

P017 Ca^{2+} -mediated changes in pancreatic islet NAD(P)H autofluorescence: Comparison of experiments and model predictions

Dan S. Luciani

Department of Cellular and Physiological Science, University of British Columbia, Canada

Simultaneous measurement of cytosolic Ca^{2+} and NAD(P)H autofluorescence in intact glucose-stimulated pancreatic islets revealed highly correlated slow (~ 5 min) oscillations which depended on voltage-gated Ca^{2+} influx. The oscillations showed a slight phase-shift with NAD(P)H leading cytosolic Ca^{2+} rises, indicating that the NAD(P)H oscillations were not shaped solely by mitochondrial Ca^{2+} uptake and activation of calcium-sensitive mitochondrial dehydrogenases (mCaDH). A more complex Ca^{2+} -NAD(P)H relationship was also suggested by the observation that prolonged KCl-induced Ca^{2+} rises augmented islet NAD(P)H autofluorescence in resting islets and in glucose-stimulated islets if respiratory flux was blocked, while it conversely lowered NAD(P)H levels in the presence of stimulatory glucose alone. These in-vitro findings were compared to simulations performed with an existing mathematical model of oscillatory beta-cell electrical activity, Ca^{2+} handling and mitochondrial metabolism (Magnus & Keizer, *Am. J. Physiol.* 274, 1998). Model and experiments agreed with respect to the relative amplitude of NADH oscillations and the critical role of Ca^{2+} entry, but the simulations showed purely out-of-phase oscillations due to a dominant Ca^{2+} -induced increase in NADH oxidation and a saturation of mCaDH. These comparisons suggest that the physiological dynamics of islet NAD(P)H autofluorescence involve a dynamic interplay of mCaDH activation and Ca^{2+} -dependent acceleration of respiration due to mitochondrial depolarization.