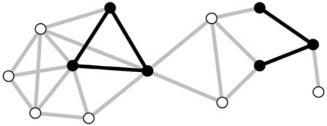
Modelling the nonrandom and dynamic structure of local cortical circuits

Felix Z. Hoffmann

Slides: bit.ly/xbcn18



Bernstein Conference 2018 Satellite Workshop:
Adaptivity and Inhomogeneity in Neuronal Networks

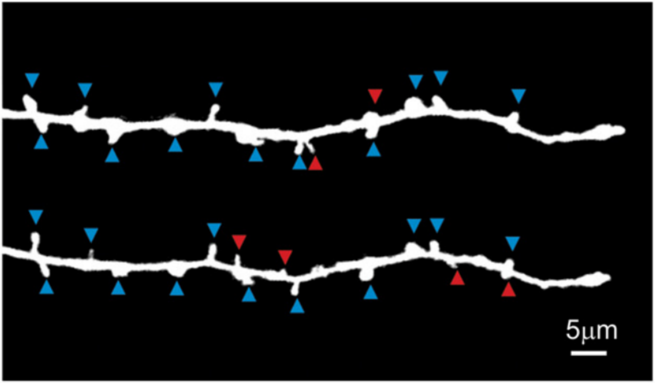
bcf

FELLOW PROGRAMM FREIES WISSEN
Wissenschaft offen gestalten

FIAS Frankfurt Institute for Advanced Studies

SPP 2041
Computational Connectomics

The dynamic connectome

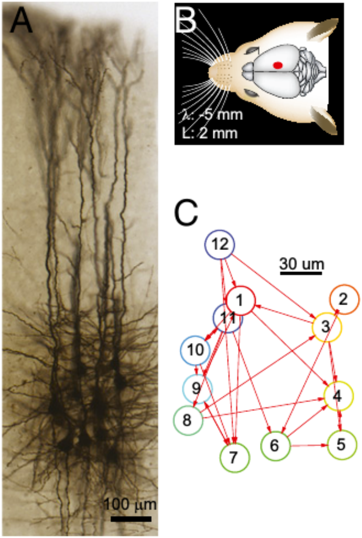


Day 0

Day 4

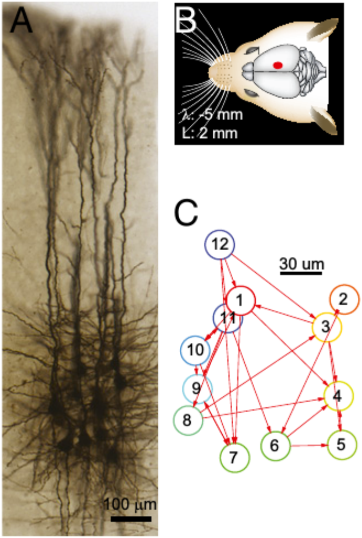
Loewenstein et al. 2015

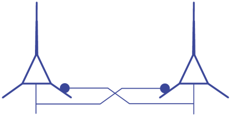
Robust nonrandom connectivity patterns



Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

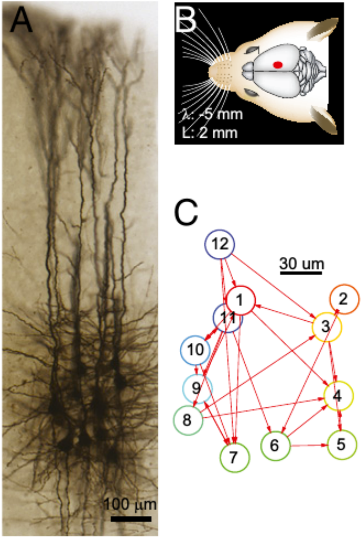
Robust nonrandom connectivity patterns

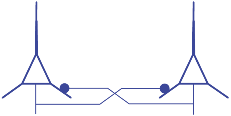


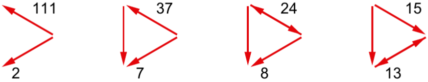


Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

Robust nonrandom connectivity patterns

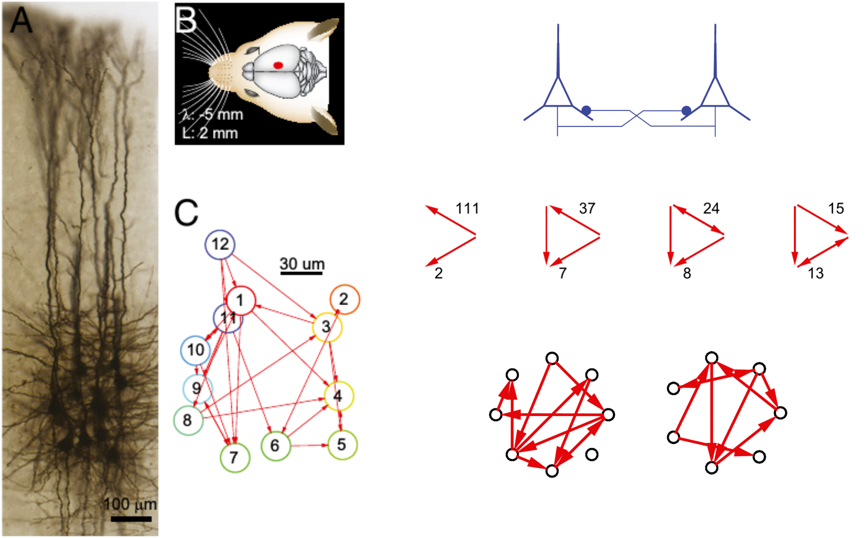






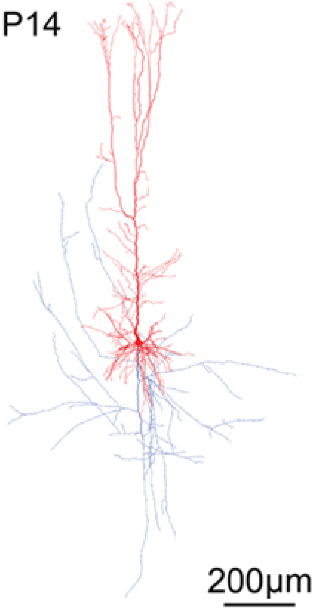
Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

Robust nonrandom connectivity patterns



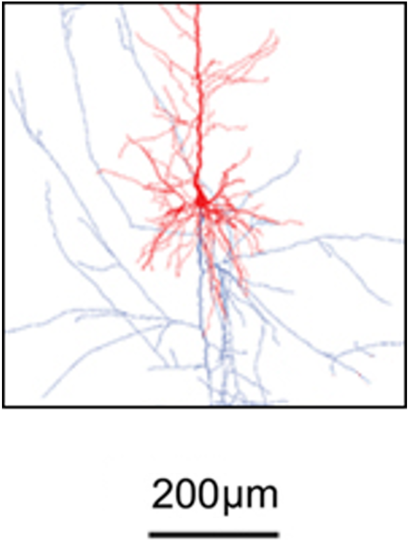
Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

Anisotropy in stereotypical axon morphology



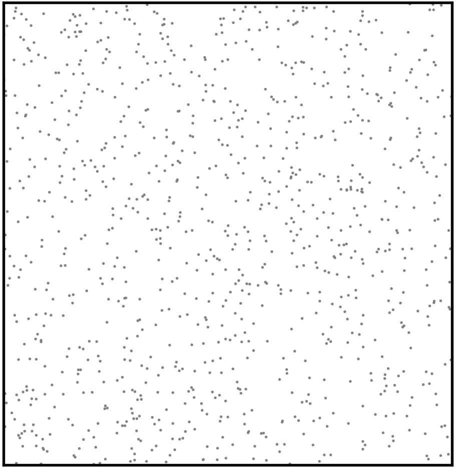
Romand et al. 2011

Anisotropy in stereotypical axon morphology



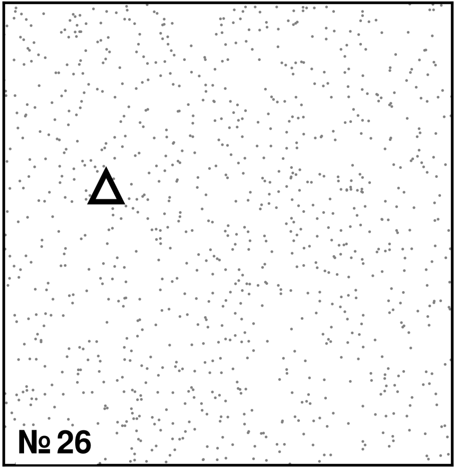
Romand et al. 2011; Stepanyants and Chklovskii 2005

Anisotropic network model



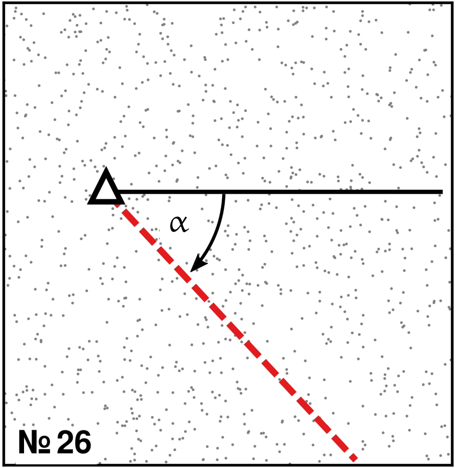
N = 1000

Anisotropic network model



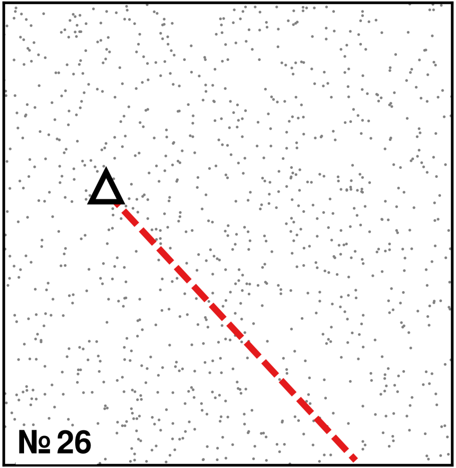
N = 1000

Anisotropic network model



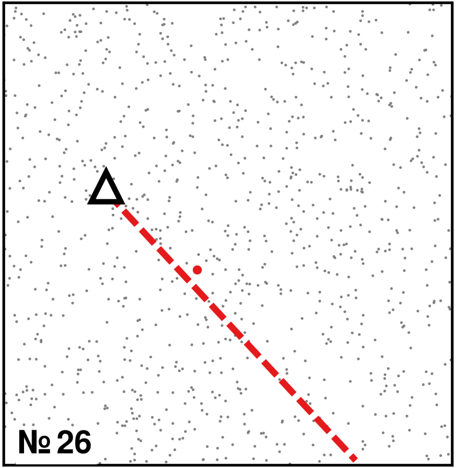
N = 1000

Anisotropic network model



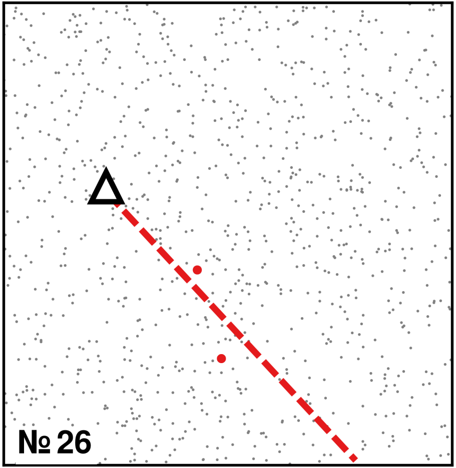
N = 1000

Anisotropic network model



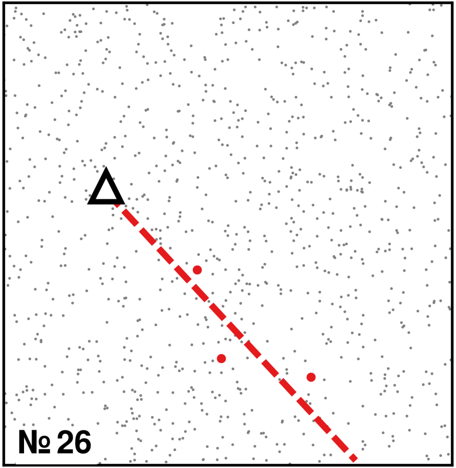
N = 1000

Anisotropic network model



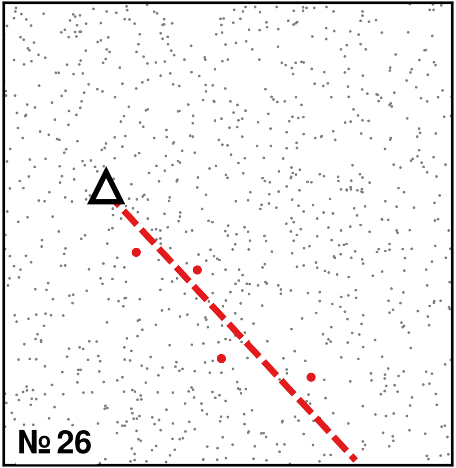
N = 1000

Anisotropic network model



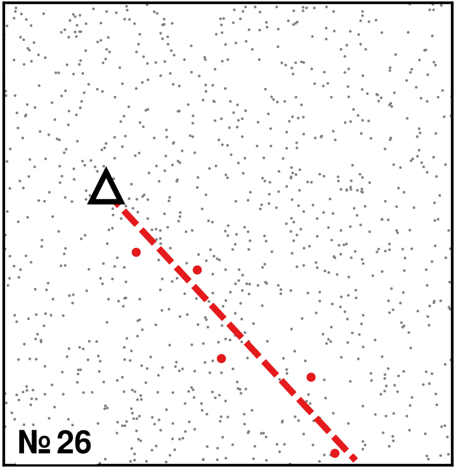
N = 1000

Anisotropic network model



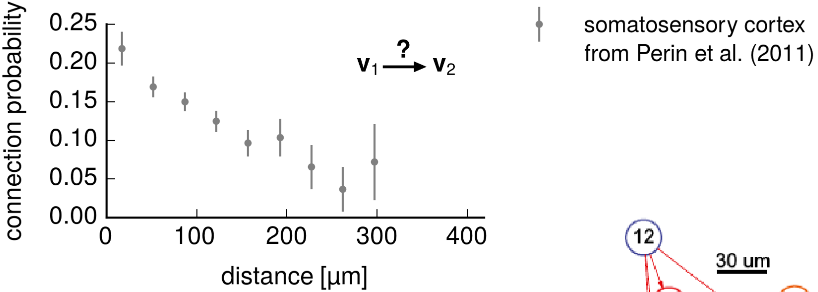
N = 1000

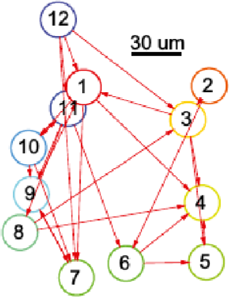
Anisotropic network model



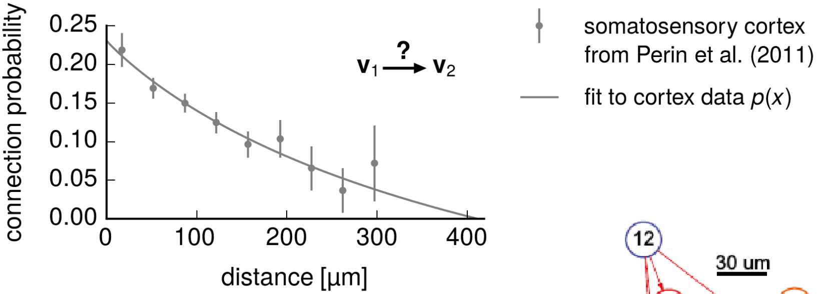
N = 1000

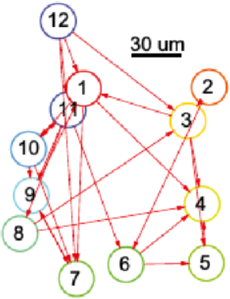
Anisotropic network model – Distance-dependency



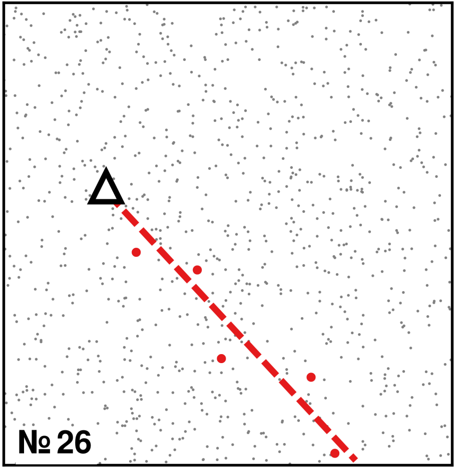


Anisotropic network model – Distance-dependency

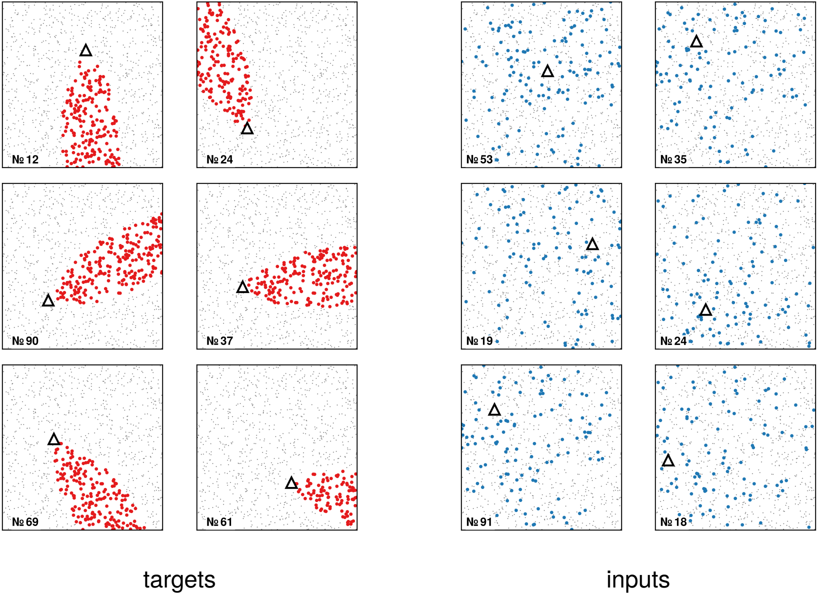




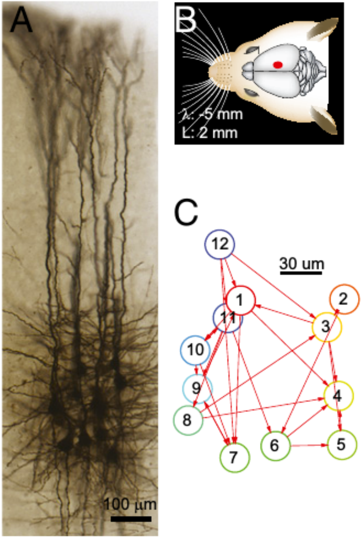
Anisotropic network model

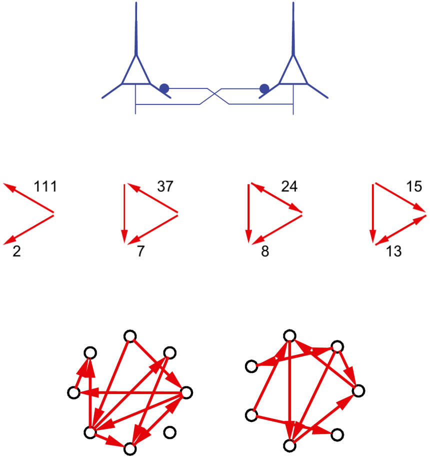


Anisotropic network model



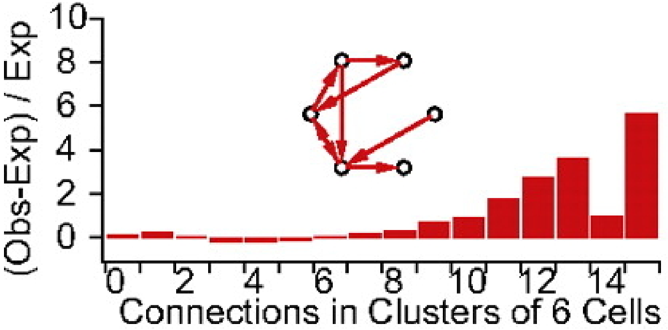
Robust nonrandom connectivity patterns





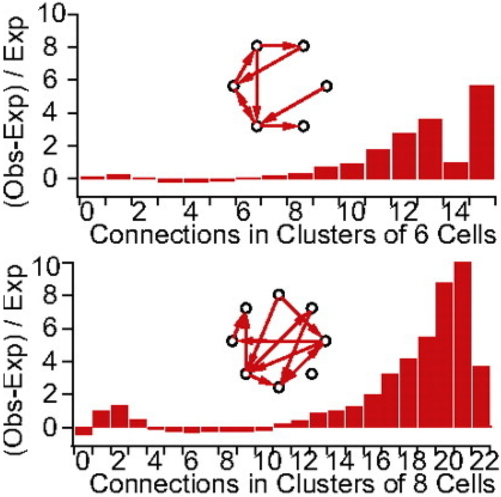
Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

Connection counts in neuron clusters



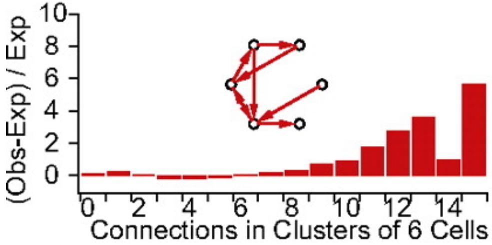
Perin et al. 2011

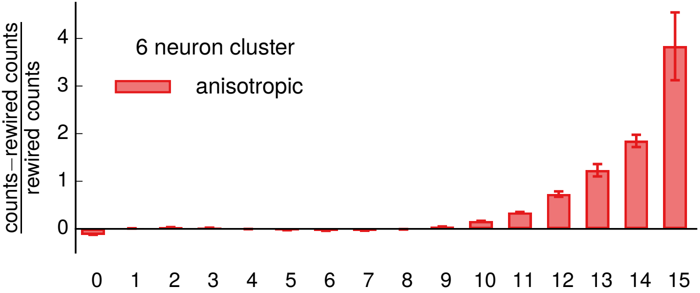
Connection counts in neuron clusters



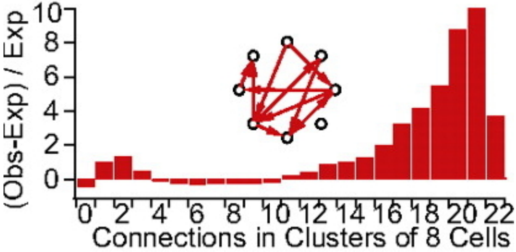
Perin et al. 2011

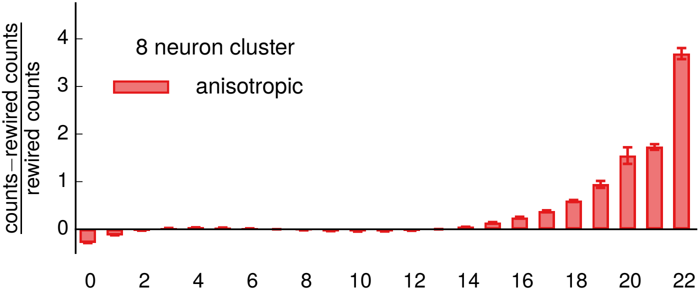
Connection counts in neuron clusters



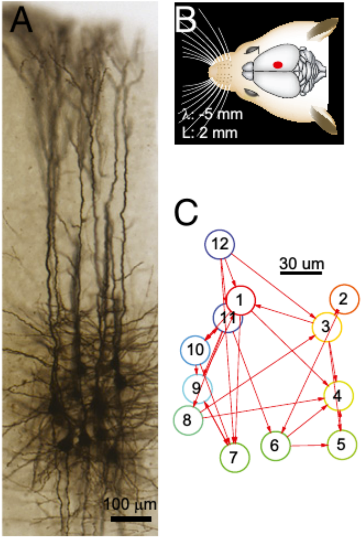


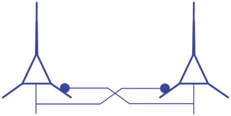
Connection counts in neuron clusters

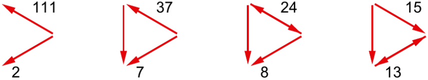


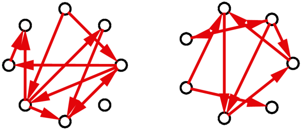


Robust nonrandom connectivity patterns



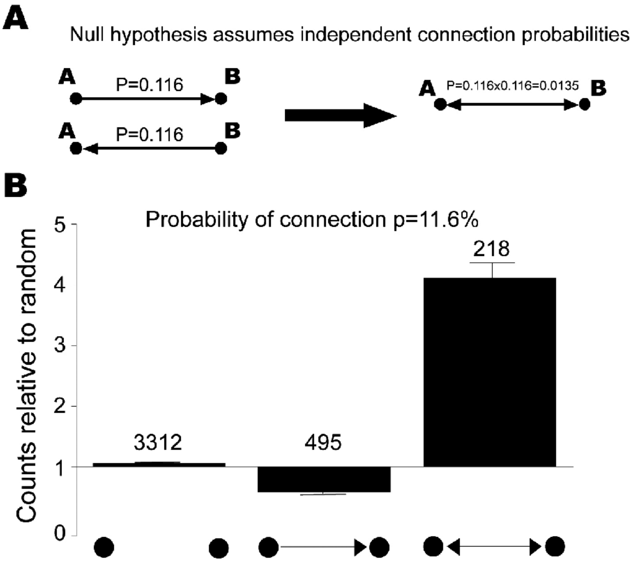






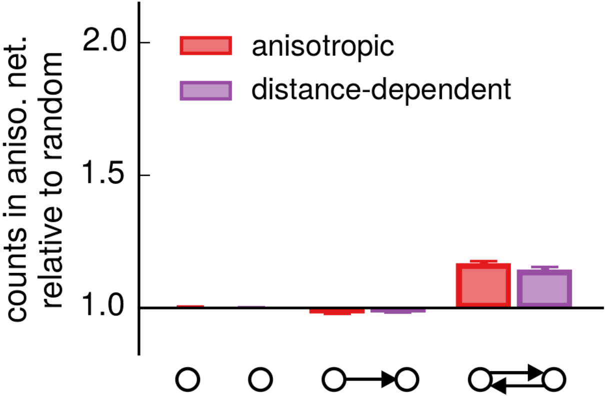
Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

Overrepresentation of reciprocal connections

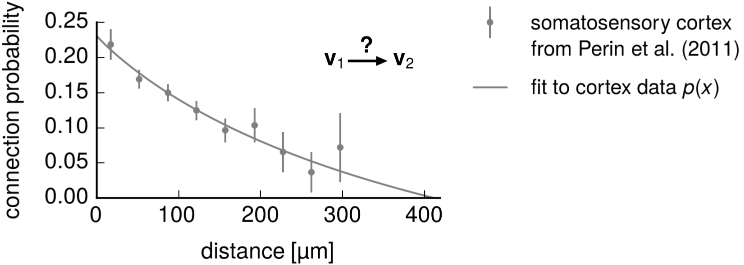


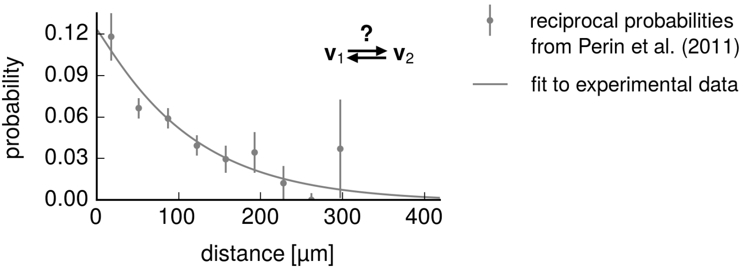
Song et al. 2005

Overrepresentation of reciprocal connections

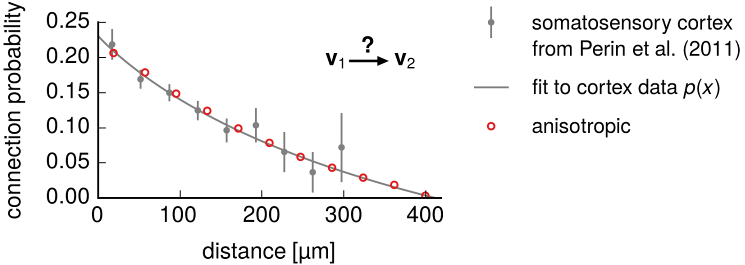


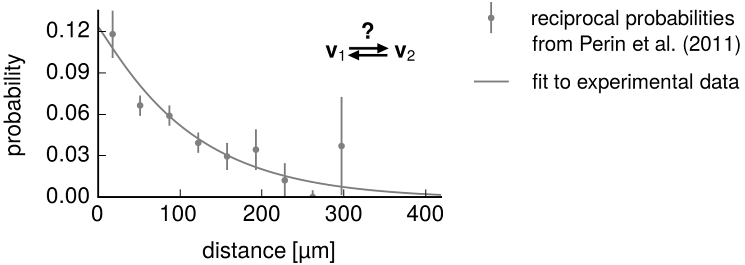
Reciprocity – Distance-dependent?



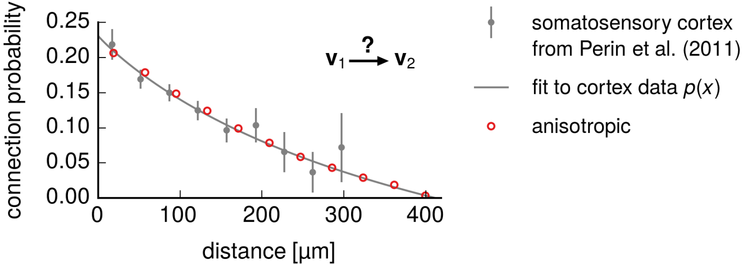


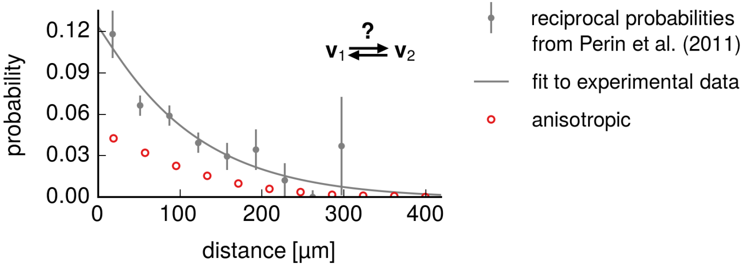
Reciprocity – Distance-dependent?



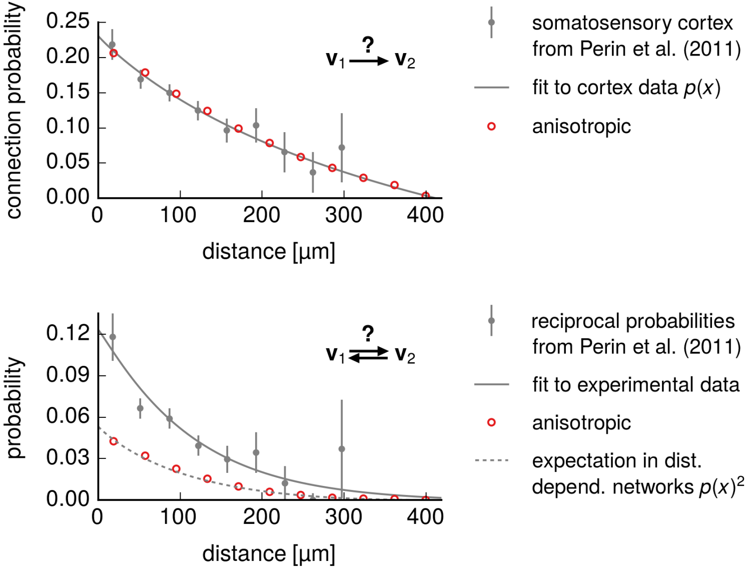


Reciprocity – Distance-dependent?

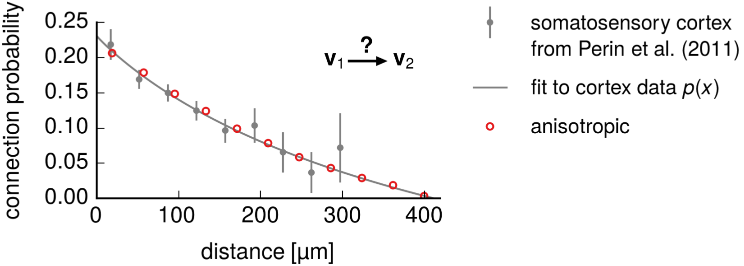




Reciprocity – Distance-dependent?

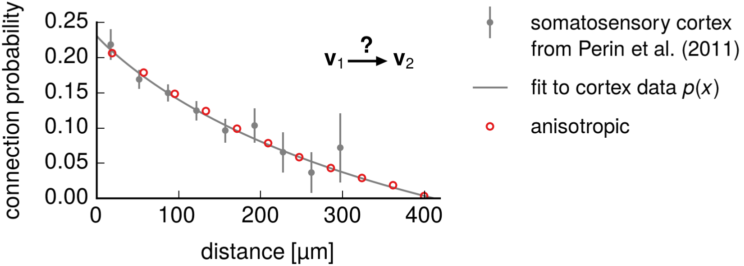


Reciprocity – Distance-dependent?



Other sources for the overrepresentation of bidirectional connections?

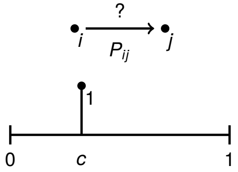
Reciprocity – Distance-dependent?



Other sources for the overrepresentation of bidirectional connections?

⇒ Hoffmann, FZ and Triesch, J (2017). Nonrandom Network Connectivity Comes in Pairs. *Network Neuroscience*

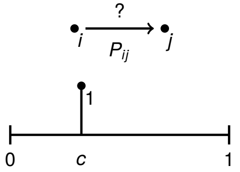
Standard random network model



Probability of connection a constant P_{ij},

$$P_{ij} = c$$

Standard random network model



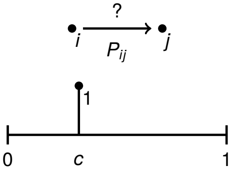
Probability of connection a constant P_{ij},

$$P_{ij} = c$$

Overall connection probability

$$\mu = P_{ij} = c$$

Standard random network model



Probability of connection a <u>constant</u> P_{ij},

$$P_{ij} = c$$

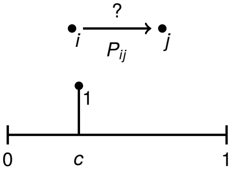
Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\text{bidir}} = P_{ij} P_{ji} = c^2$$

Standard random network model



Probability of connection a <u>constant</u> P_{ij},

$$P_{ij} = c$$

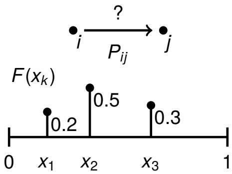
Overall connection probability

$$\mu = P_{ij} = c$$

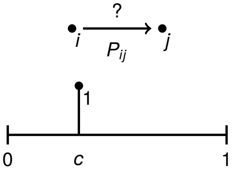
Bidirectional connection

$$P_{\text{bidir}} = P_{ij} P_{ji} = c^2$$

Varying connection probabilities



Standard random network model



Probability of connection a constant P_{ij},

$$P_{ij} = c$$

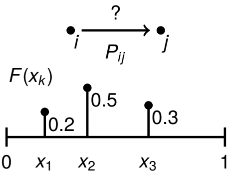
Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\text{bidir}} = P_{ij} P_{ji} = c^2$$

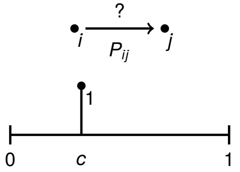
Varying connection probabilities



Probability of connection a random variable P_{ij},

$$\textbf{Prob}(P_{ij} = x_k) = F(x_k)$$

Standard random network model



Probability of connection a <u>constant</u> P_{ij},

$$P_{ij} = c$$

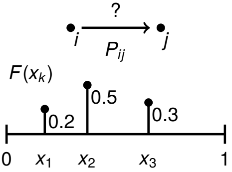
Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\mathrm{bidir}} = P_{ij} P_{ji} = c^2$$

Varying connection probabilities



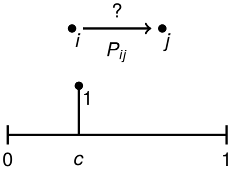
Probability of connection a <u>random variable</u> P_{ij},

$$\mathbf{Prob}(P_{ij} = x_k) = F(x_k)$$

Overall connection probability

$$\mu = \sum_{k=1}^{m} F(x_k) x_k$$

Standard random network model



Probability of connection a constant P_{ij},

$$P_{ij} = c$$

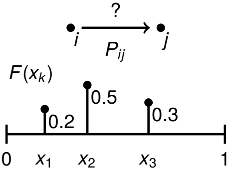
Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\text{bidir}} = P_{ij} P_{ji} = c^2$$

Varying connection probabilities



Probability of connection a random variable P_{ij},

$$\mathbf{Prob}(P_{ij} = x_k) = F(x_k)$$

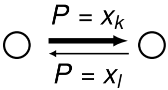
Overall connection probability

$$\mu = \sum_{k=1}^{m} F(x_k) x_k$$

Bidirectional connection

$$P_{\text{bidir}} = ?$$

Varying connection probabilities



Probability of connection a constant P_{ij},

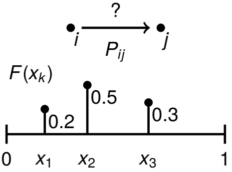
$$P_{ij} = c$$

Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\text{bidir}} = P_{ij} P_{ji} = c^2$$



Probability of connection a random variable P_{ij},

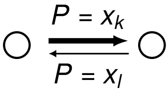
$$\mathbf{Prob}(P_{ij} = x_k) = F(x_k)$$

Overall connection probability

$$\mu = \sum_{k=1}^{m} F(x_k) x_k$$

Bidirectional connection

$$P_{\text{bidir}} = ?$$



Probability of connection a <u>constant</u> P_{ij},

$$P_{ij} = c$$

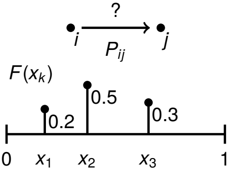
Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\text{bidir}} = P_{ij}P_{ji} = c^2$$

Varying connection probabilities



Probability of connection a <u>random variable</u> P_{ij},

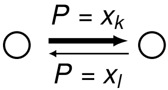
$$\mathbf{Prob}(P_{ij} = x_k) = F(x_k)$$

Overall connection probability

$$\mu = \sum_{k=1}^{m} F(x_k)x_k$$

Bidirectional connection

$$P_{\text{bidir}} = \sum_{k=1}^{m}\sum_{l=1}^{m} F(x_k)x_kF(x_l|x_k)x_l$$



Probability of connection a <u>constant</u> P_{ij},

$$P_{ij} = c$$

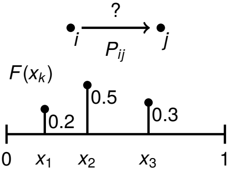
Overall connection probability

$$\mu = P_{ij} = c$$

Bidirectional connection

$$P_{\mathrm{bidir}} = P_{ij}P_{ji} = c^2$$

Varying connection probabilities



Probability of connection a <u>random variable</u> P_{ij},

$$\mathbf{Prob}(P_{ij} = x_k) = F(x_k)$$

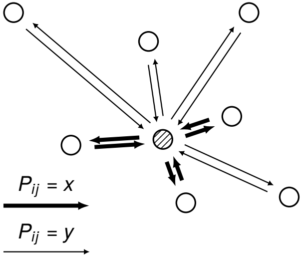
Overall connection probability

$$\mu = \sum_{k=1}^{m} F(x_k)x_k$$

Bidirectional connection

$$P_{\mathrm{bidir}} = \sum_{k=1}^{m}\sum_{l=1}^{m} F(x_k)x_k\underline{F(x_l|x_k)}x_l$$

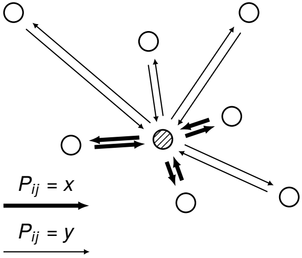
$$F(x_l|x_k) = \begin{cases} 1 & \text{if } l = k \\ 0 & \text{otherwise.} \end{cases}$$



Hoffmann and Triesch 2017

$$P_{\text{bidir}} = \sum_{k=1}^{m} \sum_{l=1}^{m} F(x_k) x_k F(x_l | x_k) x_l$$
$$= \sum_{k=1}^{m} F(x_k) x_k^2 .$$

$$F(x_l | x_k) = \begin{cases} 1 & \text{if } l = k \\ 0 & \text{otherwise.} \end{cases}$$



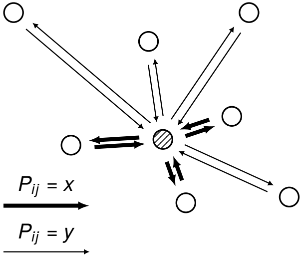
Hoffmann and Triesch 2017

$$P_{\text{bidir}} = \sum_{k=1}^{m} \sum_{l=1}^{m} F(x_k) x_k F(x_l | x_k) x_l$$
$$= \sum_{k=1}^{m} F(x_k) x_k^2 .$$

$$F(x_l | x_k) = \begin{cases} 1 & \text{if } l = k \\ 0 & \text{otherwise.} \end{cases}$$

Relative overrepresentation ρ is the fraction

$$\rho = \frac{P_{\text{bidir}}}{\mu^2} = \frac{\sum_{k=1}^{m} F(x_k) x_k^2}{\left(\sum_{k=1}^{m} F(x_k) x_k\right)^2} .$$

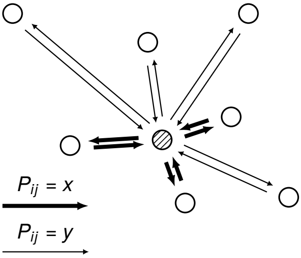


Hoffmann and Triesch 2017

$$P_{\text{bidir}} = \sum_{k=1}^{m} \sum_{l=1}^{m} F(x_k) x_k F(x_l | x_k) x_l$$

$$= \sum_{k=1}^{m} F(x_k) x_k^2.$$

$$F(x_l | x_k) = \begin{cases} 1 & \text{if } l = k \\ 0 & \text{otherwise.} \end{cases}$$



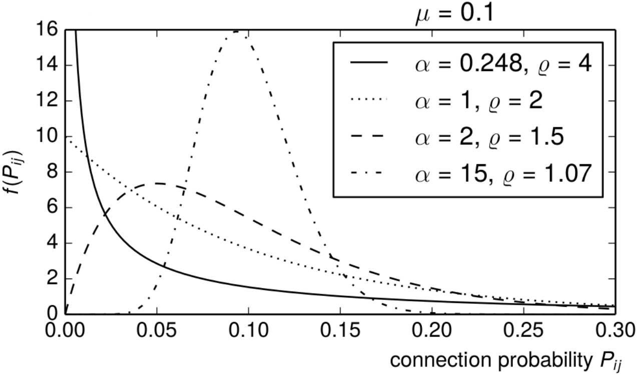
Relative overrepresentation ρ is the fraction

$$\rho = \frac{P_{\text{bidir}}}{\mu^2} = \frac{\sum_{k=1}^{m} F(x_k) x_k^2}{\left(\sum_{k=1}^{m} F(x_k) x_k\right)^2}.$$

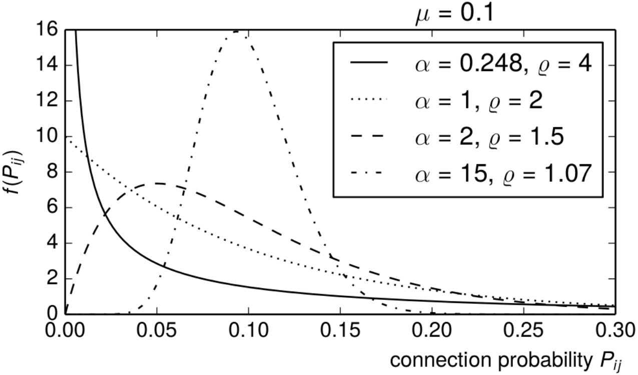
By Jensen's inequality,

$$\left(\sum_{k=1}^{m} F(x_k) x_k \right)^2 \leq \sum_{k=1}^{m} F(x_k) x_k^2 \quad \text{and thus} \quad \rho \geq 1.$$

Hoffmann and Triesch 2017

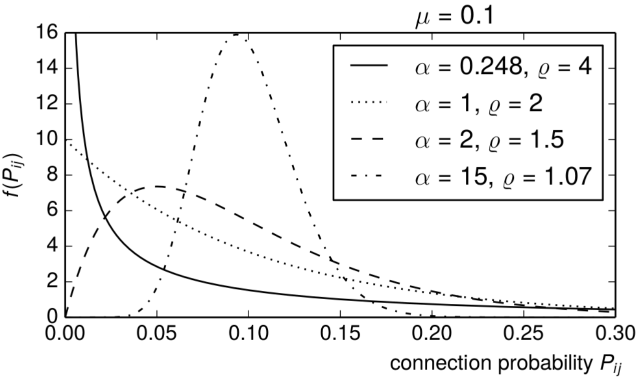


Hoffmann and Triesch 2017



– multiple neuron properties together can cause strong overrepresentation

Hoffmann and Triesch 2017

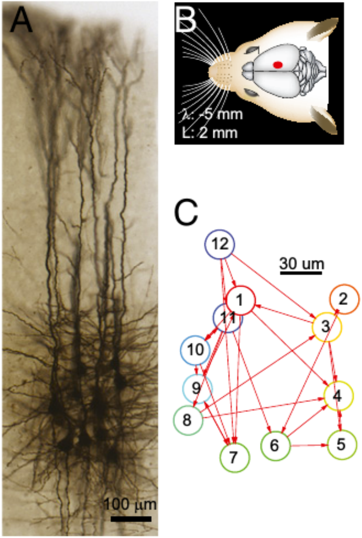


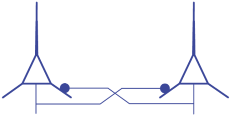
– multiple neuron properties together can cause strong overrepresentation

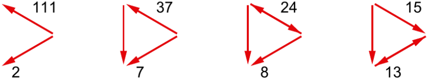
– example: higher connection probability in functionally related cells (Lee et al. 2016)

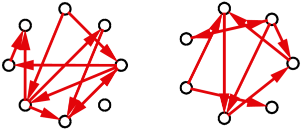
Hoffmann and Triesch 2017

Robust nonrandom connectivity patterns



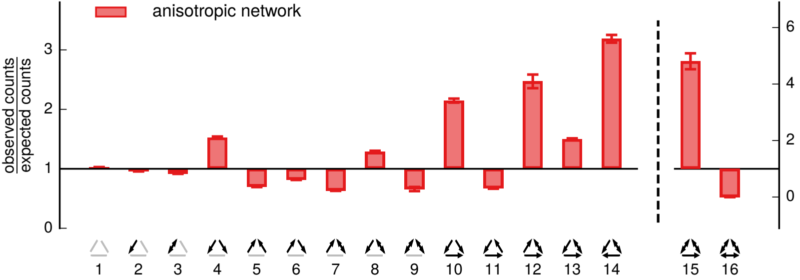






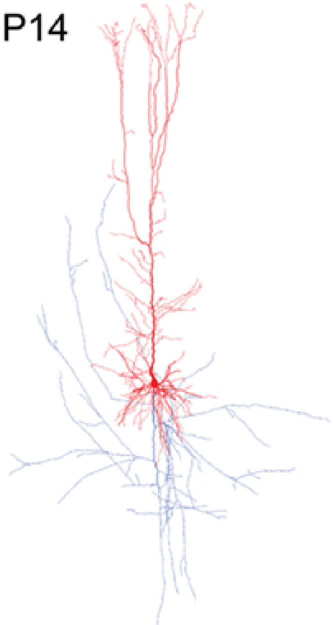
Perin et al. 2011; Song et al. 2005; Markram et al. 1997; Miner and Triesch 2016; Gal et al. 2017; Vegué et al. 2017

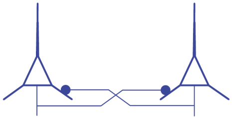
Triplet motif statistics in anisotropic networks

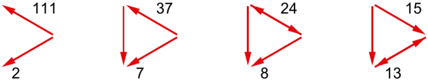


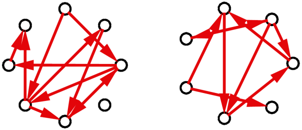
$\Rightarrow$ More aboout this: Poster W77, Wednesday!

Nonrandom connectivity from anisotropy

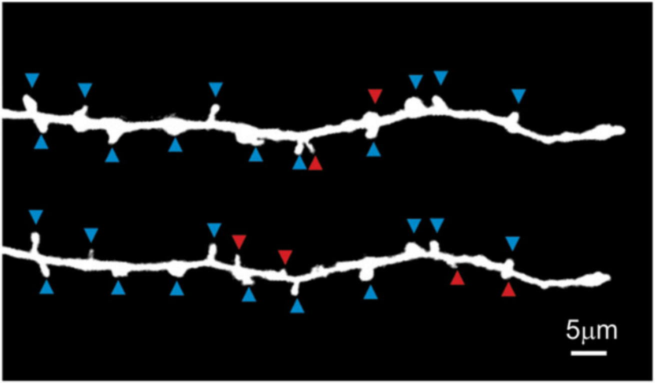








The dynamic connectome

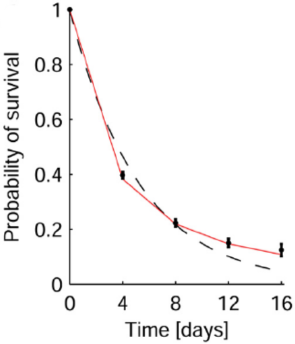


Day 0

Day 4

Loewenstein et al. 2015

The dynamic connectome

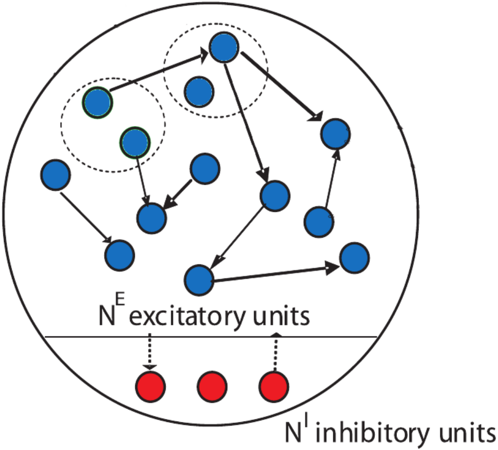


Survival probability of $\rho(t) = (t + 1)^{-\gamma}$ with $\gamma \approx 1.4$,

equivalently lifetime distribution of $f(t) = \gamma(t + 1)^{-(\gamma+1)}$

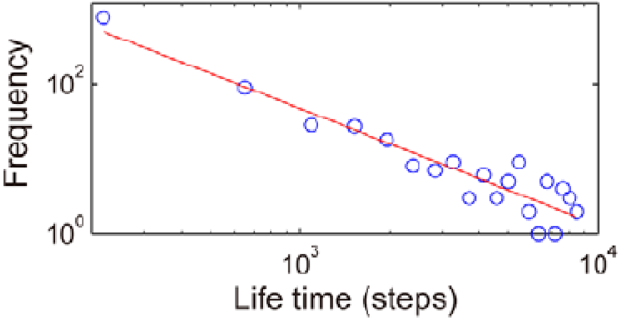
Loewenstein et al. 2015

Synapse dynamics in self-organizing recurrent networks



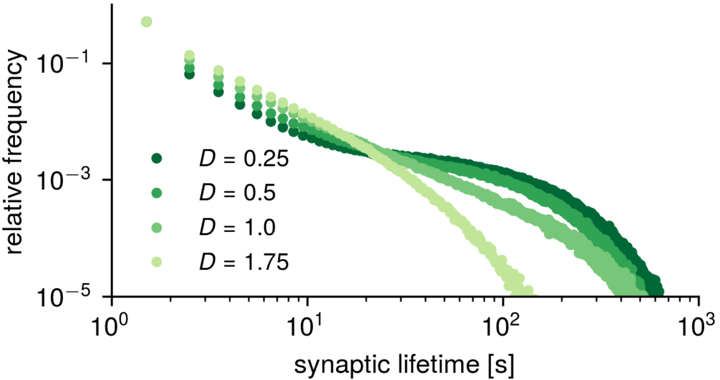
Zheng et al. 2013; Miner and Triesch 2016; Kleberg 2018

Synapse dynamics in self-organizing recurrent networks



Zheng et al. 2013; Miner and Triesch 2016; Kleberg 2018

Lifetimes in the self-organizing recurrent network



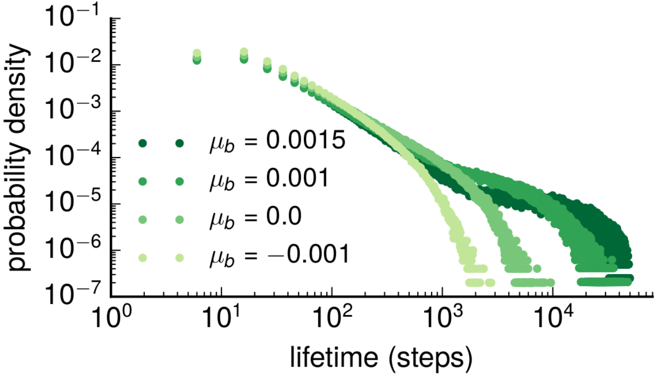
D = LTD–LTP balance

Lifetimes modelled by a stochastic process

Kesten process (Kesten 1973; Statman et al. 2014)

$$X_{n+1} = a_n X_n + b_n$$

as a model for synapse dynamics



Acknowledgements

Stefan Rotter

Jochen Triesch

Daniel Miner

Sarah Jarvis
Stefano Cardanobile

Florence Kleberg
Triesch lab

bcf

FELLOW PROGRAMM FREIES WISSEN
Wissenschaft offen gestalten

FIAS Frankfurt Institute for Advanced Studies

SPP 2041
Computational Connectomics

References

Gal, Eyal, Michael London, Amir Globerson, Srikanth Ramaswamy, Michael W. Reimann, Eilif Muller, Henry Markram, and Idan Segev (2017). Rich Cell-Type-Specific Network Topology in Neocortical Microcircuitry. *Nature Neuroscience*.

Hoffmann, Felix Z. and Jochen Triesch (2017). Nonrandom Network Connectivity Comes in Pairs. *Network Neuroscience*.

Kesten, Harry (1973). Random Difference Equations and Renewal Theory for Products of Random Matrices. *Acta Mathematica*.

Kleberg, Florence (2018).

Lee, Wei-Chung Allen, Vincent Bonin, Michael Reed, Brett J. Graham, Greg Hood, Katie Glattfelder, and R. Clay Reid (2016). Anatomy and Function of an Excitatory Network in the Visual Cortex. *Nature*.

Loewenstein, Yonatan, Uri Yanover, and Simon Rumpel (2015). Predicting the Dynamics of Network Connectivity in the Neocortex. *Journal of Neuroscience*.

Markram, Henry, Joachim Lübke, Michael Frotscher, Arnd Roth, and Bert Sakmann (1997). Physiology and Anatomy of Synaptic Connections between Thick Tufted Pyramidal Neurones in the Developing Rat Neocortex. *The Journal of Physiology*.

Miner, Daniel and Jochen Triesch (2016). Plasticity-Driven Self-Organization under Topological Constraints Accounts for Non-Random Features of Cortical Synaptic Wiring. *PLOS Computational Biology*. Ed. by Olaf Sporns.

Perin, Rodrigo, Thomas K. Berger, and Henry Markram (2011). A Synaptic Organizing Principle for Cortical Neuronal Groups. *Proceedings of the National Academy of Sciences*.

Romand, Sandrine, Yun Wang, Maria Toledo-Rodriguez, and Henry Markram (2011). Morphological Development of Thick-Tufted Layer V Pyramidal Cells in the Rat Somatosensory Cortex. *Frontiers in Neuroanatomy*.

Song, Sen, Per Jesper Sjöström, Markus Reigl, Sacha Nelson, and Dmitri B Chklovskii (2005). Highly Nonrandom Features of Synaptic Connectivity in Local Cortical Circuits. *PLoS Biol*.

Sporns, Olaf (2011). The Non-Random Brain: Efficiency, Economy, and Complex Dynamics. *Frontiers in Computational Neuroscience*.

Statman, Adiel, Maya Kaufman, Amir Minerbi, Noam E. Ziv, and Naama Brenner (2014). Synaptic Size Dynamics as an Effectively Stochastic Process. *PLOS Comput Biol*.

Stepanyants, Armen and Dmitri B. Chklovskii (2005). Neurogeometry and Potential Synaptic Connectivity. *Trends in Neurosciences*.

Vegué, Marina, Rodrigo Perin, and Alex Roxin (2017). On the Structure of Cortical Microcircuits Inferred from Small Sample Sizes. *Journal of Neuroscience*.

Zheng, Pengsheng, Christos Dimitrakakis, and Jochen Triesch (2013). Network Self-Organization Explains the Statistics and Dynamics of Synaptic Connection Strengths in Cortex. *PLOS Comput Biol*.