Building a molecular BIO-DIODE: modeling and synthesis

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The comprehension of the driving forces which determine the protein folding from a linear sequence remains a major theoretical challenge. On the other hand, we assisted to an increase of both resolved protein structures and available data. Moreover, the synthesis of peptides and of small structures has provided relevant insights, allowing to test structural hypotheses and to suggest new ones. The *ab initio* design and the synthesis of organic-biological structures has recently received a growing interest. In general, all these structures refer to soluble systems, due to the difficulties to handle membrane systems. To-date, the increasing level of understanding of natural membrane systems, together with the relevant performances of the computational platforms, allow a simulation approach on realistic model systems.

The aim of this project is to realize a synthetic bio-diode able to display the electron transfer property of the emulated natural system (i.e. the photosynthetic reaction centre of bacteria). This molecule can represent the basic element for a miniaturized bio-electronic device. The system is designed to be immobilized in a lipid membrane.

We carried out simultaneous modeling and experimental activities, using the model results to drive the complex experimental part.

The system is based on a proteic scaffold constituted by two peptidic chains. The donor-acceptor electron system is constituted by a heme group and a naphthoquinone. As the assembled structure should be placed into a lipidic system, the sequence and the length of the proteic scaffold has been purposely selected. An initial sequence based on the current know-how of protein structures has been written and built using as starting point the backbone coordinates of two natural helices assembled with an heme group. After, it has been minimized, solving special problems connected with the presence of a heme group containing an ion. The resulting pdb file has been controlled by PROCHECK and used as input for GROMACS for further minimization, in view of the insertion in a simulated membrane.

At the end of the structure optimization in vacuo, a MD simulation in a lipid bilayer will be performed to analyze the stability of the system, its adhesion property, the effects of the insertion in the physical properties. Nanosecond Molecular Dynamics simulations of membrane proteins in an explicit bilayer plus water environment are now feasible using high performance computing platforms.

At the same time, the proteic portion of the system has been synthesized by SPPS (Solid Phase Peptide Synthesis), purified and preliminary tested. The results concerning the simulation of various acceptor groups will drive in assembling the complete structure.