Dynamical Properties of the Thick Ascending Limb (TAL): A Modeling Study

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We developed a cell-based model of the TAL 2 using an empirical tubuloglomerular feedback (TGF) model to study the dynamical properties of the TAL. The cell-based TAL model tracks the time evolution and space dependence of cell volume and the luminal and cytoplasmic concentrations of major solutes including Na+, K+, Cl−, and HCO3−. The TAL segment model consists of a stack of cell models that comprise the wall. Each cell model includes detailed representations of the major transport pathways (NKCC2, KCC4, NHE3, BCE) as well as the extracellular space (ESS) and cell junctions (CJ) between the cells. We simulated the TAL wall and without the TGF system using different tubular inflow forcing schemes and compared transient excitations, and amplitude and frequency response for the TAL cells with or without the input. The forcing was done by varying the concentration of luminal sodium chloride (NaCl) (obtained with a multi-scale TAL model) that the TAL acts as a nonlinear low-pass filter with a harmonic structure and filtering properties related to the steady state transit time, and reflects the establishment of standing waves of sinusoidal forcing (see Figure 2). For K+ in the cortical region the U-O relation is positive, which implies amplification.

Conclusions

The major results of this modeling study are:

• When TAL inflow oscillates the TAL segment acts as a nonlinear low-pass filter with a characteristic harmonic structure. Such structure is derived from tubule properties like the steady-state transit time, and reflects the establishment of standing waves of Na+ and Cl− in the lumen of the TAL. This finding is consistent with both earlier modeling efforts and experimental data.

• The harmonic structure is affected by the transport properties of the solute under consideration.

• The TAL cells themselves are predicted to act as multi-input/multi-output nonlinear systems.

References