

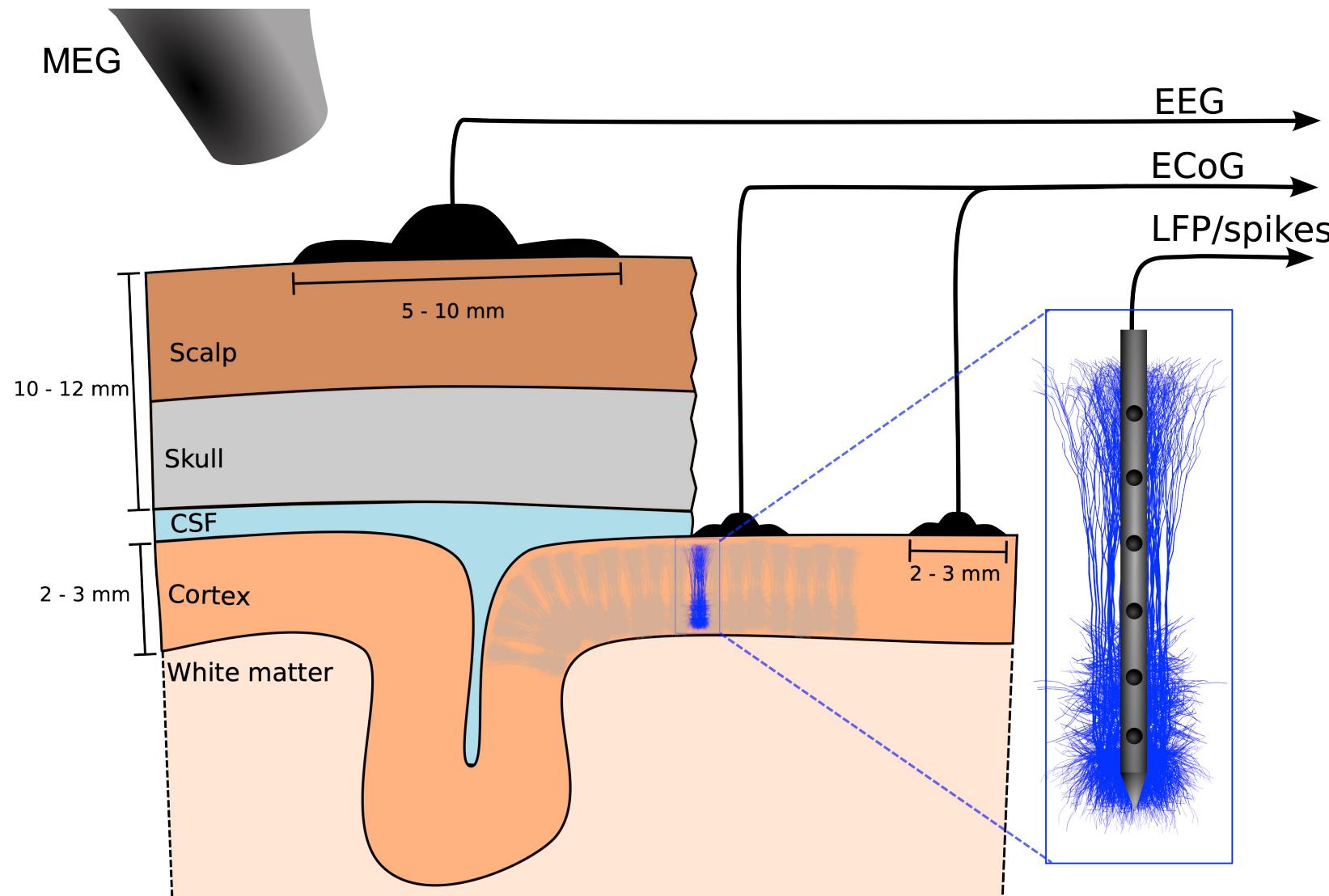
Modelling of electric and magnetic brain signals: Applications

Gaute T. Einevoll

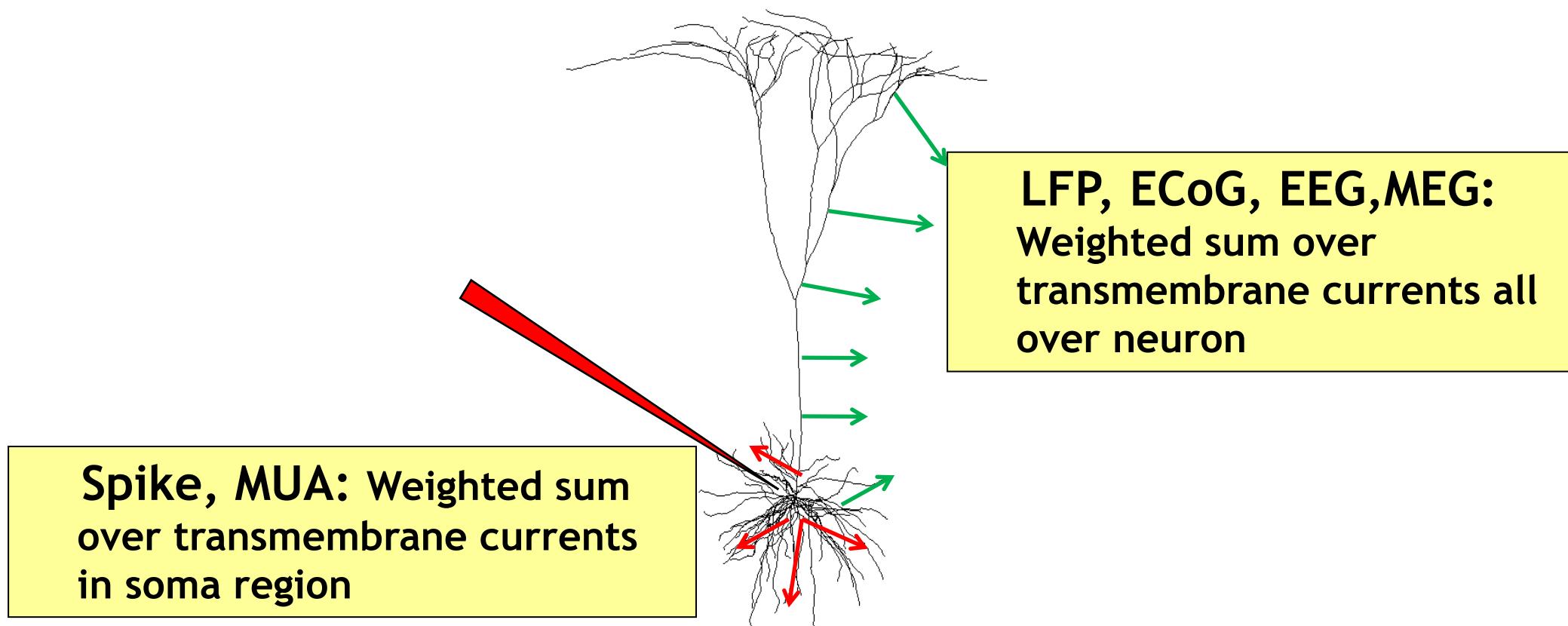
Norwegian University of Life Sciences (NMBU), Ås;
University of Oslo, Norway



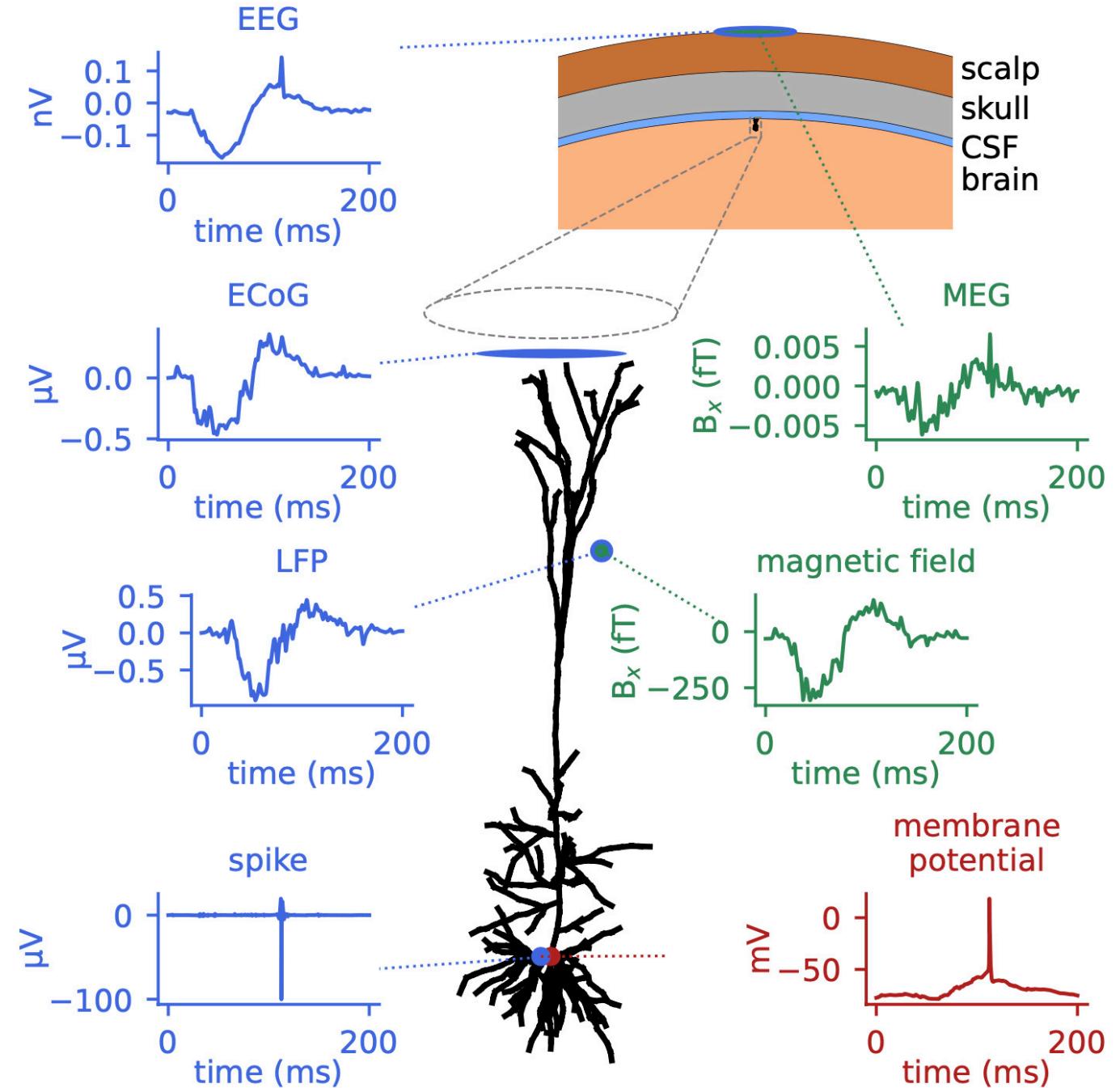
Systems level measurements of neural activity



Mechanistic modeling of electric and magnetic brain signals



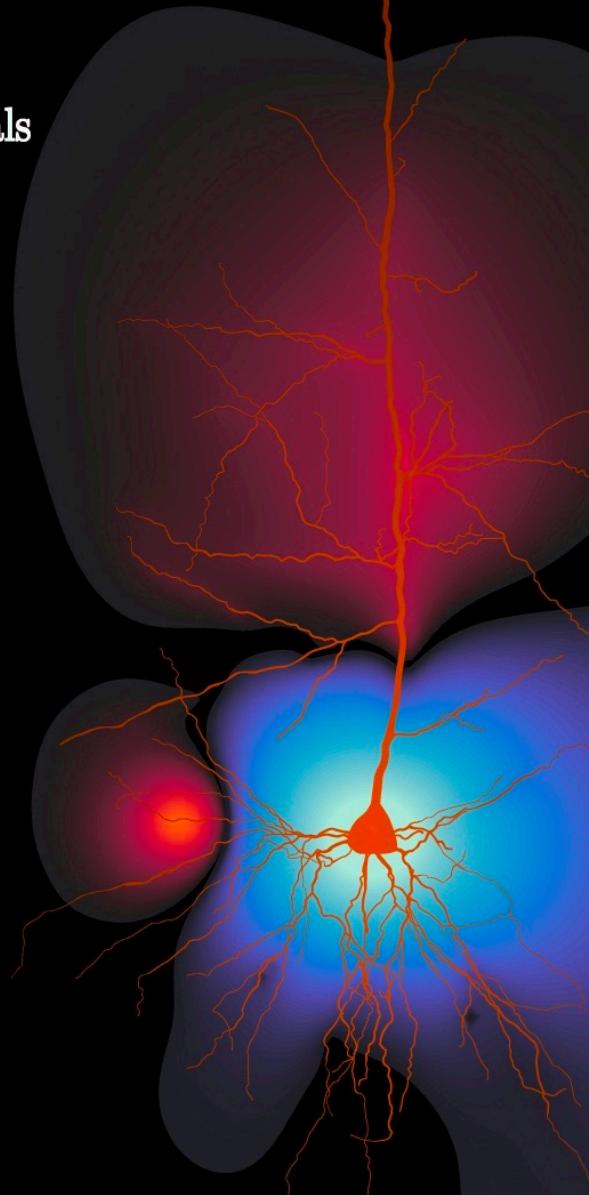
Modeled brain signals from single neuron firing action potential following synaptic inputs





Electric Brain Signals

From Neural Dynamics
to Extracellular Potentials



Geir Halnes
Torbjørn V. Ness
Solveig Næss
Espen Hagen
Klas H. Pettersen
Gaute T. Einevoll



Cambridge University
Press (2024)

Applications of forward-modeling of brain signals

Spikes

- What determines the shape and size of spikes? (Pettersen & Einevoll, 2008)
- What does spikes look like in micro-electrode arrays MEAs? (Ness et al, 2015)
- Multiunit activity in bat inferior culliculus (Luo et al, 2018)
- Spikes from axonal terminations in mouse cortex (Thunemann et al, bioRxiv, 2022)

LFPs

- How “local” are local field potentials? (Linden et al, 2010; 2011; Leski et al, 2013)
- How does active dendritic conductances affect LFPs? (Ness et al, 2016; 2017)
- What is the “unitary” LFP from a thalamocortical spike? (Hagen et al, 2017)
- Network LFPs using kernel trick (Hagen et al, 2022)
- Simplified formula for LFP modeling (Mazzoni et, 2015)

EEG/ECoG/MEG

- What is the link between EEG, LFP, ECoG and MEG? (Næss et al, 2021)
- Simplified formula for EEG modeling (Martinez-Canada et al, 2021)

Data analysis

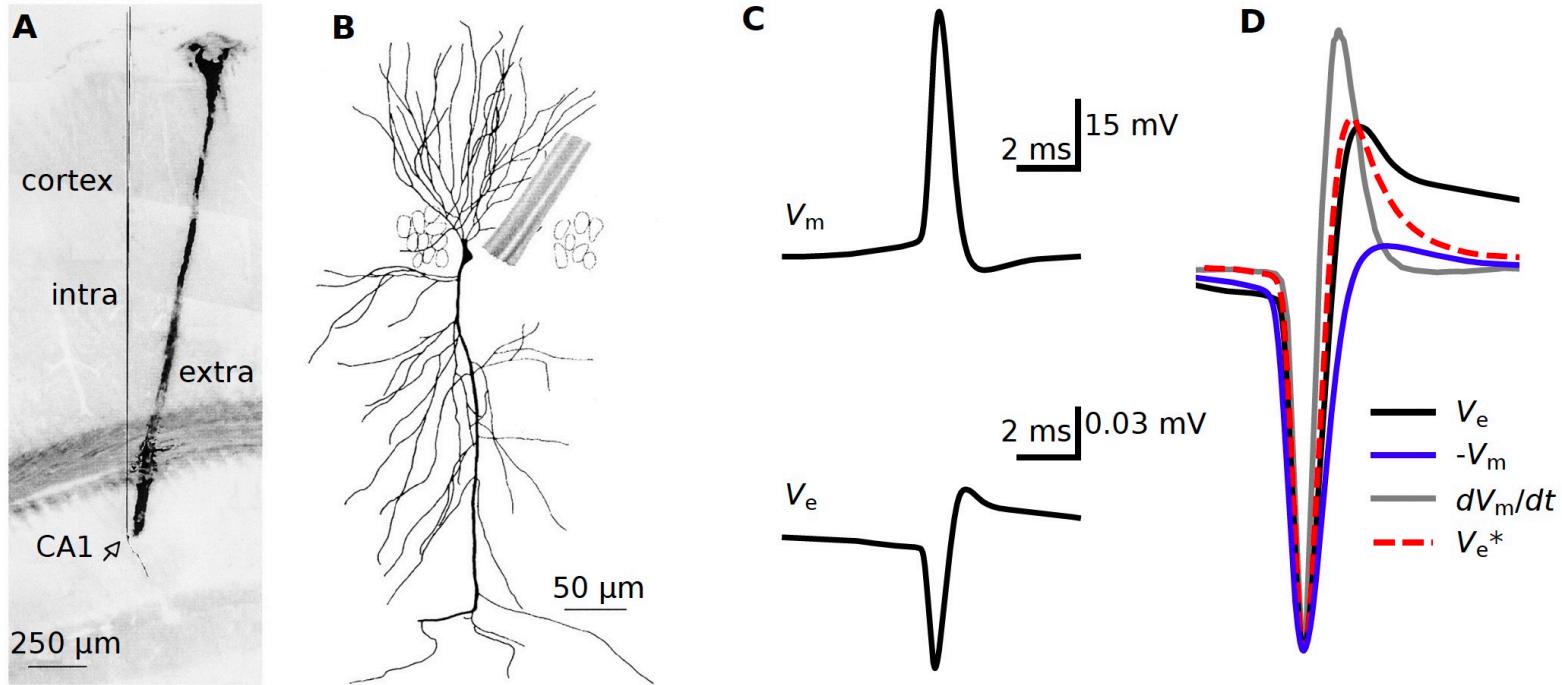
- Development and validation of iCSD method in vivo (Pettersen et al. 2006; 2008; Leski et al. 2011)
- Development and validation of iCSD method in MEAs (Ness et al. 2015)
- Benchmarking data for spike sorters (Hagen et al, 2015; Buccino & Einevoll, 2020)
- Spike-based classification and localization of neurons (Buccino et al, 2018)
- Laminar Population Analysis (LPA) for joint analysis of spikes and LFPs (Einevoll et al, 2007; Glabska et al., 2016)
- Multilinear Population Analysis (MLPA) of LFP data (Geddes et al, 2020)

Network model parameter estimation

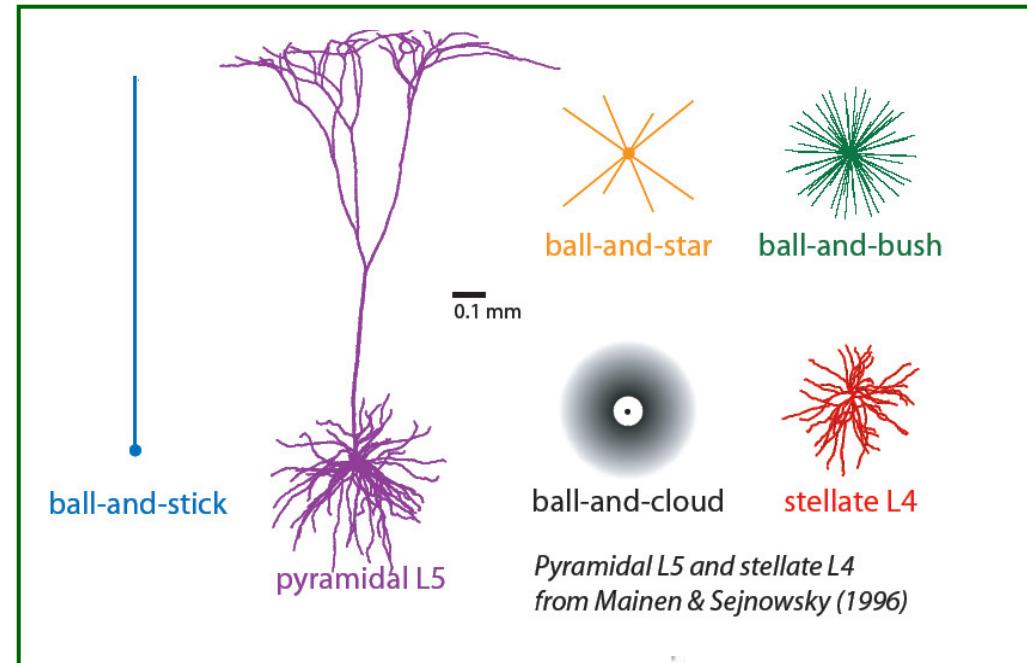
- Parameter estimation for Brunel network from LFPs with deep networks (Skaar et al, 2020)
- Parameter estimation for Brunel network from LFPs with Gaussian processes (Skaar et al, bioRxiv, 2022)
- Network parameters from spikes and LFPs for mouse V1 (Rimehaug et al, bioRxiv, 2022)

Extracellular spikes

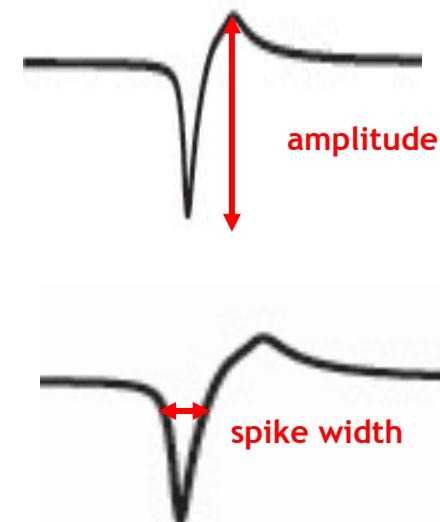
Experimental data from Henze et al (2000)



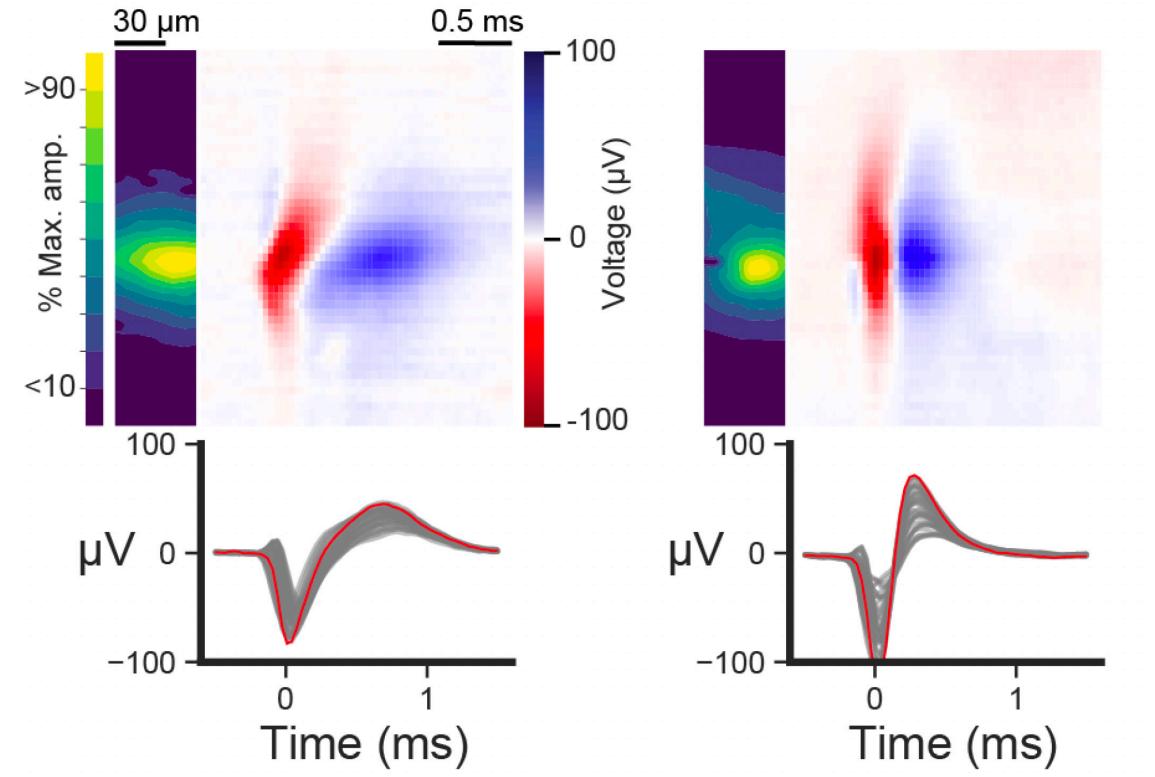
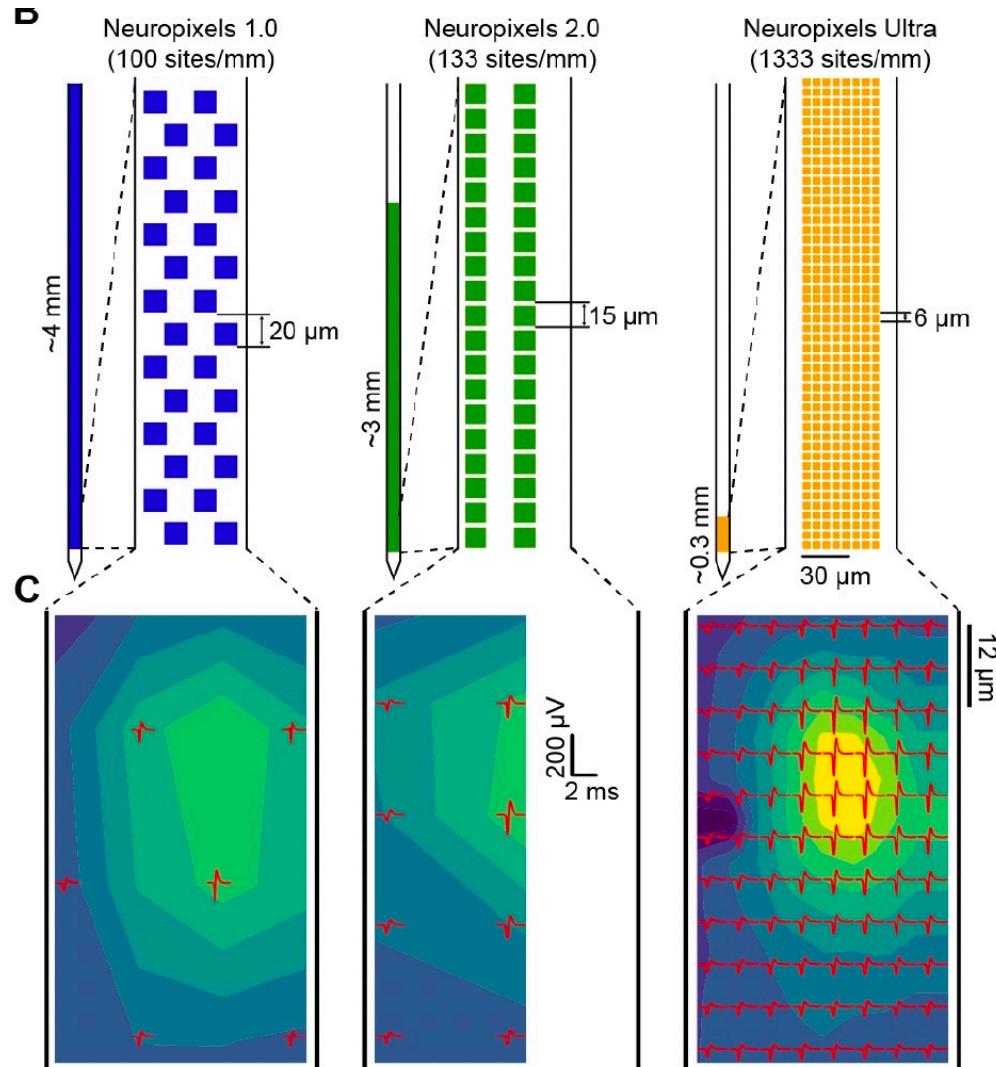
How do the extracellular spikes depend on neuronal morphology?



- Amplitude is (i) roughly proportional to *sum of cross-sectional areas* of dendrites connected to soma, (ii) independent of *membrane resistance* R_m , ...
- Spike width increases with distance from soma, i.e., high-frequency dampening also with simple ohmic extracellular medium



Neuropixel Ultra



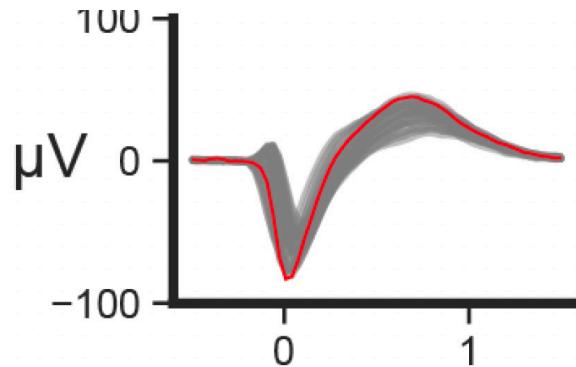
Regular-spiking cell

Fast-spiking cell

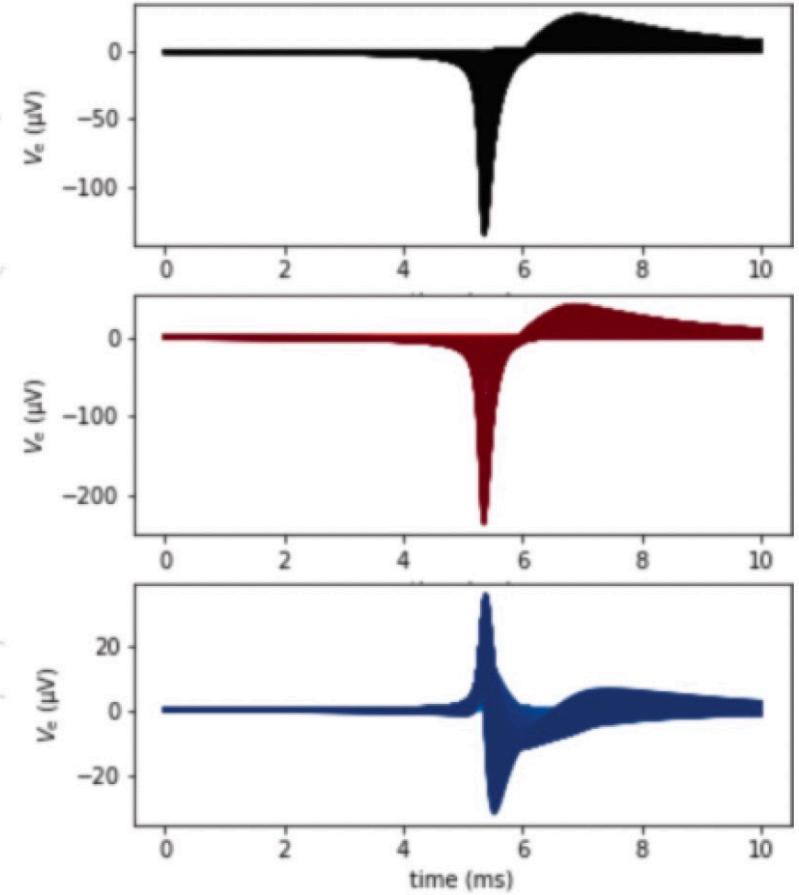
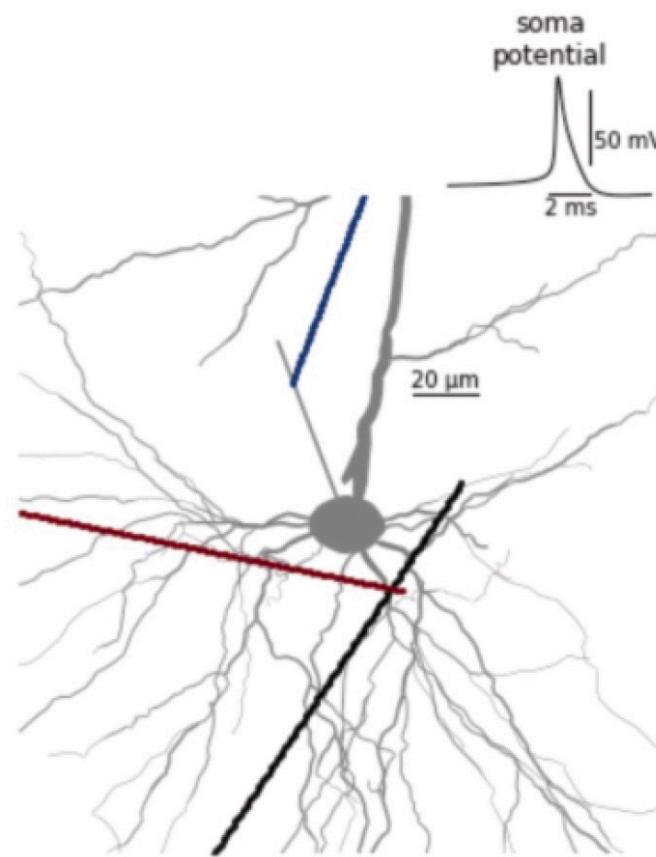
Neuropixel Ultra - computational modeling



Torbjørn
Ness



Regular-spiking cell



Imaging through wearable, transparent Windansee



Anna
Devor



Shadi
Dayeh



Martin
Thunemann



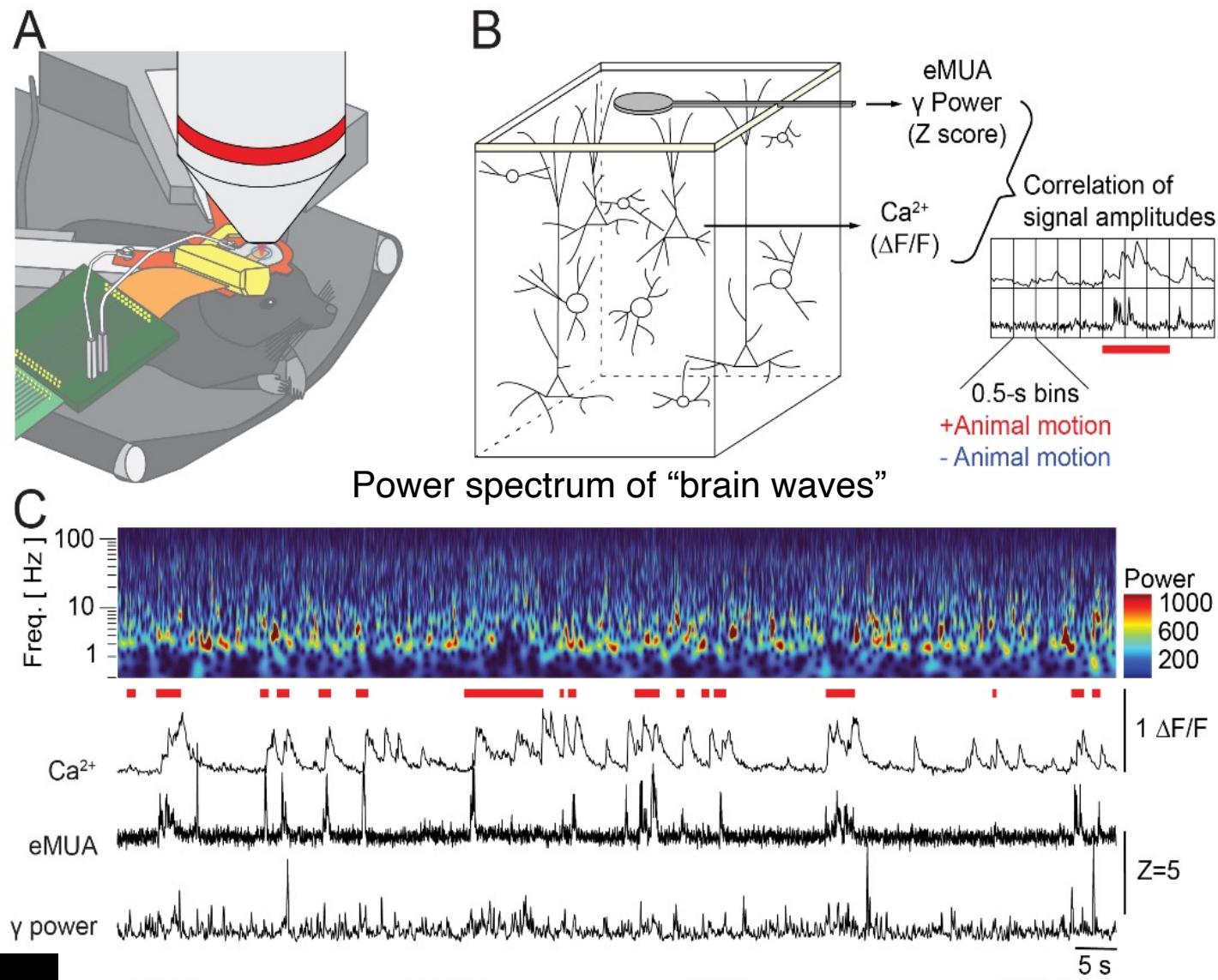
Lorraine
Hossain



Nick
Rogers



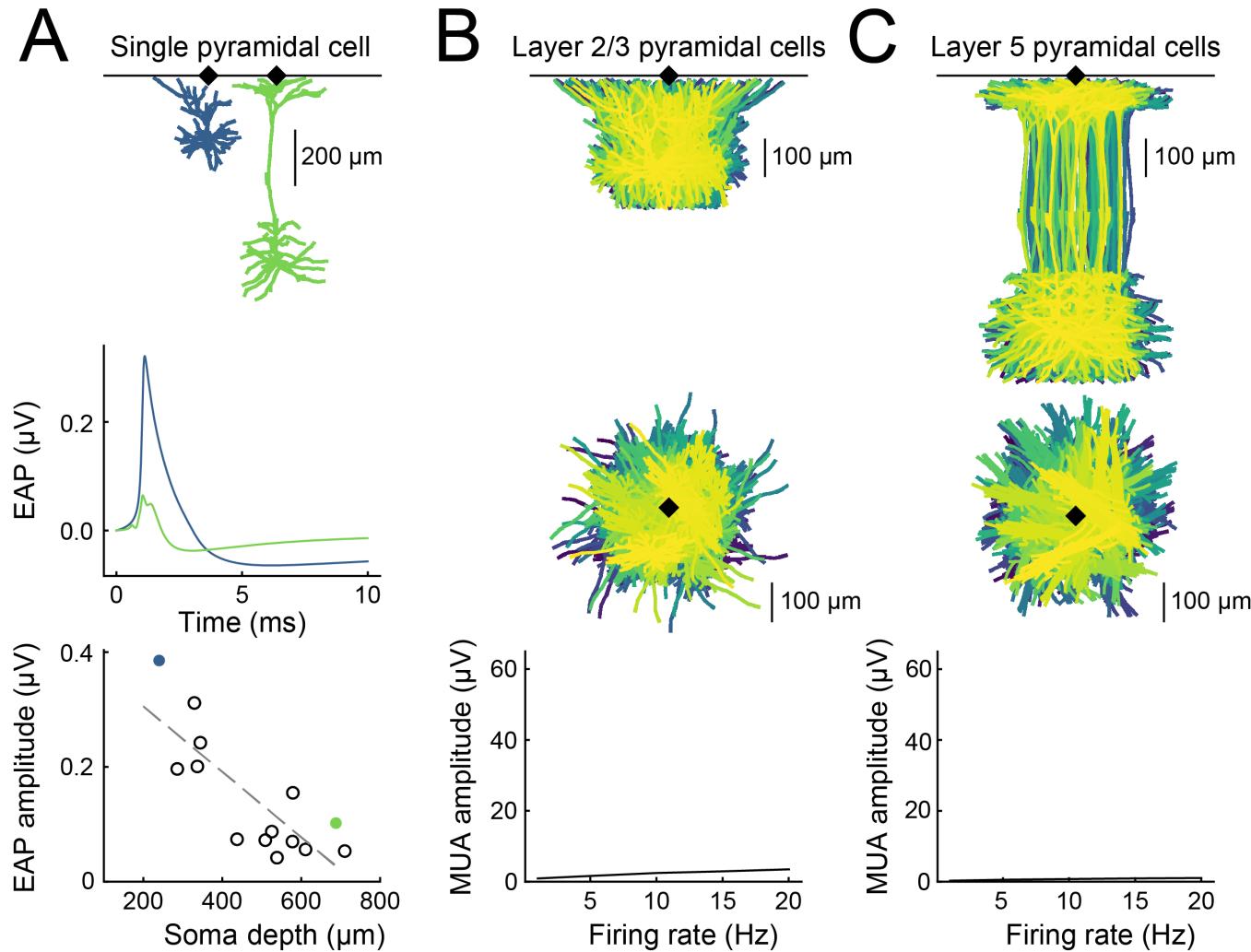
Kivilcim
KILIÇ



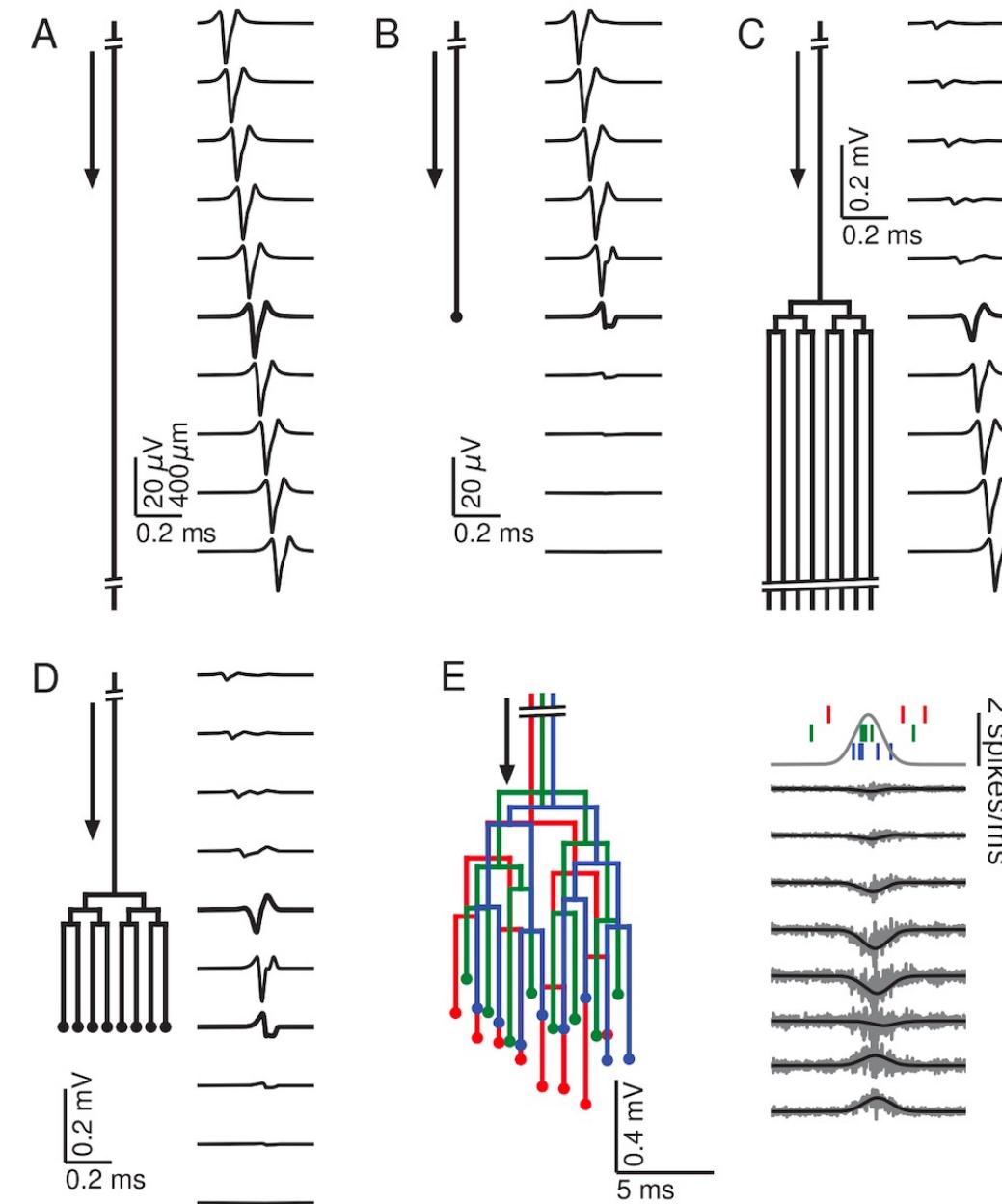


Torbjørn
Ness

What is the source of surface MUA?

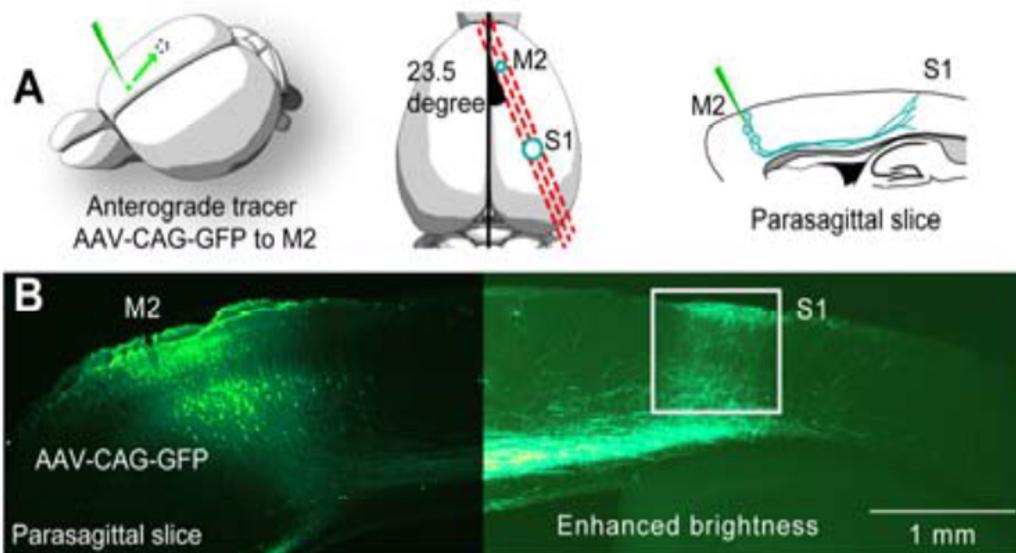


Bifurcating axons may give large EP signals



EP signals from ascending axons in S1

- Murayama (personal communication):
 - “Hindpaw stimulation to mice evokes two temporally distinct components, fast and late activity in S1. The late activity comes from M2 via top-down projection. Their axons reach to the bottom layer in S1 and then to L1, shown in Suppl.fig. S2B.”

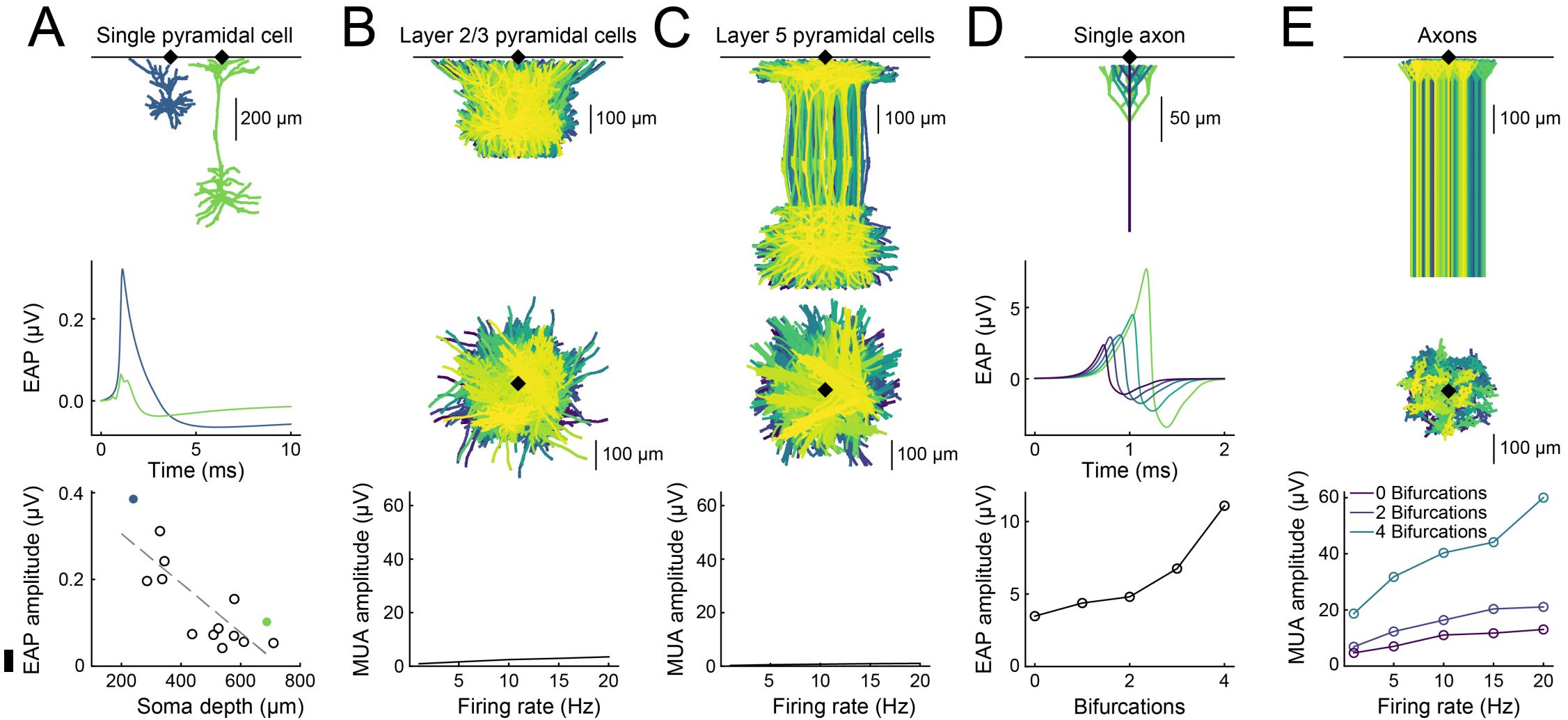


Manita et al, Neuron
(2015)

What is the source of surface MUA?

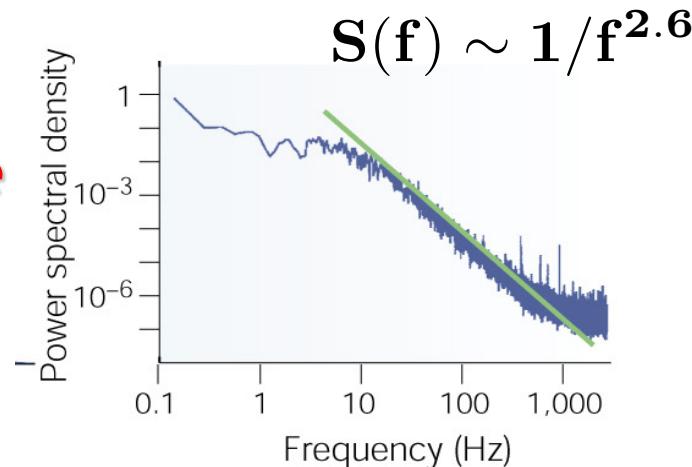


Torbjørn
Ness



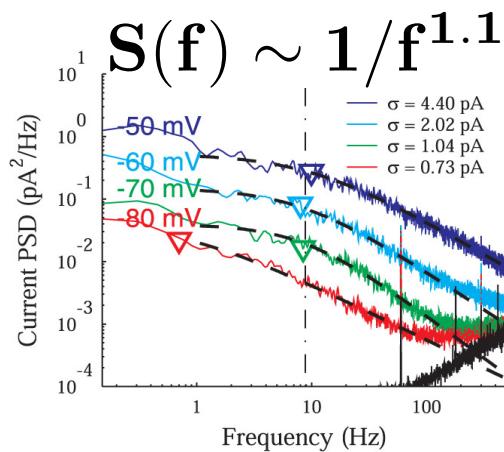
Power laws in electrical brain recordings

Soma
membrane
potential

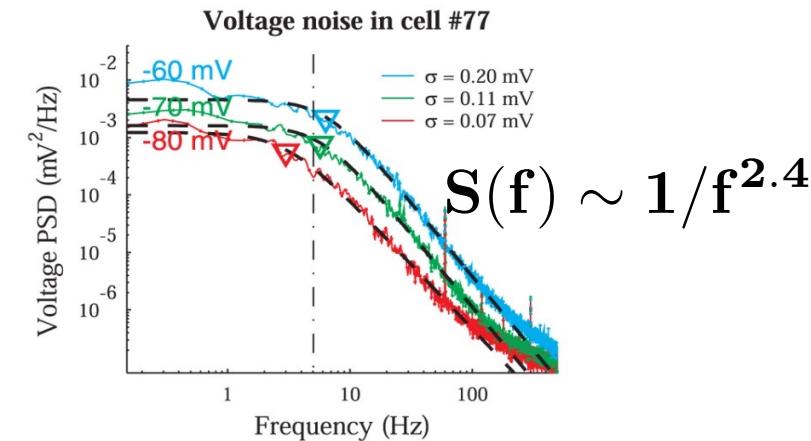


Destexhe et al., 2003

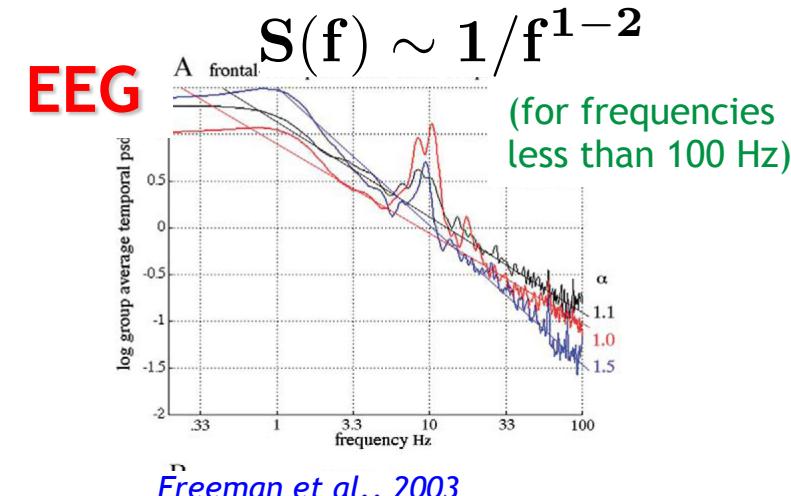
Soma
membrane
current



Diba et al. 2004

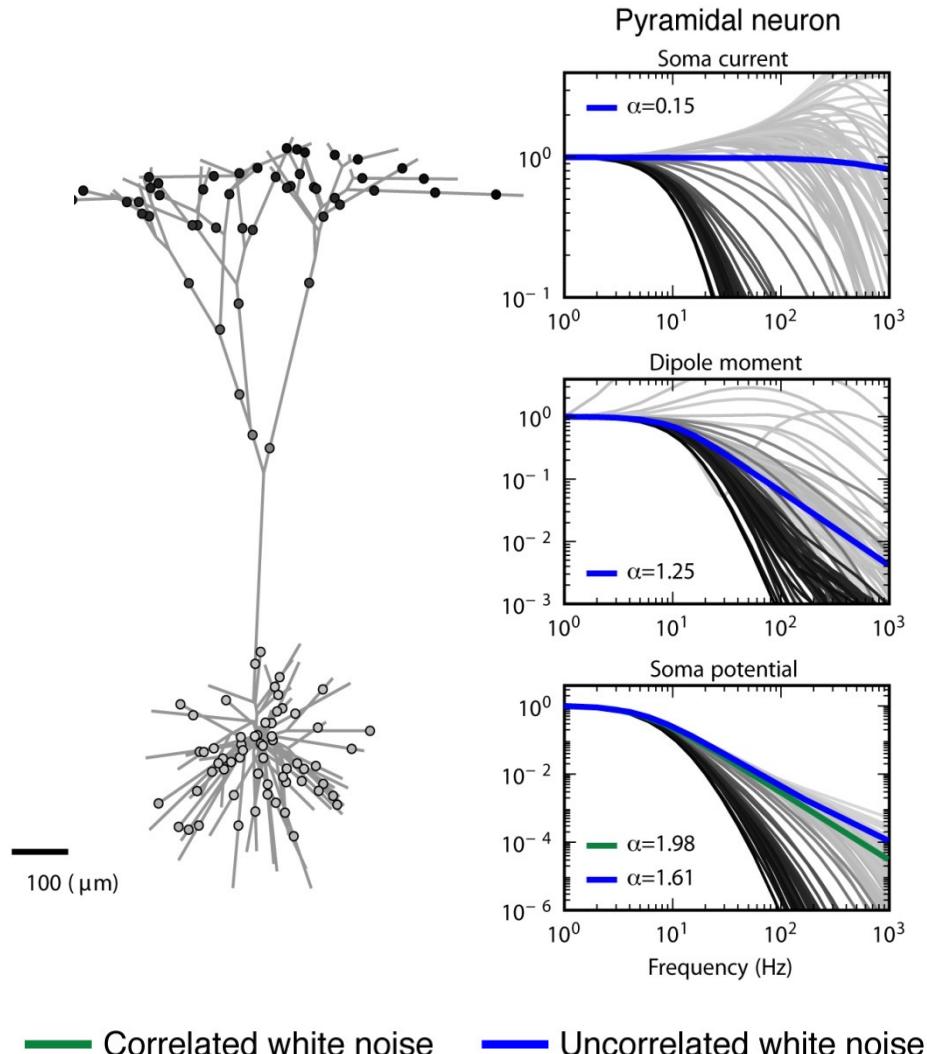


Diba et al. 2004



Power laws from cable equation with many evenly distributed membrane current inputs

- «White-noise» current injected at different positions on dendrites

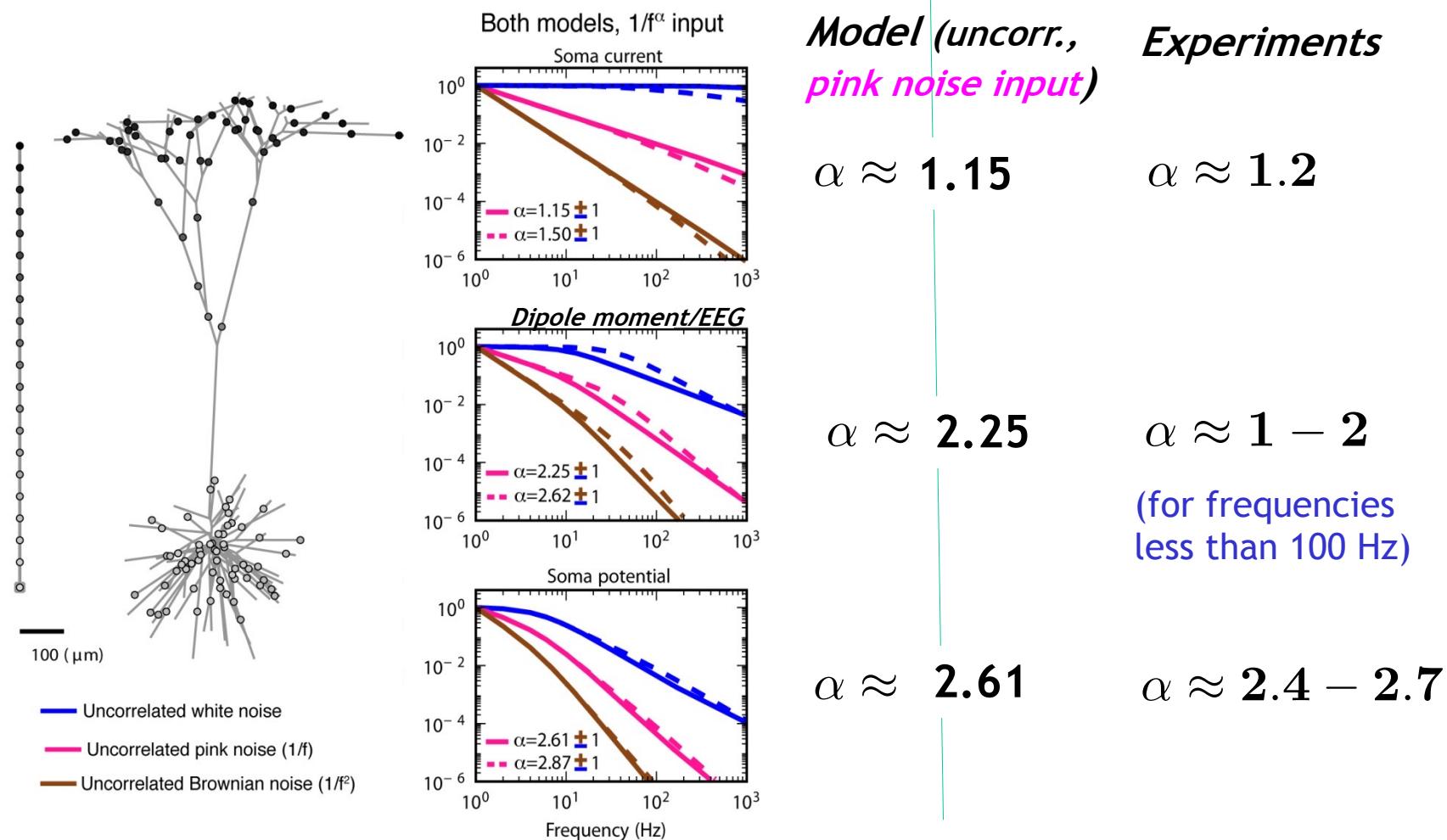


$$S(f) \sim 1/f^\alpha$$

(α is here
estimated at
1000 Hz)

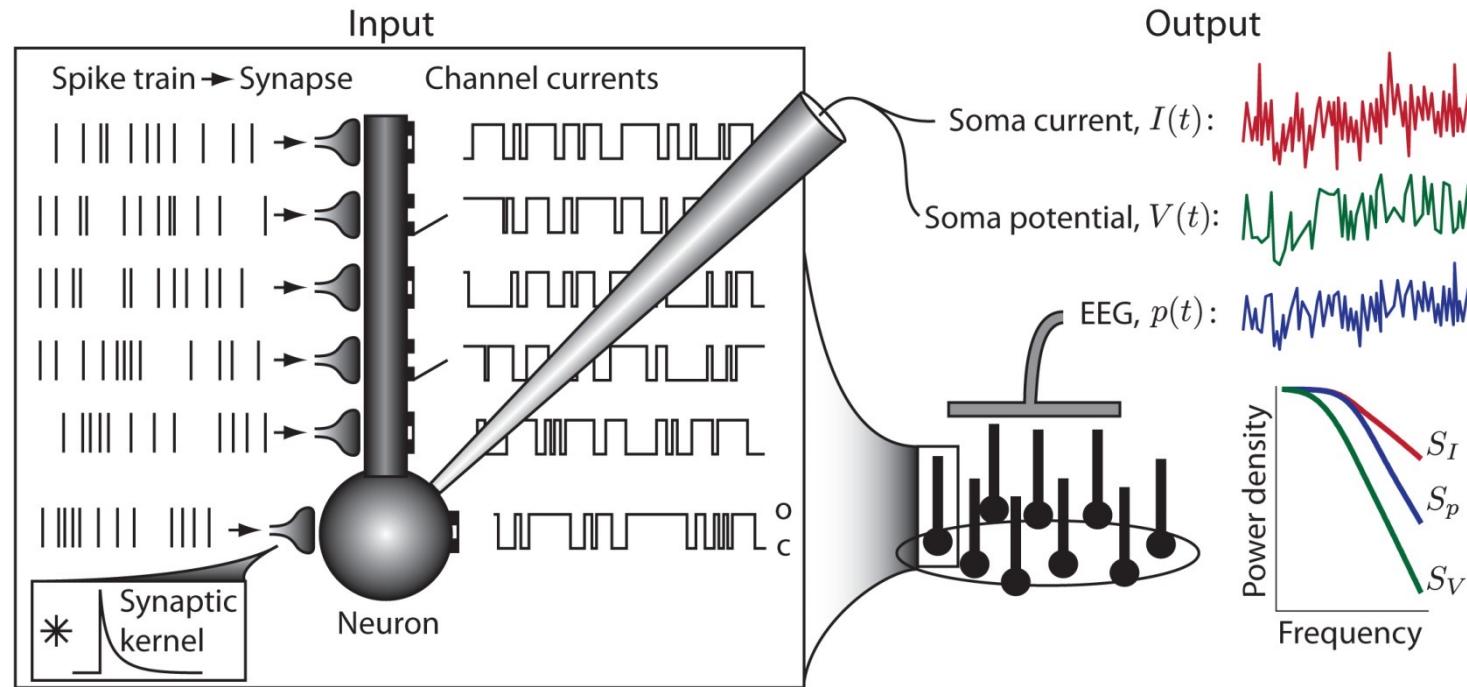
- Note: Power-law coefficients α vary between different measurements even with a common underlying noise source

Model power-law coefficients vs experiments

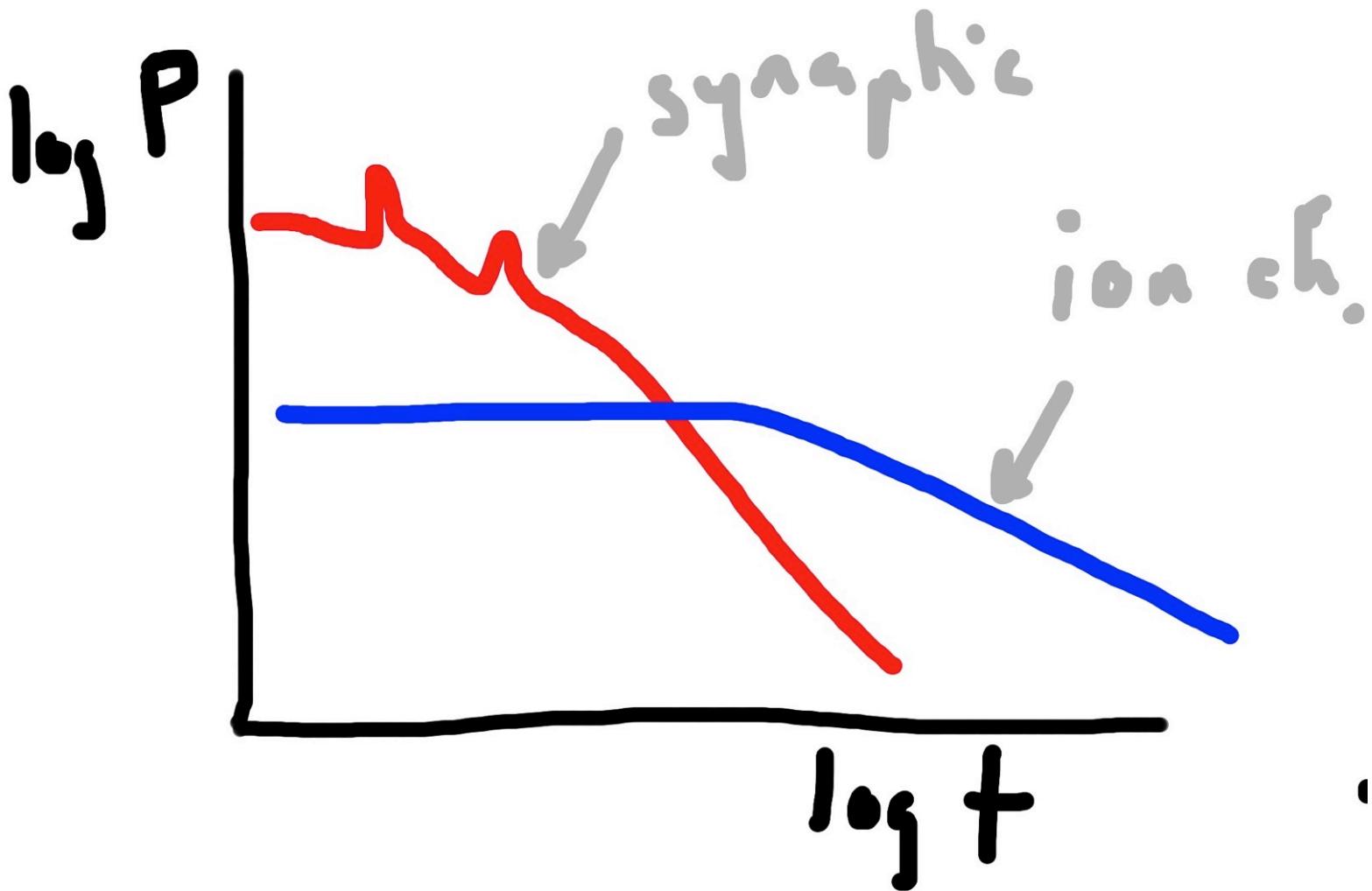


- Overall, model with (i) **uncorrelated**, (ii) **evenly distributed** input currents each with (iii) a **pink-noise ($1/f$) characteristic** seem to be compatible with experiments

Biophysical origin of current noise underlying power laws

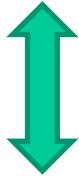


- Experiments support model with (i) **uncorrelated**, (ii) **evenly distributed** input currents with (iii) a **pink-noise ($1/f$)** spectra
- Conjecture: Intrinsic potassium ion channels dominate power-law part of spectra as
 1. potassium channels with $1/f$ spectra have been seen, and
 2. synaptic noise would give larger power-law coefficients



Models for image recognition in mouse

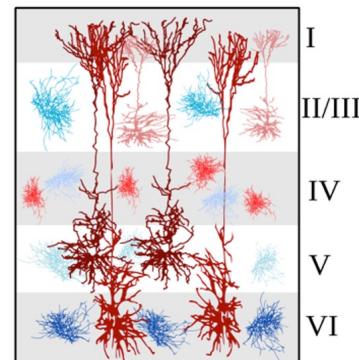
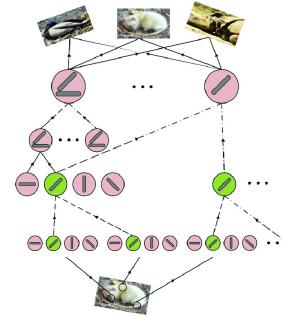
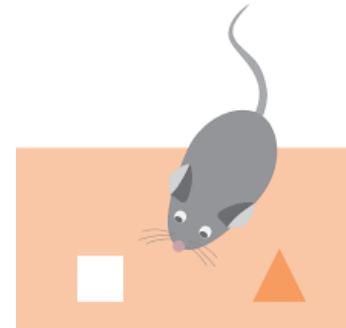
COMPUTATIONAL



ALGORITHMIC



PHYSICAL

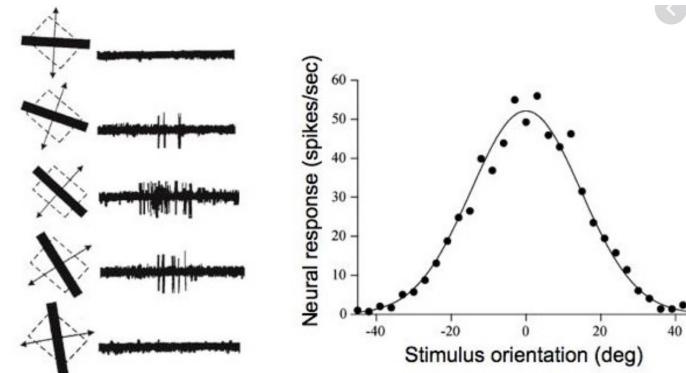


Analysis of *in vivo* experiments

- Until now: Focus mainly on neural representations

- Receptive fields in primary visual cortex

- simple/complex cells
- orientation-selective cells
- direction-selective cells
- end-stopping cells
-



Hubel & Wiesel (1960s)

Mini-Symposium

Journal of Neuroscience, 2005

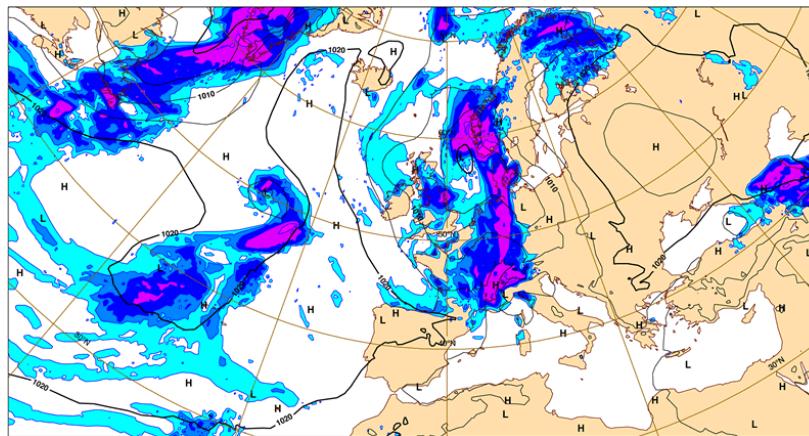
Do We Know What the Early Visual System Does?

Matteo Carandini,¹ Jonathan B. Demb,² Valerio Mante,¹ David J. Tolhurst,³ Yang Dan,⁴ Bruno A. Olshausen,⁶ Jack L. Gallant,^{5,6} and Nicole C. Rust⁷

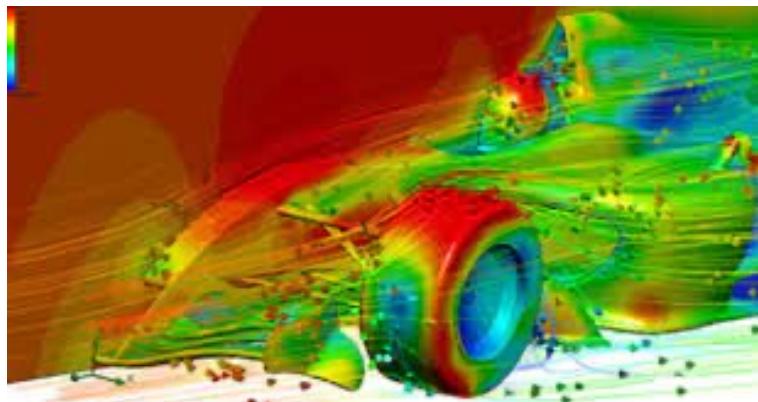
First line of abstract: *We can claim that we know what the visual system does once we can predict neural responses to arbitrary stimuli, including those seen in nature.*

Multipurpose model

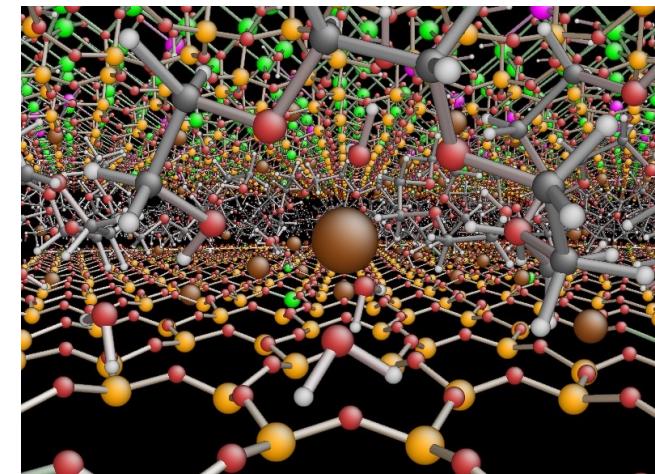
Multipurpose modeling in natural sciences



Weather forecasting



Fluid dynamics

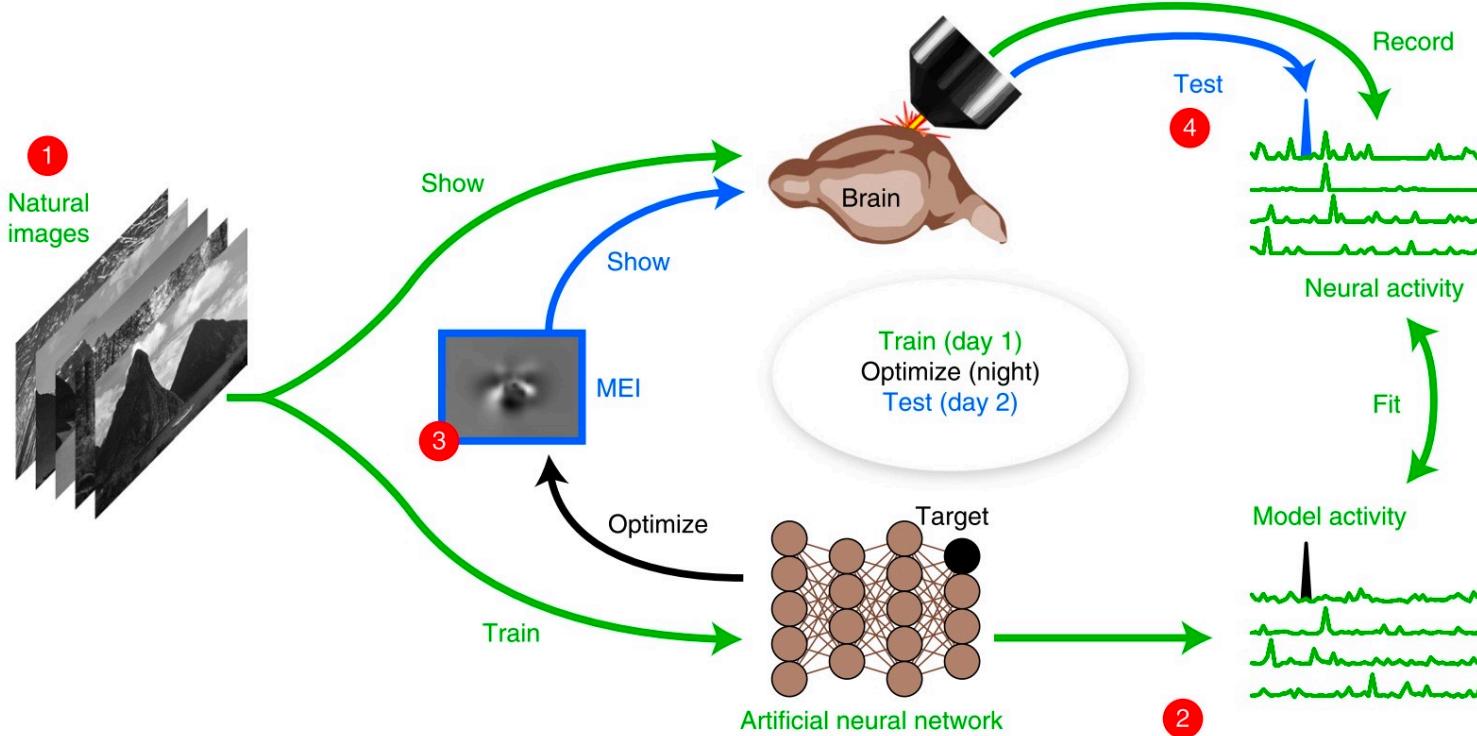


Material science

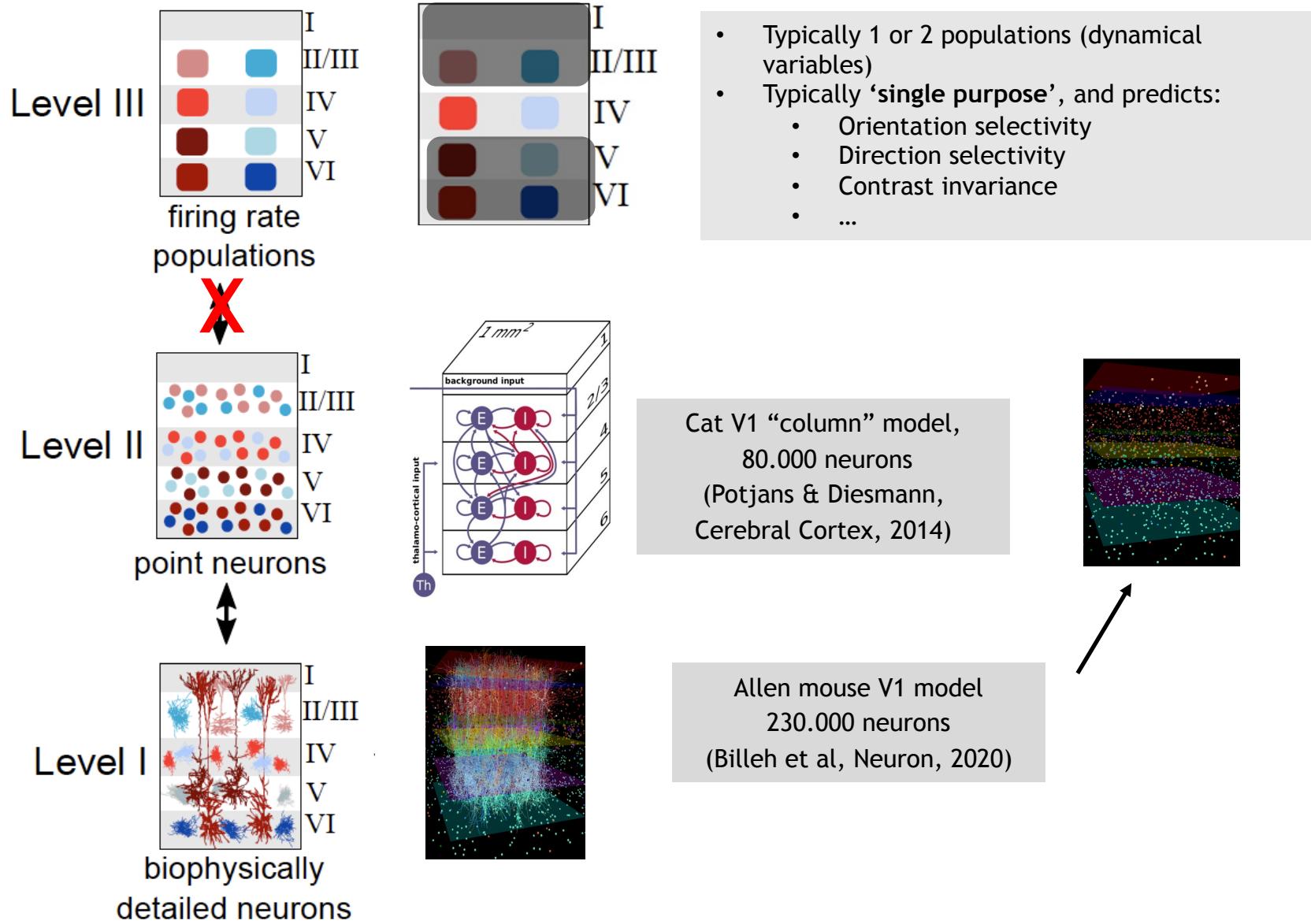
Towards multipurpose descriptive models

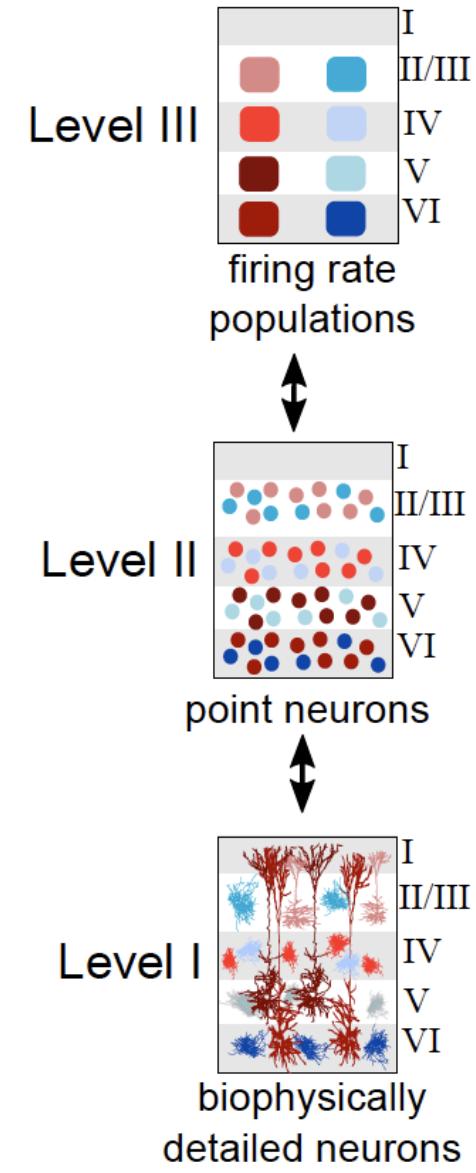
Inception loops discover what excites neurons most using deep predictive models

Edgar Y. Walker  ^{1,2,8*}, Fabian H. Sinz  ^{1,2,3,4,8*}, Erick Cobos^{1,2}, Taliah Muhammad^{1,2}, Emmanouil Froudarakis  ^{1,2}, Paul G. Fahey^{1,2}, Alexander S. Ecker  ^{1,3,5,6}, Jacob Reimer^{1,2}, Xaq Pitkow  ^{1,2,7} and Andreas S. Tolias  ^{1,2,7*}



Mechanistic modeling of primary visual cortex

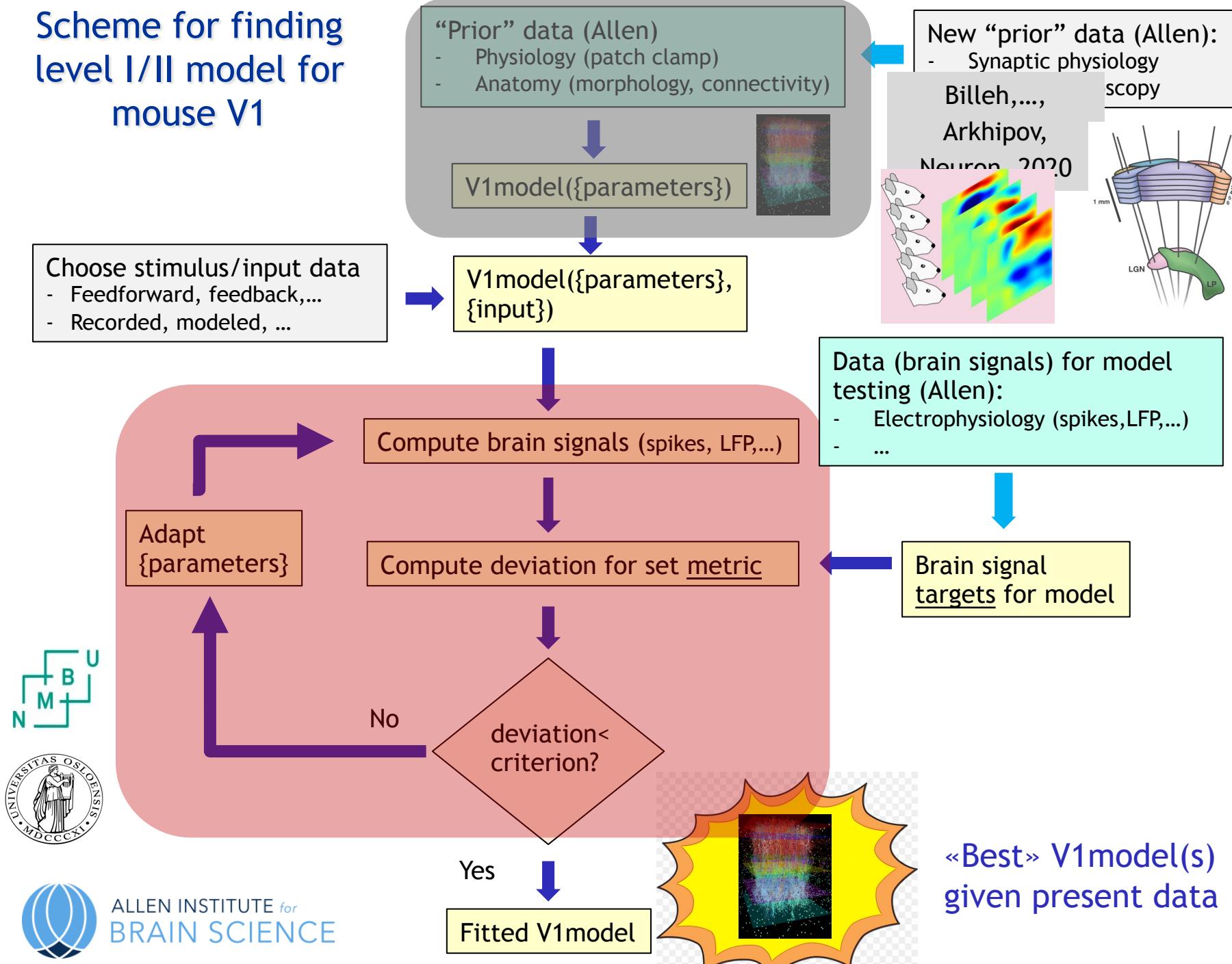




Multipurpose mechanistic modeling of primary visual cortex

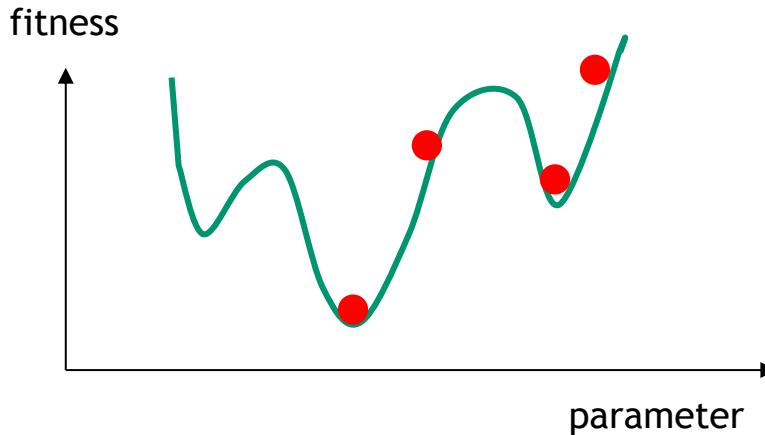
- Models that simultaneously can predict experimental data
 - for different **visual stimuli**
 - for different **measurement types**
 - for different **brain states**
- Multipurpose models
 - must likely be **high-dimensional** (like real brains)
 - should be reducible to several single-purpose **low-dimensional** models

Scheme for finding level I/II model for mouse V1



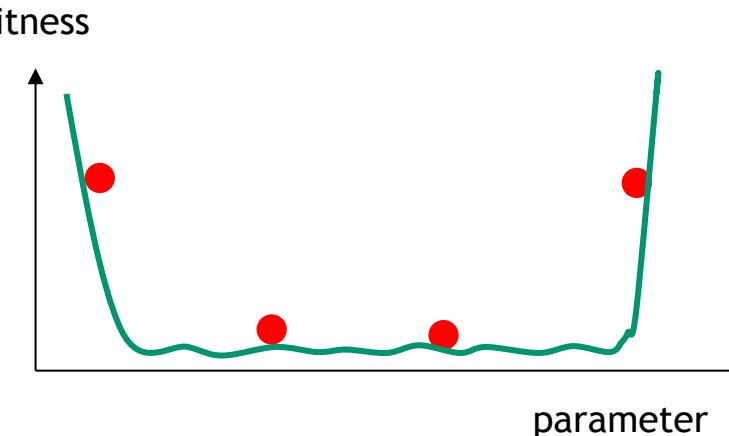
Model fitting (``adapt parameters``)

- Models with few parameters

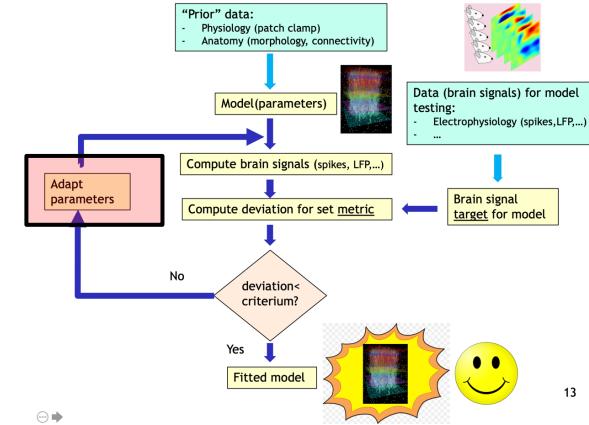


- Unique optimal model
- Gets easily stuck in local minima during fitting

- Models with many parameters (like V1 circuit)

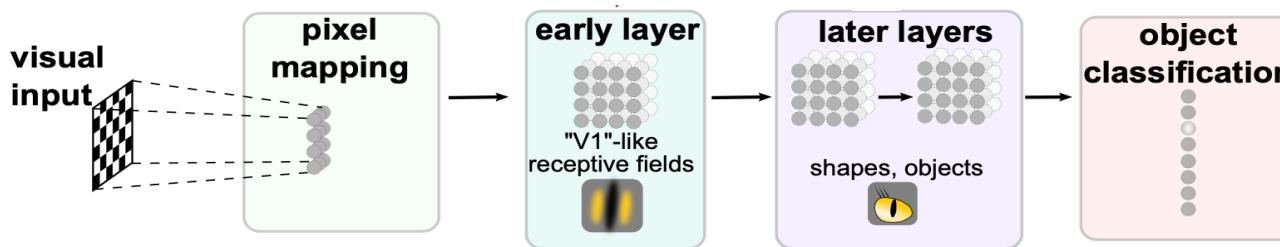


- Many ``optimal`` models
- Not easily stuck in local minima during fitting

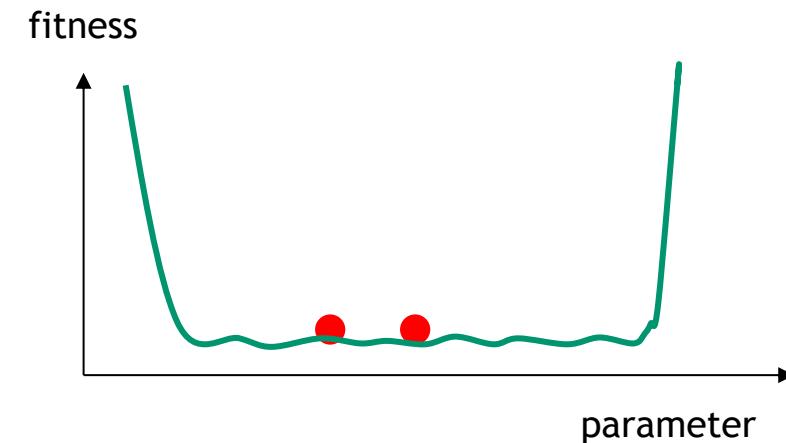


13

Why are «deep networks» working so well?



- Two identical CNNs (Convolutional Neural Networks) trained on the same images:
 - similar performance, but
 - trained parameters (weights) are different



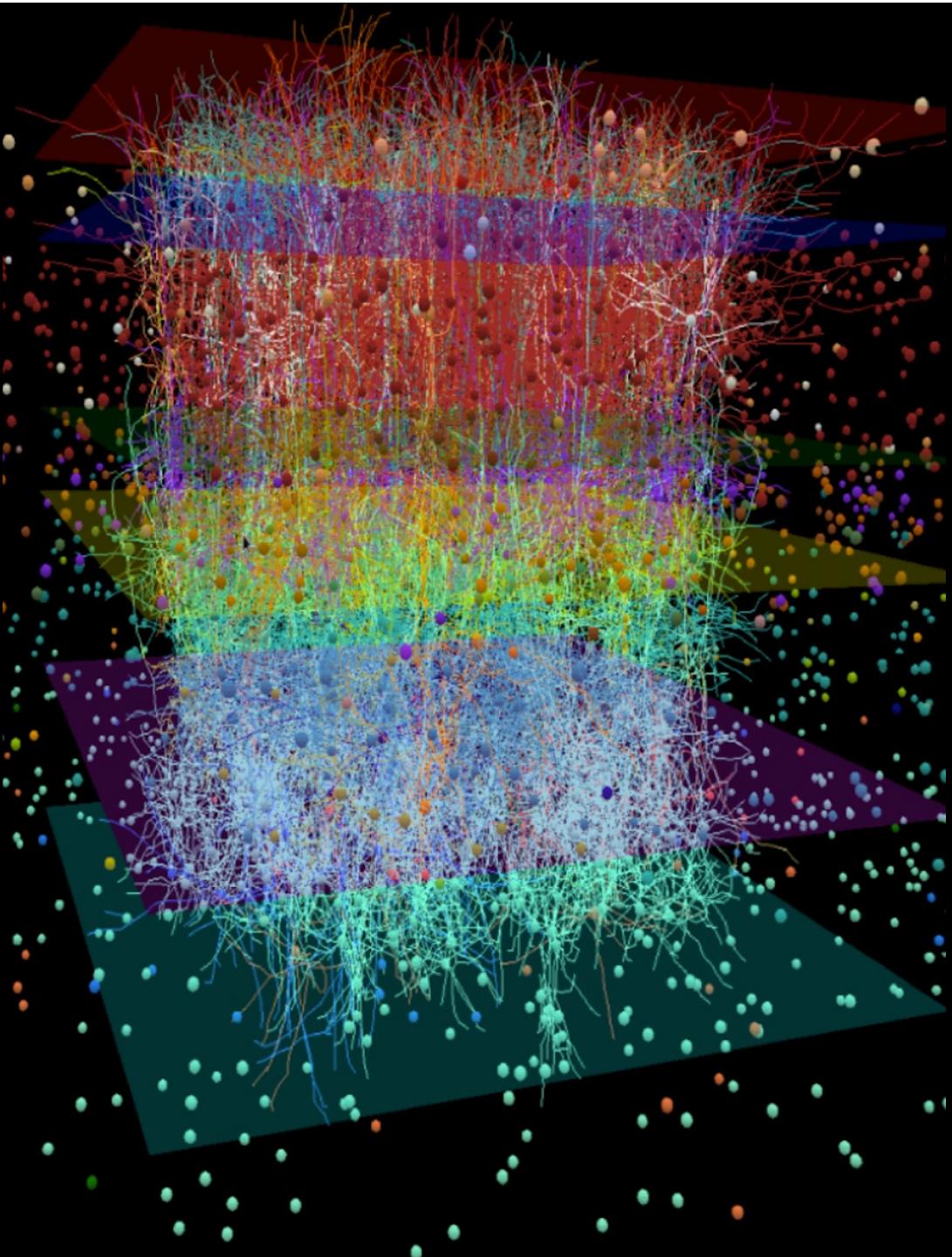
T. Sejnowski: *The Unreasonable Effectiveness of Deep Learning in Artificial Intelligence*, PNAS (2020)

Episode #2 in podcast «Sense and Science»: On AI and the underlying algorithms - with Terrence Sejnowski



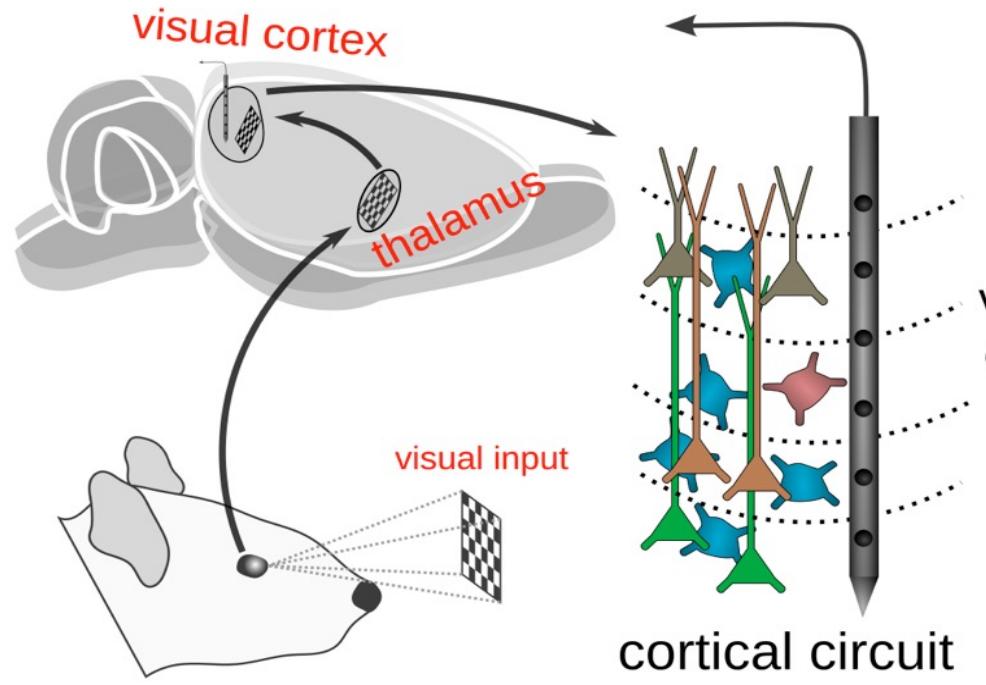
Allen model of mouse primary visual cortex

- 250000 neurons (52000 biophysically detailed)
- 21 neuron types

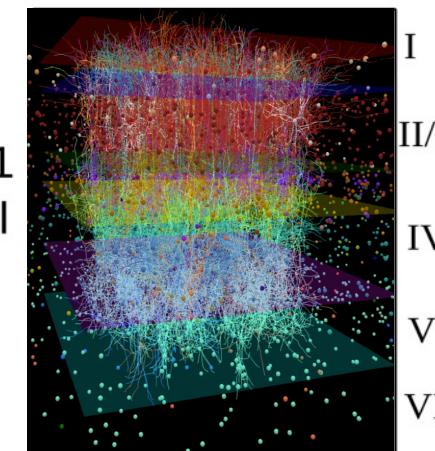


Billeh et al,
Neuron (2020)

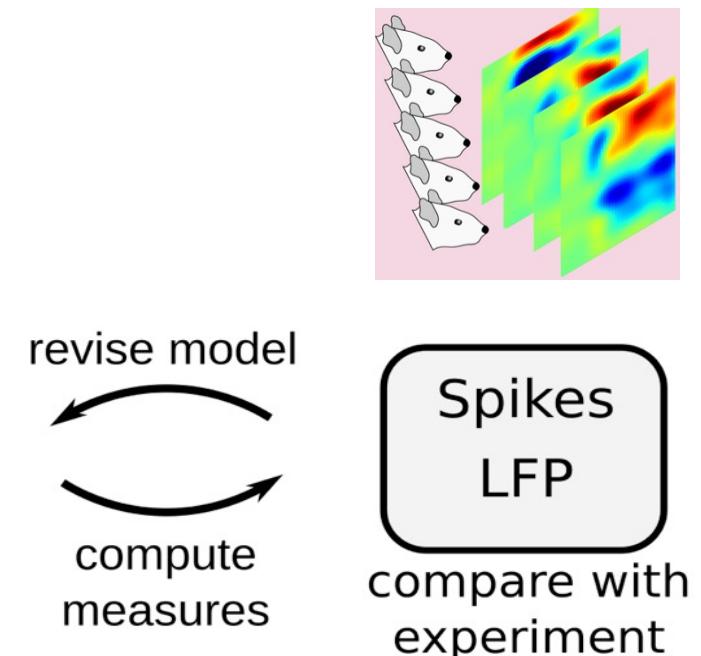
Collaborative research project



Allen V1 model



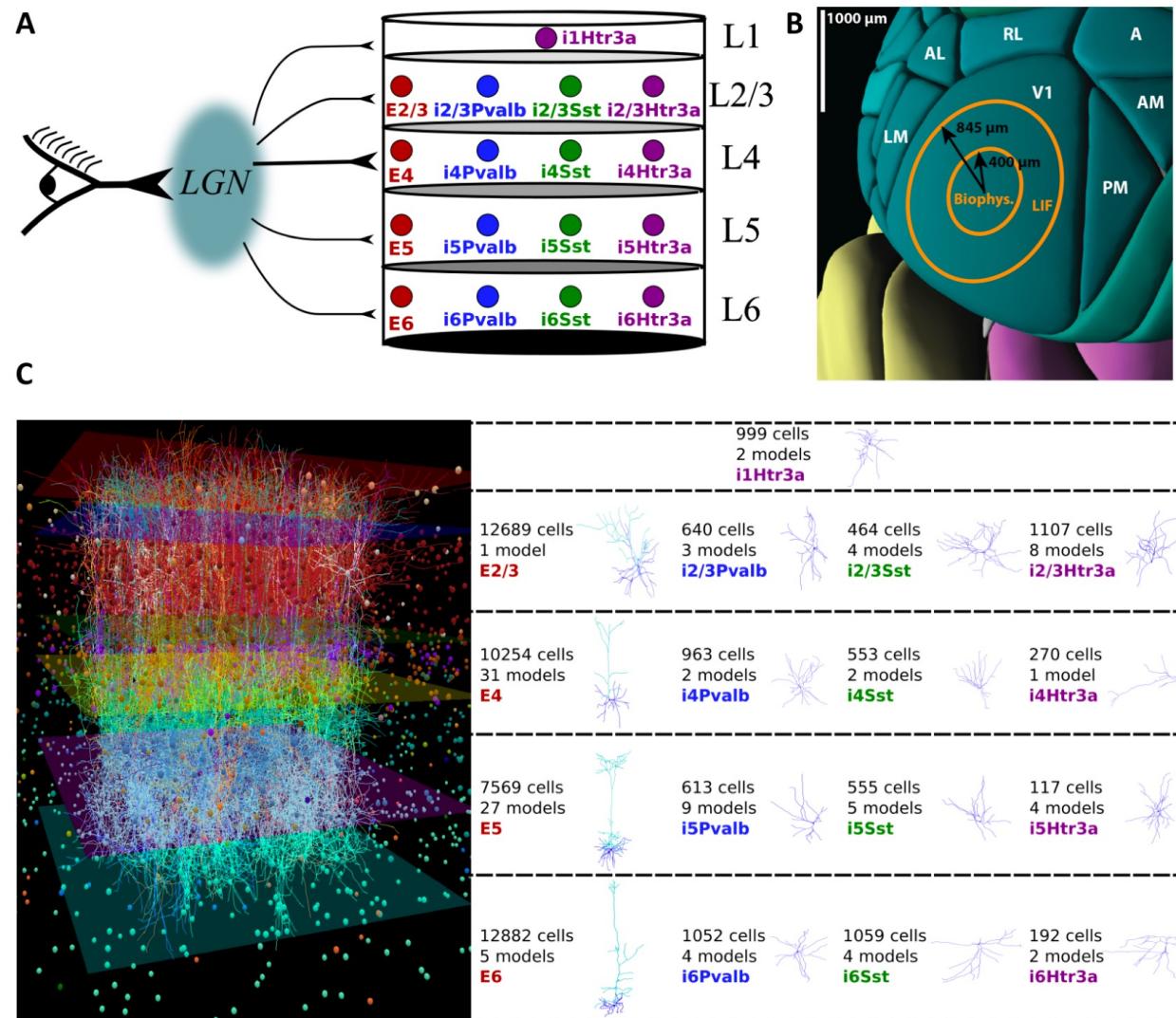
230.000 neurons
[Billeh et al, 2020]



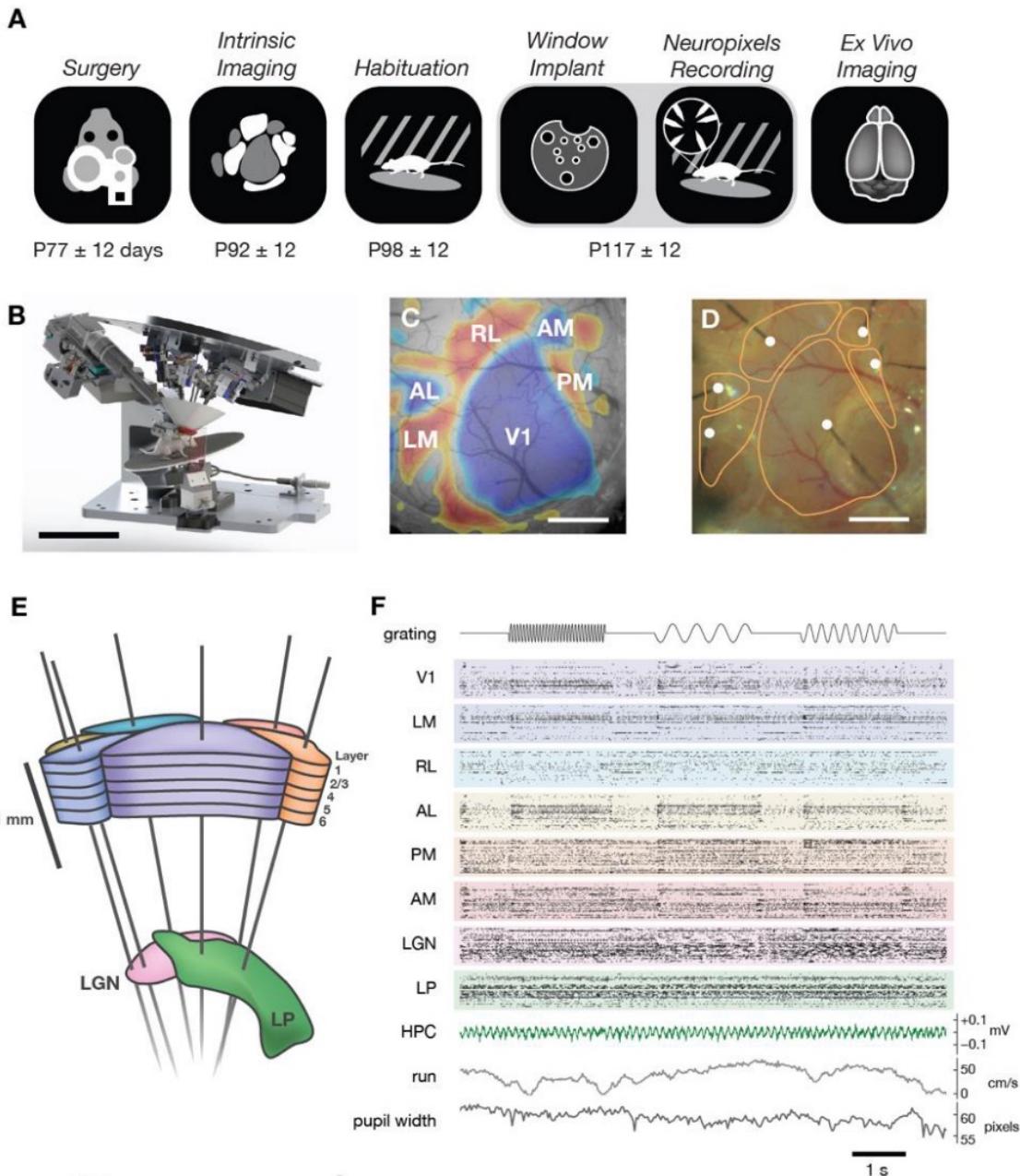
ALLEN INSTITUTE *for*
BRAIN SCIENCE

*Collaboration with groups of Anton Arkhipov, Stefan Mihalas
and Christof Koch at Allen Institute for Brain Science in Seattle*

Model

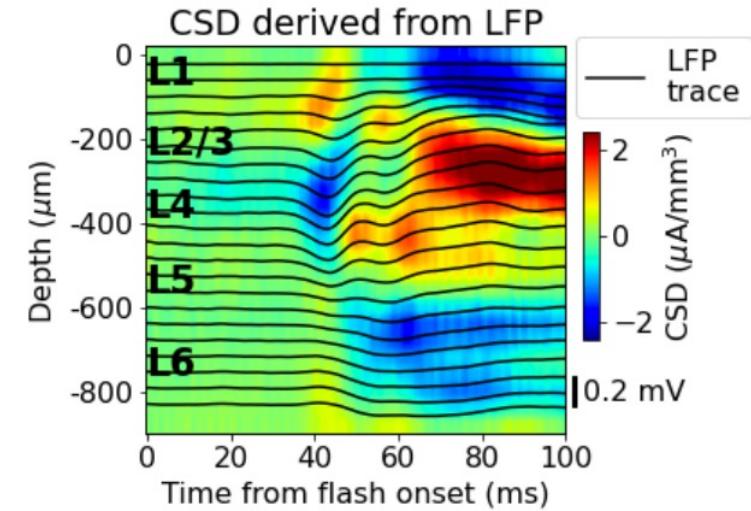
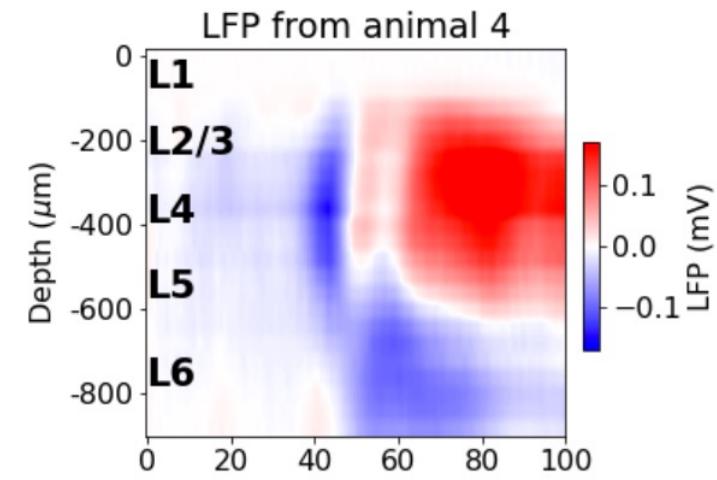
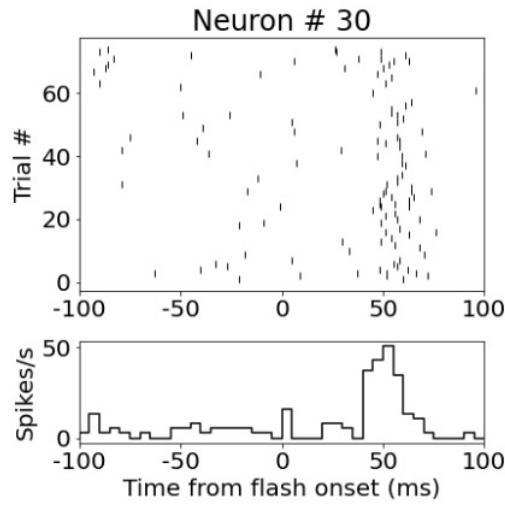
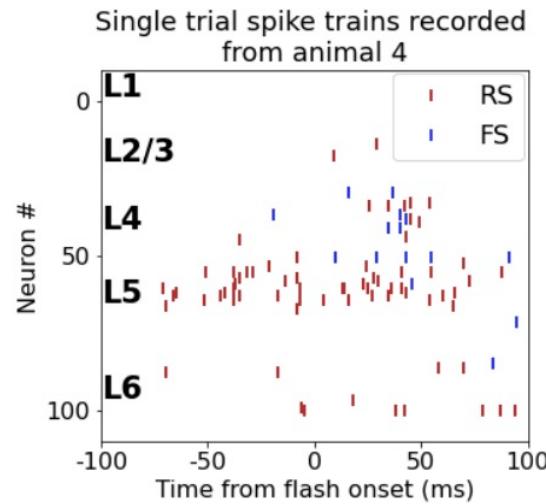


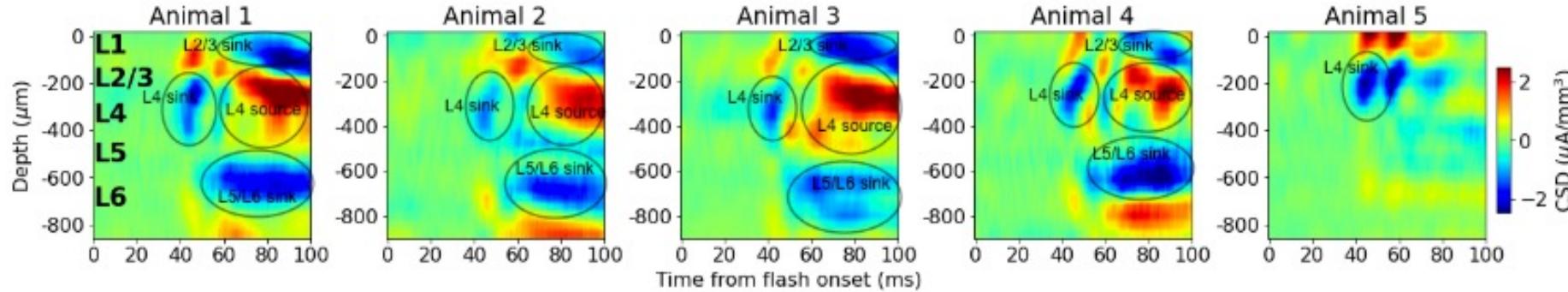
Neuropixel experiments



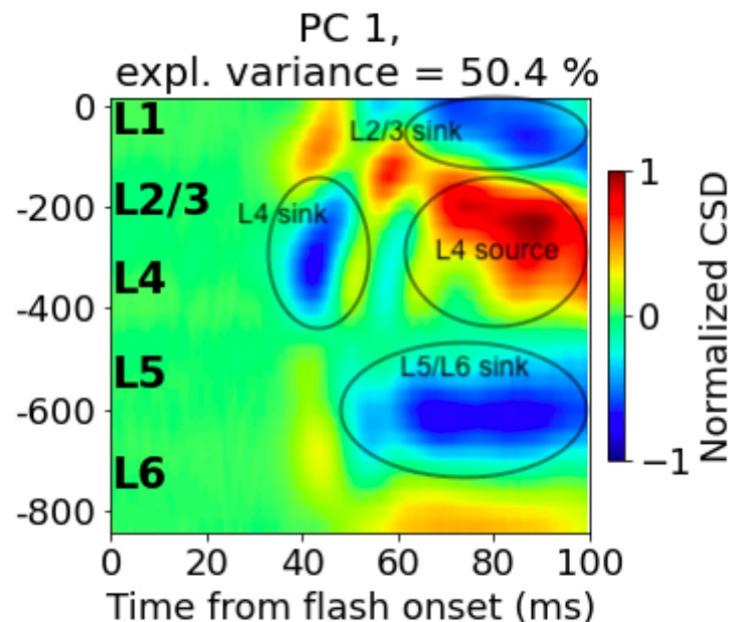
Siegle et al,
Nature, 2021

Neuropixel experiments

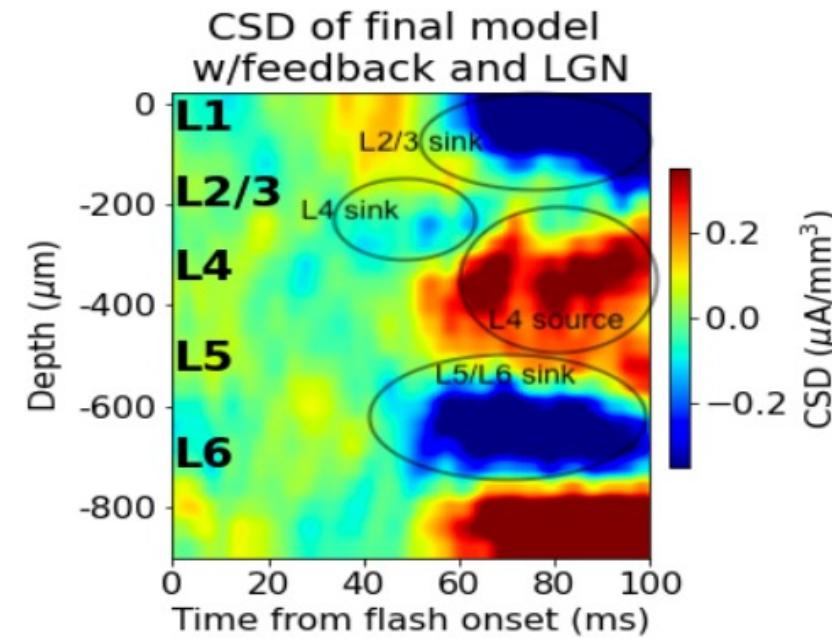




Experiment (animal average)



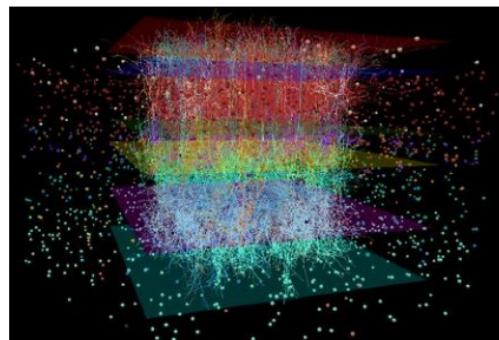
Model



Virtual workshops: «Towards multipurpose network models ...»



Anton Arkhipov



ALLEN INSTITUTE **MODELING WORKSHOP**

Towards multipurpose models of cortical circuits

Starting with the work of Hodgkin, Huxley, Cole, Rall, Katz, Eccles and others in the 1950s and 1960s, we now have a reasonably good understanding of the principles by

08/12/2020
to
08/14/2020

Bio-realistic model of the mouse primary visual cortex
Neuropixels probe for electrophysiology recordings
Image made with VND

>>>>>>>> Free online workshop

TOWARDS MULTIPURPOSE NEURAL NETWORK MODELS II:
MODEL TESTING AND MODEL FITTING

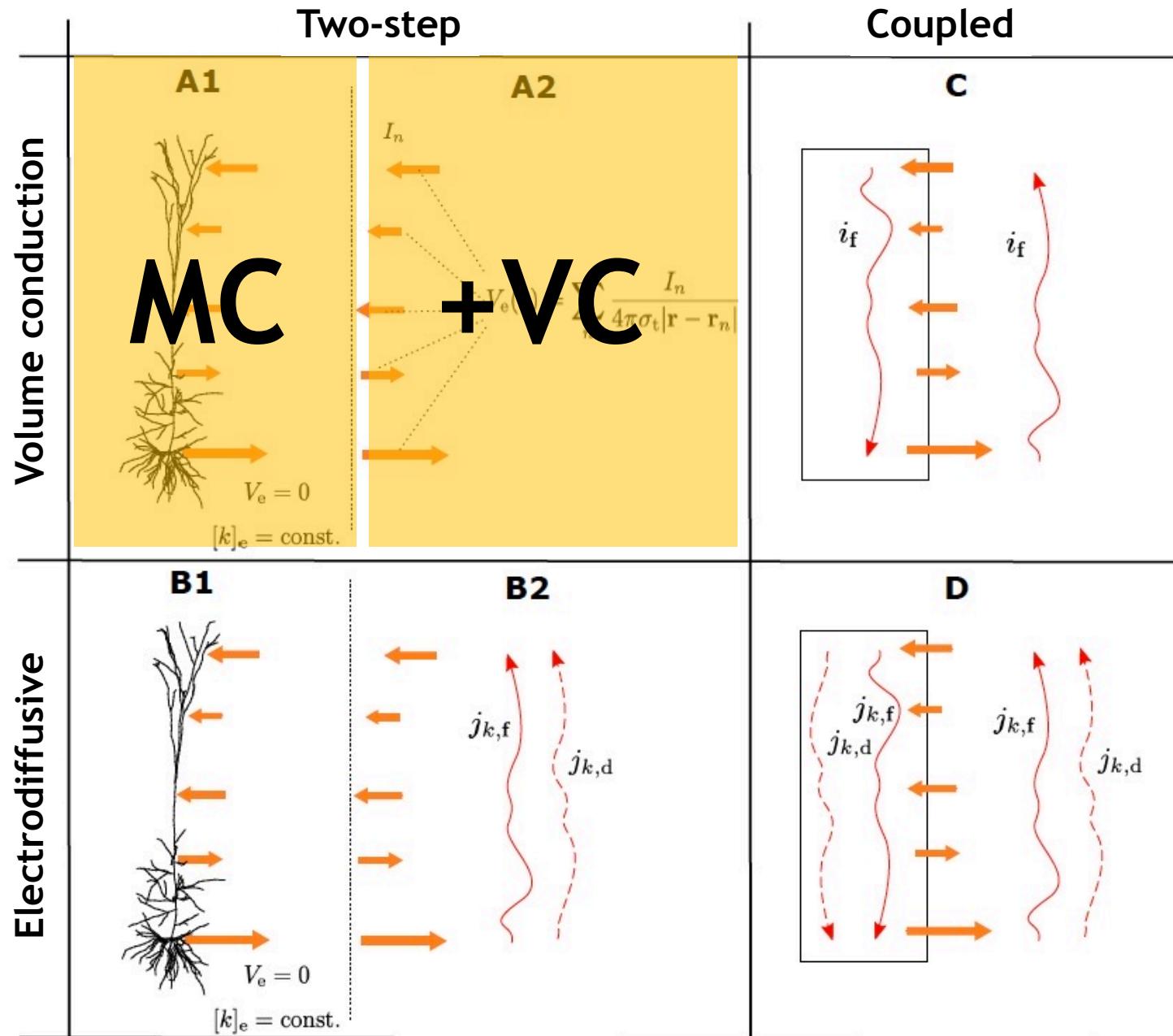
Organized by:
Anton Arkhipov
(Allen Institute, Seattle)
Gaute Einevoll
(NMBU/University of Oslo)

29 SEP 21 · 01 OCT 21
5PM · 9:15PM CET

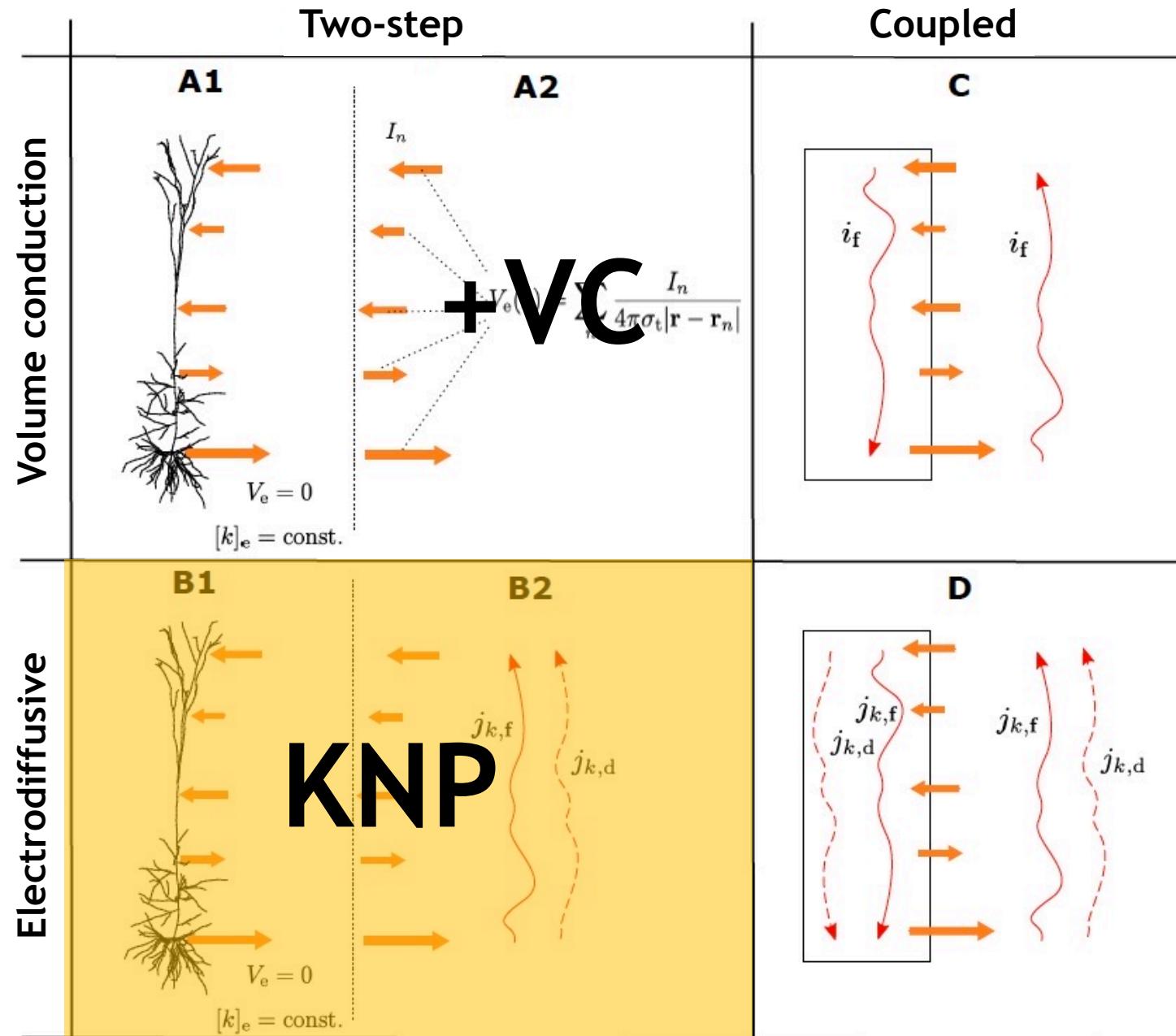
<<<<<<<< INFO AT EITN.ORG

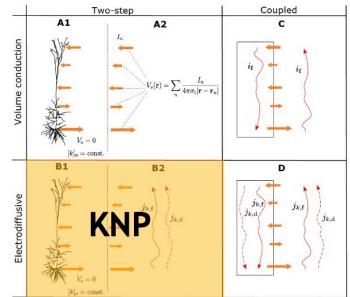
eITN Human Brain Project CNRS NeuroPSI université PARIS-SACLAY ALLEN INSTITUTE U N M B E L U Norwegian University of Life Sciences UiO University of Oslo

Differents schemes for modelling of electric dynamics in brain tissue



Different schemes for modelling of electric dynamics in brain tissue





RESEARCH ARTICLE

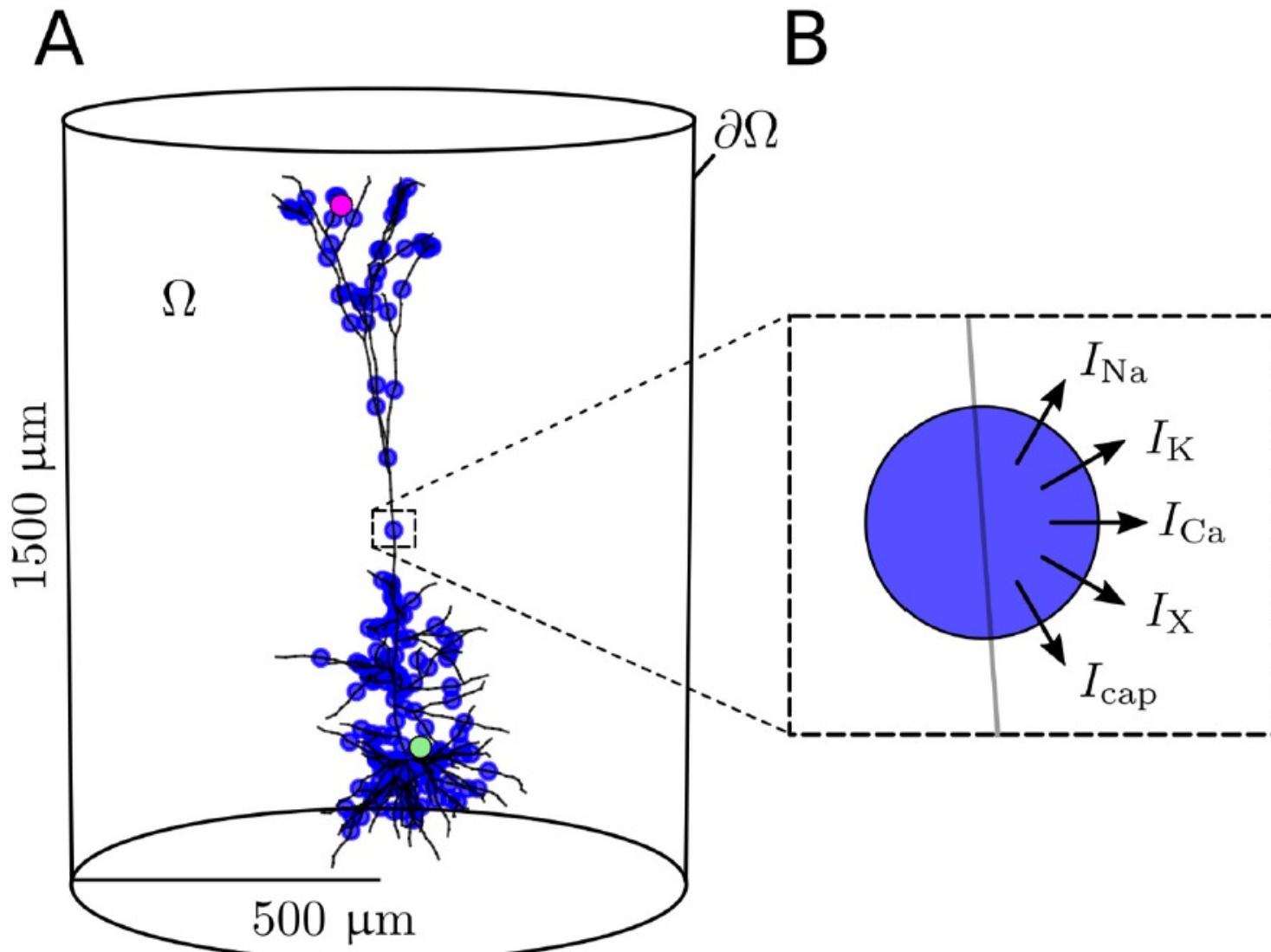
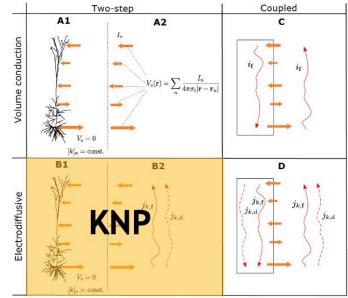
A Kirchhoff-Nernst-Planck framework for modeling large scale extracellular electrodiffusion surrounding morphologically detailed neurons

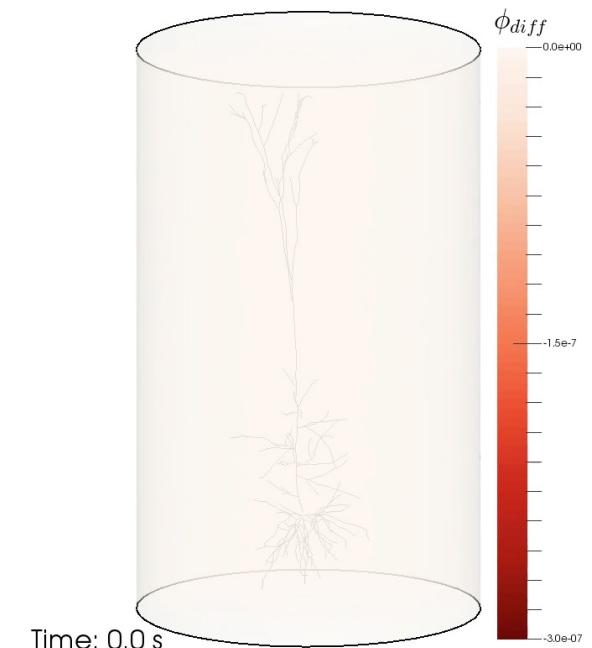
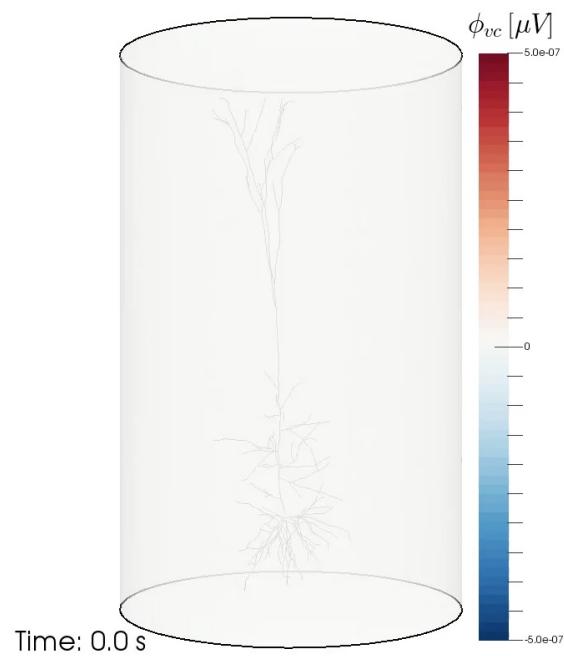
Andreas Solbrå  ^{1,2}, **Aslak Wigdahl Bergersen** ³, **Jonas van den Brink** ³,
Anders Malthe-Sørensen  ^{1,2}, **Gaute T. Einevoll**  ^{1,2,4}, **Geir Halnes**  ^{4*}

1 Center for Integrative Neuroplasticity, University of Oslo, Oslo, Norway, **2** Department of Physics, University of Oslo, Oslo, Norway, **3** Simula Research Laboratory, Fornebu, Norway, **4** Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Ås, Norway

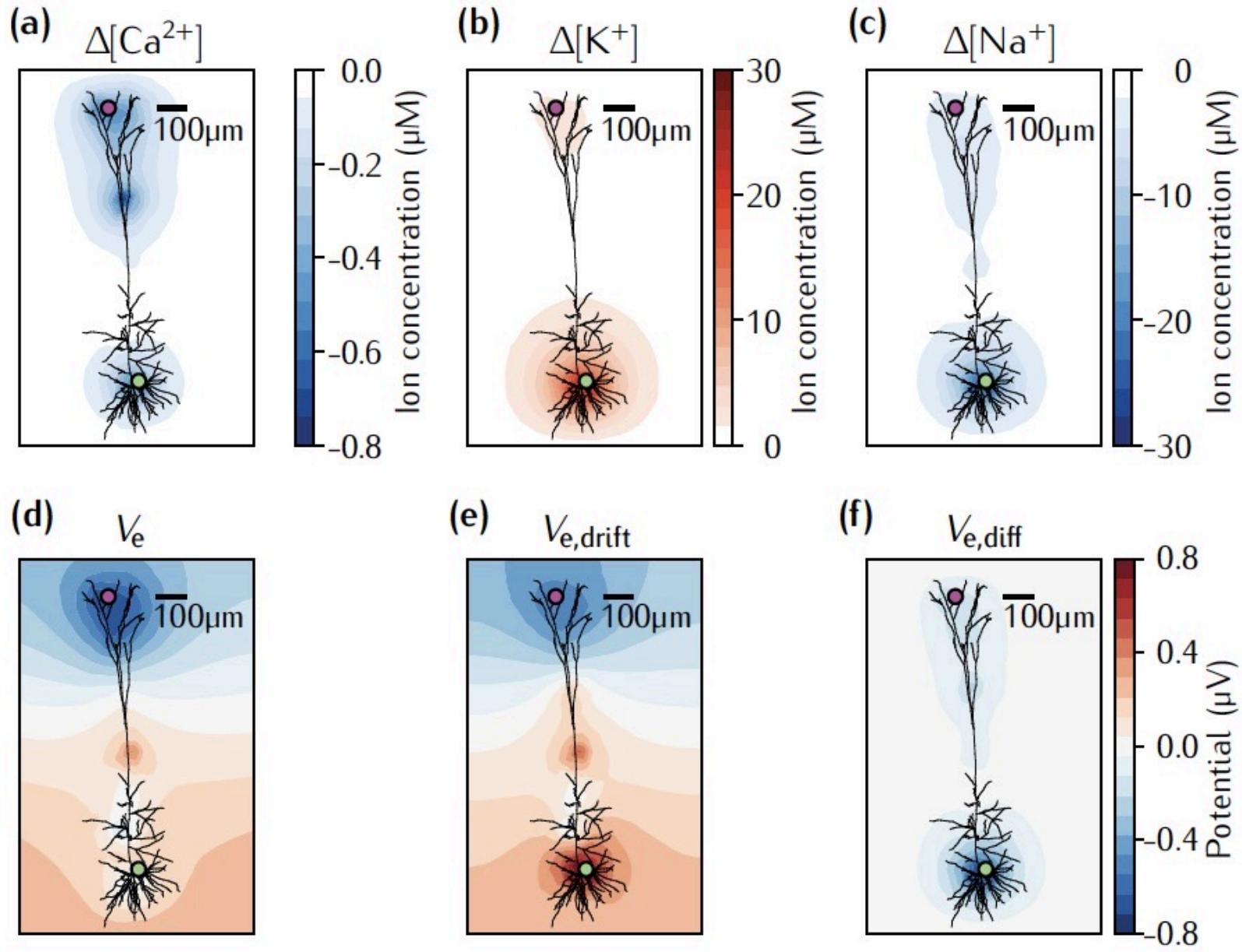
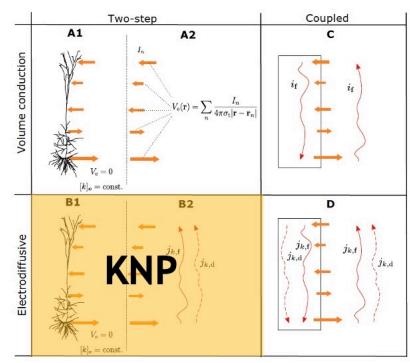
* geir.halnes@nmbu.no







The simulation was performed on standard desktop computer in 15 hours.



Electrodifusive Model for Astrocytic and Neuronal Ion Concentration Dynamics

Geir Halnes^{1*}, Ivar Østby¹, Klas H. Pettersen², Stig W. Omholt³, Gaute T. Einevoll¹

1 Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Ås, Norway, **2** Centre for Integrative Genetics, Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Ås, Norway, **3** Centre for Integrative Genetics, Department of Animal and Aquacultural Sciences, Norwegian University of Life Sciences, Ås, Norway

Abstract

The cable equation is a proper framework for modeling electrical neural signalling that takes place at a timescale at which the ionic concentrations vary little. However, in neural tissue there are also key dynamic processes that occur at longer timescales. For example, endured periods of intense neural signaling may cause the local extracellular K^+ -concentration to increase by several millimolars. The clearance of this excess K^+ depends partly on diffusion in the extracellular space, partly on local uptake by astrocytes, and partly on intracellular transport (spatial buffering) within astrocytes. These processes, that take place at the time scale of seconds, demand a mathematical description able to account for the spatiotemporal variations in ion concentrations as well as the subsequent effects of these variations on the membrane potential. Here, we present a general electrodifusive formalism for modeling of ion concentration dynamics in a one-dimensional geometry, including both the intra- and extracellular domains. Based on the Nernst-Planck equations, this formalism ensures that the membrane potential and ion concentrations are in consistency, it ensures global particle/charge conservation and it accounts for diffusion and concentration dependent variations in resistivity. We apply the formalism to a model of astrocytes exchanging ions with the extracellular space. The simulations show that K^+ -removal from high-concentration regions is driven by a local depolarization of the astrocyte membrane, which concertedly (i) increases the local astrocytic uptake of K^+ , (ii) suppresses extracellular transport of K^+ , (iii) increases axial transport of K^+ within astrocytes, and (iv) facilitates astrocytic release of K^+ in regions where the extracellular concentration is low. Together, these mechanisms seem to provide a robust regulatory scheme for shielding the extracellular space from excess K^+ .

Citation: Halnes G, Østby I, Pettersen KH, Omholt SW, Einevoll GT (2013) Electrodifusive Model for Astrocytic and Neuronal Ion Concentration Dynamics. PLoS Comput Biol 9(12): e1003386. doi:10.1371/journal.pcbi.1003386

Editor: Olaf Sporns, Indiana University, United States of America

Received April 24, 2013; **Accepted** October 24, 2013; **Published** December 19, 2013

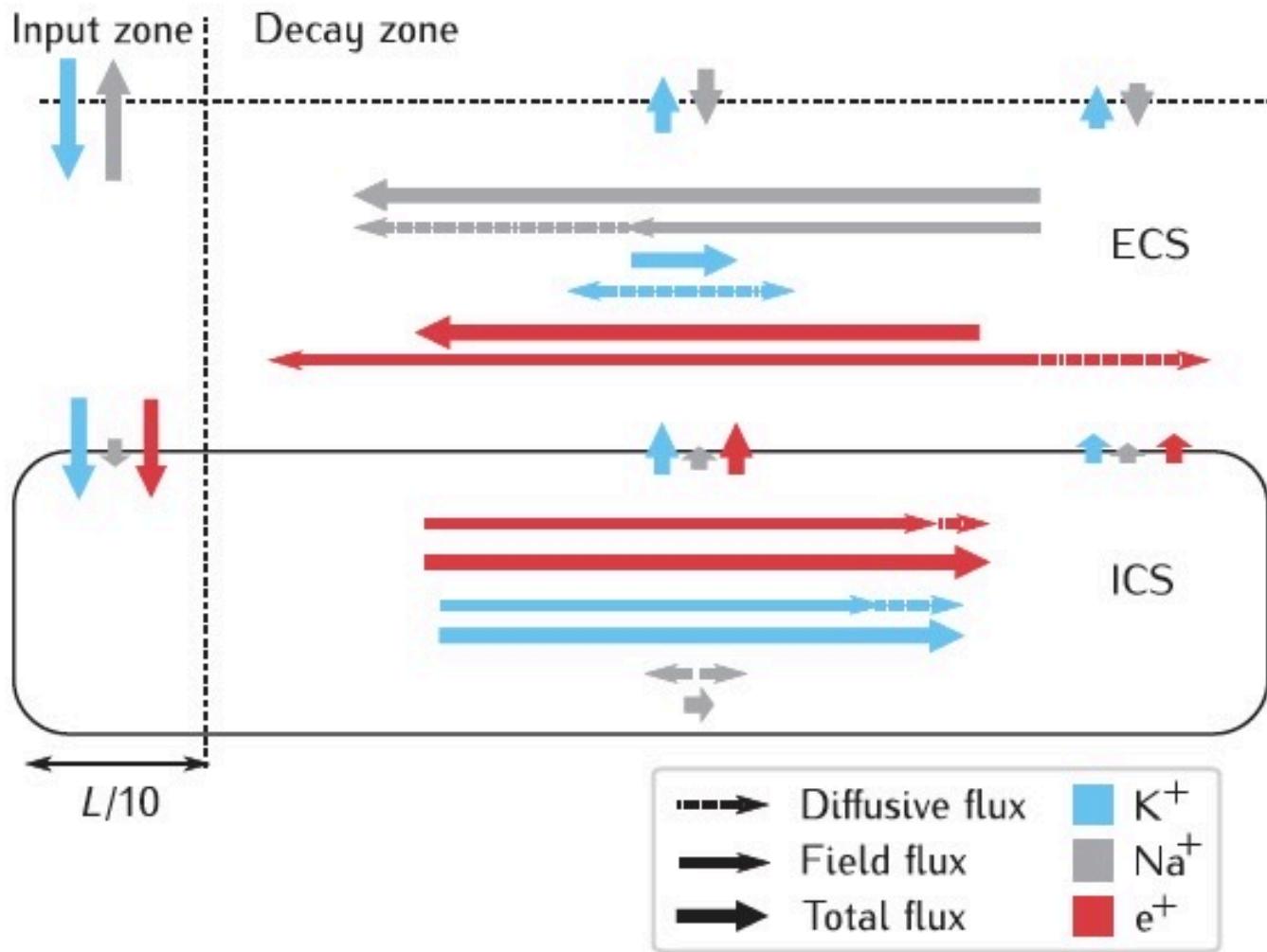
Copyright: © 2013 Halnes et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The project was supported by the Research Council of Norway (eVITA program; project numbers 178892 and 178901 and ISP-Fysikk; project number 216699), and EU Grant 269921 (BrainScaleS). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

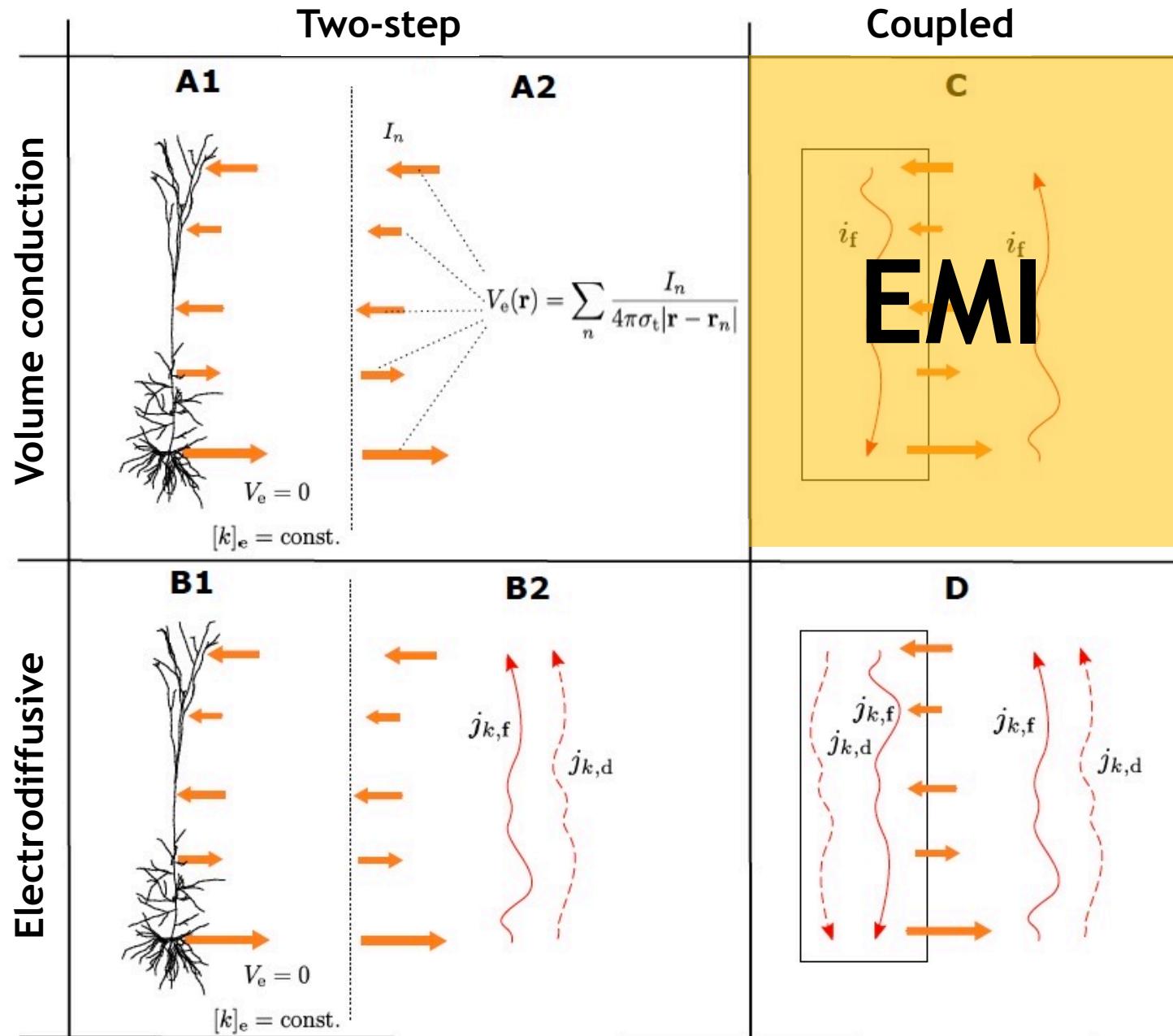
Competing Interests: The authors have declared that no competing interests exist.

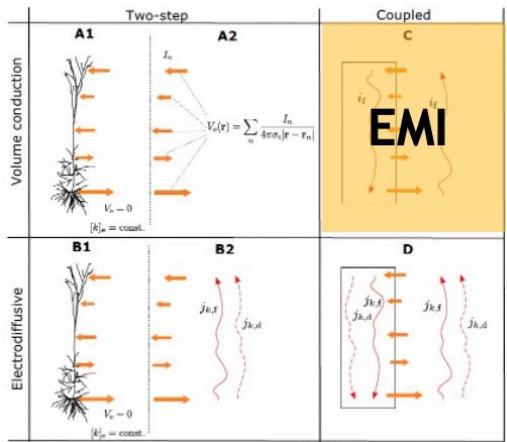
* E-mail: geir.halnes@umb.no

Fig 10.15 Results from exploration of spatial buffering of potassium in the ECS using the KNP scheme (Halnes et al., 2013). Model geometry is depicted in Figure 10.14. An $L = 300 \mu\text{m}$ section of a glial cable (ICS) is considered. The high-firing region where K^+ enters the ECS from neurons (downward pointing blue arrow in upper left corner) corresponds to the left one tenth of the cable. The model includes three ion types (K^+ , Na^+ , Cl^-) and a variety of ion channels, as well as a Na-K ion pump, embedded in the glial membrane. The flowchart summarises the main transport routes of K^+ and Na^+ at steady state, which is reached



Different schemes for modelling of electric dynamics in brain tissue





An Evaluation of the Accuracy of Classical Models for Computing the Membrane Potential and Extracellular Potential for Neurons

Aslak Tveito ^{1,2*}, Karoline H. Jæger ¹, Glenn T. Lines ¹, Łukasz Paszkowski ³, Joakim Sundnes ^{1,2}, Andrew G. Edwards ^{1,4}, Tuomo Mäki-Marttunen ⁵, Geir Halnes ⁶ and Gaute T. Einevoll ^{6,7}

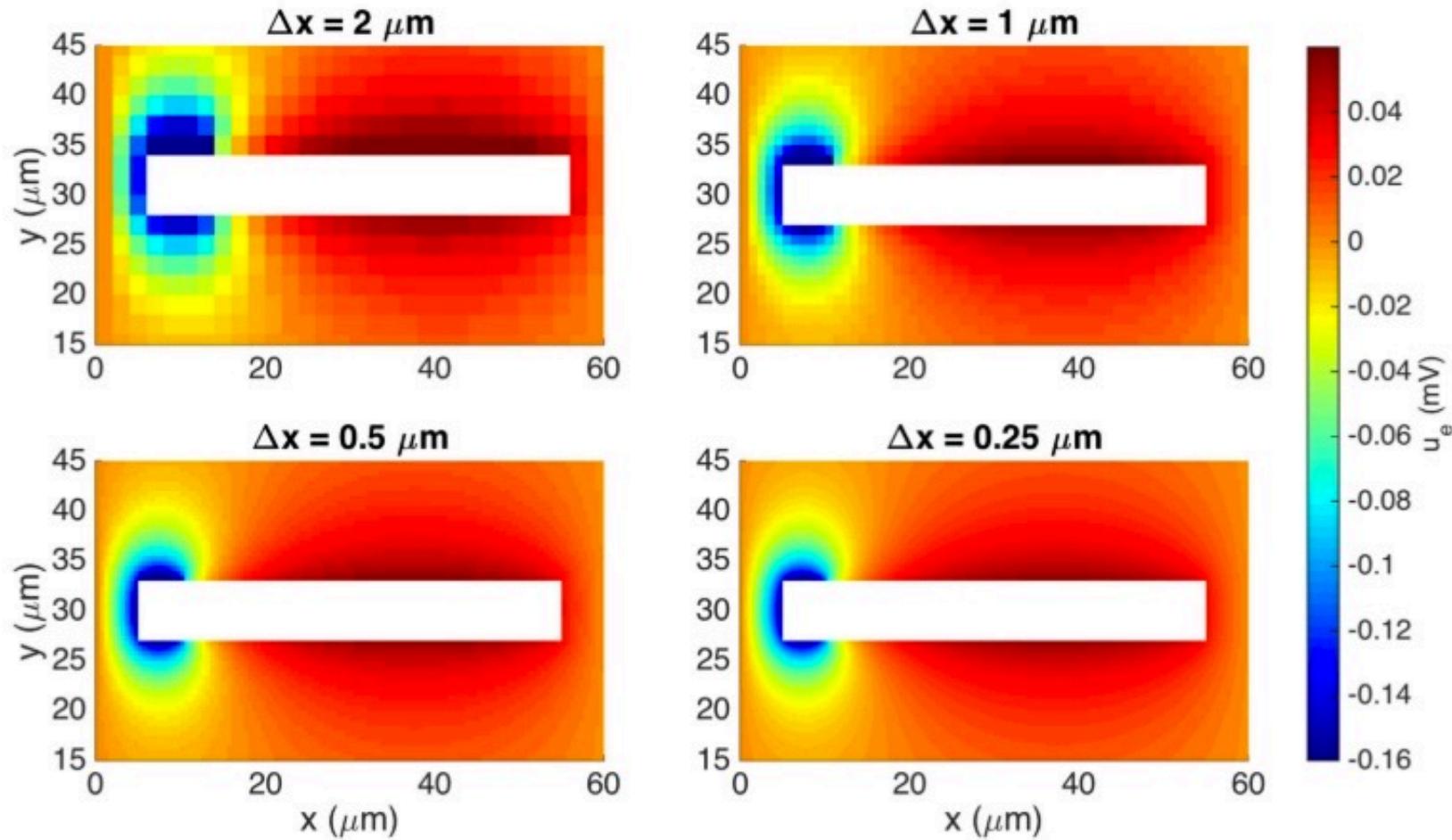
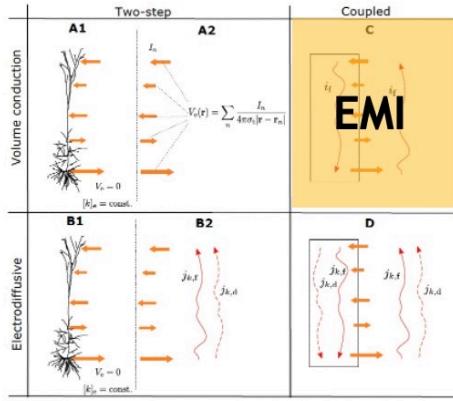
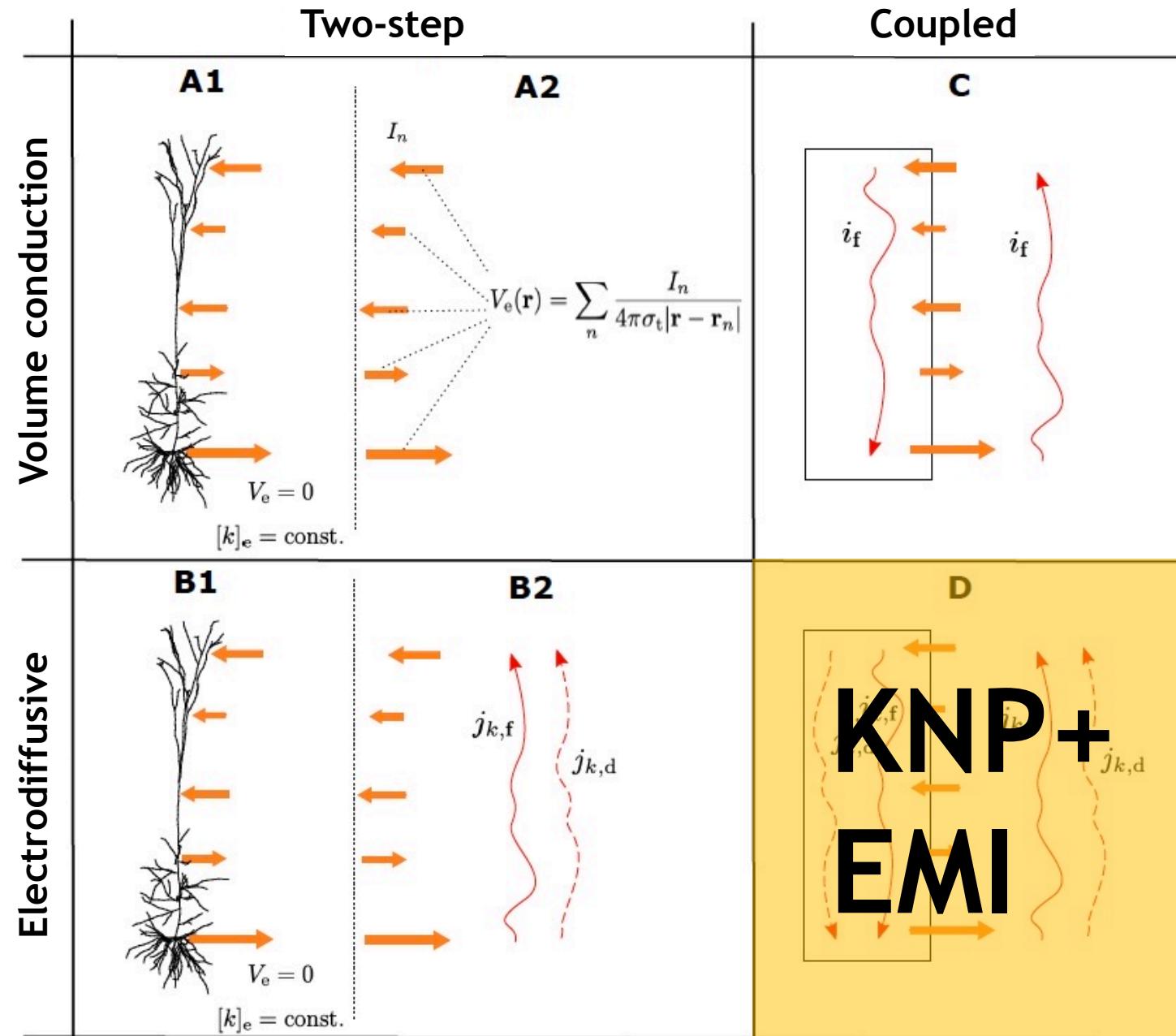


FIGURE 6 | Extracellular potential computed by the stationary EMI model for four different values of $\Delta x = \Delta y = \Delta z$. We show the solution in a rectangle of size $60 \times 30 \mu\text{m}$ on the plane in the center of the domain in the z -direction. The white area represents the cell. We use the parameters given in **Table 2** except for an increased value of $g_L = 3 \cdot 10^{-5} \mu\text{S}/\mu\text{m}^2$ and a domain of size $60 \times 60 \times 60 \mu\text{m}$.

Differents schemes for modelling of electric dynamics in brain tissue



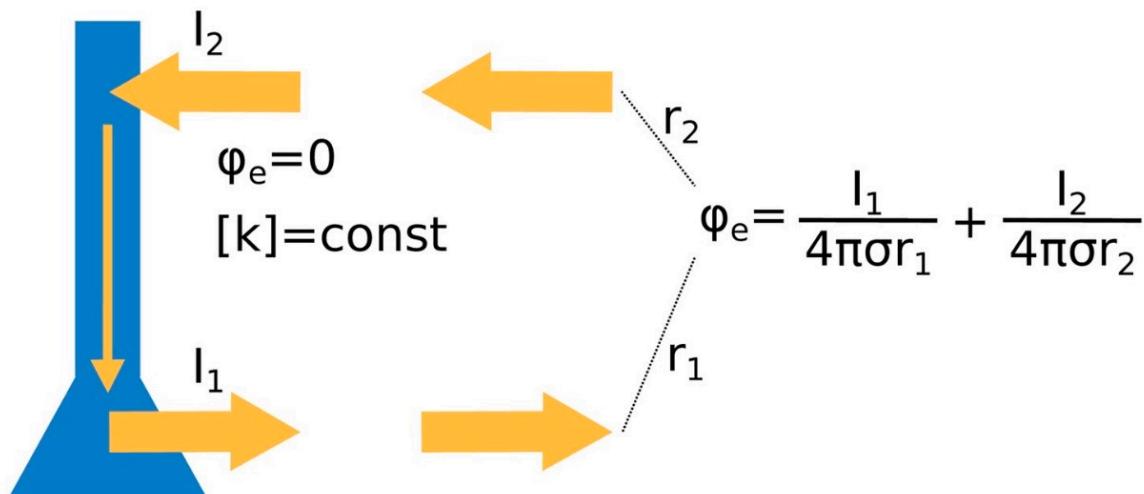
RESEARCH ARTICLE

An electrodiffusive, ion conserving Pinsky-Rinzel model with homeostatic mechanisms

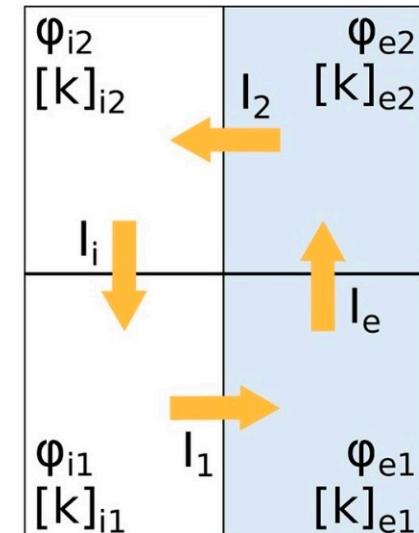
Marte J. Sætra  ^{1,2}, Gaute T. Einevoll  ^{1,2,3}, Geir Halnes  ^{1,3*}

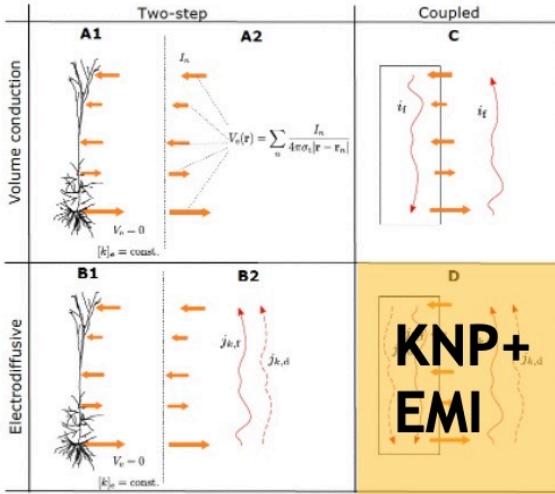
1 Centre for Integrative Neuroplasticity, University of Oslo, Oslo, Norway, **2** Department of Physics, University of Oslo, Oslo, Norway, **3** Faculty of Science and Technology, Norwegian University of Life Sciences, Ås, Norway

Two-step (MC+VC)



Coupled electrodiffusive (KNP+EMI)





Finite Element Simulation of Ionic Electrodiffusion in Cellular Geometries

Ada J. Ellingsrud^{1†}, Andreas Solbrå^{2,3†}, Gaute T. Einevoll^{2,3,4}, Geir Halnes^{2,4†} and Marie E. Rognes^{1*†}

¹ Department for Scientific Computing and Numerical Analysis, Simula Research Laboratory, Oslo, Norway, ² Centre for Integrative Neuroplasticity, University of Oslo, Oslo, Norway, ³ Department of Physics, University of Oslo, Oslo, Norway,

⁴ Faculty of Science and Technology, Norwegian University of Life Sciences, Ås, Norway

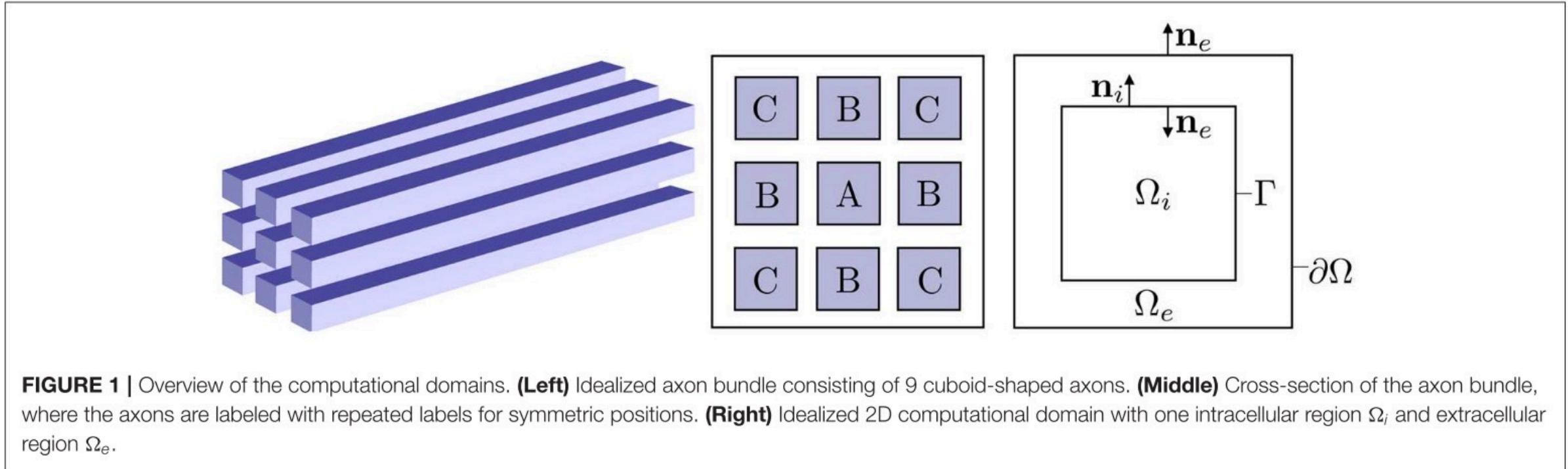
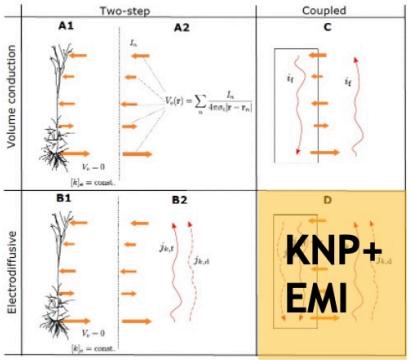
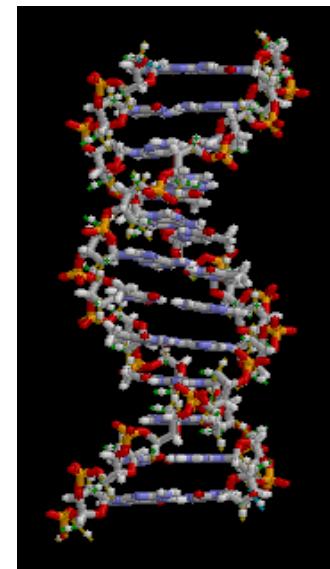
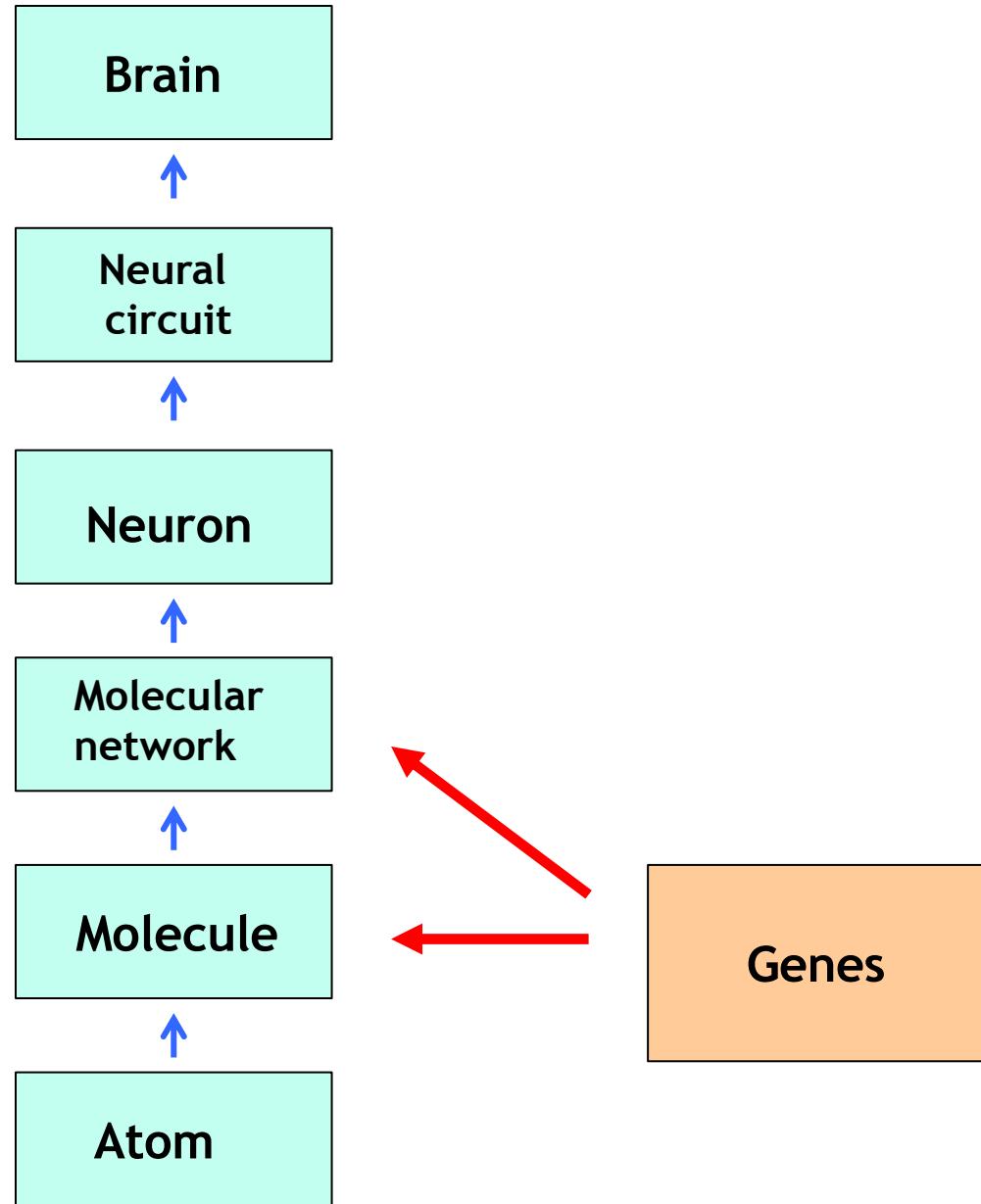
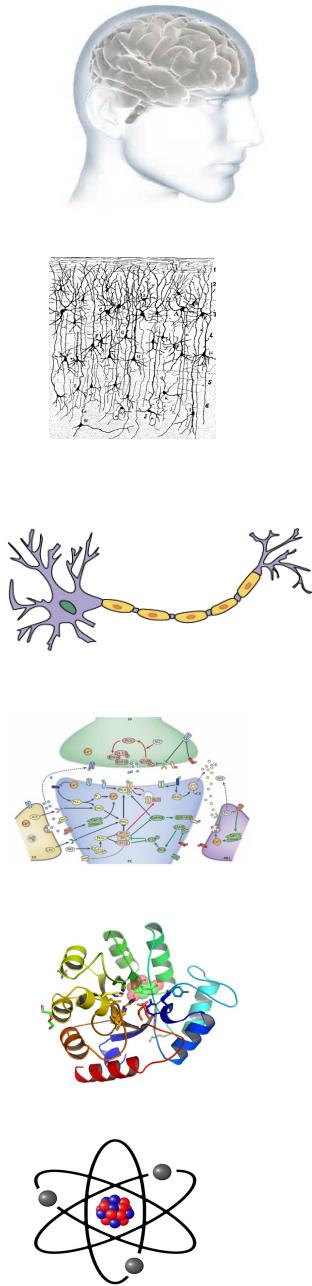


FIGURE 1 | Overview of the computational domains. **(Left)** Idealized axon bundle consisting of 9 cuboid-shaped axons. **(Middle)** Cross-section of the axon bundle, where the axons are labeled with repeated labels for symmetric positions. **(Right)** Idealized 2D computational domain with one intracellular region Ω_i and extracellular region Ω_e .





Functional Effects of Schizophrenia-Linked Genetic Variants on Intrinsic Single-Neuron Excitability: A Modeling Study

Tuomo Mäki-Marttunen, Geir Halnes, Anna Devor, Aree Witoelar, Francesco Bettella, Srdjan Djurovic, Yunpeng Wang, Gaute T. Einevoll, Ole A. Andreassen, and Anders M. Dale

Mäki-Marttunen et al. *Translational Psychiatry* (2017)7:5
DOI 10.1038/s41398-017-0007-4

Translational Psychiatry

Tuomo Mäki-
Marttunen

ARTICLE

Open Access

Pleiotropic effects of schizophrenia-associated genetic variants in neuron firing and cardiac pacemaking revealed by computational modeling

Tuomo Mäki-Marttunen^{1,2}, Glenn T. Lines², Andrew G. Edwards², Aslak Tronstad², Anders M. Dale^{3,4,5},
Gaute T. Einevoll^{6,7} and Ole A. Andreassen^{1,8}



Cerebral Cortex, February 2019;29: 875–891

doi: 10.1093/cercor/bhy291
Advance Access Publication Date: 22 November 2018
Original Article

ORIGINAL ARTICLE

Alterations in Schizophrenia-Associated Genes Can Lead to Increased Power in Delta Oscillations

Tuomo Mäki-Marttunen^{1,2}, Florian Krull², Francesco Bettella², Espen Hagen^{3,4}, Solveig Næss⁵, Torbjørn V. Ness⁴, Torgeir Moerget², Torbjørn Elvsåshagen^{2,6}, Christoph Metzner⁷, Anna Devor^{8,9,10}, Andrew G. Edwards¹, Marianne Fyhn¹¹, Srdjan Djurovic^{12,13}, Anders M. Dale^{8,9}, Ole A. Andreassen^{2,14} and Gaute T. Einevoll^{3,4}



Biophysical Psychiatry—How Computational Neuroscience Can Help to Understand the Complex Mechanisms of Mental Disorders

OPEN ACCESS

Edited by:

Cynthia H. Y. Fu,
University of East London,
United Kingdom

Tuomo Mäki-Marttunen^{1,2*}, Tobias Kaufmann², Torbjørn Elvsåshagen^{2,3}, Anna Devor^{4,5,6}, Srdjan Djurovic^{7,8}, Lars T. Westlye^{2,9}, Marja-Leena Linne¹⁰, Marcella Rietschel¹¹, Dirk Schubert¹², Stefan Borgwardt¹³, Magdalena Efrim-Budisteanu^{14,15,16}, Francesco Bettella², Geir Halnes¹⁷, Espen Hagen¹⁸, Solveig Næss¹⁹, Torbjørn V. Ness¹⁷, Torgeir Moberget², Christoph Metzner^{20,21}, Andrew G. Edwards¹, Marianne Fyhn²², Anders M. Dale^{4,5}, Gaute T. Einevoll^{17,18} and Ole A. Andreassen²

¹ Department of Computational Physiology, Simula Research Laboratory, Oslo, Norway, ² NORMENT, Division of Mental Health and Addiction, Oslo University Hospital & Institute of Clinical Medicine, University of Oslo, Oslo, Norway, ³ Department

Collaborators on modeling of extracellular potentials

Norw. Univ. Life Sci.

Torbjørn Bækø Ness

Geir Halnes

Espen Hagen

Jan-Eirik W. Skaar

Klas Pettersen (Oslo)

Henrik Lindén

Tom Tetzlaff (Jülich)

Maria Stavrinou (Oslo)

Eivind S. Norheim

Kristin Tøndel

Nicolay Haug

Alexander Stasik

UC San Diego

Anders Dale

Eric Halgren

Boston University

Anna Devor

University of Oslo

Atle Rimehaug

Solveig Næss

Andreas Solbrå

SIMULA, Oslo

Marte Julie Sætra

Ada Ellingsrud

Aslak Tveito

Marie Rognes

Eirill Hauge

FZ Jülich

Markus Diesmann

Sonja Grün

David Dahmen

Sacha van Albada

Nencki Inst, Warsaw

Szymon Leski

Daniel Wojcik

Helena Glabska

Oxford University

Chaitanya Chintaluri

Humboldt Univ Berlin

Michiel Remme

UMC Hamburg

Stefano Panzeri

SSSA (Italy)

Alberto Mazzoni

Radboud, Nijmegen

Dirk Schubert

Stephanie Miceli

Allen Institute, Seattle

Anton Arkhipov

Christof Koch

ESI, FIAS & Goethe Univ, Frankfurt

Hermann Cuntz

University of Washington

Nick Steinmetz

Funding in Norway:

Research Council of Norway

EU (BrainScaleS, Human Brain Project)

DARPA (NESD)

END

END