Automated Multimodal Correlative Microscopy for high resolution *in vivo* imaging.

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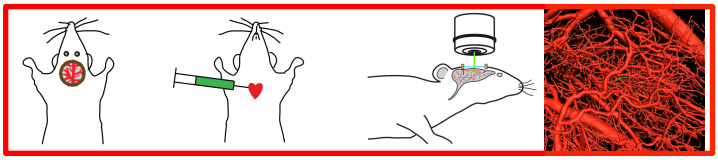
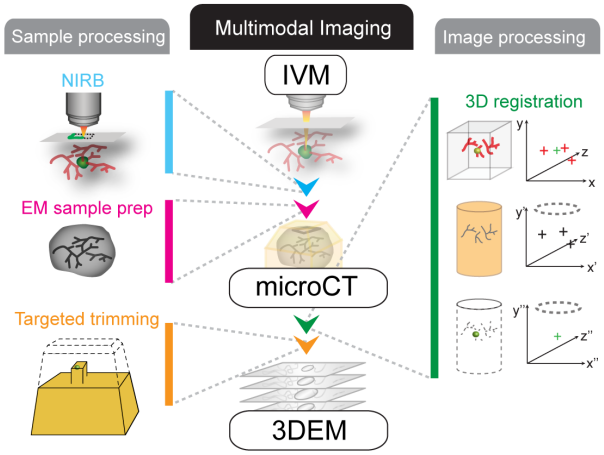
Introduction

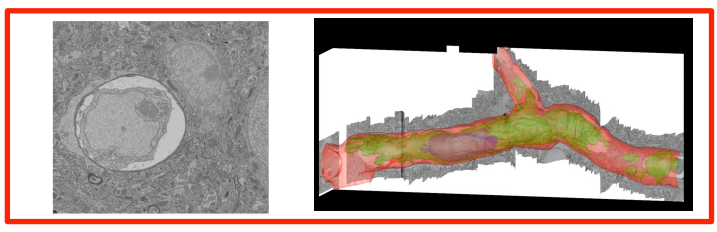
Modern research in Life Sciences is integrating multiple and diverse data from complex biological models, to understand at the molecular level, the mechanisms underlying the development, the function and dysfunction of living organisms. For this, imaging technologies are playing a crucial role. One big challenge is to record the living state (functional and dynamic) at the highest resolution possible (ultrastructural level). One of the most efficient solution is to combine and correlate on the same specimen, various imaging technologies, such as light microscopy (LM) and electron microscopy (EM). Correlative Light and Electron Microscopy (CLEM) is now an imaging field per se that covers a large spectrum of applications on multiple biological domains and models. The challenge, when it comes to correlate intravital imaging (by LM) to subcellular recordings (by EM), is to improve the targeting precision in 3D but also to enhance the speed and the resolution of the imaging. In doing so, the enhanced recording throughput is expected to enable quantitative analysis of biological phenomena.

We have recently demonstrated the power of multimodal correlative microscopy that **combines intravital imaging** of single metastatic cells **to large volume electron microscopy** (1). With this technology, it is now feasible to study the cellular mechanisms, for example of cancer spreading, in relevant models in vivo. Working closely with numerous laboratories in the Life Sciences, we are now establishing workflows for various applications in the fields of cell biology, development biology, neurobiology and physiology.

The Idea/Concept







Intravital imaging

volume
ultrastructure

Potential Impact

We aim to dramatically improve the Multimodal CLEM processes to allow even faster correlation and more importantly, to make it more accessible to non specialized laboratories. In doing so, we will answer to the needs of a growing and eager community with a unique, versatile and powerful tool to link function to structure in biologically relevant multicellular models. Achieving this goal will only be possible with key technological development to offer new instrumentation and automation in the areas of image processing (software), of sample preparation (mechanics) and of the large volume imaging (microCT, EM).

(1) M A Karreman et al., "Fast and Precise Targeting of Single Tumor Cells in Vivo by Multimodal Correlative Microscopy," Journal of Cell Science 129, no. 2 (January 15, 2016): 444–56, doi:10.1242/jcs.181842.