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Physiologically-based **biopharmaceutics** modelling for **nasal delivery**

DDL Pre-Conference Workshop

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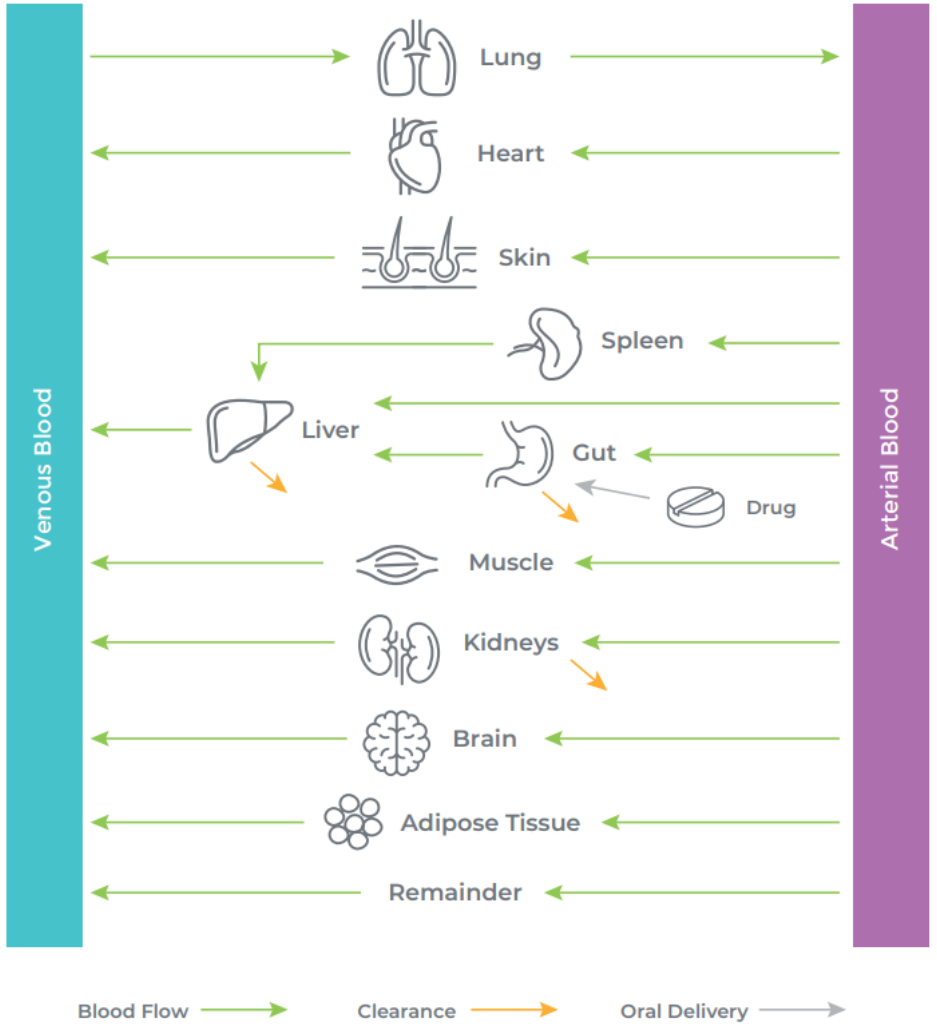
Non-Confidential

Physiologically Based **Biopharmaceutics Modelling** (PBBM) \

- **PBBM** is a specific **subset of PBPK** modelling focused on **absorption** and the **impact of formulation** on rate and extent of drug absorption
- PBBM is used extensively for oral drugs and other routes of administration informs:
  - formulation design
  - dose prediction
  - specification setting
- **PBBM** could have similar applications in **nasal delivery**



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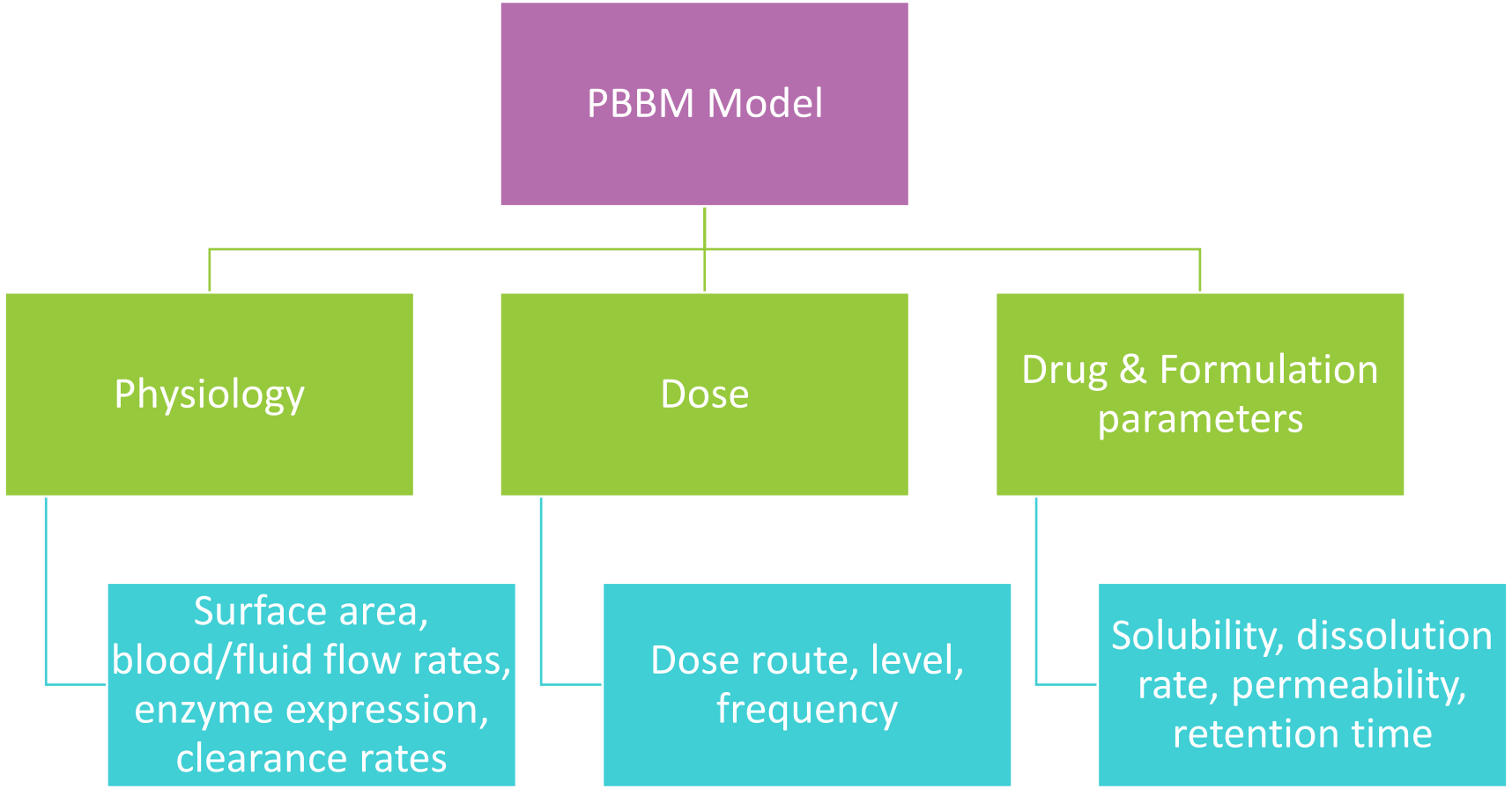
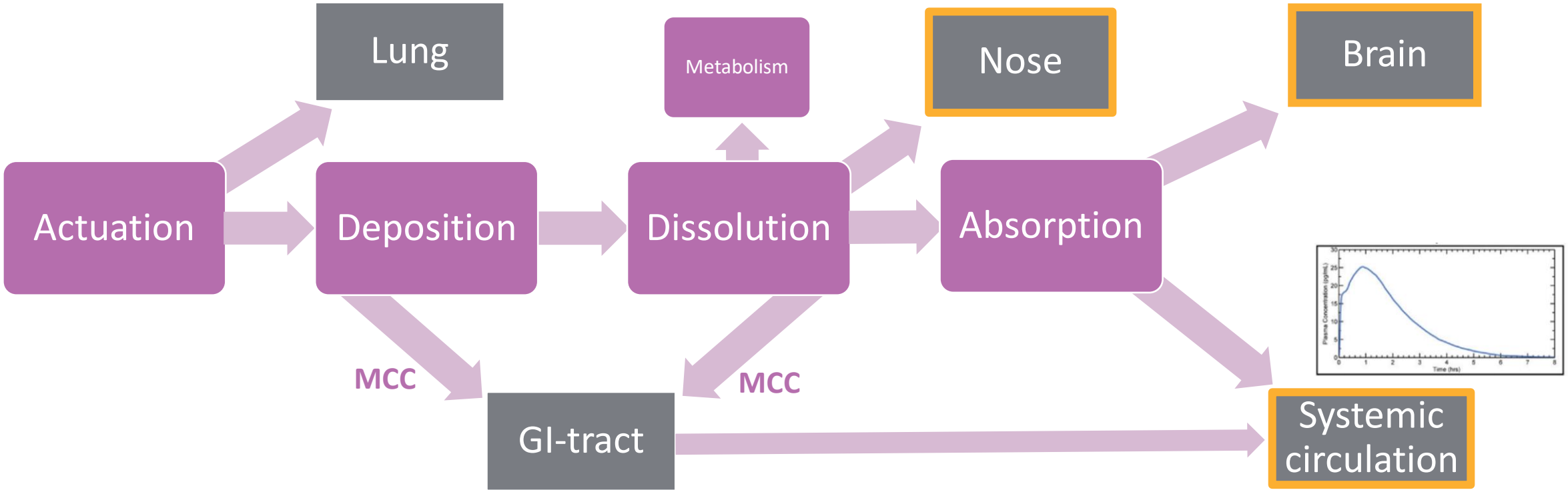
What is required to build a PBBM model? \



Processes in Nasal Drug Delivery \



Accessible Models \

- GastroPlus contains a pulmonary/intranasal absorption model in its Additional Dosage Routes Module (ADRM).
  - Limited information in the public domain.
  - Poster describes successful scaling of fitted adult nasal absorption PK profile to paediatrics by scaling physiological parameters[1]
  - Bottom up predictive capability unknown

- PKSIM (opensource PBPK and QSP platform) has no published nasal absorption models, but users have reported building a nasal compartment using Mobi (details not disclosed) to achieve IVIVC[2].

Schematic of G+ nasal-pulmonary model. See: https://www.simulations-plus.com/wp-content/uploads/nasal-pulmonary-drug-delivery.jpg

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1. APSTJ 2012 Poster (simulations-plus.com)
2. <rdf:li xml:lang=x-default/> (accp1.org)

Published In Silico Models \

- Simple pseudo compartmental model for nasal delivery (e.g. Gonda, 1998)

(https://doi.org/10.1016/S0169-409X(97)00068-9)

- Hybrid CFD-PBPK models (e.g. Dave 2022)

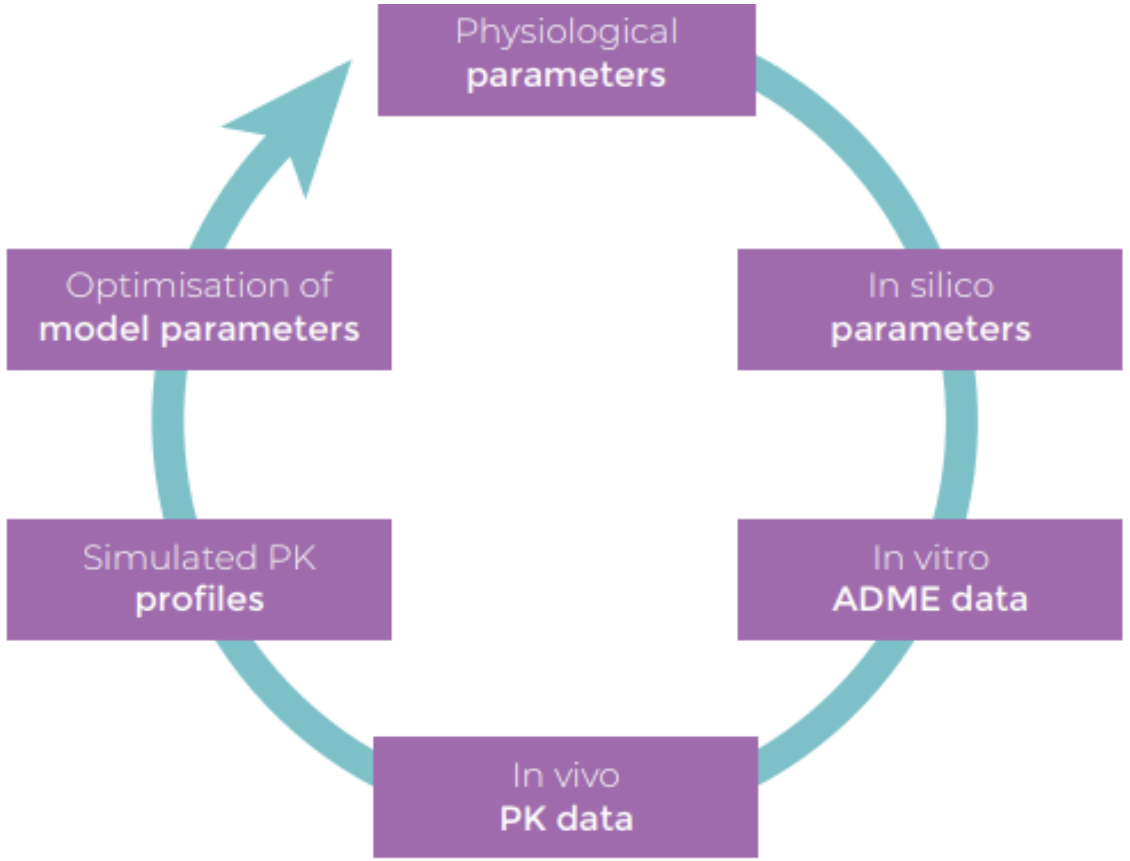
https://doi.org/10.1016/j.jaerosci.2021.105898

Open Questions/Research Needs \

- There are obvious benefits of PBBM modelling in oral delivery.

Do we want to get there for nasal, and if so, how do we.....

- generate the parameters needed to build and validate the models
- develop sufficient understanding of the processes involved in nasal delivery to develop mechanistic models?
- assess prediction accuracy
- collaborate to bring all the required elements together



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