a semi-minor axis, b, equal to the fully stretched tail length, 16.7 Å, the semi-major axis, a, is then determined to be 23.4 Å using 350 Å^3 as the steric volume of the hydrocarbon tail. The dry head group of the monomer would then occupy a volume equal to $V_H = 402 - 350 = 52$ Å^3, which corresponds to a sphere of diameter $l = 4.6$ Å. Thus, the outer layer of the micelle can be assumed to be a shell of thickness l, consisting of 78 head groups plus solvent molecules. Such a model would predict that there are ~9 water molecules in the outer layer for every one of the head group. The radius of gyration calculated from this model is $R_g = 15.2 \pm 0.2$ Å, in agreement with the experimental value. If we now allow for one solvent molecule per monomer in the core, then, taking the volume of the water molecule to be 30 Å^3, a similar calculation would give $R_g = 15.8$ Å, which disagrees with the experimental value[2].

Finally, systematic measurement of the cross-section in concentrated LDS solution[4] allowed us to fit our model equation (1) consistently well. $S(q\sigma)$, thus extracted, unambiguously gives $\sigma = 2(R + l)$, where R is calculated from the volume of a close-packed dry core and l can be anywhere in the range 4.6–5.6 Å, depending on slight variations of the micellar surface charges.

S. H. CHEN
Department of Nuclear Engineering,
Massachusetts Institute of Technology,
Cambridge,
Massachusetts 02139, USA

K. DILL
School of Pharmacy,
Department of Pharmaceutical Chemistry,
University of California,
San Francisco, California 94143, USA

1. Dill, K. A. *et al. Nature* **309**, 42-45 (1984).
2. Bendedouch, D., Chen, S. H. & Koehler, W. C. *J. phys. Chem.* **87**, 153-159 (1983).
3. Chen, S. H. & Lin, T. L. in *Methods of Experimental Physics—Neutron Scattering Vol. II* (eds Sköld, K. & Price, D. L.) Ch. 16 (Academic, New York, 1985).
4. Bendedouch, D., Chen, S. H. & Koehler, W. C. *J. phys. Chem.* **87**, 2621-2628 (1983).

Species variation in sensitivity of general anaesthesia to high pressure

BASED largely on the coincidence in crustacea of lack of pressure reversal of anaesthesia, insensitivity to strychnine and absence of glycine, and on similarities between strychnine- and high pressure-induced convulsions, Smith *et al.*[1] have proposed a hypothesis of general anaesthesia related to glycine receptors. Such an interpretation can be challenged on several grounds.

First, the authors' work[1] shows that the relative potencies of a series of general anaesthetics remain constant across a number of species, whether or not they have glycine receptors. Second, binding of strychnine at the glycine receptor in the mammalian central nervous system is unaffected by general anaesthetics[2]. Third, there is abundant neurophysiological data on the lack of interaction between anaesthetics and glycine. Short-latency, glycine-mediated synaptic inhibitions are not enhanced by general anaesthetics, whereas long-latency γ-aminobutyric acid (GABA)-mediated inhibitions are increased in both amplitude and duration[3]. In a variety of *in vivo* and *in vitro* experimental protocols, the inhibitory effects of glycine are not affected by anaesthetic doses that enhance GABA actions[4-6].

As most of the above experiments have concentrated on barbiturates, we have recently examined the effects of two other clinically useful anaesthetics on the mammalian CNS[7,8]. We found no evidence to support the view that perturbation of the glycine system is a common property of general anaesthetics. The dissociative anaesthetic ketamine did not affect responses of neurones to glycine or GABA but did selectively block activation of the neurones by the glutamate analogue, *N*-methylaspartate[7]; correlated with this, ketamine had no clear effect on synaptic inhibitions but did reduce polysynaptic reflexes[8]. When tested on spinal reflexes and inhibitions in decerebrate cats[8], the steroid anaesthetic, alphaxalone, clearly enhanced long-latency GABA-mediated inhibitions but had no effect on short-latency inhibitions, thought on other grounds to be mediated by glycine[9].

It seems, therefore, that general anaesthetics do not influence the operation of glycinergic synapses. It remains possible that an action on the glycine system underlies the effects of high pressure on vertebrates. The absence of pressure-induced hyperactivity in crustacea[1], presumably an evolutionary advantage to subaquatic species, might support this view. In this case, the present models, which assume that pressure and anaesthetics act at the same site, would need to be re-appraised.

DAVID LODGE
Department of Physiology,
The Royal Veterinary College,
University of London,
Royal College Street,
London NW1 0TU, UK

1. Smith, E. B. *et al. Nature* **311**, 56-57 (1984).
2. Snyder, S. H. & Enna, S. J. *Adv. biochem. Psychopharmac.* **14**, 81-91 (1975).
3. Weakley, J. N. *et al. Archs int. Pharmacodyn.* **171**, 385 (1968).
4. Barker, J. L. & Ransom, B. R. *J. Physiol., Lond.* **280**, 355-372 (1978).
5. Evans, R. H. & Hill, R. G. *Experientia* **34**, 1325 (1978).
6. Lodge, D. & Curtis, D. R. *Neurosci. Lett.* **8**, 125-129 (1978).
7. Anis, N. A. *et al. Br. J. Pharmac.* **79**, 565-575 (1983).
8. Lodge, D. & Anis, N. A. *Br. J. Anaesth.* **56**, 1143-1151 (1984).
9. Curtis, D. R. & Johnston, G. A. R. *Ergeon. Physiol.* **69**, 97-184 (1974).

SMITH *ET AL.* REPLY—The eloquent points raised by Lodge are both valid and stimulating. As stated in our paper[1], the finding that the pressure reversal of anaesthesia appears to be linked to strychnine sensitivity can be interpreted in more than one way.

If the extended unitary hypothesis (which presupposes that pressure and all general anaesthetics share a common mechanism) is accepted[2], our observations point to strychnine-sensitive processes as an important element in the 'loss of consciousness' in vertebrates. The most widely accepted view would then implicate glycinergic processes. Implicit in this view is that the loss of swimming activity in shrimps, at comparable anaesthetic doses, must arise via a different mechanism. Indeed, our additional finding that shrimps appear to have a dose-response curve that is less steep than that observed for anaesthesia in vertebrates would be consistent with this view.

However, we cannot exclude the possibility that the pressure reversal of anaesthesia could arise from an independent action of pressure resulting in a physiological rather than a pharmacological antagonism of anaesthesia; this is compatible with the view of Lodge, who quite rightly points out that there is no direct evidence that general anaesthetics potentiate the action of glycine-mediated inhibition, although it has been demonstrated that the anaesthetics ketamine and althesin confer substantial protection against strychnine[3]. However, if Lodge's work, at the level of the spinal cord, is considered relevant to loss of consciousness which results from the action of anaesthetics at higher levels within the neuro-axis, then the striking diversity of responses to different agents must lead to a rejection of the unitary hypothesis. This implies that different anaesthetics can act by different mechanisms. Any rejection of such a powerful generalization—the unitary hypothesis—that has provided the key to interpreting the common effects of a disparate group of anaesthetic substances, will require an unequivocal body of evidence.

Whichever interpretation of our results is correct, both are incompatible with present thinking—that general anaesthetics act by inducing a general perturbation of cellular membranes—and we believe that models involving more specific molecular interactions are more appropriate.

E. B. SMITH
F. BOWSER-RILEY
S. DANIELS
I. T. DUNBAR
C. B. HARRISON
W. D. M. PATON
Physical Chemistry Laboratory,
University of Oxford,
South Parks Road,
Oxford OX1 3QZ, UK

1. Smith, E. B. *et al. Nature* **311**, 56-67 (1984).
2. Miller, J. C. & Miller, K. W. in *Physiological and Pharmacological Biochemistry* Vol. 12 (ed. Blaschko, H. K. F.) 33-75 (Butterworths, London, 1975).
3. Wardley-Smith, B., Little, H. J. & Halsey, M. J. *Br. J. Anaesth.* **55**, 235-236 (1983).