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Towards integrative multiscale models of whole kidney structure and function

Existing models of renal function have generally focused on open questions of 'local' (i.e., intrarenal) physiology rather than on providing an overall description of renal function relevant to its role in the body and incorporating sufficient detail to address the roles of transporters and channels in each nephron segment We will present our current efforts towards a multi-organ systems model of blood pressure regulation. The resulting open-source platform will be oriented towards interactive exploration of targeted pathologies and their pharmacology. Our approach will be: (1) to complete an integrated endocrine/paracrine RAAS (renin-angiotensin-aldosterone system) model, (2) to build a whole-kidney model representing essential nephrovascular relationships in the three kidney zones and operational descriptions of specific transport processes in each nephron segment and to build up a multi-nephron model capable of addressing progressive renal failure, (3) to combine the renal and RAAS models in our modular core-model (based on the classic Guyton model), (4) to calibrate and validate the models on the basis of pre-clinical and clinical data related to physiological and pathological conditions, and finally (5) to produce a large population (>100 000) of 'virtual individuals' with randomized model parameters (analogous to genetic polymorphisms) for comparison with data from cohorts of real patients from our partner clinicians (and published clinical trials). These new tools, based on virtual physiopathological models of the kidney and RAAS, will be useful to investigate dysfunctions at the clinical level as well as at the level of scientific research and education.