

# HIGHLIGHTS

## SYNAPTIC TRANSMISSION

### Close to the edge

The idea that  $\text{Ca}^{2+}$  microdomains near the synaptic membrane are crucial for vesicle fusion is not new, but the precise relationship between such microdomains (which can be rather small, extending just over a few hundred nanometres) and the fusion of single vesicles has not been established.

A recent article in *Nature Neuroscience* addresses this issue in chromaffin cells, showing that the relative proximity between  $\text{Ca}^{2+}$  microdomains and docked vesicles regulates exocytosis at the level of individual vesicles.

In this study, Becherer *et al.* measured  $\text{Ca}^{2+}$  microdomains using dual colour evanescent field microscopy — a form of microscopy that selectively probes

the near-membrane space by generating a thin short-lived luminous field at the cytosol/glass interface of a cell in culture. Combining this technique with the tracking of single fluorescent chromaffin vesicles and with amperometric measurements of catecholamine release, the authors showed that the interaction between a vesicle and a  $\text{Ca}^{2+}$  microdomain requires their strict colocalization within 300 nm. Remarkably, only about 10% of the vesicles that were exposed to  $\text{Ca}^{2+}$  within the microdomain fused immediately with the plasma membrane, indicating that most vesicles might not be ready for exocytosis. In addition, the authors found that lower, near-membrane  $\text{Ca}^{2+}$  elevations caused the vesicles

to move closer to the  $\text{Ca}^{2+}$  entry sites, transiently increasing the probability of fusion in response to subsequent  $\text{Ca}^{2+}$  increases.

Although it will be important to test whether this strict requirement for colocalization and this new facilitatory effect of  $\text{Ca}^{2+}$  on release are also relevant at the synapse, the data of Becherer *et al.* highlight the power of evanescent field microscopy to question the vesicle fusion process at an unprecedented level of resolution.

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#### References and links

**ORIGINAL RESEARCH PAPER** Becherer, U. *et al.* Calcium regulates exocytosis at the level of single vesicles. *Nature Neurosci.* 6 July 2003 (doi:10.1038/nn1087)

