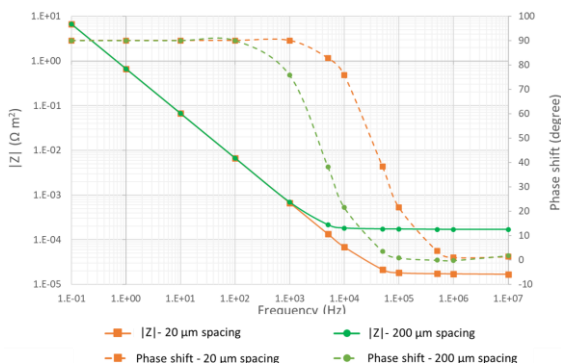


Figure 8: Impedance spectroscopy plot for electrode spacing of 20 μm and 200 μm .

The magnitude of the impedance and the phase shift are plotted against the excitation frequencies, 0.1 Hz to 10 MHz. As expected, the magnitude of impedance decreases with the increase in frequency and plateaus at higher frequencies (after the cut-off or characteristic frequency). The plateau at higher frequencies correspond to the electrolyte resistance. The electrolyte resistance and the characteristic frequency evaluated from these impedance spectroscopy plots are mentioned in Table 2. By increasing the electrode spacing 10 times from 20 μm the characteristics frequency decreases 10 times and the electrolyte resistance increases 10 times.

Table 2: Electrolyte resistance and characteristic frequency from Figure 8

Electrode spacing (μm)	Electrolyte resistance ($\Omega \text{ m}^2$)	Characteristic frequency (kHz)
20	$1.73 \cdot 10^{-5}$	40
200	$1.7 \cdot 10^{-4}$	4

Conclusions

The COMSOL model to determine the impedance between two electrodes has been built for a carbonate buffered solution. The model was based on Electrostatic (es) and Transport of dilute species (tds) of ACDC and Electrochemical module. By solving the concentration of the ion species in an applied electric field, the potential drop in the electrolyte is determined.

The model is validated first with the excitation of a step voltage. The voltage drop across the electrolyte shows an expected potential profile over time just before and after the step voltage is applied. The next validation was performed with the sinusoidal voltage excitation, which is typically used in the determination of impedance spectroscopy. The current response of the sinusoidal voltage excitation shows a phase shift of ca. 90° at lower frequencies and ca. 0° at higher frequencies.

The effect of two electrode spacing on the impedance spectroscopy is performed. The simulation shows the electrolyte resistance increases proportionally with the increase in the electrode spacing and the characteristic frequency decreases

proportionally with the increase in the electrode spacing. This will provide valuable input for electrode design knowing the operational range of the instrumentation.

This model will be further extended to 2D and 3D models to evaluate the performance of different designs (shape and area) of the impedance electrodes and verify the operational range of these sensors before realization of actual devices.

References

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Appendix

Table A: Parameter table

Parameter and symbol		Value	unit
Relative permittivity	ϵ_r	80	
Temperature	T	298	K
Electrochemical-cell length	L	20×10^{-6}	m
Stern layer thickness	λ_s	0.5×10^{-9}	m
Forward reaction rate 1	k_f^{b1}	2.23	$\text{mol}^{-1} \text{m}^3 \text{s}^{-1}$
Reverse reaction rate 1	k_r^{b1}	5.23×10^{-5}	s^{-1}
Forward reaction rate 2	k_f^{b2}	6×10^6	$\text{mol}^{-1} \text{m}^3 \text{s}^{-1}$
Reverse reaction rate 2	k_r^{b2}	1.07×10^6	s^{-1}
Water dissociation forward reaction rate	k_f^w	2.4×10^{-2}	$\text{mol m}^{-3} \text{s}^{-1}$
Water dissociation reverse reaction rate	k_r^w	2.4×10^6	$\text{mol}^{-1} \text{m}^3 \text{s}^{-1}$
Applied external potential vs reference	ϕ_M	5×10^{-3}	V
Bulk concentration (100 mM KHCO_3)	c_{bulk}	100	mol m^{-3}
CO_2 solubility (at 0.04% partial pressure)	c_{CO_2}	32	mol m^{-3}
H^+ initial bulk concentration	$c_{\text{H}^+ \text{ bulk}}$	0.00014	mol m^{-3}
K^+ initial bulk concentration	$c_{\text{K}^+ \text{ bulk}}$	100	mol m^{-3}
OH^- initial bulk concentration	$c_{\text{OH}^- \text{ bul}}$	7.1×10^{-5}	mol m^{-3}
CO_3^{2-} initial bulk concentration	$c_{\text{CO}_3^{2-} \text{ bu}}$	0.039	mol m^{-3}
HCO_3^- initial bulk concentration	$c_{\text{HCO}_3^- \text{ b}}$	99.92	mol m^{-3}
Charge number H^+	z_{H^+}	+1	
Charge number K^+	z_{K^+}	+1	
Charge number OH^-	z_{OH^-}	-1	
Charge number CO_3^{2-}	$z_{\text{CO}_3^{2-}}$	-2	
Charge number HCO_3^-	$z_{\text{HCO}_3^-}$	-1	
H^+ diffusion coefficient	D_{H^+}	9.3×10^{-9}	$\text{m}^2 \text{s}^{-1}$
K^+ diffusion coefficient	D_{K^+}	1.957×10^{-9}	$\text{m}^2 \text{s}^{-1}$
OH^- diffusion coefficient	D_{OH^-}	5.3×10^{-9}	$\text{m}^2 \text{s}^{-1}$
CO_3^{2-} diffusion coefficient	$D_{\text{CO}_3^{2-}}$	0.923×10^{-9}	$\text{m}^2 \text{s}^{-1}$
HCO_3^- diffusion coefficient	$D_{\text{HCO}_3^-}$	1.19×10^{-9}	$\text{m}^2 \text{s}^{-1}$