PROFESSOR HENRY J. MARKRAM, PhD

Founder, Brain Mind Institute Founder-Director, Blue Brain Project Founder, Human Brain Project

Born: South Africa, 28th March 1962 Nationality: South African & Israeli Permanent Resident: Switzerland

Languages: English, Hebrew, Afrikaans, basic German



BIOGRAPHICAL SUMMARY

Henry Markram is a Professor of Neuroscience at the Swiss Federal Institute for Technology (EPFL). He finished school at Kearsney College and thereafter began his research career in South Africa in the early 1980s. He studied Medicine and Neuroscience at the University of Cape Town, South Africa (1988), later moving to Israel where he obtained a PhD in Neuroscience at the Weizmann Institute (1991). After which, he completed postdoctoral work as a Fulbright Scholar at the National Institute of Health (1992) in the USA and as a Minerva Fellow at the Max-Planck Institute (1994) in Germany. In 1995, he started his own lab at the Weizmann Institute. Later on, in 2000, he spent a year sabbatical conducting research at the University of California, San Francisco and two years later, moved to EPFL to found and direct the Brain Mind Institute. In 2005, he founded the Blue Brain Project (BBP) to develop a radical and innovative approach to Neuroscience – algorithmic and digital reconstruction and simulation of the brain using supercomputers. In 2009, the project completed a cellular level model that provides a detailed picture of the whole column and offers new insights into basic principles of brain design: in particular, the role of neural morphology in the determination of cortical connectivity and the role of "Hebbian Assemblies". The Blue Brain Project today, is a team of around 100 scientists and engineers and receives 20 million CHF a year in Swiss Federal funding.

In 2010, Henry led an EU Coordinating Action to study the feasibility of a large-scale European research initiative on the Human Brain. Thereafter in 2011, he began the formation of a consortium, including 112 universities and together developed a proposal for the Human Brain Project (HBP). The HBP was initiated to scale the BBP up, to the reconstruction and the eventual simulation of the human brain. In 2013, the Human Brain Project was awarded a \leq 1 billion grant, over 10 years, by the European Commission.

From an early stage in his work, he focused on neural microcircuitry, applying a broad range of anatomical, physiological, biophysical and molecular techniques. He also pioneered the multi-neuron patch-clamp approach. His best-known discoveries are the principles of Spike Timing Dependent Plasticity (STDP), Redistribution of Synaptic Efficacy (RSE), and Long-Term Microcircuit Plasticity (LTMP). He has worked with theoreticians to develop the concept of "liquid computing", a novel technique for handling real time continuous input to recurrent neural networks. A recent and major milestone reached, is the publication of the first digital copy of a part of the neocortex, displaying brain-like properties when simulated on supercomputers. The milestone marks the beginning of the digital neuroscience era, as a new path to understanding the brain. In January 2013, the HBP was selected as one of the European Union's two FET Flagship Projects. In addition to his work in the HBP, he has also been active in autism research. Here, he has demonstrated an association between "autistic" behaviours and hyper-connectivity, hyper-reactivity and hyper-plasticity in the neocortex and amygdala. With this research, he co-developed the "Intense World Theory of Autism".

Henry also co-founded the first fully digital model for academic publishing with Kamila Markram, in 2008 – Frontiers Media SA. In only 8 years, Frontiers has become one of the largest Open Access academic publishing companies in the world, with around 60'000 internationally distributed leading scientists as editors and publishing well over 50'000 scientific papers to date, as well as being cited more than 22'000 times. In his career, Henry has published over 130 peer-reviewed scientific papers, been invited to present his work at over 300 conferences and meetings, received numerous awards and has been featured on multiple news networks (over 200 traditional, social and TV news reports and documentaries around the world). An example of his international presence shows in that his TED lecture on brain simulation has been viewed over 1 million times.

RESEARCH FOCUS

Overview

Professor Markram's laboratory adopts a multidisciplinary approach to the structure and function of the neocortex. The neocortex constitutes a large fraction of the mammalian brain and is made of a repeating stereotypical microcircuit of neurons. This neural microcircuit lies at the heart of the information processing capability of the neocortex, the capability of mammals to adapt to a rapidly changing environment, memory, and higher cognitive functions. The goal of the laboratory has been to derive the blue print for this microcircuit. The neocortical microcircuit exhibits pluripotent computational capabilities, meaning that the same microcircuit of neurons can simultaneously partake in a seemingly unlimited number of tasks. The neocortex can be parcellated into multiple overlapping functional vertical columns (0.3-0.5 m in diameter) that form the foundation of functional compartmentalization of the neocortex. In order to derive the blue print of this microcircuit, we study the components (the neurons) of the microcircuit, how the neurons are interconnected (anatomical properties of connections) and the functional structure of the microcircuitry (physiological & plasticity properties of connections). A neocortical column contains several thousand neurons that form a local microcircuitry of neurons delineated vertically by the axonal reach of the largest neuron, which is typically the large, layer 5, pyramidal neuron.

To study the different types of single neurons we employ whole-cell patch clamp studies in neocortical slices to obtain the electrophysiological profile of neurons, to aspirate cytoplasm for single cell multiplex RT-PCR studies and to load the neurons with dyes to allow subsequent 3D anatomical computer reconstruction of each neuron. This approach enables us to derive the electrophysiological behaviour, the anatomical structure, as well as the genetic basis of the anatomy and physiology of each type of cell. The microcircuit contains more than 9 main morphological types of inhibitory interneurons, in 7 main morphological types of pyramidal cells and a local circuit excitatory interneuron, called a spiny stellate cell. Neurons can express 13 major electrophysiological classes and over 60 different gene expression patterns. Precise anatomical and physiological rules operate to connect the different types of neurons. In order to derive these rules, we obtain multiple patch-clamp recordings from preselected neurons. This allows repeated analysis of the major connections and derivation of the signatures of connectivity, as well as the physiological and plasticity principles for these connections.

The laboratory has also developed a multidisciplinary approach to studying diseases such as Autism. So far, we have developed an insult-based animal model of Autism (the Valproic acid animal model) and currently study the gene expression changes (using DNA microarray analysis, multiplex RT-PCR and qRT-PCR), protein expression (using immunostaining approaches, Western Blotting), single molecule dysfunction (ion channel screening), synaptic malfunctioning (using multineuron patch-clamping), circuit malfunctioning (multi-electrode array stimulation and recording), whole brain malfunctioning (using *in vivo* multi-unit recordings) and behavioural alterations (using a battery of behavioural tests).

Methods

Professor Markram's Laboratory of Neural Microcircuitry (LNMC) is specialized in the technologies required to reverse engineer neural microcircuits. These include:

- Multi-neuron patch-clamp technologies: these allow up to 12 simultaneous neuron patch clamps, thus, making it possible to morphologically and electrically characterize neurons and to rapidly dissect synaptic pathways and dynamics of small networks.
- **Single neuron gene expression:** to better understand the relationship between the transcriptome and phenotype.
- A variety of imaging systems including fast CCD imaging for measuring Ca2+ dynamics, confocal
 microscopy to monitor the activity of multiple neurons and 2-Photon laser scanning microscopy to study the
 fine structural changes in axons and dendrites.
- Multi-electrode stimulation arrays: to study microcircuit responses to electrical stimulation.
- **Photo-activation:** of caged glutamate to study neuronal responses to real-time stimulation.
- **3D reconstruction:** to build and analyse morphometric models of neurons.
- **Informatics tools:** to database the elements of the microcircuit and their interactions.
- Supercomputers: to simulate and visualize model reconstructions of the microcircuits.

KEY FINDINGS

LINKING EFFECTS OF ACETYLCHOLINE ON MEMORY TO EFFECTS OF NMDA ON SYNAPTIC PLASTICITY

1. H. Markram and M. Segal. (1990). Long-Lasting Facilitation of Excitatory Postsynaptic Potentials in the Rat Hippocampus by Acetylcholine. *J Physiol*, **427**, pp. 381-393.

Dynamic Synaptic Transmission (short-term plasticity) - Tsodyks-Markram Model

2. M. Tsodyks and H. Markram. (1997). The Neural Code Between Neocortical Pyramidal Neurons Depends on Neurotransmitter Release Probability. *PNAS*, **94**, pp. 719-723.

Residtribution of Synaptic Dynamics - Plasticity of Short-Term Dynamics

3. H. Markram and M. Tsodyks. (1996). Redistribution of Synaptic Efficacy Between Neocortical Pyramidal Neurons. *Nature*, **382**, pp. 807-810.

Spike Timing Dependent Plasticity - Spike Times Matter

4. H. Markram, J. Lubke, M. Frotscher and B. Sakmann. (1997). Regulation of Synaptic Efficacy by Coindence of Postsynaptic APs and EPSPs. *Science*, **275**, pp. 213-215.

Network Timing Plasticity – Timing of the Network Matters

5. V. Delattre, D. Keller, M. Perich, H. Markram and E. B. Muller. (2015). Network-timing-dependent plasticity. *Frontiers in Cellular Neuroscience*, **9**, pp. 220.

LONG-TERM CIRCUIT PLASTICITY - CIRCUITS REWIRE

6. J. –V. Le Be and H. Markram. (2006). Spontaneous and Evoked Synaptic Rewiring in the Neonatal Neocortex. *PNAS*, **103**(35), pp. 13214-9.

Comprehensive Anatomical and Physiological Map of a Neocortical Synaptic Pathway

7. H. Markram, J. Lubke, M. Frotscher, A. Roth and B. Sakmann. (1997). Physiology and Anatomy of Synaptic Connections Between Thik Tufted Pyramidal Neurones in the Developing Rat Neocortex. *J Physiol*, **500**, pp. 409-440.

Different Types of Synapses on the Same Axon

8. H. Markram, Y. Wang, M. Tsodyks. (1998). Differential Signaling via the Same Axon of Neocortical Pyramidal Neurons. *PNAS*, **95**, pp. 5323-5328.

Inhibitory Synapses of the Neocortex

9. A. Gupta, Y. Wang and H. Markram. (2000). Organizing Principles for a Diversity of GABAergic Interneurons and Synapses in the Neocortex. *Science*, **287**(5451), pp. 273-8.

PLASTICITY OF INHIBITORY SYNAPSES

10. J. V. Raimondo, H. Markram and C. J. Akerman. (2012). Short-Term Ionic Plasticity at GABAergic Synapses. *Frontiers in Synaptic Neuroscience*, **4**, pp. 5.

The Common Neighbor Rule for Synaptic Connectivity – Connection Probability and Connection Strength can be Predicted

11. R. Perin, T. K. Berger and H. Markram. (2011). A Synaptic Organizing Principle for Cortical Neuronal Groups. *PNAS*, **108**(13), pp. 5419-24.

DERIVING THE CONNECTOME OF MICROCIRCUITS – EMERGENCE OF HEBBIAN ASSEMBLIES

12. S. L. Hill, Y. Wang, I. Riachi, F. Schürmann and H. Markram. (2012). Statistical Connectivity Provides a Sufficient Foundation for Specific Functional Connectivity in Neocortical Neural Microcircuits. *PNAS*, **109**(42), pp. e2885-94.

- 13. N. Kalisman, G. Silberberg and H. Markram. (2005). The Neocortical Microcircuit as a Tabula Rasa. *PNAS*, **102**(3), pp. 880-5.
- 14. M. W. Reimann, J. G. King, E. B. Muller, S. Ramaswamy and H. Markram. (2015). An Algorithm to Predict the Connectome of Neural Microcircuits. *Frontiers in Computational Neuroscience*, **9**, pp. 120.

Comprehensive Anatomical and Physiological Map of ~36 Million Neocortical Synapses

15. H. Markram, E. Muller, S. Ramaswamy, M. W. Reimann, M. Abdellah *et al.* Reconstruction and Simulation of Neocortical Microcircuitry. *Cell*, **163**(2), pp. 456-492.

Calcium Transients in Dendrites - Evoked by EPSPs and Back Propagating APs

- 16. H. Markram and B. Sakmann. (1994). Calcium Transients in Apical Dendrites Evoked by Single Sub-Threshold Excitatory Post-Synaptic Potentials via Low Voltage-Activated Calcium Channels. *PNAS*, **91**, pp. 5207-5211.
- 17. H. Markram, P. J. Helm and B. Sakmann. (1995). Dendritic Calcium Transients Evoked by Single Back-Propagating Action Potentials in Rat Neocortical Pyramidal Neurons. *J Physiol*, **485**, pp. 1-20.

Morphological Diversity Imparts Invariants and Robustness to Distribution of Synaptic Properties

18. S. Ramaswamy, S. L. Hill, J. G. King, F. Schürmann, Y. Wang *et al.* Intrinsic Morphological Diversity of Thick-Tufted Layer 5 Pyramidal Neurons Ensures Robust and Invariant Properties of *In Silico* Synaptic Connections. *J Physiol*, **590**, pp. 737-52.

Excessive Synaptic Connectivity and Over Expression of NMDA-R in Animal Model of Autism

- T. Rinaldi, K. Kulangara, K. Antoniello, H. Markram. (2007). Elevated NMDA Receptor Levels and Enhanced Postsynaptic Long-Term Potentiation Induced by Prenatal Exposure to Valproic Acid. *PNAS*, 104(33), pp. 13501-6.
- 20. T. Rinaldi, G. Silberberg and H. Markram. (2008). Hyperconnectivity of Local Neocortical Microcircuitry Induced by Prenatal Exposure to Valproic Acid. *Cereb Cortex*, **18**(4), pp. 763-70.
- 21. K. Markram, T. Rinaldi, D. La Mendola, C. Sandi and H. Markram. (2008). Abnormal Fear Conditioning and Amygdala Processing in an Animal Model of Autism. *Neuropsychopharmacology*, **33**(4), pp. 901-12.
- 22. T. Silva, J. -V. Le Bé, I. Riachi, T. Rinaldi, K. Markram *et al.* (2009). Enhanced Long-Term Microcircuit Plasticity in the Valproic Acid Animal Model of Autism. *Frontiers in Synaptic Neuroscience*, **1**, pp. 1.
- 23. F. Monica Regina, D. La Mendola, J. Meystre, D. Christodoulou, M. Cochrane *et al.* (2015). Predictable Enriched Environment Prevents Development of Hyper-Emotionality in the VPA Rat Model of Autism. *Frontiers in Neuroscience*, **9**(127).
- 24. K. Markram and H. Markram. (2010). The Intense World Theory a Unifying Theory of the Neurobiology of Autism. *Frontiers in Human Neuroscience*, **4**, pp. 224.

Neural Coding - Synaptic Dynamics Matter

- 25. M. Tsodyks and H. Markram. (1997). The Neural Code Between Neocortical Pyramidal Neurons Depends on Neurotransmitter Release Probability. *PNAS*, **94**, pp. 719-723.
- 26. M. Tsodyks, A. Uziel and H. Markram. (2000). Synchrony Generation in Recurrent Networks with Frequency-Dependent Synapses. *J Neurosci*, **20**(1), pp. 50.
- 27. T. K. Berger, G. Silberberg, R. Perin and H. Markram. (2010). Brief Bursts Self-Inhibit and Correlate the Pyramidal Network. *PloS Biol*, **8**(9), pp. e1000473.
- 28. T. K. Berger, R. Perin, G. Silberberg and H. Markram. (2009). Frequency-Dependent Disynaptic Inhibition in the Pyramidal Network: a Ubiquitous Pathway in the Developing Rat Neocortex. *J Physiol*, **587**, pp. 5411-5425.
- 29. O. Melamed, O. Barak, G. Silberberg, H. Markram and M. Tsodyks. (2008). Slow Oscillations in Neural Networks with Facilitating Synapses. *J Comput Neurosci*, **25**(2), pp. 308-16.
- 30. G. Fuhrmann, I. Segev, H. Markram and M. Tsodyks. (2002). Coding of Temporal Information by Activity-Dependent Synapses. *J Neurophysiol*, **87**(1), pp. 140-8.
- 31. M. Tsodyks, K. Pawleslik and H. Markram. (1998). Neural Networks with Dynamic Dynapses. *Neural Computation*, **10**(4), pp. 821-35.

LIQUID COMPUTING - PERTURBATIONS MATTER

32. W. Maass, T. Natschläger, and H. Markram. (2002). Real-Time Computing Without Stable States: A New Framework for Neural Computation Based on Perturbations. *Neural Computation*, **14**(11), pp. 2531-2560.

EDUCATION

1993-1994	Postdoctoral: Max-Planck Institute for Medical Research, Department of Cell Biology.		
	Laboratory of Professor B. Sakmann.		
1992-1993	Postdoctoral: National Institute of Health, USA. National Institute of Neurological		
	Disorders and Strokes. Fulbright and NIH Visiting Fellow, Laboratory of Dr E. F. Stanley.		
1988-1991	Doctoral Studies: The Weizmann Institute of Science, Israel. The Feinberg Graduate		
	School, Department of Neurobiology, PhD. Advisor Professor M. Segal.		
1985-1986	Postgraduate: University of Cape Town, Faculty of Science, Department of Physiology,		
	BSc (Honours). Advisor: Dr R. Douglas.		
1986-1987	Undergraduate: University of Cape Town, Faculty of Medicine, MBCHB-III.		
1980-1984	Undergraduate: University of Cape Town, Faculty of Science, Department of Physiology,		
	BSc. Majors: Physiology, History and Philosophy of Science.		
1975-1980	High School: Kearsney College, Kwa-Zulu Natal, South Africa.		

POSITIONS

2007-present	Founder, Human Brain Project, EPFL, Lausanne, Switzerland	
2007-2015	Director, Human Brain Project, EPFL, Lausanne, Switzerland	
2006-2007	CELEST (SNF, Centre of Excellence, Boston University) Review Board	
2005-present	Founder & Director, Blue Brain Project, Brain Mind Institute, EPFL	
2005	RIKEN Review Board	
2002-2007	Co-ordinator, BMI-Nestle Flavour Perception Group, EPFL	
2002-2005	Director, Centre for Neuroscience & Technology, EPFL	
2002-2005	Chairman, Brain Mind Institute Search Committee, EPFL	
2002-2005	Director, Brain Mind Institute, EPFL	
2002-present	Founder, Brain Mind Institute, EPFL	
2002	Tenured Full Professor, Brain Mind Institute, EPFL	
1999-2000	Visiting Professor, University of California San Francisco, USA	
1998-2000	Associate Professor (Tenured) The Weizmann Institute for Science, Rehovot, Israel	
1995-1997	Senior Scientist, Department of Neurobiology, The Weizmann Institute, Israel	
1993-1994	Minerva Fellow, Max-Planck Institute, Heidelberg, Germany	
1992-1993	Fulbright Scholar, National Institute of Health (NIH), USA	
1992-1993	NIH Visiting Scientist, NINDS, NIH, USA	

ACADEMIC RESPONSIBILITIES

- Hungarian Academy of Science, Review Board
- ➤ HFSP Grant Review Board
- EPFL High Performance Computing Committee

HONORS AND AWARDS

- ➤ Bell Labs Shannon Visionary Award (2016)
- Ottorino Rossi Award, "Founders of Neuroscience" Series (2013)
- Prix Alliance de l'invention, Alliance Foundation (2006)
- Ebner Science Prize of \$750,000, Weizmann Institute for Science, Israel (2001)
- James Heinemann Research Award, Germany (2000)
- Abramson Research Prize, Weizmann Institute for Science, Israel (1999)
- Excellent Young Investigator Award, European Society for Neurochemistry (1998)
- Levinson Biology Prize, Scientific Council of the Weizmann Institute for Science, Israel (1997)
- Senior Fulbright Scholar, J. William Fulbright Foreign Scholarship Board, USA and the United States-Israel Educational Foundation, Israel (1991)
- Elhana Bondi Memorial Prize for excellence in a PhD, Steering Committee of the Feinberg Graduate School (1991)

- > C.F. Wyndham Science Prize at the Annual Conference of the Physiological and Pharmacological Societies of South Africa, for the best paper presented at the conference entitled, "Muscarinic and nicotinic responses in pontomedullary reticular formation neurons", Pretoria, South Africa (1985)
- BSc (Honours) degree and thesis awarded with distinction, UCT, Cape Town, South Africa (1985)
- Class Medalist in Physiology, UCT, Cape Town, South Africa (1984)
- BSc degree awarded with distinction in Physiology, UCT, Cape Town, South Africa (1984)

OTHER

- > Co-founder, Frontiers Research Foundation, Switzerland
- > Co-founder, Frontiers Media SA, Switzerland

FRONTIERS MEDIA SA - Open Access Journal www.frontiersin.org



Henry Markram co-founded Frontiers Media SA with Kamila Markram. In only 8 years, Frontiers has become one of the largest Open Access publishers in the world, boasting over 60'000 internationally distributed leading scientists as editors, publishing around 20'000 scientific papers per year.

Frontiers is at the forefront of building the ultimate Open Science platform. By taking publishing entirely online, Frontiers has so far successfully: driven innovations and developed new technologies to make peer-review more efficient and transparent; provided impact metrics for articles and researchers; merged open-access publishing and looped a research network platform to catalyse collaboration and research dissemination. Frontiers avails the most up-to-date and latest research to the public, reaching young school minds to leading researchers alike. Their mission – "to increase the reach and impact of articles and their authors".

Frontiers, today, publishes several of the most cited Open-access journals in the world and is comfortably, one the largest and fastest-growing open-access publishers. It receives over a million article downloads per month and received the ALPSP Gold Award for Innovation in Publishing in 2014. Frontiers has established agreements with many universities as well as collaborating with the Nature Publishing Group, Scientific American, Digital Science, OpenAire, CrossRef, OASPA, COPE, Jacobs Foundation and others, who share the vision to advance Open Science worldwide.

MAJOR GRANT SUPPORT

EU FET Flagship, 2013-2023
Marie-Curie, 2010-2013
Fonds National Suisse, 2010-2012
Stoicescu Research Grant, 2009-present
EU Synapse Grant, 2006-2009
EU Facets Grant, 2006-2008
ENITNET Grant, 2006-2007
Swiss Fonds National Grant, 2002-2006
EU- Microcircuits Grant, 2001-2004
Levinson Foundation, 2000
National Alliance for Autism Research, 1999-2001
Ebner Research Prize, 1999

AFIRST, 1998-2001
EU 5th Framework, 1998-2001
Grodetsky Foundation, 1998
Wolfson Foundation, 1998
Israel Science Foundation, 1997-2000
Heinemann Foundation, 1997
Irvin Harris Foundation, 1996-2001
Binational Science Foundation, 1995-1997
US Office of Naval Research, 1994-2001
Minerva Foundation, 1994-2000
Human Frontiers Science Program, 1994-1999
German Israel Science Foundation, 1994-1999

IMPACT OF MAJOR PUBLICATIONS

Neocortical digital reconstruction

A digital reconstruction of a slice of rat somatosensory cortex providing the most complete simulation of a piece of excitable brain matter to date (2015). The model provides insight not only into structural principles of neocortical somatosensory cortex, the role of morphological and electrophysiological diversity, but also provides a tool to explore emergent network phenomena in relation to stimulation and biophysical parameters.

Neocortical microcircuitry

- Demonstration of dendritic Ca²⁺ influx triggered by single back propagating APs (1995) (230 citations) and EPSPs (1994) (243 citations).
- First extensive dual patch-clamp characterization of the physiology and anatomy of a neocortical synaptic connection (1997) (419 citations).
- Experimental demonstration of the diversity of signals transmitted by the axon of a single neocortical pyramidal neuron to its target neurons (1998) (489 citations).
- Identification of numerous electrophysiological-anatomical subclasses of GABAergic interneurons and 3 classes of GABAergic synapses. Demonstration of functional organizing principles, describing the types of synapses used when different neurons are interconnected (original article (2000), 616 citations; review article (2004), 607 citations).
- Demonstration of the heterogeneity of pyramidal neurons and connections in the mPFC and the first formal classification of 6 subclasses of synaptic dynamics (2006) (86 citations).
- First experimental evidence of all structural connectivity showing that axons need only to form boutons in order to target neurons and do not need to grow towards them (2005) (96 citations).
- First detailed characterization of the properties of a major synaptic inhibitory pathway the Martinotti cell pathway between pyramidal neurons (2004) (88 citations).

Synaptic plasticity

- Discovery of Redistribution of Synaptic Efficacy (RSE): the principal that the frequency-dependence of synaptic transmission is different from absolute synaptic efficacy and undergoes separable long-term plastic changes (1996) (520 citations).
- Discovery of Spike Timing Dependent Plasticity (STDP): the principle that the relative millisecond timing between pre- and post-synaptic action potentials, decides the direction of synaptic changes (1997) (1646 citations). This study was first published in 1995 at the SFN as an abstract.
- Long-Term Microcircuit Plasticity (LTMP): First demonstration of rewiring of neocortical microcircuitry involving the appearance and disappearance of entire functional multisynaptic connections (2006) (59 citations).

Neuromodulation

- *In vivo* demonstration of acetylcholine-mediated reorganization of polymodal receptive fields in the pontomedullary reticular formation (1986).
- Discovery that ACh modulates NMDA receptors: This was the first study that linked the role of ACh in memory to the role of NMDA receptors in synaptic plasticity (1990) (original paper, 128 citations; related papers, 296 citations).
- First characterization of the electrical and anatomical properties of cholinergic and GABAergic neurons in the medial septum diagonal band (1990) (62 citations).

Computational modeling

- One of the first simulations explaining how the speed of Ca²⁺ entry determines which proteins it binds to (1998) (47 citations).
- The Tsodyks-Markram (TM) synapse model: allows modeling of synapses displaying different forms of short-term synaptic plasticity (1998) (original article, 692 citations; related articles, 249 citations); the TM model was used to reveal the different forms of signaling possible with dynamic synapses (1998) (732 citations).
- Demonstration that neocortical rhythms can be shaped by dynamic synapses (2002) (140 citations).
- Co-development of "Liquid Computing", a new paradigm for real-time computing on time-varying inputs providing an alternative to attractor neural networks (2002) (691 citations).
- Designing and launching the Blue Brain Project (BBP) (2006) (307 citations).
- Construction of a parallel neural network simulator for supercomputers and automated building of neuron models (2006, 2007, 2008, 2009) (combined: 112 citations).

Autism

Neuromicrocircuit alteration in an animal model of autism: discovery that neocortical microcircuits are hyper-connected leading to hyper-reactivity and over expression of NMDA receptors, leading to hyper-plasticity (2007) (96 citations), behavioral studies subsequently revealed enhanced learning and memory of conditioned fears (2007, 2008) (30 citations). Intense World Theory of Autism (2007) (combined, 141 citations).

ACTIVITIES

Neocortical Microcircuitry

LNMC has focused on a detailed characterization of the neocortical microcircuitry which begun at the Max-Plank Institute and was mostly established at the Weizmann Institute. LNMC has extensively studied the microcircuitry of specific layers of the neocortex as well as a specific subset of callosal projecting layer 5 neurons, the various layer 6 cells and the microcircuitry of layer 1. This information helps to better understand the types of neurons and their connections in the neocortical column. In addition, LNMC has studied the disynaptic connections between pyramidal neurons via interneurons and the differences in the layer 5 circuitries between various neocortical areas with an emphasis on the specializations found in the medial prefrontal cortex. LNMC has also examined extensively the molecular distinctions (single cell gene expression patterns) between neocortical neurons.

Synaptic Organization and Plasticity

LNMC has studied the principles that govern how neurons choose their targets. The first study showed that the axonal arbour promiscuously forms close axo-dendritic touches with virtually all-neighbouring neurons however, forms boutons with only a small subset of all potential targets. In a second study, we found that activity can cause these connections to form and disappear – the first reporting of dynamic microcircuit rewiring. Current studies are underway to further examine the rules driving the connections between neurons and the mechanism underlying these rules. In more recent studies, LNMC used the first 12 neuron patch-clamp system to explore the extent to which synaptic connectivity is innately organized.

Gene Expression in Neocortical Neurons

LNMC conducted an exhaustive study to examine the correlated changes in electrical, morphological and gene expression of layer 5 pyramidal neurons during development (from P9 to P60). This study is in the last phases and could yield crucial insight into the transcriptome dynamics underlying changes in neuron structure and function.

Informatics

LNMC has been in charge of assembling the reverse engineered data to be data based for the Blue Brain Project and to drive experiments to fill gaps and control the quality of data. The database is now the most comprehensive database on a microcircuit possible, thereby allowing the BBP to reconstruct the first version of a neocortical column.

Iterations Between Simulations and Experiments

LNMC is engaged in the BBP in the sense that the experimenters also carry out experiments or provide data to be used by the BBP team for calibrating the reconstructed and simulated circuit. Predictions of structural and functional principles from the model can now also be rapidly tested experimentally.

Computation

Aside from the computational projects within BBP, in the initial stages of LNMC, the lab was focused on understanding how the brain can compute when electrical states are continuously changing. This gave rise to the novel concept called "Liquid Computing", which is equivalent to high entropy computing or computing of transient states of activity. The core finding here was that a neural network can generate a consistent and meaningful output, even though the underlying electrical states are constantly changing. This finding is now widely examined in the computational and robotics fields, as it provides a universal approach to perform real-time computing on time series data.

Animal model of Autism

LNMC in collaboration with LGC of Carmen Sandi validated and established the insult-based, valproic acid, animal model of autism and applied the multi-omics approach in an attempt to determine the core molecular,

cellular, synaptic, circuit, systems and behavioural alterations. The study found that animals of this model, displayed the core symptoms of autism as reported from humans and made a major new discovery that these animals display severe abnormalities in fear processing, where fear memories are enhanced, prolonged and resist extinction.

The *in vitro* brain slice experiments revealed that the neocortical microcircuitry was hyper-reactive and that the hyper-reactivity was due to hyper-connected circuits. The study also found that the circuits were hyper-plastic and found a massive enhancement of NMDA receptors and Ca²⁺ mediated signalling pathways. Based on these results, LNMC proposed a radically new theory of autism called "The Intense World Theory of Autism" in which the world of the Autistic child is proposed to be painfully intense and aversive, thereby potentially explaining many of the symptoms of Autism, without relying on a theory of mental retardation and poor brain function.

COLLABORATIONS

Collaboration within the Brain Mind Institute: -

Autism Project: Carmen Sandi's lab: EU Synapse Grant. 1 PhD student and 1 technician. Internal Funding. The project is aimed at understanding the behavioural alterations in animal models of Autism.

Nestle Project: Alan Carleton's group: 4 PhD Students across 4 laboratories, 1 in LNMC. Nestle Grant. The project explored multiple facets of flavour perception and processing and each lab was focused on a different aspect.

Nicolelis Lab: Joint project on multi-unit recording in an animal model of autism. 1 Postdoc and 1 technician. Funded internally.

Collaboration SV/EPFL/Lemanic Region: -

Joint pilot study with Prof Heinrich Hoffmann's lab to determine the feasibility of using nanoparticles to extract RNA from single cells. Performed by interns.

Joint pilot study to determine the feasibility of developing a universal, water-based electrode to record intracellular signals from the outside of cells. Performed by interns.

Autism Project: Carmen Sandi's laboratory on the Behavioral alterations in an animal model of Autism. 1 PhD student

Multi-unit recording in vivo: Miguel Nicolelis, to study alterations in discrimination processing in an animal model of autism.

Joint projects at EPFL & EPFL's Science Park for Innovation: -

"Novel Iridium-Oxide-based MEAs for electrophysiological recordings in brain slices" (LNMC + Inst. Microtechnique, Prof P. Renaud).

"Network-level electrophysiology in *in vitro* models of Huntington's Disease" (LNMC + FNGL, Prof Luthi-Carter).

"Silicon-based integrated array of microelectrodes for *in vitro* electrophysiology" (LNMC + Inst. Microelectronics, Prof Y. Leblebici).

"High-density arrays of microelectrodes for *in vitro* electrophysiology" (LNMC + Inst. Microtechnique and Ayanda Biosystems, Dr. Heuschkel).

"The olfactory bulb synaptic microcircuit" (LNMC + FPG, Dr. A. Carleton).

"Advanced Database Technology for Brain Simulations" (BBP + DIAS, Prof. Ailamaki).

Swiss-wide collaboration: -

"The dynamics of instantaneous firing probability in vitro, in computo and in silico" (LNMC + Inst. Neuroinformatics, Zurich, Dr. G. Indiveri).

"The role of sodium-currents in slow inactivation in neuronal computation" (LNMC + Inst. of Physiology, Bern, Prof H. -R. Luescher).

International Collaboration: -

Blue Brain Project: Collaboration with Prof Idan Segev, Hebrew University and Michael Hines, Yale University.

Joint anatomy project with Prof Zoltan Kisvardy, Hungary.

Collaboration with Professor Alex Thomson, University of London, School of Pharmacy,

1. "Conductive carbon nanotubes and neuronal networks" (LNMC + Univ. of Trieste, Italy, Profs Ballerini, Prato and Scoles) 2. "Autaptic microcircuitry and the dynamical response properties of cortical neurons" (LNMC + EBRI, European Brain Research Institute, Rome - Italy, Dr. A. Bacci).

Collaboration with industry: -

NRC – Flavour Perception – 3 years – CHF750'000/year.

IBM – Joint Postdoctoral student on the Blue Brain Project, 2005-2008, USD200,000/year (and a discounted supercomputer).

INNF - NRC - 3 years - USD100'000/year.

PEER-REVIEW RESPONSIBILITIES

<u>Journals:</u> Nature, Science, Neuron, Journal of Physiology (London), Journal of Neuroscience, Experimental Brain Research, Trends in Neuroscience, Journal of Comparative Anatomy, Nature Neuroscience, Journal of Neuroinformatics.

<u>Grant Foundations:</u> Wellcome Trust, Alzheimer's Foundation, Volkswagen Foundation, Australian Neurological Foundation, Medical Research Council, UK, BSI-REIKEN Program Evaluation Committee, German-Israel Research Committee, Hungarian Academy of Science Program Evaluation Committee, Chairman of the DIP (German-Israel Large Grants Organization) program evaluation committee (2004).

<u>Editorial:</u> Computation Based on Spiking Neurons. Neural Networks Special Issue, Grossberg, Maass, Markram, Eds.

Editorial: The Neocortical Column; Co-Editor, Special Issue of Cerebral Cortex, Markram & Linden Eds.

ORGANIZATION OF SPECIAL EVENTS

- **Active Dendrites:** Symposium organizer at the Annual European Neuroscience meeting, Strassbourg, France, 1996. Organizer: Markram.
- **Neocortical columns:** 57 Speakers focusing on the anatomy, physiology, plasticity and function of neocortical columns. Organizers: Markram, Sakmann & Grinvald.
- **Synaptic basis of receptive fields:** Human Frontiers Science Program Meeting: 10 speakers focusing on the synaptic basis of receptive fields. Organizers: Fregnac & Markram.
- Computation in a Neocortical Column: NIPS, Denver Colorado, 2000. Organizers: Linden & Markram.
- **Neocortical Microcircuitry:** Madrid, Spain, 2001. Organizers: Yuste, Callaway, & Markram.
- **Brain in Motion:** BMI Inauguration Conference, Lausanne, 2002. Organizer: Markram.
- Cajal Centenary Conference: The Neocortical Column, Cosmocaixia, Barcelona, Spain, 2006. Organizers: DeFelipe & Markram.
- **Neuroscapes:** The first Neuroart exhibition: Cosmocaixia, Barcelona, Spain, 2006. Organizers: DeFelipe & Markram.
- **IBRO/UNESCO School:** The Cape Town School of Advanced Computational Neuroscience, 2011. Organizers: Markram, Kellaway & Srivastava.

STUDENTS SUPERVISED

In total: 45 Visiting/Intern Students, 15 Masters Students, 24 PhD Students, 6 Postdoctoral Students.

Student	Year completed	Institute
Wang Yun	2000	Weizmann Institute
Anirudh Gupta	2001	Weizmann Institute
Gilad Sillerberg	2002	Weizmann Institute
Maria Toledo	2003	Weizmann Institute
Ofer Melamed	2004	Weizmann Institute
Jean-Vincent Le Be	2006	EPFL
Tania Rinaldi	2006	EPFL
Thomas Berger	2009	EPFL
Rodrigo Perin	2010	EPFL
Iman Riachi	2010	EPFL
Sebastien Lasserre	2010	EPFL
Luca Gambazz	2010	EPFL
Rajnish Ranjan	2011	EPFL
Georges Khazen	2011	EPFL
Srikanth Ramaswamy	2011	EPFL
Vincent Delattre	2013	EPFL
Monica Regina Favre	2013	EPFL
Michael Reimann	2014	EPFL
Farhan Tauheed	2014	EPFL
Jean-Pierre Ghobril	2015	EPFL
Renaud Luc Richardet	2015	EPFL
Ayah Khubieh	Current	EPFL
Jane Yi	Current	EPFL
Wuzhou Yang	Current	EPFL

Special mentions:

- Wang Yun Weizmann Prize, Excellence in a PhD
- Anirudh Gupta Weizmann Prize, Excellence in a PhD
- Gilad Sillerberg HFSP Young Researcher Award
- Maria Toledo The Roche Prize
- Tania Rinaldi Prix de la Fondation Chorafas

STUDENT THESES

- 1. R. L. Richardet, H. Markram and J. -C. Chappelier (Dirs.). (2016). *Agile* in-litero *Experiments: How Can Semi-Automated Information Extraction From Neuroscientific Literature Help Neuroscience Model Building?* Thèse no. 6809, EPFL, Lausanne.
- 2. J. P. Ghobril, H. Markram and F. S. Pavone (Dirs.). (2015). *Large Volume Imaging of Rodent Brain Anatomy with Emphasis on Selective Plane Illumination Microscopy*. Thèse no. 6533, EPFL, Lausanne.
- 3. F. Tauheed, A. Ailamaki and H. Markram (Dirs.). (2014). *Scalable Exploration of Spatial Data in Large-Scale Scientific Simulations*. Thèse no. 6125, EPFL, Lausanne.
- 4. M. Reimann, H. Markram and S. Hill (Dirs.). (2014). *The* in-Silico *Neocortical Microcircuit: From Structure to Dynamics*. Thèse no. 6168, EPFL, Lausanne.
- 5. M. R. Favre, H. Markram and K. Markram (Dirs.). (2013). *Hyper-Emotional Neurophysiology in a Rat Model of Autism*. Thèse, EPFL, no. 5996, Lausanne.
- 6. V. Delattre and H. Markram (Dir.). (2013). Network Activity and Plasticity. Thèse, EPFL, no. 5901, Lausanne.
- 7. S. Muralidhar and H. Markram (Dir.). (2013). Synaptic and Cellular Organization of Layer 1 of the Developing Rat Somatosensory Cortex. Thèse, EPFL, no. 5902 Lausanne.
- 8. S. Ramaswamy, H. Markram and S. L. Hill (Dirs.). (2011). *Emergent Properties of* in Silico *Synaptic Transmission in a Model of the Rat Neocortical Column*. Thèse no. 5208, EPFL, Lausanne.
- 9. R. Ranjan and H. Markram (Dir.). (2011). *Engineering Neuron Models: from Ion Channels to Electrical Behavior*. Thèse no. 5129, EPFL, Lausanne.

- 10. G. Khazen and H. Markram (Dir.). (2011). *Predictive Engineering the Membrane Composition of Neocortical Neurons*. Thèse no. 5067, EPFL, Lausanne.
- 11. M. A. Jan, H. Markram and F. Schürmann (Dirs.). (2011). *A Pipeline Based Approach for Experimental Neuroscience Data Management*. Thèse no. 4863, EPFL, Lausanne.
- 12. L. Gambazzi and H. Markram (Dir.). (2010). *Impact of Carbon-Nanotube Substrate Coating in Neuronal Networks*. Thèse no. 4713, EPFL, Lausanne.
- 13. R. d. C. Perin and H. Markram (Dir.). (2010). Emergent Dynamics in Neocortical Microcircuits. Thèse no. 4705, EPFL, Lausanne
- 14. I. Riachi and H. Markram (Dir.). (2010). *Emergent Connectivity Principles in the Neocortex*. Thèse no. 4631, EPFL, Lausanne.
- 15. T. Berger and H. Markram (Dir.). (2009). Properties of Neocortical Microcircuits. Thèse no. 4454, EPFL, Lausanne.
- 16. M. Pignatelli, H. Markram and A. Carleton (Dirs.). (2009). *Structure and Function of the Olfactory Bulb Microcircuit*. Thèse no. 4275, EPFL, Lausanne.
- 17. J. -V. Le Bé and H. Markram (Dir.). (2007). Structure and Dynamics of the Neocortical Microcircuit Connectivity. Thèse no. 3802, EPFL, Lausanne.
- 18. T. Rinaldi and H. Markram (Dir.). (2006). *Altered Neocortical Microcircuitry in the Valproic Acid Rat Model of Autism*. Thèse no. 3701, EPFL, Lausanne.

ALL PUBLICATIONS

- H. Markram, E. Muller, S. Ramaswamy, M. W. Reimann, M. Abdellah, C. A. Sanchez, A. Ailamaki, L. Alonso-Nanclares, N. Antille, S. Arsever, G. A. A. Kahou, T. K. Berger, A. Bilgili, N. Buncic, A. Chalimourda, G. Chindemi, J. -D. Courcol, F. Delalondre, V. Delattre, S. Druckmann, R. Dumusc, J. Dynes, S. Eilemann, E. Gal, M. E. Gevaert, J.-P. Ghobril, A. Gidon, J. W. Graham, A. Gupta, V. Haenel, E. Hay, T. Heinis, J. B. Hernando, M. Hines, L. Kanari, D. Keller, J. Kenyon, G. Khazen, Y. Kim, J. G. King, Z. Kisvarday, P. Kumbhar, S. Lasserre, J.-V. Le Bé, B. R. C. Magalhães, A. Merchán-Pérez, J. Meystre, B. R. Morrice, J. Muller, A. Muñoz-Céspedes, S. Muralidhar, K. Muthurasa, D. Nachbaur, T. H. Newton, M. Nolte, A. Ovcharenko, J. Palacios, L. Pastor, R. Perin, R. Ranjan, I. Riachi, J.-R. Rodríguez, J. L. Riquelme, C. Rössert, K. Sfyrakis, Y. Shi, J. C. Shillcock, G. Silberberg, R. Silva, F. Tauheed, M. Telefont, M. Toledo-Rodriguez, T. Tränkler, W. Van Geit, J. V. Díaz, R. Walker, Y. Wang, S. M. Zaninetta, J. DeFelipe, S. L. Hill, I. Segev, and F. Schürmann. (2015). Reconstruction and Simulation of Neocortical Microcircuitry. Cell, 163(2), pp. 456-492.
- 20. M. Abdellah, A. Bilgili, S. Eilemann, H. Markram and F. Schürmann. (2015). Physically-based *in silico* Light Sheet Microscopy for Visualizing Fluorescent Brain Models. *BMC Bioinformatics*, **16**(Suppl 11):S8.
- 21. S. Ramaswamy, J. -D. Courcol, M. Abdellah, S. R. Adaszewski, N. Antille, S. Arsever, G. Atenekeng, A. Bilgili, Y. Brukau, A. Chalimourda, G. Chindemi, F. Delalondre, R. Dumusc, S. Eilemann, M. E. Gevaert, P. Gleeson, J. W. Graham, J. B. Hernando, L. Kanari, Y. Katkov, D. Keller, J. G. King, R. Ranjan, M. W. Reimann, C. Rössert, Y. Shi, J. C. Shillcock, M. Telefont, W. Van Geit, J. Villafranca Diaz, R. Walker, Y. Wang, S. M. Zaninetta, J. DeFelipe, S. L. Hill, J. Muller, I. Segev, F. Schürmann, E. B. Muller and H. Markram. (2015). The Neocortical Microcircuit Collaboration Portal: A Resource for Rat Somatosensory Cortex. *Frontiers In Neural Circuits*, 9, pp. 44.
- 22. M. W. Reimann, J. G. King, E. B. Muller, S. Ramaswamy and H. Markram. (2015). An Algorithm to Predict the Connectome of Neural Microcircuits. *Frontiers In Computational Neuroscience*, **9**, pp. 120.
- 23. V. Delattre, D. Keller, M. Perich, H. Markram and E. B. Muller. (2015). Network-Timing-Dependent Plasticity. *Frontiers in Cellular Neuroscience*, **9**, pp. 220.
- 24. S. Ramaswamy and H. Markram. (2015). Anatomy and Physiology of the Thick-Tufted Layer 5 Pyramidal Neuron. *Frontiers In Cellular Neuroscience*, **9**, pp. 233.
- 25. D. Keller, N. Babai, O. Kochubey, Y. Han and H. Markram *et al.* (2015). An Exclusion Zone for Ca2+ Channels around Docked Vesicles Explains Release Control by Multiple Channels at a CNS Synapse. *PLoS Computational Biology*, **11**(5), pp. e1004253.
- 26. I. Costantini, J.-P. Ghobril, A. P. Di Giovanna, A. L. A. Mascaro and L. Silvestri *et al.* (2015). A Versatile Clearing Agent for Multi-Modal Brain Imaging. *Scientific Reports*, **5**(9808), pp. 1-9.

- 27. R. Frackowiak and H. Markram. (2015). The Future of Human Cerebral Cartography: a Novel Approach. *Philosophical Transactions of the Royal Society of London*, **370**(1668), pp. 20-32.
- 28. M. R. Favre, D. La Mendola, J. Meystre, D. Christodoulou and M. J. Cochrane *et al.* (2015). Predictable Enriched Environment Prevents Development of Hyper-Emotionality in the VPA Rat Model of Autism. *Frontiers In Neuroscience*, **9**, pp. 127.
- 29. C. Anastassiou, R. d. C. Perin, G. Buzsaki, H. Markram and C. Koch. (2015). Cell Type- and Activity-Dependent Extracellular Correlates of Intracellular Spiking. *Journal of Neurophysiology*, **114**(1), pp. 608-23.
- 30. S. Camacho, S. Michlig, C. De Senarclens-Bezencon, J. Meylan and J. Meystre *et al.* (2015). Anti-Obesity and Anti-Hyperglycemic Effects of Cinnamaldehyde via Altered Ghrelin Secretion and Functional Impact on Food Intake and Gastric Emptying. *Scientific Reports*, **5**, pp. 7919.
- 31. C. A. Pozzorini, S. Mensi, O. Hagens, R. Naud and C. Koch *et al.* (2015). Automated High-Throughput Characterization of Single Neurons by Means of Simplified Spiking Models. *PLoS Computational Biology*, **11**(4), pp. e1004275.

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- 32. M. Toledo-Rodriguez and H. Markram. (2014). Single-Cell RT-PCR, a Technique to Decipher the Electrical, Anatomical and Genetic Determinants of Neuronal Diversity. *Methods in Mol Biol*, **1183**, pp. 143-58.
- 33. J. Defelipe, E. Garrido and H. Markram. (2014). The Death of Cajal and the End of Scientific Romanticism and Individualism. *Trends in Neurosciences*, **37**(10), pp. 525-527.
- 34. M. Pezzoli, A. Elhamdani, S. Camacho, J. Meystre and S. M. Gonzalez *et al.* (2014). Dampened Neural Activity and Abolition of Epileptic-Like Activity in Cortical Slices by Active Ingredients of Spices. *Scientific Reports*, **4**, pp. 6825.
- 35. S. Muralidhar, Y. Wang and H. Markram. (2014). Synaptic and Cellular Organization of Layer 1 of the Developing Rat Somatosensory Cortex. *Frontiers in Neuroanatomy*, **7**(52), pp. 1-17.
- 36. W. F. Podlaski, A. Seeholzer, R. Rajnish, T. Vogels, H. Markram *et al.* (2014). Visualizing the Similarity and Pedigree of NEURON Ion Channel Models Available on ModelDB. COSYNE 2014, Utah, USA.
- 37. F. Tauheed, T. Heinis, F. Schürmann, H. Markram and A. Ailamaki. (2014). OCTOPUS: Efficient Query Execution on Dynamic Mesh Datasets. *30st International Conference on Data Engineering (ICDE '14)*, pp. 1000-11.

- 38. R. Perin and H. Markram. (2013). A Computer-Assisted Multi-Electrode Patch-Clamp System. *J Vis Exp*, **18**(80), pp. e50630.
- 39. Markram, H. (2013). Seven Challenges for Neuroscience. Functional Neurology, 28(3), pp. 145-51.
- 40. S. Druckmann, S. Hill, F. Schuermann, H. Markram and I. Segev. (2013). A Hierarchical Structure of Cortical Interneuron Electrical Diversity Revealed by Automated Statistical Analysis. *Cerebral Cortex*, **23**(12), pp. 2994-3006.
- 41. V. Delattre, D. La Mendola, J. Meystre, H. Markram and K. Markram. Nlgn4 Knockout Induces Network Hypo-Excitability in Juvenile Mouse Somatosensory Cortex *in vitro*. *Scientific Reports*, 3, pp. 2897.
- 42. M. R. Favre, T. R. Barkat, D. La Mendola, G. Khazen and H. Markram *et al.* (2013). General Developmental Health in the VPA-Rat Model of Autism. *Frontiers in Behavioral Neuroscience*, **7**(88), pp. 1-11.
- 43. M. W. Reimann, C. A. Anastassiou, R. Perin, S. L. Hill and H. Markram *et al.* (2013). A Biophysically Detailed Model of Neocortical Local Field Potentials Predicts the Critical Role of Active Membrane Currents. *Neuron*, **79**(2), pp. 375-390.
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- 45. E. Hay, F. Schuermann, H. Markram and I. Segev. (2013). Preserving Axosomatic Spiking Features Despite Diverse Dendritic Morphology. *Journal Of Neurophysiology*, **109**(12), pp. 2972-2981.
- 46. R. Perin, M. Telefont and H. Markram. (2013). Computing the Size and Number of Neuronal Clusters in Local Circuits. *Frontiers In Neuroanatomy*, **7**(1), pp. 1-10.
- 47. A. Loebel, J. -V. Le Be, M. J. E. Richardson, H. Markram and A. V. M. Herz. (2013). Matched Pre- and Post-Synaptic Changes Underlie Synaptic Plasticity over Long Time Scales. *Journal Of Neuroscience*, **33**(15), pp. 6257-6266.
- 48. J. Griggs and H. Markram. (2013). One minute with... Henry Markram. New Scientist, 217(2903), pp. 29-29.
- 49. J. DeFelipe, P. L. Lopez-Cruz, R. Benavides-Piccione, C. Bielza, P. Larranaga *et al.* (2013). New insights into the Classification and Nomenclature of Cortical GABAergic Interneurons. *Nature Reviews Neuroscience*, **14**(3), pp. 202-216.

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- 50. G. Khazen, S. L. Hill, F. Schürmann and H. Markram. (2012). Combinatorial Expression Rules of Ion Channel Genes in Juvenile Rat (*Rattus norvegicus*) Neocortical Neurons. *PloS ONE*, **7**(4), e34786, doi:10.1371/journal.pone.0034786.
- 51. H. Markram. (2012). The Human Brain Project. Scientific American, 306(6), pp. 50-5.
- 52. S. Druckmann, T. Berger, S. Hill, F. Schuermann, H. Markram and I. Segev. (2012). Revealing Hidden Dynamics of Neurons. *PNAS*, in review.
- 53. S. Lasserre, J. Hernando, S. Hill, F. Schürmann and P. d. M. Anasagasti *et al.* (2012). A Neuron Membrane Mesh Representation for Visualization of Electrophysiological Simulations. *IEEE Trans Vis Comp Graph*, **18**(2), pp. 214-27.
- 54. H. Markram, W. Gerstner and P. J. Sjöström. (2012). Spike-Timing-Dependent Plasticity: a Comprehensive Overview. *Frontiers in Synaptic Neuroscience*, **4**, pp. 2.
- 55. S. Ramaswamy, S. L. Hill, J. G. King, F. Schürmann, Y. Wang and H. Markram. (2012). Intrinsic Morphological Diversity of Thick-Tufted Layer 5 Pyramidal Neurons Ensures Robust and Invariant Properties of *In Silico* Synaptic Connections. *The Journal of Physiology*, **590**(4), pp. 737-52.
- 56. S. L. Hill, Y. Wang, I. Riachi, F. Schürmann and H. Markram. (2012). Statistical Connectivity Provides a Sufficient Foundation for Specific Functional Connectivity in Neocortical Neural Microcircuits. *PNAS*, **109**(42), pp. E2885-94.
- 57. S. Lasserre, J. Hernando, S. Hill, F. Schürmann, P. d. Miguel Anasagasti, G. Abou Jaoudé and H. Markram. (2012). A Neuron Mesh Representation for Visualization of Electrophysiological Simulations. *IEEE Trans Vis Comput Graph*, **18**(2), pp. 214-227.
- 58. J. V. Raimondo, H. Markram and C. J. Akerman. (2012). Short-Term Ionic Plasticity at GABAergic Synapses. *Frontiers in Synaptic Neuroscience*, **4**, pp. 5.
- 59. R. Ranjan, G. Khazen, L. Gambazzi, S. Ramaswamy, S. L. Hill *et al.* (2012). Channelpedia: an Integrative and Interactive Database for Ion Channels. *Frontiers in Neuroinformatics*, **5**, pp. 36.
- 60. J. DeFelipe, H. Markram and K. S. Rockland. (2012). The Neocortical Column. Frontiers In Neuroanatomy, 6, pp. 22.
- 61. F. Tauheed, T. Heinis, F. Schürmann, H. Markram and A. Ailamaki. (2012). SCOUT: Prefetching for Latent Structure Following Queries. 38th International Conference on Very Large Databases (VLDB '12), Istanbul, Turkey.
- 62. F. Tauheed, L. Biveinis, T. Heinis, F. Schürmann, H. Markram and A. Ailamaki. Accelerating Range Queries For Brain Simulations. 28th International Conference on Data Engineering (ICDE '12), Washington DC, USA.

- 63. F. Tauheed, 1 Biveinis, T. Heinis, F. Schürmann, H. Markram, and A. Ailamaki. (2011). Speeding Up Range Queries for Brain Simulations. *Conference on Very Large Data Bases (VLDB '11)*.
- 64. C. A. Anastassiou, R. Perin, H. Markram and C. Koch. (2011). Ephaptic Coupling of Cortical Neurons. *Nature Neuroscience*, **14**(2), pp. 217-23.
- 65. S. Romand, Y. Wang, M. Toledo-Rodriguez, and H. Markram. (2011). Morphological Development of Thick-Tufted Layer V Pyramidal Cells in the Rat Somatosensory Cortex. *Frontiers in Neuroanatomy*, **5**, pp: 5.
- 66. R. Perin, T. K. Berger, and H. Markram. (2011). A Synaptic Organizing Principle for Cortical Neuronal Groups. *PNAS*, **108**(13), pp. 5419-24.
- 67. H. Markram and R. Perin. (2011). Innate Neural Assemblies for Lego Memory. Frontiers in Neural Circuits, 5, pp. 6.
- 68. E. Hay, S. Hill, F. Schürmann, H. Markram and I. Segev. (2011). Models of Neocortical Layer 5b Pyramidal Cells Capturing a Wide Range of Dendritic and Perisomatic Active Properties. *PLoS Comput Biol*, **7**(7), pp. e1002107.
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- 71. S. Druckmann, T. K. Berger, F. Schürmann, S. Hill, H. Markram and I. Segev. Effective Stimuli for Constructing Reliable Neuron Models. *PloS Comput Biol*, **7**(8), pp. e1002133.
- 72. G. Miller and H. Markram. (2011). Newsmaker Interview: Henry Markram. Blue Brain Founder Responds to Critics, Clarifies his Goals. *Science*, **334**(6057), pp. 748-749.
- 73. H. Markram and K. Markram. (2011). Frontiers Research: Seek, Share & Create. *Common Knowledge: the Challenge of Transdisciplinarity*, EPFL-CHAPTER-169296, pp. 145-162.

74. H. Markram, W. Gerstner and P. J. Sjöström. (2011). A History of Spike-Timing-Dependent Plasticity. *Frontiers in Synaptic Neuroscience*, **3**(4), pp. 1-24.

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- 75. K. Markram and H. Markram. (2010). The Intense World Theory a Unifying Theory of the Neurobiology of Autism. *Frontiers in Human Neuroscience*, **4**, pp. 224.
- 76. T. K. Berger, G. Silberberg, R. Perin and H. Markram. (2010). Brief Bursts Self-Inhibit and Correlate the Pyramidal Network. *PloS Biol*, **8**(9), pp. e1000473.
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- 78. H.Markram. (2010). Handbook of Brain Microcircuits, Oxford University Press, 2010.
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- 80. L. Conboy, R. Bisaz, K. Markram and C. Sandi. (2010). Role of NCAM in Emotion and Learning. *Adv Exp Med Biol*, **663**, pp. 271-96.

2009

- 81. G. T. Silva, J. -V. Le Bé, I. Riachi, T. Rinaldi, K. Markram and H. Markram. (2009). Enhanced Long-Term Microcircuit Plasticity in the Valproic Acid Animal Model of Autism. *Frontiers in Synaptic Neuroscience*, **1**, pp. 1.
- 82. S. Gawad, M. Giugliano, M. Heuschkel, B. Wessling, H. Markram *et al.* (2009). Substrate Arrays of Iridium Oxide Microelectrodes for *In Vitro* Neuronal Interfacing. *Frontiers in Neuroengineering*, **2**, pp. 1.
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- 84. A. Loebel, G. Silberberg, D. Helbig, H. Markram, M. Tsodyks *et al.* (2009). Multiquantal Release Underlies the Distribution of Synaptic Efficacies in the Neocortex. *Frontiers in Computational Neuroscience*, **3**, pp. 27.
- 85. G. Cellot, E. Cilia, S. Cipollone, V. Rancic, A. Sucapane *et al.* (2009). Carbon Nanotubes Might Improve Neuronal Performance by Favouring Electrical Shortcuts. *Nature Nanotechnology*, **4**, pp. 126-133.
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- 89. O. Melamed, O. Barak, G. Silberberg, H. Markram, and M. Tsodyks. (2008). Slow Oscillations in Neural Networks with Facilitating Synapses. *J Comput Neurosci*, **25**(2), pp. 308-16.
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