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### SPATIAL AND TEMPORAL CRYO-TEM AND CRYO-ELECTRON TOMOGRAPHY OF MOLECULAR ASSEMBLIES AND SOFT NANOPARTICLES

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For nearly 30 years direct-imaging Cryo-TEM has made unique contributions to unfolding mysteries in colloid science and exposing primary hidden details. The technique uncovers the global supramolecular structure and local aggregate-specific details, at their hydrated state and at nanometer resolution. Information on the morphology, size and coexistence of structures is provided directly and with no further manipulation of the data. These and significant improvements in instrumentation and software placed the method as a central characterization tool in colloid, material, bio- and nano-related technologies in both academia and industry. An innovative extension to acquire 3D structural information and resolve the spatial organization of structures is cryo-electron tomography (Cryo-ET). However, this methodology that in life science is becoming a widespread technique, is still an almost unexploited in colloid science.

Our lab applies, develops and educates Cryo-EM methodologies for more than 25 years, and we invested much effort in the last 2 years in advancing Cryo-ET to make it also powerful in the field of complex fluids, where questions on morphologies and distribution of nanoparticles in the bulk are of interest. In this talk, the principles of Cryo-EM and Cryo-ET will be described [1, 2], along with examples from our own work. Examples will include analysis of micellar systems [3] in 2D and 3D, time-resolution investigations e.g., of 1D ribbons and nanotubes [4], and studies on new colloidal delivery systems e.g., to treat the Fabry disease [5] and an innovative mRNA anti Covid-19 vaccine [6].

#### References:

[1] Danino, *Curr Opin Colloid In.* (2012) 17(6), 316–329; [2] Danino and Egelman, *Curr Opin Colloid In* (2018) 34, 100-113; [3] Danino et al., *J Phys Chem Lett* (2016) 7, 1434–1439; [4] Zhang et al., *Nat Comm* 10 (1), 1-7 (2019); [5] Tomsen-Melero et al., *ACS Applied Mater Inter* (accepted); [6] Elia et al., (in review).