

PREFACE

The present thesis is comprised of two parts. In the first section the nature of hydrogen bonds in the receptor–ligand interface is addressed through statistical analysis carried out on X-ray structures of known receptor–ligand complexes. The second part of the thesis deals with the implementation of molecular modeling techniques to identify novel inhibitors for two therapeutically important targets *in silico*. Essentially the aim of the thesis is to understand the basic nature of receptor–ligand recognition through statistical and molecular modeling studies, which in turn will help to design better and safer drug molecules.

The hydrogen bond is a unique phenomenon in structural chemistry and biology. The critical role of hydrogen bonds is unanimously accepted ever since its inception about 90 years ago. Study on hydrogen bonding is an ever-green area of research in various spheres of chemistry and biology. Hydrogen bonds are manifested in a variety of ways. This multifaceted nature of hydrogen bonds fascinates scientists even today. In this context, the study of hydrogen bonding in the receptor–ligand interface is an active area of research. Chapter 1 gives an overview of strong and weak hydrogen bonds in biology. Chapter 2 describes a software for the analysis of hydrogen bonds in X-ray structures of macromolecules. Chapters 3, 4, and 5 respectively examine the nature of hydrogen bonds in a diverse set of protein–ligand complexes, complexes within the kinase family, and drug–DNA complexes, using this software.

The recent advancements in computational power and a better understanding of the molecular world have revolutionized present day’s research in chemistry and biology. Molecular modeling and its application in drug design has reached great heights in the past few decades. The second part of the thesis deals with the optimal use of a collection of rational drug design techniques to identify potential drug candidates. Chapter 6 provides an overview of molecular modeling methods with special emphasis on pharmacophore modeling. Chapters 7 and 8 portray application of pharmacophore modeling and virtual screening in two therapeutically important targets, namely cancer and Alzheimer’s disease. Chapter 9 is a brief conclusion of the work and gives some future perspectives.

The extended information related to chapters 3, 7, and 9 is presented in appendix I, II, and III respectively.

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