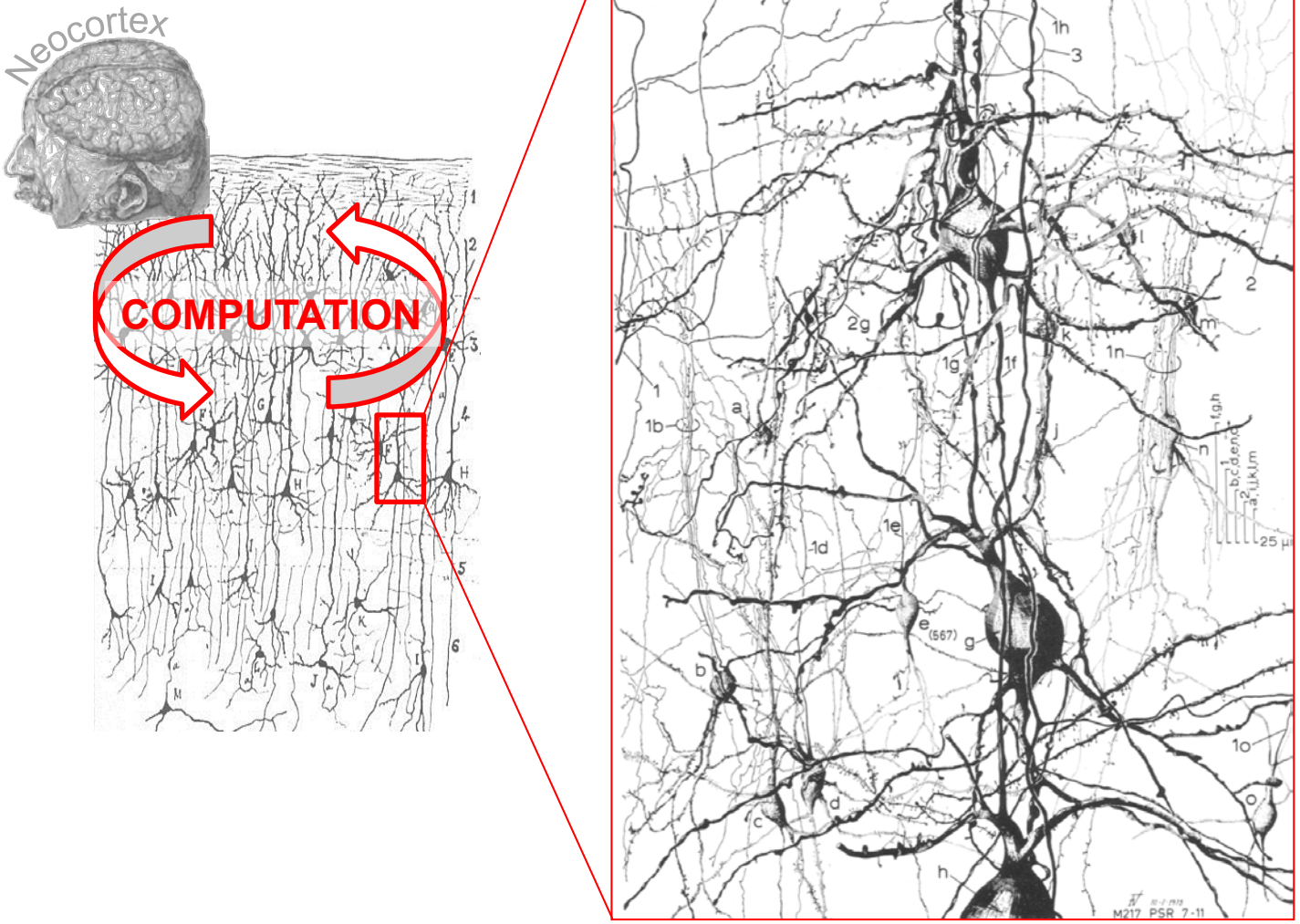
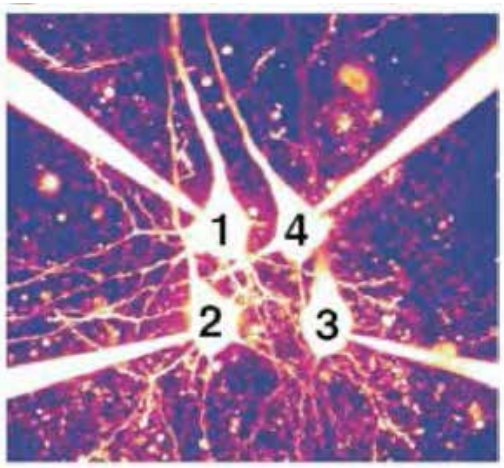
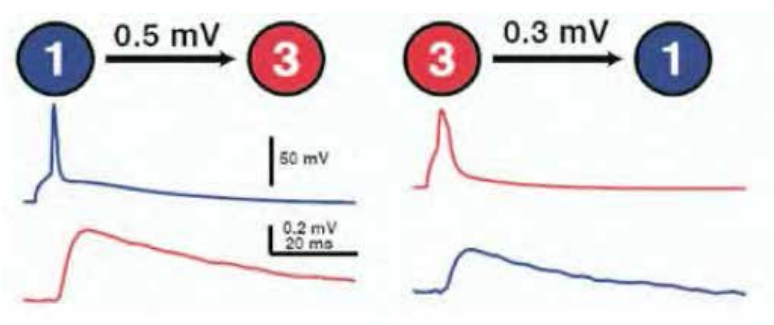
How does function constrain synaptic connectivity?

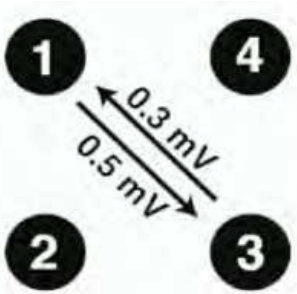


Valverde (J Neurocytology 1976)

Multiple whole-cell recordings to assay connections between cell pairs





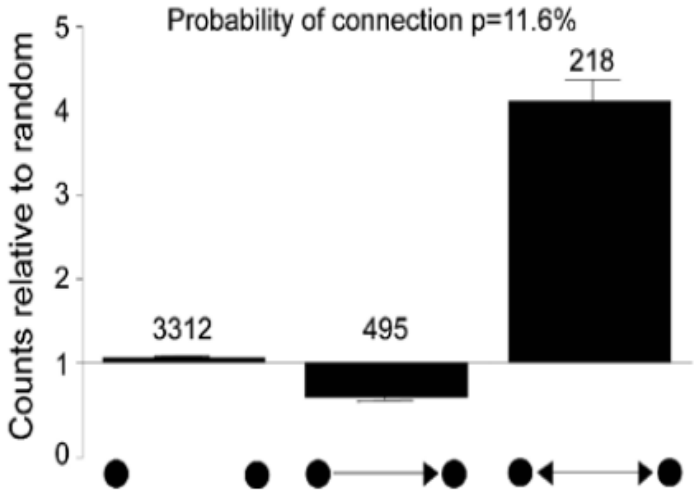


- Information about the presence and strength of connections
- But false negatives due to slicing artefacts

Song, Sjöström, Reigl, Nelson & Chklovskii (PLoS Biology 2005)

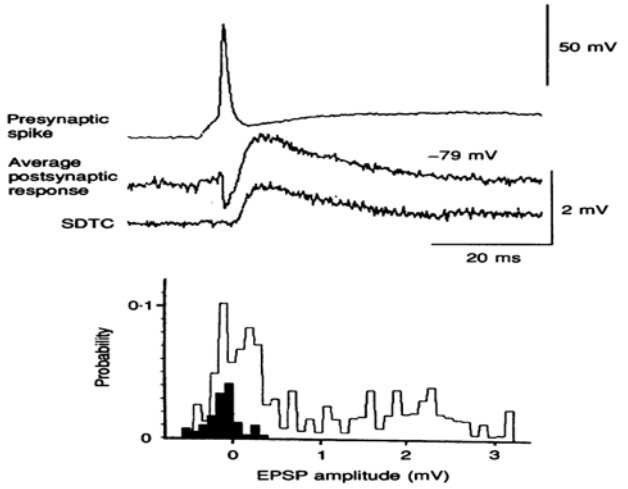
Excitatory connectivity in the neocortex is neither uniform nor random

Overrepresentation of bidirectional motifs



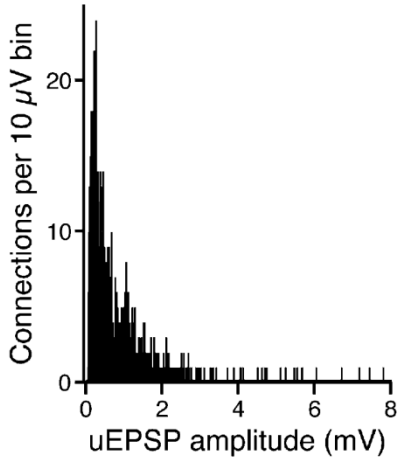
L5 pyramidal cells, Song et al. (2005)

Connection strengths are variable and their distribution has a long tail



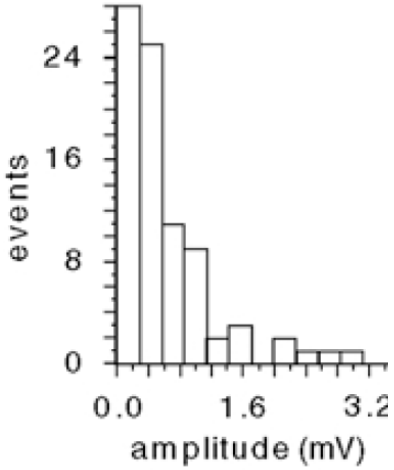
L5/6 pyramidal cells, Deuchars, West, Thomson (1994)

Vibrissa cortex, all excitatory connections



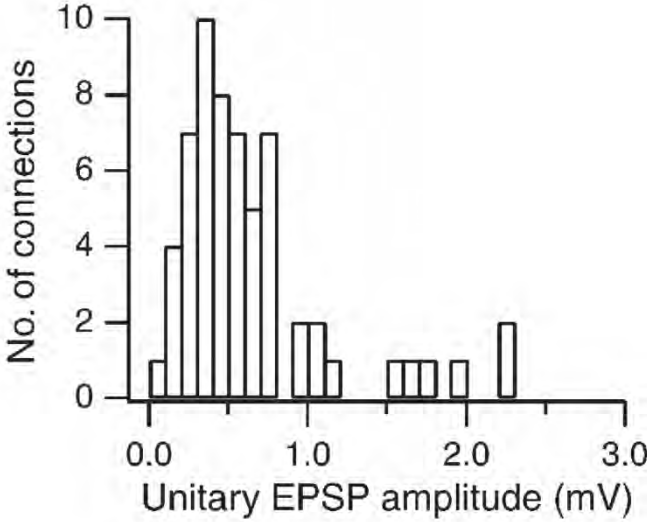
Lefort et al 2009

Visual cortex, L2/3 → L2/3 pyramid



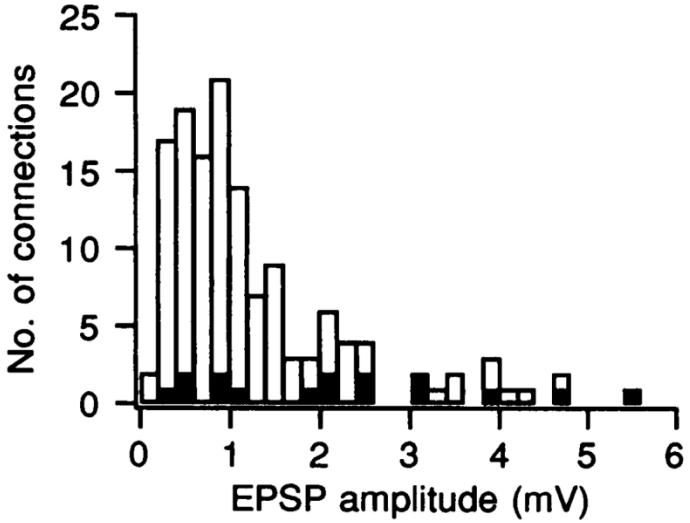
Holmgren et al 2003

Vibrissa cortex, L4 stellate → L2/3 pyramid



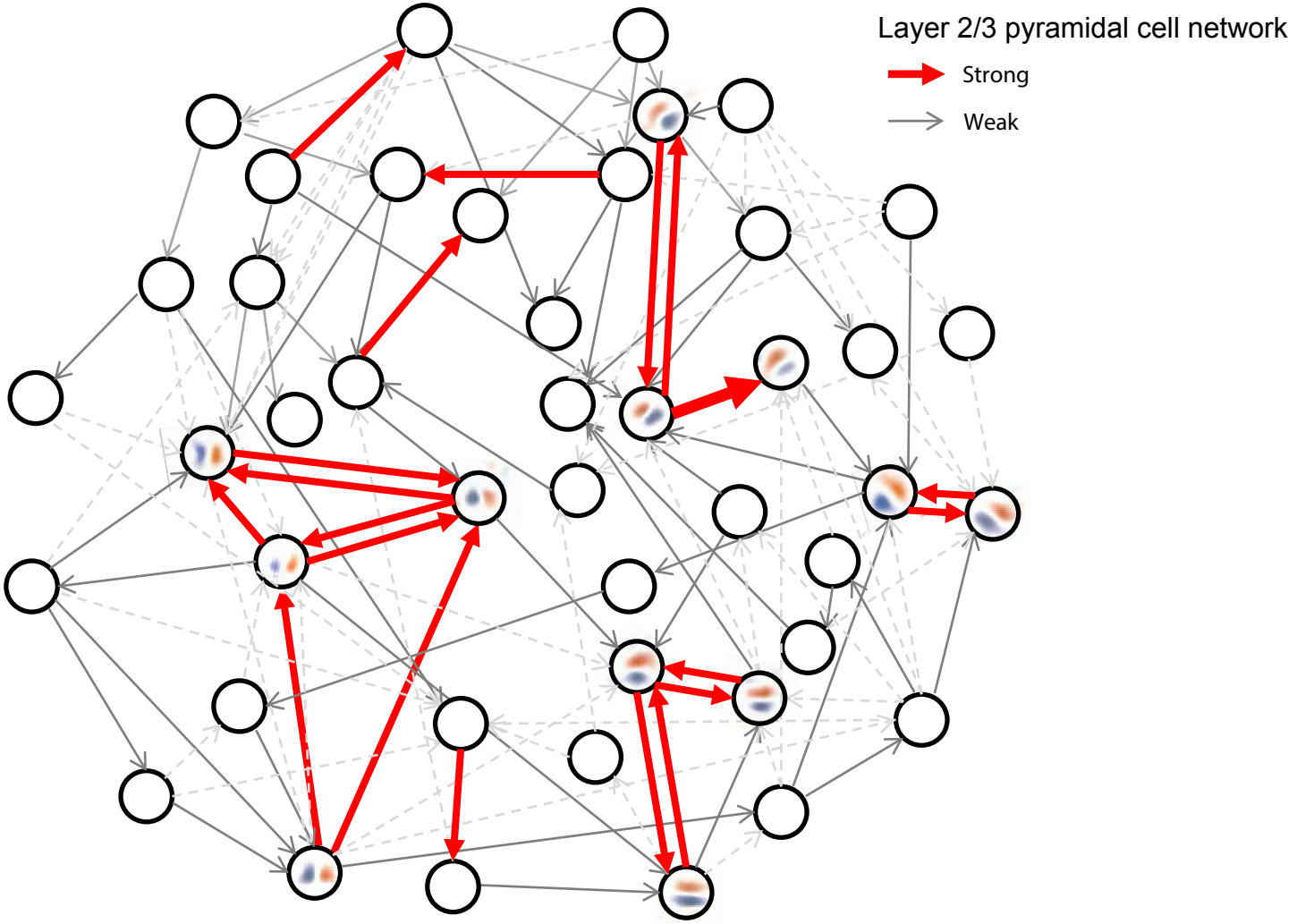
Feldmeyer et al 2002

Vibrissa cortex, L5 → L5 pyramid



Markram et al 1997

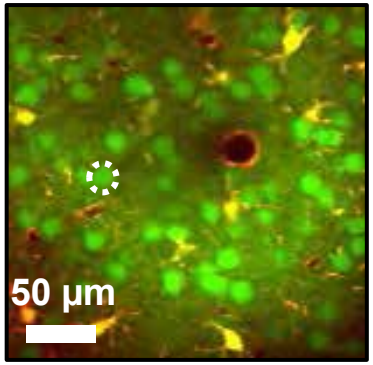
Are neurons connected by few strong synapses in a sea of weak synapses?



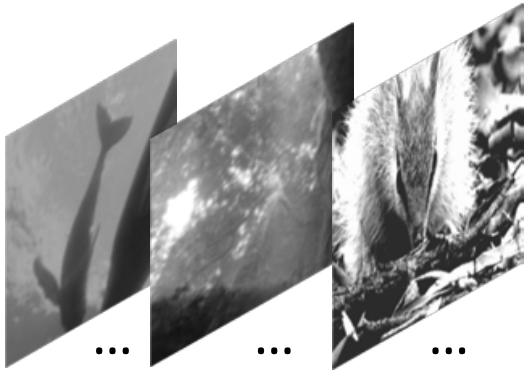
Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)

Mapping receptive fields with two-photon calcium imaging and reverse correlation

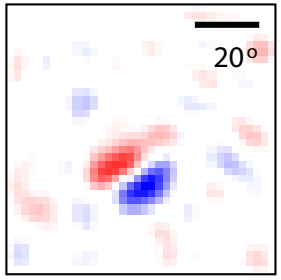
Example cell



Stimuli

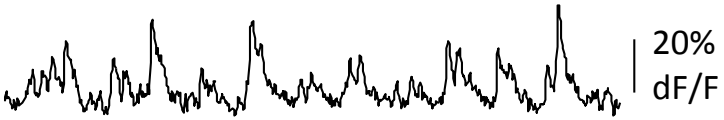


Linear receptive field

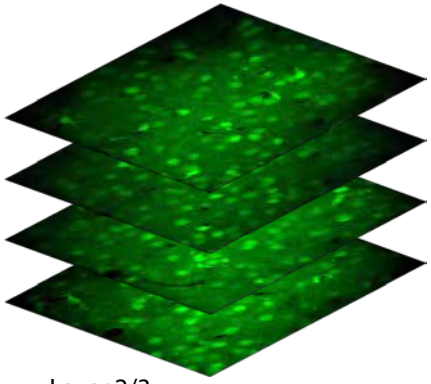


Quiescence Spike

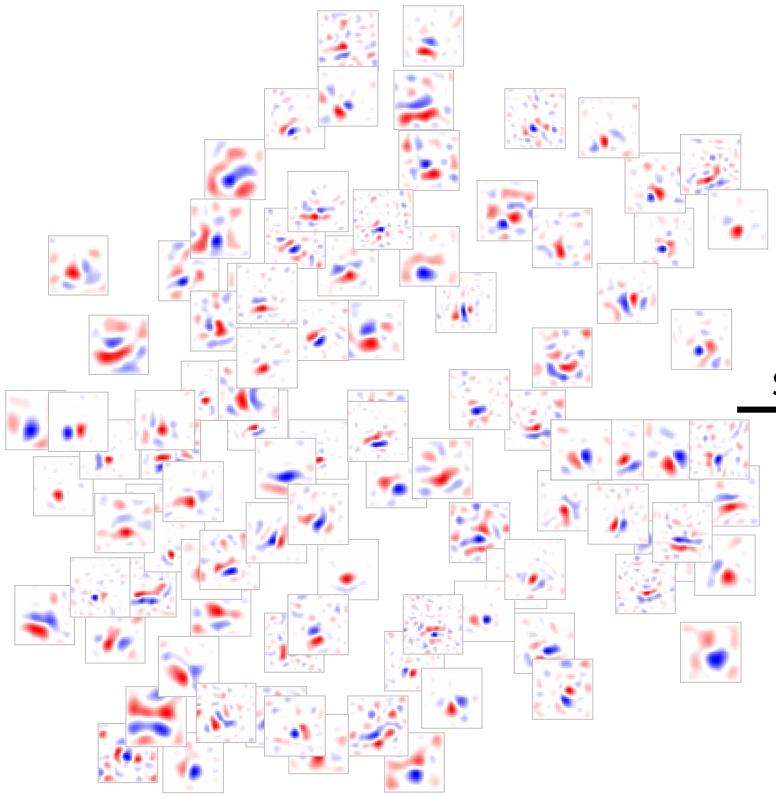
Calcium response



Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)

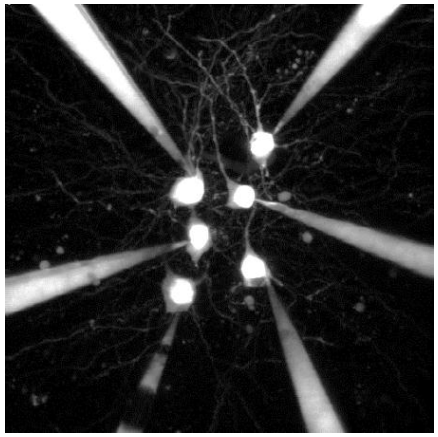


Layer 2/3
300 µm x 300 µm x 56 µm



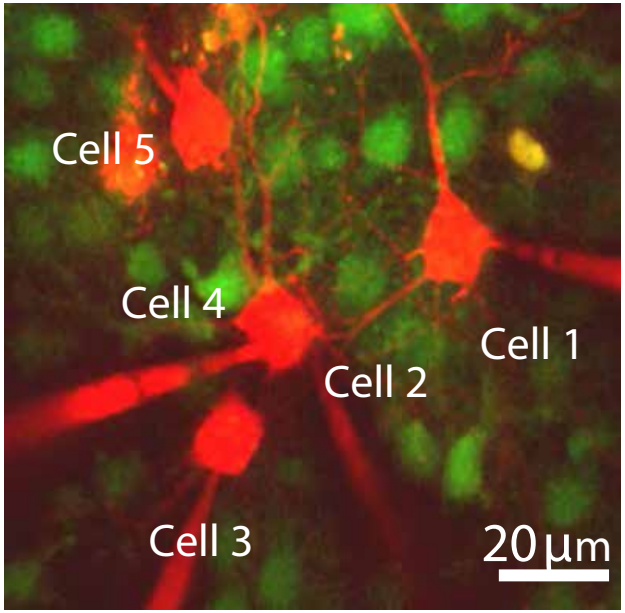
slice

Mutiple patch clamp

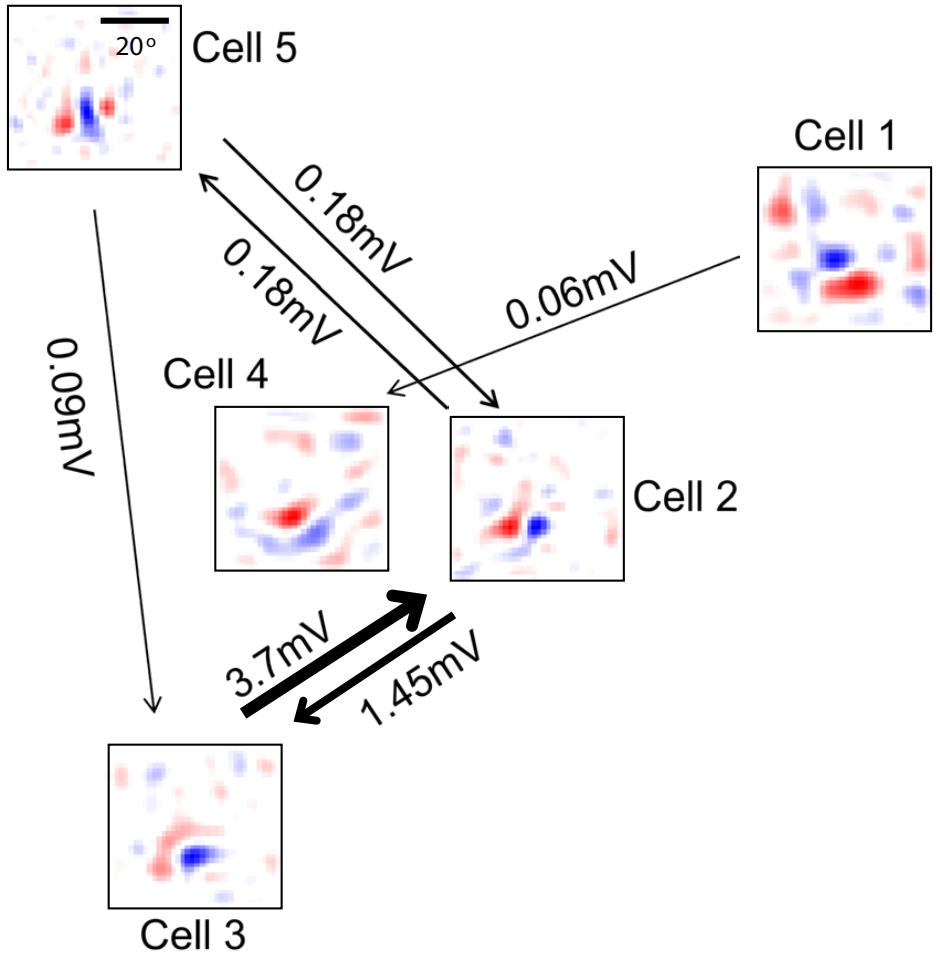


Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)

Relating synaptic connections to receptive fields

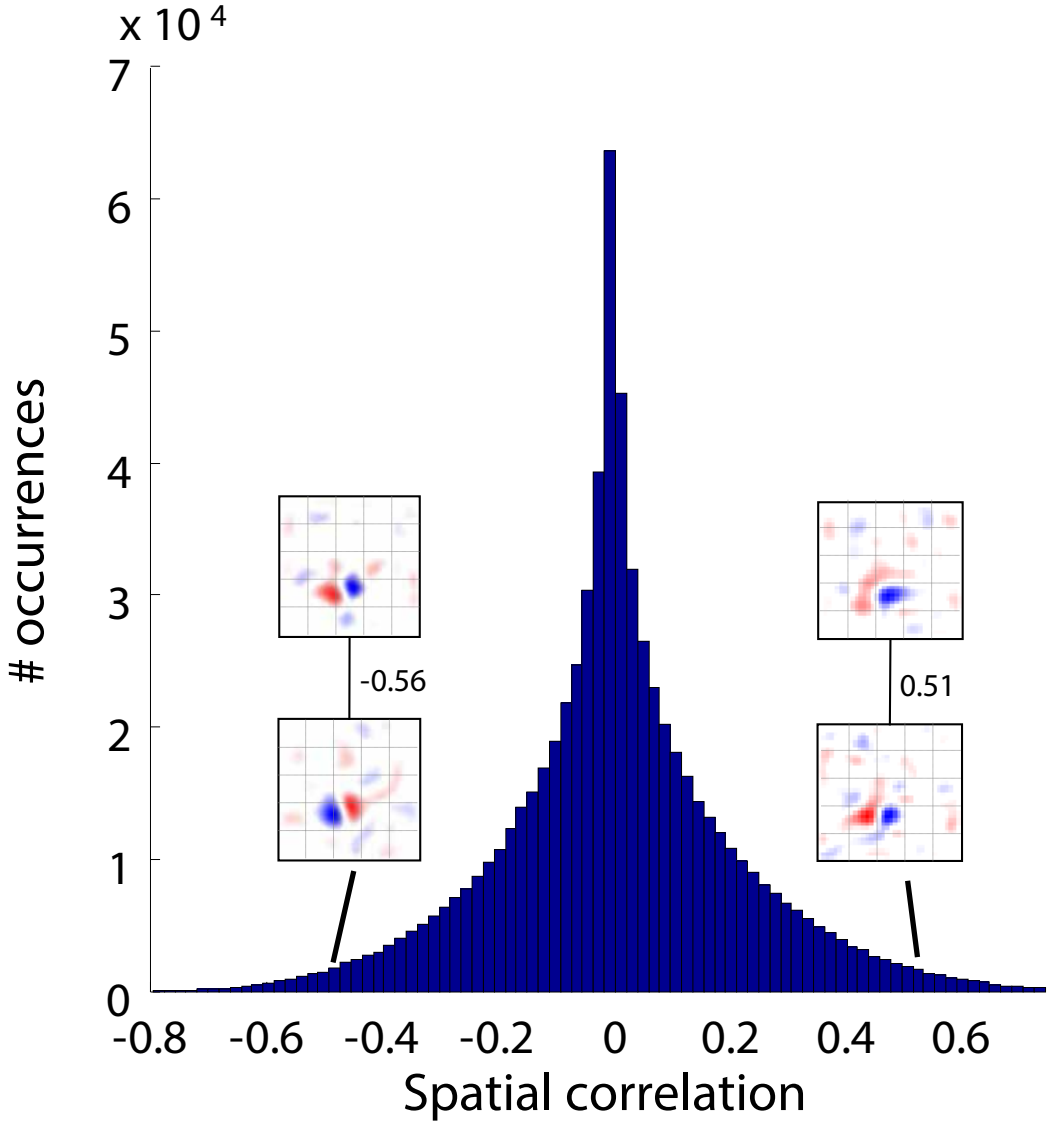


Exp : 20130522, Motif 2



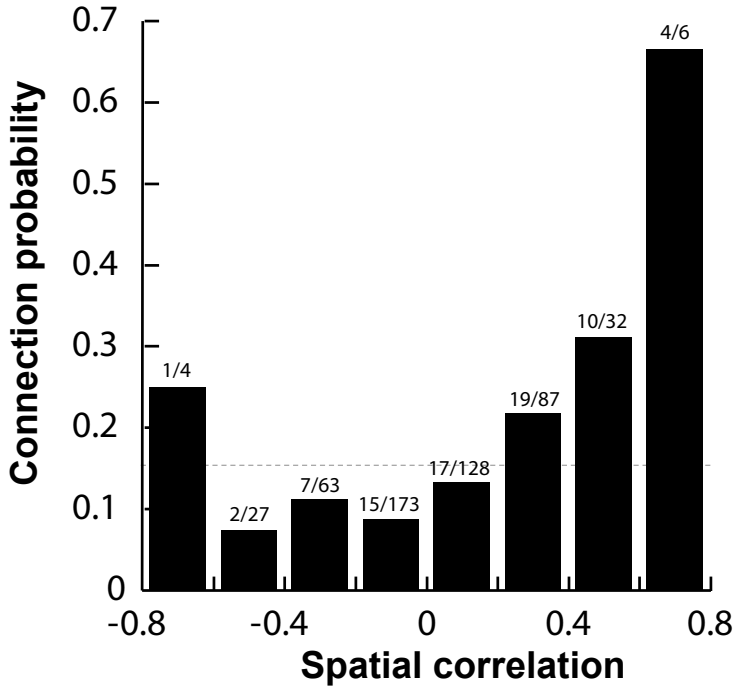
Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)

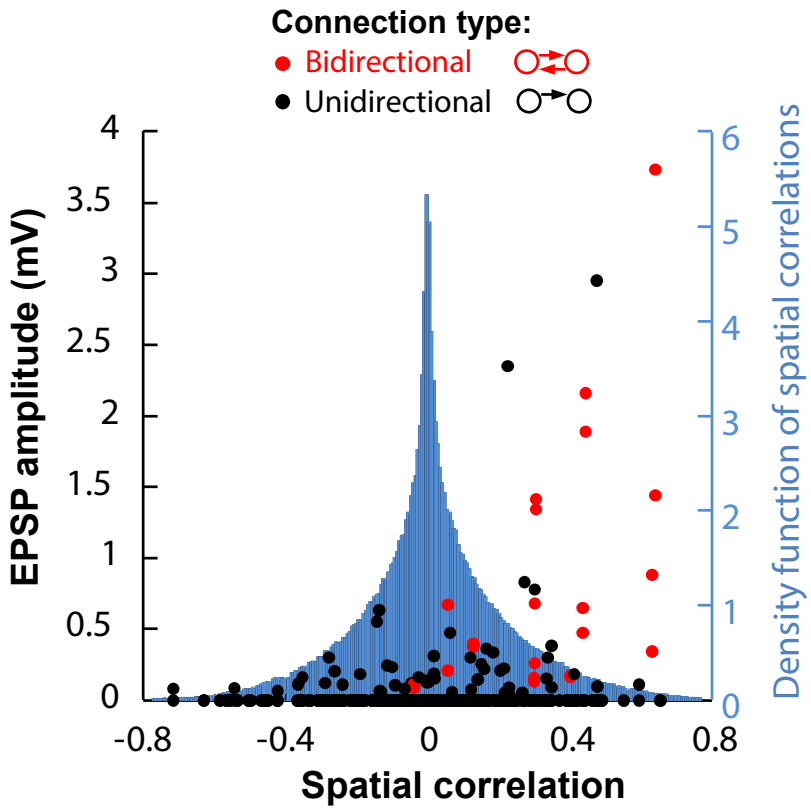
Spatial correlation of the receptive fields as a measure of cell-to-cell similarity



Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)

Similarity of receptive fields predicts probability, strength, and reciprocity of synaptic connections

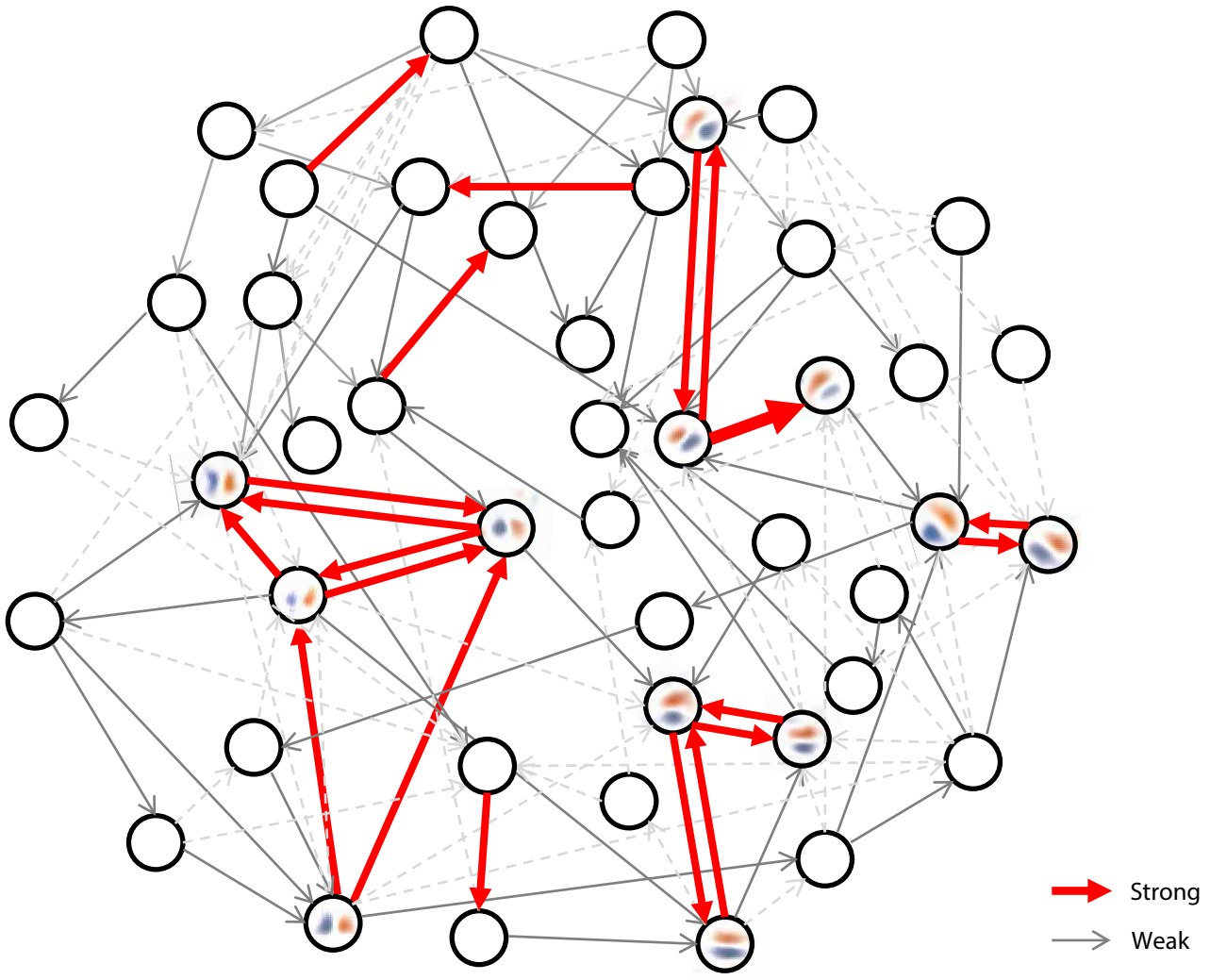




- Spatial correlation is a strong predictor of connectivity
- Cell pairs with positive correlations are more likely to connect with strong connections
- Reciprocal connections are stronger and exist between cell pairs with similar receptive fields

Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)

At least in primary visual cortex, the evidence implies that neurons are connected by a few strong synapses in a sea of weak synapses



Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)