Chapter 24. Some questions without answers

Can we say that the results of the article of Nature of 1988 on high dilutions have been reproduced?

In other words, can we say that “Benveniste was right”?

The results of the experiments intended to confirm or not the effects of high dilutions (i.e. the study coordinated by M. Roberfroid and published in 2004 in *Inflammation Research*, the study of J. Benveniste and A. Spira of the *Comptes Rendus de l’Académie des sciences* of 1991and the study of Hirst *et al* published in *Nature* in 1993) remind us of the story about the glass being half full or half empty depending on an optimistic or pessimistic view point. For some people, there was certainly a statistically significant difference, but the results were incomplete: what happened to the smart “sinusoidal” curves that fascinated so much? For other people: “Undoubtedly, one did not really find the famous oscillations again, but nevertheless the experiments were overall statistically significant. It is thus the proof that there was a real effect of high dilutions!”

For those who attended the first experiments where high dilutions appeared to defy all controls (including blind tests), the results of these “reproductions” are – one must agree –disappointing at first sight. Indeed, the regular curves, the mountainous profiles on the horizon of a new world full of promises are now partially fainted in the mists of the large-scale blind experiments and their statistical analyses. The analyses now compare “noise vs. noise”. The fact that a statistically significant difference remains is however very disturbing. But it is also disturbing to observe that “blinding the experimenter” modifies the results. The only word which could qualify the state of mind of an observer who would try to be impartial is perplexity.

Contrary to appearances, reproducibility is a very difficult issue from an epistemic point of view. Indeed, what are we talking about? What is supposed to be reproduced? Is it necessary to reproduce the experiments of *Nature* of 1988 in their slightest details? We know that it is always practically impossible. J. Benveniste did not hesitate to raise methodological differences when experiments performed by other teams were negative. When the observed results fitted with the “expected” results, this last one was prone to see on the contrary a confirmation of his own results. In this case, the methodological differences ceased to be a problem. It it must be recognized that a “positive” experiment does not have the same status as a “negative” one. But, somewhere

in the universe, is there a big book which lists all possible experiments and indicates if they must be considered as "positive" or "negative"? In fact, it is the reading grid of the scientists which decides this. As a consequence, the race for the "crucial experiment" does not make sense.

Moreover, a study such as the one of *Nature* of 1988 has a scientific interest only if the result can be generalized and is not limited to a unique experimental model. We cannot blame researchers for not having tried to reproduce it literally but to have verified if this claim was not restricted to basophils by using experimental models that they knew well.

Nevertheless, one must be cautious because there are many discoveries in the history of science that are accepted today and which, in those days, had difficulties being recognized because there were issues to reproduce them. We can quote the decomposition of colours by Newton's prism or the measure of the electrostatic forces using Coulomb's torsion balance. On the contrary, we can also evoke experiments which were reproduced those days by other scientists and which are today considered as errors. Thus, the experiments that "evidenced" the N-rays of Blondlot were reproduced by some laboratories at the beginning of the 20th century. In spite of these reproductions, this "discovery" is now a chapter of the history of the sciences intended to illustrate the auto-illusion of some scientists.

The answer to the initial question of this part is thus: in blind controlled conditions, statistically significant variations of the counts of basophils in the presence of high dilutions were reported after 1988 in other laboratories. It is an important point.

What kind of "memory" are we talking about?

The compounds which are highly diluted in the experiments are often complex mixtures. Thus, *Apis mellifica* is made of whole bee macerated in alcohol; *Lung-histamine* is prepared from an extract of lung of guinea pig after an allergic shock. Even anti-IgE antiserum contains not only anti-IgE immunoglobulins but also numerous constituents of plasma. Furthermore, a molecule such as anti-IgE is a huge protein. If water has a "memory", it should keep the "trace" not only of the molecule involved in the experiment but also those of all other dissolved molecules. Furthermore, when one uses solutions containing thousands of different molecules, as for example in an extract of crushed bee, how the "memory" of these numerous molecules with all their details would be stored? How do these various "traces" not interfere?

We do not have an answer to this question (assuming that this question has a meaning and is relevant). It is often said that water is poorly known and that

there is no explanation on the liquid state of water at usual temperature. One can only subscribe to this assertion, but one must recognize at the same time that this does not prove that "memory of water" exists. To explain the properties of high dilutions, J. Benveniste frequently quoted the studies of Giuliano Preparata and Emilio Del Giudice in theoretical physics which suggested that water molecules could organize in "coherent domains" around the dissolved compounds.[1] However, this theory has never been used to improve Benveniste's experiments or to build hypotheses in the framework of these experiments. This physical theory frequently served as argument from authority ("physicists showed that…"). This theory moreover seems to envisage only a single type of molecule. What happens in the presence of "soups" of molecules that are frequent in biology? What then become the "coherent domains" in front of a mountain of information which must be stored?

Even if we forced ourselves about not raising the issue of homeopathy as therapeutics, a question deserves nevertheless to be raised because it concerns the physical properties of high dilutions. Indeed, homeopathic medicines sold in pharmacy are most often in the form of granules. The latter are constituted by lactose on which a homeopathic solution has been pulverized. Undoubtedly, "memory of lactose" has poetic effects which are less powerful than "memory of water", but it is nevertheless mainly under this form that the homeopathic products are administered. Yet, if we break these granules, they seem as dry as a sugar cube. Are we still speaking of "memory of water"? The answer of the homeopathy manufacturers concerning this paradox is generally the following one: it is in fact very difficult to evaporate all water molecules adsorbed on a surface and temperature much higher than ordinary temperature would be required for all water molecules to escape from the granule. This is quite possible, but concentration of water is then very weak and few water molecules are adsorbed on the surface of a solid. Is water in these conditions not completely destructurated? Where could be stored the "information" in these "almost dry" conditions? Is "information" transferred to the lactose of the granule?

Moreover, the manufacturers of homeopathic medicines insist on the numerous quality controls which take place throughout the production of granules, but nothing is said (and one can understand why…) on the ultimate and essential control which would be to verify that a biologic activity is present in a few samples of a batch. In the absence of such controls, are some batches sometimes recalled, for example because of an absence of efficiency noticed by homeopath doctors? In the area of health, the homeopathic industry is probably the only one where there is no control of the finished product.[2]

To end, let us imagine by a thought experiment that a facetious goblin systematically replaced each tube of homeopathic pills which leaves the factory by a tube of "neutral" granules with nevertheless the same "label". How much time would it take for the subterfuge to be noticed? Would one ever notice it?

Why is there no simple and reproducible experiment?

As one has probably understood, J. Benveniste was not the first one to be interested in the effects of high dilutions. Today, after the publicity made around the article of *Nature* of 1988, it is difficult not to know this marginal current of research. Nevertheless, if these researches were so old, it is surprising that despite decades of research, not one simple experiment, which many laboratories would have been able to perform, was defined. No test which would have allowed quality control of homeopathic granules was invented. Nevertheless the number of biological systems which were explored is impressive, from the vegetable to the animal kingdom (not to mention the question of the clinical trials in humans or in animals).

To speak only about *in vitro* or *in vivo* biological models, one finds studies with substances at high dilutions on germination of diverse seeds, consumption of oxygen by vegetables, reaction rate of varied enzymes, contraction of the gastrocnemian muscle of frog, isolated heart of rat, liver of rat, synaptosomal preparations of rat brain, slices of rat brain, isolated intestine of rat, isolated fragments of trachea of guinea pig, isolated fragments of human bronchi, learning in rat, behavioral tests in mouse, tumoral growth in rat, proliferation of *in vitro* tumor cells, edema of rat paw, UV-induced erythema in rat, liver toxicity in rat, experimental arthritis in rat, intestinal transit in mouse, wound healing in mouse, metamorphosis in batrachians, elimination of various toxins in diverse laboratory animals, experimental diabetes in mouse, toxicity of heavy metals on cell lineages, proliferation of lymphocytes, production of diverse mediators by polymorphonuclear neutrophils, production of antibodies in mouse, etc.

Despite this list which is very far from being exhaustive, not the slightest simple experiment, not the slightest biological well-defined test on which a consensus could be built.

Did the "Benveniste affair" change anything in the field of research on high dilutions?

There are some associations or foundations that bring together researchers who study the effects of the homeopathic dilutions, most frequently in the more general frame of "complementary" medicines. The reading of the reports of the congresses or meetings organized by these groups is interesting. One indeed notices that most of the experimental studies that are reported remain phenomenological: an effect *X* is observed in a biological system Y in the

presence of high dilutions of a product *Z*. This phase of the experiment does not seem to be able to go over. It is nevertheless paradoxical, after so many years of research, that elementary results about characterization of high dilutions – for example the effect of the exposure of high dilutions to heat – are not known. There is no consensus today on what "erases" the effect of high dilutions (or even possibly what increases them). Today, we should know the action of heat, ultrasounds, electromagnetic waves or other radiations on the "traces" left in water by molecules during the dilution-agitation process. Instead of this, there are still the same types of experiments with the everlasting final wish of future investigations by other researchers. Everything is going as if the research in this domain was a never-ending beginning.

This situation does not prevent the organization of colloquiums or symposia which play probably an important social role because they allow consolidating the feeling of belonging to a small circle of "enlightened" people being right against "official science" and against the other narrow-minded scientists. Moreover, some of the researchers who attend these circles complain about the ostracism of their works since "the Affair". But, in fact, did something really change? Is it not on the contrary an ideal pretext to be in the company of all scientists who were not understood in the past but are now in the pantheon of the science (Galilee remaining the gold standard on this matter)? Did these researchers have an easier access to the high-level scientific journals before the "Benveniste affair"? This attitude also avoids raising questions on the relevance of this research area and on the real role of water in this story.

To go out of a purely phenomenological description, great expectations seem to be based on the demonstrationn of modifications of physical properties of water. Maybe this hope is due to the prestige of physics. But, after the wave of enthusiasm which invariably welcomes the promotion of new results, supposed to be a definitive answer ("is homeopathy just about to be proven and explained?"), another new physical method, generating renewed hopes, is investigated. There were thus the dielectric constant of water, infrared spectroscopy or spectroscopy Raman-laser. More recently, one could observe enthusiasm for nuclear magnetic resonance, "crystals IE" or thermoluminescence. Soon after, some issues related to reproducibility, artefacts and cruelty of blind experiments were raised. In the end, one assists to the transposition, from biology to physics, of the difficulties of high dilutions.

What can we do?

Despite these reservations, a statistically significant effect persisted in the experiments that we described in this text. This is *the* scientific fact that emerges from this story and encourages to pursue the study of the phenomenon. The

term "phenomenon" must then be understood in broader terms. Because the perspective has changed, the question is no longer "how water could have a memory", but rather "how could one obtain these results" or more exactly "how could one bias chance even in blind experiments". The hypothesis of "memory of water" would be only a hypothesis among other ones. One can discard the possibility that this hypothesis would be finally rejected. This hypothesis would have nevertheless played an important "historical" role by having crystallized around it these unusual observations. After the rejection of this hypothesis, observations awaiting a satisfactory explanation would nevertheless remain.

This approach needs to come out from a purely descriptive and pragmatic attitude ("it works, thus it is true") and at the same time not to sink into narrow-minded skepticism because these phenomenons appear at first sight to lack of credibility or because the explanation adopted by those who support them does not satisfy us ("it is impossible, thus it is false"). To sum up, there is something interesting to study, these results are not trivial, but maybe the most immediate explanation is not relevant. One could thing that there are smart circumlocutions in order not pronouncing the word "artifact". As we will see in the second part of the present text, in spite of the abandon of the basophil model, the effects of "memory of water" persisted in new experimental systems. We will consequently see that, if there is an artifact – i.e. an effect generated by the experimental procedure itself – its explanation remains a challenge which is at least as exciting as the observation of the effects attributed to the "memory of water" in its early stages.

Notes of end of chapter

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[1] E. Del Giudice, Preparata G, Vitiello G. Water as a free electric dipole laser. *Physical Review Letters* 1988; 61: 1085.

[2] There is also another difference. In contrast with pharmaceutical industry, there is no pharmacovigilance and no record of adverse events for homopathic medicines....