04-Crystallography of Biological Small Molecules

The crystal structure of SN6999 bound to the DNA sequence d(GCCGCG-ethyl-
GAATTCCG) is presented. The space group is P2₁2₁2₁ and the unit cell
dimensions are a=28.48A, b=36.11A, c=69.6A. A new lacrosse packing is observed
and the structure was solved by molecular replacement using ULTIMA. A canonical
d(GCCGCG-GAATTCCG) dodecamer crystal structure was used as the search model.
The asymmetric unit contains one dodecamer duplex, one SN6999 and 67 water
molecules. The structure was refined against 1618 mtz() reflections extending to
1.2A resolution by constrained least squares using NUCLSQ to an R-factor of
17.9%. SN6999 distorts the double helix at the C1 of the CG end. The new lacrosse
retains the interlocking interactions between the central CG base pairs in the minor
groove. The P4₁2₁ space group is solved while P4₁2₁2₁ shows a concerted
base pair.

Supported by NIH grants GM-41602 and CA-52506 to A.J.-J.W.

PS-04.02.10 CRYSTAL AND MOLECULAR STRUCTURE OF A HEXADECAYMED DNA CO-COMPLEX OF THIOINE 5’-
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Interactions between protein and nucleic acids are ubiquitous and are of fundamental
importance in molecular biology. Till now, the structure of a few protein-nucleic acid co-
complexes have been reported at low resolution. Now there is, therefore, need for elucidation
of protein-nucleic acid model interaction at atomic resolution since high resolution precision
information of unique, simple nucleotide-amino acid/peptide complexes can throw deeper insight
on the general recognition rules involved in those broad range of DNA-protein interactions
in the biological systems. Recently, we have been successful in setting the single crystal
of the co-complex of thioine 5’-Monophosphate with L-serine in adequate hydrated environment.

The physical and IR spectral investigations have clearly indicated the presence of both the parent molecules in the single crystal with other several hydrogen bonded water molecules. The co-complex has crystallized in space group P2₁ with cell dimensions a=6.09A, b=21.89A, c=12.72A and b=110.59, respectively. The structure has been solved by direct methods and the water
molecules have been located from the successive difference Fourier analysis. The electron
density map of the asymmetric unit has clearly shown the complexity of the two thioine 5’-
Monophosphate with one L-serine and six water molecules. The structure has been refined
to current R value of 0.1.

The structure consists of polar hydrophilic columns (made up of the phosphate, sugar
hydroxyl, serine, and water molecules) parallel to the a-axis, surrounded by hydrophobic columns
(generated by the stacking of the nucleotide bases). An intricate network of hydrogen
bonding among the serine groups, nucleotides, and water molecules are present in the
structure. The phosphate, 2’- and 3’-hydroxyl, and keto-oxygenes [06] as well as the purine
nitrogen (N7) of the nucleotide molecules are involved in the H-bonding scheme with the serine
molecules through phosphate oxygens... amino and 2’-hydroxyl...carbonyl groups. Strong H-bonding
is observed involving the water molecules themselves and their participation with serine

and the nucleotide functional moieties in the hydrophobic zones or channels. This structure may
suggest some plausible rationale for the interaction of proteins and nucleic acids in the biological
system.

PS-04.02.11 AMBIGUOUS PACKING OF DNA HELICES IN CRYSTALS OF d(GCCGCG)-d(GCTGCG).
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DNA oligomers are known to pack in a few well
recognized patterns in simple crystals. We report here
an unusual space group ambiguity in the crystals of the
non-self-complementary duplex d(GCCGCG)-d(GCTGCG)
grown from a drop containing 5mM DNA, 10mM sodium
cacodylate at pH 6.8, 10mM CaCl₂, equilibrated by the
hanging drop method against 25% MPD. The X-ray
diffraction pattern from a crystal of size 0.2x0.2x0.5
mm was ambiguous and indicated that the X-ray pattern
could be indexed in all the space groups given in table 1.
All of them can be apparently explained by the
same packing mode, viz, that of hexamer dumbbells
stacked on top of each other in an infinite continuous
Z-DNA helix. A continuous helix can be formed by the
repetition of two types of arrangement
1) d(GCCGCG)-d(GCTGCG) and
2) d(GCCGCG)-d(GCTGCG).
In case 1, one hexamer dumbbell is related to the other by a 2 screw
along the longest axis, while both the arrangements can
give a disordered 6 screw, with a dinucleotide duplex as the asymmetric unit. Disorder arises because of the absence of every 6th phosphate group as well as the presence of a 4-A base pair instead of 6-G base pair.

This symmetry is revealed by the systematic absence occurring in data set 1. Similar sequences have been
crystalized in space group P2₁2₁2₁. For the same packing, a suitable selection of the unit cell will
yield the cell parameters shown in the data set 2. The systematic absences of these data showed the presence
of three mutually perpendicular 2 screw axes and a C-centering. The volume of the unit cell does not
permit a C-centred orthorhombic cell. Therefore, the space group can either be P2₁2₁2₁ or C2.
In the case of P2₁2₁2₁, a full turn of helix could be forced as shown in arrangement 1, while arrangement 2 can yield
C2. The Rmerge showed more or less equal but
unconvincing possibilities for all the four space
groups. Therefore, a constrained refinement has been
carried out in the space group P1. Present R factor is
0.22 for 612 reflections of P1 within the
resolution limit 7 to 3 A.

Table 1

| CELL | ABSENCE | SPACE | R
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<tr>
<td>1</td>
<td>0 0 1, h=2n+1</td>
<td>P2₁</td>
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<tr>
<td>2</td>
<td>0 0 1, h=2n+1</td>
<td>P2₁2₁2₁</td>
<td>0.21</td>
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<tr>
<td>3</td>
<td>h=2n, k=2n+1</td>
<td>P2₁2₁2₁</td>
<td>0.22</td>
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