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Overcoming Severe Diffraction Anisotropy in Crystallographic Refinement. Michael R. Sawaya, Michael Strong, David Eisenberg, Univ. of California, Box 951570, Los Angeles, CA 90095-1570.

Diffraction anisotropy is characteristic of most macromolecular crystals used for structure determination. Moderate anisotropy can be satisfactorily modeled by anisotropic scaling factors such as those applied by REFMAC or CNS; however, such modeling has proven insufficient for 3 severe cases reported here. In the most severe case (rv2430c-rv2431c), 2.2 Å resolution is observed near the a^* and c^* cell axes, but only 3.2 Å resolution near the b^* axis. Refinement stalled at $R_{\text{work}}=32\%$ and $R_{\text{free}}=36\%$, and model building was impeded by the lack of interpretable features in the electron density map. The R factors improved after eliminating poorly measured reflections falling outside the bounds of an ellipsoid, rather than the usual sphere. However, the density remained featureless. This problem was finally reasoned to be the side effect of the anisotropic scaling algorithm in which isotropy is effected in F_{obs} not only by dampening the resolution falloff in weak diffracting direction(s), but also enhancing the falloff in the strong diffracting direction(s). That is, anisotropic scaling imposed an artificially high overall Wilson B factor. Subsequent application of a negative, isotropic B factor, facilitated model building efforts, leading to $R_{\text{work}}=24.8\%$, $R_{\text{free}}=31.3\%$.