A Drug Delivery System

Introduction

This example describes the operation of a drug delivery system that supplies a variable concentration of a water soluble drug. A droplet with a fixed volume of water travels down a capillary tube at a constant velocity. Part of the capillary wall consists of a permeable membrane separating the interior of the capillary from a concentrated solution of the drug. As the drop passes by the membrane, the drug dissolves into the water. To model this process a constant flux of the drug is assumed on the capillary wall for the duration of its contact with the membrane. By altering the droplet velocity, the final concentration of the drug in the drop can be adjusted. The principle of the device is illustrated in Figure 1.

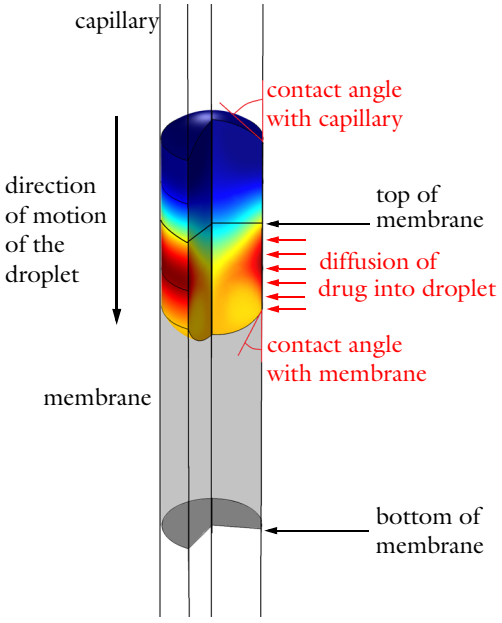

Figure 1: Diagram showing the operating principle of the drug delivery device. The color in the droplet represents drug concentration, with red indicating a higher concentration and blue indicating zero concentration. Note that the membrane length is not shown to scale.

Model Definition

The axisymmetric model geometry is shown in Figure 2. The droplet is visible near the top of the geometry. The horizontal lines across the capillary are included to assist with meshing. The drop is initially stationary at the top of the domain, but accelerates rapidly to a constant velocity before it reaches the permeable membrane. The permeable part of the capillary is not visible as part of the geometry as it is represented by a function applied to the boundary condition. It is located between z=0.6 mm and z=0.8 mm.

The droplet consists of liquid water with a density of 1000 kg/m^3 and a viscosity of 10^{-3} Pa·s. The remainder of the capillary is filled with air, with a density of 1.25 kg/m^3 and a viscosity of 2×10^{-5} Pa·s. The water air surface tension coefficient is 70 mN/m The contact angle of the droplet with the capillary wall is 135°, whilst that with the membrane is 157.5°. As the droplet passes the membrane the flux of the drug entering it is 1×10^{-3} mol/(m^2·s). The diffusion coefficient of the drug in the water is 5×10^{-9} m^2/s.

The droplet velocity past the membrane is varied between 0.1 and 1 mm/s to adjust the final concentration of the drug in the droplet.

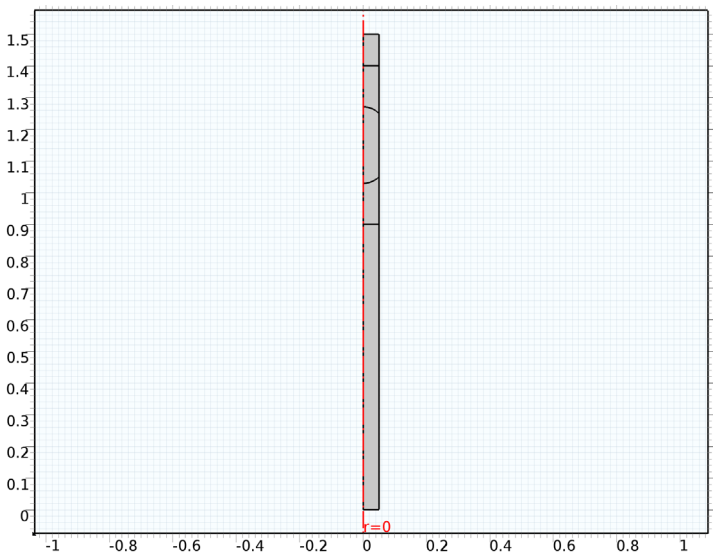

Figure 2: Axisymmetric model geometry.

Results and Discussion

The flow velocity is shown for the drop moving at 0.25 mm/s in Figure 3. The flow pattern around the interface is complex as the flow must redistribute itself from a Poiseuille flow profile away from the droplet surface, to a constant velocity flow at the surface of the droplet. Note the change in contact angle as the droplet passes the edge of the membrane at z=8 mm is apparent.

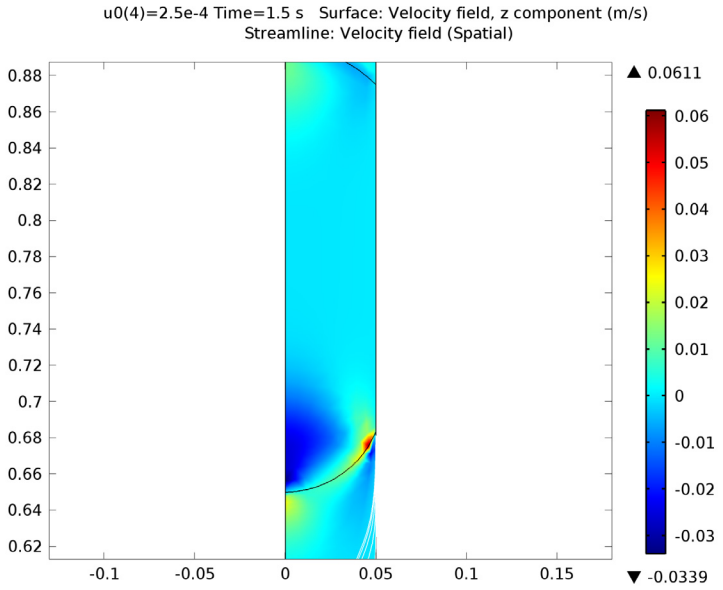

Figure 3: Flow velocity around the droplet as it travels past the edge of the permeable membrane.The droplet velocity is 0.25 mm/s.

Figure 4 shows the concentration profile for the 0.25 mm/s at the same point in time. The drug is diffusing into the droplet and is also convected by the fluid flow. A marked change in concentration is apparent between the top and the bottom of the droplet.

The total amount of drug in the droplet as a function of time is shown in Figure 5, for the drop traveling at 0.1 mm/s. The dissolved drug quantity increases with an 'S' shaped profile as the drug travels down the capillary.

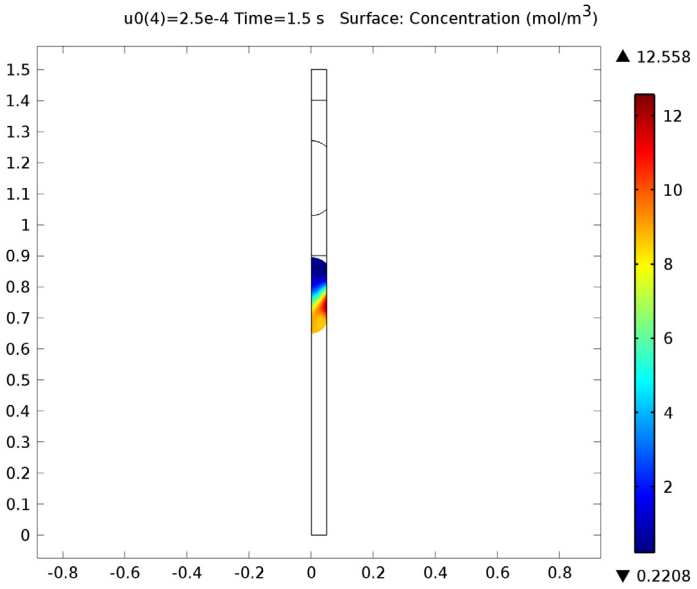

Figure 4: Drug concentration in the droplet as it travels past the edge of the permeable membrane. The droplet velocity is 0.25 mm/s.

Figure 6 shows the total amount of drug delivered against the droplet velocity. The number of moles delivered is approximately inversely proportional to the droplet velocity, which is expected as the amount of drug that diffuses into the drop will depend on time the drop takes to traverse the permeable part of the capillary.

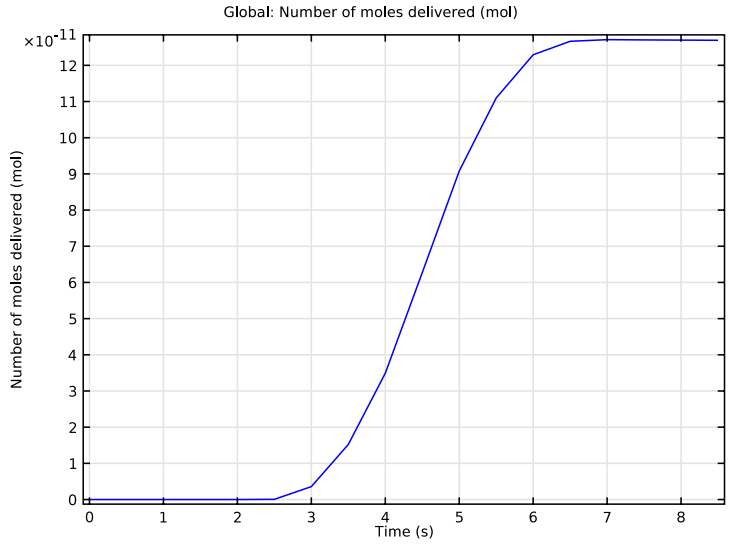

Figure 5: Total drug dose contained in the droplet as a function of time for the droplet traveling at 0.1 mm/s.

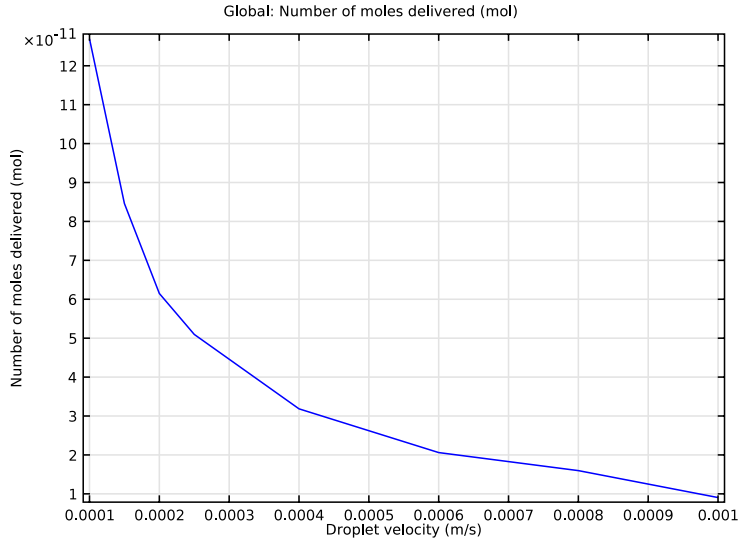

Figure 6: Total drug dose delivered shown against the droplet velocity.

Model Library path: `Microfluidics_Module/Two-Phase_Flow/drug_delivery_mm`

Modeling Instructions

NEW

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

MODEL WIZARD

1 In the **Model Wizard** window, click the **2D Axisymmetric** button.

2 In the **Select Physics** tree, select **Fluid Flow>Multiphase Flow>Two-Phase Flow, Moving Mesh>Laminar Two-Phase Flow, Moving Mesh (tpfmm)**.

3 Click the **Add** button.

4 Click the **Study** button.

5 In the tree, select **Preset Studies>Time Dependent**.

6 Click the **Done** button.

GEOMETRY 1

Import the model geometry.

1 In the **Model Builder** window, under **Component 1** click **Geometry 1**.

2 In the **Geometry** settings window, locate the **Units** section.

3 From the **Length unit** list, choose **mm**.

Import 1

1 On the **Home** toolbar, click **Import**.

2 In the **Import** settings window, locate the **Import** section.

3 Click the **Browse** button.

4 Browse to the model's Model Library folder and double-click the file `drug_delivery_mm.mphbin`.

5 Click the **Import** button.

GLOBAL DEFINITIONS

Set up a parameter for the droplet velocity.

Parameters

1 On the **Home** toolbar, click **Parameters**.

2 In the **Parameters** settings window, locate the **Parameters** section.

3 In the table, enter the following settings:

Name	Expression	Value	Description
u0	0.001[m/s]	0.001000 m/s	Droplet velocity (m/s)

Set up integration coupling variables to compute volume and point integrals.

DEFINITIONS

Integration 1

1 On the **Definitions** toolbar, click **Component Couplings** and choose **Integration**.

2 Select Domain 3 only.

Integration 2

1 On the **Definitions** toolbar, click **Component Couplings** and choose **Integration**.

2 In the **Integration** settings window, locate the **Source Selection** section.

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

4 Select Point 6 only.

Set up model variables to track drug dose and drop location. Define a function to represent the permeable part of the capillary wall.

Variables 1

1 On the **Home** toolbar, click **Variables>Local Variables**.

2 In the **Variables** settings window, locate the **Variables** section.

3 In the table, enter the following settings:

Name	Expression	Unit	Description
n_abs	intop1(2*pi*r*c)		Number of moles delivered
z_pnt	intop2(z)	m	Position of top of droplet

Create a rectangle function that is zero everywhere except at heights corresponding to the permeable membrane.

Rectangle 1

1 On the **Home** toolbar, click **Functions** and choose **Global>Rectangle**.

2 In the **Rectangle** settings window, locate the **Parameters** section.

3 In the **Lower limit** edit field, type `6e-4`.

4 In the **Upper limit** edit field, type `8e-4`.

5 Click to expand the **Smoothing** section. In the **Size of transition zone** edit field, type `5e-5`.

6 Click the **Plot** button.

Create a step function to use to ramp up the velocity from zero in the inlet boundary condition.

Step 1

1 On the **Home** toolbar, click **Functions** and choose **Global>Step**.

2 In the **Step** settings window, locate the **Parameters** section.

3 In the **Location** edit field, type `1e-4`.

4 Click to expand the **Smoothing** section. In the **Size of transition zone** edit field, type `1e-4`.

5 Click the **Plot** button.

Set constraints on the mesh displacement.

LAMINAR TWO-PHASE FLOW, MOVING MESH

Prescribed Mesh Displacement 2

1 On the **Physics** toolbar, click **Boundaries** and choose **Prescribed Mesh Displacement**.

2 Select Boundaries 2 and 11 only.

Prescribed Mesh Displacement 1

1 In the **Model Builder** window, under **Component 1>Laminar Two-Phase Flow, Moving Mesh** click **Prescribed Mesh Displacement 1**.

2 In the **Prescribed Mesh Displacement** settings window, locate the **Prescribed Mesh Displacement** section.

3 Clear the **Prescribed z displacement** check box.

The Navier Slip boundary condition must be used on the walls along which the contact line moves.

Navier Slip 1

1 On the **Physics** toolbar, click **Boundaries** and choose **Navier Slip**.

2 Select Boundaries 12–18 only.

Set the inlet boundary condition to accelerate the droplet rapidly to a constant velocity.

Inlet 1

1 On the **Physics** toolbar, click **Boundaries** and choose **Inlet**.

2 Select Boundary 11 only.

3 In the **Inlet** settings window, locate the **Boundary Condition** section.

4 From the **Boundary condition** list, choose **Laminar inflow**.

5 Locate the **Laminar Inflow** section. In the U_{av} edit field, type `u0*step1(t/1[s])`.

Apply a pressure constraint at the outlet.

Outlet 1

1 On the **Physics** toolbar, click **Boundaries** and choose **Outlet**.

2 Select Boundary 2 only.

Set up the boundary conditions for the droplet surface and the contact point.

Fluid-Fluid Interface 1

1 On the **Physics** toolbar, click **Boundaries** and choose **Fluid-Fluid Interface**.

2 Select Boundaries 19 and 20 only.

Wall-Fluid Interface 1

1 Right-click **Component 1>Laminar Two-Phase Flow, Moving Mesh >Fluid-Fluid Interface 1** and choose **Wall-Fluid Interface**.

2 In the **Wall-Fluid Interface** settings window, locate the **Wall-Fluid Interface** section.

3 In the θ_w edit field, type `3*pi*(1-rect1(z/1[m]))/4+7*pi*rect1(z/1[m])/8`.

Note: using the rectangle function in this manner makes the contact angle vary on the permeable part of the wall.

Add the Diluted Species interface to model the solute transport in the droplet.

COMPONENT 1

On the **Home** toolbar, click **Add Physics**.

ADD PHYSICS

1 Go to the **Add Physics** window.

2 In the **Add physics** tree, select **Chemical Species Transport>Transport of Diluted Species**.

3 In the **Add Physics** window, click **Add to Component**.

TRANSPORT OF DILUTED SPECIES

Ensure the drug transport occurs only in the liquid domain.

1 In the **Model Builder** window, under **Component 1** click **Transport of Diluted Species**.

2 In the **Transport of Diluted Species** settings window, locate the **Domain Selection** section.

3 Click **Clear Selection**.

4 Select Domain 3 only.

Set up convection and diffusion for the drug.

Convection and Diffusion 1

1 In the **Model Builder** window, expand the **Transport of Diluted Species** node, then click **Convection and Diffusion 1**.

2 In the **Convection and Diffusion** settings window, locate the **Model Inputs** section.

3 From the **u** list, choose **Velocity field (tpfmm)**.

4 Locate the **Diffusion** section. In the D_c edit field, type `5E-9`.

Add a boundary condition for the drug flux into droplet.

Flux 1

1 On the **Physics** toolbar, click **Boundaries** and choose **Flux**.

2 Select Boundaries 14–16 only.

3 In the **Flux** settings window, locate the **Inward Flux** section.

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

5 In the $N_{0,c}$ edit field, type `rect1(z/1[m])*0.001[mol/(m^2*s)]`.

Note: this expression ensures flux only enters the droplet as it passes the permeable membrane.

Flux 2

1 On the **Physics** toolbar, click **Boundaries** and choose **Flux**.

2 Select Boundaries 19 and 20 only.

3 In the **Flux** settings window, locate the **Inward Flux** section.

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

5 In the $N_{0,c}$ edit field, type `-c*(chds.u*chds.nr+chds.v*chds.nphi+chds.w*chds.nz)`.

This expression ensures no flux enters the domain through the walls of the moving mesh.

Add the water and air material properties to the model.

MATERIALS

Material 1

1 On the **Home** toolbar, click **New Material**.

2 In the **Material** settings window, locate the **Material Contents** section.

3 In the table, enter the following settings:

Property	Name	Value	Unit	Property group
Density	rho	1.25	kg/m³	Basic
Dynamic viscosity	mu	2e-5	Pa·s	Basic

4 Select Domains 1, 2, 4, and 5 only.

Material 2

1 On the **Home** toolbar, click **New Material**.

2 Select Domain 3 only.

3 In the **Material** settings window, locate the **Material Contents** section.

4 In the table, enter the following settings:

Property	Name	Value	Unit	Property group
Density	rho	1000	kg/m³	Basic
Dynamic viscosity	mu	1e-3	Pa·s	Basic

Mesh the geometry. The mesh is refined around the edges of the droplet.

MESH 1

Scale 1

1 In the **Model Builder** window, under **Component 1** right-click **Mesh 1** and choose **Scale**.

2 In the **Scale** settings window, locate the **Geometric Entity Selection** section.

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

4 Select Boundaries 14–16, 19, and 20 only.

5 Locate the **Scale** section. In the **Element size scale** edit field, type 0.5.

6 In the **Model Builder** window, right-click **Mesh 1** and choose **Free Quad**.

Size

1 In the **Model Builder** window, click on the **Size** node.

2 In the **Size** settings window, locate the **Element Size** section.

3 Click the **Custom** button.

4 Locate the **Element Size Parameters** section. In the **Maximum element size** edit field, type `0.01`.

5 In the **Minimum element size** edit field, type `3E-5`.

6 In the **Maximum element growth rate** edit field, type `1.1`.

7 In the **Curvature factor** edit field, type `0.2`.

8 Click the **Build All** button.

Set up the parametric sweep.

STUDY 1

Parametric Sweep

1 On the **Study** toolbar, click **Parametric Sweep**.

2 In the **Parametric Sweep** settings window, locate the **Study Settings** section.

3 Click **Add**.

4 In the table, enter the following settings:

Parameter names	Parameter value list
u0	`0.0001 0.00015 0.0002 0.00025 0.0004 0.0006 0.0008 0.001`

Step 1: Time Dependent

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

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

3 In the **Times** edit field, type `range(0,0.5,10)`.

Add a stop condition to prevent the droplet from leaving the geometry.

Solver 1

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

2 In the **Model Builder** window, expand the **Study 1>Solver Configurations** node.

3 In the **Model Builder** window, expand the **Solver 1** node.

4 Right-click **Time-Dependent Solver 1** and choose **Stop Condition**.

5 In the **Stop Condition** settings window, locate the **Stop Expressions** section.

6 Click **Add**.

7 In the table, enter the following settings:

Stop expression	Stop if	Active	Description
comp1.z_pnt<0.0004	true (>=1)	Tick	Stop expression 1

Note that the solver will stop when the real part of the stop expression is negative.

Adjust solver settings for optimum performance.

8 In the **Model Builder** window, under **Study 1>Solver Configurations>Solver 1** click **Time-Dependent Solver 1**.

9 In the **Time-Dependent Solver** settings window, click to expand the **Absolute tolerance** section.

10 Locate the **Absolute Tolerance** section. From the **Global method** list, choose **Unscaled**.

11 Click to expand the **Advanced** section. From the **Error estimation** list, choose **Exclude algebraic**.

12 On the **Home** toolbar, click **Compute**.

RESULTS

Velocity (tpfmm) 1

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

2 From the **Parameter value (u0)** list, choose **2.5e-4**.

3 From the **Time (s)** list, choose **1.5**.

4 In the **Model Builder** window, expand the **Velocity (tpfmm) 1** node.

5 Right-click **Results>Velocity (tpfmm) 1** and choose **Streamline**.

6 In the **Streamline** settings window, locate the **Streamline Positioning** section.

7 In the **Number** edit field, type 10.

8 Select Boundaries 2 and 11 only.

9 Locate the **Coloring and Style** section. From the **Color** list, choose **White**.

10 In the **Model Builder** window, under **Results>Velocity (tpfmm) 1** click **Surface 1**.

11 In the **Surface** settings window, click **Replace Expression** in the upper-right corner of the **Expression** section. From the menu, choose **Laminar Two-Phase Flow, Moving Mesh (Laminar Flow)>Velocity field (Spatial)>Velocity field, z component (w)**.

12 Click the **Zoom Extents** button on the Graphics toolbar.

13 Click the **Zoom In** button on the Graphics toolbar.

14 Click the **Zoom In** button on the Graphics toolbar.

Compare the resulting plot with that in Figure 2.

Concentration (chds)

1 In the **Model Builder** window, expand the **Results>Concentration (chds)** node, then click **Concentration (chds)**.

2 In the **2D Plot Group** settings window, locate the **Data** section.

3 From the **Parameter value (u0)** list, choose **2.5e-4**.

4 From the **Time (s)** list, choose **1.5**.

5 On the **2D Plot Group** toolbar, click **Plot**.

Compare the resulting plot with that in Figure 3.

1D Plot Group 7

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

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

3 From the **Data set** list, choose **Solution 2**.

4 From the **Parameter selection (u0)** list, choose **First**.

5 On the **1D Plot Group** toolbar, click **Global**.

6 In the **Global** settings window, locate the **y-Axis Data** section.

7 In the table, enter the following settings:

Expression	Unit	Description
n_abs	mol	Number of moles delivered

8 Locate the **x-Axis Data** section. From the **Axis source data** list, choose **Inner solutions**.

9 Click to expand the **Legends** section. Clear the **Show legends** check box.

10 On the **1D plot group** toolbar, click **Plot**.

Compare the resulting plot with that in Figure 4.

1D Plot Group 8

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

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

3 From the **Data set** list, choose **Solution 2**.

4 From the **Time selection** list, choose **Last**.

5 On the **1D plot group** toolbar, click **Global**.

6 In the **Global** settings window, locate the **y-Axis Data** section.

7 In the table, enter the following settings:

Expression	Unit	Description
n_abs	mol	Number of moles delivered

8 Locate the **x-Axis Data** section. From the **Axis source data** list, choose **Outer solutions**.

9 From the **Parameter** list, choose **Expression**.

10 In the **Expression** edit field, type u0.

11 Locate the **Legends** section. Clear the **Show legends** check box.

12 On the **1D plot group** toolbar, click **Plot**.

Compare the resulting plot with that in Figure 5.