m03.p06

”Towards Data Management for PX Structure Determination With CCP4”

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BIOXHIT (BioXtallography) is an Integrated Project within the 6th Framework Programme of the European Commission, which is coordinating scientists at all European synchrotrons alongside leading software developers in a timely and unprecedented joint effort to develop, assemble and provide a highly effective technology platform for Structural Genomics. A key part of the integrated technology platform being delivered by the BIOXHIT project is the development of automated structure determination software pipelines covering the latter stages of structure solution by protein X-ray crystallography (PX). Within such pipelines it is essential to accurately record, organise and track the data, something that becomes increasingly important as the throughput of structures solved using these procedures rises. Therefore as part of BIOXHIT, CCP4 (the Collaborative Computational Project No. 4, a UK-based software project that provides a suite of programs for the determination of macromolecular structures via X-ray crystallography) is developing a system for performing data management in order to address this need. This poster reports on recent progress towards realising this system.

m04.p01

Crosslinking of DNA duplexes: a novel binding mode by bisacridine derivatives

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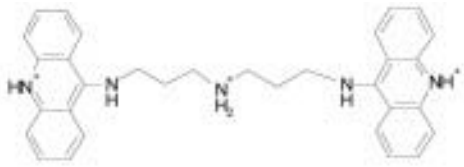
Acridine derivatives as topoisomerase inhibitors have been studied for years, they interact with DNA molecules through Π-Π interaction between their tricyclic aromatic chromophores and adjacent base pairs. Therefore, bisacridines linked through linkers with appropriate length are expected to have the highest-affinity binding by a dual intercalating mode. A number of crystallographic data have demonstrated the classic bisintercalation in which both chromophores of the bisintercalators bind to the same DNA duplex [1,2]. However, a novel crosslinking binding mode by two bisacridine derivatives has been observed in our laboratory recently, in which the bisacridines with a positively charged linker are found to be capable of crosslinking different DNA duplexes. As a direct consequence of this interaction, the DNA molecules are effectively condensed similar to their natural conformation *in vivo*. (For example, the closest distance between two phosphate oxygens is 3.5Å). The X-ray crystallographic structure of d(CGTACG) and 1,3-propanediamine, N-9-acridinyl-N'-[3-(9-acridinylamino)propyl] (Shown in the figure) was initially solved with an in-house data set by molecular replacement in space group $P6_522$ (a=25.67Å, c=78.76Å) to a resolution of 2.5Å. The difference map shows clear chromophore positions. Further refinement was carried out with synchrotron data obtained at the DESY Hamburg outstation to a resolution of 2.2Å. The structure shows the hexamer DNA duplexes are tightly tethered in a head to tail fashion with the linker emerging from the major groove at a fully extended state. Another complex of same oligonucleotide and a similar ligand with longer linker has been found crystallised in a unit cell of 29.69Å, 29.69Å, 117.63Å, 90°, 90°, 120°, which also indicates a crosslinking binding mode, though the structure is expected to be solved by a multiple wavelength dispersion experiment at the strontium edge in near the future. *In vivo*, DNA is always stored in a very compact ordered state; therefore any DNA condensation observed *in vitro* can be useful for studying its functions in living systems. The formation of compact particles can be also applied for the DNA delivery in gene therapy.



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