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***Mathematical Prediction of High Energy Metabolite Gradients in Mammalian Cells***

**Abstract:**

Described is a mathematical model that evaluates the distribution of cellular adenosine nucleotides (ATP/ADP) to test the hypothesis that local changes in the concentrations of these molecules can modulate cell function without a significant change in global cytosolic concentrations. The model incorporates knowledge of cell structure to predict the spatial concentration profiles of ATP, ADP and inorganic phosphate. The steady state was perturbed by increasing the activity of membrane bound ion transporters including the Na-K ATPase on the cell periphery or the V-type H<sup>+</sup> ATPase which serves to acidify intracellular compartments including endosomes/lysosomes. Both of these transporters utilize ATP and produce ADP and P<sub>i</sub> in the process. Both models are run over a range of cytosolic diffusivities, including local low diffusivity near the pump sites. Results suggest that local changes in the concentration of ADP (not ATP) during activation of ion transport, in particular at near membrane sites, may serve to modulate ion transport, and thereby cell behavior.