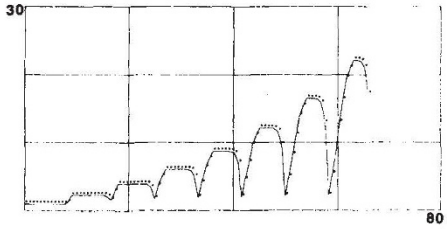

Simulation of the filling of a conventional 8 × 12 well microtitre plate. The wells are filled sequentially from left to right. Upon the addition of a unit volume of anti-IgE antiserum (having a concentration which is halved at each step), 0.001 volume units are spread equally to neighbouring wells as described in the text. Abscissa: $-ln(2^{-n})$, where n is the dilution step number. Ordinate: ratio of actual versus expected (i.e. in absence of contamination) concentration of anti-IgE.

contamination provoked by filling a given well will affect both its neighbours in adjacent columns as well as in adjacent rows. When filling the wells in a sequential order, wells in adjacent rows represent a jump by several orders of magnitude in the dilution series. Consequently, possible contamination will not merely result in a local blurring of the titration profile. To demonstrate that one expects oscillations to occur in the measured profile, we simulated the filling of a conventional 8 × 12 well microtitre plate. Using a simple model, in which upon filling a well at position (i,j), a small fraction of its contents is spread out to its immediate neighbours having plate coordinates $(i\pm1,j\pm1)$, periodicities are observed in the concentration of effector molecules (anti IgE). This is illustrated in the figure which shows the ratio of actual to expected concentration of effector molecules at each dilution step using a 0.1 per cent contamination level.

Clearly, in view of this simulation, one cannot *a priori* rule out the possibility that the periodicity in degranulation observed by Davenas *et al.* is due to a contamination effect. In particular, our contamination argument questions whether the wells at highest dilution are really devoid of any anti-IgE molecule. We therefore suggest a control experiment in which microtitre plates are substituted with individual test tubes. Alternatively, one could interlace on a given microtitre plate the anti-IgE antiserum dilution and the control anti-IgE dilution series.

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SIR—Water has been the centre of many controversies during the past 20 years or so. In particular, scientists have repeatedly proposed unusual properties for this 'universal' biological solvent. The case of 'super water' involving 'high tech' probing systems such as (15 years ago), nuclear magnetic resonancing was used to demonstrate that water could mediate special long-distance interactions. This has been proved to be due to a tricky artefact.

In the present case, I am puzzled by the fact that there has been no control of impurities (for instance by atomic absorption or neutron activation). In particular, the need for strong agitation (which is contradictory to the 'memory' hypothesis) suggests that test tubes might be involved. It seems worth recalling the experiments by Sternweis and Gilman, who have shown that the well-known fluoride effect no longer occurs when experiments are performed with pure water, in the absence of traces of aluminium[1]. Indeed, they have shown that F^- is able to extract Al^{3+} from the glass surface, generating AlF_4^- which is responsible for the effects[1,2]. Since it is well known that antibodies strongly (and often specifically) interact with surfaces, it is possible that they extract some ion (or other contaminant molecule), which in turn acts as a trigger for further extraction (in the absence of antibody). This would account for the requirement of strong agitation.

Proper control protocols should be performed before the generally efficient physicochemical laws are broken.

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1. Sternweis, P.C. & Gilman, A.G. *Proc. natn Acad. Sci. U.S.A.* **79**, 4888–4891 (1982).
2. Bigay, J. *et al. EMBO J.* **6**, 2907–2913 (1987).

SIR—In the leading article accompanying the article on an inexplicable observation about basophil degranulation by very dilute antiserum against IgE, you invite the vigilant reader to pick holes in the reported work. One obvious flaw can be seen when looking at the standard errors (s.e.) given in Table 1 of the article. According to the legend to Table 1 and to Fig. 1, the data represent the mean ± s.e. of basophil number actually counted in triplicate in a haemocytometer. The mean counts range from 27.7 to 106.7 and the s.e. are with two exceptions below 3 (2.6 per cent of the mean in average). However, according to the Poisson distribution, the s.e. of counting randomly distributed events, like cells in a haemocytometer, is equal to the square root of (mean counts/number of countings), that is, it ranges from 3 to 6 (11 per cent to 6 per cent of the means) for the triplicate counts given in Table 1. It is very unlikely that the observed s.e. of the triplicates are so much below the expected s.e. of counting.

The reason for this discrepancy is not clear. It is, however, unlikely that the s.e. given in Table 1 are the result of an erroneous calculation, as the data of 4 triplicate experiments (Tyrode's–HSA) are actually displayed in Table 1, and again the s.e. of the experimental triplicates (lower than 1 per cent) are much below the s.e. expected already from counting 3×3 times 100 cells (3.3 per cent). The only way to explain the discrepancy would be to assume that actually more basophils have been counted and that the indicated numbers are somehow calculated values. However, in order to reach the average s.e. of 2.6 per cent as published in Table 1, at least 500 basophils would have to be counted in each sample.

In conclusion, the data in Table 1 are very unlikely to be derived from flawless experimental results and are certainly not the kind of data one would need to "throw away our intellectual heritage"[1].

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SIR—I find it rather curious that a scientific journal should be so wary of non-material real phenomena as to refuse to endorse the findings of the Benveniste group research on the effect of dilution on anti-IgE antiserum! Does *Nature* expect nature to accommodate academic disciplines in order to be vindicated?

Ignorance about such non-material energetic effects as those discovered and demonstrably utilized in human medicine since the early nineteenth century by Carl Hahnemann and his successors or, more recently, thore studied by Tesla, Morell and Popp in the field of physics, is hardly to the credit of a would-be authority on science; nor does it lend credence to *Nature*'s claim of reliable and impartial reporting of significant new research. Casting doubt on findings merely because they are inconvenient to established assumptions and patterns of speculation strikes me as a poor way of advancing scientific knowledge.

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SIR—The paper demonstrating that dilutions of anti-IgE must be vortexed rather than stirred in order to retain an imprint of the antibody on the solvent elucidates another long-standing question: how James Bond could distinguish Martinis that had been shaken or stirred.

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