Topics for June 2019 Model Metrics Challenge Discussions

Statement of Goals

Identify modelling best practices and 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.

Validation metrics

1. Model geometry -- local (e.g. per-residue) and global statistics
   a. Valence geometry (bonds, angles)
   b. Ramachandran
   c. Rotamers
   d. Clashes
   e. C-alpha geometry (e.g., CaBLAM)
   f. Free energy (e.g. DFIRE)
   g. Machine learning (e.g. QMEAN, ProQ3)
2. Overall fit of model into map density
   a. Correlation coefficient
   b. Map-Model FSC
   c. EMringer overall
3. Per [chain/domain/secondary structure/residue/atom] fit of model to density
   a. Q-score
   b. EMringer
4. Comparison to "reference" structure -- local and global measures

For each metric, consider level of appropriateness for:

- automated model building
- manual (visual) model building
- automated model optimization/refinement
- final model evaluation (e.g. primary citation Table 1)
- challenge event
- public structure archive

For metrics involving maps, which map type(s) should/could be used:

- Raw map
- Modified map (e.g., segmented, filtered, masked and/or solvent flattened)
- Map represented as calculated Structure Factors
- Independent half-maps
- Local resolution or variance map
- Composite map

Best Practices for Modelling in the 1.5-4.0 Å resolution range

- B-factors (ADP)
- Occupancy and multiple conformations
- Single model vs. ensemble
- Waters, Ions
- Ligand quality/geometry
- Refining Å/pixel scale

Additional Questions
1. How can you determine whether you have overfit an EM map? (fitted to noise).
2. For the apoferritin map series, how do the maps differ from each other vs. resolution?
3. Could we calibrate/create an equivalence scale for X-ray vs. EM resolution measures? What experimental design could be used to investigate the optimal equivalence scale?

To Keep in Mind
Goodhart's law is an adage named after economist Charles Goodhart, which has been phrased by Marilyn Strathern as "When a measure becomes a target, it ceases to be a good measure." (also known as "teaching to the test).