Structure determination of biological macromolecules
by means of
X-Ray Free Electron Laser (XFEL) "Diffract-Before-Destroy" measurements

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All x-ray measurements on biological species are limited in spatial resolution due to sample damage induced by the x-ray beam itself. This damage can only be ameliorated by limiting the x-ray dose per molecule, which requires working with a large number of identical and identically oriented molecules. Hence virtually all such x-ray diffraction measurements are carried out on large single crystals. However certain critically important biomolecules are difficult or even impossible to crystallize in a size large enough for conventional synchrotron x-ray studies. This nexus has now been broken by the advent of femtosecond hard-x-ray pulses from a Free Electron Laser (XFEL). The first "hard x-ray" XFEL – the Linac Coherent Light Source (LCLS) – began operation at SLAC in Fall 2009. As in the "Back to the Future" movie, the key is to "think four-dimensionally:" The pulse from an XFEL is so intense (over 10^{12} photons/pulse) that the sample is not just damaged – it is completely annihilated! Nonetheless, the pulse is so short (under 10 fs up to several hundred femtoseconds) that elastically scattered x-rays bearing the latent diffraction pattern are on their way to the x-ray detector before the physical structure of the exploding target has significantly altered. Consequently the recorded diffraction image is that of the undisturbed structure. This "diffract-before-destroy" approach, which was completely hypothetical up until Fall 2009, has now not only been proven valid but was just named by Science as one of the top ten scientific breakthroughs of 2012 (Science is always a little slow in recognizing real science!). The ASU Physics group has been a part of the LCLS experiments since their inception, in particular developing techniques to inject fully-solvated biological macromolecules/nanocrystals in the micro- (and now nano-) focused x-ray beam in the vacuum chamber of the LCLS. After a short overall overview of LCLS biospecies research to date, this talk will discuss in some detail the micro- (and now nano-) sized liquid free-streams that make possible viable measurements on biological species in a vacuum environment.

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