
Preface

In the following the results of my Ph.D. thesis work, carried out at the Max Delbrück Center for Molecular Medicine (MDC) and at the Research Institute for Molecular Pharmacology (FMP) in the laboratories of Profs. Udo Heinemann and Hartmut Oschkinat, respectively, are presented. This dissertation is organized in five main chapters. Chapter 1 is a general introduction to molecular cell biology with a focus on cell-cycle regulation, DNA damage signaling and the molecular basis for cancer development. Chapter 2 describes the biochemical and structural biological methods with an emphasis on both the rational background and the experimental strategy. Chapters 3 and 4 show the results of the structure determination of two unrelated proteins by means of NMR spectroscopy and X-ray crystallography, respectively. Summary and concluding remarks of this thesis work are given in Chapter 5.

The results of this research work have been published in three scientific "papers" which are included in Chapter 5. The publications cover all major points of this work but additionally contain statistics and other detailed information which are not explicitly accounted for in this dissertation for reasons of brevity. Vice versa, results that made it not into the publications due to the limited space, including some new aspects of the fields, are shown and discussed in more detail in this dissertation. Thus, this dissertation on the one hand and the scientific publications on the other contain to some extent complementary information.

The Appendix represents a two-part introduction to protein structure and function. It provides additional information for the more interested reader with the focus on new developments in structural biology and related fields I encountered (and got into) during my thesis work, including some aspects hardly found yet in standard textbooks. The first part is a brief introduction to X-ray crystallography and NMR spectroscopy, covering also the principles of protein folding and the concept of energy landscapes. Cross validation methods and reliability assessment of structural models are also addressed, as well as structure prediction and design of (small) proteins. The second part briefly describes the fundamental principles of enzymatic catalysis, including the central role of RNA enzymes (ribozymes) for molecular evolution and the development of living systems on earth.

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