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Dynamics of proteins with knots, cavities and cellulosomal proteins

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The main goal of this thesis is to use theoretical methods to infer about the properties of proteins that contain either knots, or cavities, or are components of the cellulosome.

The first chapter introduces the reader to the theory of molecular dynamics used to obtain the results presented in the thesis.

In the second chapter we describe the theoretical tests of mechanical protection strategy in the protein nanomechanics. We characterize the behavior of several systems with different kinds of connectivity and we determine the conditions for the optimal application of the method. Furthermore, we interpret the experimental results on stretching.

The third chapter is about knotted proteins. At the beginning we explain what exactly knots are and how to describe them. In the next step we search for their role in proteins structures by conducting simulations of proteins stretching with constant force and by analyzing their thermostability. We examine the impact of water-air interface on proteins. Finally, we set a very ambitious goal. Namely, we try to understand the process of proteins knotting and folding and we detect the mechanisms responsible for it. We find the necessary conditions for a protein to be able to to properly fold into its knotted form. We demonstrate that this process is managed by the potential energy distribution. In the end we characterize the impact of ribosome structure presence on simulations. We show that it changes the pathways of proteins folding and we describe a new mechanism of proteins knotting.

In the fourth chapter we focus on proteins and complexes containing cavities within their structures. At the beginning we describe geometrical, thermodynamical and mechanical parameters of pathogenesis-related proteins. We try to answer the question about the cavity function. We describe the new algorithm SPACEBALL which was created for detection, description and calculation of the proteins cavity volume. In the next step we apply it to determine the volume of

cavities in virus capsids. This problem is very important because structures of this kind with cavities large enough may be candidates for a carrier of a genetic material in genetic therapy. In the end we use this program for the calculations of the amino-acids volume and we make a list of effective radii which may be used in the molecular dynamics.

The last chapter begins with a description of the biophysics of cellulosome. We introduce a new method of side chains reconstruction based on statistical approach. Next, we describe a new method of fixing the structure of cohesin domain c7A of scaffolding in *Clostridium thermocellum*. In the last step we characterize our efforts to improve the mechanical and thermodynamical biocatalyst stability.

The dissertation is briefly summarized in the last chapter where we refer to the published but not described in the main text results.

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