tions from 0 to 10. For a point lying halfway along this scale, the measured radioactivity divided by 10^3 c.p.m. gives 5, so the datum is clearly 5×10^3 c.p.m.

The approaches favoured by Liébecq and Luykx appear to have a common drawback. If on a graph or in a table one uses the heading, "velocity $\times 10^2$ (ms^{-1}), there is always the risk of some confusion. Should a reading on the graph or in the table of "48.5" be read as a velocity of 48.5×10^2 ms^{-1}, or as 48.5×10^{-2} ms^{-1}? Mathematical logic tells us it is the latter, but many people seem to get confused, some authors included. The use of the solidus, as exemplified above, has the advantage that the factor one needs to insert is the same factor as appears on the axis or at the head of a column, that is, "velocity/10^{-2} ms^{-1}". Being completely unambiguous, this method is consequently less error-prone.

S. R. Logan
Department of Chemistry,
University of Ulster at Coleraine,
Coleraine,
Co. Londonderry BTS2 1SA, UK

More help required on T and B cells

Sir—I read with great interest a recent letter[1] and a *News and Views* article[2], concerning immunological help. It was reported that a B lymphocyte can pinocytose free toxin that it binds to and present digested fragments of it on its surface. It was also reported that a helper T lymphocyte which binds to these digested fragments can help the presenting B lymphocyte to differentiate to plasma cell form in which it secretes large quantities of antibody. In the *News and Views* article several unresolved questions relating to immunological help were raised. I thought of some questions which were conspicuously absent and will here raise them and suggest hypothetical answers.

First, how is a B lymphocyte helped if it binds to a surface antigen of a pathogen? B lymphocytes might find it difficult to pinocytose a surface of any pathogen unwilling to facilitate its own destruction, and B lymphocytes are not specialized to safely phagocytose a live pathogen. Digested fragments of a pathogen presented by macrophages would not be an adequate substitute since they would not include many of the original surface antigens. Perhaps when a B lymphocyte binds to an antigen that it is unable to pinocytose, it attracts a macrophage to come and phagocytose the attached pathogen or cell, and remains with the macrophage until it places digested fragments (of the antigen and the rest of the pathogen or cell) on its surface and the B lymphocyte's surface.

Second, how is it assured that B lymphocytes will be helped if and only if they bind to nonself antigen, while still allowing pseudorandom generation of T lymphocyte antigen receptors? Perhaps helper and suppressor T lymphocytes are clones of T lymphocytes which differentiated prenatally to helper or suppressor forms according to whether they did not or did bind to digested fragments of materials presented by macrophages then.

Third, how is it assured that B lymphocytes will not be helped if they bind to B or T lymphocyte antigen receptors? The diversity of helper T lymphocytes might be greatly restricted if there could be none that bound to the many different digested fragments of these receptors. Perhaps macrophages have a special ability to recognize B and T lymphocyte antigen receptors and do not present digested fragments of them; either prenatally or postnatally.

Fourth, how is it assured that B lymphocytes will not cause serious damage to self materials during an infection if they bind to an antigen common to self and pathogen? Perhaps since activated T lymphocytes would be concentrated near the pathogens, so also would their mediating chemicals, the B lymphocytes they helped, the antibodies of those B lymphocytes and the leukocytes which destroy antibody coated objects.

I wish researchers would devise experiments which clearly address the questions raised and possibly test some of the hypothetical answers suggested.

James Shifflett
218 Stanton Avenue,
Apartment 16,
Ames, Iowa 50010, USA

1. Lanzavecchia, A. *Nature* **314**, 537 (1985).
2. Howard, J.C. *Nature* **314**, 494 (1985).

Hormone receptor–effector complex evolution

Sir—I wish to propose a theory for the evolution of receptor–effector complexes where the effector is a protein or peptide hormone. Recently, there has been much interest in the evolutionary relationship between peptide hormone effectors and their receptors. Hales proposed that peptide effectors are produced by proteolytic cleavage of membrane proteins that are evolutionarily related to receptors[1]. Several recent findings concerning the peptide hormone epidermal growth factor (EGF) are consistent with this hypothesis. EGF is cleaved from a large precursor protein (prepro-EGF) that may reside in the membrane and appears to share some sequence homology with the human low-density-lipoprotein (LDL) receptor[2,3].

In a recent paper[4] Baldwin noted that there was also sequence homology between the coding region in the oncogene c-*mos* and the precursor protein for EGF. This homology did not extend into the part of the polypeptide that was cleaved into the hormone. c-*mos* is functionally related to the avian oncogene v-*erb-B* and presumably evolved from the same gene[5,6]. In turn, v-*erb-B* has substantial homology to the EGF receptor protein[7]. This means by virtue of the relationship of c-*mos* to v-*erb-B*, the precursor protein for EGF (prepro-EGF) would have to be distantly related to its receptor as well as contain the EGF peptide.

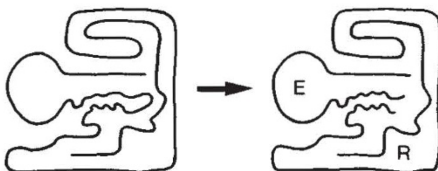

Fig. 1. A single polypeptide progenitor (left) becomes a two-polypeptide complex of receptor (R) and effector (E).

The structure of prepro-EGF leads me to extend Hales' ideas[1] and propose a model for the evolution of receptor-effector complexes. The model is based on the fact that receptors and their effector proteins form complexes due to protein–protein interactions. When a single polypeptide chain folds, different parts of the chain interact intimately with other parts of the same chain (Fig. 1). I propose that some of the genes encoding receptor–effector complexes began as single genes that encoded single polypeptide chains that were capable of intimate folding interactions. Receptors and their effectors then evolved due to changes in the DNA that split and sometimes duplicated the progenitor gene into two genes capable of encoding two distinct polypeptides, one the receptor and one the effector, that were still capable of interacting or folding with each other. For EGF and its receptor I envision that the progenitor gene was first duplicated. The copy that became the receptor deleted the domain encoding the hormone leaving a pocket for the missing domain encoded by the duplicated gene.

However, only gene-splitting, and not gene duplication, is obligatory of the general mechanism that I have proposed. After the gene is split, differential gene expression in different cell types could then induce the synthesis of each part of the original pro-polypeptide. The interaction of the two protein parts would lead to the formation of a complex capable of performing a biological task.

The interaction of these polypeptides could effectively lead to a cell–cell or hormone–cell interaction. Regardless of whether the relationship between prepro-EGF, v-*erb-B* and a c-*mos* is real or coincidental, the simplicity of this model bears further consideration as a general mechanism for the evolution of receptor–effector complexes.

David B. Kaback
Department of Microbiology,
UMDNJ-New Jersey Medical School,
Newark, New Jersey 07103, USA

1. Hales, C. N. *Nature* **314**, 20 (1985).
2. Rall, L. B. *Nature* **313**, 228-231 (1985).
3. Pfeffer, S. & Ullrich, A. *Nature* **313**, 184 (1985).
4. Baldwin, G. S. *Proc. natn. Acad. Sci. U.S.A.* **82**, 1921-1925 (1985).
5. Yamamoto, T. *et al. Cell* **35**, 71-78 (1983).
6. Gilmore, T., DeClue, J. E. & Martin G. S. *Cell* **40**, 609-618 (1985).
7. Ullrich, A. *et al. Nature* **309** 418-425 (1984).

©1985 Nature Publishing Group