

PhD Thesis Defense: Single-Molecule Spatiotemporal Dynamics of Protein Export from the Endoplasmic Reticulum

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November 12, 2026

15:00

ICFO Auditorium

The secretory pathway is a crucial process for cellular homeostasis, responsible for the synthesis, processing, and trafficking of approximately a third of all proteins to their final destinations. Newly synthesized secretory proteins enter the endoplasmic reticulum (ER) and, after proper folding, are sorted into and exported from specific ER subdomains named ER exit sites (ERES). As the first trafficking step, ER protein export plays a crucial role in ensuring the correct flow of proteins to downstream compartments, and defects result in a variety of pathological conditions. Unraveling its organization in space and time is essential to understanding its mechanisms. Despite the origins of this research field dating to the late

1960s, it was not until the widespread adoption of fluorescence microscopy techniques in the past three decades that rapid progress was made in how we conceptualize ER protein export in living cells. Yet, up until now, researchers have mostly relied on population-averaged measurements, which provide limited information on the molecular heterogeneity inherent in biology. Insights into molecular dynamics, transient interactions, short-lived states, or nanoscale distribution of secretory pathway proteins in living cells have largely remained veiled. Developing a complete view requires characterizing the process at the single-molecule level.

In this thesis, we develop and apply a quantitative framework based on single-molecule fluorescence microscopy to dissect the dynamic organization of the early secretory pathway at the molecular level. By leveraging recent technological advances in fluorescent dyes, functional assays, gene editing, and machine learning tools, our approach enables the detection, monitoring, and analysis of individual cargo protein molecules as they are exported from ERES with high spatial precision (~20-30 nm) and temporal resolution (~10 ms). Our characterization provides novel insights into the orchestration of the early secretory pathway, allowing us to revisit conflicting ideas in the field. Overall, this thesis provides a generalizable methodology and an updated, more accurate view of a fundamental intracellular trafficking process.

Thursday November 12, 15:00 h. ICFO Auditorium

Thesis Director: Prof. Dr. Maria Garcia Parajo and Dr. Felix Campelo Aubarell

Hosted by: Academic Affairs