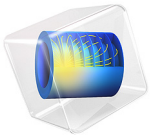


# Electrochemical Treatment of Tumors

## *Introduction*

The electrochemical treatment of tumors implies that diseased tissue is treated with direct current through the use of metallic electrodes inserted in the tumor. When tissue is electrolyzed, two competing reactions take place at the anode: oxygen evolution and chlorine production. The oxygen-evolution reaction also produces $H^+$ ions, which lower the pH close to the anode. It should be stressed that chlorine production also leads to lowered pH through the hydrolysis of chlorine. One effect of low pH is the permanent destruction of hemoglobin in the tissue, which results in destruction of tumor tissue.

$$\begin{aligned} 2Cl^- &= Cl_2(g) + 2e^- \\ 2H_2O &= 4H^+ + O_2(g) + 4e^- \end{aligned} \tag{1}$$

One challenge in developing this method of cancer treatment is in predicting the doses required for tumor destruction. One possible tool for dose planning is by modeling the reactions that take place close to the electrodes.

This example presents a first simple model for the development of dose-planning methods. More advanced models for dose planning, including secondary effects of chlorine, are found in Ref. 1, which also presents and solves models for the cathode.

## *Model Definition*

This model uses the Tertiary Current Distribution, Nernst-Planck interface to predict the transport and reaction in the electrolysis of tumor tissue in a liver. A needle electrode is placed in the tumor, and transport is assumed to take place radially to and from this electrode. Because you can assume rotational symmetry, the computational domain reduces to a line ($r_a$, $r_r$) where $r_a$ is 1 mm and $r_r$ is 6 cm (see Figure 1).

The species you consider in the model are the protons, chloride, and sodium. At the surface of the anode you account for the chlorine and oxygen evolution reactions; see Equation 1.

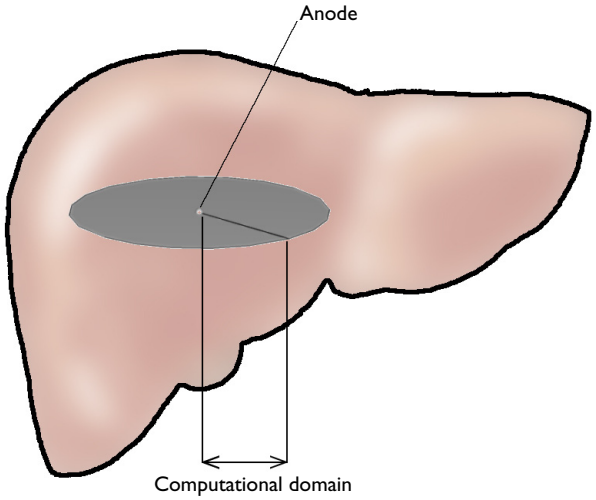



*Figure 1: Diagram of the cylindrical modeling domain inside a tumor.*

This simplified model considers only a 1D model of the transport between two points, that is, between the two electrodes. The material balance for the species $i$ is given by

$$\frac{\partial c_i}{\partial t} + \nabla \cdot (-D_i \nabla c_i - z_i u_{\mathrm{m}i} F c_i \nabla \phi_l) = R_i$$

where $c_i$ is the concentration (SI unit: mol/m$^3$), $D_i$ give the diffusivities (SI unit: m$^2$/s), $z_i$ equals the charge, $u_{\mathrm{m}i}$ represents the mobility (SI unit: (mol·m$^2$)/(J· s)), and $R_i$ is the production term for species $i$ (SI unit: mol/(m$^3$·s)), $F$ denotes Faraday's constant (SI unit: C/mol), and $\phi_l$ is the electrolyte potential (SI unit: V). The mobility, $u_{\mathrm{m}i}$, can be expressed in terms of $D_i$, $R$, and $T$ as

$$u_{\mathrm{m}i} = \frac{D_i}{RT}$$

The conservation of electric charge is obtained through the divergence of the current density:

$$\nabla \cdot \left( F\sum_i z_i^2(-D_i\nabla c_i - z_i u_{\mathrm{m}i} F c_i \nabla \phi_l) \right) = 0$$

At the electrode surface ($r = r_a$) you use the Electrode Surface boundary node to specify the electrode reactions and the resulting fluxes for the ionic species that are included in the electrode reactions, $H^+$ and $Cl^-$. For the inert ionic species, $Na^+$, the transport through the electrode surface equals zero. The expressions for molar fluxes at the boundary are based on the electrode reaction currents according to

$$\mathbf{N}_i \cdot \mathbf{n} = \sum_j \frac{\nu_{ij} j_j}{n_j F}$$

where $\mathbf{N}_i$ is the flux, $\nu_{ij}$ represents the stoichiometric coefficient for the ionic species $i$ in reaction $j$, and $n_j$ is the number of electrons in reaction $j$.

You can express the current densities for the two reactions using the Electrode Reaction nodes. Introducing dimensionless pressure, $P = p/p_b$, and concentration, $C = c/c_b$, (where $b$ denotes the reference concentration), the current density for the oxygen evolution is

$$j_{\mathrm{I}} = j_{\mathrm{I},0}\left\{ e^{\frac{F\eta_{\mathrm{I}}}{2RT}} - (P_{\mathrm{O}_2})^{1/4} C_{\mathrm{H}^+} e^{-\frac{F\eta_{\mathrm{I}}}{2RT}} \right\}$$

where $j_{\mathrm{I}0,}$ is the exchange current density (SI unit: $\mathrm{A/m^2}$) and $\eta_I$ is the overpotential for the oxygen evolution reaction, defined as

$$\eta_{\mathrm{I}} = \phi_s - \phi_l - E_{\mathrm{eq,\,I}}$$

where $E_{\mathrm{eq,I}}$ (SI unit: V) is the equilibrium potential for the oxygen evolution reaction.

Set the electrode potential to

$$\phi_s(t) = \left(0.4977 + 0.2567 \cdot \ln\left(100 + \frac{t}{1\,\mathrm{s}}\right)\right)\ \mathrm{V}$$

where $t$ denotes time.

The chlorine evolution reaction is similarly given by the expression

$$j_{\mathrm{II}} = j_{\mathrm{II},0}\left\{C_{\mathrm{Cl}^-}\, e^{\frac{F\eta_{\mathrm{II}}}{2RT}} - (P_{\mathrm{Cl}_2})^{1/2} e^{-\frac{F\eta_{\mathrm{II}}}{2RT}}\right\}$$

Using the input values $n_{\mathrm{I}} = n_{\mathrm{II}} = 1$, $\nu_{\mathrm{H,I}} = -1$, and $\nu_{\mathrm{Cl,II}} = 1$, gives the fluxes at the electrode surface:

$$N_{\mathrm{H}} \cdot \mathbf{n} = \frac{-j_{\mathrm{I}}}{F}$$

$$N_{\mathrm{Cl}} \cdot \mathbf{n} = -\frac{j_{\mathrm{II}}}{F}$$

At the exterior boundary, assume the concentration is constant, $c_i = c_{i0}$, and ground the electrolyte potential.

The initial concentration is constant: $c_i = c_{i0}$.

## *Results and Discussion*

The plot in Figure 2 shows the pH for different time steps. You can see that values below pH 2 are reached somewhere between 1800 and 2400 s. A closer examination reveals that

it occurs after 2000 s. At this pH, tumor destruction starts to occur very rapidly according to the experimental and theoretical findings in Ref. 1.

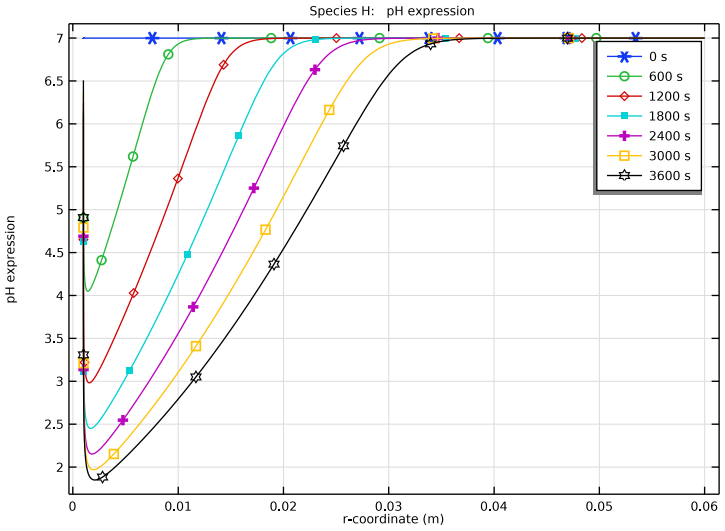



*Figure 2: pH-profiles at different time steps during the treatment.*

The corresponding $H^+$ profile in Figure 3 shows that the concentration maximum is not at the anode surface.

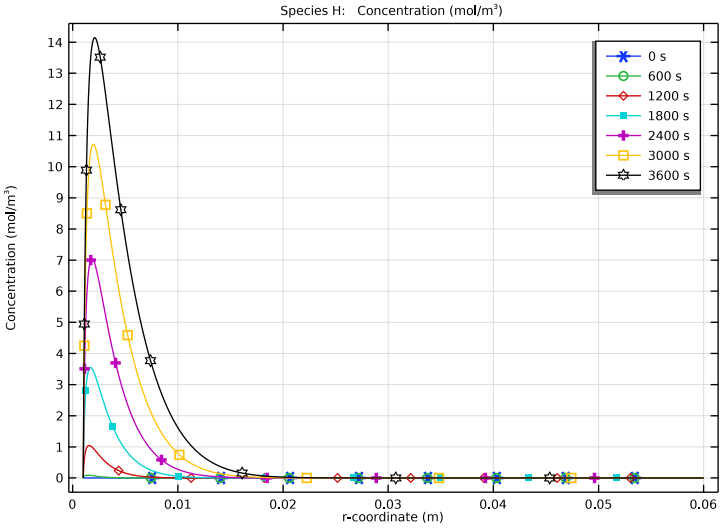



*Figure 3: Proton concentration in the domain at different time steps.*

This result arises because the current density is not constant over time. At high current densities, large amounts of protons are produced and this front moves inward in the domain as the current density is lowered.

The corresponding plot for chloride (Figure 4) shows a continuous decrease of chloride concentration close to the anode surface. This in turn decreases the production of chlorine and increases oxygen evolution.

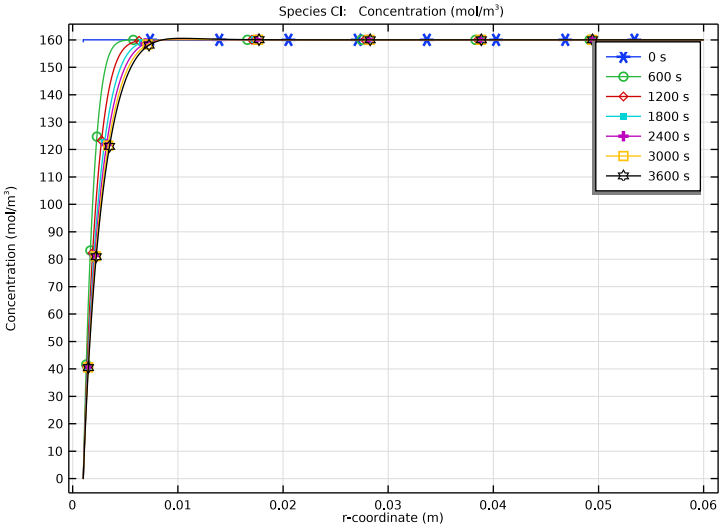



*Figure 4: Chloride concentration at different time steps.*

The current-density plot in Figure 5 shows that the total current decreases rapidly as the concentration overvoltage for chlorine formation increases, due to lowered chloride

concentration at the anode surface. The potential is then increased, which results in an increase in total current through increased oxygen evolution.

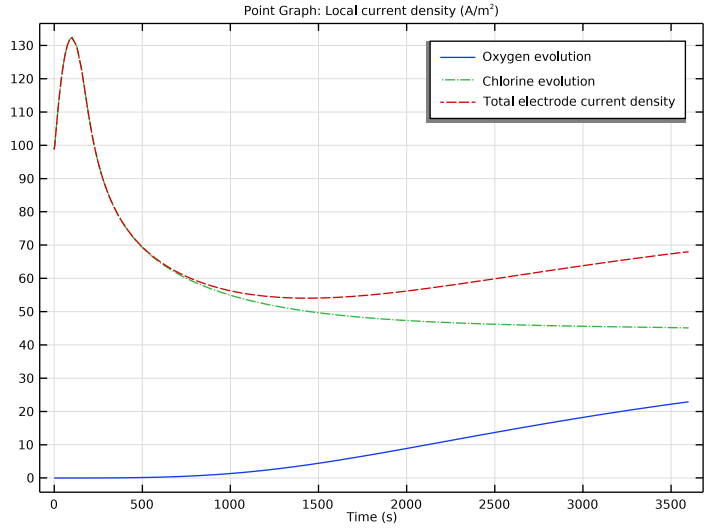



*Figure 5: Total current density and current density for the competing reactions on the anode surface. Oxygen evolution is the lowest graph.*

## *Reference*

1. E. Nilsson, *Modelling of the Electrochemical Treatment of Tumors*, PhD. thesis, Dept. Chemical Engineering and Technology, Royal Inst. of Technology, Stockholm, Sweden, 2000.

**Application Library path:** `Electrochemistry_Module/Electrochemical_Engineering/tumor`

## *Modeling Instructions*

From the **File** menu, choose **New**.

**NEW**

In the **New** window, click **Model Wizard**.

### MODEL WIZARD

1 In the **Model Wizard** window, click **1D Axisymmetric**.

2 In the **Select Physics** tree, select **Electrochemistry>Tertiary Current Distribution, Nernst-Planck>Tertiary, Electroneutrality (tcd)**.

3 Click **Add**.

4 In the **Number of species** text field, type 3.

5 In the **Concentrations** table, enter the following settings:

| |
|---|
| Na |
| H |
| Cl |

6 Click **Study**.

7 In the **Select Study** tree, select **General Studies>Time Dependent**.

8 Click **Done**.

### GLOBAL DEFINITIONS

Start by loading the model parameters and variables from text files.

*Parameters 1*

1 In the **Model Builder** window, under **Global Definitions** click **Parameters 1**.

2 In the **Settings** window for **Parameters**, locate the **Parameters** section.

3 Click **Load from File**.

4 Browse to the model's Application Libraries folder and double-click the file `tumor_parameters.txt`.

### DEFINITIONS

*Variables 1*

1 In the **Home** toolbar, click **Variables** and choose **Local Variables**.

2 In the **Settings** window for **Variables**, locate the **Variables** section.

3 Click **Load from File**.

4 Browse to the model's Application Libraries folder and double-click the file `tumor_variables.txt`.

### GEOMETRY 1

Create the geometry as a single interval.

*Interval 1 (i1)*

1 In the **Model Builder** window, under **Component 1 (comp1)** right-click **Geometry 1** and choose **Interval**.

2 In the **Settings** window for **Interval**, locate the **Interval** section.

3 In the table, enter the following settings:

| Coordinates (m) |
| --- |
| r_a |
| r_ext |

4 Click **Build Selected**.

5 Click the **Zoom Extents** button in the **Graphics** toolbar.

### TERTIARY CURRENT DISTRIBUTION, NERNST-PLANCK (TCD)

Now start with the physics, begin with the electrolyte settings.

*Species Charges 1*

1 In the **Model Builder** window, under **Component 1 (comp1)>Tertiary Current Distribution, Nernst-Planck (tcd)** click **Species Charges 1**.

2 In the **Settings** window for **Species Charges**, locate the **Charge** section.

3 In the $z_{Na}$ text field, type `z_Na`.

4 In the $z_{H}$ text field, type `z_H`.

5 In the $z_{Cl}$ text field, type `z_Cl`.

*Electrolyte 1*

1 In the **Model Builder** window, click **Electrolyte 1**.

2 In the **Settings** window for **Electrolyte**, locate the **Diffusion** section.

3 In the $D_{Na}$ text field, type `D_Na`.

4 In the $D_{H}$ text field, type `D_H`.

5 In the $D_{Cl}$ text field, type `D_Cl`.

*Electrolyte Potential 1*

Now ground the potential of the exterior end, and then define the concentration at the same location.

1 In the **Physics** toolbar, click **Boundaries** and choose **Electrolyte Potential**.

2 Select Boundary 2 only.

*Concentration 1*

1 In the **Physics** toolbar, click **Boundaries** and choose **Concentration**.

2 Select Boundary 2 only.

3 In the **Settings** window for **Concentration**, locate the **Concentration** section.

4 Select the **Species H** check box.

5 In the $c_{0,\mathrm{H}}$ text field, type `H0`.

6 Select the **Species Cl** check box.

7 In the $c_{0,\mathrm{Cl}}$ text field, type `Cl0`.

*Electrode Surface 1*

Now set up the anode, and the anode reactions.

1 In the **Physics** toolbar, click **Boundaries** and choose **Electrode Surface**.

2 Select Boundary 1 only.

3 In the **Settings** window for **Electrode Surface**, locate the **Electrode Phase Potential Condition** section.

4 In the $\phi_{\mathrm{s,ext}}$ text field, type `E_cell`.

*Electrode Reaction 1*

1 In the **Model Builder** window, click **Electrode Reaction 1**.

2 In the **Settings** window for **Electrode Reaction**, locate the **Stoichiometric Coefficients** section.

3 In the $\nu_{\mathrm{H}}$ text field, type `-1`.

4 Locate the **Equilibrium Potential** section. In the $E_{\mathrm{eq,ref}}(T)$ text field, type `E_eqI`.

5 Click to expand the **Reference Concentrations** section. In the table, enter the following settings:

| Electrolyte species | Reference concentrations (mol/m^3) |
|---|---|
| H | H0 |

6 Locate the **Electrode Kinetics** section. In the $i_{0,\mathrm{ref}}(T)$ text field, type `j_I0`.

*Electrode Surface 1*

In the **Model Builder** window, click **Electrode Surface 1**.

*Electrode Reaction 2*

1 In the **Physics** toolbar, click **Attributes** and choose **Electrode Reaction**.

2 In the **Settings** window for **Electrode Reaction**, locate the **Stoichiometric Coefficients** section.

3 In the $\nu_{Cl}$ text field, type `1`.

4 Locate the **Equilibrium Potential** section. In the $E_{eq,ref}(T)$ text field, type `E_eqII`.

5 Locate the **Reference Concentrations** section. In the table, enter the following settings:

| Electrolyte species | Reference concentrations (mol/m^3) |
|---|---|
| Cl | `Cl0` |

6 Locate the **Electrode Kinetics** section. In the $i_{0,ref}(T)$ text field, type `j_II0`.

*Initial Values 1*

1 In the **Model Builder** window, under **Component 1 (comp1)>Tertiary Current Distribution, Nernst-Planck (tcd)** click **Initial Values 1**.

2 In the **Settings** window for **Initial Values**, locate the **Initial Values** section.

3 In the *H* text field, type `H0`.

4 In the *Cl* text field, type `Cl0`.

## GLOBAL DEFINITIONS

*Default Model Inputs*

Set up the temperature value used in the entire model.

1 In the **Model Builder** window, under **Global Definitions** click **Default Model Inputs**.

2 In the **Settings** window for **Default Model Inputs**, locate the **Browse Model Inputs** section.

3 In the tree, select **General>Temperature (K) - minput.T**.

4 Find the **Expression for remaining selection** subsection. In the **Temperature** text field, type `T`.

## MESH 1

Create a user defined mesh with a very fine resolution close to the anode.

1 In the **Model Builder** window, under **Component 1 (comp1)** click **Mesh 1**.

2 In the **Settings** window for **Mesh**, locate the **Sequence Type** section.

3 From the list, choose **User-controlled mesh**.

*Size*

1 In the **Model Builder** window, under **Component 1 (comp1)>Mesh 1** click **Size**.

2 In the **Settings** window for **Size**, locate the **Element Size** section.

3 From the **Predefined** list, choose **Extra fine**.

*Size 1*

1 In the **Model Builder** window, right-click **Edge 1** and choose **Size**.

2 In the **Settings** window for **Size**, locate the **Geometric Entity Selection** section.

3 From the **Geometric entity level** list, choose **Boundary**.

4 Select Boundary 1 only.

5 Locate the **Element Size** section. Click the **Custom** button.

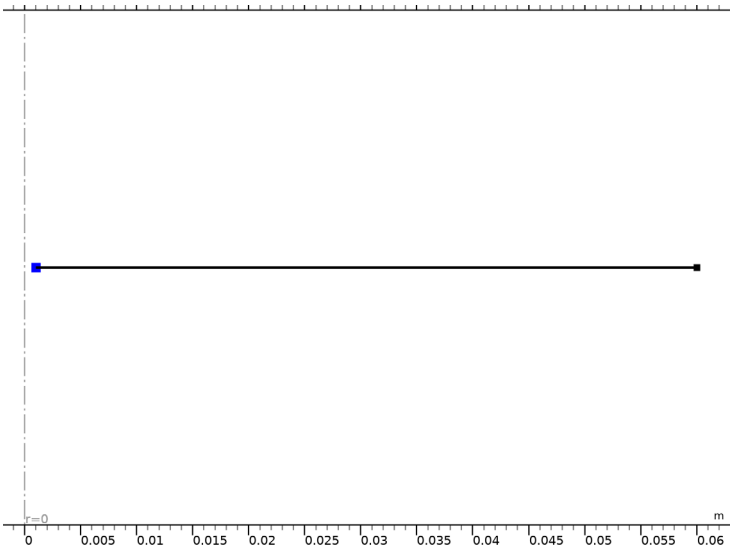
6 Locate the **Element Size Parameters** section.

7 Select the **Maximum element size** check box. In the associated text field, type `1e-8`.

8 Select the **Maximum element growth rate** check box. In the associated text field, type `1.1`.

9 Click **Build All**.

The finalized mesh should now look as follows:




## STUDY 1

*Step 1: Time Dependent*

Modify the default solver to store all steps taken by the solver, and solve the problem.

1 In the **Model Builder** window, under **Study 1** click **Step 1: Time Dependent**.

2 In the **Settings** window for **Time Dependent**, locate the **Study Settings** section.

3 In the **Output times** text field, type `0 3600`.

*Solution 1 (sol1)*

1 In the **Study** toolbar, click **Show Default Solver**.

Store the actual steps taken by the solver to avoid interpolation issues in the stored solution.

2 In the **Model Builder** window, expand the **Solution 1 (sol1)** node, then click **Time-Dependent Solver 1**.

3 In the **Settings** window for **Time-Dependent Solver**, locate the **General** section.

4 From the **Times to store** list, choose **Steps taken by solver**.

5 In the **Study** toolbar, click **Compute**.

## RESULTS

*Concentration, H (tcd)*

The following instructions show how to create the plots shown in Figure 3 to Figure 5.

1 In the **Model Builder** window, under **Results** click **Concentration, H (tcd)**.

2 In the **Settings** window for **1D Plot Group**, locate the **Data** section.

3 From the **Time selection** list, choose **Interpolated**.

4 In the **Times (s)** text field, type `range(0,600,3600)`.

*Line Graph 1*

1 In the **Model Builder** window, expand the **Concentration, H (tcd)** node, then click **Line Graph 1**.

2 In the **Settings** window for **Line Graph**, click to expand the **Legends** section.

3 Select the **Show legends** check box.

4 Click to expand the **Coloring and Style** section. Find the **Line markers** subsection. From the **Marker** list, choose **Cycle**.

5 From the **Positioning** list, choose **Interpolated**.

6 In the **Concentration, H (tcd)** toolbar, click **Plot**.

Compare the plot with that shown in Figure 3.

*Concentration, Cl (tcd)*

1 In the **Model Builder** window, under **Results** click **Concentration, Cl (tcd)**.

2 In the **Settings** window for **1D Plot Group**, locate the **Data** section.

3 From the **Time selection** list, choose **Interpolated**.

4 In the **Times (s)** text field, type `range(0,600,3600)`.

*Line Graph 1*

1 In the **Model Builder** window, expand the **Concentration, Cl (tcd)** node, then click **Line Graph 1**.

2 In the **Settings** window for **Line Graph**, locate the **Legends** section.

3 Select the **Show legends** check box.

4 Locate the **Coloring and Style** section. Find the **Line markers** subsection. From the **Marker** list, choose **Cycle**.

5 From the **Positioning** list, choose **Interpolated**.

6 In the **Concentration, Cl (tcd)** toolbar, click **Plot**.

Compare with the plot in Figure 4.

*pH*

1 In the **Model Builder** window, right-click **Concentration, H (tcd)** and choose **Duplicate**.

2 In the **Settings** window for **1D Plot Group**, type `pH` in the **Label** text field.

*Line Graph 1*

1 In the **Model Builder** window, expand the **pH** node, then click **Line Graph 1**.

2 In the **Settings** window for **Line Graph**, locate the **y-Axis Data** section.

3 In the **Expression** text field, type `pH`.

4 In the **pH** toolbar, click **Plot**.

The plot should look like that in Figure 2.

*Electrode reaction current densities*

1 In the **Home** toolbar, click **Add Plot Group** and choose **1D Plot Group**.

Finally, reproduce the plot shown in Figure 5.

2 In the **Settings** window for **1D Plot Group**, type `Electrode reaction current densities` in the **Label** text field.

*Point Graph 1*

1 Right-click **Electrode reaction current densities** and choose **Point Graph**.

2 Select Boundary 1 only.

3 In the **Settings** window for **Point Graph**, click **Replace Expression** in the upper-right corner of the **y-Axis Data** section. From the menu, choose **Component 1 (comp1)> Tertiary Current Distribution, Nernst-Planck>Electrode kinetics>tcd.iloc_er1 - Local current density - A/m²**.

4 Click to expand the **Legends** section. Select the **Show legends** check box.

5 From the **Legends** list, choose **Manual**.

6 In the table, enter the following settings:

| Legends |
| --- |
| Oxygen evolution |

*Point Graph 2*

1 Right-click **Point Graph 1** and choose **Duplicate**.

2 In the **Settings** window for **Point Graph**, locate the **y-Axis Data** section.

3 In the **Expression** text field, type `tcd.iloc_er2`.

4 Click to expand the **Title** section. From the **Title type** list, choose **None**.

5 Click to expand the **Coloring and Style** section. Find the **Line style** subsection. From the **Line** list, choose **Dash-dot**.

6 Locate the **Legends** section. In the table, enter the following settings:

| Legends |
| --- |
| Chlorine evolution |

7 In the **Electrode reaction current densities** toolbar, click **Plot**.

*Point Graph 3*

1 Right-click **Point Graph 2** and choose **Duplicate**.

2 In the **Settings** window for **Point Graph**, click **Replace Expression** in the upper-right corner of the **y-Axis Data** section. From the menu, choose **Component 1 (comp1)> Tertiary Current Distribution, Nernst-Planck>Electrode kinetics>tcd.itot - Total interface current density - A/m²**.

3 Locate the **Coloring and Style** section. Find the **Line style** subsection. From the **Line** list, choose **Dashed**.

4 Locate the **Legends** section. In the table, enter the following settings:

| Legends |
| --- |
| Total electrode current density |

5 In the **Electrode reaction current densities** toolbar, click **Plot**.