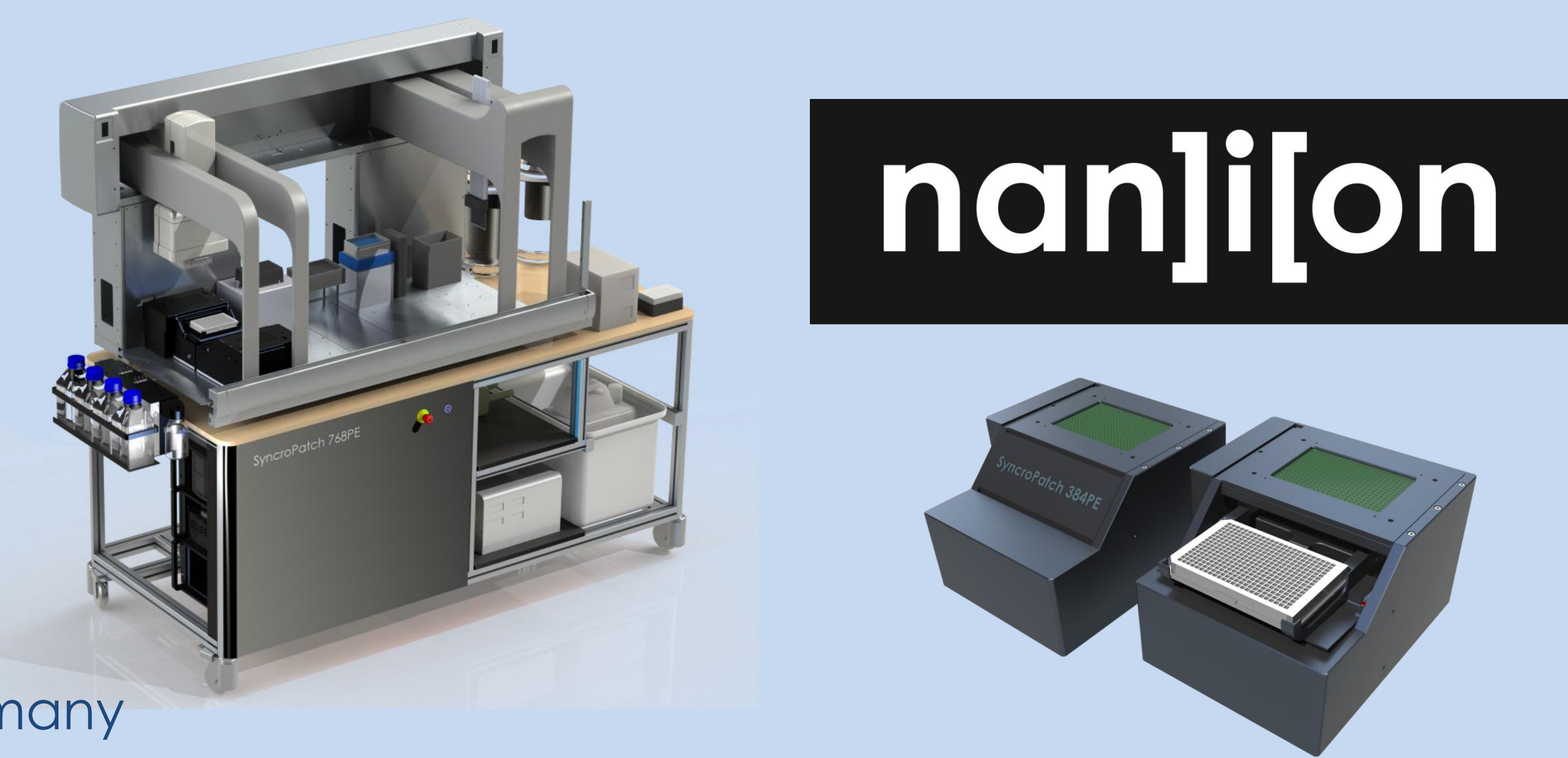


High throughput automated patch clamp of ion channels important in cardiac safety and drug discovery

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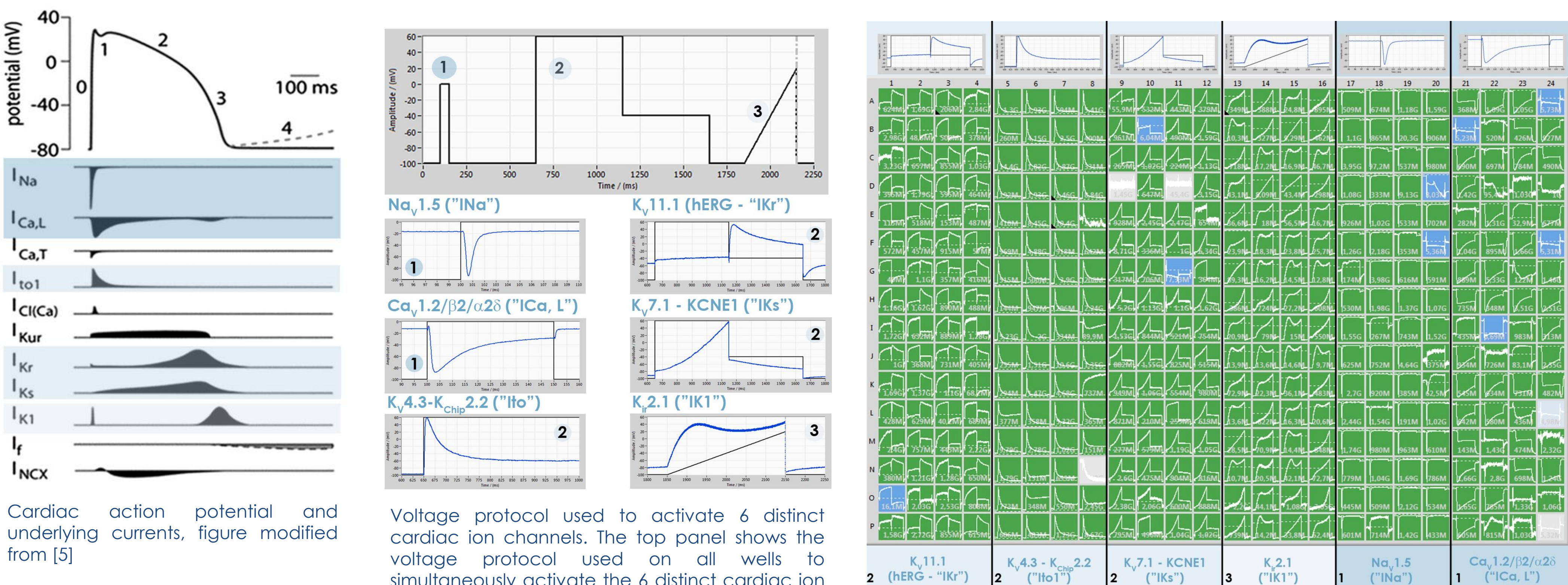


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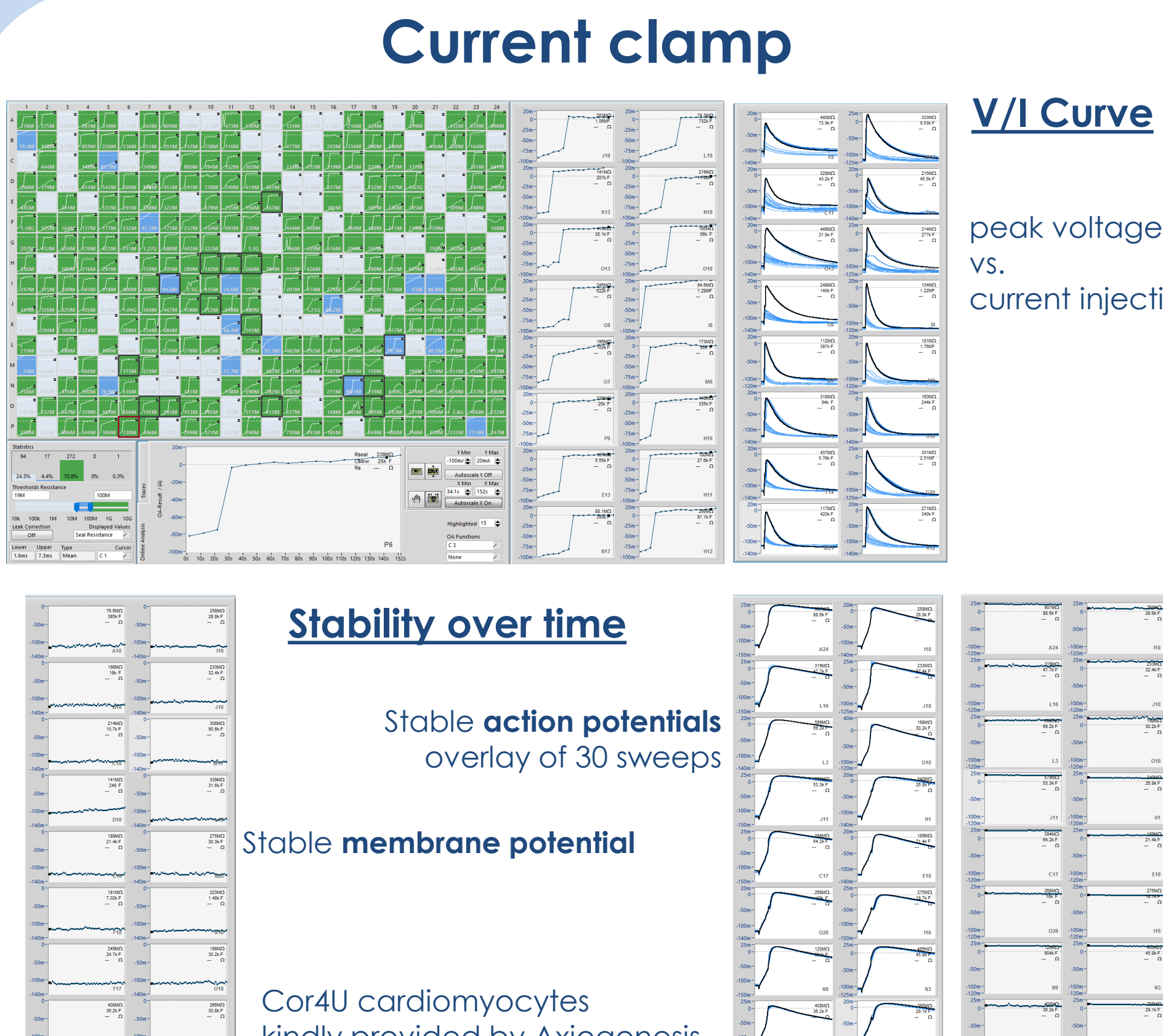
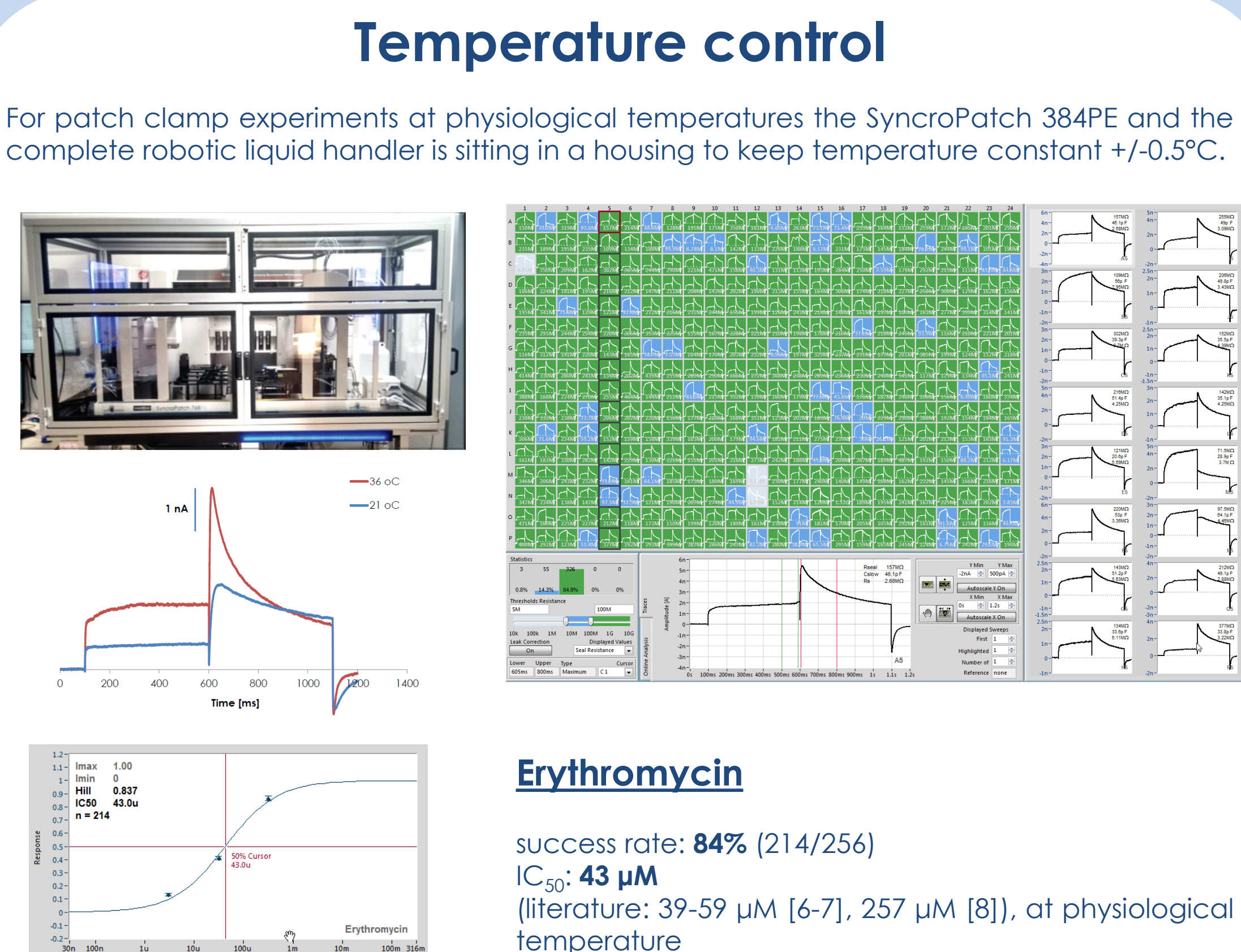
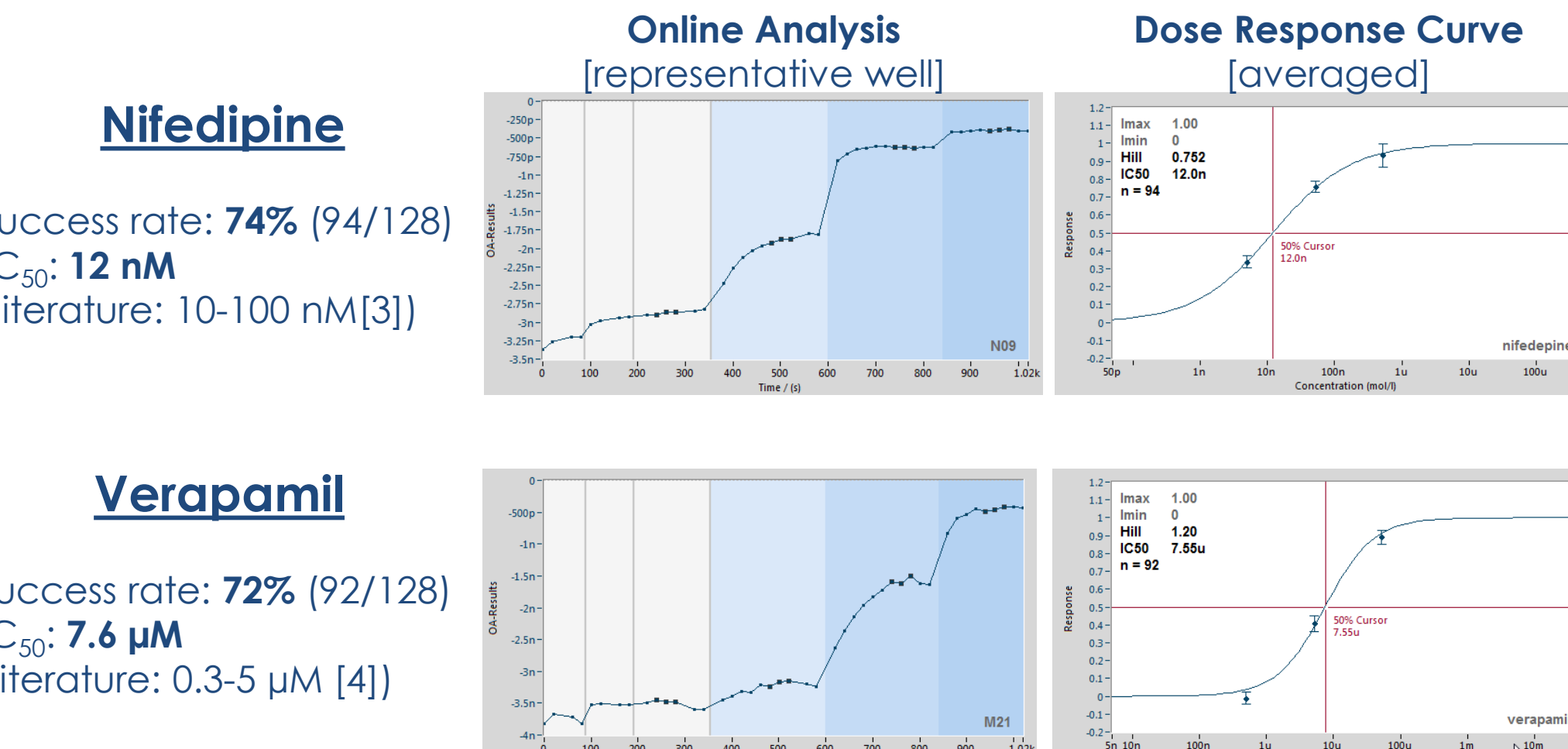
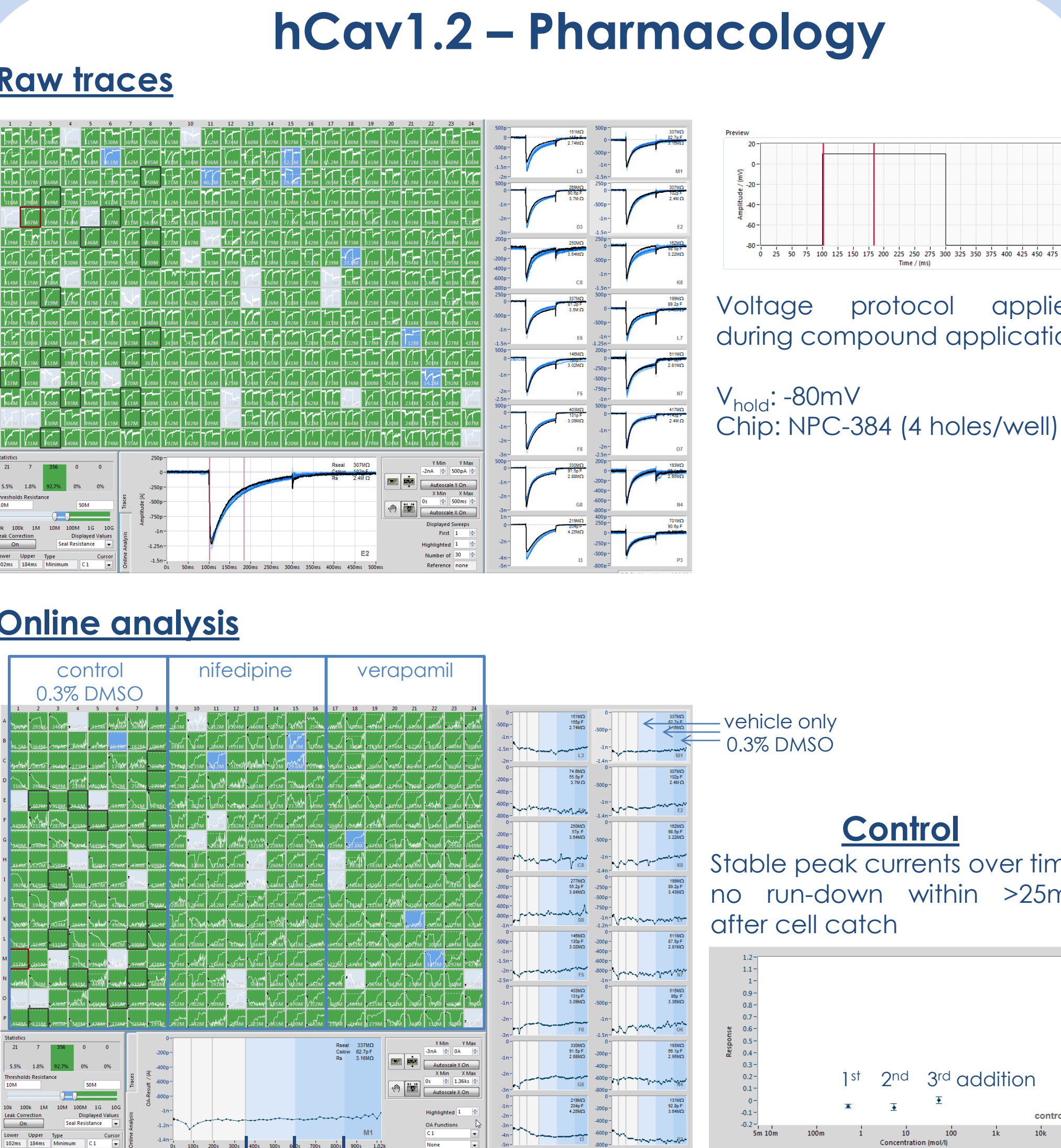
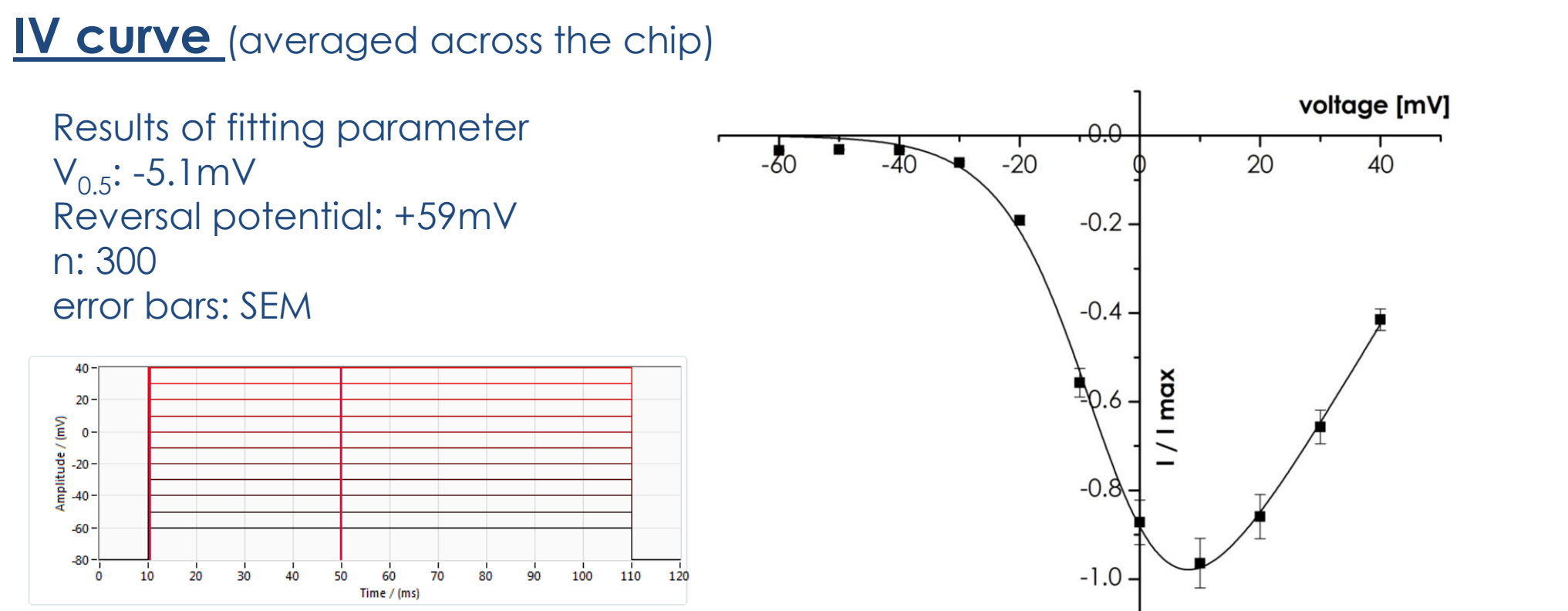
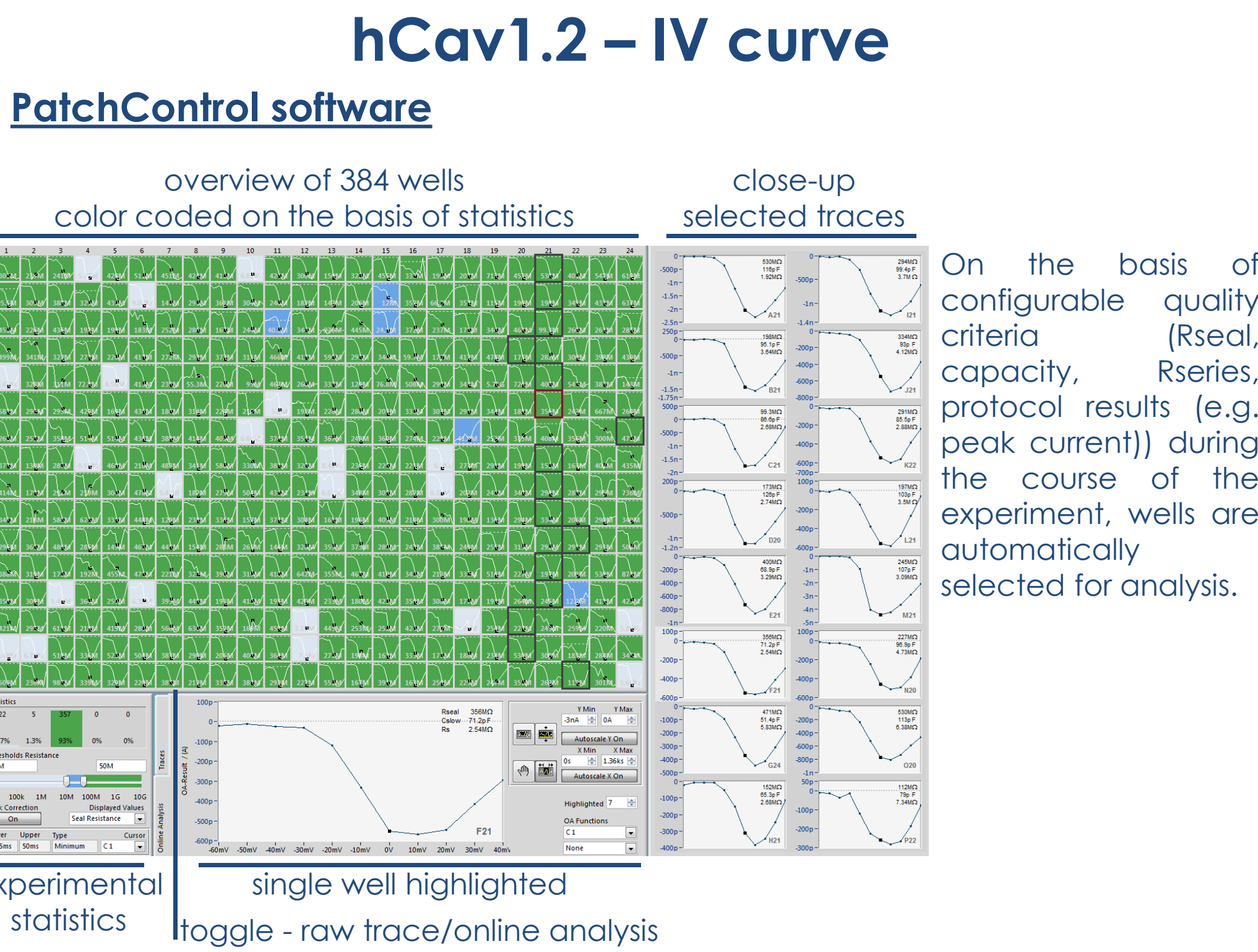
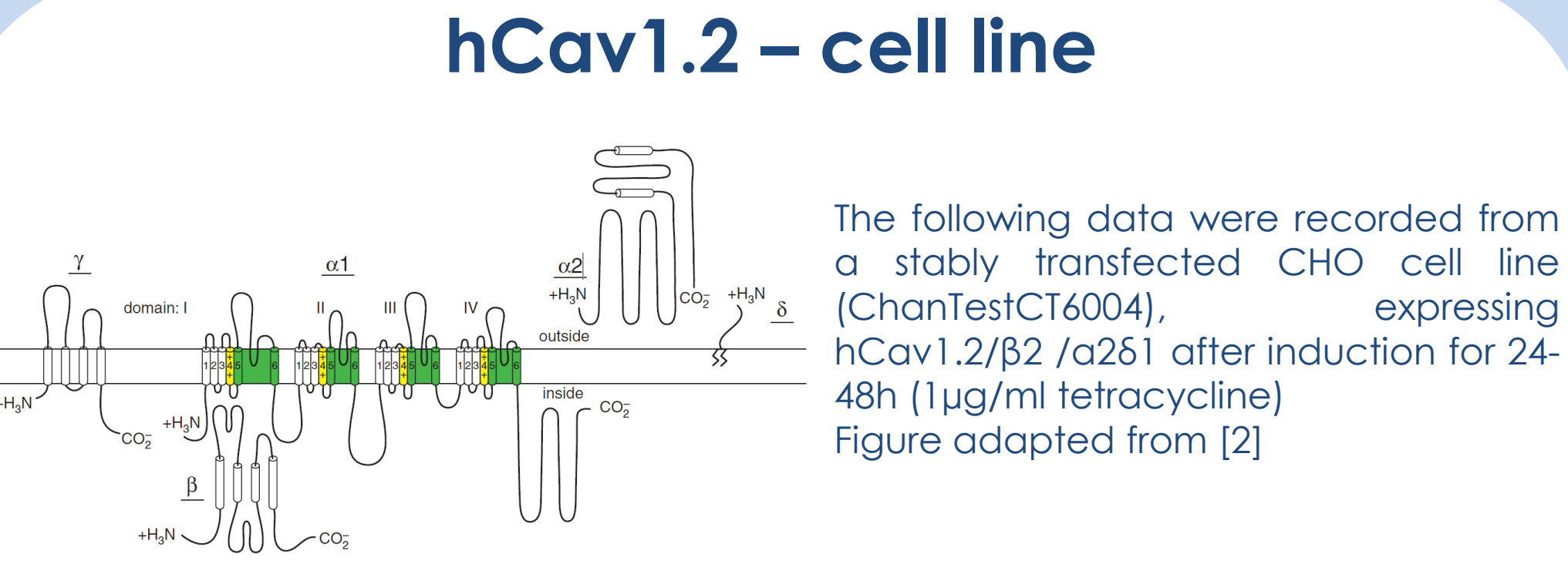
Abstract

One important part of the drug discovery process is the early assessment of a drug's safety profile. The new paradigm in cardiac drug safety screening, the Comprehensive In-vitro Proarrhythmia Assay (**CIPA**) initiative, is being introduced to provide a more complete assessment of proarrhythmic risk by evaluating and implementing currently available high throughput methods. An important part of this is an extension of the electrophysiological evaluation of ion channels beyond hERG to include other cardiac channels such as Na_v1.5, Ca_v1.2, KV-LQT1 (K_v7.1) and Kir2.1. The ion channel **Ca_v1.2**, however, is not only found in cardiac tissue but also in the CNS and smooth muscle cells, amongst others. It is thought to play a role in CNS function, cardiac and smooth muscle contraction, neuroendocrine regulation and a multitude of other processes (Hofmann, Flockerzi, Kahl, & Wegener, 2014). Blockers of Ca_v1.2 are used for the treatment of hypertension and angina and pharmacology of two such compounds (verapamil and nifedipine) are shown here. In this study, HEK or CHO cells expressing the ion channels **hERG**, **Na_v1.5**, **Ca_v1.2**, **KV-LQT1 (K_v7.1)**, **K_v4.3** and **Kir2.1** were recorded simultaneously on an automated patch clamp instrument recording from 384 cells in parallel. Additionally, CHO cells expressing Ca_v1.2 were recorded using multi-hole chips and pharmacology of verapamil and nifedipine will be shown.

Simultaneous recording of 6 cardiac ion channels [hERG, Na_v1.5, Ca_v1.2, KV-LQT1 (K_v7.1), K_v4.3 and Kir2.1]



Six different cardiac channels recorded simultaneously on the SyncroPatch 384PE. Shown is a screenshot of the data acquisition and analysis software showing an experiment recording six different cardiac channels at once. A representative image of the current recording for each ion channel is shown at the top.



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