an inflexion at magnitude 4.5, and a concave downward slope thereafter. One might even be tempted to fit two straight lines to the data above and below M_L 4.5, if it were not for the fact that the discrete frequency–magnitude plot shows a gaussian peak (in the inferred length distribution) rather than a simple break in slope above this magnitude. The peak magnitude corresponds to a seismic source roughly equal to the 2 km depth of the seismogenic zone in the volume above the magma chamber. This figure also highlights the importance of plotting both discrete and cumulative frequency data before the type of curve fit is chosen in the first place.

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Electrical bursting in islet β cells

SIR — Ämmälä *et al.*[1] presented a novel theory to account for the bursting pattern of glucose-induced membrane electrical activity in pancreatic β cells. They show that exposure of clusters of cultured mouse β cells to carbamylcholine (CCh) or to dibutyryl cyclic AMP (db-cAMP) triggers repetitive membrane hyperpolarizations. These waves of hyperpolarization are attributed to activation of low conductance calcium-activated K channels by the transient release of calcium from endoplasmic reticulum stores controlled by inositol 1,4,5-trisphosphate. The authors conclude that the burst pattern of β-cell electrical activity depends on this periodic release of intracellular calcium and on the presence of intra-islet hormones (such as glucagon) and neurotransmitters (such as acetylcholine). Although this theory may explain hyperpolarizations in their cultured β cells, the relevance of these observations to the electrophysiology of β cells in intact islets of Langerhans is not apparent.

First, rather than potentiating β-cell responses to glucose, Ämmälä *et al.* find that both db-cAMP and CCh hyperpolarize the membrane and inhibit membrane electrical activity. The depolarizing and potentiating effect of these, or pharmacologically comparable, agents on β-cell electrical activity has been well established by several groups[2–7]. A well-documented alternative ionic mechanism for muscarinic effects[8] is not discussed by Ämmälä *et al.*

Second, Ämmälä *et al.* point out that the intracellular calcium transients and K-channel activation are independent of membrane potential and calcium influx, yet they propose to explain a bursting mechanism which is clearly voltage-dependent in intact mouse islets. As recently reviewed[9], electrical stimuli as brief as 50 ms during a burst of spikes interrupts the burst and triggers an all-or-none silent phase indistinguishable in voltage trajectory and duration from endogenous silent phases. Similarly, stimuli as brief as 1 s during silent phases triggers all-or-none bursts of spikes. In both cases, the subsequent bursting rhythm is immediately and completely reset by these brief electrical stimuli. It is not evident how voltage-independent calcium release from intracellular stores could possibly explain this clear voltage-dependence of bursting.

It is difficult to reconcile the mechanism proposed by Ämmälä *et al.* with the published observations and, hence, the importance of the proposed mechanisms for pancreatic β-cell electrical activity and insulin secretion is questionable. It is disappointing that the cultured mouse β-cell preparation, the only culture system capable of intermittent electrical activity, appears to achieve bursting by a mechanism unrelated to that used by β cells in intact islets.

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RORSMAN AND BERGGREN REPLY — Although CCh and cAMP analogues are normally depolarizing in intact pancreatic islets, repolarizing effects — particularly at high concentrations — have been reported[1,2]. It is possible that the failure of CCh, for example, to exert a stimulatory action in the cultured β cells results from the loss of the ion channels (probably Na^+ conducting[3]) mediating this response and the inhibitory action prevails.

As to Cook's second point, phospholipase C, the enzyme catalysing the production of $InsP_3$, is Ca^{2+}-dependent in the β cell[4]. The Ca^{2+} influx occurring during electrical activity can consequently be envisaged to result in stimulation of $InsP_3$ formation, mobilization of intracellular Ca^{2+} and activation of K^+ channels, thus providing a direct connection between regulation of intracellular Ca^{2+} stores and electrical activity. Another mechanism that may be significant in this context is Ca^{2+}-induced Ca^{2+} release[5]. The observation that the oscillatory rhythm in intact pancreatic islets can be reset by current injections[6] does therefore not exclude the involvement of intracellular Ca^{2+} pools in regulation of membrane excitability in the β cell.

We disagree with Cook's statement that the proposed mechanism is "unrelated to that used by β cells in intact islets" because the mechanism evoking bursting in intact islets is not known. Many processes are thought to be involved, for example inactivation of the Ca^{2+} current[3,6] and variations of the activity of ATP-regulated K^+ channels[7]. Although such processes may well be important, direct experimental evidence for their involvement has not yet been provided. On the other hand, activation of the current we described in our paper[8] clearly represents one mechanism capable of producing membrane potential oscillations in cultured β cells. Considering that the hormones and neurotransmitters required for its activation are present and released within the pancreatic islet, it seems reasonable to assume that this mechanism is operating in the intact tissue and thus contributes to the bursting pattern. Mechanisms similar to those we reported for the β cell have now been demonstrated to underlie rhythmic hyperpolarizations also in pituitary cells[9].

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