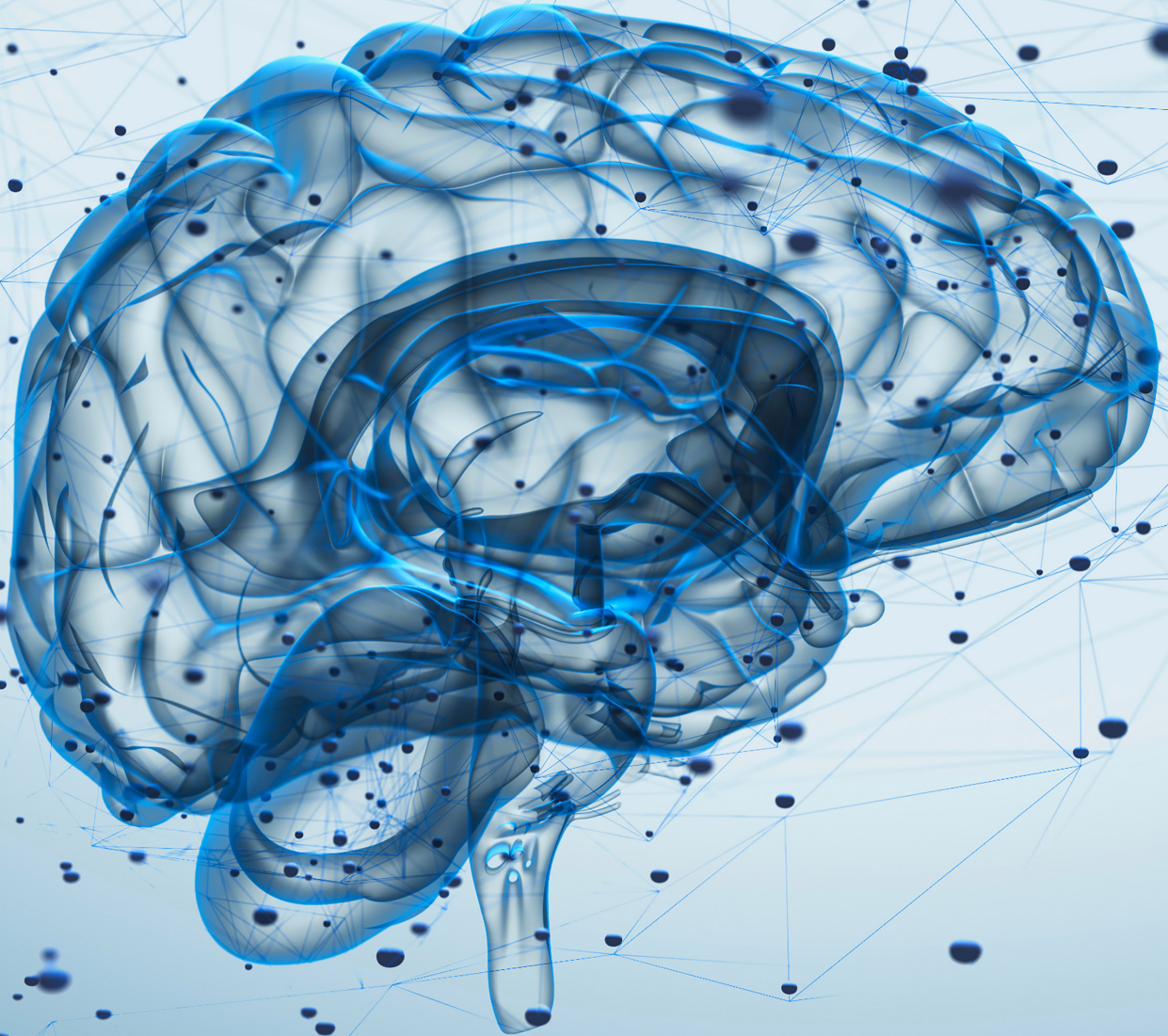




CELL
Microsystems®



IonFlux Mercury

Automated Patch Clamp Systems

Unmatched Compound Delivery And Washout Speed

Automated patch clamp systems have enhanced our understanding of ion channels in the brain, heart, and other excitable tissue. However, limitations in fluid control have hindered drug discovery by bringing complicated discovery and screening assays to a halt.

IonFlux Mercury automated patch clamp systems from Cell Microsystems have been designed to eliminate drug delivery limitations that plague complicated ion channel assays.

Benefits of IonFlux Mercury:

- High-quality recordings
- Rapid data collection
- Little to no cell desensitization
- High throughput



Ion channels make up over 25% of available drug targets

“Despite their attractiveness as drug discovery targets ion channels remain an under-exploited target class, which is in large part due to the labour-intensive and low-throughput nature of patch-clamp electrophysiology.”

Dunlop, J. et al.

Nature Reviews Drug Discovery: 7, 358-368

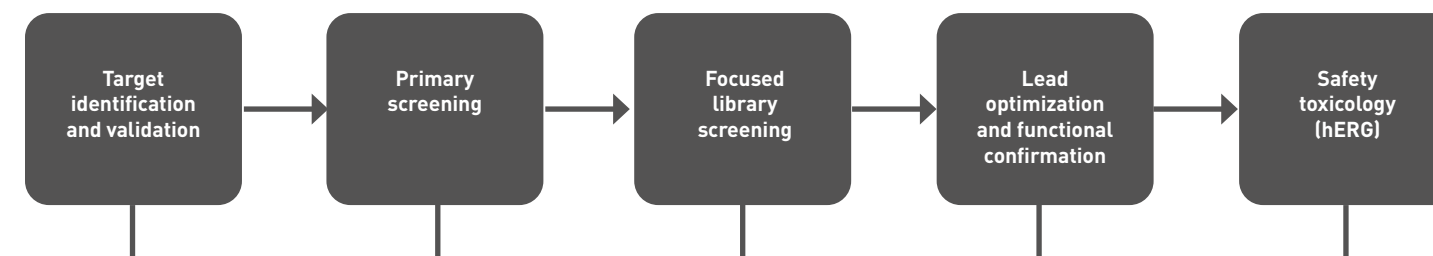
Flexibility & Scalability

IonFlux Mercury systems offer scalable solutions for automated electrophysiology, providing 16 to 256 parallel channel recordings. Providing one of the lowest costs per data point, well-plate simplicity, user-friendly software, and a space-saving footprint, IonFlux Mercury systems are ready to meet all of your ion channel research and drug discovery needs.

Common IonFlux Mercury Application Areas

- Functional expression of ion channels
- Compound profiling
- Mutant and cell line screening
- Recording from primary cells
- Transient transfection

Ion channels represent a major classification of targets for drug discovery. Ion channels play critical roles in various diseases, including epilepsy, Alzheimer’s disease, and cardiovascular diseases. **Patch clamp measurements are essential to drug discovery and are currently required for the approval of pharmaceuticals by the United States Food and Drug Administration (FDA).**

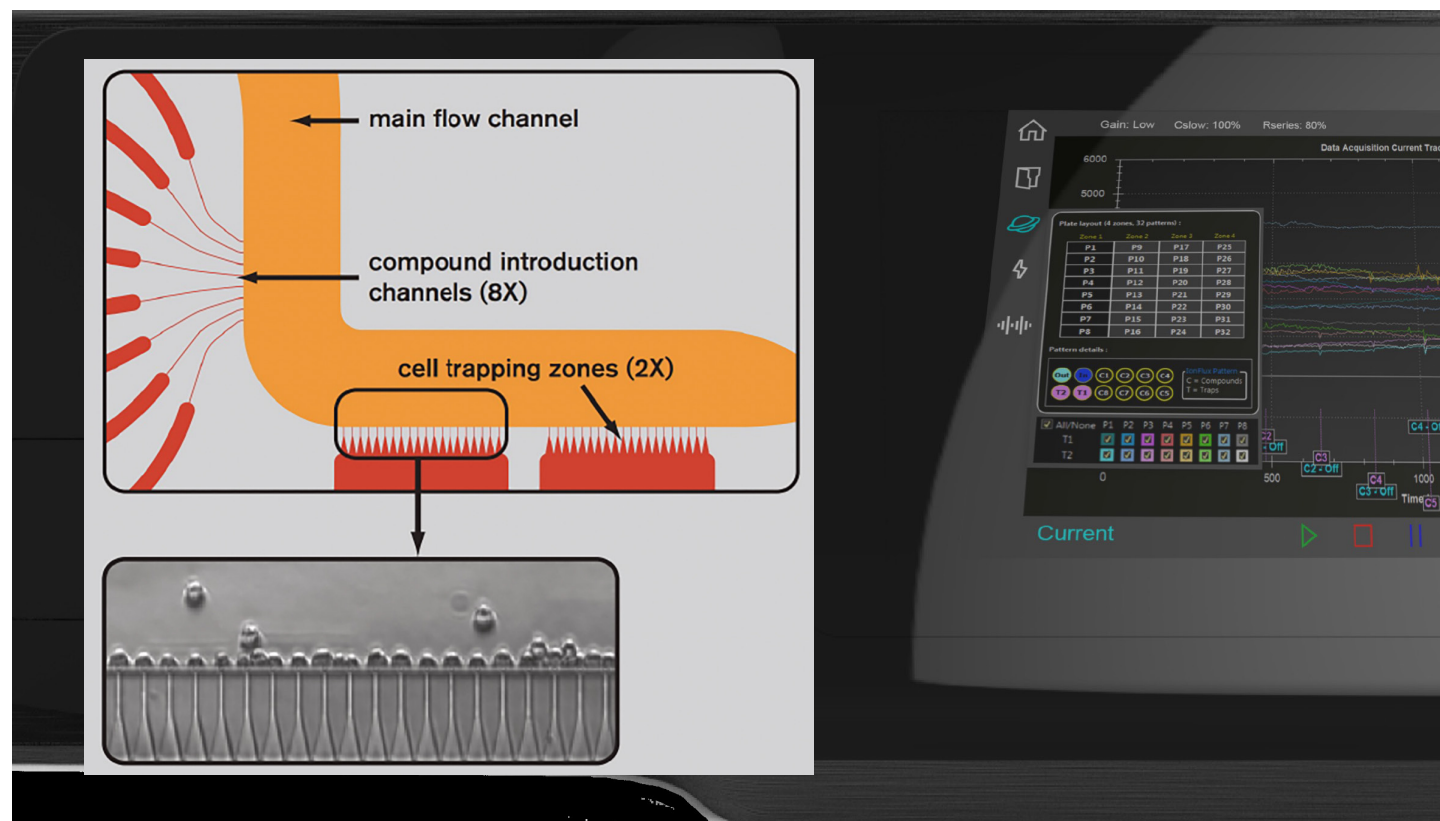


IonFlux Mercury in Drug Discovery & Development

IonFlux Mercury systems provide the highest throughput at the lowest operating cost of any automated patch clamp system available.

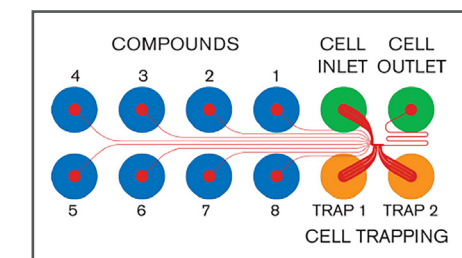
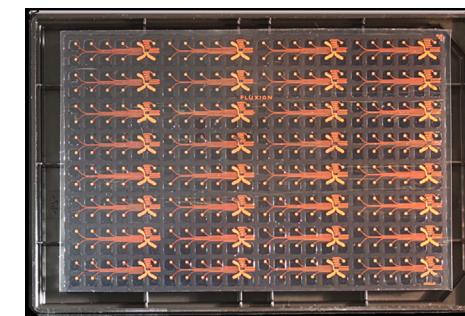
System Features

IonFlux Mercury systems operate using unique microfluidic plates, making them the only systems available where all cell recordings and liquid exchanges are performed within the plate. Without the hindrance of liquid handlers during data collection, IonFlux Mercury systems enable specialized high throughput assays, which would be impractical or impossible using other asynchronous systems.



Microfluidic Plates

IonFlux Mercury systems harness the power of microfluidic technology to embed micron-scale fluidic channels on the bottoms of Society for Biomolecular Screening (SBS) standard well plates. With available 96 and 384-well plates, IonFlux Mercury systems are compatible with existing laboratory equipment while still providing a high degree of functionality and flexibility.



Each experimental pattern on an IonFlux plate is comprised of 12 wells:

- 8 compound wells
- 2 cell trap wells
- 2 cell inlet and outlet wells

Simple Plate Preparation

1. Load cells into inlet wells
2. Load buffer into trap wells
3. Load up to 8 unique compounds or concentration series into the compound wells

Cells are pushed through the main flow channel using pneumatic pressure. An ensemble of 20 cells (ensemble plate) or a single cell (single cell plate) is trapped in small channels. Two recordings per experimental pattern are exposed to the same group of 8 compounds/ concentrations, **providing 8 data points in duplicate for enhanced data fidelity.**

Electrodes from the instrument are placed in fluidic contact with the cells. Current is measured using discrete patch clamp amplifiers. Compounds can be applied across the cells with complete washout between compound applications.

- 16 to 256 independent recordings with 8 to 128 parallel experiments provide **fast execution of the most demanding assays**
- Continuous flow of solutions and compounds with integrated wash steps for **maximum assay stability**
- In-plate solution exchange **eliminates the need for compound pipette stacking**
- Single-cell giga-ohm seal recordings and ensemble recordings (20 cells), with no artificial averaging, **increase experimental success rates**
- Available integrated temperature control (ambient to 40°C) **enhances similarity to in vivo physiology**
- Independent cell sources allow for **multiple cell types to be screened at the same time**
- Included liquid handler **automates stock dilution and plate filling**
- Integrated software **simplifies assay development and analysis**

Key Applications

Ligand-Gated Ion Channels

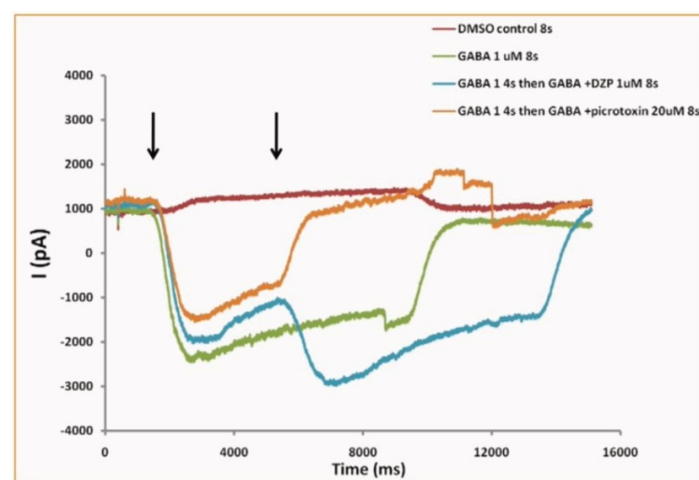
IonFlux Mercury's microfluidic plate technology enables industry-leading flexibility and unmatched synchronous compound additions across the entire plate. Rapid fluidic introductions and washouts enhance throughput by reducing operating time (~8 minutes per plate for ligand-gated ion channel targets; determined by compound incubation times). Continuous liquid perfusion prevents cell desensitization by dramatically improving ligand washout, enabling the study of difficult targets, such as the NMDA receptor.

Benefits

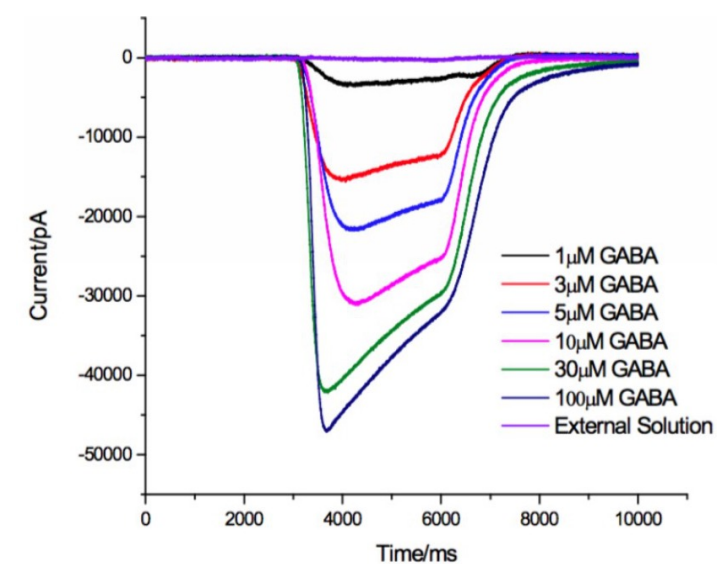
- Continuous perfusion
- Extensive and precise control over liquid addition
- Complete compound washout due to microfluidics
- Unmatched protocol flexibility

Tested Ligand-Gated Applications

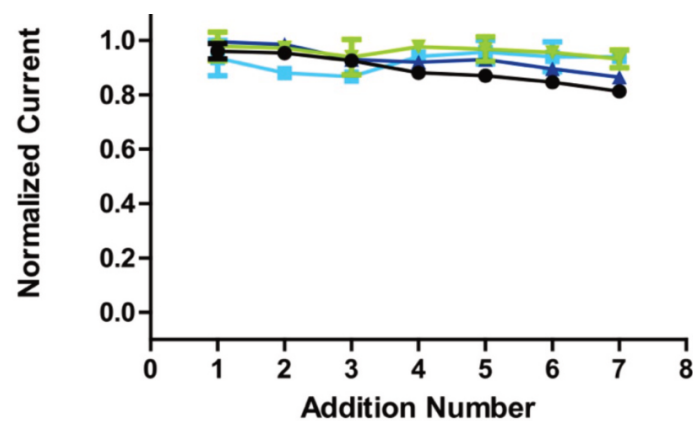
- GABA receptor agonist screens
- NMDA receptor screens
- Nicotinic receptor studies
- P2X purinergic receptor



Rapid change of solutions during GABA current activation producing potentiation or antagonism.



Inward Cl⁻ current from one ensemble of cells exposed to increasing concentrations of GABA (1 μ M to 100 μ M).



Stable serial currents from multiple nicotinic acetylcholine receptors (data from a Eurofins/CMS webinar).

Voltage-Gated Ion Channels

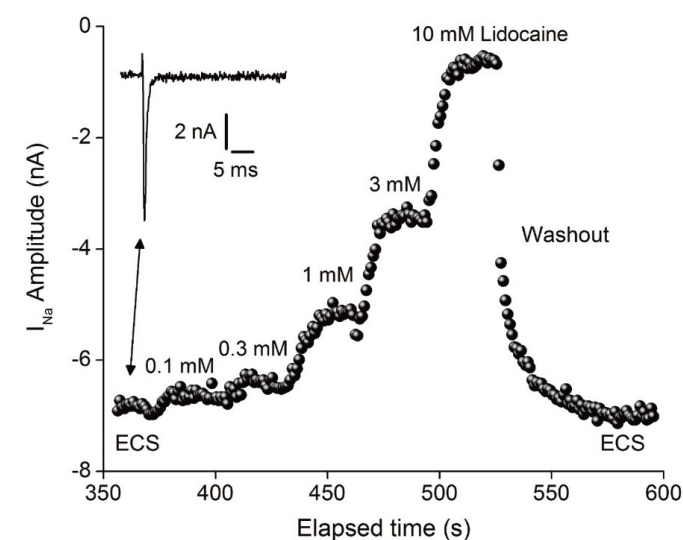
The unique microfluidic construction of IonFlux plates provides a superior concentration clamp due to continuous liquid perfusion. The concentration clamp combined with high success rates from ensemble recordings and giga-seal quality data, make IonFlux Mercury systems ideal for studying voltage-gated ion channels, such as action potentials neurons and cardiomyocytes.

Benefits

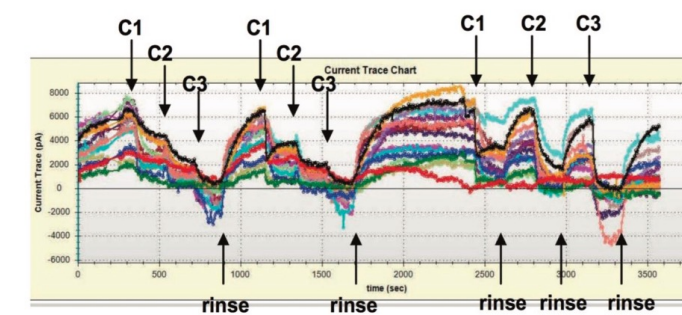
- Superior concentration clamp due to continuous perfusion
- Increased success rates from ensemble recordings
- Giga-seals enhance recording stability
- Temperature control

Tested Voltage-Gated Applications

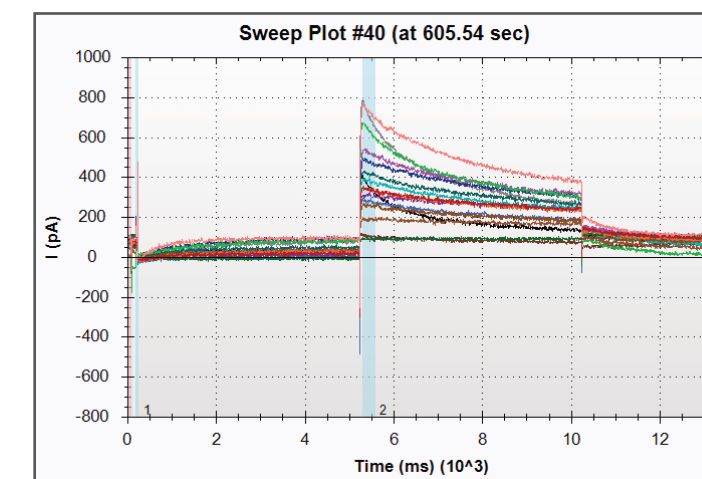
- CiPA safety pharmacology
- Sodium channel screening
- Potassium channel research
- Calcium channel research



Nav1.7 Lidocaine effect.



Serial hERG recording and two types of compound application sequences. A blocker was applied at different doses. That was followed by a wash step before adding a second blocker.



Superimposed CHO hERG current from single cells (single cell mode).

Ionflux Mercury Systems

IONFLUX MERCURY 16

The most cost-effective medium throughput automated patch clamp system available.

Standard Features:

- 16 independent amplifiers
- Continuous liquid flow
- Touch-screen operation (no PC required)
- Temperature control
- High-speed solution exchange



IONFLUX MERCURY HT

4X the number of recording channels make the HT system the lowest cost per data point among medium to high throughput automated patch clamp systems.

Standard Features

- 64 independent amplifiers
- Continuous liquid flow
- Touch-screen operation (no PC required)
- Temperature control
- 384 well plate compatibility
- 4 independent zones
- Automated liquid handler (for plate setup)

IONFLUX MERCURY ULTRA

Ideal for ultra-high throughput ion channel research and drug screening.

Standard features

- 128/256 independent amplifiers
- Continuous liquid flow
- Temperature control
- 384 well plate compatibility
- Asynchronous/synchronous operation
- Centralized data analysis
- Remote operation



System Specifications

	IonFlux Mercury 16	IonFlux Mercury HT	IonFlux Mercury Ultra
Design	Benchtop	Benchtop	Floor
Amplifiers	16	64	256
Data points/hr	~700	~2500	~10,000
Maximal sweep length (@0.5 KHz)	300 seconds	300 seconds	300 seconds
Maximal sampling rate (KHz)	20	20	20
Plate format	96 well	384 well	384 well
Minimum data points per plate	144	575	576/plate (2,304 using 4 plates)
Solution flow	Continuous	Continuous	Continuous
Asynchronous assays	1	1	Up to 4
Independent experiments/plate	8	32	128
Independent compounds	64/run	256/run	1,024/run
Liquid exchange rate	25 ms at EC50	25 ms at EC50	25 ms at EC50
Assay modes	Single cell / 20 cell ensemble	Single cell / 20 cell ensemble	Single cell / 20 cell ensemble
Intracellular solutions per run	16	64	256
Rs/Cslow compensation	80/100	80/100	80/100
Mode	Voltage / Current (optional)	Voltage / Current (optional)	Voltage Clamp
Temperature control	Ambient to 40°C	Ambient to 40°C	Ambient to 40°C
Cooling	Yes	Yes	No

Automation

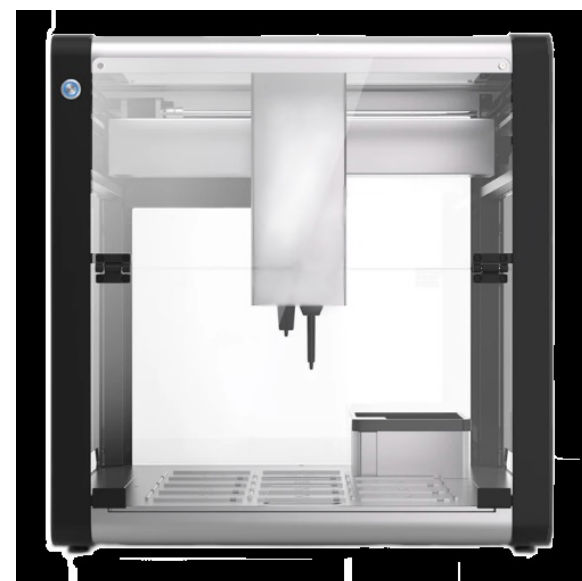
Reduce Hands-on Time with Automated Liquid Handling

A liquid handling system is provided with IonFlux Mercury HT and ULTRA systems to prepare compound concentrations as well as to fill IonFlux 384-well plates. Liquid handling is fully integrated into the IonFlux Mercury HT and ULTRA workflows and can easily be programmed to fit most drug screening needs.

Benefits of liquid handling

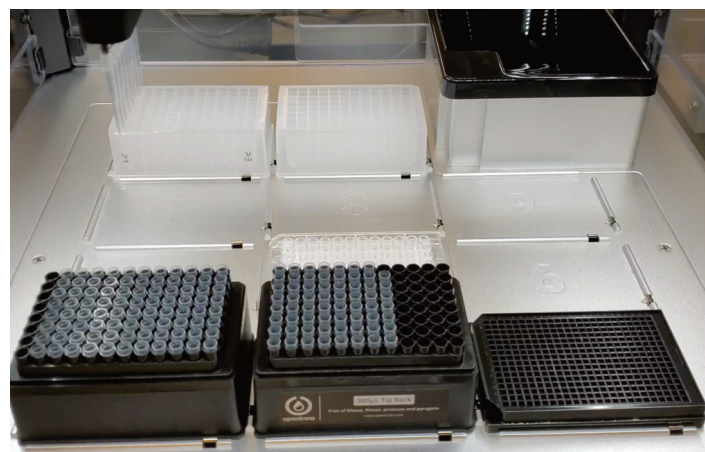
- Dilution from stock solutions
- Preparation of different concentrations
- Drug mixing

* Liquid handler workflow scripts are available from Cell Microsystems



Optimized operation for ionflux

- Simple experimental setup with preconfigured scripts for automated drug dilutions.
- Saves money by using standard nest reservoirs for solutions and diluents
- Reduces hands-on time by performing all IonFlux plate filling, including water rinsing
- Easily programmable with a graphical web-based application
- Enhance operational flexibility by controlling via direct computer access or remotely
- Expand throughput by including additional pipetting systems



Software

Operational simplicity

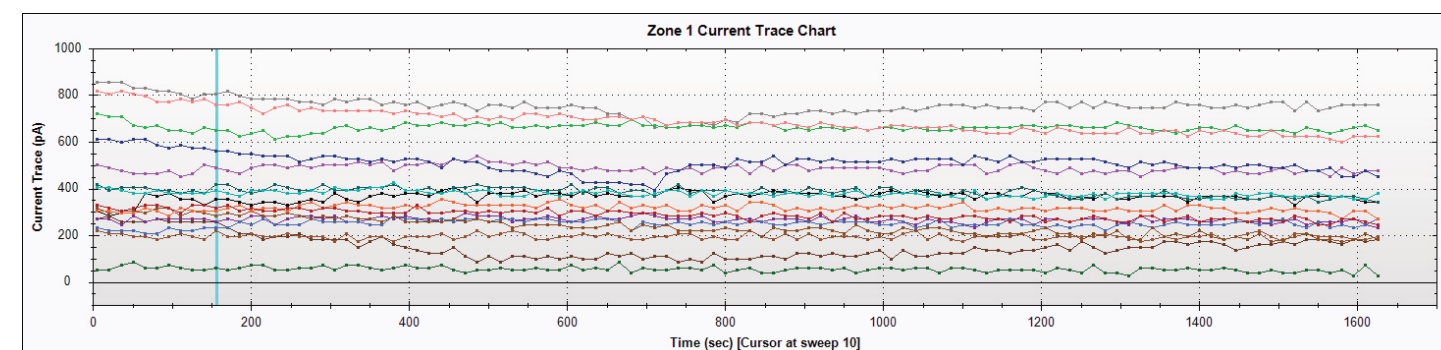
IonFlux Mercury 16 and HT systems are designed with integrated touch screens to facilitate operation without the need for an external computer. As data is collected, live current versus time plots are automatically generated using predefined cursors. This simplicity allows any lab personnel to seamlessly operate the system.

Convenient Assay Development

Assay development is done using an extensive graphical interface. IonFlux software provides all the necessary tools to build and implement complicated experimental protocols. IonFlux software can be loaded onto any PC for convenient assay development. Once developed, assay protocols can either be loaded locally onto an IonFlux system or sent remotely for execution.

Extensive Data Analysis

Initial analysis of peaks and means can be performed using the included IonFlux Data Analysis software. Additionally, data can be structured into templates to further analyze IC50/EC50 and Z Prime values.



IT plot for hERG tail currents from 16 different cells recorded in single cell mode

Ionflux Plates

Plate	Number of Wells	Operation Mode	System Compatibility	Part Number
IonFlux Plate 16 (ensemble)	96	20-cell ensembles	IonFlux 16 / IonFlux Mercury 16	910-0054
IonFlux Plate 16 (single cells)	96	Single cell	IonFlux 16 / IonFlux Mercury 16	910-0058
IonFlux Plate HT (ensemble)	384	20-cell ensembles	IonFlux HT / IonFlux Mercury HT/ IonFlux Mercury ULTRA	910-0055
IonFlux Plate HT (single cells)	384	Single cell	IonFlux HT / IonFlux Mercury HT/ IonFlux Mercury ULTRA	910-0059

Automated Patch Clamp Systems Made to Enhance Your Workflow

The IonFlux Mercury systems combined with IonFlux analysis software are powerful and intuitive, enabling:

- Unbeatable compound washout to quickly generate accurate dose-response curves for ligand-gated ion channel testing
- Continuous concentration clamp for superior voltage-gated data collection
- Superior voltage-gated data collection due to continuous compound perfusion
- Experimental flexibility with single-cell and 20-cell ensemble recordings
- Usage by everyone in the lab, thanks to user-friendly software and touchscreen accessibility
- Saving precious lab space with a low-profile design

For more information on the presented data or IonFlux Technology, visit cellmicrosystems.com