Most of chemical compounds that we know are organic molecules, so that they consist of carbon and hydrogen atoms as the basic building blocks. Besides of them, oxygen, nitrogen and sulfur are the other important elements. They form, together with carbon and hydrogen, so-called functional groups, i.e. connections of atoms accounting for activity and functionality of given molecules, e.g. amino acids, carbohydrates, vitamins, etc. A sizeable part of functional groups is able to reversible process of binding and releasing of hydrogen atom in solution, thereby they may occur in the neutral or charged forms. In the case of groups defined as acidic, the neutral form has a bounded hydrogen, and after its losing (dissociation) the negatively charged form is created. The basic groups, in turn, are positively charged after binding of hydrogen and neutral after its losing. Ability of given group to undertake this process, in other words the strength of hydrogen binding by this group in solution, is characterized by the acid dissociation constant – pK_a. It tells us in which state the group occurs at the given pH of environment. pK_a value is one of the crucial parameters that characterizes physicochemical properties, e.g. solubility of molecules or capability to interactions with other molecules. The pK_a value is valid for particular functional group in particular molecule, and it may change upon interactions with other compounds that result in formation of the specific interconnection (complex). The aim of this project is examination of possible changes in pK_a values for the chosen compounds, and identification of basic factors that have a bearing on these phenomena (explanation of their mechanism).

The basic research planned in this project will consist in optimization and application of new methods for examination of pK_a variability and determination of related parameters, as dissociation enthalpy and entropy. To this aims, the capillary electrophoresis will be used as an experimental tool. The Applicant specializes himself in development of new bioanalytical methods utilizing capillary electrophoresis. The pK_a shifts will be studied for 3 classes of compounds: coumarin derivatives, cathinone derivatives and the chosen synthetic dyes. Cyclodextrins, cucurbiturils, calixarenes (so-called macrocycles) and albumins (natural serum proteins) will be applied as the pK_a shifts inducers (partners of interactions). The selection of these molecules has been made carefully, to provide a good model for examination of specific structural effects accounting for pK_a shifts, as e.g. formation of intramolecular non-covalent interactions. Some of the chosen compounds, in addition, have not been characterized yet as regards their pK_a value in the free state.

The subject matter of this research project has been chosen, for the reason that current knowledge on mechanisms governing pK_a shifts upon formation of intermolecular complexes is relatively little and incomplete. Especially, the project is aimed to examine how these effects depend on chemical nature of compounds, how big are differences between structurally similar molecules, and what is the role of so-called enthalpic and entropic factors. Partial answering to these questions might be crucial in future designing of fully predictable systems, i.e. in strategic pK_a tuning. Inventing of novel drug delivery systems to enhance drugs bioavailability and effectivity, tuning of properties of known substances e.g. indicators of some chemical processes, development of highly innovative separation methods, and potential advances in so-called molecular architecture, are prospective very promising applications of pK_a tuning.