Haemoglobin structure

A clam with a difference

from Max Perutz

ALL vertebrate haemoglobins are tetramers made up of two pairs of unlike polypeptide chains, termed alpha and beta, each chain forming a basket for one haem. But on page 227 of this issue W. E. Royer Jr, W. E. Love and F. F. Fenderson demonstrate that haemoglobin of the clam *Scapharca inaequivalvis* has a quite different form of subunit assembly.

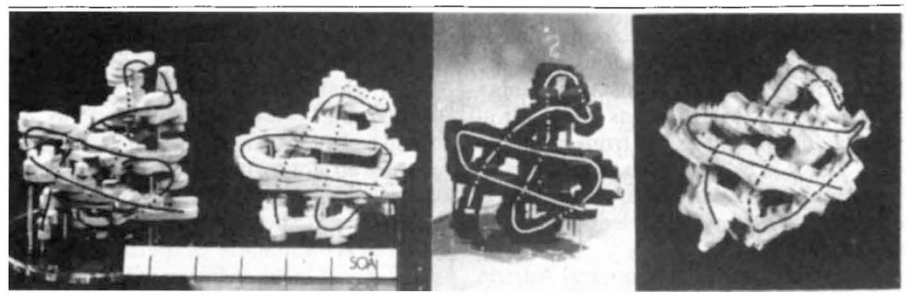
In vertebrate haemoglobins, the alpha chain is coiled into seven helical and six non-helical segments, and the beta-chain is coiled into eight helical and six non-helical segments. The tertiary structures of both the alpha and beta chains are similar to each other and to myoglobin, and the residues lining the haem pockets are largely homologous. The vertebrate tetramer has pseudo-tetrahedral symmetry with one true dyad axis running through a central water-filled cavity and two pseudo dyads at right angles to each other and to the true dyad. Assembly occurs in two stages: first, one alpha and one beta chains form a tightly bound dimer; and second, two such dimers combine to form a tetramer. The allosteric change between deoxyhaemoglobin and oxyhaemoglobin consists in a large rotation and slight translation of the two alpha–beta dimers relative to each other.

The haemoglobins of two primitive vertebrates, lampreys and lungfish, are monomeric when oxygenated and oligomeric when deoxygenated; the monomer has a tertiary structure similar to myoglobin. The same is true for all the invertebrate haemoglobins whose structure has been determined and for the haemoglobin found in the root nodules of leguminous plants, suggesting that the myoglobin fold is a universal pattern (see figure) that has evolved to provide the surround for an oxygen-carrying haem.

A suspicion that the quaternary structure of invertebrate haemoglobins may be different from that of vertebrates arose from the observation that one of the larval haemoglobins (component X) of the fly *Chironomus thummi thummi* has a marked Bohr effect coupled to a dimeric structure at *p*H 5.5 and to a monomeric structure at *p*H 7.0. Bohr effects probably arise from the ionization of histidines, but no histidine in this haemoglobin is at at position corresponding to subunit contacts in vertebrate haemoglobins.

Royer *et al.* now show that haemoglobin of the blood clam *S. inaequivalvis* has a tertiary structure similar to myoglobin, but with one additional helix at the amino end which lies parallel to the carboxy-terminal helix H and brings the terminal amino group close to the terminal carboxy group. It is in its quaternary structure that the clam haemaglobin is exceptional. Two like monomers assemble to form dimers, not by contact between helices G and H as in vertebrates, but by contact between the haem-linked helices E and F, so that the haem pockets lie on the inside of the tetramer, as Pauling once imagined, rather than on the outside, as in vertebrates. Two chemically different dimers join to form a tetramer; as far as one can make out from Fig. 2 of Royer *et al.*, the tetramer is formed by contact between helices A, and between the non-helical segments NA and GH. The dyad axes of each of the individual dimers make angles of 75° with the dyad joining the two dimers, so that there is no tetrahedral symmetry.

The structure solved is that of the carbonmonoxy-derivative which is probably isomorphous with the oxy-derivative. Oxygen binding is cooperative with a Hills coefficient of 2.1, and loss of oxygen is linked with polymerization of the tetramer. It will be interesting to see if solution of the deoxy-structure reveals the mechanism that triggers this polymerization. □



The universal tertiary structure of, from left to right, sperm-whale myoglobin, horse haemoglobin alpha chains, horse haemaglobin beta chain and haemoglobin of the clam *Glycera dibranchiata*. In each picture the amino end is on the left.

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X-ray astronomy

A new breed of oscillator

from N. E. White

THE first short timescale periodic oscillations from a bright galactic centre X-ray source (GX5−1) are reported by van der Klis *et al.* on page 225 of this issue. These quasi-periodic oscillations (QPOs) probably indicate the presence of an accreting neutron star that is rotating with a period of a few milliseconds. This discovery may provide timely support for recent models for the evolution of low-mass X-ray binary stars (LMXBRs) into millisecond radio pulsars. Furthermore, the oscillations themselves display intriguing characteristics requiring some ingenuity from theorists seeking to explain them.

An accreting neutron star will only be seen as an X-ray pulsar if its surface magnetic-field strength is high enough to funnel the inflowing material from its companion star onto the magnetic pole. The spin-down properties of radio pulsars suggest that neutron star magnetic fields decay on a timescale of 10^6-10^7 years. If neutron stars are born with the same surface field of 10^{12}–10^{13} Gauss, then those located in the X-ray binaries should show a range of field strengths depending on their age. X-ray pulsars are usually associated with young population I objects (OB stars). In contrast, the older population II LMXRB systems (where the mass-losing star is of a late special type) rarely contain X-ray pulsars.

Any material that flows between components in a binary system must lose angular momentum before it can fall onto a compact object. It may form an accretion disk which will mediate the flow and, by exerting torque, will spin the neutron star up to equilibrium period at which its rotation period is equal to that of the innermost keplerian period of the disk. If a strong magnetic field is present this is determined by the radius at which the magnetic pressure disrupts the disk; for a typical X-ray pulsar with a field of $\sim 10^{12}$ Gauss the equilibrium period is a few seconds. If the field is less than 10^8 Gauss this disk will extend to the neutron star surface and the equilibrium period is ~ 1 ms. It takes only 10^6-10^7 years to spin a neutron star up to this period.

This scenario has encouraged the search for millisecond periodicities from LMXRBs but with no success until van der Klis *et al.*, using the European Space Agency X-ray observatory (EXOSAT) because it is probably more sensitive to millisecond periodicities than previous X-ray satellites, searched again for milli-