# Seminar

# Atomic resolution molecular imaging based on soft-landing electrospray ion beam deposition

## Stephan Rauschenbach

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**Time: 9:30 am, Aug.27, 2025 (Wednesday)**

**时间：2025年8月27日（周三）上午9:30**

**Venue: Room w563, Physics building, Peking University**

**地点：北京大学物理楼，西563会议室**

## Abstract

Soft-landing Electrospray ion beam deposition (ESIBD), the deposition of intact molecular ions created by electrospray ionisation onto solid surfaces in vacuum, has been introduced in our lab as a tool for the handling of large and complex, usually non-volatile molecules.[1] Initially, the high-resolution singlemolecule imaging by scanning probe microscopy (SPM) has been the major application. For this ESIBD proved successful in the investigation of structure, conformation, and properties of proteins, peptides, saccharides, and synthetic molecules.[2,3]

ESIBD's high level of control over molecular ion beam and environment opens new avenues in molecular imaging.ESIBD together with native electrospray ionisation enables the chemically selective enrichment of folded proteins and proteins complexes for structural investigation by electron microscopy imaging (cryoEM)[4,5], and low energy electron holography (LEEH).[6]

Optimized conditions for native deposition promote imaging of individual proteins at a resolution sufficient for the construction of atomic models from cryoEM data.[5] The structure obtained from cryoEM after embedding the landed proteins in ice grown from the gas phase shows a fold and subunit arrangement which is remarkably similar to the solution structure. Small conformational changes cause differences mostly at the protein surface and interfaces. We find the closing of cavities and crevices' due to self-interaction in absence of water, a change reversed in MD simulations to find the native structure again.

References:

[1] Rauschenbach, **Annu Rev Anal Chem** 9 (2016) 16.1-16.26.
[2] Wu, SR ..., **Nature** 582 (2020) 375–378.
[3] Anggara, SR, ..., **Science** 382 (2023) 219-223.
[4] Esser, ..., SR **PNAS Nexus** 1 (2022) pgac153.
[5] Esser, ..., SR **Science Advances** 10 (2024) eadl4628.
[6] Ochner, SR ... **PNAS** (2021) pg. e2112651118

## About the speaker

Professor Stephan Rauschenbach is a leading expert in single-molecule microscopy and preparative mass spectrometry. He holds an Associate Professorship in Physical Chemistry at the University of Oxford and serves as Tutorial Fellow at Wadham College. His research focuses on developing novel instrumentation combining electrospray ion beam deposition (ESIBD) with high-resolution imaging methods including scanning probe microscopy, electron microscopy, and cryo-EM to investigate individual molecules and molecular assemblies.

Rauschenbach obtained his doctorate in Physics from EPFL (2007) and served as Senior Scientist and Group Leader at the Max Planck Institute for Solid State Research, Stuttgart (2007-2017) before joining Oxford. He has pioneered the integration of mass spectrometry with single-molecule imaging, enabling unprecedented structural analysis of individual molecules, native proteins, and biomolecular complexes.

His research focuses on instrumentation development of ESIBD and its application in scanning probe microscopy (SPM), electron microscopy (EM) and low energy electron holography. This work resulted in 56 peer-reviewed publications with some notable achievements including the first real-space imaging of a complex glycan in using noncontact AFM, demonstrating remarkable atomic resolution imaging of gas-phase protein structure in cryo-EM, and the discovery of selective hyperthermal reaction mechanisms in molecule-surface collisions. For his work in developing preparative mass spectrometry into a viable method for sample preparation for microscopy, he was awarded the prestigious Mattauch-Herzog Award by the German Society for Mass Spectrometry (2017).