Model created in COMSOL Multiphysics 6.4

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.

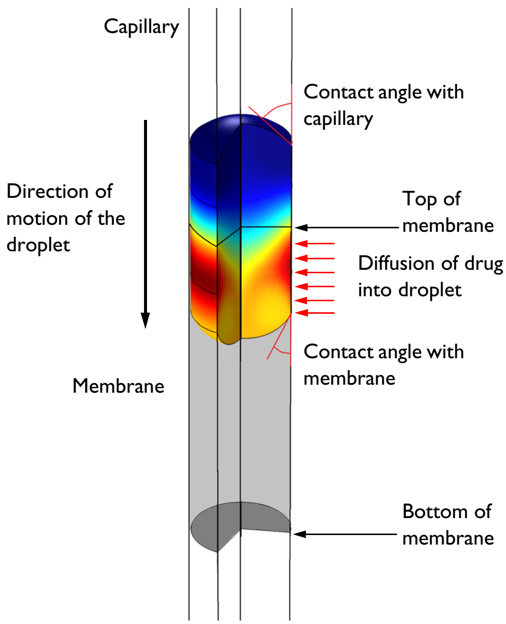

Figure 1: Diagram showing the operating principle of the drug delivery device. The color in the droplet represents drug concentration, with red indicating a higher concentration and blue indicating zero concentration. Note that the membrane length is not shown to scale.

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 of density 1000 kg/m^3 and viscosity 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.

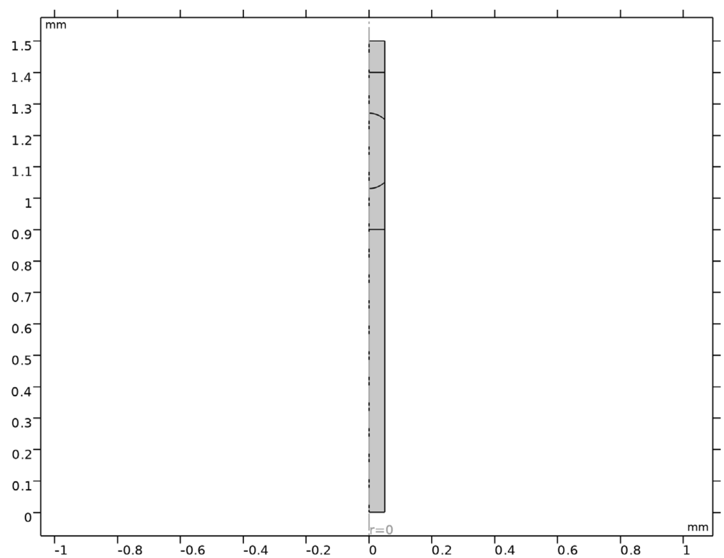

Figure 2: Axisymmetric model geometry.

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. Notice that the change in contact angle as the droplet passes the edge of the membrane at z = 8 mm is apparent.

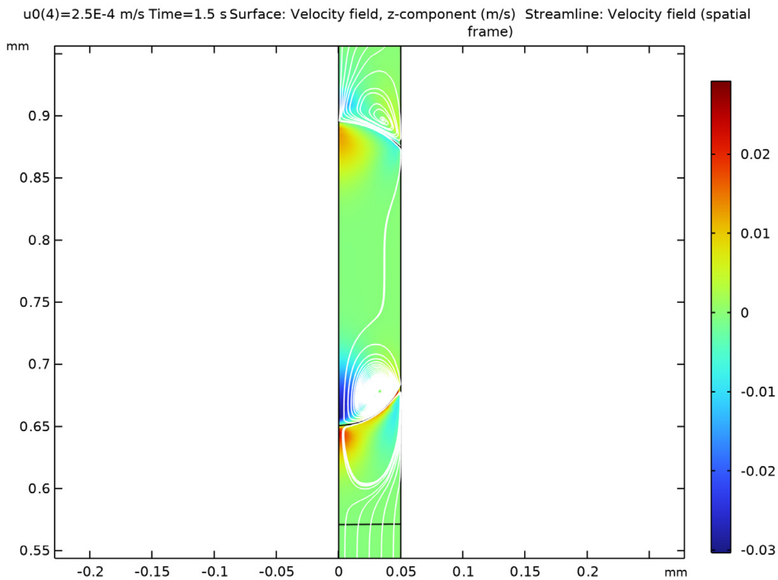

Figure 3: Flow velocity around the droplet as it travels past the edge of the permeable membrane. The droplet velocity is 0.25 mm/s.

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.

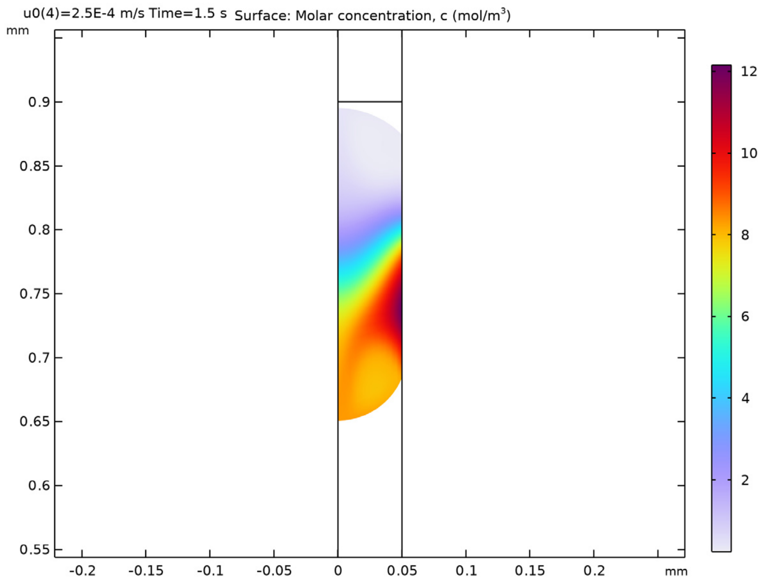

Figure 4: Drug concentration in the droplet as it travels past the edge of the permeable membrane. The droplet velocity is 0.25 mm/s.

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 depends on the time the drop takes to traverse the permeable part of the capillary.

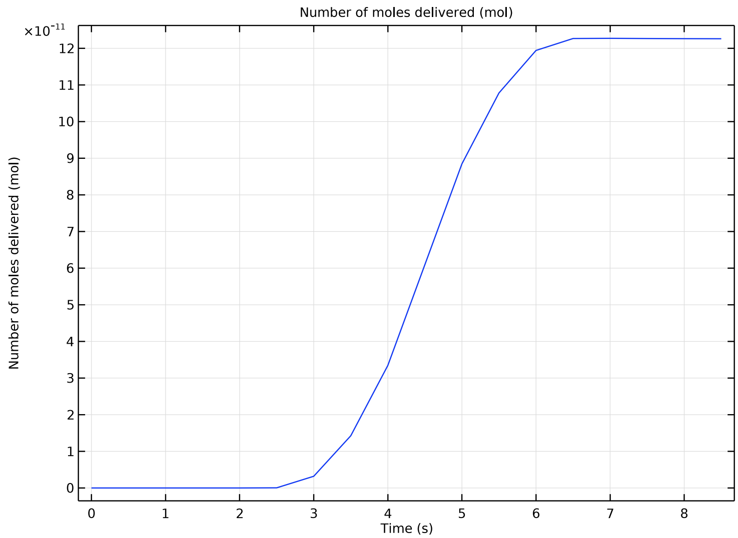

Figure 5: Total drug dose contained in the droplet as a function of time for the droplet traveling at 0.1 mm/s.

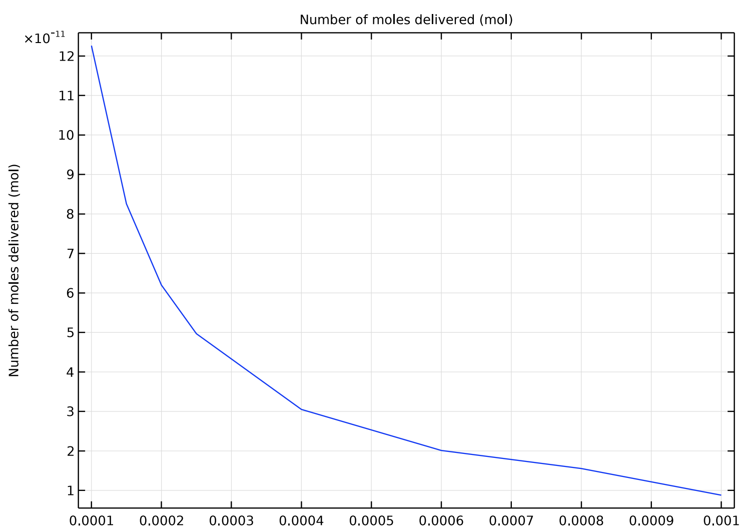

Figure 6: Total drug dose delivered shown against the droplet velocity.

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

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 **2D Axisymmetric**.

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

3 Click **Add**.

4 Click **Study**.

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

6 Click **Done**.

GEOMETRY 1

For convenience, the device geometry is inserted from an existing file. You can read the instructions for creating the geometry in the Appendix — Geometry Instructions.

1 In the **Geometry** toolbar, click **Insert Sequence** and choose **Insert Sequence**.

2 Browse to the model's Application Libraries folder and double-click the file `drug_delivery_mm_geom_sequence.mph`.

3 In the **Geometry** toolbar, click **Build All**.

GLOBAL DEFINITIONS

Set up a parameter for the droplet velocity.

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 In the table, enter the following settings:

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

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

DEFINITIONS

Integration 1 (intop1)

1 In the **Definitions** toolbar, click **Nonlocal Couplings** and choose **Integration**.

2 Select Domain 3 only.

3 In the **Settings** window for **Integration**, locate the **Advanced** section.

4 Clear the **Compute integral in revolved geometry** checkbox.

Integration 2 (intop2)

1 In the **Definitions** toolbar, click **Nonlocal Couplings** and choose **Integration**.

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

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

4 Select Point 4 only.

5 Locate the **Advanced** section. Clear the **Compute integral in revolved geometry** checkbox.

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 In the **Definitions** toolbar, click **Local Variables**.

2 In the **Settings** window for **Variables**, 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 (rect1)

1 In the **Definitions** toolbar, click **More Functions** and choose **Rectangle**.
2 In the **Settings** window for **Rectangle**, locate the **Parameters** section.
3 In the **Lower limit** text field, type `6e-4`.
4 In the **Upper limit** text field, type `8e-4`.
5 Click to expand the **Smoothing** section. In the **Size of transition zone** text field, type `5e-5`.
6 Click **Plot**.

Create a step function to ramp up the velocity from zero in the **Inlet** boundary condition.

Step 1 (step1)

1 In the **Definitions** toolbar, click **More Functions** and choose **Step**.
2 In the **Settings** window for **Step**, locate the **Parameters** section.
3 In the **Location** text field, type `1e-4`.
4 Click to expand the **Smoothing** section. In the **Size of transition zone** text field, type `1e-4`.
5 Click **Plot**.

Set constraints on the mesh displacement.

MOVING MESH

Symmetry/Roller 1

1 In the **Moving Mesh** toolbar, click **Symmetry/Roller**.
2 Select Boundaries 1, 3, 5–7, and 10–14 only (lateral boundaries).

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

LAMINAR FLOW (SPF)

Wall 2

1 In the **Physics** toolbar, click **Boundaries** and choose **Wall**.
2 Select Boundaries 10–14 only.
3 In the **Settings** window for **Wall**, locate the **Boundary Condition** section.
4 From the **Wall condition** list, choose **Navier slip**.

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

Inlet 1

1 In the **Physics** toolbar, click **Boundaries** and choose **Inlet**.
2 Select Boundary 9 only.
3 In the **Settings** window for **Inlet**, locate the **Boundary Condition** section.
4 From the list, choose **Fully developed flow**.
5 Locate the **Fully Developed Flow** section. In the U_{av} text field, type `u0*step1(t/1[s])`.

Apply a **Pressure** constraint at the **Outlet**.

Outlet 1

1 In 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 In the **Physics** toolbar, click **Boundaries** and choose **Fluid-Fluid Interface**.
2 Select Boundaries 15 and 16 only.
3 In the **Settings** window for **Fluid-Fluid Interface**, locate the **Surface Tension** section.
4 From the **Surface tension coefficient** list, choose **User defined**. Locate the **Normal Direction** section. Select the **Reverse normal direction** checkbox.

Contact Angle 1

1 In the **Model Builder** window, expand the **Fluid-Fluid Interface 1** node, then click **Contact Angle 1**.
2 In the **Settings** window for **Contact Angle**, locate the **Contact Angle** section.
3 In the θ_{w} text 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.
4 Locate the **Normal Wall Velocity** section. Select the **Constrain wall-normal velocity** checkbox.

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

ADD PHYSICS

1 In the **Home** toolbar, click **Add Physics** to open the **Add Physics** window.
2 Go to the **Add Physics** window.
3 In the tree, select **Chemical Species Transport > Transport of Diluted Species (tds)**.
4 Click the **Add to Component 1** button in the window toolbar.

5 In the **Home** toolbar, click **Add Physics** to close the **Add Physics** window.

TRANSPORT OF DILUTED SPECIES (TDS)

Ensure the drug transport occurs only in the liquid domain.

1 In the **Settings** window for **Transport of Diluted Species**, locate the **Domain Selection** section.

2 Click **Clear Selection**.

3 Select Domain 3 only.

Set up convection and diffusion for the drug.

Fluid 1

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

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

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

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

Add a boundary condition for the drug flux into droplet.

Flux 1

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

2 Select Boundary 12 only.

3 In the **Settings** window for **Flux**, locate the **Inward Flux** section.

4 Select the **Species c** checkbox.

5 In the $J_{0,c}$ text 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.

Add the water and air material properties to the model.

MATERIALS

Material 1 (mat1)

1 In the **Model Builder** window, under **Component 1 (comp1)** right-click **Materials** and choose **Blank Material**.

2 In the **Settings** window for **Material**, locate the **Material Contents** section.

3 In the table, enter the following settings:

Property	Variable	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 (mat2)

1 Right-click **Materials** and choose **Blank Material**.

2 Select Domain 3 only.

3 In the **Settings** window for **Material**, locate the **Material Contents** section.

4 In the table, enter the following settings:

Property	Variable	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 **Mesh** toolbar, click **More Attributes** and choose **Scale**.

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

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

4 Select Boundaries 12, 15, and 16 only.

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

Free Quad 1

In the **Mesh** toolbar, click **Free Quad**.

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 `0.01`.

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

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

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

8 Click **Build All**.

Set up the parametric sweep.

STUDY 1

Parametric Sweep

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

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

3 Click **Add**.

4 In the table, enter the following settings:

Parameter name	Parameter value list	Parameter unit
u0 (Droplet velocity (m/s))	`0.0001 0.00015 0.0002 0.00025 0.0004 0.0006 0.0008 0.001`	`m/s`

Step 1: Time Dependent

1 In the **Model Builder** window, 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(0,0.5,10)`.

Use a strict time step to avoid interpolation of the concentration field at output times, and add a stop condition to prevent the droplet from leaving the geometry.

Solution 1 (sol1)

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

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**, click to expand the **Time Stepping** section.

4 From the **Steps taken by solver** list, choose **Strict**.

5 Right-click **Study 1** > **Solver Configurations** > **Solution 1 (sol1)** > **Time-Dependent Solver 1** and choose **Stop Condition**.

6 In the **Settings** window for **Stop Condition**, locate the **Stop Expressions** section.

7 Click **Add**.

8 In the table, enter the following settings:

Stop expression	Stop if	Active	Description
`comp1.z_pnt<0.0004`	True (>=1)	√	`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.

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

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

11 From the **Global method** list, choose **Unscaled**.

12 Click to expand the **Output** section. Clear the **Store the first time derivative** checkbox.

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

RESULTS

Velocity (spf)

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

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

3 From the **Parameter value (u0 (m/s))** list, choose **2.5E-4**.

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

Streamline 1

1 Right-click **Velocity (spf)** and choose **Streamline**.

2 In the **Settings** window for **Streamline**, locate the **Streamline Positioning** section.

3 In the **Number** text field, type `10`.

4 Select Boundaries 2 and 9 only.

5 Locate the **Coloring and Style** section. Find the **Point style** subsection. From the **Color** list, choose **White**.

Surface

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

2 In the **Settings** window for **Surface**, locate the **Expression** section.

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

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

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

6 Click the **Zoom In** button in the **Graphics** toolbar.

7 In the **Velocity (spf)** toolbar, click **Plot**.

Compare the resulting plot with that in Figure 2.

Arrow Surface 1

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

2 Right-click **Arrow Surface 1** and choose **Disable**.

Concentration (tds)

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

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

3 From the **Parameter value (u0 (m/s))** list, choose **2.5E-4**.

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

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

Compare the resulting plot with that in Figure 3.

1D Plot Group 7

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

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

3 From the **Dataset** list, choose **Study 1/Parametric Solutions 1 (sol2)**.

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

Global 1

1 Right-click **1D Plot Group 7** and choose **Global**.

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

3 In the table, enter the following settings:

Expression	Unit	Description
n_abs	mol	Number of moles delivered

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

5 Click to expand the **Legends** section. Clear the **Show legends** checkbox.

6 In the **1D Plot Group 7** toolbar, click **Plot**.

Compare the resulting plot with that in Figure 4.

1D Plot Group 8

1 In the **Results** toolbar, click **1D Plot Group**.
2 In the **Settings** window for **1D Plot Group**, locate the **Data** section.
3 From the **Dataset** list, choose **Study 1/Parametric Solutions 1 (sol2)**.
4 From the **Time selection** list, choose **Last**.

Global 1

1 Right-click **1D Plot Group 8** and choose **Global**.
2 In the **Settings** window for **Global**, locate the **y-Axis Data** section.
3 In the table, enter the following settings:

Expression	Unit	Description
`n_abs`	`mol`	`Number of moles delivered`

4 Locate the **x-Axis Data** section. From the **Axis source data** list, choose **Outer solutions**.
5 From the **Parameter** list, choose **Expression**.
6 In the **Expression** text field, type `u0`.
7 Locate the **Legends** section. Clear the **Show legends** checkbox.
8 In the **1D Plot Group 8** toolbar, click **Plot**.

Compare the resulting plot with that in Figure 5.

Appendix — Geometry Instructions

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

NEW

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

ADD COMPONENT

In the **Home** toolbar, click **Add Component** and choose **2D**.

GEOMETRY 1

1 In the **Settings** window for **Geometry**, locate the **Units** section.
2 From the **Length unit** list, choose **mm**.

Rectangle 1 (r1)

1 In the **Geometry** toolbar, click **Rectangle**.
2 In the **Settings** window for **Rectangle**, locate the **Size and Shape** section.

3 In the **Width** text field, type `0.05`.

4 In the **Height** text field, type `1.5`.

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

Layer name	Thickness (mm)
Layer 1	0.9
Layer 2	0.5

Ellipse 1 (e1)

1 In the **Geometry** toolbar, click **Ellipse**.

2 In the **Settings** window for **Ellipse**, locate the **Size and Shape** section.

3 In the **a-semiaxis** text field, type `0.09`.

4 In the **b-semiaxis** text field, type `0.12`.

5 Locate the **Position** section. In the **y** text field, type `1.15`.

6 Locate the **Object Type** section. From the **Type** list, choose **Curve**.

Partition Objects 1 (par1)

1 In the **Geometry** toolbar, click **Booleans and Partitions** and choose **Partition Objects**.

2 Select the object **r1** only.

3 In the **Settings** window for **Partition Objects**, locate the **Partition Objects** section.

4 Click to select the **Activate Selection** toggle button for **Tool objects**.

5 Select the object **e1** only.

Form Union (fin)

In the **Geometry** toolbar, click **Build All**.