



Assessing the effect of pneumonia on tigecycline lung exposure using physiological-based pharmacokinetic modelling



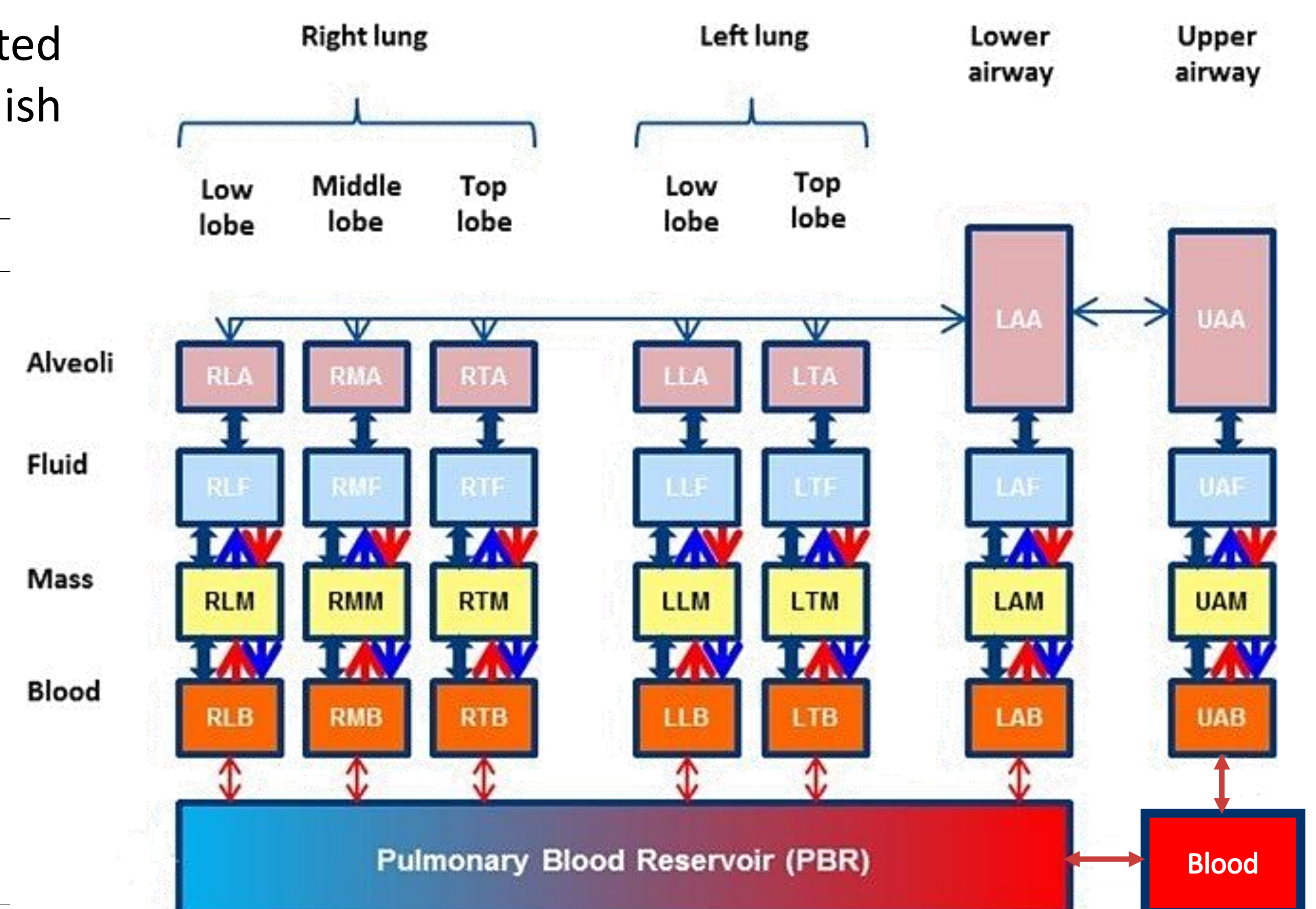
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Introduction

- Pneumonia** is a major global cause of infection-related mortality, with **tigecycline** commonly used for treatment.
- Lung exposure** is crucial for tigecycline's efficacy against pneumonia, while tigecycline exposure varies across different lung compartments, such as epithelial lining fluid (ELF) and alveolar cells (ACs), in pneumonia patients¹⁻³.
- Elucidating the mechanism underlying tigecycline distribution between ELF and ACs could help optimize tigecycline dosage regimens.
- Aim: To assess how physiological conditions associated with pneumonia affect lung tigecycline exposure using PBPK modelling to facilitate tigecycline dosage regimens optimization in pneumonia patients.**

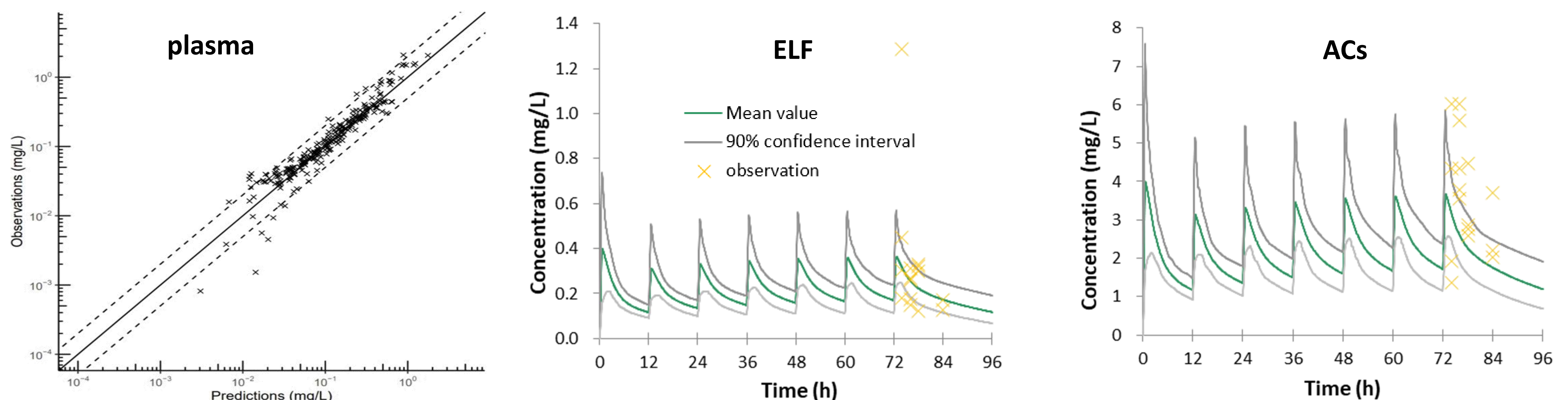
Methods

- Multicompartment permeability-limited lung model⁴ was incorporated in Simcyp population-based PBPK simulator (version 21) to establish the PBPK model of tigecycline.



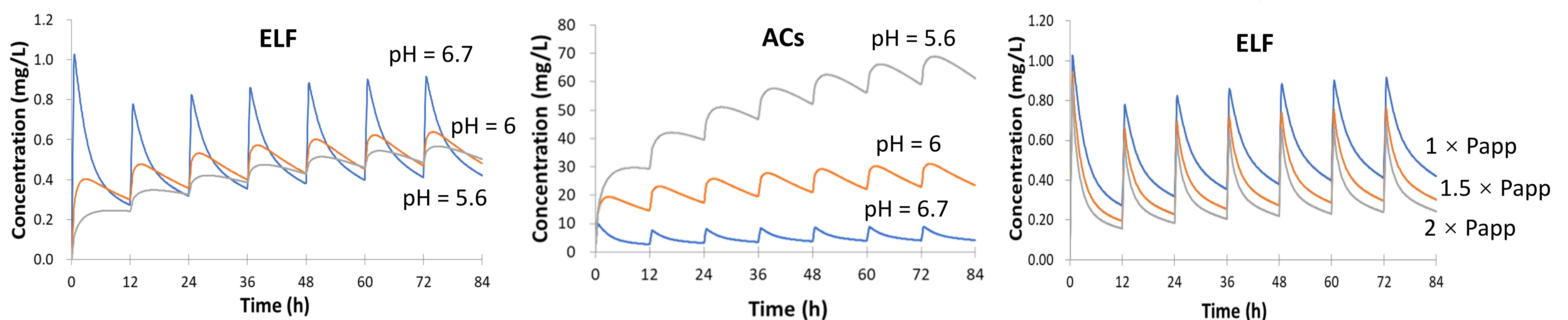
Results – Predictive Performance of the Permeability-Limited Lung PBPK model

- The developed tigecycline PBPK model demonstrated robust predictive accuracy in plasma, ELF and ACs exposure in healthy adults.



Results – Evaluation of the Impact of Pneumonia on Tigecycline Lung Exposure

- Changes in pulmonary mass pH and pulmonary permeability associated with pneumonia can alter tigecycline exposure in ELF and ACs.



Conclusion

- A decrease in pulmonary mass pH could significantly alter tigecycline lung exposure.**
- The developed tigecycline PBPK model highlights the importance of considering lung-specific physiological conditions to optimize tigecycline regimens for pneumonia patients.**

References

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