Model components in neuroscience

model = structure + dynamics
(anatomy) (activity)

emerging network activity

plasticity
Integrative Loop

- Experimental Structural Data
- Experimental Functional Data
- Data Analysis
- Validation
- Simulation
- Model Building
- Theory

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Top-down and bottom-up

the computer analogy:

<table>
<thead>
<tr>
<th>system</th>
<th>computer</th>
<th>brain</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>top</td>
<td>multiplication</td>
<td>maze navigation</td>
<td>system-level behavior</td>
</tr>
<tr>
<td></td>
<td>↓ logical algorithm</td>
<td>↓ TD-learning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ electrical circuit</td>
<td>↑ neuronal network</td>
<td>system-level theory</td>
</tr>
<tr>
<td></td>
<td>↑ transistor</td>
<td>↑ I&amp;F neuron model</td>
<td></td>
</tr>
<tr>
<td>bottom</td>
<td>↑ electrons</td>
<td>↑ spikes</td>
<td>(bio)physics</td>
</tr>
</tbody>
</table>

comparison between levels: compatibility and consistency
Interactions between neurons

- 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
Minimal layered cortical network model

- 1 mm³
- 1 billion synapses, 100,000 neurons
- 2 populations of neurons per layer:
  - E: Excitatory
  - I: Inhibitory
- E and I identical neuronal dynamics
- Laterally homogeneous connectivity
- Layer- and type-specific $C_{ij}^{xy}$
Anatomical data sets

in vivo anatomy

in vitro physiology

Type of connection | Connectivity ratio
--- | ---
L5 pyramid to L5 pyramid | 1:11 (15:163)
L2/3 pyramid to L2/3 pyramid | 1:4 (65:247)
L4 excitatory to L4 excitatory | 1:10 (8.11)
L3 pyramid to L5 pyramid (P.styapic apical dendrite) | 1:1.8 (16.29)
L5 pyramid to L3 pyramid | 1:1 (2:2)
L4 excitatory to L3 pyramid | 1:3.6 (7.75)
(Presynaptic spiny stellate) (n = 4) | 1:10 (7.70)
L5 pyramid to L5 interneuron | 1:10.4 (7.73)
L5 interneuron to L5 pyramid | 1.8 (5.73)

(Binzegger et al. 2004)

(Thomson et al. 2002)
Target specificity

- correction for bias in anatomical method
Convergence and divergence

- dominated by within-layer connections
- $e \rightarrow e$ divergence reflects "standard" loop
- $e \rightarrow i$ divergence reflects target-specific feedback
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

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
Response to transient inputs

Sakata and Harris (2009) Neuron
Response to transient inputs

- \( T = -0.4 \)

- \( T = +0.4 \)
Hypothesis on cortical flow of activity

- handshaking between layers

Building block for mesoscopic studies

- collaboration with Gaute Einevoll (UMB, Norway)


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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.

Human cortex:

- $10^{10}$ neurons
- $10^{14}$ synapses
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)?
Simulation Technology: the NEST Initiative

collaborative effort and community building

- origins in 1994, collaboration of several labs (since 2001)
- registered society (since 2012)
- teaching in international advanced courses:
  - Okinawa Computational Neuroscience Course OCNC, Japan
  - Advanced Course in Computational Neuroscience ACCN, Europe
  - Latin American School on Computational Neuroscience LASCON, South America

Major goals:
- systematically publish new simulation technology
- produce public releases under GPL

www.nest-initiative.org

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- network simulator of Human Brain Project
  e.g.: Morrison et al. (2005) *Neural Computation*
  Zaytsev, Morrison (2013) *Frontiers in Neuroinformatics*
Supercomputers ready for use as discovery machines for neuroscience

Moritz Helias\textsuperscript{1,2*}, Susanne Kunke\textsuperscript{1,3,4}, Gen Masumoto\textsuperscript{5}, Jun Igarashi\textsuperscript{6}, Jochen Martin Eppler\textsuperscript{1}, Shin Ishii\textsuperscript{7}, Tomoki Fukai\textsuperscript{6}, Abigail Morrison\textsuperscript{1,3,4,8} and Markus Diesmann\textsuperscript{1,2,4,9}

\textsuperscript{1} Institute of Neuroscience and Medicine (INM-6), Computational and Systems Neuroscience, Jülich Research Centre, Jülich, Germany
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\textsuperscript{4} Bernstein Center Freiburg, Albert-Ludwig University of Freiburg, Freiburg, Germany
\textsuperscript{5} Bernstein Center Freiburg, Albert-Ludwig University of Freiburg, Freiburg, Germany

Spiking network simulation code for petascale computers

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

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

makes supercomputers accessible for neuroscience

provides the evidence that neuroscience can exploit petascale systems
3\textsuperscript{rd} generation simulation kernel

(released with NEST 2.2 in December 2012)

- up to $10^8$ neurons on K (and JUQUEEN)
- 11,250 synapses per neuron (exc-exc STDP)
- using up to $MT=196,608$ threads and $T=8$ threads per node
- 16 GB of memory per node

Model of memory usage of NEST

- describes the memory usage per MPI process

\[
M(M, T, N, K) = M_0(M) + M_n(M, N) + M_c(M, T, N, K)
\]

\[
M_c(M, T, N, K) = TNm_c^0 + TN_c^0 m_c^0 + T(N - N_c^0) m_c^+ + K_M m_c
\]

- \(M\) total number of MPI processes
- \(T\) number of threads per MPI process
- \(N\) total number of neurons
- \(K\) number of incoming connections per neuron

Previous connection infrastructure (3g)

- required on each process

  neurons with local targets

  sparse table

  inner data structure

- from 10,000 nodes on collapse along 2 dimensions
3rd generation simulation kernel

analysis of contributions to total memory usage

- in the regime of 10k processes and beyond the inner data structure causes severe overhead
3rd generation simulation kernel

analysis of contributions to total memory usage

- adapt the model to account for short target lists
- potential solution: low-overhead data structure on supercomputers
New adaptive connection infrastructure (4g)

- Low overhead per synapse on supercomputers
- Full flexibility on laptops and moderately sized clusters

Diagram details:
- Neurons with local targets
- Cases 1, 2, and 3
- Synapse types:
  - Hom Connector 16B
  - Hom Connector 40B
  - Vtable 8B
  - Last spike 8B
  - STL vector 24B

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Comparison of 4g to 3g kernel

3g kernel

4g kernel

more than one synapse stored

one synapse stored

memory usage (GB)

infrastructure

sparse table

synapses

$MT$
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 simulation software developed at INM-6/IAS-6
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
Feasibility and necessity

- Can we do simulations at the brain scale? ✔
- Do we need to simulate full scale (at cellular resolution)?
Measure of neural interaction: Cross-Correlation

The cross-correlation represents the probability of finding any spike in train $s_2$ as a function of time before or after a spike in train $s_1$: $\rho(\tau) = \int s_1(t)s_2(t - \tau)dt$

Perkel et al, 1967
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Cross-Correlation

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Perkel et al, 1967
Cross-Correlation Histogram: Binning

The cross-correlation histogram results by binning of the cross-correlation function

Perkel et al, 1967
Cross-Correlation Histogram (CCH)

- number of coincidences for each time delay $\tau$
- often task of neuroscientist: significance of correlation
Perception Related Correlation


- Simultaneous recording of two single units (stereotrodes) from different columns of visual cortex (A17) of cat
- Long bar condition induces synchronized spike responses
- Dual bar condition: absence of synchronization
  → interpretation: Gestalt perception requires binding (by synchrony)
Functional Correlation

- two simultaneously recorded neurons in CA1 of a rat performing an auditory or visual discrimination task
- task related correlation only for visual task (although spike rates in same range in both tasks)
  → interpretation: these two neurons belong to a cell assembly processing visual information

Mechanisms at finite size differ from limit

inhomogeneous connectivity \( \begin{pmatrix} J_{EE} & J_{EI} \\ J_{IE} & J_{II} \end{pmatrix} \)

homogeneous connectivity \( \begin{pmatrix} J_E & J_I \\ J_E & J_I \end{pmatrix} \)

Full theory

\[ c^{\text{int}} \]
\[ c^{\text{int}} + c^{\text{ext}} \]
\[ c^{\text{ext}} \]

External Renart et al. 2010 Science

Intrinsic biologically relevant range of model convergence of \( c^{\text{ext}} \)

Biologically relevant range of model

\[ c_{EE} \]
\[ c_{II} \]
\[ c_{EI} \]

No convergence \( c^{\text{ext}}_{\alpha\alpha} \) approx 0


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What are finite size effects?

local cortical circuit  →  cortical area  →  human brain  →  1 mol

10^5  10^7  10^{11}  N  10^{24}

local cortical network

→ simulated network

deviation = finite size effect

simulated crystal of network

theory of network

crystal

deviation = finite size effect

error of simulation

theory of crystal

enable simulation

N

gain analytical insight

∞
Networks generally not reducible

Scalability of asynchronous networks is limited by one-to-one mapping between effective connectivity and correlations

Sacha Jennifer van Albada, Moritz Helias, Markus Diesmann

(Submitted on 18 Nov 2014 (v1), last revised 4 Jul 2015 (this version, v3))

Network models are routinely downscaled compared to nature in terms of numbers of nodes or edges because of a lack of computational resources, often without explicit mention of the limitations this entails. While reliable methods have long existed to adjust parameters such that the first-order statistics of network dynamics are conserved, here we show that limitations already arise if also second-order statistics are to be maintained. The temporal structure of pairwise averaged correlations in the activity of recurrent networks is determined by the effective population-level connectivity. We first show that in general the converse is also true and explicitly mention degenerate cases when this one-to-one relationship does not hold. The one-to-one correspondence between effective connectivity and the temporal structure of pairwise averaged correlations implies that network scalings should preserve the effective connectivity if pairwise averaged correlations are to be held constant. Changes in effective connectivity can even push a network from a linearly stable to an unstable, oscillatory regime and vice versa. On this basis, we derive conditions for the preservation of both mean population-averaged activities and pairwise averaged correlations under a change in numbers of neurons or synapses in the asynchronous regime typical of cortical networks. We find that mean activities and correlation structure can be maintained by an appropriate scaling of the synaptic weights, but only over a range of numbers of synapses that is limited by the variance of external inputs to the network. Our results therefore show that the reducibility of asynchronous networks is fundamentally limited.

- downscaling works well for first order statistics like spike rate
- severe constraints already for second order like spike correlation
- spike correlation directly interacts with plasticity
- in press at PLoS Computational Biology
Effective connectivity and correlations

\[
\begin{align*}
\text{Susceptibility} &\quad S_i(\mu, \sigma) \\
\times & \\
\text{Connectivity} &\quad J_{ij}K_{ij} \\
= & \\
\text{Effective connectivity} &\quad W_{ij}
\end{align*}
\]

\[
\begin{align*}
\text{Correlations} &\quad c_{ij} \\
\equiv & \\
\text{Effective connectivity} &\quad W_{ij}
\end{align*}
\]

One-to-one under:
- fixed single-neuron parameters and delays
- stationarity
- diffusion approximation
- absence of degeneracies
Uniqueness of effective connectivity

- for single-population binary network with \( d = 0 \),

\[
c(\Delta) = \frac{a}{N(1-W)} e^{\frac{W-1}{\tau} |\Delta|}
\]

\( \rightarrow \) \( W \) uniquely determines temporal structure

- more generally, \( C_{ij}(\omega) = \sum \tilde{f} \left( W_{kl} \frac{e^{\pm i \omega d_{kl}}}{1+i \omega \tau_k} \right) \)

\( \rightarrow \) each \( W_{kl} \) determines unique \( \omega \)-dependence unless some delays are equal

- narrower set of exceptions when transfer functions are identical
Feasibility and necessity

- Can we do simulations at the brain scale? ✓
- Do we need to simulate full scale (at cellular resolution)? ✓
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
V. Thalamic 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 $3.2 \cdot 10^6$ neurons and $3 \cdot 10^{10}$ synapses

Architectural types provided by C. Hilgetag (private communication)

From Dombrowski et al. (2001), Cereb Cortex
Availability of cortico-cortical connectivity

labeling: y-axis: odd areas
x-axis: even areas

Markov et al. (2012)
Cereb Cortex
Laminar patterns

Sending side

From Markov et al. (2014), J. of Comparative Neurology

Receiving side

- synapse layer: CoCoMac database
- receiving synapse type: Computed from Binzegger et al. (2004)

Fraction of cortico-cortical synapses in each layer

<table>
<thead>
<tr>
<th>Cell body location</th>
<th>23E</th>
<th>23I</th>
<th>4E</th>
<th>4I</th>
<th>5E</th>
<th>5I</th>
<th>6E</th>
<th>6I</th>
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<td>0.85</td>
<td>0.15</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

From Binzegger et al. (2004), J Neurosci
Multi-area model: Dynamical results

- Maximilian Schmidt
- Sacha van Albada
- Rembrandt Bakker

**Goal of the study:**
- achieve a realistic ground state with low firing rates and heterogeneous laminar patterns
- study interactions and slow oscillations between areas

Experimental data provided by Kelly Shen and Gleb Bezgin
Model 2: spatially organized, meso

- parallel study
- network of 4mmx4mm covers size of 100 electrode Utah array
- spike correlation structure, LFP
- experimentally, formation and breakdown of waves observed in relation to behavior

- about 1 million neurons with 10 billion synapses
- requires supercomputing but not incredible resources

Johanna Senk
Espen Hagen

S Kunkel

data: INT/Juelich

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Summary

- full-scale model explains prominent features of network activity
- is building block of further studies (www.opensourcebrain.org)
- need for brain scale models
  - increase self consistency
  - compute meso- and macroscopic measures of activity
- need for full scale models
  - irreducibility: already 2nd order statistics affected
  - verify mean-field results
- require memory only available on supercomputers
- machines ready for use by neuroscience (www.nest-initiative.org)