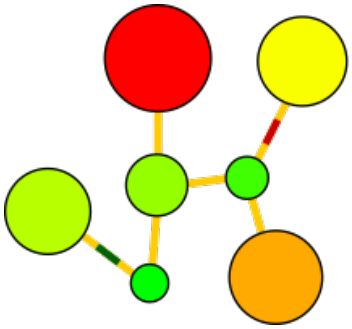

aRMSD

aRMSD is an open toolbox for the structural comparison of two constitutionally identical molecules. The data are read from common file formats (e.g., *.xyz, *.pdb, etc.) by default, or by assistance of openbabel.[1] The results may be accessed interactively as 3D rendering with vtk[2] and exported. The development started with Arne Wagner during his PhD thesis in the Himmel group (University of Heidelberg) and made available on https://github.com/armsd/aRMSD.

Contrasting to said original branch, *this* fork develops aRMSD under Linux (Debian 10 / Buster, currently testing / Sid), since it was used side-by-side with other programs already deployed successfully in Linux. Specific to Linux: I liked to have a Python script resolving the dependencies of aRMSD instead of a somewhat manual download, and installation anticipated for Windows. Other than this, changes made within this fork, however, should work equally in other operating systems.

1 What may aRMSD do for you – an appetizer

As shown in the figure below, aRMSD may be used to align the models (a) and reorder the atom order by the Hungarian algorithm (b). Subsequently, the superposition is optimized by minimization of the RMSD according to the Kabsch algorithm.

In a newly designed representation (c), the differences between the two models may be accessed visually: atoms drawn with larger diameter indicate a larger *relative* contribution to the final RMSD determined for the complete model. The color scaling, corresponding to the scale at the side, corresponds to the *absolute* difference – in Angstroms – of said atom for both models in the optimized superposition.

In addition, the program compares the corresponding bond lengths of model and reference indicates either by green or red color encoding if the one by the model is shorter, or lengthier than the corresponding bond in the reference. Not shown here, but aRMSD allows the interactive readout of the differences found for selected bond lengths, angles, and dihedral angles, too.

Equally, the program offers you an interactive 3D rendering of model and reference with the optimized superposition (d). This "best fit" determined may be saved in *.xyz files.

[1] Open Babel, http://openbabel.org/wiki/Main_Page. For further details, see by O'Boyle, N. M.; Banck, M.; James, C. A.; Morley, C.; Vandermeersch, T.; Hutchison, G. R. Open Babel: An open chemical toolbox. *J. Cheminf.* 2011, 3:33 (doi: 10.1186/1758-2946-3-33).

[2] http://www.vtk.org

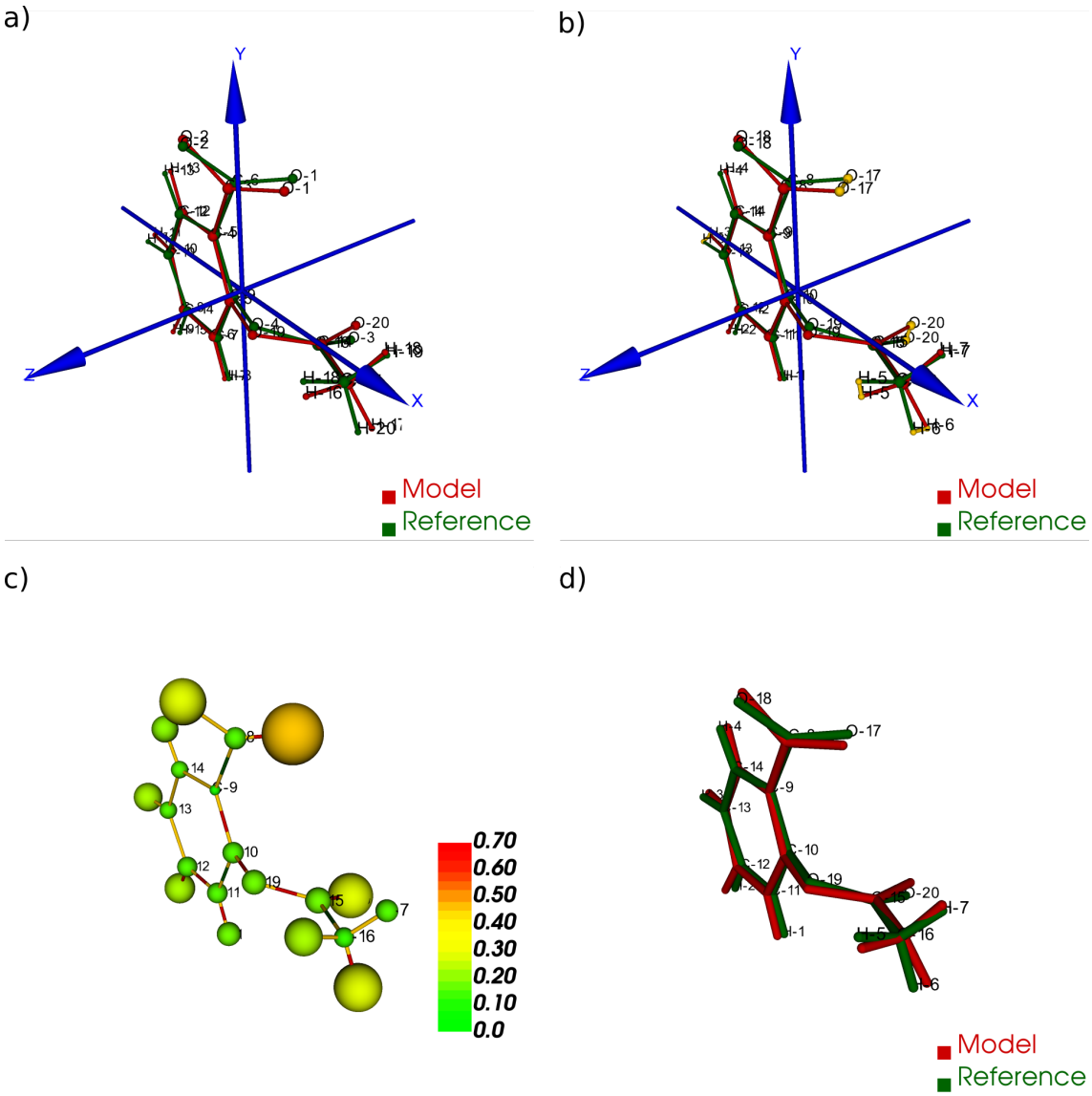

Figure 1: Subsequent stages comparing two models of the aspirinate anion with aRMSD: a) user-assisted alignment, b) re-ordering of atoms by the Hungarian algorithm, c) interactive difference rendering, d) interactive refined superposition of the models.

On an operational system including `matplotlib`, `aRMSD` may complement the scrutiny by computing and plotting selected statistics. The scaling may be altered by the user, equally in charge to select the file format of export (`*.png`; `*.ps`, `*.eps` `*.pdf`, `*.svg`; `*.tkiz`).

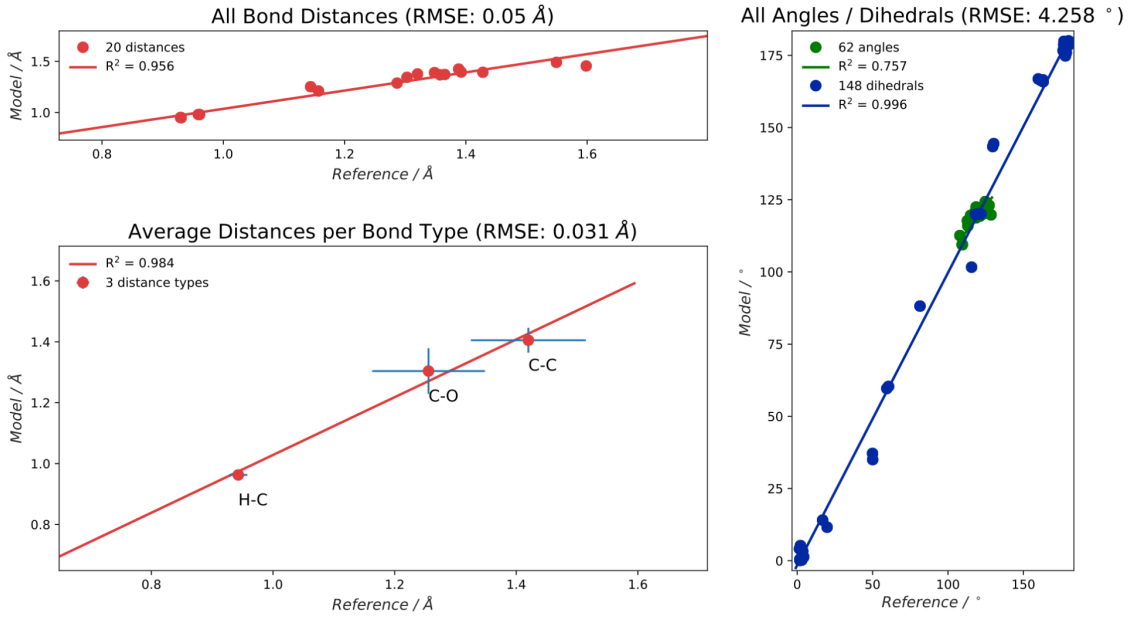

Figure 2: Statistical plots drawn by `aRMSD` about said comparison of two aspirinate model data.

Besides the results of the Kabsch test, supplementary similarity figures of merit like the cosine similarity or the GARD values may be stored permanently in plain ASCII (`aRMSD_logfile.out`).

Altogether with a few test data (sub-directory `examples`), an illustrated primer in sub-directory `docs` will guide you through setting-up the program and detail out how to perform a basic analysis.

2 Where stands aRMSD, relatively to other programs?

`aRMSD` emerges from the pair-wise comparison of (crystallographic, but not limited to this) models with significant user-interaction. This offers you multiple levels to check and adjust the progress of the analysis. As such, a batch-wise comparison of models is not foreseen.

Note, however, that an automate, batch-wise scrutiny of two model data may yield wrong results. One potential pitfall is how the model information is handled prior to the refinement of the structure alignment, where `aRMSD` uses the Hungarian algorithm. To quote Kildgaard:[3]

> "The RMSD can be minimized by translating and rotating one set of coordinates (the other is held fixed) because the molecules are invariant under these operations.

[3] Kildgaard, J. V.; Mikkelsen, K. V.; Bilde, M.; Elm, J. Hydration of Atmospheric Molecular Clusters: A New Method for Systematic Configurational Sampling. *J. Phys. Chem. A* 2018, 122, 5026−5036 (doi: 10.1021/acs.jpca.8b02758).

> This will lead to the two molecules being superimposed but can also lead to a false RMSD value if the atoms are not ordered identically."

Independent from this problem, the conventional RMSD optimization accounts only for *atom connectivity*, neglecting *bond order*. As demonstrated (and illustrated) by Temeslo[4], this may yield to results questionable from a chemists point of view.

3 History & Credits

`aRMSD` was developed in Windows by Arne Wagner during his PhD thesis in the Himmel group (University of Heidelberg, Germany). It is described briefly in his PhD thesis submitted in 2015.[5] The program was presented in further detail in

> Wagner, A.; Himmel, H.-J. aRMSD: A Comprehensive Tool for Structural Analysis. *J. Chem. Inf. Model.*, 2017, *57*, 428–438 (doi: 10.1021/acs.jcim.6b00516)

and originally deposit as open source code with the permissible MIT license to the public under

```
https://github.com/armsd/aRMSD
```

As by November 2018, his last public github-commit regarding aRMSD was on April 5, 2017. My subsequent work on `aRMSD` is based on this release.

◇

[4] Temeslo, B.; Mabey, J. M.; Kubota, T.; Appiah-Padi, N.; Shields, G. C. ArbAlign: A Tool for Optimal Alignment of Arbitrarily Ordered Isomers Using the Kuhn-Munkres Algorithm. *J. Chem. Inf. Model.* 2017, 57, 1045–1054 (doi: 10.1021/acs.jcim.6b00546).

[5] Wagner, A. Synthese und Koordinationschemie guanidinatstabilisierter Diboranverbindungen. (Synthesis and Coordination Chemistry of Guanidinate-Stabilised Diboranes) PhD thesis (2015), University of Heidelberg (Germany). Written in German including an English summary. The pdf of this document may be found at the doi 10.11588/heidok.00019018.