How do function and projection targets constrain synaptic connectivity?
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

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, L4 stellate $\rightarrow$ L2/3 pyramid

Visual cortex, L2/3 $\rightarrow$ L2/3 pyramid

Vibrissa cortex, all excitatory connections

Visual cortex, L5 $\rightarrow$ L5 pyramid

Feldmeyer et al 2002

Holmgren et al 2003

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)
Acuity (cycle/°)
Human 46
Mouse 0.5
Mapping receptive fields with two-photon calcium imaging and reverse correlation

Example cell

Stimuli

Linear receptive field

Calcium response

Quiescence Spike

Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)
Layer 2/3
300 μm x 300 μm x 56 μm

Mutiple patch clamp

Cossell, Iacaruso, Muir, Houlton, Sader, Ko, Hofer & Mrsic-Flogel (Nature 2015)
Relating synaptic connections to receptive fields

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.