# Connectomics and ZEISS MultiSEM – the fastest scanning electron microscope in the world enables extreme-scale electron microscopy

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Connectomics is a still new discipline in the Neurosciences to study complex synaptic networks assembled by billions of neurons with the ultimate goal of a better understanding of neuronal functions. One way to shed some light on the structural and therefore functional organization of these networks is serial array tomography. Ultrathin slices are prepared from blocks of tissue embedded in resin, followed by imaging these series of sections using scanning electron microscopes (SEM). After aligning and merging all acquired section images into a 3D volume, human trained computer algorithms delineate and visualize the fine structure of neurons. The result is a detailed 3D map of the brain: the Connectome. However, at a sufficient resolution, the imaging might take more time than most researchers can dedicate to a single experiment or project, as current single beam SEMs are limited in their ultimate data acquisition rate at a given resolution by electron interactions and detector bandwidth. Scanning multiple electron beams in parallel circumvents the limitations in scan speed of single beam SEMs. Such a multi-beam SEM can image areas of several $mm^2$ at nanometer pixel size within hours. The dramatic increase of imaging speed opens the door for electron microscopy to applications where both high resolution and large scan area are of key importance.

With the advent of automated sample preparation devices [1] and the first commercially available multi-beam SEM [2], dense reconstructions of larger brain volumes at nanometer resolution are now within reach. Whereas the imaging of one $mm^3$ of tissue with the required pixel resolution would take ~6 years with a conventional single-beam SEM, the 61-beam ZEISS MultiSEM 505 could do the same task in merely 4 months. A second variant of the multi-beam SEM from ZEISS with 91 beams and a higher current per beam [3] increases the imaging throughput even further. A net acquisition rate of up to two TeraPixel per hour is now achievable, therefore enabling extremely large-scale imaging experiments. The presentation will give an overview of the current state of the technology, its potential application space and the challenges in data handling imposed by the enormously increased data rate.

References:

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2. Eberle AL, Schalek R, Lichtman JW, et al. (2015) Multiple-Beam Scanning Electron Microscopy. Microscopy Today, 23 (2):12–19

3. Crosby K, Eberle AL, Zeidler D (2016) Multi-beam SEM Technology for High Throughput Imaging. MRS Advances, 1 (26):1915–1920