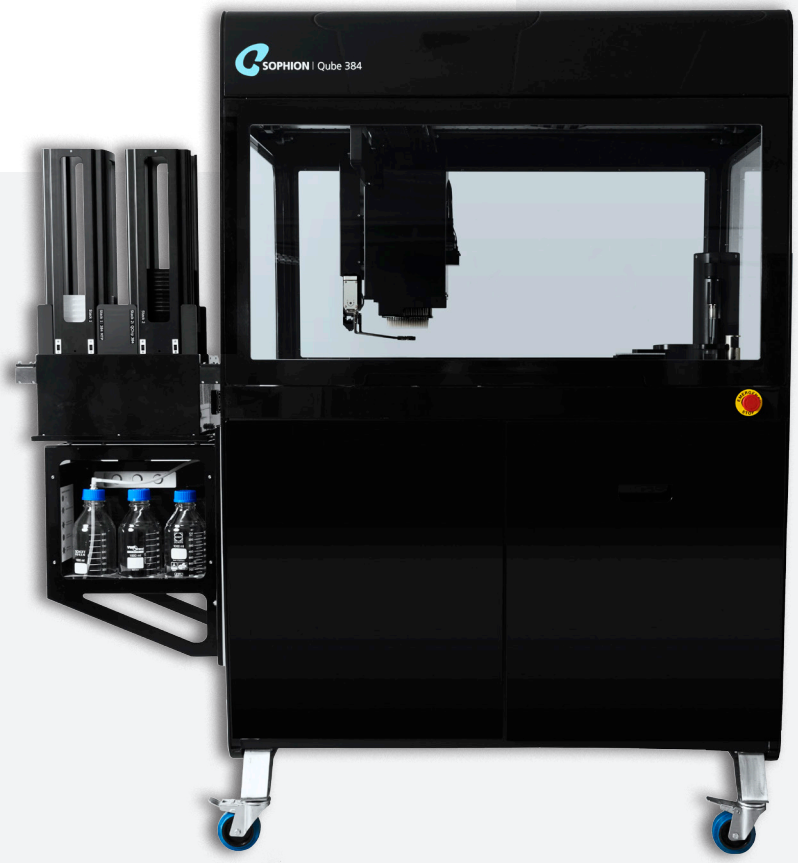
SOPHION
BIOSCIENCE

Product Specification

Qube 384
Automated Patch Clamp Systems

- From HTS to support of extensive medicinal chemistry programs
- Unattended operation to ensure high laboratory efficiency
- Advanced consumables ensure consistent high fidelity data
- Well documented success rates, repeatability and reproducibility
- Intuitive software - Powerful data analysis
- One vendor solution



Bridging the gap between high throughput screening and high fidelity in ion channel research and discovery

Qube 384 is a high-throughput, automated patch clamp system for whole-cell and perforated-patch measurements on ion channels. Qube runs unattended and thus requires minimal work load while generating high fidelity data. Time is freed up to digest the data that are automatically analyzed in Sophion Analyzer. Data can be exported to in-house databases so next steps in the drug discovery program can be planned efficiently and the chemist can get valuable and accurate information quickly. Bringing electrophysiology into the primary screening means that hit validation can be omitted and lead characterization can be started earlier than with traditional fluorescence based screening[1].

1 Chambers et al. VOL 4 NO. 2 MARCH 2016 ASSAY and Drug Development technologies.

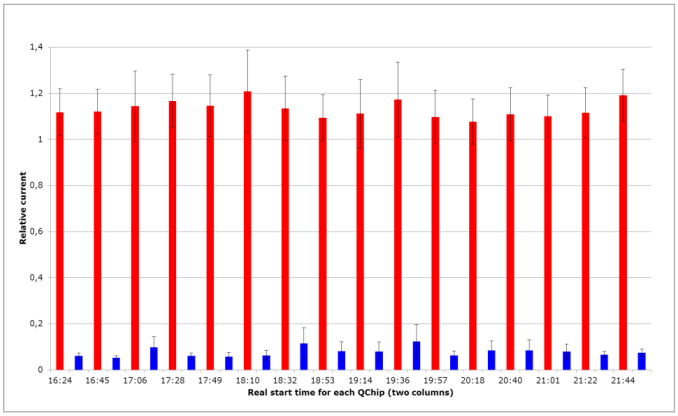


Fig. 1: Unattended Qube run with 16 QChips in a row. $Na_V1.4$ was exerted to a two pulse protocol. Half of the test substance was 30 µM tetracaine (blue columns) and the other half was vehicle (red columns). One red and one blue column belong to one QChip.

Support of medicinal chemistry programs is also possible with Qube with both cumulative and non-cumulative dose response experiments .

- Accurate **voltage clamp** is ensured with full R_S-compensation[2]
- **Ligand** exposure time down to 0.8 s to prevent desensitization
- Physiological behavior is measured with **current clamp**, which can be combined with voltage clamp in the same sweep for extra experimental control
- Thermal dependence is investigated with **temperature control** at the recording site, and can both heat and cool

Both during the primary screening and the lead optimization Qube ensures automatic and full traceability of compounds. All compound information is handled by lists in combination with reading barcodes on the compound plates.

Qube utilizes a 384-well measurement plate and records from all 384 channels in parallel with an equal number of amplifiers and pipettes.

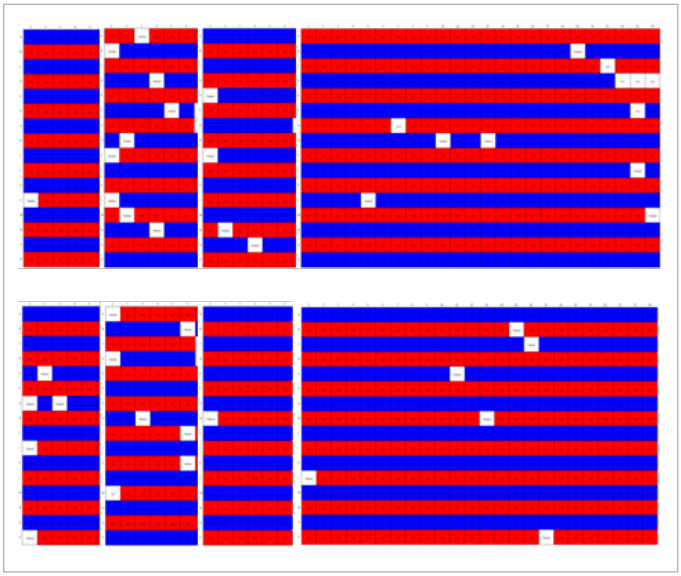


Fig. 2: $Na_V1.4$ screen with 16 compound plates tested (6144 wells). The overall success rate was 93%. Analysis of eight plates is shown. There was no false positive/negative. Blue means 30 µM Tetracaine giving block and red means control. The white sites are those that are automatically failed by the quality filters.

Advanced consumables ensure consistent high quality data

The planar patch clamp chip, the QChip, is designed for stable and maximum performance, which is required in HTS. Success rates well above 90% is a prerequisite and are obtained due to the combined action of Qube and the unique features of the QChip.

- Giga-Ohm seals and thereby excellent voltage control in recordings
- Microfluidic channels in the QChip provide fast and complete liquid exchange during the experiment (τ < 40 ms)
- Integrated and maintenance-free electrodes with one set of electrodes per measurement site decrease any risk of drift in results (< 0.01 mV/min)
- One- and ten-hole QChips as standard and varying number of holes 1-36 for assay development
- Custom-made number of holes as well as hole sizes

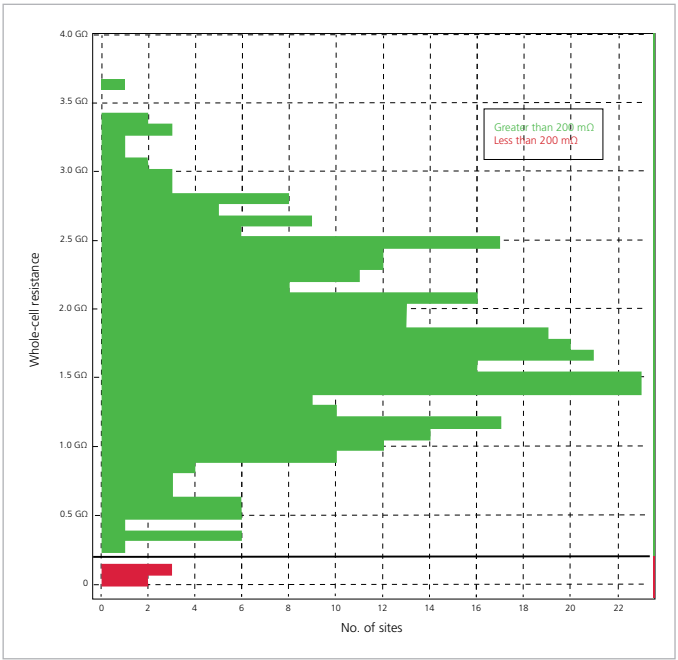


Fig. 3: Distribution of single cell resistances across a QChip 384X. Cells were TE671 which endogenously express $Na_v1.4$. The Viewpoint software is equipped histograms that have dividers and a range of color grading to highlight the distribution. In this case the lower limit for seal quality has been set at 200 MΩ.

Qube generates data with high degree of reproducibility and repeatability

Table 4: hERG pharmacology with three reference compounds. Experiments on two different Qubes gave very similar results

Compound	Qube A	Qube B	Ratio Max/Min
Cisapride	51 nM n=93	55 nM n=85	1.08
Terfenadine	298 nM n=96	301 nM n=88	1.01
Verapamil	548 nM n=84	756 nM n=85	1.38

Modular with throughput to fit any need

Qube 384 is built of modules and can be fitted to meet any need for throughput. All Qube configurations[2] are solely provided by Sophion to ensure stable operation and with only one point of contact for application support and technical service.

- Integrated cell hotel and patented cell-preparation unit increase cell viability
- Plate stacker and autofill reservoirs ensure up to 10 hours of unattended operation
- Temperature control to both cool and heat the recording site
- Across-plate or cumulative dose-response experiments
- Just-in-time dilution of stock solution to mitigate adherence of compound when screening many compound plates

Qube can also be integrated with any third-party instrument for absolutely minimal hands-on time, and can act both as slave and master is such a setup.

2 May not apply if integrated with third party equipment in an automation line in which case Sophion can provide scheduling interface

Easy setup and analysis

ViewPoint, the software for controlling Qube, is intuitive and flexible to allow customer specific screening scenarios.

- Learn to operate Qube in less than one day
- Simple user interface to eliminate human errors
- Powerful engine – your Application Scientist can quickly adapt for special operations

Sophion Analyzer is the imbedded software that is designed to handle the massive amount of data generated by high fidelity electrophysiology.

- Project analysis – after initial setup, all subsequent runs are analyzed automatically
- Export of user defined results for third party applications or company data bases
- Data security with automatic back up routines
- Easy move of data for sharing, segmenting or for creating more storage space on Qube

In fig. 4 are shown the steps from raw traces to the fully analyzed data with hit detection filter applied. Data can also be exported to third-party software and customized to different laboratory information systems upon request.

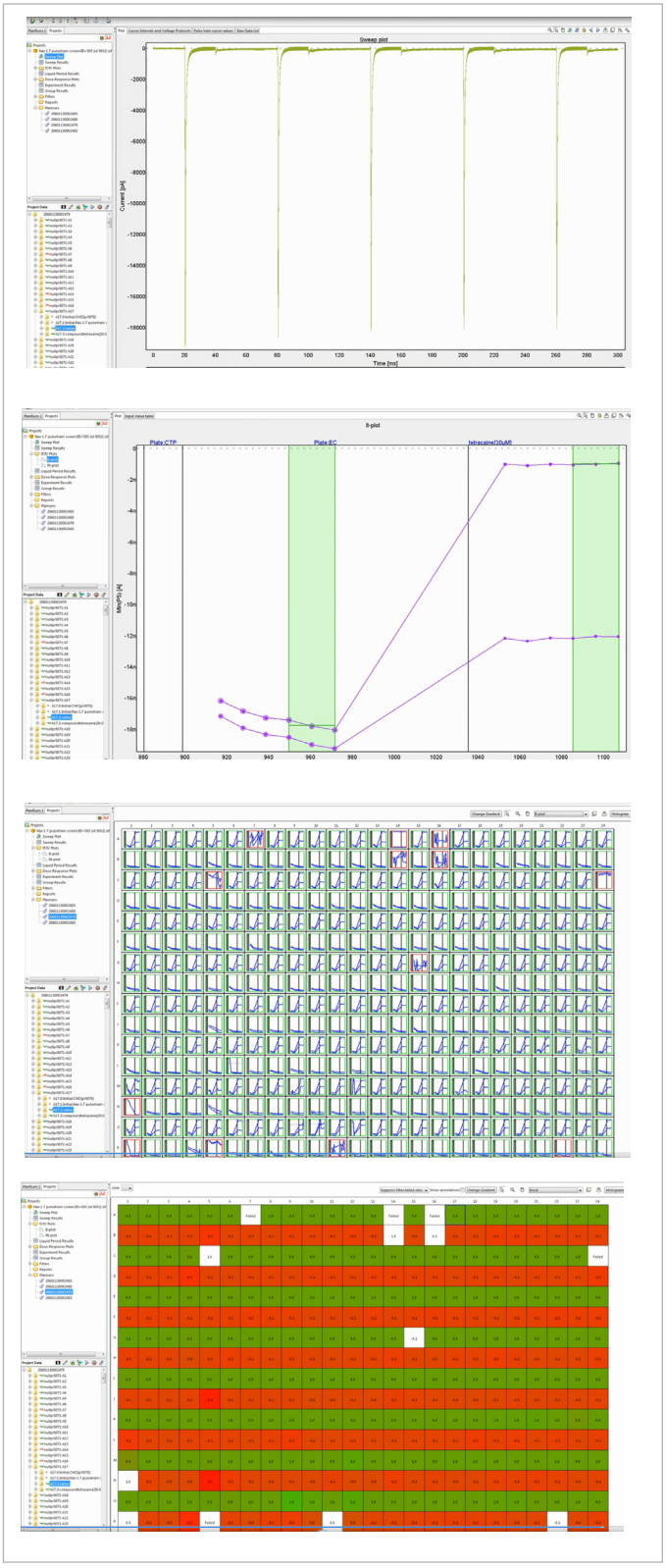
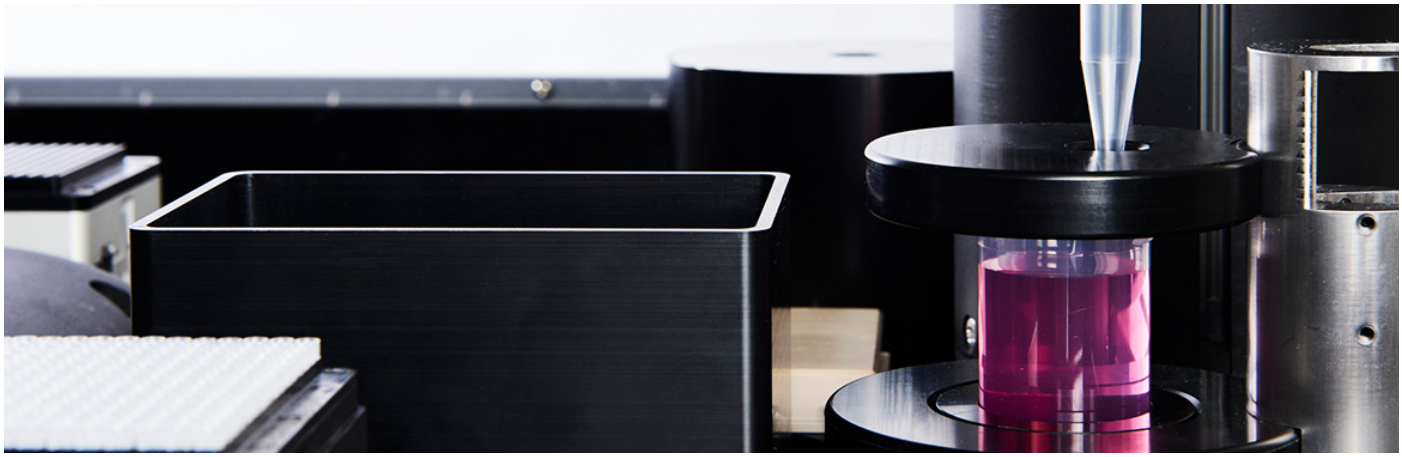


Fig. 4: Screen prints from Sophion Analyzer demonstrating the analysis from the raw current traces that are responses to a five-pulse train, through a current vs. time plot (IT-plot of peak 1 and peak 5 for a single site), the plate-view of the IT-plot for a whole plate to the final analysis of hits/no-hits as color coded for a whole plate.

Performance/features	Qube 384	Qube 384 with stacker	Qube 384 integrated
Hardware modules	Automatic cell preparation (always included) Stacker and autofill reservoir (optional) Third party integration (optional) Temperature control; heating/cooling at recording site (optional)		
Unattended operation	Up to 4 hours	Up to 10 hours	∞
Target throughput per month	<100,000	<400,000	>400,000
Success rate (incl. pharmacology and quality filtering), typical	>93%		
Consumable/compound handling	Pre-loaded in Qube workplane	In the stacker	Third party instrumentation
Just-in-time dilution of stock solution	√		
Resuspension of compound	√		
Liquid handler tips	Disposable Washable onboard, water + optional solvent Automatic exchange at user-defined intervals		
Number of extracellular liquid additions	∞		
Liquid exchange rate	τ < 40 ms		
Number of different intracellular solutions	24		
Automatic exchange of intracellular solution	√		
Stimulation mode	Voltage-gated Ligand-gated Current clamp		
Free combination of stimulation modes in same sweep	√		
Shortest/longest voltage-segment	1 ms / 2h 47m		
Shortest exposure time in ligand-gated experiments	0.8s		
Resolution of current injection	0.6 pA		
Recording configuration	whole-cell / perforated patch		
Cell types applicable	Cell lines Stem cells Primary cells		
QChip compatibility	Single-hole Multi-hole Variable hole number Variable hole size		
Maintenance of electrodes	None		
Electrode stability	Electrode drift < 0.01 mV/min		
User maintenance of instrument	None		
Giga Ohm seals	√		
R_{series} compensation*	√		
C_{cell}, C_{slow} and leak compensation	√		
Data security and traceability	Automated backup Full log of activity User-hierachy		

Dimensions	Qube 384 Basic	Qube 384 with stacker	Qube 384 integrated
Width	128 cm	195 cm	128 cm + external
Depth	85 cm	85 cm	85 cm + external
Height	187 - 206 cm (open)	187 - 206 cm (open)	187 - 206 cm (open)
Weight	600 kg	630 kg	600 kg + external
Point pressure	≤1kg/cm²	≤1kg/cm²	≤1kg/cm² (Qube)
Requirements			
Power supply	100-240 V 50-60 Hz Max. 6A	100-240 V 50-60 Hz Max. 6A	100-240 V 50-60 Hz Max. 6A
Pressure	6 - 8 Bar	6 - 8 Bar	6 - 8 Bar
Vacuum	900 - 620 mBar	900 - 620 mBar	900 - 620 mBar
Network	100 BaseT (100 Mbit)*	100 BaseT (100 Mbit)*	100 BaseT (100 Mbit)*

*Qube uses gigabit switch internally which data transfer can benefit from



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