



# SCIPION

## A Software Framework for Integration, Reproducibility and Validation in Cryo-EM

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### How to install, tutorials, videos, theory and practice

GitHub, Inc. (US) | <https://github.com/I2PC/scipion/wiki>

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Carlos Oscar S. Sorzano edited this page 2 minutes ago · 25 revisions



Scipion is an image processing framework for obtaining 3D models of macromolecular complexes using Electron Microscopy (3DEM). It integrates several software packages and presents a unified interface for both biologists and developers. Scipion allows you to execute workflows combining different software tools, while taking care of formats and conversions. Additionally, all steps are tracked and can be reproduced later on.

#### Getting Started

- Follow this step-by-step guide about **How to Install Scipion**.
- Complete the **Mix-and-Match Tutorial** illustrating how to use several packages.
- Take a look at the list of **current Integrated Packages and Protocols** (more than 150).
- Take a look at our **tutorial videos**.
- Know more about the theory and practice behind Image Processing in EM.

Scipion is open-source and freely available at <http://scipion.cnb.csic.es>



**Integration, Reproducibility and Analysis**

Scipion is an image processing framework to obtain 3D models of macromolecular complexes using Electron Microscopy.

Download

#### Documentation

Find out more information about Scipion for both users and developers. Check how to install Scipion, the list of integrated packages and some introductory tutorials. Learn how to use Scipion, more alignment and local resolution (Restack).

#### Web Tools

Give a try to our online processing workflows, which are a subset of the protocols in Scipion to provide a first try with any local installation. Current web-tools include: 3D reconstruction, motion correction, image alignment and local resolution (Restack).

#### News and Events

Keep an eye on latest Scipion news. Check out about bugfixes, new features and release plan. Don't miss the next Scipion workshop, or any related event. Don't hesitate to contact us for more information, or if you want to organize a workshop at your institution.

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J.M. de la Rosa-Treviñ, A. Quintana, L. del Cano, A. Zaldívar-Peraza, I. Foche, J. Gutiérrez, J. Gómez-Blanco, J. Burguet-Castells, J. Cuenca-Alba, V. Abrishami, J. Vargas, J. Olón, G. Sharov, J.L. Vilas, J. Navas, P. Conesa, M. Kazemi, R. Marabini, C.O.S. Sorzano, J.M. Carazo. Scipion: a software framework toward integration, reproducibility, and validation in 3D Electron Microscopy. *J. Structural Biology*, 195: 93-99 (2016)



## Use of Scipion

#### Wiley Online Library

Discover open access

Share your research where, when, and anywhere

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Full compliance with institutional funder mandates

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#### PROTEIN SCIENCE

#### Reviews

### Determination of the ribosome structure to a resolution of 2.5 Å by single-particle cryo-EM

Zheng Liu, Cristina Gutierrez-Vargas, Jia Wei, Robert A. Grassucci, Ming Sun, Noel Espina, Susan Madison-Antenucci, Liang Tong, Joachim Frank

First published: 26 October 2016 Full publication history

DOI: 10.1002/pro.3068 View/save citation

Cited by (CrossRef): 2 articles Check for updates Citation tools

Volume 26, Issue 1  
January 2017  
Pages 82-92



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Special Issue:  
Special Issue:  
Electron Microscopy





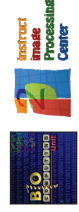
## Collaboration with other developers

- **Example 1:** Spider-MDA (with T. Shaikh)
- **Example 2:** NMA and flexible fitting (with S. Jonic)
- **Example 3:** Refactoring of ResMap (with A.Kucukelbir and H.Tagare)
- **Example 4:** Localized Reconstruction (with S.Ilca and J.Huiskonen)
- **Example 5:** SIMPLE protocols (with H.Elmlund)
- **Example 6:** Spring (with C. Sachse)

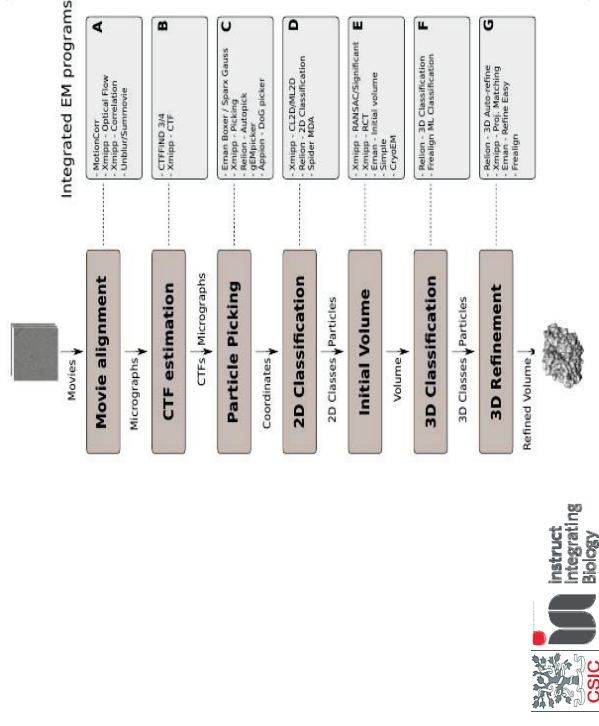


## Current packages (153 prots)

- Xmipp (75)
- Scipion (26)
- Relion (13)
- Spider (10)
- Grigorieff (8)
- Eman (5)
- Bsoft (2)
- Imagic (2)
- Opic (2)
- Appion (1)
- Simple (1)
- CryoEM (1)
- Atsas (1)
- Gautomatch (1)
- Gcft (1)
- Igbmc (1)
- Ispyb (1)
- Motioncorr (1)
- Resmap (1)



## SPA workflow and Scipion integrated programs

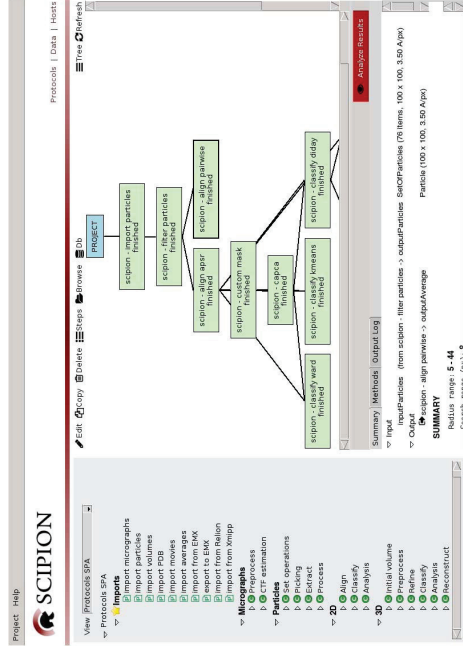


**Goal 2:** Full project traceability,  
improving reproducibility.

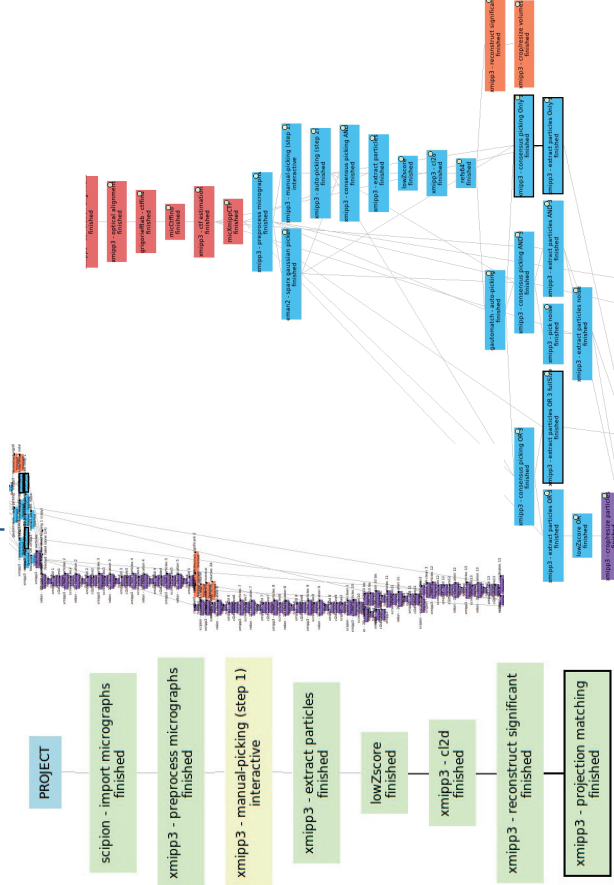




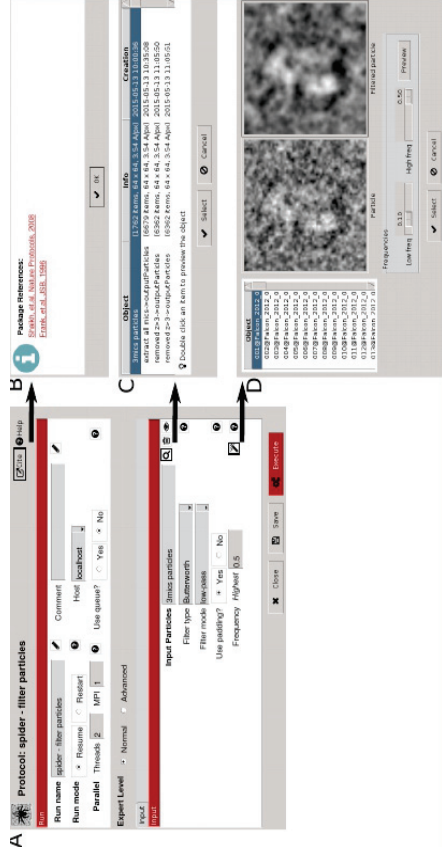
We track all the steps performed in a project



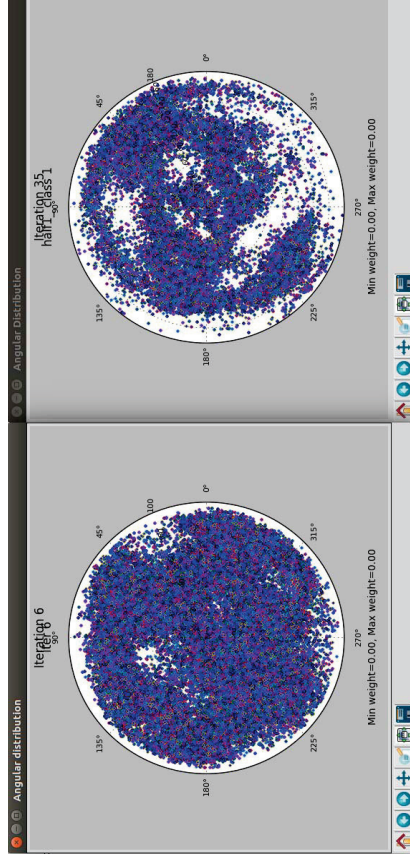
### Complex workflows



All parameters are also stored

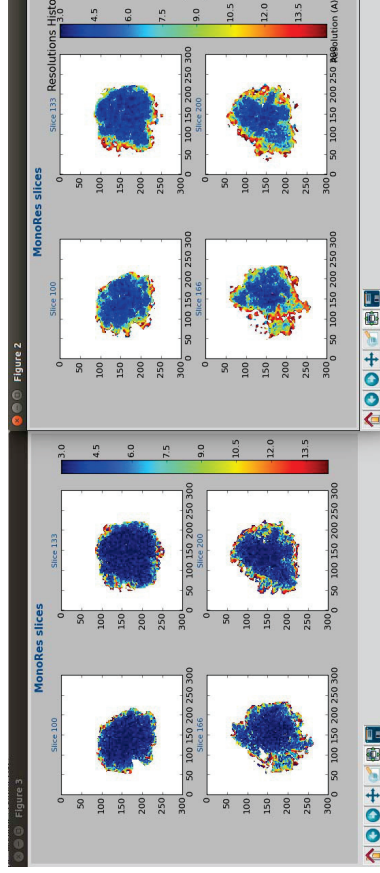


### Better angular coverage

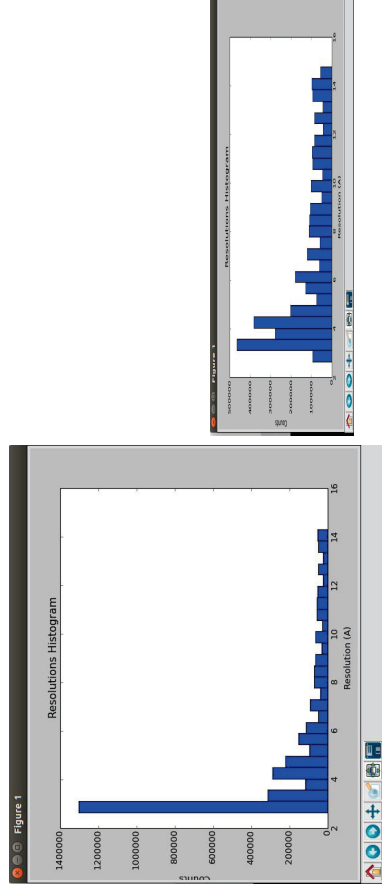




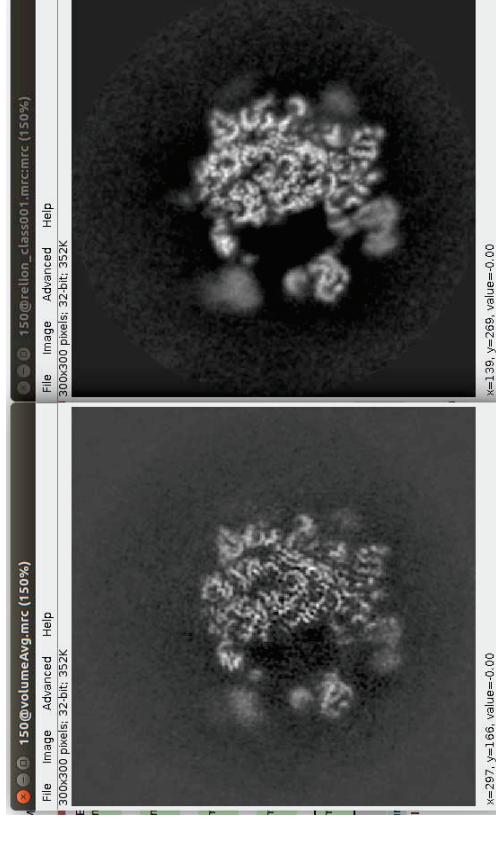
## Better local resolution



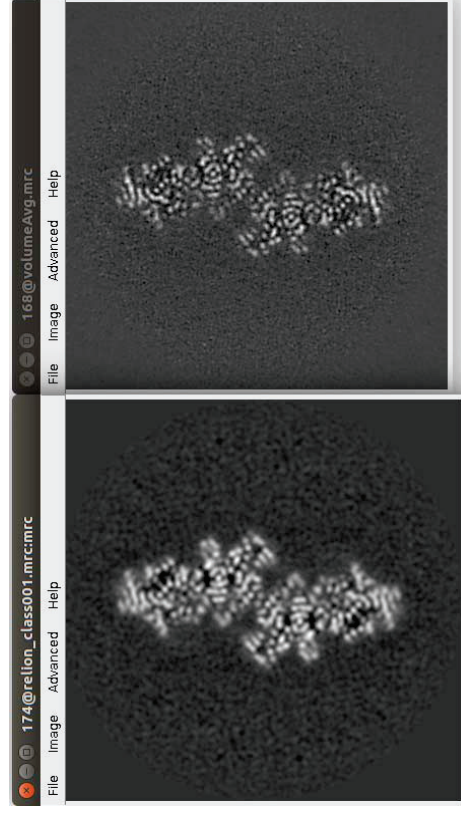
## Better local resolution



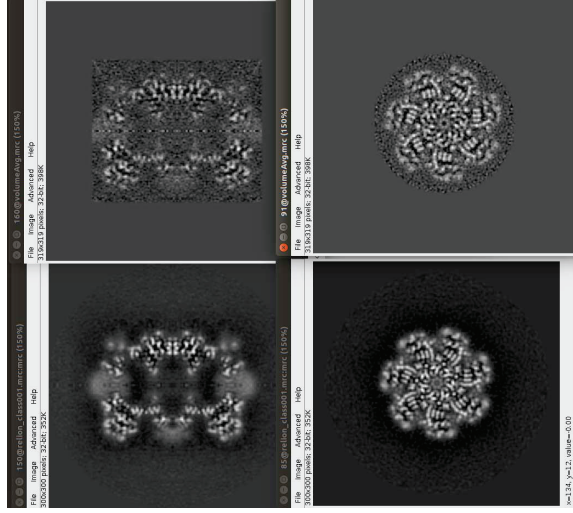
## Results ribosome



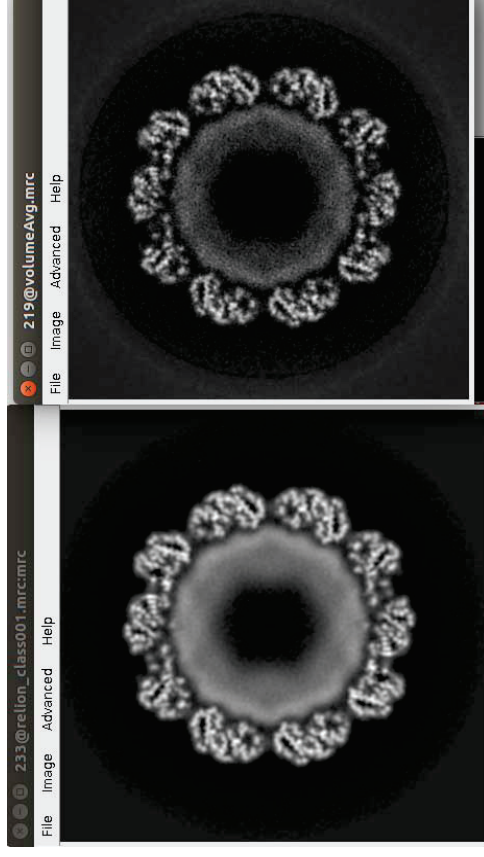
## Results galactosidase



## Results proteasome

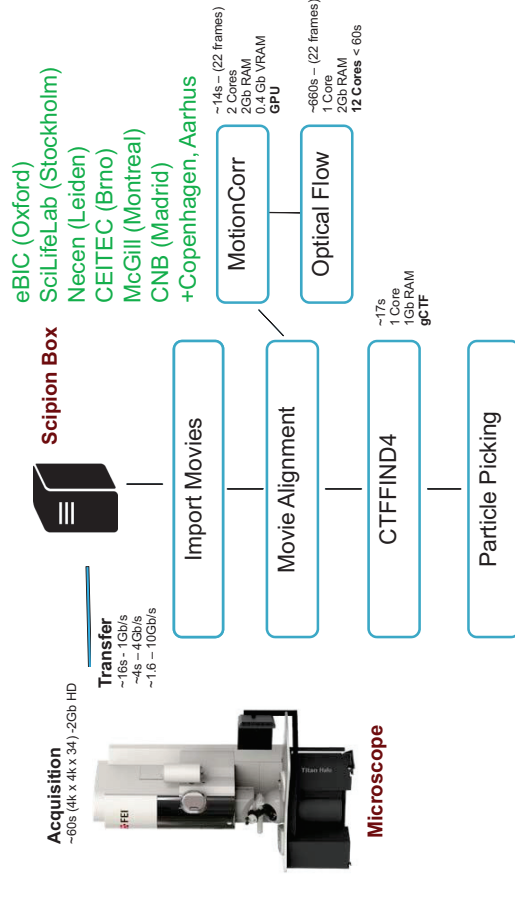


## Results virus



## Goal 3: Execute complete workflows in an automated manner.

### Run workflows automatically in streaming

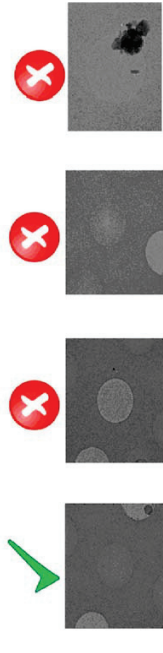




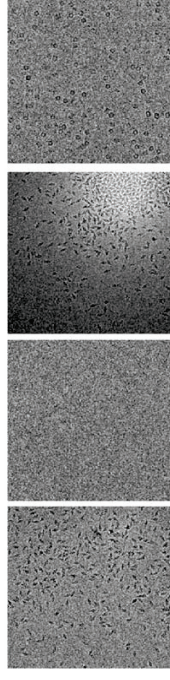
# Scipion Cloud



# Feedback to the microscope



Foil-hole images



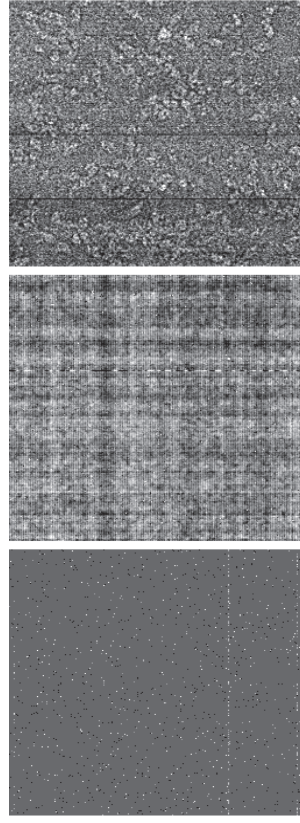
Data images

Dataset	Num	% Bad	ErrorDI	ErrorFH	FH1 - DI
β-Gal	43	(D)81% (FH)81%	0%	2%	0%
	41	(D)32% (FH)34%	0%	3%	3%
	156	(D)5% (FH)6%	0%	1%	1%
GroEL	128	(D)21% (FH)27%	0%	1%	0%
	105	(D)32% (FH)27%	1%	5%	0%
	140	(D)1% (FH)3%	0%	0%	0%
Hemoglobin	204	(D)12% (FH)11%	1%	3%	2%

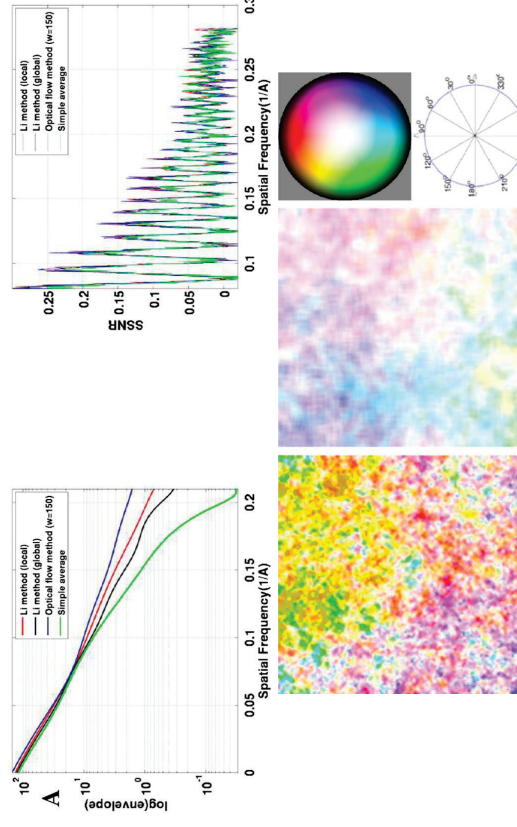
J. Vargas, E. Franken, J. Gómez-Bianco, R. Schoenmakers, A. J. Koster, C.O.S. Sorzano, J.M. Carazo, Semi-automatic and automatic foil-hole and data images quality assessment in 3DEM. J. Structural Biology 196: 515-524 (2016)



# Blind estimation of camera gain



# Optical flow

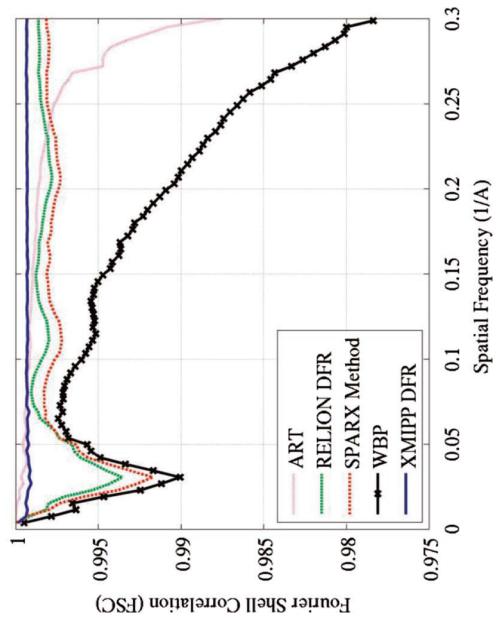






V. Abishami, J. Vargas, Y. Cheng, X. Li, R. Marabini, C.O.S. Sorzano, J.M. Carazo. Alignment of direct detector device micrographs using a robust optical flow approach. J. Structural Biology, 189: 163-176 (2015)





## Fourier Reconstruction



V. Abrishami, J.R. Bilbao-Castro, J. Vargas, R. Marabini, J.M. Carazo, C.O.S. Sorzano. A fast iterative convolution-based weighing approach for direct Fourier three-dimensional reconstruction. *Ultramicroscopy*, 157: 79-87 (2015)

## Statistical Analysis in Fourier space

**FSC=0.5**  $\Rightarrow$   $SNR_C=1$   
 $E\{FSC\} \approx \frac{SNR_C}{1+SNR_C}$   
**FSC=0.3**  $\Rightarrow$   $SNR_C=1$


**The approximations come after an order 0 Taylor approximation, and they are true on average.**

$$E\{FSC(R, \Delta R)\} \approx \frac{SNR_C^{(half)}}{1+SNR_C^{(half)}} = \frac{SNR_C^{(full)}}{2+SNR_C^{(full)}}$$





$$E\{FSC^{(full)}(R, \Delta R)\} \approx \frac{2E\{FSC(R, \Delta R)\}}{1+E\{FSC(R, \Delta R)\}}$$

**FSC=0.143=1/7**  $\Rightarrow$  **FSC<sub>ref</sub>=0.5**

$$f_1(\mathbf{r}) = x(\mathbf{r}) + n_1(\mathbf{r}) \text{ and } f_2(\mathbf{r}) = x(\mathbf{r})$$

$$E\{FSC_{ref}(R, \Delta R)\} \approx \sqrt{\frac{2SNR_C}{2SNR_C+1}}$$

$$E\{FSC_{ref}(R, \Delta R)\} \approx \sqrt{\frac{2E\{FSC\}}{1+E\{FSC\}}}$$







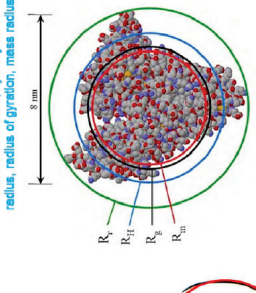
C.O.S. Sorzano, J. Vargas, J. Olón, V. Abrishami, J.M. de la Rosa-Trevin, J. Gómez-Blanco, J.L. Vilas, R. Marabini, J.M. Carazo. A review of resolution measures and related aspects in 3D Electron Microscopy. *Progress in Biophysics and Molecular Biology* (in press)

## Statistical Analysis in Fourier space

**Guinier approximation**  
 $\frac{\sin(Rr)}{Rr} \approx 1 - \frac{R^2 r^2}{6} + \frac{R^4 r^4}{100} - \dots$


$|F(R)|^2 \approx \int_0^D \int_0^D \gamma^2 \Phi_f(r) dr - R^2 \int_0^D \int_0^D \frac{r^4}{6} \Phi_f(r) dr$   
 $= \int_0^D \gamma^2 \Phi_f(r) dr \left( 1 - R^2 \int_0^D \frac{r^4}{6} \Phi_f(r) dr \right)$   
 $= F_0^2 \left( 1 - \frac{R^2}{3} F_2^2 \right)$









**For infinitely small atoms**  
 $F_0^2 = |F(0)|^2 = \sum_{i=1}^{N_{atoms}} \sum_{j=1}^{N_{atoms}} w_i w_j \delta(\|\mathbf{r}_i - \mathbf{r}_j\|)$

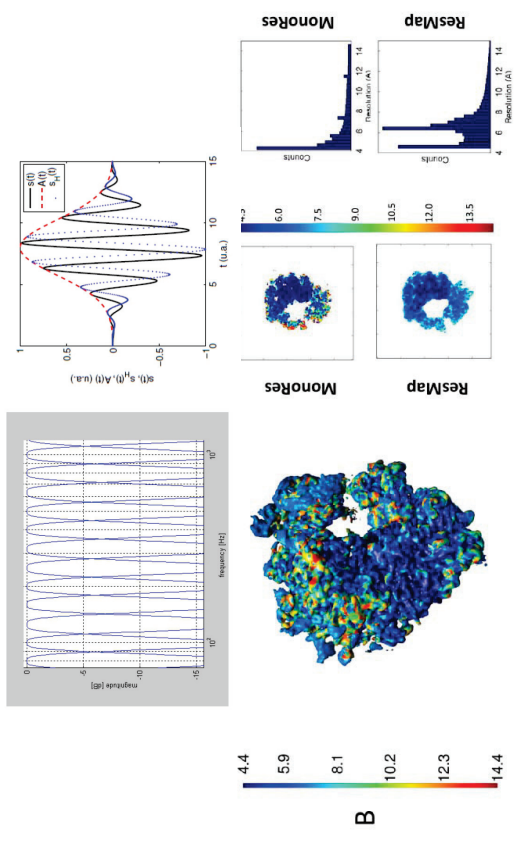
**Same as Wilson**



**If all atoms have equal weight, it is the number of atoms**  
**Rosenthal, P. B. J. Molecular Biology, 2003, 333, 721-745**







C.O.S. Sorzano, J. Vargas, J. Olón, V. Abrishami, J.M. de la Rosa-Trevin, J. Gómez-Blanco, J.L. Vilas, R. Marabini, J.M. Carazo. A review of resolution measures and related aspects in 3D Electron Microscopy. *Progress in Biophysics and Molecular Biology* (in press)

## (Monogenic) Local resolution





J.L. Vilas, J. Gómez-Blanco, J.M. de la Rosa-Trevin, R. Melero, J. Cuenca, R. Marabini, J.M. Carazo, J. Vargas, C.O.S. Sorzano. MonoRes: Local resolution for electron microscopy maps using monogenic signals. *Structure* (in press)

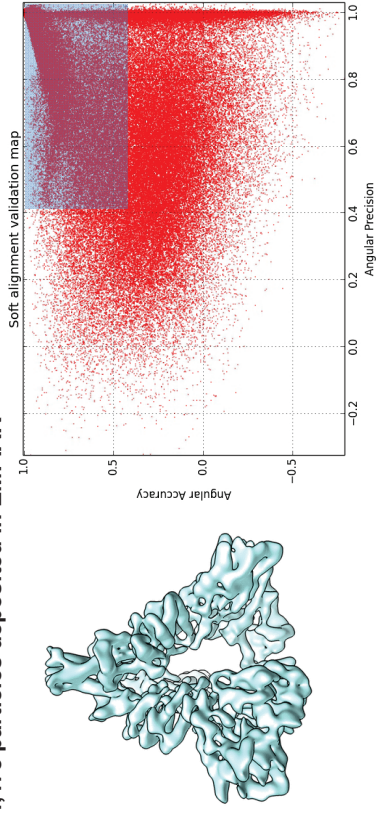






## Volume validation: Precision

124,478 particles deposited in EMPIAR



75% particles align with precision

45% particles align with accuracy

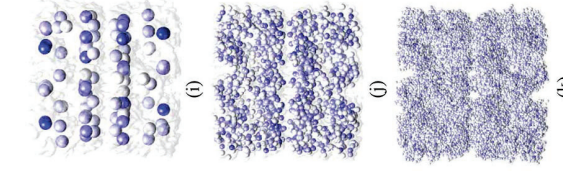
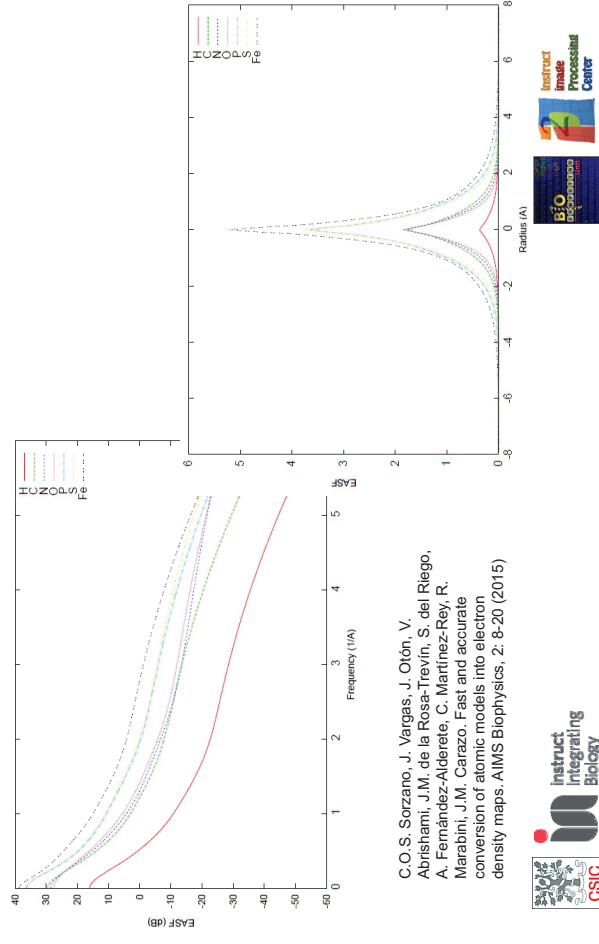
38% particles align with accuracy and precision



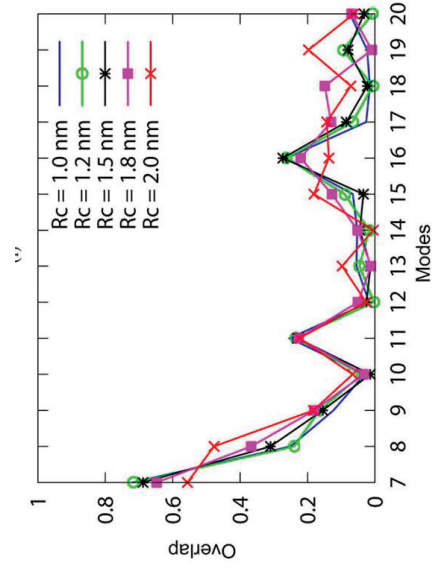
C.O.S. Sorzano, J. Vargas, J. Otón, V. Abrishami, J.M. de la Rosa-Trevín, S. del Riego, A. Fernández-Alderete, C. Martínez-Rey, R. Marabini, J.M. Carazo. Fast and accurate conversion of atomic models into electron density maps. *AIMS Biophysics*, 2: 8-20 (2015)



## From PDB to electron densities



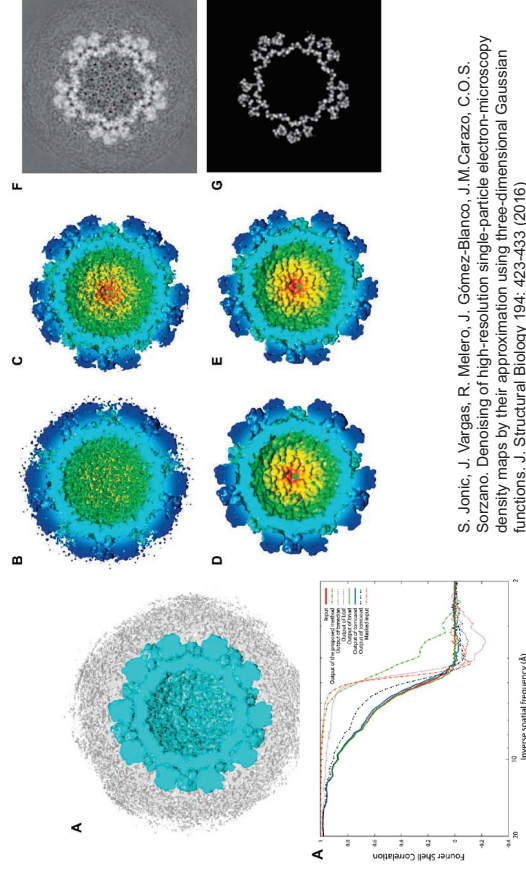
... and back



S. Jonic, C.O.S. Sorzano. Coarse-graining of Volumes for Modeling of Structure and Dynamics in Electron Microscopy: Algorithm to Automatically Control Accuracy of Approximation. *IEEE J. Selected Topics in Signal Processing*, 10: 161-173 (2016)



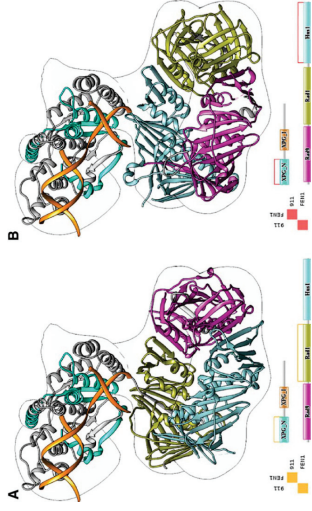
## Denoising



S. Jonic, J. Vargas, R. Melero, J. Gómez-Blanco, J.M. Carazo, C.O.S. Sorzano. Denoising of high-resolution single-particle electron-microscopy density maps by their approximation using three-dimensional Gaussian functions. *J. Structural Biology* 194: 423-433 (2016)



## Hybrid modelling validation



**A** **DDI Sequence Analysis**

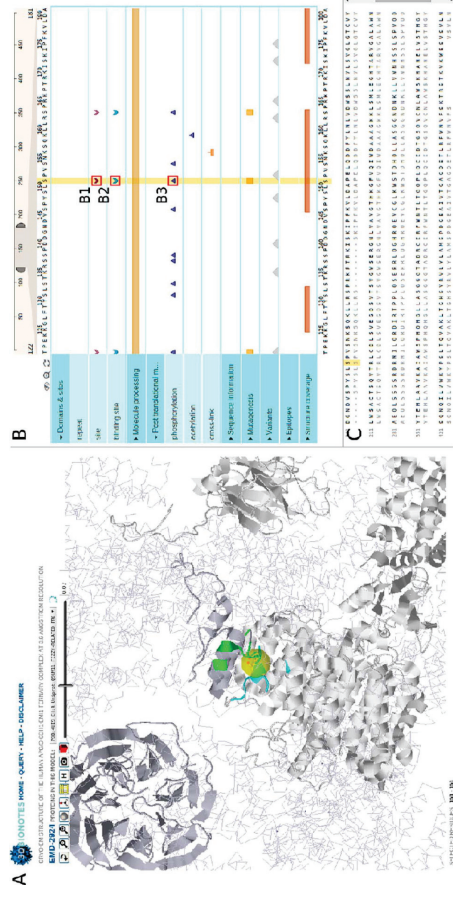
**B** **EXPAND TABLE TO ALL POSSIBLE DOMAINS**

Domain	Start	End	e-value	Start	End	e-value	IP score	Struct. Map
Helix	13	246	7.6E-05	NPGL_N	1	108	1.5E-36	X
Helix	13	246	7.6E-05	NPGL_I	146	232	4E-29	LCP
Helix	257	407	1E-01	NPGL_N	1	108	1.5E-36	X
Helix	257	407	1E-01	NPGL_I	146	232	4E-29	LCP
Helix	515	772	1.2E-01	NPGL_N	1	108	1.5E-36	X
Helix	515	772	1.2E-01	NPGL_I	146	232	4E-29	LCP

J. Segura, R. Sánchez-García, D. Tabas-Madrid, J. Cuenca-Alba, C.O.S. Sorzano, J.M. Carazo. 3D/IANA: 3D Domain Interaction Analysis. A toolbox for quaternary structure modelling. *Biophysical J.* 110: 766-775 (2016)



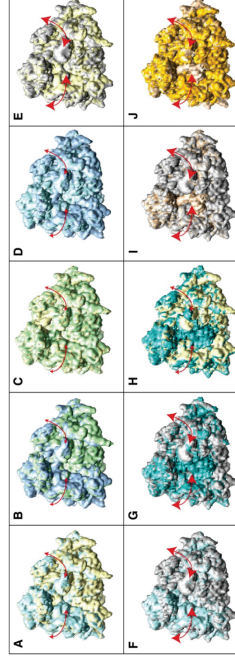
## Hybrid modelling validation through annotations



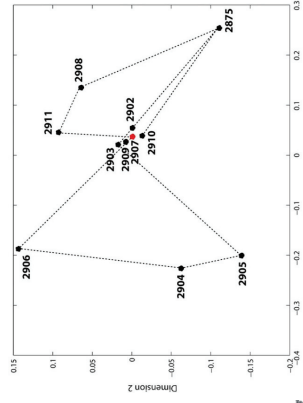
D. Tabas-Madrid, J. Segura, R. Sánchez-García, J. Cuenca-Alba, C.O.S. Sorzano, J.M. Carazo. 3DBioNotes: A unified, enriched and interactive view of macromolecular information. *J. Structural Biology* 194: 231-234 (2016)



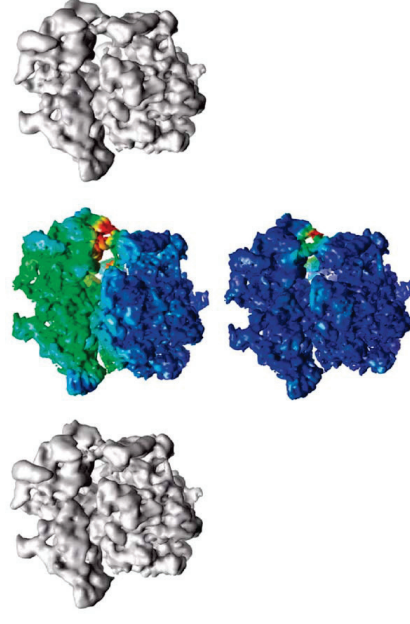
## Sorting discrete states



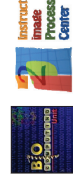
C.O.S. Sorzano, A.L. Álvarez-Cabrera, M. Kazemi, J.M. Carazo, S. Jonic. StructMap: Elastic distance analysis of electron microscopy maps for studying conformational changes. *Biophysical J.* 110: 1753-1765 (2016)



## Analysis of local forces



C.O.S. Sorzano, A. Martín-Ramos, F. Prieto, R. Mejero, J. Martín-Benito, S. Jonic, J. Navas-Calvente, J. Vargas, J. Olón, V. Abrishami, J.M. de la Rosa-Trevín, J. Gómez-Blanco, J.L. Vilas, R. Marabini, J.M. Carazo. Local analysis of strains and rotations for macromolecular electron microscopy maps. *J. Structural Biology*, 195: 123-128 (2016)





# Web tool page layout

## Obtain your initial volume

To obtain an initial 3D map from your average images several methods are available from different packages (Xmipp3 and Eman2). At the end of the processing you will be able to compare the output volumes from the different methods, downloading the selected ones. It is recommended to read the ["Initial model estimation" tutorial](#) before using this portal.

### Choose your project

- Create an empty project [Create](#)
- Create a project with Test data [Test data](#)
- Explore project with Test data (read-only) [Explore](#)



# Example of a web tool

SCIPION Project GroelTestData [None left] [Home](#)

Workflow View: [initial\_Volume] [Edit](#) [Copy](#) [Delete](#) [Small Tree](#) [List](#) [Refresh](#) [Help](#)

**1. Upload data**


- import averages
- Create a 3D volume
  - xmipp3 - ransac
  - eman2 - initial volume
  - xmipp3 - significant
- Align volumes.
  - xmipp3 - align volumes


**PROJECT**

```





    graph TD
      A[import averages (groel) finished] --> B[xmipp3 - ransac finished]
      A --> C[eman - initial vol finished]
      A --> D[xmipp3 - significant finished]
      B --> E[align volumes finished]
      C --> E
      D --> E
    
```

**Summary** **Methods** **Output Logs** **Analyze Results** **Download Results**


**Input**  
 inputSet (from 103.inputSet.116)  SetOfAverages (31 items, 64 x 64, 1.00 Apx)

**Output**  
 outputVolumes  SetOfVolumes (10 items, 64 x 64 x 64, 1.00 Apx)

**Summary**  
 Input Images: 2 outputAverages: 47  
 Output Initials volumes: None

# Google: 3DEM Methods (Wiki+Mail list)

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**Main Page**

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- 4 Single particles
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  - 4.2 2D Preprocessing
  - 4.3 2D Alignment
  - 4.4 2D Classification and clustering
  - 4.5 3D Alignment
  - 4.6 3D Reconstruction
  - 4.7 3D Heterogeneity
  - 4.8 Resolution
  - 4.9 Sharpening of high resolution information
  - 4.10 CTF estimation and restoration
  - 4.11 CTF estimation and restoration
  - 4.12 Segmentation
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  - 5.4 3D reconstruction
  - 5.5 Noise reduction

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- 6 Related methods
- 7 Comments

**Citation [edit]**  
 Liu, J., Li, H., Zhang, L., Rames, M., Zhang, M., Yu, Y., Peng, B., Celsi, C. D., Xu, A.,

**Abstract [edit]**  
 Knowledge of three-dimensional (3D) structures of each individual particles of asyn provides a tool for imaging a single and unique biological object from a series of 2D images. This method could reduce the accumulation of beam error of the target object center during the tilting process through a closed-loop prop comparable capability to other ET methods in tracking target proteins while maintain

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**Links [edit]**  
<http://www.nature.com/articles/ncisp20231>

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