

## **Crystallographic studies on the ribosome, a large macromolecular assembly exhibiting severe nonisomorphism, extreme beam sensitivity, and no internal symmetry**

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Crystals, diffracting best to around 3 Å, have been grown from intact large and small ribosomal subunits. The bright synchrotron radiation necessary for the collection of the higher-resolution x-ray diffraction data introduces significant decay, even at cryogenic temperatures. Nevertheless, due to the reasonable isomorphism of the recently improved crystals of the small ribosomal subunits, reliable phases have been extracted at medium resolution (5–6 Å) and an interpretable five-derivative multiple isomorphous replacement (MIR) map has been constructed. For the crystals of the large subunits, however, the situation

is more complicated because at higher resolution (2.7–7.0 Å), they suffer from substantial radiation sensitivity, a low level of isomorphism, instability of the longest unit-cell axis, and nonisotropic mosaicity. The 8 Å MIR map, constructed to gain insight into this unusual system, may provide feasible reasoning for the odd combination of the properties of these crystals, as well as hints for future improvement. Parallel efforts, in which electron-microscopy-reconstructed images are being exploited for molecular-replacement studies, are also discussed.