

The Role of Neuronal Identity in Synaptic Competition

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Summary (1)

- Neonatal mammalian muscle- ***Polyneuronal Innervation***
- ***Synaptic Competition*** => Survival of one axon branch, withdrawal of the others (*irregularly*- i.e. not together, at the same time)
- Why does one *specific* branch survive? Why do some competitions last longer than others?

Summary (2)

- Neuron axon branches = axonal **arbor**
- Arbor is involved in *many* competitions along neuron
- Neurons with *larger* arborisations fare worse against neurons with *smaller* arborisations

Aims

- To demonstrate whether the fate of axons at co-innervated junctions is related to the properties of the competing axon or its parent neuron
- Thus, to determine whether *Competitive Vigour* is a *local* or *global* phenomenon
 - i.e. A property of the axon branch? Or its environment?

Hypothesis (1)

- An axonal branch is influenced by a competing axon (and not its parent neuron) if, when the two branches co-innervate the same target cells, the outcome of the competition favours the same axon at every target.

Hypothesis (2)

- As competitive vigour depends on a globally distributed resource (neurotransmitter), larger motor units- with larger arborisations- are at a competitive disadvantage when compared to smaller motor units

Two competing motor units

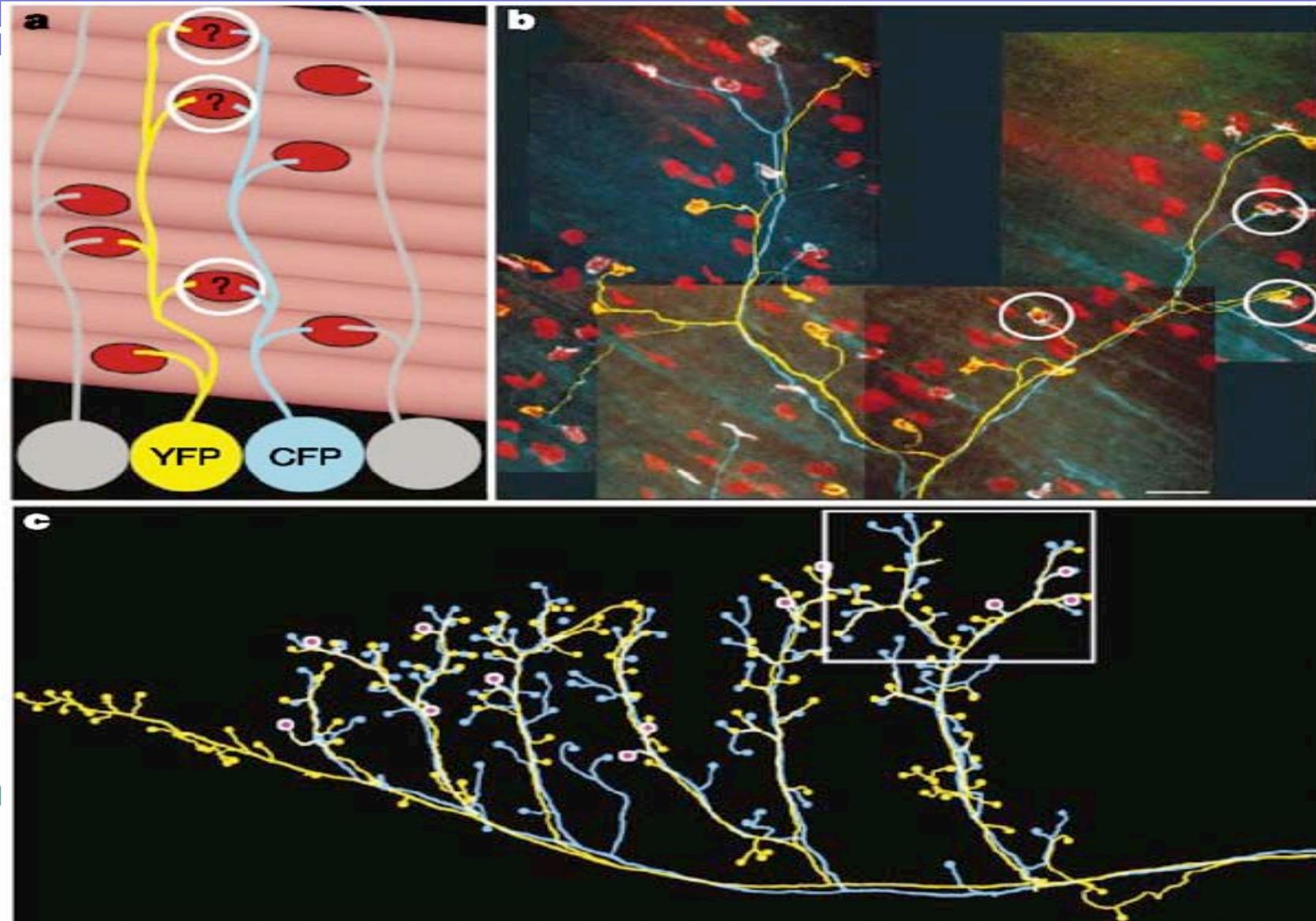
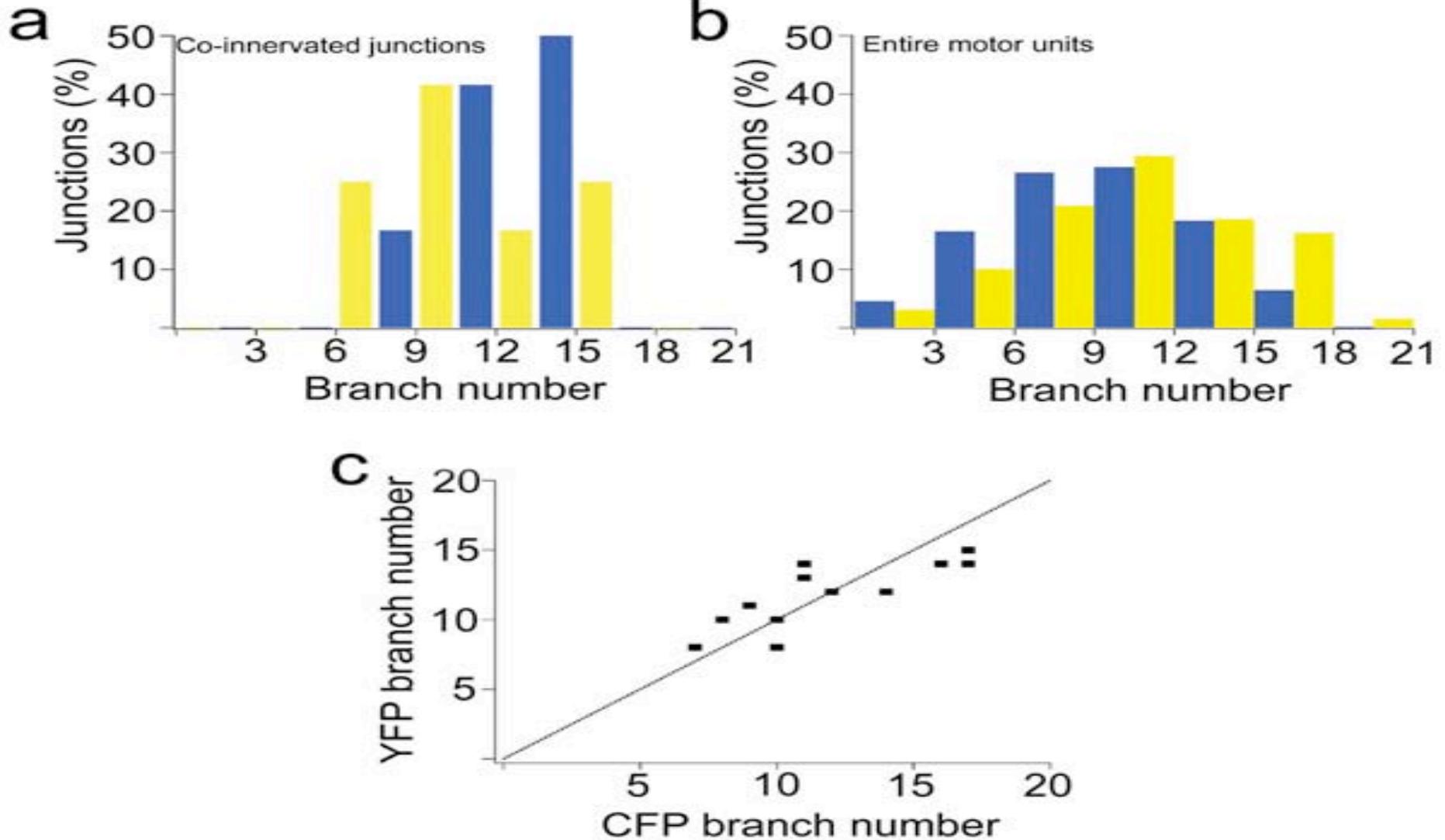


Figure 1- Kasthuri et al, 2003

Distribution & Numbers of Axonal Branches

Lichtman supplemental figure 1



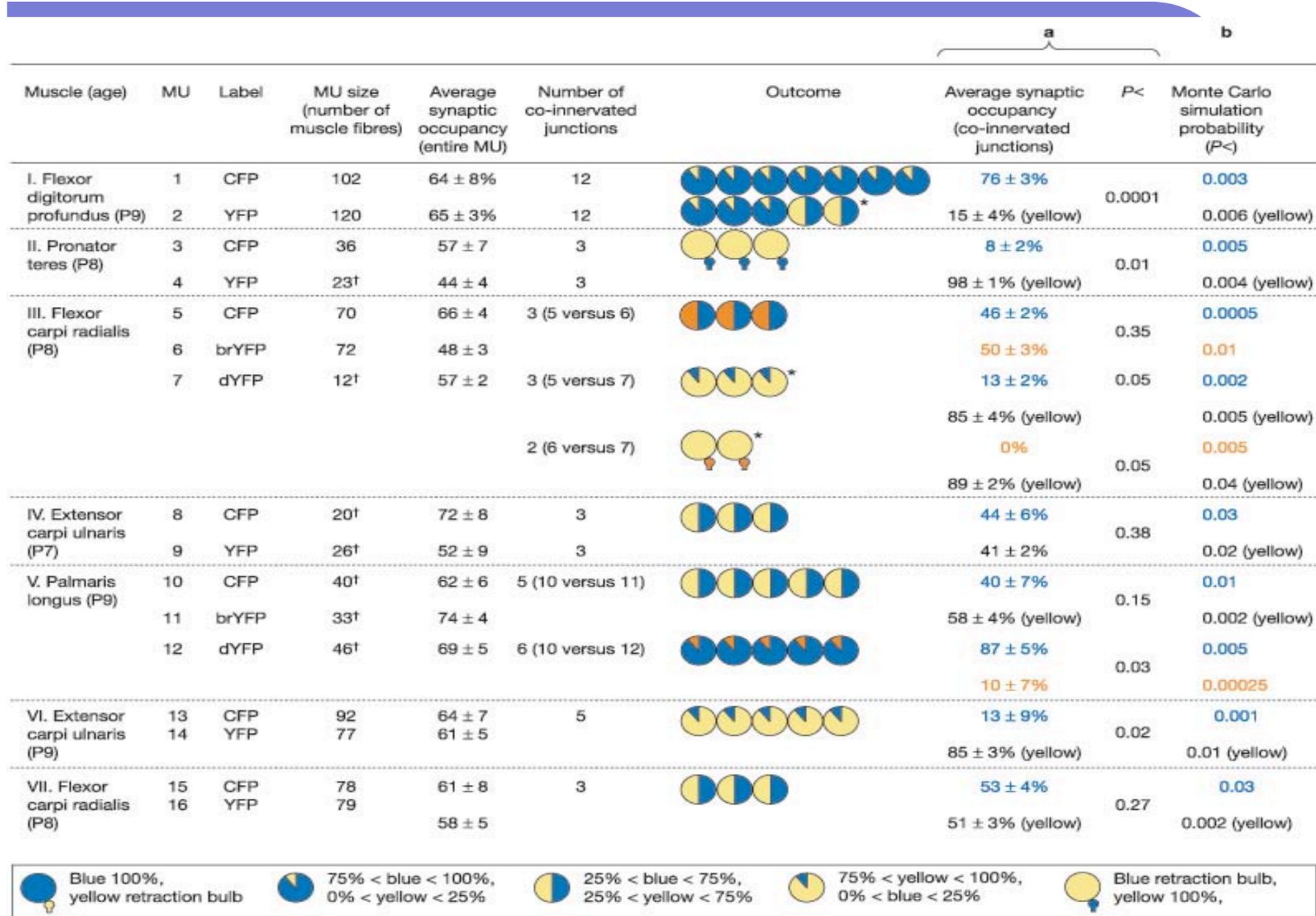


Figure 2- Kasthuri et al, 2003

Co-innervated NMJs

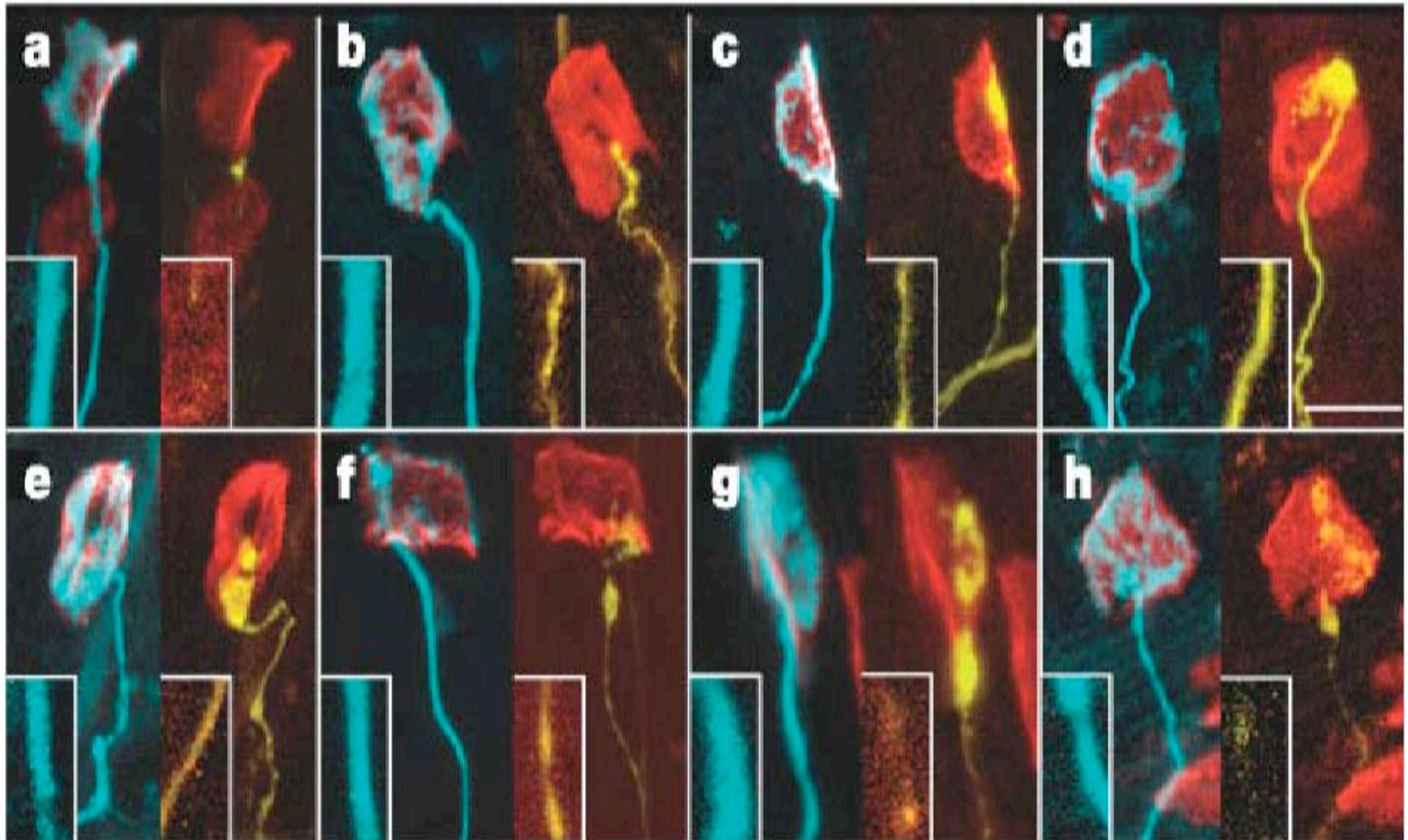


Figure 3a-h- Kasthuri et al, 2003

Co-innervated & Normal NMJs (contd.)

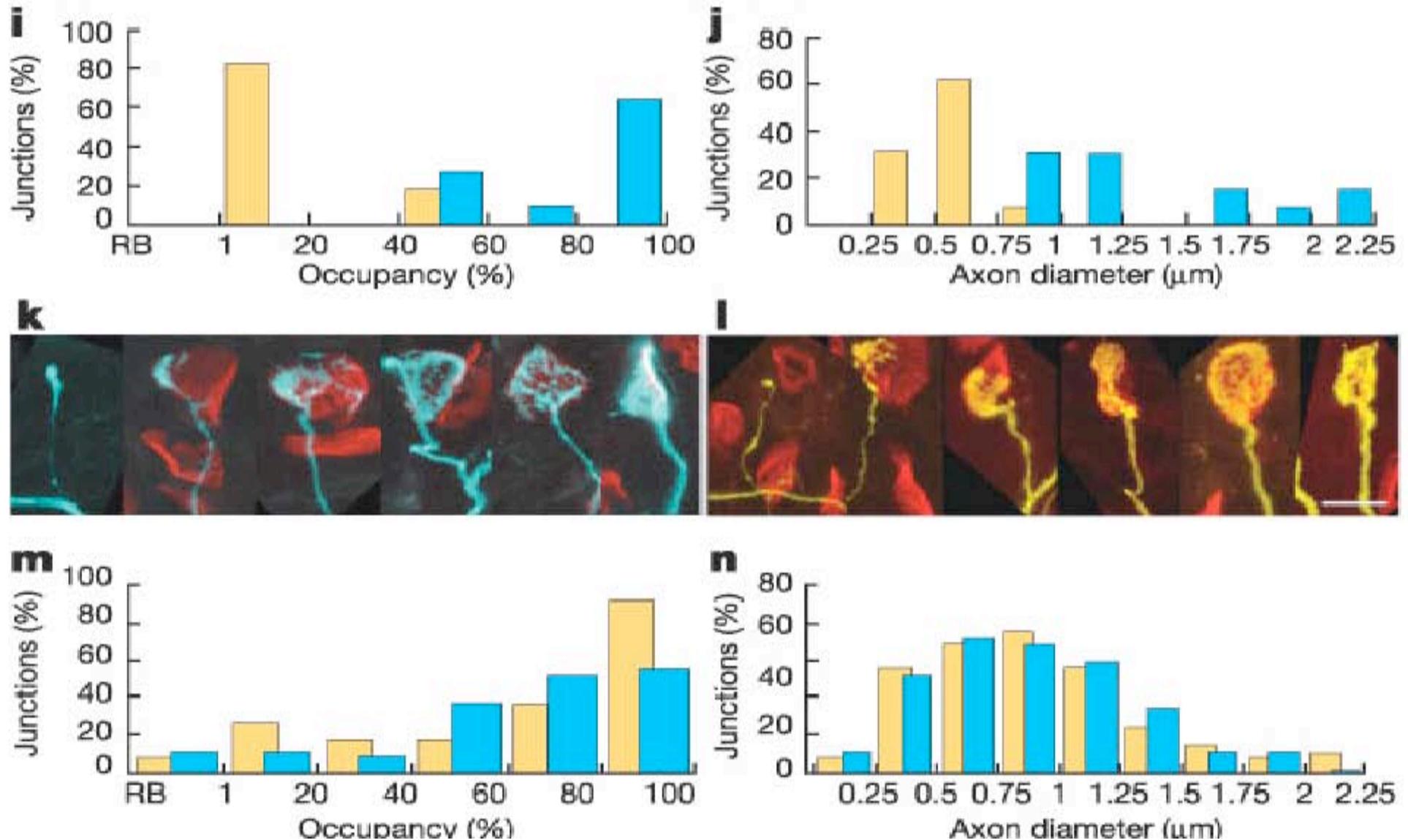


Figure 3i-n- Kasthuri et al, 2003

Synapse Elimination

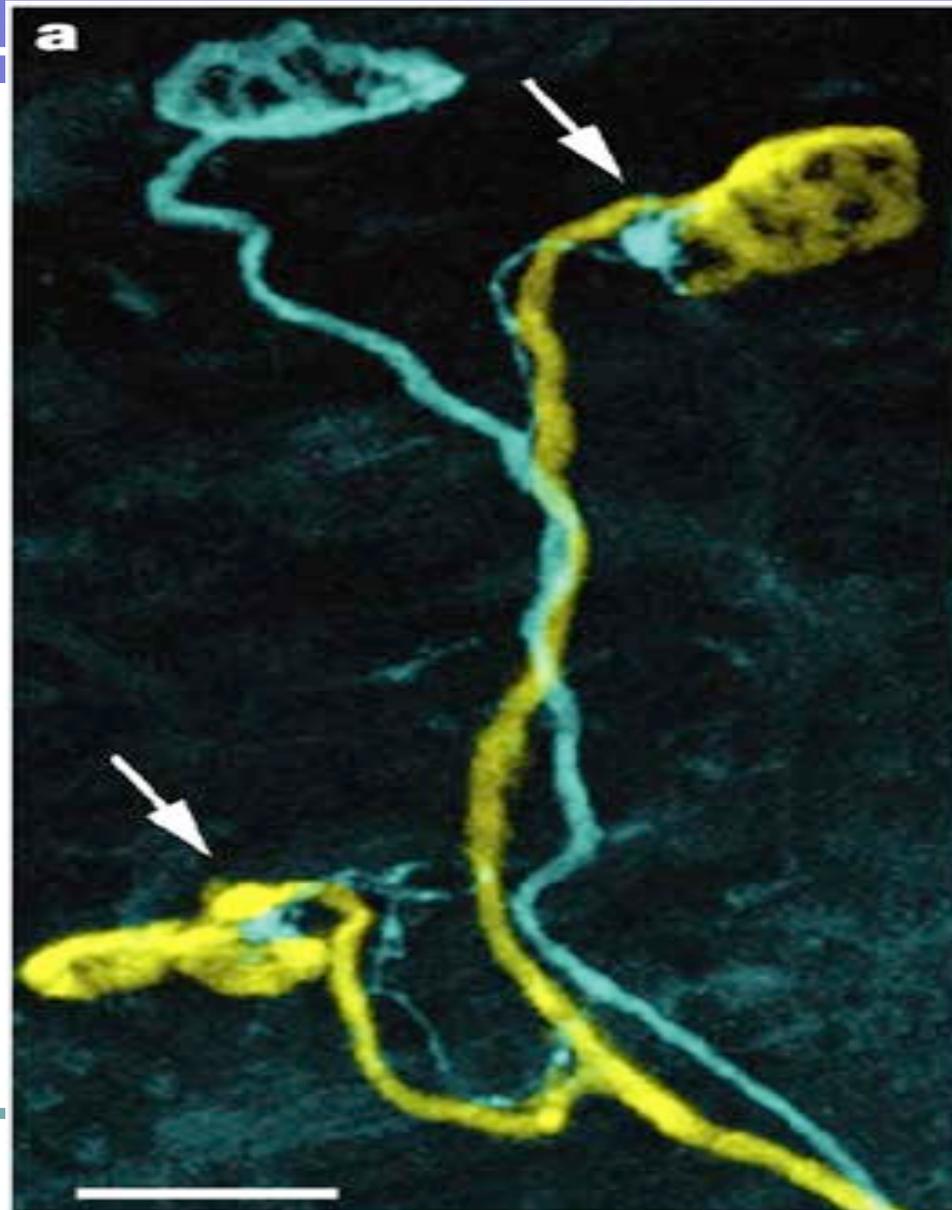


Figure 4a- Kasthuri et al, 2003

Synapse Elimination & Competitive Vigour

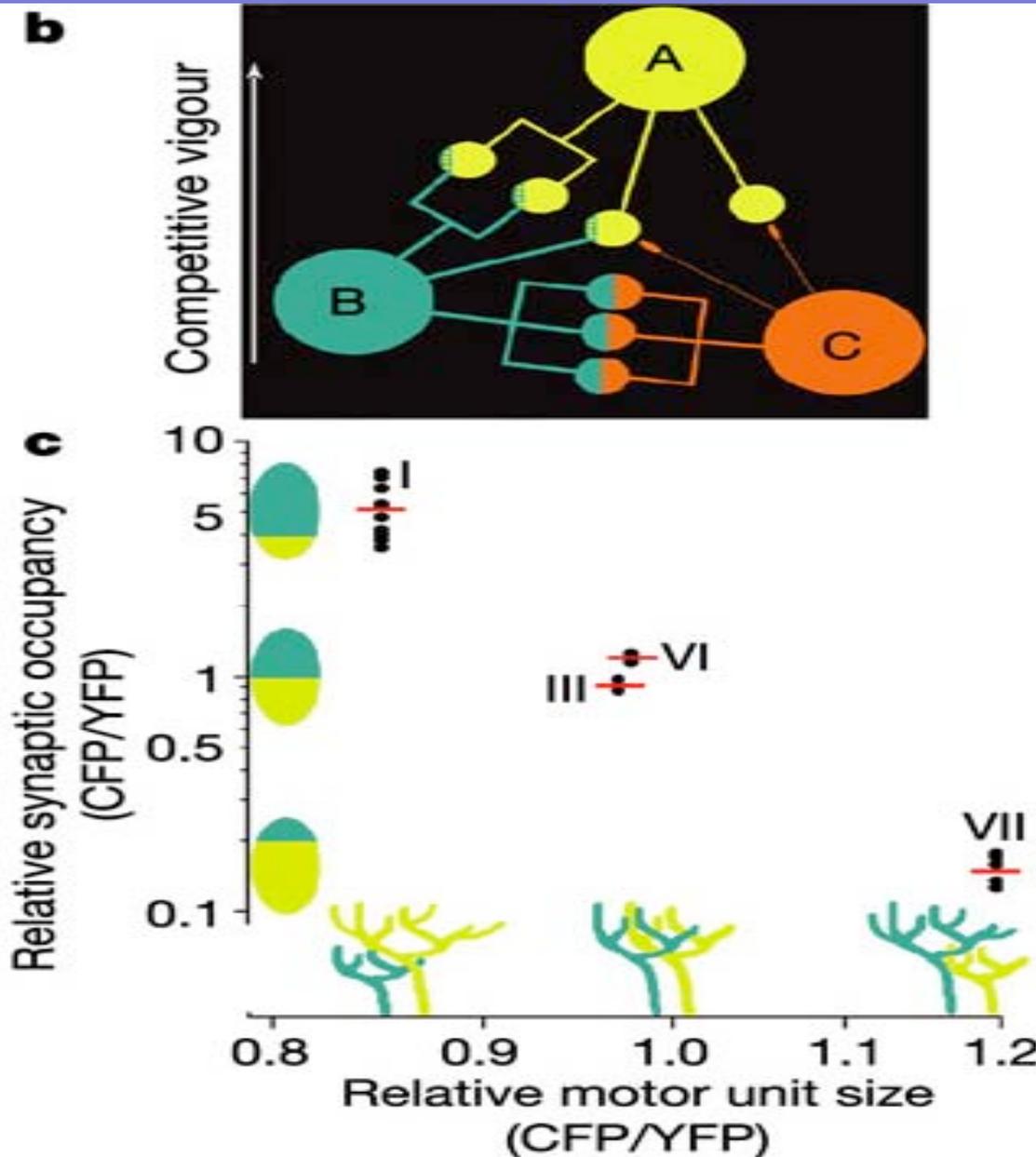


Figure 4b-c- Kasthuri et al, 2003

Conclusions (1)

- The pace & outcome of synaptic elimination are determined by the **opposing axon** at a co-innervated synaptic cell:
 - Buffelli et al. confirm that the opposing axon's *level, pattern & timing* of *Axonal Activity* (and *amount of neurotransmitter* released) are entirely responsible for the pace & outcome of synaptic elimination
- Hypothesis: the opposing axon IS responsible for synaptic elimination because the results prove that when two neurons co-innervate several target cells, the outcome IS skewed in favour of the SAME axon at all common targets

Conclusions (2)

- The reasons why one axonal branch will survive and another will withdraw are **unlikely** to be due to *chance* or *local factors*
- This study demonstrates that competitive vigour is reliant on a limited, global resource:
 - Larger arborisations/motor units have **less** *competitive vigour*- meaning that they will be at a ***competitive disadvantage***
 - Thus, as the size of axonal arbor INCREASES, the synaptic occupancy of its branches DECREASES
 - Buffeli et al. confirm this because those axons with greater *competitive vigour* destabilise those axonal branches with less of this resource

Strengths

- Very clear, detailed and bright images obtained by the *'Laser Scanning Confocal Microscope'*
- Such microscopes are widely available and relatively inexpensive

Limitations (1)

- Only 7 different muscles were studied
- Only ages P7-P9 were studied...
 - no long term, developmental analysis possible
 - Does synaptic competition differ when there is polyneuronal innervation with more than two axonal branches? i.e. at earlier ages than in this study
- Method is limited to only 2 colours

Limitations (2)

- Labour-intensive process; two breeds of transgenic mice are required to produce the ‘double-subset expressing mice’ examined in this study
- Possibility of Human Error:
 - In measuring the Branch Number (Supplementary Figure 1)?

- Questions?