

# High performance ion channel screening

npi electronic has revolutionized automated drug screening with the launch of the ScreeningTool, an automated system for screening of voltage- or ligand-gated ion channels in *Xenopus* oocytes, with millisecond resolution and high speed voltage clamping. The innovative instrument depends on a Tecan OEM liquid handling system for automated drug delivery, integrated with a miniature chamber design and unique amplifier to provide unprecedented speed, reproducibility and efficiency for high quality drug screening applications.

The ScreeningTool was developed through a collaboration between npi electronic and Prof Steffen Hering from the Department of Pharmacology and Toxicology at the University of Vienna, who originally invented the miniature recording chamber (patent pending). It was designed to automate the standard, two-electrode, voltage clamp screening procedure in a 15  $\mu\text{l}$  bath, covered by a glass plate with a funnel for precise, automated drug application by the liquid handling system. This set-up allows very fast solution changes and requires only minimal amounts of sample for the procedure. The design depends on

one of npi electronic's TURBO TEC amplifiers, which are specially developed for recording of bioelectrical signals from *Xenopus* oocytes, and Tecan's MSP9250 liquid handling system.

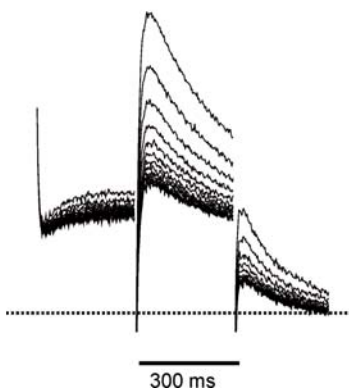
"The Tecan liquid handling system is ideal for the ScreeningTool because it has all the necessary features. In particular, the time it takes to apply the drug and the time it takes in between applications is very short," explained Mr Hans Reiner Polder, managing director of npi electronic. "Automating the drug application helps to get more reproducible data as the reliability of the instrument, based on the features of the Tecan liquid handling

system, is excellent. The uptake of the drug into the pipette and the wash-in and wash-out procedures are also fully automated, further increasing the reliability. This completely avoids cross-contamination between individual applications and the quality of the experiment is improved considerably. The system can be easily programmed by the customer, using scripting language that was developed in cooperation with Tecan."

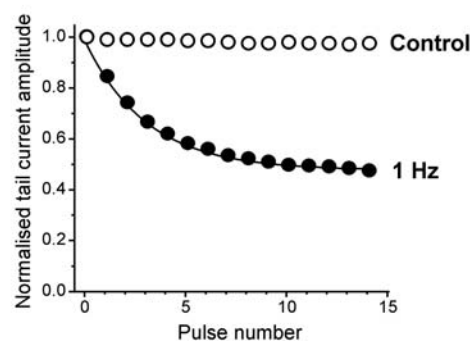
Using the Tecan liquid handling system means that only the pipette tip head needs to be filled with solution (~100  $\mu\text{l}$ ), so the ScreeningTool requires just fractions of the amount of sample that other instruments need to perform a complete experiment. All alternative instruments are based on tubing, which has to be filled with solution, resulting in a lot of sample wastage and considerable time delays. Another important feature is that this system can be programmed to ensure that cells are always kept at the same ionic milieu in between applications, which increases the reliability of the experiments as well as maintaining the cell's condition. Instead of using only a few solutions for one cell, more than a hundred solutions can be used on one single cell, allowing many more experiments to be performed in a shorter period of time.

## hERG channel inhibition by 10 $\mu\text{M}$ Amiodarone (black filled circles) at 1 Hz

Superimposed hERG currents at 1 Hz



Peaks of hERG currents plotted against numbers of pulses





Automated, high speed ion channel screening with millisecond resolution



The Screening Tool is automated using Tecan's MSP9250

"Combining the Tecan MSP9250 with Prof Hering's special chamber makes this instrument unique and very specialized for its applications; there is no competing instrument that could fulfil all these parameters at the same time," said Hans Reiner.

Voltage clamping is performed using npi's TURBO TEC series of amplifiers, as Hans Reiner explained, "The npi amplifiers are based on a unique, sophisticated design that we developed years ago and their high speed of response makes them superior to similar systems. The amplifiers also have a very high degree of precision, so they are ideal for Prof Hering's chamber design."

The ScreeningTool's flexible fluid application and high performance voltage clamp make it highly suitable for drug screening on ligand and voltage gated ion channels. The system is specifically designed for *Xenopus* oocytes, which are widely used for drug screening and for pharmacological safety tests. *Xenopus* oocytes are often used to analyze the interaction between certain

drugs and ion channels or receptors that could be expressed in the oocytes, such as investigations of the hERG channel - a special potassium channel derived from the heart. Some drugs affect this channel and alter the heart beat, causing arrhythmia, and such cases would not normally be suitable for further development.

This is the first time that npi electronic has used a Tecan OEM component for one of their products and Hans Reiner is very impressed with the collaboration service, "We had a lot of support from Tecan and established a good relationship, which helped us to produce a professional version of the software that is suitable for use in the pharmaceutical industry, within a very short time period."

"In the future we plan to develop other versions of the ScreeningTool designed for different cell types and are very interested to continue the collaboration with Tecan. We had a very good experience with this product and I have already recommended Tecan to all our partner companies."

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