

# 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<sup>3</sup> and a viscosity of 10<sup>-3</sup> Pa·s. The remainder of the capillary is filled with air, with a density of 1.25 kg/m<sup>3</sup> and a viscosity of  $2 \times 10^{-5}$  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  $1 \times 10^{-3}$  mol/(m<sup>2</sup>·s). The diffusion coefficient of the drug in the water is  $5 \times 10^{-9}$  m<sup>2</sup>/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: CFD\_Module/Multiphase\_Flow/drug\_delivery\_mm

# Modeling Instructions

From the File menu, choose New.

#### NEW

In the New window, click 🙆 Model Wizard.

# MODEL WIZARD

- I 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  $\bigcirc$  Study.
- 5 In the Select Study tree, select General Studies>Time Dependent.
- 6 Click 🗹 Done.

## GEOMETRY I

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.

- I 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

- I In the Model Builder window, under Global Definitions click Parameters I.
- 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)

- I 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 check box.

# Integration 2 (intop2)

- I 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 check box.

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

#### Variables I

- I In the **Definitions** toolbar, click **a= 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	<pre>intop2(z)</pre>	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)

- I In the **Definitions** toolbar, click f(x) 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 I (step I)

- I In the **Definitions** toolbar, click f(X) **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.

# COMPONENT I (COMPI)

# Symmetry/Roller 1

- I In the Definitions toolbar, click Moving Mesh and choose Boundaries>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

- I In the Model Builder window, under Component I (compl) right-click Laminar Flow (spf) 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

- I 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 I

- I 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

- I 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** check box.

#### Contact Angle 1

- I In the Model Builder window, expand the Fluid-Fluid Interface I node, then click Contact Angle I.
- 2 In the Settings window for Contact Angle, locate the Contact Angle section.
- 3 In the  $\theta_w$  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** check box.

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

#### ADD PHYSICS

I In the Physics 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 Add to Component I in the window toolbar.
- 5 In the Physics 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.

- I 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.

Transport Properties 1

- I In the Model Builder window, under Component I (comp1)> Transport of Diluted Species (tds) click Transport Properties I.
- 2 In the Settings window for Transport Properties, 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 I

- I 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** check box.
- **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 I (mat1)

I In the Model Builder window, under Component I (compl) 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)

- I 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 I

#### Scale 1

- I In the Mesh toolbar, click A 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  $\frown$  Free Quad.

# Size

- I 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 I

Parametric Sweep

- I 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

- I In the Model Builder window, click Step I: 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).

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

Solution 1 (soll)

- I In the Study toolbar, click **The Show Default Solver**.
- 2 In the Model Builder window, expand the Solution I (soll) node.
- **3** Right-click **Study I>Solver Configurations>Solution I (sol1)>Time-Dependent Solver I** and choose **Stop Condition**.
- 4 In the Settings window for Stop Condition, locate the Stop Expressions section.
- 5 Click + Add.

6 In the table, enter the following settings:

Stop expression	Stop if	Active	Description
comp1.z_pnt<0.0004	True (>=I)		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.

- 7 In the Model Builder window, under Study I>Solver Configurations>Solution I (soll) click Time-Dependent Solver I.
- 8 In the Settings window for Time-Dependent Solver, click to expand the Absolute Tolerance section.
- 9 From the Global method list, choose Unscaled.
- **10** Click to expand the **Time Stepping** section. Click to expand the **Output** section. Clear the **Store time derivatives** check box.
- II In the **Study** toolbar, click **= Compute**.

# RESULTS

Velocity (spf)

- I 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

- I 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

- I 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  $\longleftrightarrow$  **Zoom Extents** button in the **Graphics** toolbar.
- **5** Click the  $\bigcirc$  **Zoom In** button in the **Graphics** toolbar.
- 6 Click the 🔍 Zoom In button in the Graphics toolbar.
- 7 In the Velocity (spf) toolbar, click **I** Plot.

Compare the resulting plot with that in Figure 2.

#### Streamline 1

- I In the Model Builder window, expand the Results>Concentration (tds) node.
- 2 Right-click Streamline I and choose Disable.

Concentration (tds)

- I 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 **O** Plot.

Compare the resulting plot with that in Figure 3.

## ID Plot Group 6

- I In the Home toolbar, click 🚛 Add Plot Group and choose ID Plot Group.
- 2 In the Settings window for ID Plot Group, locate the Data section.
- 3 From the Dataset list, choose Study I/Parametric Solutions I (sol2).
- 4 From the Parameter selection (u0) list, choose First.

Global I

- I Right-click ID Plot Group 6 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 check box.
- 6 In the ID Plot Group 6 toolbar, click 🗿 Plot.

Compare the resulting plot with that in Figure 4.

#### ID Plot Group 7

- I In the Home toolbar, click 🚛 Add Plot Group and choose ID Plot Group.
- 2 In the Settings window for ID Plot Group, locate the Data section.
- 3 From the Dataset list, choose Study I/Parametric Solutions I (sol2).
- **4** From the **Time selection** list, choose **Last**.

## Global I

- I Right-click ID 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 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 check box.
- 8 In the ID Plot Group 7 toolbar, click i 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 I

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

#### Rectangle 1 (r1)

- I 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 I (el)

- I 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 (parl)

- I In the Geometry toolbar, click 🛑 Booleans and Partitions and choose Partition Objects.
- 2 Select the object rl only.
- 3 In the Settings window for Partition Objects, locate the Partition Objects section.
- **4** Find the **Tool objects** subsection. Click to select the **Delta Activate Selection** toggle button.
- **5** Select the object **e1** only.

Form Union (fin)

In the Geometry toolbar, click 🟢 Build All.

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