Our work is focused on the development of methods that enable high-resolution snapshots of dynamic events or of subcellular structures in cells and multicellular organisms. To achieve that, correlating light and electron microscopy is a powerful solution. By improving targeting strategies, we are successfully combining live imaging and electron microscopy on various sample types, allowing the correlation in three dimension of rare events in cultured cells, nematodes, zebrafish embryos and mouse tissues.

A generalized way to achieve the correlation and to trace the objects of interest across the switch in imaging modalities is to rely on specific landmarks that are used to navigate into the sample, to specifically collect sections at the site of interest and to register the acquired images. With cultured cells, we utilize coordinates systems etched at the surface of the culture substrate, a widespread solution that is compatible with a large variety of sample preparation techniques for electron microscopy (e.g. chemical fixation, high-pressure-freezing). On multicellular organisms, the targeting to the region of interest is performed by the combined use of anatomical cues and of engineered landmarks that are recognizable in both light and electron microscopy. By imaging the sample in 3D, maps of its volume can be generated. These maps are then utilized to navigate the block and to target the sectioning precisely to the region of interest.

With the widespread use of easy-to-implement but efficient sample preparation methods, we believe that correlative light and electron microscopy has the potential to serve as a powerful tool to achieve single cell recordings in heterogeneous systems allowing to link functional imaging with ultrastructural analysis.