SUMMARY OF THE THESIS

This habilitation thesis presents the results of computational biology. These results can be grouped into four categories: contributions to highlighting nonlinear dynamics of proteins, contributions to elucidating aspects of the fractal structure of proteins, contributions to emphasizing specific aspects of diffusion and biochemical reactions in crowded environments and contributions to molecular modeling of proteins-ligands interactions and bioinformatics analysis of structural aspects of proteins respectively. Not least, among my concerns is also an ongoing contribution to develop the field of computational biochemistry in Romania by disseminating, illustrating and facilitating the understanding of teaching methods of this area at the university level.

My contributions to highlight nonlinear dynamics of proteins consist in revealing the applicability of the nonlinear dynamics concepts for studying structural and functional proprieties of proteins. The results refer to the evidence of the presence of long-range correlations in the physico-chemical properties of the amino acids in protein sequences and the presence of attractors for the series of the spatial coordinates of the atoms in the main chains of different proteins and also for the flexibility parameters and the temperature factors of the protein chains. All these results reveal that packing of the spatial structure of proteins and the spatial fluctuations of their atoms are nonlinear dynamic processes.

The contributions to elucidate the fractal aspects of the structure of proteins refer to highlighting the fractal aspects of proteins backbones that are different locally and globally illustrating that the rules governing the local and global packaging of protein structure are distinct. They also emphasize the fractal aspects associated to the mass of proteins that allow appreciation of the packing degree of protein structure and also the fractal aspects of protein surfaces, illustrating the packing density of the protein structure and the interactions that the protein may develop. The revealed fractal aspects of investigated proteins correspond to their structural and functional classes illustrating the applicability of the fractal geometry concepts for studying the structure and dynamics of proteins.

Concerning the contributions in the field of diffusion and biochemical reactions taking place in crowded environments, they have resulted in proposing a new equation to describe the fractal-like kinetics of enzymatic reactions and in the adaptation of the algorithm for simulation of biochemical reactions in 2D and 3D lattices with obstacles and *off lattice* simulations respectively. They also contributed to revealing the effects of the concentration, size and mobility of the obstacles on the diffusion and biochemical reactions taking place in

crowded environments. We have also exposed that in crowded environments, the diffusing particles have fractal trajectories. Furthermore, I have participated in experimental studies that reveal peculiarities of the enzyme kinetics in crowded environments.

My contributions to the field of molecular modeling of protein-ligand interactions and bioinformatics analysis of structural aspects of proteins are the followings: (i) the development of knowledge regarding interactions of proteins with lipids present in the cell membrane underlining the main forces that govern these interactions; (ii) the prediction of the interactions of enzymes present in the soil with pesticides revealing the inhibitory potential of pesticides on the enzymatic activity in the soil and underlying the need to use pesticides with caution; (iii) the prediction of the interactions of the subfamily 2C of the human cytochrome P450 with xenobiotics illustrating the inhibitory potential of xenobiotics with direct implications on the metabolism of various drugs used for the treatment of cardiovascular diseases, cancer, diabetes, and other diseases; (iv) the illustration of the advantage obtained by the use of NMR structural assemblies to take into account the flexibility of the protein in molecular docking studies; (v) the prediction of secondary structure elements and disordered regions of proteins that do not have three dimensional structures and to obtain homologous structural models for them, characterization of the structure and surfaces of various classes of proteins, identification and characterization of the properties of the cavities on the proteins surfaces with application for understanding and predicting the interactions with various ligands.

Although fewer, my studies on the development of the field of computational biochemistry have resulted in the dissemination of experience in the use of databases and the teaching methods for computational biochemistry in order to facilitate the understanding of these methods and to contribute to enhancing the Romanian community activating in this field.