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Editorial

Towards Three-dimensional Chemical Imaging of Cells

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Editorial

Our perception of the world has evolved considerably from the archaic flat Earth model to the modern vision of the terrestrial sphere, but nevertheless, the global vision of the surface of our planet has not been achieved until it was observed from the outer space. Thus, Earth observation from the space provides access to the distribution and dynamic of its different geographical and atmospheric layers. Similarly, the vision of life has substantially progressed from the drawings of the structure of cork, published by Robert Hooke [1], to the three-dimensional description of sub-cellular components although, once again, it might be completed by the study of the distribution and dynamic of the cellular chemical components. This can now be reached by the combination of chemical mapping approaches, widely applied for analytical characterization of non-biological materials, with tomographic reconstruction methods, used more and more often for the study of sub-cellular components [2]. Thus, three-dimensional chemical mapping has been recently used to address biological questions, such as the understanding of chromatin structure and nuclear sub-compartmentalization [3]. From another point of view, the increased of the use of metallic nanoparticles (MNPs) in therapy, diagnosis, drug delivery and cosmetics among other biological applications [4, 5], will led to a need for the development of methods, such as three-dimensional chemical imaging, allowing their intracellular tracking and characterization.

Current methods suitable for three-dimensional chemical imaging with in cells, at nanometric resolution, are traditionally based on electron microscopy frequently applied in material sciences. That is the case with tomography combined with Z-contrast by scanning transmission electron microscopy (STEM) and with energy-filtered transmission electron microscopy (EFTEM) [6]. In addition, the recent development of synchrotron tomography imaging is an attractive alternative to the classical electron microscopy approaches. Thus, in spite of its current limited spatial resolution, synchrotron radiation X-ray fluorescence is becoming a promising tool because of their accuracy in elemental mapping [7, 8]. This may be also true for other imaging approaches, such as secondary ion mass spectroscopy (NanoSIMS) [9, 10]. NanoSIMS, even if it is not really appropriated for three-dimensional studies because of the erosion required by the method that cannot be easily calibrated, offers scope for isotopic characterization inaccessible by other methods. Thus, in combination with atomic force microscope, that allows erosion calibration; NanoSIMS is now becoming to be adapted for three-dimensional chemical imaging studies [11].

In spite of the significant advances performed in adapting chemical imaging acquisition systems to biological samples an important bottle neck is still remaining. Since the biological material is mainly composed by water, the observation of cells in their native hydrated state defies the traditional chemical imaging methods, initially developed for dehydrated materials. This issue is addressed by quickly cooling the cells at liquid nitrogen temperatures and by observing them in a frozen-hydrated state where the generated amorphous ice is preserved. While it is true that the aforementioned approach has been widely validated in tomographic structural studies of cellular components in both, transmission electron microscopy [12, 13] and soft X-ray synchrotron radiation imaging [14, 15]; its use for three-dimensional chemical imaging is still in a developmental stage and continues to face significant technological problems to be solved. Thus, to obtain images from samples having several microns of thickness, such as is the case of eukaryotic cells, and to prevent the damage induced by the radiation on frozen-hydrated samples, are open questions. Nevertheless, promising results recently obtained have demonstrated the feasibility of tomography in frozen hydrated samples by scanning transmission electron microscopy [16]. Moreover, the first results on frozen-hydrated whole cells, obtained by hard X-ray fluorescence, have been recently reported [17].

To sum up, combining the chemical information with three-dimensional visualization of cells opens up new horizons for their ultra-structural depiction and for the understanding of their interactions with the environment. The next challenges are now to improve the resolution and the accuracy of the three-dimensional chemical maps, and to increase the sensitivity of the different chemical imaging methods, in order to advance in the completion of our perception of eukaryotic entire cells close to their native hydrated state.

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