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## Modeling the multiscale functionality of the (mammalian) kidney

### Abstract:

In all animals, the main organ responsible for maintaining water balance is called a kidney. In mammals, the kidneys manage not only this key function of water balance but are also responsible for maintaining salt balance and nitrogen (in the form of urea) balance, plus a number of other functions. This unique triple role explains why only mammals need to excrete a concentrated urine (in order to maintain salt and nitrogen balance without dehydrating the animal), and is responsible for a number of structural features that are peculiar to mammalian kidneys. The function of mammalian kidneys is thus highly complex, with interacting subsystems that span not only multiple time and spatial scales but also span a number of functional modes, such as countercurrent multiplication of water and solute transport inter-related with metabolic consequences of structurally hypoxic regions. I will give an overview of multiscale kidney function from a modeler's point of view, ranging from kinetics of individual cell membrane transporters and channels to the key role of the key role in blood pressure regulation.

### Short Bio:

S. Randall Thomas is the leader of WP2 in the VPH Network of Excellence (FP7) and was a partner in the STEP Roadmap project (FP6). He received his M.A. in Biology from Swarthmore College (1973), a Ph.D. in Physiology at Medical College of Virginia, Richmond (1977), and the HDR from Univ. Paris 5 (1990). After postdocs at the French Atomic Energy Commission (Biology Dept.) at Saclay (1979) and in the Dept. of Physiology at Univ. Texas Med. Center, Houston (1980-81), he became Chargé de Recherche with the CNRS, France (1982), where he is now a Director of Research. He currently works at IR4M UMR8081 CNRS & Univ. Paris-Sud at Orsay and Villejuif. His research centers on mathematical modeling of integrated transport systems in renal and cardiovascular physiology and on the development of related databases and physiome infrastructure; he is international coordinator of the Renal Physiome. He serves or has served on the editorial board of the journals *Frontiers in Computational Physiology and Medicine*, *Systems & Synthetic Biology*, *Nephron Physiology*, and *Philosophical Transactions of the Royal Society A*. He is also Section Head of Integrative Physiology/Homeostasis in the Faculty of 1000.



### Several relevant publications:

- Thomas, S. R. (2009). "Kidney Modeling and Systems Physiology." *Wiley Interdisciplinary Reviews: Systems Biology and Medicine* 1: 172-190.
- Moss, R., T. Grosse, I. Marchant, N. Lassau, F. Gueyffier and S. R. Thomas (2012). "Virtual Patients and Sensitivity Analysis of the Guyton Model of Blood Pressure Regulation: Towards Individualised Models of Whole-Body Physiology." *PLoS Comp. Biol.* 8(6):e1002571. DOI: doi:10.1371/journal.pcbi.1002571.
- Hernandez, A. I., V. Le Rolle, D. Ojeda, P. Baconnier, J. Fontecave-Jallon, F. Guillaud, T. Grosse, R. G. Moss, P. Hannaert and S. R. Thomas (2011). "Integration of detailed modules in a core model of body fluid homeostasis and blood pressure regulation." *Prog Biophys Mol Biol* 107(1): 169-182. DOI: S0079-6107(11)00055-1 [pii] 10.1016/j.pbiomolbio.2011.06.008.
- Thomas, S. R., P. Baconnier, J. Fontecave, J. P. Francoise, F. Guillaud, P. Hannaert, A. Hernandez, V. Le Rolle, P. Maziere, F. Tahi and R. J. White (2008). "SAPHIR: a physiome core model of body fluid homeostasis and blood pressure regulation." *Philos Transact A Math Phys Eng Sci* 366(1878): 3175-3197.
- Thomas, S. R. (2000). "Inner medullary lactate production and accumulation: A vasa recta model." *American Journal of Physiology Renal* 279: F468-F481.
- Hervy, S. and S. R. Thomas (2003). "Inner medullary lactate production and urine-concentrating mechanism: a flat medullary model." *Am J Physiol Renal Physiol* 284(1): F65-81.
- Thomas, S. R. (1998). "Cycles and separations in a model of the renal medulla." *American Journal of Physiology Renal* 275: F671-F690.
- Bali, M. and S. R. Thomas (2001). "A modelling study of feedforward activation in human erythrocyte glycolysis." *Comptes Rendus de l'Académie des Sciences* 324: 185-199.