Preface

Transmissible spongiform encephalopathies (TSEs), also known as prion-related diseases, are a group of infectious, fatal neurodegenerative disorders for which there is no cure, treatment, or early diagnosis. TSEs are dramatic diseases that rapidly, progressively, and inexorably destroy the cognitive, motor, and sensorial skills that are the essence of human beings. At the molecular level, the disease is likely caused by the misfolding of the prion protein, which accumulates in the brain and produces neurodegeneration. Several unprecedented scientific findings, which have directly confronted popular dogmas in biology, have put prion research in the spotlight. The experimental evidence strongly supports an entirely novel disease mechanism, involving disease transmission by replication of the misfolding of a single protein in the absence of nucleic acids. The popularity of prion diseases is also due to the panic produced by the recent appearance of a new human disease (variant Creutzfeldt-Jakob disease) that is transmitted by eating meat contaminated by bovine spongiform encephalopathy (BSE), better known as mad cow disease. Because of insufficient information available regarding the incubation time and the actual level of exposure to the contaminated material, it is impossible to make any well-founded prediction about the future of this nascent epidemic.

This book attempts to combine a detailed and up-to-date description of the state of the knowledge in the field with an intriguing but tempered speculation of the putative implications of the findings to our current understanding of biology. During the last few years we have begun to perceive the broader implications of the heretically attractive prion concept of transmission of biological information by propagation of alternative protein folding. I hope that this book can contribute to liberating the imagination of the reader to see the new scientific world opened by prions, which impact broader areas of biology, public health, and biotechnological strategies for therapy and diagnosis.

Although I regretted it many times during the long process of preparing this book, I decided to write it entirely myself in order to give continuity to the text, maintain a homogenous style, and provide an appropriate connection between chapters. The decision was also guided by a desire to avoid important gaps and repetitions, which are frequent in multiauthored books. I could not have completed this book without the constant support of my

family, lab members, and close collaborators. To them I extend my sincere gratitude for their patience, help, and illuminating discussions.