Spreadsheet analysis of ion transport in epithelia

R.B. Patuzzi, Discipline of Physiology, School of Anatomy, Physiology and Human Biology, The University of Western Australia, WA 6009, Australia.

An understanding of the concerted action of the transport proteins in any cell or complex epithelium requires mathematical modelling of the solute and water transport through the cells' membranes. This is true for the resting electrical potentials within the cells, or the ion/solute flow through them. While detailed models of the function of specific epithelia have appeared, they are implemented in dedicated programs and are therefore not generally available. However, an understanding of difficult asymmetric cells is readily accessible using equivalent spreadsheet analysis, which allows us to: (i) solve for the voltage-steady state; (ii) solve for the ionic and osmotic steady-states; (iii) simulate changes in transport rates; (iv) work backwards (reverse engineer) from steady-state experimental conditions to transporter densities; (v) investigate cell design generally; (vi) solve the more complex equations for a cell's dynamic response; and (vii) analyse multi-layered and non-homogenous epithelia, and the role of intercellular or intracellular compartments. Overall, spreadsheet analysis makes it possible to readily model complex epithelial structures to gain insight into the importance of a particular cell topology, and the role the properties of specific ion transporter have on cell and organ function.

The steps in spreadsheet modelling of cell solute flow include: (a) the specification of the transport properties of individual transport proteins (pores, ports and pumps); (b) the statement of the major constraint equations governing cellular and epithelial transport; and (c) the solving of these constraint equations given initial conditions using spreadsheet/s (*e.g.* Microsoft Excel) and the optimization software contained within them (*e.g.* Solver within Excel). The interactions between multiple cells in a complex epithelium like *stria vascularis* in the cochlea can be analysed, using a spreadsheet to represent each cell type, with all spreadsheets linked so that they share their environmental (extracellular) constraints. Alternatively, multi-cellular epithelia can be analysed cell-by-cell, using what is known in engineering as a free-body analysis, where one sub-system of a complex whole can be considered in isolation, with its complex surroundings replaced by a minimal definition of its essential environmental variables. In ion transport, the free-body might be a particular transport protein in a particular membrane, a particular membrane of a particular cell, one cell in a complex epithelium, or one epithelium in the complex organ. If the important variables of the free body's environment are defined (potentials and concentrations in this case), the analysis can proceed. To explain spreadsheet analusis, we need the current-voltage (IV) characteristics of the three main categories of transport proteins (pores, ports and pumps), and the constraint equations that apply under various conditions (the voltage or ionic steady states in the open- and closed-circuit conditions). Consistent cell models can be developed by either trial-and-error (adjusting the density of transport proteins manually) or by reverse engineering the cell design. Either way, similar cell topologies are found. The circulation of K^+ within the cochlea, and the chloride, salt and water balance of *scala media* and *stria vascularis* is one systen that has been successfully elucidated in this way.