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Polymorphisms in Helical Polymers: A New Perspective

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Many important biological macromolecules exist as helical polymers. Examples are actin, tubulin, myosin, RecA, Rad51, flagellin, pili, and filamentous bacteriophage. Helical objects have also occupied an important place in methods development in electron microscopy, since the first application of three-dimensional reconstruction from electron microscopic images was to a helical polymer[1]. A number of laboratories today are using helical tubes of integral membrane proteins for solving the structure of these proteins in the electron microscope at near atomic resolution. We have developed a method to analyze and reconstruct electron microscopic images of macromolecular helical polymers, the Iterative Helical Real Space Reconstruction (IHRSR) algorithm[2]. We can show that when there is disorder or heterogeneity, when the specimens diffract weakly, or when Bessel functions overlap, we can do far better with our method than can be done using traditional Fourier-Bessel approaches. In many cases, structures that were not even amenable to analysis can be solved at fairly high resolution using our method. The problems inherent in the traditional approach will be discussed, and examples are presented illustrating how the IHRSR approach surmounts these problems.

One of the most important outcomes of applying the IHRSR method is that heterogeneity can be resolved, rather than averaged away. Thus, in many instances one might have no information indicating that a helical polymer is polymorphic, but this polymorphism can be clearly seen using the IHRSR approach. For one helical filament, F-actin, it was suggested before using these new methods that multiple interfaces must exist in the filament to accommodate large variations in the rotation between subunits[3]. We can show, using the IHRSR method, how additional insights into this polymorphism can be gained. But we can now show that F-actin is not unique, and higher resolution studies of filamentous bacteriophage and bacterial Type Three Secretion System components reveal that a multiplicity of interfaces may be much more common than has been assumed.

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