Supplementary Information

SAMPL5: Distribution Coefficient Predictions with SOMD

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August 23, 2016

Datasets

Fig. 1 shows the dataset extracted from the Minnesota Database [1]. The dataset was chosen in order to simulate the most typical moieties present in the SAMPL5 batch.

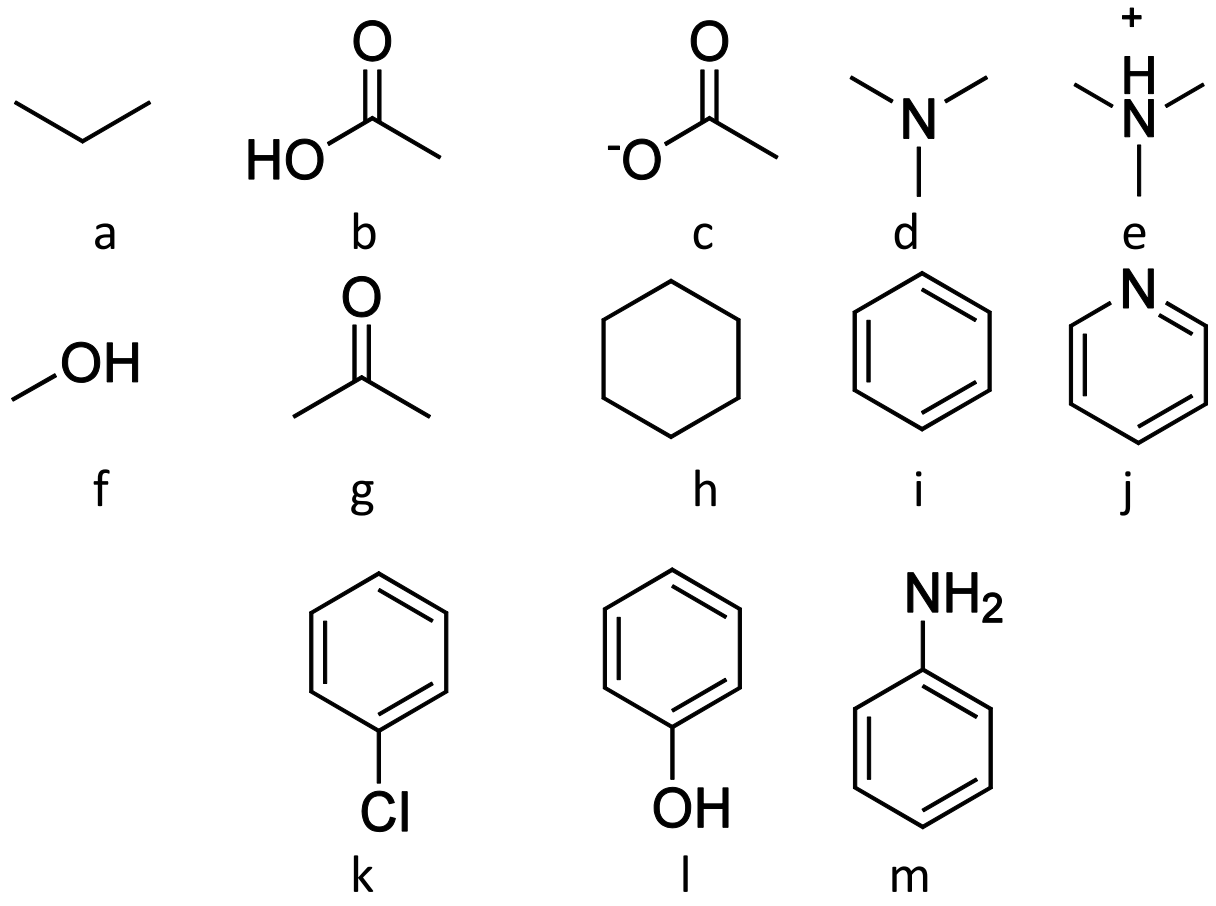
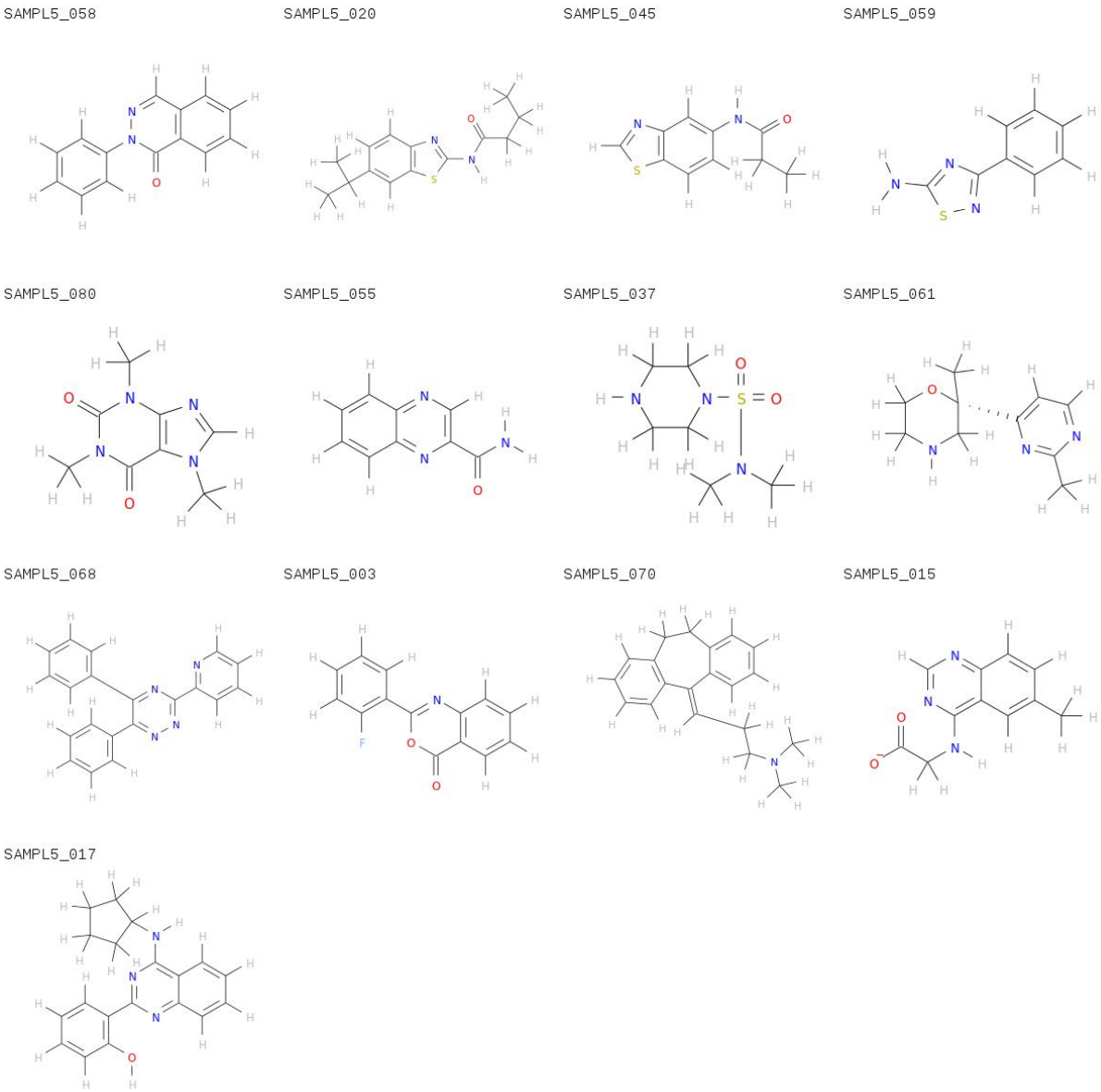
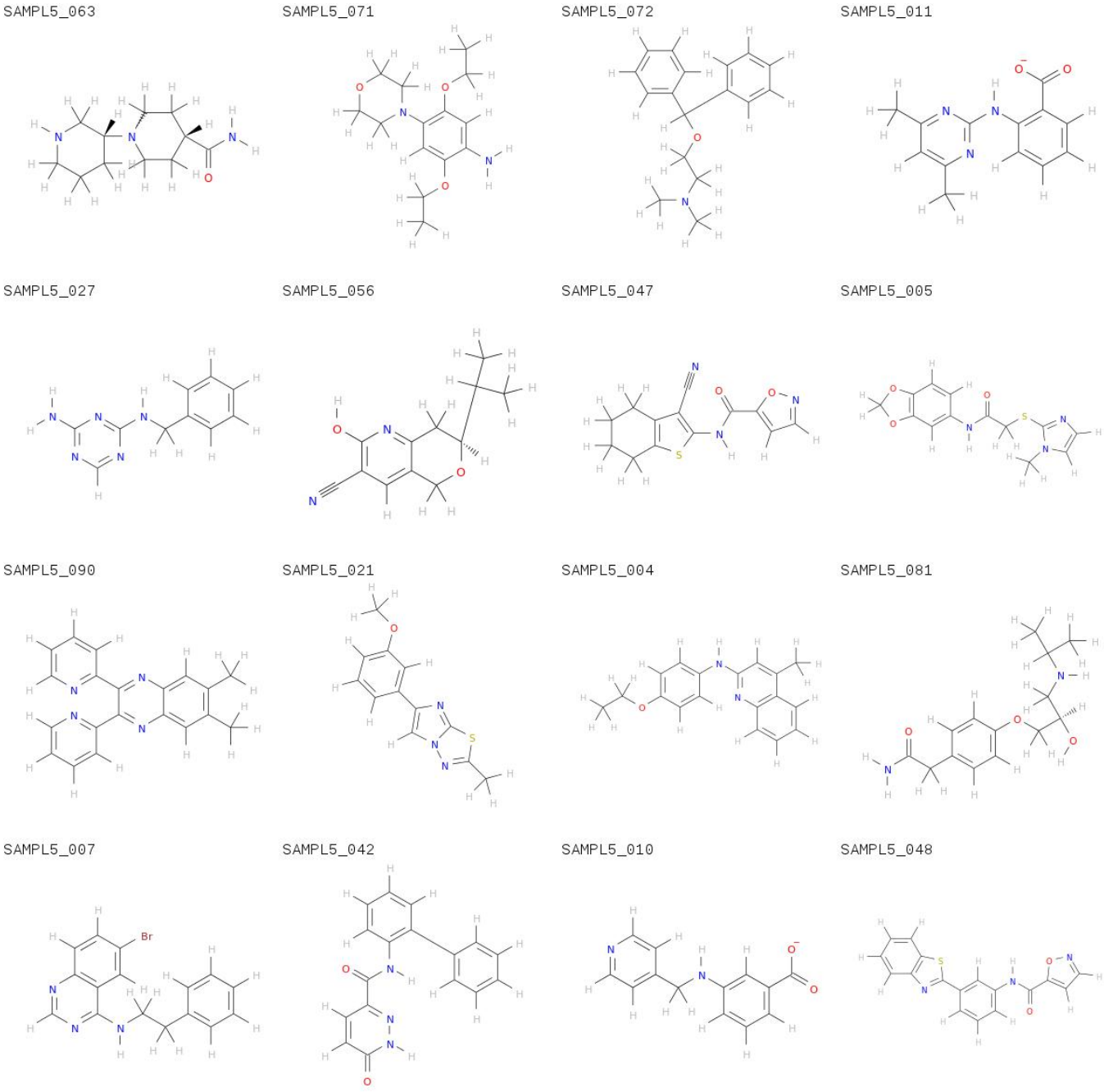


Figure 1: Dataset of molecules selected from the Minnesota Database [1]: a) n-propante, b) acetic acid c) acetate d) trimethylamine e) trimathylammonium f) methanol g) acetone h) cyclohexane i) benzene j) pyridine k) chlorobenzene l) phenol m) aniline

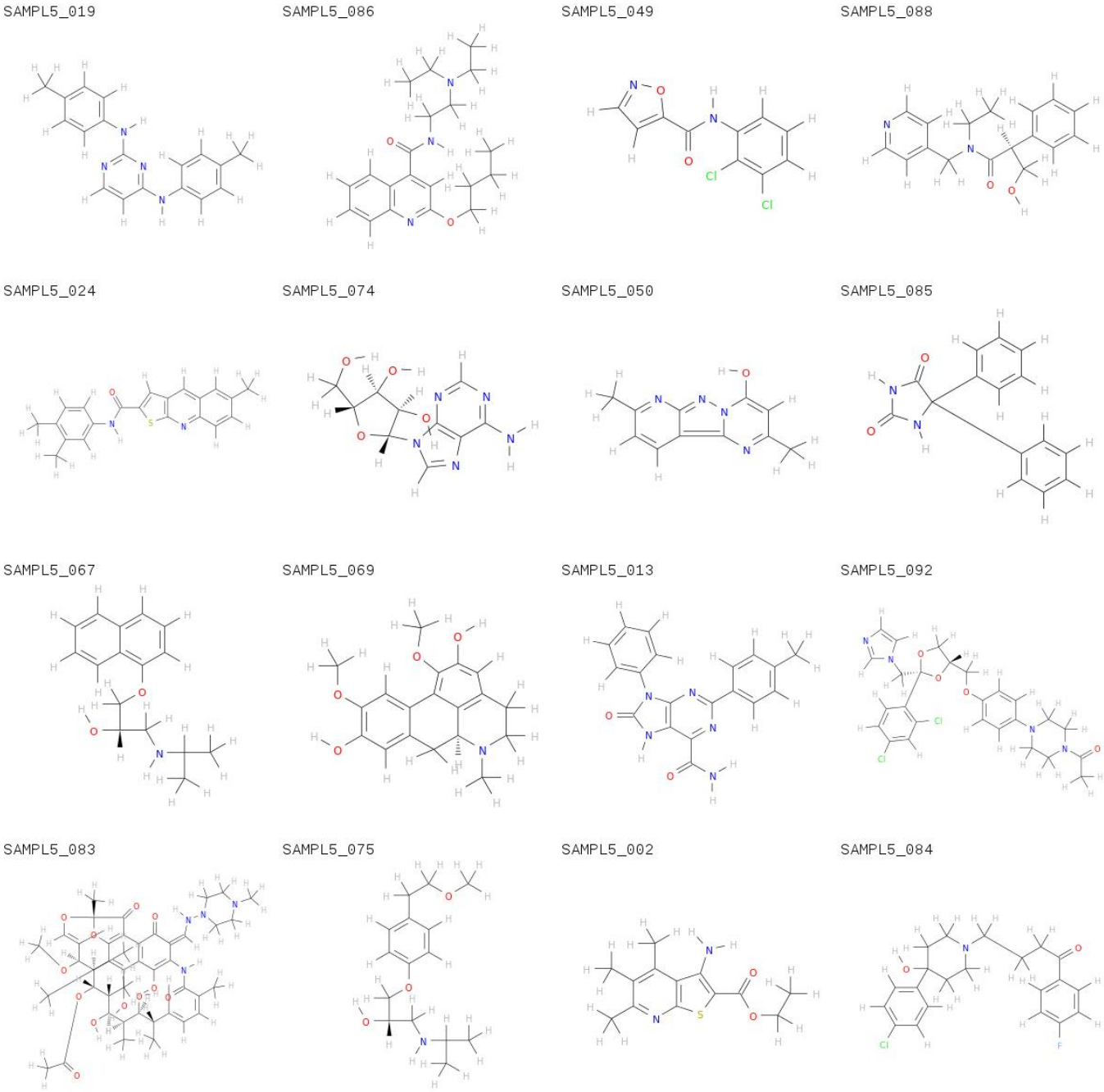


(a) SAMPL5 distribution coefficient molecules of batch 0

Fig. 2a, 2b, 2c show the 53 molecules of SAMPL5 dataset divided in batch 0, batch 1 and batch 2



(b) SAMPL5 distribution coefficient molecules of batch 1



(c) SAMPL5 distribution coefficient molecules of batch 2

Chemical structures for the charged species are represented in fig. 3

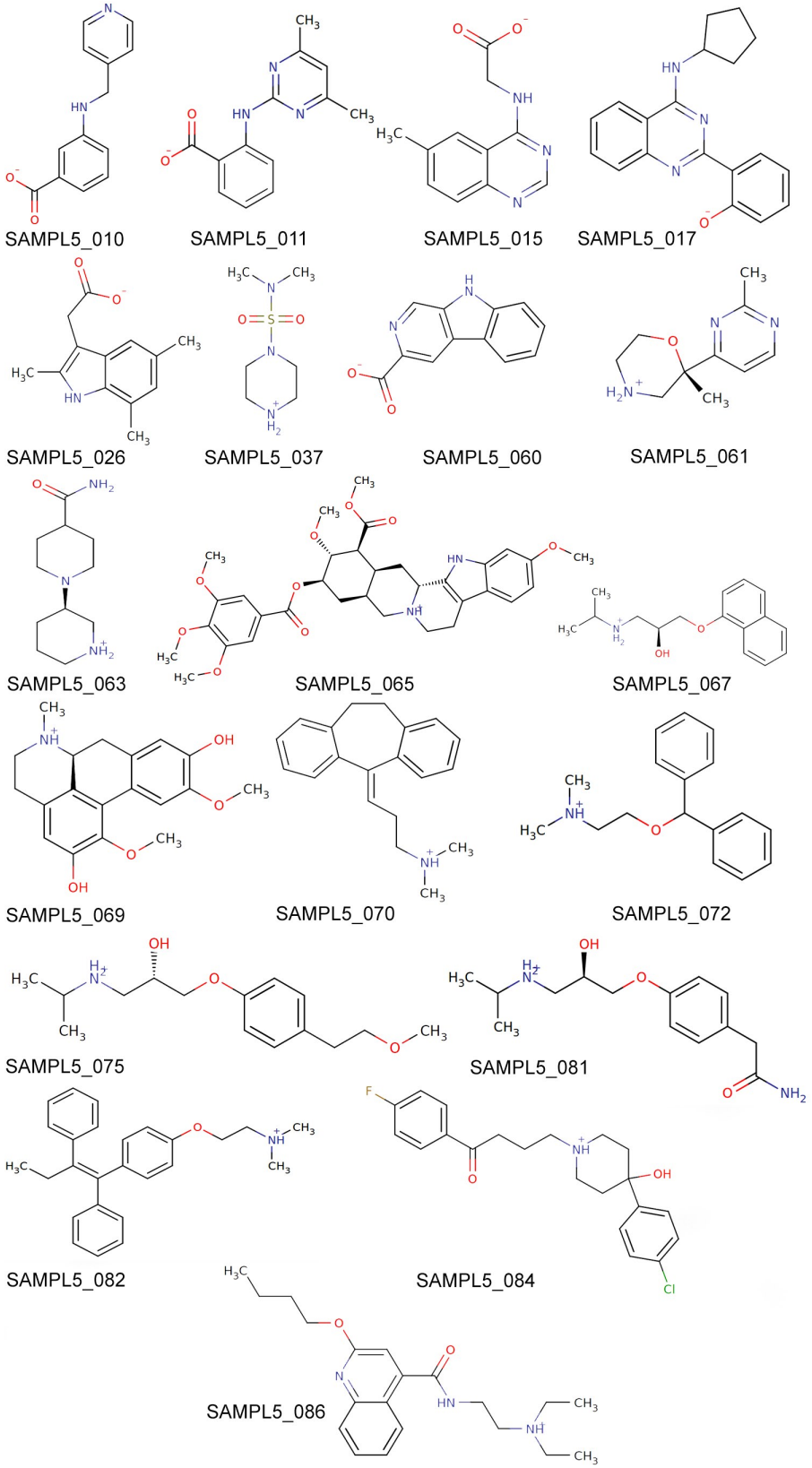


Figure 3: Chemical structure for the compounds modeled as charged

Statistical analysis of the different models

The statistical significance of *model A, B, C* and *D* of the **dominant-species model** is shown in fig. 4. Overlap betwween notches is present in *model A* and *B*, denoting a similar behavior in $\log$ D estimations. *Model C* is the less statistical significant with the lowest R^2 and τ and highest MUE.

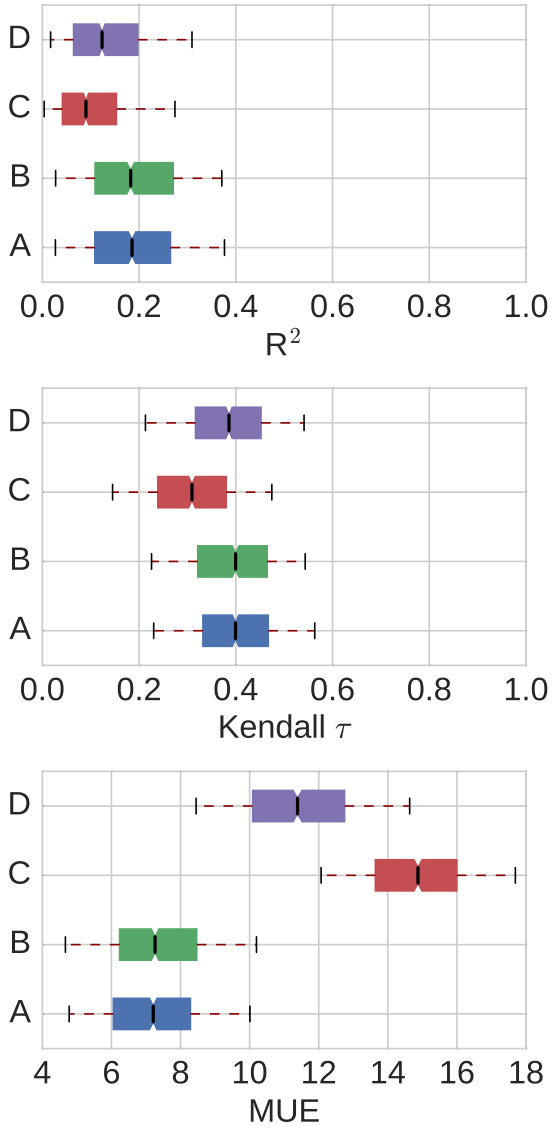


Figure 4: Comparison of determination coefficient R^2 (top), Kendall τ (middle) and mean unsigned error (MUE) (bottom), between *model A, B, C* and *D* for $\log$ D estimation with **dominant-species model**. Results show in box plot form with the 5th 95th percentile, the median and the notch.

Results are improved if the **two-species model** is adopted and statistical significance of *model A, B, C* and *D* is shown in fig. 5

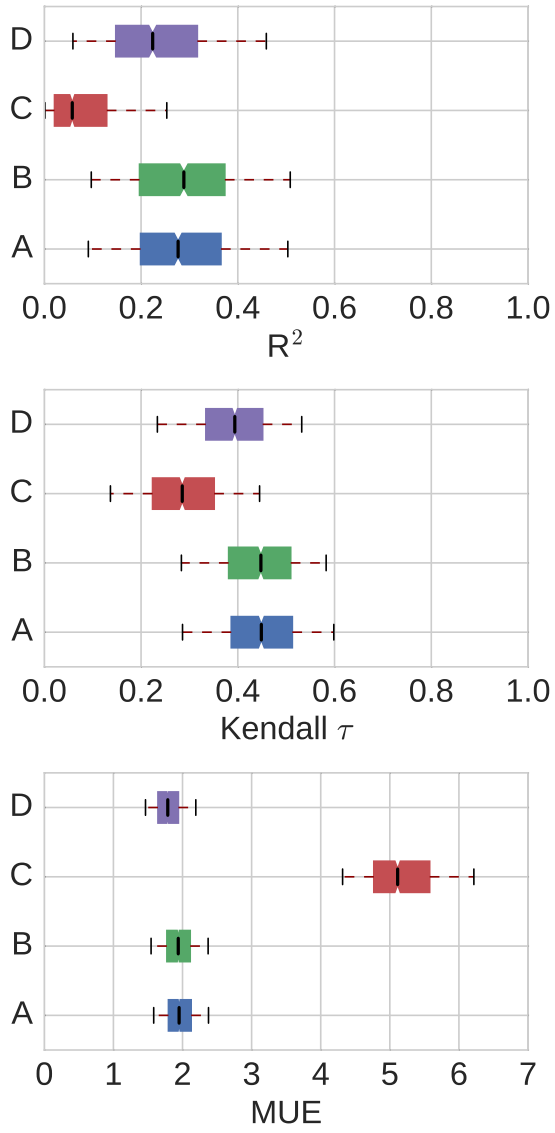


Figure 5: Comparison of determination coefficient R^2 (top), Kendall τ (middle) and mean unsigned error (MUE) (bottom), between *model A, B, C* and *D* for $\log$ D estimation with **two-species model**. Results show in box plot form with the 5th 95th percentile, the median and the notch.

The archive dominant_species.zip contains:

- logD folder: the predicted $\log$ D are stored into csv files along with the standard error for *model A* (A.csv), *B* (B.csv), *C* (C.csv) and *D* (D.csv)
- solv_energies folder: this folder contains the solvation free energies for each model and standard error for cyclohexane (cyclohexane_solv.csv) and hydration free energies (water_solv.csv)

The archive two_species.zip contains:

- Comparison_methods.csv : a comparison between two species equation (eq.19) and eq.20 [2] to test the efficacy of the effective pKa assumption
- Concentration.csv: the concentration used to calculate the $\log$ D with eq.19, retrieved from ChemAxon [3]
- logD_charged.csv: the predicted $\log$ D for each charged species according to *model A, B, C* and *D* for the two species approach
- pKa.csv: the pKa used to calcualte the $\log$ D with eq.19, retrieved from ChemAxon [3]

References

[1] Aleksandr V. Marenich, Casey P. Kelly, Jason D. Thompson, Gregory D. Hawkins, Candee C. Chambers, David J. Giesen, Paul Winget, Christopher J. Cramer, and Donald G. Truhlar. *University of Minnesota, Minneapolis*, 2009.

[2] Robert A. Scherrer, Susan M. Howard, *J. Med. Chem.*, 1977, 20(1), 53-58

[3] Chemaxon, www.chemicalize.org.