Cryo-EM Archives, Challenges and Validation

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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
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

2004: Dictionary Development Workshop

2011, 2012, 2015: Data Management Workshops

2016: Map Challenge, 2nd Model
Challenge

EM Standards / Validation Development

2010: 1\textsuperscript{st} Model Challenge, Validation Task Force Workshop

2019: 3\textsuperscript{rd} 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
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.


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, Liguo Wang, Frank DiMaio, Matt Baker
- EMDataResource: Andriy Kryshtafovych, 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
http://model-compare.emdataresource.org

Andriy Kryshtafovych UC Davis

1.8 Å 2.3 Å 3.1 Å

**Apo ferritin vs EM map:**

**Map-Model FSC**

**Apo ferritin:** 1.8 Å

**Model-Only Statistics Summary Plots**
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 Molprobity molprobity.biochem.duke.edu
Nucleic Acid conformation DNATCO dnatco.org
“backbone
bumpiness” EMRinger emringer.com (@UCSF)
See also: www.emdataresource.org/validation.html

Unified Data Resource for 3DEM
References


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