Nanion Technologies

Bridging the gap between primary and secondary screening with the Syncropatch

Rodolfo Haedo Vice President Nanion Technologies Inc., North Brunswick, NJ



Company Background

- Nanion Technologies was founded in January 2002
- Currently >60 employees in central Munich
- Launch of first product (Port-a-Patch©) in 2003/Q4
- Nanion achieves break even in 2004
- Nanion's Patchliner was launched in 2006/Q1
- Nanion's SyncroPatch (96 channel) launched in 2011
- >500 systems installed globally
- In-house production of devices and chips
- 2013-2014 launch of the Syncropatch 384 Patch Engine

and CardioExcyte 96!



Global Company



Nanion's Product Range

The Port-a-Patch

The Patchliner

nanjijon patchiner The SyncroPatch 96





5000 dp / d

50 dp / d

500 dp / d

Developed to cover requirements in ion channel research and drug discovery.



Nanion's product range



Orbit 16[®]

CardioExcyte96®



SURFER N96









Measure More Membrane

12 years of patch clamping and more to come





Simultaneous recordings of (A) impedance and (B) electric field potential. (C) Average traces of impedance signals with standard deviation envelope curves (grey) (D) average traces of EFP signals with standard deviation envelope curves (grey).

Electrical stimulation of cell monolayers

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Cells can be successfully stimulated on the CardioExcyte96: (A) impedance traces prior to stimulus application and (B) cells adapt to the beat rate imposed by the stimulus application.

Patchliner[®]. Unlimited experimental freedom.



+ accurate pharmacology!



Stem cell derived cardiomyocytes





SyncroPatch[®] 96. Get more throughput.





Stem cell derived cardiomyocytes





The PatchEngine – 100 % integration in HTS environment:



The PatchEngine – the core of the SyncroPatch 384PE

- Fits into commercially available liquid handler
- Up to two PE's per robot
- Open design allows integrations into fully robotic environments
- Used successfully with

Beckman Coulter's Biomek



SyncroPatch 384PE – Integrated into the Biomek FX (Beckman Coulter)



Open design allows for seamless integration into robotic HTS-workstations

SyncroPatch 384PE – clearly makes you happy...





SyncroPatch 384PE – Integrated into Felix (Cybio)





- One 384 PE module integrated (=384 amplifier channels)
- Felix compatible with full robotic environments
- Very small footprint
- ✓ 384 pipettor head



SyncroPatch 384 PE – Consumables NPC-384

Available as single and multi-hole borosilicate plates:



The PatchEngine -

The Revolution in APC-based Ion Channel Drug Screening

Key features

- ✓ 384 or 768 cells in parallel (384 or 768 amplifier)
- ✓ 384 pipettor head
- ✓ Up to 20,000 data points per day per module
- ✓ Integrates easily into an HTS environment
- ✓ Cost per data point: \$ 0.24
- ✓ 85 % success rates routinely obtained
- Excellent results with voltage-gated & ligand-gated ion channels
- Modular approach easy upgrade & integration
- ✓ Single- and multi-hole recording substrates



Overview Experiment Window



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CHO-hKv1.3 cells were kindly provided by Evotec

SyncroPatch 384 PE – quick priming and short experiments



Total experiment length for 4 – 5 additions: **15 – 20 minutes**

Experiment length is exposure time dependent.



SyncroPatch 384 PE – Assay compatibility examples

The SyncroPatch 384 PE has been validated with:

- CHO, HEK, LTK and RBL-1 cells
- Cor.4U[®] iPSC Derived Human Cardiomyocytes and CDI iCells
- A variety of voltage-gated ion channels including hNav1.5, hNav1.7, hKv1.3, Kir2.1, Cav3.2, hERG
- A variety of ligand-gated ion channels including hGABA_A α₁, β₂, γ₂, hGlycine α₁, hGluR2



Current Voltage Relationship of hKv1.3 (CHO cells)





CHO-hKv1.3 cells were kindly provided by Evotec

Current Voltage Relationship of hKv1.3 (CHO cells)



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CHO-hKv1.3 cells were kindly provided by Evotec

SyncroPatch 384PE Solution Application: Mix and Read



Stability of Giga Ω seal during compound application



Applications: control + three concentrations Four additions took about 500 s

Success rate: 85.2 %

IV-Current Voltage Relationship of hNav1.7 (CHO cells)



Nav1.7 a very popular pain target, fast,

inward sodium channel

CHO-hNav1.7 cells were kindly provided by Anaxon



Current Voltage Relationship of hNav1.7 (CHO cells)



Nav1.7 IV or current voltage graph with a click of a

button in real-time

CHO-hNav1.7 cells were kindly provided by Anaxon



hNav1.7 block by Tetracaine (5 μM , 50 μM and 500 μM)



Setup a voltage protocol step to 0 mV, and then run the

assay at max activation of channel, and titrate 3

concentrations of compound

Current over Time block by Tetracaine (5 μ M, 50 μ M and 500 μ M)



Exp length: 15 minutes

Success rate: 86.2 %

Tetracaine IC50: 49.6µM

CHO-hNav1.7 cells were kindly provided by Anaxon



DataControl 384: A fast and easy way of data analysis





hKv1.3 (outward potassium channel) block by Quinidine



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CHO-hKv1.3 cells were kindly provided by Evotec

hKv1.3 block by Quinidine (5 μM , 50 μM and 500 μM)



Exp length: 16 minutes

Success rate: 85.2 %

Quinidine IC50: 18.9µM

CHO-hKv1.3 cells were kindly provided by Evotec



SyncroPatch 384PE Ligand Gated channels: Stacked Solutions



Repeat exposure of hGABAA a1, β2, γ2 (HEK 293)



Three GABA-applications (5 µM)

Four-hole chip

 \checkmark

 \checkmark

Dose response on hGABAA α1,β2,γ2 (HEK 293)



Four GABA concentrations: 100n, 1u, 3u, 10u Four-hole chip

 \checkmark

 \checkmark

Dose response on hGABAA α1,β2,γ2 (HEK 293)



Four GABA concentrations: 100n, 1u, 3u, 10u Four-hole chip

 \checkmark

 \checkmark

Ongoing project: HTS screening of Induced Pluripotent Stem cells IPSC Cor.4U (human) cells!



- ✓ 384 scd cardiomyocytes (Cor.4U) in parallel!
- Cell consumption: 333 cell (in 10 μL/well)
- One T-75 Flask with 1.5 Mio cells is sufficient for 10 x 384-patch clamp plates

Ongoing project: HTS screening of Cor.4U cells!



Possible questions, e.g.:

CaV current densities of in diverse batches, ages of cells, etc.



Data Control 384 – Outstanding data handling and export 📷





DataControl 384 – intuitive & easy-to-use featuring:

- Intuitive, quick & easy-to-use setup of exps
- Powerful data analysis functions
- Compound view
- Automated data export
- ✓ PDF-reporting



Raw data traces of 384 hKv1.3 current responses

Nanion Technologies – 10 years ago introducing the Port-a-Patch



Reducing a set-up that takes up an entire room to something so small that you can hold in your hand.



The Port-a-Patch

- Makes patch clamp accessible to non-experts
- Increases throughput 5 10 x
- Allows quick tests of compounds and cells



Nanion Technologies – still increasing the throughput & reducing size



Each PatchEngine:

- ✓ 384 cells in parallel
- ✓ 2 units possible
- ✓ Integrates easily in HTS



SyncroPatch 384PE – Superior Ion Channel Drug Screening

- Giga-seal recordings
- 384 or even 768 simultaneous whole-cell recordings
- Multiple units per liquid handler
- High success rates 85 %
- Up to 20,000 data points per day
- Voltage- and ligand-gated ion channels
- Competitive price per data point ~ \$0.24
- Customized hole sizes and multi-hole chips







Nanion Customer Reference

- a global customer base distributed between industrial and academic laboratories

Companies:

- Abbott
- Almirall Prodesfarma
- AstraZeneca
- Amgen
- Aurigene Discovery Technologies, Ltd.
- Axiogenesis

Bayer

- Bionomics
- Boehringer Ingelheim
- Bristol-Myers Squibb
- Center for New Drug Safety Evaluation and Research (NCDSER),
 Chromocell
- Chromocell
 conoGenetix biosciences GmbH
- Evotec
- Genionics
- GlaxoSmithKline
- Grünenthal
- Hofman La Roche
- Hvdra Biosciences
- Japanese Tobacco
- Lupin Limited
- Merck
- Merch Serano
- Novartis
- Novo Nordisk
- Nycomed
- Ono Pharmaceutical
- Orion Pharma
- Pfizer
- Pierre Fabre
- Regeneron Pharmaceuticals
- Rytmion
- Sanofi-Aventis
- Shinogi
- Siena Biotech
- SK Holding, Co Ltd
- Sundia MediTech Company, Ltd.
- Suven Life Sciences Ltd, Hyderabad, India
- Syngenta
- UCB Pharma
- Vertex Pharmaceuticals
- Vimta Labs Life Sciences, Hyderabad, India
- WyethXention

Research institues and universites:

- Cambridge University, Cambridge, UK
- Charité Universitätsmedizin Berlin, Germany
- Consiglio Nazionale delle Ricerche, Povo (Trento), Italy
- Copenhagen University, Denmark
- Cornell University, Geneva, NY, USA
 Eberhard Karls Universität Tübingen,
- GermanyFMP, Berlin, Germany
- FMF, Benn, Germany
 Forschungszentrum Caesar, Bonn, Germany
- Forschungszentrum Jülich GmbH, Jülich, Germany
- Friedrich-Schiller-Universität Jena, Germany
- Georg-August-Universität Göttingen, Germany
- Griffith University, Nathan, Australia
- GSF Forschungszentrum für Umwelt und Gesundheit, GmbH, Neuherberg,
- GermanyHasselt University, Diepenbeek ,Belgium
- Hertie Institute for Clinical Brain
- Research, GermanyHoward Florey Institute, USA
- Howard Hughes Medical Institute, Ashburn, VA, USA
- Institute of Genomics and Integrative Biology, Delhi, India
- IPBS-CNRS, Tolouse, France
- Istituto Italiano di Tecnologia, Genova, Italy
- Jacobs University, Bremen, Germany
- JNCASR, Bangalore, IndiaJulius von Sachs Institut, Würzburg,
- Germany
- Karolinska Institute, Stockholm, Sweden
 Kingdati Organizationen
- Kiserleti Orvostudomanyi Kutatointezet, Budapest, Hungary
- Korea Institute of Science and Technology (KIST), Seoul, South Korea
- Laboratorio Especial de Toxinologia Aplicada CAT-CEPID, Sao Paolo, Brazil
- Ludwig Maximillian Universität, München, Germany
- Lund University, Lund, SwedenMax Planck Institut, Göttingen,
- GermanyMedizinische Hochschule Hannover,

Germany

Research institues and universites: (cont.)

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· University of North Carolina, Wilmington,

University of Tennessee Health Science

University of Valladolid and Spanish

National Research Council (CSIC),

University of Wisconsin, Madison, WI,

Universitatea Lucian Blaga din Sibiu,

Universität für Bodenkultur, Wien, Austria

University of Queensland, Brisbane,

University of Rochester, NY, USA

University of Washington, USA

Universität Zürich, Switzerland

Universität Augsburg, Germany

Universität Freiburg, Germany

Universität Heidelbera, Germany

Vanderbilt Medical School, Nashwille,

Yale University, New Haven, CT, USA

• Inje University, Busan, South Korea

Virginia State University, Blacksburg, VA,

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Universität Hohenheim, Germany

Universität Osnabrück, Germany

• X-Lab, Göttingen, Germany

· University of Michigan, Ann Arbor, MI,

Università degli Studi di Napoli -

Federico II, Napoli, Italy

USA

NC, USA

Australia

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USA

Romania

TN. USA

USA

Center, USA

Valladolid, Spain

- Nanjing University, Nanjing, China
- Nanyang Technological University, Singapore
- National University of Singapore, Singapore
- National Center for New Drug Safety Evaluation and Research (NCDSER), Shanghai, China
- National Heart Center, Singapore
- National Jewish Medical and Research Center, Denver, CO, USA
- NIH/NINDS, Bethesda, MD, USA
- NIST, Gaithersburg, MD, USA
- New York University, NY, USA
- RMIT University, Bundoora, Australia
- Ruhr-Universität Bochum, Germany
- Shanghai Institute of Materia Medica, Shanghai, China
- Simon Fraser University, Burnaby, Canada
- Southampton General Hospital, Southampton, UK
- Stiftung Alfred-Wegener-Institut für Polar- und Meeresforschung, Bremerhaven, Germany
- Syracuse Univerity, NY, USA
- Technische Universität Ilmenau, Germany
- Technische Universität Darmstadt, Germany
- Technische Universiät München, Germany
- Uppsala University, Uppsala, Sweden
- UNESCO, Bahía Blanca, Argentina
- Universidade Federal de Sao Paulo, Brazil
- Università degli Studi di Genova, ItalyUniversitatea Lucian Blaga Din Sibiu,

University of California, Los Anaeles,

University of Cambridge, UK

University of Groningen, the

University of Leeds, UK
Universidade de Lisboa, Portuaal

University of Cincinnati, OH, USA

University of California, San Diego, CA,

Romania

CA, USA

Netherlands

USA

SyncroPatch 384 PE – Allosteric Modulation, fast and easy



HEK Gaba, 2µM GABA + 10 µ M

Double stack technique: Harnessed from Syncro96 technology





