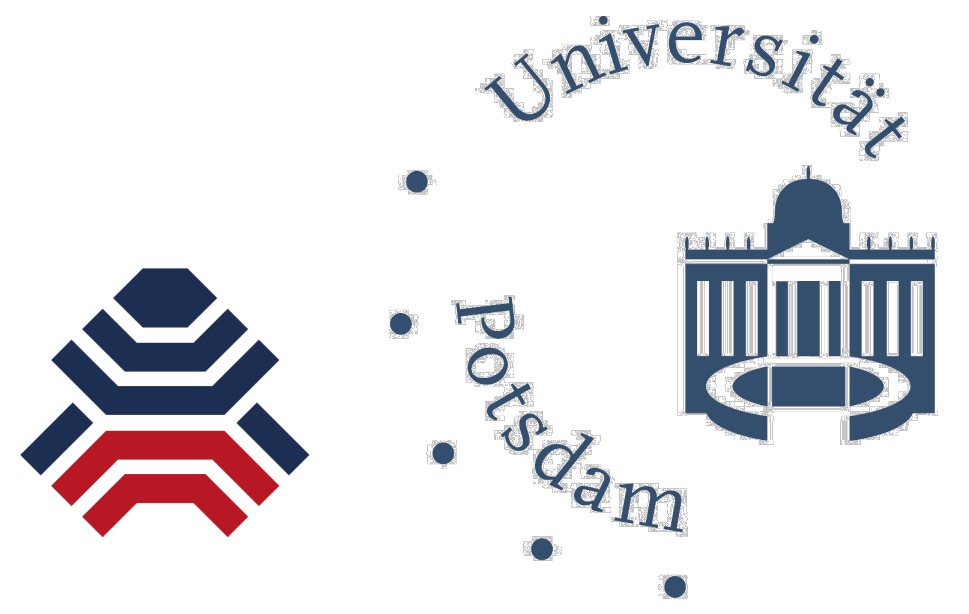


Physiologically-based toxicokinetic modelling of aluminium exposure in humans

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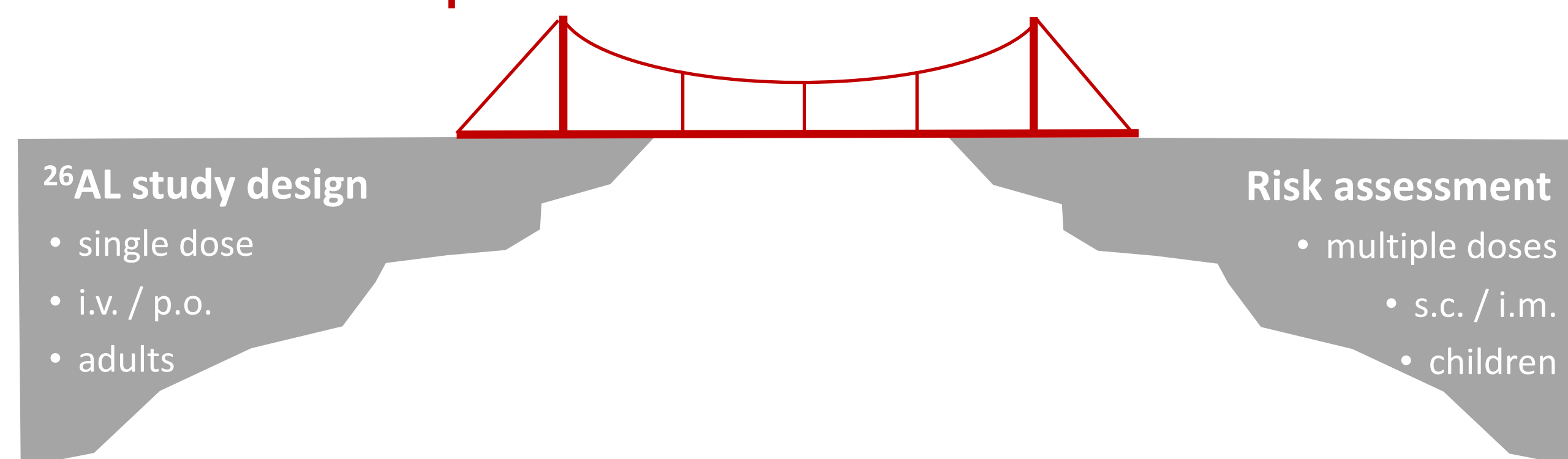
Summary

Background

- Aluminium (Al) is toxic on bone, brain and liver at elevated exposure levels → detailed understanding of Al toxicokinetics is crucial for risk assessment (food, water, medicinal products) [1]
- We recently established a mixed-effects physiologically-based toxicokinetic (PBTk) model for Al, built on a comprehensive set of ²⁶Al radiotracer data [2]

Aims

- Model extension (administration routes, children's physiology)
- Model validation in larger scope

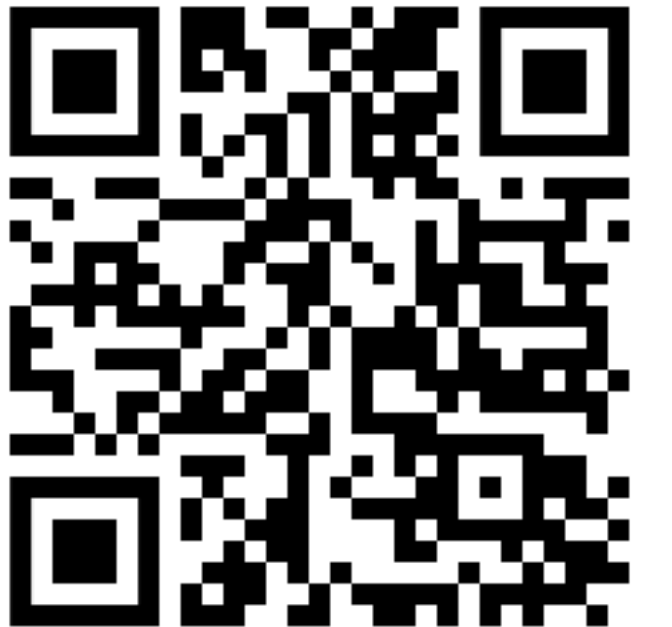


Conclusion

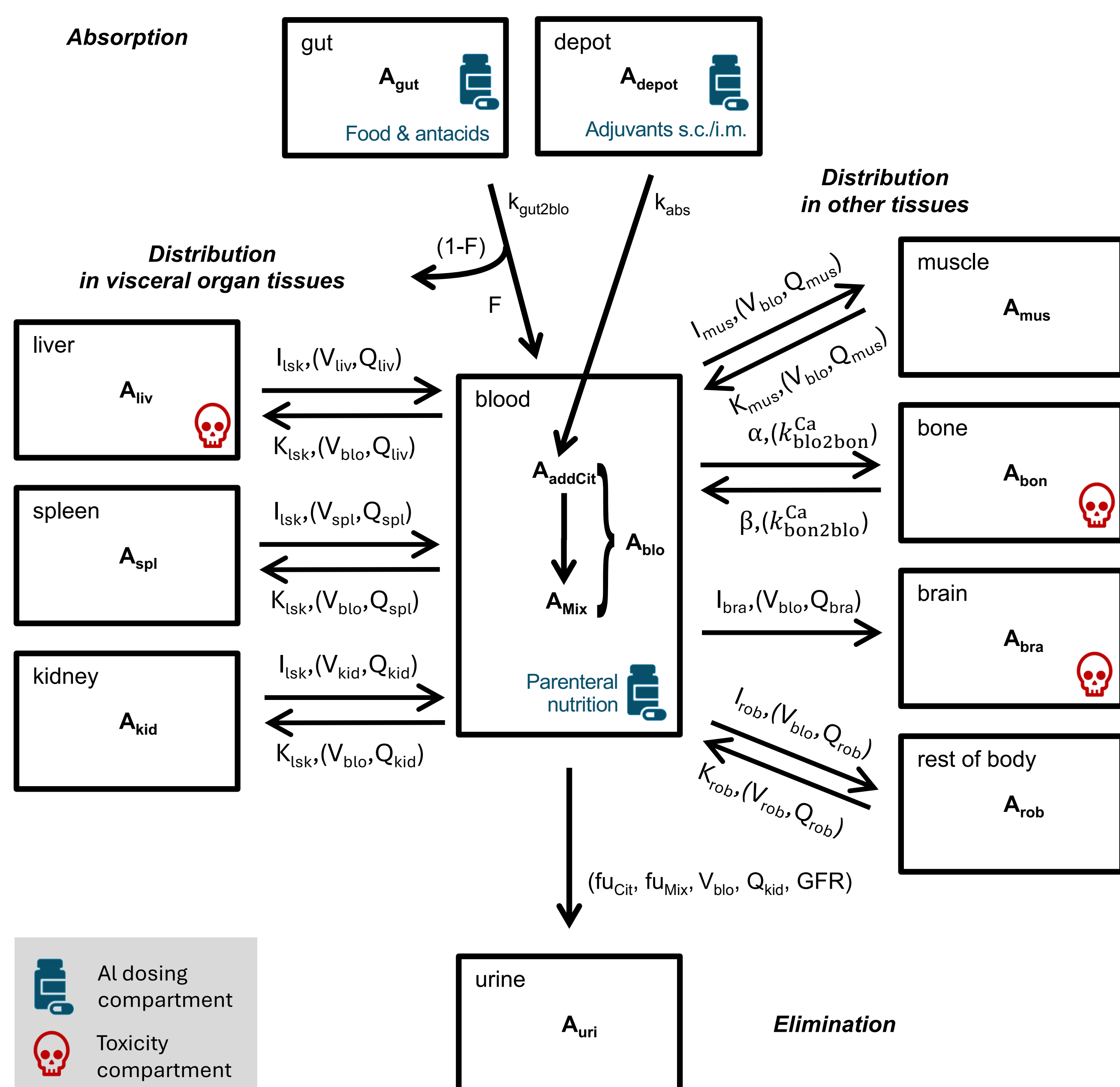
Successful development and validation of **first Al PBTk model suitable for simulations of Al exposure in humans**

- from birth to adulthood
- from various sources
- short-term or lifelong

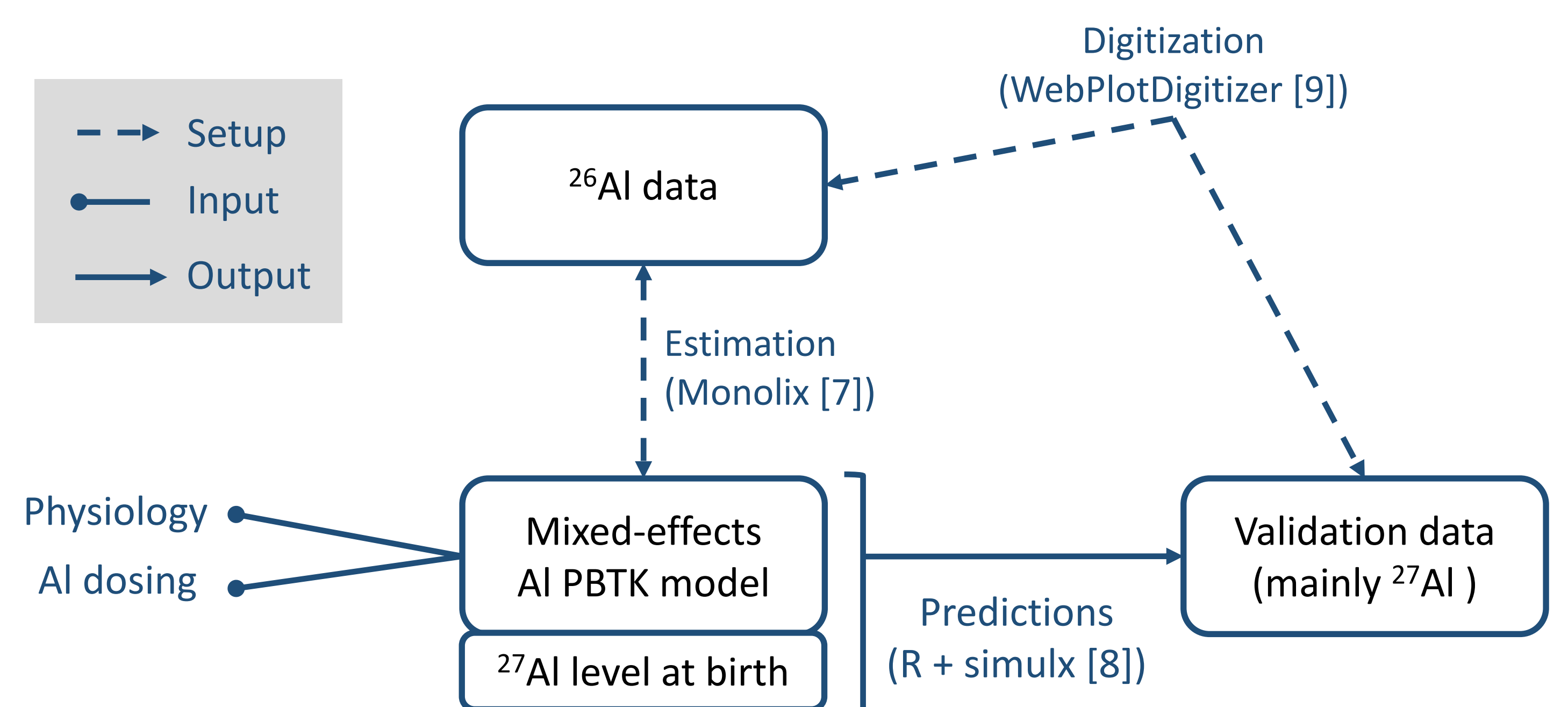
Article [3] →



Mixed-effects Al PBTk model



Workflow

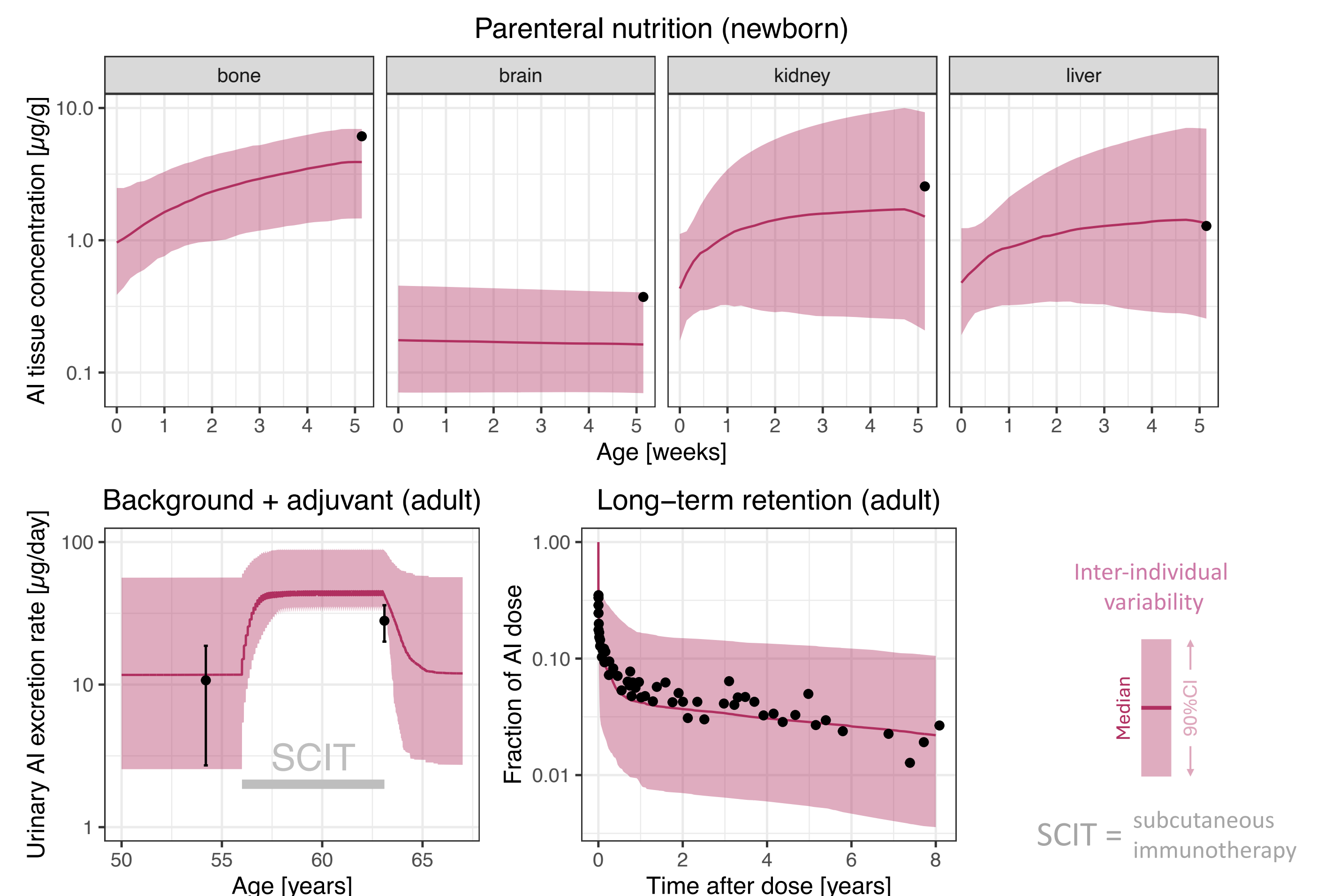
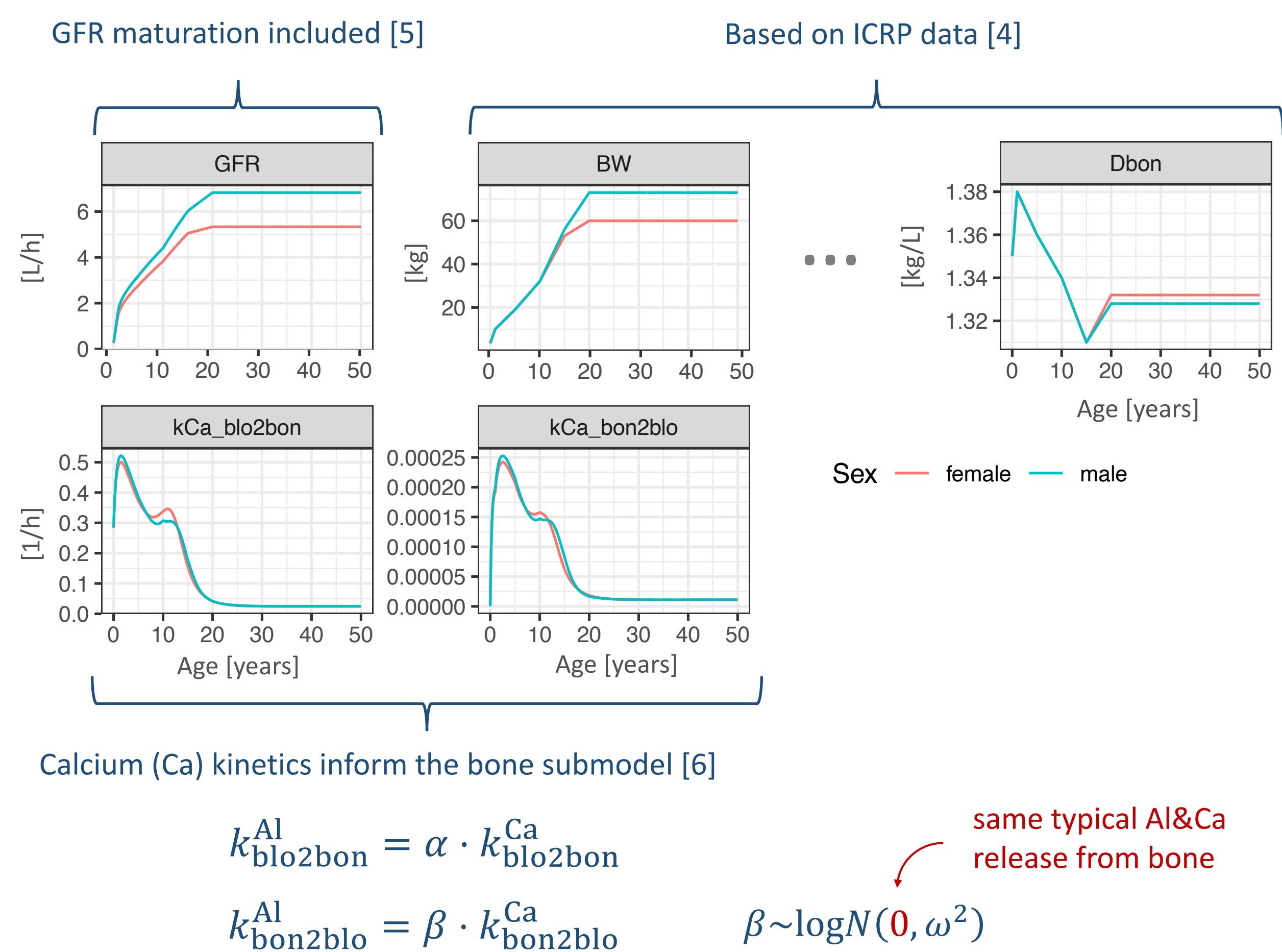


Model validation

Al source	Population	Route	No. studies	Measurement sites
Food	Adult	p.o.	11	blo, bon, bra, liv, kid, spl, mus
Adjuvants	Adult, rats	i.m./s.c.	3	blo, bon, bra, uri
Parenteral nutrition (PN)	Newborn to adult	i.v.	5	blo, bon, bra, liv, kid, uri
PN + antacid	Adult	i.v. + p.o.	1	blo, uri
Injection	Adult	i.v.	2	ret (=blo+...+rob)

Age-dependent physiology (growth, maturation, bone turnover)

Selected validation datasets [10,11,12]



References

- [1] Krewski D et al. J. Toxicol. Environ. Health B 10(sup1):1-269, 2007
- [2] Hethey C et al. Arch. Tox. 95(9):2977-3000, 2021
- [3] Hartung N et al. Arch. Tox., 2025, DOI: 10.1007/s00204-025-04031-1

- [4] Valentin J et al. Ann. ICRP 32(3-4):1-277, 2002
- [5] Rhodin M et al. Pediatr. Nephrol. 24(1):67-76, 2009
- [6] Hartung N et al. Bone 189:117254, 2024
- [7] Monolix version 2019R2. Antony, France. Lixoft SAS, 2019
- [8] Lavielle M et al. (2021). mlxR: Simulation of Longitudinal Data (R package version 4.2.0). [online] <https://CRAN.R-project.org/package=mlxR>

- [9] Rohatgi A (2022) WebPlotDigitizer. [online] <https://automeris.io/WebPlotDigitizer>
- [10] Moreno A et al. Acta Paediatrica 83(1):25-29, 1994
- [11] Hiller J et al. Int J Hyg Environ Health 258:114337, 2024
- [12] Newton D et al. Hum Exp Toxicol 31(12):1195-1198, 2012

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