Prediction of stability constants of coordination compounds from their molecular graphs

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Abstract. Every molecular structure can be regarded as a graph, and each graph can be transformed into characteristic scalar – topological index. There are many, over 1000 topological indices used by chemists, but they are not equally successful in solving specific problems. For the prediction of stability of coordination compounds valence molecular connectivity index of the 3rd order ($3\chi_v$) proved best. Stability of these compounds was expressed as $\log K$ ($K$ stays for stability constant), which is proportional to the Gibbs free energy of reaction between metal (or metal complex) and ligand. Various molecular graphs were checked, from a simple graph of ligand, to the graphs of various metal-ligand complexes (aqua complex, complex with additional bonds etc.) leading to conclusion that chemically sounder graphs generally yield better models. The best results were obtained for the systems of one metal, measured at the same experimental conditions. However, our graph-theoretical approach enables development of models for the simultaneous prediction of stability constants of few metals.

1. Topological indices in chemistry

Application of topological indices in chemistry commenced in 1947 when H. Wiener introduced path number $W$, later known as Wiener number or Wiener index [1,2]. The path number was defined as the number of bonds between all pairs of atom in an acyclic molecule, i.e.:

$$W(G) = \frac{1}{2} \sum D_{ij}(G)$$

where $D_{ij}(G)$ are off-diagonal elements of (topological) distance matrix $D(G)$. Wiener correlated his path number with physical parameters of acyclic hydrocarbons, and this problem occupy the chemists and mathematicians till our days; i.e. most of the papers in mathematical chemistry deal with modelling boiling points of hydrocarbons by using a variety of topological indices [3,4]. Later, topological indices (now, there are more than thousand of them) were used for prediction of many physico-chemical properties (QSPR, quantitative structure-properties relationships) [5-7] and biological activity (QSAR, quantitative structure-activity relationship) [8] of many kinds of molecules. Among the hundreds of topological indices [9] very few, however, found its application in chemistry. In our first paper in application of these indices for the estimation of stability of coordination compounds [10], we found the best fit with the Wiener index, $W$, and three valence connectivity
indices, $\chi^1$, $\chi^2$, and $\chi^3$. The last one, the valence molecular connectivity index of the 3rd order, later proved to be the best of all indices, is defined by relation [11,12]:

$$3\chi^v(G) = \sum [\delta(i)\delta(j)\delta(k)\delta(l)]^{-0.5} \quad (2)$$

where $\delta(i)$, $\delta(j)$, $\delta(k)$, and $\delta(l)$ are weights (valence values) of vertices (atoms) $i$, $j$, $k$, and $l$ making up the path of length 3 (three consecutive chemical bonds) in vertex-weighted molecular graph, $G$.

2. The stability of coordination compounds

The stability of coordination compounds is usually measured by log $K$ values, where $K$ is equilibrium constant of reaction between metal (M) and ligand (L):

$$M + L \underset{K_1}{\overset{K_2}{\rightleftharpoons}} ML$$

$$ML + L \underset{K_3}{\overset{K_4}{\rightleftharpoons}} ML_2$$

which are related to the Gibbs energy of reaction, i.e. stability of the complex ($\Delta G = -RT \ln K$). There are many models aimed at prediction of log $K_1$, log $K_2$, and log $\beta_2$ ($= \log K_1 + \log K_2$) [13], but there is yet no general model for this purpose. Problem is that stability of coordination compounds is determined by many diverse factors which are not easy to calculate, and, as an additional obstacle, stability constants of coordination compounds were measured at different conditions (temperature, ionic strength, solvent composition, etc.). Our approach is, however, based on quantitative comparison of structural (constitutional) similarity of molecules of coordination compounds, via their topological indices, assuming that more related molecules should have closer values of stability constants [14].

3. Influence of molecular graph

There are many possibilities to correlate log $K$ with topological index $3\chi^v(G)$, because there are many possibilities to write a graph, $G$, representing a molecule. $G$ may represent ligand (L), and many forms of complexes $ML$ and $ML_2$. Exact structure of the complex in solution is not known; it could be generally denoted as $(H_2O)_nML$ or $(H_2O)_nML_2$, where $n$ may be anything from 0 to maximal coordination number (Figure 1). However, more chemically sound structures (graphs) gave better correlations: $L < ML < ML^{n_1} \approx ML^{n_2}$ [15].

![Figure 1. Four kinds of graphs used to estimate stability constants of coordination compounds (M = metal, L = butyldiaminoethane): L (1), ML (2), ML$^{n_1}$ (3), and ML$^{n_2}$ (4).](image-url)

An another approach to proper graph of coordination compounds is based on the segmentation of molecule (graph) to its fragments (subgraphs). This approach was applied to copper(II) complexes of dipeptides, tripeptides and higher peptides [16,17]. Both approaches are original in graph-theoretical analysis, because researchers usually try many topological indices of the same, well defined graph. We, however, have tried the same topological index, $3\chi^v$, but of the different graphs.
4. Reliability of method
Stability constants predicted from regression of log $K$ on $\chi_v$ usually gave $\text{rms} \ (\log K) < 0.3$, and even $0.05$ [18,19]. In judging these numbers, it has to bear in mind that according to IUPAC recommendation constants determined with $\text{SD} (\log K) \leq 0.05$ were regarded as recommended, and the ones determined with $0.05 \leq \text{SD} (\log K) \leq 0.2$ were denoted as “tentative” [20]. However, it is not uncommon that the constants for the same system, measured at the same experimental conditions, differ more than 0.5 log units.

To check the validity of our method we applied our models on the constants $K_1$ and $\beta_2$ of copper(II) complexes with glycine and alanine, and their $N$-alkylated derivatives [21]. We compared log $K_1$ and log $\beta_2$ values measured by two experimental methods (glass electrode potentiometry, GEP, and square wave voltammetry, SWV) and various linear models based on different sets of stability constants and different molecular graphs (ML and MLaq). It was found that the theoretical method reproduces experimental constants in the error range commensurable to the differences between GEP and SWV values. Moreover, it was found that theoretical values for log $K_1$ fit better GEP constants, and the opposite is true for SWV log $\beta_2$ values. This is in accordance with general statement that $K_1$ constants are better determined with GEP, and $\beta_2$ constants with SWV. That means that our theoretical method should be usable for checking experimental data.

5. Modeling the complex systems
Most of our models deals with one metal, usually copper(II) or nickel(II), and one class of ligands, usually amino acids, their $N$-alkylated derivatives, and diamines. However, in our recent paper [18] we developed models for mono- and bis-complexes of glycine, alanine, valine, and leucine with bivalent transition metals (Ni, Co, Fe, and Mn) by using the equations (Figure 2):

$$\log K_1 = a_1 [\chi_v (\text{ML}) - \chi_v (\text{NiL})]^2 + a_2 [\chi_v (\text{ML}) - \chi_v (\text{NiL})] + a_1 \chi_v (\text{NiL}) + b$$

(3)

$$\log \beta_2 = a_1 [\chi_v (\text{ML}_2) - \chi_v (\text{NiL}_2)]^2 + a_2 [\chi_v (\text{ML}_2) - \chi_v (\text{NiL}_2)] + a_1 \chi_v (\text{NiL}_2) + b$$

(4)

![Figure 2](attachment:image.jpg)  

Figure 2. Experimental vs. theoretical (fit) log $\beta_2$ for Mn$^{2+}$, Fe$^{2+}$, Co$^{2+}$, and Ni$^{2+}$ complexes with glycine, alanine, valine, and leucine, $r = 0.998$, $\text{rms} = 0.11$. 

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6. Conclusion
Application of topological indices for the prediction of values of stability constants of coordination compounds provides a simple and efficient tool for evaluating experimental data and planning future experiments. We hope that this short introduction will move the chemists, engaged in determination of stability constants, to use our method.

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