The dielectric function (and the dynamic structure factor) could be measured by applying, for a brief time, a spatially periodic field and detecting the temporal oscillation of the charge density[7]. ❐

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FREE-ELECTRON LASERS

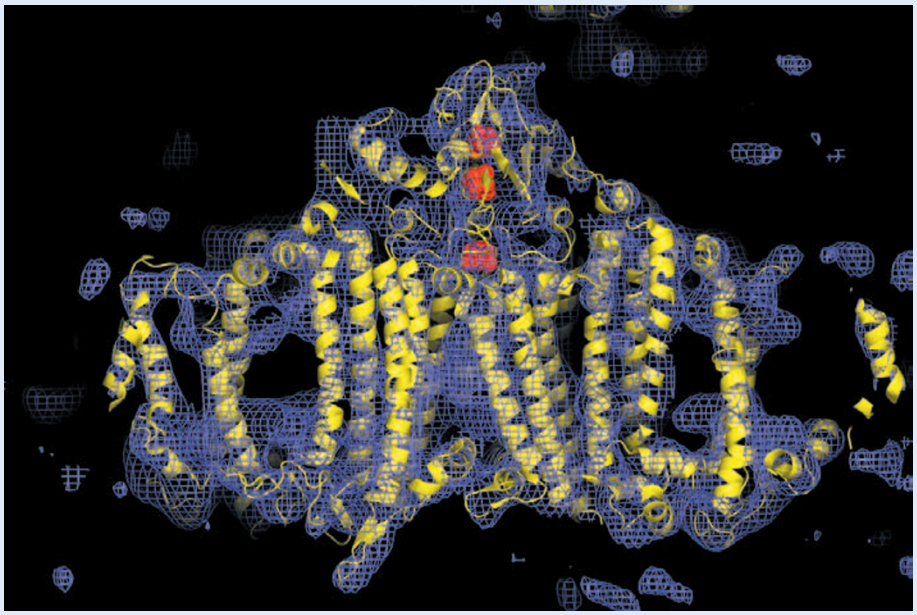
X-ray crystallography goes viral

It's no exaggeration to say that the invention of X-ray crystallography was one of the most important developments of the twentieth century. It revolutionized our understanding of the material world and enabled us to reveal the molecular structure of the building blocks of life. Yet conventional X-ray crystallography is only capable of probing the structure of a minor fraction of all the proteins that living organisms produce and use.

That should change with the advent of X-ray free-electron lasers, which produce short, intense bursts of X-rays. Two studies published in *Nature* by an international consortium of scientists demonstrate the use of X-rays generated by the free-electron laser of the Linac Coherent Light Source (LCLS), at the SLAC laboratory in California, to determine the structure of microscopic organic structures that have previously been challenging, or even off-limits, for X-ray analysis.

The problem with using X-rays to probe the structure of small organic compounds is the damage they cause. When X-rays scatter off the atoms in a compound they can dislodge them from their natural position in its structure. Moreover, to get an accurate picture of the compound's structure, a great many X-rays must be scattered and collected. But the damage causes the information to degrade and eventually become meaningless.

The problem is usually overcome by sampling X-rays scattered from millions of copies of a molecule arranged in a crystal. This reduces the amount of damage per copy and increases the number of scattered X-rays — and therefore the amount of structural information — sampled from it. Unfortunately, most organic molecules don't readily form large, well-ordered crystals.



The solution is a combination of extreme intensity and speed: use an X-ray free-electron laser to expose individual molecules (or small crystals of molecules) to an extreme flux of X-rays but over a short period of time, of the order of femtoseconds. This way, it should be possible to collect enough X-rays to reconstruct a molecule's natural structure before the molecule disintegrates in the intense beam of radiation.

The authors of the *Nature* studies have put this into practice, and have built a detailed picture of the structure of the protein complex, photosystem I, a component of the photosynthetic machinery of plants, algae and light-harvesting bacteria (H. N. Chapman *et al. Nature* **470,** 73–77; 2011). Although crystals of this complex have been formed, growing large crystals that are free from defects is a difficult task. Instead, the authors used a stream of smaller crystals suspended in a liquid jet, which they passed through the beam of the LCLS. Combining the data from 15,000 individual X-ray pulses resulted in a picture of the protein (shown here) that compares well to that built from much larger crystals by conventional X-ray crystallography.

To explore the potential of the technique further, in their second study the group imaged the structure of a mimivirus — one of the largest types of virus known and one that doesn't form crystals of any size (M. M. Seibert *et al. Nature* **470,** 78–81; 2011). This time, the researchers injected a stream of virus particles into the LCLS beam in the form of an aerosol, and, by combining the results of thousands of X-ray pulses, formed an image of its gross structure. Doing so by conventional techniques would normally require meticulous sample preparation that could affect the natural state of the virus.

ED GERSTNER