

# BILBAO

## SPAIN

# Stephan Schaller

## Bio



Stephan is the Founder and Managing Director of ESQlabs GmbH, a mid-size biosimulation solutions and services CRO and holds a PhD in Computational Engineering. He has > 15 years of industry experience with a focus on Model-Based Drug Development (MIDD) and Next-Generation Risk Assessment (NGRA). His scientific career is focused on advancing knowledge- and mechanism-based modeling approaches such as PBK, and QSP/T for decision-making support to R&D teams in the Life Sciences. Stephan is the current chair of [www.Open-Systems-Pharmacology.com](http://www.Open-Systems-Pharmacology.com), an initiative to democratize and develop open-source computational tools for physiologically- and mechanism-based analysis of disease and kinetics and effect of drug therapies and chemicals. Stephan is coordinator and PI of a number of German national and European multinational public grant research projects

## Abstract

New modalities are rapidly increasing their share in the discovery and development of biologics. These new modalities introduce uncertainties with respect to their pharmacokinetics (PK), target interactions, and consequentially their pharmacodynamics (PD). The prediction of PD for new modalities in the absence of prior clinical or preclinical in vivo data is challenging, especially when the involved biological networks are not precisely known. However, the prediction of PK and target engagement can be based on PBPK models that contain the influence of the molecular properties in which the new modality differs from previously tested modalities. Such parameters are often available, especially in platform PBPK models that have been applied to small and large molecule drugs, large molecules of different sizes, in different species, for different targets, and for different diseases. The value of integrated PBPK and QSP models is illustrated by the example of FcRn inhibitors, where the new modality could be described by the existing PK-Sim large molecule model structure after updating the model implementation with preclinical model data. The value of target engagement models within whole-body PBPK models for biologics is illustrated by a recent investigation that demonstrated the impact of tissue volume, target turnover, target binding, and molecular size on tissue concentrations and target occupancy. A range of literature values for these parameters can be used for novel modalities where the system-specific parameters are unknown. We conclude that the integration of PBPK and QSP models offers valuable information and insight into the most relevant molecular and system-specific properties of (novel) biologic modalities in drug discovery and development.

