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STEROID-HORMONE MESOGENS

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For elucidation of the mesogenic characteristics and abilities of steroid hormones, a number of enantiomeric and racemic coil-like estrogens and some of their rod-like artificial analogs have been synthesized. The mesogenic patterns of these simple thermotropics might be regarded as primitive models for bioregulatory operation modes of their hormonal standards.

1. INTRODUCTION

Though we appear to understand the gross features of the widespread activities of steroids[1] as bioregulators,[2] detailed knowledge concerning their definite structure-function relationships is in most cases still lacking. Independently of whether they serve as sterol constituents of cell membranes, sex and adrenal cortical hormones, bile acids, or cardiotonic agents, their unique molecular designs that rendered them both competitors and interaction partners of nearly all biopolymeric species confront our efforts for elucidation of their ac-

tivity patterns with an as yet hardly approachable complexity that might well be an expression of a more general biological uncertainty principle[2]. In view of these difficulties occupying the central scene, unconventional concepts of modelling those molecular strategies of information processing might be of at least partial use[3].

1.1. Steroid Hormones

Steroid hormones and cholesterol (Figs. 1 and 2) present themselves towards their different interaction partners double-faced: a flat and from estrogens via androgens

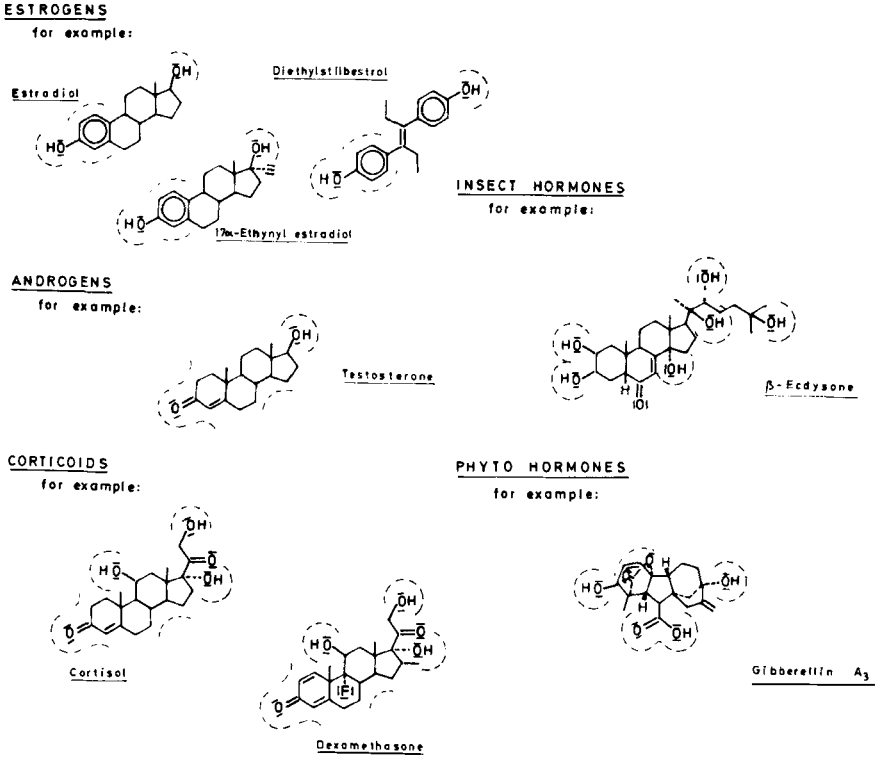


FIGURE 1 Steroid (and analogs) hormone patterns.

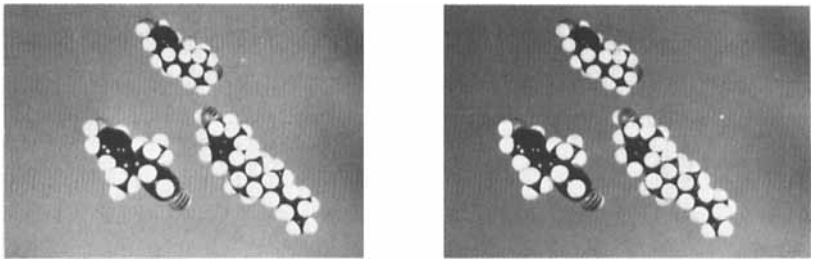


FIGURE 2 Representatives of bioregulatory steroids: cholesterol in comparison with ß-estradiol and its synthetic analog diethylstilbestrol.

and corticoids to insect moulting hormones increasingly twisted α- and, just within the same sequence, more and more distorted ß-face[4,5,6].

1.2. Thermotropic Derivatives

The coil-like shape (Figs. 3 and 4) of the majority of these compounds favored them, nevertheless, as candida-

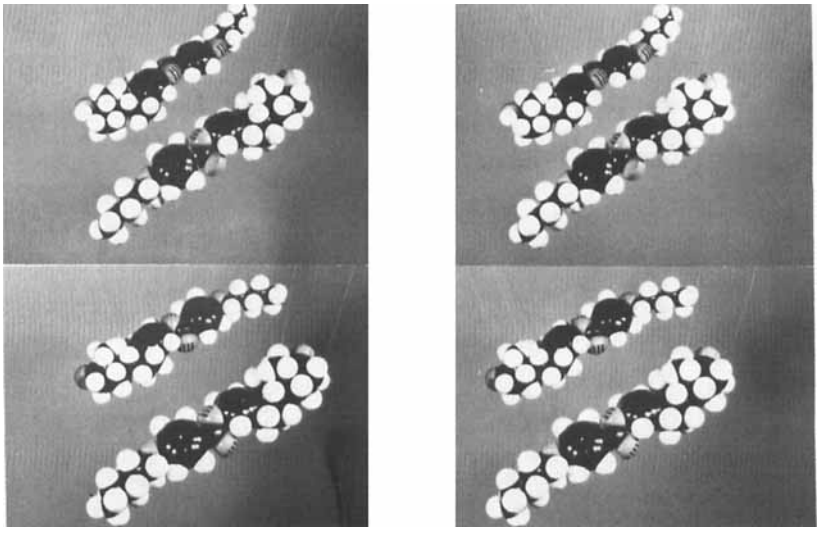


FIGURE 3 Monotropic cholesterics of 3-monoacylated enantiomeric ß-estradiols and estrones[7].

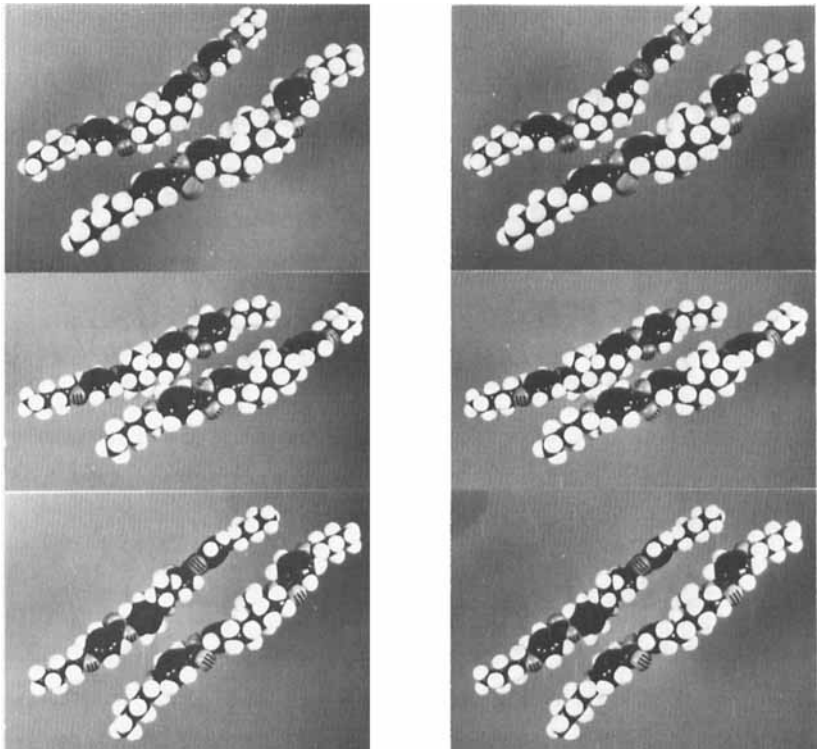
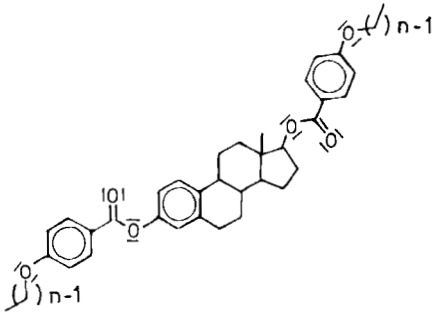
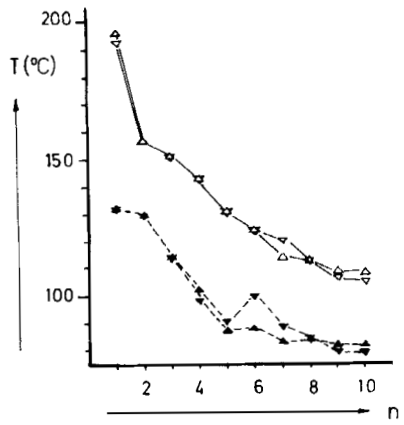
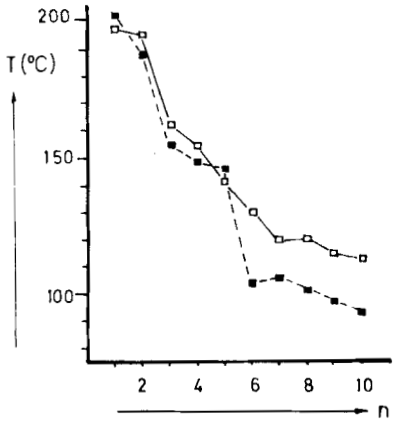


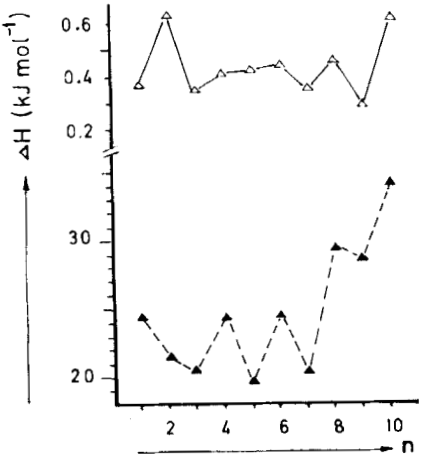
FIGURE 4 Enantiotropic cholesterics of 3,17-bisacylated enantiomeric ß-estradiols and estrones - in comparison with diethylstilbestrol nematics[7-11].

tes for central parts of suitably designed thermotropics. From its very beginning, the whole area has been dominated by the aptness of cholesterol[12]. Before in our days interest shifted to the more stable chiral side-chain cholesterics, only a few other steroid moieties, mainly androgen derivatives,[13] had further joined the circle. When we entered the field with the so far surprisingly forgotten estrogens (Figs. 3 - 7)[2-5,8-11], we had been interested not so very much in the possible technical applications of these thermotropics, but in their fore-









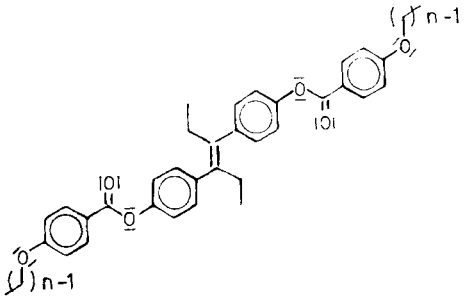
transition temperatures and enthalpies of homologous 3,17ß-bis-(4-n-alkoxybenzoyloxy)-1,3,5(1o)-estratrienes:

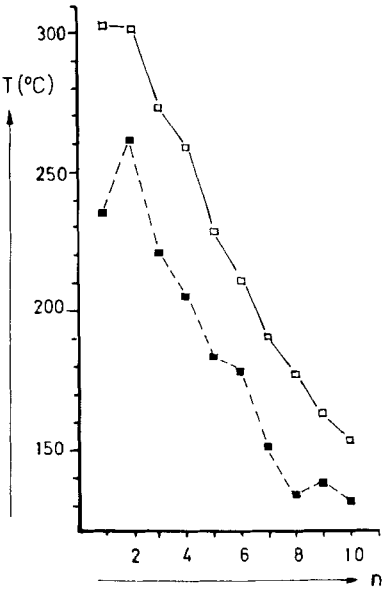
native ß-estradiols:
C - Ch ▲ ; Ch - I △

enantiomeric ß-estradiols:
C - Ch ▼ ; Ch - I ▽

racemic ß-estradiols:
C - N ■ ; N - I □

FIGURE 5 Thermotropic ß-estradiol derivatives[7,1o,11].



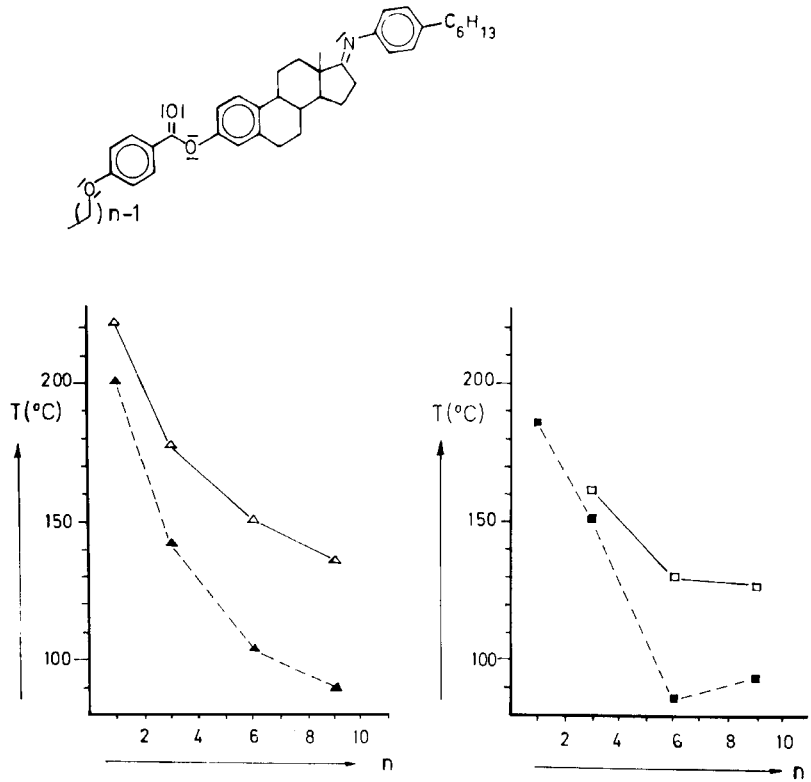


transition temperatures of homologous 4,4'-bis-(4-n-alkoxybenzoyloxy)-trans-7,7'-diethyl-stilbenes:

C - N ■ ; N - I □

FIGURE 6 Thermotropic diethylstilbestrol derivatives[7]

seeable facilities of modelling regulatory aspects of their central part standards in directing biomesogen phase and domain organizations[2-5]. We started with common 3,17-elongation strategies of ß-estradiols (Fig. 5) and estrones (Fig. 7), comparing them, simultaneously, with synthetic analogs (Fig. 6)[7,10]. While this program that has by this way proved the qualification of some



transition temperatures of homologous (only even-membered alkyls given) 3-(4-n-alkoxy-benzoyloxy)-17-(4-n-hexyl-phenyl-imino)-1,3,5(1o)-estratrienes:
native estrones: C - Ch ▲; Ch - I △
racemic estrones: C - N ■; N - I □

FIGURE 7 Thermotropic estrone derivatives[7,1o,11].

new central parts[7] and has, meanwhile, also introduced some unconventional terminals[7,14] is slowly underway in our laboratory, we tried to narrow the gap between thermotropic model aspects and biomesogenic regulation strategies by establishing a suitable structure-function leitmotiv[2-5,15]. As a reasonable approach appeared to us the "negative modelling"[15] of structural and functional patterns (Figs. 8 and 9) of steroidal moieties to select

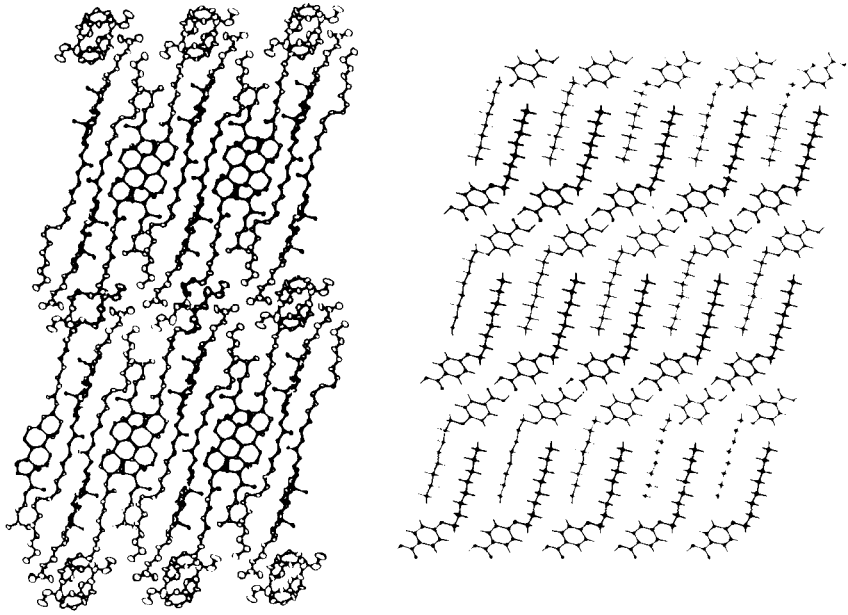


FIGURE 8 Characteristic crystal packing patterns of cholesterics[16] and smectics[17].

for potential complementary adaptation patterns of mate biopolymeric species (Figs. 1o - 15). Such a procedure

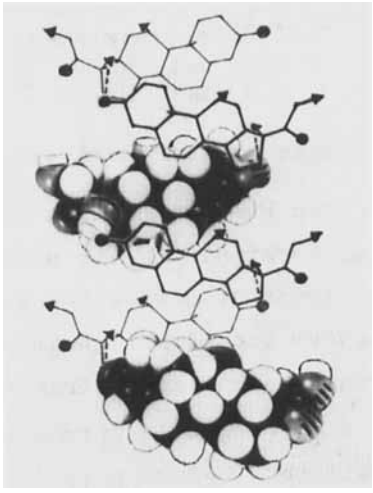


FIGURE 9 Helical crystal packings of cortisol[4,6].

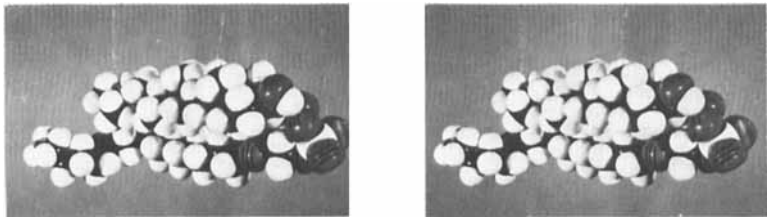


FIGURE 1o Cholesterol fitting phospholipid head and tail design[2-5,18].

seems the more justified as steroid conformations observed in the solid closely approximate the most probable structures regardless of environment[6].

1.3. Biomesogenic Standards

While the adaptation of cholesterol to the head-tail interfaces of membranes offers pictures (Fig. 1o) supported by accumulating experimental evidence,[18] the even more important visualization of proteinic grasp at steroidal hormone geometries still remains in its infancy[19] (Fig. 11). Nucleic acids as further possible receptor candidates experienced an initial period of enthusiasm, followed, however, by a long controversial debate and persisting doubts. Nevertheless, these informational macromolecules offer a spectrum of striking structural

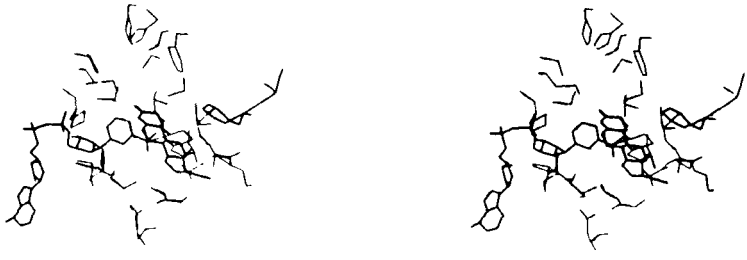


FIGURE 11 ADH-NAD complex fitting steroids[19].

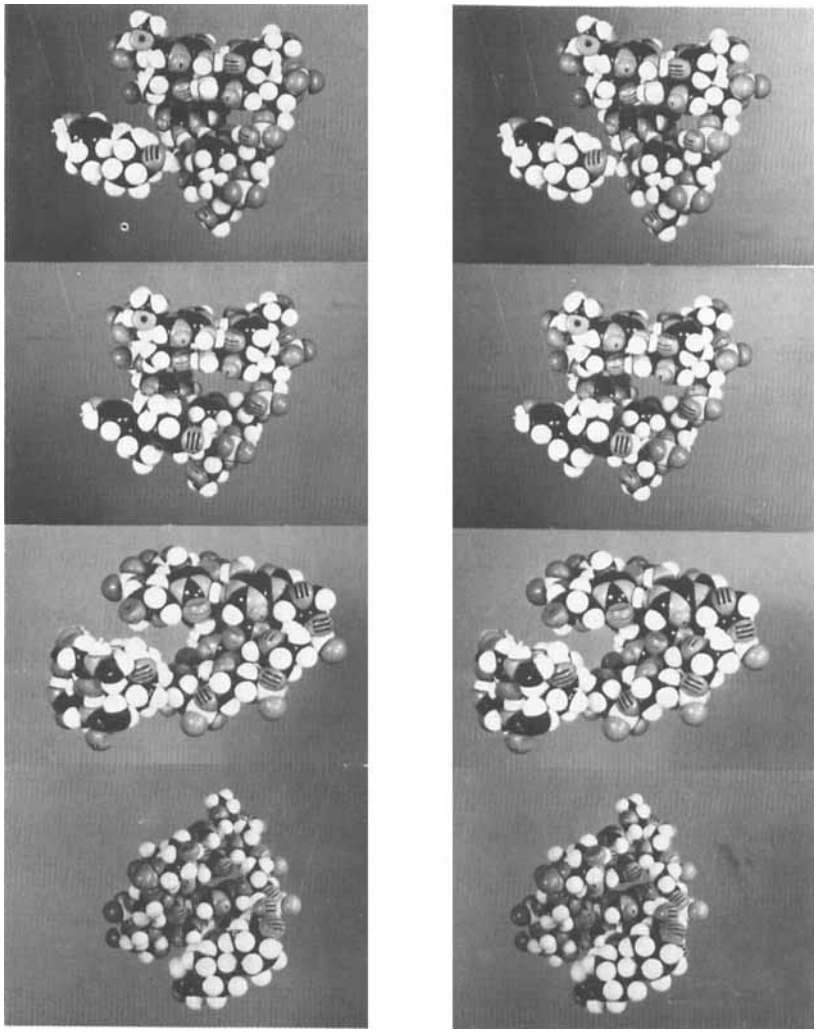


FIGURE 12 ß-Estradiol, diethylstilbestrol, testosterone and cortisol facing cavities of B-DNA design[4,5].

complementarities to important classes of steroid hormones (Figs. 12 - 15). Estrogens, preferentially crystallizing in layered arrangements,[6] might well be accommodated for by the intercalation geometries of B-DNA[20].

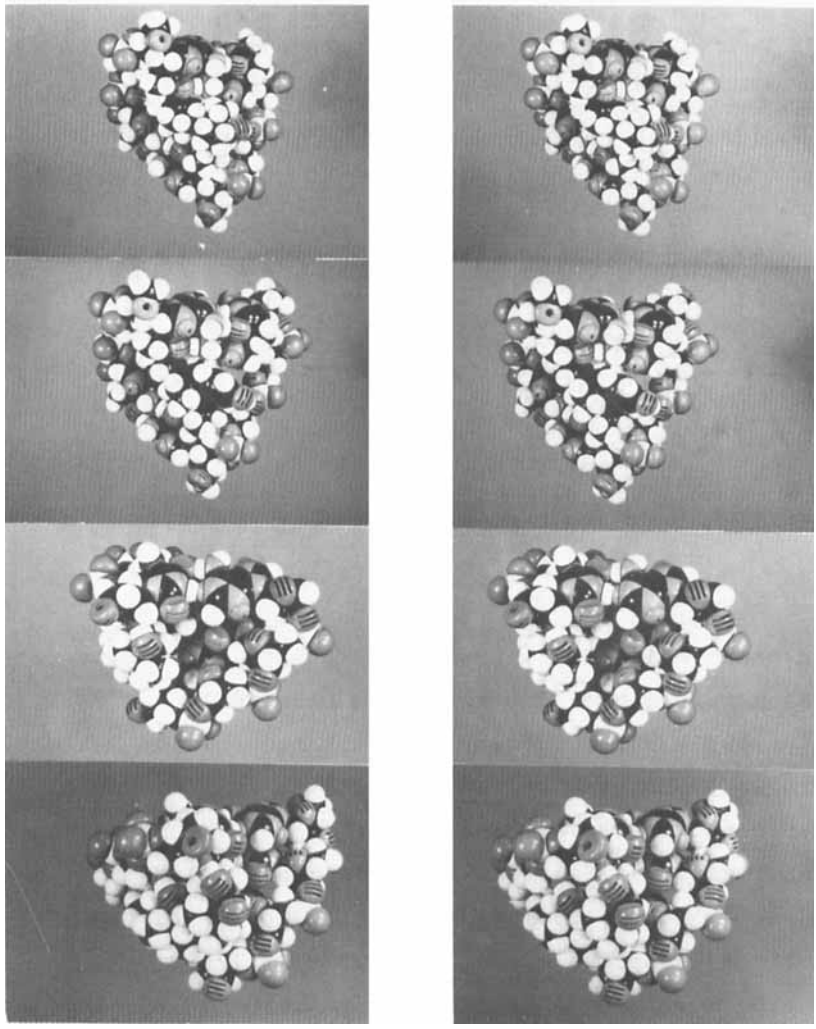


FIGURE 13 ß-Estradiol and diethylstilbestrol occupying intercalation sites, testosterone and cortisol fitting the minor groove of B-DNA[4,5].

Their terminal hydroxy groups fit, as it is also the case with stilbestrol, the strand phosphates. Testosterone and cortisol, preferring screw axis arrangements within their crystal packings, hydrophobically smooth

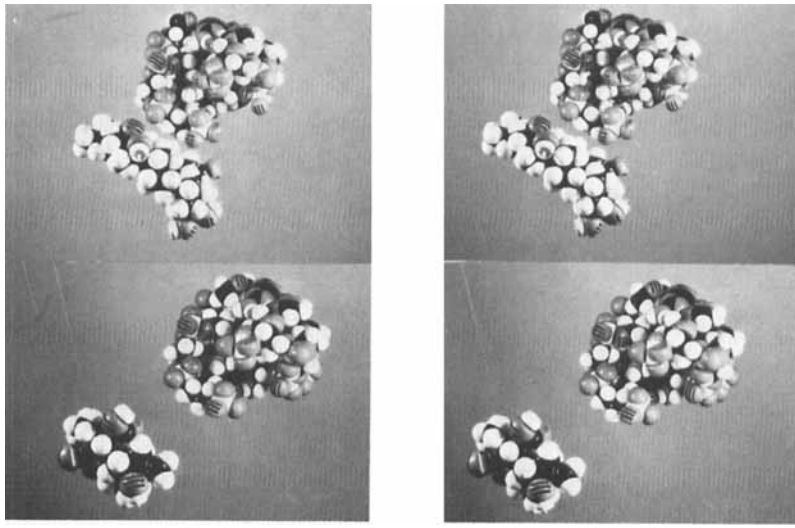


FIGURE 14 ß-Ecdysone and gibberellin A_3 facing Z-DNA deep groove[4,5].

with their chirally twisted α-faces into the cavity of B-DNA minor groove. The distorted steroidal ß-faces simultaneously offer suitable protein recognition designs. Hydrogen bonds, in the case of cortisol a whole network interconnecting both DNA-strands, assist the hydrophobic annealing. Visualizations of B-DNA minor groove molecular electrostatic potentials[20] intriguingly confirm the negatively modelled steroid-acceptor patterns.

The more complex structural patterns of the insect moulting hormone ß-ecdysone and the phytohormone gibberellin A_3, both crystallizing in screw axis arrangements,[21,22] can surprisingly be met by the deep groove design of Z-DNA[23]. Neat hydrophobic contacts and networks of hydrogen bonds provide matrix fits for the steroidal insect hormone and the far phyto-analog.

Though all this need not be of any relevance to the native functionalism within the chromatin, it is not

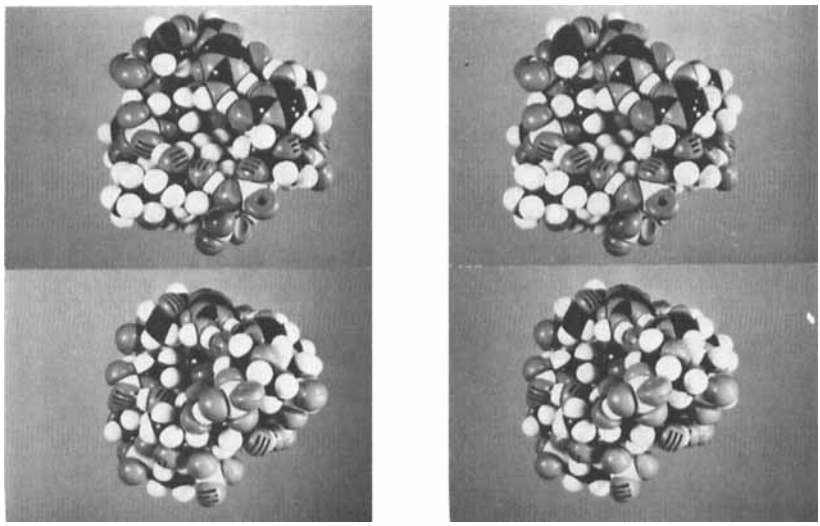


FIGURE 15 ß-Ecdysone and gibberellin A_3 fitting Z-DNA deep groove[4,5].

contradictory to the at present accepted schemes[24] of hormonal efficiencies between nuclear hormone receptors and the DNA-partner.

2. CONCLUSIONS

Mesogenic activities of regulatory steroids in directing and modulating complex biomesogenic order-disorder patterns[25] offer an intriguingly coherent view of quite different and multi-level operation modes in signal generation, transduction and amplification.

Thermotropic and lyotropic characteristics in general and complex guest-host relationships in particular might forward useful approaches (Fig. 16) in modelling the complex roles of steroidal bioregulators in organismic information processing.

By this the field will contribute to a better understanding of (bio)mesogens statics and dynamics.

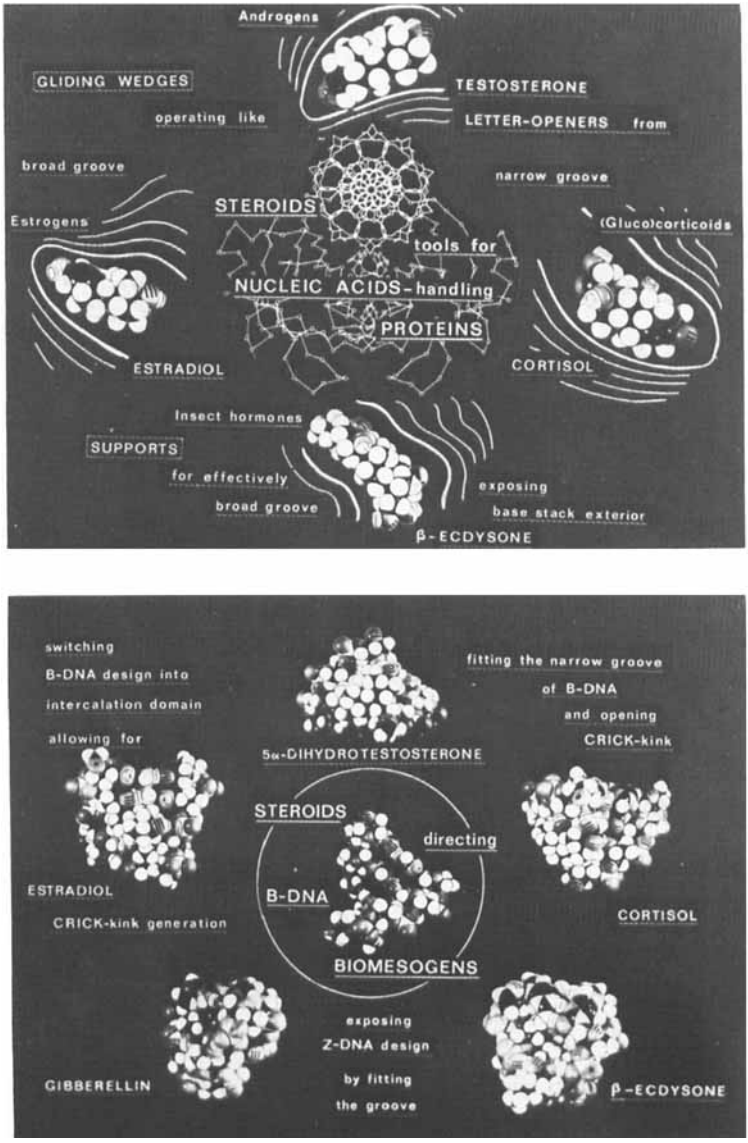


FIGURE 16 Hypothetical biomesogemic activities of steroidal and non-steroidal hormones within the chromatin.

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