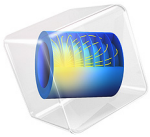

# Liquid Chromatography

## Introduction

Chromatography is an important group of methods to separate closely related components of complex mixtures. The following example simulates the separation of species in High Performance Liquid Chromatography (HPLC). In this technique an injector introduces a sample as a zone in a liquid mobile phase. The mobile phase containing the sample zone is pumped through a column containing a solid stationary phase; Figure 1 shows a diagram of such an instrument.

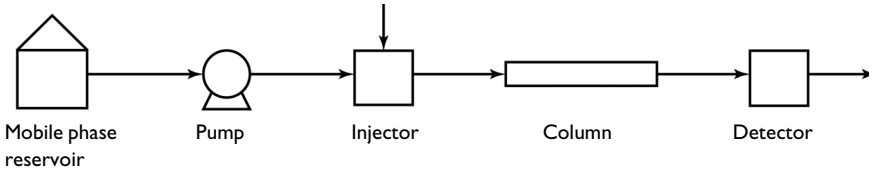


*Figure 1: Diagram of an HPLC system.*

The mobile and stationary phases are chosen so that the samples are distributed to varying degrees between the two phases. Those components that strongly adsorb to the stationary phase move only slowly with the flow of the mobile phase, and those that are weakly adsorbed move more rapidly. As the sample zones progress through the column, the components are separated into discrete zones that are recognized by a detector, situated beyond the outlet of the column.

## Model Definition

This model studies the separation of two species under conditions of nonlinear chromatography in a 1D geometry. The Transport of Diluted Species in Porous Media interface is used, with convection and adsorption in porous media accounted for.

The equation for analyte transport through a chromatographic column, with constant porosity, is computed by:

$$(\varepsilon + \rho k_{\mathrm{P},i})\frac{\partial c_i}{\partial t} + \mathbf{u}\cdot\nabla c_i = \nabla\cdot\left[\left(D_{\mathrm{D},i} + \frac{\varepsilon}{\tau_{\mathrm{F},i}}D_{\mathrm{F},i}\right)\nabla c_i\right] + R_i + S_i \qquad (1)$$

Here, $c_i$ is the concentration of component $i$ (SI unit: mol/m$^3$), $\varepsilon$ is the porosity, $\rho$ is the density of the media within the column (for the mix of liquid and solid matrix, SI unit: kg/m$^3$), $k_{\mathrm{P},i}$ is an adsorption isotherm, and $\mathbf{u}$ is the volume average velocity of the fluid phase (SI unit: m/s). The second term on the right-hand side describes the mixing of the

solutes, including mechanical mixing (dispersion) and molecular diffusion. The two last terms on the right-hand side are a reaction rate term and a fluid source term.

Equation 1 comes from the following derivation:

First, consider the dispersion of the chromatographic zone to be negligible as it progresses through the column. The mass transport equation will then take the form:

$$S\frac{\rho_p(1-\varepsilon)}{\varepsilon}\cdot\frac{\partial n_i}{\partial t}+\frac{\partial c_i}{\partial t}=-\frac{v}{\varepsilon A}\cdot\frac{\partial c_i}{\partial x}$$

where $S$ denotes the specific surface area of the particles in the column (SI unit: $m^2/kg$), $\rho_p$ denotes the density of the solid particles (SI unit: $kg/m^3$), $\varepsilon$ equals the column porosity, $A$ gives the inner area of the column tube, $n_i$ equals the analyte concentration in the stationary phase of component $i$ (SI unit: $mol/m^2$), $v$ describes the mobile phase flow (SI unit: $m^3/s$), and $c_i$ equals the analyte concentration in the mobile phase of component $i$ (SI unit: $mol/m^3$).

Equation 1 is defined according to the ideal model for chromatography that assumes that the equilibrium for the analyte between the mobile and stationary phases is immediate, that is:

$$\frac{\partial c_{\mathrm{P},i}}{\partial t}=\frac{\partial c_{\mathrm{P},i}}{\partial c_i}\cdot\frac{\partial c_i}{\partial t}=k_{\mathrm{P},i}\left(\frac{\partial c_i}{\partial t}\right)$$

where $c_{\mathrm{P},i}$ is the concentration of the component adsorbed to the solid (moles per dry unit).

The mass transport equation for the ideal chromatography model therefore becomes:

$$\left(1+S\frac{\rho_p(1-\varepsilon)}{\varepsilon}\cdot\frac{dn}{dc}\right)\cdot\frac{\partial c_i}{\partial t}=-\frac{v}{\varepsilon A}\frac{\partial c_i}{\partial x}$$

The dispersion or band broadening of the analyte zone is a result of a great number of random processes that the analyte experiences (for example, inhomogeneous flow and diffusion in pores and the mobile phase). It is therefore possible to formally express the band broadening as a diffusion process with an effective diffusion constant, $D_{\mathrm{eff}}$. Thus, $D_{\mathrm{eff}}$ is a measure of the chromatographic system's efficiency for a particular analyte. This constant is closely related to the concept of the height equivalent of a theoretical plate, $H$, that is customarily used in chromatographic practice. It can be shown that:

$$D_{\mathrm{eff}}=\frac{Hv_{zi}}{2}$$

where $v_{zi}$ is the migration velocity of the analyte zone through the column. A mass balance that includes the zone-dispersion term gives the following equation:

$$\left(1 + \Phi \cdot \frac{dn}{dc}\right) \cdot \frac{\partial c_i}{\partial t} = -v_l \frac{\partial c_i}{\partial x} + D_{\text{eff}} \frac{\partial^2 c_i}{\partial x^2}$$

Here $\Phi = S\rho(1 - \varepsilon)/\varepsilon$ denotes the phase ratio of the column (SI unit: $m^2/m^3$), $v_l = v/(\varepsilon A)$ gives the linear velocity of the mobile phase in the column (SI unit: m/s), and $D_{\text{eff}}$ is the effective diffusion constant (SI unit: $m^2/s$).

This first example covers two components. The adsorption isotherm for both components is assumed to follow a Langmuir adsorption isotherm, that is,

$$n_i = \frac{n_{0i} K_i c_i}{1 + K_i c_i}$$

and

$$\frac{dn_i}{dc_i} = \frac{n_{0i} K_i}{(1 + K_i c_i)^2}$$

where $K_i$ is the adsorption constant for component $i$ (SI unit: $m^3/mol$), and $n_{0i}$ is the monolayer capacity of the stationary phase for component $i$ (SI unit: $mol/m^2$).

Using an effective zone-dispersion term and the $k_{P,i}$ adsorption isotherm notation gives Equation 1 without the reaction rate and a fluid source terms:

$$(\varepsilon + \rho k_{P,i}) \frac{\partial c_i}{\partial t} + u \frac{\partial c_i}{\partial x} = \frac{\partial}{\partial x}\left(D_{\text{eff},i} \frac{\partial c_i}{\partial x}\right)$$

## INPUT DATA

This example looks at the progress of the chromatographic zone within the column. The physical data for the column correspond to a 12 cm-by-4 mm inner diameter column filled with 5 μm porous particles. The rest of the input data appear in Table 1.

TABLE 1: INPUT DATA.

| NAME | VALUE |
|---|---|
| $S$ | 100 $m^2/g$ |
| $\rho_p$ | 2300 $kg/m^3$ |
| $\varepsilon$ | 0.6 |
| $v_l$ | 1.322 mm/s |

TABLE 1: INPUT DATA.

| NAME | VALUE |
|---|---|
| $D_{eff1}$ | $1 \cdot 10^{-8}$ $m^2/s$ |
| $D_{eff2}$ | $1 \cdot 10^{-8}$ $m^2/s$ |
| $K_1$ | 0.04 $m^3/mol$ |
| $K_2$ | 0.05 $m^3/mol$ |
| $n_{01}$ | $1 \cdot 10^{-6}$ $mol/m^2$ |
| $n_{02}$ | $5 \cdot 10^{-7}$ $mol/m^2$ |

The injector concentrations for the two components are described by a normal distribution and are set up with the help of a Gaussian pulse function with an amplitude of 1 (Figure 2).

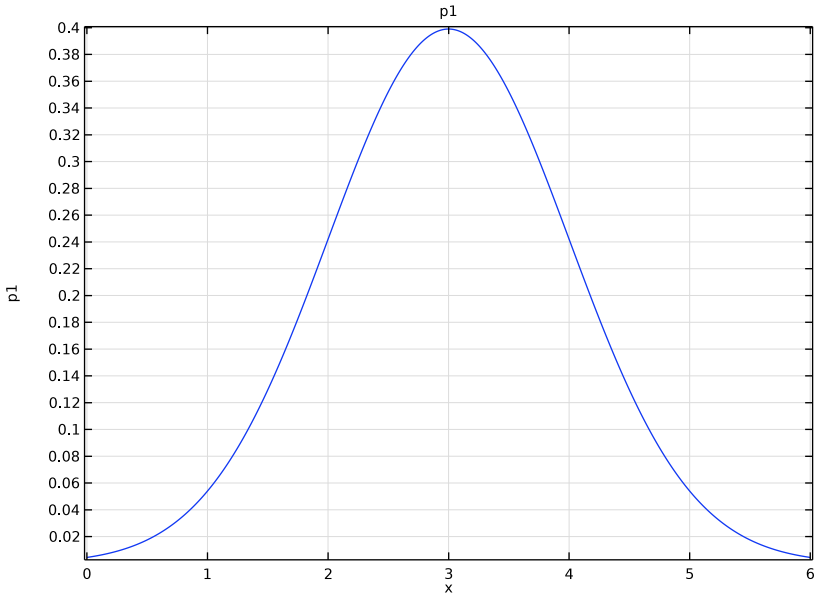


*Figure 2: Injection pulse with amplitude 1.*

The maximum inlet concentrations are 1 $mol/m^3$ and 10 $mol/m^3$ for components 1 and 2, respectively.

Figure 3 shows the mobile concentration zones of component 1 at various times. Initially, the concentration is zero in the column and at approximately 5 s the whole component mixture has been injected through the leftmost boundary (the inlet). At approximately 385 s, the first trace of component 1 exits the rightmost boundary (the outlet). The zones are nearly symmetrical and normally distributed, indicating that the solution is affected by an almost linear adsorption isotherm.

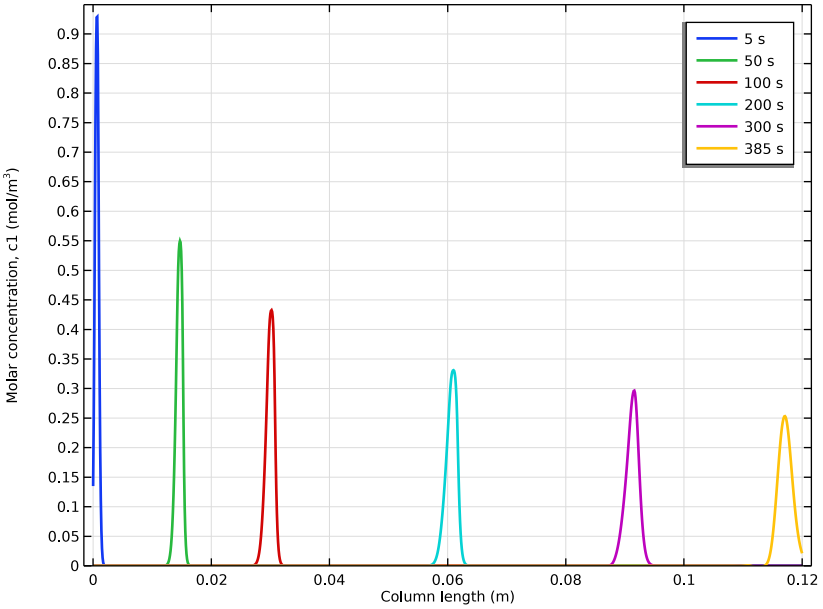


*Figure 3: The concentration of component 1 in the mobile phase at various times.*

In Figure 4, the zones for both of the components are displayed at various times. For the present conditions a clear separation of the two components occurs within the column; the component zones do not overlap as they reach the outlet. As an example, at $t = 300$ s, component 2 is no longer present in the mobile phase of the column, while most of component 1 still remains. Here, it is shown that component 2 depends on a nonlinear

adsorption isotherm, quickly obtaining an asymmetrical mobile concentration zone (compare with Figure 2).

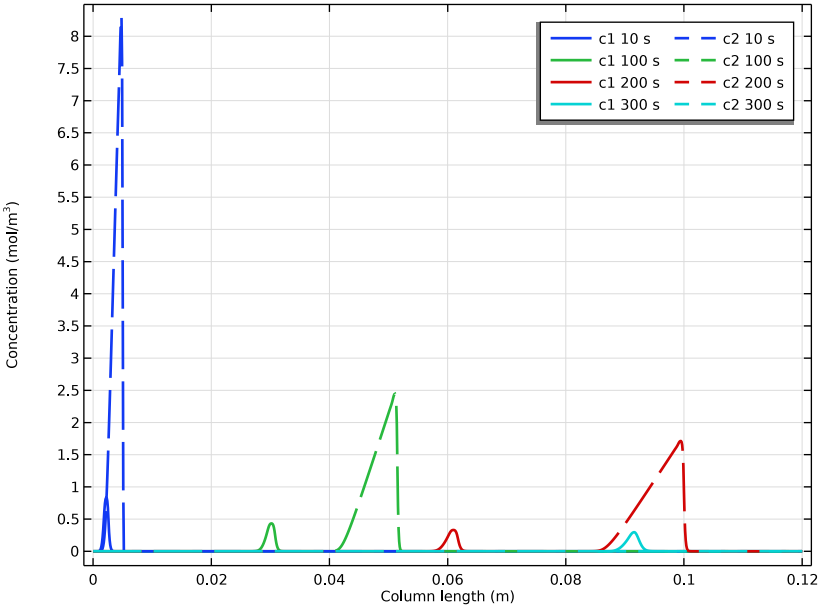


*Figure 4: The concentrations of components 1 (solid) and 2 (dashed) in the mobile phase at various times.*

The concentrations that are registered over time by the detector unit in the HPLC system are displayed in Figure 5. The first peak is that of component 1 and the second that of component 2.

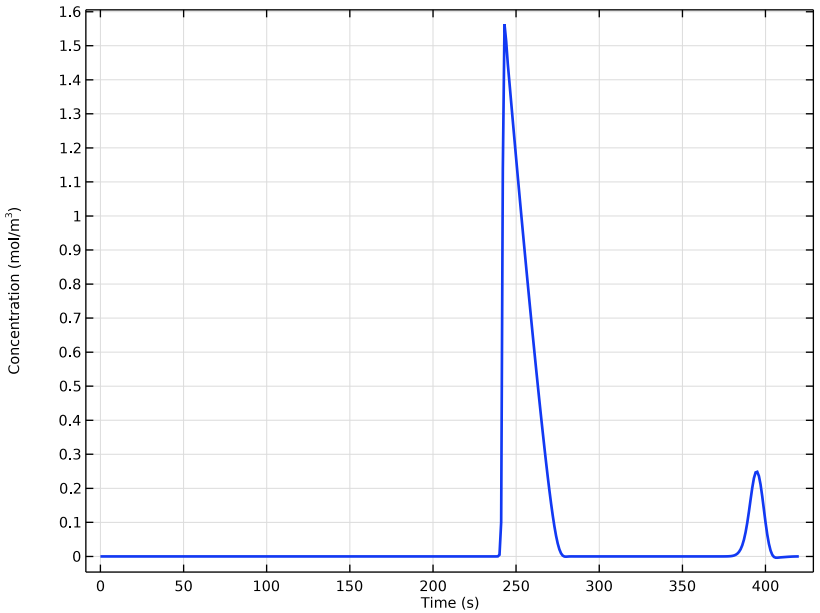


*Figure 5: Concentration at the outlet of the column, that is, the concentration monitored by the system detector.*

## *References*

1. D. DeVault, "The Theory of Chromatography," *J. Am. Chemical Soc.*, vol. 65, pp. 532–540, 1943.

2. S. Golshan-Shirazi and G. Guiochon, "Analytical solution for the ideal model of chromatography in the case of a Langmuir isotherm," *Analytical Chemistry*, vol. 60, no. 21, pp. 2364–2374, 1988.

3. B. Lin and G. Guiochon, *Modeling for Preparative Chromatography*, Elsevier Publishing, Amsterdam, 2003.

**Application Library path:** `Chemical_Reaction_Engineering_Module/Mixing_and_Separation/liquid_chromatography`

## *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**.
2. In the **Select Physics** tree, select **Chemical Species Transport** > **Transport of Diluted Species in Porous Media (tds)**.
3. Click **Add**.
4. In the **Number of species** text field, type 2.
5. Click **Study**.
6. In the **Select Study** tree, select **General Studies** > **Time Dependent**.
7. Click **Done**.

### ROOT

Add the model parameters from a text file.

### GLOBAL DEFINITIONS

*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 `liquid_chromatography_parameters.txt`.

The injection of the sample into the column is modeled with a **Gaussian pulse**.

*Injection Pulse*

1. In the **Home** toolbar, click **Functions** and choose **Global** > **Gaussian Pulse**.

2 In the **Settings** window for **Gaussian Pulse**, type `Injection Pulse` in the **Label** text field.

3 In the **Function name** text field, type `p1`.

4 Locate the **Parameters** section. In the **Location** text field, type `3`.

5 Click **Plot**.

*Variables 1*

1 In the **Model Builder** window, right-click **Global Definitions** and choose **Variables**.

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

3 In the table, enter the following settings:

| Name | Expression | Unit | Description |
|---|---|---|---|
| pulse_inj | 2.5*p1(t/1[s]) | | Time-dependent injection pulse with amplitude 1 |
| rho_c | rho_p*(1-eps_p) | kg/m³ | Density media in column |

## GEOMETRY 1

*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) |
|---|
| 0 |
| L_c |

4 Click **Build All Objects**.

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

## TRANSPORT OF DILUTED SPECIES IN POROUS MEDIA (TDS)

*Porous Medium 1*

In the **Model Builder** window, under **Component 1 (comp1)** > **Transport of Diluted Species in Porous Media (tds)** click **Porous Medium 1**.

*Adsorption 1*

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

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

3 Select the **Species c1** checkbox.

4 Select the **Species c2** checkbox.

5 Locate the **Matrix Properties** section. Find the **Density** subsection. From the ρ list, choose **User defined**. In the associated text field, type `rho_c`.

6 Locate the **Adsorption** section. In the $K_{L,c1}$ text field, type `K1`.

7 In the $c_{P,max,c1}$ text field, type `S*n01`.

8 In the $K_{L,c2}$ text field, type `K2`.

9 In the $c_{P,max,c2}$ text field, type `S*n02`.

*Fluid 1*

1 In the **Model Builder** window, expand the **Porous Medium 1** node, then click **Fluid 1**.

2 In the **Settings** window for **Fluid**, locate the **Convection** section.

3 Specify the **u** vector as

| | |
|---|---|
| `v_1` | `x` |

4 Locate the **Diffusion** section. In the $D_{F,c1}$ text field, type `D_1`.

5 In the $D_{F,c2}$ text field, type `D_2`.

*Porous Matrix 1*

1 In the **Model Builder** window, click **Porous Matrix 1**.

2 In the **Settings** window for **Porous Matrix**, locate the **Matrix Properties** section.

3 From the $\varepsilon_p$ list, choose **User defined**. In the associated text field, type `eps_p`.

*Inflow 1*

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

The investigated sample is injected at the leftmost boundary.

2 Select Boundary 1 only.

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

4 In the $c_{0,c1}$ text field, type `c01*pulse_inj`.

5 In the $c_{0,c2}$ text field, type `c02*pulse_inj`.

*Outflow 1*

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

2 Select Boundary 2 only.

## MESH 1

### *Edge 1*

In the **Mesh** toolbar, click  **Edge**.

### *Size*

1. In the **Model Builder** window, click **Size**.
2. In the **Settings** window for **Size**, locate the **Element Size** section.
3. Click the **Custom** button.
4. Locate the **Element Size Parameters** section. In the **Maximum element size** text field, type `1e-4`.
5. Click  **Build All**.

## STUDY 1

### *Step 1: Time Dependent*

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 `range(0,1,420)`.
4. From the **Tolerance** list, choose **User controlled**.
5. In the **Relative tolerance** text field, type `0.0010`.

### *Solution 1 (sol1)*

1. In the **Study** toolbar, click  **Show Default Solver**.
2. In the **Model Builder** window, expand the **Solution 1 (sol1)** node.
3. In the **Model Builder** window, expand the **Study 1** > **Solver Configurations** > **Solution 1 (sol1)** > **Dependent Variables 1** node, then click **Concentration (comp1.c1)**.
4. In the **Settings** window for **Field**, locate the **Scaling** section.
5. From the **Method** list, choose **Manual**.
6. In the **Scale** text field, type `c01`.
7. In the **Model Builder** window, under **Study 1** > **Solver Configurations** > **Solution 1 (sol1)** > **Dependent Variables 1** click **Concentration (comp1.c2)**.
8. In the **Settings** window for **Field**, locate the **Scaling** section.
9. From the **Method** list, choose **Manual**.
10. In the **Scale** text field, type `c02`.

11 In the **Model Builder** window, under **Study 1** > **Solver Configurations** > **Solution 1 (sol1)** click **Time-Dependent Solver 1**.

12 In the **Settings** window for **Time-Dependent Solver**, click to expand the **Absolute Tolerance** section.

13 From the **Tolerance method** list, choose **Manual**.

14 In the **Absolute tolerance** text field, type `1e-4`.

15 In the **Study** toolbar, click = **Compute**.

### RESULTS

Follow these steps to reproduce the plot in Figure 4:

*Concentrations, All Species (tds)*

1 In the **Model Builder** window, under **Results** click **Concentrations, All Species (tds)**.

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 `10 100 200 300`.

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

6 Locate the **Plot Settings** section.

7 Select the **x-axis label** checkbox. In the associated text field, type `Column length (m)`.

8 Locate the **Axis** section. Select the **Manual axis limits** checkbox.

9 In the **y minimum** text field, type `0`.

10 Locate the **Legend** section. In the **Number of columns** text field, type `2`.

*Species c1*

1 In the **Model Builder** window, expand the **Concentrations, All Species (tds)** node, then click **Species c1**.

2 In the **Settings** window for **Line Graph**, click to expand the **Coloring and Style** section.

3 From the **Width** list, choose **2**.

4 Click to expand the **Legends** section. Find the **Include** subsection. Select the **Solution** checkbox.

*Species c2*

1 In the **Model Builder** window, click **Species c2**.

2 In the **Settings** window for **Line Graph**, click to expand the **Coloring and Style** section.

3 Find the **Line style** subsection. From the **Line** list, choose **Dashed**.

4 From the **Color** list, choose **Cycle (reset)**.

5 From the **Width** list, choose **2**.

6 Locate the **Legends** section. Find the **Include** subsection. Select the **Solution** checkbox.

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

8 In the **Concentrations, All Species (tds)** toolbar, click  **Plot**.

Follow these steps to reproduce the plot in Figure 3:

*Concentration, c1 (tds)*

1 In the **Model Builder** window, under **Results** click **Concentration, c1 (tds)**.

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 `5 50 100 200 300 385`.

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

6 Locate the **Plot Settings** section.

7 Select the **x-axis label** checkbox. In the associated text field, type `Column length (m)`.

8 Locate the **Axis** section. Select the **Manual axis limits** checkbox.

9 In the **y minimum** text field, type `0`.

*Line Graph 1*

1 In the **Model Builder** window, expand the **Concentration, c1 (tds)** node, then click **Line Graph 1**.

2 In the **Settings** window for **Line Graph**, click to expand the **Coloring and Style** section.

3 From the **Width** list, choose **2**.

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

5 In the **Concentration, c1 (tds)** toolbar, click  **Plot**.

*Concentration, c2 (tds)*

1 In the **Model Builder** window, under **Results** click **Concentration, c2 (tds)**.

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 `5 50 100 200 300 385`.

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

6 Locate the **Plot Settings** section.

7 Select the **x-axis label** checkbox. In the associated text field, type `Column length (m)`.

8 Locate the **Axis** section. Select the **Manual axis limits** checkbox.

9 In the **y minimum** text field, type `0`.

10 Locate the **Legend** section. From the **Layout** list, choose **Outside graph axis area**.

*Line Graph 1*

1 In the **Model Builder** window, expand the **Concentration, c2 (tds)** node, then click **Line Graph 1**.

2 In the **Settings** window for **Line Graph**, click to expand the **Coloring and Style** section.

3 From the **Width** list, choose **2**.

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

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

6 In the **Concentration, c2 (tds)** toolbar, click **Plot**.

Follow these steps to reproduce the plot in Figure 5:

*Detected Concentration*

1 In the **Results** toolbar, click **1D Plot Group**.

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

3 Locate the **Title** section. From the **Title type** list, choose **None**.

*Point Graph 1*

1 Right-click **Detected Concentration** and choose **Point Graph**.

2 Select Boundary 2 only.

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

4 In the **Expression** text field, type `c1+c2`.

5 Click to expand the **Coloring and Style** section. From the **Width** list, choose **2**.

*Detected Concentration*

1 In the **Model Builder** window, click **Detected Concentration**.

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

3 Select the **y-axis label** checkbox. In the associated text field, type `Concentration (mol/m<sup>3</sup>)`.

4 In the **Detected Concentration** toolbar, click **Plot**.

Last, an animation of the liquid chromatography process can be set up in the following manner:

*Liquid Chromatography Animation*

1 In the **Results** toolbar, click **Animation** and choose **File**.

2 In the **Settings** window for **Animation**, type `Liquid Chromatography Animation` in the **Label** text field.

3 Locate the **Scene** section. From the **Subject** list, choose **Concentrations, All Species (tds)**.

4 Locate the **Target** section. From the **Target** list, choose **Player**.

5 Locate the **Animation Editing** section. From the **Time selection** list, choose **Interpolated**.

6 Click **Range**.

7 In the **Range** dialog, type `0` in the **Start** text field.

8 In the **Step** text field, type `2`.

9 In the **Stop** text field, type `420`.

10 Click **Replace**.

11 Click the **Play** button in the **Graphics** toolbar.