KN-7 Electron nanodiffraction for structural biology

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Cryo-electron microscopy (cryo-EM) is a powerful technique for studying the structure of macromolecular complexes. Radiation damage by the electron beam limits image contrast, and thus the resolution. But an EM can be switched to diffraction mode and recent experiments indicate that this delivers ten times better data with an electron dose that is 100 times lower, when using a hybrid pixel quantum area detector originally developed for high-energy physics. This allows full atomic structure determination using just a single protein nano-crystal with a diffracted volume of 0.03 cubic micrometer. The physics that explain this vast improvement equally applies to non-crystalline samples. These results indicate that switching to diffraction may allow structure determination of single macromolecules in solution, and ultimately in complex environments like those of the living cell. But collecting electron scattering data does have a major disadvantage: the phase information that is required for structure determination can only be inferred indirectly. For electron scattering data of crystals, methods that were originally developed for X-ray crystallography have proven to work. But in order to extend the method to non-crystalline samples, alternative phasing strategies have to be considered.

Keywords: Cryo-electron microscopy, Electron nanodiffraction

KN-8 Driving Forces of Phase Transitions in Molecular Materials

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In two essays published in the March 2015 issue of *IUCrJ* Dunitz and Desiraju and co-workers present contrasting views of the way in which intermolecular interactions in crystal structures should be interpreted. Dunitz's view emphasises the importance of whole-molecule interaction energies, whereas Desiraju promotes the importance of individual atom-atom interactions, associating short atom–atom distances with specific intermolecular bonding. The contrast in between views, which is extremely important in the analysis of phase stability and the rationalisation of phase transitions, forms the subject of this Keynote. For example, application of pressure to trigonal γ glycine yields the monoclinic ε phase, and we have studied this transition using neutron powder diffraction. Packing energy calculations using both the PIXEL method and symmetry-adapted perturbation theory yield consistent results which can be interpreted using Hirshfeld surface analysis and full interaction maps. The calculations provide detailed characterisation of the factors which promote the stability of the two phases under different external conditions, enabling the principal thermodynamic driving forces of the forward and reverse transitions to be identified. The crystal structures of amino acids have generally been interpreted in terms of strong NH…O hydrogen bond formation between the ammonium and carboxylate groups of the zwitterionic molecules, supported by weaker dispersion or CH…O interactions. The packing energy calculations reveal that this view should be modified substantially, to take into account the large *repulsive* intermolecular interactions (as promoted by Dunitz) which are associated with apparently highly-stabilising hydrogen bond geometry (emphasised by the Desiraju model).

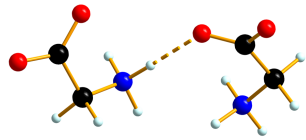

Figure 1. Repulsive H-bonded dimer in γ-glycine. NH…O = 1.95 Å, <NH…O = 179°, Energy = +18.5 kJ mol^{-1}.

Keywords: Hydrogen bonding, high pressure, amino acids, phase transitions, intermolecular energies