Explanation of Benveniste

The following letters are triggered by an article by Davenas et al. (*Nature* **333**, 816–818; 1988).

SIR—The article stating that high dilutions of a protein (containing no protein molecules) are biologically active has all the traditional properties of homoeopathic claims: insufficient description of the methods used (what is the source of the 0.1 per cent human serum proteins in the diluent?), suggestive hearsay ("similar results were obtained in other laboratories (Toronto, preliminary results)") and wild statements with no data shown ("our results can be summarized as"; "we can confirm that").

This will turn out to be yet another case of artefacts (or worse) but the harm has already been done; worldwide recognition of this important paradigm of homoeopathy by a major scientific journal. The homoeopathic industry (supplying for example 15 per cent of all medicines in France) will not care about a short retraction in *Nature* (which will get much less attention in the popular press than the original claims).

Nature should have insisted on an independent confirmation of these results before and not after publication.

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SIR—Scientific belief belongs on a flat earth. There is no danger, no threat to science, in the restatement of the drug-diluent paradox — we need only apply the scientific method and then seek the verdict of experience.

In this way the inquiry by me and my colleagues reluctantly judged the placebo hypothesis redundant and homoeopathic dilutions active[1]. We agree with Benveniste's suggestion that his results relate to ours and we consider that both teams' research represents a development from homoeopathic science. Those who adopt the position that there is no such link are standing on ice so thin that even the weight of the author list will crack it — there are at least three homoeopathic doctors on it. It may be deep water but we must face the facts that homoeopathic physicians introduced and developed this area and that those wishing to examine this 'new' discovery will be well served by homoeopathic history. Fifty years before *Nature* had the courage to publish, Boyd began to demonstrate in a series of classical scientific experiments similar on/off effects up to 10^{-56} in biological assays such as mercuric chloride affecting starch diastase[2]. His methods were scientific but his results 'unbelievable' and so they joined a body of experience accumulated and ignored over the very same 200-year period that you invoke in your leading article (*Nature* **333,** 787; 1988). If we now rise to this challenge, we have nothing to lose. If we prove the observations wrong, we will have exposed homoeopathy as one of medical science's greatest misadventures — a folly so massive it will merit study in itself — why have 1 in 4 French doctors prescribed it[3]? If confirmed, we open up a vista of fundamental discovery and development. If this strikes at the heart of some current scientific models, that will be good for science. Right or wrong, such cross-fertilization has yielded benefit in the past. Some claim it laid the foundation of modern immunology[4], certainly tangible benefits to medicine accrued when homoeopaths proved pollen the cause of hay fever[5] and introduced low-dose allergen desensitization[6].

Moving from experiment to speculation, how are we to conceptualize memory in water? (If it *is* there, then the later stages of reaction with biological systems are easier to imagine with the models of pheromones, receptor sensitivity and biological amplification.) As a point of departure for criticism, I have visualized this first link in the chain as 'liquid snowflakes' modelled from the parent drug — one concentration but with unique biophysical information or pattern, 'seeded' in the new diluent in the reorganizing post-vibrational phase like liquid crystals growing in the order after chaos. But my snowflake analogy melts if we become fixed on the idea of 'shape' — best to say for now that the quality and nature of this ghost in the machine is unknown. And what of sinusoidal change in activity? Might the first generation antagonist grow in dominance through successive dilutions until at a critical threshold (concentration?) it itself becomes the template for a second generation agonist, the relative activity of these opposing patterns alternating in a sinusoidal curve as one continues the process of dilution/vibration — an agonist/antagonist template shift. In this respect, other work by Poitevin, Davenas and Benveniste[7] shows that certain dilutional points are not just ineffective as agonists but show an opposite inhibitory effect on the action of a second agonist. Similarly, we have shown clinically that although most patients reacting to a homoeopathic allergen dilution improve, unpredictably some aggravate and then improve while others only aggravate without subsequent improvement. In clinical practice, this raises questions of safety but in this context it suggests that Benveniste's agonist/antagonist curve may correlate with clinical responses. We are already exploring this possibility of *in vitro* and *in vivo* overlap.

This landscape is so unfamiliar that perhaps we cannot see around our favourite biochemical landmarks to the horizon beyond. Doctors already observe the altered nuclear spin of diseased tissue in their patients with magnetic resonance imaging. Now Franco Bruno of Citta Universitaria Rome has communicated (OMHI Conference, Rome, April 1988) apparent confirmation of earlier work[8] that the nuclear magnetic resonance spectra of homoeopathic dilutions are altered. Here may be glimpses of the territory we seek.

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SIR—Davenas *et al.* (*Nature* **333,** 816–818; 1988) demonstrate that degranulation can be triggered at dilutions of anti-IgE antiserum in which not a single anti-IgE molecule is expected. In view of the revolutionary nature of this finding it is of the utmost importance to discuss all possible controls. As we feel an important control experiment has been overlooked, we would like to draw attention to a potential problem in the interpretation of the data of Davenas *et al.*

As described in the 'Methods' section of their article, Davenas *et al.* use microtitre plates to assay the basophil degranulation. Interestingly, these authors observe a periodicity in the basophil degranulation as a function of anti-IgE antiserum dilution. One might wonder to what extent this observation can be accounted for by contaminating, for example by aerosol, the contents of adjacent wells when filling the microtitre plate. As a contamination at the level of a single anti-IgE molecule might in principle corrupt the relevance of the findings, this criticism must be taken seriously.

In a microtitre plate, a contamination between adjacent wells will not result in a simple blurring of the measured titration profile. As the wells in a microtitre plate are placed in a matrix organization, any