D3R
Overview of Results

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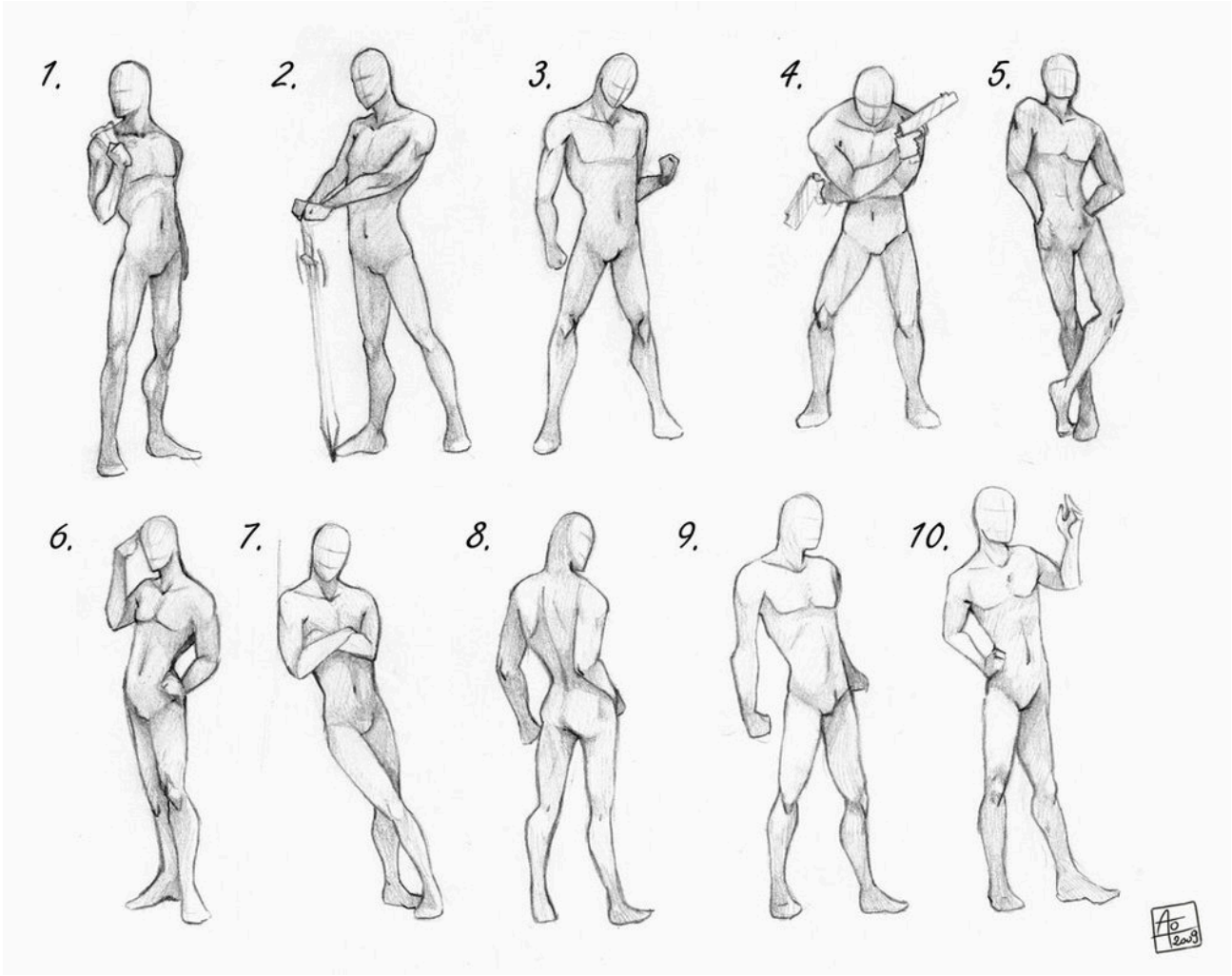
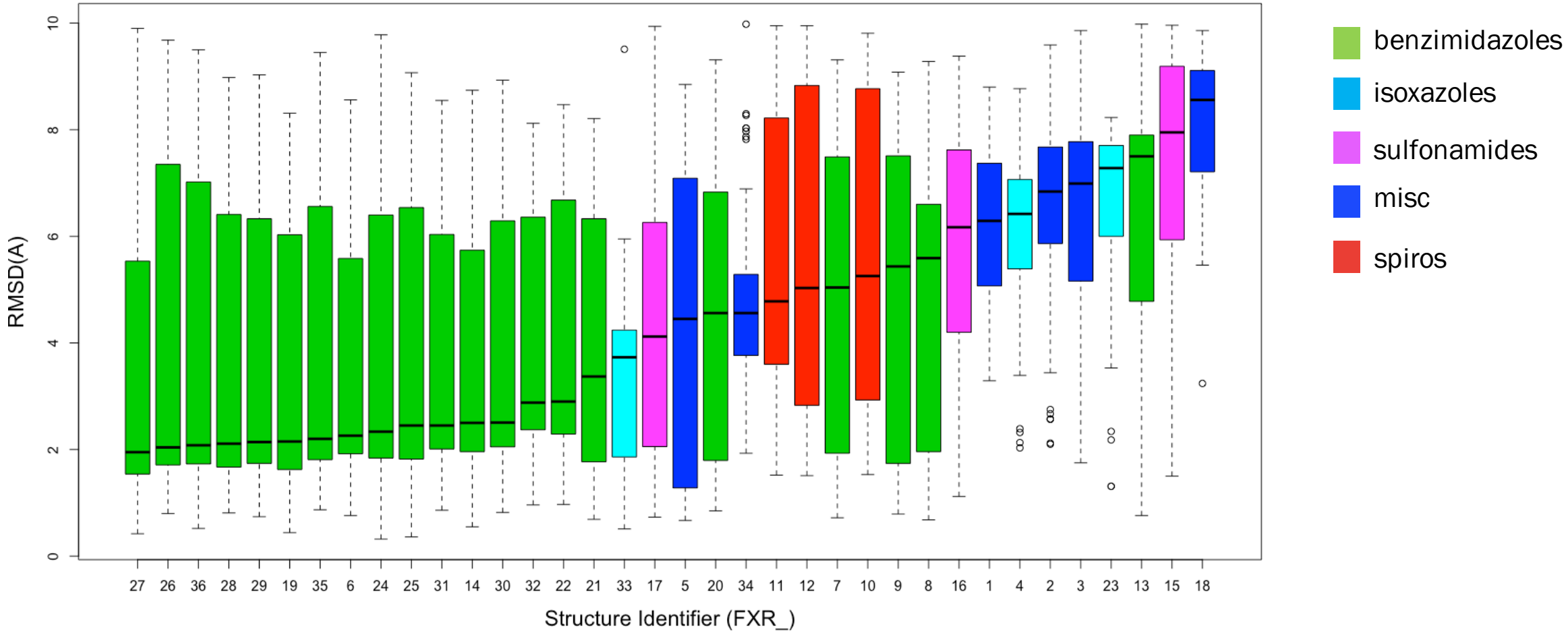
Operational Details

- Submissions independently evaluated by Shuai Liu and Pat Walters
  - *Compared for consistency*
- Docking submissions much easier to process than D3R Grand Challenge 2015
  - *Molfiles were a great improvement over PDB files*
- Still a few issues made RMS comparisons of docking submissions difficult
  - *Bond orders were incorrect or all set to 1 in 31% of submissions*
  - *Worked around this with maximum common substructure or substructure search*
  - *Input molfiles may simplify the situation next time*
- Scoring and free energy results were well formatted

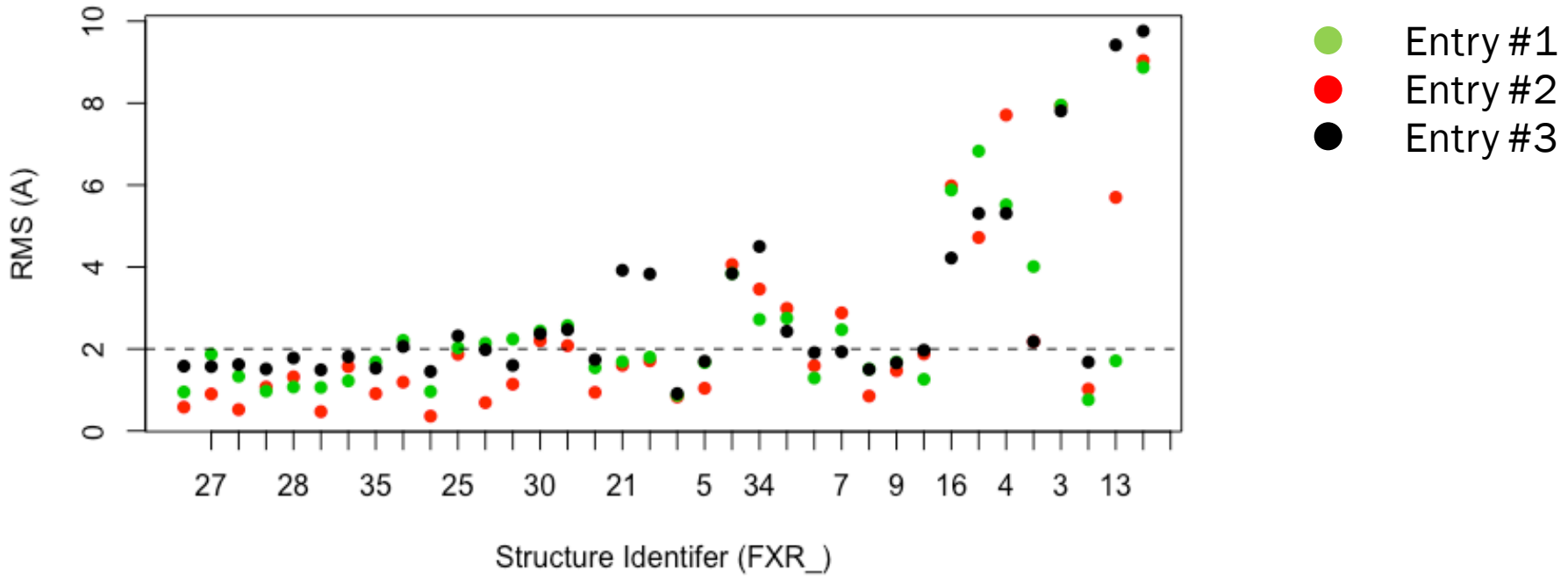
Pose Prediction



Comparing RMS Distributions



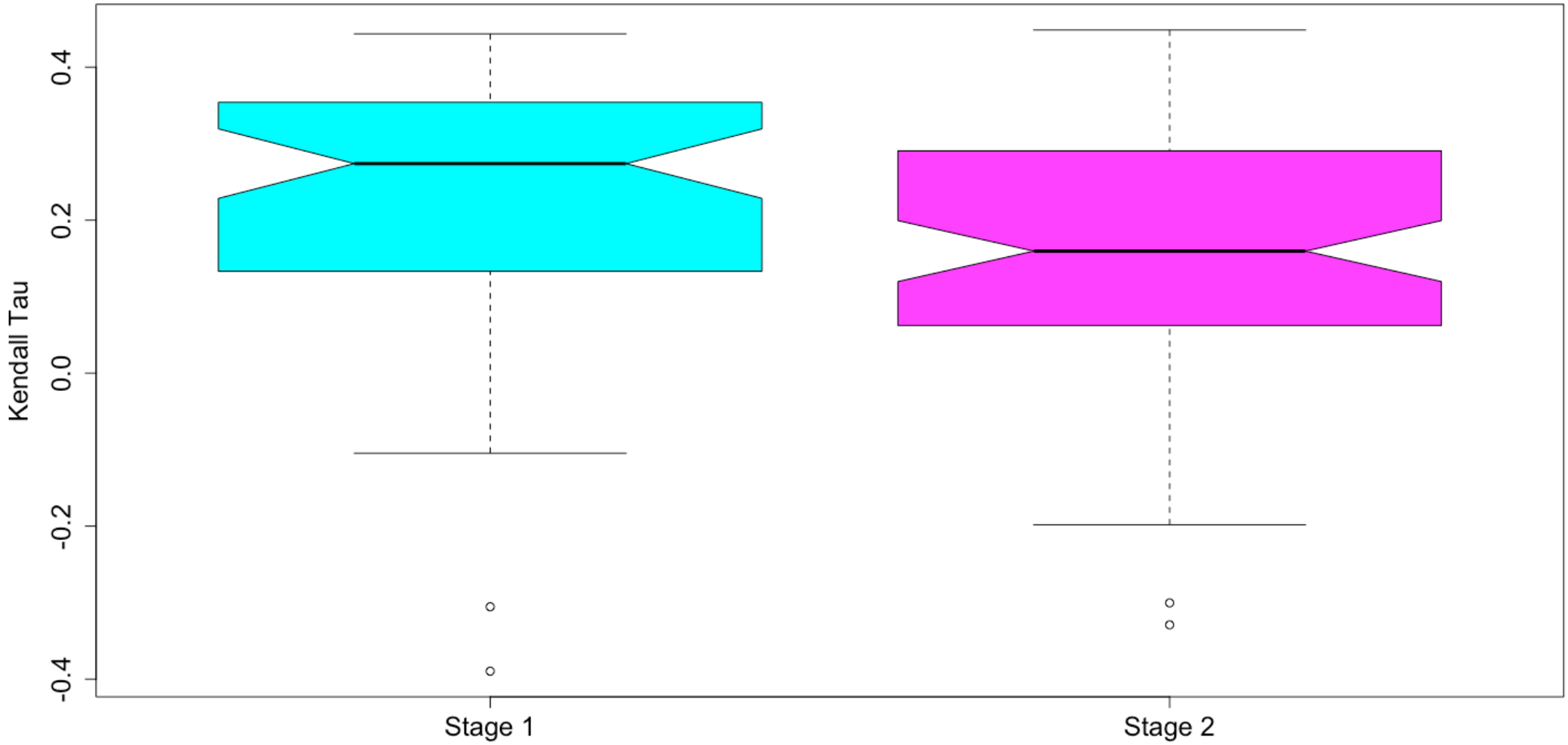
Pose Prediction – State of the Art



- Just showing the 3 top scoring pose prediction methods
  - Many others statistically equivalent
- Different methods used – commercial, academic, MD, visual inspection
- High correlation between correctly and incorrect predicted structures
  - A follow-up discussion would be very informative

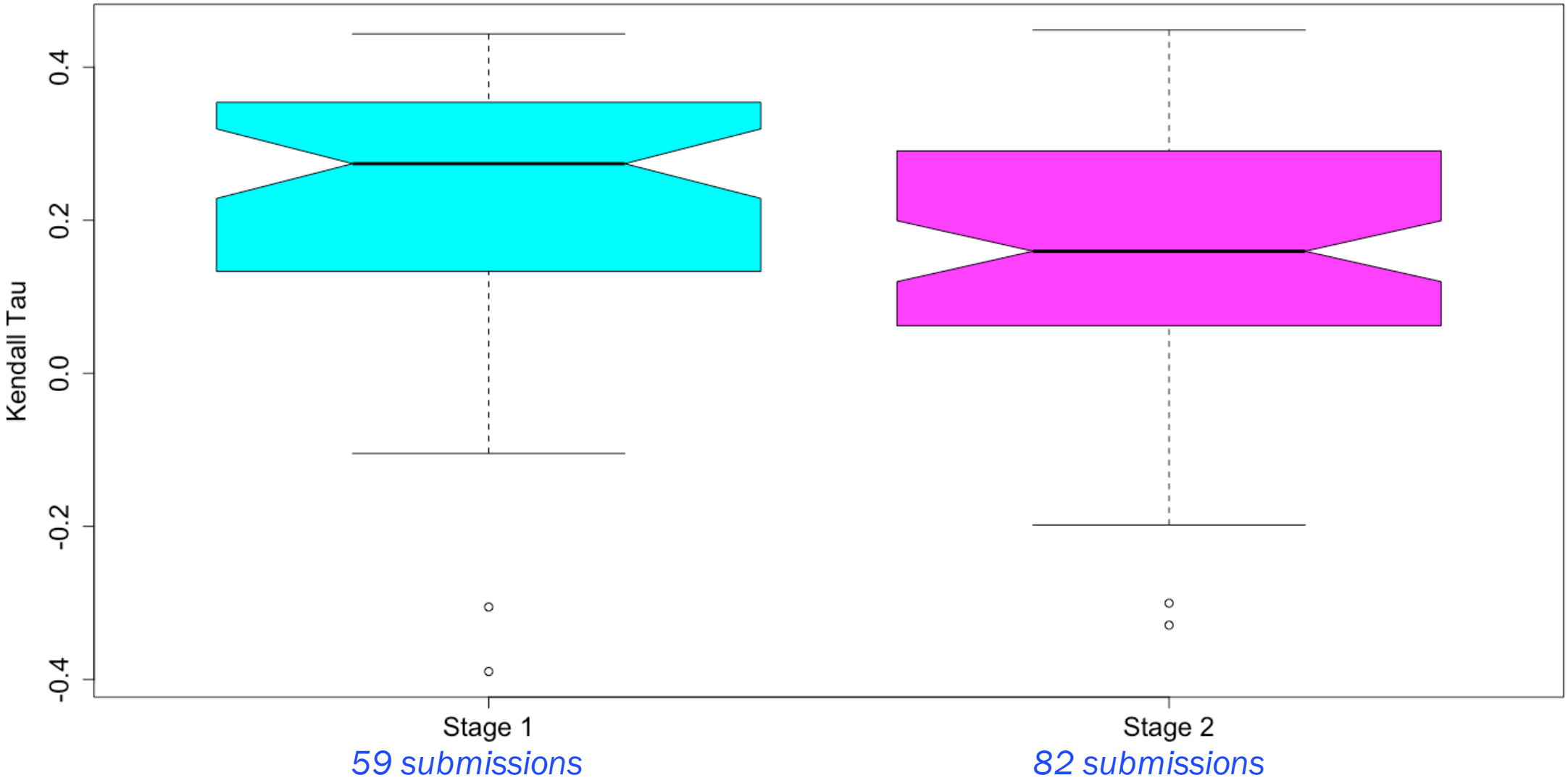
Scoring

Scoring – Stage 1 vs Stage 2



Scoring – Stage 1 vs Stage 2

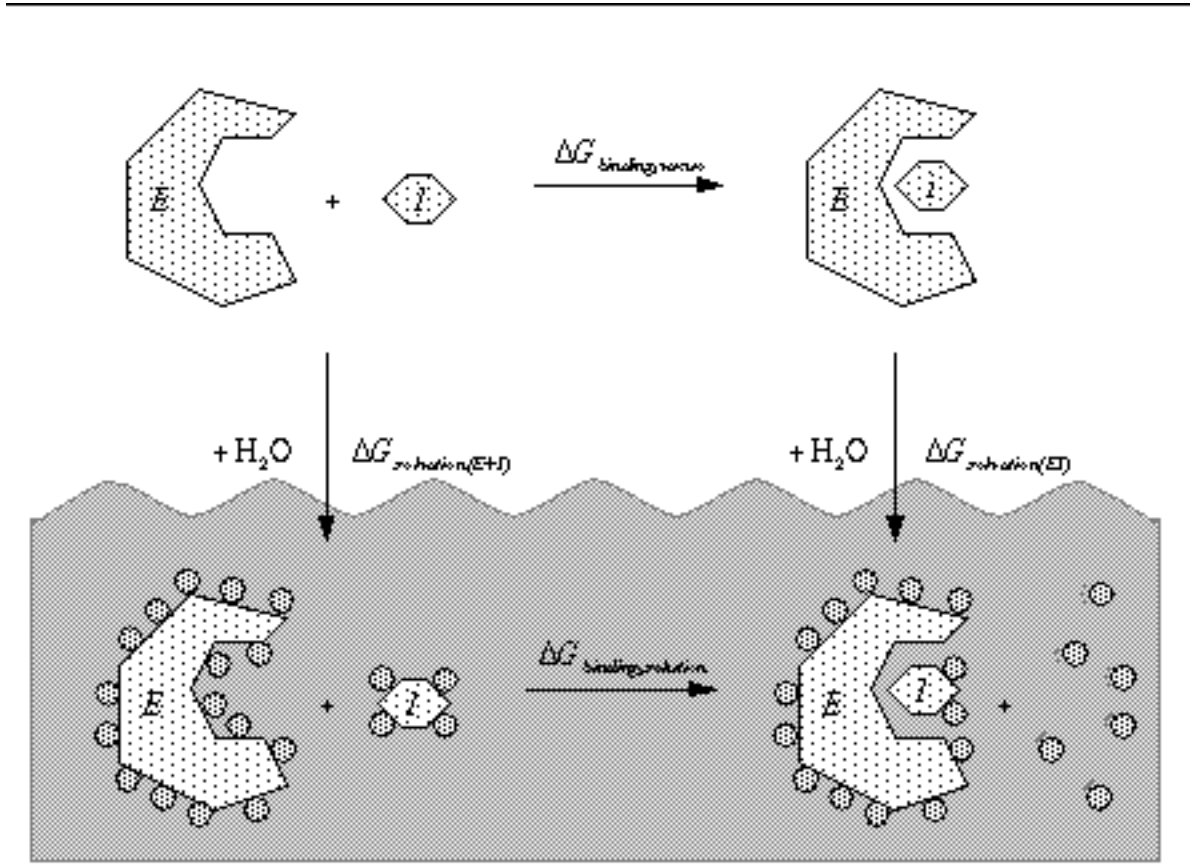
Differences may be deceiving



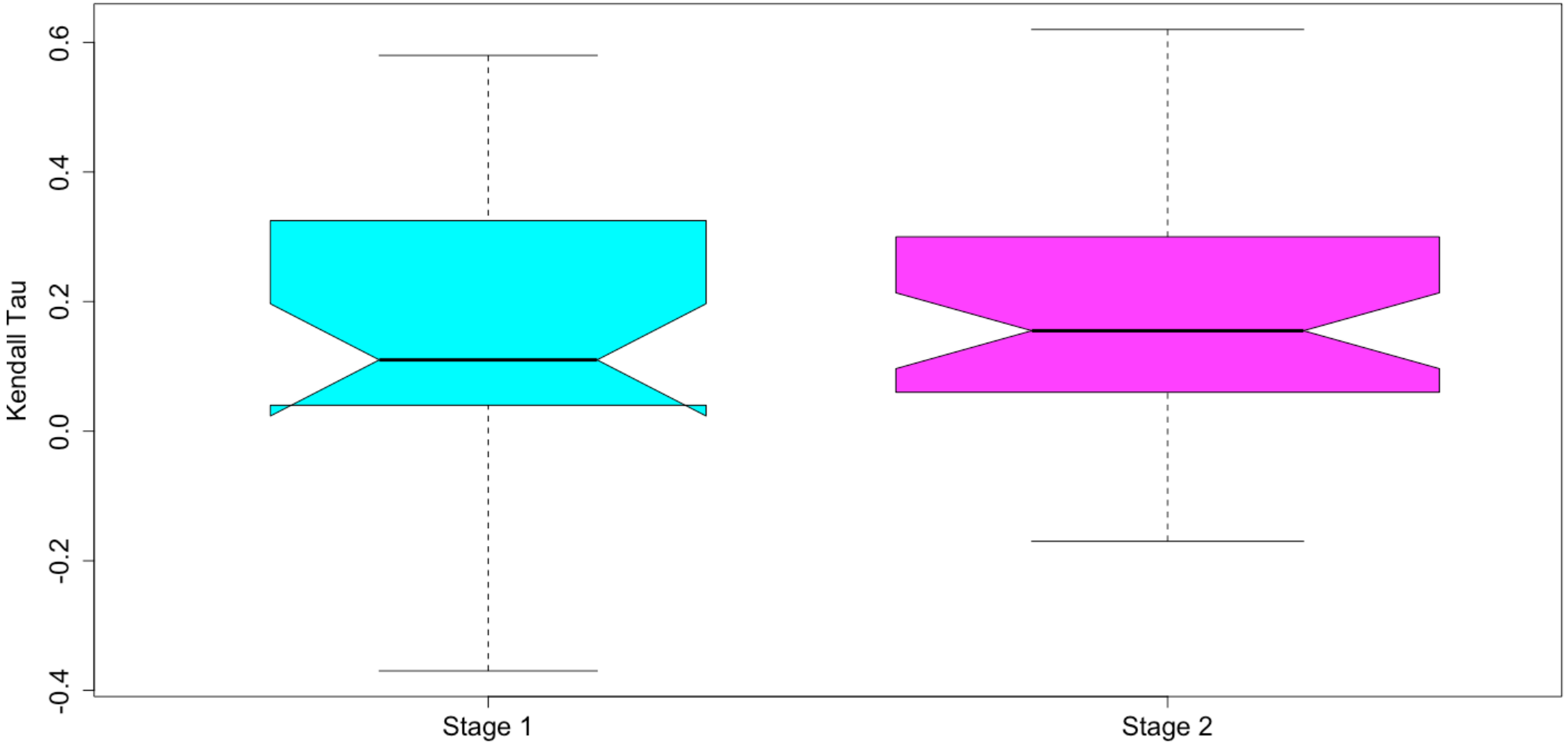
59 submissions

82 submissions

Free Energy



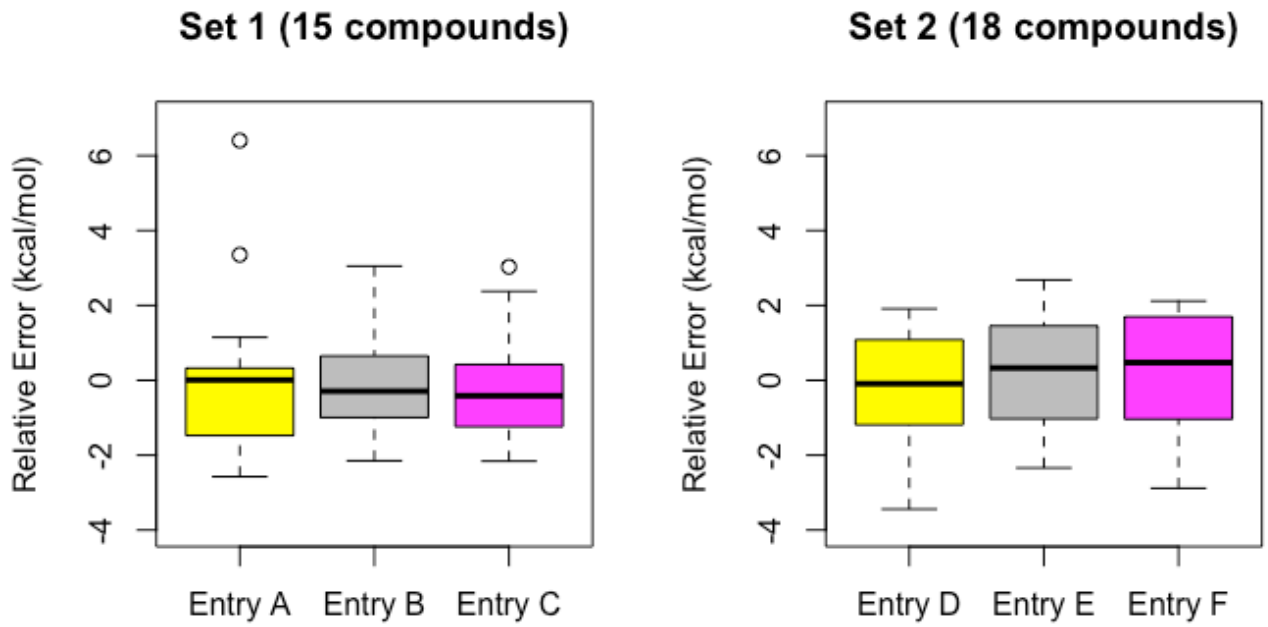
Free Energy – Stage 1 vs Stage 2



27 submissions

42 submissions

Free Energy – State of the Art



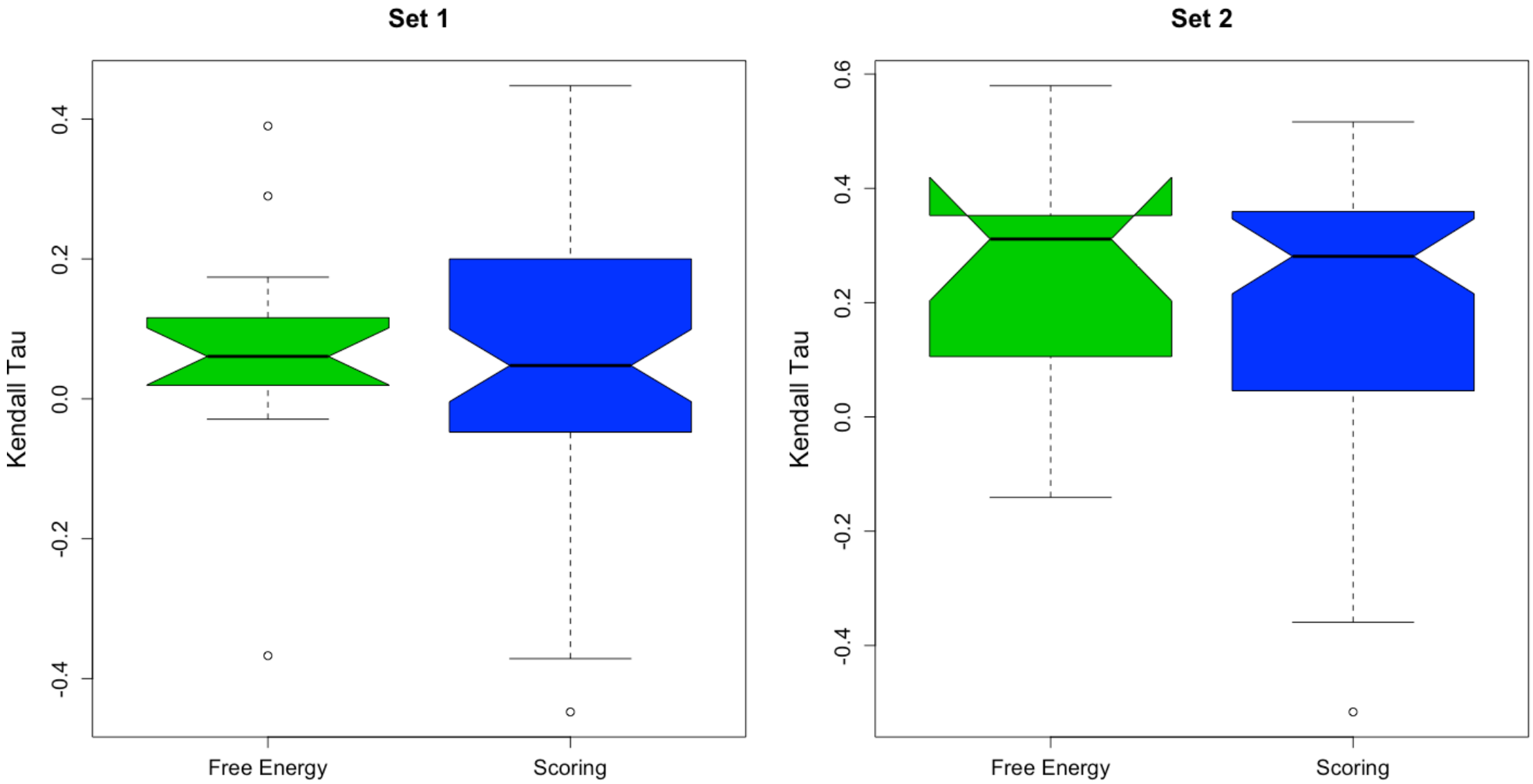
- Top entries had very low RMS Error
  - Set1 had 6 entries with RMSD < 1.5 kcal/mol
  - Set2 had 8 entries with RMSD < 1.5 kcal/mol

Comparing Free Energy and Scoring

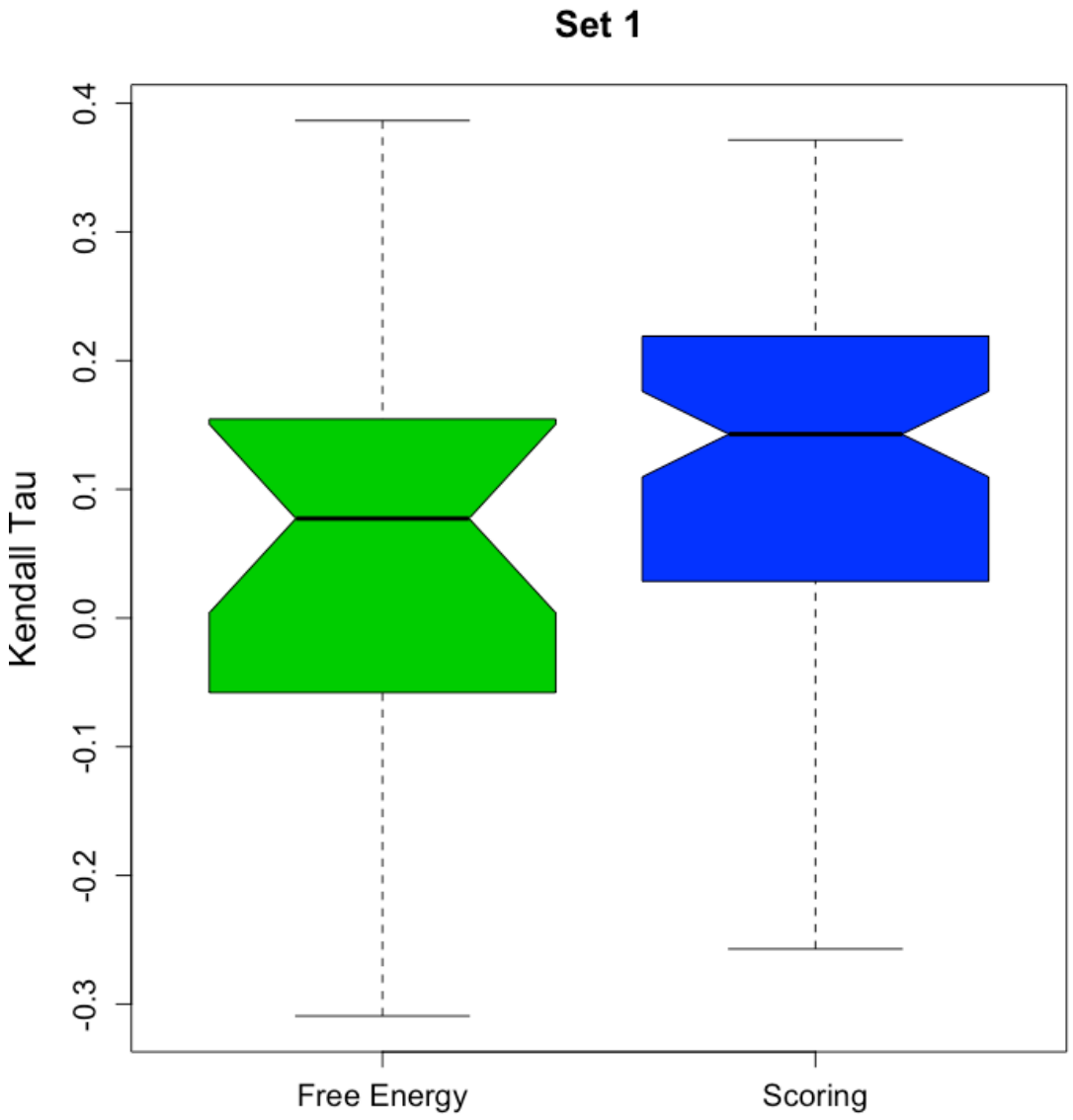
- All comparisons were carried out on the same subsets
- Set1 - 15 compounds
- Set2 – 18 compounds

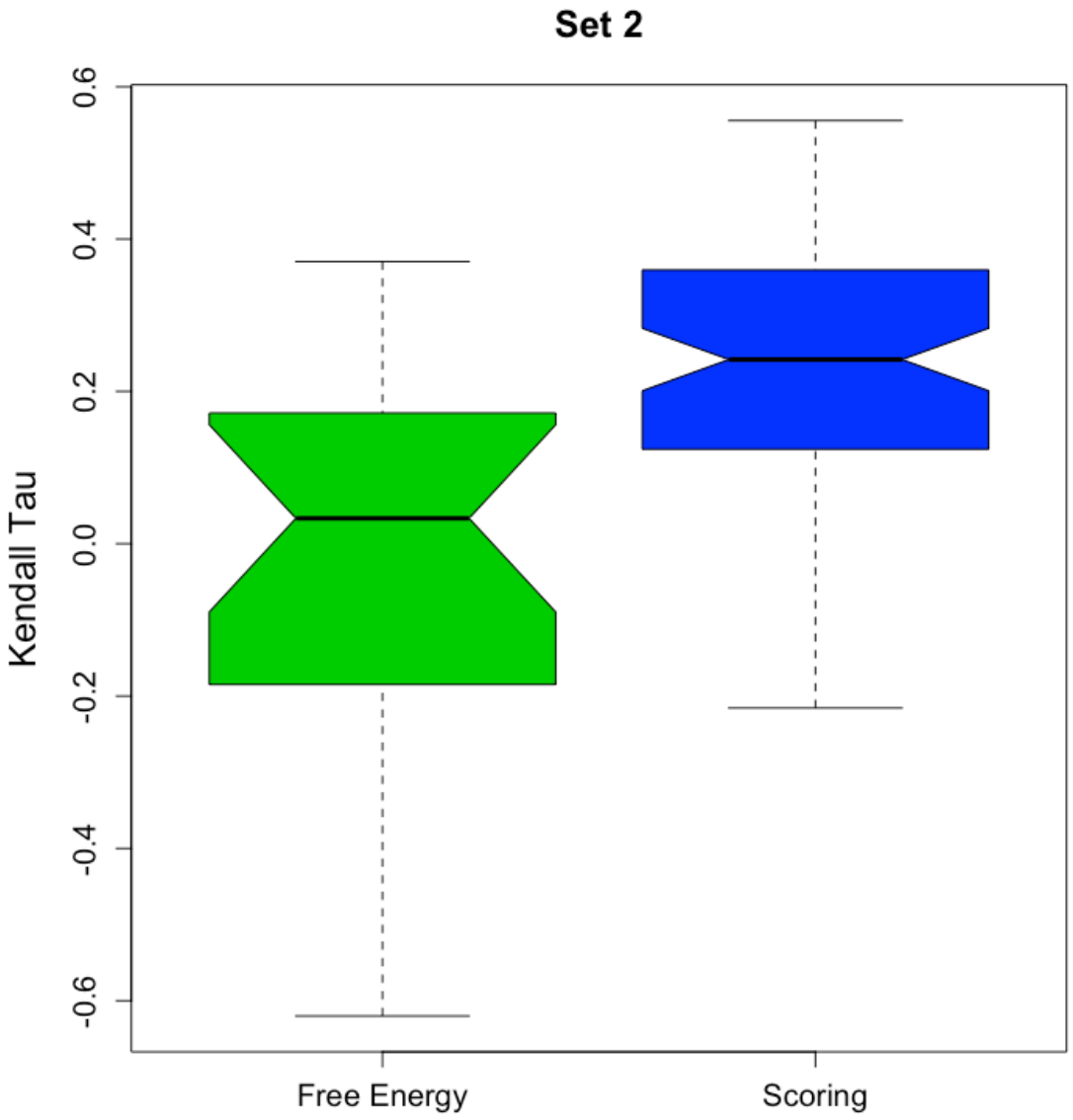
- Comparisons were based on Kendall Tau

Free Energy vs Scoring – Stage 1



Free Energy vs Scoring – Stage 2





Conclusions

- A variety of methods performed well in the pose prediction challenge
  - *Approx half the compounds were predicted with in 2 $\AA$ by the best methods*
  - *Examination of poorly predicted compounds should be informative*
- Free energy methods provided good predictions of relative binding energy
  - *Multiple entries with RMS < 1 kcal/mol*
  - *Need to understand error sources for outliers*
- Correlations from scoring competitive with free energy
  - *Compare ranks for poorly predicted molecules*
  - *How can one field learn from the other?*

Acknowledgements

- Shuai Liu
- Mike Gilson
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