

Dielectrophoretic Separation of Platelets from Red Blood Cells

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 of particles in a non-uniform electric field due to the interaction of the particles' induced dipoles with the spatial gradient of the electric field norm.

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:

$$\mathbf{F}_{\mathrm{ext}} = 2\pi r_{p}^{3} \varepsilon_{0} \operatorname{real}(\varepsilon_{f}^{\star}) \operatorname{real}\left(\frac{\varepsilon_{p}^{\star} - \varepsilon_{f}^{\star}}{\varepsilon_{p}^{\star} + 2\varepsilon_{f}^{\star}}\right) \nabla \left|\mathbf{E}_{\mathrm{rms}}\right|^{2}$$

where ϵ_f^\star (dimensionless) is the complex relative permittivity of the fluid, ϵ_p^\star (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** subnode can be added to the **Dielectrophoretic Force** node to model the dielectrophoretic force on particles with thin dielectric 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:

$$\varepsilon_{\text{eq}}^{\star} = \varepsilon_{s}^{\star} \frac{\left(\frac{r_{0}}{r_{i}}\right)^{3} + 2\left(\frac{\varepsilon_{p}^{\star} - \varepsilon_{s}^{\star}}{\varepsilon_{p}^{\star} + 2\varepsilon_{s}^{\star}}\right)}{\left(\frac{r_{0}}{r_{i}}\right)^{3} - \left(\frac{\varepsilon_{p}^{\star} - \varepsilon_{s}^{\star}}{\varepsilon_{p}^{\star} + 2\varepsilon_{s}^{\star}}\right)}$$

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^\star (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 µm/s) than the upper inlet $(154 \,\mu\text{m/s})$ in order to focus all the injected particles toward the upper outlet.

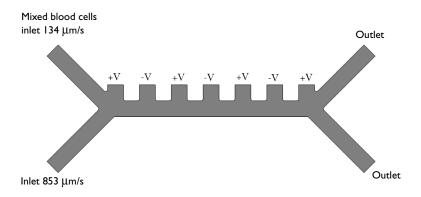


Figure 1: Two dimensional geometry of the modeled device. Details are presented in Ref. 1. The inlet velocity for the bottom inlet is significantly higher than the upper inlet to focus all the injected particles toward the upper outlet (Flow Focusing).

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. When no dielectrophoretic force is applied, the red blood cells and platelets follow the same path and exit through the same outlet, as shown in Figure 3. When the dielectrophoretic force is applied, the two species are separated due to the differences in their dielectric properties, as shown in Figure 4.

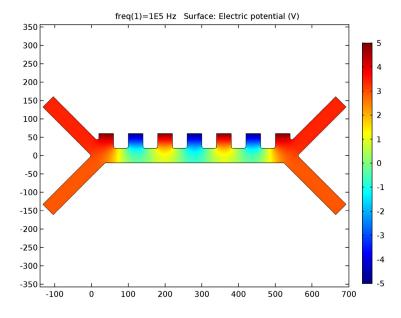


Figure 2: Spatial variation of the electric potential in the microfluidic channel.

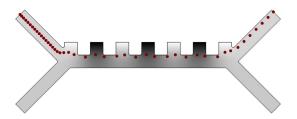


Figure 3: Particle trajectories without dielectrophoretic force applied. The RBCs are displayed in red and the platelets in blue. Since the particles are released at the same time and follow a similar path, the platelets are hidden behind the RBCs on the figure.

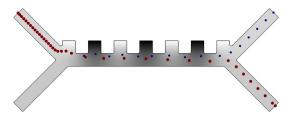


Figure 4: Particle trajectories with dielectrophoretic force applied. The RBCs are displayed in red and the platelets in blue. For sake of visualization, the relative size of the RBCs has been divided by two.

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

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

Insert the prepared geometry sequence from file. You can read the instructions for creating the geometry in the appendix.

- I On the Geometry toolbar, click Insert Sequence.
- **2** Browse to the application's Application Libraries folder and double-click the file dielectrophoretic_separation_geom_sequence.mph.

GLOBAL DEFINITIONS

Parameters

- I On the Home toolbar, click Parameters.
 - Load the model parameters from a file.
- 2 In the Settings window for Parameters, locate the Parameters section.
- 3 Click Load from File.
- 4 Browse to the application's Application Libraries folder and double-click the file dielectrophoretic_separation_parameters.txt.

ELECTRIC CURRENTS (EC)

Electric Potential I

- 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)

In the Model Builder window, under Component I (compl) click 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.
- 5 In the Model Builder window, click Particle Tracing for Fluid Flow (fpt).

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 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 I.

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

In the Model Builder window, under Component I (compl) right-click Materials and choose Blank Material.

Material I (mat I)

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

ADD STUDY

- I On the Home toolbar, click Add Study to open the Add Study window.
- **2** Go to the **Add Study** window.
- 3 Find the Studies subsection. In the Select Study tree, select Preset Studies.
- 4 Find the **Physics interfaces in study** subsection. In the table, clear the **Solve** check box for Electric Currents (ec) and Particle Tracing for Fluid Flow (fpt).
- 5 Find the Studies subsection. In the Select Study tree, select Preset Studies>Stationary.
- **6** Click **Add Study** in the window toolbar.
- 7 On the Home toolbar, click Add Study to close the Add Study window.

STUDY I

Frequency Domain

On the Study toolbar, click Study Steps and choose Frequency Domain>Frequency Domain.

Step 2: Frequency Domain

- I In the Settings window for Frequency Domain, locate the Study Settings section.
- 2 In the Frequencies text field, type f0.
- 3 Locate the Physics and Variables Selection section. In the table, clear the Solve for check box for Creeping Flow (spf) and Particle Tracing for Fluid Flow (fpt).
- 4 On the Study toolbar, click Compute.

RESULTS

Electric Potential (ec)

Click the **Zoom Extents** button on the **Graphics** toolbar. Compare the resulting plot to Figure 2.

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

ADD STUDY

- I On the Study toolbar, click Add Study to open the Add Study window.
- **2** Go to the **Add Study** window.
- 3 Find the Studies subsection. In the Select Study tree, select Preset Studies.

- 4 Find the Physics interfaces in study subsection. In the table, clear the Solve check box for Electric Currents (ec) and Creeping Flow (spf).
- 5 Find the Studies subsection. In the Select Study tree, select Preset Studies>Time Dependent.
- 6 Click Add Study in the window toolbar.
- 7 On the Study toolbar, click Add Study to close the Add Study window.

Change the relative tolerance for better accuracy.

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, 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. Find the Values of variables not solved for subsection. From the Settings list, choose User controlled.
- 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 a plot of the particule trajectories and use it to plot the particles while solving for them.

Particle Trajectories (fpt)

On the Study toolbar, click Get Initial Value.

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

RESULTS

Particle Trajectories (fpt)

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

Particle Trajectories 1

- I In the Model Builder window, expand the Results>Particle Trajectories (fpt) node, then click Particle Trajectories 1.
- 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).

Color Expression 1

- I In the Model Builder window, expand the Particle Trajectories I node, then click Color Expression 1.
- 2 In the **Settings** window for Color Expression, locate the **Expression** section.
- 3 In the Expression text field, type fpt.dp.
- 4 Locate the Coloring and Style section. From the Color table list, choose Wave.

Particle Trajectories (fbt)

In the Model Builder window, under Results right-click Particle Trajectories (fpt) and choose Surface.

Surface I

- I In the Settings window for Surface, locate the Coloring and Style section.
- 2 From the Color table list, choose GrayScale.
- 3 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 (fbt)

Click the **Zoom Extents** button on the **Graphics** toolbar. The plot should look like Figure 3.

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

ADD STUDY

- I On the Study toolbar, click Add Study to open the Add Study window.
- 2 Go to the Add Study window.
- 3 Find the Studies subsection. In the Select Study tree, select Preset Studies.
- **4** Find the **Physics interfaces in study** subsection. In the table, clear the **Solve** check box for Electric Currents (ec) and Creeping Flow (spf).
- 5 Find the Studies subsection. In the Select Study tree, select Preset Studies>Time Dependent.
- 6 Click Add Study in the window toolbar.
- 7 On the Study toolbar, click Add Study to close the Add Study window.

STUDY 3

Step 1: Time Dependent

- I In the Model Builder window, under Study 3 click Step 1: 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. Find the Values of variables not solved for subsection. From the Settings list, choose User controlled.
- 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/cucn1)**.
- **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 1

In the Model Builder window, under Component I (compl)>Particle Tracing for Fluid Flow (fpt) right-click Dielectrophoretic Force I and choose Duplicate.

Dielectrophoretic Force 2

- In the Settings window for Dielectrophoretic Force, locate the Particle Properties section.
- **2** In the $\varepsilon_{r,p}$ text field, type epsilon_p2.
- **3** In the σ_p text field, type sigma_p2.
- 4 Locate the Advanced Settings section. From the Affected particle properties list, choose Override Properties 1.

Shell 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

Particle Trajectories (fpt) I

On the Study toolbar, click Get Initial Value.

RESULTS

Particle Trajectories 1

- I In the Model Builder window, expand the Particle Trajectories (fpt) I node, then click Particle Trajectories 1.
- 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).

Color Expression 1

- I In the Model Builder window, expand the Particle Trajectories I node, then click Color Expression 1.
- 2 In the Settings window for Color Expression, locate the Expression section.
- 3 In the Expression text field, type fpt.dp.
- 4 Locate the Coloring and Style section. From the Color table list, choose Wave.

Particle Trajectories (fpt) I

In the Model Builder window, under Results right-click Particle Trajectories (fpt) I and choose Surface.

Surface I

- I In the Settings window for Surface, locate the Coloring and Style section.
- 2 From the Color table list, choose GrayScale.
- 3 On the Particle Trajectories (fpt) I toolbar, click Plot.
- 4 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 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) 1.
- 5 On the Home toolbar, click Compute.

RESULTS

Particle Trajectories (fbt) I

- I In the Model Builder window, click Particle Trajectories (fpt) I.
- 2 On the Particle Trajectories (fpt) I toolbar, click Plot.
- 3 Click the **Zoom Extents** button on the **Graphics** toolbar. Compare the resulting plot to Figure 4.

Appendix - Geometry Instructions

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

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 I (r I)

- I On the Geometry toolbar, click Primitives and choose Rectangle.
- 2 In the Settings window for Rectangle, locate the Size and Shape 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 and Shape 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 (mirl)

- 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 I (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 (arr I)

- I On the Geometry toolbar, click Transforms and choose Array.
- **2** Select the object **sq1** 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 **uni1**, select Points 5, 6, 8, 9, 11, 13, 15, 17, 19, 22, 24, 26, 28, 30, 32, 34, 35, and 37 only.
- 3 In the Settings window for Fillet, locate the Radius section.
- 4 In the Radius text field, type 5.
- 5 Click Build All Objects.