Imaging molecules using X-ray free-electron lasers

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X-ray free-electron lasers are large-scale facilities that produce intense X-ray pulses of femtosecond duration about a billion times brighter than achievable at synchrotrons. These pulses can be used to determine the three-dimensional structure of biological objects such as macromolecules or virus particles. They overcome the problem of radiation damage that plagues all forms of high-resolution imaging of soft matter and which limits the achievable resolution or requires large well-diffracting protein crystals. The X-ray FEL pulses completely vaporise the sample, but they are so brief that individual single-shot diffraction patterns can be obtained from a sample before significant radiation damage occurs. We have developed and employed this "diffraction before destruction" method to determine the structures of proteins that cannot be grown into large enough crystals or are too radiation sensitive for high-resolution crystallography, using the Linac Coherent Light Source (LCLS) at SLAC. Ultrafast pump-probe studies of photoinduced dynamics in proteins or other materials can also be studied. Our experiments and modelling suggest that it should be possible to obtain 3D atomic-resolution structural information from even smaller crystals, perhaps all the way down to single molecules. These method have the potential to vastly increase the rate at which structures can be solved.