Epstein *et al.* assume that the 'white points' reported in our paper¹ are artefacts produced by gold sputtering alone, because gold aggregates also appear on undoped (CH)_x.

However, we have never observed white points on undoped gold coated material in any of our experiments. We have examined the effects of three iodine doping methods:

(1) Liquid-phase (I₂ in pentane solution) doping; (2) vapour-phase doping at room temperature; (3) vapour-phase doping at low temperature (Epstein method²), associated with several techniques for excess dopant desorption:

- (i) liquid phase desorption (pentane);
- (ii) dynamical pumping (10⁻² torr);
- (iii) Epstein method.

Using the same 80-Å gold coating alone, the aspect of the doped samples, obtained by these various methods, is different.

With the method (2ii), we nearly always observe 'white points', with size increasing according to the dopant level. When the sample is dedoped using method (i) we notice a more homogeneous fibrillar aspect. Using the Epstein process (3iii), we generally do not observe large white points.

Consequently we think that the different observations may be due to the various different ways of preparing the experimental samples. Taking into account that the gold-coated undoped (CH)_x do not show white points, the gold coating is not responsible for the modifications related to the iodine presence. As the largest white points distribution appears when using the roughest doping and dedoping method (2ii), we can assume that the iodine distribution is often inhomogeneous (corroborated by our transmission electronic microscopy observations³). On the other hand, rough pumping can produce a local desorption of iodine with a fibril bursting and iodine heaps appearing on the surface.

Gold may be preferably deposited on the highly-iodinated sites and consequently could exhibit the inhomogeneous iodine distribution.

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Note added in proof by Rommelmann et al.: Secondary electron yield is a weak erratic function of atomic (*Z*) number¹⁴ compared with its strong dependence on surface topography. It is, therefore, incorrect to conclude that white areas on a highly structured surface, such as cross-sections of polyacetylene samples, are due to the high *Z* number of the dopant moiety. As has been shown in detail in ref. 13 these white areas are either agglomerates of coating particles and/or fibrils (or bundles of fibrils) being viewed end-on under extremely high contrast. As we have concluded previously^{9,10,13}, the diameter of these fibrils may be a function of dopant and doping procedure.

Furthermore, the transmission electron microscope results referred to by Rolland and Cadene are not under question, nor are they an appropriate corroboration as the inhomogeneities reported occur on a much smaller scale than may be resolved using SEM.

Asymmetric ligand binding by haemoglobin

WEBER has presented an interesting hypothesis about the origins of the asymmetry of the oxygenation curves of human haemoglobin¹. However, it is important to point out the significance of an assumption that is essential to his analysis—that the energetics of a boundary or interface are defined only by the presence or absence of ligand on the subunits involved in the interface. Constraints which are termed third and fourth order are specifically ignored. Weber fails to make note of the fact that this assumption excludes consideration of all models that invoke concerted transitions in quaternary structure. Such models permit asymmetric ligand binding without the need for dissimilar subunits. The two-state model of Monod *et al.*² is intrinsically asymmetric, being symmetric only in the special case when $1/L = c^{n/2}$, where *n* is equal to the number of binding sites per molecule. For a tetrameric structure it is positively asymmetric when $1/L < c^2$. If more than one quaternary state is possible, the free energy of interaction between two subunits will depend not only on the presence or absence of ligand on these subunits, but also on the particular quaternary state of the entire molecule. This is the equivalent of saying that the constants *K*_{BB} and *K*_{AB} of the square model of Koshland *et al.*³ will have as many different values as there are quaternary states. Such a feature, when added to the sequential model of these authors, introduces asymmetry even when the subunits are identical.

Thus the conclusions reached by Weber, although valid for systems that are properly described by simple sequential mechanisms, are not necessarily true for all systems. As they lack such general-

ity, it remains uncertain that the presence of dissimilar subunits in the haemoglobin molecule is a necessary condition for asymmetric oxygen binding. Although few would argue that haemoglobin can be properly described by a simple two-state model, the occurrence of alterations in quaternary structure, in addition to sequential changes in the tertiary structures of the subunits, seems very likely.

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WEBER REPLIES—Any phenomenological description of oxygen binding by haemoglobin can accommodate asymmetric titration curves if the variation allowed to the binding constants is sufficiently large. In the two-states description negative, zero or positive binding asymmetry may be accommodated according to whether *Lc*² is, respectively, smaller than, equal to or greater than unity. But, how are *L* and *c* chosen? Certainly not by appeal to any principles that involve the physical characteristics of the system, but because they are the best values in the fitting of experimental data. If Curie's principle¹—as I interpret it—is correct it follows that *Lc*² ≠ 1 shows the existence of asymmetric causes. Failure of Curie's principle would require the observation (not simply the postulation) of systems of identical subunits showing asymmetric binding. Until this is found, I prefer to believe that an asymmetric cause (difference in the diagonal interactions of the subunits) underlies the asymmetric binding by haemoglobin.

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