## **USER GUIDE**

This code was developed by Dr. Julio Sotelo, associated professor at Universidad de Valparaiso, Valparaiso, Chile. In this toolbox also collaborate the professor Dr. Sergio Uribe, from the Pontificia Universidad Católica de Chile. It is also part of the contribution developed by the Center for Biomedical Imaging (www.mri.cl) and Nucleo Milenio CardioMR (https://cardiomr.cl/). We have developed a methodology for the non-invasive quantification of hemodynamics and geometrical parameters from 4D flow data sets based on Finite Elements methods.

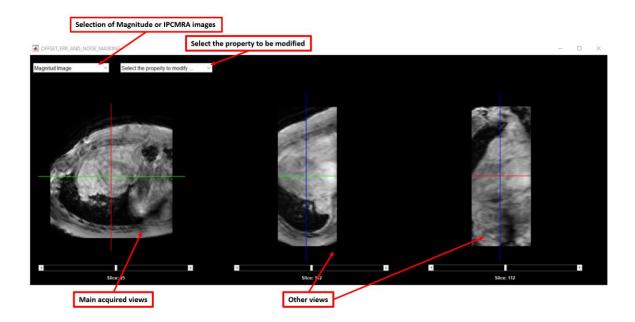
The application run on Windows, macOS, and Linux. To generate the finite element mesh we make use of iso2mesh opensource toolbox (http://iso2mesh.sourceforge.net/cgibin/index.cgi?Home).

The 4D Flow MRI data set need to be loaded as MATLAB structure file (in the same orientation that was acquired), with the following format:

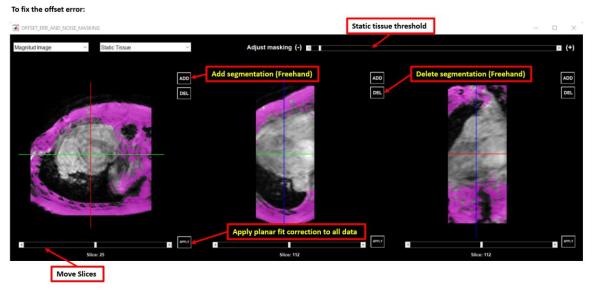
- a) The file need to be named data.mat, and saved in a single folder.
- b) The data.mat file contain the following:
  - data.MR\_FFE\_FH = magnitude image (4D matrix with: rows, columns, slices, cardiac phases)
  - data.MR\_FFE\_AP = magnitude image (4D matrix with: rows, columns, slices, cardiac phases)
  - data.MR\_FFE\_RL = magnitude image (4D matrix with: rows, columns, slices, cardiac phases)
  - data.MR\_PCA\_FH = velocity image in cm/s (4D matrix with: rows, columns, slices, cardiac phases)
  - data.MR\_PCA\_AP = velocity image in cm/s (4D matrix with: rows, columns, slices, cardiac phases)
  - data.MR\_PCA\_RL = velocity image in cm/s (4D matrix with: rows, columns, slices, cardiac phases)
  - data.voxel\_MR = voxel size (row,columns,slices)
  - data.VENC = velocity encoding
  - data.heart\_rate = cardiac frequency in bpm
  - **data.type** = you can write 'DCM' in this variable.
  - If you need more information to save you can add more data.XXX variables.

## **STEPS:**

- **1.-** To execute the app, go to the app folder and write "run GUIDE\_4D\_FLOW.m" in the MATLAB command windows.
- **2.-** Go to File/Load/Load Folder, and select the folder with the structure file "*data.mat*". Wait until the next windows is open, this window allows the background phase offset correction via planar fits of the static tissue. Also allow noise masking and selection of a region of interest.



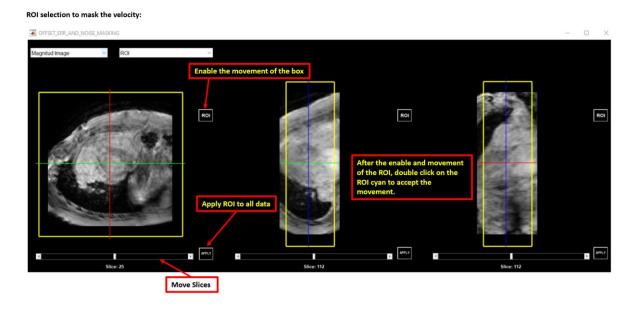
If you want to correct the offset error, select the property "Static Tissue". Move the threshold to leave only static tissue, improve the segmentation by adding or removing regions of the segmentation for different slices if desired, once done apply the correction to all cardiac phases.



If you want to remove some noise of the image, select the property "Noise". Move the threshold and improve the segmentation by adding or removing regions of the segmentation for different slices if desired, once done apply the noise masking to all cardiac phases.



If you want to select an ROI of the image, select the property "ROI". Enable the ROI movement for each view individually, change the size of the ROI and then press double click in any border of the ROI, move the other ROIs if you want, once done, you can apply the ROI masking to all cardiac phases.



You can close the windows and then wait until the message with the information about the views appears and close it.

## **3.-** The main windows contain:

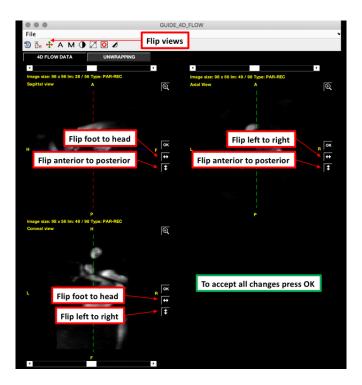


It is important that the axial, coronal, and sagittal views appear in the same orientation given in the view titles. On the other hand, the anterior (A), posterior (P), foot (F), head (H), left (L) and right (R) directions also need to be adjusted.

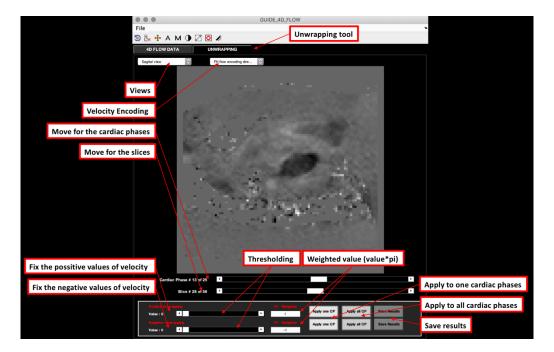
To change the views orientations (axial, sagittal and coronal), press the button "Change views", please remember always press Ok when you finish the adjustment, and the buttons will disappear.



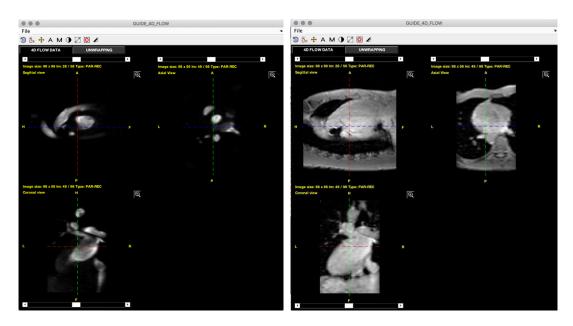
To Flip the views orientations (F to H, A to P or L to R), press the button "Flip views", please remember always press Ok when you finish the adjustment, and the buttons will disappear.



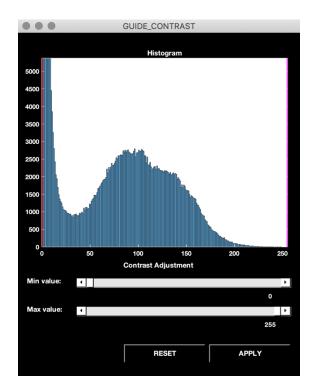
To fix the aliasing, use the unwrapping windows tools: Remember always save all your data.



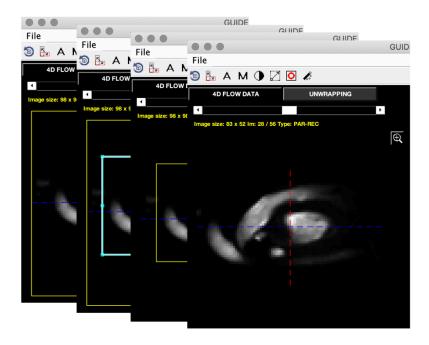
**4.**- The tools A and M change between angiographic and magnitude image.



**5.-** If you want to change the contrast of the image, press the contrast button . Then, move the slider to adjust the thresholding and press apply (all images change automatically). If you want to save this result, close this window. If you want to discard the results press reset button before closing the window.

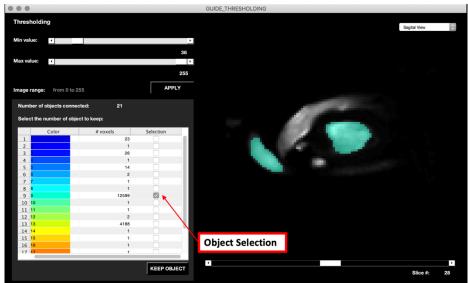


buttons appear ( and ), press the first of them, to enable the movement of the box. The box change to cyan color when it's enabling. Move the box edges and then if you are agreed with the size of the new box, press double click in the edge of this (and the color automatically change to yellow). Change the size of the others views if you want, and finish pressing the OK button (All boxes need to be in yellow color after press OK) and all resizing buttons are removed.

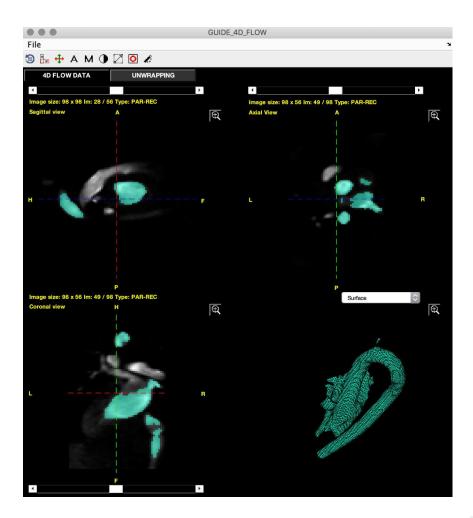


**7.-** Press the thresholding button  $\bigcirc$ . A new window is opened. Adjust the minimum and maximum values of the thresholding, and then press Apply button. Select in the table the color of the vessel of interest and press keep object. Then, close the windows and the segmentation is saved.

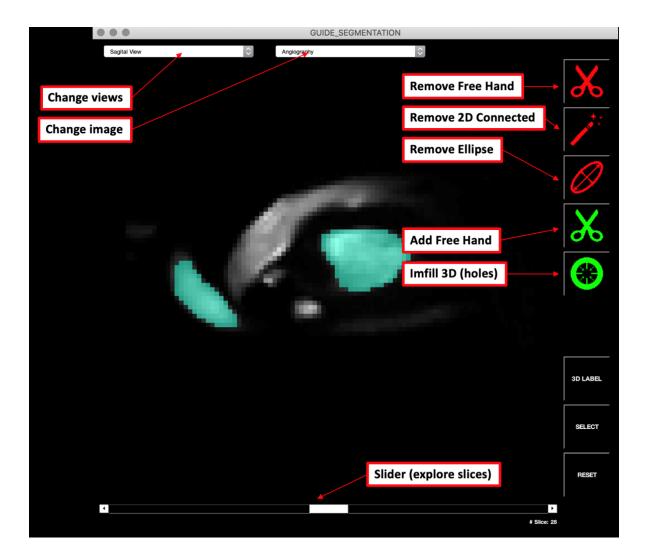




After closed the thresholding windows, a new popup-menu is available in the main windows. This button permits the exploration of the 3D maps and surfaces.



**8.-** The next step is the manual correction of the segmentation. Press the button and a new window is open. In this window you can select different views, and anatomical images, you can also remove (red button tools) or add (green button tools) section to the segmentation. When you are agreed with the results, press 3D Label button and select, and keep the section that you want (see the description in the point 7). If you are not agreed press reset button to obtain the original segmentation. You can repeat this process all times that you need to clean the segmentation. Finally, to save the final segmentation, close the window.



## The buttons are:



Draw a closed line in the region that you want to remove.



One click in one or multiples 2D segmentations that you want yo remove from an specific slice, then press enter.



Draw a closed ellipse in the region that you want to remove.

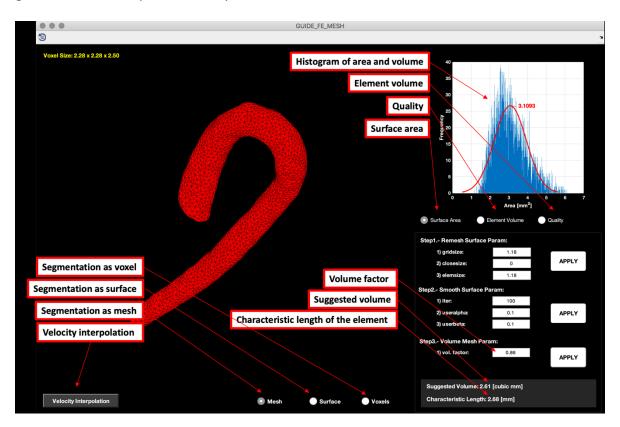


Draw a closed line in the region that you want to add, this region need to be in contact with other segmentation.



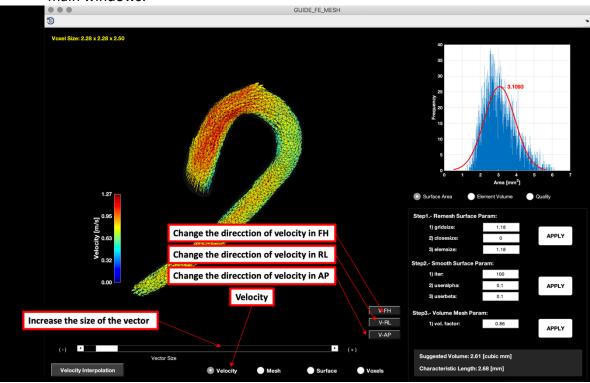
Double click in the 3D segmentation with multiples holes, if those holes, are closed for all sides, those are filled.

**9.-** To generate the tetrahedral finite element mesh, click on MESH button. Then press the button apply of the "Step 1: Remesh Surface Param" and then press the apply button of the "Step 2: Smooth Surface Param". The tetrahedral mesh was generated in the "Step 3: Volume Mesh Param", press apply and see the element volume in the histogram (top right), we suggest an element volume equal to the 20% of the voxel volume, if you want adjust the volume, change the vol. factor and press apply again. In the histogram you can see the area of the surface elements, the volume of the tetrahedral elements and the quality of the mesh (bigger that 0.8 is a good quality). For Windows system also appear in the step 3, the keep ratio option, that means the percentage of node that you want to keep from the surface generate in the Step 2, necessary to run TetGen.



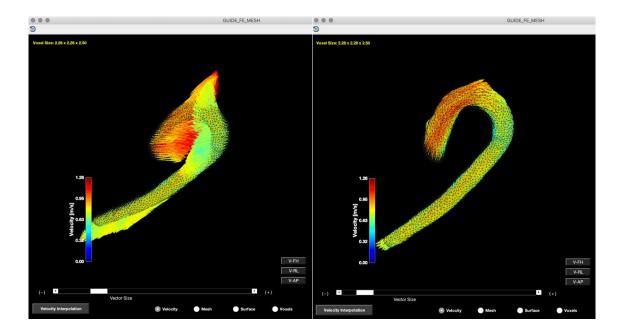


After the step 3, a new button appears (velocity interpolation), press and the velocity interpolation to each node of the mesh is generated. If the velocity vectors are in the correct orientation, close the window and the velocity will be transferred to the main windows.

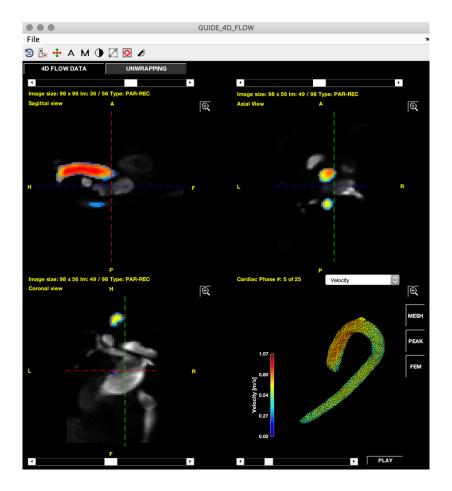


If the velocity vectors are wrong as in the next example (The wrong orientation of the vectors are in AP and RL). Increase the vector size with the slider, to see correctly which vector orientation is wrong and press the button that correspond to that direction (V-FH, V-RL or V-AP) to fix this. In the example we press V-RL and V-AP to

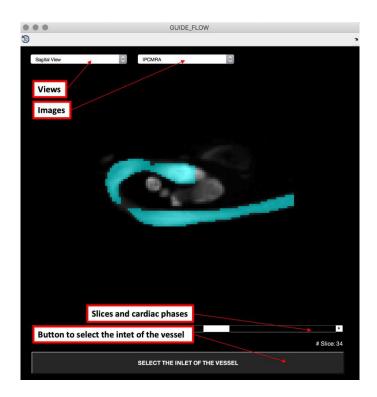
fix the orientation. Then close the window and the velocity will be transferred to the main windows.



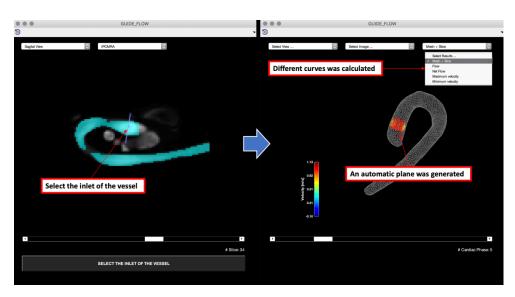
**10.-** To see the velocity in the main window, select this from the popup-menu, in the main windows app.



**11.**- A new button appears in the main window (PEAK button), press this button to calculate properly the peak flow. If you close this window the peak flow was calculated as the cardiac phase with maximum mean velocity.



11.1.- Press the button and draw a line at the inlet of the vessel. An automatic 2D slice perpendicular to the wall was generated in the three-dimensional mesh, and different curves was calculated (flow, net flow, maximum velocity and minimum velocity)



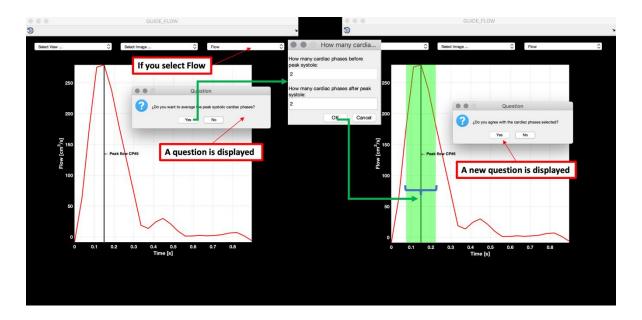
11.2.- If you select Flow in the third popupmenu, a new question is displayed. Do you want to average the peak systolic cardiac phases?.

If the answer is yes, you need to select the number of cardiac phases before and after the peak systole, and then, the cardiac phases selected in the flow curve are

colored. The last question, if you are agreed with the selection press yes, and then, the cardiac phases selected are replaced by the average value of all of them.

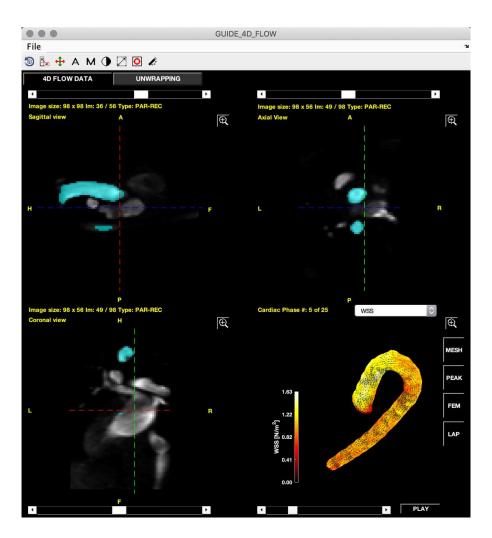
Please, not use here the Oscillatory Shear Index and the Regurgitant Flow for the final analysis, because those values depend of the time variation of velocity.

*If the answer is no*, each cardiac phase is processed independently, and the quantification of Oscillatory Shear Index and the Regurgitant Flow are properly calculated because those values depend of the time variation of velocity.



Close the windows to finish.

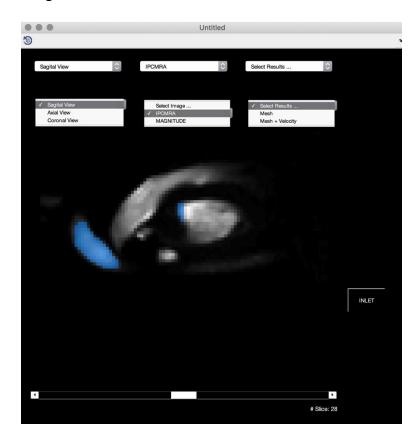
**12.-** A new button appears in the main window (FEM button), press this button and some global hemodynamics parameters are calculated (WSS, OSI, Vorticity, Helicity Density, relative Helicity Density, Viscous Dissipation, Energy Loss and Kinetic Energy) with our least square projection method. Select any of them from the popup-menu.



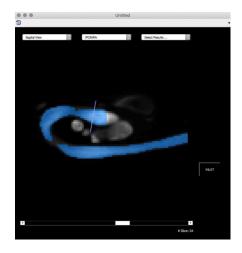
- **13.** A new button appears in the main window (LAP button), this button applies our Laplacian algorithm, press this button and a new window appears.
  - 13.1.- The warning windows indicate if you want load the inlet and outlet nodes ID form a .csv file obtained by PARAVIEW Software (this is recommended where the selection of inlet or outlet nodes is very difficult, necessary for complex geometries), with the mesh previously saved.



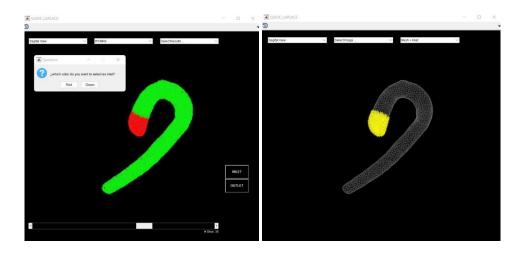
13.2.- In you press No, you can generate the selection of the inlet and outlet region with our application. Using the first two popup-menu select the orientation and the background image.



13.3.- Press Inlet button and drag a line over the inlet section, then press double click over the line.



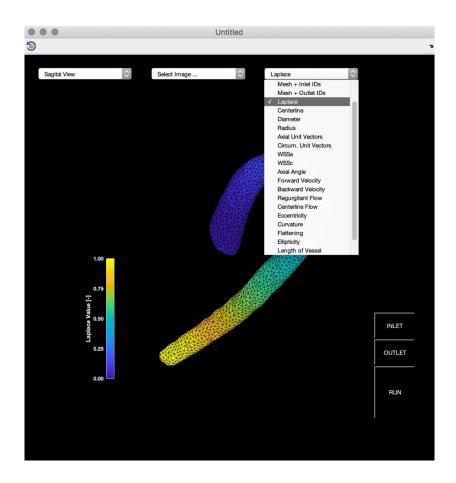
Then the 3D mesh was loaded, with the nodes colored green and red. Then you need to select the color that corresponds to the input, and those nodes was changed to yellow color.



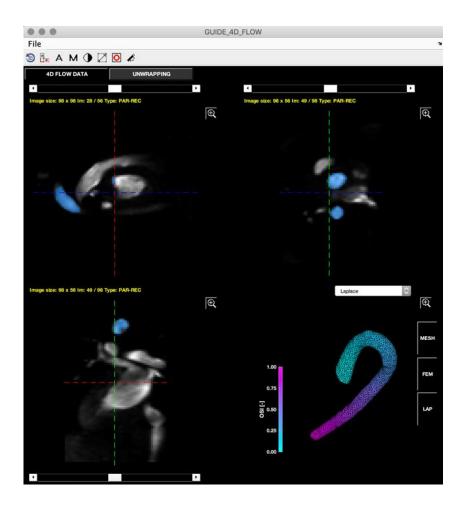
Then select again from the popup menu the IPCMRA image and apply the same process to select the outlet nodes.



13.4.- Press the RUN button and the Laplace quantification start. All parameters calculated in this window will be available in the popup-menu.



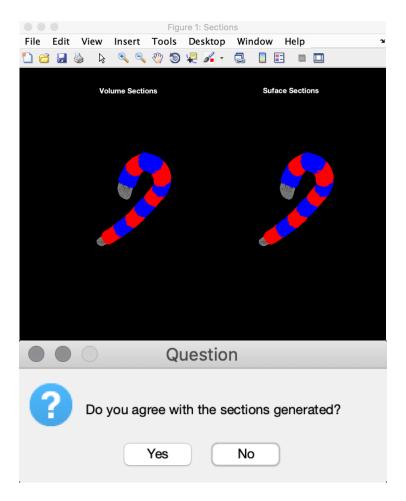
13.5. Close the window and the information will be transferred to the main window. (All parameters are now available in the popup-menu of the main window)



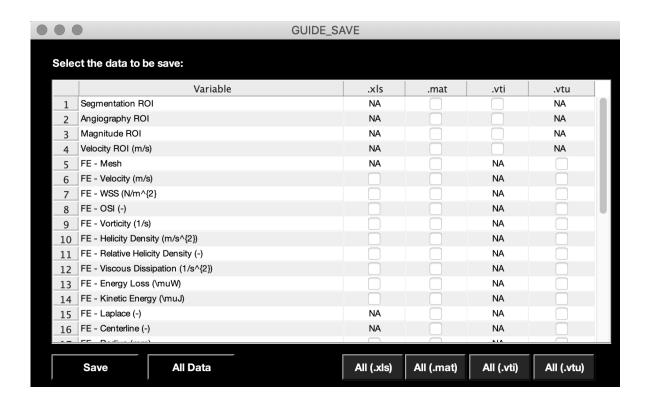
- **14.-** To save the data go to File/Save/Save Data.
  - 14.1.- A new option appears (Would you like save an excel file?), if you want automatically to divide the vessel in multiples or one sections, using the Laplace distribution, and save the results in excel file, press YES.



14.2.- Then enter the number of section and press OK, a new window appears with the volumetric and surface sections, automatically generated. If you are agreed with the section generated press YES.



13.3.- Then you can save the data in multiples format, Excel files (.xls), Matlab files (.mat) and visualization toolkit format to load these in PARAVIEW Software (.vti and .vtk). select the format that you want and save it.



**15.-** Finally if you want to load a previously saved segmentation, you can load it. Go to File/Load/Load SEG and select the SEG file in the MATLAB FILES/ Segmentation ROI/SEG.mat.

IF YOU NEED ANY ADDITIONAL INFORMATION OR HELP WITH PARAVIEW (I RECCOMMENDED THE VERSION 5.4.1), LET ME KNOW (julio.sotelo@uv.cl)