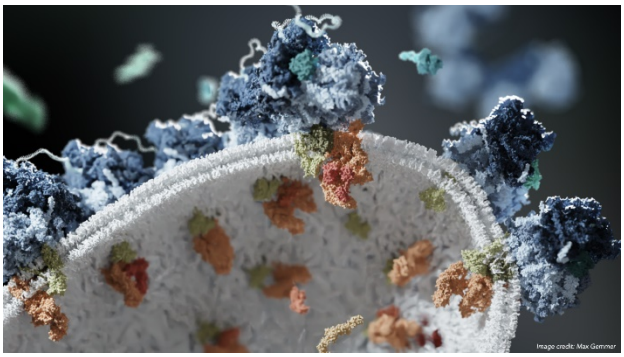
– Special Seminar –



Friday, June 9, 2023

Seminar 2:00 – 3:00 PM

Juliette Fedry

Structural Biochemistry
Bijvoet Center for Biomolecular Research
Utrecht University, Utecht, The Netherlands

SEMINAR LOCATION:

New York Structural Biology Center
Seminar Room A-11
89 Convent Avenue
New York, NY

THE SEMINAR WILL ALSO BE AVAILABLE VIA ZOOM:

Click here for Zoom link
Meeting ID: 870 5022 4531
Passcode: 165802

HOST:

Amédée des Georges
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Molecular visualization of cellular processes in mammalian cells

New insights into mRNA translation and the dynamics of the Nuclear Envelope under stress

ABSTRACT To understand cellular processes, it is important to visualize the proteins catalyzing the corresponding biochemical reactions. Over the last decades, X-ray crystallography has allowed the very detailed visualization of purified proteins, importantly contributing to our understanding of their functions and mechanisms of action. Recent method developments in the field of cryo electron tomography (cryoET) now open the door to structural studies of macromolecular complexes in a more biologically relevant context, such as vesicles for membrane complexes or ultimately directly within the cell.

In my recent work, I visualized the mRNA translation process in situ, in intact mammalian cells and analyzed its reorganization under persistent collision stress. My results highlight the presence of a Z-site bound tRNA on 80S complexes, increased under stress and stabilized on collided disomes, as well as the accumulation of an off-pathway 80S complex likely resulting from collision splitting events. We further observe the apparition of tRNAbound aberrant 40S complexes shifting with the stress timepoint, suggesting a succession of different initiation inhibition mechanisms over time.

To visualize the translocation of secretory protein nascent chains into the Endoplasmic Reticulum (ER) on native membranes, we used cryoET on vesicles derived from the rough ER of mammalian cell lines. We characterized the distinct populations of translocon complexes assembled in the ER membrane and revealed their clustering according to polysomes translating different types of nascent chains. We obtained a subtomogram average of the most abundant translocon variant at subnanometer resolution and built the corresponding atomic model, revealing new interactions between its main components.

Finally, I investigated the dynamics of the nuclear envelope under ER stress and recovery. I visualized this process in mammalian cells, shedding light on how autophagy processes proceed to the specific degradation of outer nuclear membrane portions.

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