03.X-01 DRUG-NUCLEIC ACID COMPLEXES: AN OVERVIEW. By Helen M. Berman, The Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia, Pa. 19111.

In an effort to understand the structural basis for intercalation, neighbor exclusion and helical unwinding, the structures of crystalline complexes of drugs and fragments of nucleic acids have been determined by researchers in several laboratories. For intercalation of simple planar chromophores into dinucleoside phosphates, it has been established that the geometry is characterized by an alternation between low and high anti conformations around the glycosidic bonds and that the 3' end of the dimer is flexible. Understanding of conformational changes induced by intercalators with large substituents must await future structural determinations of complexes with these drugs. The structures of the dimer complexes have also been used to build models that explain neighbor exclusion and unwinding. The characteristics of these models will be described and compared with results obtained from nucleic acid polymers.

The structures of the dimer complexes are highly hydrated and as such contain much sought after information about the water structures in nucleic acids. In one example, a very elegant network of edge-linked pentagons of water molecules that resemble semi clathrate structures has been observed. The implications of this pentagonal structure with respect to nucleic acid hydration will be discussed.

This research was supported by NIH Grants GM 21589, CA06927, RR055390, CA22780 and by an appropriation from the Commonwealth of Pennsylvania.

03.X-02 ASPECTS OF CYCLIC AND LINEAR OLIGOPEPTIDES. By Isabella L. Karle, Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, D. C. 20375, U.S.A.

Peptides are composed of the same amino acid residues as proteins but they differ in several important respects. Both D and L residues can be present, there may be cis amide bonds, and occasionally there are ester linkages instead of amide linkages (depsipeptides). Furthermore, cyclic peptides as well as linear peptides occur naturally. Peptides have diverse biological functions including antibiotic, antitoxic, and analgesic activity, and ion transport. Bond lengths and bond angles are quite similar in all peptides but there is little regularity in conformation of these extremely flexible molecules. Some peptides assume classic conformations such as a fragment of an antiparallel pleated sheet or an α-helix while other peptides adopt nearly chaotic conformations. The two mechanisms associated with ion transport through membranes by peptides, channel formation and encapsulation of the charged particles, will be examined. Examples will be shown of channels, both polar and hydrophobic, formed in crystals of several diverse peptides that have appropriate dimensions and characteristics for ion transport. Other examples will be shown of the various modes of complexation of alkali and alkaline earth ions with peptides, such as infinite sandwiches, discrete sandwiches and encapsulation. Drastic changes in conformation of the cyclic peptides accompany complexation.

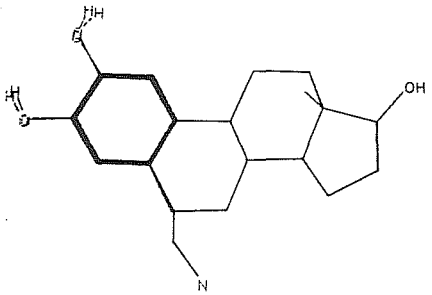
03.1-01 STEROID STRUCTURE, PROTEIN BINDING AND BIOLOGICAL ACTIVITY. By W.L. Duax, J.F. Griffin, D.C. Rohrer and C.M. Weeks, Medical Foundation of Buffalo, Inc., 73 High Street, Buffalo, New York 14203, U.S.A.

On the basis of the analysis of the crystallographic data on hundreds of natural and synthetic steroid hormones and their functional analogues we have postulated that, for estrogens and progestins, the A-ring end of the steroid initiates receptor binding and the D-ring end controls hormonal response. We have been attempting to prepare complexes of steroids with amino acids that may explain the high affinity that steroids have for binding to receptor proteins. Ultraviolet difference spectra suggest interaction between the Δ^4-3-keto chromophore and tryptophan residues when progestins are bound to progesterone binding globulin (PBG). A two to one complex of indole and progesterone was prepared as a model for progesterone tryptophan interaction. The crystals are orthorhombic [$P2_12_12_1$; a=12.237(2), b=34.954(5), c=7.2317(8)Å] and the structure was solved by direct methods. An indole molecule is hydrogen bonded to each of the carbonyl oxygens, O(3) and O(20). The indole molecule hydrogen bonded at O(3) exhibits a two-fold disorder. There is no stacking of the indole molecules over each other or over the Δ^4-3-one chromophore. No significant differences in bond lengths, valence angles, torsion angles, overall conformation or 17-side chain orientation have been detected when the progesterone molecule in the complex is compared with that in either of two isomorphous crystal forms of progesterone itself. We conclude that the hydrogen bonding between indole and progesterone may resemble progesterone tryptophan interaction in the PBG complex but that the chromophore shift is dependent upon an additional interaction of progesterone with other amino acids in the binding site. Research supported in part by USPHS Grant No. AM-26546.

03.1-02 A CRYSTALLOGRAPHIC COMPARISON OF SOME CATECHOLAMINES WITH A CATECHOLESTROGEN, By D.C.Swenson, W.L. Duax and P.D. Strong, Medical Fndn. of Buffalo, Inc., Buffalo, NY 14203 and J. Weisz, M. S. Hershey Medical Center, Hershey, PA, USA.

It has been recently shown that 1,3,5(10)-estratrien-2,3,17β-triol (2-hydroxyestradiol) stereospecifically binds to an enriched membrane fraction isolated from the rat anterior pituitary gland (Schaefer, *et al*, J. Biol. Chem. (1980) 255, 9838-9843). Dopamine and spiroperidol competitively inhibit the binding of 2-hydroxyestradiol. The crystal structure of 2-hydroxyestradiol ($P2_12_12_1$, a=12.086(2), b=20.140(4), c=6.179(1)Å, Z=4) is reported here and its solid state conformation is compared to the solid state conformations of the catecholamines dopamine (Giesecke, Acta Cryst. (1980) B36, 178-181) and apomorphine (Giesecke, Acta Cryst. (1973) B29, 1785-1791). The catechol portions of these molecules are very similar as shown by the figures below.

Research supported by Grant No. AM-26546 from NIAMDD.



Superposition of catechol portions of 2-hydroxyestradiol and dopamine