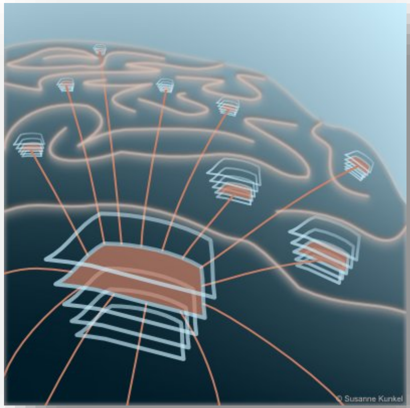


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# Necessity and feasibility of brain-scale simulations at cellular and synaptic resolution

February 22-23 2016
6th AICS International Symposium
RIKEN AICS, Kobe, Japan

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Institute of Neuroscience and Medicine (INM-6)
Institute for Advanced Simulation (IAS-6)
Jülich Research Centre

www.csn.fz-juelich.de
www.nest-initiative.org

# History of brain-scale simulations on K computer

- work reported started in 2006
- Next-Generation Supercomputing project of MEXT
- group at RIKEN Brain Science Institute (BSI)  2006-2011
- from March 2011 Juelich Research Centre

- special thanks to
    - Ryutaro Himeno
    - Mitsuhisa Sato
    - Naoya Maruyama

Diesmann, M (2012) Proceedings of the 4th Biosupercomputing Symposium Tokyo 83–85

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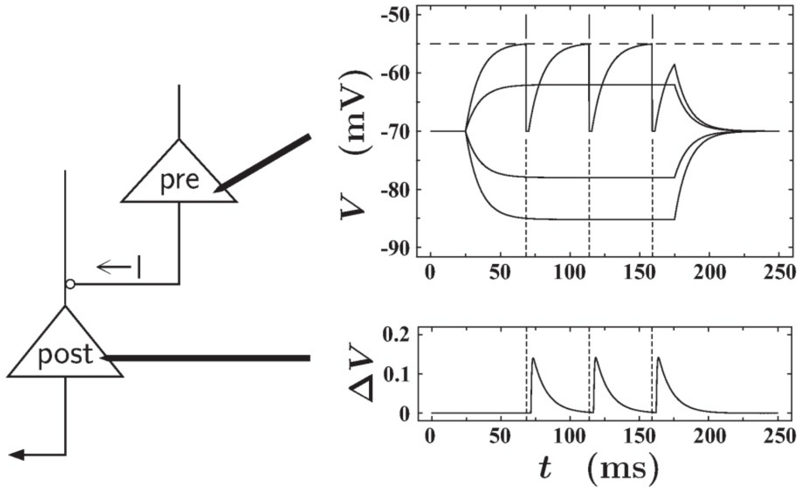
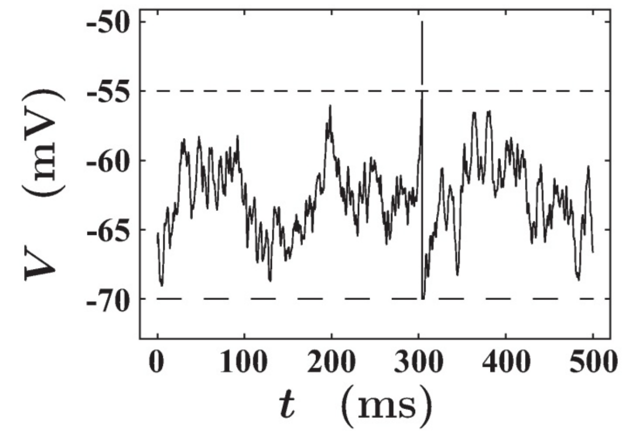
# Fundamental interaction between neurons

in vitro




in vivo



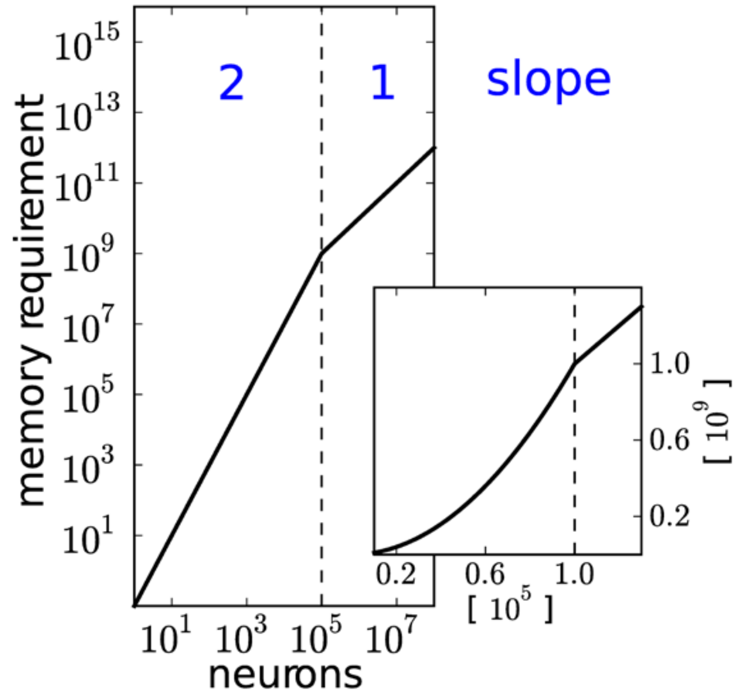

- current injection into pre-synaptic neuron causes excursions of membrane potential
- supra-threshold value causes spike transmitted to post-synaptic neuron
- post-synaptic neuron responds with small excursion of potential after delay
- inhibitory neurons (20%) cause negative excursion

- each neuron receives input from 10,000 other neurons
- causing large fluctuations of membrane potential
- emission rate of 1 to 10 spikes per second

# Realistic local cortical networks

- connectivity $c = 0.1$
- synapses per neuron = $10^4$

⇒ minimal network size = $10^5$




- network $N = 10^5$
  - considered elementary unit
  - corresponding to $1\ \mathrm{mm}^3$

- total number of synapses = $(cN) \cdot N$

⇒ possible

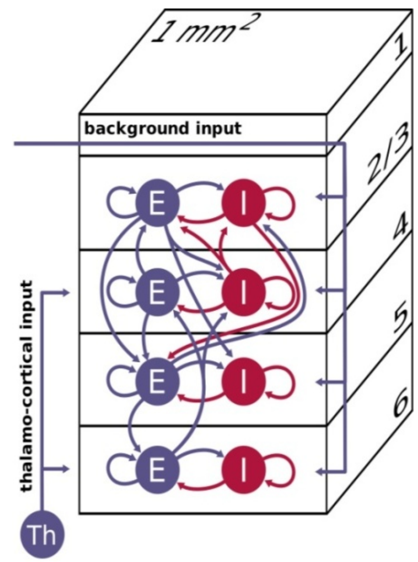
Morrison A, Mehring C, Geisel T, Aertsen A, Diesmann M (2005) Neural Comput 17(8):1776-1801

Morrison A, Straube S, Plesser HE, Diesmann M (2007) Neural Comput 19(1):47-79

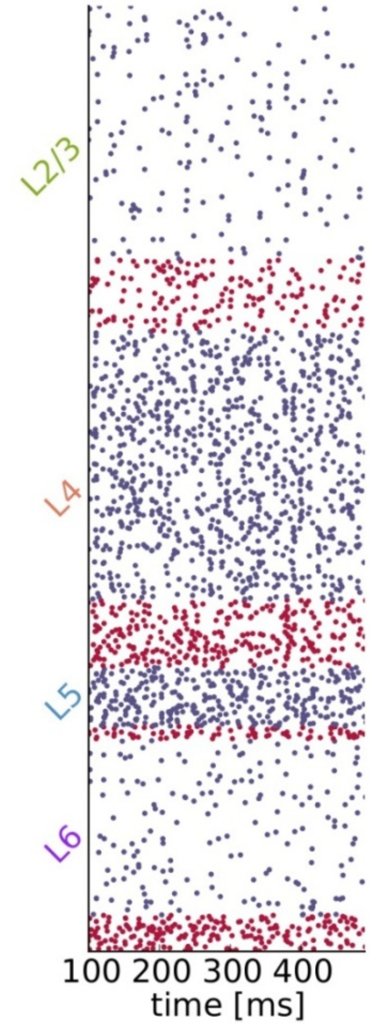
# Local cortical microcircuit

taking into account layer and neuron-type specific connectivity is sufficient to reproduce experimentally observed:

- asynchronous-irregular spiking of neurons
- higher spike rate of inhibitory neurons
- correct distribution of spike rates across layers
- integrates knowledge of more than 50 experimental papers




$10^5$ neurons
$10^9$ synapses

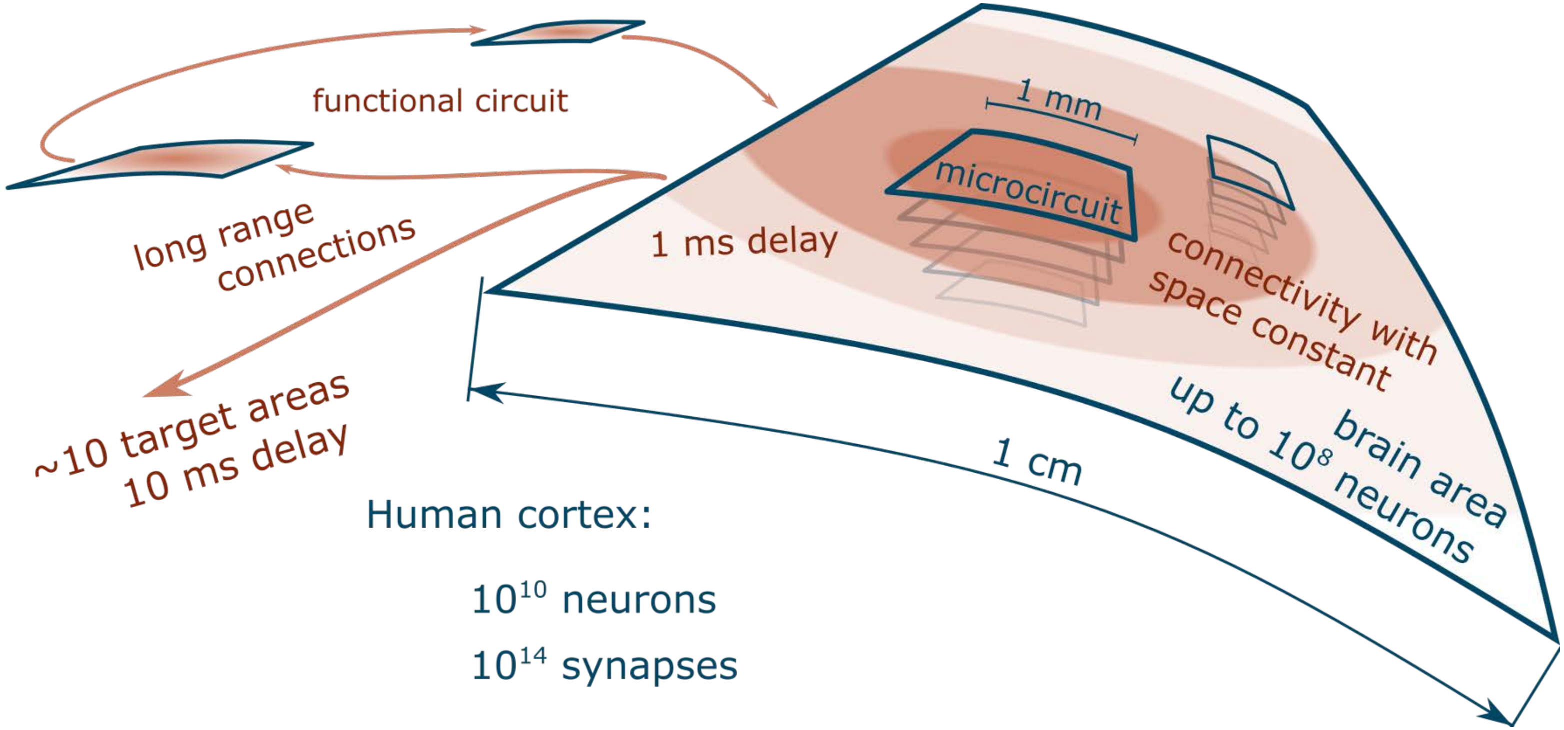



Potjans TC & Diesmann M (2014) The cell-type specific connectivity of the local cortical network explains prominent features of neuronal activity. *Cerebral Cortex* 24 (3): 785-806

available at: www.opensourcebrain.org

# Critique of local network model

**a network of networks** with at least three levels of organization:




- neurons in local microcircuit models are missing 50% of synapses
- e.g., power spectrum shows discrepancies, slow oscillations missing
- solution by taking brain-scale anatomy into account

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# Meso- and macro-scale measures

brain-scale networks basis for:

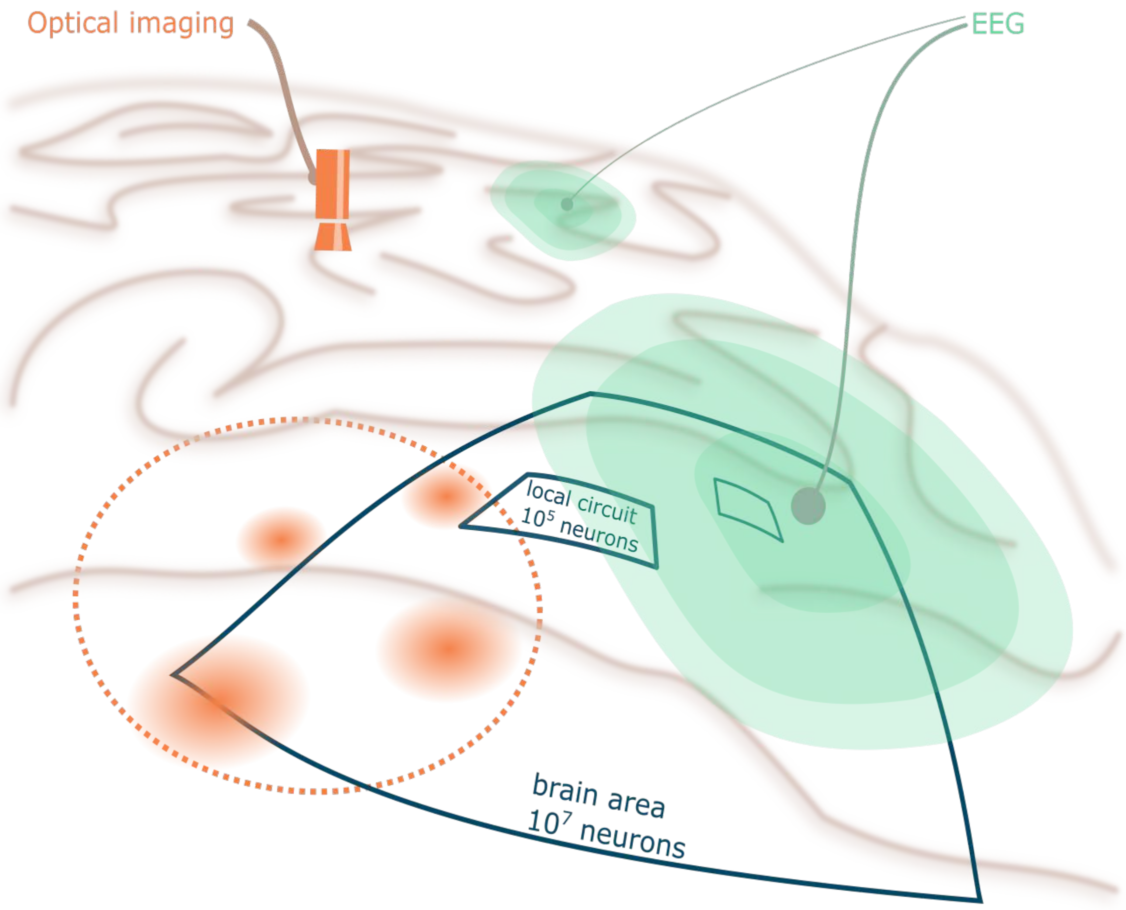
- further measures by forward modeling
- comparison with mean-field models

mesoscopic measures

- local field potential (LFP)
- voltage sensitive dyes (VSD)

and macroscopic measures

- EEG, MEG
- fMRI resting state networks



# Feasibility and necessity

- Can we do simulations at the brain scale?
- Do we need to simulate full scale (at cellular resolution)?

frontiers in NEUROINFORMATICS

ORIGINAL RESEARCH ARTICLE
published: 02 November 2012
doi: 10.3389/fninf.2012.00026

# Supercomputers ready for use as discovery machines for neuroscience

***Moritz Helias[1,2]*, Susanne Kunkel[1,3,4], Gen Masumoto[5], Jun Igarashi[6], Jochen Martin Eppler[1], Shin Ishii[7], Tomoki Fukai[6], Abigail Morrison[1,3,4,8] and Markus Diesmann[1,2,4,9]***

[1] *Institute of Neuroscience and Medicine (INM-6), Computational and Systems Neuroscience, Jülich Research Centre, Jülich, Germ...*
[2] *RIKEN Brain Science Institute, Wako, Japan*
[3] *Simulation Laboratory Neuroscience – Bernstein Facility for Simulation and Database Technology, Institute for Advanced Simulation, Jülich Aa... Alliance, Jülich Research Centre, Jülich, Germany*
[4] *Bernstein Center Freiburg, Albert-Ludwig University of Freiburg, Freiburg, Germany*

makes supercomputers accessible for neuroscience

provides the evidence that neuroscience can exploit petascale systems

frontiers in NEUROINFORMATICS

ORIGINAL RESEARCH ARTICLE
published: 10 October 2014
doi: 10.3389/fninf.2014.00078

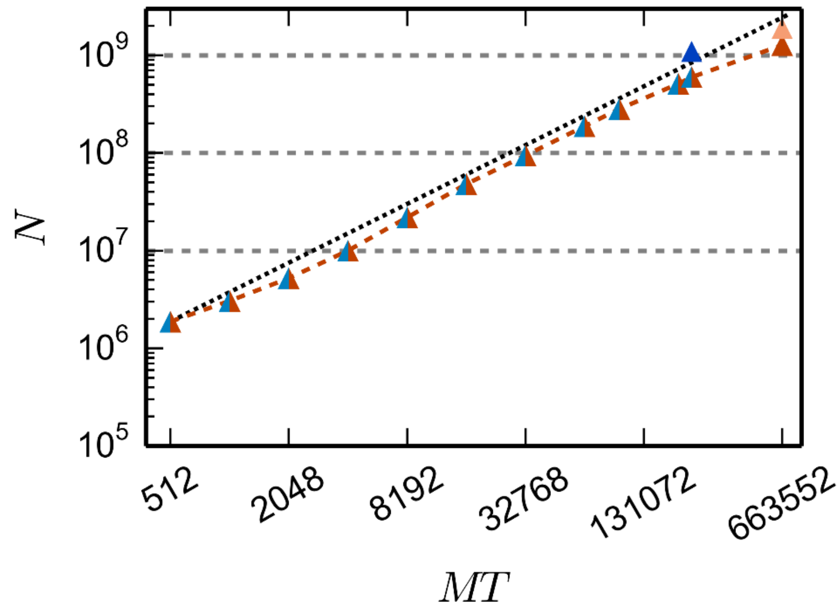
# Spiking network simulation code for petascale computers

***Susanne Kunkel[1,2]*, Maximilian Schmidt[3], Jochen M. Eppler[3], Hans E. Plesser[3,4], Gen Masumoto[5], Jun Igarashi[6,7], Shin Ishii[8], Tomoki Fukai[7], Abigail Morrison[1,3,9], Markus Diesmann[3,7,10] and Moritz Helias[2,3]***

[1] *Simulation Laboratory Neuroscience – Bernstein Facility for Simulation and Database Technology, Institute for Advanced Simulation, Jülich Aachen Research Alliance, Jülich Research Centre, Jülich, Germany*
[2] *Programming Environment Research Team, RIKEN Advanced Institute for Computational Science, Kobe, Japan*
[3] *Institute of Neuroscience and Medicine (INM-6), Institute for Advanced Simulation (IAS-6), Jülich Research Centre and JARA, Jülich, Germany*
[4] *Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Aas, Norway*

# NEST – Maximum network size

- using 663,552 cores of K
- using 229,376 cores of JUQUEEN
- worst case: random network
- exc-exc STDP




- largest general network simulation performed to date:
- $1.86 \times 10^9$ neurons, 6000 synapses per neuron
- $1.08 \times 10^9$ neurons, 6000 synapses per neuron

nest::

**NEST simulation software**

JARA|BRAIN Human Brain Project JÜLICH FORSCHUNGSZENTRUM

# European Human Brain Project

- simulation engines in ramp-up phase

nest:: initiative

www.nest-initiative.org

**NEURON**

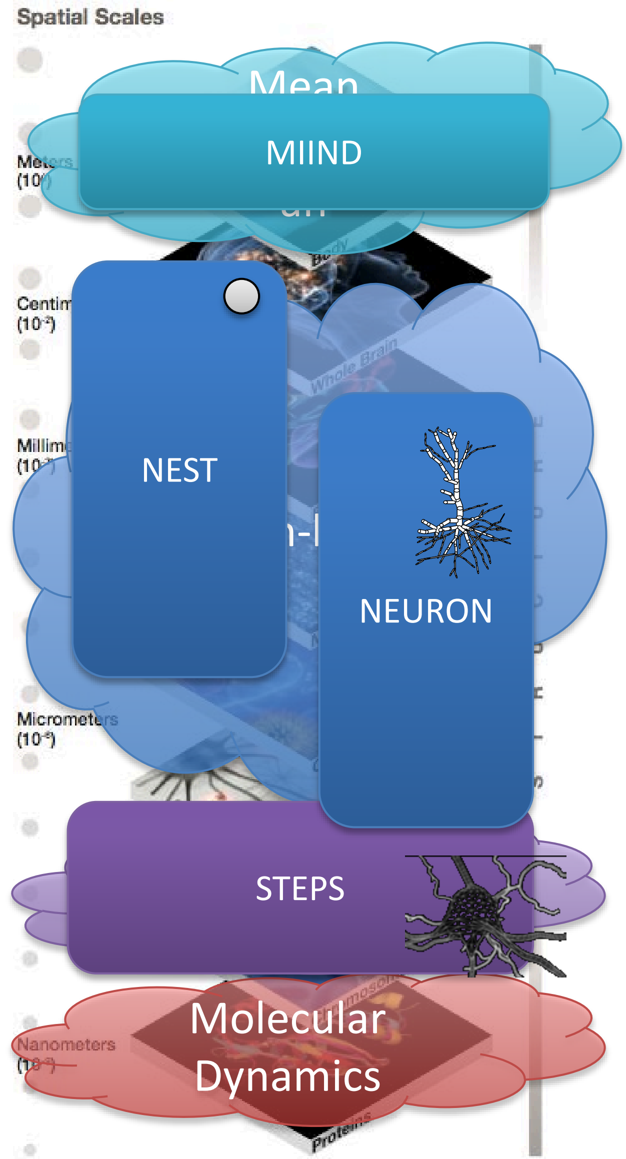
for empirically-based simulations of neurons and networks of neurons

www.neuron.yale.edu

**STEPS**

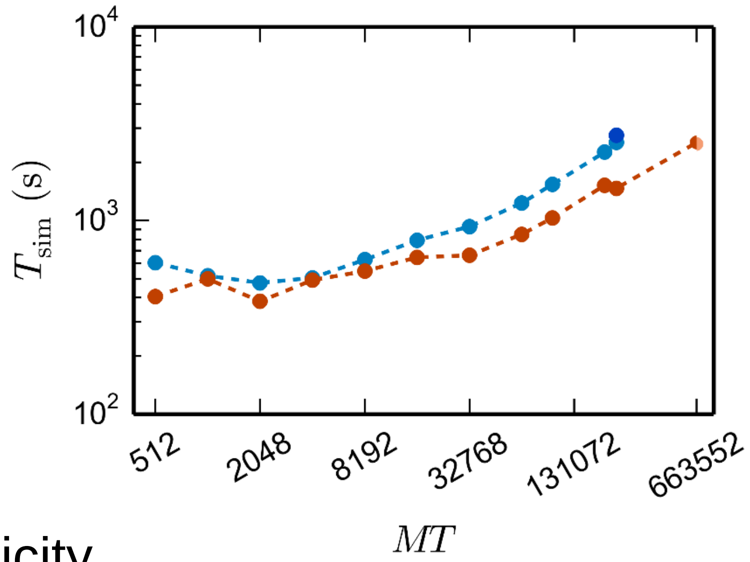
STochastic Engine for Pathway Simulation

Erik De Schutter (OIST Okinawa)



# NEST – Scaling of run time

- runtime for 1 second biological time:
- between 6 and 42 min on K computer
- between 8 and 41 min on JUQUEEN
- wiring: between 3 and 15 min




- still not fast enough for studies of plasticity
- need to increase multi-threading on compute nodes

- is self-contained benchmark application for HBP prototype system

# Feasibility and necessity

- Can we do simulations at the brain scale? ✓
- Do we need to simulate full scale (at cellular resolution)?

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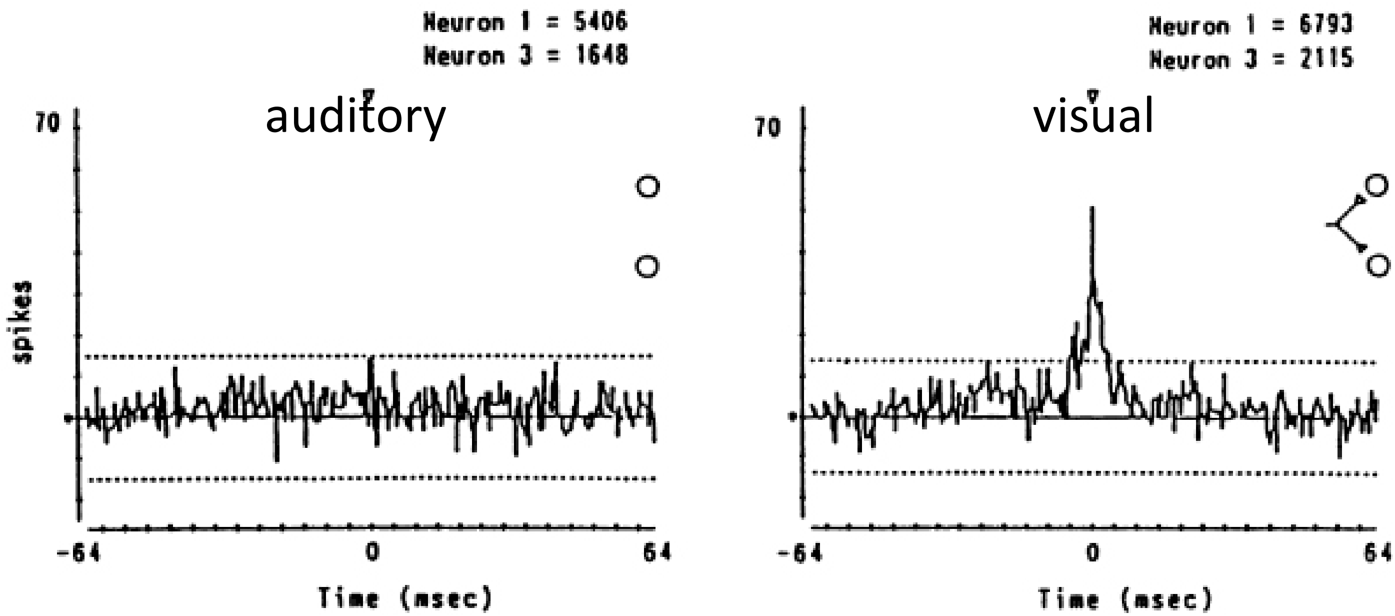
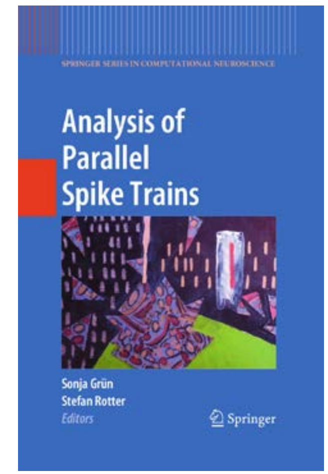
# Functional Correlation




Sakurai, Y. (1999) Neuroscience & Biobehavioral Reviews 23: 785-796




- two neurons in CA1 of a rat performing an auditory or visual discrimination task
- cross-correlation function: probability of neuron 2 emitting spike at delay after 1
- task related correlation only observed for visual task

⇒ interpretation: neurons belong to a cell assembly processing visual information

# Networks generally not reducible

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RESEARCH ARTICLE

## Scalability of Asynchronous Networks Is Limited by One-to-One Mapping between Effective Connectivity and Correlations

Sacha Jennifer van Albada, Moritz Helias, Markus Diesmann

Published: September 1, 2015 • DOI: 10.1371/journal.pcbi.1004490

Article | Authors | Metrics | Comments | Related Content

- downscaling works well for first order statistics like spike rate
- severe constraints already for second order like spike correlation
- spike correlation drives mesoscopic measures like LFP and EEG

# Feasibility and necessity

- Can we do simulations at the brain scale? ✓
- Do we need to simulate full scale (at cellular resolution)? ✓

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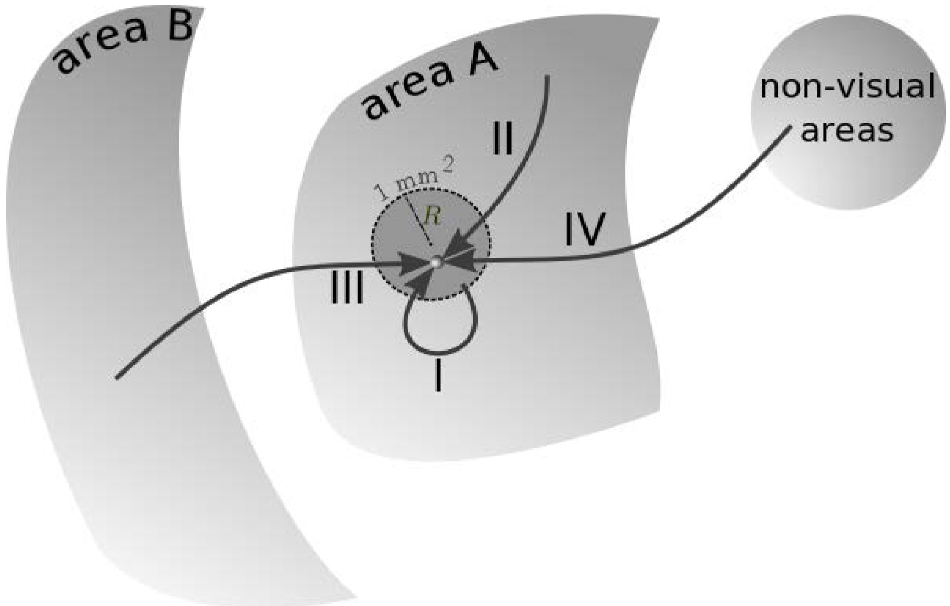
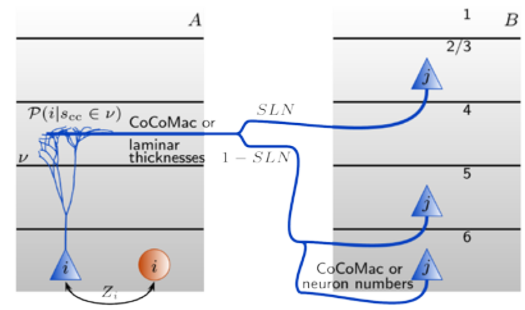
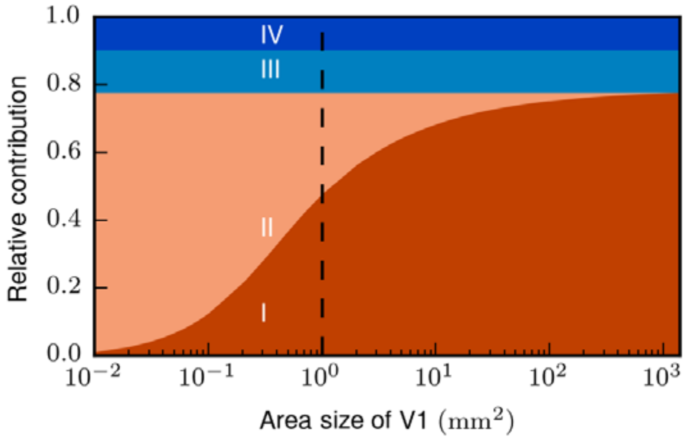
# Toward a self-consistent model



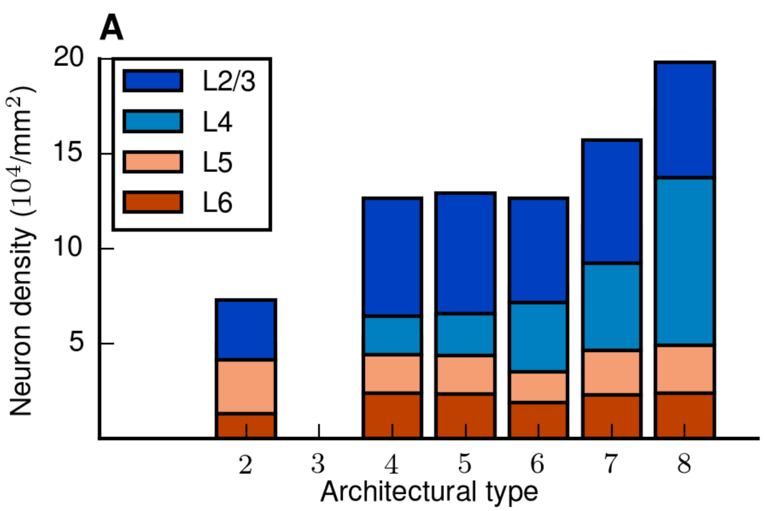




**I. Intra-areal synapses**
**II. Intra-areal synapses replaced by random input**
**III. Cortico-cortical synapses**
**IV. External input represented by random input**

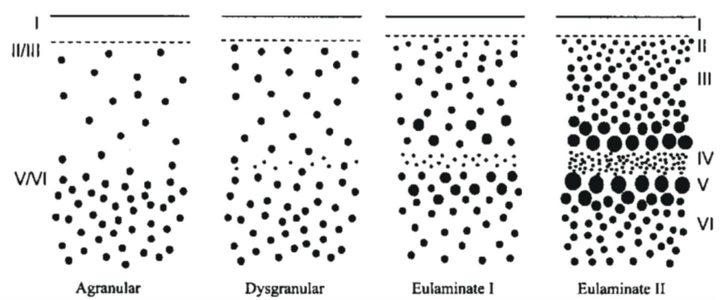
- Sacha van Albada
- Maximilian Schmidt
- Rembrandt Bakker

# Multi-area model of macaque visual cortex

- rich anatomical data sets available (e.g CoCoMac)
- close to human
- 32 areas structured in layers comprising $8 \cdot 10^8$ neurons
- downscaled model with $4.1 \cdot 10^6$ neurons and $3.9 \cdot 10^{10}$ synapses

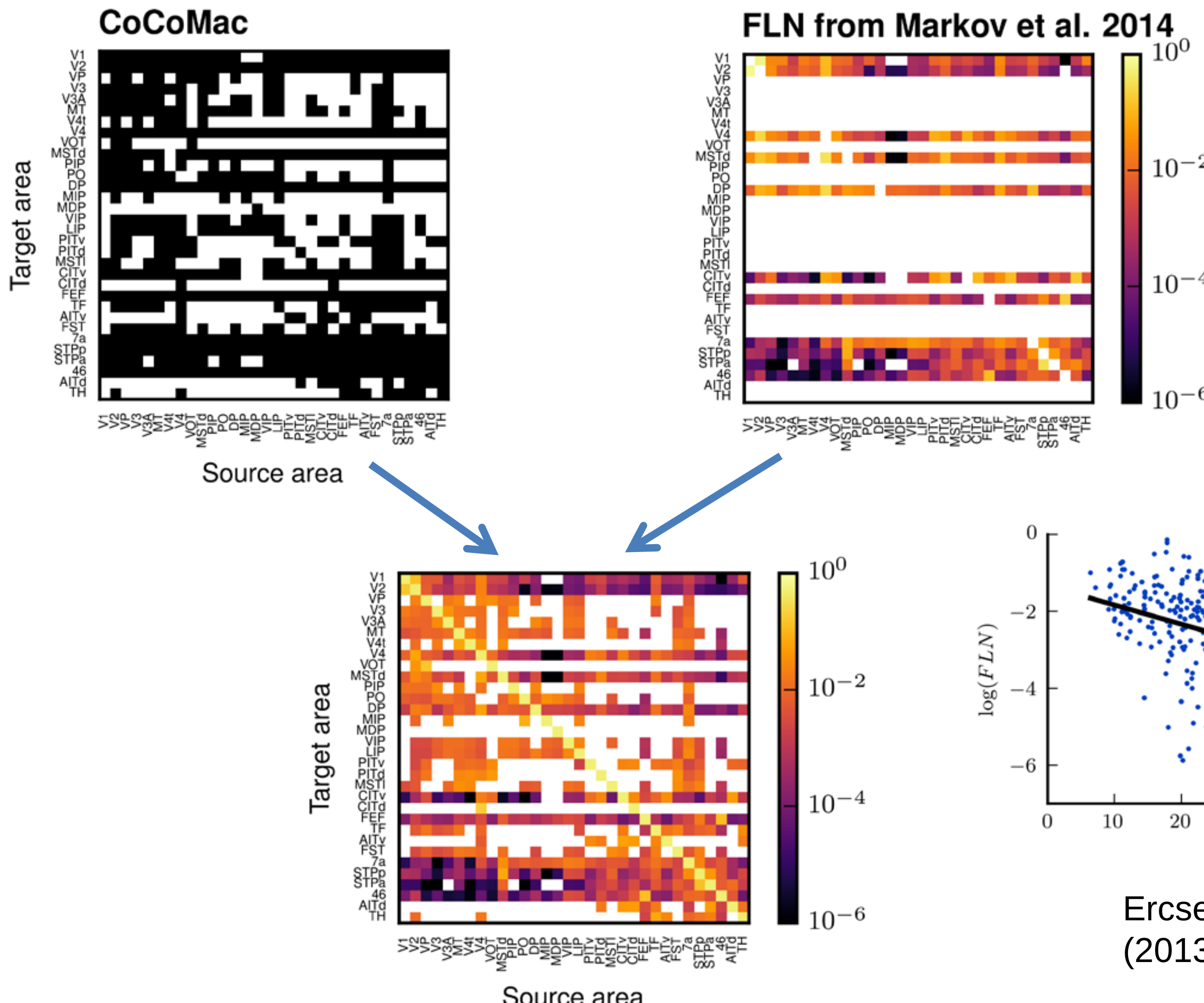


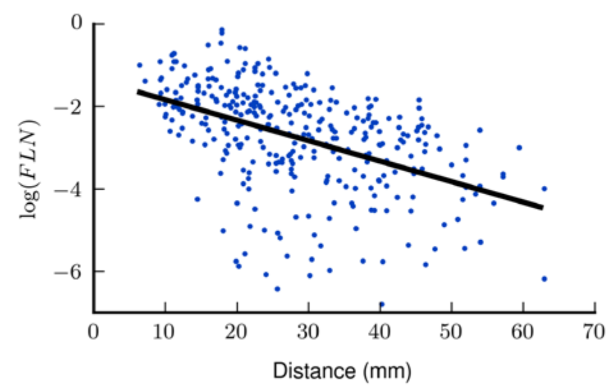

architectural types from Hilgetag et al. (2015)
with data by Helen Barbas




From Dombrowski et al. (2001), Cereb Cortex

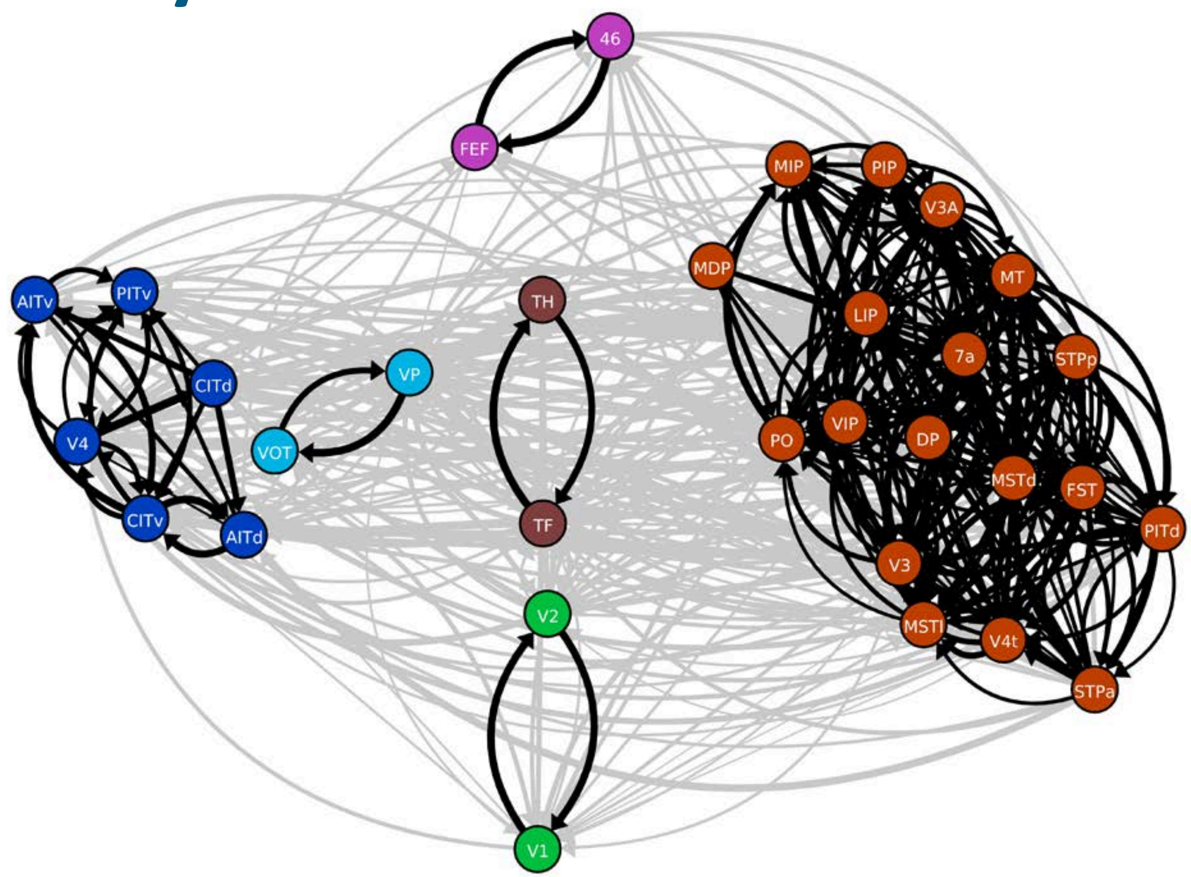
# Construction of cortico-cortical connectivity




Ercsey-Ravasz et al. (2013), Neuron

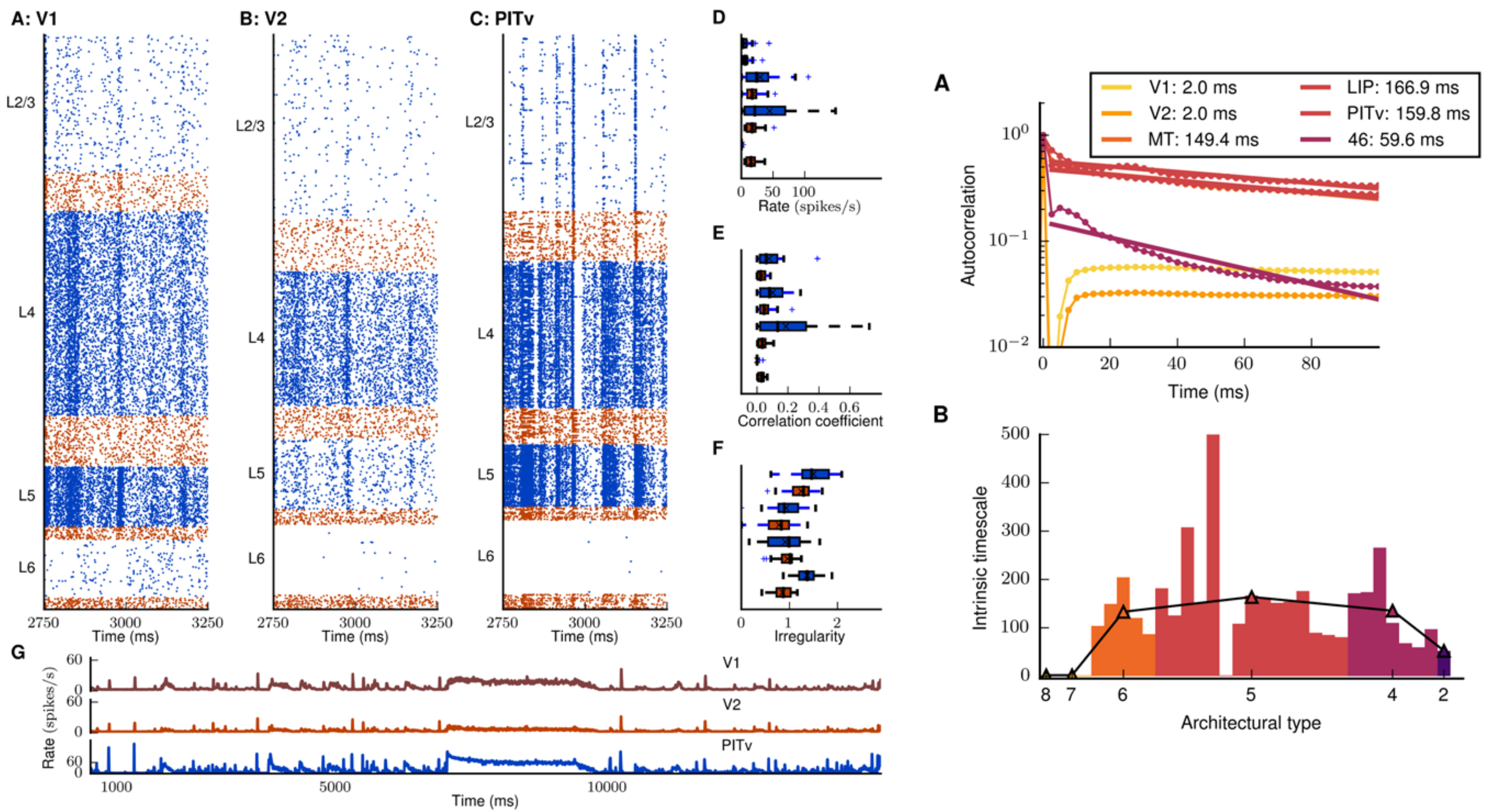
# Structural connectivity reveals functionally relevant community structure




clustering by map equation method (Rosvall et al. 2010)

# Multi-area model: Dynamical results

- stable resting state with heterogeneous laminar rate patterns and irregular firing
- cortico-cortical interactions trigger increased time scales in higher visual areas



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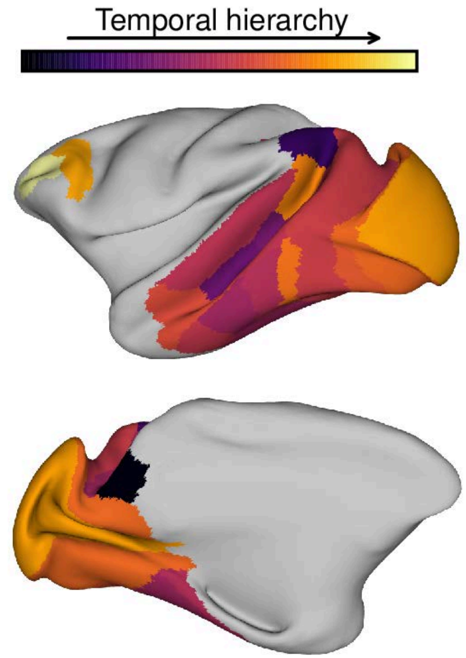
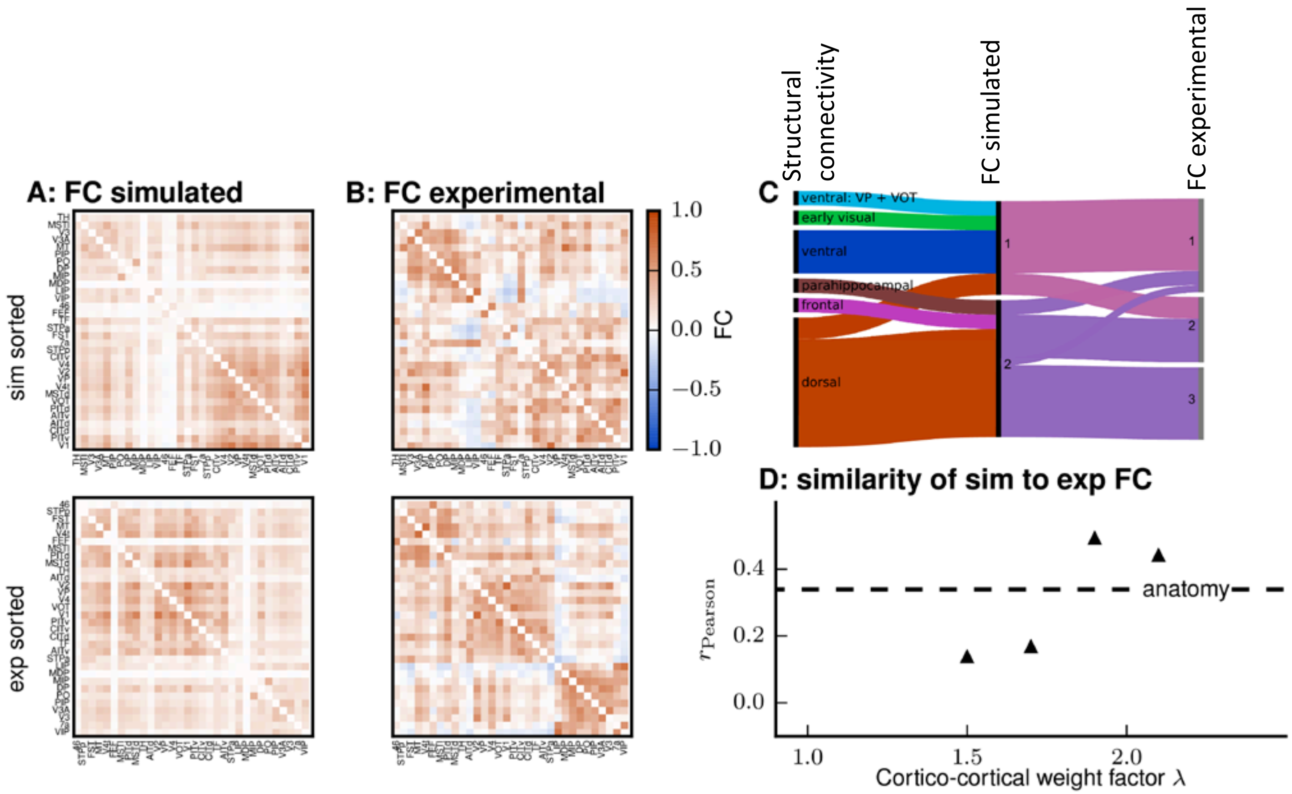
# Multi-area model: Dynamical results

- activity propagates in feedback direction
- inter-area interactions mimic experimental resting-state fMRI




FC sorted according to Louvain clustering (Blondel et al. 2008)

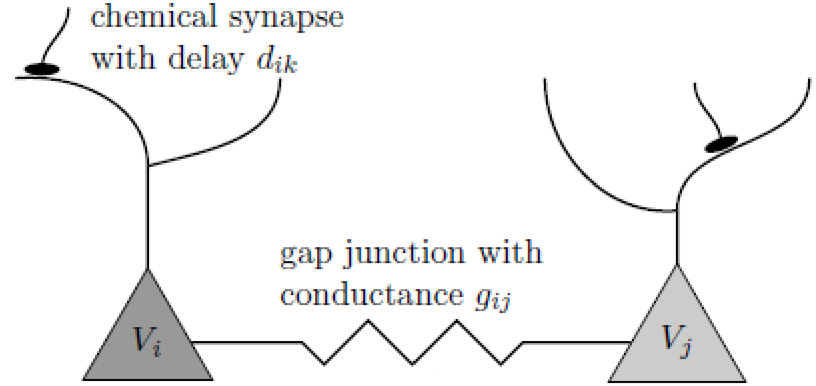
Schmidt M, Bakker R, Shen K, Bezgin G, Hilgetag CC, Diesmann M, van Albada SJ (2016) arXiv:1511.09364

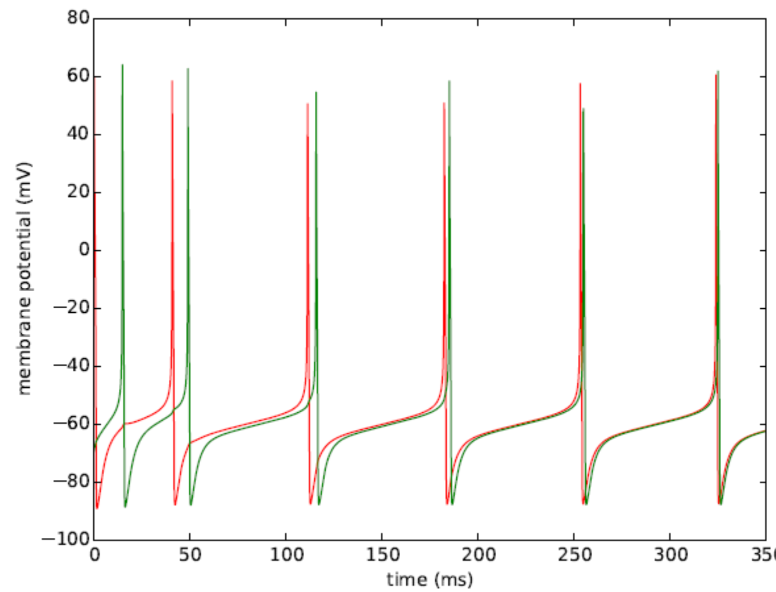
# Biophysics of gap junctions

- electrical synapses between neurons
- widespread in nervous system
- crucial for synchronization and generation of rhythmic activity
- mechanism: instantaneous gap current

$$I_{\mathrm{gap}}(t) = g_{ij}\,(V_i(t) - V_j(t))$$

- only very small networks studied so far




time evolution of the membrane potentials of two neurons with constant current input and gap-junction coupling

# Gap junctions in NEST simulator

## A unified framework for spiking and gap-junction interactions in distributed neuronal network simulations

frontiers in Neuroinformatics

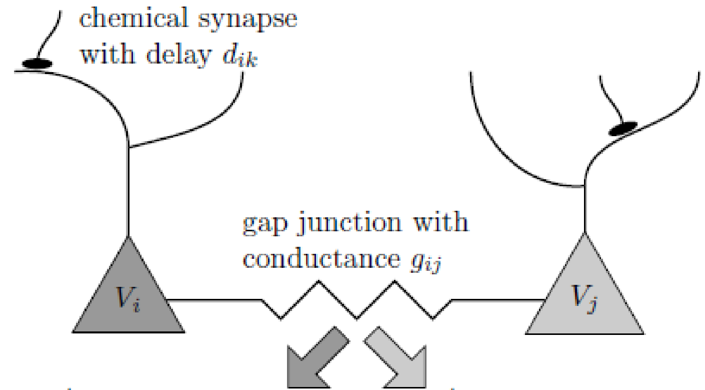
*Jan Hahne[1]*, Moritz Helias[2, 3], Susanne Kunkel[3, 4], Jun Igarashi[5, 6], Matthias Bolten[1], Andreas Frommer[1] and Markus Diesmann[2, 7, 8]*

*[1] Department of Mathematics and Science, Bergische Universität Wuppertal, Wuppertal, Germany, [2] Institute of Neuroscience and Medicine (INM-6), Institute for Advanced Simulation (IAS-6), JARA BRAIN Institute I, Jülich Research Centre, Jülich, Germany, [3] Programming Environment Research Team, RIKEN Advanced Institute for Computational Science, Kobe, Japan, [4] Simulation Laboratory Neuroscience, Bernstein Facility for Simulation and Database Technology, Institute for Advanced Simulation, Jülich Aachen Research Alliance, Jülich Research Centre, Jülich, Germany, [5] Neural Computation Unit, Okinawa Institute of Science and Technology, Okinawa, Japan, [6] Laboratory for Neural Circuit Theory, RIKEN Brain Science Institute, Wako, Japan, [7] Department of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, RWTH Aachen University, Aachen, Germany, [8] Department of Physics, Faculty 1, RWTH Aachen University, Aachen, Germany*

- technology included in NEST 2.10.0
- collaboration of K computer and JUQUEEN teams
- benchmarking with Itaru Kitayama (AICS) and Brian Wylie (JSC Juelich)

# Distributed solver for gap-junction dynamics

- instantaneous interaction couples ODE-systems of single neurons
- iterative approach based on waveform relaxation technique required
- cubic approximation of membrane potentials



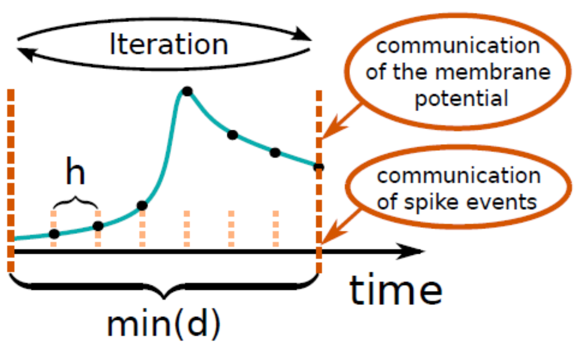

$I^i_{\text{gap}} = g_{ij}(V_j - V_i)$ $\quad$ $I^j_{\text{gap}} = g_{ij}(V_i - V_j)$

**Neuron $i$ (hh_psc_alpha_gap)**

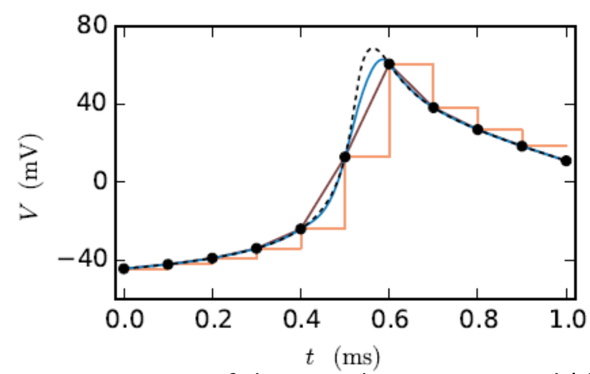
$$\frac{\dot{V}_i}{C_m} = -I^i_{\text{ionic}}(V_i, m_i, h_i, n_i, p_i) + I^i_{\text{applied}}(I^i_{\text{ex}}, I^i_{\text{in}}) + I^i_{\text{gap}}(V_i, V_j)$$

**Neuron $j$ (hh_psc_alpha_gap)**

$$\frac{\dot{V}_j}{C_m} = -I^j_{\text{ionic}}(V_j, m_j, h_j, n_j, p_j) + I^j_{\text{applied}}(I^j_{\text{ex}}, I^j_{\text{in}}) + I^j_{\text{gap}}(V_j, V_i)$$




membrane potential evolution during minimal delay of spike interactions, solved repeatedly until stopping criterion is met

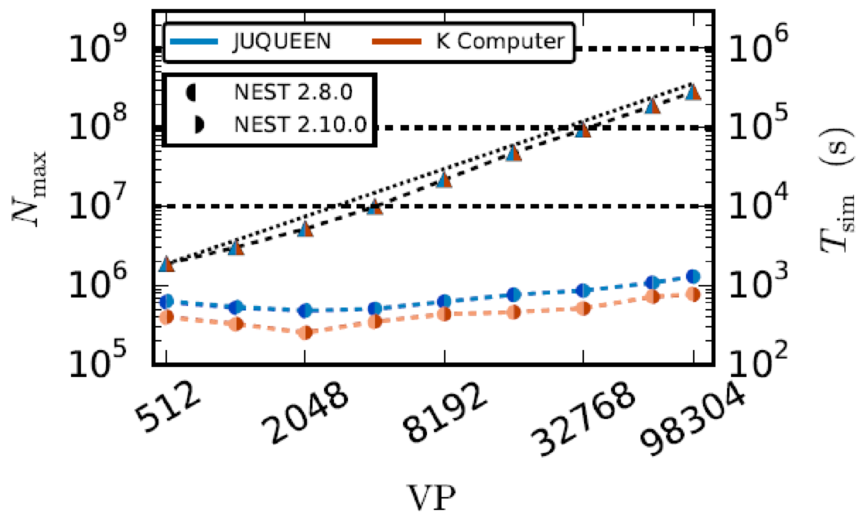



possible approximations of the membrane potential (dashed black curve) representing an action potential (spike), black dots indicate grid points

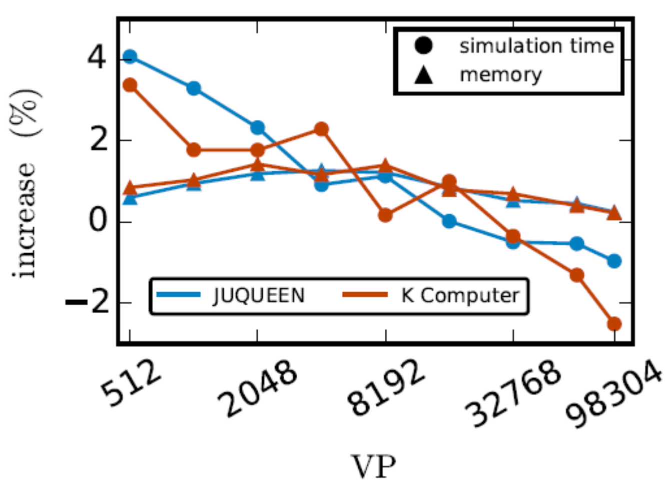
# Performance of gap junction code

## influence on simulations w/o gap junctions

max-filling of (Brunel, 2000) network

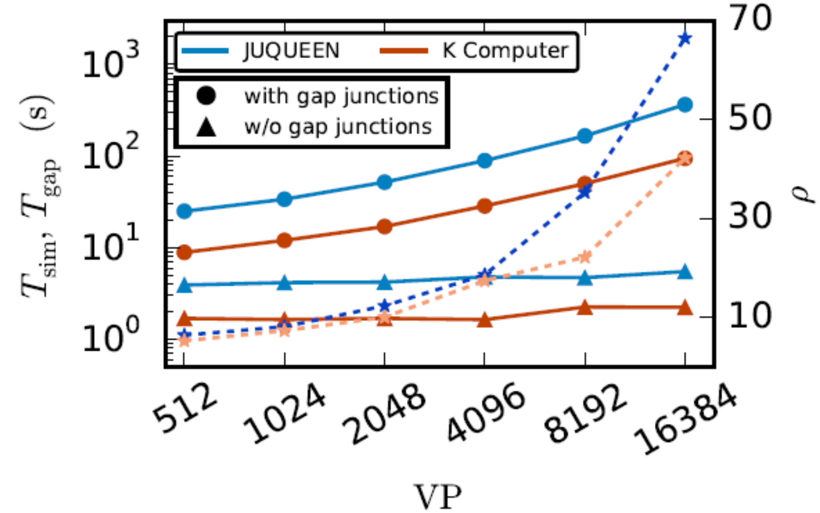



increase of memory/time in percent

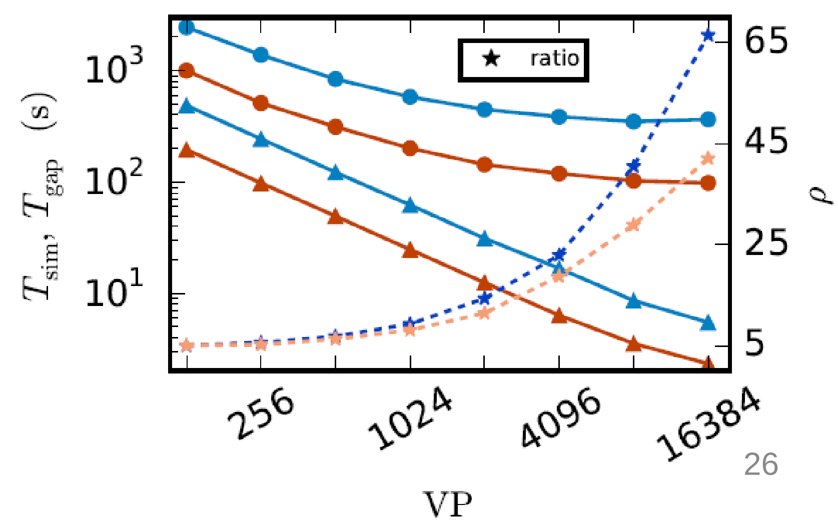



## costs of gap-junction dynamics

weak scaling with N = 185 x VP




strong scaling with N = 3,031,040



# Summary

- need for brain-scale models
  - increase self consistency
  - compute meso- and macroscopic measures of activity
- need for full-scale models
  - irreducibility of second order statistics
  - verify mean-field results
- machines ready for use by neuroscience (www.nest-initiative.org)
- K computer and JUQUEEN well suited for brain simulations
- neuroscience results for model of macaque monkey visual cortex
- biological mechanism “gap junction” (electrical synapse) available
  - hard problem due to continuous interaction
  - evaluated in MoU AICS–Jülich

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van Albada SJ, Helias M, Diesmann M PLoS Comput Biol (2015) 11(9):e1004490

Hahne J, Helias M, Kunkel S, Igarashi J, Matthias B, Frommer A, Diesmann M (2015) Front Neuroinform 9:22

Schuecker J, Schmidt M, van Albada SJ, Diesmann M, Helias M (2016) arXiv:1509.03162

Schmidt M, Bakker R, Shen K, Bezgin G, Hilgetag CC, Diesmann M, van Albada SJ (2016) arXiv:1511.09364