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.

Model Definition

The axisymmetric model geometry is shown in Figure 1. 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=6 mm and z=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.

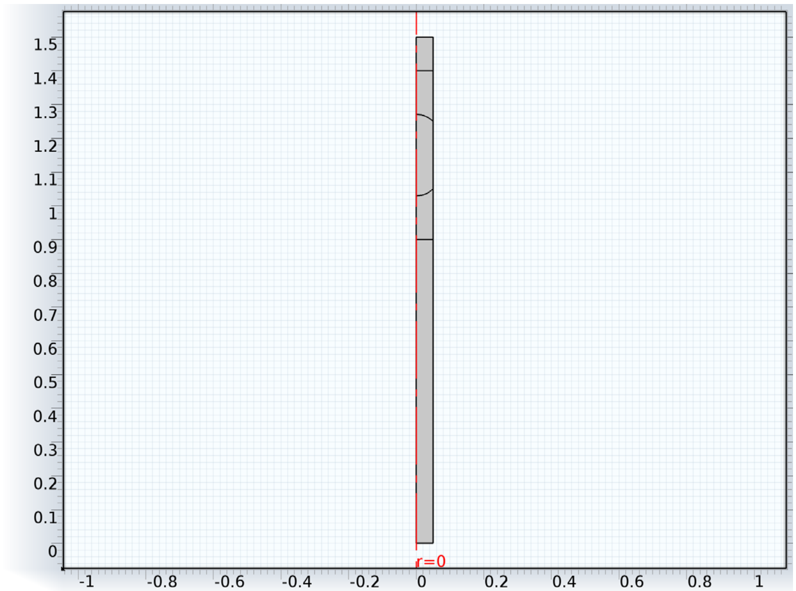

Figure 1: Axisymmetric model geometry.

Results and Discussion

The flow velocity is shown for the drop moving at 0.25 mm/s in Figure 2. 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.

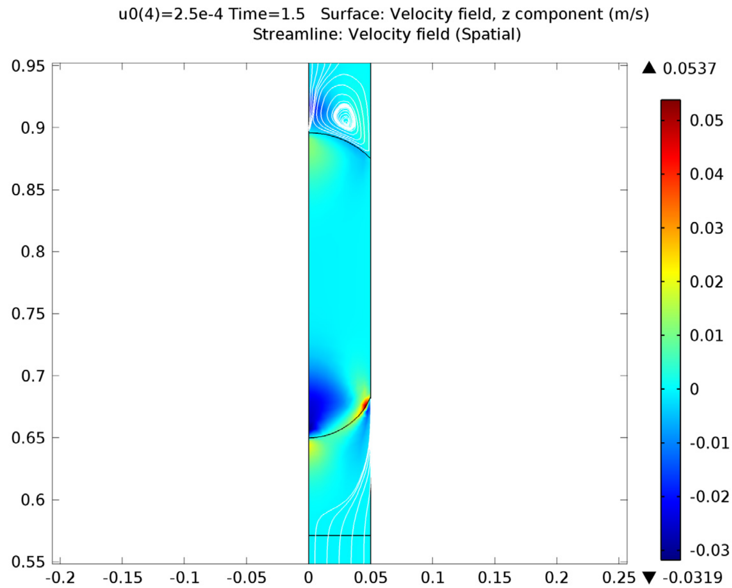

Figure 2: Flow velocity around the droplet as it travels past the edge of the permeable membrane.The droplet velocity is 0.25 mm/s.

Figure 3 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 4, for the drop travelling at 0.1 mm/s. The dissolved drug quantity increases with an 'S' shaped profile as the drug travels down the capillary.

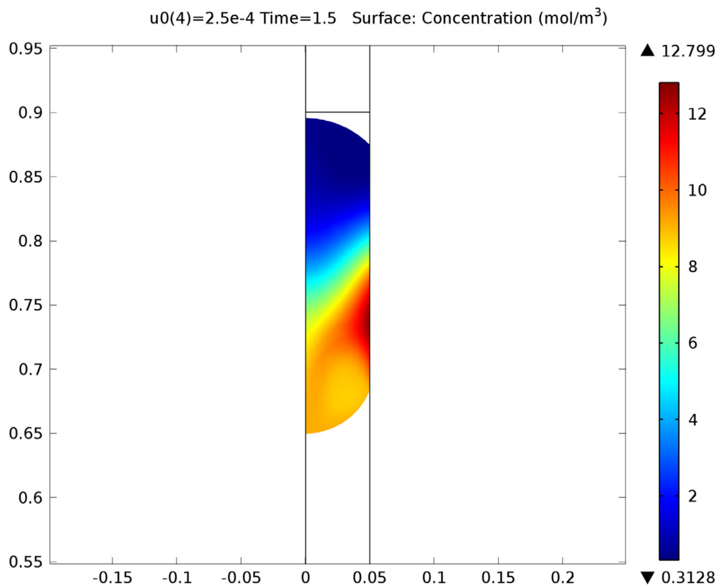

Figure 3: Drug concentration in the droplet as it travels past the edge of the permeable membrane. The droplet velocity is 0.25 mm/s.

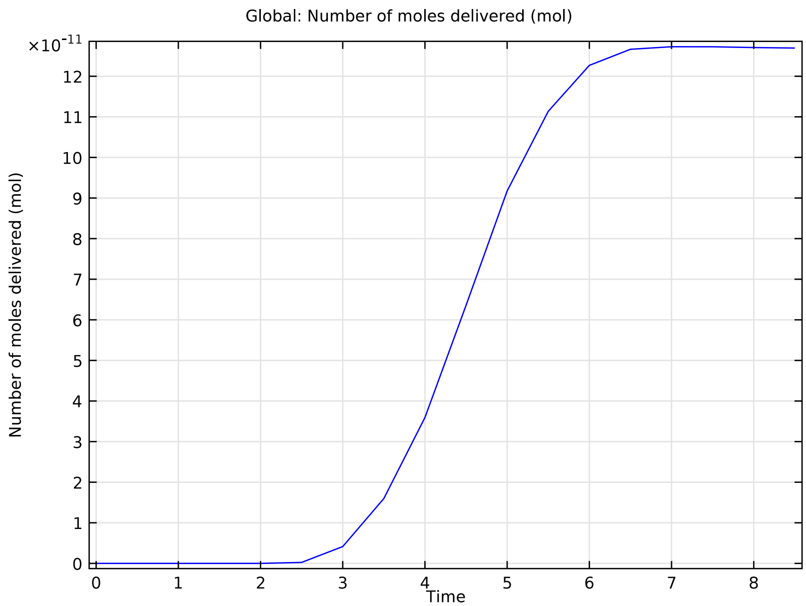

Figure 4: Total drug dose contained in the droplet as a function of time for the droplet travelling at 0.1 mm/s.

Figure 5 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.

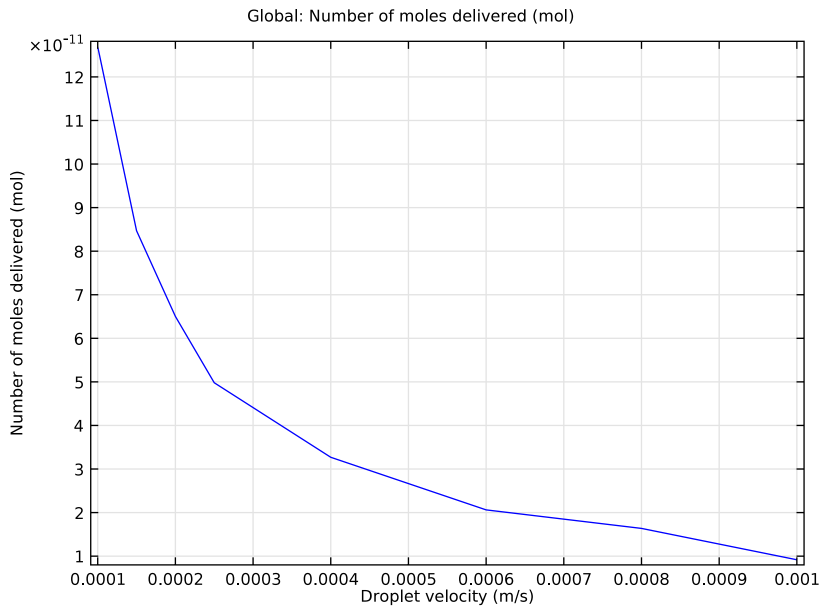

Figure 5: Total drug dose delivered shown against the droplet velocity.

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

Modeling Instructions

MODEL WIZARD

1. Go to the **Model Wizard** window.
2. Click the **2D axisymmetric** button.
3. Click **Next**.
4. In the **Add physics** tree, select **Fluid Flow>Multiphase Flow>Two-Phase Flow, Moving Mesh>Laminar Two-Phase Flow, Moving Mesh (tpfmm)**.
5. Click **Next**.
6. Find the **Studies** subsection. In the tree, select **Preset Studies>Time Dependent**.

7 Click **Finish**.

GEOMETRY 1

Import the model geometry.

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

2 Go to the **Settings** window for Geometry.

3 Locate the **Units** section. From the **Length unit** list, choose **mm**.

Import 1

1 Right-click **Geometry 1** and choose **Import**.

2 Go to the **Settings** window for Import.

3 Locate the **Import** section. 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 In the **Model Builder** window, right-click **Global Definitions** and choose **Parameters**.

2 Go to the **Settings** window for Parameters.

3 Locate the **Parameters** section. In the **Parameters** table, enter the following settings:

NAME	EXPRESSION	DESCRIPTION
`u0`	`0.001[m/s]`	`Droplet velocity (m/s)`

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

DEFINITIONS

Integration 1

1 In the **Model Builder** window, right-click **Model 1>Definitions** and choose **Model Couplings>Integration**.

2 Select Domain 3 only.

Integration 2

1 In the **Model Builder** window, right-click **Definitions** and choose **Model Couplings>Integration**.

2 Go to the **Settings** window for Integration.

3 Locate the **Source Selection** section. 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 In the **Model Builder** window, right-click **Definitions** and choose **Variables**.

2 Go to the **Settings** window for Variables.

3 Locate the **Variables** section. In the **Variables** table, enter the following settings:

NAME	EXPRESSION	DESCRIPTION
n_abs	intop1(2*pi*r*c)	Number of moles delivered
z_pnt	intop2(z)	Position of top of droplet
wallfn	flc2hs(z/1[m]-0.0006,5e-5)-flc2hs(z/1[m]-0.0008,5e-5)	Function to define location of membrane

The above expression makes `wallfn` a smoothed square wave that is zero everywhere except at heights corresponding to the permeable membrane.

Set constraints on the mesh displacement.

LAMINAR TWO-PHASE FLOW, MOVING MESH

1 In the **Model Builder** window, expand the **Model 1>Laminar Two-Phase Flow, Moving Mesh** node.

2 Right-click **Laminar Two-Phase Flow, Moving Mesh** and choose the boundary condition **Moving Mesh>Prescribed Mesh Displacement**.

Prescribed Mesh Displacement 2

Select Boundaries 2 and 11 only.

Prescribed Mesh Displacement 1

1 In the **Model Builder** window, click **Prescribed Mesh Displacement 1**.

2 Go to the **Settings** window for Prescribed Mesh Displacement.

3 Locate the **Prescribed Mesh Displacement** section. Clear the **Prescribed z displacement** check box.

Navier Slip 1

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

1 In the **Model Builder** window, right-click **Laminar Two-Phase Flow, Moving Mesh** and choose **Navier Slip**.
2 Select Boundaries 12–18 only.

Inlet 1

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

1 In the **Model Builder** window, right-click **Laminar Two-Phase Flow, Moving Mesh** and choose the boundary condition **Laminar Flow>Inlet**.
2 Select Boundary 11 only.
3 Go to the **Settings** window for Inlet.
4 Locate the **Boundary Condition** section. From the **Boundary condition** list, choose **Laminar inflow**.
5 Locate the **Laminar Inflow** section. In the U_{av} edit field, type `u0*tanh(1E4*t/1[s])`.

Outlet 1

Apply a pressure constraint at the outlet.

1 In the **Model Builder** window, right-click **Laminar Two-Phase Flow, Moving Mesh** and choose the boundary condition **Laminar Flow>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 **Model Builder** window, right-click **Laminar Two-Phase Flow, Moving Mesh** and choose **Fluid-Fluid Interface**.
2 Select Boundaries 19 and 20 only.

Wall-Fluid Interface 1

1 Right-click **Fluid-Fluid Interface 1** and choose **Wall-Fluid Interface**.
2 Go to the **Settings** window for Wall-Fluid Interface.
3 Locate the **Wall-Fluid Interface** section. In the θ_w edit field, type `3*pi*(1-wallfn)/4+7*pi*wallfn/8`. Using the wall 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.

MODEL WIZARD

1 In the **Model Builder** window, right-click **Model 1** and choose **Add Physics**.
2 Go to the **Model Wizard** window.
3 In the **Add physics** tree, select **Chemical Species Transport>Transport of Diluted Species (chds)**.
4 Click **Add Selected**.
5 Click **Finish**.

Ensure the drug transport occurs only in the liquid domain.

TRANSPORT OF DILUTED SPECIES

1 In the **Model Builder** window, click **Model 1>Transport of Diluted Species**.
2 Go to the **Settings** window for Transport of Diluted Species.
3 Locate the **Domain Selection** section. 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 Go to the **Settings** window for Convection and Diffusion.
3 Locate the **Model Inputs** section. From the $\mathbf{u}$ list, choose **Velocity field (tpfmm/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 In the **Model Builder** window, right-click **Transport of Diluted Species** and choose **Flux**.
2 Select Boundaries 14–16 only.
3 Go to the **Settings** window for Flux.
4 Locate the **Inward Flux** section. Select the **Species c** check box.
5 In the $N_{0,c}$ edit field, type `wallfn*0.001[mol/(m^2*s)]`.

   This expression ensures that flux only enters the droplet as it passes the permeable membrane.

Flux 2

1 In the **Model Builder** window, right-click **Transport of Diluted Species** and choose **Flux**.
2 Select Boundaries 19 and 20 only.
3 Go to the **Settings** window for Flux.
4 Locate the **Inward Flux** section. 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 that no flux enters the domain through the walls of the moving mesh.

MATERIALS

Add the water and air material properties to the model.

Material 1

1 In the **Model Builder** window, right-click **Model 1>Materials** and choose **Material**.
2 Go to the **Settings** window for Material.
3 Locate the **Material Contents** section. In the **Material contents** table, enter the following settings:

PROPERTY	NAME	VALUE
Density	rho	1.25
Dynamic viscosity	mu	2e-5

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

Material 2

1 In the **Model Builder** window, right-click **Materials** and choose **Material**.
2 Select Domain 3 only.
3 Go to the **Settings** window for Material.
4 Locate the **Material Contents** section. In the **Material contents** table, enter the following settings:

PROPERTY	NAME	VALUE
Density	rho	1000
Dynamic viscosity	mu	1e-3

MESH 1

Mesh the geometry. Use a refined mesh around the edges of the droplet.

Scale 1

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

2 Go to the **Settings** window for Scale.

3 Locate the **Geometric Entity Selection** section. 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 **Size**.

2 Go to the **Settings** window for Size.

3 Locate the **Element Size** section. 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 `3.0E-5`.

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

7 In the **Resolution of curvature** edit field, type `0.2`.

8 Click the **Build All** button.

STUDY 1

Set up the parametric sweep.

In the **Model Builder** window, expand the **Study 1** node.

Parametric Sweep

1 Right-click **Study 1** and choose **Parametric Sweep**.

2 Go to the **Settings** window for Parametric Sweep.

3 Locate the **Study Settings** section. Under **Parameter names**, click **Add**.

4 Go to the **Add** dialog box.

5 In the **Parameter names** list, select **u0 (Droplet velocity (m/s))**.

6 Click the **OK** button.

7 Go to the **Settings** window for Parametric Sweep.

8 Locate the **Study Settings** section. In the **Parameter values** edit field, type `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, click **Study 1>Step 1: Time Dependent**.
2 Go to the **Settings** window for Time Dependent.
3 Locate the **Study Settings** section. In the **Times** edit field, type `range(0,0.5,10)`.
4 In the **Model Builder** window, right-click **Study 1** and choose **Show Default Solver**.

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

Solver 1

1 In the **Model Builder** window, expand the **Study 1>Solver Configurations>Solver 1** node.
2 Right-click **Time-Dependent Solver 1** and choose **Stop Condition**.
3 Go to the **Settings** window for Stop Condition.
4 Locate the **Stop Condition** section. In the **Stop expression** edit field, type `mod1.z_pnt-0.0004`. The solver will stop when the real part of this expression is negative.

   Adjust solver settings for optimum performance.
5 In the **Model Builder** window, click **Time-Dependent Solver 1**.
6 Go to the **Settings** window for Time-Dependent Solver.
7 Click to expand the **Absolute Tolerance** section.
8 From the **Global method** list, choose **Unscaled**.
9 Locate the **Advanced** section. From the **Error estimation** list, choose **Exclude algebraic**.
10 In the **Model Builder** window, right-click **Study 1** and choose **Compute**.

RESULTS

2D Plot Group 1

1 In the **Model Builder** window, expand the **Results>2D Plot Group 1** node, then click **2D Plot Group 1**.
2 Go to the **Settings** window for 2D Plot Group.
3 Locate the **Data** section. From the **Parameter value (u0)** list, choose **2.5e-4**.
4 From the **Time** list, choose **1.5**.
5 Right-click **2D Plot Group 1** and choose **Streamline**.
6 Go to the **Settings** window for Streamline.
7 Locate the **Streamline Positioning** section. In the **Number** edit field, type `10`.

8 Select Boundaries 2 and 11 only.

9 Go to the **Settings** window for Streamline.

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

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

12 Go to the **Settings** window for Surface.

13 In the upper-right corner of the **Expression** section, click **Replace Expression**.

14 From the menu, choose **Laminar Two-Phase Flow, Moving Mesh>Velocity field, z component (w)**.

15 Click the **Plot** button.

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

17 Click the **Zoom In** button on the Graphics toolbar twice.

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 Go to the **Settings** window for 2D Plot Group.

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

4 From the **Time** list, choose **1.5**.

5 Click the **Plot** button.

Compare the resulting plot with that in Figure 3.

1D Plot Group 7

1 In the **Model Builder** window, right-click **Results** and choose **1D Plot Group**.

2 Go to the **Settings** window for 1D Plot Group.

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

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

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

6 Go to the **Settings** window for Global.

7 Locate the **y-Axis Data** section. In the table, enter the following settings:

EXPRESSION	UNIT	DESCRIPTION
n_abs	mol	Number of moles delivered

8 Click to expand the **Legends** section.

9 Clear the **Show legends** check box.

10 Click the **Plot** button.

Compare the resulting plot with that in Figure 4.

1D Plot Group 8

1 In the **Model Builder** window, right-click **Results** and choose **1D Plot Group**.

2 Go to the **Settings** window for 1D Plot Group.

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

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

5 Right-click **Results>1D Plot Group 8** and choose **Global**.

6 Go to the **Settings** window for Global.

7 Locate the **y-Axis Data** section. 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 **Solutions** list, choose **Outer**.

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 Click the **Plot** button.

Compare the resulting plot with that in Figure 5.