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Frodo and the ribosome: how to display low resolution structural models with Frodo

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The molecular graphics display program Frodo[1] implemented for the Evans & Sutherland PS300, has recently been extended with a new display object, which is called Bones[2]. The Bones object consists of a set of points and a link list describing how the points are connected. In addition, each point is assigned a level on the basis of which it is possible to select parts for displaying and to differentiate the points by colouring. Although Bones was introduced to display skeletonized electron density, it was clear to us that it could be used to display almost anything. The ribosome interacts with a large number of macromolecules, both proteins and nucleic acids, during the protein synthesis. Locations of functional sites, binding sites and locations of the ribosomal constituents have been suggested. To be able to get a view of the spatial implications of these hypotheses, we have made a Bones file containing these structures. Each of the two subunits of the ribosome were made as contours obtained from a replica of a plaster model based on data from electron microscopy. The backbones of the known structures of elongation factor Tu, C-terminal fragment of L7/L12, $tRNA^{Phe}$ and a mRNA in helical conformation were made as Bones objects as well. The full structures may be obtained by using the 3D structure recognition options when using the atomic coordinates of the proteins in question as a database. Positions of ribosomal proteins determined by neutron scattering and immuno electron microscopy are defined in the Frodo coordinate file. They can be displayed as dotted spheres generated by the Mol option Surf. The location of functional sites and binding sites can be visualized in the same way.

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A liquid crystal stereo viewer for use with computer display systems and television transmissions

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In a recent publication[1] we described a new high speed liquid crystal shutter which could be used with computer display systems to provide a 3D image. In essence, left and right eye views of a molecule or other object are displayed alternately and in rapid succession; the shutters, which are worn as spectacles, are synchronized with the displayed images so that the left eye only sees the left image and the right eye only sees the right image, the observer perceiving a fully-coloured 3D picture. We have now developed the system further so that *real* objects can be televised and the televised picture (as a video recording, closed-circuit television picture, or broadcast picture) can be viewed in 3D. For example, it is possible to make a television recording of a lecture or demonstration in which CPK, Labquip, or other molecular models are being used and to show this in 3D. Video recordings taken from a computer display system can be edited into the television recording and also viewed in 3D. The system involves two synchronized, but otherwise, standard television cameras which are mounted side-by-side. The output signals are combined so that successive interlaced frames show the views seen by the two cameras alternately. The television picture is viewed with the liquid crystal shutters in the same way as for computer display systems.

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Conformational analysis and an NMR study of a trisaccharide, constituting a model for branching points in polysaccharides

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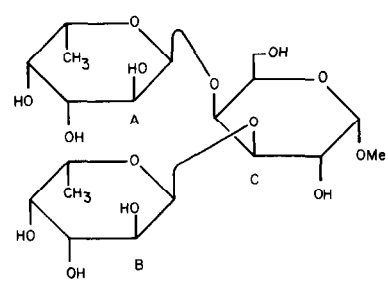
NMR-spectroscopy has become one of the most versatile techniques for structural studies of bacterial polysaccharides which are built of oligosaccharide repeating units. Information on residues, substituents and mode of linkages is obtained without destruction of the material. In order to understand all provided by NMR-spectra a comprehensive chemical shift database, and a set substitution rules for all types of linkages are required. Our present database, including disaccharides, is now extended to comprise also information on sterically hindered trisaccharides. Such oligosaccharides can be found in branched polysaccharides. To study this phenomenon several trisaccharides, *inter alia* **1**, were synthesized together with the disaccharides B–C and A–C.



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Conformational analysis using the HSEA-program[1], (basically Van de Waals energies) indicates that the conformations of B–C and A–C are very similar to those found in the trisaccharide. Comparison of the rotational freedom of B–C and A–C shows that the latter is more flexible. NMR-spectra, on the other hand, show large changes in chemical shifts for unit A. Thus from these results it can be concluded that several factors including conformational changes are responsible for the changes of the chemical shifts.

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Three-dimensional and electronic analysis of Na^+-dependent antidopaminergic agents: tropapride and zetidoline

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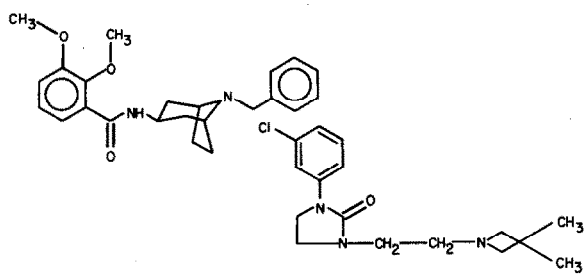
'Tropapride' belongs to a well-known neuroleptic class: the benzamide nortropanes whose most significant feature is a selective binding to D_2 receptors in a highly Na^+-dependent manner[1]. A first 3D and electronic analysis of several analogues of tropapride has lead us to suggest a model of three pharmacophoric elements, a basic nitrogen lone pair, a phenyl ring, and a carbonyl function, for ligands at the D_2 receptor[2]. In order to confirm this model, a comparison will be made of tropapride to zetidoline, the lead compound of a new neuroleptic family with the same biochemical properties as other atypical neuroleptics[3].



Using a user-interactive flexible molecular fitting program, IFMFIT, zetidoline has been shown to possess the three pharmacophoric elements observed for benzamides. In addition, both show a similar steric hindrance. Molecular electrostatic potential maps obtained at the *ab initio* SCF-LCAO-MO level for zetidoline show that it has two well-defined regions in common with tropapride: the negative and positive regions lie on opposite sides of the carbonyl and methoxy groups respectively.

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Computer assisted investigation of structure activity relationship in α_2 adrenoceptor ligands

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The aim of this work was to investigate within a set of molecules the common minimal structural features required to elicit α_2 adrenoceptor affinity in radioligand displacement experiments. *In vitro* radioligand binding assays were carried out using standard published procedures using *p*-aminoclonidine as the radioligand[1]. The set of compounds was composed of reference drugs (rauwolscine[2], mianserine[2], idazoxan[3], 1-methyl-4-<3-fluoro-2-pyridinil>-piperazine[2]) and original compounds from Continental Pharma's collection (CP2953[4], CP3848) displaying, to different extents, *in vitro* α_2 adrenoceptor affinity. Modelling studies were performed using a software package developed in FUNDP[5]. The workstation consists of a Megatek 7210 graphic processor connected to a host CPU processor PDP 11/60. Rauwolscine has been used as a reference template. We have been able to find good superpositions for a phenyl ring and a nitrogen atom (sp^2 or sp^3 hybridized) common to all compounds. The 3D structures used for modelling studies were obtained either from X-ray data of the molecule itself or fragment assembly from the Cambridge Crystallographic Data File. For the flexible molecules, we have found different conformations with acceptable internal energy that allow superpositions. Thus all the molecules with affinity to the α_2 adrenoceptors have at least one conformation in which a N-atom is at a fixed position in space relative to an aromatic ring: the mean distance is 5.6 ± 0.15 Å with the nitrogen atom roughly lying in the same plane as the phenyl ring.

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