PREDICTIVE MODEL FOR HYDROGEN BONDED COMPLEXES WITH SINGLE AND COOPERATIVE HYDROGEN BONDS

Glavatskikh M.V.,[a,b] Madzhidov T.I.,[b] Solov'ev V.P.,[c] Horvath D.,[a] Marcou G.,[a] Varnek A.A.[a,b]

[a]University of Strasbourg, Strasbourg, 67008, France
[b]Kazan (Volga region) Federal University, Kremlyovskaya, 4/5, Kazan, 420111, Russia, e-mail: mvglavatskikh@gmail.com
[c]A.N. Frumkin Institute of Physical Chemistry and Electrochemistry, RAS, Leninsky prospekt, 31, Moscow, 119071, Russia

This work is devoted to building a QSPR model for the prediction of Hydrogen Bond (HB) complexation strength. Hydrogen Bonding is the most investigated and the most important type of intermolecular interaction. The instances in which Hydrogen Bond plays a fundamental role are varied and span from drug-ligand interaction to self-assembling systems. Thus, the necessity of quick and precise calculations of the Halogen Bond thermodynamic parameters which reflect the strength of the interaction is in high demand.

The data used herein is based on Gibbs energy *dG* for 1:1 hydrogen bond complexation of various organic donors and acceptors in CCl4 at 298K[1-3]. Models based on ISIDA local descriptors were performed using Support Vector Machine (SVM) and Multiple Linear Regression (eMLR) methods on a set of 3388 organic complexes and validated in 3-fold cross validation. A consensus model returning the mean of values predicted by the most successful individual SVM models, based on various ISIDA fragmentation schemes[4,5], and including applicability domain assessment strategies (bounding box, standard deviation of consensus prediction) was challenged to predict Δ*G* for the HB complexation of an external test set of 641 complexes with single HBs and a set of 22 complexes of cooperative HBs, and its subsets. Different strategies of model validation have been suggested in order to investigate various scenarios with respect to presence / absence of the same H-bond acceptors and donors in the training and test sets The *RMSE* value of 2.17 kJ/mol for the most robust predicted class is within the experimental uncertainties.

References

1. Raevskii O.A., Solov'ev V.P., Grigor'ev V.Y. *Thermodynamic Characteristics of Hydrogen Bond of Phenols with Organic Bases*, VINITI, Moscow, 1988
2. Laurence C., Gal J.-F. *Lewis Basicity and Affinity Scales. Data and Measurement*, John Wiley & Sons Ltd, Chichester, 2010
3. Terent'ev V.A. *Thermodynamics of Hydrogen Bond*, University of Saratov Kuibyshev, 1973
4. Varnek A., Fourches D., Hoonakker F., Solov'ev V.P. J. Computer-Aided Mol. Design, *2005, 19, 693-703*
5. Ruggiu F., Solov'ev V., Marcou G., Horvath D., Graton J., Le Questel J-Y., Varnek A. *Mol. Informatics,* 2014*,* 33, 477 – 487