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Intracellular pH Regulation in Cardiac Myocytes

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Intracellular pH(pH_i) regulation is very important to regulate the cellular functions of cardiac myocytes such as contractility, signal transduction, ion regulation, cell volume, and energy production etc. The resting pH_i was maintained at about 7.07 and strictly regulated within the range of ± 0.1. Primary defence mechanism for pH_i change is the intracellular proton buffers. Intracellular proton buffering power consists of two different components such as intracellular intrinsic buffering power (β_i) and CO_2-dependent buffering power(β_{CO2}). β_i inversely varied with pH_i in a manner consistent with two principal intracellular buffers of differing concentration and pK. The value of β_{CO2} monotonically increased with pH_i and β_{CO2} was consistent with buffering in a cell fully open to CO_2. Recently, it was discovered four types of sarcolemmal carriers contributes the intracellular pH regulation in cardiac myocytes. Two of these are acid-equivalent extruders (Na^+-H^+ exchange, NHE and Na^+-HCO_3^- symport, NBC) while two are acid-loaders (Cl^--HCO_3^- exchange, AE and Cl^--OH^- exchange, CHE). In 5% CO_2/HCO_3^--buffered conditions, the acid extrusion on NHE and NBC increased as pH_i was reduced below the resting pH_i, with the greater increase occurring through NHE at $pH_i < 6.90$. The acid influx on AE and CHE was increased as pH_i was raised above the resting pH_i. NHE, with the greater increase occurring through AE at

pH_i > 7.15. At the resting pH_i, all four carriers were activated equally, albeit at a low rate (about 0.15 mM/min). β_{CO2} was developed slowly because of low carbonic anhydrase activity and CO_2 hydration rate increased only 3.7 times compared to natural hydration rate. The pH_i dependence of flux through the transporters, in combination with the pH_i and time dependence of intracellular buffering ($\beta_i + \beta_{CO2}$), was used to predict mathematically the recovery of pH_i following an intracellular acid or base load. Under several conditions the mathematical predictions compared well with experimental recordings, suggesting that the model of dual acid influx and acid efflux transporters in sufficient to account for pH_i regulation in the cardiac cell. Key properties of the pH_i control system will be discussed.