



Universiteit
Leiden
The Netherlands

Model-informed design of antibiotic therapy against antimicrobial resistance

Tandar, S.T.

Citation

Tandar, S. T. (2026, May 27). *Model-informed design of antibiotic therapy against antimicrobial resistance*. Retrieved from <https://hdl.handle.net/1887/4304248>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/4304248>

Note: To cite this publication please use the final published version (if applicable).

Model-informed design of antibiotic therapy
against antimicrobial resistance

Cover design: Sebastian Tandar

Thesis lay-out: Sebastian Tandar

Printed by: ProefschriftMaken | www.proefschriftmaken.nl

© Sebastian Tandar, 2026

ISBN: 978-94-6534-402-7

All rights reserved. No part of this book may be reproduced in any form or by any means without permission of the author.

Model-informed design of antibiotic therapy against antimicrobial resistance

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof.dr. S. de Rijcke,
volgens besluit van het college voor promoties
te verdedigen op woensdag 27 mei 2026
klokke 10.00 uur

door

Sebastian Tommi Tandar

Promotor Prof. dr. J. G. C. van Hasselt
Co-promotor Dr. L. B. S. Aulin
Promotiecommissie Prof. dr. M. van Eck
Prof. dr. E. C. M. de Lange
Prof. dr. B. C. P. Koch
University Medical Center Groningen
Prof. dr. R. Regoes
ETH Zürich
Prof. dr. D. E. Rozen
Prof. dr. C. A. J. Knibbe

The research described in this thesis was performed at the Systems Pharmacology and Pharmacy division of the Leiden Academic Centre for Drug Research (LACDR), Leiden University (Leiden, The Netherlands). The research was financially supported by the Lung Foundation (Longfonds).

Contents

Chapter 1 Introduction	3
Section I: The Pharmacodynamics of Antibiotics and Resistance Evolution	
Chapter 2	Teicoplanin dose individualization: insights from the hollow fibre infection model 15
Chapter 3	Semi-mechanistic modeling of resistance development to β -lactam and β -lactamase-inhibitor combinations 41
Chapter 4	Interspecies interactions alter the antibiotic sensitivity of <i>Pseudomonas aeruginosa</i> 65
Section II: From PK-PD to Clinical Dose Optimization	
Chapter 5	Model-based optimisation for teicoplanin dosing in patients undergoing maintenance haemodialysis 99
Chapter 6	Physiologically-based modelling framework for prediction of pulmonary pharmacokinetics of antimicrobial target site concentrations 121
Chapter 7	Computational Framework for Multi-Objective Optimization of Population Dosing Regimens 143
Section III: Collateral Sensitivity	
Chapter 8	Clinical prevalence of collateral sensitivity: a systematic exploration of multi-center antimicrobial surveillance data 175
Chapter 9	Divergent spontaneous antibiotic-resistance evolution confers reciprocal and exploitable collateral sensitivity effects 201
Chapter 10	Collateral sensitivity-based antibiotic combination regimens to prevent resistance in <i>Pseudomonas aeruginosa</i> 231
Chapter 11 General Summary and Discussion	259
Synopsis	275
Samenvatting	279
Acknowledgement	282
Curriculum Vitae	283
List of Publications	284

