

Deliverable D7.6: EM quality assurance workflow

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Deliverable written by Laura del Cano

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1 Executive summary

The image end result of a cryo-EM study is a three-dimensional density map in which the different parts of the volume may present different degrees of quality (resolution) as a result of, most typically, flexibility or compositional differences of the macromolecule under consideration. Consequently, maps are better described using the concept of local (per voxel) resolution, rather than by a single global value. However, the concept of what resolution truly means is not simple, and several approaches have been proposed to measure resolution (for a review on resolution measures in cryo-EM, see 1).

The existence of different methods to calculate resolution, each included in different software packages, provided a very good case for Scipion Web Tools, a web application built over Scipion framework software that offers access to predefined image processing workflows over the web.

2 Project objectives

With this deliverable, the project has reached or the deliverable has contributed to the following objectives:

No.	Objective	Yes	No
1	Provide analysis solutions for the different Structural Biology approaches	X	
2	Provide automated pipelines to handle multi-technique datasets in an integrative manner		X
3	Provide integrated data management for single and multi-technique projects, based on existing e-infrastructure	X	
4	Foster best practices, collaboration and training of end users	X	

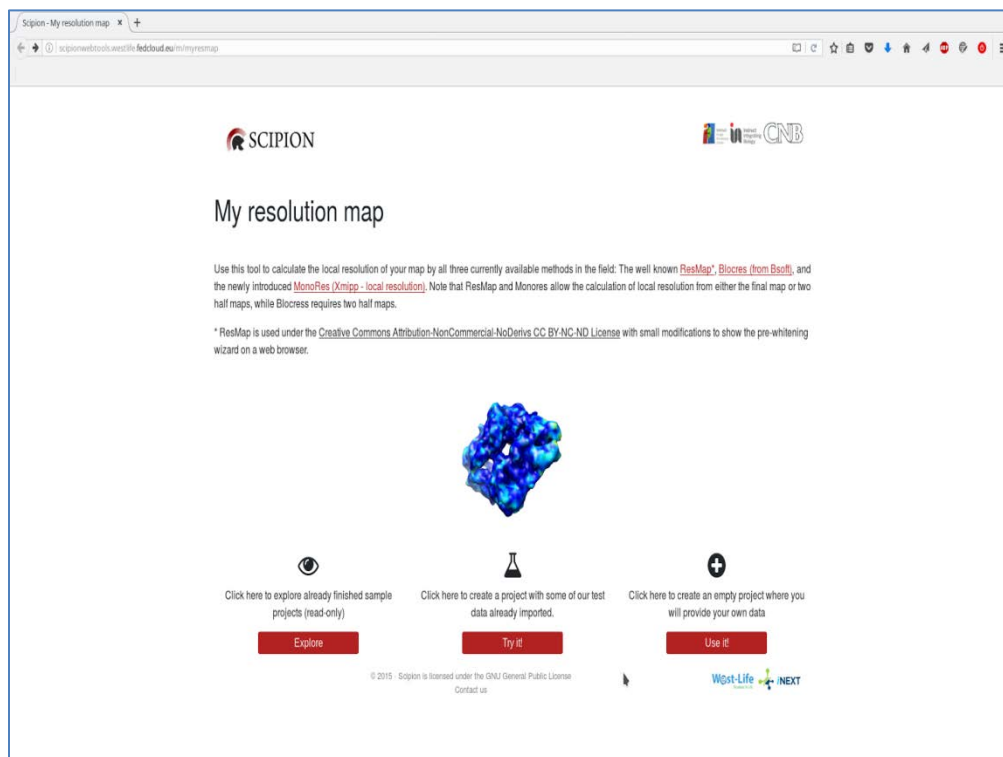
3 Detailed report on the deliverable

With this deliverable we aimed at providing a web tool for any structural biologist who want to calculate the local resolution of his/her final map using three different methods: Resmap, Blocres, and a novel algorithm developed at CNB-CSIC, MonoRes.

3.1 Web tool My resolution map

Of the three methods Resmap (2) is the most popular approach, Blocres (3) was the first one to be introduced in the field, and MonoRes (Vilas et al., 2017, Structure, in press the newest with an almost automatic processing.

The following image shows the entry page of the “My resolution map” tool, running on the EGI Federated Cloud (<http://scipionwebtools.westlife.fedcloud.eu/m/myresmap>) as described on M5.3.



1 My resolution map Web Tool

Like for the other tools, there are two learning entry points: “Explore” and “Try it!”. The first one provides users with three read-only, already executed projects using different input data, where they can explore how data, parameters and results are handled by the tool. The second one, “Try it”, offers the user these same input data sets with a predefined workflow to be run step by step, allowing the user to focus on the way they are run and possibilities of the graphical interface. The third option the user has is “Use it!”, which creates an empty project with a predefined workflow, where users should upload their own data and define and run everything from the beginning.

Note that Bloccress, by the very essence of the algorithm that it uses, requires the user to supply two “half maps” and not just the final map; for simplicity, test data sets provided by SWT only refer to the case of calculating the local resolution of a final map and, therefore, only ResMap and MonoRes are shown in test mode.

Three example datasets are provided:

Example projects

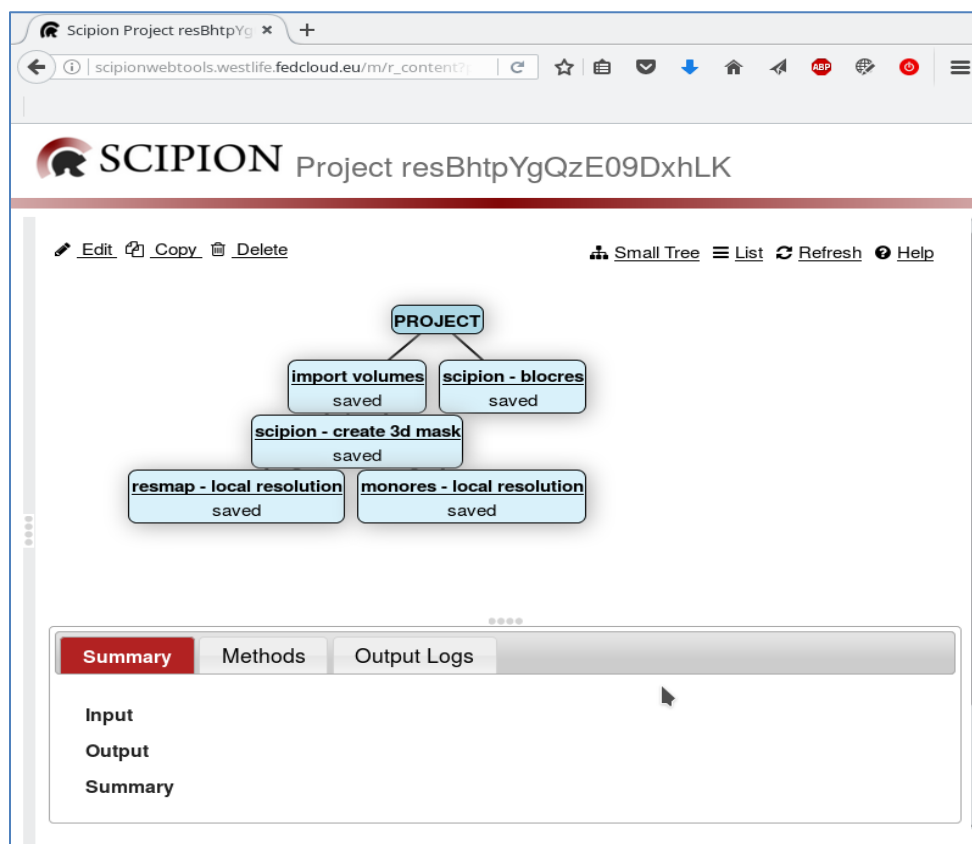
Select the **Test data**:

- Feline calicivirus virus-like particles** (Resolution 14 Å , [from Burmeister WP et al. PLoS One, 2015](#))
- β-galactosidase** (Resolution 2.2 Å , [from A. Bartesaghi et. al. Science. 2015](#))
- T20S Proteasome** (Resolution 2.8 Å , [from Campbell MG et al. eLIFE, 2015](#))

2 Example datasets on the tool

All are described and properly referenced to acknowledge the data producers.

This is the typical workflow that a user will get when creating its own “My resolution map” project:



3 My resolution map workflow

First thing a user needs to do is to upload the input data, in this case a density map obtained from a typical cryo-EM reconstruction project, and import it into the project. Next step on the workflow is to create a 3D mask needed both by Resmap and Monores (and optionally for Blocres). Finally, the user can execute each of the three resolution methods.

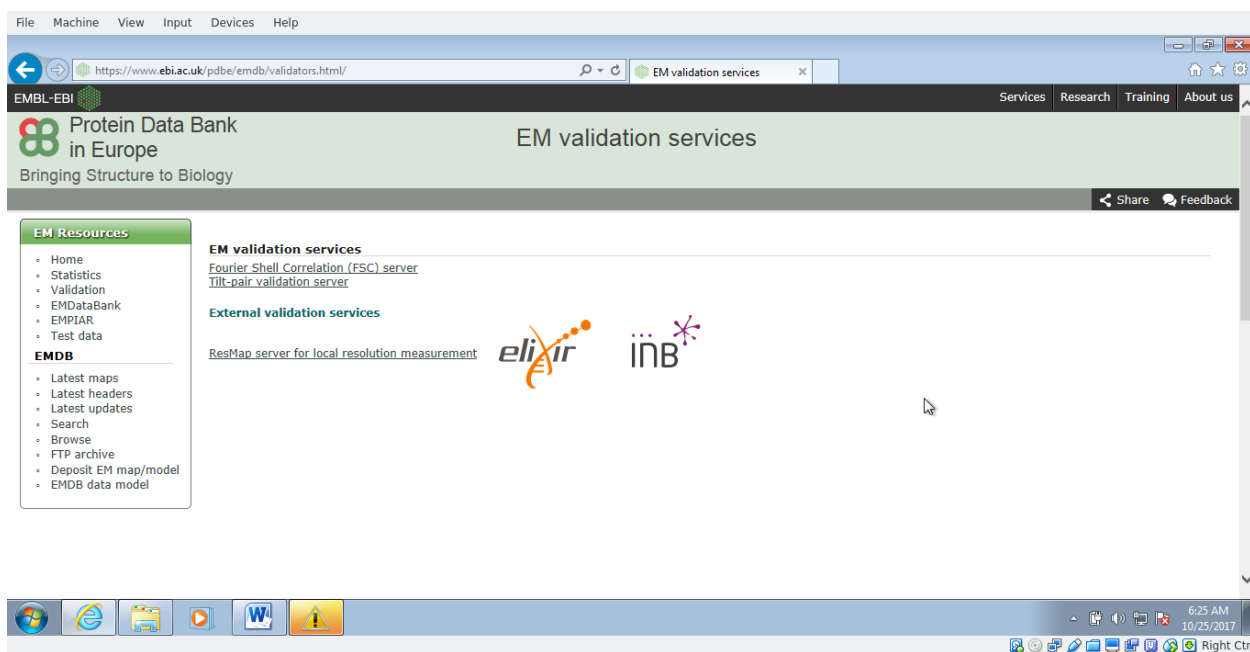
Note that, as mentioned above, Blocres requires the user to supply two "half maps".

3.2 Tutorials and support

Westlife VRE compiles a set of tutorials and webinars related to different services offered, among them a webinar dedicated to 'My resolution map' tool (<https://youtu.be/sfSRhP3mX14>).

3.3 Integration of the tool in the EMBL-EBI web site

Several teleconferences took in place to see if there was a way to integrate this service with Electron Microscopy Data Base (EMDB) at the European Bioinformatics and it was decided to start by having a link at EMDB pointing to the service (<https://www.ebi.ac.uk/pdbe/emdb/validators.html/>), as shown on the picture below. A possible future integration, would be to add an extra entrypoint in the 'My resolution map' to receive a map/url and, in a single step, create a project, import the map and run as many automatic steps as possible. The very likely need of user input for any of the methods make a fully automatic approach impossible to achieve. This underlines the importance of the user training described above.



4 Integration of the service with EMBL-EBI

3.4 Architecture

Like the already existing web tools, the service relies on scipion framework to take care of all the Cryo-EM functionality and wraps it, using a django server. The addition of this redesigned resolution webtool triggered the update of the scipion version running in the background from v1.0.1 to the latest released on June 2017, v1.1. Server is currently running on the [federated](#)

[cloud](#) as described on milestone M5.3. The whole site is been redesigned and some of the frontend technologies used updated like [bootstrap](#), now running 4.0 version.

References cited

1. C. Sorzano, J. Vargas, , J. Otón, V. Abrishami, J.M. Rosa-Trevín, J. Gómez-Blanco, J.L. Vilas, R. Marabini, and J. Carazo. A review of resolution measures and related aspects in 3d electron microscopy. *Progress in Biophysics and Molecular Biology*, 124:1–30, 2017.
2. A. Kucukelbir, F.J. Sigworth, and Tagare H.D. Quantifying the local resolution of cryo-em density maps. *Nature Methods*, 11:63–65, 2014.
3. G. Cardone, J.B. Heymann, and A.C. Steven. One number does not fit all: Mapping local variations in resolution in cryo-em reconstructions. *J Struct Biol*, 184:226–236, 2013.