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# Self-consistent molecular modelling approach for receptor identification and drug design: Basis and data base needs*

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**Abstract**

The central problem in drug design is the lack of understanding of the molecular structural features of receptors. In this work, a new self-consistent molecular modelling approach, based on drug-(model) receptor interaction studies, is developed to aid in the identification of receptor's active site structure and the design of drugs. For a given molecule, be it a drug, nutrient, model receptor, biomolecule or moiety likely to form part of an active site structure of a receptor model, the data base holds the following information: the cartesian coordinates and net charges on all the atoms including hydrogens, complete all-valence electron (CNDO) wavefunctions and energies in a coordinate system fixed at a convenient point on the molecule. The methodology can also be employed to understand, at the molecular level, drug-drug, drug-nutrient interactions and the molecular origin of adverse effects of drugs.

**Key words:** Data base, drug design, receptors, drug-receptor, drug-nutrient interactions, molecular modelling.

## 1. Introduction

Biological activity of a drug is the result of its interaction with receptor(s). All drugs taken in higher dosages or for longer duration have adverse effects. Something like the Newton's third law of motion, the beneficial effect of any drug is always accompanied by its side effects. It is the dream of every drug design group to develop ideal drugs–those with none or least side or adverse effects. The advent of modern computers, be it PCs or minis or work stations or supers, coupled with sophisticated 3D-graphic systems, has led to the era of molecular modelling. Here one pictures, on the video graphic terminal, the possible mode of binding of drugs at the receptor sites in cases where the receptor structures are known. Receptor models considered in these cases are usually enzymes or proteins whose crystal structures have already been solved. It is reported[1] that significant reductions in research and development costs are possible in the chemical and drug industry by the application of a molecular modelling approach. Almost all the leading chemical and pharmaceutical industries in the west have groups actively involved in using computers and molecular orbital methods. Many successes have been reported in obtaining newer candidate drugs, whose discovery would not have been possible without the aid of molecular modelling[2–6]. Although drug design is essentially an experimental

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science, molecular modelling procedures demand scientists with a theoretical background to interact with the experimentalists. Thus, the role of theoreticians is beginning to gain its due place in this vital sector. In fact, a molecular theorist has co-authored the patent of a recent pharmaceutical product in Europe[7]. However, in India there appears to be no active group either in the industry or in research institutions in this area. The little that is attempted in academic institutions is said to be often desultory in nature[8].

Our approach envisages a self-consistent molecular modelling, based on drug-(model)receptor interaction studies. Before going into an outline of our approach, it is appropriate to mention here the cost and time involved in bringing a new drug to market and some facts about drug action. It costs about US $ 40 to 90 million, according to 1986 estimates, together with an initial investment of US $ 50 to 150 million. The time consumed being around 7–10 years, after a lead is found. Only one out of nearly 10,000 newly synthesized compounds is likely to become a drug! Further satisfactory therapy is available to only about one-third of all ailments!. *i.e.* for 66% of ailments we have no drugs of choice. Some facts on drug action are that a majority of drugs bir d reversibly at the receptor sites, with weak binding energies, their molecular mechanism of action not being understood. Further, the moiecular and structural features of a majority of receptors are unknown. As an analogy, we can compare the current understanding of receptors to, something similar to, the description of an elephant by a group of blind persons. Despite intense efforts[9–12], receptors are today where enzymes were 25 years ago! It is this lack of understanding of the molecular structural features of receptors that constitutes the central problem in drug design and the consequential high costs and delay in the arrival of safer drugs to the market.

## 2. The approach

We have initiated an entirely different approach, based on the following premises, to solve the dilemma.

### *2.1. All drug-receptor interactions can essentially be regarded as an exercise in quantum mechanical intermolecular perturbation theory.*

As an analogy to drug-receptor interaction, we can look upon it as a clap by hands, the sound being related to the strength of interaction. No matter how well we look at one of the hands, which incidentally can assume any allowed shape, we cannot say anything about the sound or strength of the clap (fig. 1). We have to look at both the partners, if we have to arrive at any understanding of the drug action. Quantum mechanics is the only theory which has many successes in the understanding of the molecular structure and activities of atoms and molecules. It also provides an ideal tool, the perturbation method, to study the weak interactions between two systems. We apply this tool in the understanding of drug-receptor interactions as a majority of drug-receptor bindings are weak and the processes are reversible.

It is fairly easy to understand that as the molecule approaches its receptor site, there is some optimal distance at which a weak (reversible) complex is formed (fig. 2) where,

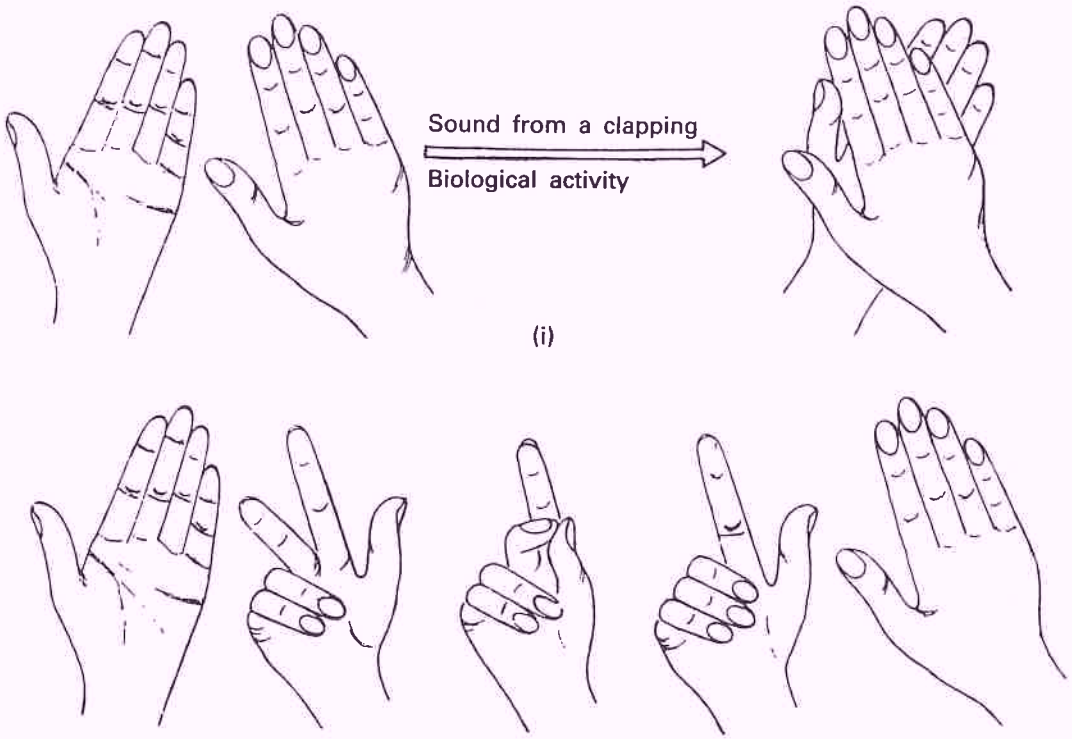



FIG. 1. An analogy to drug-receptor interactions, the sound being related to the strength of interaction *viz.* biological activity (i), and no matter how well we look at one of the partners (ii), we cannot say anything about the strength/sound of a clap. Hence, any correlation of activity to structure or property of either one of the partners is less effective towards understanding the mechanism of action.

there is a net balance between the repulsive and attractive forces, with the latter in a dominant role. Thus, the drug-receptor binding refers to the interactions in the medium-range, with a small intermolecular overlap and a mixed combination of energies of repulsive and attractive kinds.

According to the quantum mechanical theory of intermolecular forces in regions of small orbital overlap[13], the binding energy of a drug-receptor complex (fig. 3) can be split into the following components.

1. Electrostatic energy–the interaction energy between net charges on various atoms of the two molecules. In an MO picture, the situation refers to interaction between electrons in the occupied orbitals of the two molecules. The net effect could either be attractive or repulsive and the effect is operative at all intermolecular separations–*i.e.* at all ranges.
2. Exchange repulsion energy,
3. Polarisation energy,

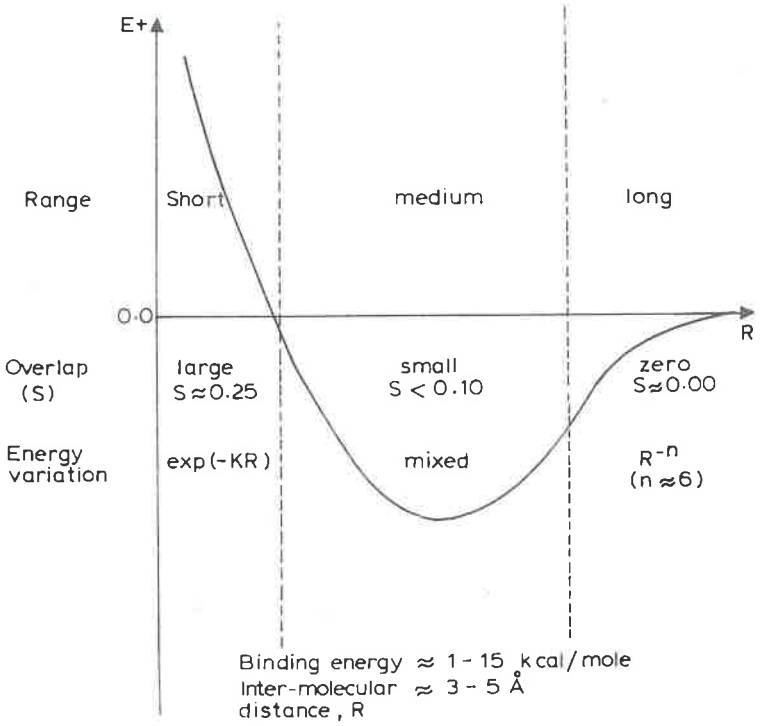



FIG. 2. A typical spherically averaged intermolecular potential energy curve, together with the common terminologies employed in discussion on intermolecular affairs. The drug-receptor binding process falls in the category of interactions in the medium range.

4. Dispersion energy, and
5. Charge transfer energy.

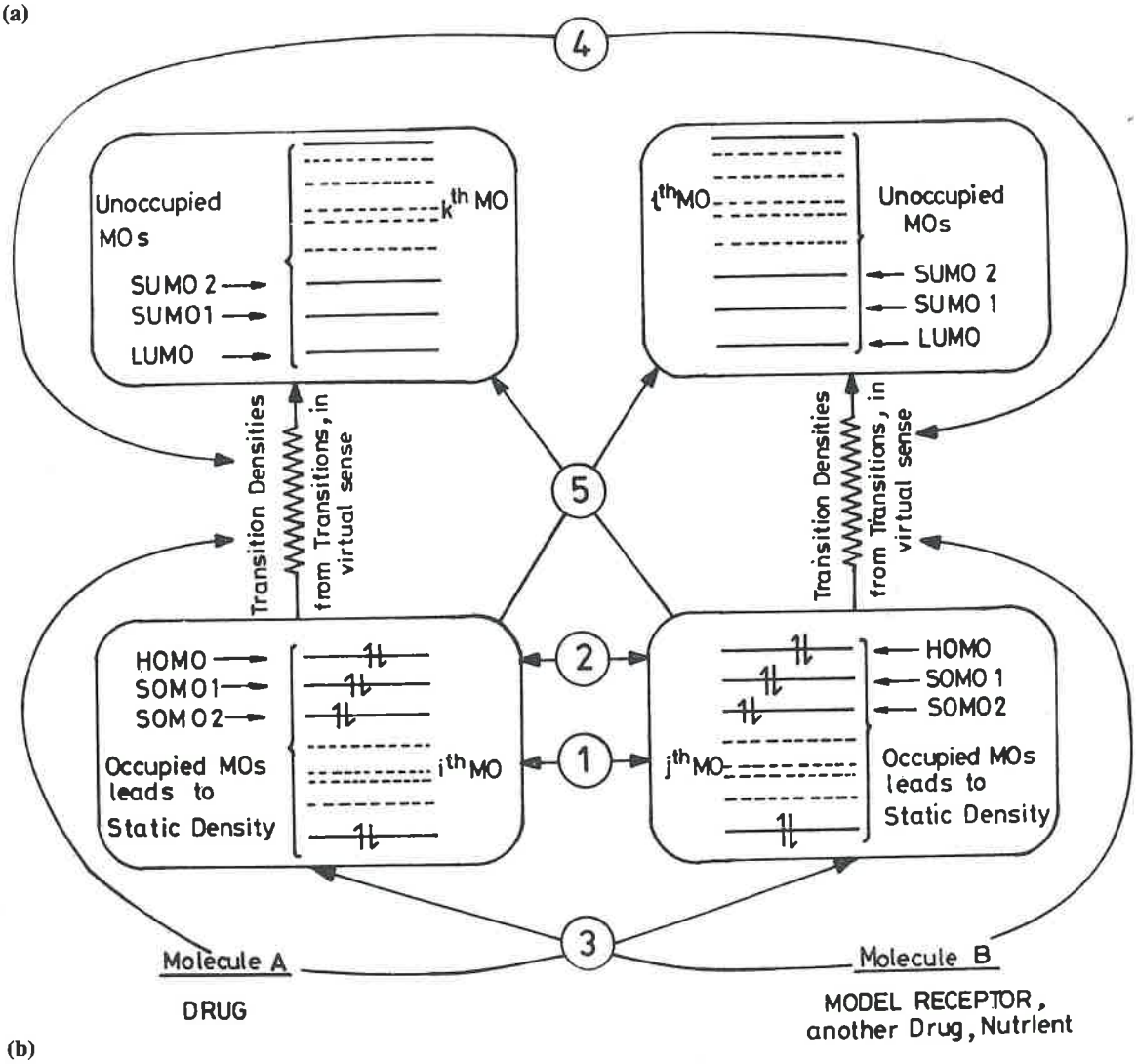
The interaction energy program in FORTRAN, developed by us, computes these terms for any given geometry of the complex, thus facilitating an explicit analysis of the relative role played by various terms in the binding process.

*2.2. Starting with a crude model for a receptor, with the repeated use of the interaction energy program and varying the geometry and composition of the model receptor a self-consistent (refined) model for the receptor can be achieved!*

Although the receptor as a whole could be a complex molecule, as far as the drug activity is concerned, only a portion of the molecule will be involved in the interaction with the drug. In fact, our experience with large molecules clearly suggests that at distances greater than 7 Å no significant interaction occurs between molecules, or pairs of atoms or functional groups. This important factor reduces the complexities of the systems (drug or receptor) to manageable sizes when computing their interaction energies, thereby facilitating this modelling approach.

Smaller molecular units like nucleic acid bases, free amino acids, small peptides and nucleotides, likewise, can be employed as models for the active site of the receptor.

(a)




(b)

| Type | Range | Attractive/ repulsive | Pairwise additive |
|---|---|---|---|
| 1. Electrostatic | long | either | yes |
| 2. Exchange | short | repulsive* | nearly |
| 3. Polarisation | long | attractive | no |
| 4. Dispersion | long | attractive | yes |
| 5. Charge-transfer | short | attractive | nearly |

*Except possibly for the interaction between two anions.

FIG. 3. Features of the various components of molecular interaction, (a) in terms of interaction and mixing of Molecular Orbitals (MOs) and (b) their characteristic properties. *H*ighest *O*ccupied *M*olecular *O*rbital (HOMO), its immediate neighbours–*S*ubjacent *O*ccupied *M*olecular *O*rbitals (SOMO-1 & SOMO-2) and the *L*owest *U*noccupied *M*olecular *O*rbital (LUMO), its immediate neighbours–*S*ubjacent *U*noccupied *O*rbitals (SUMO-1 & SUMO-2), play a dominant role in interaction studies.

Consequently, a feature of the approach, is that the computational exercise forces one to think (or enhance one's understanding) of the structural features necessary for the drug as well its effector–receptor, concurrently and on equal footing. Such an advantage is non-existent in any of the currently followed drug design efforts[14,15].

The approach in quest of receptor(s) consists of two stages:

2.2.1. In the first stage, as outlined in scheme 1, the wavefunctions and energies of drugs, their derivatives or metabolites and model receptors are generated which form the zeroth order basis set for the intermolecular perturbative interaction energy calculations. These data are stored in the data base.

Another feature of the approach is that the data is computed only once and can be reused. No repetition of computations is necessary and results in a big saving in computational cost and time. This feature is essential in view of the fact that a functional group or a moiety appears in a variety of positions/situations, in the search for receptor identity.

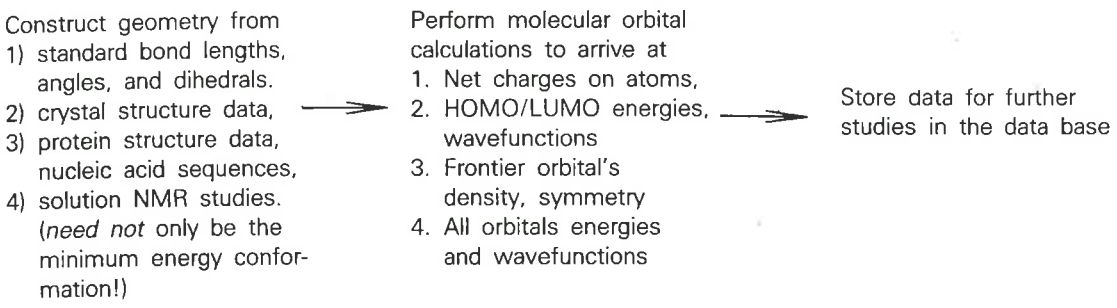
2.2.2. In the second stage (scheme 2) the interaction energy calculations between a given drug and a set of models for the active site structure of a receptor are carried out to arrive at a self-consistent model of the receptor which can lead to a new classification of receptors based on their own identity.

*2.3. Not only drug-receptor interactions but also drug-interactions, drug-nutrient interactions and toxicities can be analysed using the same methodology/program.*

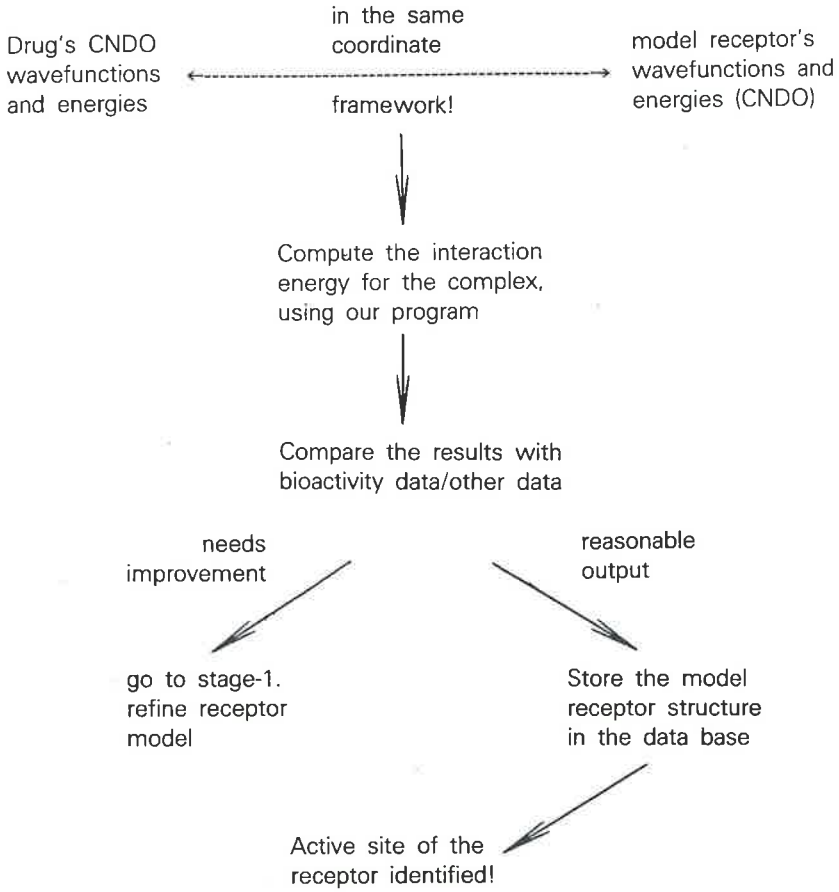
This is feasible in view of the plausibility that a given active site structure acting as a therapeutic site for one drug, could as well act as a toxicity or an antagonist or an inactive centre for another drug, its derivative(s) or metabolite(s). One can easily perform a computational exercise to see how a given receptor site interacts with various other drugs and *vice versa*. Such an effort may suggest newer experiments as a challenge to the experimentalists or can act as a complementary tool, something like Raman spectroscopy complementing infrared spectroscopy. So, as an added bonus, the approach opens the door to understanding the molecular origin of adverse effects of drugs[16,17], drug interaction[18–21], etc., all under the umbrella of the data stored in the data bank and the interaction energy program. Further, in the future it may become possible to answer questions like whether a given receptor for a drug is same in the infectious or disease state and in the normal state, *i.e.* the methodology may help in characterising, at the molecular level, the disease state and the mechanism of drug (especially antibiotics) resistance.

*2.4. The methodology in relation to drug action and drug design.*

Our efforts are concerned with the pharmacodynamic phase in drug action (scheme 3), the phase wherein the drug is purely or exclusively involved in interaction with the receptor. This is something similar to the interaction between two molecules in the gas

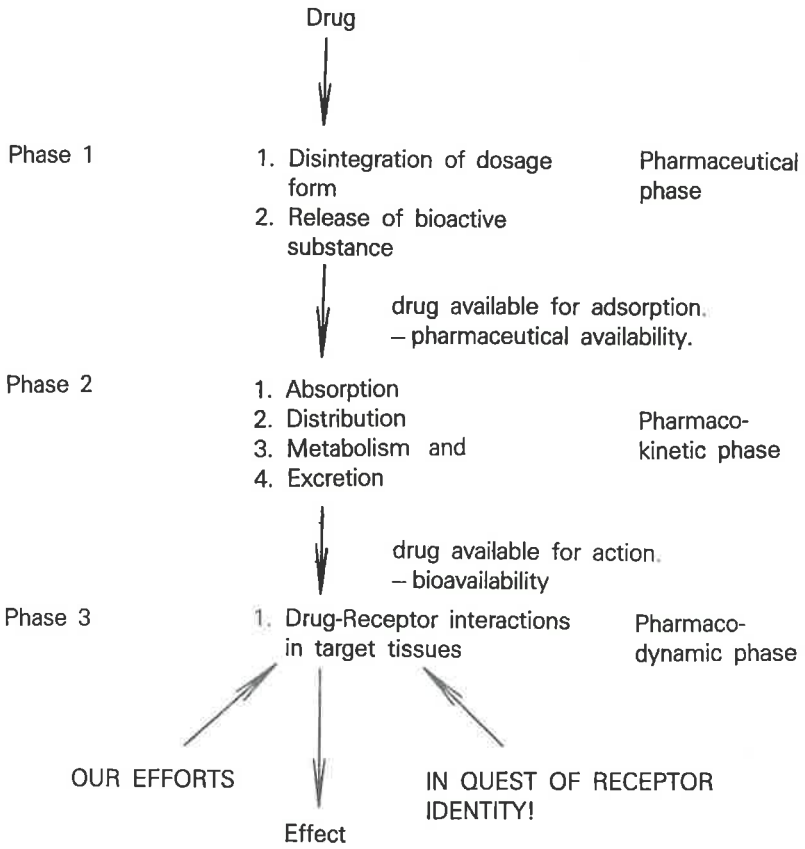



Scheme 1. The sequence of steps involved in generation and storage of molecular wavefunctions and energies of drugs, their derivatives or metabolites, nutrients and model receptors in the data base.




Scheme 2. The sequence of steps involved in arriving at the active site structure of a receptor in our approach.

phase without any interference of either media or other molecules. Although, interactions do occur *in vivo*, the classification of the term or situation – pharmacodynamic phase – refers solely to that part of events where the drug actually meets the




**Scheme 3. Role of our methodology in relation to the various phases of drug action.**

receptor. It is to this vital zone in drug action that the outlined theoretical methodologies apply.

What is provided here is an *alternative tool* to the conventional computational methods *viz.* QSAR[22,23] extensively used in drug design. Current QSAR methods require a series of test compounds with determined biological activity data known before hand and use complicated statistics[24] to arrive at a better candidate drug. They tell nothing about the receptor's molecular structural features. On the other hand, in the approach outlined here, it is possible to get at the active site structure of a receptor. Once this is done, it is obvious that the enormous cost and time involved in drug design efforts is reduced. Hence, the approach has the potential to aid in drug design efforts.

## 3. The data base

We have begun constructing a data base consisting of molecular geometries, net charges, complete CNDO[25] wavefunctions and energies for a number of compounds, drugs, and biomolecules likely to act as receptors. Currently we have the data for the following compounds:

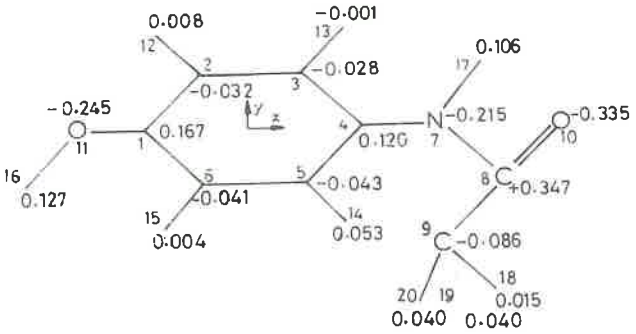
**Table I**
**Cartesian coordinates of atoms in aspirin and paracetamol (fig. 4)**

| Drug | Aspirin | | | Paracetamol | | |
|---|---|---|---|---|---|---|
| Atom no. | X | Y | Z | X | Y | Z |
| 1 | −1.400 | 0.000 | 0.000 | −1.400 | 0.000 | 0.000 |
| 2 | −0.700 | 1.212 | 0.000 | −0.700 | 1.212 | 0.000 |
| 3 | 0.700 | 1.212 | 0.000 | 0.700 | 1.212 | 0.000 |
| 4 | 1.400 | 0.000 | 0.000 | 1.400 | 0.000 | 0.000 |
| 5 | 0.700 | −1.212 | 0.000 | 0.700 | −1.212 | 0.000 |
| 6 | −0.700 | −1.212 | 0.000 | −0.700 | −1.212 | 0.000 |
| 7 | 2.760 | 0.000 | 0.000 | 2.830 | 0.000 | 0.000 |
| 8 | 3.440 | −1.178 | 0.000 | 3.539 | −1.227 | 0.000 |
| 9 | 4.960 | −1.178 | 0.000 | 5.065 | −1.227 | 0.000 |
| 10 | 2.830 | −2.234 | 0.000 | 2.924 | −2.292 | 0.000 |
| 11 | 1.430 | 2.477 | 0.000 | −2.760 | 0.000 | 0.000 |
| 12 | 0.820 | 3.533 | 0.000 | −1.240 | 2.148 | 0.000 |
| 13 | 2.790 | 2.477 | 0.000 | 1.240 | 2.148 | 0.000 |
| 14 | 1.240 | −2.148 | 0.000 | 1.240 | −2.148 | 0.000 |
| 15 | −1.240 | −2.148 | 0.000 | −1.240 | −2.148 | 0.000 |
| 16 | −2.480 | 0.000 | 0.000 | −3.300 | −0.935 | 0.000 |
| 17 | −1.240 | 2.148 | 0.000 | 3.335 | 0.875 | 0.000 |
| 18 | 3.103 | 1.569 | 0.000 | 5.427 | −0.199 | 0.000 |
| 19 | 5.323 | −0.664 | 0.890 | 5.427 | −1.741 | 0.890 |
| 20 | 5.323 | −2.206 | 0.000 | 5.427 | −1.741 | 0.890 |
| 21 | 5.323 | −0.664 | −0.890 | | | |

1. Paracetamol, $C_8H_9NO_2$, antipyretic/analgesic/anti-inflammatory.
2. Acetylsalicylic acid, $C_9O_4H_8$, antipyretic/analgesic/anti-inflammatory.
3. Phenacetin, $C_{10}H_{13}NO_2$, anti-inflammatory.
4. Naproxen, $C_{14}H_{14}O_3$, anti-inflammatory.
5. Ibuprofen, $C_{13}H_{18}O_2$, anti-inflammatory.
6. Mefenamic acid, $C_{15}H_{15}NO_2$, anti-inflammatory.
7. Flufenamic acid, $C_{14}H_{10}F_3NO_2$, anti-inflammatory.
8. Enfenamic acid*, $C_{15}H_{15}NO_2$, anti-inflammatory.
9. Naphthalene nitrenium ion, $C_{10}H_8N$, model aromaticamine carcinogen.
10. Porphin, $C_{20}H_{14}N_4$, model for heme ring current.
11. Benzene, $C_6H_6$, a model for aromatic ring.
12. Guanine,
13. Adenine,
14. Thymine,
15. Uracil,
16. Cytosine.

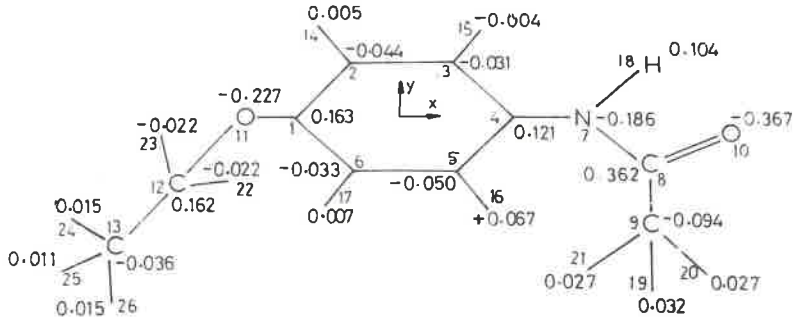
} components of DNA/RNA, for modelling the 'active sites' of receptor(s).

*This drug is an Indian contribution in recent times. It was synthesized by Raiz Hashim and P. B. Sattur at the Regional Research Laboratory, Hyderabad, in 1964. After extensive clinical trials, it was released to the market, under the trade name TROMARIL by Unichem in 1981. Like the fenamates, its side effects are skin rashes, itching and diarrhoea. Many other contributions are in the offing[8].



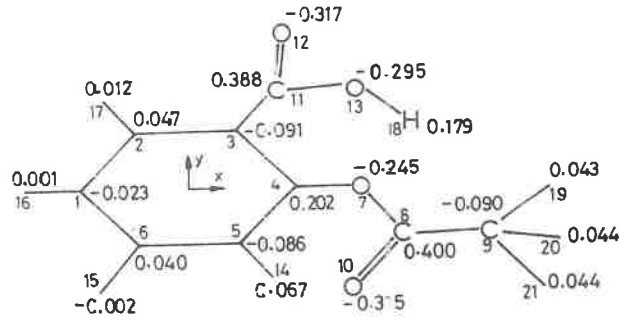

HOMO (29th MO) $\varepsilon = -10.78201$ ev ($\pi$ type)
LUMO (30th MO) $\varepsilon = +3.84764$ ev ($\pi$ type)

## PARACETAMOL $C_8H_9NO_2$



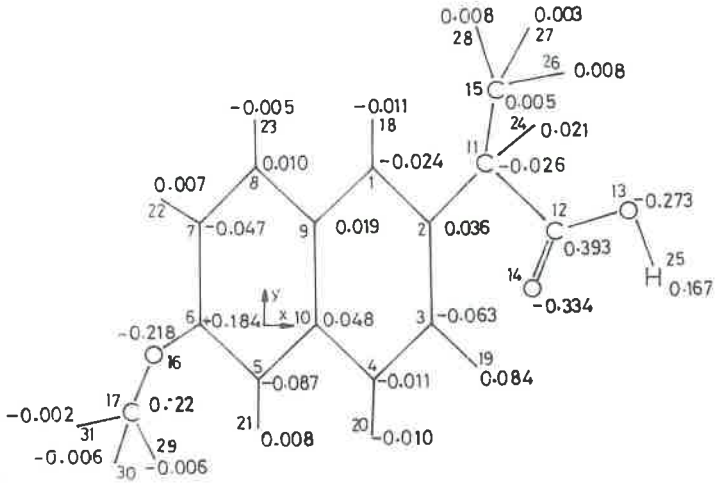

HOMO (35th MO) $\varepsilon = -10.67081$ ev ($\pi$ type)
LUMO (36th MO) $\varepsilon = +3.90078$ ev ($\pi$ type)

## PHENACETIN $C_{10}H_{13}NO_2$



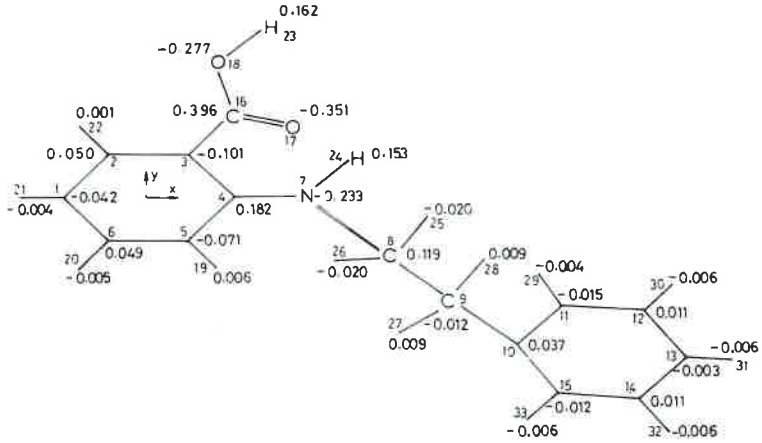

HOMO (34th MO) $\varepsilon = -12.28014$ ev ($\pi$ type)
LUMO (35th MO) $\varepsilon = +2.31844$ ev ($\pi$ type)

## ASPIRIN $C_9H_8O_4$



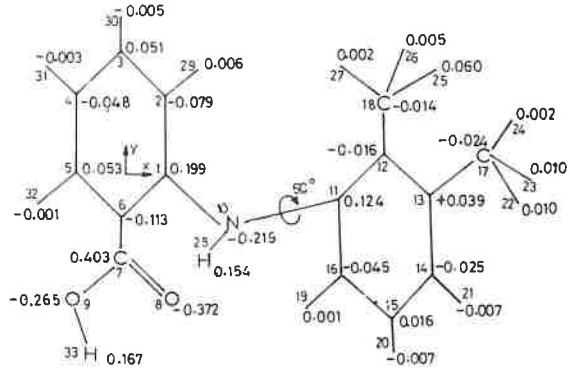

HOMO (44th MO) $\varepsilon = -10.41127$ ev ($\pi$ type)
LUMO (45th MO) $\varepsilon = +2.01812$ ev ($\pi$ type)

## NAPROXEN $C_{14}H_{14}O_3$



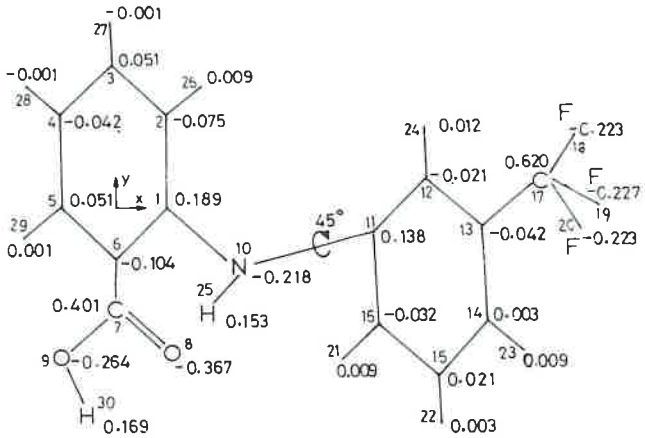
HOMO (46th MO) $\varepsilon = -11.11069$ ev ($\pi$ type)
LUMO (47th MO) $\varepsilon = +2.48474$ ev ($\pi$ type)

ENFENAMIC ACID $C_{15}H_{15}NO_2$



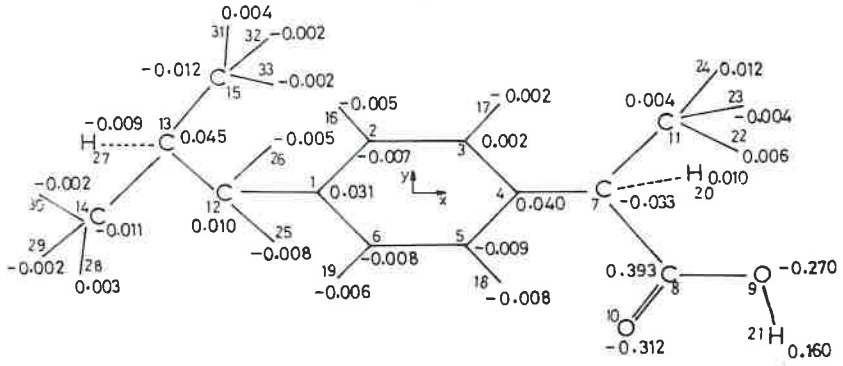
HOMO (46th MO) $\varepsilon = -10.53285$ ev ($\pi$ type)
LUMO (47th MO) $\varepsilon = +2.50966$ ev ($\pi$ type)

MEFENAMIC ACID $C_{15}H_{15}NO_2$



HOMO (52nd MO) $\varepsilon = -10.88397$ ev ($\pi$ type)
LUMO (53rd MO) $\varepsilon = +2.28888$ ev ($\pi$ type)

FLUFENAMIC ACID $C_{14}H_{10}F_3NO_2$



HOMO (41th MO) $\varepsilon = -11.85714$ ev ($\sim\pi$ type)
LUMO (42th MO) $\varepsilon = +3.72909$ ev ($\sim\pi$ type)

IBUPROFEN $C_{13}H_{18}O_2$

FIG. 4. The net charges on all atoms in the various drugs together with the HOMO/LUMO energies (CNDO method). See Tables I–IV for their corresponding cartesian coordinates.

Presenting a complete data file for each of the above molecules, consisting of cartesian coordinates in a convenient molecule-fixed coordinate system, complete CNDO wavefunctions and energies (not just the HOMO/LUMOs), and the net charges on all the atoms including hydrogens, would become too unwieldy to be included here*. Consequently, only a partial set of data for drugs mentioned above is given. The data given are: (a) the net charges on all the atoms (fig. 4), (b) the cartesian coordinates (Tables I–IV) and the corresponding highest occupied and lowest vacant molecular orbitals (Tables V–VIII).

**Table II**
**Cartesian coordinates of atoms in ibuprofen and phenacetin (fig. 4)**

| Drug | Ibuprofen | | | Phenacetin | | |
|---|---|---|---|---|---|---|
| Atom no. | X | Y | Z | X | Y | Z |
| 1 | −1.400 | 0.000 | 0.000 | −1.400 | 0.000 | 0.000 |
| 2 | −0.700 | 1.212 | 0.000 | −0.700 | 1.212 | 0.000 |
| 3 | 0.700 | 1.212 | 0.000 | 0.700 | 1.212 | 0.000 |
| 4 | 1.400 | 0.000 | 0.000 | 1.400 | 0.000 | 0.000 |
| 5 | 0.700 | −1.212 | 0.000 | 0.700 | −1.214 | 0.000 |
| 6 | −0.700 | −1.212 | 0.000 | −0.700 | −1.213 | 0.000 |
| 7 | 2.920 | 0.000 | 0.000 | 2.800 | 0.000 | 0.000 |
| 8 | 3.427 | 0.717 | 1.241 | 3.460 | −1.143 | 0.000 |
| 9 | 4.764 | 0.841 | 1.456 | 4.980 | −1.143 | 0.000 |
| 10 | 2.627 | 1.184 | 2.051 | 2.850 | −2.200 | 0.000 |
| 11 | 3.433 | 0.726 | −1.257 | −2.760 | 0.000 | 0.000 |
| 12 | −2.920 | 0.000 | 0.000 | −3.475 | 1.238 | 0.000 |
| 13 | −3.433 | 0.726 | 1.257 | −4.989 | 0.957 | 0.000 |
| 14 | −4.973 | 0.726 | −1.257 | −1.240 | 2.148 | 0.000 |
| 15 | −2.920 | 0.000 | −2.515 | 1.240 | 2.148 | 0.000 |
| 16 | −1.240 | 2.148 | 0.000 | 1.239 | −2.149 | 0.000 |
| 17 | 1.240 | 2.148 | 0.000 | −1.241 | −2.148 | 0.000 |
| 18 | 1.240 | −2.148 | 0.000 | 3.305 | 0.875 | 0.000 |
| 19 | −1.240 | −2.148 | 0.000 | 5.343 | −0.629 | 0.890 |
| 20 | 3.283 | −1.028 | 0.000 | 5.343 | −2.171 | 0.000 |
| 21 | 5.387 | 0.476 | 0.824 | 5.343 | −0.629 | −0.890 |
| 22 | 3.070 | 1.753 | −1.257 | −3.212 | 1.810 | −0.890 |
| 23 | 4.523 | 0.726 | −1.257 | −3.212 | 1.810 | 0.890 |
| 24 | 3.070 | 0.212 | 2.147 | −5.252 | 0.385 | 0.890 |
| 25 | −3.283 | 0.514 | 0.890 | −5.534 | 1.901 | 0.000 |
| 26 | −3.283 | −1.027 | 0.000 | −5.252 | 0.385 | −0.890 |
| 27 | −3.070 | 1.753 | −1.257 | | | |
| 28 | −5.337 | 1.240 | −0.367 | | | |
| 29 | −5.337 | 1.240 | −2.147 | | | |
| 30 | −5.336 | −0.302 | −1.257 | | | |
| 31 | −3.283 | −1.028 | −2.515 | | | |
| 32 | −3.283 | 0.514 | −3.405 | | | |
| 33 | −1.830 | 0.000 | −2.515 | | | |

*Limited copies of the data can be had from the author on request.

**Table III**
**Cartesian coordinates of atoms in mefenamic acid and enfenamic acid (fig. 4)**

| Drug | Mefenamic acid | | | Enfenamic acid | | |
|---|---|---|---|---|---|---|
| Atom no. | X | Y | Z | X | Y | Z |
| 1 | 1.025 | 0.000 | 0.000 | −1.400 | 0.000 | 0.000 |
| 2 | 1.025 | 1.400 | 0.000 | −0.700 | 1.212 | 0.000 |
| 3 | −0.188 | 2.100 | 0.000 | 0.700 | 1.212 | 0.000 |
| 4 | −1.400 | 1.400 | 0.000 | 1.400 | 0.000 | 0.000 |
| 5 | −1.400 | 0.000 | 0.000 | 0.700 | −1.212 | 0.000 |
| 6 | −0.188 | −0.700 | 0.000 | −0.700 | −1.212 | 0.000 |
| 7 | −0.188 | −2.160 | 0.000 | 2.800 | 0.000 | 0.000 |
| 8 | 0.878 | −2.775 | −0.000 | 3.535 | −1.273 | 0.000 |
| 9 | −1.331 | −2.820 | 0.000 | 5.049 | −0.992 | 0.000 |
| 10 | 2.203 | −0.680 | 0.000 | 5.809 | −2.308 | 0.000 |
| 11 | 3.501 | −0.129 | 0.000 | 5.109 | −3.520 | 0.000 |
| 12 | 3.908 | 0.703 | 1.050 | 5.809 | −4.733 | 0.000 |
| 13 | 5.197 | 1.250 | 1.050 | 7.209 | −4.733 | 0.000 |
| 14 | 6.078 | 0.965 | 0.000 | 7.909 | −3.520 | 0.000 |
| 15 | 5.671 | 0.133 | −1.050 | 7.209 | −2.308 | 0.000 |
| 16 | 4.382 | −0.414 | −1.050 | 1.430 | 2.477 | 0.000 |
| 17 | 5.639 | 2.152 | 2.190 | 2.650 | 2.477 | 0.000 |
| 18 | 2.951 | 1.011 | 2.190 | 0.750 | 3.655 | 0.000 |
| 19 | 4.067 | −1.055 | −1.860 | 1.240 | −2.148 | 0.000 |
| 20 | 6.350 | −0.086 | −1.860 | −1.240 | −2.148 | 0.000 |
| 21 | 7.072 | 1.387 | 0.000 | −2.480 | 0.000 | 0.000 |
| 22 | 5.904 | 3.133 | 1.795 | −1.240 | 2.148 | 0.000 |
| 23 | 6.506 | 1.714 | 2.685 | 1.380 | 4.379 | 0.000 |
| 24 | 4.825 | 2.257 | 2.907 | 3.305 | 0.875 | 0.000 |
| 25 | 2.781 | 2.087 | 2.240 | 3.272 | −1.845 | −0.890 |
| 26 | 3.383 | 0.668 | 3.130 | 3.272 | −1.845 | 0.890 |
| 27 | 2.004 | 0.501 | 2.018 | 5.312 | −0.420 | 0.890 |
| 28 | 2.203 | −1.690 | 0.000 | 5.312 | −0.420 | −0.890 |
| 29 | 1.960 | 1.940 | 0.000 | 4.029 | −3.520 | 0.000 |
| 30 | −0.188 | 3.180 | 0.000 | 5.269 | −5.668 | 0.000 |
| 31 | −2.335 | 1.940 | 0.000 | 7.749 | −5.668 | 0.000 |
| 32 | −2.335 | −0.540 | 0.000 | 8.989 | −3.520 | 0.000 |
| 33 | −1.146 | −3.772 | 0.000 | 7.749 | −1.373 | 0.000 |

Many more are in the process of being added to the above list. These include: (a) all the amino acids, (b) model di-, tri-, and penta-peptides relevant to CNS activity, (c) models of A-, B-, Z- DNAs, as possible models for receptor sites, (d) models of receptors built from amino acid sequences, (e) all the possible 200 essential drugs, (f) newer model anticarcinogens, antivirals, antibacterial drugs, etc.

With the protein data base and the nucleic acid sequence data base becoming available in India, under the National Biotechnology Board (NBTB) program, many more

**Table IV**
**Cartesian coordinates of atoms in flufenamic acid and naproxen (fig. 4)**

| Drug | Flufenamic acid | | | Naproxen | | |
|---|---|---|---|---|---|---|
| Atom no. | X | Y | Z | X | Y | Z |
| 1 | 1.024 | 0.000 | 0.000 | 2.237 | 2.100 | 0.000 |
| 2 | 1.024 | 1.400 | 0.000 | 3.450 | 1.400 | 0.000 |
| 3 | −0.188 | 2.100 | 0.000 | 3.450 | 0.000 | 0.000 |
| 4 | −1.400 | 1.400 | 0.000 | 2.237 | −0.700 | 0.000 |
| 5 | −1.400 | 0.000 | 0.000 | −0.188 | −0.700 | 0.000 |
| 6 | −0.188 | −0.700 | 0.000 | −1.400 | 0.000 | 0.000 |
| 7 | −0.188 | −2.170 | 0.000 | −1.400 | 1.400 | 0.000 |
| 8 | 0.878 | −2.785 | 0.000 | −0.186 | 2.100 | 0.000 |
| 9 | −1.331 | −2.830 | 0.000 | 1.025 | 1.400 | 0.000 |
| 10 | 2.220 | −0.690 | 0.000 | 1.025 | 0.000 | 0.000 |
| 11 | 3.527 | −0.162 | 0.000 | 4.766 | 2.160 | 0.000 |
| 12 | 3.855 | 0.895 | 0.857 | 5.921 | 1.172 | 0.000 |
| 13 | 5.153 | 1.420 | 0.857 | 7.203 | 1.626 | 0.000 |
| 14 | 6.123 | 0.887 | 0.000 | 5.698 | −0.027 | 0.000 |
| 15 | 5.796 | −0.170 | −0.857 | 4.848 | 3.045 | −1.257 |
| 16 | 4.497 | −0.694 | −0.857 | −2.578 | −0.680 | 0.000 |
| 17 | 5.502 | 2.545 | 1.770 | −2.578 | −2.110 | 0.000 |
| 18 | 5.310 | 2.175 | 3.012 | 2.237 | 3.180 | 0.000 |
| 19 | 6.760 | 2.870 | 1.600 | 4.385 | −0.540 | 0.000 |
| 20 | 4.743 | 3.578 | 1.500 | 2.237 | −1.780 | 0.000 |
| 21 | 4.245 | −1.510 | −1.519 | −0.188 | −1.780 | 0.000 |
| 22 | 6.544 | −0.581 | −1.519 | −2.335 | 1.940 | 0.000 |
| 23 | 7.125 | 1.292 | 0.000 | −0.188 | 3.180 | 0.000 |
| 24 | 3.107 | 1.306 | 1.519 | 4.824 | 2.787 | 0.890 |
| 25 | 2.220 | −1.700 | 0.000 | 7.807 | 0.879 | 0.000 |
| 26 | 1.960 | 1.940 | 0.000 | 4.019 | 3.754 | −1.257 |
| 27 | −0.188 | 3.180 | 0.000 | 5.792 | 3.590 | −1.257 |
| 28 | −2.335 | 1.940 | 0.000 | 4.790 | 2.419 | −2.147 |
| 29 | −2.335 | −0.540 | 0.000 | −1.550 | −2.473 | 0.000 |
| 30 | −1.146 | −3.782 | 0.000 | −3.091 | −2.473 | 0.890 |
| 31 | | | | −3.091 | −2.473 | −0.890 |

interesting set of model receptor geometries can be built in the near future. So we foresee the need and growth of the data base for drug design in the imminent future, to a level something similar to the currently popular Cambridge crystallographic data base. The latter data base started in the 60s with crystal structure data for about 200 organic molecules, grew[26] to about 2000 entries by 1975 and currently to around 50,000 entries. This represents a collection of data from worldwide publications in the area.

Some interesting observations are noted from the data given in fig. 4. Consider the net charges on the various functional groups (Table IX). The charges on these groups are nearly constant, especially on the hetero atoms, independent of the position or group to

**Table V**
**HOMO and LUMO wavefunctions and energies (CNDO) in aspirin and paracetamol**

| Drug | | Aspirin | | | Paracetamol | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −12.280 | 2.318 | | −10.782 | 3.848 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 1 | S | C | 0.008 | −0.000 | C | 0.000 | 0.000 |
| | PX | | 0.028 | −0.000 | | 0.000 | 0.000 |
| | PY | | −0.194 | −0.000 | | 0.000 | 0.000 |
| | PZ | | 0.000 | 0.161 | | −0.405 | −0.090 |
| 2 | S | C | 0.001 | 0.000 | C | −0.000 | −0.000 |
| | PX | | 0.008 | 0.000 | | 0.000 | 0.000 |
| | PY | | 0.123 | 0.000 | | −0.000 | −0.000 |
| | PZ | | 0.000 | −0.349 | | −0.236 | −0.449 |
| 3 | S | C | −0.015 | −0.000 | C | 0.000 | 0.000 |
| | PX | | −0.007 | −0.000 | | −0.000 | 0.000 |
| | PY | | −0.317 | −0.000 | | 0.000 | 0.000 |
| | PZ | | −0.000 | −0.425 | | 0.278 | 0.545 |
| 4 | S | C | 0.009 | 0.000 | C | 0.000 | −0.000 |
| | PX | | −0.037 | 0.000 | | 0.000 | 0.000 |
| | PY | | 0.257 | −0.000 | | −0.000 | 0.000 |
| | PX | | −0.000 | 0.327 | | 0.390 | −0.110 |
| 5 | S | C | 0.017 | −0.000 | C | −0.000 | 0.000 |
| | PX | | 0.071 | −0.000 | | −0.000 | 0.000 |
| | PY | | −0.314 | −0.000 | | 0.000 | −0.000 |
| | PZ | | −0.000 | 0.195 | | 0.271 | −0.430 |
| 6 | S | C | −0.026 | 0.000 | C | 0.000 | −0.000 |
| | PX | | −0.088 | −0.000 | | 0.000 | 0.000 |
| | PY | | 0.144 | −0.000 | | −0.000 | 0.000 |
| | PZ | | 0.000 | −0.482 | | −0.240 | 0.523 |
| 7 | S | O | −0.014 | 0.000 | N | 0.000 | −0.000 |
| | PX | | 0.057 | 0.000 | | −0.000 | −0.000 |
| | PY | | −0.236 | −0.000 | | −0.000 | 0.000 |
| | PZ | | 0.000 | −0.062 | | −0.490 | −0.008 |
| 8 | S | C | 0.021 | −0.000 | C | −0.000 | 0.000 |
| | PX | | −0.119 | −0.000 | | 0.000 | 0.000 |
| | PY | | 0.036 | −0.000 | | −0.000 | 0.000 |
| | PZ | | 0.000 | −0.104 | | −0.014 | 0.113 |
| 9 | S | C | −0.056 | 0.000 | C | 0.000 | −0.000 |
| | PX | | 0.160 | −0.000 | | −0.000 | 0.000 |
| | PY | | 0.009 | −0.000 | | 0.000 | 0.000 |
| | PZ | | −0.000 | −0.013 | | 0.006 | 0.023 |
| 10 | S | O | −0.075 | −0.000 | O | −0.000 | 0.000 |
| | PX | | 0.426 | 0.000 | | 0.000 | −0.000 |

**Table V** (*contd.*)

| Drug | | Aspirin | | | Paracetamol | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −12.280 | 2.318 | | −10.782 | 3.848 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| | PY | | −0.170 | 0.000 | | 0.000 | −0.000 |
| | PZ | | −0.000 | 0.079 | | 0.259 | −0.075 |
| 11 | S | C | −0.065 | 0.000 | O | 0.000 | 0.000 |
| | PX | | 0.076 | 0.000 | | 0.000 | 0.000 |
| | PY | | 0.185 | −0.000 | | −0.000 | −0.000 |
| | PZ | | 0.000 | −0.351 | | 0.335 | 0.025 |
| 12 | S | O | −0.004 | −0.000 | H | −0.000 | 0.000 |
| | PX | | −0.190 | −0.000 | | | |
| | PY | | −0.277 | 0.000 | | | |
| | PZ | | 0.000 | 0.364 | | | |
| 13 | S | O | −0.004 | 0.000 | H | 0.000 | −0.000 |
| | PX | | −0.116 | −0.000 | | | |
| | PY | | −0.141 | 0.000 | | | |
| | PZ | | −0.000 | 0.126 | | | |
| 14 | S | H | 0.277 | −0.000 | H | −0.000 | −0.000 |
| 15 | S | H | −0.152 | −0.000 | H | 0.000 | 0.000 |
| 16 | S | H | −0.034 | −0.000 | H | −0.000 | −0.000 |
| 17 | S | H | 0.169 | −0.000 | H | −0.000 | −0.000 |
| 18 | S | H | 0.059 | 0.000 | H | 0.000 | 0.000 |
| 19 | S | H | 0.028 | 0.032 | H | 0.009 | −0.039 |
| 20 | S | H | 0.016 | 0.000 | H | −0.009 | 0.039 |
| 21 | S | H | 0.028 | −0.032 | | | |

For hydrogen S is the 1*s* atomic orbital; for atoms S, PX, PY and PZ refer to the $2s$, $2p_x$, $2p_y$ and $2p_z$ valence atomic orbitals respectively.

which they are attached to in the various drugs. This result suggests that during interaction with a given receptor, the above groups interact with nearly the same strength in all the above drugs. As electrostatic interactions are of long range and as hydrogen bonds are predominantly electrostatic in nature, it is reasonable to expect that the above observation can play a significant role in simplifying the search of receptor identity.

Preliminary analysis of interaction of the above drugs with guanine as a possible active site of a receptor, indicates the possibility of formation of a rotated sandwich complex with weak binding energy. Based on this *apriori* information, we looked for possible binding of ibuprofen with DNA. It was gratifying to observe that this drug binds in a unique manner with DNA, unlike the well established minor or major groove binding

**Table VI**
**HOMO and LUMO wavefunctions and energies (CNDO) in ibuprofen and phenacetin**

| Drug | | Ibuprofen | | | Phenacetin | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −11.857 | 3.729 | | −10.671 | 3.901 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 1 | S | C | 0.011 | 0.002 | C | −0.000 | −0.000 |
| | PX | | −0.053 | −0.004 | | −0.000 | −0.000 |
| | PY | | 0.007 | 0.000 | | −0.000 | −0.000 |
| | PZ | | −0.445 | −0.547 | | 0.394 | 0.092 |
| 2 | S | C | 0.002 | 0.003 | C | 0.000 | 0.000 |
| | PX | | 0.023 | −0.002 | | −0.000 | −0.000 |
| | PY | | 0.003 | −0.002 | | 0.000 | 0.000 |
| | PZ | | −0.257 | 0.298 | | 0.228 | 0.449 |
| 3 | S | C | 0.004 | 0.000 | C | −0.000 | −0.000 |
| | PX | | −0.025 | 0.001 | | −0.000 | −0.000 |
| | PY | | −0.005 | −0.001 | | −0.000 | −0.000 |
| | PZ | | 0.240 | 0.243 | | −0.281 | −0.549 |
| 4 | S | C | −0.000 | 0.001 | C | −0.000 | 0.000 |
| | PX | | 0.020 | 0.001 | | −0.000 | −0.000 |
| | PY | | 0.006 | −0.000 | | 0.000 | −0.000 |
| | PZ | | 0.446 | −0.550 | | −0.381 | 0.118 |
| 5 | S | C | 0.001 | 0.001 | C | 0.000 | −0.000 |
| | PX | | −0.038 | −0.002 | | 0.000 | −0.000 |
| | PY | | −0.006 | −0.002 | | 0.000 | 0.000 |
| | PZ | | 0.255 | 0.311 | | −0.257 | 0.426 |
| 6 | S | C | −0.006 | −0.003 | C | −0.000 | 0.000 |
| | PX | | 0.038 | 0.003 | | −0.000 | −0.000 |
| | PY | | −0.012 | −0.004 | | 0.000 | −0.000 |
| | PZ | | −0.253 | 0.236 | | 0.245 | −0.526 |
| 7 | S | C | −0.013 | −0.009 | N | −0.000 | 0.000 |
| | PX | | −0.038 | −0.005 | | 0.000 | 0.000 |
| | PY | | −0.043 | −0.007 | | 0.000 | −0.000 |
| | PZ | | −0.227 | −0.039 | | 0.468 | 0.006 |
| 8 | S | C | −0.089 | 0.114 | C | 0.000 | −0.000 |
| | PX | | 0.063 | −0.005 | | −0.000 | −0.000 |
| | PY | | 0.083 | −0.048 | | 0.000 | −0.000 |
| | PZ | | 0.159 | −0.073 | | 0.021 | −0.100 |
| 9 | S | O | −0.001 | −0.023 | C | 0.000 | 0.000 |
| | PX | | −0.104 | 0.052 | | −0.000 | −0.000 |
| | PY | | −0.059 | 0.016 | | −0.000 | −0.000 |
| | PY | | −0.059 | 0.016 | | −0.000 | −0.000 |
| | PZ | | −0.103 | 0.024 | | −0.013 | −0.021 |

**Table VI** (*contd.*)

| Drug | | Ibuprofen | | | Phenacetin | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −11.857 | 3.729 | | −10.671 | 3.901 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 10 | S | O | −0.014 | −0.000 | O | 0.000 | −0.000 |
| | PX | | −0.077 | −0.007 | | −0.000 | 0.000 |
| | PY | | −0.128 | 0.002 | | −0.000 | 0.000 |
| | PZ | | −0.106 | 0.014 | | −0.293 | 0.060 |
| 11 | S | C | 0.065 | −0.083 | O | −0.000 | −0.000 |
| | PX | | −0.068 | 0.010 | | 0.000 | −0.000 |
| | PY | | −0.038 | 0.056 | | 0.000 | −0.000 |
| | PZ | | 0.144 | −0.086 | | −0.356 | −0.022 |
| 12 | S | C | −0.007 | −0.013 | C | 0.000 | 0.000 |
| | PX | | 0.065 | 0.013 | | 0.000 | 0.000 |
| | PY | | −0.024 | −0.020 | | −0.000 | 0.000 |
| | PZ | | 0.194 | −0.059 | | 0.021 | 0.017 |
| 13 | S | C | −0.060 | −0.073 | C | −0.000 | −0.000 |
| | PX | | −0.096 | −0.028 | | −0.000 | 0.000 |
| | PY | | 0.070 | 0.055 | | −0.000 | −0.000 |
| | PZ | | −0.171 | −0.081 | | −0.001 | −0.003 |
| 14 | S | C | 0.018 | 0.021 | H | 0.000 | −0.000 |
| | PX | | 0.066 | 0.030 | | | |
| | PY | | −0.023 | 0.009 | | | |
| | PZ | | 0.043 | −0.014 | | | |
| 15 | S | C | −0.003 | −0.024 | H | −0.000 | 0.000 |
| | PX | | −0.040 | −0.011 | | | |
| | PY | | −0.006 | −0.003 | | | |
| | PZ | | 0.053 | −0.010 | | | |
| 16 | S | H | −0.015 | −0.002 | H | −0.000 | 0.000 |
| 17 | S | H | −0.019 | 0.000 | H | 0.000 | −0.000 |
| 18 | S | H | −0.019 | −0.003 | H | 0.000 | 0.000 |
| 19 | S | H | −0.019 | −0.002 | H | −0.012 | 0.035 |
| 20 | S | H | 0.030 | 0.001 | H | 0.000 | 0.000 |
| 21 | S | H | 0.038 | −0.007 | H | 0.012 | −0.035 |
| 22 | S | H | 0.040 | −0.005 | H | −0.067 | −0.003 |
| 23 | S | H | −0.036 | 0.056 | H | 0.067 | 0.003 |
| 24 | S | H | −0.066 | −0.012 | H | −0.007 | 0,006 |
| 25 | S | H | 0.174 | 0.164 | H | 0.000 | 0.000 |
| 26 | S | H | −0.015 | 0.003 | H | 0.007 | −0.006 |

**Table VI** (*contd.*)

| Drug | | Ibuprofen | | | Phenacetin | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −11.857 | 3.729 | | −10.671 | 3.901 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 27 | S | H | −0.001 | 0.003 | | | |
| 28 | S | H | 0.031 | 0.007 | | | |
| 29 | S | H | −0.085 | −0.035 | | | |
| 30 | S | H | 0.019 | 0.014 | | | |
| 31 | S | H | 0.029 | 0.014 | | | |
| 32 | S | H | −0.055 | 0.001 | | | |
| 33 | S | H | −0.007 | −0.000 | | | |

**Table VII**
**HOMO and LUMO wavefunctions and energies (CNDO) in mefenamic acid and enfenamic acid**

| Drug | | Mefenamic acid | | | Enfenamic acid | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −10.533 | 2.510 | | −11.111 | 2.485 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 1 | S | C | −0.009 | −0.004 | C | −0.000 | 0.000 |
| | PX | | −0.010 | −0.005 | | −0.000 | 0.000 |
| | PY | | 0.012 | 0.003 | | −0.000 | 0.000 |
| | PZ | | −0.225 | 0.259 | | 0.412 | −0.081 |
| 2 | S | C | −0.004 | 0.000 | C | 0.000 | −0.000 |
| | PX | | −0.012 | 0.000 | | −0.000 | 0.000 |
| | PY | | −0.012 | −0.001 | | 0.000 | −0.000 |
| | PZ | | −0.314 | 0.277 | | 0.119 | −0.408 |
| 3 | S | C | 0.001 | −0.000 | C | −0.000 | 0.000 |
| | PX | | 0.004 | −0.001 | | −0.000 | 0.000 |
| | PY | | 0.004 | 0.000 | | −0.000 | 0.000 |
| | PZ | | 0.087 | −0.481 | | −0.344 | 0.383 |
| 4 | S | C | −0.002 | −0.000 | C | −0.000 | −0.000 |
| | PX | | −0.005 | −0.000 | | −0.000 | −0.000 |
| | PY | | −0.006 | 0.000 | | 0.000 | 0.000 |
| | PZ | | 0.376 | 0.071 | | −0.282 | −0.262 |
| 5 | S | C | −0.002 | −0.001 | C | 0.000 | 0.000 |
| | PX | | −0.003 | −0.001 | | 0.000 | 0.000 |
| | PY | | 0.005 | 0.001 | | −0.000 | −0.000 |
| | PZ | | 0.115 | 0.412 | | −0.312 | −0.268 |

**Table VII** (*contd.*)

| Drug | | Mefenamic acid | | | Enfenamic acid | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −10.533 | 2.510 | | −11.111 | 2.485 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 6 | S | C | 0.001 | 0.001 | C | −0.000 | −0.000 |
| | PX | | −0.001 | 0.001 | | −0.000 | 0.000 |
| | PY | | −0.010 | 0.001 | | 0.000 | 0.000 |
| | PZ | | −0.318 | −0.377 | | 0.135 | 0.482 |
| 7 | S | C | 0.005 | 0.001 | N | −0.000 | −0.000 |
| | PX | | 0.001 | 0.000 | | 0.000 | −0.000 |
| | PY | | 0.007 | 0.000 | | 0.000 | 0.000 |
| | PZ | | −0.007 | −0.377 | | 0.627 | 0.102 |
| 8 | S | O | −0.005 | −0.001 | C | 0.000 | 0.000 |
| | PX | | −0.013 | −0.001 | | −0.000 | −0.000 |
| | PY | | −0.021 | −0.002 | | 0.000 | 0.000 |
| | PZ | | 0.187 | 0.353 | | −0.086 | 0.024 |
| 9 | S | O | −0.003 | −0.000 | C | 0.000 | 0.000 |
| | PX | | −0.008 | −0.000 | | −0.000 | −0.000 |
| | PY | | −0.004 | −0.000 | | −0.000 | 0.000 |
| | PZ | | 0.022 | 0.140 | | 0.005 | 0.001 |
| 10 | S | N | 0.000 | 0.002 | C | 0.000 | 0.000 |
| | PX | | 0.005 | 0.001 | | 0.000 | −0.000 |
| | PY | | −0.028 | 0.001 | | 0.000 | 0.000 |
| | PZ | | 0.597 | −0.106 | | 0.020 | 0.001 |
| 11 | S | C | −0.007 | −0.000 | C | 0.000 | 0.000 |
| | PX | | −0.021 | −0.013 | | −0.000 | −0.000 |
| | PY | | −0.054 | 0.035 | | 0.000 | −0.000 |
| | PZ | | −0.184 | −0.023 | | 0.021 | −0.001 |
| 12 | S | C | −0.048 | 0.008 | C | −0.000 | −0.000 |
| | PX | | −0.014 | 0.004 | | 0.000 | 0.000 |
| | PY | | 0.206 | −0.021 | | 0.000 | −0.000 |
| | PZ | | 0.023 | −0.002 | | 0.011 | 0.001 |
| 13 | S | C | 0.015 | −0.005 | C | 0.000 | 0.000 |
| | PX | | −0.005 | 0.016 | | −0.000 | −0.000 |
| | PY | | −0.062 | −0.027 | | −0.000 | −0.000 |
| | PZ | | −0.021 | 0.017 | | −0.014 | 0.000 |
| 14 | S | C | 0.001 | −0.000 | C | 0.000 | 0.000 |
| | PX | | 0.055 | −0.015 | | −0.000 | −0.000 |
| | PY | | −0.126 | 0.036 | | −0.000 | −0.000 |
| | PZ | | 0.137 | −0.024 | | −0.021 | −0.001 |
| 15 | S | C | −0.016 | 0.003 | C | 0.000 | −0.000 |
| | PX | | 0.051 | −0.001 | | −0.000 | 0.000 |
| | PY | | −0.069 | −0.003 | | −0.000 | 0.000 |
| | PZ | | 0.000 | 0.001 | | −0.000 | 0.001 |

**Table VII** (*contd.*)

| Drug | | Mefenamic acid | | | Enfenamic acid | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −10.533 | 2.510 | | −11.111 | 2.485 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 16 | S | C | 0.056 | −0.010 | C | −0.000 | −0.000 |
| | PX | | −0.131 | 0.022 | | 0.000 | −0.000 |
| | PY | | 0.137 | −0.037 | | 0.000 | 0.000 |
| | PZ | | 0.020 | 0.015 | | 0.008 | 0.381 |
| 17 | S | C | −0.021 | 0.001 | O | −0.000 | −0.000 |
| | PX | | 0.014 | 0.002 | | −0.000 | 0.000 |
| | PY | | 0.045 | −0.005 | | 0.000 | −0.000 |
| | PZ | | 0.038 | −0.001 | | 0.216 | −0.366 |
| 18 | S | C | 0.031 | −0.022 | O | −0.000 | 0.000 |
| | PX | | 0.003 | 0.021 | | −0.000 | 0.000 |
| | PY | | −0.046 | 0.013 | | 0.000 | −0.000 |
| | PZ | | −0.039 | −0.000 | | 0.012 | −0.131 |
| 19 | S | H | −0.049 | 0.001 | H | 0.000 | −0.000 |
| 20 | S | H | 0.063 | −0.004 | H | −0.000 | 0.000 |
| 21 | S | H | 0.003 | −0.000 | H | −0.000 | 0.000 |
| 22 | S | H | 0.024 | 0.010 | H | 0.000 | 0.000 |
| 23 | S | H | −0.004 | −0.011 | H | −0.000 | −0.000 |
| 24 | S | H | 0.006 | 0.001 | H | 0.000 | 0.000 |
| 25 | S | H | −0.059 | 0.001 | H | 0.162 | 0.021 |
| 26 | S | H | 0.002 | 0.019 | H | −0.162 | −0.021 |
| 27 | S | H | 0.050 | −0.006 | H | 0.019 | −0.006 |
| 28 | S | H | 0.024 | 0.010 | H | −0.019 | 0.006 |
| 29 | S | H | −0.013 | 0.002 | H | 0.000 | 0.000 |
| 30 | S | H | 0.008 | 0.001 | H | −0.000 | −0.000 |
| 31 | S | H | −0.000 | −0.000 | H | −0.000 | −0.000 |
| 32 | S | H | −0.003 | 0.001 | H | 0.000 | −0.000 |
| 33 | S | H | 0.002 | 0.000 | H | −0.000 | −0.000 |

drugs. Further studies are underway to elucidate the exact nature, strength and geometry of this binding process.

## 4. Other features

Apart from its use in receptor identification and drug design, the data base can also be profitably utilised in a variety of situations, some of which are:

**Table VIII**
**HOMO and LUMO wavefunctions and energies (CNDO) in flufenamic acid and naproxen**

| Drug | | Flufenamic acid | | | Naproxen | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −10.884 | 2.289 | | −10.411 | 2.018 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| 1 | S | C | 0.005 | 0.007 | C | −0.000 | 0.001 |
| | PX | | 0.001 | 0.008 | | −0.010 | 0.001 |
| | PY | | −0.018 | −0.004 | | 0.002 | −0.001 |
| | PZ | | 0.230 | −0.277 | | −0.379 | 0.427 |
| 2 | S | C | 0.008 | 0.000 | C | 0.005 | 0.001 |
| | PX | | 0.026 | −0.000 | | 0.017 | 0.001 |
| | PY | | 0.023 | 0.000 | | 0.007 | 0.001 |
| | PZ | | 0.298 | −0.249 | | −0.340 | −0.263 |
| 3 | S | C | −0.003 | 0.001 | C | −0.006 | −0.002 |
| | PX | | −0.011 | 0.001 | | −0.016 | 0.000 |
| | PY | | −0.005 | −0.000 | | −0.002 | −0.002 |
| | PZ | | −0.092 | 0.477 | | 0.115 | −0.267 |
| 4 | S | C | 0.003 | 0.000 | C | 0.003 | 0.001 |
| | PX | | 0.010 | 0.000 | | 0.013 | 0.001 |
| | PY | | 0.010 | −0.000 | | 0.003 | 0.000 |
| | PZ | | −0.363 | −0.095 | | 0.385 | 0.400 |
| 5 | S | C | 0.002 | 0.002 | C | 0.002 | 0.000 |
| | PX | | −0.000 | 0.001 | | 0.007 | 0.000 |
| | PY | | −0.007 | −0.001 | | 0.001 | −0.000 |
| | PZ | | −0.114 | −0.392 | | −0.439 | −0.391 |
| 6 | S | C | 0.002 | −0.002 | C | −0.001 | 0.000 |
| | PX | | 0.009 | −0.003 | | −0.003 | 0.000 |
| | PY | | 0.015 | −0.001 | | 0.002 | −0.000 |
| | PZ | | 0.303 | 0.386 | | −0.325 | 0.248 |
| 7 | S | C | −0.007 | −0.001 | C | 0.001 | −0.000 |
| | PX | | −0.001 | −0.000 | | 0.003 | −0.000 |
| | PY | | −0.010 | −0.000 | | 0.000 | −0.000 |
| | PZ | | 0.003 | 0.375 | | 0.073 | 0.303 |
| 8 | S | O | 0.004 | 0.002 | C | −0.002 | 0.000 |
| | PX | | 0.015 | 0.001 | | −0.006 | 0.000 |
| | PY | | 0.023 | 0.002 | | 0.001 | −0.000 |
| | PZ | | −0.177 | −0.353 | | 0.347 | −0.439 |
| 9 | S | O | 0.004 | 0.000 | C | 0.001 | −0.000 |
| | PX | | 0.010 | 0.001 | | 0.007 | −0.000 |
| | PY | | 0.006 | 0.000 | | 0.001 | 0.000 |
| | PZ | | −0.018 | −0.140 | | 0.136 | −0.026 |
| 10 | S | N | −0.002 | −0.002 | C | −0.001 | 0.000 |
| | PX | | 0.007 | −0.003 | | −0.007 | 0.000 |
| | PY | | 0.028 | −0.001 | | 0.001 | −0.000 |

**Table VIII** (*contd.*)

| Drug | | Flufenamic acid | | | Naproxen | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | −10.884 | 2.289 | | −10.411 | 2.018 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| | PZ | | −0.602 | 0.092 | | 0.121 | 0.027 |
| 11 | S | C | 0.003 | 0.003 | C | 0.000 | −0.008 |
| | PX | | 0.007 | 0.021 | | −0.020 | −0.001 |
| | PY | | −0.045 | −0.057 | | −0.010 | −0.010 |
| | PZ | | 0.180 | 0.064 | | 0.089 | −0.017 |
| 12 | S | C | 0.032 | 0.001 | C | −0.007 | 0.002 |
| | PX | | 0.048 | −0.010 | | 0.007 | −0.003 |
| | PY | | −0.211 | 0.025 | | −0.003 | 0.002 |
| | PZ | | 0.071 | −0.002 | | −0.001 | 0.006 |
| 13 | S | C | −0.003 | −0.001 | O | 0.003 | −0.000 |
| | PX | | −0.021 | −0.016 | | −0.011 | −0.000 |
| | PY | | 0.070 | 0.047 | | −0.006 | −0.000 |
| | PZ | | −0.012 | −0.048 | | −0.004 | −0.002 |
| 14 | S | C | −0.004 | 0.003 | O | 0.005 | −0.001 |
| | PX | | −0.043 | 0.023 | | −0.022 | 0.001 |
| | PY | | 0.125 | −0.059 | | −0.001 | −0.003 |
| | PZ | | −0.193 | 0.068 | | −0.049 | 0.015 |
| 15 | S | C | 0.013 | −0.002 | C | −0.046 | −0.030 |
| | PX | | −0.046 | −0.002 | | 0.031 | −0.005 |
| | PY | | 0.057 | 0.009 | | 0.053 | 0.032 |
| | PZ | | −0.026 | −0.008 | | −0.073 | −0.039 |
| 16 | S | C | −0.046 | 0.008 | O | 0.000 | −0.000 |
| | PX | | 0.128 | −0.028 | | 0.004 | −0.000 |
| | PY | | −0.157 | 0.057 | | −0.000 | −0.000 |
| | PZ | | 0.074 | −0.055 | | 0.281 | −0.079 |
| 17 | S | C | 0.024 | −0.003 | C | 0.000 | 0.000 |
| | PX | | −0.010 | −0.003 | | −0.000 | 0.000 |
| | PY | | −0.032 | 0.011 | | 0.001 | −0.000 |
| | PZ | | −0.027 | −0.008 | | −0.023 | −0.010 |
| 18 | S | F | 0.001 | 0.007 | H | −0.001 | −0.001 |
| | PX | | 0.005 | 0.003 | | | |
| | PY | | 0.014 | −0.001 | | | |
| | PZ | | 0.004 | −0.014 | | | |
| 19 | S | F | −0.003 | 0.000 | H | −0.013 | −0.000 |
| | PX | | 0.011 | 0.000 | | | |
| | PY | | 0.011 | −0.003 | | | |
| | PZ | | 0.013 | 0.002 | | | |
| 20 | S | F | −0.005 | −0.006 | H | −0.001 | −0.001 |
| | PX | | −0.008 | −0.007 | | | |

**Table VIII** (*contd.*)

| Drug | | Flufenamic acid | | | Naproxen | | |
|---|---|---|---|---|---|---|---|
| MO-Energy (ev) | | | − 10.884 | 2.289 | | − 10.411 | 2.018 |
| Atom no. | AOs | Atom | HOMO | LUMO | Atom | HOMO | LUMO |
| | PY | | 0.027 | 0.011 | | | |
| | PZ | | 0.012 | 0.001 | | | |
| 21 | S | H | 0.033 | − 0.001 | H | 0.001 | − 0.000 |
| 22 | S | H | − 0.052 | 0.003 | H | − 0.004 | 0.000 |
| 23 | S | H | 0.006 | − 0.003 | H | − 0.000 | − 0.000 |
| 24 | S | H | − 0.061 | 0.001 | H | 0.110 | 0.074 |
| 25 | S | H | − 0.022 | − 0.015 | H | − 0.002 | 0.001 |
| 26 | S | H | 0.027 | − 0.001 | H | − 0.023 | 0.003 |
| 27 | S | H | − 0.013 | − 0.001 | H | 0.046 | 0.015 |
| 28 | S | H | − 0.003 | 0.000 | H | 0.007 | − 0.008 |
| 29 | S | H | 0.009 | − 0.002 | H | − 0.001 | 0.000 |
| 30 | S | H | − 0.004 | − 0.000 | H | − 0.047 | 0.018 |
| 31 | | | | | H | 0.048 | − 0.018 |

For a given drug/model receptor, in a given geometry, one can have from the data base the following information:

(i) Cartesian coordinates of all the atoms, including hydrogens.

(ii) The net charges on all atoms, which enables one to guess the electrophilic or nucleophilic sites of attack.

(iii) The energies of HOMO (SOMO1, SOMO2) and LUMO (SUMO1, SUMO2) data enables us to make predictions regarding the relative propensities of involvement of these orbitals with other molecules. It may be recalled here that much of the success of the now famous Woodward-Hoffmann rules on conservation of orbital symmetry during reactions in organic chemistry, is essentially based on the symmetries of the HOMO/LUMOs. It may be useful to apply the HOMO, LUMO data available from the point of the above rules, to understand the mechanism of drug-receptor interactions at the molecular level.

(iv) The availability of all the MOs of molecules, from the data base facilitates us to set up easily molecular orbital interaction patterns with any other drug or receptor molecule. Questions like stereoselectivity (d/l isomer binding), or specificities of interaction in complex formation, of which hydrogen bonding is a popular case, can be analysed using the data bank and the interaction energy program.

**Table IX**
**The net charges on the various functional groups in the given series of drugs**

(i) the $-C-O-R$ group

| *Drug* | $-C$ | $-O$ | $-R$ |
|---|---|---|---|
| Paracetamol | 0.167 | −0.245 | 0.127(H) |
| Naproxen | 0.184 | −0.218 | 0.123($CH_3$) |
| Phenacetin | 0.163 | −0.227 | 0.162($CH_2$) |
| Aspirin | 0.202 | −0.245 | 0.400(C = 0) |

(ii) the $-COOH$ group

| *Drug* | $-C$ (ar) | $-C(CO)-$ | O(CO) | $-O(OH)$ | $-H(OH)$ |
|---|---|---|---|---|---|
| Aspirin | −0.091 | 0.388 | −0.317 | −0.295 | 0.179 |
| Enfenamic acid | −0.101 | 0.396 | −0.351 | −0.277 | 0.162 |
| Mefenamic acid | −0.113 | 0.403 | −0.372 | −0.265 | 0.167 |
| Naproxen | −0.026($CH_2$) | 0.393 | −0.334 | −0.273 | 0.167 |
| Ibuprofen | −0.033 | 0.393 | −0.312 | −0.270 | 0.160 |

(iii) the $-NH-$ group

| *Drug* | $-C$ | $-N(H)$ | H(N) | $-C$ |
|---|---|---|---|---|
| Paracetomol | 0.120 | −0.215 | 0.106 | 0.347($C_{C=O}$) |
| Phenacetin | 0.121 | −0.186 | 0.104 | 0.362($C_{C=O}$) |
| Enfenamic acid | 0.182 | −0.233 | 0.153 | 0.119($C_{ar}$) |
| Mefenamic acid | 0.199 | −0.219 | 0.154 | 0.124($C_{ar}$) |

(v) The data base can serve as an educational aid as well. It can help biochemists, pharmacologists, chemists and molecular physicists to understand the concepts and features of molecular orbital theory and methods.

## 5. Conclusions

We have outlined a new computational molecular modelling approach, based on drug-(model) receptor interaction studies, to arrive at a self-consistent model for the active site structure of a receptor. Unlike the current QSAR methods, our approach is based on a sound theory, *viz.* quantum mechanics, and possesses the potential to provide a molecular level interpretation of drug action, interaction and design. The need and features of the associated data base are also highlighted. Our own results utilizing the data base will be discussed elsewhere.

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**Short Communication**

# Ibuprofen binds to DNA

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**Abstract**

Molecular modelling and UV spectrophotometric studies suggest that Ibuprofen binds to DNA with greater preference to GC than AT. The study raises the question whether ibuprofen could be a 'lead-molecule' in the search for better anti-cancer drugs.

**Key words:** Anti-cancer drugs, DNA, molecular modelling, Ibuprofen, anti-inflammatory drugs, binding.

## 1. Introduction

Ibuprofen is widely used as an analgesic and anti-inflammatory drug[1,2]. The molecular mechanism of its action, like other anti-inflammatory drugs, is believed to be in the inhibition of prostaglandin biosynthesis in the body[3,4]. However, other mechanisms may be there, but are as yet not well established[4]. We pose the question whether anti-inflammatory action of these drugs can arise from binding to DNA or more simply how do these agents interact with DNA as there is an urgent need to look for novel leads to cancer therapy.

In two recent communications from one of us[5,6], a new molecular modelling approach was outlined which can enable one to arrive at the geometry of the active site of a receptor. As part of an ongoing research in the application of this new procedure, here we report of an experimental work carried out after a suggestion, from theoretical modelling studies, that ibuprofen can weakly bind to DNA in a pseudo-intercalative manner. The results are presented in two stages. First, the theoretical calculations performed on ibuprofen interacting with nucleic-acid components, followed by UV spectroscopic studies on the binding of ibuprofen with calf-thymus DNA, poly(dA-dT) and poly(dG-dC).

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## 2. Theoretical studies

The binding energy of a drug-(model) receptor complex comprises electrostatic, induction, dispersion (long-range forces) and non-bonded repulsion (exchange repulsion), and charge-transfer energy terms (short-range forces). As we are primarily interested in the pharmaco-dynamic phase of this drug's action, we exclude the discussion of the 'ill-defined' term of hydrophobic interactions. Of the long-range terms, only the electrostatic term can either be attractive or repulsive. If this term is attractive, then it is likely that the drug may bind at the receptor site. On this premise, we computed the electrostatic interaction energy for interaction between ibuprofen with guanine, thymine, cytosine and adenine, in the sandwich conformation of the complex at inter-planar distances of 3 to 5 Å (Fig. 1).

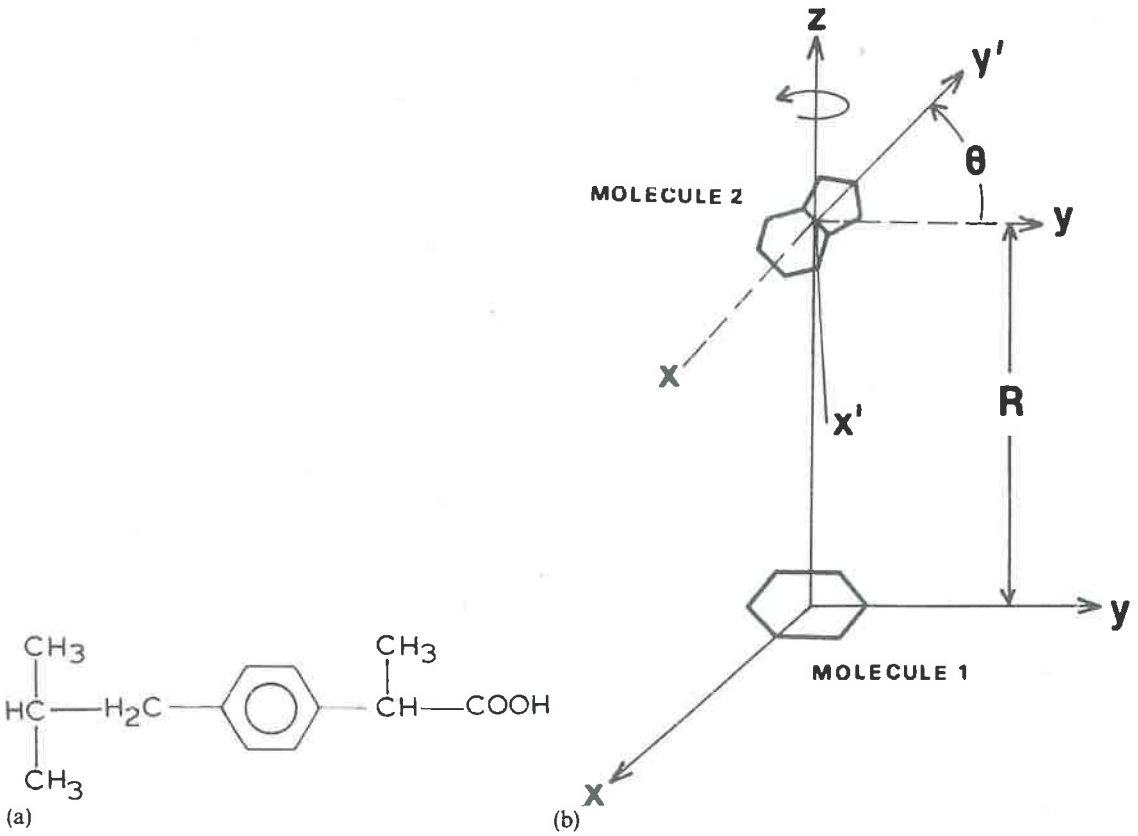


FIG. 1. Structure of the molecular complex considered in the present work.

The geometries of the molecules and the net charges on all the atoms were taken from the data bank drug design and receptor identification. It is noted (Table I) that interaction is favouring the formation of the complex with more binding to GC than AT. Based on this, we carried out UV spectroscopic studies to check whether ibuprofen binds with DNA.

**Table I**
**Electrostatic interaction energy between ibuprofen and nucleic acid bases** (fig. 1 for geometry)

| Base | R(Å) | O°(deg.) | Energy (kcal/mole) |
|---|---|---|---|
| Guanine | 3.5 | 210 | −0.98 |
| Thymine | 3.5 | 60 | −1.00 |
| Adenine | 3.5 | 90 | −0.35 |
| Thymine | 3.5 | 300 | −0.51 |

## 3. Material and methods

Poly(dA-dT) and poly(dG-dC) (Pharmacia P. L.) were used without further purification. Ibuprofen was a gift from Dr. S. Chandrasekhar (IISc) and c.t. DNA (Sigma) was deproteinated by phenol extraction and extensively dialysed against 20 mM NaCl, pH 7.1, before use. The concentrations of the drug and polynucleotides are expressed in terms of moles per litre, and measured using molar extinction coefficients ($nm^{-1}\,cm^{-1}$) poly(dA-dT) $\varepsilon_{260} = 6.7$, poly(dG-dC) $\varepsilon_{254}$ 8.4, c.t. DNA $\varepsilon_{260}$ 6.6 and Ibuprofen $\varepsilon_{263}$ 0.38.

Ibuprofen stock solution was made in 60% methanolic buffer solution and dilution to required concentration with 20 mM NaCl solution, pH = 7.1. All the experiments were carried out at room temperature of 20°C employing a Beckman DU8B spectrophotometer using 1-cm quartz cuvettes.

Figure 2 shows the changes in the UV spectrum of the drug on addition of c.t. DNA. The appearance of a new peak between 290 and 295 nm clearly indicates the binding of the drug with DNA. Further, the interaction of ibuprofen with polynucleotides and c.t. DNA are characterised (fig. 3) by an increase in absorption of DNA with a small blue shift in the peak position of DNAs on addition of the drug.

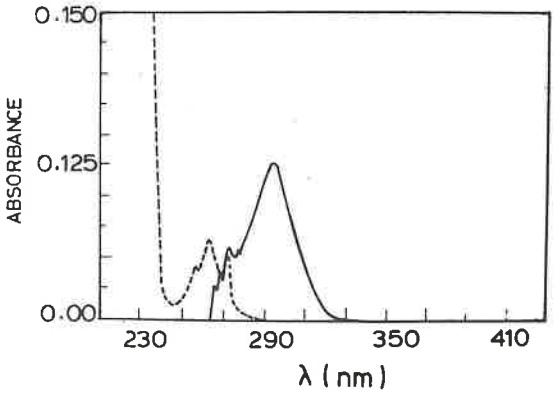


FIG. 2. UV absorption spectrum of ibuprofen alone (----) (130 μm) and in the presence of c.t. DNA (448 μm) (——). Note the appearance of a peak at 295 nm on drug-DNA complexation.

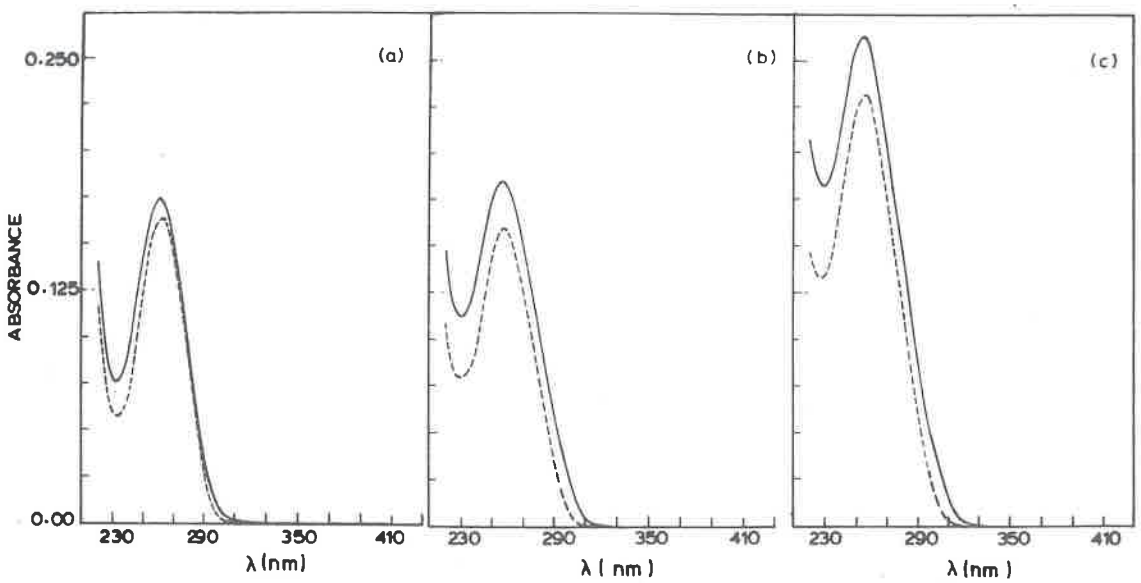


FIG. 3. UV absorption spectra of DNA alone (25 $\mu$m) (----) and in the presence of ibuprofen (5 $\mu$m) (——) a) Poly d(dA-dT), b) Calf-thymus c.t. DNA, c) Poly d(dG-dC).

These results indicate the binding of the drug with DNA, but not of any base specificity. We tried to monitor the reaction with CD spectroscopy, but the drug-DNA complex did not show any induced band in the DNA non-absorption region, *i.e.*, above 300 nm. However, the difference spectra of the drug-DNA complex and DNA showed weak positive band in 300–305 nm region (figure not shown).

This result raises several questions of fundamental importance to the understanding of the basis of all drug action, principally among them: If binding is the criteria for activity, then how do we distinguish binding to an active from those with inactive or antagonist sites. What is the optimal geometric nature of the bound complex? Electrostatic energy term being a long-range force, normally one expects it to be a facilitator for an 'early recognition' of binding site and in this perspective will an analog of ibuprofen form a better anti-cancer agent? or can we think of utilising ibuprofen as a model 'lead' molecule in the quest for less toxic and more effective anti-cancer drugs? Perhaps, detailed calculations of all the terms, 2D-nmr and crystallographic studies are likely to provide answers to many of these queries.

## Acknowledgements

We are grateful to Prof. V. Sasisekharan for facilities and encouragement. EKB thanks CSIR for a research associateship and BSS thanks ICMR for a supernumerary position.

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INDIRA GANDHI NATIONAL OPEN UNIVERSITY

# Ekalavya

NEWSLETTER

## CONTENTS



# IGNOU'S STUDY CENTRES - SOME FUNCTIONS

In a distance education or open university system, the learner is independent, highly motivated and self-disciplined. The system demands that a student work mainly at home. Still, the face-to-face interaction has not been totally discarded from the system. Learners at distance need, besides the self-learning packages, the support of other services such as advising, counselling and tutoring. Support services aim at personalising and humanising the distance teaching system. Student support services are varied and broad. The nature of support services depends on the philosophy, resources and organisational structure of the distance education institution.

The normal structure of the institution for providing student support services, besides the central office of the institution, is its network of Regional and Study Centres. IGNOU has, to this day, established 155 Study Centres throughout the country, in areas of high population as well as in the educationally backward areas. The Study Centres, are the focal point for the meeting of students with the Academic Counsellors. Though the attendance of the students at the Study Centres is not a compulsory component of the system, these meetings are an important element of the programme at all the levels, especially at the undergraduate level.

The main purpose of this contact between the students and the Academic Counsellor is to remedy any academic weakness or deficiencies of understanding on the part of the student, and to support, the individual student's overall progress, through counselling sessions.

The Study Centres of IGNOU are mainly based in existing institutions of higher learning, such as colleges, training institutions, etc. The University attaches great importance to the Study Centres.

## Organisation

Every Study Centre of IGNOU is headed by a senior academic, designated as the "Coordinator". His/her selection is made out of the existing staff members from the same institution where the Study Centre is established. The Coordinator of the Study Centre may be termed as an all-in-one, i.e., as an Administrator, Manager, Supervisor and an Organiser. The Coordinator manages the smooth functioning of the Study Centre under the overall supervision of the head of the institution where the Study Centre is located.

The Coordinator coordinates the work of the Academic Counsellors and acts as a link between the University, the Regional Centre and the Study Centre. Where the student enrollment exceeds a particular limit, some Coordinators are assisted by Assistant Coordinators. Both the functionaries are part-time employees of the University. The Study Centre is also supported by some ministerial part-time staff to assist the Coordinator in his work.

ESSAY

# Health Science Education in an Open University System

*Dr.B.S.Sudhindra,Regional Director (Hqs,RSD)*

## 1. Introduction

If Health is Wealth, then think of it first!

We briefly outline below areas of activity that can be fruitfully performed under the School of Health Sciences in an Open University System with special reference to the health scene in India. Some regard Health Science to be synonymous with Medical Education, which in turn, is looked upon essentially as patient care with little attention to understand the origin of the disease and its curative mechanism. However, we regard Health Science to be a more broad based, multifaceted activity where faculties of scientists, engineers and management personnel play significant roles in maintaining the health care system. For the purpose of continuity, we first will briefly discuss the concept of the Open University System (OUS) and then build up the main topic.

## 2. Open University System (OUS)

* Open University System shatters the myth that higher academic knowledge can be acquired only by enrolling as day-scholars in premier institutes. While there is no single well defined/accepted way of describing the openness of OUS, we regard the following features of the OUS that distinguish it from the "regular or day-scholar university system" :

## Open University :

***Operation flood knowledge for the thirsty !***

**independent of your age (no upper limit),location and status!**

## 3. *Health Science Programmes*

We suggest the following plan of activities that can be performed effectively in an OUS framework :

| Leisure-time Scholars (OUS) | Day-time Scholars (Univ./IIT set up) |
|---|---|
| 1. Learn mainly through Self-study. | Mainly by attending classes and study |
| 2. Optional attendance at counselling sessions. | Compulsory attendance to teaching sessions. |
| 3. Syllabus not explicitly defined, but the content is covered in material specially prepared to suit independent study. | Syllabus is defined along with a recommended list of books. Lectures cover the study areas. |
| 4. Provision to select a combination of subjects | Generally a fixed combination of subjects. |
| 5. Choice of study-media, English or Hindi. Some courses even in regional languages. eg.Gujarati. | No such choices |
| 6. Caters mainly adult clientele. Age 20 +. (no upper age limit) | Generally youngsters in the age 16-20 only. |
| 7. Provides uniform pattern of quality education irrespective of student's location and economic status. | Varies from institution to institution. |
| 8. Employs print, audio- video- & TV media as aids to Self-study efforts of the student | Mainly verbal(class-room) communication with texts available from book shops. |
| 9. Practicals are conducted for a week or two at one stretch during the course. | Practicals are for few hours per week through-out the course. |

3.1. *Developing a Certificate course in General Self-Health Care Education for all adults.*

Need: Discussed further below. (Section 4)

3.2. *Developing a Certificate course for Medical Laboratory Assistantship.*

Need: There are a number clinical/pathology laboratories but the number of skilled personnel working in such much advertised set up are few. This course is suggested to provide well trained skilled workers in the area, which meets a real need of the society.

3.3. *Developing a Certificate Course in Small-Hospital/Nursing-Home Administration.*

Need: It is a common sight in cities and towns to see the growth of many "Nursing Homes ". But how well they are equipped and managed is an open question. It is a dream of every medical graduate to start his own clinic. OUS can fill-in the vacuum existing in this area by providing " all you need to keep/ have to run a 10-bed facility ".

3.4. *Developing a Certificate course on Drug Information/Sale for Medical Representatives and Chemists.*

Need: In our country and like many other developing countries, the market is flooded with a host of "combinations" and drug formulations. Many of these are either unnecessary or dangerous. There is need to educate the promoters/ distributors with factual information on drugs.

3.5. *Certificate course in Med-/Bio-informatics targeted to practicing Physicians, Students in Medical/ Biological-background to increase their awareness on the use of large DATA BASES like MEDLAR, GENE Sequences, etc.*

Need: Very little attention is paid in medical schools to prepare the future generation doctors to knowledge pouring-in/around the world in this changing pattern in

medical diagnosis, therapy and management. Much of such an information now appears in the form of data bases and through use of on-line facility. In order to effectively use such facilities one needs to get acquainted with the various data bases, now available in India through the ICMR-NIC project. OUS can effectively provide this much needed training.

3.6. *Developing Graduate Medical Degree course for Scientists and Engineers so as to improve the "content" of medical education with contributions from interdisciplinary specialists.*

Need: In our country where entry to medical schools are characterised by "donations" and other non-merit criteria, much of the talent takes up other professions. If one looks at the advancements like CT-Scan, Whole-body MRI, and other non-invasive techniques diagnostic tools, these are necessarily due to efforts of other professionals deeply committed to improving the health-care system. Once again, OUS can provide "a lost-opportunity" to the talented non-medicos to serve the nation in improving the quality of health-care system in the country.

3.7. *Certificate course in Computers in Clinics, Hospitals, Patient-Care and Management.*

Need: When our country is taken by the wave of computers for homes, offices and entertainment, should not the medical professionals learn and use this technology ? IGNOU has launched courses in the use of computers in Office Management. There exists already much material which can used to prepare a course specifically aimed at the medical profession.

3.8. *Encourage studies/programmes in Molecular Medicine.*

Need: Modern chemotherapeutic agents are the outcome of efforts of multi-disciplinary group involving chemists, physicists, pharmacologists, statistists, plant engineers and doctors. Current approaches rely strongly on the fact that better medicines (less toxic, without side-effects) can be arrived at only by a clear understanding of the basic molecular mechanisms of normal physiology and disease patho-genesis. Computer Assisted Molecular Modelling of these processes are in the forefront Medicinal Research in the west. This tool is similar to what CAD is for engineers. OUS provides an ideal platform to educate the talents in our country both medicals and others professionals in these developments. (Section 5)

3.9. *Updates in Medicine: Certificate courses for practicing physicians, in collaboration with Medical Council of India and other Premier Institutes like AIIMS/PGIMER/JIPMER, etc.*

Need: While continuing medical education programmes are being imparted by MCI at premier institutes, the number of doctors who attend such courses are far less when compared to the vastness of our country. When such materials are prepared in distance education format and conducted by OUS, the number of medicos benefited will obviously be in large numbers. This activity requires co-operation of other educational organisation.

3.10. *Certificate course in Pharmacology in Nursing.*

Need: Much of the routine bed-side patient-care in hospitals are done by this group. With advances in delivery systems and multitudes of combination drugs, etc., it is necessary to up-date knowledge on drug profiles to nurses.

NONE of the above areas (except 9 & 10) are covered in any of Medical Schools TODAY in India. Open University has the tremendous potential to fill-in the vacuum. We must act today and pursue from NOW ON!

While some of the activities (like 3,5,7) may be encroached by the use of certain terminology into activities of other schools, as the primary content of the materials fall within the realm of the Health Science — programme, the faculties of other schools can contribute to the course materials. The philosophy presented here is to highlight the multifaceted nature of Health Science and *not to repeat* the mistakes present in the conventional education system today. For the purpose of illustration we look at item no.1 and 8 above, in some detail.

## 4. *Self-Health-Care Education*

A Certificate Course in General Health Science Education to meet common problems of frequent occurrence by citizens.

Audience: Any literate adult.

Scope: To provide general information on how to face day-to-day health problems and how to take care of them yourself (to the extent possible).

*A diploma course* in Health-care suitable to Para-medics can be formulated using the above material along with some more technical information on basic human physiology and patho-physiology and pharmacology material. The format of presentation could be as under :

### Common health problems: How to treat at home and when to go to a Doctor.

1. / Complaint : /
2. / Home treatment : /
3. / When to go to Doctor : /
4. / Precautions to take : /
5. / How does this drug help:/
6. / Dosage and interval :/
7. / Likely side effects :/
8. / Adverse effects :/
9. / Do not use if ..../
10. / Remember : Preventive measures /

This format will be followed for all cases.

*Areas to be covered are :*

-(i) Respiratory Problems
- 1. Colds & flu
- 2. Cough
- 3. Sore throat
- 4. Allergic rhinitis
- 5. Respiratory symptomsfor direct referral

-(ii) Gastrointestinal tract Problems
- 6. Mouth ulcers
- 7. Heartburn
- 8. Indigestion
- 9. Nausea and Vomiting
- 10. Constipation
- 11. Diarrhoea
- 12. Haemorrhoids

-(iii) Skin Conditions
- 13. Acne
- 14. Warts and Verrucae
- 15. Common Childhood rashes

-(iv) Painful Conditions
- 16. Headache
- 17. Sprains

- (v) Womens' Problems
- 18. Urinary tract infections
- 19. Period pains.

-vi) Eye and Ear
- 20. Eye problems
- 21. Common ear problems

-(vii) Childhood Conditions
- 22. Napkin rash
- 23. Head lice
- 24. Threadworms

*Appendices include :*

11. Drug Interaction alert chart.
12. Alphabetical list of complaints.
13. Alphabetical list of commonly used (WHO short list) drugs each with dosage chart seperate for:
    a) adults 12+
    b) children 5 - 12 years
    c) children 2 - 5 years
    d) children 1 - 2 years
    e) babies upto 12 months

14. Alphabetical list of brand names and their relation to non-proprietary names.

15. Home Pharmacy: List medicines and other items.

16. Immunisation chart/schedule.

17. Medicine literature references for the inquisitive.

18. Medical terms: how they are formed.

19. First aid: Elements of...

20. Special topics: Alert situations like

a) convulsion cases,

b) sudden collapse/dizziness in diabetics.

c) pregnant women

d) heart attack cases

e) Looking after elderly people (Geriatrics)

f) etc. (?)

21. Daily intake diet requirements: Elements of nutrition.

22. Food intake during sickness period.

23. How to measure temperature, types of thermometers.

24. Common tests/ routine laboratory investigations.Urine, blood, stools. (Normal values, variation and their extent of significance)

25. Sub-area faculties

## 5. *Molecular Medicine*

There is an "Untold Emergency" in the area of Medicine as :

(i) we do not know, the precise structure and interactions of many bio-molecules involved in normal physiology and disease patho-genesis.

(ii) we do not know, for a majority of drugs, their molecular mechanism of actions, and

(iii) we do not have safe drugs of choice for nearly two-third's (66%) of diseases !

A possible way out of this "crisis" is the aim of the thrust area of the research work - Molecular Medicine.

The principal reason for this thrust of activity is the increasing realisation of the fact that better patient care can only come from better understanding of the basic biology, patho-physiology, drug action/ interactions, etc. at the molecular level. Current trend in medicinal research in the West, especially in the chemotherapy area, is to arrive at safer, less toxic drugs by employing a combination of tools of medicinal chemistry, molecular pharmacology, molecular modelling using computers and color graphic facilities. To cite an example, NMR was until recently, primarily used in basic science research activity, but now has emerged as a powerful non-evasing diagnostic tool(CAT-SCAN) to the physicians. Likewise, in the coming decade, the field of molecular medicine is expected to become an integral part of under-graduate and postgraduate medical education. As an excerpt from this new discipline of activity, we present here a short account of how a therapeutic molecule is arrived at. ( See Scheme 1)

The whole process involves extensive cooperative interaction with as many as 80 different disciplines. Consequently, it is not surprising that the cost involved in putting a new drug into the market is of the order Rs.50 to 100 crores! It is a fact that newer agents are being developed, at the same time lack of knowledge on the molecular architecture of the receptors makes the search for new agents a fantasy !

The relevance of such an activity in India is as under: Majority of drugs and their formulation used in our country are of outside collaboration, for we have no manpower trained to utilise advances in Computer Aided Molecule Design techniques now in use in the West by pharmaceutical companies. OUS can easily develop such knowledge imparting programme wherein chemists/ pharmaceutists in industry get exposed to these developments and thereby help in improving the drugs availability in our country.

The Molecule of a nation state is the individual. What is the state of this molecular India? If we understand this, then only can we understand the question of brain-drain/ development, and the optimum utilisation of science in our country.

## 6. *Related Open Question*

When we wish to embark on such a line of action many questions arise. Principal among them are :

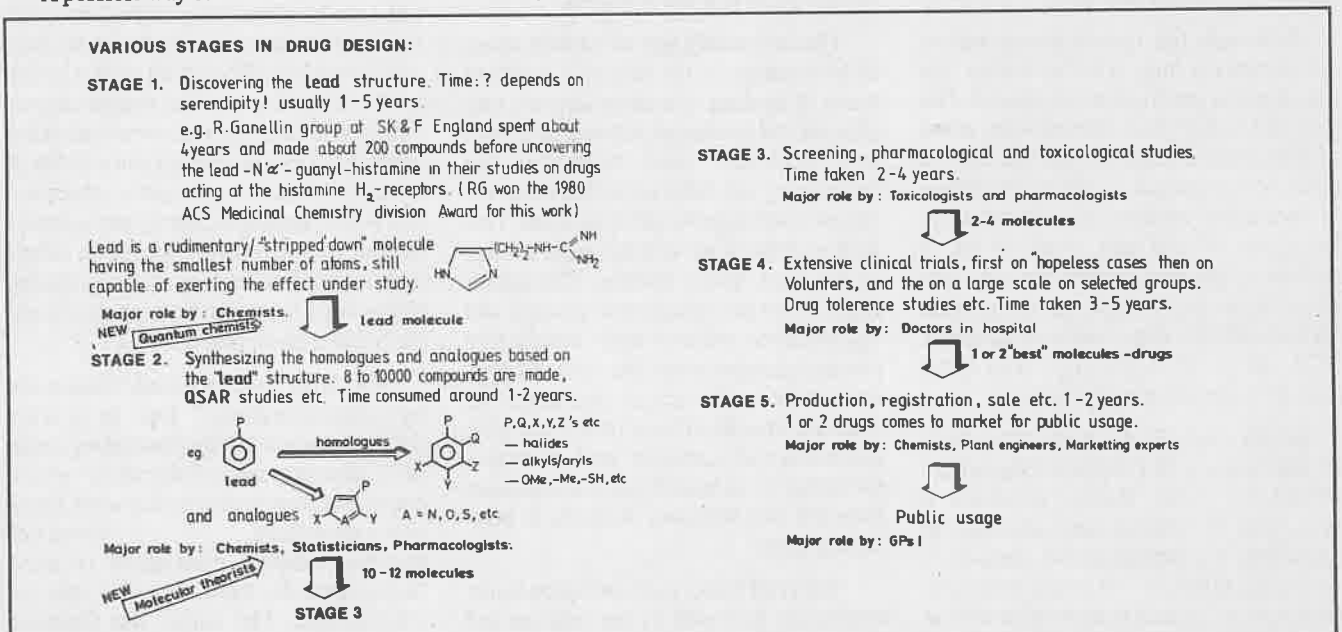
(i) whether sufficient enrollment can be expected ?

(ii) will it benefit the student(age no bar) ?

(iii) will it brighten his employment prospects ?

Obviously activities such as items 1, 2, & 7 can attract high enrollment, on the other hand, items like 3,4 & 5 meets vacuum existing in our present education pattern although it improves the quality of service of the health care system.

While items 6 & 8 are revolutionary in nature and require elaborate planning and discussion, may well fit for M.Phil. & Ph.D. programmes benefitting the country in the long run. Should we not be aware of/get prepared for such activities today? Open university needs to offer both the foundation as well all advanced courses to meet the aspirations of wide spectrum of the society. Let's act today with confidence and dedication to meet these challenges facing Education Today !




Molecular Medicine: Better health care can only come through better understanding of drug action and receptors, at the Molecular level.

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## CONTENTS



# PROF. G. RAM REDDY IS THE NEW CHAIRMAN OF THE UGC

It is gratifying to note that our former Vice-Chancellor Prof. G. Ram Reddy has been selected by the Govt. of India as the Chairman of the University Grants Commission. This is in recognition of his yeoman services in the field of education.

Formerly he was the Vice-Chancellor of Osmania University (1977-82) and then the founder Vice-Chancellor of Andhra Pradesh Open University (1982-85), the first of its kind in the country, and also Indira Gandhi National Open University (1985-89).

For Prof. Reddy, distance education is a matter of commitment to democratise education in our country. Under his stewardship, IGNOU was able to launch several innovative courses such as Diploma in Distance Education, Diploma in Creative Writing, Certificate Courses in Rural Development and Food & Nutrition, in addition to the Diploma Courses in Management leading to M.B.A. and the Bachelor's Degree Programme — all within a short period of four years. As Vice-Chancellor of IGNOU, Prof. Reddy set the pace for the establishment of open universities in the country. He enthused the state governments to launch their own open universities to meet the growing demands for higher education, particularly from the people in the rural and backward areas. Exchange of courses and credit transfers between different open universities had been his major concern. He believed that this would avoid duplication and promote uniformly high standards. He repeatedly pointed out that many institutions in the country were not in a position to provide access to all eligible students. He has constantly stressed that only distance education can provide this access and, to this extent, he has become the chief exponent and proponent of the open university system in the country. He was instrumental in the setting up of the Kota Open University of Rajasthan, the Nalanda Open University of Bihar and the Y. B. Chavan Maharashtra Open University. Recently, he led a team of experts to Bangladesh to help the government to set up a National Open University at Dacca.

*Prof. G. Ram Reddy*

Later, when Prof. Ram Reddy was appointed as the Vice-President of Commonwealth of Learning (Vancouver, Canada), he saw to it that inter-institutional cooperation between the different commonwealth countries became a reality. In particular, the COL, during the short period that he was there, organised several working group meetings in order to devise new courses for distribution across the continents. Under the aegis of the COL, several cooperative programmes have been recently undertaken to train personnel in education. He advocated the training and exchange of faculty and experts between sister institutions of different commonwealth countries. The COL played a facilitating role in this endeavour.

As Chairman of the UGC Prof. Ram Reddy is likely to extend his support to strengthen and expand the distance education system in the country.

# WHITHER HEALTH SCIENCE ? (A Programme for Family Physicians & Biomedics/ Molecular Medicinists)

*Dr. B. S. Sudhindra, Regional Director (RSD).*

## 1. Introduction

What is Health Science? Is it pure Medical Education i.e. one dealing with generation of MBBS, MD doctors? Or is it devoted to generation of Paramedics? Or Nurses or manpower in the area of village Health Workers? Does it include research and development activities related to drug discovery and delivery systems? These and many other questions come to one's mind when one speaks/hears of a School of Health Science. A holistic view of the problem was taken and a set of courses suitable to practical situation in our country was presented in an earlier issue of this journal (Ekalavya, Sept.-Oct. 1990). Here we outline a strategy that helps in generation of manpower in the inter-disciplinary area of Biomedics and Family physicians.

The situation of Health Care Delivery System for the public, in our country, is much below the minimum standards from all angles. Coupled with this is the problem of non-uniformity of MBBS courses offered at various medical colleges across the country and the opposing views of various bodies which look after the quality of medical profession across the country viz. MCI, DGHS, NBE and IMA. Even in the premier medical institutes like AIIMS etc. patient care aspect needs to be improved. A way out of this complex and chaotic situation (from public viewpoint) is to make learning of these professional courses possible through the Open University System.

## 2. Newer Programmes in Health Sciences

We emphasise here the need to start Open University courses in the following areas:

i) Generation of Manpower of Family Physicians, viz. Post Graduate Diploma in Family Medicine (After MBBS).

The basic reason for this course is that most of the fresh Medicos are not thoroughly oriented in dealing with common problems of patients that come to Primary Health Centres (PHCs) or to a General Practitioner's office. This fact is fairly well known among (academic) medical fraternity and is a hot topic of discussion as how to improve under-graduate medical education programme (for a recent review one may see the proceedings and recommendationsof the IMA meeting of Dec. 1990). It has been realised that a thorough grounding in dealing around 80 diseases/cases is all that is required to run an efficient PHC or a GP office! Current syllabi of degree courses hardly lay any stress on these topics as they concentrate more on advanced techniques/topics of interest to those aspiring to go-in for specialisation, viz. MDs.

ii) Generation of Biomedical/ Molecular Medicine Personnel, viz. Post Graduate Diploma/Degree programmes in Basic Medicine for Scientists and Engineers (entrants with MSc/BE degree).

Much of the present day advances in diagnostics and treatment can in all fairness be attributed to the advances in Therapeutics and Instrumentation. The former is due to efforts of Molecular Medicinists, Chemists and Pharmacologists, while the latter is due to Engineers. In the words of a young scientist, "Even if you put 1,000 doctors to look at alleviating a disease, no improvement or solution to it can be arrived at if a medicine is not already available to the doctors. Whereas if you put 1,000 Biomedics to look at a disease, you are likely to get a solution for therapy! John Blake could do in a laboratory what doctors at the bedside could not".

The contents of a programme run by the universities are normally based on recommendations of an expert committee. In the following sections, we outline broadly the titles which such a programme must have as seen by an outsider. The choice of these programmes is based on our conviction that the prime responsibility of diagnosis and use of a therapy routine is done by this group of professionals only. The paramedics or the nursing or any allied health worker fraternities are *NOT* involved in these vital matters. Hence, any programme or course that will aid in improving the quality ( & quantity) of such professional group is of vital importance to a developing nation and therefore it must form an integral part of Open University programme. Fairly obvious is also the fact that Medical Profession, as compared to other professions, is more closed or "eminently maintains isolation" from interaction with any other professionals. Progress in Medicine & Health care is occurring in such centres where this barrier is being broken!

## 3. Post-graduate Diploma Programme in Family Medicine

This may be structured on the following pattern:

| | |
|---|---|
| 1. Clinical Diagnosis | - 8 credits |
| 2. Children (2+) | - 4 credits |
| 3. Adolescents (10+) | - 4 credits |
| 4. Adults (18+) | - 4 credits |
| 5. Older people (60+) | - 4 credits |
| 6. Medical Informatics | - 4 credits |

7. Disaster Medicine - 4 credits

The classification may appear a bit strange to many, but it has been presented with a view that different age groups of patients come up with unique complaints. Therapy regime may be same but precautions (ability to cope with adverse reactions) are different.

IMA College of General Practitioners, Delhi, conduct a fellowship programme through correspondence in this area. However, their infrastructural facilities are limited and cannot cope with vastness of our country. Their course materials are not in distance education format and have no audio/video support.

### 4.Post-graduate Programme in Biomedics/Molecular Medicinists

This two-year programme can be made modular and have in the First Year (Compulsory)

1. Clinical Diagnosis with Anatomy, Physiology, Pathophysiology. 8 credits
2. Laboratory methods: 8 credits
3. Medical Informatics: 4 credits
4. Medical Instrumentation-I: 8 credits
5. Disaster Medicine: 4 credits

Second Year ( Total 32 credits)

(i Choose any one of the following:

a) Computer aided Molecule Design-16 credits

b) Computer aided Organ design-16 credits

c) Medical Instrumentation-II- 16 credits

d) Clinical chemistry/bio-chemistry/microbiology- 16 credits

e) Clinical pharmacology- 16 credits

(ii) Compulsory:

f ) Project work in the chosen area- 16 credits

Here again we emphasise that structuring such a course may vary from one expert group to another. However the basic strategy being that the whole effort should be to expose the interdisciplinary nature of medical science. Such an effort would enable future generation of professionals to more easily appreciate and solve problems related to the well being of man.

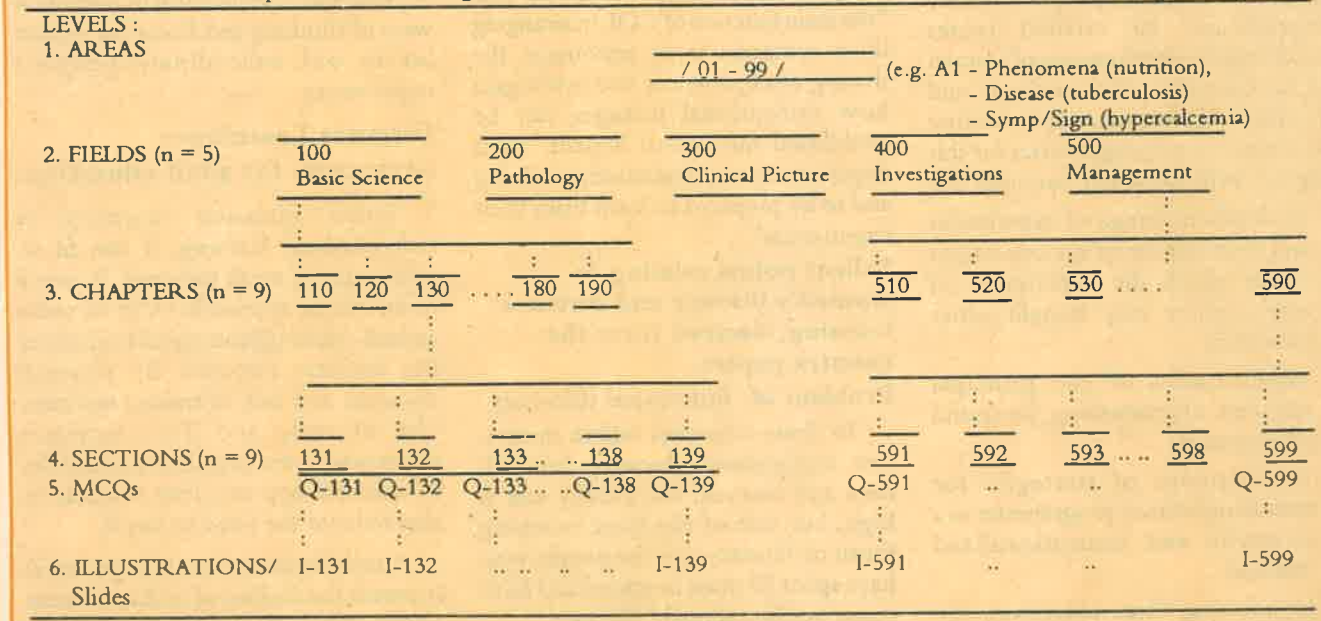
### 5. Integrated Presentation using Computers

Irrespective of the choice of topic to be included in such a course, an integrated view of the topic can be presented, such as the one given in Flow Chart below [ J. Distance Education (University of Jammu *3* (3), 13-20 (1991) ]. A computer assisted instruction material is an ideal way to achieve such an integration. These can be effectively carried on with the "low-end" systems such as PC-XTs and DOS environment. However a good collection of books (International editions and some journals) at all Centres where the programmes are activated is a must, for achieving success and credibility of the efforts.

### 6. Conclusion

All said and done, much depends on the academic and political will of the Open University System to take advantage of launching such needed and demanding courses. While break-throughs in science have occurred due to efforts of individual vision, launching of new programmes demands unusual strength from the authorities of the Open University. Time alone can tell about future actions in these areas.

Flow Chart for Computer Assisted Integrated Modular Self-Instructional Learning in Health Science Programmes.




Note : one-Screen view area = one Section,
9 section = one chapter,
9 chapters = one field, and
5 fields = one area i.e. 9 (section) x 9 (chapters) x 5 (fields) = 405 sections for each area.
i.e. 405 sections = one area.

It is recommended to hold one area per floppy with flexibility to move across & vertical from any section to any section within a given area/floppy.

IN HOUSE MAGAZINE

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# EMPOWERING THE "NEGLECTED MAJORITY"

**Prof. Dr.B.S.Sudhindra**
Regional Director
IGNOU Regional Centre, Pune

## ABSTRACT:

*An Open University System (OUS) is set up essentially to meet the higher education needs of the **"Neglected Majority"** Some new approaches to empower this lot of Distance Learners to succeed in their studies are presented in this work. Topics discussed include*

*1. What are COMMANDMENTS in Distance Learning?*

*2. How to study to ensure 100% success in every subject? Along with the familiar **"SQ3R"** procedure for reading skills, new approaches like **"NEED-IPS"** procedure for writing skills and **"FOLK-CAP"** procedure for success in Maths are documented.*

*3. What the University provides and what the student has to do, are given in **Display Sheets**. The concept of "Space Time Management" is introduced in "My Study Time Table"*

*4. How to keep track of last dates with respect to submission of assignments, filling of Examination forms etc. are given in a handy pocket-sized booklet christened **"MEMORABILIA",***

*5. The slogan **IGNOU: "Every Family's University"** has been introduced to popularise IGNOU among the public.*

*6. Suggestions towards improving the quality of Student Support Services to make it more "Distance-Learner-Oriented" are also cataloged. Some major items being:*

*a) Make 24 credits/year as the standard norm for all Open University programmes.*

*b) Self-Instructional materials (SIMS) should:*
- *i) be reduced from A4 size to a lower size.*
- *ii) have two column-wise printing.*
- *iii) Use multi-colour diagrams*

*to enhance the learners attention to studies.*

*c) Telecast timing should be rescheduled to morning 5am to 6.30 am and at night 9.30 to 11 pm.*

*d) All Assignments should be made available on E-mail/Internet.*

*e) Saturdays and Sundays should be normal working days for the OUS.*

## 1. Introduction :

Only about 5% of the population in our country is getting the benefit of Higher education. The rest of the 95% forms the "Neglected Majority" deprived of opportunities of acquiring Higher Education. An Open University System (OUS) is essentially set up to meet the Higher Educational needs of "the Neglected Majority".

The concept of Open University is now well known in our country with the arrival of National (IGNOU) and State Open Universities (BRAOU, KOU,Bhoj OU (MP), AOU (Gujarat), KOU (Karnataka) etc). There are many facets in the conduct of Open University Education. viz.

1. Pre-entry information/guidance
2. Guidance during the course of study
3. Conduction of Examinations and declaration of results.

There are many varieties of personnel involved at Divisions/Schools providing the necessary inputs and outputs to the student. As the number increases, the scenerio becomes a fertile land for "operational lapses" or "mismatch" in the delivery of OUS. The student, in general a working adult - who is normally busy during the day (8 to 5)-, passionately interested to improve his educational qualifications, to move higher-up in life, needs explicit guidance to successfully complete the course he has enrolled for.

There are many "grey areas of operation" where improvements can be effected to facilitate the distance learner. Some efforts made at Regional Centre Pune, are discussed below.

## 2. COMMANDMENTS In Distance Learning:

There is no dearth of materials, books, brochures etc on Distance Education. Every Programme Guide of IGNOU describes it. However, it has been our experience at the Regional Centre that numerous queries on the DE concept are asked every day. It was felt that a need exists to put the whole matter in some "rules" for the benefit of the learner regarding the concept of DE. This resulted in formulating the concept of **"COMMANDMENTS"** in Distance Learning. viz.

1. In the Distance Education Mode,
   Your speaking is through your
   our our

   Writing. So you have to cultivate the
   we

   habit of writing in simple term
   (without presuming but starting explicitly).

2. Nothing can be achieved without some sacrifice.
   Success comes to those who cultivate
   i) a good reading habit
   ii) a good writing habit and
   iii) a logical problem solving habit..

3. Cultivate the habit of attending counselling sessions organised at the Study Centres. You get to know your fellow students and teachers.

You can extend them further !

## 3. How to Study ?

Everyone accepts that IGNOU print materials are well prepared content wise. Inspite of this, the percentage of students passing out annually is still not very high.

Even in the most popular programme like MBA the number of students passing within the stipulated minimum time of two and half years is a single digit figure ! This area is a fertile land for pro/contra discussion. Our effort is to take the by-pass route, namely let us inform all Distance Learners on "How to study"- the result being formulations of some new procedures like NEED-IPS, and FOLK-CAP described in details below. What has been done in effect is empowering "every Distance Learner" with information that is available only to a section of the academic community!

A good reading habit can be cultivated by following the **"SQ3R procedure".**

This involves

| | | |
|---|---|---|
| **a.** | Survey | } |
| **b.** | Question | } |
| c. | Read | for every topic discussed |
| d. | Recall | in the Self-Instructional |
| e. | Review | Material |

A good writing habit can be cultivated by following the "NEED IPS" procedure.

a. Noting down/outlining the essential points that need to be covered for the topic

b Elaborating each of the points into small paragraphs

c. Editing the above developed paragraphs into a sequential order by
   i. giving an introduction to the theme
   ii. putting the paragraphs developed in order
   iii. giving a brief summary/conclusion with your comments.

d. The draft so prepared may be further edited checking for spelling and grammatical errors with the help of a dictionary and Roget's Thesaurus.

How to succeed in Maths?
"FOLK-CAP" procedure can be cultivated to solve problems.

Figure - Out the Logic with Knowledge of Current And Previous chapters

Step 1 Be aware of previous chapters/years maths data w.r.t. Definitions, Theorems and properties of figures, relations etc.

- Please note down all of them in a book, for your easy reference.
- e.g. B.Com./B.Sc./B.C.A.students need to note only maths covered upto 10+2 level.
- BPP students only upto 10th Std.
- In this revision process you will have become familiar with the vocabulary and script that are unique to maths.

Step 2 Read the text/unit and spend some time in "Figuring-Out the Logic" (F-O-L) used in "solved example" in the unit/text.

- Add to your collection the newly read topic's important results and new vocabulary learnt.

Step 3 For any given problem, note down
I. data already given and
II What is to be found/determined clearly.

Step 4 Try to "Figure - Out the Logic/steps" with knowledge of Current (data given) and Previous chapters to solve the problem.

- Stretch/strain your mind and Imagination to get at the solution in stages.
- If you can not "figure-out" at the first go, put it aside.
- Keep thinking about it and come back to it.
- Review again the steps/logic used
- Try again !

Step 5 If you can finally solve it on your own, isn't the feeling great?

- In this process you will have learned to think critically !
- The hard work done now, multiplies your ability in many spheres of life later on.
- There are no short cuts to solve a problem.
- You can not have hop, skip and jump approach to study maths.
- You have to study in the sequence presented and solve all problems given in the text.
- Only then will you have gained confidence in Maths.

Like in the initial stages of learning "bicycling" the above procedures may appear difficult, but as you go by the whole Reading/Writing/Maths process becomes easy.

You will have cultivated good habits !

## 4. Display Sheets :

These are :
i) Myself
ii) My Study Time Table
iii) From IGNOU

These are self-explanatory. i) & iii) have been in use since 1994 and ii) is a new addition. (1996+) The need to inform the reader in simple terms of information already available in the bulky programme guides and other materials was felt because of innumerable queries that used to come at the Regional and Study Centres. Lack of man-power & repeat nature of queries forced us to bring out them. These are in vogue in Maharashtra region and the number of queries being received have greatly reduced after introduction of these Display Sheets. Latest addition being the "Spare-Time Management" schedule for Self-study by the Distance Learner.

## 5. Memorabilia :

In order to help the Distance Learner in keeping track of his commitments, like last dates for submission of assignments, filling examination forms and numerous other "last date deadlines", a small pocket sized and distinctive color booklet christened "Memorabilia" was developed. The product has been of immense utility. Again only students attached to Maharashtra Region have benefitted by this innovation.

Every programme/course should have/develop such Memorabilias highlighting the most essential points of theory and practicals to the benefit of the recipients.

## 6. IGNOU : Every Family's University

In order to attract more students into our system and in line with many premier setups like IBM, WILEY, YCMOU,

BRAOU all having some "eye catchy slogan" to highlight their organisation. Looking into the power and jurisdiction of IGNOU, the following slogan was introduced

"IGNOU : Every Family's University"

The reasoning being as follows : A family is the basic unit in the socio-cultural context in our country. All members in the family (18 and above) can enroll in IGNOU. At least there is one programme (CFN) which can be taken without any hindrance. In other words every father/mother, parents-in-law, son/daughter, daughter-in-law can enroll for IGNOU programmes. They may be residing anywhere in India, independent of their status (economic, social, gender etc). That's the power of IGNOU and its commitment to meet the needs of the "Neglected Majority". This slogan is in vogue since 1993. Every letter and communication from Maharashtra Regional & Study Centers are involved in this "silent & cost - less" effort to spread the concept of OUS in Maharashtra.

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