

Cryo-EM Archives, Challenges and Validation

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2019

Unified Data Resource for 3DEM

Stanford University/SLAC ^{Rutgers University}

European Bioinformatics

Institute

- Established 2007 under NIGMS Support (R01GM079429)

- Develop Data Archives for 3DEM (EMDB + PDB)

- Promote Community Development of Validation and Standards

www.emdataresource.org

<https://www.emdataresource.org>

Project Website

Growth of EM

Structures

Statistics updated every week:

www.emdataresource.org/statistics.html

CryoEM (R)Evolution

Molecular Shapes Traceable Densities

2011 2016

EMDB maps by year and

resolution

www.emdataresource.org/statistics.html

Cryo-EM Structure Deposition

EMDB, PDB

wwPDB OneDep System

- X-ray, NMR, and EM Methods
(since 2016)
- EM Methods: Deposit map to
EMDB with associated model to

PDB

- Validation report produced

File uploads for 3DEM joint map/model submission in OneDep FSC Curve Upload

- Create xml format file using a software package (e.g., Relion, EMAN), or...
- Use PDBe's Server:
PDBe.org/FSC

Current Validation Report for EM Structures

- Resolution value reported by depositor
- Model statistics

Coming soon to EM Validation Reports:

- Orthogonal images of map, map + model
- Atom inclusion at recommended contour level
- Plots: deposited FSC curves, Atom inclusion vs. contour level, rotationally

averaged power spectrum

CryoEM Validation Challenges

**2011, 2012,
2015:** Data
Management
Workshops

2004:

Dictionary
Development
Workshop

2016: Map
Challenge, 2nd
Model

Challenge

EM Standards /

Validation Development

2010: 1st Model Challenge,

Validation Task Force Workshop

2019: 3rd Model Challenge

EM Validation Task Force 2010 Recommendations

- Full FSC curve from independent half-maps
- Model Stereochemistry (same as X-ray / NMR)
- Other Metrics: **More Research Needed**

Henderson *et al.* (2012) *Structure* **20**, 205-214

<http://www.ncbi.nlm.nih.gov/pubmed/22325770>

vtf.emdataresource.org

Challenges Outcomes Published in JSB Special Issue: December 2018

- 18 peer-reviewed articles +editorial summarizing the outcomes of the Oct workshop
- Recommended best practices as well as novel methods for Cryo-EM structure determination and assessment

Apoferritin 3.1 vs 3.5 Å

← Which is which? →

- Different expert practitioners can arrive at different resolution estimates for same level of map detail
- Question: Could the community agree on a standard for resolution estimation?

Frontiers in Cryo-EM Validation Workshop

- January 14-15 at EMBL-EBI in

Hinxton, UK

- Organized by CCP-EM Project
- Key recommendation: EMDB-calculated resolution based on deposited (unmasked, minimally filtered) half-maps

2019 Model Metrics Challenge

- **Goal:** Identify metrics most suitable for evaluating and comparing fit of atomic coordinate

models into cryo-EM maps for specimens in the 1.5-4.0 Å reported overall resolution range.

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[http://challenges.emdataresource.org/?q=model-](http://challenges.emdataresource.org/?q=model-metrics-challenge-2019)

[metrics-challenge-2019](http://challenges.emdataresource.org/?q=model-metrics-challenge-2019)

Model Challenge

Meeting @ Stanford/SLAC June 2019

- External Advisors/Assessors: Peter Rosenthal, Paul Emsley, Jane Richardson, Paul Adams, James Fraser, Frank DiMaio, Pavel Afonine, Tom Terwilliger, Mark Herzik
- Challengers: Soon Wen Hoh, Gunnar Schroeder, Andrea Vaiana, Grzegorz Chojnowski, Daisuke Kihara, Pavel Afonine, Abishek Singharoy, Xiaodi Yu, Ligu Wang, Frank DiMaio, Matt Baker
- EMDataResource: Andriy Kryshchak, Cathy

Lawson, Wah Chiu, Greg Pintilie, Helen Berman

Challenge Process 2019

63* model submissions from 13 challengers

targets assembled Submissions and assessment data released (blinded)

expert

initial Full advisors advertising Recruited

/sign-up

Complete model-compare analysis

*Most models (51) were created using *ab initio* methods

submission workflows Released/unblinded

Development Challenge Assessment Write Up March April May June

September

October

Model Compare Pipeline

- “Laboratory” for evaluating assessments

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<http://model-compare.emdataresource.org>

Andriy Kryshatovych UC Davis

1.8 Å 2.3 Å 3.1 Å

Apoferritin vs EM map: Map-Model FSC

Apoferritin: 1.8 Å

**Model-Only Statistics Summary
Plots**

2.3 Å

3.1 Å

Observations/Highlights

- Target maps at 2-3 Å have excellent information content
- *Ab initio* modeling strategies work amazingly well for these cases
- Some manual/expert intervention still needed to fully optimize

- B-factors for Cryo-EM: meaning is different, needs clarification

EM Structure Validation Servers

Overall Shape & Hand Tilt-Pair
pdbe.org/tiltpair Resolution by FSC FSC pdbe.org/FSC
Local Resolution 3DFSC 3dfsc.salk.edu Local Resolution
Scipion scipion.cnb.csic.es/m/myresmap#

Stereochemistry, compare
with all PDB structures

wwPDB validate.wwpdb.org

Stereochemistry Molprobit molprobit.biochem.duke.edu

Nucleic Acid conformation DNATCO dnatco.org

“backbone
bumpiness” EMRinger emringer.com (@UCSF)

See also: www.emdataresource.org/validation.html

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References

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[10.1016/j.str.2011.12.014](https://doi.org/10.1016/j.str.2011.12.014)

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