Work in electron-based macromolecular structure determination has grown in importance with the recent developments in rotation electron crystallography [1]. It was recently shown that serial electron crystallography (serialED) can be implemented within an electron microscope (TEM) to recover structures from nanocrystalline inorganic molecules [2]. This raises questions on the applicability of serialED to organic macromolecules. Such materials present challenges, notably in terms of dose sensitivity and beam quality. Moreover, TEMs have their own limitations: spatial constraints forbid large-travel high-precision stages or equipment for dynamics triggering.

We present the design of a dedicated electron beamline for serialED in development. A Schottky field emitter filtered by a 50-μm aperture creates a highly-coherent beam. Sub-μs pulses are generated through pulsing of the extraction potential and beam blanking. Properties of the beamline are explored through particle-tracking simulations based on realistic representations of the optics from finite-element methods. Macromolecular structures determination in a high-current regime is discussed: considering a fluence threshold of 5 e-/Å², simulations show that a repetition rate of the order of 100 Hz is achievable.

Data processing is explored in a proof-of-principle experiment within a TEM. Using softwares developed for x-ray diffraction, such as CrystFEL4 and CCP4, the structures of hen-egg lysozyme, and granulovirus are recovered at a resolution of 2 Å and 1.8 Å, respectively.