

# EMDB and EMPIAR – resources for EM data

Workshop on Computational Methods in Bio-imaging Sciences, IMS/NUS,  
Singapore

*January 8, 2018*

Ardan Patwardhan



# Plan

- Introduction to EM, EMDB and EMPIAR
- Trends in the field
- Overview of web resources for searching, visualisation and validation
- Planned initiatives and developments

**Nature Methods – Method of the Year 2015**

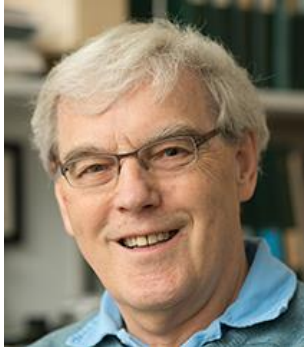
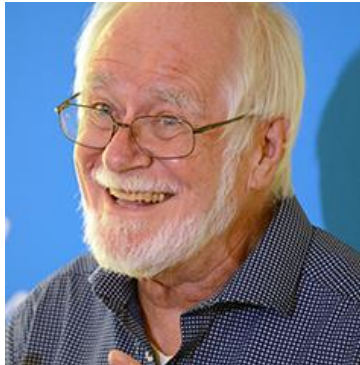
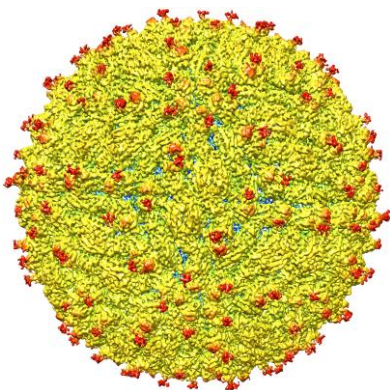
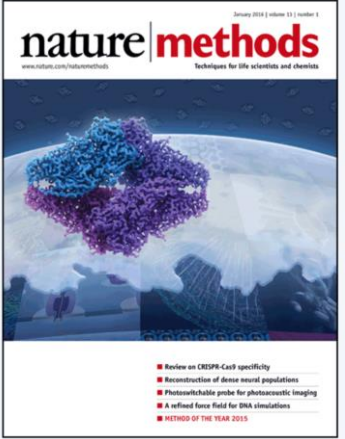
The end of 'blob-ology': single-particle cryo-electron microscopy (cryo-EM) is now being used to solve macromolecular structures at high resolution.

**MRC May 2016** - Researchers at the MRC Laboratory of Molecular Biology in partnership with US high-performance microscopes company FEI, five pharmaceutical companies (Astex Pharmaceuticals, AstraZeneca, GlaxoSmithKline, Heptares Therapeutics and UCB) and the University of Cambridge's Nanoscience Centre have formed the Cambridge Pharmaceutical Cryo-EM Consortium to assist early-stage drug discovery research

**Zika virus at 3.8Å – EMD-8116**

Scientists revealed a molecular map of the Zika virus, which could help scientists develop new treatments for the disease ([Daily Mail; July 2016](#))

**2017 Nobel Prize in Chemistry** - Jacques Dubochet, Joachim Frank, Richard Henderson  
for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution

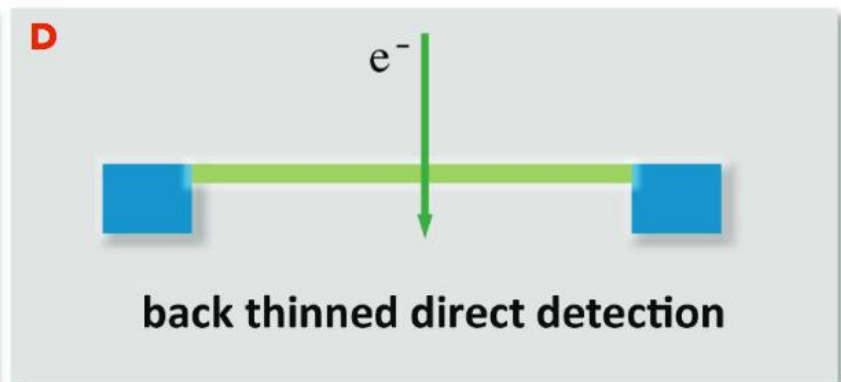
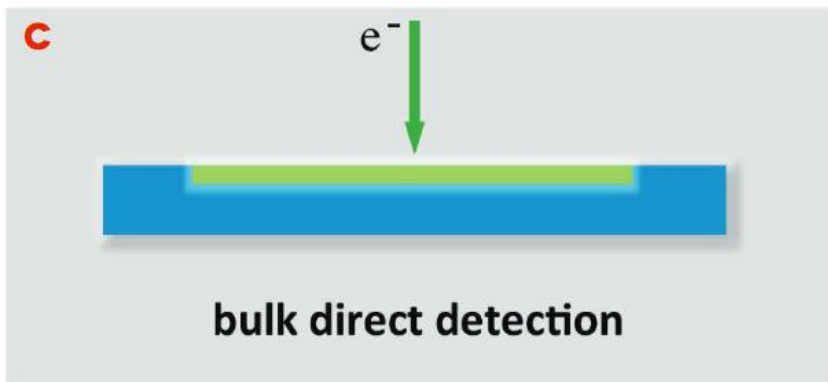
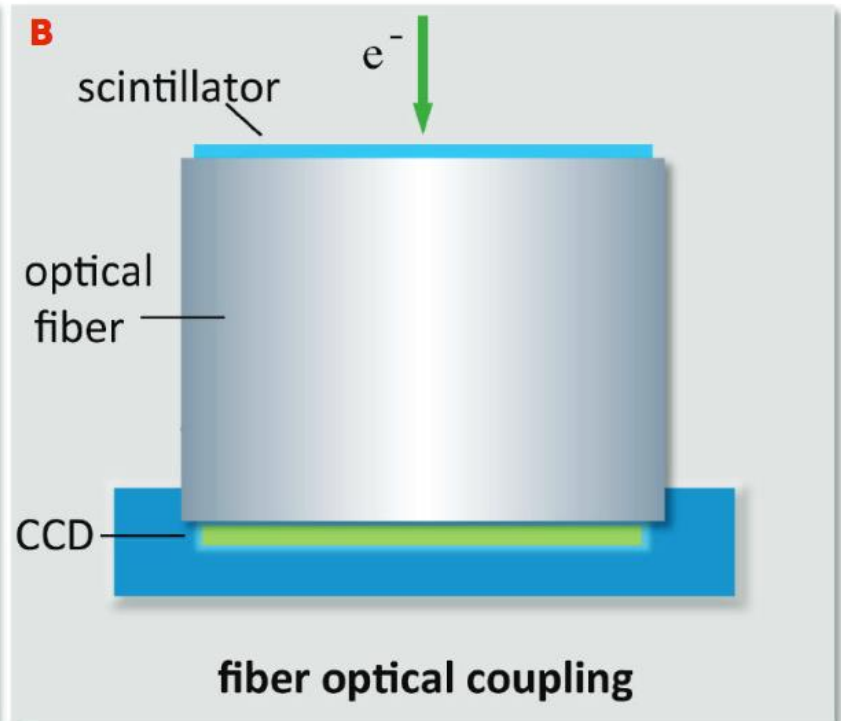
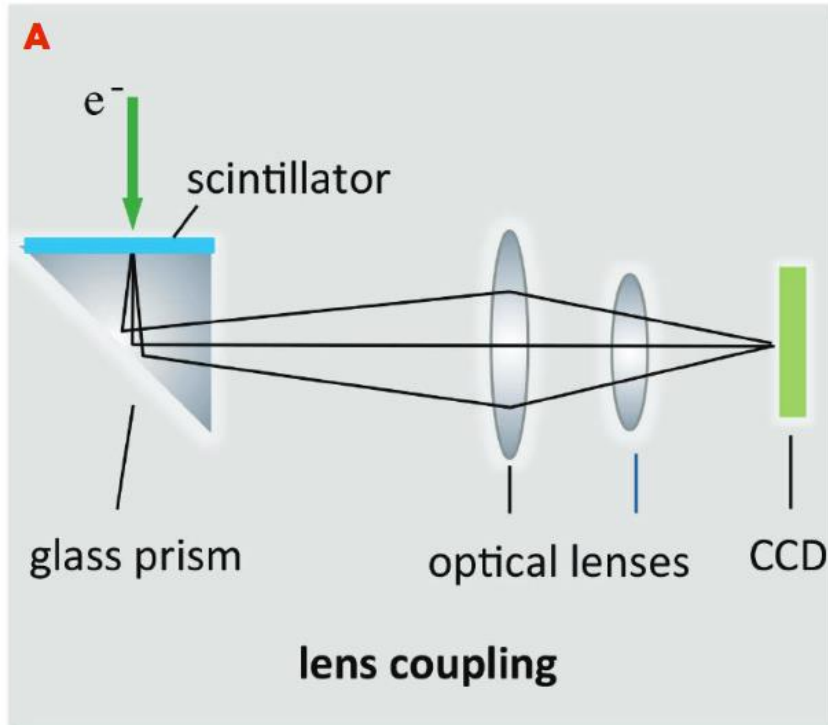


# Transmission Cryo-Electron Microscopy

A tool used by structural biologists to study  
molecular nanomachines

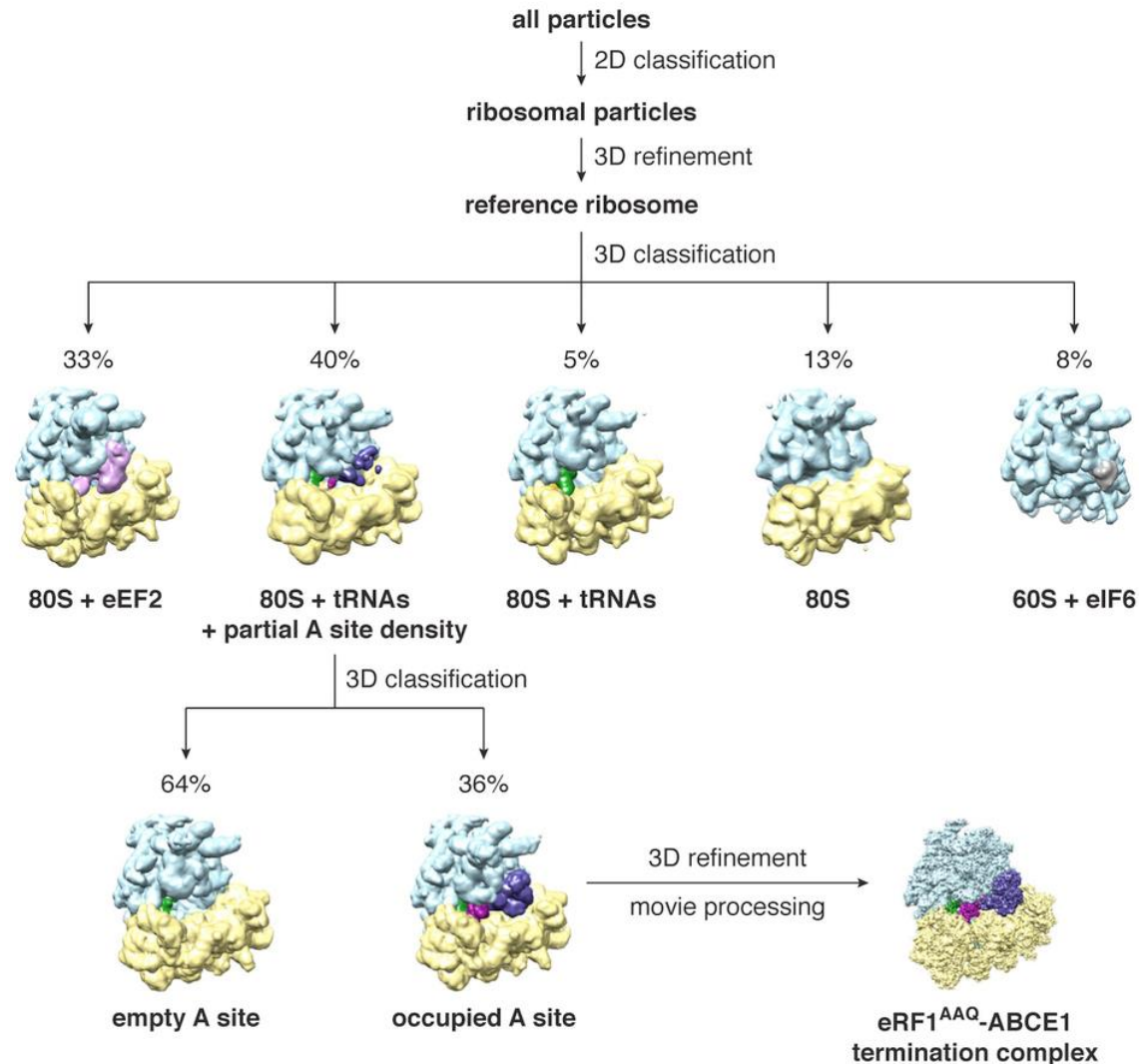
# Major advances – direct electron detector

- Gatan K2, FEI Falcon II



# Major advances – 3D classification

- Samples are rarely completely structurally homogeneous
- Use 3D classification techniques, e.g., in Relion to split original dataset into smaller, more homogeneous datasets
- **E.g.: Structural basis for stop codon recognition in eukaryotes**, Alan Brown, Sichen Shao, Jason Murray, Ramanujan S. Hegde & V. Ramakrishnan Nature 524, 493–496  
doi:10.1038/nature14896





# Major advances – improved microscopy

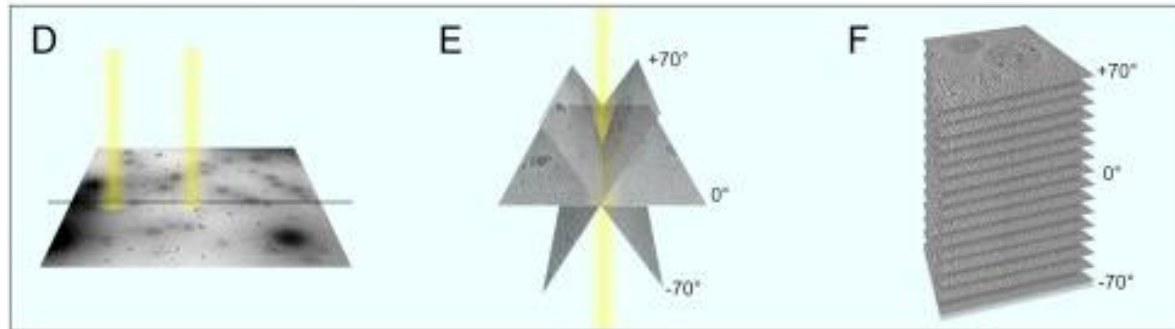
- FEI Titan Krios



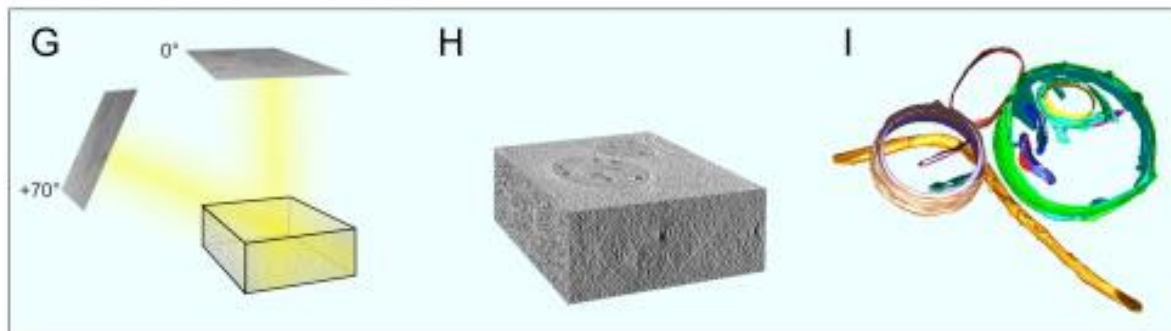
# Electron tomography

- Examine molecular assemblies in the cellular context
- 3D reconstructions of unique samples

Low dose image acquisition

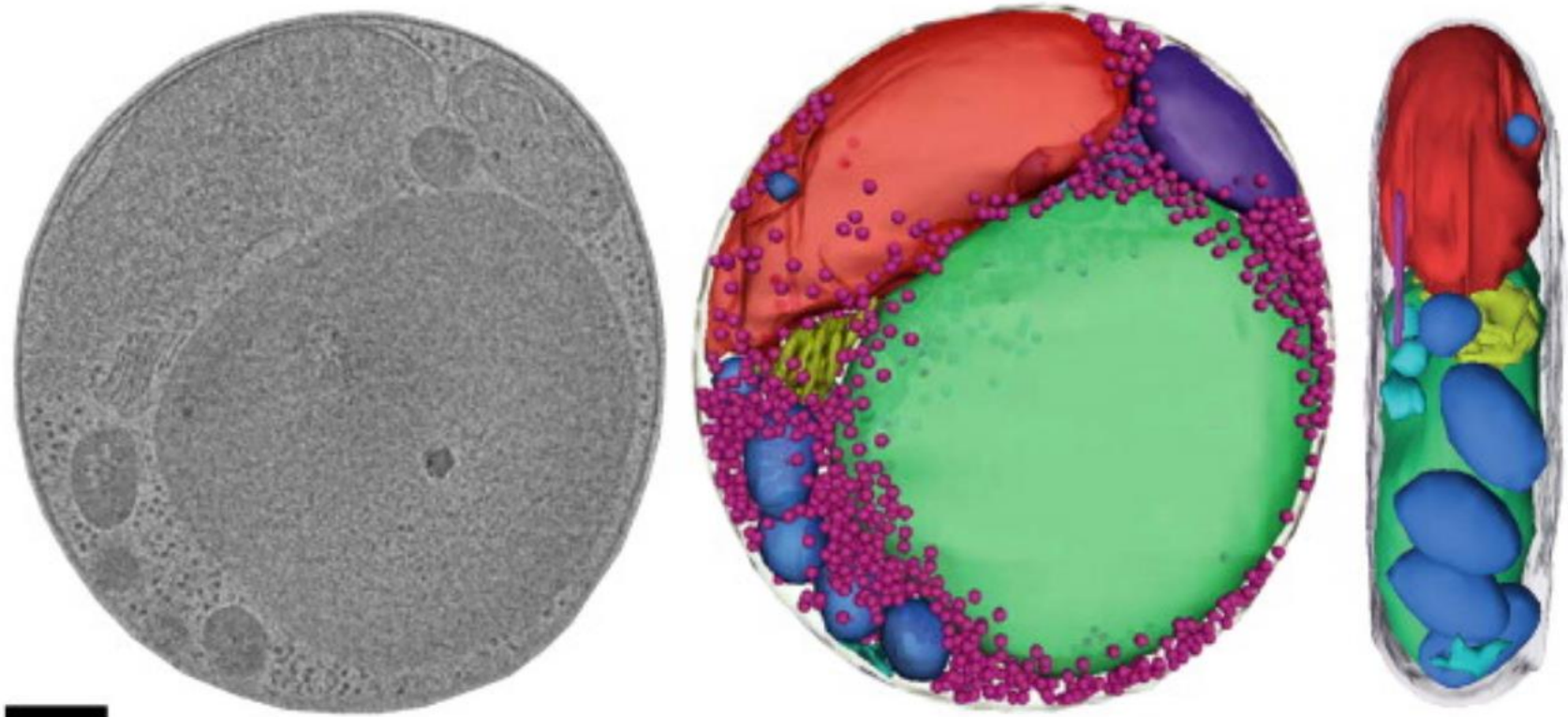


Reconstruction and visualization



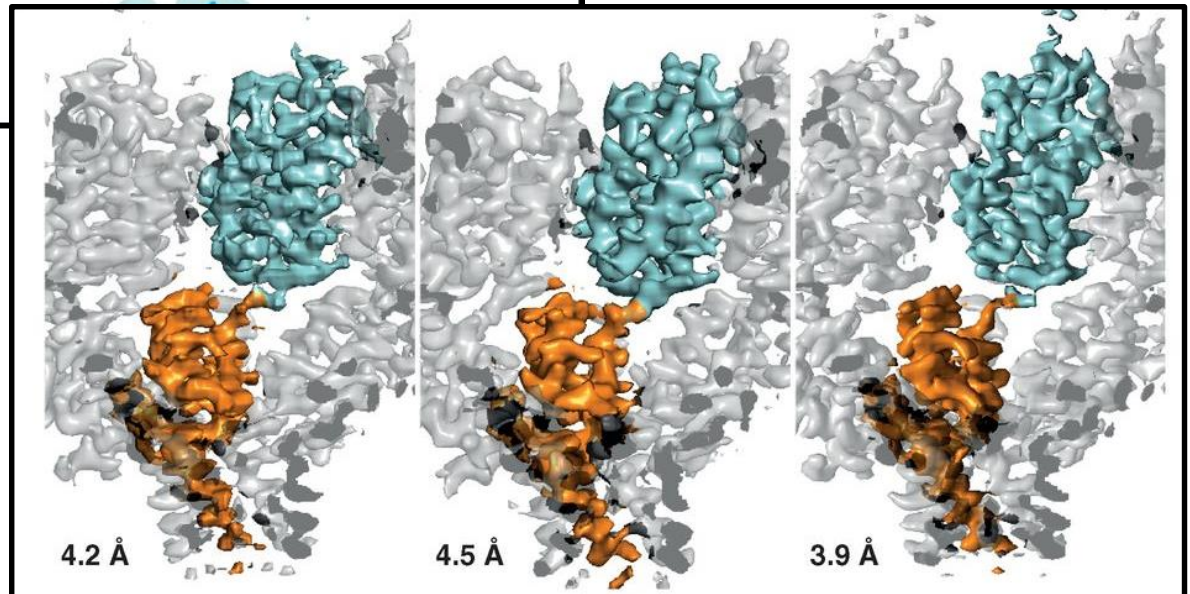
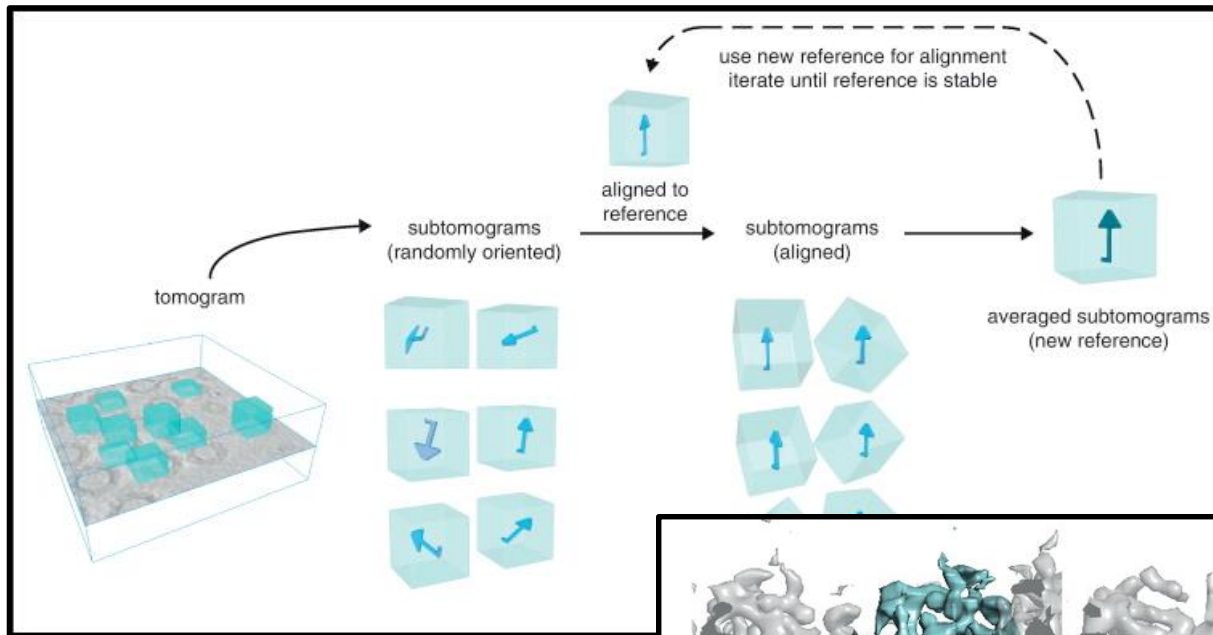


# 3D segmentation



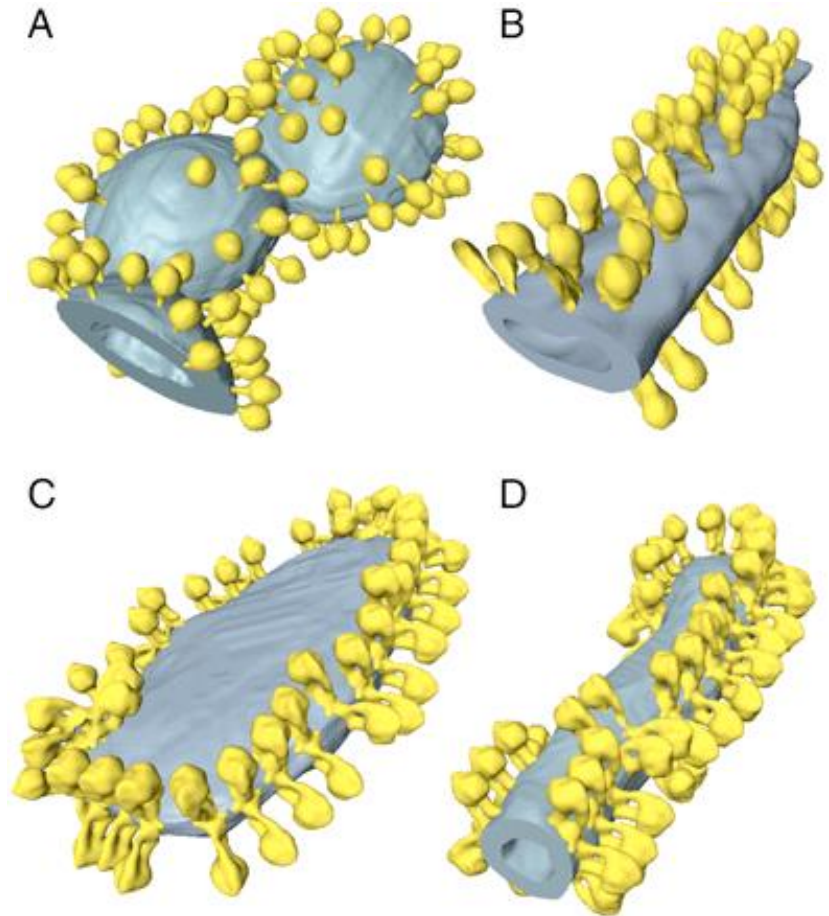
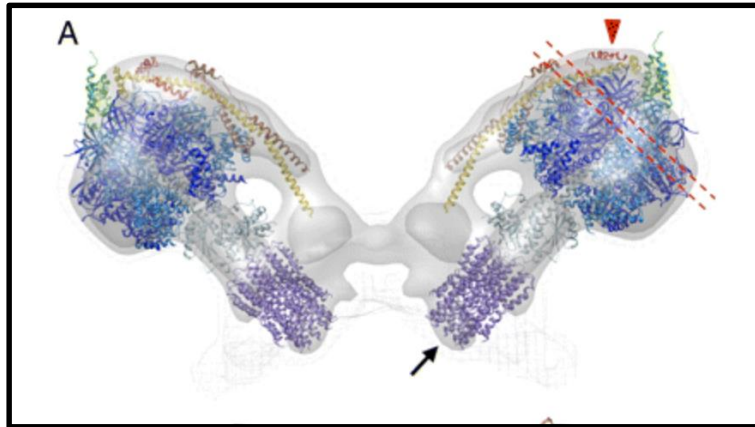
# Sub-tomogram averaging

- averaging of similar structure yields improved resolution

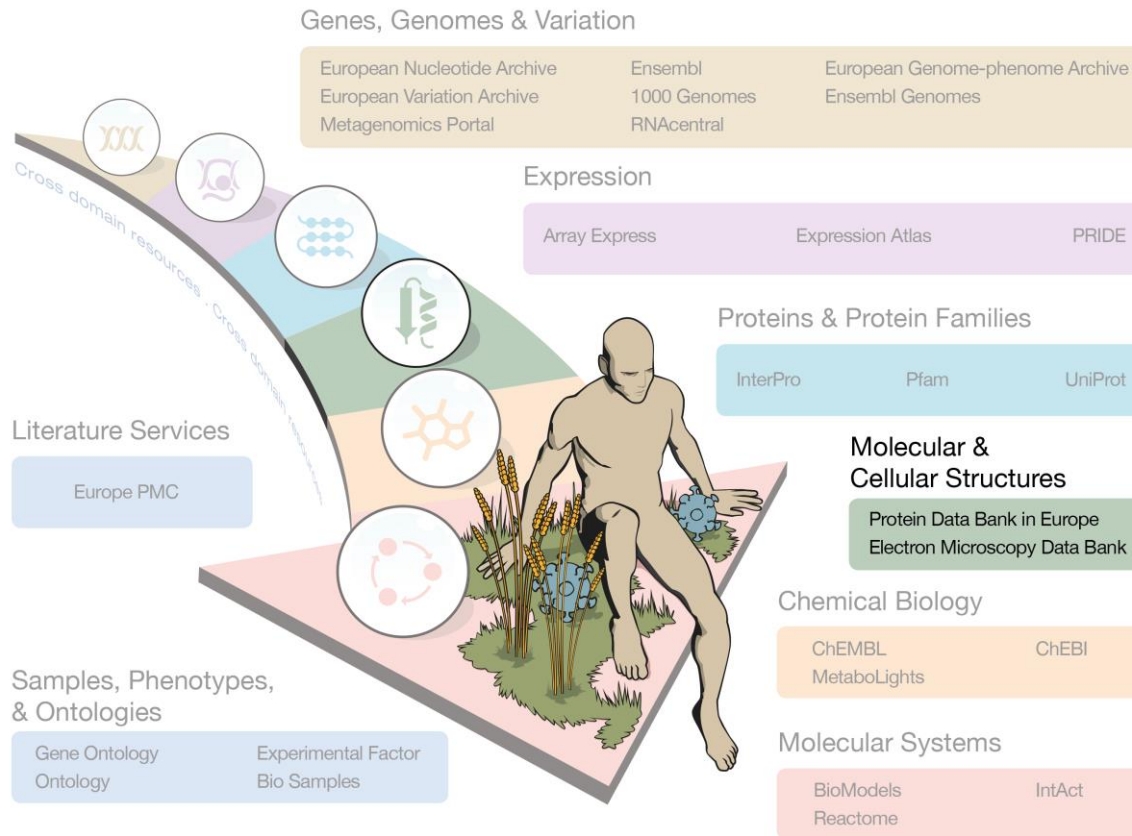


# The cellular context

- Placing sub-tomogram averages back into original positions provides additional information about organization and interactions in the cellular environment



# Cellular Structure and 3D Bioimaging Team

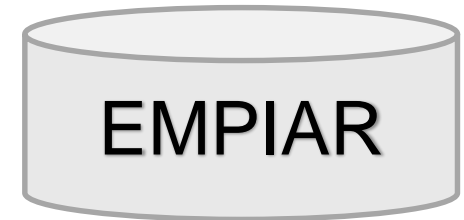
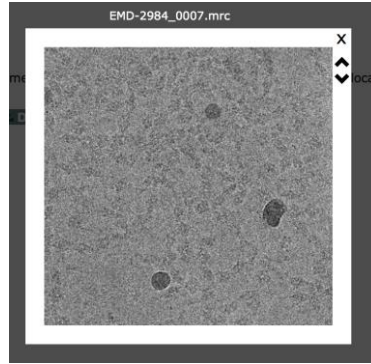


- Maintain and manage archives
  - EMDB for 3DEM reconstructions
  - EMPIAR for 3DEM raw data
- Develop and maintain web-services – searching, visualisation and validation
- Facilitate community-wide initiatives
- Key themes – integration (with other bioinformatics resources and imaging scales), validation, data-mining

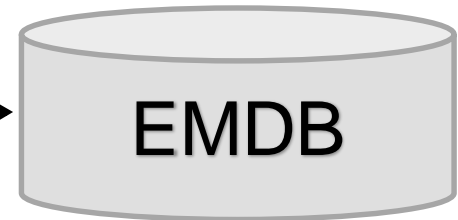
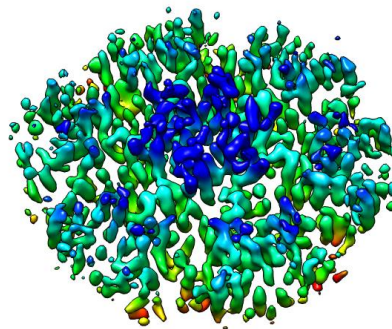


# Data: What data is found where...

2D Raw  
image



3D Volume



Fitted model



# Comparison of archives

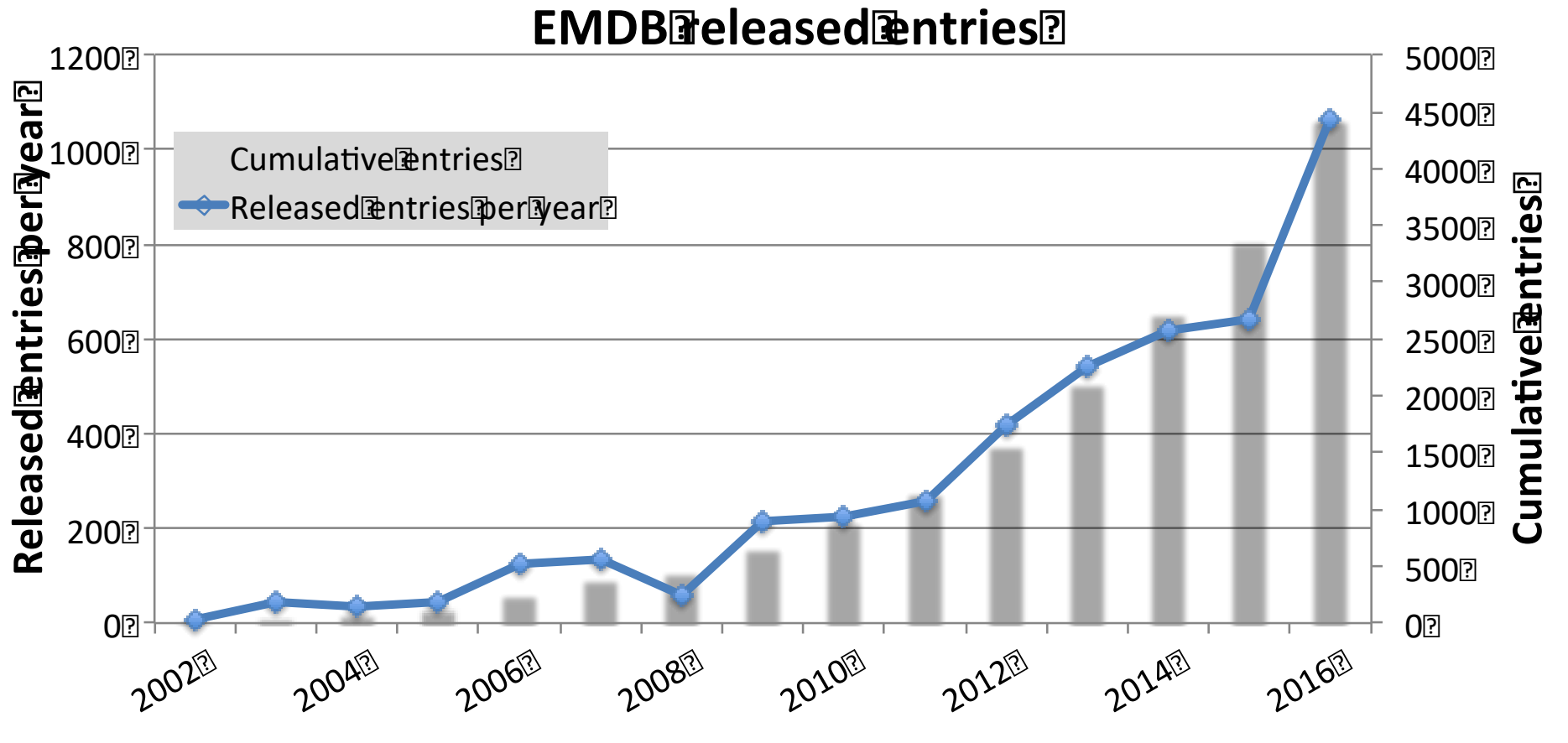
	PDB	EMDB	EMPIAR
Inception	1971	2002	2014
Number of entries	133589 (2297 EM)	5163 (1068 in 2016)	84
Archive size	1 GB	489 GB	48 TB
Mandatory deposition	Coordinates (1989) Structure factors (2008)	Single particle and sub-tomogram averaged structures (2012)  Representative tomogram strongly recommended	-



# EMDB Deposition Discussion at 3DEM GRC 2017

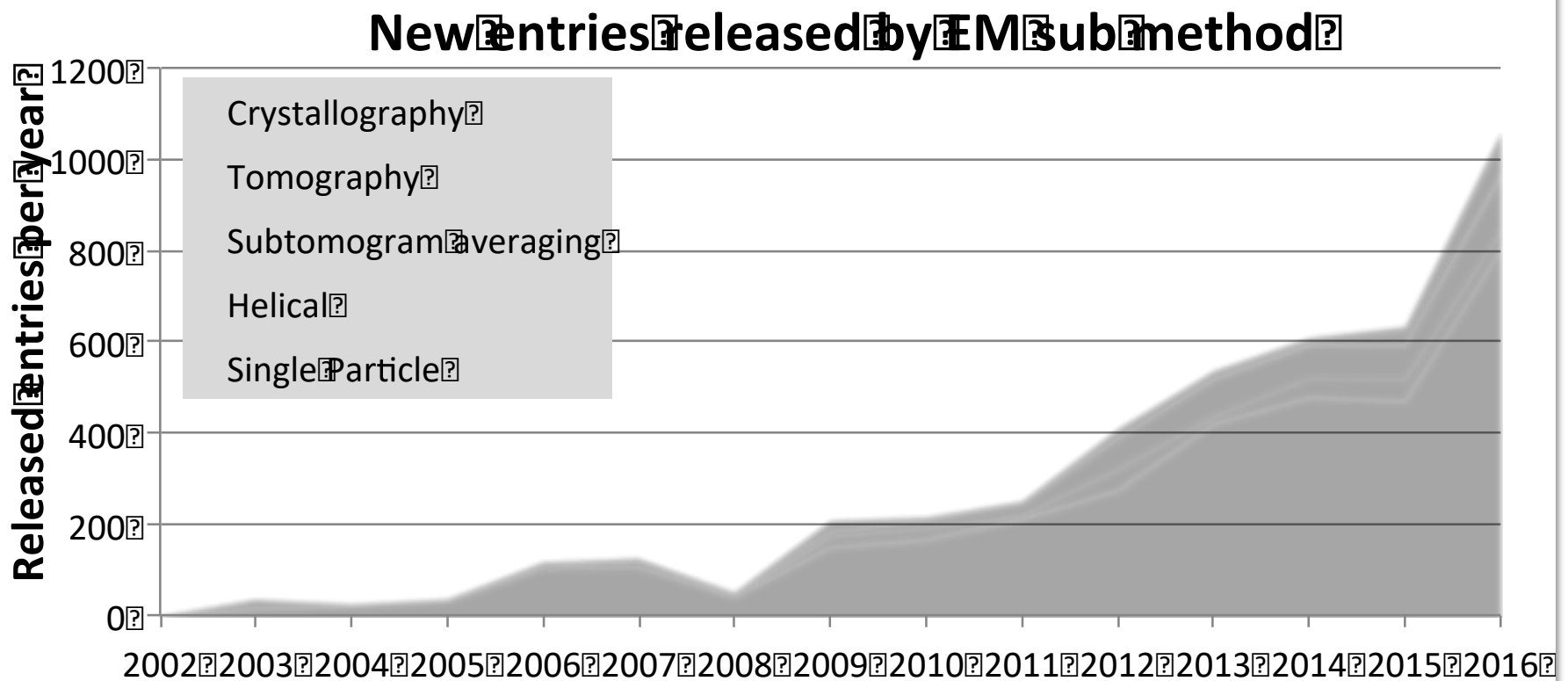
- Following changes were voted on with overwhelming majority (few abstentions and none against)
  - For all tomography-based studies, the deposition of representative tomographic reconstructions should be made mandatory. All tomographic reconstructions that are depicted in published figures (as orthoslices, renderings or similar), should be deposited
  - The deposition of un-modified half-maps should be mandatory in cases where half-maps have been used to assess resolution

# EMDB trends: released entries



# EMDB trends: EM sub-methods

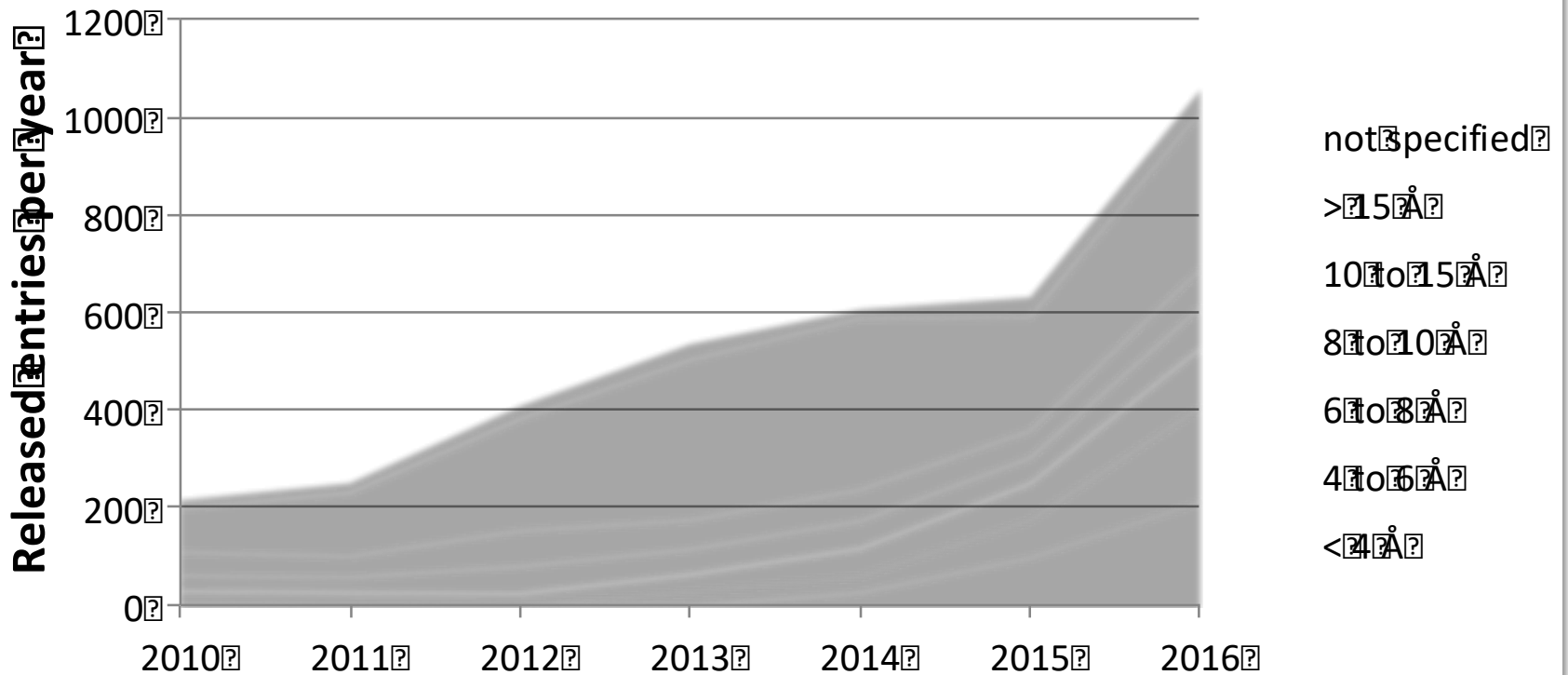
- ~20% from tomography in 2016



# EMDB trends: resolution

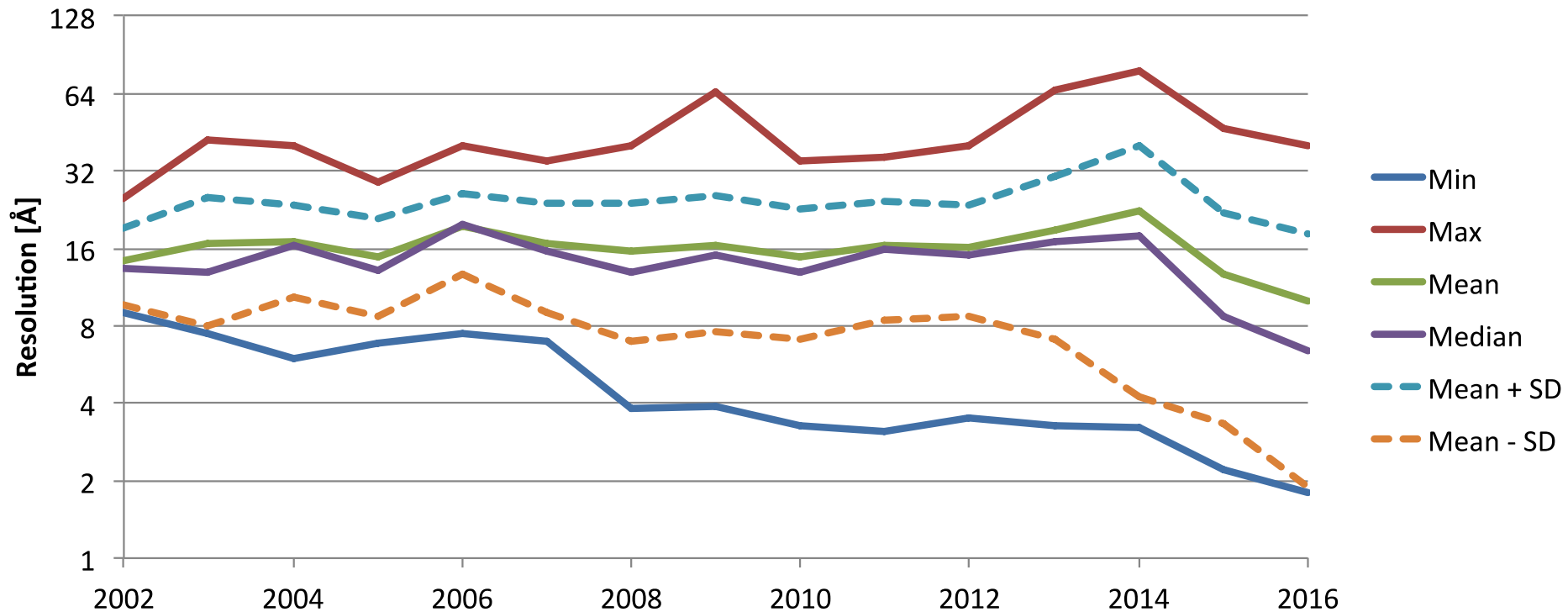
- Strong growth of better than 4Å structures

Resolution trends of released EMDb entries



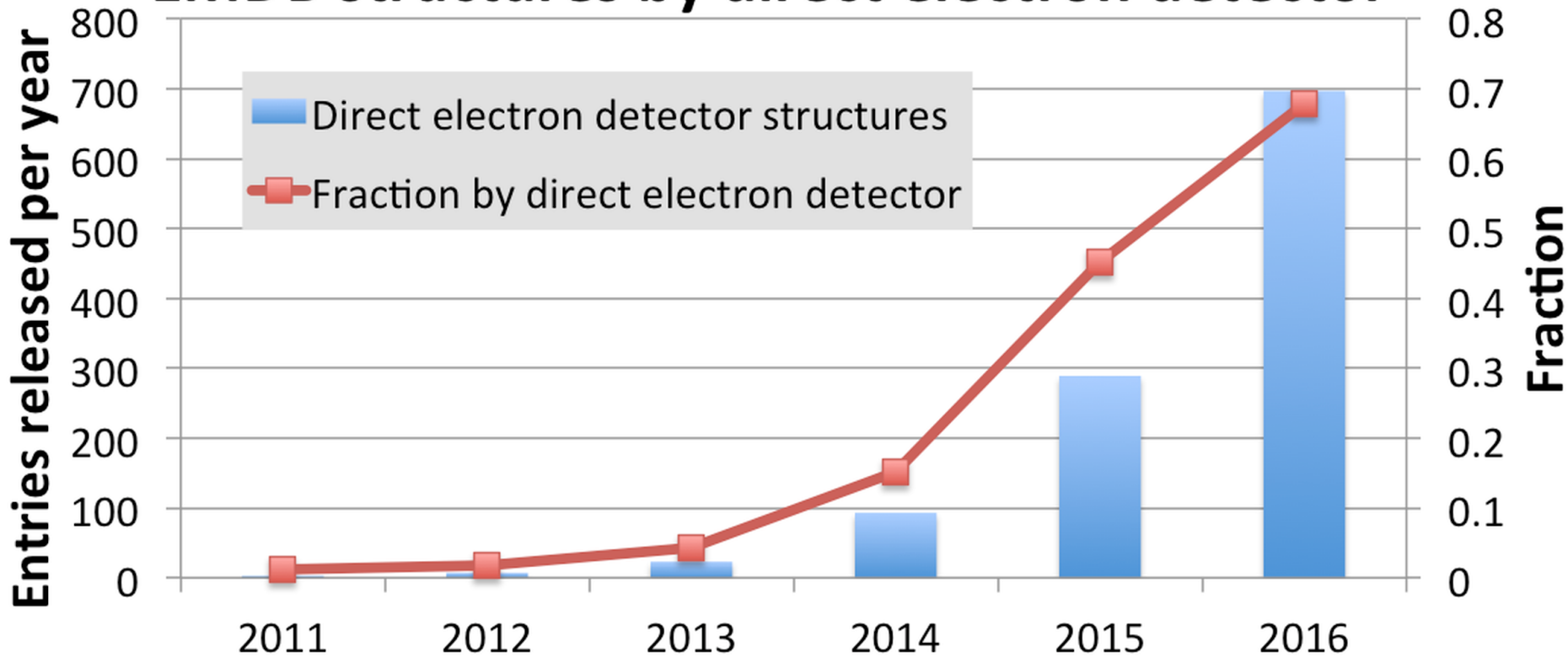
# EMDB trends: resolution of single-particle entries

Analysis of resolutions of released single particle entries



# EMDB trends: direct electron detectors

## EMDB structures by direct electron detector





# EMDB trends: geographic spread

- Analysis of author affiliations of EMDB-associated publications
- USA, Germany, UK continue to lead
- Strong growth in China
- Many more countries up and coming
- Patwardhan A., *Trends in the Electron Microscopy Data Bank (EMDB)*, Acta D **73**(6), 503-508

Country	2010	2011	2012	2013	2014	2015	2016	Sum
USA	55	50	86	116	139	135	162	743
Germany	19	25	20	22	42	53	53	234
UK	14	10	27	16	42	51	62	222
China	3	4	3	10	13	29	39	101
France	8	4	6	8	16	16	23	81
Japan	6	7	4	6	11	11	20	65
Spain	4	7	11	7	8	7	10	54
Canada	1	5	3	2	10	14	17	52
Switzerland	2	2	8	8	6	15	11	52
The Netherlands	0	1	1	3	9	15	16	45

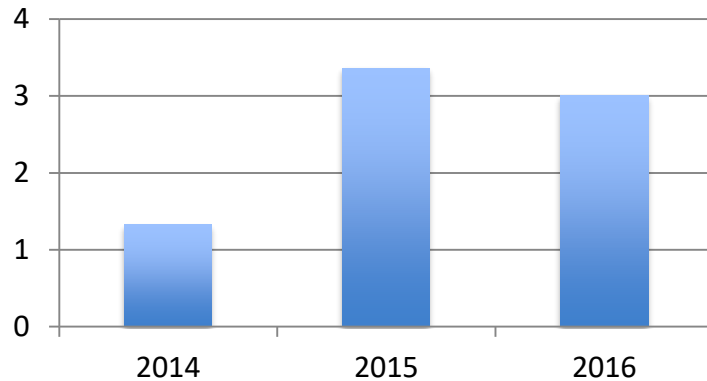
# EMPIAR Raw image data archive for EM

- Started in 2014 – strong community support
- Control growth by requiring deposition of 3D to EMDB
- Usage: validation, development, testing, teaching and...
  - Safe storage of your data!
  - Was source for data in EMDatabank Map Validation Challenge
- Multi-frame micrographs, averaged micrographs, particle-stacks, tilt series
- Uses Aspera, Globus, ftp, http for data transfers

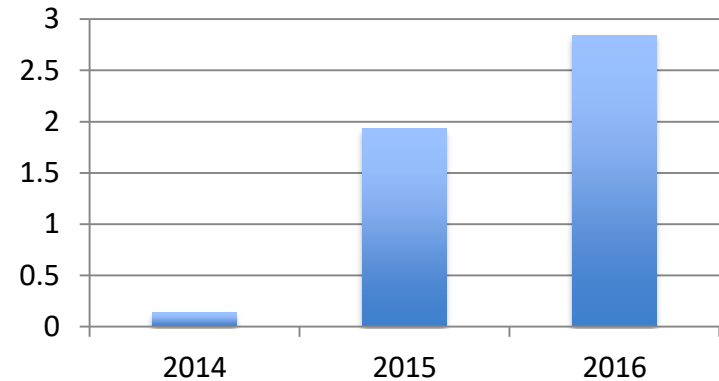
# EMPIAR metrics

- Number of entries: 84 (~50TB; average size ~ 600GB)
- 12 datasets greater than 1 TB; one 10TB+ dataset
- Transfer speed: uploads 1-2 TB/24h (Europe, US, Australia)
- “empiar” cited 50+ times in full-text open-access papers
- Nature Methods publication (Iudin et al., 2016)

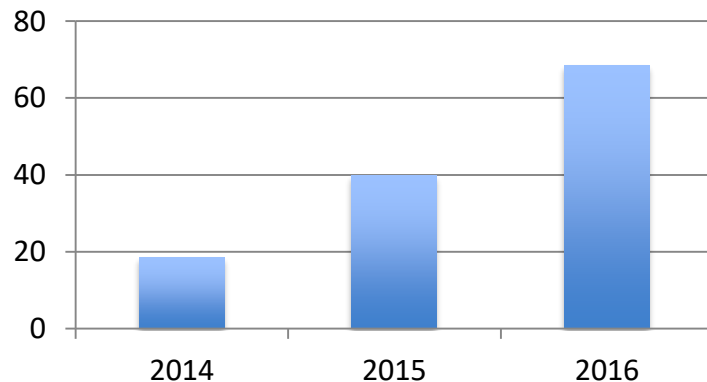
Aspera uploads/month (users)



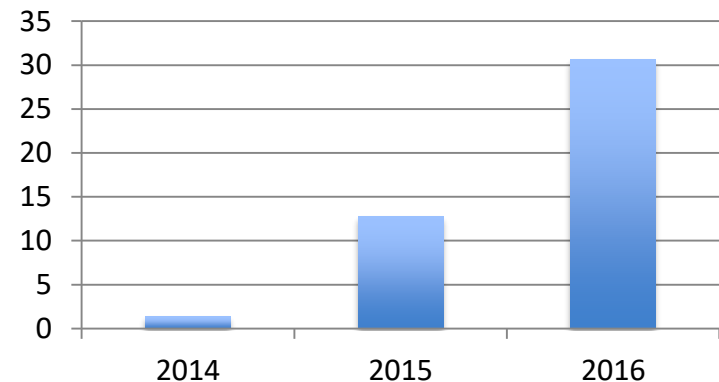
Aspera uploads/month (TB)



Total downloads (users)



Total downloads (data)



# Searching EMDB

Latest entries

Quick access

**EM Resources**

- Home
- Statistics
- Validation
- EMDataBank
- EMPIAR
- Test data

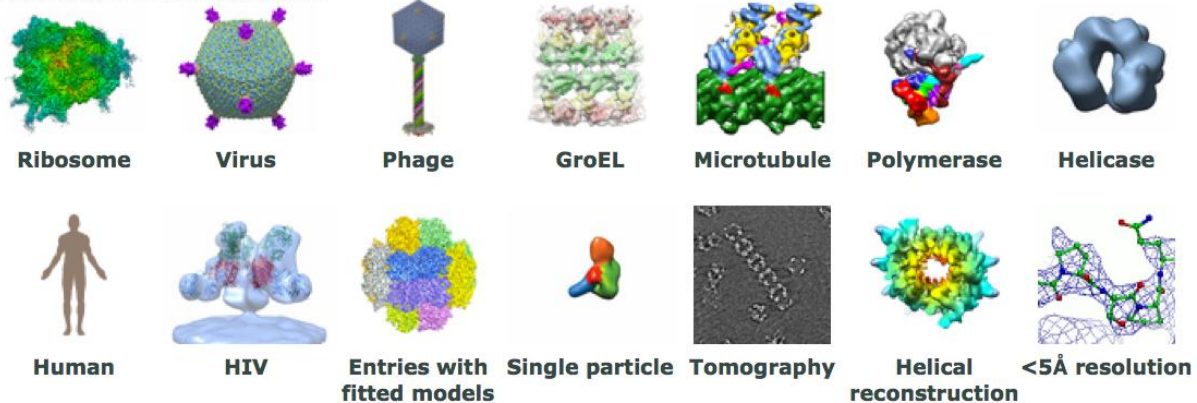
**EMDB**

- Latest maps
- Latest headers
- Latest updates
- Search
- Browse
- FTP archive
- Deposit EM map/model
- EMDB data model

## The Electron Microscopy Data Bank (EMDB) at PDBe

### Quick access

Click on one of these categories:



or enter 4-digit EMDB entry number:

[Entry summary](#)

[Visual analysis of map](#)

[Volume viewer](#)

Form search/browse

### Introduction

The Electron Microscopy Data Bank (EMDB) is a public repository for electron microscopy density maps of macromolecular complexes, including single-particle analysis, electron tomography, and electron (2D) crystallography.

The EMDB was founded at EBI in 2002, under the leadership of Kim Henrick. Since 2007 it has been operated jointly by the PDBe Bioinformatics (RCSB PDB) as a part of EMDataBank which is funded by a joint NIH grant to PDBe, the RCSB and the National Center

# EMStats – EMDB statistics

- Dynamically generated charts based on the current state of the archive

## Charts

---

### General

[Map releases](#)

[Map size statistics for released maps](#)

[Distribution of maps released based on EM technique used](#)

[Trends and distribution of microscope usage for released maps](#)

[Trends and distribution of software package usage for released maps](#)

[Molecular weight statistics of single-particle released maps](#)

[Sample taxonomy statistics for released maps](#)

### Resolution

[Trend of highest resolutions achieved annually for released maps](#)

[Number of released maps achieving given resolution levels](#)

[Single-particle released maps - resolution trends](#)

[Single-particle released maps - resolution versus acceleration voltage and source type](#)

[Single-particle released maps - resolution versus microscope type and software package used](#)

[Single-particle released maps - resolution versus number of projections](#)

[Tomography - resolution trends for released maps](#)

### Publications

[Trend for publications associated with released maps](#)

[Journal distribution of articles associated with released maps](#)

[Publication trends and distribution for different microscope types](#)

[Publication trends and distribution for different software packages](#)

### FTP downloads

[Monthly FTP downloads](#)

[Top 10 FTP downloads](#)

### EMPIAR

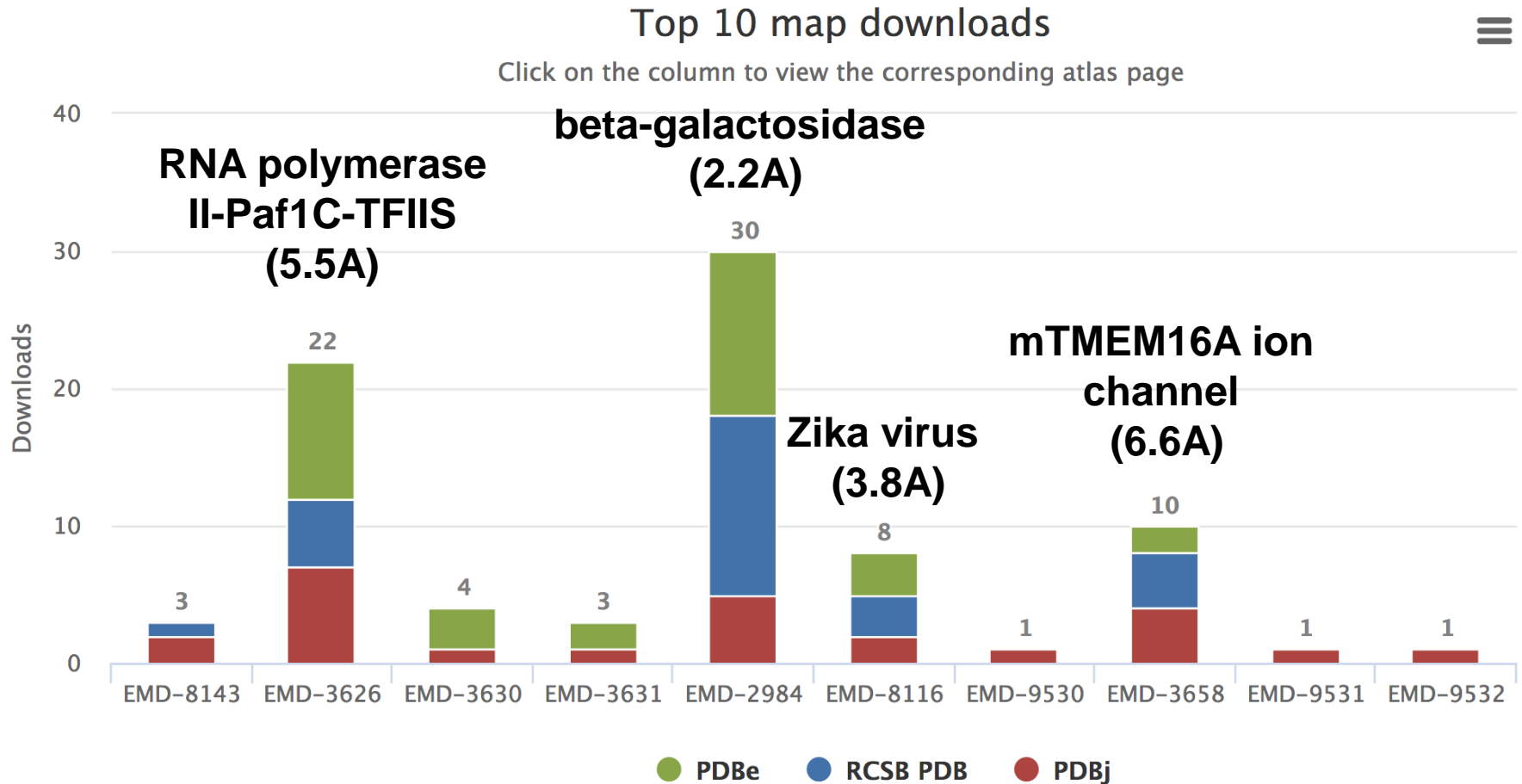
[Entry releases](#)

[Entry size statistics for released entries](#)

[EMPIAR transfer statistics](#)

# EMStats – map downloads

- Downloads stats for the past two years





# EMDB entry pages

- Displays summary info about entry
- Download header file (extensive meta-data), map, FSC etc
- Visual analysis pages and visualisation options

## EMDB › EMD-2852

Electron cryo-microscopy of mitochondrial ATP synthase dimers

**Source organism:** [Polytomella](#) [3049]

**3Dbionotes:** [available for this entry](#)

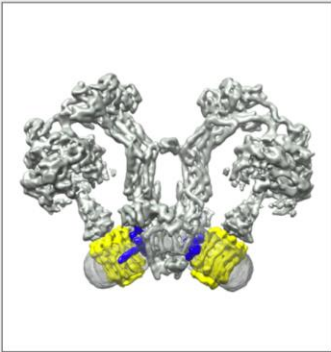
**Related EMPIAR entry:** [EMPIAR-10023](#)

**Primary publication:**  
Horizontal membrane-intrinsic alpha-helices in the stator a-subunit of an F-type ATP synthase  
Allegretti M, Klusch N, Mills DJ, Vonck J, Kuehlbrandt W, Davies KM  
*NATURE* **521** 237-240 (2015)  
PMID: [25707805](#)

**Single particle reconstruction**  
**7.0Å resolution**

**Map released:**  
2015-03-04

**Last modified:**  
2015-05-13



### Quick links

- [EMD-2852 overview](#)
- [Function and Biology](#)
- [Experiments and Validation](#)
- [View](#)
- [Downloads](#)
- [Volume viewer](#)
- [Volume slicer](#)
- [Visual analysis](#)

### Related entries

- [By authors](#)
- [By sample](#)
- [By organism](#)

### Function and Biology

**Sample name:** Polytomella ATP-synthase

**Protein:** Mitochondrial F-type ATP-synthase

### Experimental Information

**Resolution:** 7.0Å

**Resolution method:** FSC 0.143, gold-standard

**Applied symmetry:** C2

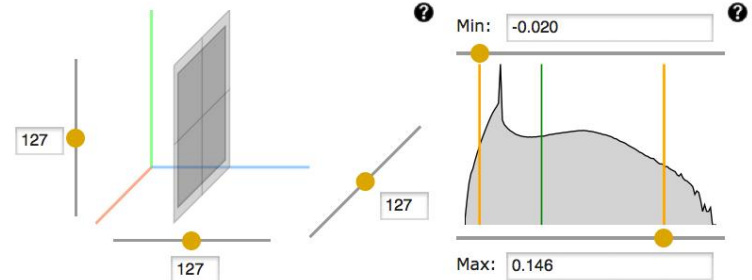
# Volume slicer

- Orthogonal slices in three directions
- Interactive 3D navigation

## EMD-2852 > Volume Slicer

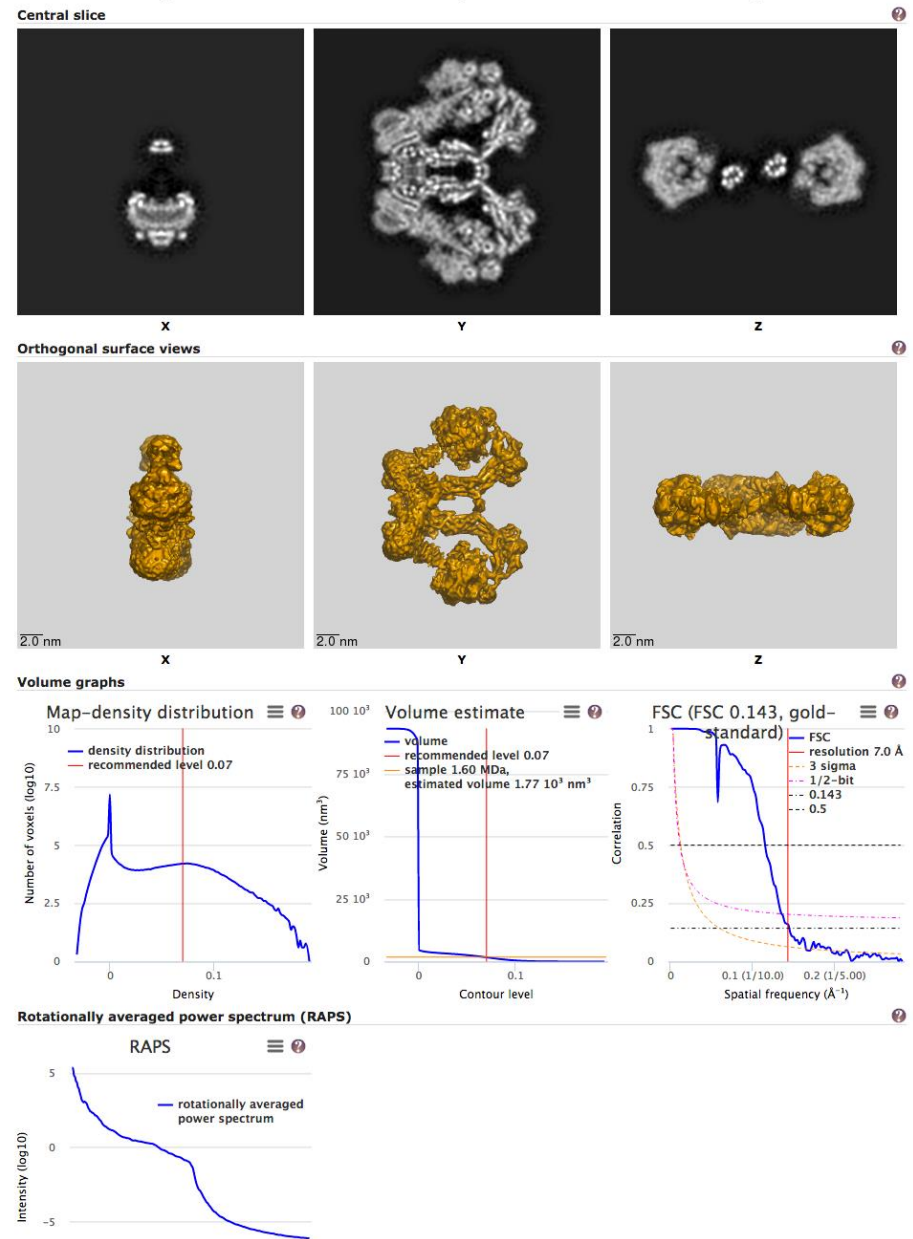
Electron cryo-microscopy of mitochondrial ATP synthase dimers

**Sample name:** Polytomella ATP-synthase  
**Method:** Single-particle  
**Resolution:** 7.0Å (FSC 0.143, gold-standard)



# Visual analysis

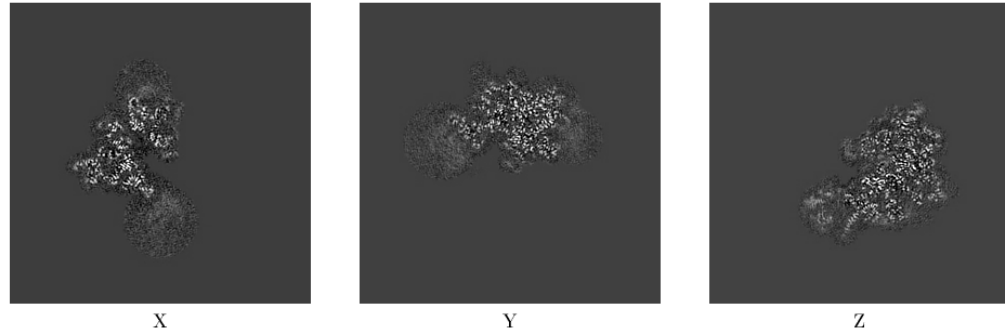
- Basic sanity checking info
- FSC curves shown if available



# Visual analysis: images

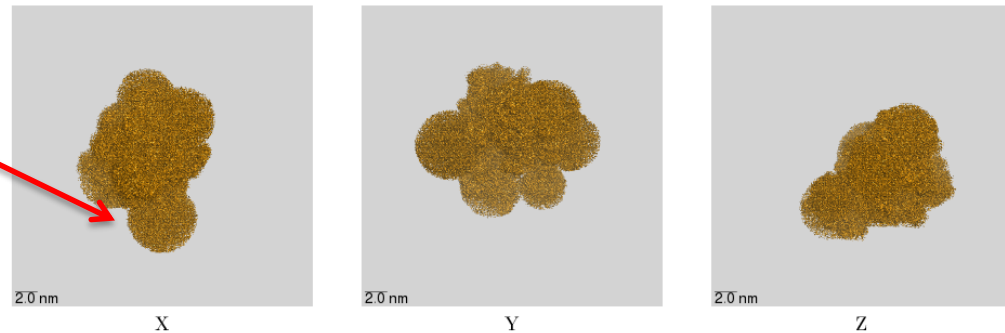
- Surface rendering shows that contour level is too low

## 5.3 Central slices [i](#)



Contour level defines  
the mask!!

## 5.4 Orthogonal surface views [i](#)

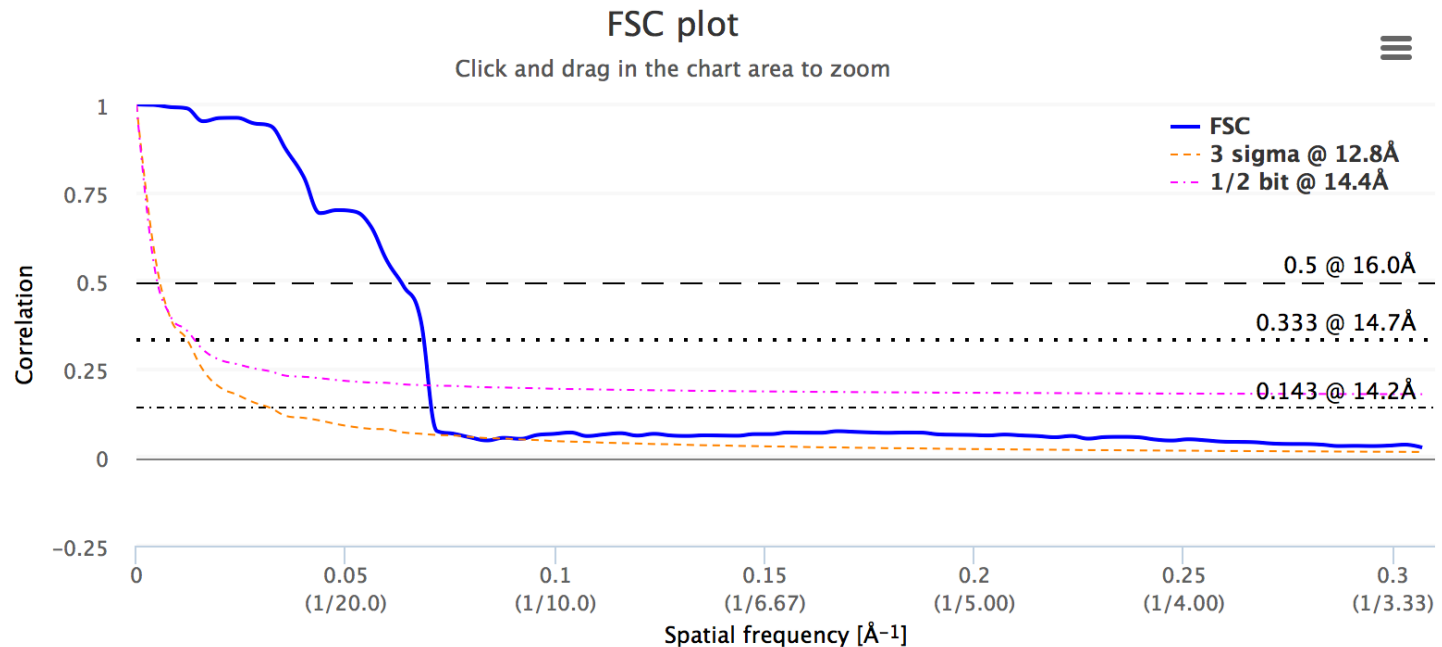


# Stand-alone validation servers

- Convenience
- Promote use and reporting
- Work with software developers to develop standards for capturing validation data

# Fourier shell correlation (FSC) server

- User uploads two maps -> server calculates FSC curve
- FSC curve can be deposited to EMDB
- Automated calculation of thresholds
- Bsoft, Relion and EMAN2 generate FSC curves that can be deposited






# EMDB API

- Programmatically access EMDB meta-data
- e.g., [ebi.ac.uk/pdbe/api/emdb/entry/all/EMD-6007](http://ebi.ac.uk/pdbe/api/emdb/entry/all/EMD-6007)

```
    }  
  ],  
  "imaging": [  
    {  
      "electronSource": "FIELD EMISSION GUN",  
      "imagingMode": "BRIGHT FIELD",  
      "illuminationMode": "SPOT SCAN",  
      "specimenHolder": "Eucentric",  
      "microscope": "FEI/PHILIPS CM200FEG",  
      "specimenHolderModel": "GATAN LIQUID NITROGEN",  
      "acceleratingVoltage": {  
        "value": 160.0,  
        "units": "kV"  
      }  
    }  
  ],  
  "imageAcquisition": [  
    {
```

# EMPIAR website - [empiar.org](http://empiar.org)

- Search, browse EMPIAR entries and download and deposit data

 **EMPIAR** Electron Microscopy Public Image Archive

EMPIAR home | Deposition | REST API | FAQ | About EMPIAR

Share | Feedback


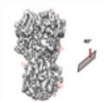

EMPIAR, the Electron Microscopy Public Image Archive, is a public resource for raw, 2D electron microscopy images. Here, you can browse, upload, and download and reprocess the thousands of raw, 2D images used to build a 3D structure. [More ...](#)

[Deposit your data](#) in EMPIAR to share it with the structural biology community.

Browse and [download](#) EMPIAR datasets using the table below.

Show  entries

Search:

Dataset	Title	Authors	Related EMDDB/PDB entries	Size
<a href="#">EMPIAR-10107</a> 	The Structure of the Yeast Mitochondrial Ribosome [stack of 2524 particles in MRCS format]	Desai N, Brown A, Amunts A, Ramakrishnan V [Pubmed: <a href="#">28154081</a> ] [DOI: <a href="#">10.1126/science.aal2415</a> ]	<a href="#">EMD-3551</a> , <a href="#">EMD-3552</a> , <a href="#">EMD-3553</a> , <a href="#">EMD-3554</a> , <a href="#">EMD-3555</a> , <a href="#">EMD-3556</a> , <a href="#">5mrc</a> , <a href="#">5mre</a> , <a href="#">5mrf</a>	138.6 GB
<a href="#">EMPIAR-10097</a> 	40 Degree Tilted Single-Particle CryoEM of Highly Preferred Orientated Influenza Hemagglutinin Trimer [multiple data sets in MRC and ASSORTED formats]	Tan YZ, Lyumkis D		1.8 TB
<a href="#">EMPIAR-10096</a> 	Untilted Single-Particle CryoEM of Highly Preferred Orientated Influenza Hemagglutinin Trimer [multiple data sets in MRC and ASSORTED formats]	Tan YZ, Lyumkis D		1.2 TB

### Quick links

- [EMDB](#)
- [PDBe](#)
- [EMDataBank](#)
- [EMPIAR: Quick tour](#)

### EMPIAR citations

[Parasitophorous vacuole poration precedes its rupture and rapid host erythrocyte cytoskeleton collapse in Plasmodium falciparum egress.](#)  
Hale VL et al. (2017)

[Accurate model annotation of a near-atomic resolution cryo-EM map.](#)  
Hryc CF et al. (2017)

[Using the Volta phase plate with defocus for cryo-EM single particle analysis.](#)  
Danev R et al. (2017)

[Accelerated cryo-EM structure determination with parallelisation using GPUs in RELION-2.](#)  
Kimanus D et al. (2016)

[Structural basis for dynamic regulation of the human 26S proteasome.](#)  
Chen S et al. (2016)


[See all citations](#)

# EMPIAR entry pages

- Browse more info on entry
- View thumbnail images before downloading
- Select images to download


**EMPIAR-10030**

Cryo-EM micrographs of microtubules in GDP-state obtained by copolymerization with EB3

**Publication:** Mechanistic Origin of Microtubule Dynamic Instability and Its Modulation by EB Proteins  
Zhang R, Alushin GM, Brown A , Nogales E  
*Cell(Cambridge,Mass.)* **162** 849-859 (2015)  
PMID: [26234155](#)  
DOI: [10.1016/J.CELL.2015.07.012](#)

**Related PDB entry:** [3jar](#)  
**Related EMDB entry:** [6351](#)


**Deposited:** 8 Jul 2015  
**Released:** 12 Aug 2015  
**Last modified:** 12 Aug 2015  
**Dataset size:** 426.0 GB  
**Dataset DOI:** [10.6019/EMPIAR-10030](#)





**Contains:**  
 micrographs

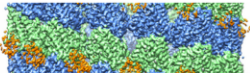
**Image sets**

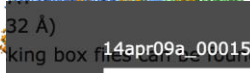
Unaligned multi-frame micrographs of microtubules in GDP-state

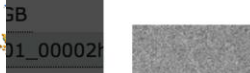
**Category:** micrographs - multiframe  
**Image format:** MRC  
**No. of images or tilt series:** 383  
**Frames per image:** 20  
**Image size:** (3710, 3710)  
**Pixel type:** 32 BIT FLOAT  
**Pixel spacing:** (1.32 Å, 1.32 Å)  
**Details:** Particle-picking box files can be found under /data/boxfiles

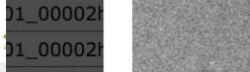
☒  unaligned\_movies 406.3 GB [Download](#)


☒  14apr09a\_00015sq\_v01\_00002hl\_00003en\_st.mrc 1.1 GB  
☒  14apr09a\_00018sq\_v01\_00002hl\_00002en\_st.mrc 1.1 GB  
☒  14apr09a\_00018sq\_v01\_00002hl\_00003en\_st.mrc 1.1 GB  
☒  14apr09a\_00018sq\_v01\_00002hl\_00004en\_st.mrc 1.1 GB




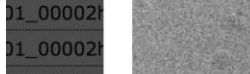


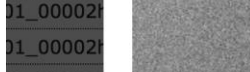


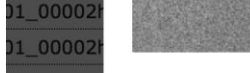


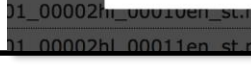






















































































































































































































































































































































































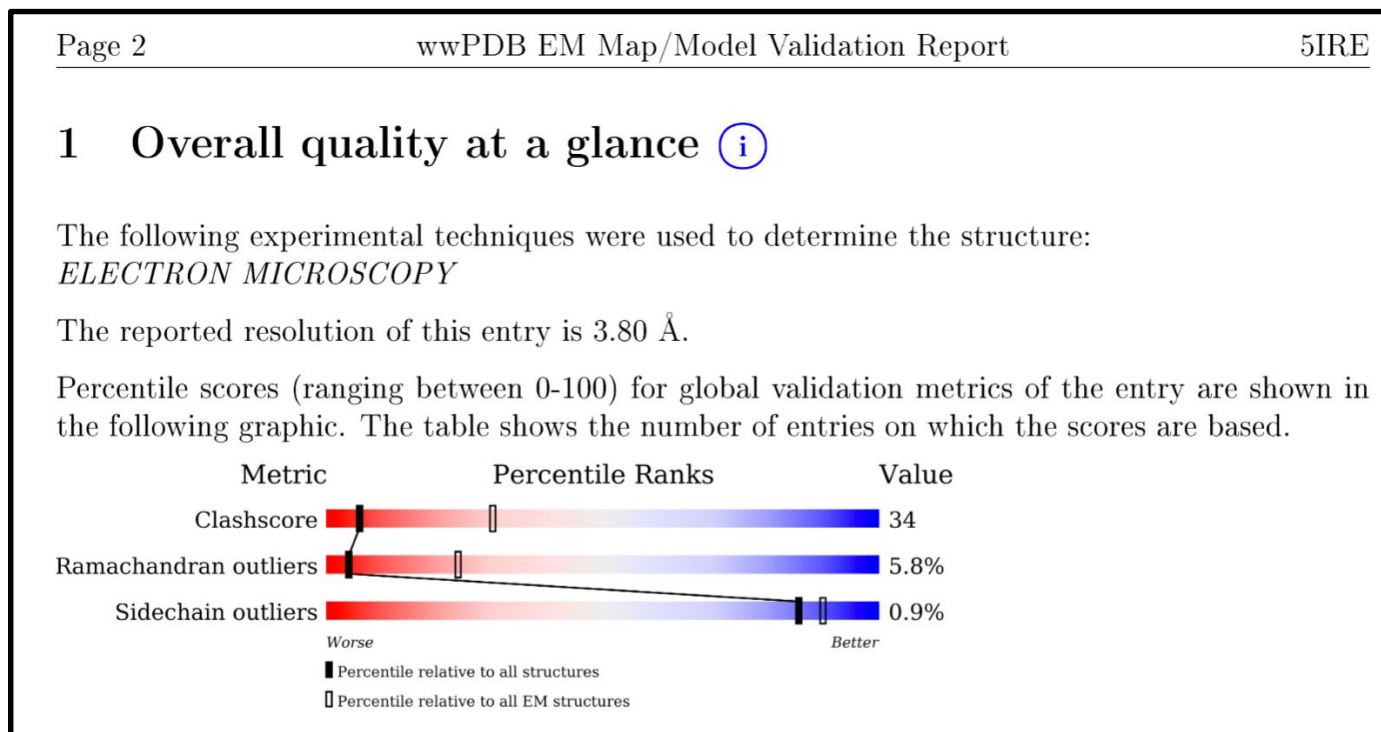




# Planned developments

# EM validation reports

- In production: mainly info relating to EM models
- Validation report for PDB EM models calculated and available from ftp sites





# Expert workshop on “Data-Management Challenges in 3D Electron Microscopy”



- Recommendations:

- Work with tomography community to encourage deposition
  - **Set up an archive for raw image data**
  - Develop and promote standardisation of file formats to capture richer content
  - Promote and encourage good practices w.r.t validation by providing web-based validation services
- Patwardhan, A. *et al.* *Nat Struct Mol Biol* **19**, 1203-1207 (2012).



# Expert workshop on “A 3D Cellular Context for the Macromolecular World”



- Meeting report: Patwardhan, A. *et al. Nat Struct Mol Biol* **21**, 841-845 (2014).
- Recommendations:
  - **Set up archiving for 3DSEM and SXT**
  - **Capture correlative LM in public archive(s)**
  - **Biologically-annotated segmentations are essential for integrating cellular imaging data with other biological (structure) resources**
  - **Integrated multi-scale viewers will be important for making molecular and cellular data accessible to a wider audience**
  - **Set up archiving facility for movies**



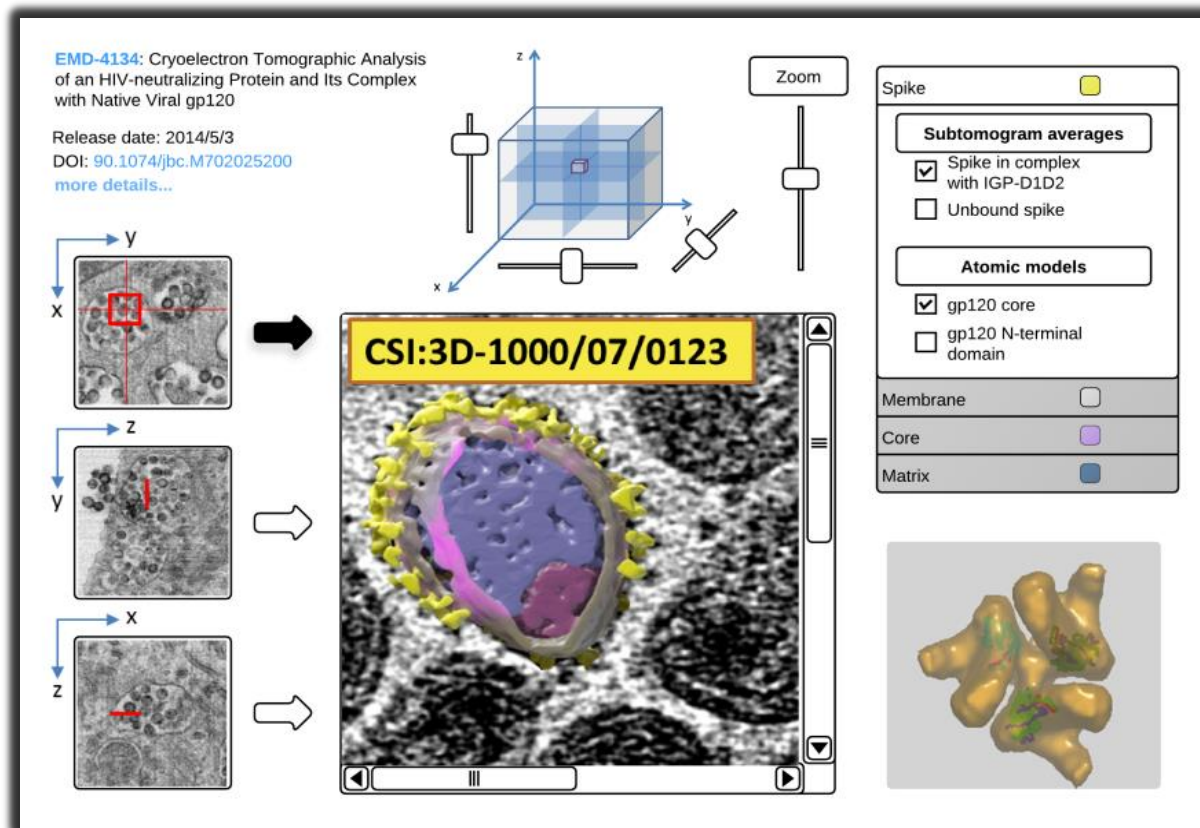


# Project: Integrating 3D biological data on scales from molecules to cells

- MRC/BBSRC funded for 36 months from October 2014 for 2 FTE
- Aims
  - Build pilot image archive for image data related to EMDB structures (EMPIAR)
  - Build a web-based volume browser for integrated web-based visualisation of cellular and molecular data
  - Build a segmentation annotation tool – tool to facilitate the addition of biological annotations to segmentations

# Volume browser – the idea

- Integrated visualisation of structural data
- Spanning scales from cells to molecules

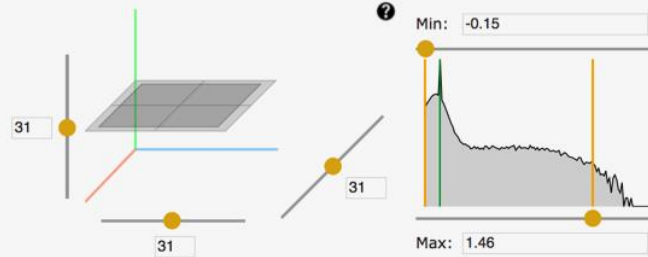


# Volume browser – the reality (almost there!)

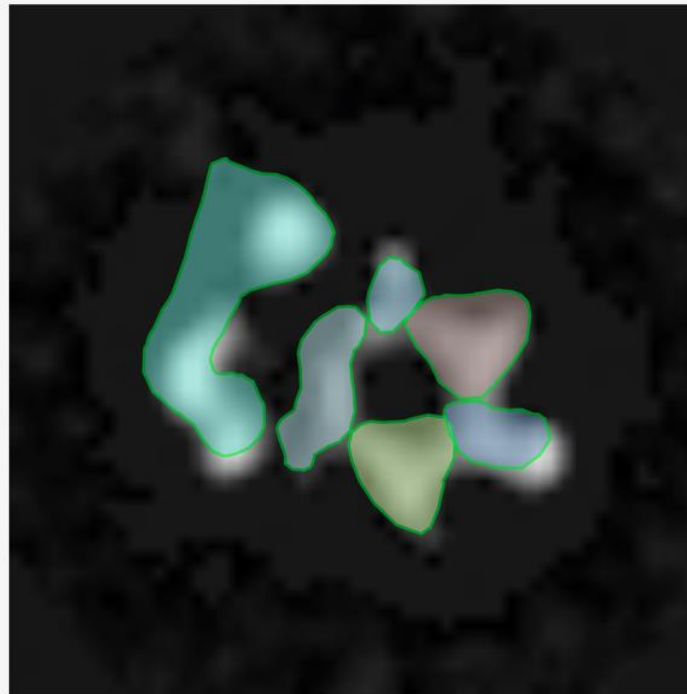
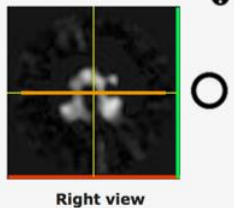
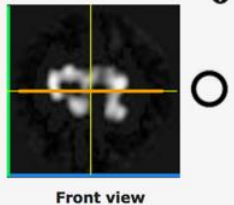
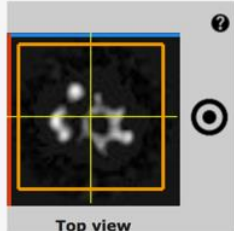
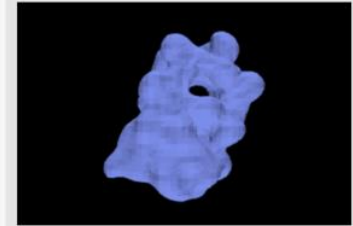
## EMD-1832 > Volume slicer

**Drosophila melanogaster CMG complex bound to ADP.BeF3**

**Sample name:** Drosophila melanogaster CMG complex bound to ADP.BeF3  
**Method:** Single-particle  
**Resolution:** 28Å (FSC 0.5)



3D Viewer [↗](#)



Annotated Segments [👁](#) [↓](#)

- ▼ DNA replication licensing factor MCM3... [👁](#) (1)
- ▼ DNA replication licensing factor MCM6 [👁](#) (1)
- ▼ DNA replication licensing factor MCM7 [👁](#) (1)
- ▼ DNA replication licensing factor MCM2 [👁](#) (1)
- ▼ DNA replication licensing factor MCM4 [👁](#) (1)
- ▼ GINS + Cdc45 [👁](#) (1)

[i](#) Details

[i](#) Related Entries

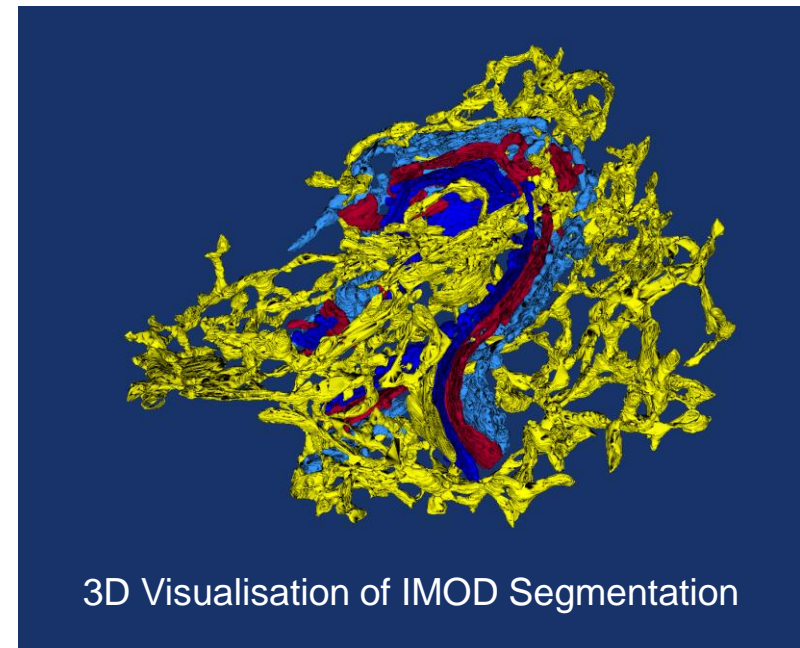
# EMDB-SFF (Segmentation File Format)

- Expert workshop on “3D segmentations and transformations - building bridges between cellular and molecular structural biology”, Dec 2015
  - Patwardhan et al., ***Cutting Edge: Building bridges between cellular and molecular structural biology***, eLife 2017;6:e25835 doi: [10.7554/eLife.25835](https://doi.org/10.7554/eLife.25835)
- Working group to advise on development
- EMD-SFF supports structured biological annotation linking segments to ontologies and other bioinformatics resources
- Implementations in XML, HDF5 and JSON
- Also capable of supporting transforms between subtomogram averages and tomograms



# EMDB-SFFTK (toolkit)

- Available from CCP-EM SVN: <http://bit.ly/2oQnvxd>
- Contains code for manipulating EMD-SFF
  - Translators support external formats
    - IMOD
    - Segger
    - Amira (AmiraMesh and Amira HxSurface)
    - STL
    - EMD MAP masks
  - Annotation utilities
    - Search ontologies (OLS hosted at EBI)
    - View, add, edit, delete annotations
- Output formats: XML, HDF5, JSON
- Create and load ROIs into OMERO



# SAT – Segmentation Annotation Tool


localhost:8000/sat/paul/annotate/9/

Annotate Segmentation: Map Mask

[Login](#) | [Logout](#)

Segmentation metadata

Schema version: 0.6.0a3



Segments 5

Annotations 2

Find terms

Reset

Done

Save

© 2017 EMBL-EBI. All rights reserved.

# EMBL-EBI Expert Workshop on Bioimaging, January 2017

- Molecular, cellular and organism level imaging represented
- EMBL-EBI to consider setting up a general biological imaging archive
  - potential home for LM data from correlative experiments
- Different fields will need to consider what is reference data and what needs to be archives
- Useful conceptually to distinguish between archive and added value resources

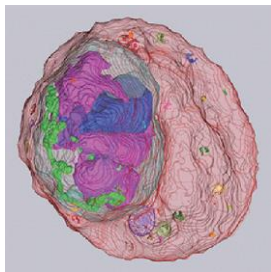


# Project: Public archiving and data integration in the era of multi modal imaging

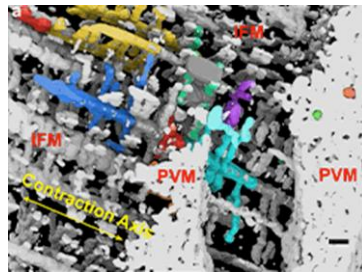
- MRC/BBSRC funded for 36 months from October 2017 for 3 FTE
- Project aims:
  - Archiving for related imaging modalities including – 3DSEM, SXT and CLEM
  - **Data-harvesting and submission pipelines to EMDB and EMPIAR**
  - **Visualisation of and standards for correlative imaging and for relating sub-tomogram averages to tomograms**

# Beyond molecular cryo-EM

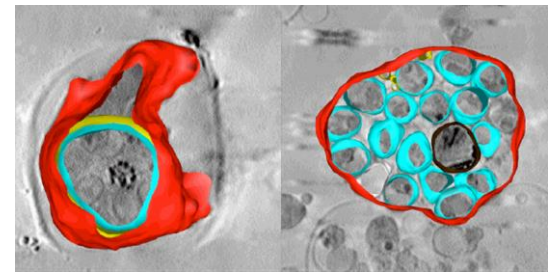
- We have already expanded EMPIAR beyond molecular cryo-EM, e.g.,
  - EMPIAR-10052/3/4/5: SBF-SEM
  - EMPIAR-10070: FIB-SEM
  - EMPIAR-10087: soft X-ray tomography
  - Discussion with integrative hybrid modelling community on deposition of related EM data
- Expand data models – workshop December 2017
- Work with communities on data deposition



EMPIAR-10054



EMPIAR-10070



EMPIAR-10087

# Future outlook

- Archiving for related imaging modalities including – 3DSEM, SXT and CLEM
- Data-harvesting and submission pipelines to EMDB and EMPIAR
- Visualisation of and standards for correlative imaging and for relating sub-tomogram averages to tomograms
- Validation
- Crowd sourced annotation of segmentation
- Automated segmentation – deep learning
- Fast archive-wide sub-structure volumetric (or shape-based) searches

# Cellular Structure and 3D Bioimaging Team



**Sanja Abbott**



**Andrii Iudin**



**Paul Korir**



**Sriram Somasundharam**

- PDB/EMDB annotation staff
- Former members: E Sanz Garcia, C Lugo, J Salavert Torres (UPV), I Lagerstedt (Lilly)
- Former students: M Holmdahl, V Lysenkov, I Solanes Valero
- Several positions available...

# Collaborations & acknowledgements

- Birkbeck College (Elena Orlova, Maya Topf, Helen Saibil)
- Baylor (Wah Chiu)
- Chinese Academy of Sciences (Fei Sun)
- CNB Madrid (Jose Maria Carazo)
- Dundee (Jason Swedlow)
- EMBL-EBI (Helen Parkinson, Alvis Brazma, Ugis Sarkans)
- Francis Crick (Lucy Collinson, Raffa Carzaniga, Peter Rosenthal)
- Osaka University (Genji Kurisu)
- MRC-LMB (John Briggs, Paula da Fonseca, Wanda Kukulski, Garib Murshudov)
- RCSB (Cathy Lawson)
- STFC (Martyn Winn)
- University of Manchester (Alan Roseman)
- And many more...!

# Websites

- [emdb-empiar.org](http://emdb-empiar.org)
- [empiar.org](http://empiar.org)
- [pdbe.org](http://pdbe.org)
- [emdatatabank.org](http://emdatatabank.org)

# References

1. Patwardhan A., *et al.* "Data management challenges in three-dimensional EM". *Nat Struct Mol Biol*, **19**, 1203-1207 (2012).
2. Gutmanas A., Oldfield T., Patwardhan A., Sen S., Velankar S. and Kleywegt G. "The role of structural bioinformatics resources in the era of integrative structural biology". *Acta Cryst*, **D69**, 710-721 (2013).
3. Lagerstedt I., Moore W.J., Patwardhan A., Sanz-Garcia E., Best C., Swedlow J.R. and Kleywegt G.J. "Web-based visualisation and analysis of 3D electron-microscopy data from EMDB and PDB". *J Struct Biol*, **184**, 173-181 (2013).
4. Patwardhan A., *et al.* "A 3D cellular context for the macromolecular world". *Nat Struct Mol Biol*, **21**, 841-845 (2014).
5. Wood C., Burnley T., Patwardhan A., Scheres S., Topf M., Roseman A. and Winn M. "Collaborative computational project for electron cryo-microscopy". *Acta Crystallogr D Biol Crystallogr*, **71**, 123-126 (2015).
6. Iudin A., Korir P.K., Salavert-Torres J., Kleywegt G.J. and Patwardhan A. "EMPIAR: A public archive for raw electron microscopy image data". *Nature Methods*, **13**, 387-388 (2016).
7. Patwardhan A. and Lawson C.L. "Databases and Archiving for CryoEM". *Methods Enzymol*, **579**, 393-412 (2016).
8. Salavert-Torres J., Iudin A., Lagerstedt I., Sanz-Garcia E., Kleywegt G.J. and Patwardhan A. "Web-based volume slicer for 3D electron-microscopy data from EMDB". *J Struct Biol*, **194**, 164-170 (2016).
9. Patwardhan A. "Trends in the Electron Microscopy Data Bank (EMDB)". *Acta Crystallographica Section D*, **73**, (2017).