1 Research project objectives/ Research hypothesis

This project aims to initiate research that can solve the problem of measuring the geometry of the molecules in solution through the use of appropriate dynamic combinatorial library (DCL) with advanced data analysis using artificial neural networks (ANN). In this project, a set of model compounds (templates) will consist of dicarboxylates, and DCL will provide a set of multiple macrocyclic anion receptors systematically varying in size. The changes in the composition of the library induced by the addition of the template reflect the interactions between library products and the template, while this interactions depend on the molecular geometry attainable by the template. The structure of the template can thus be translated in a simple experiment into the composition of DCL.

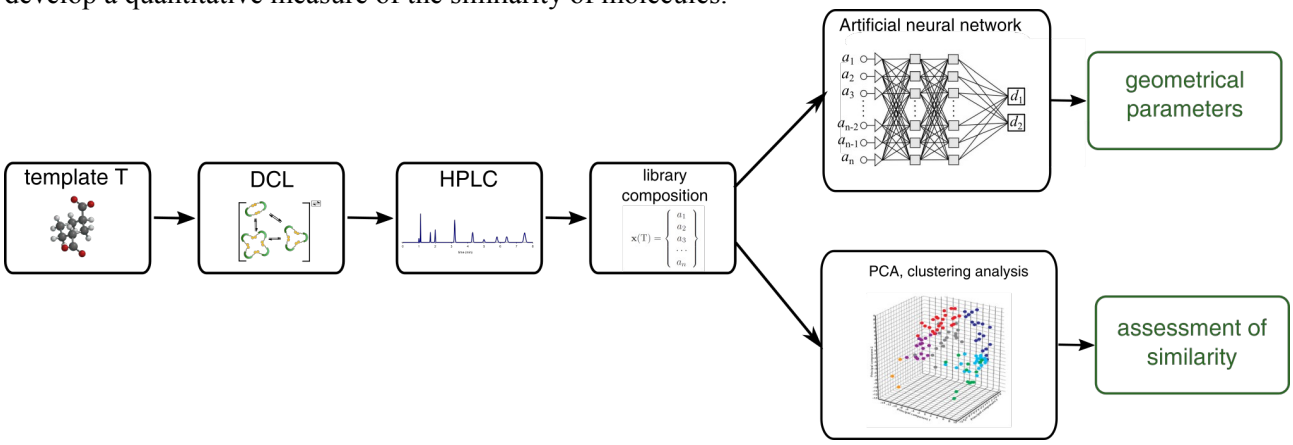
In this project I plan to determine the mathematical method (neural network) that allows to decode the geometrical parameters of any dicarboxylate based on its impact on the DCL. In addition, using data mining techniques I will describe the similarities between different dicarboxylates based on induced library compositions.

2 Research project methodology

Dynamic combinatorial library will consist of macrocyclic oligomeric anion receptors formed of simple building blocks which are consecutive homologues. The equilibrium in the system will be obtained via disulfide exchange. The various components of the library, in particular dimers, will form a series of macrocycles which systematically differ in size. The template (dicarboxylate) will be effectively bound only by the selected components of the library, whose concentration in the library will thus increase. The composition of native and templated library will be determined by HPLC.

In the first stage of the project a set of 15 templates with a rigid structure and a well-defined geometry will be used. By analyzing their impact on the DCL I will create and train a neural network method for decoding the template's geometrical parameters from the library composition. Next, this method will be applied to the group of dicarboxylates with flexible linkers between their functional groups to validate the effectiveness the method.

The results obtained for all templates will undergo data mining. By using the methods of cluster analysis (k-means and principal component analysis) I will be able to determine classes of compounds which interact similarly with DCL components, which means that they may have some common properties. I will also develop a quantitative measure of the similarity of molecules.



3 Expected impact of the research project on the development of science, civilization and society

Accurate knowledge of the geometry of the molecules in solution and in conformations favorable for intermolecular interactions is crucial in the search for new biologically active substances and in material science. None of the existing spectroscopic or computational methods can accurately determine the geometry of flexible molecules with high conformational freedom. The combination of dynamic combinatorial chemistry with artificial neural network suggested in this project, should solve this problem and provide information about the spatial structure of molecules interacting with the library. Ultimately, this will create a method of analysis characterized by unambiguity, high precision and high throughput which will extend the existing database used in medicinal chemistry and material science.

In addition, the results of the project will significantly increase our knowledge on supramolecular interactions, especially the geometrical match between the components of the complexes. It will also develop the branch of organic chemistry dealing with dynamic and reversible systems, which are crucial for fully understanding the biochemical processes.