LETTERS

'Dynamic clamp' in cardiac electrophysiology

In the recent study 'Role of the transient outward current (I_{to}) in shaping canine ventricular action potential – a dynamic clamp study' by Sun & Wang (2005), the authors used the 'dynamic clamp' technique to inject a computer-calculated current into an isolated ventricular myocyte under current-clamp conditions, thus simulating an ion channel conductance in real time. This technique enabled them to nicely demonstrate how I_{to} modulates the ventricular action potential. The 'dynamic clamp' technique was introduced in neurobiology by Sharp *et al.* (1992, 1993*a*,*b*) to create an artificial electrical synapse between two isolated neurones or insert an artificial membrane conductance in a single isolated neurone. Similar techniques were independently developed by Robinson & Kawai (1993) and Hutcheon *et al.* (1996), presented as 'conductance injection' and 'reactive current clamp', respectively. The 'dynamic clamp' has become a widely used tool for the study of neural systems at the cellular and circuit levels, inserting artificial conductances in individual neurones (Sharp *et al.* 1993*a*; Hutcheon *et al.* 1996), coupling biological neurones (Sharp *et al.* 1992; Elson *et al.* 1998), and coupling model and biological neurones (Le Masson *et al.* 1995; Manor & Nadim, 2001).

In their paper, Sun & Wang (2005) state that 'the dynamic clamp was first developed as a neurobiological tool over a decade ago' and that 'the dynamic clamp is a new and effective tool to study the ionic basis of the electrical properties of cardiac cells'. I would like to place these statements in the proper historical context. The dynamic clamp is certainly an effective but not a new tool in cardiac electrophysiology. Actually, the technique was first developed over 25 years ago by Scott (1979) who used it as a tool to study the mutual synchronization of two small clusters of spontaneously beating embryonic chick ventricular cells. He created an 'Ersatz Nexus' by injecting an ionic current into each cluster corresponding to the current that would have flown if the clusters would have been physically coupled by gap junctions. One decade later, a related technique was independently developed by Joyner and coworkers to study the electrical interactions of isolated cardiomyocytes through an artificial gap junction (Tan & Joyner, 1990; Joyner *et al.* 1991). Initially, this 'coupling clamp' technique, which has been adopted by other groups (e.g. Watanabe *et al.* 1995; Huelsing *et al.* 2001), was implemented by an analog circuit, but in subsequent studies a computer-based system was used, which allowed one of the myocytes to be replaced with a real-time simulation of such cell (Wilders *et al.* 1996*a*,*b*). The system has also been modified to insert a simulated conductance in an isolated cardiomyocyte (e.g. Wagner *et al.* 2004), as in the study by Sun & Wang (2005). Recently, Berecki *et al.* (2005) extended this technique by effectively replacing a native ionic current of a ventricular myocyte with wild-type or mutant current recorded from a HEK-293 cell that is voltage-clamped by the free-running action potential of the ventricular myocyte ('dynamic action potential clamp'). In summary, the dynamic clamp started its life in cardiac electrophysiology as early as 1979 and has proven to be an effective tool since then.

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