Dielectrophoretic Separation of Platelets from Red Blood Cells

Introduction

By exploiting the fact that platelets are the smallest cells in blood, it is possible to perform size-based fractionation of blood (that is, separate platelets from red blood cells) using dielectrophoresis. This model demonstrates the continuous separation of platelets from red blood cells (RBCs) using the dielectrophoretic force feature available in the Particle Tracing for Fluid Flow interface.

This model also requires one of the following: CFD Module, Microfluidics Module, or Subsurface Flow Module.

Model Definition

Dielectrophoresis is the movement characterizing particles placed in a non-uniform electric field due to the interaction of the particles' induced dipoles and spatial gradient of the electric field.

When the electric field is computed in the frequency domain, the Dielectrophoretic Force feature adds the following contribution to the total force applied on the particles:

$$\mathbf{F}_{\text{ext}} = 2\pi r_p^3 \varepsilon_0 \text{real}(\varepsilon_f^*) \text{real}\left(\frac{\varepsilon_p^* - \varepsilon_f^*}{\varepsilon_p^* + 2\varepsilon_f^*}\right) \nabla |\mathbf{E}_{\text{rms}}|^2$$

where ε_f^* (dimensionless) is the complex relative permittivity of the fluid, ε_p^* (dimensionless) is the complex relative permittivity of the particle, and \mathbf{E}_{rms} is the root mean square electric field. For fields that are computed in the frequency domain, the complex permittivity can be expressed as

$$\varepsilon^* = \varepsilon - \frac{i\sigma}{\omega}$$

where ε is the permittivity, σ is the electrical conductivity, and ω is the angular frequency of the electric field.

The Shell feature can be added to the Dielectrophoretic Force node to model the dielectrophoretic force on particles with thin shells. The complex permittivity of the shell can differ from the complex permittivity of the rest of the particle. When computing the dielectrophoretic force, the complex permittivity of the particle is replaced by the equivalent complex relative permittivity ϵ^*_{eq} of a homogeneous particle comprising both the shell and the interior of the particle:

$$\varepsilon^*_{eq} = \varepsilon^*_s \frac{\left(\frac{r_0}{r_i}\right)^3 + 2\left(\frac{\varepsilon^*_p - \varepsilon^*_s}{\varepsilon^*_p + 2\varepsilon^*_s}\right)}{\left(\frac{r_0}{r_i}\right)^3 - \left(\frac{\varepsilon^*_p - \varepsilon^*_s}{\varepsilon^*_p + 2\varepsilon^*_s}\right)}$$

where r_0 and r_i (SI unit: m) are the outer and inner radii of the shell, respectively; ε_p^* (dimensionless) is the complex relative permittivity of the particle, and ε_s^* (dimensionless) is the complex relative permittivity of the outer shell. For this model, the shell parameters for platelets and RBCs are respectively obtained from Ref. 2 and Ref. 3.

The present model is based on a lab-on-a-chip device described in detail in Ref. 1. It consists of two inlets, two outlets and a separation region in which a non-uniform electric field created by an arrangement of electrodes of alternating polarity alter the particle trajectories. Figure 1 shows the schematic of the modeled geometry. As seen on the figure, the inlet velocity for the lower inlet is significantly higher (853 μ m/s) than the upper inlet (154 μ m/s) in order to focus all the injected particles toward the upper outlet.

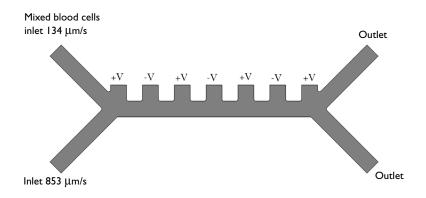


Figure 1: Two dimensional geometry of the modeled device. Details are presented in Ref. 1. The inlet velocity for the bottom inlet is significantly higher than the upper inlet to focus all the injected particles toward the upper outlet (Flow Focusing).

The model uses the following physics interfaces:

- I Creeping Flow (Microfluidics Module) to model the fluid flow,
- 2 Electric Currents to model the electric field in the microchannel, and
- **3** Particle Tracing for Fluid Flow (Particle Tracing Module) to compute the trajectories of RBCs and platelets under the influence of drag and dielectrophoretic forces

Three studies are also used:

- I Study 1 solves for the steady state fluid dynamics and frequency domain (AC) electric potential.
- **2** Study 2 uses a Time Dependent study step which utilizes the solution from Study 1 and estimates the particle trajectories without the dielectrophoretic force, as a result of which all particles (platelets and RBC) are focused to the same outlet.
- **3** Study 3 computes the particle trajectories while including the effect of the dielectrophoretic force.

Results and Discussion

Figure 2 shows the electric potential in the microfluidic device.

Figure 3 shows the particle trajectories in the absence of the dielectrophoretic force. All of the particles follow the same path and exit through the outlet in the top-right quadrant of the modeling domain.

Figure 4 shows the particle trajectories when the particles are subjected to the dielectrophoretic force. Due to differences in the particle properties, the RBCs and platelets exit the domain through different outlets.

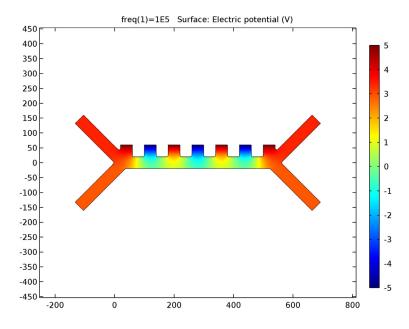


Figure 2: Spatial variation of the electric potential in the microfluidic channel.

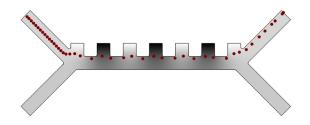


Figure 3: Particle trajectories without dielectrophoretic force applied. The RBCs are displayed in red and the platelets in blue. Since the particles are released at the same time and follow a similar path, the platelets are hidden behind the RBCs on the figure.

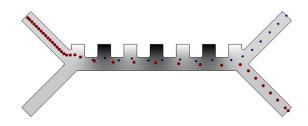


Figure 4: Particle trajectories with dielectrophoretic force applied. The RBCs are displayed in red and the platelets in blue. For sake of visualization, the relative size of the RBCs has been divided by two.

References

1. N. Piacentini, G. Mernier, R. Tornay, and P. Renaud, "Separation of platelets from other blood cells in continuous-flow by dielectrophoresis field-flow-fractionation," *Biomicrofluidics*, vol. 5, 034122, 2011.

2. M. Egger and E. Donath, "Electrorotation measurements of diamide-induced platelet activation changes," *Biophysical Journal*, vol. 68, pp. 364–372, 1995.

3. S. Park, Y. Zhang, T.H. Wang, and S. Yang, "Continuous dielectrophoretic bacterial separation and concentration from physiological media of high conductivity," Supplementary information, *Lab on a Chip*, vol. 11, pp. 2893–2900, 2011.

Application Library path: Particle_Tracing_Module/Fluid_Flow/ dielectrophoretic_separation

Modeling Instructions

From the File menu, choose New.

NEW

I In the New window, click Model Wizard.

MODEL WIZARD

- I In the Model Wizard window, click 2D.
- 2 In the Select physics tree, select AC/DC>Electric Currents (ec).
- 3 Click Add.
- 4 In the Select physics tree, select Fluid Flow>Single-Phase Flow>Creeping Flow (spf).
- 5 Click Add.
- 6 In the Select physics tree, select Fluid Flow>Particle Tracing>Particle Tracing for Fluid Flow (fpt).
- 7 Click Add.
- 8 Click Done.

GEOMETRY I

- I In the Model Builder window, click Geometry I.
- 2 In the Settings window for Geometry, locate the Units section.
- 3 From the Length unit list, choose µm.

Rectangle 1 (r1)

- I On the Geometry toolbar, click Primitives and choose Rectangle.
- 2 In the Settings window for Rectangle, locate the Size section.
- 3 In the Width text field, type 560/2.
- **4** In the **Height** text field, type 40.
- **5** Locate the **Position** section. In the **y** text field, type -20.

Rectangle 2 (r2)

- I On the Geometry toolbar, click Primitives and choose Rectangle.
- 2 In the Settings window for Rectangle, locate the Size section.
- **3** In the **Width** text field, type 40.
- 4 In the **Height** text field, type 200.
- 5 Locate the **Position** section. In the **x** text field, type 9.

6 In the y text field, type -9.

7 Locate the Rotation Angle section. In the Rotation text field, type 45.

Mirror I (mir I)

- I On the Geometry toolbar, click Transforms and choose Mirror.
- 2 Select the object r2 only.
- **3** In the **Settings** window for Mirror, locate the **Normal Vector to Line of Reflection** section.
- **4** In the **x** text field, type **0**.
- **5** In the **y** text field, type **1**.
- 6 Locate the Input section. Select the Keep input objects check box.

Mirror 2 (mir2)

- I On the Geometry toolbar, click Transforms and choose Mirror.
- 2 Click in the **Graphics** window and then press Ctrl+A to select all objects.
- 3 In the Settings window for Mirror, locate the Input section.
- 4 Select the Keep input objects check box.
- 5 Locate the Point on Line of Reflection section. In the x text field, type 560/2.

Square 1 (sq1)

- I On the Geometry toolbar, click Primitives and choose Square.
- 2 In the Settings window for Square, locate the Size section.
- **3** In the **Side length** text field, type 40.
- 4 Locate the **Position** section. In the **x** text field, type 20.
- **5** In the **y** text field, type **20**.

Array I (arr1)

- I On the Geometry toolbar, click Transforms and choose Array.
- 2 Select the object sql only.
- 3 In the Settings window for Array, locate the Size section.
- 4 In the x size text field, type 7.
- 5 Locate the **Displacement** section. In the **x** text field, type 80.

Union I (uni I)

I On the Geometry toolbar, click Booleans and Partitions and choose Union.

Use the select box icon to select all the geometry objects.

- 2 Click the Select Box button on the Graphics toolbar.
- 3 Click in the Graphics window and then press Ctrl+A to select all objects.
- 4 In the Settings window for Union, locate the Union section.
- 5 Clear the Keep interior boundaries check box.

Fillet I (fill)

- I On the Geometry toolbar, click Fillet.
- **2** On the object **unil**, select Points 5, 6, 8, 9, 11, and 13 only.
- **3** On the object **unil**, select Points 5, 6, 8, 9, 11, 13, 15, 17, 19, and 22 only.
- **4** On the object **unil**, select Points 5, 6, 8, 9, 11, 13, 15, 17, 19, 22, 24, 26, 28, 30, 32, 34, 35, and 37 only.
- 5 In the Settings window for Fillet, locate the Radius section.
- 6 In the Radius text field, type 5.
- 7 Click the Build All Objects button.

GLOBAL DEFINITIONS

Parameters

I On the Home toolbar, click Parameters.

2 In the Settings window for Parameters, locate the Parameters section.

3 In the table, enter the following settings:

Name	Expression	Value	Description
f0	100[kHz]	IE5 Hz	Frequency of the electric field
sigma_f	55[mS/m]	0.055 S/m	Fluid medium conductivity
epsilon_f	80	80	Fluid relative permittivity
rho_f	1000[kg/m^3]	1000 kg/m ³	Fluid density
mu_f	1e-3[Pa*s]	0.001 Pa·s	Fluid dynamic viscosity
rho_p	1050[kg/m^3]	1050 kg/m ³	Particle density (RBCs and platelets)
dp1	1.8[um]	1.8E-6 m	Particle diameter: platelets
dp2	5[um]	5E-6 m	Particle diameter: RBCs

Name	Expression	Value	Description
sigma_p1	0.25[S/m]	0.25 S/m	Particle conductivity: platelets
sigma_p2	0.31[S/m]	0.31 S/m	Particle conductivity: RBCs
epsilon_p1	50	50	Particle relative permittivity: platelets
epsilon_p2	59	59	Particle relative permittivity: RBCs
sigma_s1	1e-6[S/m]	IE-6 S/m	Shell electrical conductivity: platelets
sigma_s2	1e-6[S/m]	IE-6 S/m	Shell electrical conductivity: RBCs
epsilon_s1	6	6	Shell relative permittivity: platelets
epsilon_s2	4.44	4.44	Shell relative permittivity: RBCs
th_s1	8[nm]	8E-9 m	Shell thickness: platelets
th_s2	9[nm]	9E-9 m	Shell thickness: RBCs

ELECTRIC CURRENTS (EC)

Electric Potential 1

- I On the Physics toolbar, click Boundaries and choose Electric Potential.
- 2 In the Settings window for Electric Potential, locate the Electric Potential section.
- **3** In the V_0 text field, type 5.
- 4 Select Boundaries 8, 17, 26, and 34 only.

Electric Potential 2

- I On the Physics toolbar, click Boundaries and choose Electric Potential.
- 2 In the Settings window for Electric Potential, locate the Electric Potential section.
- **3** In the V_0 text field, type -5.
- 4 Select Boundaries 13, 21, and 30 only.

CREEPING FLOW (SPF)

Inlet I

I On the Physics toolbar, click Boundaries and choose Inlet.

- 2 Select Boundary 3 only.
- 3 In the Settings window for Inlet, locate the Velocity section.
- 4 In the U_0 text field, type 134[um/s].

Inlet 2

- I On the Physics toolbar, click Boundaries and choose Inlet.
- 2 Select Boundary 1 only.
- 3 In the Settings window for Inlet, locate the Velocity section.
- 4 In the U_0 text field, type 853[um/s].

Outlet I

- I On the Physics toolbar, click Boundaries and choose Outlet.
- 2 Select Boundaries 40 and 41 only.

PARTICLE TRACING FOR FLUID FLOW (FPT)

Wall I

- I In the Model Builder window, expand the Particle Tracing for Fluid Flow (fpt) node, then click Wall I.
- 2 In the Settings window for Wall, locate the Wall Condition section.
- 3 From the Wall condition list, choose Bounce.

Particle Properties 1

- I In the Model Builder window, under Component I (compl)>Particle Tracing for Fluid Flow (fpt) click Particle Properties I.
- 2 In the Settings window for Particle Properties, locate the Particle Properties section.
- **3** In the ρ_p text field, type rho_p.
- **4** In the d_p text field, type dp1.

Override Properties 1

- I On the Physics toolbar, click Global and choose Override Properties.
- **2** In the **Settings** window for Override Properties, locate the **Particle Properties** section.
- **3** In the ρ_p text field, type rho_p.
- **4** In the d_p text field, type dp2.

Inlet I

I On the Physics toolbar, click Boundaries and choose Inlet.

- 2 Select Boundary 3 only.
- 3 In the Settings window for Inlet, locate the Release Times section.
- **4** In the **Release times** text field, type range(0,0.05,3).
- **5** Locate the **Initial Position** section. From the **Initial position** list, choose **Uniform distribution**.
- 6 Locate the Initial Velocity section. From the **u** list, choose Velocity field (spf).

Inlet 2

- I Right-click Component I (comp1)>Particle Tracing for Fluid Flow (fpt)>Inlet I and choose Duplicate.
- 2 In the Settings window for Inlet, click to expand the Inherit properties section.
- **3** Locate the Inherit Properties section. From the Inherit properties list, choose Override Properties 1.

Outlet I

- I On the Physics toolbar, click Boundaries and choose Outlet.
- **2** Select Boundaries 40 and 41 only.

Drag Force 1

- I On the Physics toolbar, click Domains and choose Drag Force.
- 2 Select Domain 1 only.
- 3 In the Settings window for Drag Force, locate the Drag Force section.
- 4 From the **u** list, choose Velocity field (spf).

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	Name	Value	Unit	Property group
Electrical conductivity	sigma	sigma_f	S/m	Basic
Relative permittivity	epsilonr	epsilon_f	I	Basic
Density	rho	rho_f	kg/m³	Basic
Dynamic viscosity	mu	mu_f	Pa∙s	Basic

Add a Stationary and a Frequency Domain study step to respectively solve the fluid flow and electric potential in the channel.

ROOT

On the Home toolbar, click Windows and choose Add Study.

ADD STUDY

- I Go to the Add Study window.
- 2 Find the Studies subsection. In the Select study tree, select Preset Studies.
- **3** Find the **Physics interfaces in study** subsection. In the table, enter the following settings:

Physics	Solve
Electric Currents (ec)	
Particle Tracing for Fluid Flow (fpt)	

- 4 Find the Studies subsection. In the Select study tree, select Preset Studies>Stationary.
- 5 Click Add Study in the window toolbar.

STUDY I

Step 2: Frequency Domain

- I On the Study toolbar, click Study Steps and choose Frequency Domain>Frequency Domain.
- 2 In the Settings window for Frequency Domain, locate the Study Settings section.
- 3 In the Frequencies text field, type f0.
- **4** Locate the **Physics and Variables Selection** section. In the table, enter the following settings:

Physics interface	Solve for	Discretization
Creeping Flow (spf)		physics
Particle Tracing for Fluid Flow (fpt)		physics

5 On the Study toolbar, click Compute.

RESULTS

Electric Potential (ec)

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

2 Compare the resulting plot to Figure 2.

Add a new Time Dependent study to compute the trajectories of the particles without the Dielectrophoretic Force feature.

ROOT

On the Home toolbar, click Windows and choose Add Study.

ADD STUDY

- I Go to the Add Study window.
- 2 Find the Studies subsection. In the Select study tree, select Preset Studies.
- **3** Find the **Physics interfaces in study** subsection. In the table, enter the following settings:

Physics	Solve
Electric Currents (ec)	
Creeping Flow (spf)	

- 4 Find the Studies subsection. In the Select study tree, select Preset Studies>Time Dependent.
- 5 Click Add Study in the window toolbar.

Change the relative tolerance for better accuracy.

STUDY 2

Step 1: Time Dependent

- I In the Model Builder window, under Study 2 click Step I: Time Dependent.
- 2 In the Settings window for Time Dependent, locate the Study Settings section.
- 3 In the Times text field, type range(0,0.05,3).
- 4 Select the **Relative tolerance** check box.
- **5** In the associated text field, type **1.0E-3**.

Check the values of variables not solve for in order to get access to the velocity field and electric potential computed in the first study.

- 6 Click to expand the Values of dependent variables section. Locate the Values of Dependent Variables section. Select the Values of variables not solved for check box.
- 7 From the Method list, choose Solution.

8 From the Study list, choose Study I, Frequency Domain.

Get the initial solution. The purpose is to generate plot of the particle trajectories and use it to display the particles as the model solves.

9 On the Study toolbar, click Get Initial Value.

Modify the plot to display the particle size and electric potential.

RESULTS

Particle Trajectories (fpt)

To facilitate visualization use an if statement to display the RBCs with a diameter two times smaller than their real size.

- I In the Model Builder window, expand the Results>Particle Trajectories (fpt) node, then click Particle Trajectories I.
- 2 In the Settings window for Particle Trajectories, locate the Coloring and Style section.
- 3 Find the Point style subsection. In the Point radius expression text field, type if(fpt.dp==dp2,dp2/2,dp1).
- 4 In the Model Builder window, expand the Results>Particle Trajectories (fpt)>Particle Trajectories | node, then click Color Expression |.
- 5 In the Settings window for Color Expression, locate the Expression section.
- 6 In the **Expression** text field, type fpt.dp.
- 7 Locate the Coloring and Style section. From the Color table list, choose Wave.
- 8 In the Model Builder window, right-click Particle Trajectories (fpt) and choose Surface.
- 9 In the Settings window for Surface, locate the Coloring and Style section.
- **IO** From the **Color table** list, choose **GrayScale**.

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

Plot the particle trajectories while solving. Note that the dielectrophoretic force isn't applied in this study, so all of the particles appear follow approximately the same trajectory.

STUDY 2

Step 1: Time Dependent

- I In the Model Builder window, under Study 2 click Step 1: Time Dependent.
- **2** In the **Settings** window for Time Dependent, click to expand the **Results while solving** section.

- 3 Locate the Results While Solving section. Select the Plot check box.
- 4 From the Plot group list, choose Particle Trajectories (fpt).
- 5 On the Study toolbar, click Compute.

RESULTS

Particle Trajectories (fpt)

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

Compare the resulting plot to Figure 3.

2 On the Particle Trajectories (fpt) toolbar, click Plot.

Now add another Time Dependent study to compute the effect of the dielectrophoretic force on the particle trajectories.

ROOT

On the Home toolbar, click Windows and choose Add Study.

ADD STUDY

- I Go to the Add Study window.
- 2 Find the Studies subsection. In the Select study tree, select Preset Studies.
- **3** Find the **Physics interfaces in study** subsection. In the table, enter the following settings:

Physics	Solve
Electric Currents (ec)	
Creeping Flow (spf)	

- 4 Find the Studies subsection. In the Select study tree, select Preset Studies>Time Dependent.
- 5 Click Add Study in the window toolbar.

STUDY 3

Step 1: Time Dependent

- I In the Model Builder window, under Study 3 click Step I: Time Dependent.
- 2 In the Settings window for Time Dependent, locate the Study Settings section.
- 3 In the Times text field, type range(0,0.05,3).
- 4 Select the **Relative tolerance** check box.

- **5** In the associated text field, type **1.0E-3**.
- 6 Click to expand the Values of dependent variables section. Locate the Values of Dependent Variables section. Select the Values of variables not solved for check box.
- 7 From the Method list, choose Solution.
- 8 From the Study list, choose Study I, Frequency Domain.

COMPONENT I (COMPI)

In the Model Builder window, expand the Component I (compl) node.

PARTICLE TRACING FOR FLUID FLOW (FPT)

Dielectrophoretic Force 1

- I On the Physics toolbar, click Domains and choose Dielectrophoretic Force.
- **2** Select Domain 1 only.
- **3** In the **Settings** window for Dielectrophoretic Force, locate the **Dielectrophoretic Force** section.
- 4 From the **E** list, choose **Electric field (ec/cucn I)**.
- **5** Locate the **Particle Properties** section. In the $\varepsilon_{r,p}$ text field, type epsilon_p1.
- **6** In the σ_p text field, type sigma_p1.
- 7 Locate the Advanced Settings section. Select the Use piecewise polynomial recovery on field check box.
- 8 From the Particles to affect list, choose Single species.

Shell I

- I On the Physics toolbar, click Attributes and choose Shell.
- 2 In the Settings window for Shell, locate the Shell Properties section.
- **3** In the t_s text field, type th_s1.
- **4** In the $\varepsilon_{r,s}$ text field, type epsilon_s1.
- **5** In the σ_s text field, type sigma_s1.

Dielectrophoretic Force 2

- I In the Model Builder window, under Component I (compl)>Particle Tracing for Fluid Flow (fpt) right-click Dielectrophoretic Force I and choose Duplicate.
- **2** In the **Settings** window for Dielectrophoretic Force, locate the **Particle Properties** section.
- **3** In the $\varepsilon_{r,p}$ text field, type epsilon_p2.

- **4** In the σ_p text field, type sigma_p2.
- 5 Locate the Advanced Settings section. From the Affected particle properties list, choose Override Properties 1.

Shell I

- I In the Model Builder window, expand the Dielectrophoretic Force 2 node, then click Shell I.
- 2 In the Settings window for Shell, locate the Shell Properties section.
- **3** In the *t_s* text field, type th_s2.
- **4** In the $\varepsilon_{r,s}$ text field, type epsilon_s2.
- **5** In the σ_s text field, type sigma_s2.

Get the initial solution in order to view the particle trajectories while running the study.

STUDY 3

On the Study toolbar, click Get Initial Value.

RESULTS

Particle Trajectories (fpt) 1

- I In the Model Builder window, expand the Particle Trajectories (fpt) I node, then click Particle Trajectories I.
- 2 In the Settings window for Particle Trajectories, locate the Coloring and Style section.
- **3** Find the **Point style** subsection. In the **Point radius expression** text field, type if(fpt.dp==dp2,dp2/2,dp1).
- 4 In the Model Builder window, expand the Results>Particle Trajectories (fpt) I>Particle Trajectories I node, then click Color Expression I.
- 5 In the Settings window for Color Expression, locate the Expression section.
- **6** In the **Expression** text field, type fpt.dp.
- 7 Locate the Coloring and Style section. From the Color table list, choose Wave.
- 8 In the Model Builder window, right-click Particle Trajectories (fpt) I and choose Surface.
- 9 In the Settings window for Surface, locate the Coloring and Style section.
- **IO** From the **Color table** list, choose **GrayScale**.
- II Click the Zoom Extents button on the Graphics toolbar.

Plot the particle trajectories while solving. Note that the dielectrophoretic force separates the particles.

STUDY 3

Step 1: Time Dependent

- I In the Model Builder window, under Study 3 click Step I: Time Dependent.
- **2** In the **Settings** window for Time Dependent, click to expand the **Results while solving** section.
- 3 Locate the **Results While Solving** section. Select the **Plot** check box.
- 4 From the Plot group list, choose Particle Trajectories (fpt) I.
- **5** On the **Study** toolbar, click **Compute**.

RESULTS

Particle Trajectories (fpt) 1

I Click the Zoom Extents button on the Graphics toolbar.

Compare the resulting plot to Figure 4.

Solved with COMSOL Multiphysics 5.1