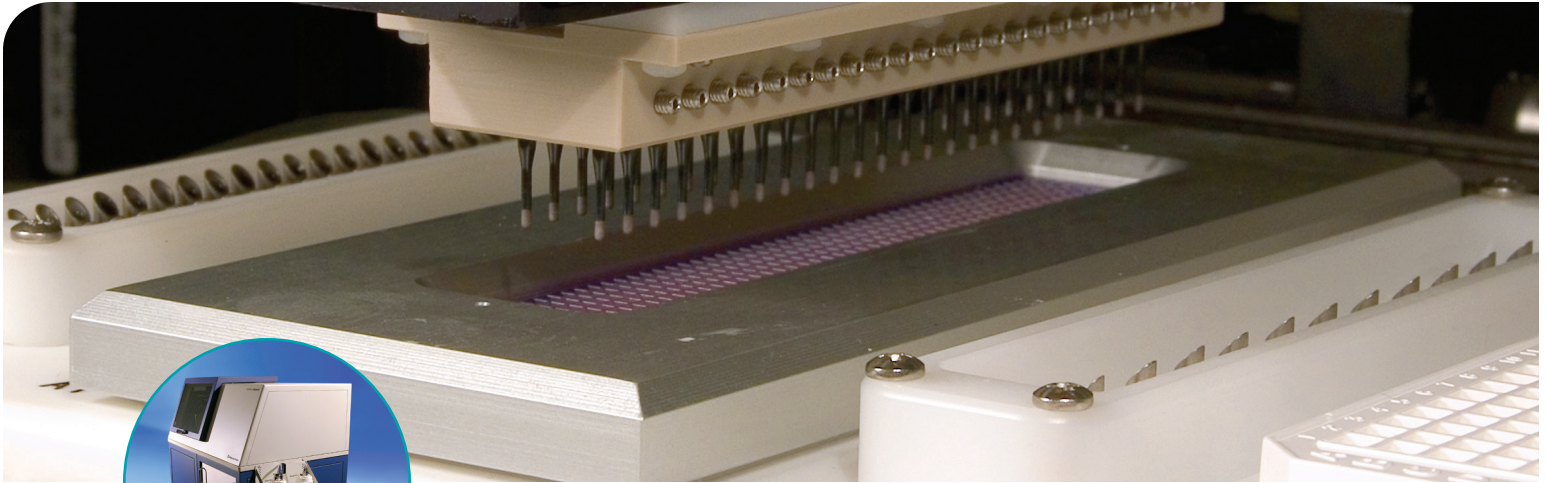


IonWorks Quattro System

A HIGH-THROUGHPUT SYSTEM FOR ELECTROPHYSIOLOGICAL SCREENING



→ **POPULATION PATCH CLAMP TECHNOLOGY**

→ **USED FOR DIRECTED SCREENS, HIT CONFIRMATION, SAFETY PROFILING, PHARMACOLOGY**

→ **EASY SET-UP AND OPERATION**

→ **COMPLETE TURNKEY SOLUTION**

Voltage-gated ion channels represent a largely untapped portion of the drug target market. Until recently, voltage-gated ion channels have been studied using either conventional patch clamp techniques or indirect higher throughput methods, which include assays such as radioligand binding, ion flux or fluorescent indicators of membrane potential or intracellular calcium. Although these methods have high throughput, they lack direct voltage control and cannot drive ion channels to specific conformational states. Therefore, the informational content of these screens is not as biologically relevant as conventional patch clamping.

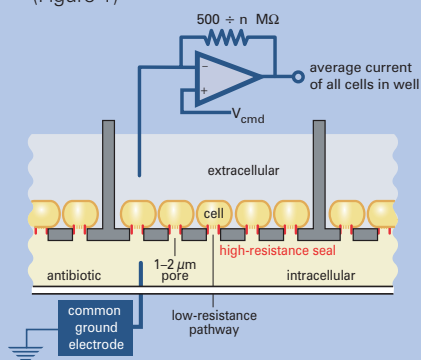
The throughput of conventional patch clamping is extremely low, which creates a severe bottleneck in the follow-up of HTS assays from the indirect techniques. To address this bottleneck, Molecular Devices introduced the IonWorks Quattro™ System in 2005. The system offers higher throughput than conventional patch clamping, making it perfect for secondary screening of hits from HTS, primary screening of directed libraries, early safety profiling and pharmacology assays.

POPULATION PATCH CLAMP TECHNOLOGY

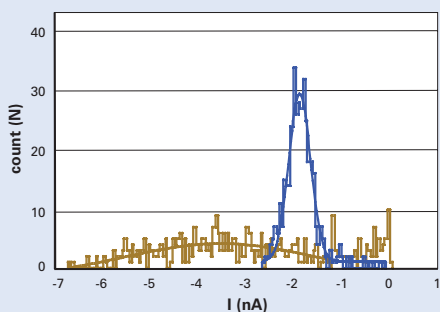
The IonWorks Quattro System utilizes a new PatchPlate™ substrate with Population Patch Clamp™ (PPC) Technology that contains multiple recording sites per well. (See Figure 1.) The measured ion channel current from each well is an ensemble-average of a population of cells. With PPC Technology, well-to-well variability is dramatically reduced. (See Figure 2.) In addition, the success rate of obtaining a current measurement from each well utilizing the new PatchPlate PPC Consumable is nearly perfect (> 95%). As a result, subsequent IC₅₀ determinations are highly consistent (Figure 3) with robust Z' factors. Hence the throughput of the IonWorks Quattro System is increased four-fold over the IonWorks® HT System—already the highest throughput electrophysiology screening system on the market. The cost per data point is also significantly reduced by more than 50% compared to the IonWorks HT System. The IonWorks Quattro System with Population Patch Clamp Technology is yet another innovative and revolutionary advance in ion channel screening instrumentation from Molecular Devices.

Population Patch Clamp Technology

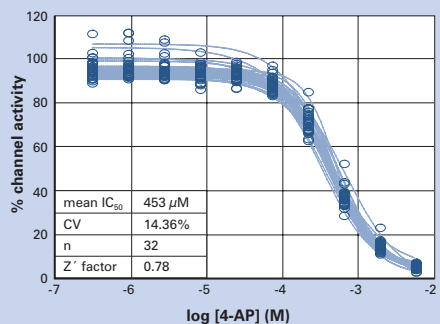
(Figure 1)



The IonWorks Quattro System employs a new PatchPlate PPC Substrate that contains multiple recording sites per well. Thus, ion channel currents are ensemble-averaged from a population of cells. As a result, success rates using PatchPlate PPC are nearly perfect (> 95%) and the recordings and subsequent IC_{50} determinations are highly reproducible.

Data Consistency of the IonWorks Quattro System (Figure 2)

Comparison of $Na_v1.5$ peak currents measured in the IonWorks Quattro (blue) and IonWorks HT (orange) Systems. The tighter data distribution of the peak current variability indicates that the IonWorks Quattro System significantly reduces the impact of biological variability. Cell line: Chinese Hamster Lung (CHL).

Robust and Consistent Pharmacology (Figure 3)

Pharmacology of 4-aminopyridine (4-AP) inhibition of $K_v1.3$ expressed in CHO cells on the IonWorks Quattro system. A 384-well compound plate was used consisting of 32 replicate 10-point titrations of 4-AP and four sets of positive and negative control columns. The IC_{50} curves for each column were plotted individually and the average IC_{50} value obtained for all 32 replicates was 445–453 μ M (95% confidence interval). The success rate of this experiment was 99.7% and the Z' was 0.78. Data is plotted as the mean \pm SEM, and indicates the extremely tight distribution of the data.

SCREEN VOLTAGE-GATED ION CHANNELS

The IonWorks Quattro System uses cell lines expressing voltage-gated ion channels, such as K_v , Na_v and Ca_v channels. Additional channel types, such as chloride channels, K_{ir} and slow, non-desensitizing ligand-gated ion channels, can also be used.

SIGNIFICANTLY REDUCED COST PER DATA POINT

The IonWorks Quattro System performs direct functional assays at throughput levels needed for ion channel drug discovery. The cost for indirect assays is approximately 15¢ per data point, but subject to much higher rates of false positives and false negatives, therefore the true costs are much higher. In contrast, the IonWorks Quattro System generates high quality electrophysiological data and has considerably lower rates of false hits with only a small increase in the cost-per-data-point (75¢ per data point) compared to indirect assays. The IonWorks Quattro System can generate over 400,000 data points per year.

EASY TO SET UP AND RUN EXPERIMENTS

The IonWorks Quattro System is easy to set up and operate—routine day-to-day operations do not require a trained electrophysiologist. The IonWorks Quattro System software allows the user to define assay protocols, control the system and analyze data through the intuitive and flexible PC graphical user interface.

TECHNICAL SPECIFICATIONS

Dimensions (in.): 55.6 (H) x 58.1 (W) x 32.5 (D)
 Dimensions (cm): 141.2 (H) x 147.6 (W) x 82.6 (D)
 Weight (lbs.): 550 (250 kg)
 Vacuum req.: Min. 120 mbar @ 0.6 m³/hr.
 26 in. Hg @ 1,200 cfm
 Microplate formats: 96- and 384-well
 Read time: < 60 minutes/384-wells
 (protocol-dependent)
 Consumables: Supports both standard
 PatchPlate and PatchPlate
 PPC Substrates

Integrated fluidics with 12-channel pipettor

Integrated 48-channel voltage clamp amplifier,
 switchable between standard and Population
 Patch Clamp modes

ORDERING INFORMATION

IonWorks Quattro System:

Part Number: QUATTRO

→ IonWorks Quattro Instrument

→ PC with Windows Operating System

→ Accessories

→ IonWorks Quattro System operating software
 and manuals

PatchPlate (for IonWorks HT & IonWorks Quattro):

Part Number: 9000-0688

→ (50) plates per case

PatchPlate PPC (for IonWorks Quattro only):

Part Number: 9000-0902

→ (50) plates per case

SALES OFFICES

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→ China (Shanghai) +86-21-6887-8820

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