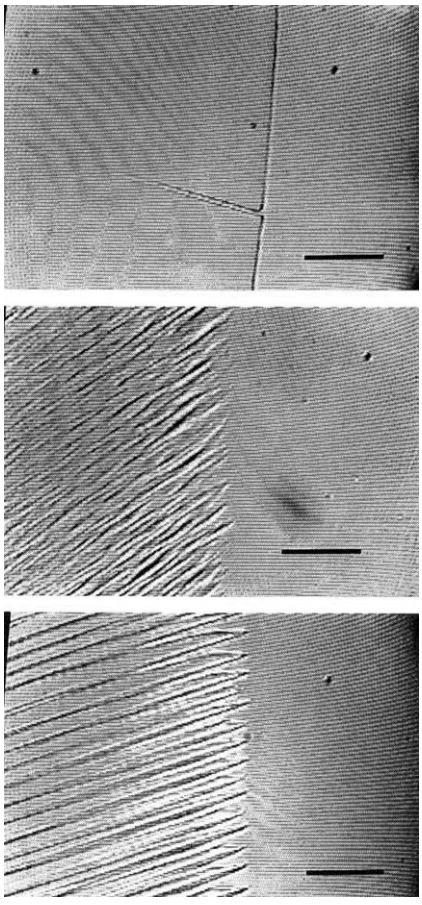

Freezing is from left to right; isotherms are vertical; scale bar, 50 um. See text for details.

dent of crystallographic orientation. The centre panel shows the spicular ice structure that forms in a 0.71 mM solution (a typical physiological concentration in fish) of sea raven antifreeze proteins in distilled water. This spicular structure is thought to result from the unique ability of antifreeze proteins to bind to the nonbasal planes of ice crystals and inhibit growth on these planes. This property has not been observed in other protein types[3].

The lower panel obtained for a solution of 0.71 mM rattlesnake venom lectin in distilled water clearly shows faceted ice crystals. It is obvious that this ice-crystal morphology is not caused by the phenomenon of freezing interface instability, which is associated with rejection of solutes by ice, colligative depression of freezing temperature and constitutional supercooling, because the inorganic salt and the sugar controls produced planar freezing interfaces at much higher concentrations. Furthermore, the cellular and dendritic structures caused by interface instability are smooth and non-faceted, indicating a rough interface on an atomic or molecular scale[7]. The ice crystals that form in the presence of the lectins are faceted, indicating that the ice-crystal facet seen is smooth on the atomic scale and is the slowest growing ice-crystal plane.

The results suggest that the lectins inhibit ice growth along this plane, a property thought to be unique to antifreeze proteins. The mechanism resulting in this effect is probably similar to that of the antifreeze proteins. The fact that only one crystallographic orientation is affected by the lectins, whereas the antifreeze proteins seem to affect all nonbasal planes, may explain why we did not observe any depression in freezing temperatures with lectins. However, if the ability to inhibit ice growth along particular crystallographic planes is common among all C-type lectin CRDs, then the CRDs are good prototype structures from which an AFP could have evolved. This may explain the evolution of type II AFP in three divergent fish groups. Furthermore, as the snake venom lectin, a protein that is not an antifreeze, appears to have the ability to modify the structure of ice crystals by interacting with specific ice-crystal planes, this property may be more common to proteins than had previously been thought.

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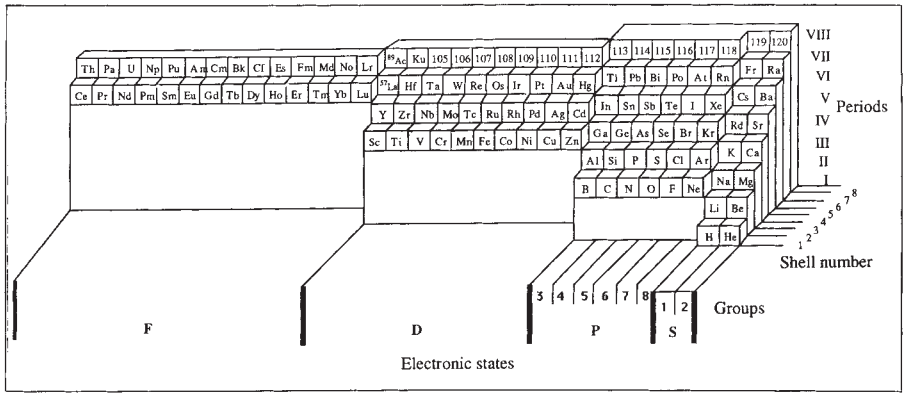
A three-dimensional periodic table

SIR — More than 50 years ago, Linus Pauling suggested his classic idea of introducing another index, namely electronegativity of atoms, to the periodic table[1]. Recently, Allen[2] introduced a third index into the periodic table, configuration energy (CE), and demonstrated its usefulness. As Maddox[3] puts it, the question of whether "...CE resolves enough of the inconsistencies in the periodic table to win the hearts and minds of men with an interest in these matters" still remains to be answered.

We propose a genuinely three-dimensional periodic table, based on quantum mechanics and Hund's rules (the latter proposed as early as 1926; ref. 4), namely, that the term of largest S and among these the term of largest L is lowest in energy. In this case the number of chemical elements in periods is the following: 2, 2, 8, 8, 18, 18, 32, 32, ...

Therefore, for instance, in period number 1 only hydrogen and helium are present, the second period consists of only Li and Be, the third has eight elements from B to Mg, the fourth again contains 8 elements from Al to Ca, and so on.

The three-dimensional picture, in which the third dimension is periodic number $(n+1)$, is shown in the figure. All the elements on the same level have equal $n+1$. Such subdivision seems absolutely natural. The only obstacle is tradition. Since Mendeleev, every period begins with s-electrons of the previous level, so that it includes electrons from two levels, that is, s-electrons from the level n–1, and all the rest of the electrons from the level n. This mixing, from the point of view of quantum mechanics, is confusing.



Periods correspond to passing from one chemical element to another one at the same height from left to right. Group numbers are traditional ones. Two elements, La and Ac, are placed according to their traditional places, although they

could also be placed in the left-most position.

When projecting in the x-direction (number of shell), the three-dimensional table degenerates into two dimensions. When projecting down along the z-axis (axis of periods), we get a two-dimensional realization of Hund's rule.

In conclusion, we believe that our three-dimensional representation is a useful tool for visualizing properties of chemical elements and is in complete accord with quantum mechanics.

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Eradication of rabies in Europe

SIR — To complete the story described by Brochier *et al.*[1], we would like to explain what had already been done in Europe since 1978, when oral vaccination of foxes against rabies began, as well as to mention a recent development concerning improvement of vaccinal strains.

Investigations of oral immunization of foxes began in Switzerland about 20 years ago, after US and Canadian workers had demonstrated that orally administered attenuated rabies strain SAD could immunize foxes[2]. By 1978, a system was ready for field use, consisting of 1.8 ml of SAD (Bern) at a titre of 10^7 $TCID_{50}$ per ml (where TCID is tissue culture infectious dose), included in small crushable plastic containers (blisters) fixed under the scalp of chicken heads. The baits were manually distributed.

After a first successful trial on a 335-km^2 area, vaccination zones were gradually extended over the Swiss midlands and finally the Jura mountains bordering France. One after the other, the infected regions were freed from rabies by immunizing their fox populations through the distribution of 12–15 vaccine baits per km^2. The epidemiological effect of vaccination was most dramatically demonstrated in eastern Switzerland, where high rabies prevalence lasting for 18 years came to a sudden end after only three vaccination campaigns covering the whole region[3].

Five years after the first trial in Switzerland, Germany began to use the same method with SAD B19, a derivative of the Swiss vaccine strain. In 1985 the Germans developed an 'artificial bait' based on tallow and fish meal that could be mechanically produced[4], which considerably simplified the preparation, storage and distribution of the vaccine.

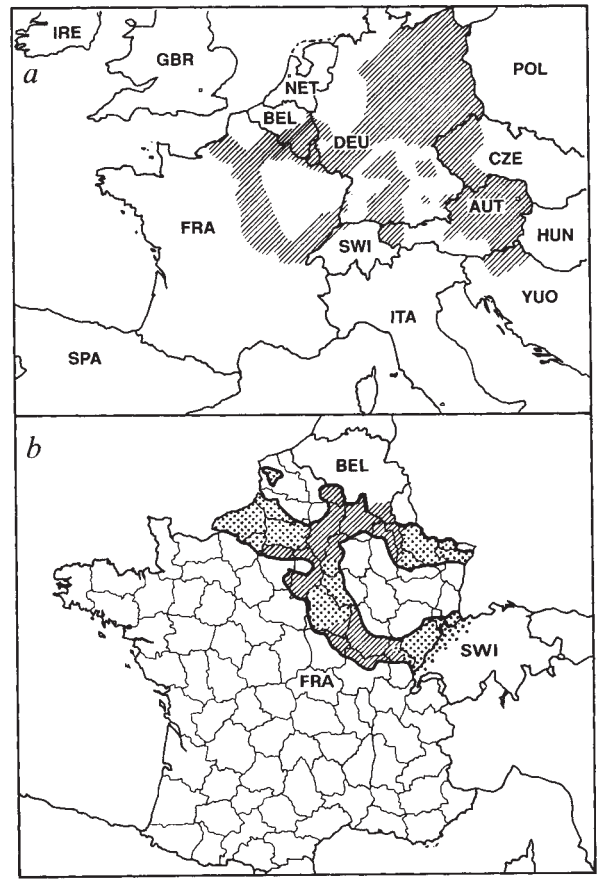
After 1983, field trials were begun in several other European countries and in Canada. In Europe alone, a total of around 300,000 km^2 was treated in the spring and autumn of 1991 (*a* in the figure) representing about 9 million baits dropped by planes and helicopters or distributed by hand, leading to a consistent reduction in the number of cases of rabies.

Although poorly virulent by intramuscular or oral inoculation routes, fixed strains used for vaccination of foxes exhibited residual pathogenicity, at least for rodents[5], and this was a matter of concern for the authorities.

Previous work on the molecular basis of rabies virulence has shown that avirulent mutants could be isolated from virulent strains, using appropriate monoclonal antibodies[6]. We isolated several of those antibodies that neutralize SAD (Bern) or derivatives but do not neutralize mutants with a substitution in position 333 of the viral glycoprotein, a mutation which abolishes viral virulence for adult mice[7–9]. One of those monoclonals was used to select SAG1, a mutant of SAD (Bern) which had a serine in position 333 instead of an arginine and, as expected on the basis of previous results, was avirulent for adult mice, whatever the dose and the route of inoculation. When administered orally or by the mucosal route it also failed to induce any pathology in foxes, in non-target carnivora (badgers, ferrets, polecats), in crows and birds of prey, and in several species of wild rodents[10].

SAG1 strain was found to be as immunogenic as the parental strain: 100% survival was achieved for doses equal to or higher than 10^6 plaque-forming units given orally to foxes. Lower doses still induced some protection. This mutant was found to be fairly stable and did not revert to virulence after three successive intracerebral inoculations of suckling mice, unlike a similar avirulent mutant (Arg→Ser) isolated from another fixed strain of rabies, CVS (ref. 8). The reason for this difference is not clear, but it could be due either to a lower mutation rate of the SAD (Bern) polymerase or to a lower selective advantage of the revertants in this genetic background. More recently, a further step toward complete safety of the vaccine was accomplished by the selection of a double avirulent mutant, SAG2, which has two mutations in the codon of Arg 333. This mutant is under trial at present.

In France, the SAD B19 has gradually



Oral vaccination of foxes against rabies. *a*, In Europe. Hatched area; vaccination campaigns in 1991 (subject to a few possible modifications not yet registered by WHO). (Adapted from *The work of WHO 1990–1991: Biennial Report of the Director General* by permission of the World Health Organisation, which retains the copyright.) *b*, In France (FRA), Belgium (BEL) and Switzerland (SWI). Dotted area, vaccination with the Virbac vaccine; hatched area, vaccination with the Rhône–Mérieux vaccine.

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