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Nota di contenuto	 Biosimulation in Drug Development; Contents; Preface; List of Contributors; Part I Introduction; 1 Simulation in Clinical Drug Development; 1.1 Introduction; 1.2 Models for Simulations; 1.3 Simulations in Clinical Drug Development: Practical Examples; 1.3.1 Predicting the Outcome of Phase I Studies of Erythropoietin Receptor Agonists; 1.3.2 Simulations for Antimicrobial Dose Selection; 1.3.3 Optimizing the Design of Phase II Dose Finding Studies; 1.3.4 Predicting the Outcome of Phase III Trials Using Phase II Data; 1.4 Conclusions; 2 Modeling of Complex Biomedical Systems; 2.1 Introduction 2.2 Pulsatile Secretion of Insulin2.3 Subcutaneous Absorption of Insulin; 2.4 Bursting Pancreatic -Cells; 2.5 Conclusions; 3 Biosimulation of Drug Metabolism; 3.1 Introduction; 3.2 Experimental Approaches; 3.2.1 Animal Test Models; 3.2.2 Microbial Models; 3.3 The Biosimulation Approach; 3.4 Ethical Issues; 3.5 PharmBiosim - a Computer Model of Drug Metabolism in Yeast; 3.5.1 General Concept; 3.5.1.1 Chemical Abstraction; 3.5.1.2 Biological Abstraction; 3.5.2

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	Initial Steps - Experimental Results; 3.5.2.1 Dehalogenation (Pathways II and III); 3.5.2.2 Retro-Claisen Condensation (Pathway IV) 3.5.2.3 Ester Hydrolysis (Pathway VI)3.5.2.4 Competing Pathways and Stereoselectivity; 3.6 Computational Modeling; 3.6.1 Selection of the Modeling Software; 3.6.2 SBML-compatible Software; 3.6.2.1 Cellware; 3.6.2.2 Copasi; 3.6.2.3 Ecell; 3.6.2.4 JigCell; 3.6.2.5 JSim; 3.6.2.6 Systems Biology Workbench; 3.6.2.7 Virtual Cell; 3.6.2.8 XPPAUT; 3.6.3 CellML-compatible Software; 3.6.4. X Kinetic Model; 3.6.4.1 Methods; 3.6.4.2 Model Derivation; 3.6.4.3 Results; 3.6.5 Stoichiometric Model; 3.6.5.1 Methods; 3.6.5.2 Model Derivation; 3.6.5.3 Results 3.7 Application of the Model to Predict Drug Metabolism3.8 Conclusions; Part II Simulating Cells and Tissues; 4 Correlation Between In Vitro, In Situ, and In Vivo Models; 4.1 Introduction; 4.2 Biophysical Models of Intestinal Absorption; 4.2.1 Colon; 4.2.2 Small Intestine; 4.2.3 Stomach; 4.3 Influence of Surfactants on Intestinal Permeability; 4.3.1 Absorption Experiments in Presence of Surfactants; 4.3.1.1 Colon; 4.3.1.2 Intestine; 4.3.1.3 Stomach; 4.4 Modeling and Predicting Fraction Absorbed from Permeability Values; 4.4.1 Mass Balance, Time- independent Models 4.4.2 Prediction of the Fraction of Dose Absorbed from In Vitro and In Situ Data4.4.3 Prediction from In Situ Absorption Rate Constant Determined with Closed Loop Techniques; 4.4.5 Prediction from Permeabilities Through Caco-2 Cell Lines; 4.4.5 Prediction from Permeabilities Through Caco-2 Cell Lines; 4.4.5 Prediction from Parameters; 4.5.1 In Situ Parameter Estimation; 4.5.2 In Vitro-In Situ Correlation; 5 Core-Box Modeling in the Biosimulation of Drug Action; 5.1 Introduction; 5.2 Core-Box Modeling; 5.2.1 Shortcomings of Gray- Box and Minimal Modeling 5.2.1.1 Full-Scale Mechanistic Gray-Box Modeling
Sommario/riassunto	This first comprehensive survey to cover all pharmaceutically relevant topics provides a comprehensive introduction to this novel and revolutionary tool, presenting both concepts and application examples of biosimulated cells, organs and organisms.Following an introduction to the role of biosimulation in drug development, the authors go on to discuss the simulation of cells and tissues, as well as simulating drug action and effect. A further section is devoted to simulating networks and populations, and the whole is rounded off by a look at the potential for biosimulation in industrial dru