The goal of this research project is to apply advanced techniques and develop new computational approaches for drug design, biophysics, and energy research. Three main research topics will be investigated with the intent to create more accurate methods and more efficient algorithms: rare events, non-equilibrium, and mixed quantum-classical dynamics. Progress in these areas is crucial to fulfill the potential of computer simulation as a reliable and cost-effective tool that can assist technological developments by providing microscopic understanding of the behavior of complex systems and suggesting atomic or molecular changes to steer their properties in desired directions. Enhancing computational performances and creating tools and models with this goal is one of the main objectives of the Platform Computation in the IIT scientific plan. Furthermore, the fundamental research that we propose will be developed to study a set of problems of interest in other Platforms included in the IIT scientific plan. Rare events methods will be used in combination with ab initio calculations of the electronic structure to characterize materials for solid state hydrogen storage and to understand the mechanism of their dissociation reactions (Energy storage, Platform Energy). Our simulations will aim at suggesting improvements of the operational features of these materials to match the standards required to make hydrogen an economically viable sustainable energy carrier. To accurately tackle this problem, however, existing rare events methods must be combined with quantum statistical mechanics and new methods are needed to do so effectively and accurately: developing such methods is one of the goals of our research. Mixed quantum-classical methods will be employed to understand how biological photosynthetic centers maintain and exploit quantum coherence to achieve their remarkable efficiency in capturing and storing solar energy (Energy harvesting, Platform Energy). This understanding is the first step towards developing biomimetic energy photonic devices, but it can only be obtained via advanced mixed quantum-classical methods that can describe the time evolution of the full (i.e. diagonal and off-diagonal elements) electronic density matrix including non-adiabatic effects. These methods have been recently developed in our group, and, in the course of this project, we intend to extend the investigation of their formal properties and to improve the algorithms for their implementation so as to substantially increase their efficiency. The same improved algorithms will also be used to investigate the non-adiabatic relaxation dynamics of basis of nucleic acids and amino acids pairs after photo-excitation with ultrafast UV lasers. Controlling this relaxation process might lead to designing sequences of laser pulses resulting in a very high yield of bound pairs and this, in turn, could be exploited (when the pairs are linked to DNA and proteins) to develop a highly efficient method for studying stable DNA-protein interactions (Predicting biomolecular interactions, Platform Drug Discovery, Development and Diagnostic).Non-equilibrium and rare event techniques will also be combined with bioinformatic approaches to devise original and effective strategies for rational drug design and to find novel therapeutic possibilities for existing drugs with obvious advantages for the safety of the patients and for the cost of drug's production and testing (Platform Drug Discovery). The successful completion of this project will produce methodological advances that

will be made available to the community both via their publication and by coding of the corresponding algorithms in open source packages. The results of the different applications that we will pursue will instead contribute to the specific applicative goals stated for each one of them.