In this issue

Designing anti-HIV drugs

Rational drug design requires detailed structural characterization of target macromolecules on pathogenic organisms, followed by computer-aided design of low molecular weight inhibitors, leading eventually to chemical synthesis and clinical testing of potential therapeutics. Although relatively few products of this 'rational' approach have reached the marketplace, there is little doubt that the years to come will witness many more successes. No disease in recent times has evoked as much scientific attention as acquired immunodeficiency syndrome (AIDS), largely as a consequence of its dramatic surfacing in the United States. Despite an enormous effort, no sure cure is as yet available for human immunodeficiency virus (HIV) infection. The field of rational design of inhibitors of HIV growth is wide open and a variety of enzyme targets may be explored. An aspartic protease, HIV-PR, is crucial for proper maturation of the virions. Inactivation of this enzyme could neutralize the infectivity of the viral particles. The attractiveness of the HIV-PR as a target for drug design has led to an intense flurry of activity on high-resolution crystal structure determination of this enzyme in the free-form and also in complexes with synthetic inhibitors.

Sathyanarayana and Wlodawer review this burgeoning field on **page 835**. At the time of writing, over 160 complexes of HIV-1-PR have been studied, resulting in an unparalleled wealth of structural data on enzyme–inhibitor interactions. However, the compulsions of pharmaceutical development and the attendent secrecy of research in private companies means that much of this research may never find its way into the scientific literature. The authors conclude with a plea for the free flow of information in an area of great public interest.

G Proteins

One of the most important fields of research in cell biology today is the area of understanding the molecular mechanisms of signal transduction – the phenomenon by which binding of an external effector to a membrane-bound receptor results in transmission of a message to the cell interior, thereby affecting physiological functions. A major role in signalling pathways is ascribed to a family of proteins that are coupled to diverse receptor families, viz. the G proteins, which derive their name from their ability to specifically bind guanine nucleotides. The G proteins, a heterotrimeric class of molecules remarkably conserved over evolution, have been the focus of extensive investigations over the past few years. Gautam (**page 848**) reviews the molecular biology of mammalian G proteins, emphasizing their role in neuronal signalling and development and in human disease.

P. B.

Evidence for a novel structure of $C_{60}H_{36}$

Birch reduction of C_{60} was among the first chemical reactions on fullerenes to be reported. The major product was identified as $C_{60}H_{36}$. Since Birch reduction of planar aromatic compounds leads to unconjugated products, a T_h structure with an isolated double bond in each of the pentagons of C_{60} was proposed. Alternative isomeric structures for $C_{60}H_{36}$ have been considered independently by different groups on the basis of symmetry considerations, qualitative analysis of residual conjugative stabilization and semi-quantitative MO calculations. An aesthetically pleasing geometry for $C_{60}H_{36}$ involves four benzenoid rings in a tetrahedral array on the spheroidal C_{60} framework. The possibility that the Birch reduction product has the corresponding T symmetry structure is evaluated by A. Govindaraj (**page 868**). The key evidence assembled to support the presence of aromatic rings in the Birch reduction product are the UV spectrum with bands at 218 and 275 nm and observation of a charge transfer band for $C_{60}H_{36}$ with tetracyanoethylene. Further, the FT-IR spectrum is shown to have a closer correspondence with the computed vibrational spectrum for the T structure. The study should trigger additional chemical and structural efforts towards obtaining clinching proof for the proposed structure.

J. C.