S. Jonic - Tutorial 2
Structural Mapping (StructMap) within Scipion

StructMap [1] can be used to analyze a set of EM density maps of the same molecular complex, to detect differences between them in terms of continuous conformational changes [2]. We use nine density maps that were used to show the StructMap protocol in Xmipp [1], but we resize them here to make the processing faster. The synthesis of the data set is fully described in [1] and, here, only in brief.

In [1], we discretized two distinct synthetic trajectories of continuous conformational changes of RyR1. The two synthesized trajectories are completely fictional and may not exist or coexist in the experimental case. The sequences of discrete states 3-2-1-4-5 and 5-4-1-2-3 describe symmetrical opening and closing of the complex, respectively, whereas the sequence 7-6-1-8-9 (or 9-8-1-6-7) describes asymmetrical opening or closing of the complex (one side of the complex opens while the other side closes).

The pseudoatomic model of the EM density map of the closed conformation of RyR1 (EMDB:EMD-1606) and its normal modes 8 and 9 were used to compute 8 additional pseudoatomic models. The displacement in mode 8 produces symmetrical opening or closing of the complex, whereas the displacement in mode 9 produces asymmetrical opening or closing of the complex. The state referred to as 1 corresponds to the nondisplaced initial pseudoatomic model (i.e., zero displacement amplitudes in all modes). The states referred to as 2, 3, 4, and 5 correspond to the displacement of the initial pseudoatomic model in mode 8 using displacement amplitudes of 300, 500, -300, and -500 (no units), respectively, and zero displacement amplitudes in other modes. The states referred to as 6, 7, 8, and 9 correspond to the displacement of the initial pseudoatomic model in mode 9 using displacement amplitudes of 300, 500, -300, and -500 (no units), respectively, and zero displacement amplitudes in other modes.

The density maps obtained from the nine pseudoatomic models were projected to obtain 500 randomly oriented projections for each density map. The projections had a uniform angular distribution, a size of 128 × 128 pixels, and a pixel size of 3.94 Å × 3.94 Å. Each projection was modified by adding simulated experimental noise and contrast transfer function, simulated for a 200 kV microscope with a spherical aberration of 2 mm, defocus of 1 mm, and signal/noise ratio of 0.2. Finally, each of the nine sets of simulated images was used to compute the corresponding 3D reconstruction (density-map size: 128 × 128 × 128 voxels, voxel size: 3.94 Å × 3.94 Å × 3.94 Å).

Here, we show processing of these nine density maps after their resizing to the size of 64 x 64 x 64 voxels (voxel size: 7.88 Å × 7.88 Å × 7.88 Å). The distances among the maps were obtained using 20 normal modes computed for each of the maps (for each of their pseudoatomic models).

REFERENCES

1. Sanchez Sorzano CO, Alvarez-Cabrera AL, Kazemi M, Carazo JM, Jonic S: **StructMap: Elastic Distance Analysis of Electron Microscopy Maps for Studying Conformational Changes**. *Biophys J* 2016, **110**:1753-1765.

2. Jonic S: **Computational methods for analyzing conformational variability of macromolecular complexes from cryo-electron microscopy images**. *Curr Opin Struct Biol* 2017, **43**:114-121.

1. In Scipion, create a new project and check that "Protocols SPA" is displayed in "View" menu at left. Then, double click on "import volumes" in the menu:
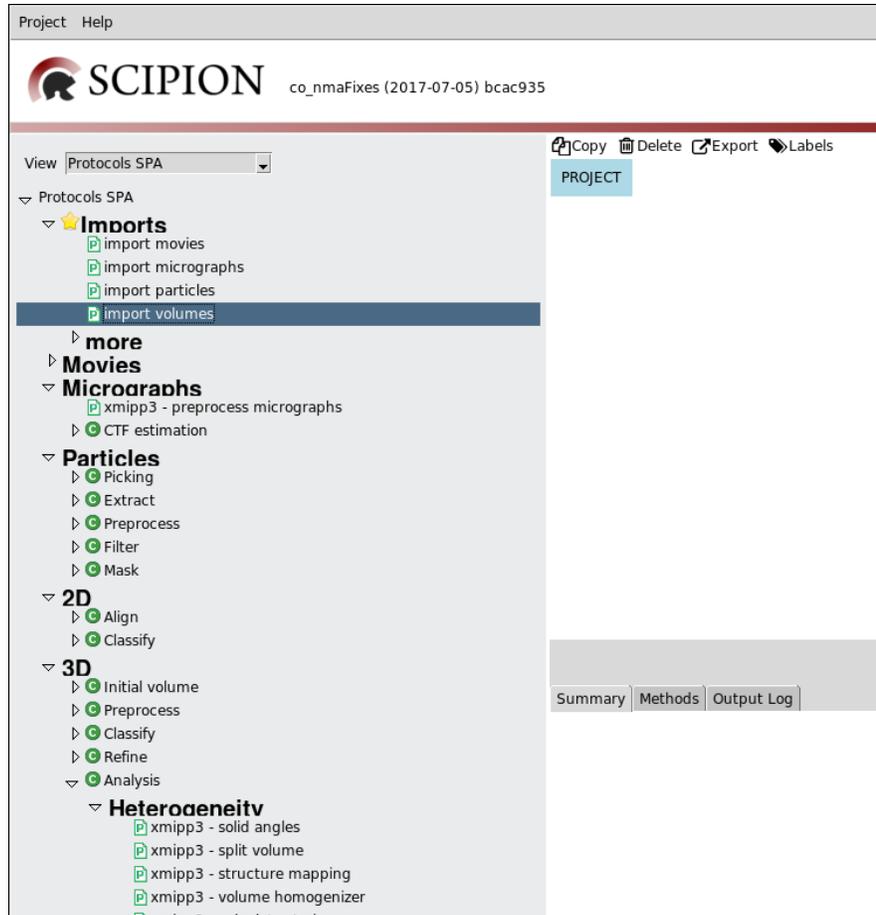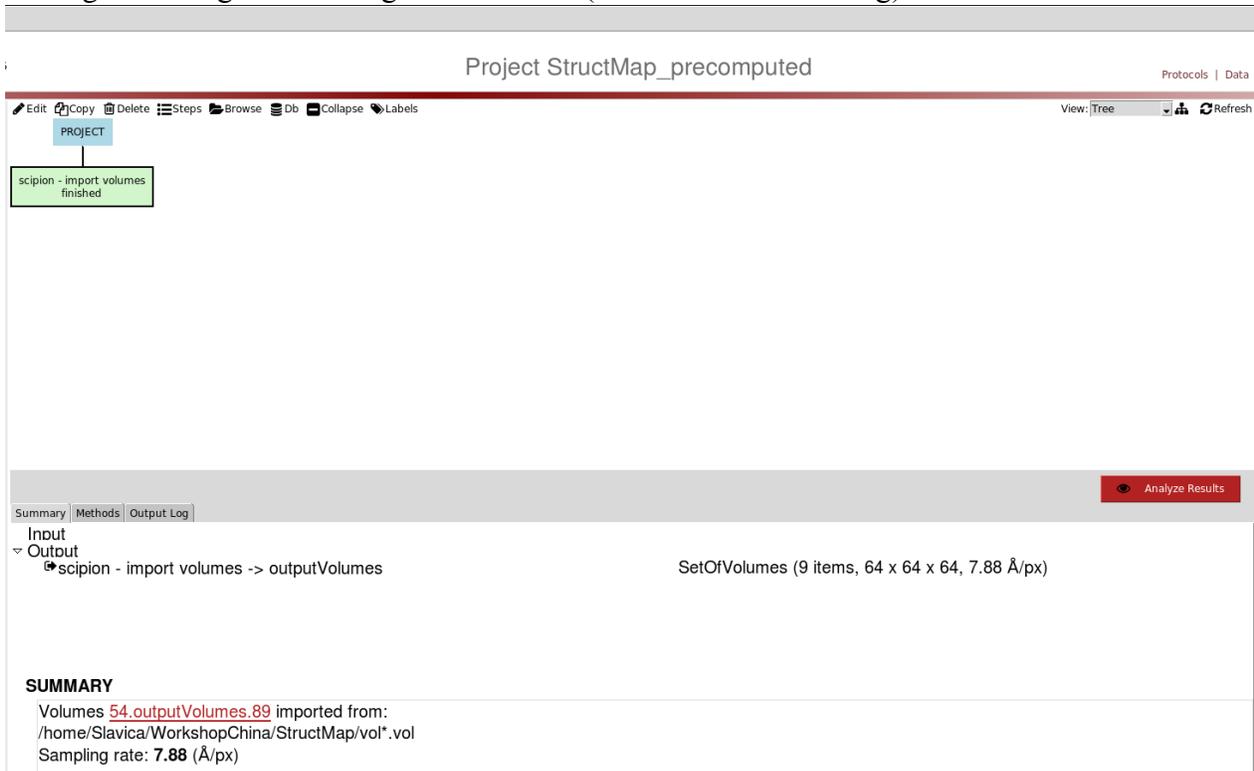
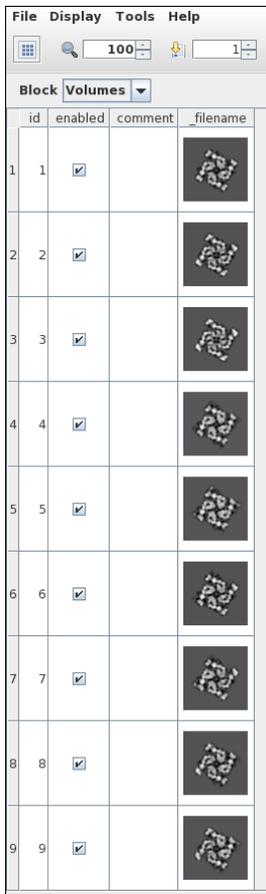

2. Import a set of EM density maps:

Dialog to import a set of EM density map (after a double click on "import volumes"):
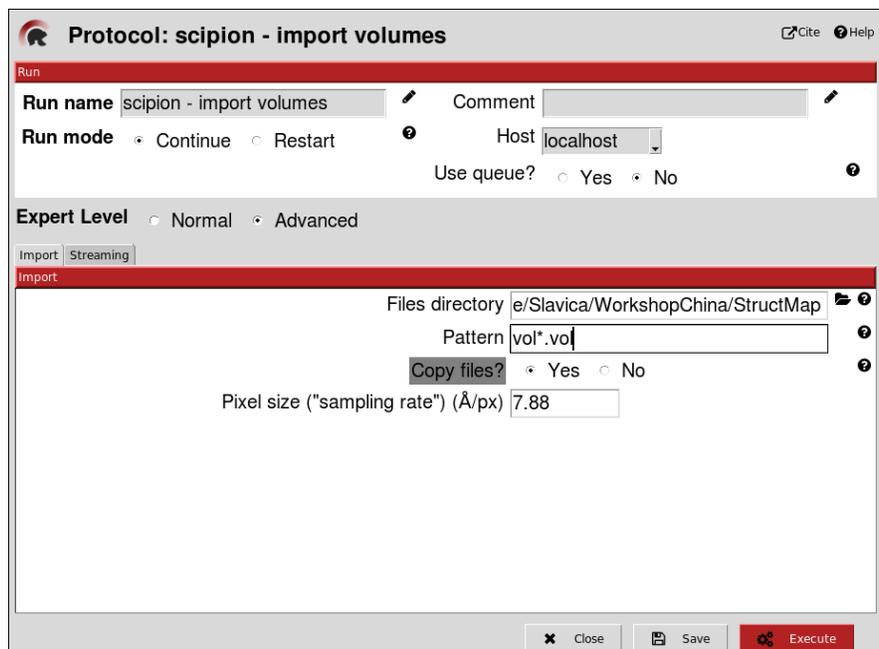
After filling the dialog and clicking on "Execute" (red button in the dialog):

The imported data can be checked (visualized) by first clicking on the "scipion – import volumes finished" box and then on "Analyze Results" (red button).

This opens a table (left) whose number of rows corresponds to the number of imported density maps. The slices of a volume can be visualized by double clicking on this volume in the table ("_filename" column of the table):
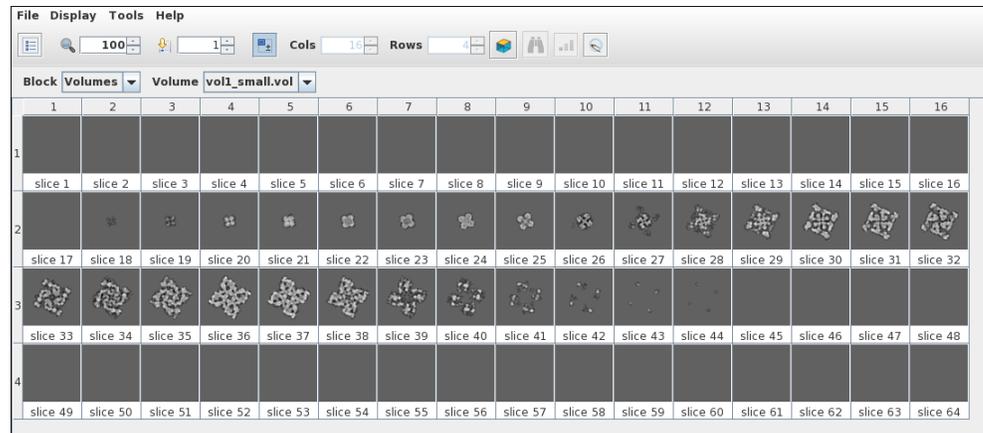
3. Perform "Structure Mapping" (double click on "xmipp3 – structure mapping" in the menu at left)
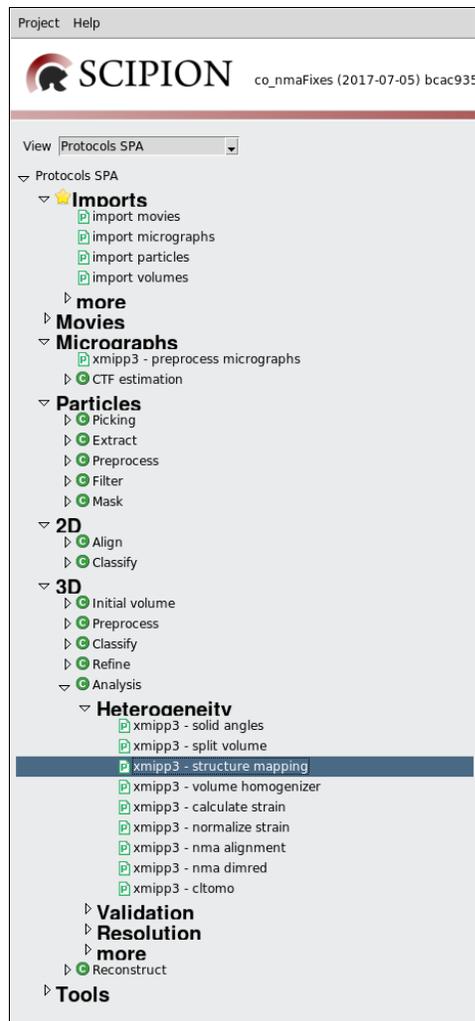
This opens a dialog box that consists of the following three tabs: "Input", "Pseudoatom", and "Normal Mode Analysis".

"Input" tab:

"Pseudoatom" tab :

"Normal Mode Analysis" tab :

To execute, click on "Execute" (red button).
After executing:

Project StructMap_precomputed

Edit Copy Delete Steps Browse Db Collapse Labels   View: Tree

PROJECT

scipion - import volumes
finished

xmipp3 - structure mapping
finished

Analyze Results

Summary | Methods | Output Log

▽ Input
    001 (from scipion - import volumes -> outputVolumes [outputVolumes])   SetOfVolumes (9 items, 64 x 64 x 64, 7.88 Å/px)
    Output

SUMMARY
Volumes to calculate StructMap: **9**

StructMap projects density maps onto a space of distances (differences) among them. The dimension of this space is given by the number of the imported density maps. For visualization purposes, StructMap also reduces this dimension to 1, 2, and 3. The results can be visualized by first clicking on the "xmipp3 – structure mapping finished" and then on the "Analyze Results" button. This opens a dialog box in which they can be viewed in the space of 1, 2 or 3 dimensions:

Protocol: xmipp3 - viewer validate_overfitting Cite Help

Show StructMap

Show StructMap

Number of dimensions 2

Display the StructMap 👁

✖ Close

In the "Number of dimensions" field, enter 1, 2, or 3 to see the results in the space of a reduced dimension (here, "2" for displaying results in a 2D space). Then, click on the eye icon next to "Display the StructMap".

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The results obtained with the 9 density maps imported here are as follows:

Visualization in the space of 3 dimensions:
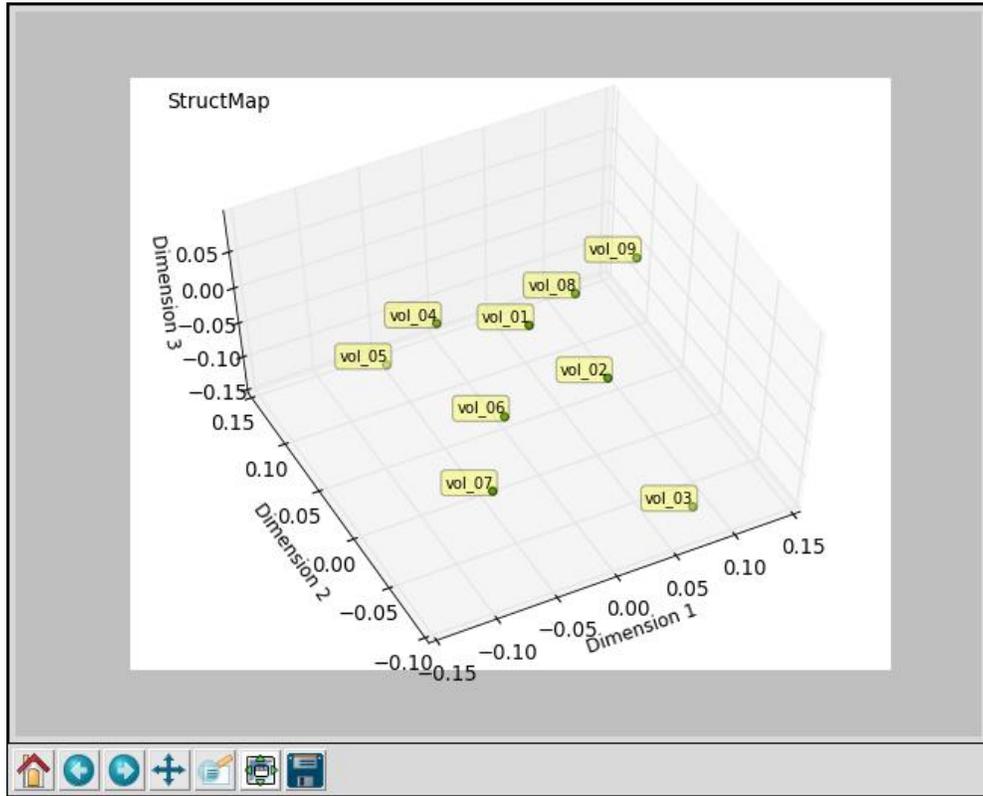
Visualization in the space of 2 dimensions:
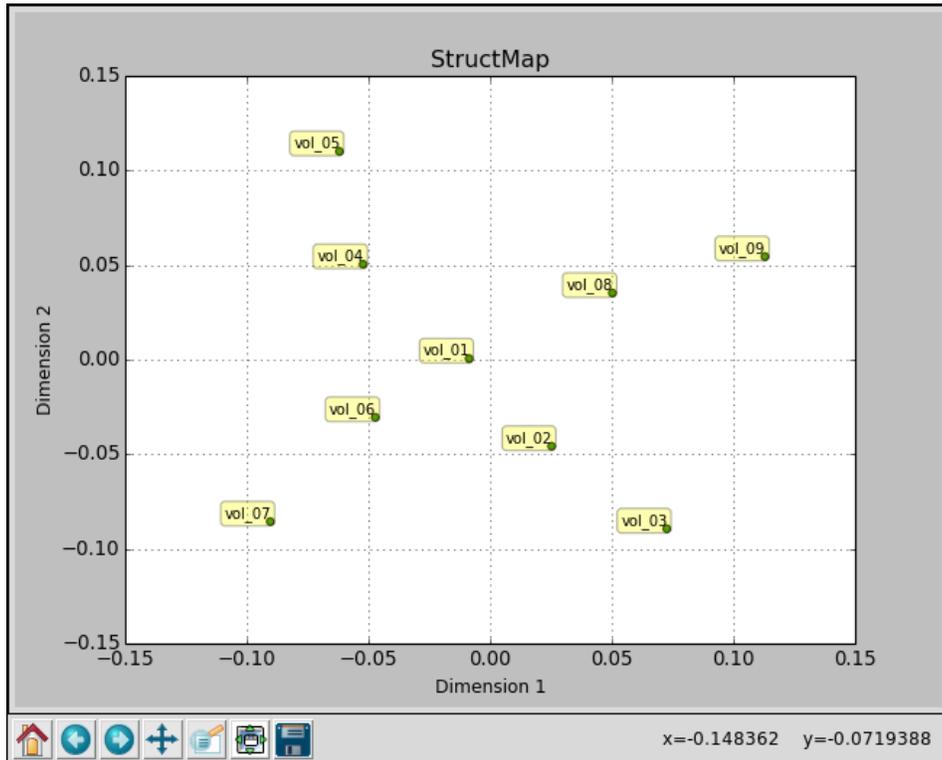
Visualization in the space of 1 dimension: