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PREDICTING STABILITIES OF METAL -ORGANIC LIGAND COMPLEXES

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This presentation concerns the **COMET** (***CO***mplexation of ***MET***als) project devoted to development of chemoinformatics tools able to predict stability constants for the M:L = 1:1 ($\log K_1$) and M:L = 1:2 ($\log\beta_2$) complexes of metal cations (M) with organic ligands (L) in water.

Two approaches were used: (*i*) quantitative structure – property modeling and (*ii*) linear free energy relationships. The first one concerns theoretical calculations with the *ISIDA* (In SIlico design and Data Analysis) software[1–9] which builds quantitative structure-property relationships (QSPR) using fragment descriptors and different machine-learning techniques: multi-linear regression, support vector machine, artificial neural networks, *k* nearest neighbors. All developed models are then simultaneously applied to predict $\log K_1$ ($\log\beta_2$) values for new ligands. Generally a *consensus model* calculated as arithmetic mean of values obtained with different models leads to more reliable predictions than any individual QSPR model. Model's applicability domain concept was also used in order to improve the robustness of predictions.

The second approach is based on empirical correlations between stability constants for the complexes of the given set of ligands with two different metals M_i and M_j. This approach is more restrictive than the previous one because it can be applied only for already known ligands.

In order to train structure-property models, the experimental data on complexation stability constants from the IUPAC Stability Constants Database (SC-DB) were used. Thus, from 80000 records of SC-DB including 8600 ligands, we have selected more than 13600 $\log K_1$ and 4300 $\log\beta_2$ values corresponding to the complexes 78 metals in their 140 cationic forms with 2962 organic ligands. Then, these data scaled for standard temperature 298 K and ionic strength 0.1 M were used for the modeling.

Application of the developed software tools to the complexes alkaline-earth cations, transition metals and lanthanides with organic ligands is discussed.

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