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Directional explosion. A hybrid simulation study

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Single particle imaging (SPI) using X-ray pulses has become increasingly attainable with the advent of high-intensity free electron lasers. SPI overcomes the need of a crystalline sample, but the extreme intensity of the X-ray pulse causes severe radiation damage to the molecule, leading to coulombic explosion [1]. Diffraction patterns are thus obtained from separate exposures of identical molecules, each in their own random orientation. Hence, a single diffraction pattern reflects a single view of the particle. The unknown orientation of the particle renders its 3D reconstruction problematic, complicated and expensive – in terms of large sample consumption and beam-time required. If additional information about the orientation of the protein in the instant of X-ray exposure could be recorded, it would be beneficial for the algorithms that find the relation between the diffraction images.
One way to control proteins orientation prior to the interaction with the X-ray pulses is to make them interact with external electric field [2]. Unfortunately, in some cases, the field can be destructive for the protein structures, as positively and negatively charged moieties will be pulled in opposite directions, potentially leading to unfolding and therefore to artefacts on the reconstructed images. It has also been proposed that by measuring the directions of the ejected ions from the Coulomb explosion of the protein, the orientation of the protein could be determined a posteriori [3]. In our previous simulation study, it has been shown how the sulphur atoms from a lysozyme protein tend to follow similar trajectories in 150 independent simulations. Since lysozyme is a rather small protein, and most of the sulphurs are closed to the surface of the protein, it is hard to draw any conclusions of how well defined the trajectories of atoms heavier than N, C and O from a larger protein would be. To test if the findings from the simulations agrees with what happens in an experiment, one needs to design an experiment to test this aspect. In such experiment it is necessary to know how the distance from the surface of the protein affects the direction of the ion path. In the present study we are addressing this specific question. By placing a sulphur atom at different distances from a water surfaces, and measure sulphur trajectories we aim at understanding how close to the surface of a biomolecule an atom can be to give reliable orientation information. To this end, we developed a hybrid simulation approach employing a combination of non-local thermodynamic equilibrium and extensive classical molecular dynamics simulations. Based on our findings, we conclude that explosion data can aid spatial orientation in SPI experiments and could substantially improve the capabilities of the SPI technique.

[1] Chapman, Henry N., Carl Caleman, and Nicusor Timneanu. “Diffraction before destruction.” Philosophical Transactions of the Royal Society B: Biological Sciences 369.1647 (2014): 20130313.
[2] Sinelnikova, Anna, et al. “Protein orientation in time-dependent electric fields: orientation before destruction.” Biophysical Journal 120.17 (2021): 3709-3717.
[3] Östlin, Christofer, et al. “Reproducibility of single protein explosions induced by X-ray lasers.” Physical Chemistry Chemical Physics 20.18 (2018): 12381-12389.

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