

An introduction to PK-Sim[®]: the open source platform for PBPK modeling

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AGENDA (50 min)

Open Systems Pharmacology website
PK-Sim[®]: small molecule structure and parameterization
Building block philosophy
Making a simulation
Populations and pediatrics
What is MoBi[®]?
Q&A (10 min or more...)

www.open-systems-pharmacology.org

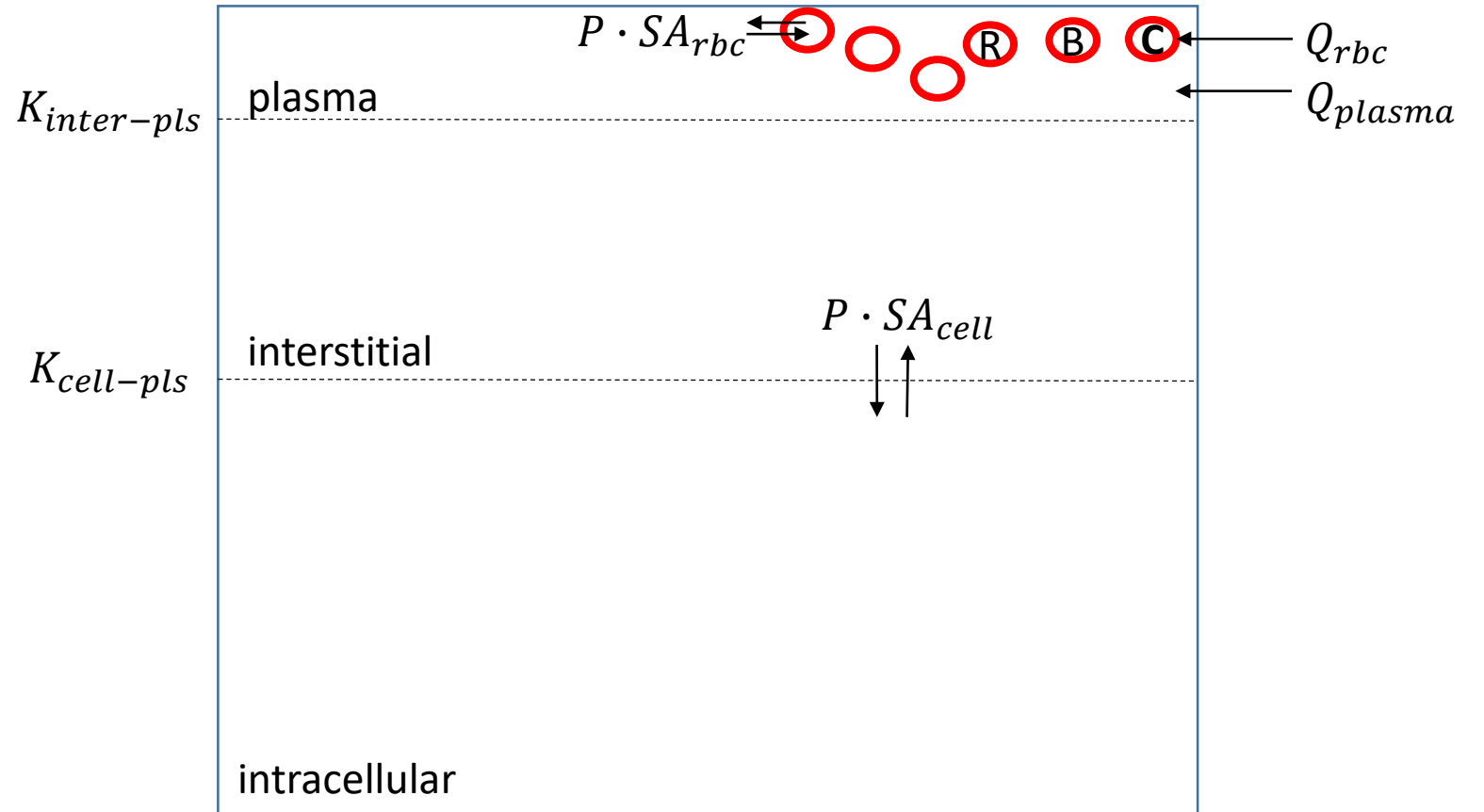
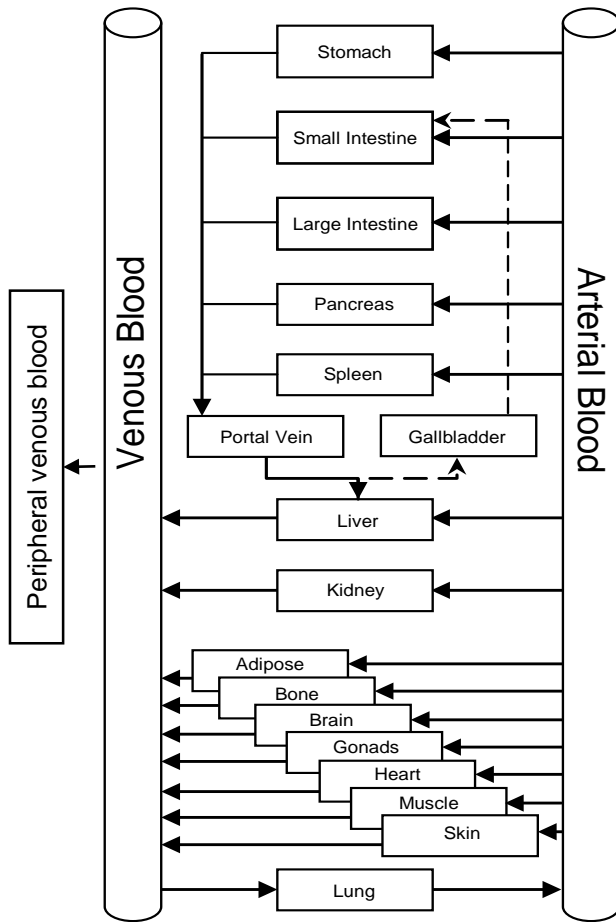
A (GitHub) place to

- Download PK-Sim[®], MoBi[®] and the GENEDBhuman (MatLab and R-toolboxes as well)
- Access source code (if you're savvy like that)
- Find the manuals
- Watch/access tutorials
- View qualification documents
- Ask and answer questions on the community FORUM
- See the bug reports and fixes (ISSUES in PK-Sim or MoBi)



Website

Small molecule structure



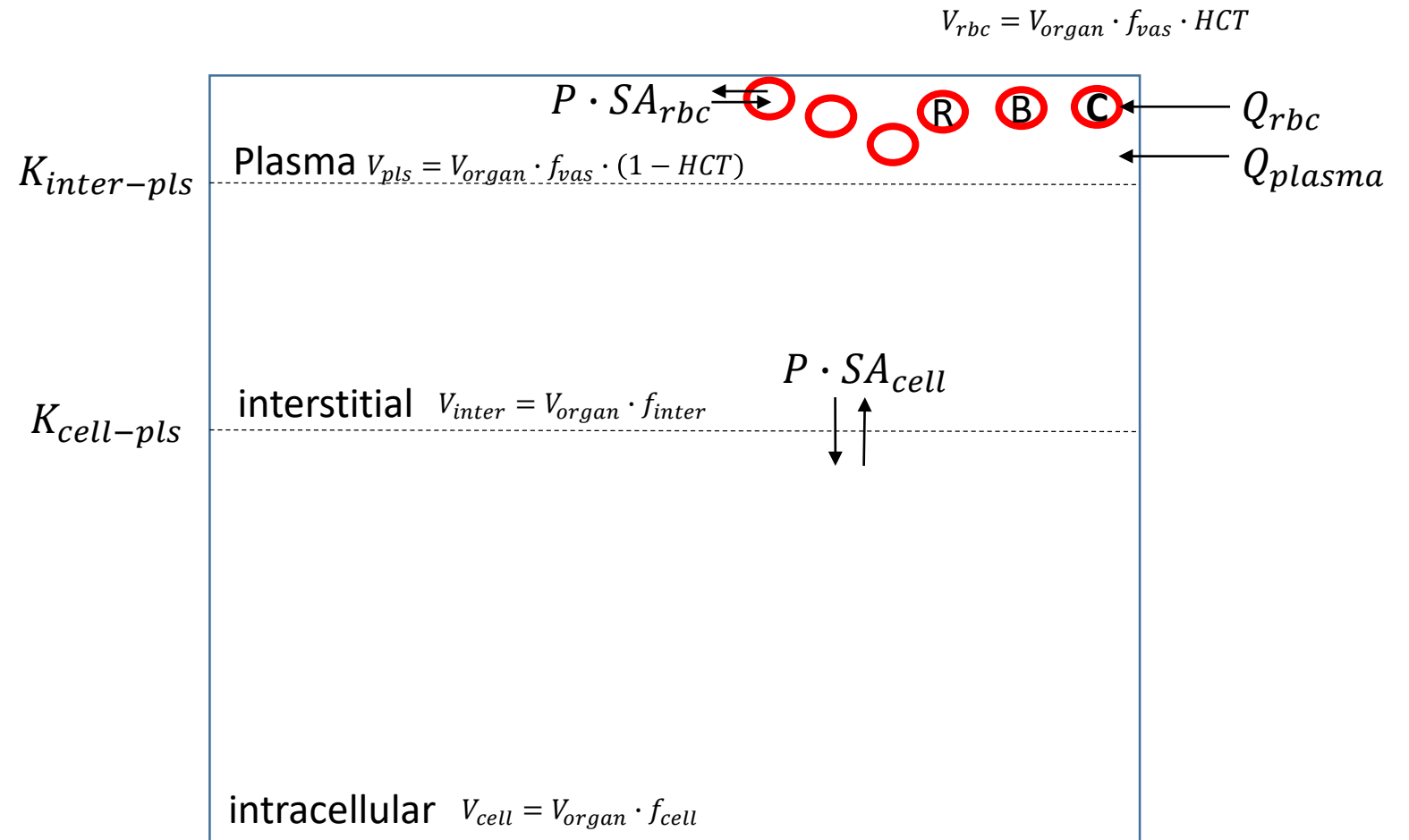
Small molecule structure

$K_{inter-pls}$: partition coefficient defined by binding protein concentration differential across endothelium

$K_{cell-pls}$: defined by tissue: plasma partition coefficient algorithms (tissue composition based: lipophilicity, charge, fu)

P : cellular permeability defined by algorithm using lipophilicity, molecular weight and charge (predicts permeability-limited vs. well stirred conditions)

SA : Surface area, quantified



Inhalation & dermal absorption

- Not included but can apply in lung or skin via user defined application
- There are numerous mechanistic models in the literature, they could be incorporated with MoBi
- Create a model in MoBi and generate a plug-in (the future of MoBi modeling – see Forum Issue #52)
- Plug-ins could be reused with any underlying PK-Sim model



Pediatrics in PK-Sim®

- Basic pediatric (term +) parameters:

Edginton AN et al. 2006. Development and evaluation of a generic physiologically based pharmacokinetic model for children. *Clin Pharmacokinet.* 45(10):1013-34.

- Preterm (IV only)

Claassen K et al. 2015. Development of a physiologically-based pharmacokinetic model for preterm neonates: evaluation with in vivo data. *Curr Pharm Des.* 21(39):5688-98

- Clearance scaling:

Edginton AN et al. 2006. A mechanistic approach for the scaling of clearance in children. *Clin Pharmacokinet.* 45(7):683-704

- Updated maturation functions for enzymes and binding protein concentrations in documentation on GitHub

- Pregnancy

Dallmann A et al. 2017. Gestation-specific changes in the anatomy and physiology of healthy pregnant women: an extended repository of model parameters for physiologically based pharmacokinetic modeling in pregnancy. *Clin Pharmacokinet.* in press.

