

# Getting to the heart of drug safety testing

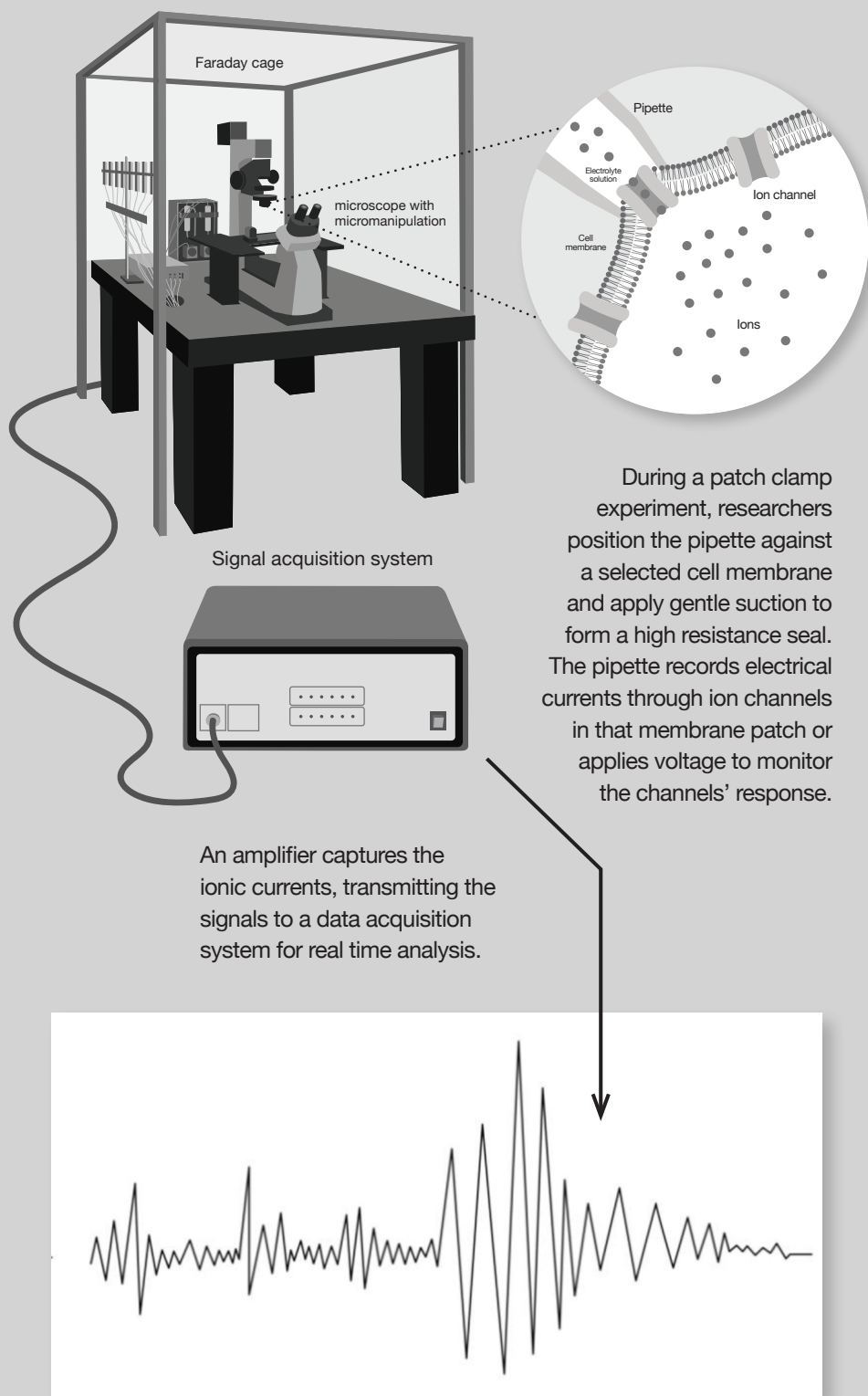
High throughput optical scanning illuminates cardiac toxicology with precision and speed.

Every heartbeat is a finely tuned process mediated by ion channels in cardiac cells. These channels control the flow of sodium, potassium, and calcium ions, generating the electrical impulses that regulate heart function. Measuring transmembrane ion channel activity provides vital insights into the heart's response to modulators such as pharmaceutical agents.

Drug-induced cardiotoxicity, a common adverse effect arising from altered heart electrical activity due to drug interactions with cardiac ion channels, poses significant challenges in drug development. Accurate cardiac physiology is crucial in assessing drug safety, understanding mechanisms of action, and predicting clinical outcomes.

## Traditional patch clamp analysis

The patch clamp technique is a classic electrophysiological method to measure ion currents in individual cells. A standard patch clamp setup consists of a Faraday cage for electromagnetic shielding, a fine-tipped glass pipette filled with an electrolyte solution, a micromanipulator for precise pipette positioning, a microscope for visual observation, and a signal acquisition system for data collection.

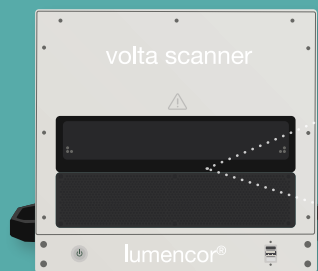


During a patch clamp experiment, researchers position the pipette against a selected cell membrane and apply gentle suction to form a high resistance seal. The pipette records electrical currents through ion channels in that membrane patch or applies voltage to monitor the channels' response.

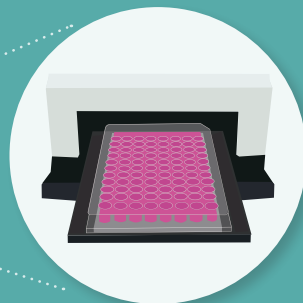
An amplifier captures the ionic currents, transmitting the signals to a data acquisition system for real time analysis.

## High throughput optical scanning

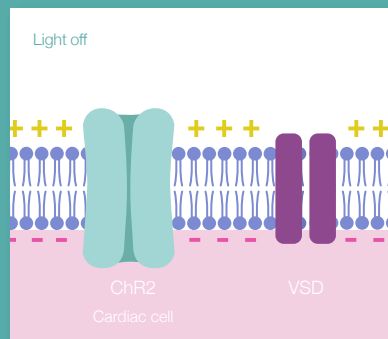
Lumencor's VOLTA Scanner is an automated kinetic plate reader, a turnkey solution to facilitate traditionally challenging electrophysiology assays. VOLTA simultaneously scans 96-wells with the power and sensitivity of optical detection. Leveraging the clean and quiet nature of light, VOLTA can detect electrophysiological changes at sub-millisecond speeds in a manner compatible with high-throughput analysis. VOLTA leverages bright lasers and fluorescence dyes to reveal the secrets of ion channels with VOLTA Scanner.



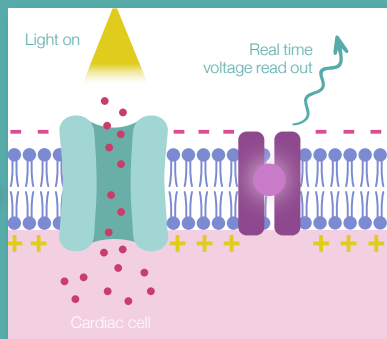
VOLTA scanner



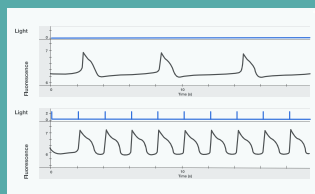
96 or 384-well compatible



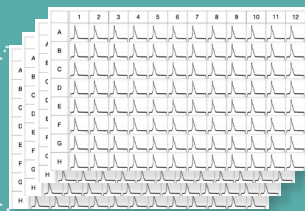
VOLTA activates cardiac cells that express channelrhodopsin-2 (ChR2) ion channels using light. In the presence of a voltage-sensitive fluorescent dye (VSD), membrane voltage changes are detected optically.



When a brief pulse of 462 nm light is applied, the ChR2 channels are stimulated to open, allowing ions to flow across the cell membrane, causing changes in the membrane potential. The VSD reports the change in ion flux as a fluorescence change, indicating the cells' responses in real time.



Using light to stimulate ChR2 channels enables optical pacing of cardiomyocytes, offering a more reliable and artifact-free method than electrical stimulation.



In the presence of drugs acting as agonists or antagonists of ion-channel activity, pharmacokinetics and dynamics may be studied. Multiwell plates can be used to report precise kinetic parameters. Detailed, quantitative, high throughput analysis is simple and fast.

**Technical complexity**  
**Noisy data lacking reproducibility**  
**Prone to errors**  
**Time consuming**  
**Limited throughput**

**Quiet, reproducible scans**  
**Effortless**  
**Accurate, robust**  
**<2-min 96-well simultaneous reads**  
**High throughput with 384-well scans**

## Not for the faint of heart

Throughout the process, researchers must have specialized expertise and skills to constantly monitor the setup's stability and frequently adjust the pipette's position and suction as needed. The technique is notoriously susceptible to noise and inconsistencies in electronic transduction, limiting its throughput and making it difficult to test large numbers of cells or compounds.

## Safer drug development ahead

The VOLTA Scanner utilizes 96 or 384-well plates to generate hundreds of data points for calibration curves and kinetic analyses, enabling fast evaluation of cardiovascular events. This improves the accurate identification and quantitative characterization of compounds of interest, supporting more informed decision-making in drug discovery, development, and pharmacosafety.