Direct evidence - the digital approach

Historically, the importance of calcium was discovered when experiments were performed in the presence and absence of calcium. Thus, Sidney Ringer discovered the essential role of calcium in the process that is now named excitation–contraction coupling (ECC)[1]. Ringer performed experiments with tap water and distilled water and identified the presence of calcium as a necessary requirement for ECC. This early experiments hinted that the physiologically relevant calcium concentration is rather small and is in the μM range. For Ringer, the »contamination« of the tap water with calcium was sufficient for his discovery. Because the contamination of all types of chemicals with small amounts of calcium is quite common, a nominally calcium-free solution cannot be regarded as being completely calcium-free; the solution requires an appropriate amount of a calcium-sequestering buffer, such as ethylene glycol tetraacetic acid (EGTA), ethylenediaminetetraacetic acid (EDTA) or 1,2-bis(o-aminophenoxy) ethane-N,N,N',N'-tetraacetic acid (BAPTA).

In red blood cells, George Gardos observed a breakdown of the potassium gradient in the presence of calcium under certain conditions[6,7]. This equilibration of the potassium gradient could be inhibited by calcium chelators[7]. Aside from the fact that the question of whether red blood cells contain calcium has a long history[8-10], this initial publication by Gardos inspired membrane function-related calcium investigations in red blood cells.

Although this digital approach is the most direct way to probe for the involvement of calcium, it generally lacks quantitative information. Nevertheless, experiments in the presence and absence of calcium are still popular and valid for performing negative or positive control experiments[11-14].

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