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Automated ion channel screening: patch clamping made easy

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Efficient high resolution techniques are required for screening efforts and research targeting ion channels. The conventional patch clamp technique, a high resolution but low efficiency technique, has been established for 25 years. Recent advances have opened up new possibilities for automated patch clamping. This new technology meets the need of drug developers for higher throughput and facilitates new experimental approaches in ion channel research. Specifically, Nanion's electrophysiology workstations, the Port-a-Patch and the Patchliner, have been successfully introduced as high-quality automated patch clamp platforms for industry as well as academic users. Both platforms give high quality patch clamp recordings, capable of true giga-seals and stable recordings, accessible to the user without the need for years of practical training. They also offer sophisticated experimental possibilities, such as accurate and fast ligand application, temperature control and internal solution exchange. This article describes the chip-based patch clamp technology and its usefulness in ion channel drug screening and academic research.

Keywords: automated patch clamp, drug screening, ion channel, Patchliner, Port-a-Patch

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1. Introduction

Ion channels are transmembrane protein pores present in most cells throughout the human body. They serve as means for intra- and intercellular communication. Their actions underlie every movement, thought and heartbeat. Consequently, ion channels are important targets for the pharmaceutical industry as well as for academic research, because their dysfunction is directly or indirectly involved in many severe disorders, such as cardiac arrhythmia, epilepsy, migraine, chronic pain, cystic fibrosis and hypertension [1].

Historically, ion channel drug discovery has been hampered by the lack of high-throughput methods for functional screening of relevant compounds. Several indirect techniques with high-throughput capabilities are available, with binding assays, voltage-sensitive fluorescence resonance energy transfer and flux assays being the most predominantly used techniques. Although these methods are compatible with primary screening formats, they sacrifice high data quality for high-throughput. Because of the low information content and high rate of false-negative and false-positive results, subsequent testing and evaluation of the hits are required, using techniques providing more detailed information, such as electrophysiological techniques.

Another aspect of drug development and ion channel drug screening is the safety assessment of potential drug candidates. An important example is the channel encoded by the human *ether-à-go-go*-related gene (hERG), expressed in cardiomyocytes, which has shown to be very promiscuous in its interactions with drugs. A blocking effect of hERG can, in the worst case, lead to cardiac arrest and death, which has been the reason for the withdrawal of several would-be 'blockbuster' drugs from the market.

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Today, all new drugs must go through safety assessment studies as stipulated by the FDA, the Europeam Medicines Agency and the International Conference on Harmonization. Having a compound withdrawn from the market or from late phase development is costly and inefficient; therefore, safety testing is conducted faster and earlier in the drug development process. Here as well, the patch clamp technique provides the best data on the safety profile of a compound.

Ion channel research performed in the academic setting also requires increased throughput capabilities, but at the same time, has higher demands on experimental flexibility due to the wide variety of ion channel targets under investigation. Also, experiments on primary cells that are widely used instead of immortalised cell lines are often more technically demanding.

2. Patch clamping – the gold standard for ion channel analysis

All of the above-mentioned areas of ion channel drug development and research require reliable methods for electrophysiological characterisation. Here, the patch clamp technique is the gold standard. Patch clamping is the only technique for obtaining functional and highly resolved information in real time about ion channel function and regulation. In fact, actions of single ion channel proteins can be monitored because of the high temporal resolution (sub-ms) and the high sensitivity of patch clamping, allowing measurements of currents in the subpA range [2]. The first patch clamp recordings were made in the late seventies in the pioneering work by Erwin Neher and Bert Sakmann (Nobel Prize in Physiology or Medicine 1991). A glass microelectrode was pressed against the cell surface and the ionic current passing through the enclosed ion channels was measured. A key requirement for performing such recordings is the so-called giga-seal. 'Giga' refers to the high ohmic resistance (> $10^9\,\Omega$) that is established between the lipid membrane and the tip of the recording glass pipette [3]. Resistances of several GΩ are essential for low noise recordings and resolution of the minute currents passing through single ion channels.

Sakmann and Neher performed recordings in the cell-attached configuration in order to study the actions of single channels. However, by applying further suction, the patch of membrane covering the pipette tip can be ruptured, which results in direct access to the interior of the cell. This allows for voltage-control of the entire cellular membrane. In this configuration, currents are measured from the whole ion channel population present in the cellular membrane, therefore, referred to as the whole-cell configuration.

Although providing excellent data quality, throughput in patch clamping suffers severely from its laborious nature. A highly trained and patient experimenter is required, as well as the technical means to visually and mechanically control the pipette and to shield the recordings from vibrations and electromagnetic noise. Typically, only a few compounds can be analysed per week. Therefore, it has not been feasible to rely on patch clamping for the electrophysiological characterisation of ion channel active substances in other than tertiary screening efforts, where only a limited number of compounds are left for functional characterisation.

3. Increasing the throughput in patch clamping

In recent years, automated patch clamp techniques have emerged primarily to allow and facilitate faster and better screening and optimisation of ion channel drug candidates. Automated patch clamping aims at extracting functional data on ion channel active compounds, ideally with a 1000- to 10,000-fold higher throughput than possible with conventional patch clamping.

Several automated platforms are commercially available, the first one on the market being the Ionworks (Molecular Devices Corporation) followed by the PatchXpress (MDC, formerly Axon Instruments) and Nanion's Port-a-Patch [4]. Other automated patch clamp devices are Sophion's Qpatch [4], Flyion's Flyscreen and Nanion's Patchliner. Most automated patch clamp platforms on the market today have replaced the glass microelectrode with a chip cartridge, containing parallel recording wells. Each recording well comprises a μm-sized aperture where a cell is automatically and blindly positioned, sealed and recorded from.

The true giga-seal patch clamp recording platforms are the PatchXpress, Port-a-Patch, Patchliner, Flyscreen and the Qpatch. The Ionworks Quattro, although not achieving giga-seals, offers the highest throughput, by recording from 48 out of 384 chambers at a time. Sophion's 48-channel system also records from 48 chambers at a time, which thereby might prove to be a high quality screening platform.

Parallelisation of patch clamp recordings gives higher throughput in characterisation of compounds and ion channels [5]. The electrophysiologist can generate and manage a lot more data in less time for screening and safety profiling, which is very likely to cut the time to market in the development of drugs. At the same time, automated patch clamp platforms are restricted to using cell lines for expression of ion channels where the quality of the cell suspension is crucial for acceptable success rates. A cell is caught randomly from a cell suspension, which means that the expression must be homogenous within the suspension and most cells must be healthy. For most systems on the market it is, therefore, not feasible to use primary or transiently transfected cells with low expression rates because of the blind approach of catching cells.

Apart from Nanion's two systems, the available automated patch clamp platforms are only designed to meet the needs of the pharmaceutical industry for secondary drug screening efforts and safety profile characterisation of, for example, the ion channel coded by *h*ERG. The Port-a-Patch and the Patchliner are exceptions because they are flexible research platforms providing high quality data as well as increasing the

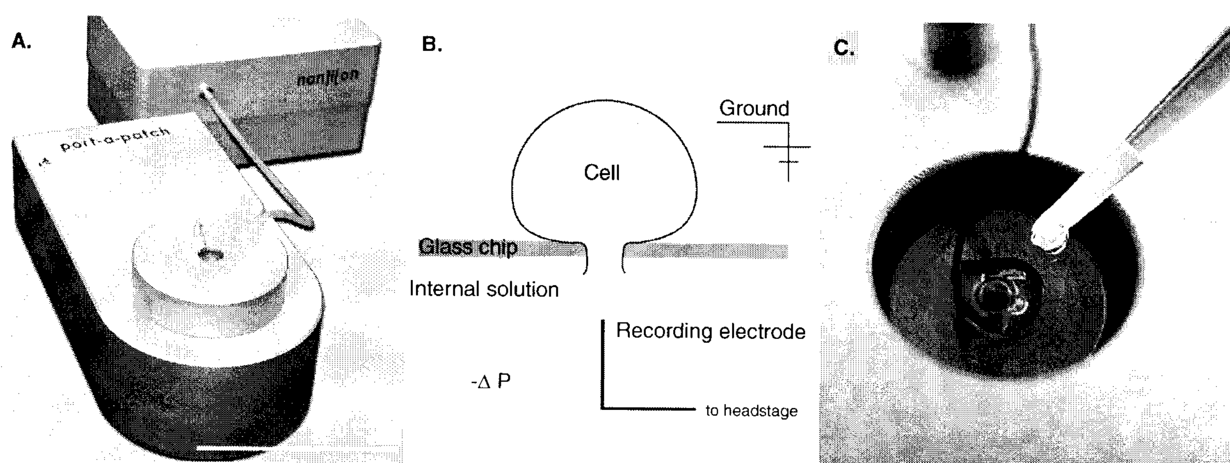

Figure 1. The Port-a-Patch. A. The Port-a-Patch is a miniaturised set up for high quality patch clamp recordings. **B.** A cell is automatically sealed to borosilicate glass chip and recordings can be performed in cell-attached, whole-cell and the perforated patch configuration. **C.** Drug application can be performed manually as shown here or by using a dedicated perfusion system.

throughput and accessibility of patch clamp to non-electrophysiologists. With these platforms, the user can interrupt and directly control the experiments at any time. Protocols can be changed or extended on-the-fly, according to the user's judgment. For many academic scientists, this is preferable over other robotic systems, which only run through predefined protocols. No adaptations other than breaking the entire run are possible in those systems.

The Port-a-Patch and the Patchliner have also been tested with a limited number of different primary cells with encouraging results.

4. The Port-a-Patch

In 2003, Nanion launched the Port-a-Patch (**Figure 1A**) a semiautomated, high data quality patch clamp device providing comparable data quality as pipette-based patch clamping. The system has been used for various cell types, with high success rates (~ 80%) in obtaining GΩ seals (1 – 5 GΩ) and stable whole cell recordings (> 20 min) with low series resistances (< 10 MΩ).

The Port-a-Patch uses borosilicate glass chips (called NPC-1 chips) for the patch clamp recordings because of their excellent dielectric properties and clearly distinguishable stray capacitances [6]. Another benefit of using untreated glass is the very long shelf life. NPC-chips can be stored at room temperature for up to 2 years with unaltered success rates for obtaining giga-seals and whole-cell recordings.

In the centre of the micromachined glass chip there is a µm-sized aperture, on which the cell is positioned automatically by application of suction (**Figure 1B**). Using a graphical user interface, the suction protocol is preprogrammed and computer controlled. The software adapts the applied negative pressure to parameters such as pipette resistance, series resistance and slow capacitance. This way, the programme can determine if a cell has been sealed to the chip and whether the parameters correspond to the cell-attached or the whole-cell recording configuration.

One chip is used at a time and the user adds solutions, cell suspension and compounds using a manual pipette (**Figure 1C**). Dose-response curves are obtained by manual addition of the drugs (5 – 50 µl) to the recording chamber or by using a dedicated perfusion system. The perfusion system contains a computer controlled, 8-channel magnetic valve control panel and a dedicated flow chamber that is mounted on the Port-a-Patch before use. With this system, external solutions can be exchanged in the order of 100 ms, which is sufficient for most ion channels. Solutions on the internal side of the membrane can be exchanged by unmounting the chip, exchanging the droplet and remounting the chip. In most cases the seal remains intact and the recordings can be continued [5].

The cells in suspension remain viable for up to four hours, stored at room temperature. Normally, cell suspensions are prepared twice a day, once in the morning and once after lunch. A cell preparation takes ~ 20 min each time and as such, has not been shown to be a limitation for the throughput of the Port-a-Patch or the Patchliner.

The Port-a-Patch was developed to increase the throughput and to simplify patch clamp measurements. The increased throughput comes from the high success rates and ease-of-use in combination with short cycle times, which results in an increased number of successful recordings per day.

The system is used around the globe for studies of ion channels that activate by a change of the transmembrane-voltage (voltage-gated ion channels), as well as ion channels activated

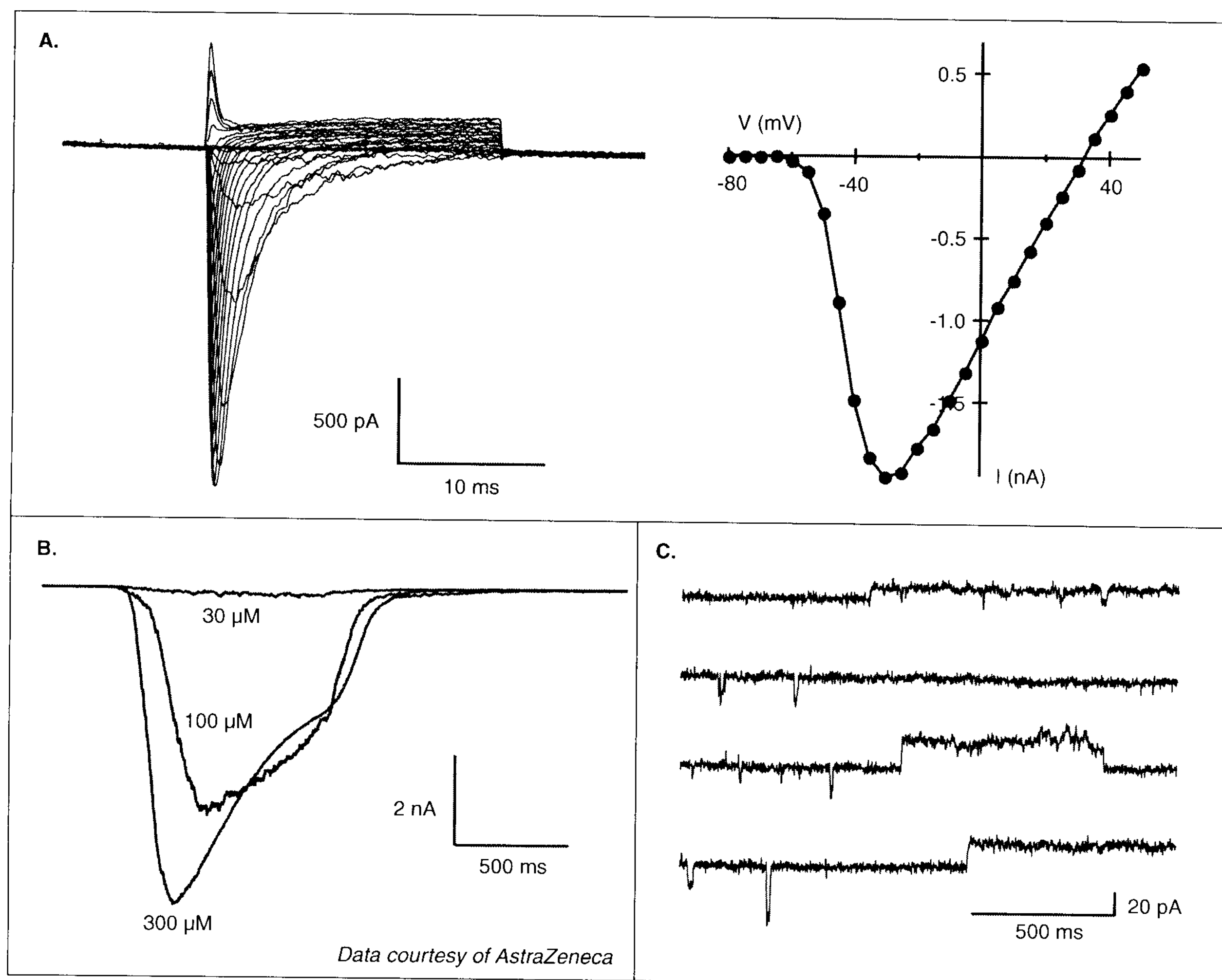

Figure 2. Data from the Port-a-Patch. A. A HEK cell expressing $Na_V1.5$-channels was patch clamped in the whole-cell configuration (holding potential -100 mV), and the I/V-characteristics were investigated. Because of the low access resistance (< 10 MΩ), good voltage-control of the membrane is obtained. Cells were kindly provided by Cytomyx. **B.** Glycine responses were investigated from LTK cells expressing the hα1 glycine receptor. The EC_{50} was determined as 89 µM (compared with EC_{50} = 136 µM obtained by conventional patch clamping, as reported by AstraZeneca). **C.** Single channel recordings in the cell-attached configuration were obtained from a freshly isolated erythrocyte.
HEK: Human embryonic kidney.

by addition of compounds (ligand-gated ion channels). Both ion channel types are important and interesting from an academic and industrial perspective.

Data examples can be seen in **Figure 2**, showing the current–voltage relationship of sodium channels ($hNa_V1.5$) expressed in human embryonic kidney (HEK) cells (**Figure 2A**) and the dose-dependent activation of human glycine ion channels expressed in a mouse fibroblast cell line (LTK) (**Figure 2B**). Glycine applications and wash steps were preprogrammed and executed automatically, with exposure times to glycine set to 800 ms, followed by a 30-second wash cycle in between every agonist exposure. Experiments in the two examples where performed in the whole-cell configuration.

To accommodate specific requirements of different cell preparations (e.g., the use of very small cells), Nanion supplies chips with custom-sized apertures. This makes Nanion's automated patch clamp workstation broadly applicable, even to conventionally difficult to patch cell types such as erythrocytes. Red blood cells are small and very flexible, which makes them difficult to work with in conventional patch clamping. Nanion's apertures facilitate a high sealing success rate (~ 80%) and high quality recordings even from primary erythrocytes as can be seen from the single channel recordings in **Figure 2C**. Also, a variety of other primary cells, such as human endothelial cells, dorsal root ganglia, cultured mouse cardiac fibroblasts, and myocytes from beating areas of

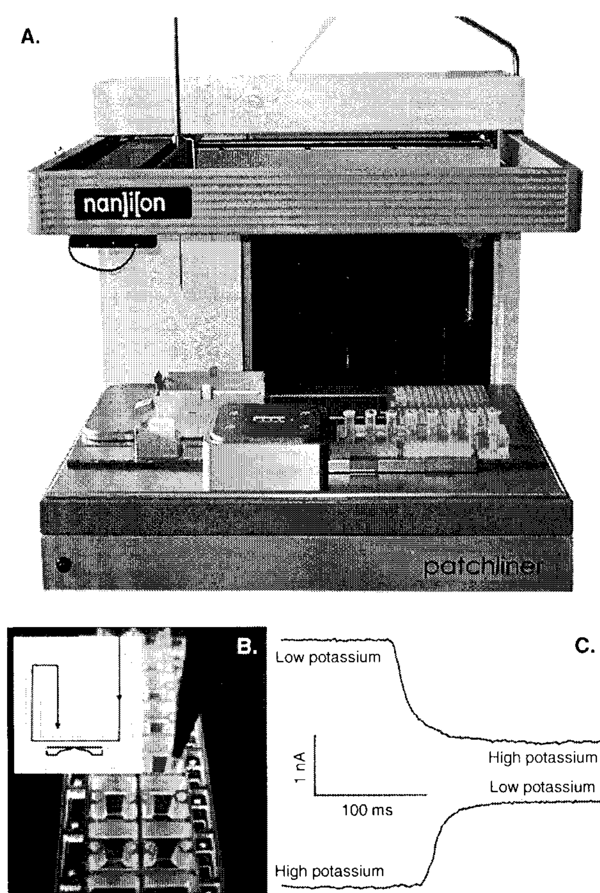

Figure 3. The Patchliner. The Patchliner (**A**) is a fully automated patch clamp platform using NPC-16 chips (**B**) for recordings in the cell-attached or whole cell configuration. The microchannels integrated in the patch clamp chip, allow for fast switching of the external and internal solution. **C.** When adding external solution high in potassium, there is an immediate current increase through potassium channels endogenously expressed in rat basophilic leukaemia cells. Solution exchange is obtained within 50 ms.

cultured and differentiated stem cells have been tested with Nanion's workstations with encouraging results. However, it is too early to predict the overall feasibility and success rates for planar patch clamping methods with primary cells, but ongoing research projects will validate this further.

4.1 Temperature control

To make patch clamp recordings at physiologically relevant temperatures possible, Nanion has implemented a temperature control add-on for the Port-a-Patch. Performing experiments at physiological temperatures increases the physiological relevance of the collected data, because open probabilities change with temperature and some channels also show temperature-dependent levels of activation, for example, transient receptor potential (TRP) channels such as TRPM8 and TRPV1. Also, many patch clampers prefer to perform experiments on hERG at physiological temperatures, as compound blocking characteristics may change with temperature in an unpredictable manner [7]. The temperature in Port-a-Patch is reliably controlled with a standard deviation of 0.5°C around the mean for all solutions added throughout an experiment.

5. The Patchliner

The Patchliner, shown in Figure 3A, is a fully automated patch clamp platform that addresses the need for higher throughput, without compromising data quality or experimental flexibility. As with the Port-a-Patch, borosilicate glass chips are used for seal formation and patch clamp recordings. Recordings are performed in a parallel fashion, from up to eight different recording wells at a time. The chip cartridge, containing 16 recording wells in total (and hence called NPC-16 chip), is a three-part structure in which a rectangular glass plate containing 16 micromachined apertures is sandwiched between two pieces containing the microchannel structures. These microchannel structures ensure rapid delivery of solution to the internal and external side of each aperture (Figure 3B). Three 16-chamber chips can be loaded into the Patchliner at a time, which means that up to 48 experiments can be preprogrammed and executed, either under supervision or in stand-alone mode. The type of experiment conducted, dictates the time it takes to run 48 experiments. As an estimate, recording from four cells at a time, making a four-point dose-response curve of an activator or blocker with a 1-min incubation time of the drug, it would take ~ 200 min to run through the 3 NPC-16 chips. The chips have very long shelf lives (up to 2 years) and can be stored at room temperature.

A robotic pipetting arm does all the liquid handling. It adds solutions, cell suspension and compounds to the chip and removes the waste. The external microchannel allows fast switching of the solution environment surrounding the patch-clamped cells, with measured switch times of 50 ms, as seen from the whole cell traces in Figure 3C. With every solution addition, the solution in the microchannel spills over into a waste reservoir, which is emptied throughout the experiment. This way, the chip imposes no restrictions on the number of solution applications that can be made to a cell during an experiment. In certain types of experiments, for example, when investigating the effect of positive modulators or antagonists acting on ligand-gated ion channels, many compound additions are required to obtain the EC_{50}-value because of necessary control, preincubation and wash steps and so on. From a data quality perspective, it is always desirable to collect full dose-response curves from a single cell in order to minimise the error due to cell-to-cell variations.

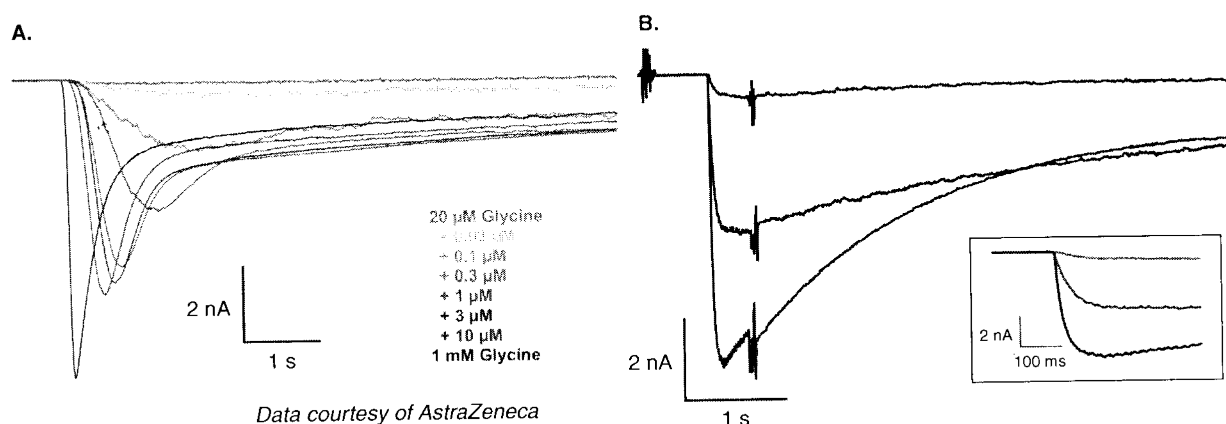

Figure 4. The Patchliner has been used to investigate the effects of agonists, antagonists, and positive modulators on various ligand-gated ion channels. In (**A**) the response to 20 µM glycine was facilitated by increasing concentrations of a positive modulator. Two positive controls were used, one at the start of the experiment, applying only 20 µM glycine and a final application of 1 mM glycine. **B.** Increasing concentrations of GABA were applied to a patch-clamped HEK cell expressing $GABA_A$ receptors. As seen from the insert, application is fast and the onset of current is as expected.
HEK: Human embryonic kidney.

6. Rapid solution exchange

In order to attain correct pharmacology, it is extremely important that the solution environment surrounding a cell is fully controlled and known throughout the entire experiment. In that sense, ligand-gated ion channels are somewhat more demanding to study than voltage-gated ion channels. Firstly, a ligand must be added in order to see whether the cell expresses the ion channel. Secondly, many ligand-gated ion channels enter a closed state despite constant ligand stimulation, a process called desensitisation. Cells normally recover from desensitisation after removal of the ligand followed during a prolonged wash step. To be able to study rapidly desensitising ion channels, fast solution exchange is crucial for obtaining reproducible and relevant data.

Because of the small dimensions of the microchannels in the NPC-16 chip, solution exchange around the cell is complete on the addition of 40 µl. For example, the solution exchange characteristics of the NPC-16 chips on the Patchliner were investigated using rat basophilic leukaemia cells patch-clamped in the whole cell configuration. The extracellular recording solution was exchanged for solution containing a higher concentration of potassium, which increases the current through the endogenous potassium channels. Under optimal conditions, solution switching is achieved within 50 ms (**Figure 3C**). This makes the Patchliner suitable for studies on for example ligand-gated ion channels, where additions of drugs or wash solution must be fast so that the cell is not exposed to a concentration landscape before the maximum concentration is reached.

Both, the Port-a-Patch and the Patchliner, have been used to investigate several ligand-gated ion channels such as $GABA_A$, glycine and P2X for the action of agonists, antagonists and positive modulators. An example of the latter can be seen in **Figure 4A**, showing the dose-dependent facilitation of glycine activated hα1 receptors expressed in a mouse fibroblast cell line (LTK). Initially, 20 µM glycine was added as a first positive control to see the approximate response at EC_{20} for that particular cell. Increasing concentrations of a positive modulator were co-administered with 20 µM glycine to determine the EC_{50} of the modulator and the degree of maximum potentiation of the glycine response. Eventually, 1 mM of glycine was added as a second positive control to stimulate full response. The ion channels desensitises rather quickly upon drug application, which can be seen from the patch clamp traces. As the drugs are removed and the cell resides in drug-free buffer solution, the ion channels 'resensitises' within the order of 10 seconds. Therefore, wash steps are required in between every new compound addition in order to record currents from the entire ion channel population. In total, 18 solution additions were made to the cell during the shown experiment, which lasted ~ 20 min. Recordings were made from two cells in parallel for determination of the EC_{50} and the degree of potentiation of the drug. Results correlated very well with data obtained with conventional patch clamping (data courtesy of AstraZeneca).

The Patchliner has also been used to study the dose-dependent activation of $GABA_A$ receptors expressed in HEK cells. The expected onset of the response was obtained, as can be seen from the inset in **Figure 4B**.

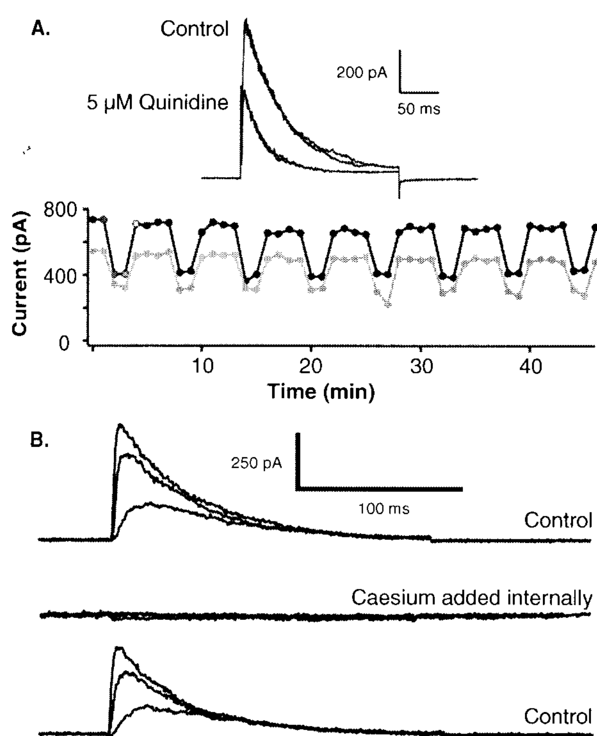

Figure 5. Reproducibility and stability of the recordings. A. Reproducibility and stability of patch clamp recordings were tested by the repeated current block by and wash out of quinidine. Recordings were made from two cells simultaneously for a time period of > 40 min. In this example, Jurkat cells, expressing $K_V1.3$-channels were used. The current amplitude was monitored when stepping the membrane voltage from a holding potential of -60 mV to +20 mV. The current traces (top) show the effect of block caused by 5 μM of quinidine and the plot (bottom) shows the peak current amplitude over time modulated by quinidine block and intermittent wash out. **B.** Currents through $K_V1.3$ channels in another Jurkat cell were blocked by the internal administration of caesium. The currents recovered after washout of the caesium-containing solution.

7. High quality recordings

The Patchliner has been used with various types of cells and ion channels, with high success rates regarding seal formation (60 – 80%) and subsequent stable whole-cell recordings. The stated success rates are valid for all tested cell lines so far, where the cells can be dissociated to yield a cell suspension of at least 75% viable cells and minimal amount of debris in solution. If those criteria are met, success rates are surprisingly independent of the used cell line.

The recordings are stable (> 20 min) so that in most cases entire dose-response curves can be extracted from the single cells. The stability comes from the fact that it is a one entity system where vibrations cause all parts to move synchronously. No additional isolation from vibrations is required for either the Port-a-Patch or Patchliner. As can be seen from Figure 5A, a cell was used for recordings over a prolonged period of time, in this case > 40 min. Jurkat cells, endogenously expressing $K_V1.3$ channels, were repeatedly perfused with quinidine and intermittently washed with normal recording solution, reversing the block and regaining the current. The procedure was repeated eight times, showing reproducible current block and wash out. The image shows data from two simultaneous recordings.

Apart from whole cell and perforated patch recordings, the Port-a-Patch as well as the Patchliner have been used for single channel recordings. To be able to perform single channel recordings, high seal resistance and low dielectric noise properties of the chip are required. Single channel events were measured from a freshly isolated erythrocyte in the cell-attached configuration, shown in Figure 2B.

A low series resistance is important to attain precise control over the voltage-clamp of the cell membrane. This is especially important when studying rapidly activating and inactivating ion channels, for example the $Na_V1.5$-channel shown in Figure 2C. Here, a poor voltage-control would result in deleterious effects that could be interpreted as compound block. Because of the geometry of the NPC-1 and NPC-16 chips, low series resistances (10 MΩ) are routinely obtained, which ensures correct voltage-clamp conditions of the patch clamped cell.

8. Compound control

Another important aspect regarding data quality and accuracy is the control of compound loss due to substance adsorption. Many compounds affecting the hERG-channel have shown to be problematic because they are often very hydrophobic and thereby tend to stick to surfaces. Sticky compounds with a known effect on hERG were chosen to obtain dose-response curves with both of Nanion's systems. No potency shifts were detected for either one of the platforms [101,102]. The compound storage area of the Patchliner can be equipped with various types of plates and vials, so that different storage materials (e.g., glass) can be used depending on the nature of the compounds.

9. Internal perfusion

A unique feature of Nanion's automated patch clamp platforms is the possibility to exchange the intracellular solution: even after the whole cell configuration has been established. With conventional patch clamping this is difficult because of the tiny dimensions of the pipette tip and the long tapered shaft and thus the diffusion limitation of the liquid exchange. With Nanion's systems, ion channels regulated by second messengers acting on internal binding sites can be modulated simultaneously by compound additions to the external side of the membrane. This allows for novel and complex experiments on interactions between ion channels and drugs. Another aspect of internal

perfusion is the possibility to add membrane-permeable drugs directly to the inside of the cell and thereby speed up the time course of the experiments.

With the Port-a-Patch, the internal solution can be exchanged by un-mounting the chip and manually making additions to the internal side of the chip. The Patchliner has even further possibilities for automated, multiple and reliable exchange of the intracellular solution. There are virtually no limitations on how many intracellular additions can be made in one experiment. In both systems the intracellular solution can be exchanged within tens of seconds. An example can be seen in **Figure 5B**, where the normal internal solution was exchanged for caesium-containing solution, which blocked the endogenous $K_V1.3$ currents in the patch-clamped Jurkat cell. The block was reversed when the internal solution was switched back to normal caesium-free internal solution.

As the internal solution is so easily exchanged using the Port-a-Patch and Patchliner, both platforms are ideally suited for experiments using the perforated patch technique [5]. Here, pore-forming molecules are used to perforate the membrane patch in order to obtain electrical control over the membrane. Thus, the cell interiors remain intact and the cytosolic constituents that can be important for ion channel function are preserved. The cell can be sealed without the interference of the pore formers, which are then added to the internal side of the chip. Once the pore former has been added, electrical access is obtained quite rapidly as the pore forming agent has to diffuse a shorter distance on the chip compared with distances in a conventional patch pipette.

10. Expert opinion

Platforms for patch clamp based ion channel screening are starting to mature. Products on the market focus mainly on increasing the throughput in screening or in pharmacological characterisation of potential drug candidates and targets. The ambition of both providers and users is to use high-quality screening methods, such as automated patch clamping, earlier and earlier in the drug discovery process. With automated patch clamping, the data provided would reveal more details about the compounds. Valuable hits that would not be detected using more indirect methods can be picked up with automated patch clamping. However, for this dream to come true, users argue that consumable pricing has to decrease in order to make screens of tens of thousands of compounds affordable. On the other hand, one needs to consider that using these more sophisticated methods would result in a more qualified hit list of drug candidates and it would likely cut time to market for developed drugs. Also, the highly trained patch clamper would be able to run multiple machines and thereby increase the efficiency thousand-fold in terms of obtainable dose-response curves per week.

However, what needs to be thoroughly considered is the handling and analysis of information-rich data, because data analysis in patch clamping is, if not as then almost as labour-intensive as performing the patch clamp experiments themselves. Methods for automated analysis and interpretation of data will be required.

At present, automated patch clamp technology is employed in safety pharmacology (hERG screening) and secondary screening efforts, where it certainly is a decisive factor for the increase in efficiency. It shortens cycle times to get results (e.g., on the safety profile of a compound) and it also allows for better qualification of hits, which overall decreases the dropout rate in late phase drug development and shortens the time to market for new drugs.

It is the authors' firm belief that currently there is a paradigm shift when thinking in terms of how patch clamp recordings can and should be carried out. A general acceptance is starting to spread in the electrophysiology communities for automated patch clamping. This is probably due to the fact that people have seen what some of the patch clamp machines are capable of and the relative maturity of the products. Seeing these platforms can be perceived as a possibility or a threat to women and men of the craft as a machine can take over what took years of training to learn. 'These machines will put me out of a job' is a common reaction. The authors think it is the other way around, because the interest in ion channel screening and research is constantly growing in terms of efforts made and increased funding within industry as well as increased interest in ion channel pharmacology and function in academic research.

A prosperous future of ion channel screening and research requires a spectrum of products covering the demands for higher throughput as well as experimental freedom. The platforms described in this article are flexible enough to suit the type of experiments performed in a more academic setting, as well as in screening when the demand is high on data quality and experimental possibilities such as fast solution switching, temperature control and the unique feature of internal solution exchange.

Automated electrophysiology has been a great success so far, with a surprising rapid implementation of what only five years ago were scientific proofs of concepts. As a result, a nice portfolio of different established instruments is available to the user today.

For the future, of course, even higher throughput is demanded by the drug development community, as well as more flexibility in setting up more demanding experiments required by academic users. Automated patch clamping will certainly move forward in both directions, with even higher quality and throughput. It will eventually become the standard tool for ion channel research in the development of ion channel modulating drugs.

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