

# Joint Challenges Workshop Summary

Oct 8, 2017

## Summaries of Action Plan

### 1. Meeting summary manuscript: targeted for submission on Dec 31, 2017

Impact on training students at both undergraduate and graduate levels involved in development of new tools and testing new tools (targets and submitted data to remain available for further/future analyses).

Outcome of meeting could include recommendations for mandatory data items to include in map/model submissions to EMDB/PDB data archives.

#### a. Map Challenges:

- i. Improvements to software packages were made.
- ii. All software packages are at ~same stage, *capable* of producing maps of good/same quality (though not near the “end point”). Biggest variable is the user (knowledge of how to use package is key). Even with a large N of users, software package results were variable (e.g., Relion maps).
- iii. The assessors were able to rank users but not able to rank packages (because of uneven distribution of software package use).
- iv. Masking is still a problem and needs normalization across packages. Filtering too.
- v. Need to learn best practices.
- vi. Work is needed to develop bullet-proof packages that follow best practices.
- vii. Need a way to rank the maps.
- viii. Even with similar FSC's (e.g. proteasome), maps differed (e.g. in side-chain quality). Modelling is one way to evaluate map quality.
- ix. Need useful standard/best practices for sharpening maps.
- x. There were some improvements made in resolution and map quality relative to target reference structures, but at this point the mystery remains for how to produce well behaved homogeneous structures. Seems likely that this involves knowing which particles to select rather than squeezing more resolution out of the map.
- xi. A heterogeneous structure would be a good candidate for the next challenge.
- xii. Need other metrics to evaluate maps as well as FSC. Reslog plots? (would require having readable particle information for each submission -- was not achieved this time around).
  1. **Have assessors work together following workshop to compare results--create overall summary.**

## **b. Model Challenges:**

- i. There are many outstanding modeling (ab initio, fitting, refinement) tools. Some allow you to start with very little prior knowledge and do quite well getting a significant portion of the model correct. Some need more manual work (segmenting etc.) but can get almost all of the model correct. Results are still dependent on map resolution and uncertainty/disorder in the map. Refinement category not designed in optimal way (better to provide a minimal starting point).
  1. Suggest that we present the range of performance for each category (ab initio, fitting, refinement) - rather than how each particular software performed (suggest to label entries as to their category on the website).
  2. Suggest that we show how the challenge spurred development, and where possible, examples of the improvement in performance (TomT: all development spurred by challenge--other examples?).
- ii. There is still a need for the development of new workflows for automatic model generation
  1. This may be quicker if developers have mechanisms to work together (collaborative projects?).
  2. Attention needs to be paid by developers to usability
- iii. Review of the metrics that were used in this challenge by assessors -- which ones were useful?
- iv. New metrics are needed to assess the map and model at the residue level
  1. It is promising that new methods have been developed, e.g. EMRinger, CaBlam and others, to assess models, and models with maps
- v. Future perspectives:
  1. What are the current best practices, and what can be improved?
  2. What are the current limits of performance (e.g. vs. resolution), and what would be the limit of performance with more developments?
  3. Can we reliably assess uncertainty, and if so, can we distinguish between uncertainty and significant differences in conformation?

## **2. Nature Methods or Science Summary Article**

- a. Overview of Map and Model challenges
- b. Outcomes
- c. Future Directions
- d. Recommendations

## **3. Special JSB issue: targeted for submission by 1st of March.**

- a. Summary manuscripts (targeted to *Nature Methods*):
  - i. Challenges Overview
  - ii. Map Challenge
  - iii. Model Challenge
- b. Assessor and Challenger individual manuscripts:

- i. Methods
- ii. Results
- iii. Update since submission

4. **Disseminate our activities**

a. **in upcoming meetings**

- i. NYSBC workshop
- ii. Gordon Research Conference
- iii. Keystone Meeting
- iv. Biophysical Society
- v. ACA/CryoEM SIG

b. **Set of slides that others can use to disseminate.**

5. **Possibility: seek EM targets for CASP (ideally high resolution).**

6. **Next challenges for the next 12 months**

**Organization: Advisory committee; assessors and challengers**

**The challenges are to engage the community willing to participate; students and postdoc involved with incentive; workshops**

- a. ~~Separate~~ vs merged map and model committees
- b. Who are the targeted challengers: software developers; users
- c. Collaborative project approach?
- d. Category for novices? Recruit from cryoEM courses?
- e. Important considerations:
  - 1. What question do we want to answer
  - 2. Availability of “ground truth” (could be one of the submitted models)
  - 3. Minimal requirements/standards for map and coordinate file submissions
  - 4. Have analysis software pipeline “ready to go”
- f. Types of benchmark data
  - 1. Membrane protein
  - 2. Large complex
  - 3. Complex with heterogeneous compositions and conformations
  - 4. Maps with different resolutions: 2-3 Å vs 4-7 Å vs 7-9 Å
  - 5. Specimens of unknown structures for competition
  - 6. Best practices target + target with multiple conformations
  - 7. Best practices target could be re-do of target with most variable results from this challenge (beta-gal?)
  - 8. Small target (e.g. hemoglobin; aldolase)
  - 9. Pre-existing model refinement: more “minimal” starting point

d. 1-2 challenges each time: Turn around time 6 months (3 for map challenge, then 3 for modellers to pick up maps for model challenge)

e. Face to face vs virtual meetings : before or after national meetings (ACA; Biophysical Society)

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\*Suggestions/Comments from GK:

Tom T could run his automated procedure on all maps to construct consistent best-effort automatic models and then assess: what %-age of CA atoms can be built to within 2 Å (half a CA-CA distance)? What %-age of those can be assigned the correct sequence? What %-age of those have well-resolved side chain density?

Attempt to improve angle assignments using preliminary model? (Model bias?)

Ewan Callaway is the Nature journalist who has been covering EM and integrative SB in recent years

Perhaps "hackathons" could be organised virtually with good conferencing software to keep costs down. Alternatively, they could be organised at the regional or national level with a virtual wrap-up workshop?