

Basophil and high diluted bio-active molecules: What lies beneath?

Comment to:

Adrenaline inhibits the immunological activation of human basophils at pharmacological and ultra-low doses
Pier Francesco Mannaioni, Rosanna Mastroianni, Domenico Mastrangelo
Med Sci Monit 2010; 16(7): BR227–232

Dear Editor,

The recently published article by Mannaioni PF and colleagues represents another encouraging evidence on the functioning of biomolecules which underwent high dilution process in aqueous solutions. In the last 20 years very few Italian [1] and other European groups [2–5] have shown the phenomenon in which doses of histamine diluted beyond Avogadro's number retained an inhibitory function on basophils quite comparable to that from usual pharmacological dose ranges. Very highly diluted pharmacological substances act also on mouse models [6]. Although seemingly puzzling by the currently accepted chemistry principles, this evidence has raised up two mandatory questions: why basophils are so sensitive to ultra-high dilutions and what means, strictly within a physico-chemical point of view, the awkward concept of ultra-high dilution. While someone skates at the idea that there is a mysterious nature of water so suggesting that this liquid can be fully understood only by an atomic-molecular perspective [7], much evidence has raised the issue about the existence of a hidden property of water which might throw a light on unexplainable phenomena in cell biology and pharmacology. According to Finney two major aspects of water in biological systems seem to be particularly relevant to design a theoretical or experimental approach aiming at the improvement of our understanding of solvent effects [8]: if we take into account that the system solvent-solute is a complex system, this complexity implies that a panoply of techniques are needed to probe both perturbations of the bio-molecular system by the solvent and perturbations of the solvent by the bio-molecular solute [8]. The latter issue would be the real topic of any debate about the nature of ultra-high dilutions. Elia and co-workers has shown that water can build up dissipative structures by seeding an energetic input on the fluid such as strong mechanical forcing, then suggesting that this dissipative behavior reminds to many primitive forms of life [9]. Recent papers has introduced also the role of electromagnetic energies in doing nanosized and long-range organized structures into waters, structures able to inform cells and to result in a biological action [10]. Water is sensitive to low energy fields [11], produces spontaneously luminescence [12], reacts to static electric fields [13] and behaves as a magnetic tape [14]. But if this evidence appears as an interesting curiosity on the incredible nature of water, what's new for the biologist? Apart from some interesting model on receptor-ligand dynamics when ligand is in the attomolar-zeptomolar (10^{-18} – 10^{-21} M) concentration range [15] and the concept of hormesis, which should not be erroneously mismatched with homeopathy [16], a theoretical model of the biological response to an improbable solvent-water "modified" by serially processed dilutions of a bioactive solute has not yet been forwarded. In fact, while it seems quite likely to set up an explanatory model for solute concentrations up to 1.66 $\mu\text{mol/L}$, a molecular model of the active sub-

stance cannot be taken into account for doses below 10^{-23} M. We do not know whether other receptive structures might be involved (cell membrane, cytoskeleton, intracellular calcium oscillation) [17] whose perturbation due to water-bearing information turn to the ability to elicit receptor-intracellular signaling, but certainly, I am in agreement with the Authors, that an attomolar concentrated substance is diluted in bloodstream many and many times to reach an infinitesimal local concentration that is theoretically far beyond its molecular traceability. High diluted substances are, hence, the normality [18]. I think that time is ripe, research on water behavior in living organisms and in cells is of paramount importance and deserves a much more close and productive cooperation between chemists, physics and biologists in the next future.

Sincerely,

Salvatore Chirumbolo,
Department of Pathology and Diagnostics,
University of Verona, Verona, Italy,
e-mail: salvatore.chirumbolo@univr.it

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Received: 2010.10.19