Gap Junctions. Edited by M. V. L. BENNETT, DAVID C. SPRAY. Cold Spring Harbor, New York: Cold Spring Harbor Laboratory. 1985. 409 pages. $70 in USA; $84 elsewhere. ISBN 0 87969 187 5.

This volume represents the proceedings of a conference held at the Banbury Centre of Cold Spring Harbor Laboratory in October 1984. I am not in general an enthusiastic purchaser of volumes of symposium proceedings, which so often are collections of unrefereed manuscripts on tenuously related subjects which have been overtaken by subsequent developments long before publication. Such criticisms cannot, however, be levelled at this volume, in which leading experts in various aspects of the study of gap junctions concisely review their immediate area of interest and present their most recent, frequently unpublished work. The result is a coherent synthesis which can still be regarded as summarizing the 'state of the art' at the time of writing this review: indeed, there are a number of interesting new developments with which I became acquainted for the first time from its pages.

It has been clear for some time that the gap junction provides channels for the movement of small molecules between the cytoplasm of two apposed cells without equilibration with the extracellular space. However, detailed molecular understanding of its behaviour is still incomplete, as is our comprehension of the factors controlling the formation and permeability of gap junctions and, indeed, their role in non-excitable tissues. These are some of the questions which this book addresses.

The contributions are organised into six sections. Firstly there are five papers describing structural studies. X-ray diffraction and electron microscopic studies of isolated liver gap junctions are covered by Makowski and by Zampighi and Simon respectively. These provide evidence for two distinct quarternary states of the junctional channels which were originally interpreted as the open and closed conformations. However, as discussed by Hanna, Orberg and Reese, it is now clear from freeze–fracture analysis of rapidly frozen gap junctions that the transition between the two conformations does not accompany the permeability change but is a secondary consequence of it. The remaining papers raise the question of inter-tissue variability. Lens fibres contain a protein, MIP or MP26, whose relationship to gap junctions is unclear. It is, however, well characterised and predictions of its secondary structure based on its primary sequence are consistent with a role as a junctional channel (Revel and Yancey). Page and Manjunath discuss the biochemistry and structure of cardiac gap junctions which differ from liver junctions in ultrastructure and protein composition.

Five papers are grouped under the heading of biochemistry. Unfortunately progress here is still bedevilled by disagreement about the molecular weight of the gap junction protein. The main candidates are a 27 kD species present in related but distinct forms in different tissues as shown by antibody probes (Hertzberg and Spray, Willecke *et al.*) and a 16 kD species found in vertebrate junctions which appears to correspond to an 18 kD protein present in arthropod junctions (Finbow *et al.*). The question of the lens MP26 protein is again taken up by Johnson *et al.*, and Paul demonstrates that antibody against liver 27 kD protein cross-reacts with a 54 kD species whose relationship to the 27 kD molecule is not yet clear.

The third section, biophysics, begins with four papers (Brink; Spray *et al.*; Ramon *et al.*; Wojtczak) covering the effects of various agents on junctional permeability, including gating by voltage, pH and calcium ion. Of particular interest in this section are the remaining two papers which describe cell-free reconstituted systems for the analysis of junctional permeability. Hall and Zampighi demonstrate that protein from lens junctions induces channels in planar lipid bilayers, and Peracchia and Girsch study the gating of the permeability of lens junctional protein incorporated into liposomes, demonstrating a requirement for calmodulin in pH- and calcium ion-dependent gating. It is not yet clear in either system whether the structures one is studying span a double bilayer, as does a gap junction *in vivo*, or represent hemichannels spanning only a single bilayer. Nevertheless these reconstituted systems represent a significant advance and will without doubt lead to a more detailed understanding of channel permeability in molecular terms.

The fourth section is entitled 'Control of Formation'. This may however be somewhat misleading, as the events described in the first paper by Atkinson and Sheridan, namely changes in coupling in virally transformed cells, are shown by temperature-shift experiments with *ts* mutants to occur within minutes, so that they probably relate to changes in the permeability of established junctions rather than in junction formation. Cole and Garfield discuss factors influencing coupling in uterine smooth muscle and the section is completed by two papers on electronic synapse formation. Kessler *et al.* discuss factors regulating this process in cultured sympathetic neurones, and Kater *et al.* present evidence from the study of cultured identified neurones from snail buccal ganglia that specificity in electrical synapse formation involves two selection events, one in the initial formation of electrical connections and a second involving the stabilization of some of these connections and the breaking of others.

There is then a discussion of the role of intercellular communication and development. Two papers (Lo; Caveney and Safranyos) cover the relationship between communication compartments and developmental compartments in insects. Warner describes developmental anomalies which result from the injection of antibodies raised against the 27 kD protein

into *Xenopus* embryos. Larsen discusses gap junction population dynamics, and the roles of the gap junction in oocyte maturation and in secretory epithelia are the subject of contributions by Beers and Olsiewski and by Peterson respectively.

The book is completed by six papers on electrotonic synapses. Electrical interactions and synchronization of cortical neurones are discussed by Dudek and Snow. Llinas deals with the role of the electrical synapse in the mammalian central nervous system. Bennett *et al.* discuss the interaction of electrical and chemical synapses. The crayfish rectifying synapse is the subject of the paper by Giaume and Korn, and the effects of neurotransmitters on electrical synapses are presented by Neyton *et al.* and by Lasater and Dowling.

As one has come to expect of books published by Cold Spring Harbor Laboratory, the book is well produced if expensive. In my opinion it is a volume which no laboratory carrying out work in the area of gap junctions can afford to be without. Indeed, I had already bought a copy for use by my group before being offered my review copy. Would anyone like to make me an offer for a second-hand volume in mint condition?

MARTIN HOOPER
Department of Pathology
University of Edinburgh
Teviot Place
Edinburgh EH8 9AG

Frequencies of Hemoglobin Variants. By FRANK B. LIVINGSTONE. Oxford: Oxford University Press. 1985. 526 pages. £29.00. ISBN 0 19 503634 4.

Ever since the discovery by Pauling in 1946 that sickle cell anaemia was a disease that could be explained entirely in terms of a mutant protein, the haemoglobin (Hb) loci have been at the forefront of advances in human biochemical genetics. At the last count there were more than 400 known Hb variants, while amongst the alpha- or beta-thalassaemias (syndromes with deficient alpha- or beta-chain synthesis) some fifty to sixty separate point mutations have been described. If one includes the glucose-6-phosphate dehydrogenase (Gd) locus with its 250 known mutants, one has a set of red cell polymorphisms and rare variants which show remarkable heterogeneity. And yet the frequencies are all determined to a greater or lesser extent by heterozygote advantage in the face of the falciparum malaria parasite.

Interest in population and racial frequencies of the Hb and Gd variants comes mainly from anthropologists and others studying the migration patterns of ethnic groups. Thus, the frequency of *Hb S* genes amongst American blacks shows that they probably come from three major areas in Africa: Benin in Nigeria, Central Africa and Senegal. Hb E is found at high frequencies to the east of Calcutta, *Hb S* to the west; the border of these distributions corresponds to the major ethnic interface between Indo-European speakers to the west and Tibeto-Burman speakers to the east. The virtual absence of red cell variants amongst Amerindians confirms their migration from the Bering Strait into a malaria-free world.

The collecting and cataloguing of human genetic variants is a valuable but thankless activity. Mourant and his colleagues did it for the blood groups and other red cell and plasma polymorphisms. The second and (probably) last edition of *The Distribution of Human Blood Groups* appeared in 1976, and could not have made much profit for Oxford University Press. It is to this publisher's credit that they have again performed a service in supporting another huge compilation of essential genetic data.

The raw statistics of Frank Livingstone's book tell their own story. He has surveyed the Hb and Gd variants and the incidence of thalassaemia, ovalocytosis and Gd deficiency in 150 different ethnic and geographical groups around the world. There are over 8000 entries set out in dictionary-style, and no less than 2000 references. One imagines that it is all there. My only criticism is that he might well have followed Mourant's lead and imposed some meaning on the data by setting them out in maps or flow-charts of migration.

D. J. H. BROCK
Human Genetics Unit
University of Edinburgh

Essential Medical Genetics. By J. M. CONNOR and M. A. FERGUSON-SMITH. Oxford: Blackwell Scientific Publications. 280 pages. 1984. £7.50. ISBN 0 632 01331 1.

There are at present some 40 genetic counselling centres in Britain (compared with 450 in the USA), and this number, though rising, appears to be still inadequate. In the West of Scotland the authors counsel about 1000 families annually from a population of 3 million, and consider that another 2000 families need genetic counselling, of whom 'a substantial number' do not receive it.

In the UK the Congenital Disabilities (Civil Liability) Act of 1976 means that legal action can be brought against a person whose breach of duty to parents results in a child being born disabled, abnormal or unhealthy; so medical practitioners need training in medical genetics – at least to the stage where they can recognise problems which need referral to a clinical geneticist, though preferably not to the stage where they consider they know all the answers themselves. Most medical and dental training now includes a course in medical genetics, and this book is designed for such students, based on the teaching and counselling experience of the authors in Glasgow.

The first 10 chapters (120 pages) cover the basic