Correlative Microscopy in Life and Materials Science

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Correlated fluorescence and 3D electron microscopy temporally resolves ultrastructural changes during endocytosis

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The application of fluorescence and electron microscopy to the very same specimen has the potential to reveal ultrastructural details of dynamic and rare cellular events. We have developed a correlative approach combining high accuracy of correlation, high sensitivity as well as robustness to permit large dataset collections. Using a fiducial-based correlation, signals of fluorescent proteins can be mapped into 3D electron tomograms. The versatility of the approach was demonstrated by application to various cellular systems. Recently, we used it to describe how the plasma membrane is reshaped during endocytosis in a time-resolved manner. We systematically located 211 endocytic intermediates, assigned each of them to one of nine defined time windows during endocytosis, and reconstructed their ultrastructure in 3D. Combined with a quantitative analysis of the membrane shapes, correlative microscopy allowed us to produce a virtual 4D-movie of how protein-mediated shape changes occur during transition from a plane membrane into a tubular invagination and to scission of a vesicle. This study demonstrates the capability of our simple, robust correlative microscopy approach to answer structure-function related questions in cell biology.