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Evidence for a Role of Dendritic Filopodia in Synaptogenesis and Spine Formation

Does dendritic filopodia actively initiate synaptogenic contacts, and thereafter evolve into dendritic spines ?

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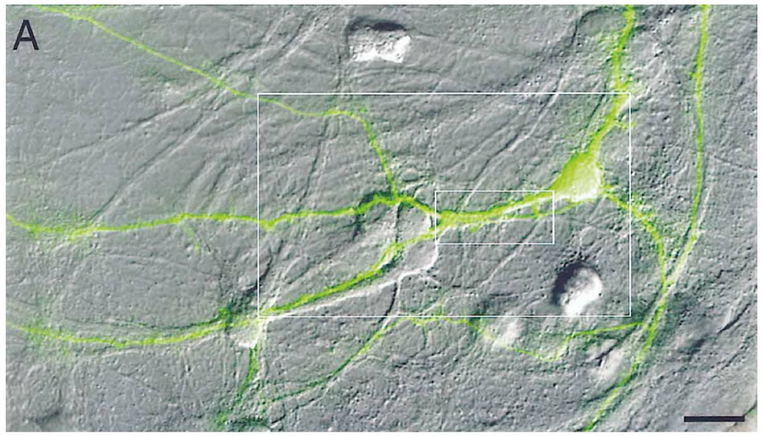
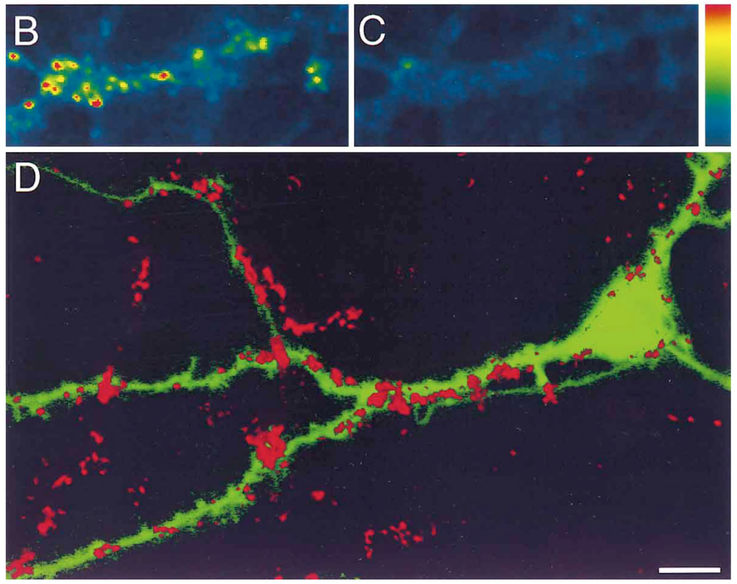


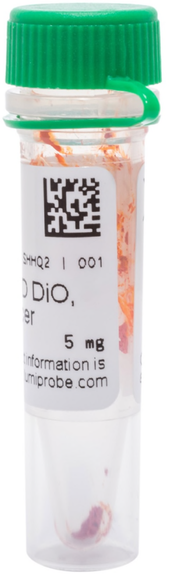


Cell cultures of live rat hippocampal neurons

Fast- DIO fluorescent liphofilic dye

FM4-64 fluorescent endocytotic marker

Time-lapse recordings of dendritic structures



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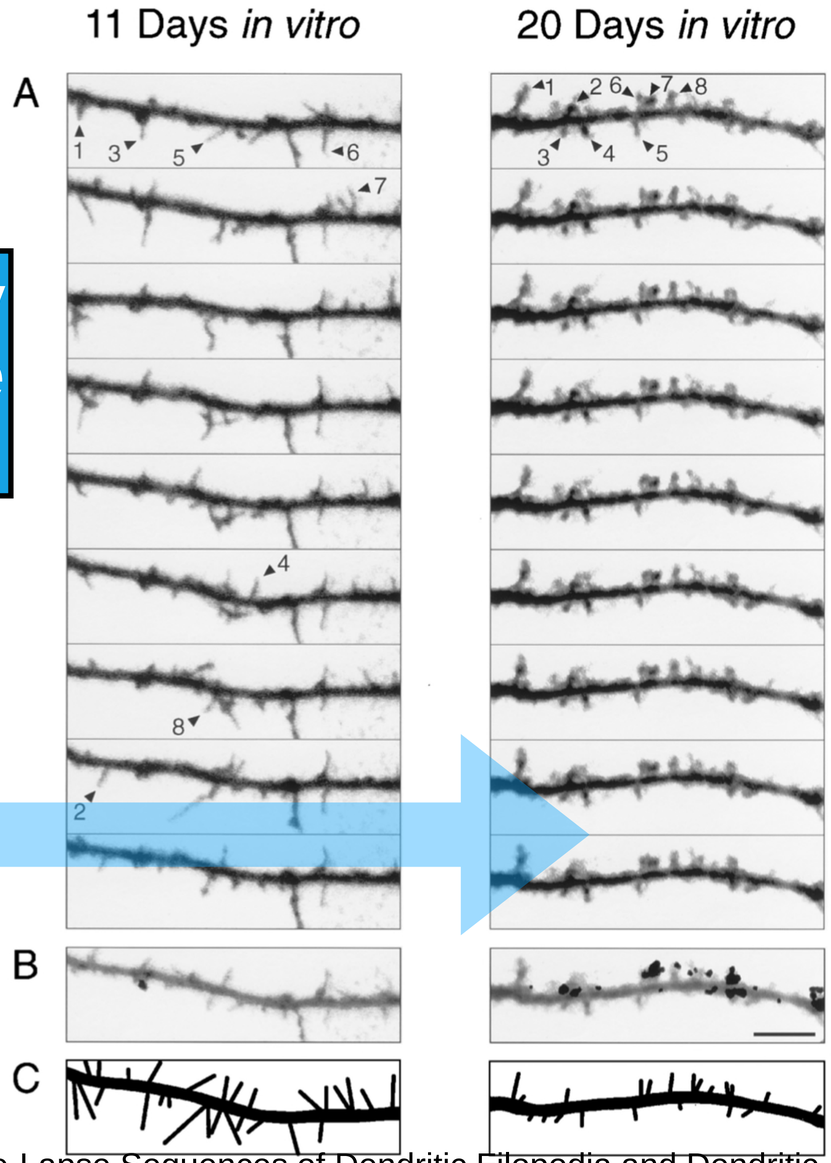
Dendritic Filopodia Exhibit Protrusive Motility Patterns Consistent with a Role in Short-Range Exploration and Contact Initiation

Most of the protrusion on the younger dendrite are transient structures

Dendritic protrusions of the older neurons are persistent structures

Cumulative representation of all spines or filopodia in the 9 frames



Time-Lapse Sequences of Dendritic Filopodia and Dendritic Spines

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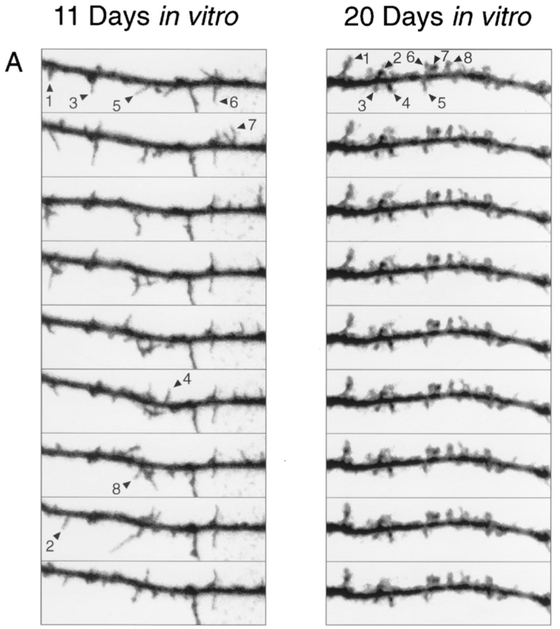
Dendritic Filopodia Are Formed in Sufficient Numbers to Account for the Entire Spine Population

Based on any single timepoint, one might conclude that there are many more spines on the dendrite of the older neuron than filopodia on the younger dendrite.



Each filopodium or spine is represented by a line proportional to the peak length

When this comparison is based on images representing the cumulative appearance of transient filopodia during an extended period, even as short as 1 hr, the filopodium density easily exceeds the spine density in the older neuron.

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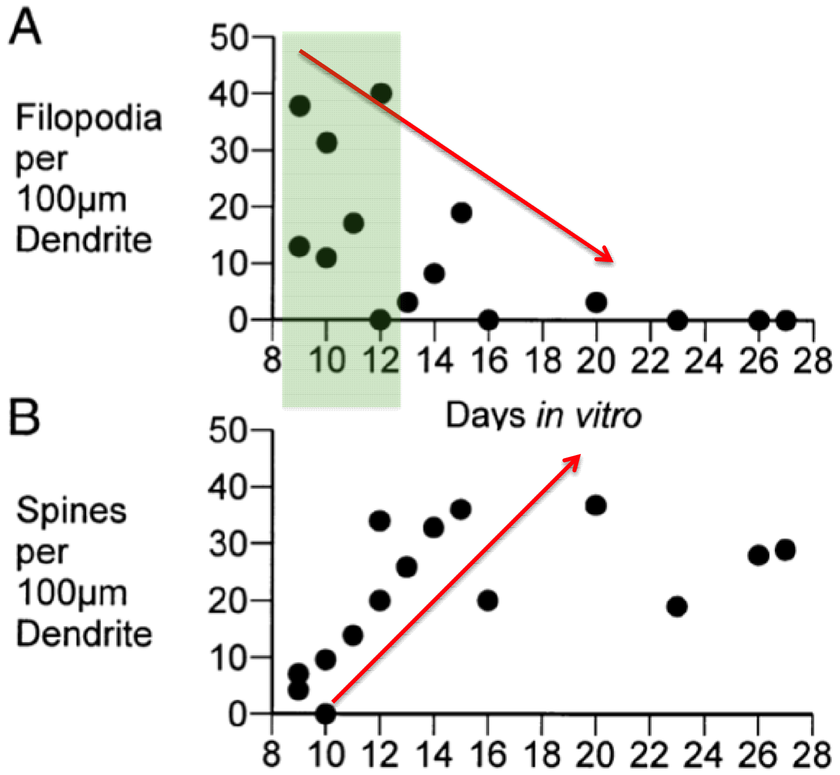
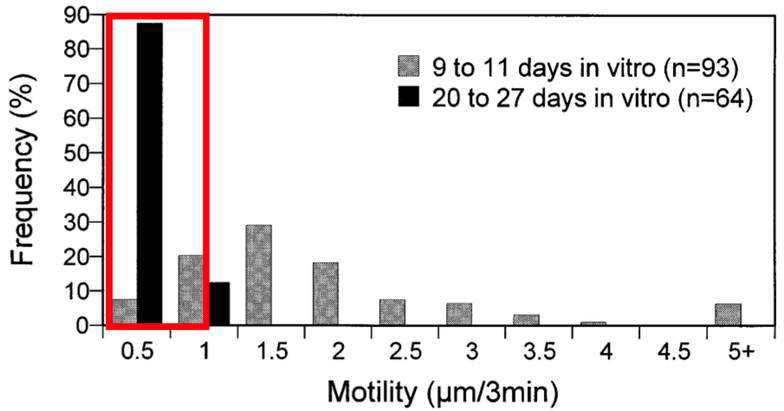
Are dendritic filopodia the direct precursor of dendritic spine?

density



time

FILOPODIA = motility score > 1 um/3 min



STABLE SPINES = motility score =< 1 um/3 min

The complementary time courses of filopodium and spines densities seem consistent with the proposal that dendritic spines are formed by the stabilization of motile dendritic filopodia.

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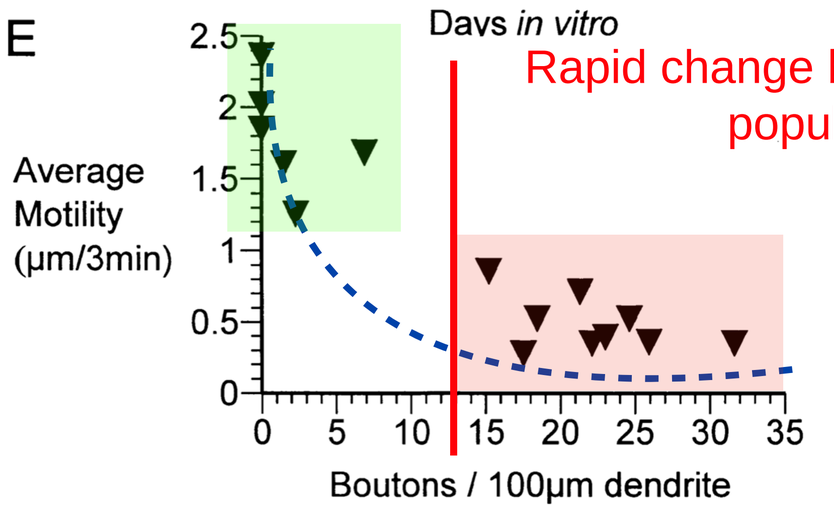
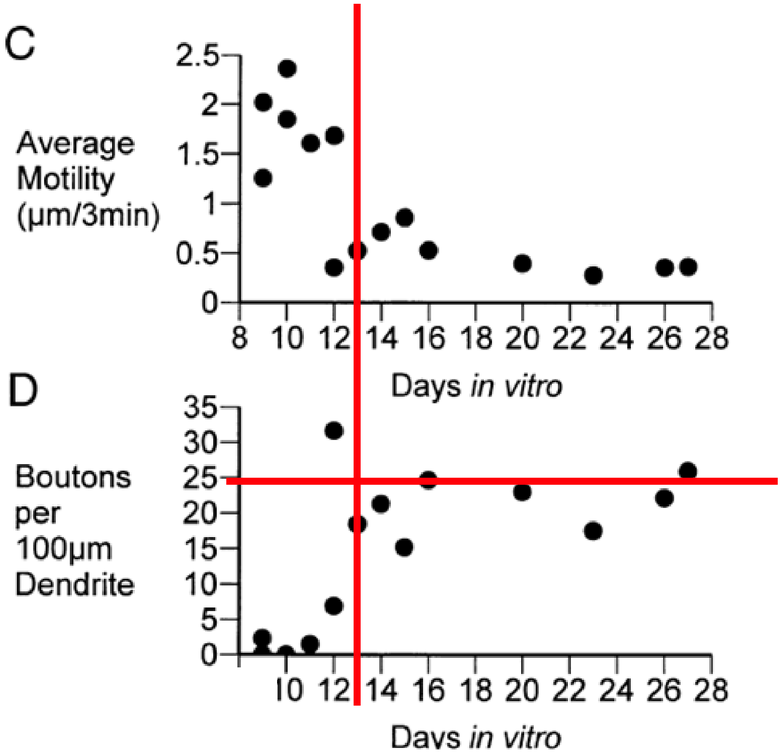
Spine Appearance Is Associated with the Appearance of Functional Synapses

Dendritic protusive activity



Rapid change between the two populations



sparsely innervated neurons with highly motile dendritic protrusions

densely innervated neurons with stable dendritic protrusions

FILOPODIA ARE INSTRUMENTAL TO ESTABLISH AXON-DENDRITIC CONTACT

Reduction of motility AND of additional spines

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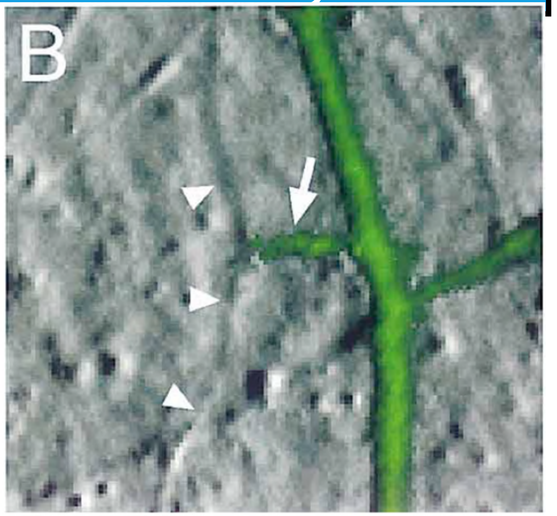
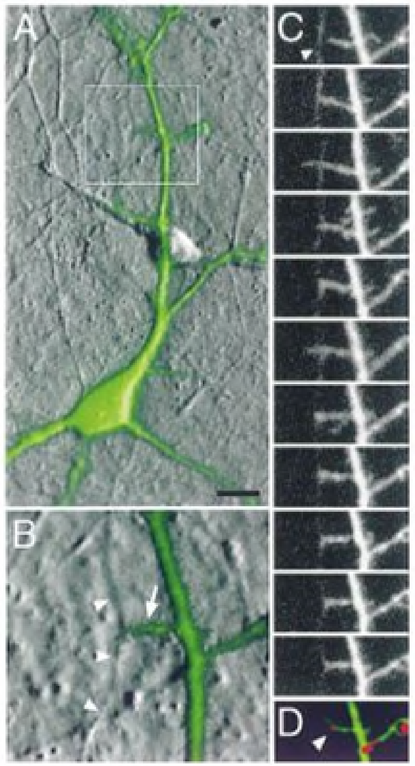
Synapses May Be Found at Contact Sites between Dendritic Filopodia and Nearby Axons

?

- How to observe ? fluorescence and DIC (differential interference contrast) images
- presynaptic bouton
- How were the contacts between the axon and the parallel dendrite established?
- it seems most likely that the filopodia spanned the 5–7 mm gap between the two neurites and that synapses subsequently formed at the contact sites.





90 min from the time of contact formation

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Conclusion:

These observations are therefore consistent with the hypothesis that dendritic filopodia can actively initiate synaptogenic contacts with axons, and, at least in some cases, evolve into dendritic spines.

strengths	*weaknesses*	*opportunities*	*threats*
• The study provides evidence that dendritic filopodia may serve as precursors to dendritic spines • Time-lapse recordings • Usage of live hippocampal cell cultures • Usage of scanning fluorescence and DIC images	• The study was conducted in vitro, which may limit the generalizability of the findings to in vivo systems. • The study did not investigate the molecular mechanisms underlying dendritic filopodia formation and synaptogenesis. • Observational Duration • Classification of old vs young neurons	• Development of further research into the dynamics of dendritic protrusions. • Some stable dendritic protrusion did not appear with a presynaptic bouton. This may reflect an ongoing process of axonal degeneration. • The study could lead to a better understanding of the molecular mechanisms underlying dendritic filopodia formation and synaptogenesis.	• The study may be limited by the availability of live hippocampal cell cultures and the difficulty of imaging dendritic filopodia and synaptogenesis in vivo. • Limitations in the representation of stable spines, as the potential evolution over time may not be fully captured in the recordings. • Some stable dendritic protrusion did not appear with presynaptic boutons.

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