A Challenging 90 Residue Problem for X-ray Crystallography: the ^{2}F1-^{3}F1 Module Pair of Human Fibronectin

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Human fibronectin (Fn) is a large multidomain protein found in the extracellular matrix and plasma. It is involved in many cellular processes. The ability to bind Fn is a characteristic that has been demonstrated for a number of pathogens. Although the structures of two F1 module pairs have been determined by NMR, no X-ray structures have been reported so far.

Fibronectin crystals of the ^{2}F1-^{3}F1 module pair diffracting to 1.7 Å were obtained but they exhibited symptoms of possible twinning (1). Initially, we attempted to solve the structure by MR using different ensembles of the NMR models, but after many different strategies failed, we moved on to MIR methods. A number of different derivative datasets were collected, and all showed partially occupied sites but did not give interpretable maps. In-house data were collected for the sulphur SAD method, but this also failed. RIP was tried next, and although a large signal from the breakage of the 4 disulphide bonds was obtained, the maps were again uninterpretable.

We then collected highly redundant S-SAD data to a highest resolution of 2.15 Å. A sulphur signal was measured, but yet again the maps were uninterpretable. Eventually, the structure was solved when the phase information from the S-SAD and RIP data were combined.

Data were collected at the ESRF, beamlines ID 14-4 and BM 14, and at the SRS, station 9.6.

[1] Rudiño-Piñera E., Schwarz-Linek U., Potts J. R., Garman E. F., *Acta Cryst.*, 2004, D**60**, 1341-1345.

Keywords: fibronectin, RIP, sulphur SAD, twinning