# Abstract of Habilitation Thesis

This habilitation thesis presents the main scientific achievements of the candidate since 2008, when he sustained his PhD thesis at the Budapest University of Technology and Economics, in the field of biomedical engineering. The new scientific contributions represent the achievements of two postdoctoral assignments. The first one was performed at the Petru Maior University of Târgu Mureș (October 2011 – March 2013), while the second one took place at the University of Fribourg, Switzerland (April 2013 – March 2014), and was supported by the Swiss Scientific Exchange Program (Sciex).

The thesis is organized on two sections. The first chapter entitled "Unsupervised classification of protein sequence databases using the fast Markov clustering method" presents new ways to efficiently and accurately solve the problem of clustering large protein sequence data sets, based on previously evaluated pair-wise similarity criteria. This task was achieved by proposing several enhancing modifications to the TRIBE-MCL method.

The second chapter entitled "A patient specific multi-level electro-mechanical heart model" presents a patient specific deformable heart model, whose behavior is evaluated for normal and various pathological cases. The main goal was to enhance the precision, accuracy, robustness, and execution speed of the spatial heart modeling. This task had to be accomplished by an accurate simulation and visualization of the monitored biological parameters that otherwise could not have, or hardly could have been measured.

The main scientific achievements presented in this thesis are the following:

Chapter I:

- A detailed analysis of the TRIBE-MCL algorithm was given, presenting generalization schemes for all operations performed in the main loop, aiming at efficient execution.

- An optimal scheme for reordering rows and columns in the similarity matrix was proposed, transforming it into a matrix with several compact blocks along the diagonal, and zero similarities outside the blocks. This method was named matrix splitting version of TRIBE-MCL.

- An efficient version for the TRIBE-MCL algorithm was proposed, which employed sparse matrix representation based on double chained lists. This version of the algorithm is suitable for parallel execution.

- A special sparse matrix structure (SSM) was proposed which stored nonzero similarity values in arrays. The Markov clustering algorithm based on this novel structure reduced the total runtime by two orders of magnitude.

- Several optimization schemes of the previous solution were introduced, which modified SSM in terms of efficiently handling most operations of the main loop.

- Taking advantage of the symmetry of the similarity matrix, an asymptotically faster sparse matrix squaring formula was developed to facilitate the time consuming expansion.

- A quick and memory-efficient implementation of the TRIBE-MCL clustering algorithm was developed that is suitable for accurate classification of large-scale protein sequence data sets.

- An ultimate efficient approach to the graph-based TRIBE-MCL clustering method was proposed, enabling a regular personal computer to process a graph of one million nodes in reasonable time.

- A novel method was proposed to create synthetic test data sets for the TRIBE-MCL algorithm. This is a useful tool at testing the clustering on data sets of any desired size. Based on a thorough investigation of the SCOP95 protein data set, the proposed method can generate sparse similarity matrices of any reasonable size, which holds the properties of the SCOP95 similarity matrix (BLAST), without having actual protein sequences at the foundation.

Chapter II:

- It was developed a regulation model of ionic concentrations for hypoxia. Using this model the effects of deep hypoxia on ventricular cell metabolism and activation potential were investigated.

- It was investigated the phenomena of ion conductance modification, generated by the improper functionality of the ion channels in case of hypoxia. It was established that these malfunctions may yield dangerous modification in activation potential function.

- It was realized a new energetic extension of the Luo-Rudy cardiac cell model that may throw new light upon the development process of ischemia that can enforce various cardiac rhythm malfunctions such as ventricular fibrillation.

- It was demonstrated by cellular metabolism modeling the imperial role of mitochondria. The development of a mitochondria model enhanced the understanding of deep hypoxia phenomena.

- It was performed the computerized simulation of fibroblasts that provides a better estimation of cardiac excitation, which may help to uncover the formation steps of arrhythmia. This non-invasive tool may elucidate the development of dangerous arrhythmias.

- It was emphasized the importance of aging phenomena in the cardiac activity. The created simulation environment illuminates the most important anatomical and physiological changes occurred with aging, such as reduced pumping activity and increased mechanical load, caused by the stiffed cardiac muscle and reduced arterial flexibility.

- It was created a simulation environment to show the effects of artificial cardiac tissue. From the results of this simulation it was concluded that the artificial tissue may

enhance the cardiac pumping function, but also may increase the chance to develop arrhythmias.

- It was modeled the development phenomena of spiral waves that yields ventricular fibrillation. Computerized simulation of SW represents a non-invasive visualization tool than helps to understand the inner cardiac depolarization-repolarization process in normal and various pathological cases. An adequate simulation platform may select the most endangered patients by a non-invasive method that can enhance the efficiency of health care.

- The proposed computerized simulation of cardiac dynamics, using various spatial and temporal resolutions, provides a better appreciation of cardiac excitation and reentry wave development. An adequate simulation platform may be used to recognize the most dangerous situations, thus contributing to the efficiency of computerized health care.