the first two and competition and rivalry among the companies.

A few words on 'me-too' drugs, which are condescending if not denigratory terms for 'look-alikes'. The international research director of a MNC probably put it in proper perspective when he termed them as products of 'molecular evolution' (earlier, manipulation) as against breakthrough drugs which are from 'molecular revolution'. The latter represent quantum jumps while the former afford incremental improvements. We must understand that the patenting of a 'me-too' drug has to satisfy the criterion of novelty; since this is not possible in terms of chemical structure, it must do so in its biological profile. Further the 'me-too' ness of the 'look-alike' does not shorten the process of its development, which goes through detailed biology, toxicology, metabolism, pharmacokinetics and clinical trials.

The contribution of Indian chemists to the synthesis of bulk (known) drugs is very significant, having made these available at low prices, in some cases because of improvements to available processes. While we should be justly proud of this achievement made possible for brand new drugs by the existing patent regimen, we must not lose sight of realities—much of the cost of drugs abroad arises from the ever-soaring cost of developing a new drug. A second factor is undoubtedly cheaper Indian labour. A last but not least important factor is the heavier expenses incurred abroad for pollution containment in bulk drug production processes. Increasing emphasis on the last parameter in the coming years is bound to push up our prices as well.

Apart from process development of synthetic drugs, it must be noted that some of our capable scientists have ventured successfully into the synthesis of biologically active molecules in the areas of cancer, AIDS and bacterial infections. It was common knowledge that these would never become cost-effective processes; but it was however felt that the approaches could produce newer and cheaper analogues. It was evident at that time, and it has been confirmed in retrospect, that this was wishful thinking since neither the desire nor the mechanisms to have the new molecules screened properly have been in place.

In conclusion, the development of a new drug is a complex conglomeration of many activities. While this has been a desirable national objective so far, it has become imperative in the light of the expected changes to our patent laws. Fully realizing the enormity of the task, the country can undertake it optimistically and we should congratulate the larger Indian drug companies venturing into this area. Chemistry, which is but one of the many disciplines involved, has demonstrated its ability in the synthesis of drugs. Expertise in other disciplines like different areas of biology, drug metabolism, toxicology, etc. are both scarce and currently, not focused to the task in this country. Success in new drug development will smile on those institutions where these disciplines are knit into a cohesive team by an understanding management with defined targets and adequate resources.

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SCIENTIFIC CORRESPONDENCE

Graphical representation of long DNA sequences

Apropos the article on a new graphical representation and analysis of DNA sequences[1], it has been brought to my attention recently that a similar technique was presented by M. A. Gates[2] some time ago.

Gates had proposed to plot the DNA sequence in a simple metric space to enable visualization by choosing a C–G, A–T axes system based on the redundancy of the genetic code; it generates sequence maps that *a priori* resemble the maps we had independently proposed in our paper. However, when analysing genome length DNAs, it is not codon degeneracy but macro aspects like, e.g. purine-pyrimidine abundances, distribution of bases, etc. that are important. The non-trivial choice of a symmetric purine-pyrimidine axes system plotting A–G, C–T along the two axes introduces subtle differences in the new sequence representation which give more significant information of current biological interest

For instance:

– In the light of recent interest in long range correlation effects in long DNA sequences as observed by Peng *et al.*[3] by an analysis of purine-pyrimidine abundances, we have shown[4] that the maps of the myosin heavy chain genes in our representation can be taken as pointers to a possible source of the long-range correlation effects;

– At a more direct level, our graphical representation serves to explicitly demarcate purine and pyrimidine abundances as in the case of the gamma globins where the alternating A, G runs are seen to be clearly superposed on a strong pyrimidine backbone (Figure 2 in Ref. 1);

– In this particular choice of axes, transition types of evolutionary changes are suppressed leading to easier identification of significant evolutionary developments in the gene sequences;

– As we show also[4], detailed analysis of the maps in our representation can lead to indications of regions of gene duplication and repetition.

Thus, while the graphing technique is similar in Gates and our case, our choice of particular axes system based on macroscopic aspects provides an effectively new representation and approach to analysis of DNA sequence composition and distribution that is potentially of significant biological interest.

1. Nandy, A., *Curr Sci.*, 1994, **66**, 309–314.
2. Gates, M. A., *J. Theor Biol.*, 1986, **119**, 319–328.
3. Peng, C–K, *et al.*, *Nature*, 1992, **356**, 168–170.
4. Nandy, A. and Nandy, P., 1994, communicated.

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