Electronic Supplementary Material (ESI) for Lab on a Chip.

Supplementary material for the manuscript « Positional Dependence of Particles and Cells in Microfluidic Electrical Impedance Flow Cytometry: Origin, Challenges and Opportunities »

Impedance signals obtained when a particle is flowing inside a microfluidic chip between two electrodes can be simulated by FEM. In order to be able to compare the two most widely spread configurations of electrodes used for impedance sensing in microsystems, the facing and the coplanar electrode designs, FEM simulations were performed using Comsol Multiphysics 5.5 and the AC/DC Module.

Comsol tutorials usually cover the basics. The aim of this supplementary material is to present key tips needed to improve the quality of the simulations related to simulating impedance measurements while reducing computation time.

Here two different Comsol files have been used to compare the impedance signal obtained for coplanar and facing electrodes when a particle is flowing through. While constructing such simulations different aspects must be carefully taken into account:

- **Particle: material definition**

The method used to define a particle was inspired by the tutorial “Electric Impedance Sensor” available on Comsol website:
https://www.comsol.com/model/electric-impedance-sensor-7704

A spherical particle is defined as a change in material properties instead of a geometrical entity. This definition enables to mesh the entire geometry only once thus reducing computational time. A parametric sweep is used to move the particle center (coordinate x0, y0 and z0) along the channel.

A variable, rsq, is used to compute the distance from the center of the particle:

rsq=((x-x0)^2+(y-y0)^2+(z-z0)^2)

and the electrical properties of the material in the channel are defined as follow:

Electrical conductivity = sigma_par+(sigma_sol-sigma_par)*(rsq>r0^2)
Relative permittivity = eps_r_par+(eps_r_sol-eps_r_par)*(rsq>r0^2)

where sigma_par, sigma_sol, eps_r_par and eps_r_sol are respectively the electrical conductivity and the relative permittivity of the particle and the solution and r0 is the radius of the particle.

The expression (rsq>r0^2) is a comparison, evaluated to 1 (for TRUE) outside the particle and 0 (for FALSE) inside the particle. The above-mentioned settings result in the particle properties inside the particle (centered in (x0,y0,z0) and with a radius of r0), and the properties of the solution outside of it.

- **Meshing**

Meshing using only elements size calibrated for the general physics, even with the "Extremely fine" setting can have some limitations. One possible workaround is to reduce the "Maximum element size" in the Custom settings.

Another possibility is to use a swept mesh which, in our case, will represent more accurately the geometry and the solution. Controlling the "Maximum element size" in accordance to the size of the particles and the geometry will improve the quality of the results obtained while reducing the calculation time.

In our simulations, since particles of 4 µm are used, a Maximum element size of 1 µm was used.

For more info on swept mesh see https://www.comsol.com/blogs/improving-your-meshing-with-swept-meshes/

- **Relative tolerance**

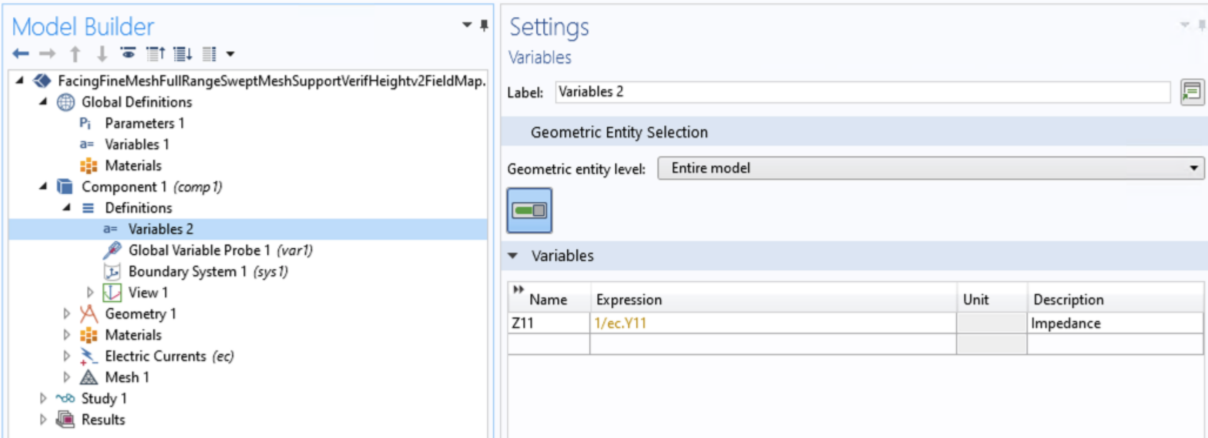
The Relative tolerance describes how well the solution converges. Convergence is reached if the relative difference between two consecutive solutions is smaller than the set relative tolerance.

In our case, since the intrinsic value behind the calculation of the impedance is the electric current of the order of the µA, a relative tolerance of 1e-7 was used as a tradeoff between precision and computation time.

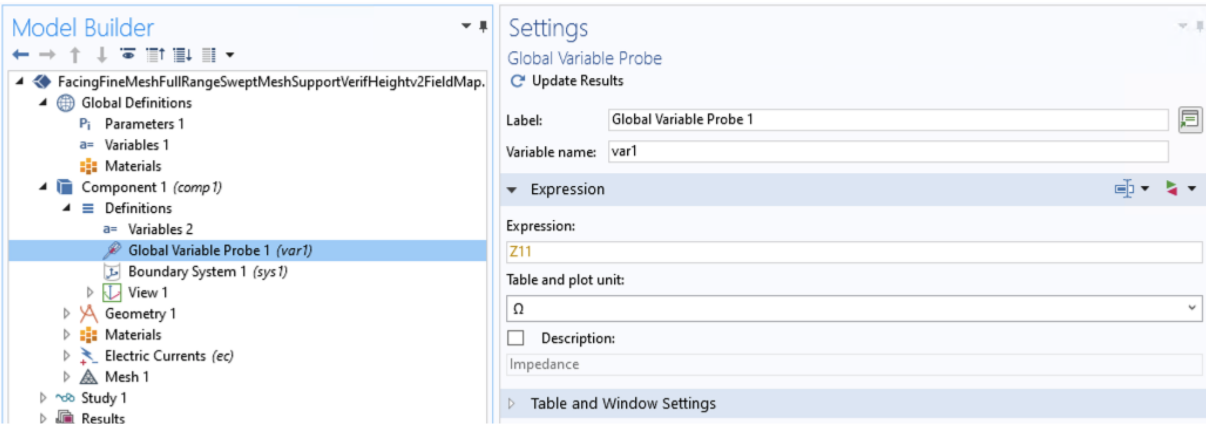
- **Impedance**

Impedance values are not directly accessible in Comsol. To obtain this value, a variable should be defined:

Z11 = 1/ec.Y11



To be able to plot the impedance during the simulation, the created variable Z11 can be accessed via a "Global Variable Probe"

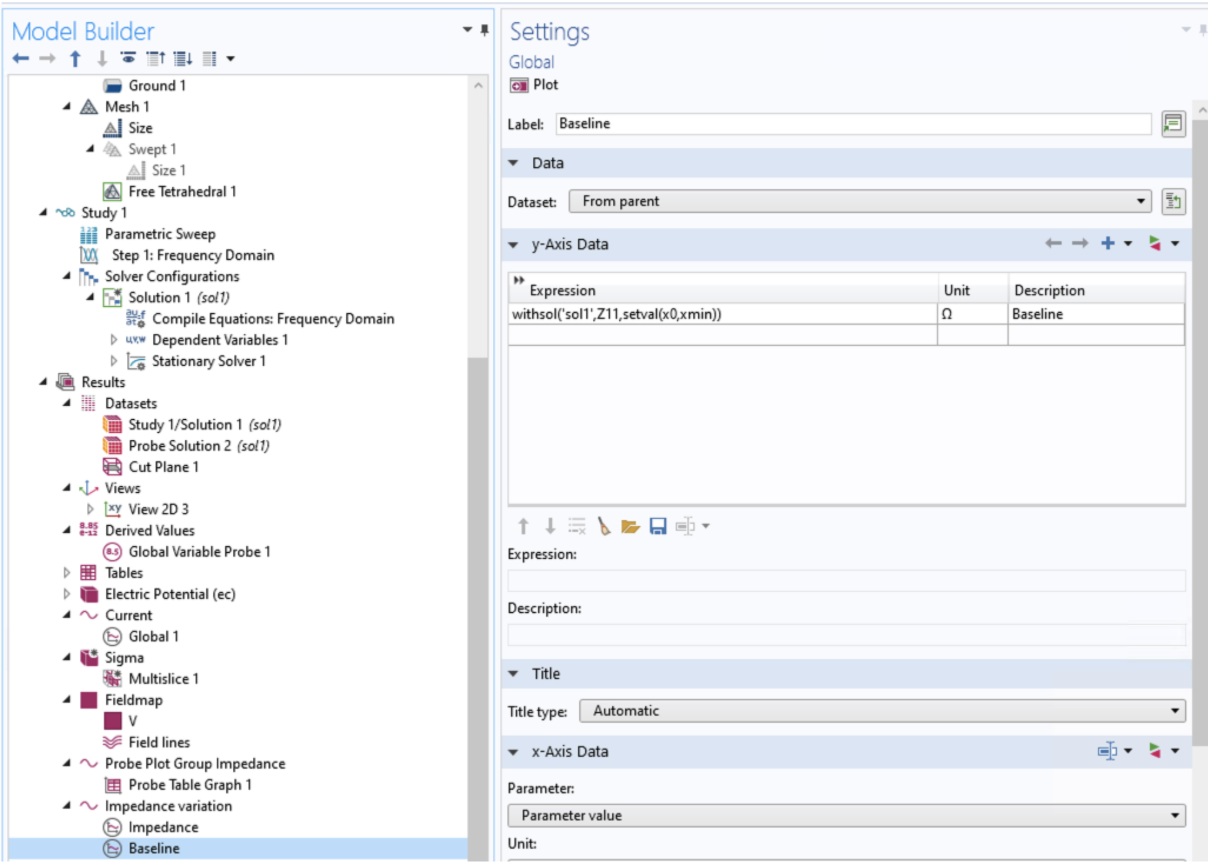


- **Calculation of the relative variation of impedance**

To access the value of the relative impedance, the baseline which is the value of the impedance when the particle is not in the sensing zone (typically in the inlet or outlet) should be accessed. This value can be accessed using the "withsol" operator.

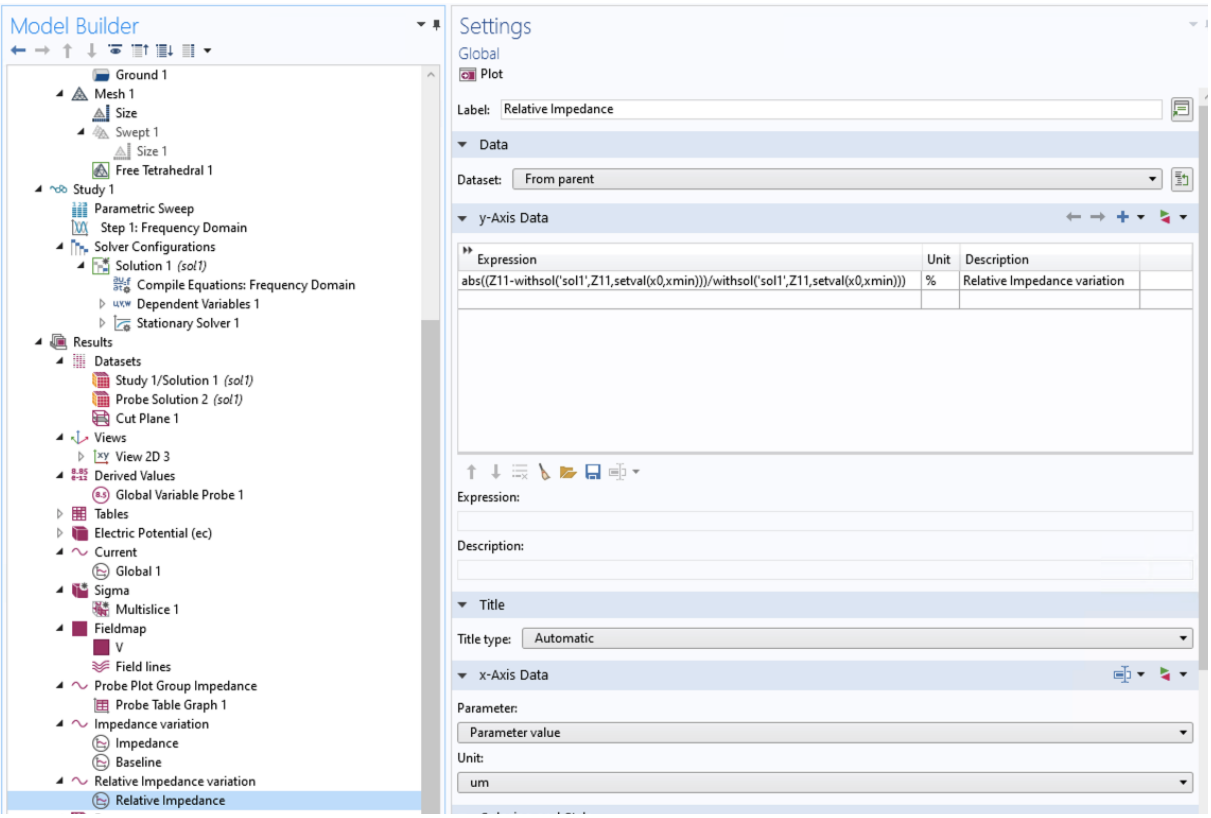
If x0= xmin corresponds to position of the inlet far from the sensing zone, the value of the baseline impedance is accessed, using a global evaluation with

withsol('sol1',Z11,setval(x0,xmin))



The relative impedance variation can be similarly defined as:

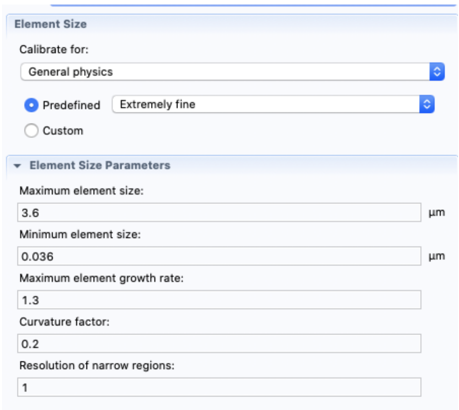
abs((Z11-withsol('sol1',Z11,setval(x0,xmin)))/withsol('sol1',Z11,setval(x0,xmin)))



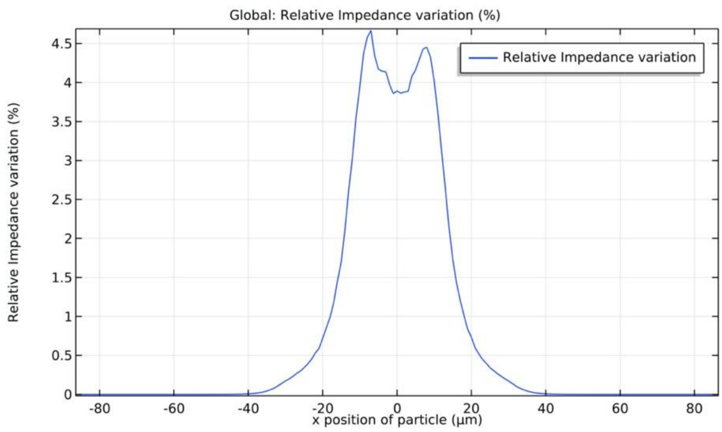
- **Complements to the meshing discussion**

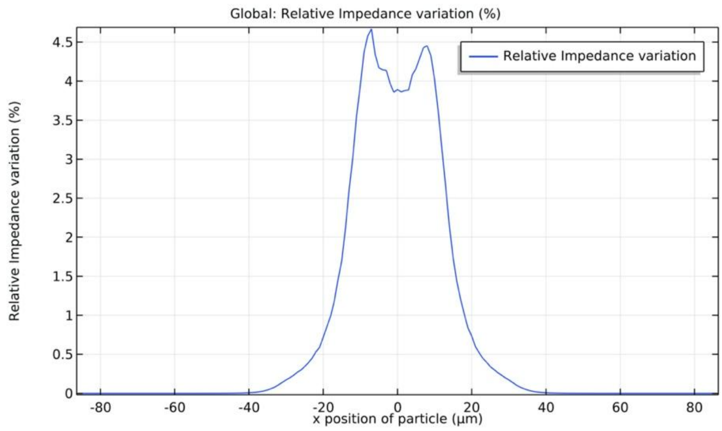
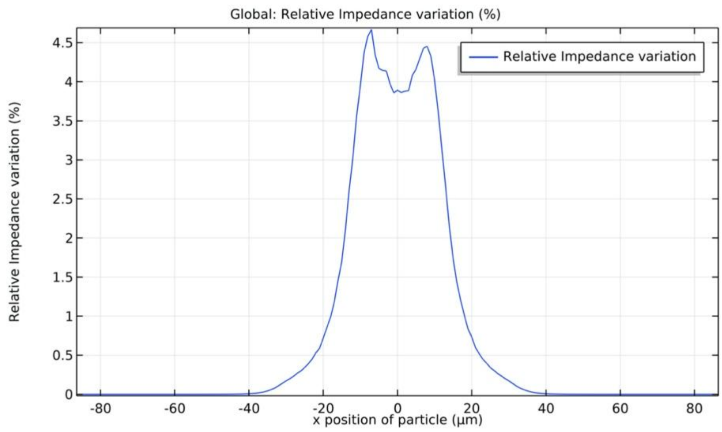
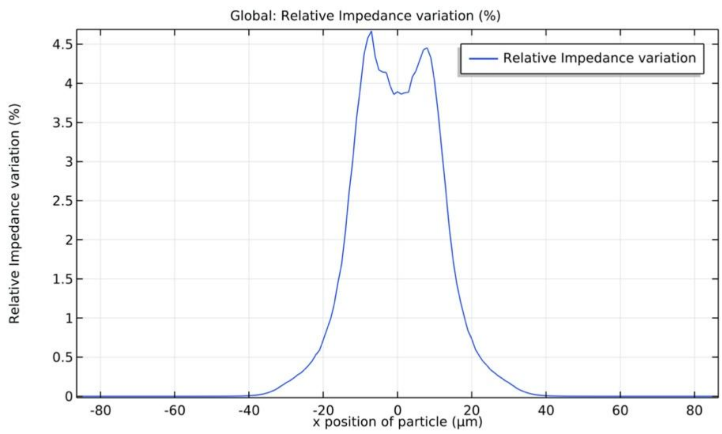
The computer used for the simulation was MacBook Pro running macOS Catalina with a 2.3 GHz 8-Core Intel Core i9 processor and 32 GB 2400 MHz DDR4 of memory.

Using the automatic meshing option from Comsol, for the specific dimensions involved in both the facing and the coplanar design leads to the following settings for the mesh, for the size setting “Extremely fine”



For the a “Extremely fine”mesh, the following results were obtained:

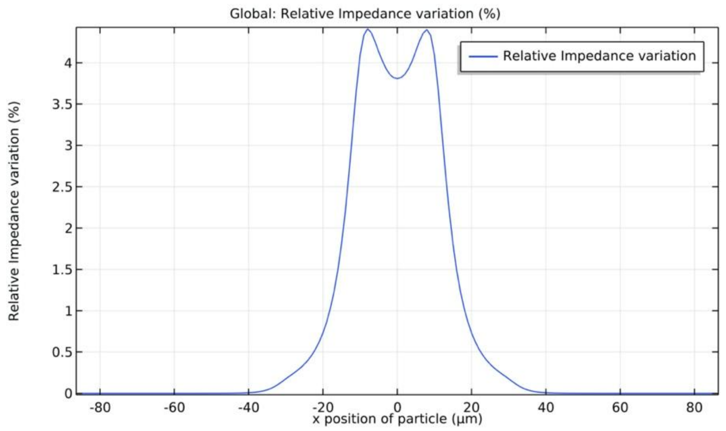
Auto Mesh: Extremely fine (Maximum element size: 3.6 µm)		
Number of degrees of freedom solved: 37 222		
Tolerance	Computational time (dd:hh:mm:ss)	Result
1E-6	00:00:06:55	

1E-7	00:00:06:44	
1E-8	00:00:07:12	
1E-9	00:00:06:46	

Regardless of the tolerance set for the simulation, because of the too wide mesh, the result obtained is asymmetric, thus not consistent with the physics

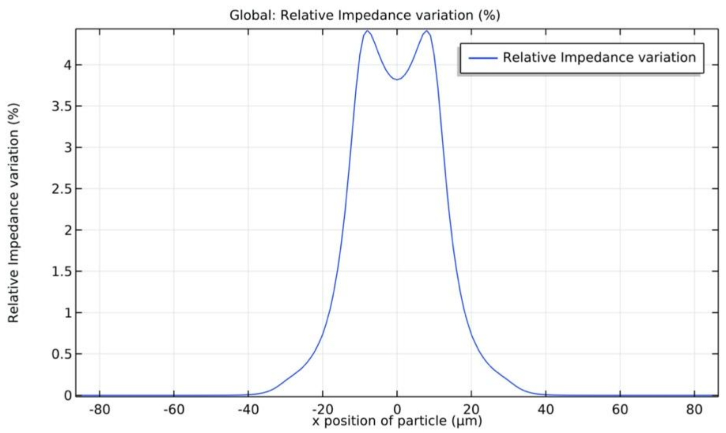
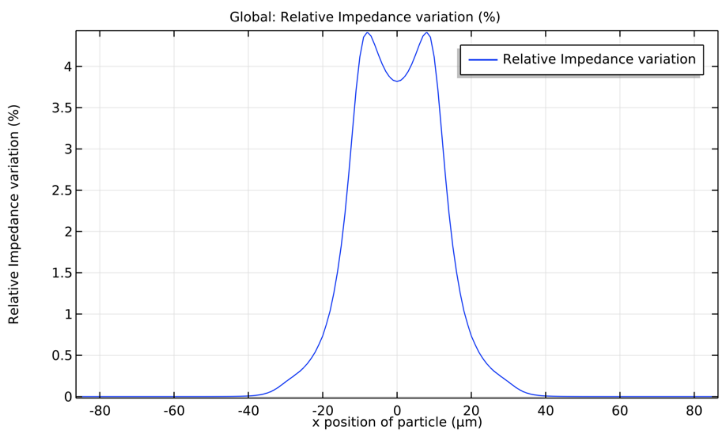
A possibility to improve the obtained result could be to modify only the Maximum Element Size from 3.6 µm to for example 1 µm. The result obtained is the following:

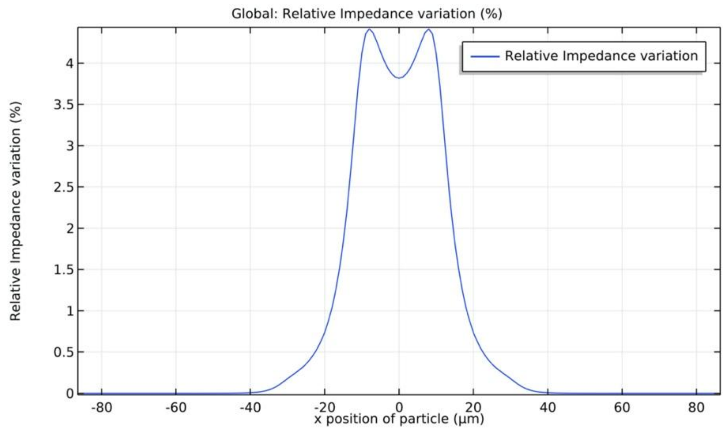
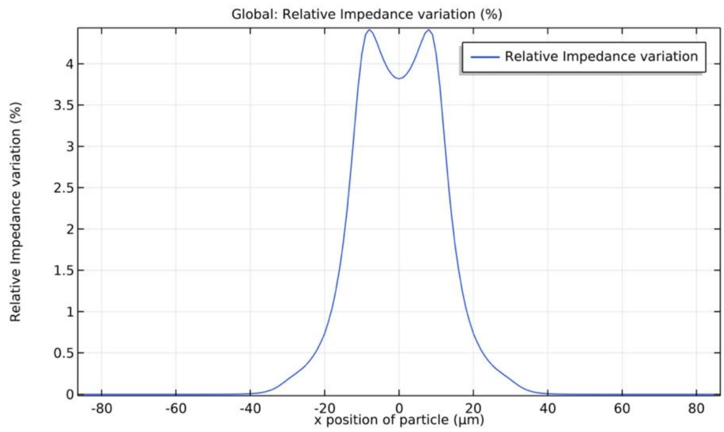
Auto Mesh: Extremely fine (Maximum element size: 1 µm)		
Number of degrees of freedom solved: 1 664 789		
Tolerance	Computational time (dd:hh:mm:ss)	Result

1E-6	01:21:16:10	

However, the time necessary for the simulation (1 day 21 hours 16 minutes 10 seconds) is extremely long.

By controlling the swept mesh with element size of 1 µm, the following results were obtained:

Swept Mesh: Element size 1 µm		
Number of degrees of freedom solved: 613 565		
Tolerance	Computational time (dd:hh:mm:ss)	Result
1E-6	00:05:30:27	
1E-7	00:06:30:38	

1E-8	00:08:08:38	
1E-9	00:10:27:44	

The swept mesh therefore proves its ability to perform simulations with a high accuracy while reducing the computational time compared to using only the approach where the Maximum Element Size is decreased.