

Virtually all physical and chemical phenomena concerning atoms and molecules are a result of electrostatic interactions. These interactions manifest themselves in many various forms, which is quite surprising given the simplicity of the Coulomb force (which depends only on the charges and the distances between the interacting species) and a small variety of particles (electrons and atomic nuclei) interacting *via* them. The strongest manifestation of the Coulomb force, originating from the interaction of overlapping electron clouds of neighboring atoms, is known as the chemical bond. The strength and stability of chemical bonds are to a large extent determined by electronic configurations of the participating atoms. In some cases (e.g., for nitrogen, oxygen, or carbon) the energetic effects of the atomic cloud overlap are particularly large and lead to atomic aggregates known as molecules, whereas in other cases (e.g., noble gases or mercury), they are rather weak. The extent of the electron cloud overlap is determined by the energy profile of this process usually visualized in the scientific literature in a form of a potential energy maps. The stability of molecules and their ability to take part in physical (e.g., ionization) or chemical processes (e.g., isomerization or dissociation) are determined to a large extent by the shape of the potential energy maps near the local minima corresponding to equilibrium structures of stable molecules. It turns out that also stable chemical systems (i.e., molecules) can interact with one another and undergo further chemical reactions (e.g., dimerization, $\text{NO}_2 + \text{NO}_2 \rightleftharpoons \text{N}_2\text{O}_4$ or substitution reactions, $\text{AB} + \text{CD} \rightleftharpoons \text{AD} + \text{BC}$) or physical processes (e.g., solvation or condensation). The latter phenomena, usually referred to as intermolecular interactions, lead to rather small energetic benefits. However, their ubiquity and omnipresence lead to creation of diverse aggregate structures and to appearance of various molecular phenomena such as formation of clusters in the gas phase, vapor condensation, stability of liquids, formation of molecular crystals and many more. Usually, the intermolecular interactions can be well represented considering the condensed phase as a collection of pairs of molecules; the resulting two-body (or pair) potentials constitute a standard, effective tool in studying such interactions. Indeed, for many systems such an approach is correct and does not lead to significant errors. On the other hand, there are some important classes of systems, such as liquid water, where the pair interactions are known to be responsible for only about 80% of the total interaction energy whereas the remaining portion is known to result from so-called many-body (or nonadditive) interactions, where more than two molecules have to be considered at a time. Neglecting the many-body effects leads to substantial computational errors in simulating melting or boiling points of liquid water of the order of a few dozen degrees Celsius. Since water is a very important solvent, playing an important role in many physical processes and participating in majority of chemical and biological reactions, including those in living organisms which happen in a very narrow range of temperatures (of the order of a few degrees Celsius), computational errors of the order of tens of degrees Celsius effectively disqualify the two-body model for studying biological phenomena. In case of molecular crystals formed from organic molecules, the non-additive effects are usually weaker. Pair interactions are responsible for about 95% of the total interaction energy, leading to a plausible conclusion that the non-additive effects could be safely neglected. However, molecular crystals can be packed in various arrangements that differ significantly in structure but not very much in energy. These different packing arrangements are usually characterized by quite different magnitude of non-additive effects. Only simulation methods that are able to resolve these subtle many-body effects and recover accurate energy differences between different packing structures of molecules inside a molecular crystal (so-called polymorphs), can be used for reliable prediction of the polymorphic structure that is the most stable and naturally emerges in the process of crystallization. Since molecular crystals and, more generally, molecular aggregates are materials commonly utilized in modern nanotechnology, development of a computational technique suitable for efficient and accurate modeling of non-additive effects in such systems does seem a natural next step in the development of theoretical simulation of molecules and molecular systems.

In the current proposal, we plan to develop a methodology of modeling intermolecular interactions in large systems. The first step of the proposal suggests calculating interactions in various types of molecular systems. A direct application of the developed collection of data would be a critical evaluation of usefulness of available quantum chemical methods for the purpose of modeling non-additive interaction energies in molecular aggregates. We would also develop a novel technique for computationally efficient and accurate predictions of energetic effects in such many-body interactions. Details of such a novel technique, being a natural extension of the existing models used for two-body dispersive interactions, are elucidated in the body of the proposal. The next step would involve application of the developed methodology for studying practical molecular systems, for which non-additive effects play an important role. The main role of these applications would be a clear demonstration of usefulness of the developed technique for practical usage in nanotechnology and in computer simulations of molecular systems. We hope that the computational methodology developed in this way will become useful in molecular engineering based on the methods of quantum chemistry and would lead to new exciting developments in this field.