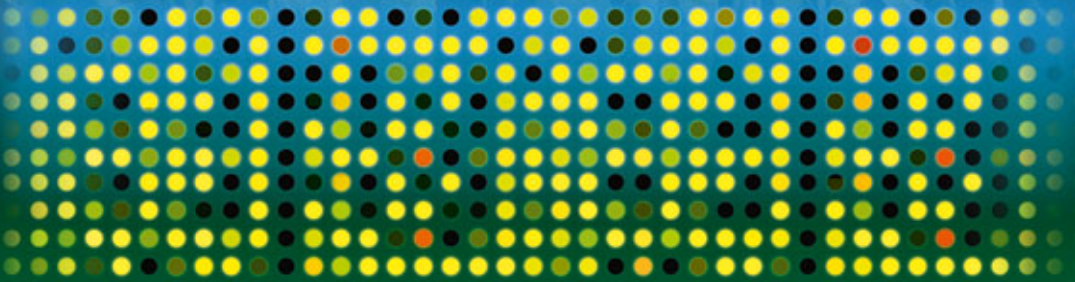


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*Edited by Peter Jeschke, Wolfgang Krämer,
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Modern Methods in Crop Protection Research



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Preface

Today, modern agriculture is facing an enormous challenge – namely, that it ensure that sufficient high-quality food is available to meet the needs of a continuously growing population.

In 2011, the world's population exceeded seven billion people, and a prognosis by the United Nations has suggested that by the year 2050 – assuming moderate birth rates – this will increase to as many as 9.1 billion.

Beyond that, losses of agriculturally usable land, climate change, and changes in the eating habits of the peoples of newly industrialized countries will require major improvements to be made in agricultural productivity. In addition to the increasing demand for food in general, people are today requesting a greater protein intake, especially in countries undergoing transition, and this in turn will lead to a higher consumption of the cereals required as feed used for meat production. Coincidentally, these changing food demands are meeting new requests for bioenergy to be produced via agriculture. Climatic changes that influence the distribution of weeds, pests, and diseases, and their prospective consequences for agriculture, represent a further challenge for crop protection. Change in seed breeding and genetically modified (GM) crops demonstrate progressive solutions for better supplies of food by employing technological innovations from both biochemistry and biotechnology. Nevertheless, the traditional research and development of crop protection compounds remains the most effective method for combating losses in agricultural yields. Currently, such losses are in the range of 14% due to competition by weeds, 13% due to damage by fungal pathogens, and 15% by insect damage.

Another very important reason for employing crop protection compounds is to improve the quality of food. For example, mycotoxins produced by species of *Fusarium* (a fungus that causes damage to the ears of wheat) lead to increasing problems in food production. In addition, changes in rainfall, temperature, and relative humidity can each favor the growth of fungi that produce mycotoxins, so that crops such as groundnuts, wheat, maize, rice, and coffee may become unsuitable for consumption by both humans and animals. Thus, the need for effective research into new crop protection compounds can be fulfilled only by introducing new scientific approaches within the methodology of seeking new active ingredients, by improving the identification process of new targets, by studying aspects of

bioavailability, and by improving the tools applied to risk assessment studies of toxicological and ecotoxicological aspects, utilizing new technologies.

This book, which is based partly on *Part IV: New Research Methods* of the First Edition of the textbook *Modern Crop Protection Compounds* (Wiley-VCH, 2007), provides details of the progress that has been made during the past few years towards new methods in modern crop protection research. This includes progress not only in chemical synthesis but also in physico-chemical research, the use of biological research progress and the knowledge and application of genetics and proteomics, and the use of mathematical methods in the design and risk assessment of new active ingredients. Consequently, this book will reflect the exclusively broad field of research in the areas of chemistry, biology, biochemistry, formulation research, toxicology, and ecotoxicology that have been used to identify and develop new chemical tools, such that “green” technology can enjoy further success.

The book, which provides a broad overview of a range of current methods used in modern crop protection research, is divided into four Parts that incorporate 15 chapters, each written by renowned experts at the R&D divisions of major agrochemical companies.

Part I presents methods for the design and optimization of new active ingredients. By using modern research techniques and serendipitous, highly specific biological screening systems, significant progress has been achieved during the past 25 years in computational methods for lead identification and optimization, based on molecular structure information and/or quantum chemistry. Additionally, *in-silico* toxicology approaches to estimate specific risk profiles of agrochemicals will have an emerging impact in the future. In the search for a so-called “optimal product” in modern crop protection in terms of efficacy, environmental safety, user friendliness, and economic viability, the halogen substitution of active ingredients is increasingly recognized as a very important tool.

In Part II are described new methods for identifying the modes of action of active ingredients. Reverse-genetic approaches such as RNA interference (RNAi) offer useful tools to elucidate modes of action, to identify novel targets for exploitation, or to help create new generations of crop protection technologies. For several years, the rapid identification of herbicidal modes of action has been possible via gene expression profiling, using DNA chips. An elucidation of the target sites of neuromuscular insecticides at an early stage in their discovery and development can play an important role in the prioritization of selected candidates. However, despite great technological progress having been made, the targeted discovery of novel fungicides remains an immense challenge because of the restrictions that have been posed on new active ingredients by the obligatory physico-chemical properties permitting a sufficient bioavailability that will, in turn, guarantee fungicidal activity.

In Part III, new methods are examined to improve the bioavailability of the active ingredients. According to novel trends in application technologies, an innovative formulation comprises a mixture of various molecules, besides the active ingredient. In this context, the influence of polymorphism and the organic solid state on the quality and efficiency of agrochemicals plays an important role. Molecular

descriptors, as defined by Abraham, can be used to set up linear free energy relationships (LFERs) of relevance to agrochemical research and environmental fate.

Finally, modern methods for risk assessment are addressed in Part IV. Today, many tools are available that can be used to assimilate the knowledge required to evaluate human health and environmental safety, such as exposure modeling, *in vitro* models to evaluate phenotypic and gene expression changes, computational toxicology, bioinformatics, and systems biology. Despite its complexity and a lack of experience of its use, environmental effect modeling has a great potential for regulatory risk assessments with modern crop protection products, although at present its use is not yet fully accepted. In Chapter 14, entitled *Safety Evaluation of New Pesticide Active Ingredients: Enquiry-Led Approach to Data Generation*, attention is focused heavily on advances in molecular biology and biotechnology, and how these may be used in conjunction with computational toxicology and bioinformatics to make toxicity testing more relevant to low-level human exposures, to reduce the need for *in-vivo* testing in animal models, and to make the whole process of hazard data generation quicker and less expensive. In parallel, an evaluation of the endocrine disruption definition and screening aspects in light of the European Crop Protection Law has led to a proposal for decision criteria for endocrine-disrupting compound (EDC) regulatory agencies. This aspect is discussed, taking into consideration the scientific needs of the near future.

We hope that this book will prove to be an invaluable source of information for all of those people working in crop protection science – whether as governmental authorities, as researchers in agrochemical companies, scientists at universities, conservationists, and/or managers in organizations and companies involved with making improvements in agricultural production – to help nourish a continuously growing world population, and to advance the production of bioenergy.

Note

Within this book the authors have named the products/compounds preferably by their common names. Although, occasionally, registered trademarks are cited, their use is not free for everyone. In view of the number of trademarks involved, it was not possible to indicate each particular case in each table and contribution. We accept no liability for this.

May 2012

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