Model-informed design of antibiotic therapy against antimicrobial resistance

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Curriculum Vitae

Sebastian Tandar was born in Palembang, Indonesia, in 1995. He obtained his Bachelor's degree in Bioengineering from Osaka University, Japan, in 2019, where he worked on a thesis entitled Optogenetic switch for controlling the central metabolic flux of Escherichia coli under the supervision of Prof. Hiroshi Shimizu and Dr. Yoshihiro Toya.

In 2019, he moved to The Netherlands to pursue a Master's degree in Bio-Pharmaceutical Sciences at Leiden University. During this programme, he joined the Quantitative Pharmacology group under the supervision of Prof. dr. Coen van Hasselt and Dr. Linda Aulin. His Master's thesis focused on semi-mechanistic modeling of resistance development to β-lactam and β-lactamase inhibitor combinations. During his Master's programme, he also completed an internship at Galapagos BV, where he worked on pharmacokinetic-pharmacodynamic (PK-PD)-based biomarker characterization in a clinical study. In addition, he served as the mathematical modeling lead of the 2019-2020 Leiden International Genetically Engineered Machines (iGEM) team, contributing to the development of Rapidemic, a versatile and label-free DNAzyme-based platform for visual nucleic acid detection.

In 2021, Sebastian continued in the Quantitative Pharmacology group at Leiden University as a PhD candidate, focusing on model-informed design of antibiotic therapy against antimicrobial resistance. His PhD research was conducted in collaboration with the Institute of Biology Leiden, Radboud University Medical Center (Radboudumc), Ghent University Hospital (UZ Ghent), and the Infectieziekten Surveillance Informatie Systeem-Antibiotica Resistentie (ISIS-AR) study group of the National Institute for Public Health and the Environment (RIVM). As part of his doctoral work, he presented the development of a computational framework for multi-objective optimization of population dosing regimens at the PAGE Meeting 2025 in the Stuart Beal Methodology Session. In addition to his scientific activities, he was also involved in laboratory automation development within the Quantitative Pharmacology group. Since February 2026, he has been working as an Associate MIDD Consultant at Pharmetheus.

List of Publications

Publications Related to This Thesis

Aulin, L. B. S., Tandar, S. T., van Zijp, T., van Ballegooie, E., van der Graaf, P. H., Saleh, M. A. A., Välitalo, P., & van Hasselt, J. G. C. (2022). Physiologically Based Modelling Framework for Prediction of Pulmonary Pharmacokinetics of Antimicrobial Target Site Concentrations. Clinical pharmacokinetics, 61(12), 1735–1748. https://doi.org/10.1007/s40262-022-01186-3

Tandar, S. T., Aulin, L. B. S., Leemkuil, E. M. J., Liakopoulos, A., & van Hasselt, J. G. C. (2024). Semi-mechanistic modeling of resistance development to β-lactam and β-lactamase-inhibitor combinations. Journal of pharmacokinetics and pharmacodynamics, 51(3), 199–211. https://doi.org/10.1007/s10928-023-09895-3

Koumans, C. I. M., Tandar, S. T., Liakopoulos, A., & van Hasselt, J. G. C. (2024). Interspecies interactions alter the antibiotic sensitivity of *Pseudomonas aeruginosa*. Microbiology spectrum, 12(12), e0201224. https://doi.org/10.1128/spectrum.02012-24

Tandar, S. T., De Clercq, A., Aulin, L. B. S., Van Biesen, W., Delanghe, S., Vanommeslaeghe, F., De Paepe, P., van Hasselt, J. G. C., De Cock, P. A., & Eloot, S. (2026). Model-based optimisation for teicoplanin dosing in patients undergoing maintenance haemodialysis. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 32(3), 466–473. https://doi.org/10.1016/j.cmi.2025.11.035

Tandar, S. T., Zwep, L. B., Woudt, S. H. S., Schoffelen, A. F., Smits, W. K., Aulin, L. B. S., Liakopoulos, A., van Hasselt, J. G. C., & Infectious Diseases Surveillance Information System–Antimicrobial Resistance Study Group (2026). Clinical prevalence of collateral sensitivity: a systematic exploration of multicentre antimicrobial surveillance data. The Lancet. Microbe, 7(4), 101274. https://doi.org/10.1016/j.lanmic.2025.101274

Other Publications

Tandar, S. T., Senoo, S., Toya, Y., & Shimizu, H. (2019). Optogenetic switch for controlling the central metabolic flux of *Escherichia coli*. *Metabolic Engineering*, *55*, 68–75. https://doi.org/10.1016/j.ymben.2019.06.002

Senoo, S., Tandar, S. T., Kitamura, S., Toya, Y., & Shimizu, H. (2019). Light-inducible flux control of triosephosphate isomerase on glycolysis in *Escherichia coli*. *Biotechnology and Bioengineering*, *116*(12), 3292–3300. https://doi.org/10.1002/bit.27148

Straub, V. M., Barti, B., Tandar, S. T., Stevens, A. F., van Egmond, N., van der Wel, T., Zhu, N., Rüegger, J., van der Horst, C., Heitman, L. H., Li, Y., Stella, N., van Hasselt, J. G. C., Katona, I., & van der Stelt, M. (2025). The endocannabinoid 2-arachidonoylglycerol is released and transported on demand via extracellular microvesicles. Proceedings of the National Academy of Sciences of the United States of America, 122(8), e2421717122. https://doi.org/10.1073/pnas.2421717122