KN11 **Combining crystallography and electron microscopy for virus structure determinations.**
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The first three-dimensional structures of spherical viruses were of small (diameters less than about 350Ĺ), icosahedral viruses. These structure determinations used X-ray crystallography as their primary structural tool. However larger, more complex, viruses generally contain a lipid membrane, stolen from the host cell at the time of assembly. Many of these viruses also have icosahedral symmetry and can sometimes be crystallized, although, in general, crystals of enveloped viruses do not diffract better than about 20Ĺ resolution. For such viruses cryo-electron microscopy can be used to establish their structures to maybe 15Å resolution and in some favorable cases to about 4.5Å resolution. The structure of the component viral proteins can often be determined by X-ray crystallography and fitted into the lower resolution cryo-electron microscopy density maps of the whole virus to give a "pseudo-atomic" resolution structure. Even more complex viruses are frequently pleomorphic with only the structural building blocks being the same in different virus particles. Currently methods are being developed to use cryo-electron tomography combined with crystallography to determine the structure of pleomorphic viruses. An example will be given from the structure determination of Newcastle disease virus, a virus similar to mumps and measles viruses, belonging to the paramyxovirus family.

Keywords: virus structure determination; pleomorphic viruses; Newcastle disease virus

KN12 **Picometer Electron Microscopy.**
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During the nineties, i.e. more than sixty years after the invention of the electron microscope, it became at last possible to realize aberration-corrected electron optics [1]. In the past decade this has revolutionized electron microscopy. The Rayleigh resolution increased to about 50 picometers, and it has become possible to measure individual atom displacements in the order of 1 picometer. This means genuine atomic resolution [2,3]. On this basis the electron microscope has become a unique high-precision measurement tool allowing the direct correlation of macroscopic physical properties with individual atomic position measurements. However, in contrast to common believe, optical resolution is just one of the pre-requisites of atomic resolution work. The world of atoms is that of quantum physics, and there the term 'image' looses its conventional meaning. The electron waves sent through a crystal in order to provide us with information on the object are subject to quantum-mechanical interaction with the atomic scattering potential as described by a relativistically corrected Schrödinger equation. The resulting complex wave function at the exit plane of the specimen does not lent itself to an intuitive interpretation. And this holds true even more so, when the additional quite complex phase shift behaviour of an electron lens are taken into account in addition. In order to understand the images and to push the frontiers of electron microscopy to single-atom site picometer precision it is therefore unavoidable that the highly non-linear quantum-mechanical imaging process is inverted numerically on a computer [4]. This is done in two steps. In the first the electron exit-plane wave function is retrieved. In the second the atomic positions and the nature of the atoms are determined by means of an iterative atomic modelling procedure. In this the atom positions are adjusted atom by atom with picometer precision striving for a 1:1 fit of the calculated to the experimental wave function. Since in quantum-mechanical dimensions neither the specimen thickness nor an unavoidable small sample tilt can be measured independently these have likewise to be treated as fitting variables. The potential of this technique for applications in materials science has been demonstrated in recent years by numerous examples, in particular in the field of oxide research [5]. Here atom relaxations and compositional variations in connection with lattice defects or surfaces could be measured, and, in ferroelectrics, since picometer microscopy allows direct access to the electric dipole strengths on the unit cell level, atomic details of polarization domain boundaries could be investigated [6,7].

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Keywords: electron optics; high-resolution TEM; oxides ferroelectric