## Electron tomography of hydrated beam-sensitive samples

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Beam sensitive samples, such as hydrogels or biological objects, are challenging samples for electron microscopy characterizations. Up to now, it has always been almost impossible to study them in native states by electron tomography. Of course, such materials are characterized in 3D but in cryo or embedded in a resin.

We will present the development of electron tomography of beam sensitive materials close to their native state. Here, the samples are not enclosed in an environmental cell, they are instead preserved in liquid state by cooling the sample at around 1-4°C, while 7-10 mbar of water vapor are insert in the chamber of an environmental electron microscope. [1] We will show developments made to analyze in 3D a full hydrated NIH-3T3 cell. The cell was cultivated on a gold TEM grid and then fixed – but not stained- and imaged in 3D as an entire and fully hydrated object (Figure 1 a)). [2]

Because low beam electron tomography requires fast manipulation of the microscope that become difficult even for most experimented users, we will also describe the principles of a Python code dedicated to fast electron tomography at multi scale at low electron dose. The code is compatible with both E-SEM and E-TEM electron microscopes and enables the 3D characterization of electron beam sensitive materials in native states (Figure 1 b)). Examples will be shown and discussed. [3]

## References

- [1] X Jiao, L Roiban, G Foray, K Masenelli-Varlot, Micron, 117 (2019) 60-67.
- [2] Akkiz Bekel, Louis-Marie Lebas, Lucian Roiban, Cyril Langlois, Mayra Yucely Beb Caal, Sounkalo Dembélé, Nadine Piat, Claire Gaillard, Bérangère Lesaint, Karine Masenelli-Varlot, Microscopy and Microanalysis, 27, S2, 1 (2021), 9–10.
- [3] The authors acknowledge the CLYM (www.clym.fr) for the access to Quattro ESEM and Titan ETEM (80-300 keV) electron microscopes. This work was funded by ANR (project ANR-20-CE92-0014-01).

## Figures



**Figure 1: a)** 3D model of a full hydrated NIH-3T3 cell obtained by BF-STEM electron tomography by using a dedicated E-SEM. **b)** Front image of a Python script developed for low beam electron tomography images recording for E-SEM and E-TEM enabling environmental electron tomography at multi scale.