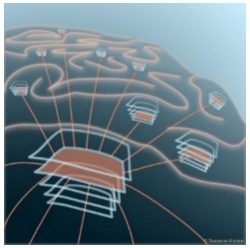
LARGE-SCALE SPIKING NEURAL NETWORK MODELING OF PRIMATE CEREBRAL CORTEX

OSB workshop, 6 Sep 2019 | Sacha van Albada

Institute of Neuroscience and Medicine (INM-6), Jülich Research Centre

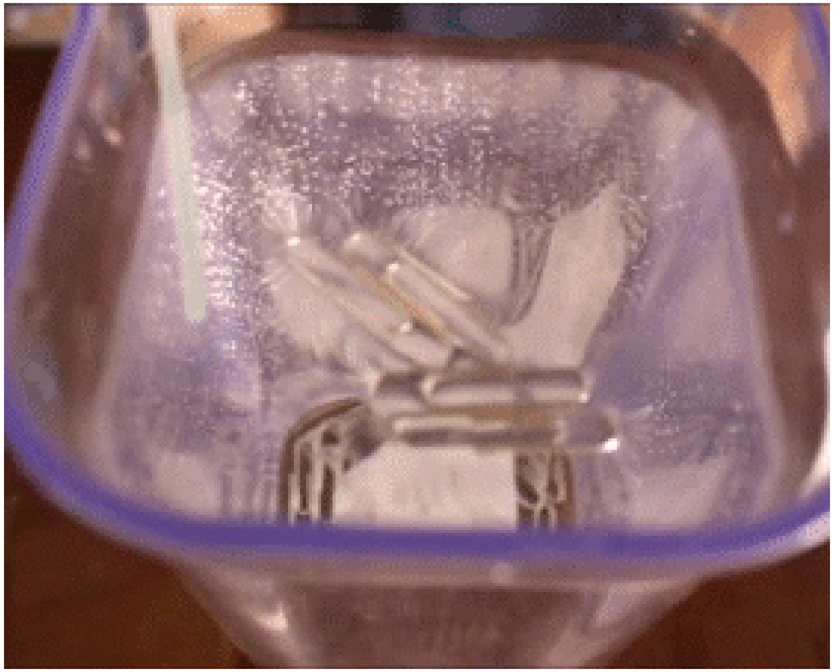


JÜLICH
Forschungszentrum

WHY BASIC BRAIN MODELS

as a stepping stone toward understanding brain function

Explaining how a water strider stays afloat requires knowledge of a basic property of water: surface tension.



In the wrong parameter regime (say, soapy water) we would predict that the water strider would sink.

Analogously, we need a good basic model of the brain as a physical system to gain insight into its function and dysfunction.

JÜLICH Forschungszentrum

NEED FOR MULTI-SCALE MODELS: LINKS TO EXPERIMENT

brain-scale networks basis for various measures by forward modeling

mesoscopic measures

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

and macroscopic measures

- EEG, MEG
- fMRI resting-state networks

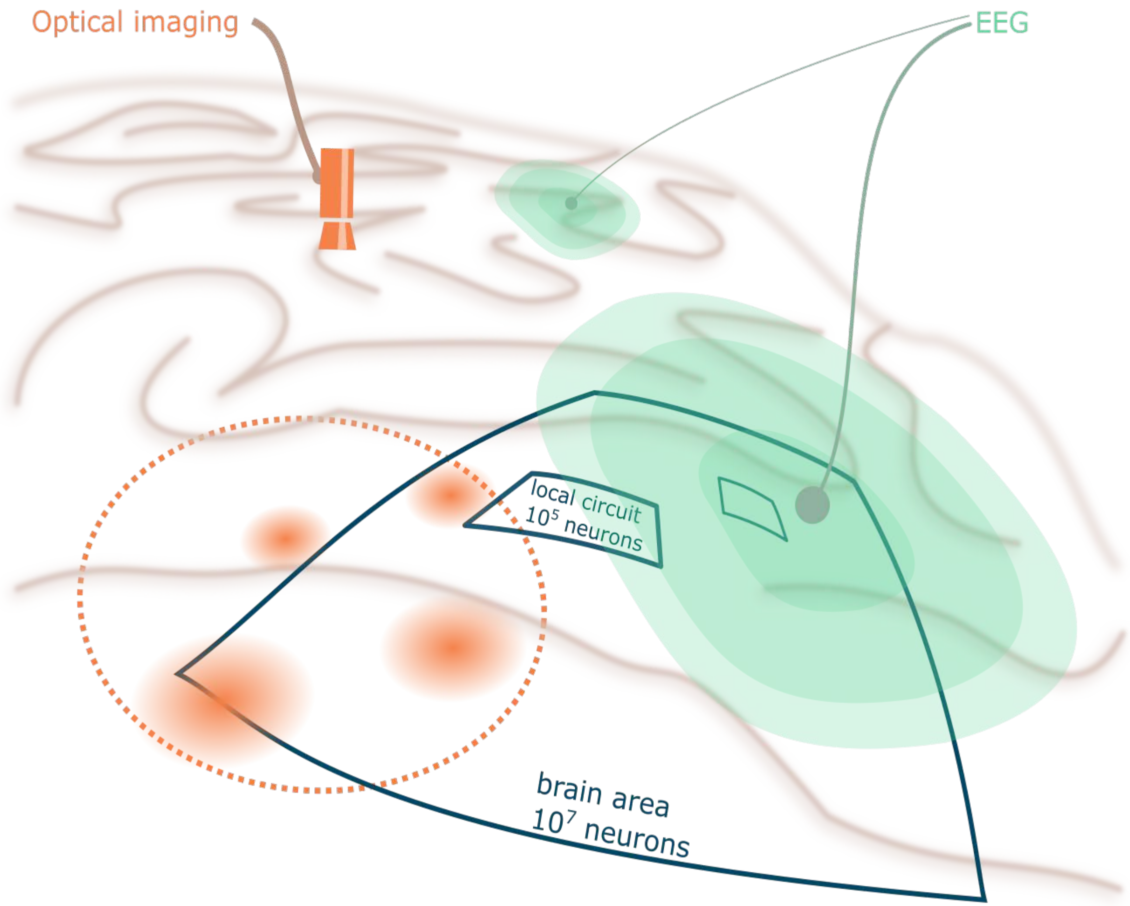
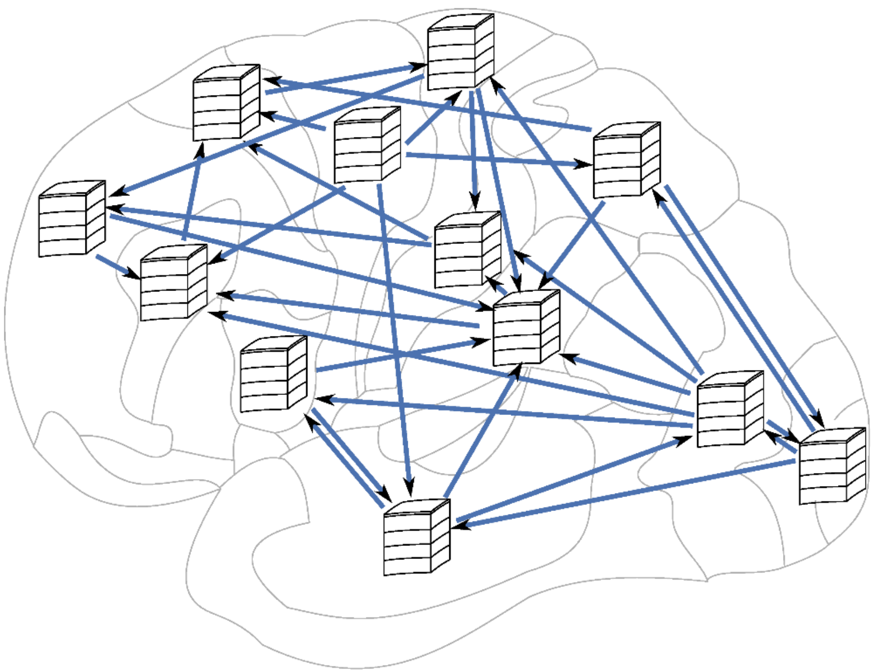


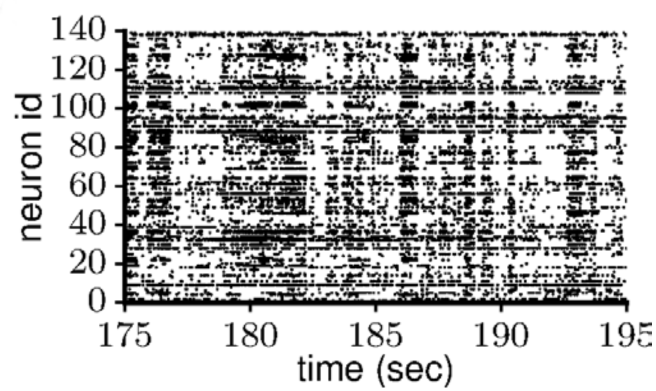
Figure by Susanne Kunkel

GOAL

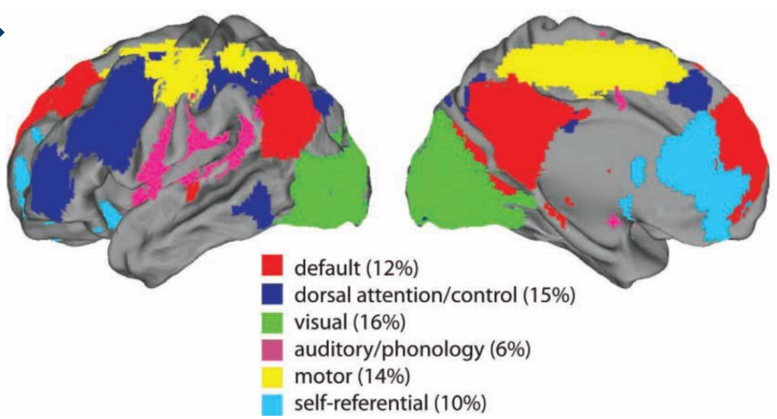


cortical connectivity

?



Chu et al. (2014) *Vision Res*

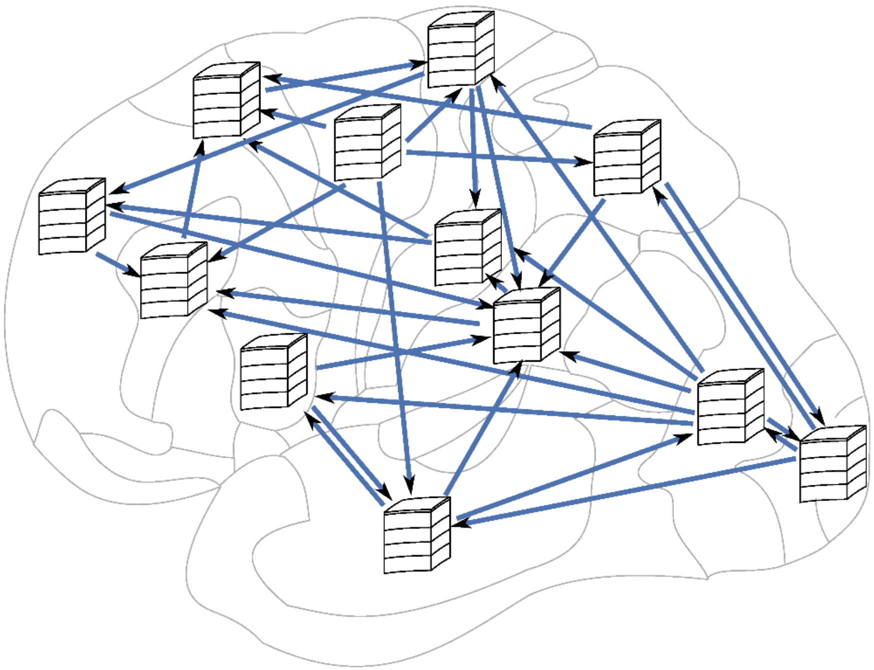


Deco and Corbetta (2011)
The Neuroscientist

multi-scale resting-state dynamics

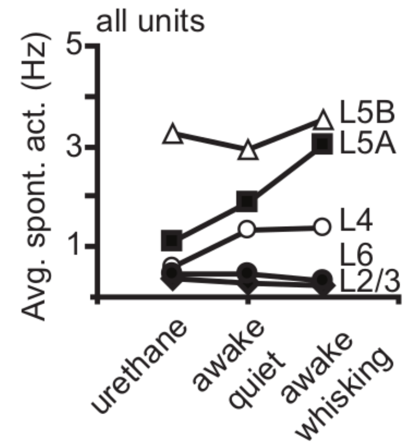
JÜLICH Forschungszentrum

GOAL



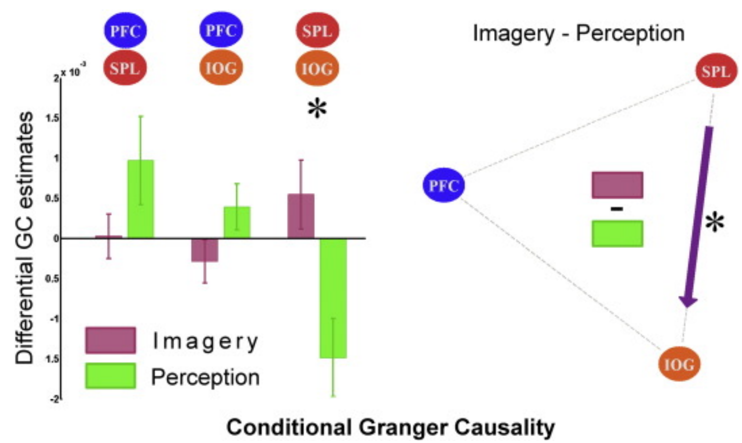
cortical connectivity

?



De Kock & Sakmann (2009) *PNAS*

cell-type specific spike rates



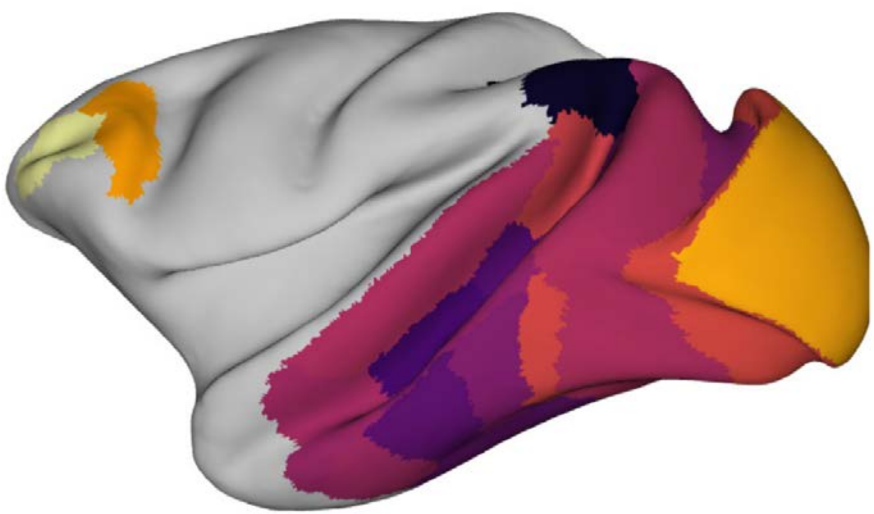
Dentico et al. (2014) *NeuroImage*

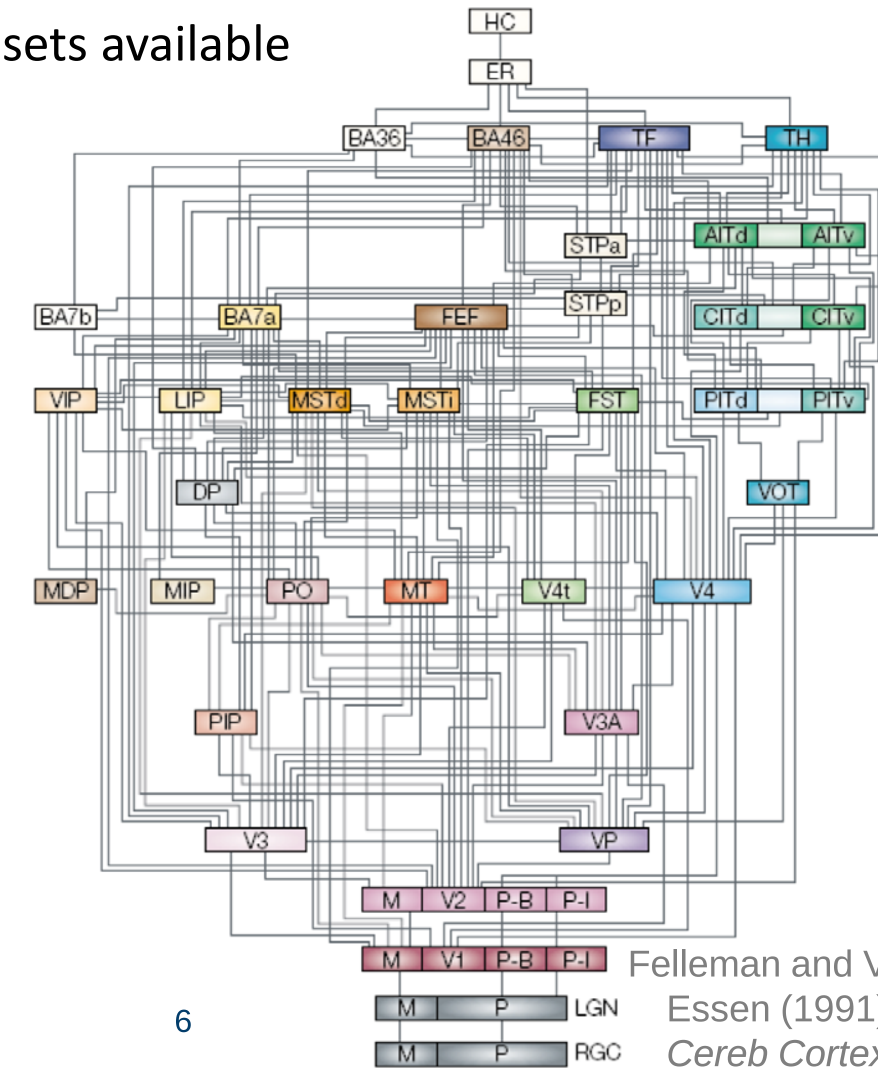
inter-area propagation

JÜLICH Forschungszentrum

MULTI-AREA MODEL OF MACAQUE VISION-RELATED CORTEX

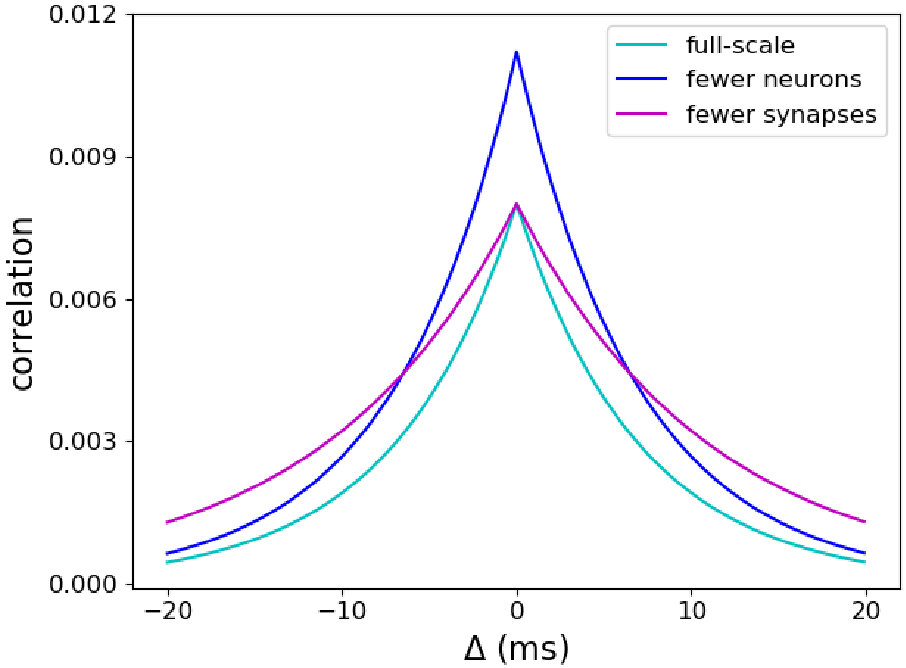
- rich anatomical and physiological data sets available
- stepping stone to human
- regularities of organization





Felleman and Van Essen (1991) *Cereb Cortex*

IRREDUCIBILITY OF NETWORK MODELS



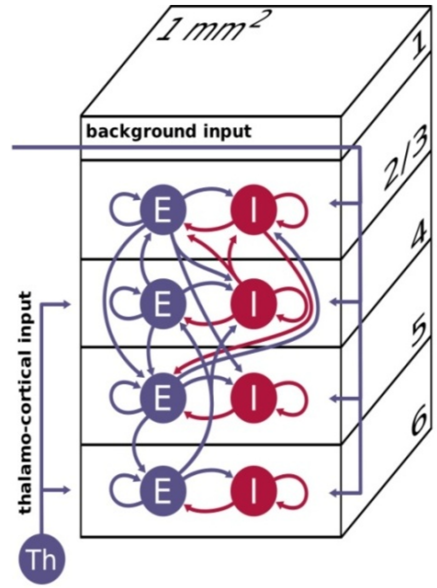
- downscaling changes dynamics
    - reducing number of neurons increases correlations
    - reducing number of synapses changes correlation shapes

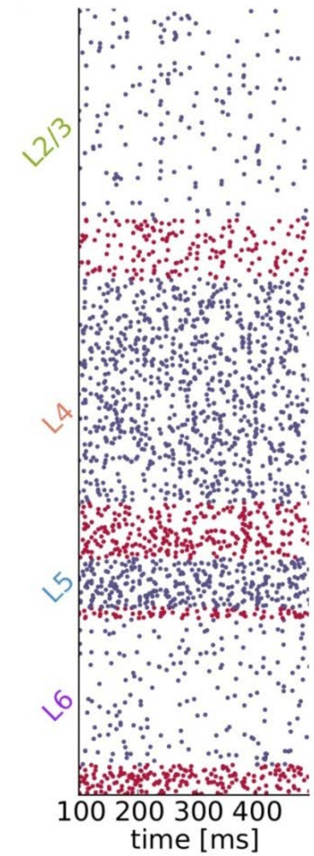
van Albada SJ, Helias M, Diesmann M (2015) *PLOS CB*

JÜLICH Forschungszentrum

MINIMAL LAYERED CORTICAL NETWORK MODEL

- 1 mm^2 cortical surface
- excitatory (E) and inhibitory (I) populations of point neurons in each layer
- layer- and type-specific connection probability
- integrates knowledge of > 50 experimental papers





available as a part of NEST and PyNN, and at www.opensourcebrain.org Gleeson et al. (2019) *Neuron*

reproduced with Brian and NetPyNE/NEURON Shimoura et al. (2018) *ReScience*
https://github.com/ceciliaromaro/PD_in_NetPyNE

ported to SpiNNaker
van Albada et al. (2018) *Front Neurosci*

Cerebral CORTEX

The Cell-Type Specific Cortical Microcircuit: Relating Structure and Activity in a Full-Scale Spiking Network Model

Tobias C. Potjans, Markus Diesmann

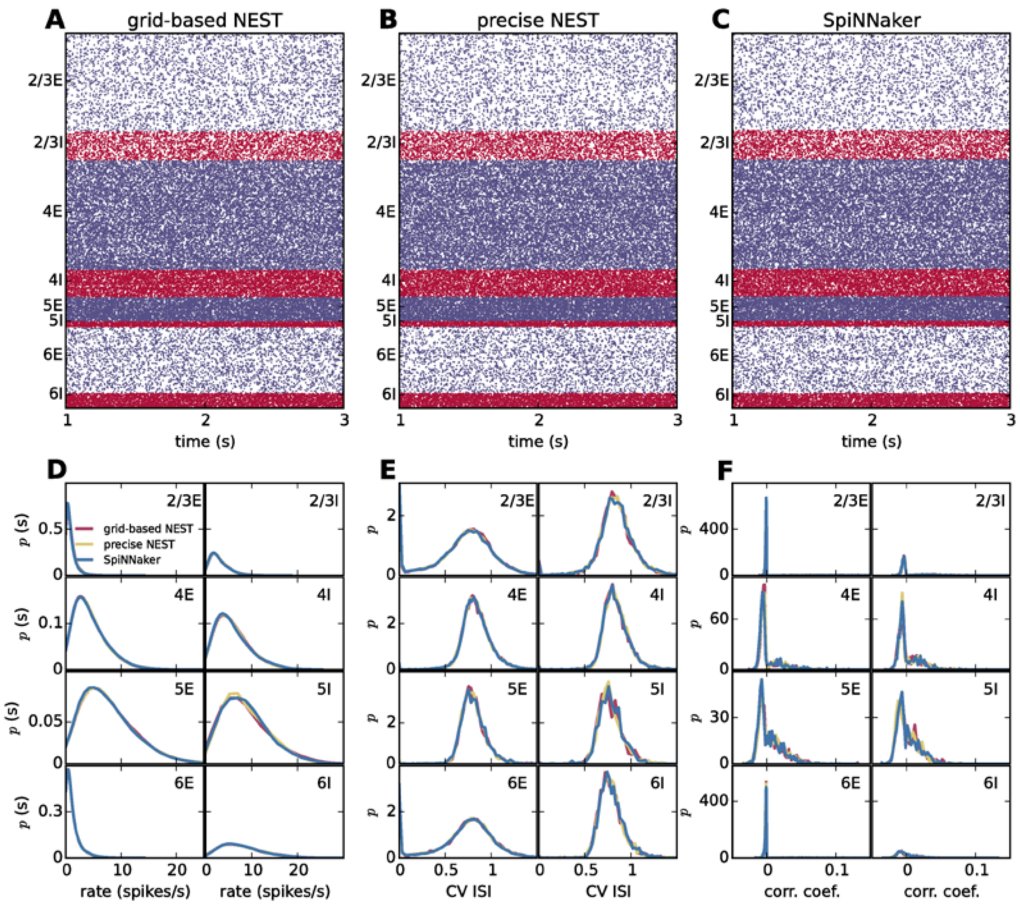
Cerebral Cortex, Volume 24, Issue 3, 1 March 2014, Pages 785–806,
https://doi.org/10.1093/cercor/bhs358

nest::

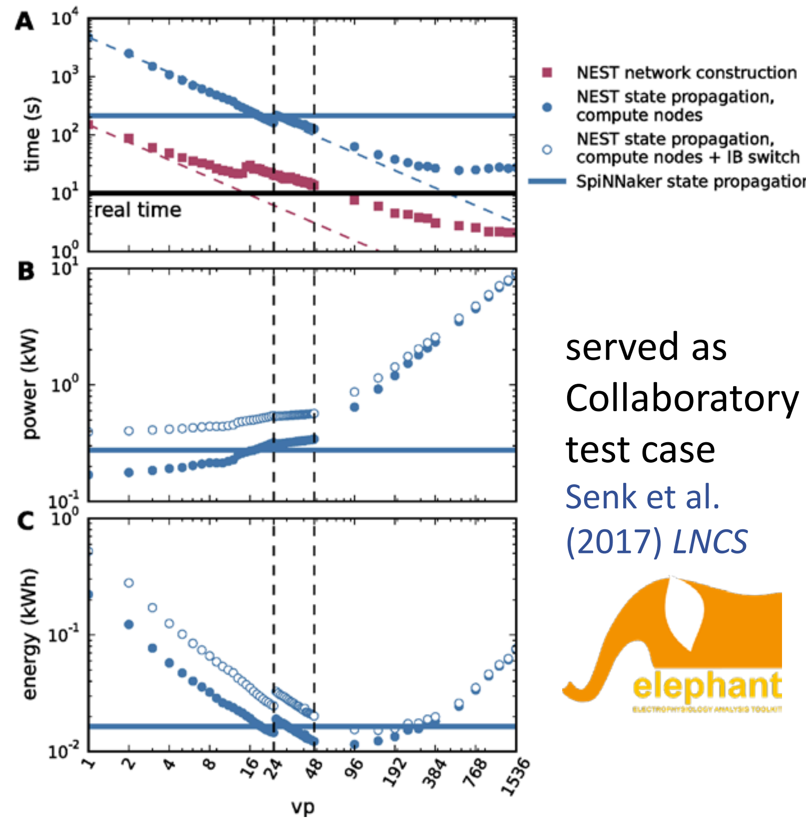
JÜLICH Forschungszentrum

MICROCIRCUIT PORTED TO SPINNAKER

first full-density simulation of cortical microcircuit on SpiNNaker (6 boards)



van Albada, Rowley, Senk, Hopkins, Schmidt, Stokes, Lester, Diesmann, Furber (2018) *Front Neurosci*

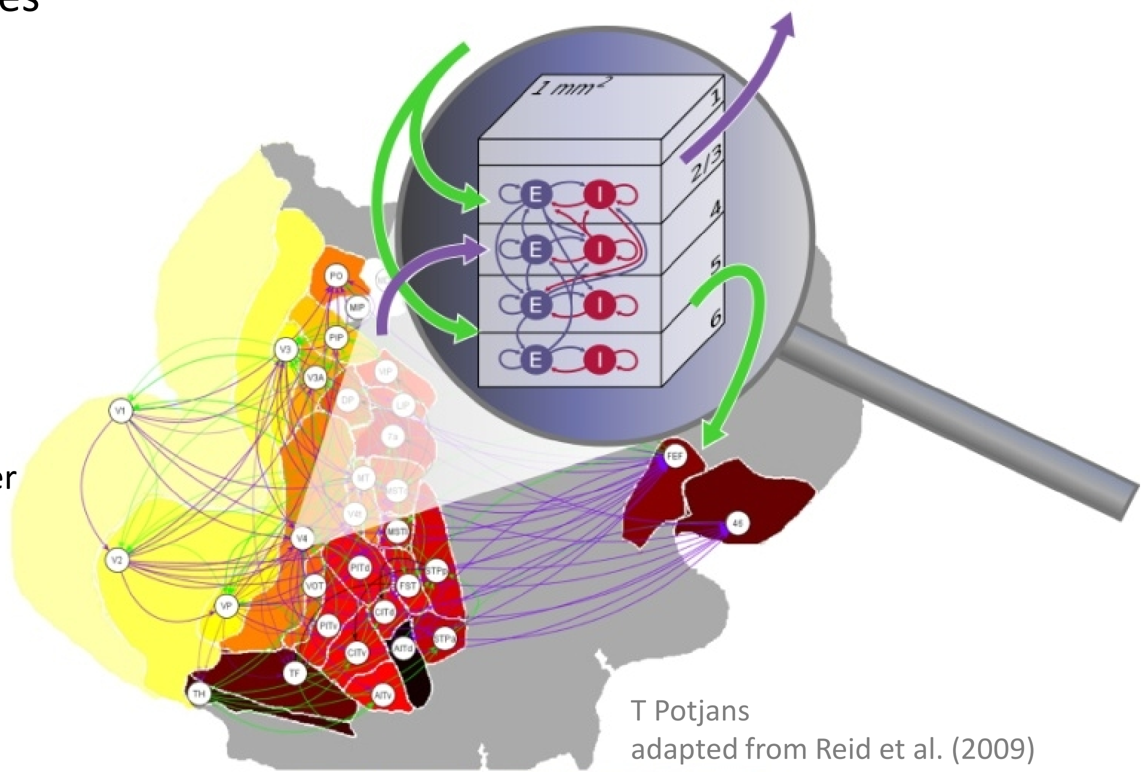


served as Collaboratory test case
Senk et al. (2017) *LNCS*

SpiNNaker and optimally parallelized NEST have comparable total energy consumption during run phase

MULTI-AREA MODEL OF MACAQUE VISUAL CORTEX

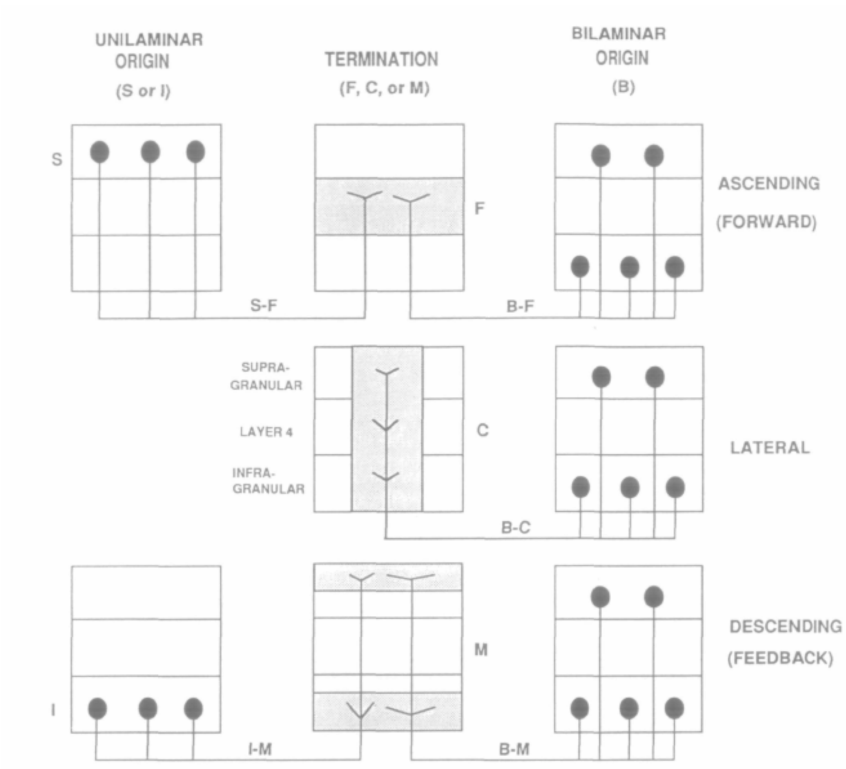
- 800 million neurons in one hemisphere
- 32 areas in Felleman & Van Essen parcellation
- representing each area by a 1 mm^2 microcircuit
- $4{\cdot}10^6$ neurons and $2.4{\cdot}10^{10}$ synapses
- simulated using NEST on Jülich supercomputers
  - $\sim 10^3$ MPI processes, multi-threaded
  - a few minutes for 1 s of simulation
  - largest version we ran: $2 \cdot 10^7$ neurons
  - simulating all 800 million neurons would approximately fill an entire supercomputer

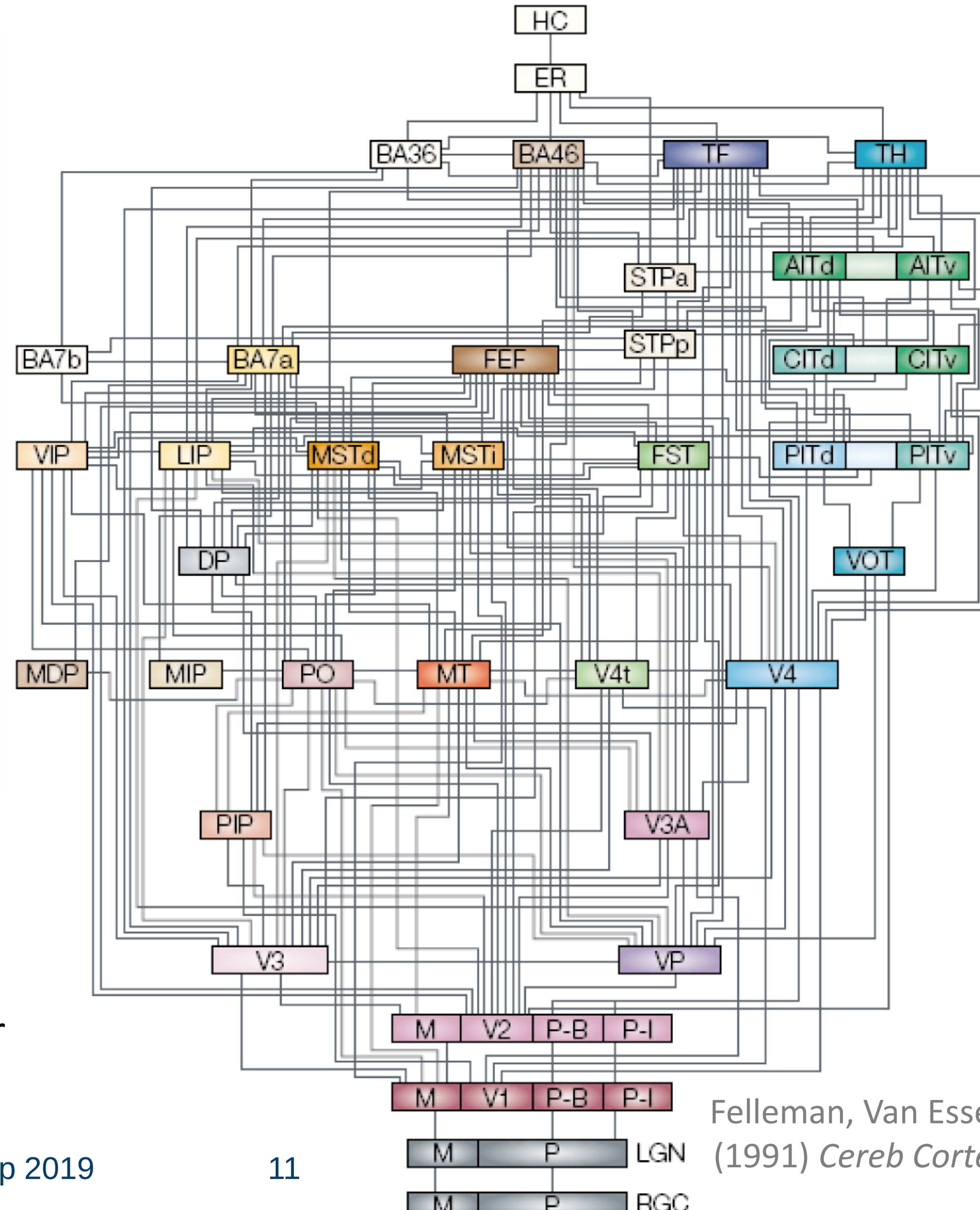


T Potjans
adapted from Reid et al. (2009)

Schmidt M, Bakker R, Shen K, Bezgin G, Diesmann M, van Albada SJ (2018) *PLOS CB*

HIERARCHY OF VISUAL CORTICAL AREAS





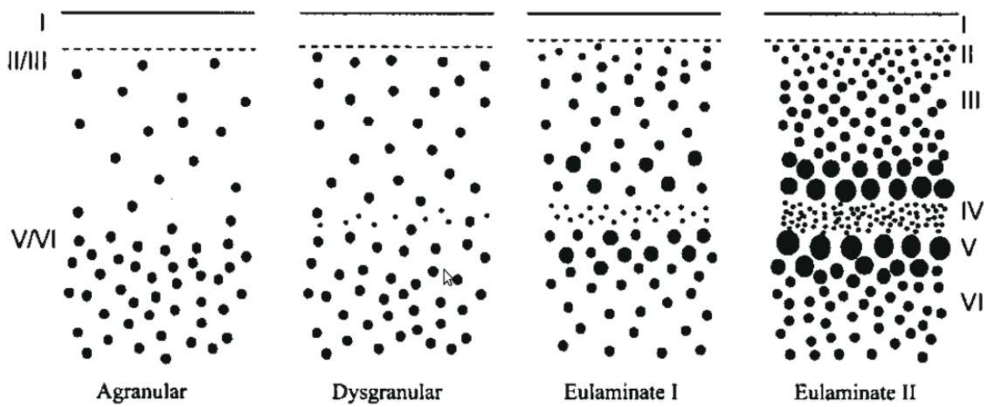
Felleman, Van Essen (1991) *Cereb Cortex*

- this is only one of thousands of possible orderings fitting the pairwise connection patterns equally well Hilgetag et al., 1996
- alternatively, can use `architectural types' or neuron densities to define hierarchy

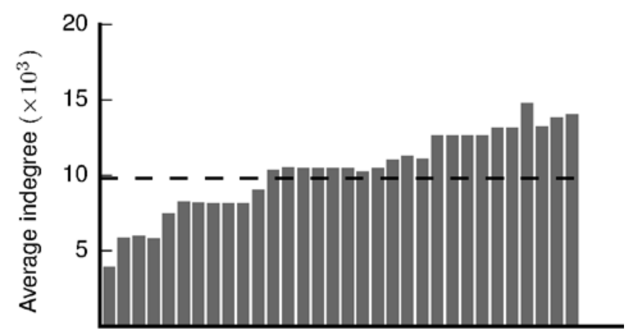
CORTICAL AREAS ARE NOT ALL THE SAME

- architectural types
  - neuron densities and layer 4 thickness decrease up the hierarchy
  - total cortical thickness increases up the hierarchy

examples of architectural types



Dombrowski et al. (2001) *Cereb Cortex*



high neuron density → low neuron density

- synapse density remains roughly constant

→ higher areas receive more synapses per neuron

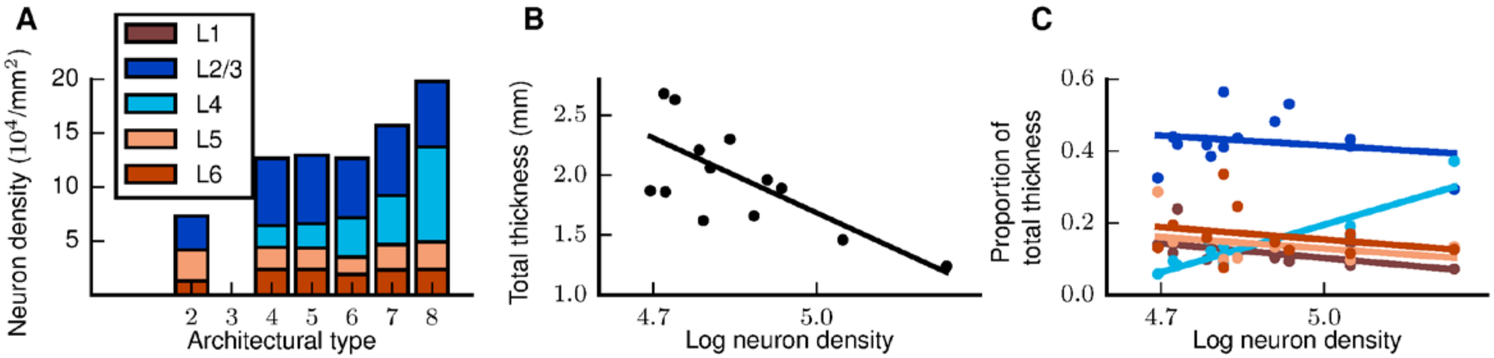
review on relationship between cortical architecture and connectivity:
Hilgetag, Beul, van Albada, Goulas (2019) *Network Neurosci*

DETERMINATION OF POPULATION SIZES

- total cortical thicknesses and overall neuron densities for 14 areas
- estimated for remaining areas based on architectural types

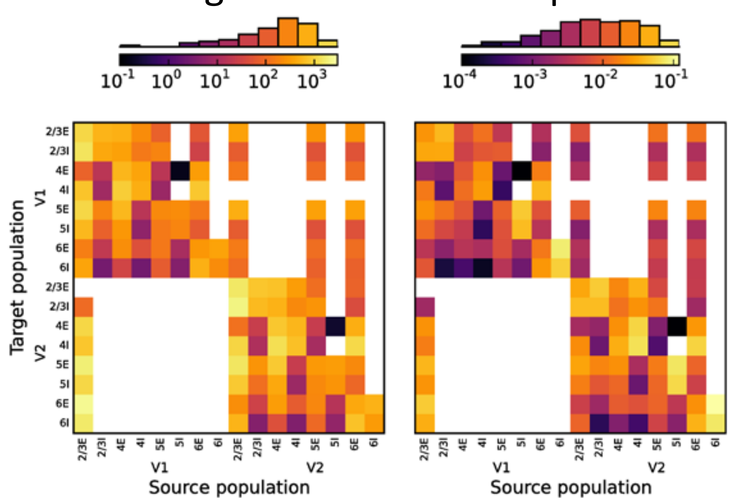
} Hilgetag et al. (2016) *NeuroImage*

- reduction in L4 thickness toward higher areas based on micrographs from the literature



- knowing population sizes is important for simulations
- enables translating between different measures of connectivity

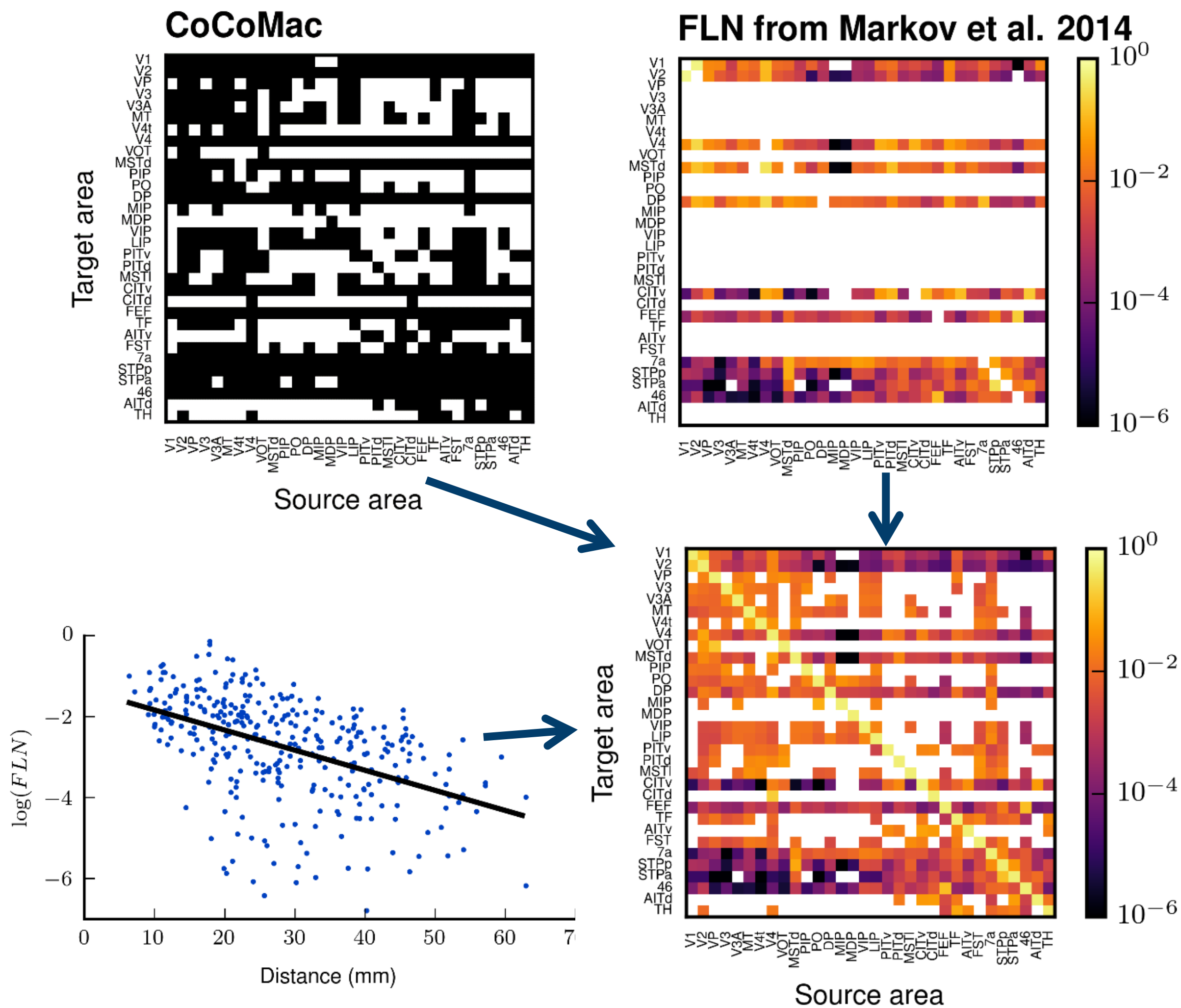
indegrees connection probabilities



JÜLICH Forschungszentrum

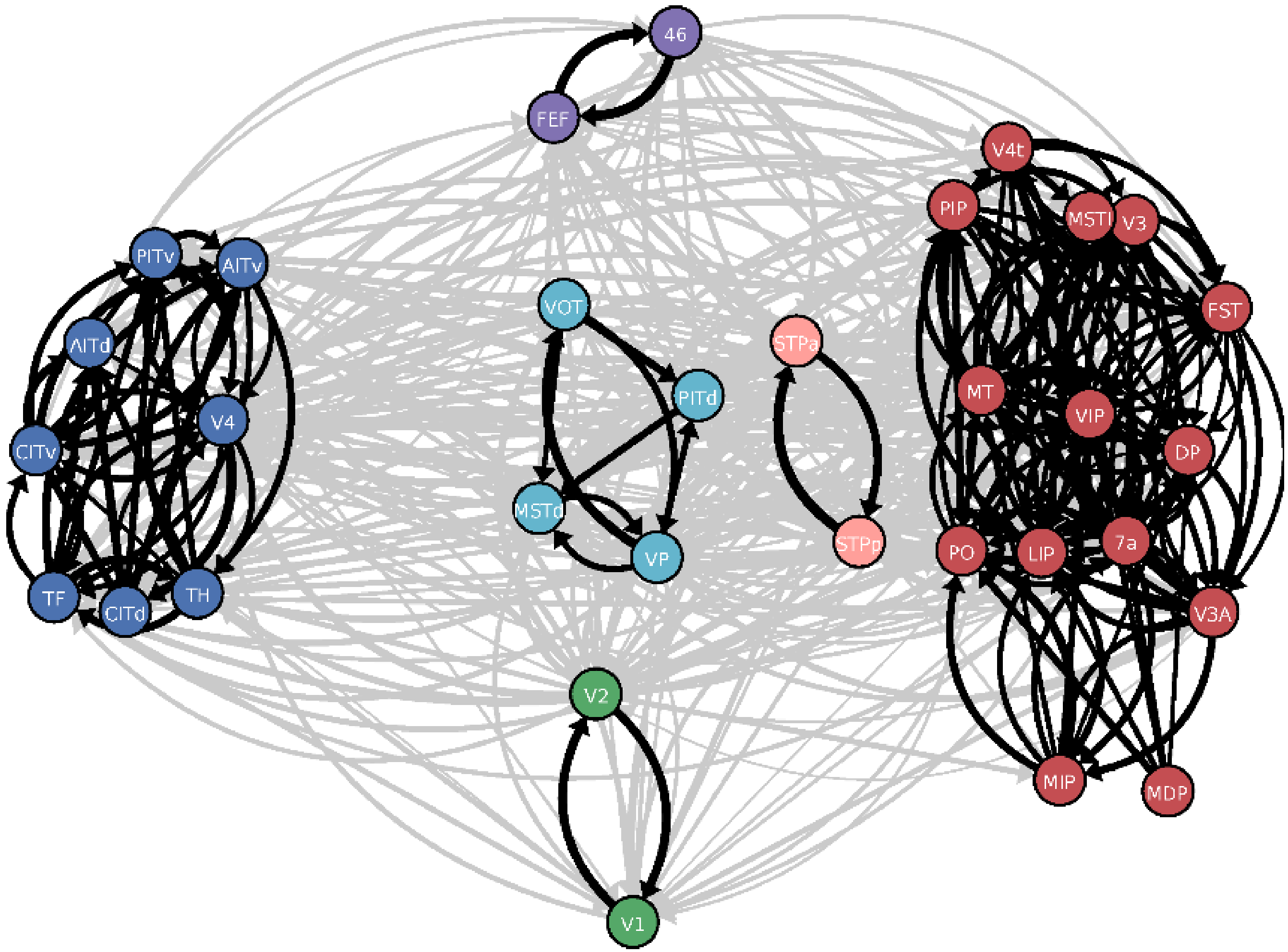
CONNECTIVITY MAP FROM TRACING DATA

- partly binary, partly quantitative data
- connection probability decays with distance also for inter-area connections
- use this decay to estimate missing data based on distance between areas
- roughly 2/3 of area pairs are connected
- more important: connection density, spanning ~6 orders of magnitude



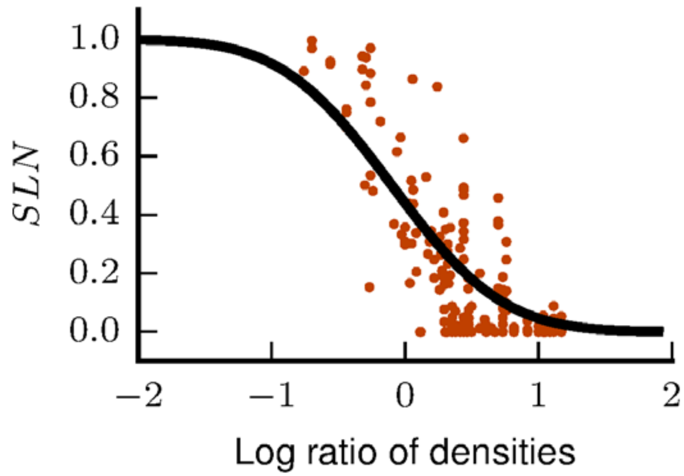
Ercsey-Ravasz et al. (2013) *Neuron*

PLAUSIBILITY CHECK

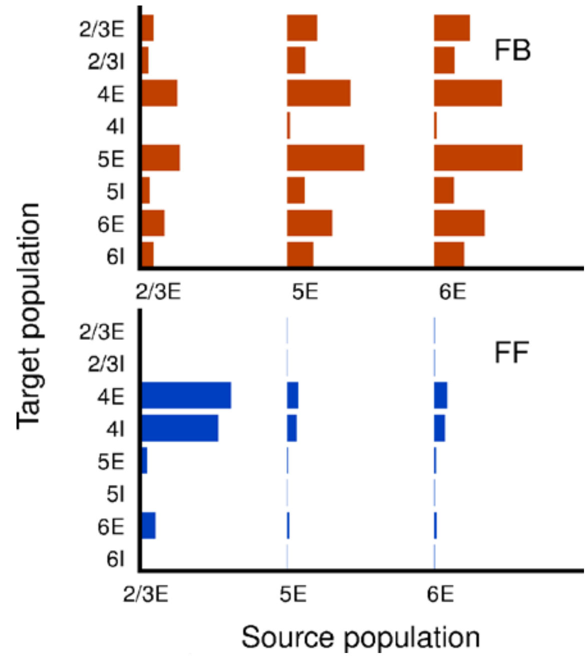


structural connectivity exhibits functionally relevant community structure

LAMINAR PATTERNS



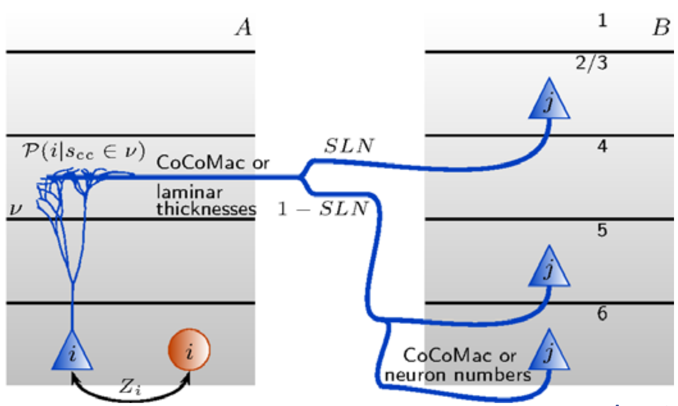
SLN = fraction of supragranular labeled neurons

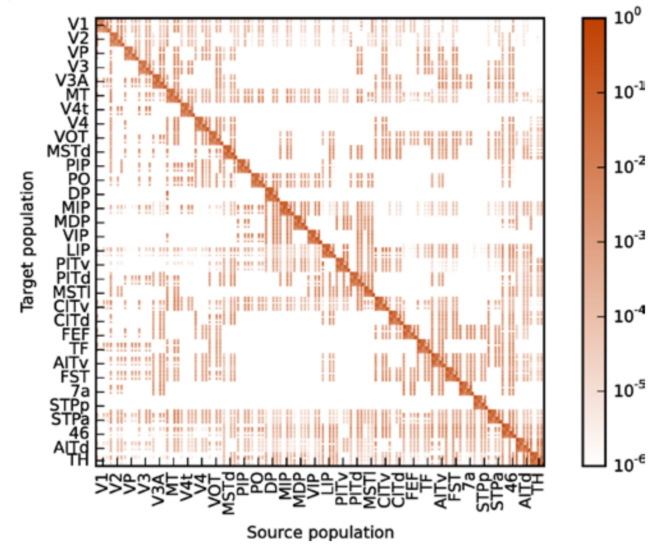


statistical mapping of synapses to target cell bodies according to Binzegger et al. (2004) cat V1 morphologies

→ substantial feedback onto L4 pyramidal neurons

realistic?

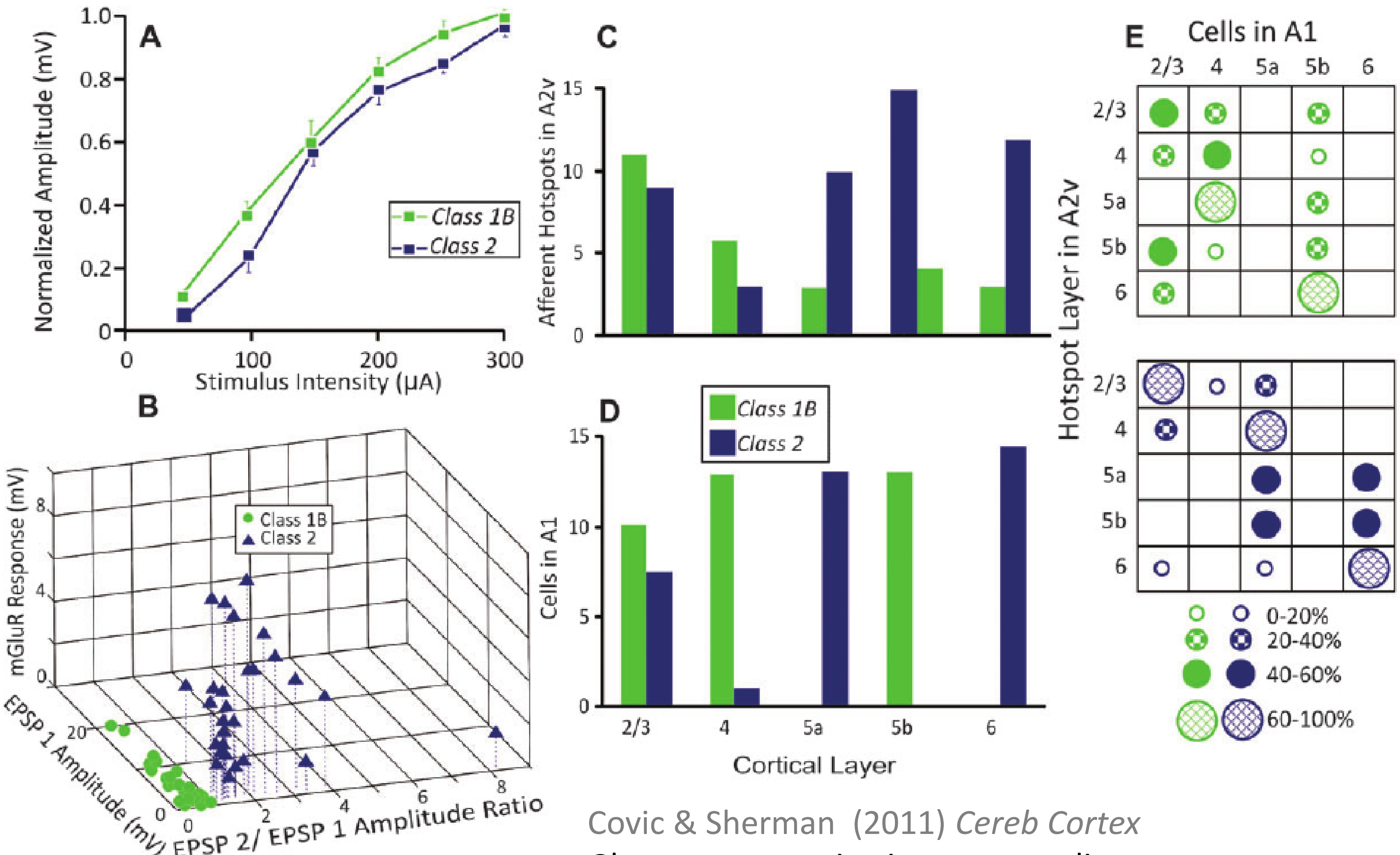




Schmidt M, Bakker R, Hilgetag CC, Diesmann M, van Albada SJ (2018) *Brain Struct Func*

JÜLICH Forschungszentrum

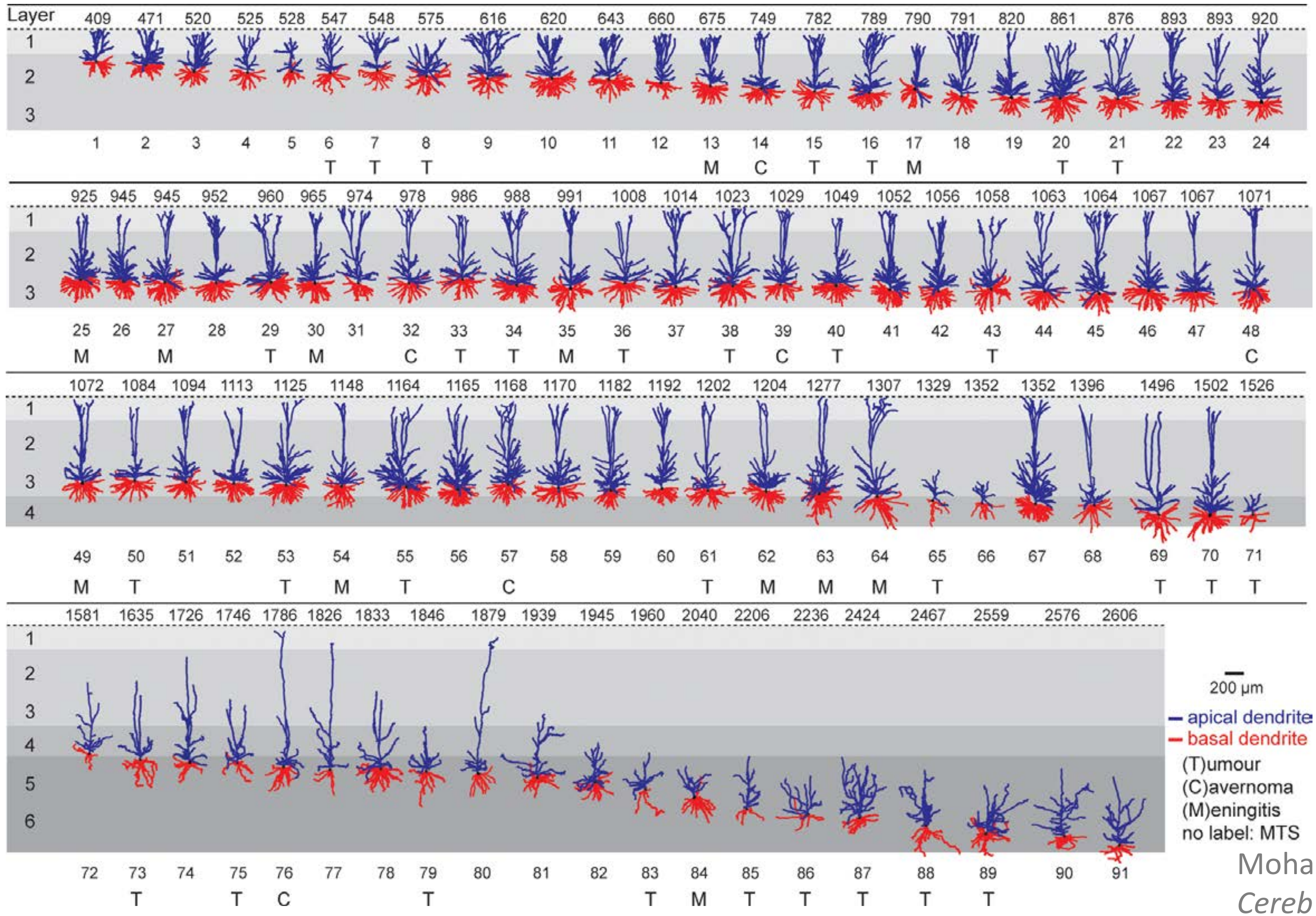
FEEDBACK ONTO L4 NEURONS IN MOUSE



Covic & Sherman (2011) *Cereb Cortex*

Glutamate uncaging in mouse auditory cortex

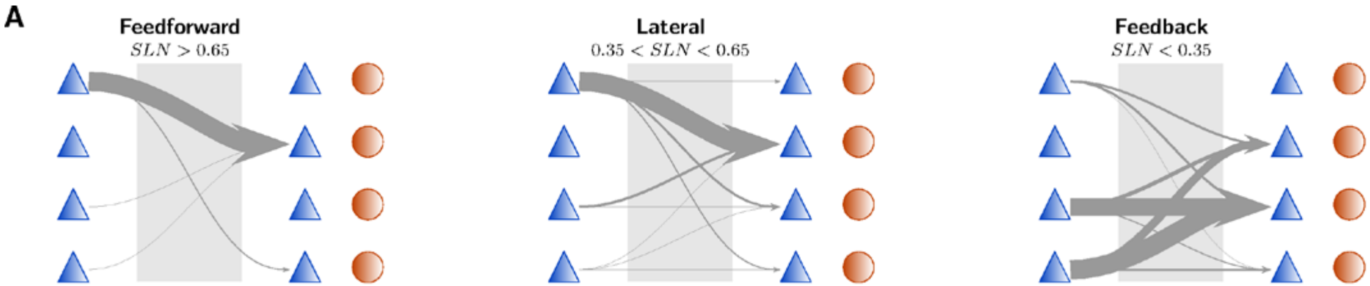
HUMAN NEURON MORPHOLOGIES



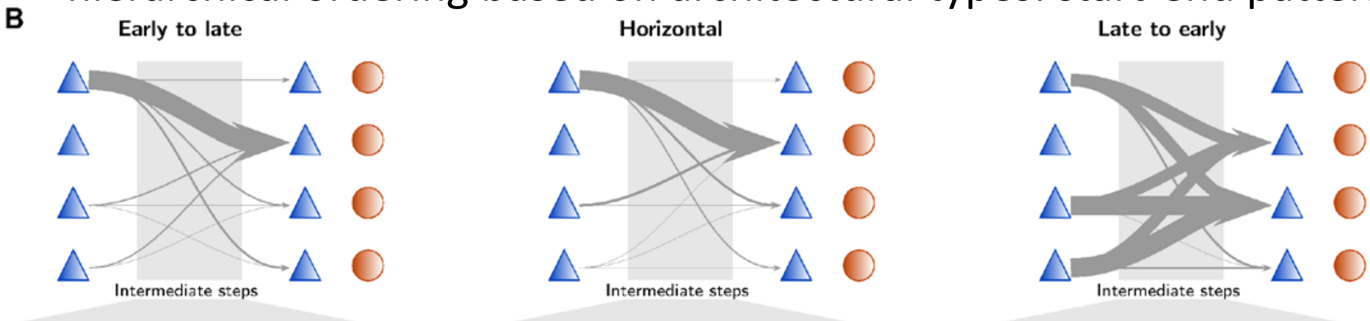
Mohan et al. (2015)
Cereb Cortex

LAYER-SPECIFIC STRONGEST PATHS

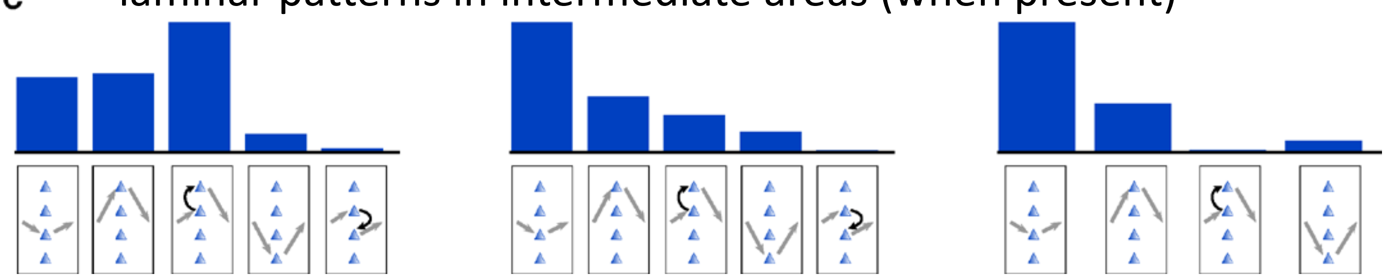
hierarchical ordering based on laminar source patterns: direct connections



hierarchical ordering based on architectural types: start-end patterns



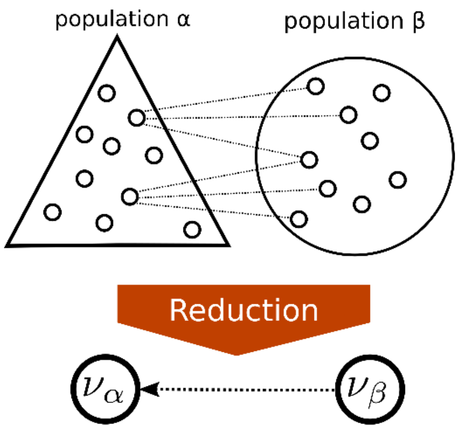
C laminar patterns in intermediate areas (when present)

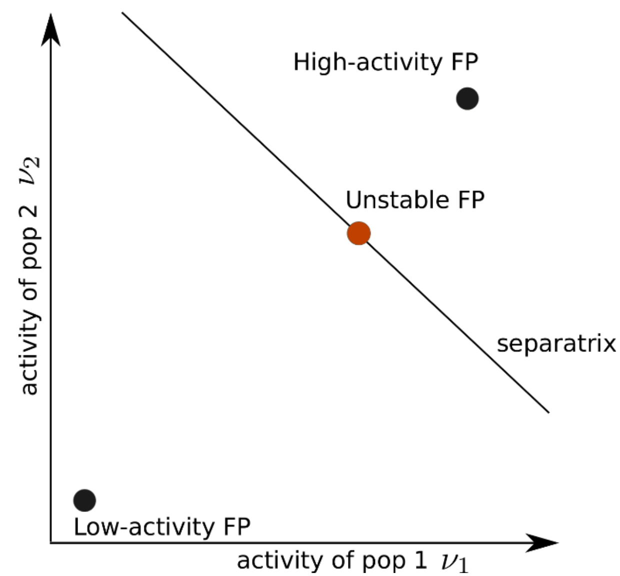


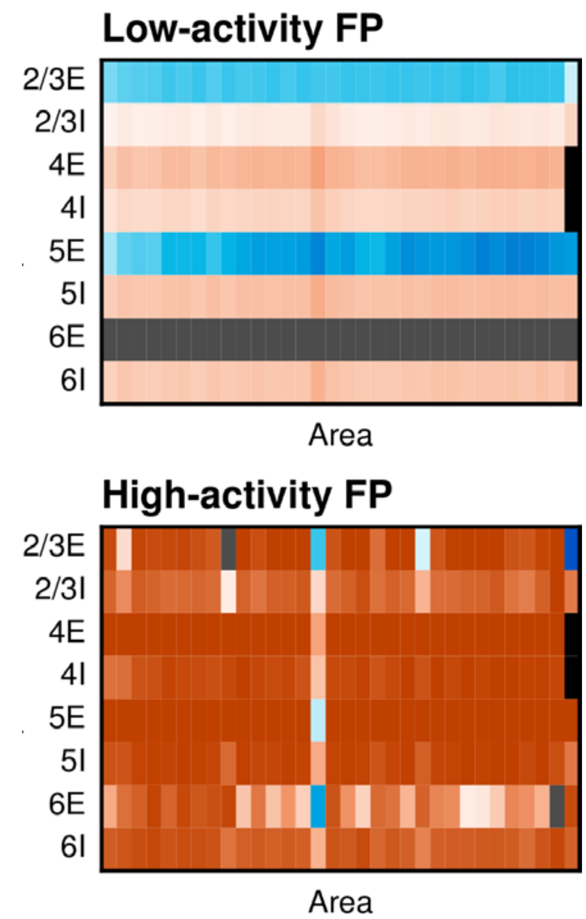
JÜLICH Forschungszentrum

BISTABLE GROUND STATE

- low rates of excitatory neurons in infragranular layers
- increasing external drive leads to high-activity state with excessive rates





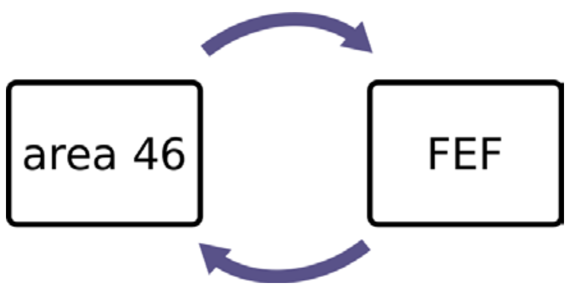


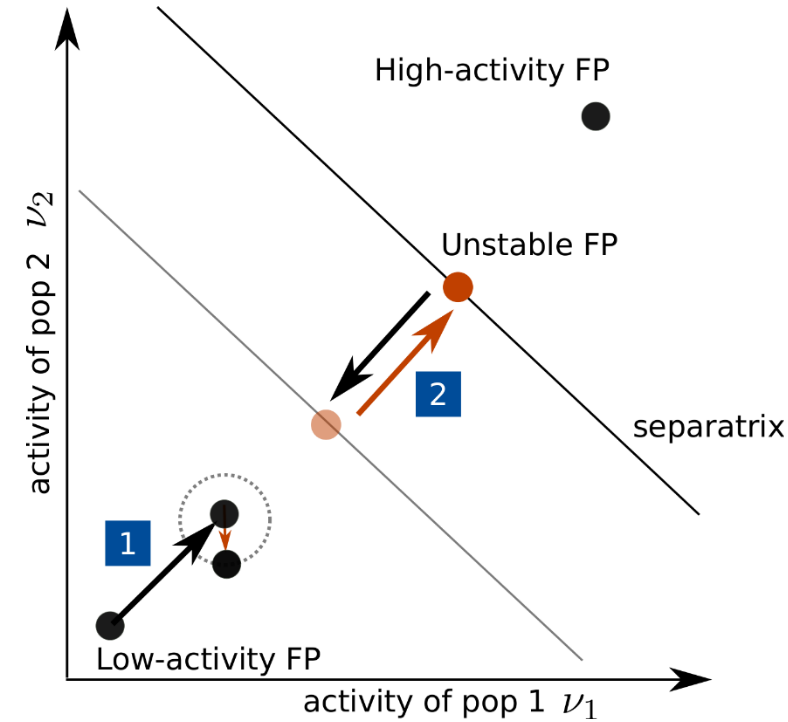
JÜLICH Forschungszentrum

STABILIZATION USING MEAN-FIELD THEORY

1) increase in external drive shifts both low-activity fixed point and separatrix
2) compensation by change in connectivity shifts back separatrix

- yields reasonable rates in all populations
- reduced connectivity in frontal loop

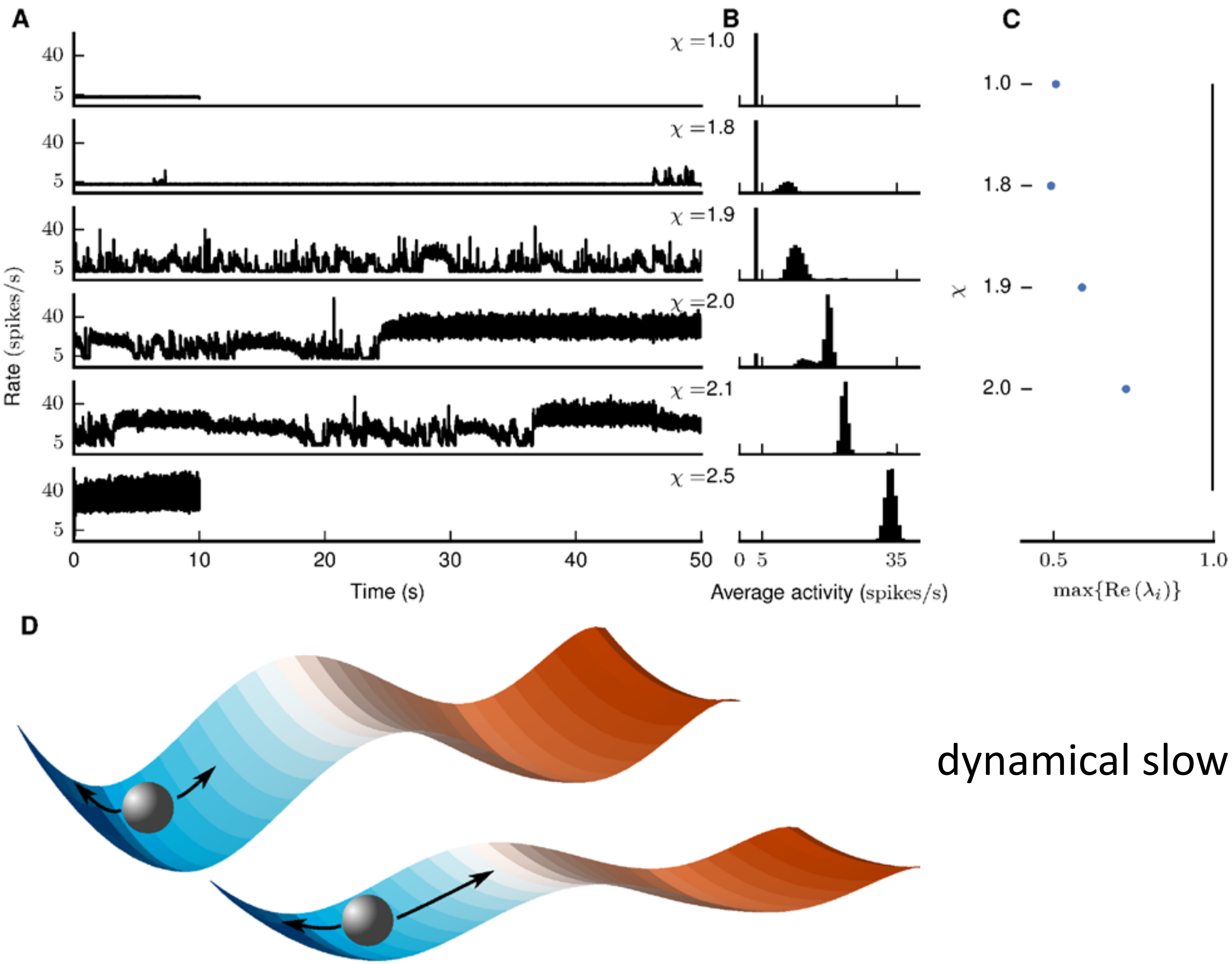




Schuecker J, Schmidt M, van Albada SJ, Diesmann M, Helias M (2017) *PLOS CB*

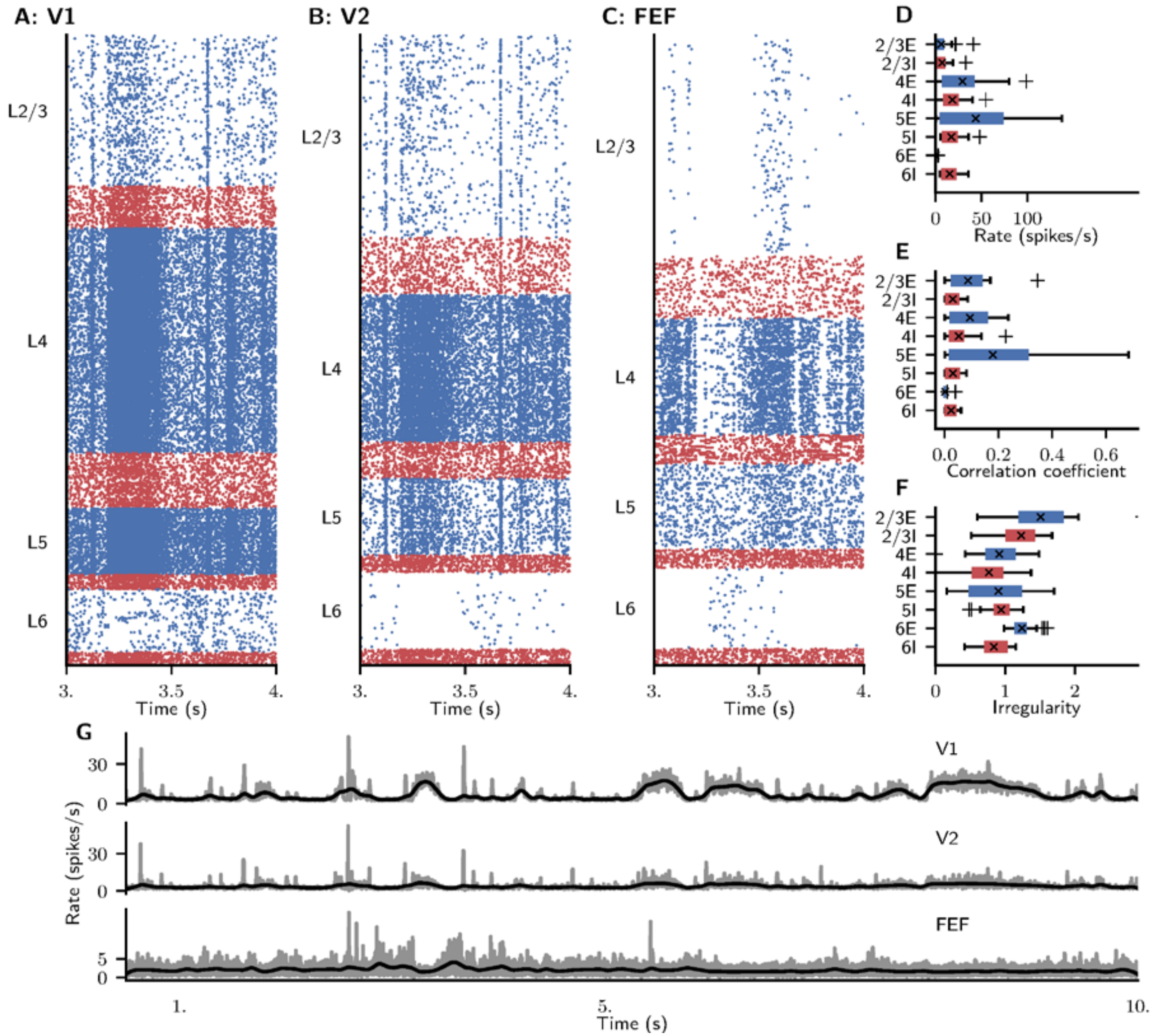
JÜLICH Forschungszentrum

INTER-AREA INTERACTIONS CAUSE SLOW FLUCTUATIONS

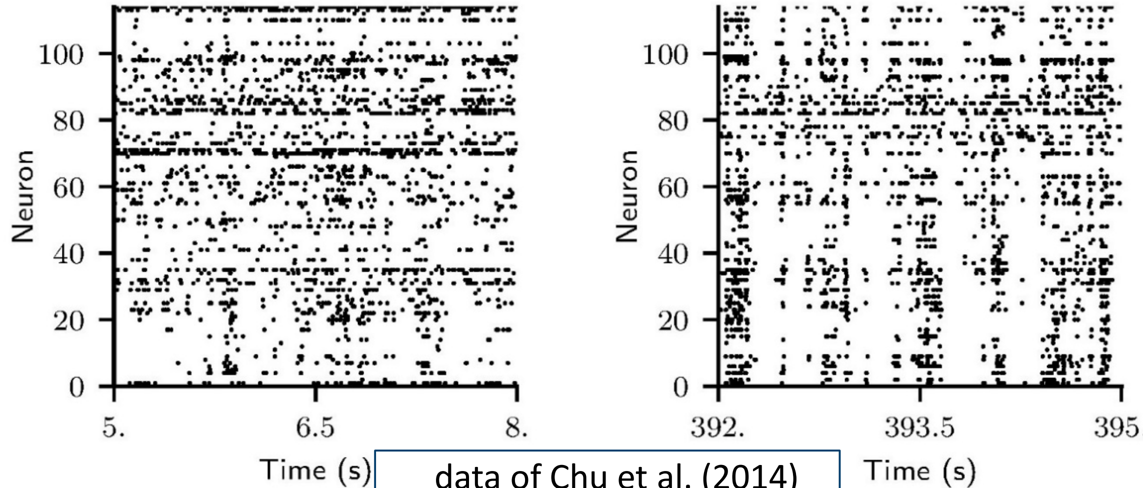


dynamical slowing near instability

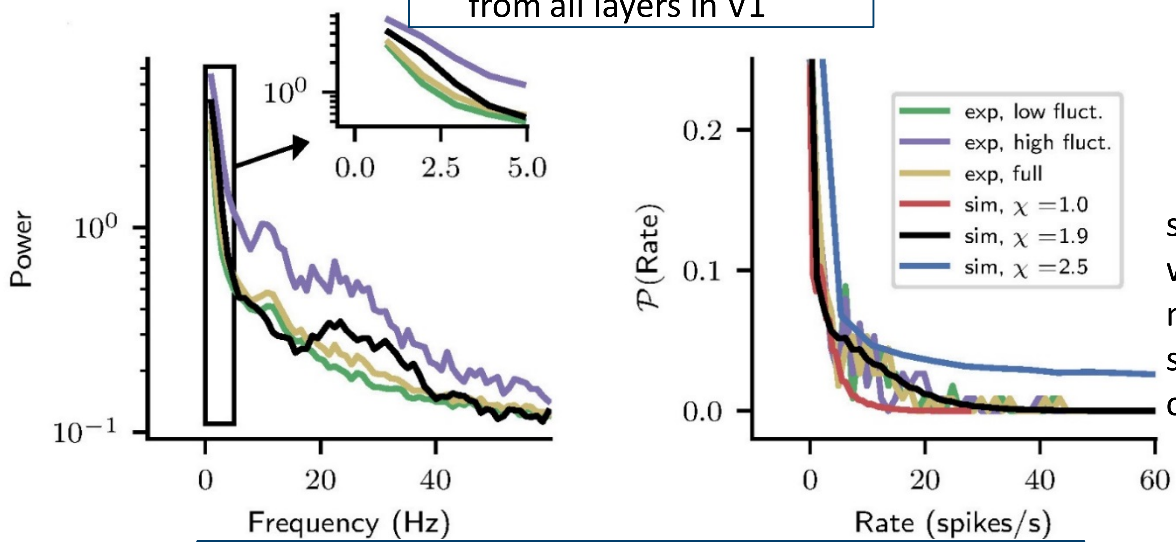
GROUND STATE WITH MULTIPLE TIME SCALES



V1 SPIKING STATISTICS



data of Chu et al. (2014)
from all layers in V1



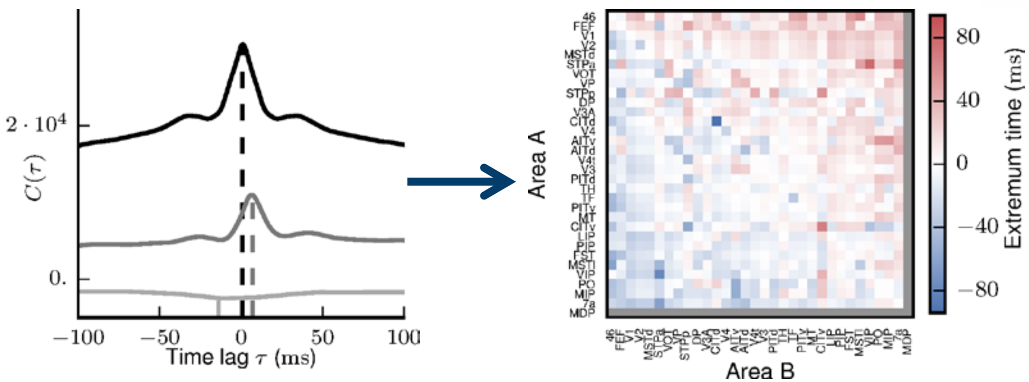
experiment
simulation

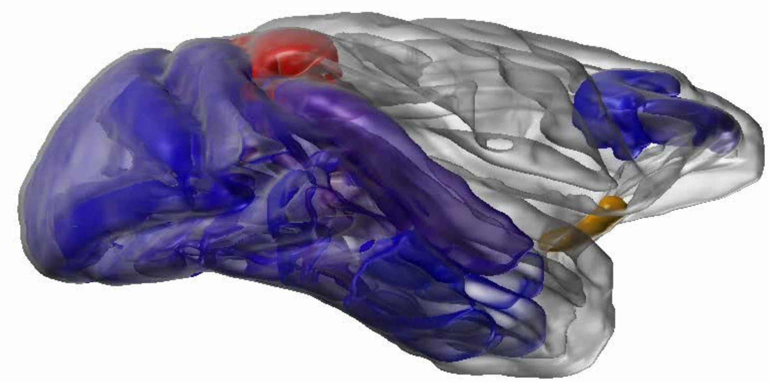
simulations with
weak (red),
medium (black/gray),
strong (blue)
cortico-cortical interactions

comparison of power spectra and rate distributions
between simulation and experiment

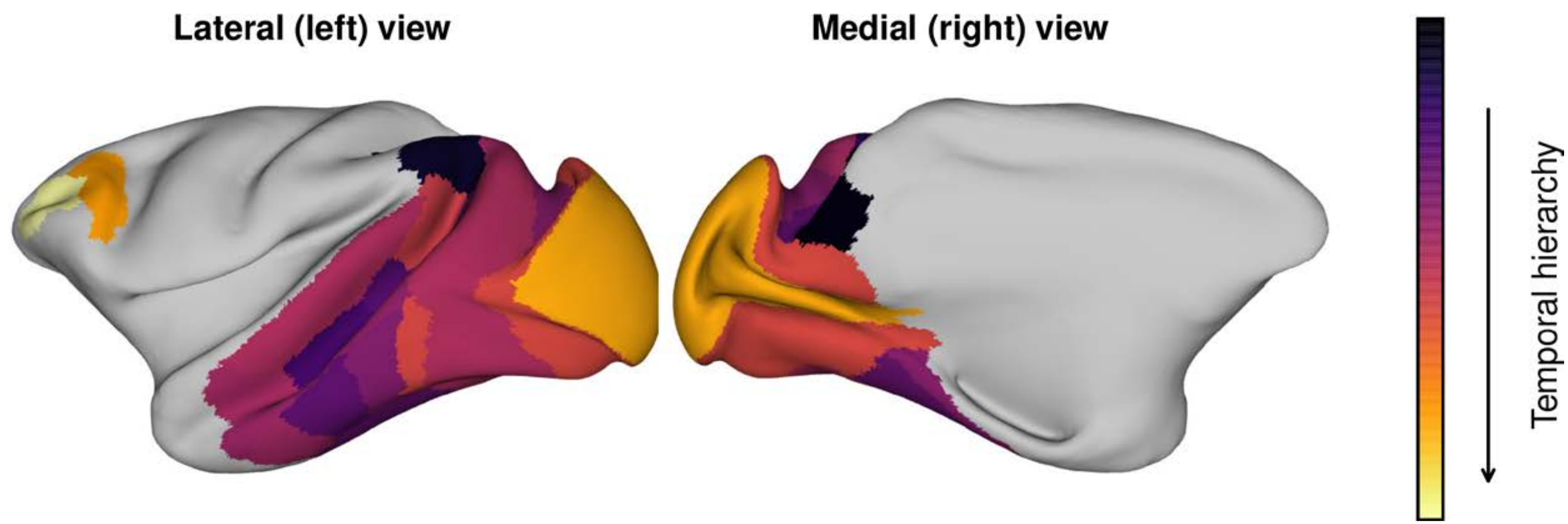
JÜLICH
Forschungszentrum

TEMPORAL HIERARCHY





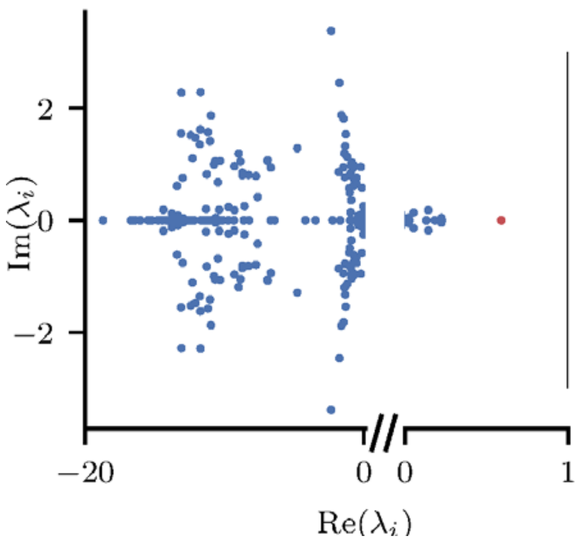
Nowke C, Schmidt M, van Albada SJ, Eppler JM, Bakker R, Diesmann M, Hentschel B, Kuhlen T (2013) *IEEE BioVis*



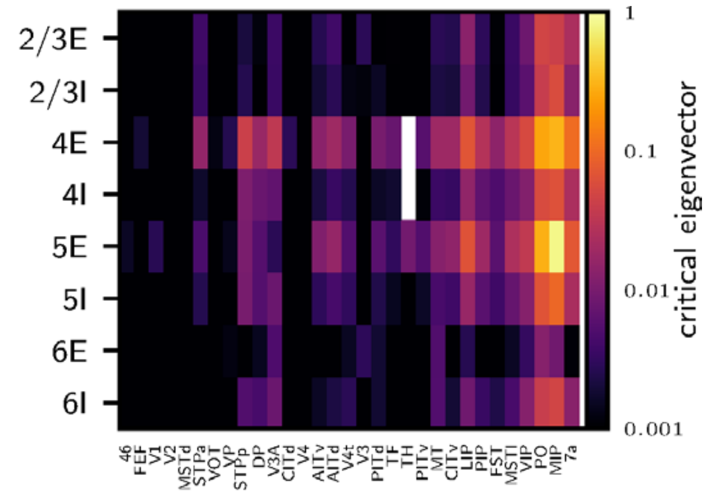
JÜLICH Forschungszentrum

LOCAL STABILITY IN NETWORK DETERMINES PROPAGATION DIRECTION

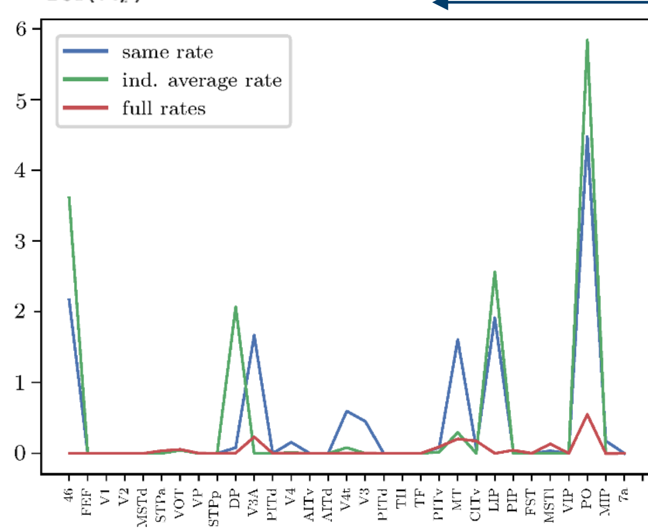
red, critical eigenvalue of effective connectivity of entire network



projection of critical eigenvector to populations and areas

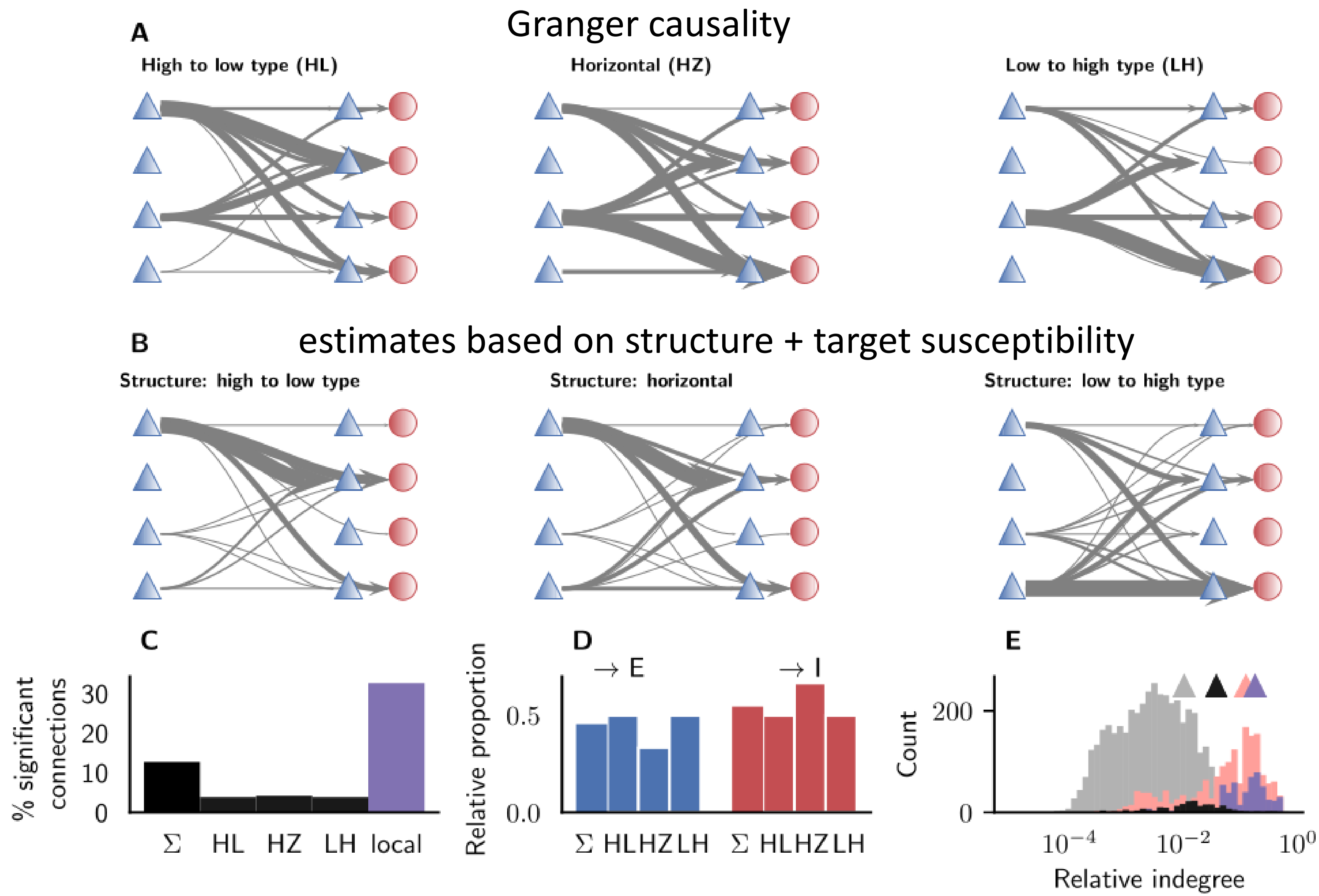


propagation direction



stability of isolated areas is not correlated with temporal hierarchy

LAMINAR INTERACTIONS



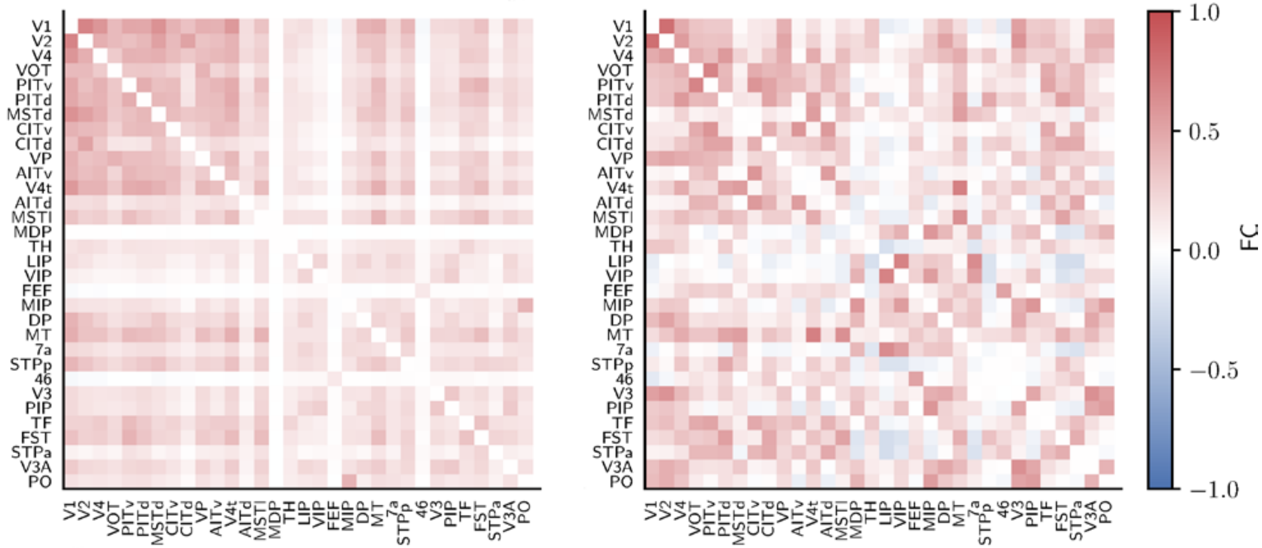
JÜLICH Forschungszentrum

FUNCTIONAL CONNECTIVITY

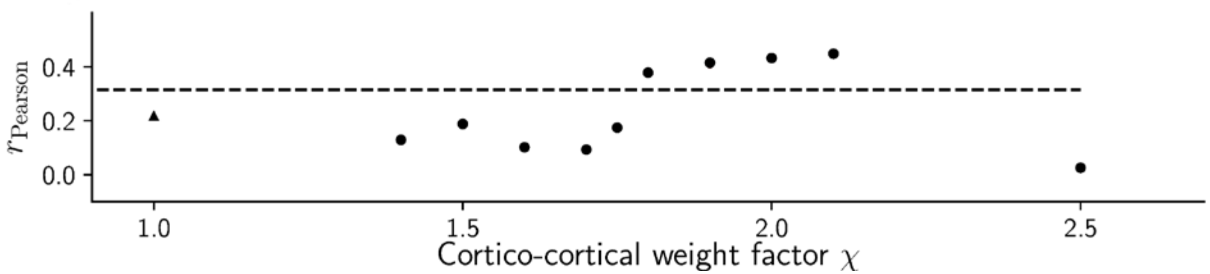
inter-area interactions in metastable state resemble experimental resting-state fMRI

correlations between simulated synaptic inputs

fMRI functional connectivity averaged over six monkeys

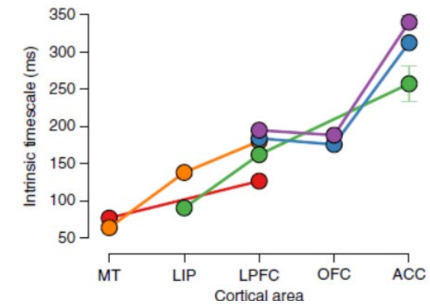


match between experiment and simulation



Schmidt M, Bakker R, Shen K, Bezgin G, Diesmann M, van Albada SJ (2018) *PLOS CB*

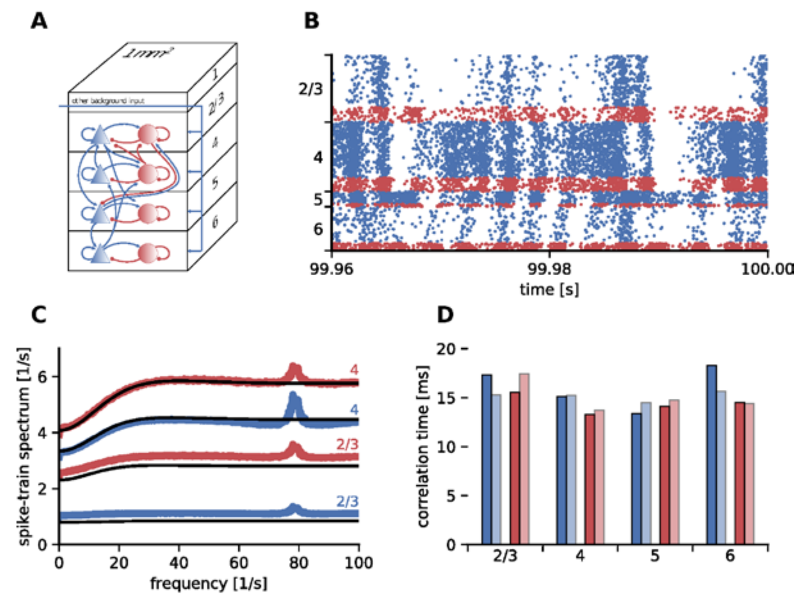
VISUAL AREAS EXHIBIT A HIERARCHY OF INTRINSIC TIMESCALES



Murray et al. (2014)
Nat Neurosci

- widths of neural autocorrelation functions are smaller closer to the sensory periphery
- thought to be relevant for hierarchical processing: different temporal integration windows
  Hasson et al. (2008) *J Neurosci*
- dynamical mean-field theory enables us to predict timescales from network parameters

  van Meegen & van Albada (arXiv preprint) A microscopic theory of intrinsic timescales in spiking neural networks



- allows the origin of the hierarchy of timescales to be studied

GITHUB REPOSITORY

https://inm-6.github.io/multi-area-model/

multi-area-model

A large-scale spiking model of the vision-related areas of macaque cortex.

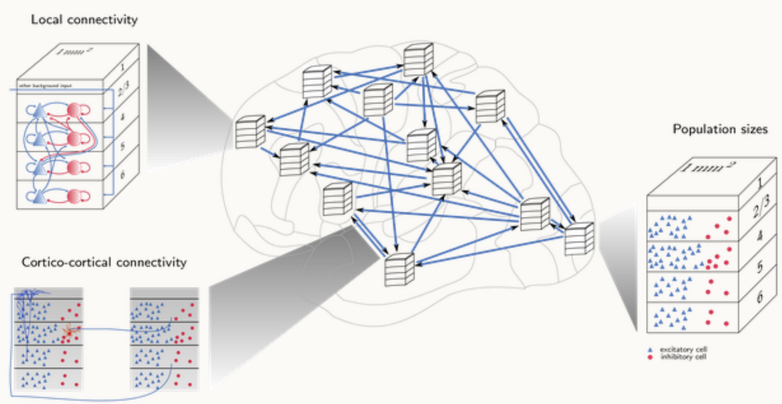
View On GitHub

This project is maintained by INM-6

Hosted on GitHub Pages

Multi-scale spiking network model of macaque visual cortex

python 3.6 | nest::simulated() | license CC BY-NC-SA 4.0



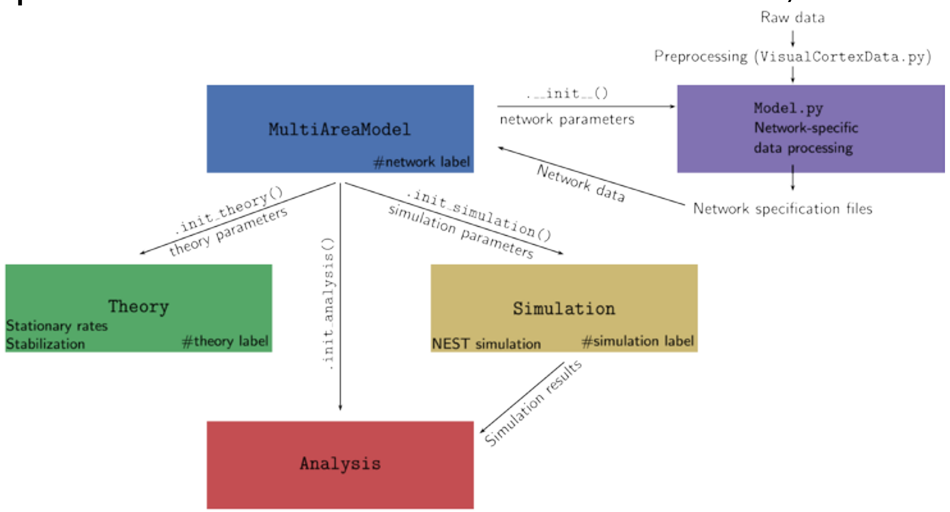
This code implements the spiking network model of macaque visual cortex developed at the Institute of Neuroscience and Medicine (INM-6), Research Center Jülich. The model has been documented in the following publications:

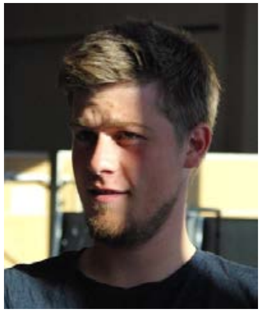
1. Schmidt M, Bakker R, Hilgetag CC, Diesmann M & van Albada SJ Multi-scale account of the network structure of macaque visual cortex Brain Structure and Function (2018), 223: 1409 https://doi.org/10.1007/s00429-017-1554-4
2. Schuecker J, Schmidt M, van Albada SJ, Diesmann M & Helias M (2017) Fundamental Activity Constraints Lead to Specific Interpretations of the Connectome. PLOS Computational Biology, 13(2): e1005179. https://doi.org/10.1371/journal.pcbi.1005179
3. Schmidt M, Bakker R, Shen K, Bezgin B, Diesmann M & van Albada SJ (accepted) A multi-scale layer-resolved spiking network model of resting-state dynamics in macaque cortex. PLOS Computational Biology, 14(9): e1006359.

JÜLICH Forschungszentrum

IMPLEMENTATION AND HURDLES

- M ported SLI code to PyNEST → more readable; new implementation from scratch enabled clean, modular setup





Maximilian Schmidt

Alexander van Meegen

- M created private GitHub repository, added files; created README; extended documentation
- M requested permission to publish data; *not yet obtained* → start from processed data
- S & especially A reviewed code → knowledge about model transferred from M to A
- mean-field integration gave different results on different machines
  - problem with package versions? → use Conda
    - problem solved by compiling NEST with different MPI compiler

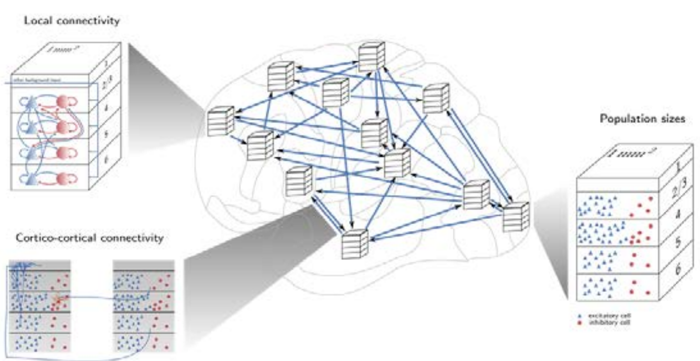
JÜLICH Forschungszentrum

DOCUMENTATION

README.md

Multi-scale spiking network model of macaque visual cortex

python 3.6 | nest | License CC BY-NC-SA 4.0



README provides all technical information needed to instantiate and run the model

instructions for running a simulation

Running a simulation

A simple simulation can be run in the following way:

1. Define custom parameters custom_params = ... custom_simulation_params = ...
2. Instantiate the model class together with a simulation class instance.

```
M = MultiAreaModel(custom_params, simulation=True, sim_spec=custom_simulation_params)
```

3. Start the simulation.

```
M.simulation.simulate()
```

software requirements

Requirements

python_dicthash (https://github.com/INM-6/python-dicthash), correlation_toolbox (https://github.com/INM-6/correlation-toolbox), pandas, numpy, nested_dict, matplotlib (2.1.2), scipy, NEST 2.14.0

Optional: seaborn, Sumatra

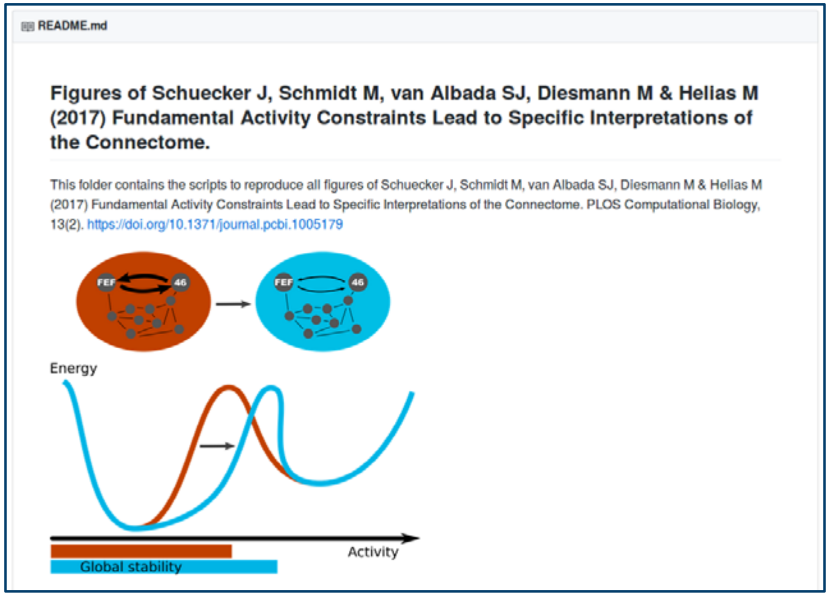
To install the required packages with pip, execute:

```
pip install -r requirements.txt
```

Note that NEST needs to be installed separately, see http://www.nest-simulator.org/installation/.

JÜLICH Forschungszentrum

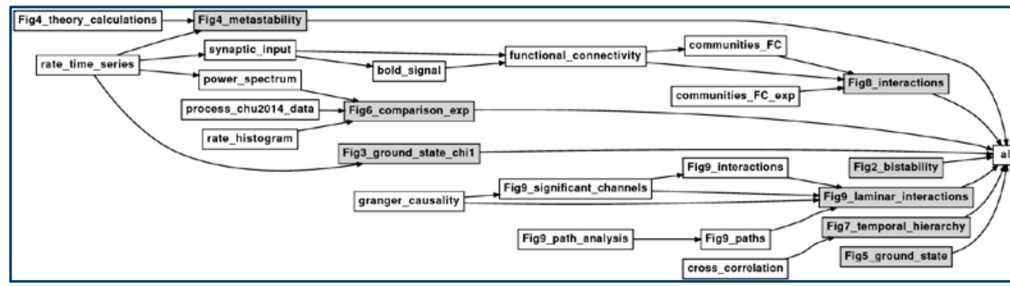
REPRODUCING FIGURES


README.md

Figures of Schuecker J, Schmidt M, van Albada SJ, Diesmann M & Helias M (2017) Fundamental Activity Constraints Lead to Specific Interpretations of the Connectome.

This folder contains the scripts to reproduce all figures of Schuecker J, Schmidt M, van Albada SJ, Diesmann M & Helias M (2017) Fundamental Activity Constraints Lead to Specific Interpretations of the Connectome. PLOS Computational Biology, 13(2). https://doi.org/10.1371/journal.pcbi.1005179

Snakemake*-based workflow to reproduce figures of Schmidt et al. *PLOS CB* (2018)



additional README with specific instructions for each publication

code snippet from the above Snakemake file

```
rule Fig4_metastability:
    input:
        expand(os.path.join(DATA_DIR, '{simulation}', 'Analysis', 'rate_time_series_full', 'rate_time_series_full_V1.npy'),
               simulation=SIM_LABELS['Fig4']),
        expand('Fig4_theory_data/results_{cc_weights_factor}.npy',
               cc_weights_factor=[1.0, 1.8, 1.9, 2., 2.1, 2.5])
    output:
        'Fig4_metastability.eps'
    shell:
        'python3 Fig4_metastability.py'
```

*Köster J, Rahmann S (2012) *Bioinformatics*

EXECUTABLE WORKFLOW

open-source material should:

- be correct

  → testing by main developer(s) and others

  great opportunity for knowledge transfer

- enable testing dependence on underlying data

  → include raw data; obtain permission early

- trace entire workflow from model construction to execution and visualization

  → include figure scripts; Snakemake removes manual steps

- be easy to understand and use

  → readable code; modularity; documentation; open-source packages

- fully specify package versions

  → Sumatra; Conda

- be provenance-tracked; enable continued development

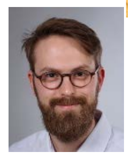
  → Sumatra; GitHub, OSB!

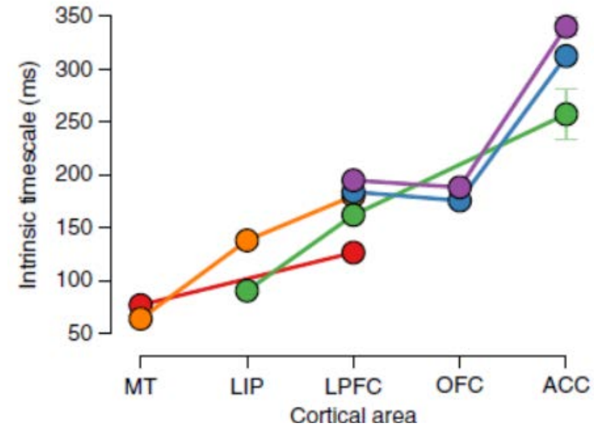
JÜLICH Forschungszentrum

CONCLUSIONS

- multi-scale point-neuron model of macaque visual cortex
  - model code available from https://inm-6.github.io/multi-area-model
  - candidate for porting to OSB!
- provides updated connectivity map incl. population sizes
  - predicts non-negligible feedback onto L4 neurons
- just below instability:
  - reproduces V1 spiking statistics
  - functional connectivity shows correspondence with fMRI
- stronger cortico-cortical connections onto inhibitory than to excitatory neurons enable stable inter-area propagation
- propagation mainly in feedback direction

OUTLOOK

- expand multi-area model with motor areas 
- explain hierarchy of intrinsic time scales  
- distinguish inhibitory cell types
- model visual attention  
- build in functional properties using learning-to-learn framework  
- model human cortex  



Murray et al. (2014) *Nat Neurosci*

ACKNOWLEDGMENTS

Jülich

modeling, theory	testing	anatomical data		theory	
					
Maximilian Schmidt **(now Tokyo)**	Alexander van Meegen	Rembrandt Bakker	Jannis Schuecker **(now Bonn)**	Moritz Helias	Markus Diesmann

fMRI data		anatomy
		
Kelly Shen **Baycrest, Toronto**	Gleb Bezgin **McGill, Montreal**	Claus Hilgetag **UKE Hamburg**

visualization

		
Christian Nowke	Bernd Hentschel	Torsten Kuhlen

RWTH Aachen University

HBP
Human Brain Project

grant JINB33 for compute time on the Jülich supercomputers