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Pandemic responses and the impact of infrastructure and technology on structural studies

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Structural biology had a major impact on the delivery of effective responses to the COVID-19 pandemic. I will give some illustrations of these from our experiences, however I will attempt to embed them in a consideration of the broader developments.

Large infrastructures allowed the high resolution structural analysis of virus proteins and particles via X-ray crystallography. For small proteins this has been honed into ultra-high throughput methods accelerating antiviral drug discovery. Circa nine years ago the field of virus structure was opened up by the resolution revolution in cryo-EM. This made complex analysis easier and revealed features that broke icosahedral symmetry. Top-end microscopes were, and remain, expensive and to democratise access we integrated them into a synchrotron facility (Diamond) and a pan-European research infrastructure (Instruct-ERIC). Technology developments have accelerated the method roughly an order of magnitude since the revolution began. Now lower voltage microscopes might take this a step further by making machines affordable by many more labs. Meanwhile the next step in structural biology, in situ analysis using electron tomography, is a reality. It remains unclear what key technology innovations will increase the reach of this method, but it is likely that the next generation or two of instruments will be increasingly expensive, and probably most should be incorporated into large facilities. Alongside these developments there are open questions about the long term impact on biology of electron ptychography and liquid phase electron microscopy. However electrons are fundamentally limited in their ability to penetrate cells and tissue, and so it is likely that imaging with light, electrons and X-rays will need to be combined to address the most challenging questions, e.g. of virus pathogenesis. There are real opportunities for large scale science infrastructures to accelerate technical innovation and markedly improve pandemic preparedness.

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