

# Optimization Problems and Algorithms for Mathematical Models of Renal Systems

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January 16, 2007

## Abstract

This talk will present optimization techniques that can be used to study the relationship between the parameters and the solutions of mathematical models of the urine concentrating mechanism (UCM). A nonlinear constrained optimization problem was used to estimate parameter sets that maximize the urine osmolality in a model of the rat inner medulla. The optimization problem was solved by means of a search-direction optimization algorithm. By allowing the parameter values to vary within ranges suggested by experimental results, the algorithm identified a set of parameters that increased urine osmolality by 42% from its base-case value and found optimal values for key parameters in the outer-inner medullary boundary, which have large uncertainties. In a second study, a nonlinear least-squares method was used to estimate parameters for a thermodynamically consistent kinetic model of ammonium transport by the NKCC2 cotransporter using published binding kinetic data. This transporter plays a central role in the UCM in the thick ascending limb of Henle where it mediates the reabsorption of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ , and  $\text{NH}_4^+$ , a process that raises interstitial osmolality to levels higher than in plasma. The nonlinear least-squares method identified a parameter set for the A isoform of the NKCC2 cotransporter that produces binding kinetic curves that agree with published data.