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Utilizing plasma physics to create biomolecular movies

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Disclaimer

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White Paper for *Frontiers of Plasma Science Panel*

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Indicate the primary area this white paper addresses by placing "P" in right column.
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1 page of references and 1 page of figures may also be included. *Submit in PDF format.*)**

- ***Describe the research frontier*** **and importance of the scientific challenge.**

In Spring of 2000, the LCLS Scientific Advisory Committee selected the top scientific experiments for LCLS [1]. One of the proposed flagship experiments is atomic-resolution three-dimensional structure determination of isolated biological macromolecules and particles, with the ultimate goal of obtaining molecular (snapshot) movies.

The key enabling insight was that radiation damage may be overcome by using x-ray pulses that are shorter than the time it takes for damage to manifest itself [2,3]. What started out as a potential revolution in biological imaging quickly became an intricate problem in plasma physics: The high-intensity x-ray free-electron laser (XFEL) radiation transforms condensed-matter macromolecules into complex nanoplasmas during the pulse with a non-Maxwellian electron-velocity distribution centered around tens of eV [4] in a mixture of partially-ionized high- and low-Z ions [5]. Experimentally-validated modeling tools to describe this transition in detail are still sorely missing to this date.

- ***Describe the approach to advancing the frontier and indicate if new research tools or capabilities are required.***

Protein crystallography performed at synchrotrons is the workhorse technique used in structural biology today. As an extension, femtosecond nanocrystallography has been demonstrated at LCLS in 2009 [6]. However, atomic-resolution three-dimensional diffractive imaging of single biological macromolecules has yet to be achieved. An important element in realizing this vision is an understanding of the structure and evolution of the associated nanoplasmas. Initial modeling of XFEL radiation damage has been mostly based on rather simplistic transport and semi-classical particle models. To do the complexity of the problem justice, experimentally-validated simulation capabilities are needed. Their development still requires significant experimental, modeling, and simulation work. For instance, chemical effects such as the initial bond breaking, localized ionization and displacement damage near high-Z atoms, as well as energy transport in the nanoplasma need to be understood. Also, it is not clear how such a partially-ionized plasma scatters x-rays, and how the scattered intensity profile relates back to the (original) electron density. Particularly challenging for plasma physics codes are (i) the transition to the plasma state which is an inherent quantum-mechanical process and (ii) describing the non-equilibrium electron distribution in the partially ionized plasma that contains both fast photo- and Auger electrons as well as slower secondaries.

- ***Describe the impact of this research on plasma science and related disciplines and any potential for societal benefit.***

X-ray tubes were critical in uncovering the structure of DNA in the 1950s [7], synchrotrons enabled protein crystallography in the 1970s [8], and XFEL's may revolutionize structural biology yet again by making possible time-resolved imaging of single isolated biological molecules, potentially bridging large systematic gaps in the database of protein structures. An important example is the class of protein molecules that are responsible for cross-membrane communication, which is vital for drug development to cure human diseases. Since this class of proteins is particularly difficult to crystallize, their structures are mostly unknown today. Beyond determining the static high-resolution structure of all these materials, the ultrashort pulses of XFELs will in addition enable time-resolved imaging and will provide the opportunity to track the dynamics of chemical reactions. The potential payoff of this technique is huge -- we "just" have to understand the plasma physics processes in XFEL-irradiated materials.

Acknowledgements

Please add "This work was performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under contract DE-AC52-07NA27344."

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