Calcium control and $InsP_4$

SIR — In their paper on page 162 of this issue[1], Bird *et al.* claim to demonstrate that inositol trisphosphate ($Ins(1,4,5)P_3$) alone can account for calcium-ion entry in stimulated cells, with no need for a contribution from the tetrakisphosphate $Ins(1,3,4,5)P_4$. But the reported experiments do not actually address the issue of the physiological role of $Ins(1,3,4,5)P_4$ *in vivo*. What the authors do show is that introducing high doses of $Ins(1,4,5)P_3$ or $Ins(2,4,5)P_3$ as a bolus into cells can cause calcium-ion entry, an observation that has been made by others in several experimental systems (see ref. 2 for review).

Under another experimental paradigm very similar to that of Bird *et al.*, $Ins(1,4,5)P_3$ did not cause calcium-ion entry, but needed help from $Ins(1,3,4,5)P_4$ (ref. 3). This phenomenon may, of course, be an artefact (an explanation implicit in the paper by Bird *et al.*), but if this is so, is it likely to be a quantitative distortion of an existing mechanism or a new phenomenon created *de novo* by experimental conditions?

Credulity in the latter alternative is stretched to the limit by the observation that the clear requirement for $Ins(1,3,4,5)P_4$ could not be substituted by $Ins(1,4,5)P_3$, $Ins(1,3,4)P_3$, $Ins(2,4,5)P_3$, $InsPS_3$, or $Ins(1,3,4,5,6)P_5$, all at concentrations five- or more-fold than the fully effective dose of $Ins(1,3,4,5)P_4$ (ref. 4), a pharmacology which matches an $InsP_4$-binding protein found in many tissues[5]. These data show clearly that $Ins(1,3,4,5)P_4$ can control calcium entry, and suggest that if this phenomenon is an artefact, it is one of degree only. Moreover, if, as Bird *et al.* claim, $(1,4,5,)P_3$ is responsible for everything in an intact cell *in vivo*, where is the selective pressure for $Ins(1,3,4,5)P_4$ (and its receptor) to evolve and remain in existence for hundreds of millions of years?

If experimental artefacts are indeed distorting the picture, I suggest that there is a more plausible alternative for their nature in the possibility that the receptors for $Ins(1,4,5)P_3$ and $Ins(1,3,4,5)P_4$ interact, and their dissociation causes calcium entry[2,6]. *In vivo*, this dissociation would be promoted by the ligands ($InsP_3$ and $InsP_4$), but any experimental manoeuvre that separates these two proteins will cause calcium entry irrespective of the presence of $Ins(1,3,4,5)P_4$. Thus one need propose only that various experimental regimes influence quantitatively the interaction between two allosteric proteins to reconcile the apparent contradictions.

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1. Bird, G. S. J., Rossier, M. F., Hughes, A. R., Shears, S. B., Armstrong, D. L. & Putney, J. W. Jr *Nature* **352**,162–165, (1991).
2. Irvine, R. F. *Bioessays* (in the press).
3. Morris, A. P., Gallacher, D. V. Irvine, R. F. & Petersen, O. H. *Nature* **330**, 653–655 (1987).
4. Changya, L., Gallacher, D. V., Irvine R. F., Potter, B. V. L. & Petersen, O. H. *J. Membr. Biol.* **109**, 85–93 (1989).
5. Theibert, A. B. *et al. Proc. natn. Acad. Sci. U.S.A.* **83**, 3165–3169 (1991).
6. Irvine, R F. *FEBS Lett.* **263**, 5–9 (1991).

Induced molecule self-organization

SIR — In his comment[1] in News and Views on our work on the encapsulation of anionic guests in inorganic host molecules, Mitchell wondered whether the vanadium oxide host shells we synthesized exist without the encapsulated species. In answer, we have no evidence that they do. We find the encapsulation is due to a new type of self-organization process leading to unusual weak repulsive interactions in molecular species and to novel topological structures.

With the self-assembly process, almost any hollow sphere (cluster shell) can be generated, depending on size, shape and charge of the encapsulated anionic species X (the template), by using square-pyramids (of OVO_4; Fig. 1) as the repeating building block. The central anion is responsible for the architecture of the system, determining the number of linked units as well as their type of linking. A new and typical example is $[H(VO)_{18}O_{26}(NO_3)]^{10-}$ (Fig. 2) with an ellipsoidal structure, which has NO_3^- as the encapsulated ion.

Characteristic of this type of species is the rather large separation between negatively charged centres (here O . . . O) due to very weak (repulsive) forces, never before reported. The weak repulsive interactions can also allow unusually high 'coordination numbers' as high as 24 (see below; the highest known conventional coordination number is 12)[2]. These types of weak interactions are probably important in the poorly understood mechanism of anion exchange through membranes which occurs very rapidly.

Interesting topological considerations should also be mentioned. By linking 18

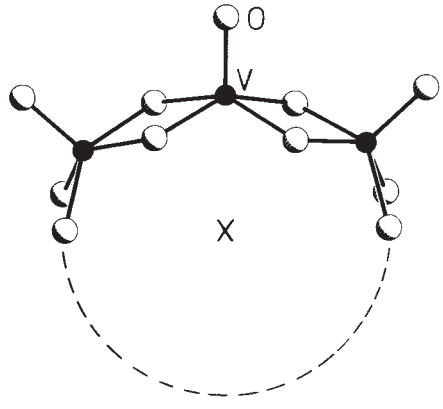

FIG. 1 Building molecular shells from OVO_4 tetrahedra.

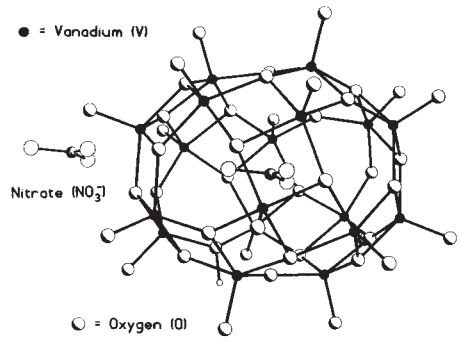

FIG. 2 The new inclusion species $[H(VO)_{18}O_{26}(NO_3)]^{10-}$, prepared by R. Rohlfing in our group. Notable in the structure is the large distance between the O atoms in shell and in the central anion, 280 picometres. With a more highly charged anion, such as CO_3^{2-}, the interaction with the V^{n+} centres in the shell is increased and the separation becomes less.

tetragonal OVO_4 pyramids, spherical hollow spheres, $[(VO)_{18}O_{24}(X)]^{n-}$, spanned by 24 O atoms can be generated[3]. Depending on the anion X the O atoms of the cluster shell with the same stoichiometry can either adapt the form of one of the 13 archimedean solids (the rhombicuboctahedron with 18 squares and 8 triangles) or the mysterious so-called fourteenth archimedean solid (or pseudo-rhombicuboctahedron). These cluster shells can be transformed into each other by rotating the upper hemisphere of the cluster by 45°.

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1. Mitchell, P. C. H. *Nature* **348**, 15–16 (1990).
2. Wells, A. F. *Structural Inorganic Chemistry* (Clarendon, Oxford, 1989).
3. Müller, A., Penk, M., Rohlfing, R., Krickemeyer, E. & Döring, J. *Angew. Chem. Int. Edn. Eng.* **29**, 926–927 (1990).

SIR — Although we were flattered to have our research cited in Mitchell's News and Views article[1] on new guest–host chemistry, the article may have left the mistaken impression that purely inorganic analogues of organic crowns and cryptands were hitherto unknown.

Inorganic crowns and cryptands have been investigated for at least 15 years. Interest was sparked initially by the biological activity of the sodium cryptate $[NaW_{21}Sb_9O_{86}]^{18-}$ (ref. 2), a species that has subsequently achieved notoriety as HPA23 in AIDS therapy. Larger, crown-shaped cryptands have been reported more recently: $[P_5W_{30}O_{110}]^{15-}$ (ref. 3); $[As_4W_{40}O_{140}]^{28-}$ (ref. 4) and $[P_8W_{48}O_{184}]^{40-}$ (ref. 5). The last two species have multiple cation binding sites in the interiors of their crown structures; the $[As_4W_{40}O_{140}]^{28-}$ cryptand even displays allosteric binding effects.

Inorganic complexes containing encapsulated anions were first characterized by Keggin[6] in 1933. Today, the number of inor-

ganic 'guest–host' complexes known to contain anions is vast[7]. Unlike the cation crown complexes just described, most of these anion complexes contain nonexchangeable ions entrapped within polyhedral cages. The $PMo_{12}O_{40}^{3-}$ ion, for example, has been described[8] as a clathrated PO_4^{3-} ion. A new type of anion complex was recently prepared, however, in which anions like Cl^- and NO_3^- are bonded to shallow basket-like inorganic frameworks[9]. These may turn out to be true guest–host as opposed to hostage–host complexes.

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MITCHELL REPLIES — I omitted heteropolys from my article on anions as guests in inorganic hosts because of space limitations and because the heteropolys are so well known. Nevertheless, my reference to the paper by Day *et al.*[10] provided a lead-in, although I ought to have added Michael Pope's excellent monograph[7].

The particular interest of Müller's work, and my concern, was the encapsulation of guest anions which were weakly bound and entities chemically distinct from the host framework. Whether a particular anion is a guest, or part of the overall structure, arises with a number of heteropolys. For the phosphomolybdates and tungstates, $[PM_{12}O_{40}]^{3-}$, the question is whether the oxygens of the phosphate are part of the framework — that is, whether the phosphate anion is a distinct entity. Clark and Hall, who solved the structure[11], do indeed refer to the phosphate as a guest species for M = Mo but not for M = W. With regard to 'anion complexes', Heinrich *et al.*[9] did not use the term 'guest–host', referring to their compounds as aggregates.

Let us agree about the questions to be asked. Which came first, the host or the guest (is the guest a template)? How far is the encapsulation of the anionic guest dependent on a structural match with the host cavity (molecular recognition)? Is the host stable without the guest? And finally, particularly important for applications, can we move the guest out of the host cavity (or is it really a 'hostage')? My article and this correspondence have provided a perspective on inorganic guest–host complexes encompassing a number of apparently disparate structural types and some familiar compounds such as the heteropolys which had not been thought of in this way. We can now look forward to developments and applications.

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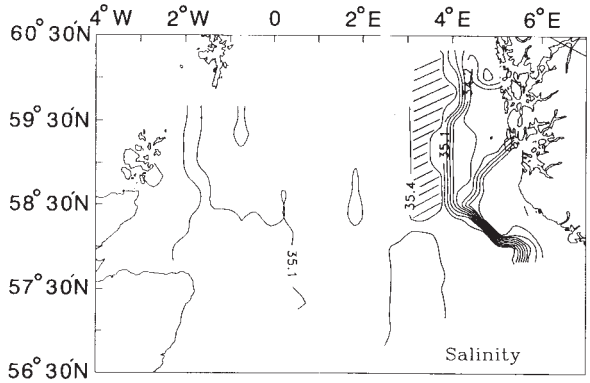
1. Mitchell, P. C. H. *Nature* **348**, 15–16 (1990).
2. Fischer, J., Ricard, L. & Weiss, R. *J. Am. Chem. Soc.* **98**, 3050–3052 (1976).
3. Alizadeh, M. H., Harmalker, S. P., Jeannin, Y., Martin-Frére, J. & Pope M. T. *J. Am. Chem. Soc.* **107**, 2662–2669 (1985).
4. Robert, F., Leyrie, M., Hervé, G. Tézé, A. & Jeannin, Y. *Inorg. Chem.* **19**, 1746–1752 (1980).
5. Content, R. & Tézé, A. *Inorg. Chem.* **24**, 4610–4614 (1985).
6. Keggin, J. F. *Nature* **131**, 908–909 (1933).
7. Pope, M. T. *Heropoly and Isopoly Oxometalates* (Springer, Berlin, 1983).
8. Boeyens, J. C. A., McDougal, G. J. & Smit, J. V. R. *J. Solid State Chem.* **18**, 191–199 (1976).
9. Heinrich, D. D., Folting, K., Streib, W. E., Huffman, J. C. & Christou, G. *J. Chem. Soc., Chem. Commun.* 1411–1413 (1989).
10. Day, V. W., Klemperer, W. G. & Yaghi, O. M. *J. Am. Chem. Soc.* **111**, 5959–5961 (1989).
11. Clark, C. J. & Hall, D. *Acta Cryst.* B**32**, 1545–1547 (1976).

High salinity in the North Sea

SIR — The salinity of sea water in the north-east Atlantic has been documented since 1902; several large-scale fluctuations have been detected. During the mid 1970s the salinity declined to low levels not encountered since 1908 (ref. 1), increasing to more usual levels during the 1980s. Atlantic water flows into the northern North Sea between the Orkney and Shetland isles, and between Shetland and Norway, and a corresponding outflow from the North Sea occurs along with Norwegian coast. Changes in salinity in the nothern North Sea during the 1970s paralleled those in the North Atlantic[2], and were correlated with changes in fish stocks and plankton composition[3,4]. We now report the discovery in January 1990 of an inflow of water of exceptionally high salinity into the northern North Sea.



Distribution of salinity at 5-m depth in the northern North Sea in January 1990 drawn from data collected at 180-s intervals throughout the survey. Shaded area, water of salinity greater than 35.40.

We conducted a survey in the northern North Sea from the vessel *British Enterprise III*. Salinity and temperature at a depth of 5 m were recorded from sensors towed alongside the ship, and water currents measured with a multiple beam echo-sounding device (acoustic doppler current profiler). The highest recorded salinities (greater than 35.45, maximum value 35.471) were found in a strip approximately 20-km wide parallel to the Norwegian coast, corresponding to the area of inflow from the Atlantic (see figure). The water currents in the high salinity region were southerly, whereas 10–20 km to the east in the lower salinity (33.5–35.0) Norwegian coastal water, the flow was northerly.

The maximum salinity was higher than any value measured in the North Sea by the Marine Laboratory, Aberdeen, since records began in 1920 (previously recorded maximum: 35.390 in August 1968). Salinities greater than 35.40 have been recorded on a number of occasions during this period in the Atlantic between Shetland and the Faroe Isles and at the edge of the continental shelf off the northwest of Scotland (in 1929, 1939, 1959, 1969, 1971, 1983–85 and 1989), but none has exceeded 35.47. It therefore seems that the salinity of the water entering the North Sea in January 1990 was perhaps the highest this century.

The late 1980s were characterized by an increasing frequency of westerly weather patterns in the North Atlantic following a minimum in the 1970s (ref. 4). It is possible that the high salinity of the water entering the North Sea in 1990 signals changes in current patterns in the Atlantic Ocean related to the changing weather conditions, bringing water from more southerly latitudes into the north-eastern Atlantic. Abundance of plankton in the northern North Sea decreased during the 1970s and has increased since 1980 (ref. 5), in parallel with the increasing incidence of westerly weather[4]. There have also been latitudinal fluctuations in the spawning of herring and sprat[3] and changes in the breeding success of some sea birds over similar timescales[4], suggesting a link between North Sea ecology and climate changes in the North Atlantic. The exceptionally high salinity in 1990 may signal the start of further changes.

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1. Dooley, H. D., Martin, J. H. A. & Ellett, D. J. *Rapp. P.-v. Reun. Cons. Int. Explor. Mer* **185**, 179–187 (1984).
2. Dickson, R. R., Jones, S. R. & Lee, A. J. *ICES CM1984/Gen: 8* (1984).
3. Corten, A. *Neth. J. Sea Res.* **25**, 227–235 (1990).
4. Aebischer, N. J., Coulson, J. C. & Colebrook, J. M. *Nature* **347**, 753–755 (1990).
5. Colebrook, J. M. *Hydrobiologia* **142**, 309–325 (1986).