# ARE THERE SOME LOOPHOLES IN EXPERIMENTAL BIOSCIENCES? THE LESSONS FROM BENVENISTE'S EXPERIMENTS

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**ABSTRACT**

The case of the "memory of water" was an outstanding scientific controversy of the end of the twentieth century which has not been satisfactorily resolved. Although an experimenter effect has been proposed to explain Benveniste's experiments, no evidence or convincing explanation supporting this assumption have been reported. One of the unexplained characteristics of these experiments was the different outcomes according to the conditions of blinding. In this article, an original probabilistic modeling of these experiments is described that rests on a limited set of hypotheses and takes into account measurement fluctuations. All characteristics of these disputed results can be described, including their "paradoxical" aspects; no hypothesis on changes of water structure is necessary. The results of the disputed Benveniste's experiments appear to be a misinterpreted epiphenomenon of a more general phenomenon. Therefore, this reappraisal of Benveniste's experiments suggests that these results deserved attention even though the hypothesis of "memory of water" was not supported. The experimenter effect remains largely unexplored in biosciences and this modeling could give a theoretical framework for some improbable, unexplained or poorly reproducible results.

**Keywords**: *Experimenter effect; Scientific controversy; Experimental artifacts; Cognition.*

## 1. INTRODUCTION

Although the notion of "memory of water" did not succeed to become taught in biology and chemistry textbooks, this scientific controversy is now a classical topic in sociological studies of science [1-4]. The early experiments reported in 1988 in *Nature* by a French team and other laboratories suggested that samples of highly diluted molecules retained the ability to activate cells [5]. Although no molecule could still be present in these high dilutions, the authors of the article claimed that the biological effect persisted in strictly controlled blind experiments. Of course, contamination was the first suggested cause to explain these unexpected results. It was argued however that appropriate controls had been done and that the number of possible contaminant molecules was too low to induce an effect of the same magnitude. Moreover, the interest of lay press – which coined the expression "memory of water" – was aroused because these results seemed the therapeutic claims of homeopathy.

Benveniste, the lead author, was not a newcomer, but was a reputed senior director of a laboratory of INSERM (the national French medical research organization). He was a member of the scientific establishment after his discovery of a new inflammatory mediator in the 1970s that was the main research topic of his laboratory [6].Therefore, he was given credit for having nothing to gain by promoting such eccentric results. The journal *Nature* played a key role in this affair. Indeed, Maddox, the Editor of *Nature*, was first reluctant to publish the data, but then changed his mind – in part due to the insistence of Benveniste – to expose and discredit what he thought to be "second rate" science in the service of the discredited homeopathy. The Benveniste-Maddox conflict is not the subject of this article and details can be found elsewhere [7-11].

Today, most scientists think that the controversy vanished after the affair with *Nature*. However, Benveniste pursued his experimental investigations, thus confirming and extending his previous results [7]. Of course, storing in liquid water the specific information that allow describing molecules – some of them as huge as immunoglobulins – appears, at first sight, quite impossible. One must also admit that direct physical evidence of a change of water structure specific of the original molecule ("ghostly imprint") has never been reported. The evidence rested on a circular reasoning: a modification of water structure was claimed to induce a change of a biological system and this change was exhibited as a proof that water structure had been modified. Actually, this research continued after the episode with *Nature* and extended overall from 1984 to 2004. After the basophil model, Benveniste's team explored other biological models. The most remarkable results were initially obtained with the isolated rodent heart model (Langendorff's apparatus) and some years later with an in vitro coagulation model that had the advantage of being possibly automated.

In 1992, Benveniste hypothesized that molecules in solution emitted electromagnetic waves that could be picked up by an electric coil, amplified and transmitted to a sample of water via another electric coil at the output of an amplifier ("electromagnetic transmission"). After confirmatory experiments, Benveniste claimed that he was now

able to "inform" samples of water through other means than high dilution (thus escaping the criticisms about homeopathy). In a further step in 1995, he reported that the alleged specific electromagnetic "signal" that was emitted by molecules in solution could be digitized, stored in a computer memory and played at will to a sample of water through an electric coil. For these last experiments, he coined the expression "digital biology". The experimental results obtained with "electromagnetic transmission" and "digital biology" have been mainly described as abstracts of congresses [12-20].

These biological and electronic devices will not be detailed in this article and information on them can be found elsewhere [7, 8]. The aim of the present paper is to expose the logic of these experiments and therefore, the experimental devices will be schematically described as simple black boxes with input and output.

## 2. SIMPLIFIED DESCRIPTION OF THE EXPERIMENTAL RATIONALE OF BENVENISTE'S EXPERIMENTS

In Benveniste's experiments, it was hypothesized that if some "memory of water" existed, then a biological change (noted "↑") above background noise (noted "↓") should be more frequently observed with samples supposed to be active (*AC*) compared with samples supposed to be "inactive" (*IN*) in biological models. Active samples were thought to have received "biological information" through high dilutions or using devices for "electromagnetic transmission" or "digital biology". In mathematical terms, we can write the aim of these experiments as a test of the following question:

$$\text{Is } \text{Prob}(\uparrow|AC) > \text{Prob}(\uparrow|IN)\,? \qquad (1)$$

Prob $(x|y)$ is the conditional probability of $A$ given $B$ (or the probability of $x$ under the condition $y$).
If modifications of water structure whatsoever were able to change a parameter of a biological system in a conventional causal relationship, it would not be different from a classical pharmacological effect. In this case, why did Benveniste's experiments fail to be fully convincing?

## 3. WHAT DID NOT WORK IN BENVENISTE'S EXPERIMENTS?

Benveniste often invited colleagues to witness his experiments. These "public demonstrations" were designed as "proof of concept" to give a definitive confirmation on the reality of "electronic transmission" or "digital biology". A protocol was defined and after the experiments were done, a report with all raw data was sent to all participants [7, 21, 22].

During these demonstrations, control samples and samples supposed to have received specific "biological information" were prepared (in some experiments of "digital biology", the "samples" were computer files) [7, 21, 22]. The sample preparation was performed in another laboratory under strict control by other scientists, and the initial labels of the samples were replaced with code numbers by participants not belonging to Benveniste's team. Open-label samples were also prepared; they were nevertheless in-house blinded. All samples were then tested in Benveniste's laboratory within the next few days after the preparation. Then the outcomes obtained with each sample were sent to the external supervisor who compared the two lists (i.e. the list of inactive/active samples vs. the list of biological effects under a code name) and who assessed the rate of "success". Note that the supervisor did not assist in the testing of the samples and remained uninformed about them until the end.

Details of these public demonstrations organized from 1992 to 1997 with the rodent isolated heart model have been given elsewhere [7, 21, 23] and one of them has been thoroughly analyzed in a recent article [22]. So what did not work in these demonstrations?

The unexpected obstacle encountered by Benveniste can be described through an illustration. Let us imagine a stage magician who presents four empty cages to the public. He covers each cage with a scarf and claims that he will predict in which cage a parrot will appear. First, he announces "cage number two" and when the cage is uncovered, a parrot is indeed present in this cage, whereas the other cages are empty. For a new trial, the cages are again covered with scarves. The magician announces "cage number four", but in fact, a parrot is present in cage number one and only in this cage. After a great number of trials, it finally appears that the magician is right with a probability which is not different from 1/4. We can conclude that the stage magician had at best a random success rate in guessing the cage number. Nevertheless, in each case, a parrot appeared by an unknown manner in a cage that was previously empty. Therefore, the apparition of a parrot – not the guessing game – is the scientific issue to be resolved.

If one replaces the parrot by the emergence of a "biological signal" from background noise, this is exactly what happened in Benveniste's experiments: In some experimental conditions such as blind "public demonstrations", the biological parameter did change, but *not at the expected places.*

## 4. THE DIFFERENT EXPERIMENTAL CONDITIONS IN BENVENISTE'S EXPERIMENTS AND CORRESPONDING OUTCOMES

Figure 1 is a graphical representation of the different experimental conditions encountered during Benveniste's experiments. Alice is the experimenter and Bob observes Alice doing the experiment; Bob can also be a supervisor in in-house blind experiments. Eve is an outside supervisor; when she participates to blind experiments, she sends to Alice the samples to be tested under a code number. After all tests have been done with the biological device, she receives the list of the observed effects ("↓" and "↑") and she calculates the rate of success. There is an essential difference with Bob: Eve neither observes Alice nor the experimental device and she has no information during the testing of the samples.

Results of Benveniste's experiments with the Langendorff apparatus are summarized in Table 1 according to different experimental conditions: (1) Alice assessed the success rate (open-label); (2) Bob assessed the success rate (Alice blind); (3) Eve assessed the success rate (Alice blind). One expects the respective probabilities of success being identical with or without Eve's assessment. Details on these experiments have been given elsewhere [7, 21-23].

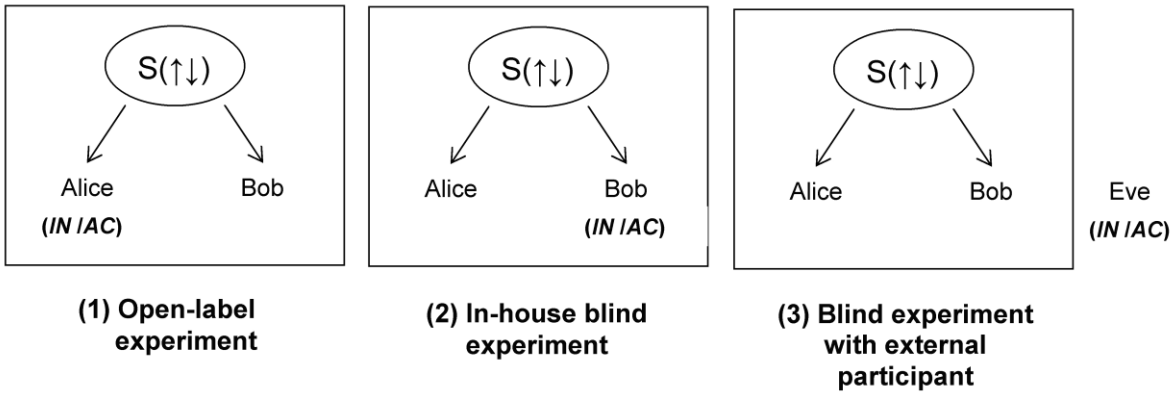



*Figure 1. Description of the different roles of the agents who participate in the experiments. Alice is the experimenter (1) and two other observers participate (if necessary) in the blind experiments. Bob is inside the laboratory, and for him who observes Alice in her environment, Alice and the experimental system (S with two possible states ↓ or ↑) are in a defined state. To control Alice's experiments, Bob can locally assess the results in blind experiments (2). This means that he replaces the initial label of each experimental sample by a code number before giving it to Alice for blind testing. Eve is outside the laboratory (3). Therefore, for Eve, Alice and the experimental system are in an undefined state until all samples have been tested and results are transmitted to Eve. When Eve participates in a blind experiment, she keeps secret the list of sample labels to be tested by Alice. After the completion of the experiments, she receives the list of outcomes of the experimental device and she compares the two lists to calculate the rate of success.*

*Table 1. Outcomes of Benveniste's experiments according to three experimental conditions.*

| Experimental situations | Number of experimental points | "Expected" outcomes | Observed outcomes (Success rate, %) | |
|---|---|---|---|---|
| | | | Outcome "↓" (resting state) | Outcome "↑" ("activated" state) |
| *Eve did not assess the success rate*:* | | | | |
| Alice assessed the success rate (Open-label) (1) | N=372 | "Inactive" | **93%** | 7% |
| | N=202 | "Active" | 11% | **89%** |
| Bob assessed the success rate (Alice blind) (2) | N=118 | "Inactive" | **91%** | 9% |
| | N=86 | "Active" | 15% | **85%** |
| *Eve assessed the success rate*:* (Alice blind) (3) | N=54 | "Inactive" | **57%** | 43% |
| | N=54 | "Active" | 44% | **56%** |

Summary of results presented in [21].
"Success" (in bold type) is defined as "Inactive" label associated with "↓" or "active" label associated with "activated" state "↑".

Without Eve's assessment, $\mathrm{Prob_A}(success) = 0.92$ (Alice's assessment) and $\mathrm{Prob_B}(success) = 0.88$ (Bob's assessment). Then Eve tried to confirm these results by supervising blind experiments with the participation of Alice (Figure 1). After receiving the results corresponding to each label, she assessed the "success" rates for the inactive and active labels and she calculated the overall rate of "success": $\mathrm{Prob_E}(success) = 0.57$. Therefore, the probability of "success" was different according to the experimental conditions (assessment of "success" rates firstly by Alice/Bob or firstly by Eve):

$$\mathrm{Prob_A}(success) \sim \mathrm{Prob_B}(success) > \mathrm{Prob_E}(success) \quad (2)$$

The remote assessment of "success" rate by Eve was associated with a decrease of this rate. Note however that the biological signal was present, but not at the "expected" place (as the parrot in the above illustration). For Benveniste, the failure of the "public experiments" did not call into question the validity of his theses on "digital biology", "electromagnetic transmission" or high dilutions, but showed that technical improvements were yet necessary. Indeed, he considered that the change of a biological parameter in his experiments was not a trivial artifact, but a proof that a discovery of great scientific value was at stake [21]. Therefore, various explanations were proposed by Benveniste and his team to try to overcome these experimental failures: water contamination, electromagnetic perturbations from the environment, spontaneous "jumps" of "electromagnetic activity" from one water sample to another one, etc. However, despite improvements of the experimental devices to prevent possible external influences, the mismatches persisted in experiments with "external" blinding [7, 22]. The impossibility to overcome this barrier was the main reason why Benveniste did not succeed to convince his peers.

These *ad hoc* explanations were indeed unsatisfying. It was difficult to explain how a simple change for blinding conditions could lead to such differences (i.e. in-house blinding *vs.* blinding by a supervisor located outside the laboratory). From this point of view, the opponents of "memory of water" were right: no causal relationship between "informed" samples and change of biological signal was convincingly established. However, in the present state of knowledge, the consistent changes that had been repeatedly observed (including after in-house blinding) remained puzzling. From this point of view, Benveniste and his team were right. In this article, we will see how a third explanation based on the involvement of the participants could make a synthesis of these apparently irreconcilable positions.

## 5. THE UNUSUAL NOTION OF "GIFTED" EXPERIMENTER

Another weird observation during the "memory of water" story was the notion of "gifted" experimenter. Indeed, in experimental sciences, the experimenter is assumed to be neutral with regard to the outcome of his/her observations. If such an influence exists, the result is called an "artifact", whatever the conditions for its production. Thus, in early experiments on the effects of high dilutions on basophils performed by Benveniste's team, one of the two experimenters of a series of blind experiments obtained results in favor of an effect of high dilutions and not the other [7, 24]. Of course, many trivial explanations were possible that could explain why one of the two experimenters was a better "measurement device" than the other; it is well known in all laboratories that some people are more skillful and dexterous. Nevertheless, these results with basophils were obtained in blind conditions. The possibility that the experimenter could disturb results, which were attributed to "memory of water" or "digital biology", was repeatedly suggested during the twenty years of research that Benveniste devoted to this topic [7].

A trivial explanation is however more difficult to hold for automated experiments that record objective measurements. Thus, in 2001, the United States Defense Advanced Research Projects Agency (DARPA) appointed a multidisciplinary team to provide expert evaluation of an automatic biological analyzer set up by Benveniste's team. This robot analyzer automatically assessed the effects of "digital biology" on plasma coagulation (more precisely fibrinogen-thrombin coagulation) with minimal human intervention. The members of the expert team reported in an article that they were unable to obtain replicable successful experiments of digital biology with the automatic biological analyzer [25]. Nevertheless, they witnessed that successful experiments had been obtained during the initial phase of the expert evaluation provided that the experimenter from Benveniste's team was present. With this automated device, the intervention of the experimenter was very limited; even the computer files to be "played" and transmitted to water through an electric coil were randomly chosen by the machine. When the machine was ready with all consumables, the experimenter pushed a button and waited for one hour before details of the results were printed. In the conclusion of their article published in 2006, the experts pointed out:

> "*[Benveniste] stated that certain individuals consistently get digital effects and other individuals get no effects or block those effects. While it is possible that other, unknown "experimenter" factors, such as the influence of chemical residues, energetic emanations or intentionality from individual experimenters could be an explanation for these findings, we did not test these hypotheses nor developed a framework that would control for such factors*" [25].

In the probabilistic modeling that we propose of Benveniste's experiments, the experimenter is not a simple neutral "observer", but is an essential component of the experimental system.

## 6. DEFINITIONS AND RULES FOR THE MODELING

In this section, some terms necessary for the formal description of Benveniste's experiments are precisely defined.

*"Inactive" and "active" labels*: Since we assume that there is no "memory of water" and that the structure of water is not modified, all samples that are assessed in the experiments are physically comparable. Samples with "inactive" and "active" labels cannot be distinguished by physical means; they only differ by their labels. As a consequence, experiments with series of samples are like comparing *repetitions* of measurements associated either with the "active" label or with the "inactive" label.

*"Success" and "failure"*: As previously defined, a "success" is defined as the association of the inactive label (*IN*) with resting state (i.e. change not different from background noise noted "↓") of the biological device or the association of the "active" label (*AC*) with a biological signal (i.e. change above background noise noted "↑"). "Failure" is defined as *AC* associated with "↓" or *IN* associated with "↑". Therefore, the aim of the modeled experiments is to establish whether the state "↑" is more frequently associated with the label *AC* than with the label *IN*.

*Macroscopic environment and measurements*: The experimental situation can be summarized as the interaction of the macroscopic environment with the mental state (perception) of the participants. The macroscopic environment consists of the experimenters/observers considered as macroscopic objects (including brain structures, sensory organs, etc.) and the experimental devices. The interactions between participants who are macroscopic structures are like measurements of the perceptions of the other participants. The knowledge of the perception of an observer is an answer to the question asked by another observer: "According to the definition, do you observe a success?" The outcome is "yes" or "no". Moreover, since these interactions are like measurements with macroscopic devices, they are subjected to fluctuations.

*Perception and objective reality*: In this modeling, an important point is that the respective perceptions of different observers are *independent*. Nevertheless, when the observers of an experiment interact, they agree on the outcomes

(*intersubjective agreement*). In other words, there is a *public space* that is the locus of the "objective reality" and there is a *private space* for each observer. Each private space (made of perceptions) independently interacts with the macroscopic environment, which constitutes the objective reality.

## 7. PROBABILISTIC MODELING OF BENVENISTE EXPERIMENTS INCLUDING THE OBSERVERS

We describe the experimental situation from the point of view of a remote observer who perfectly knows the initial conditions of the experimental situation and describes its evolution without interacting.

First, we consider the general case of the observation of an experimental relationship. One of the possible relationships is named "success" and the other one is "failure" with Prob (*success*) equal to $p$ and Prob (*failure*) equal to $q$ (with $p + q = 1$) (see definition above and Figure 2).

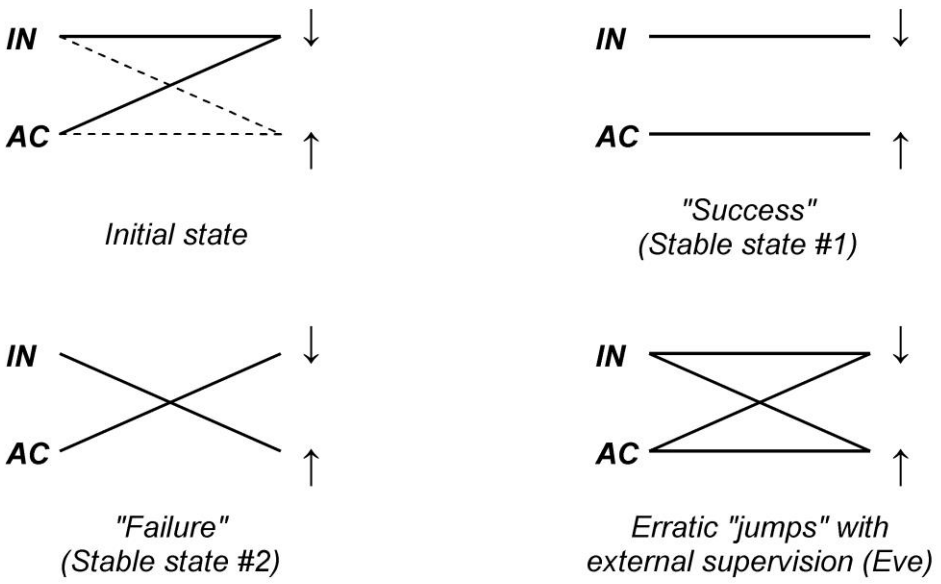



*Figure 2. The different associations of labels and states of the experimental system in Benveniste's experiments. The two labels are "inactive" (IN) and "active" (AC). There are two possible states for the experimental system: (1) "resting" state or background ("↓") and (2) "activated" state or signal above background ("↑"). The purpose of Benveniste's experiments was to answer the question: "Is Prob (↑| AC) > (↑| IN)?" In other words, were "signal" more frequently associated with the "inactive" label or with the "active" label? Note that in initial state, the probability to observe "↑" is low, but is not equal to zero (dashed line).*

When two observers assess the same outcome, they agree on their conclusion, namely "success" or "failure". An experimental situation such as "success" for one observer and "failure" for the other is not allowed. Moreover, as previously said, the interactions of the macroscopic environment with the respective cognitive states of the two observers are *independent.* Therefore, as depicted in Figure 3, the estimation of the joint probability for "success" for these two observers is:

$$\mathrm{Prob}(success) = \frac{p^2}{p^2 + q^2} \tag{3}$$

This equation can be easily generalized to a number $N$ of participants who all agree on their observations for "success":

$$\mathrm{Prob}(success) = \frac{p^N}{p^N + q^N} \tag{4}$$

In classical physics, the description of the world is independent of the presence of observers (n = 0). In the absence of any observer, the above equation has a unique value:

$$\text{Prob}(success) = \frac{p^0}{p^0 + q^0} = 1/2 \tag{5}$$

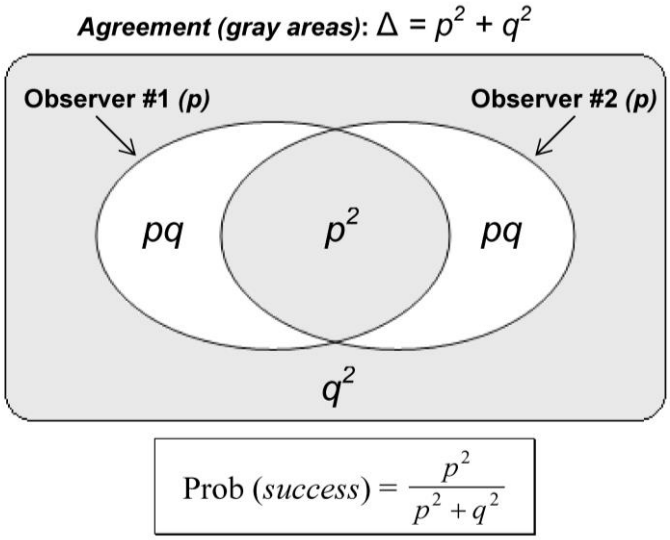



*Figure 3. Consequences of the independence of perception of "success" of each observer. In this figure, we show only two observers for simplification. Although observers' perceptions are independent, after interaction, observers nevertheless agree on the outcome of the experiment. We suppose that these two agents observe an experiment and that the rate of "success" (according to defined rules) is p and the rate of failure is q (with p + q = 1). White areas correspond to impossible situations where the outcomes are not consistent (e.g. "success" for Alice and "failure" for Bob). The white areas are consequently excluded for probability calculations. The probability that both agents observe "success" is thus the ratio of the central gray area (both Alice and Bob observe "success") divided by the probability of observing consistent outcomes (either "success" or "failure") for both observers (all gray areas).*

Prob (*success*) = 1/2 is the starting point of the modeling. For simplification, we first consider only two observers. Moreover, we take into account measurement fluctuations. As for any measurement, there are fluctuations of the interaction of the "public space" (macroscopic environment) with the "private space" (perceptions) of the observers. As a consequence, there are fluctuations of the probability to observe "success". The fluctuations of the probability of "success" are noted $\delta_i$ for one observer and $\varepsilon_i$ for the other one. $\delta_i$ and $\varepsilon_i$ are independent random numbers around zero with an absolute value << 1/2.

Since the initial probability of success is $p_0$ = 1/2, when we assess the probability of success after a first measurement, we can estimate that the probability to perceive "success" is $1/2 + \delta_1$ for the first observer and $1/2 + \varepsilon_1$ for the second observer. The introduction of measurement fluctuations implicitly means that the biological state "↑" has a probability that is very small, but not equal to zero. Indeed, Prob (*success*) slightly higher than 1/2 means that the probability to see an "active" label associated with "↑" increases and Prob (*success*) slightly lower than 1/2 means that the probability to see an "inactive" label associated with "↑" increases. In other words, the biological state "↑" is present in the background noise.

As shown above (Figure 3), the estimation of the joint probability for the two observers after a first measurement is given by the following equation:

$$\text{Prob}(success) = \frac{(1/2 + \delta_1)(1/2 + \varepsilon_1)}{\Delta} \tag{6}$$

$$\text{with } \Delta = (1/2 + \delta_1) \times (1/2 + \varepsilon_1) + (1/2 - \delta_1) \times (1/2 - \varepsilon_1) \tag{7}$$

The initial probability of success equal to 1/2 is updated with the new value, which in turn is updated after another measurement and so on in a mathematical sequence. For the measurement *n+1*, the probability $p_{n+1}$ is obtained by re-entering the probability $p_n$. The general equation of this mathematical sequence that describes Prob (*success*) is:

$$\mathrm{Prob}_{n+1}(success) = p_{n+1} = \frac{(p_n + \delta_{n+1})(p_n + \varepsilon_{n+1})}{\Delta} \quad (8)$$

$$\text{with } p_0 = 1/2 \text{ and } \Delta = (p_n + \delta_{n+1}) \times (p_n + \varepsilon_{n+1}) + (q_n - \delta_{n+1}) \times (q_n - \varepsilon_{n+1}) \quad (9)$$

Table 2 shows a detailed numerical example in order to make clear each calculation step of this mathematical sequence and to show how the transition from 1/2 to 0 or 1 emerges. The random parameters δ and ε have been chosen with relatively high values in order to obtain a transition within a few rows. In this example, a stable state was randomly achieved with Prob (*success*) = 1, but 0 could also have occurred with even probability.

*Table 2. Calculation of the mathematical sequence of Prob (success) with δ and ε randomly obtained in the interval –0.5 to +0.5 × $10^{-3}$*

| *Step n* | $\delta_{n+1}$ | $\varepsilon_{n+1}$ | $p_n + \delta_{n+1}$ | $p_n + \varepsilon_{n+1}$ | $q_n - \delta_{n+1}$ | $q_n - \varepsilon_{n+1}$ | $\mathrm{Prob}_{n+1}(success) = p_{n+1}$ |
|---|---|---|---|---|---|---|---|
| 0 | – | – | – | – | – | – | **0.50000** |
| 1 | 0.00196 | 0.00208 | 0.50196 | 0.50208 | 0.49804 | 0.49792 | **0.50404** |
| 2 | 0.00121 | 0.00243 | 0.50525 | 0.50647 | 0.49475 | 0.49353 | **0.51172** |
| 3 | -0.00408 | 0.00274 | 0.50764 | 0.51446 | 0.49236 | 0.48554 | **0.52209** |
| 4 | -0.00230 | 0.00139 | 0.51978 | 0.52348 | 0.48022 | 0.47652 | **0.54319** |
| 5 | -0.00461 | 0.00229 | 0.53858 | 0.54548 | 0.46142 | 0.45452 | **0.58348** |
| 6 | -0.00074 | -0.00016 | 0.58274 | 0.58332 | 0.41726 | 0.41668 | **0.66160** |
| 7 | -0.00341 | -0.00295 | 0.65819 | 0.65865 | 0.34181 | 0.34135 | **0.78794** |
| 8 | 0.00363 | -0.00215 | 0.79157 | 0.78579 | 0.20843 | 0.21421 | **0.93303** |
| 9 | 0.00139 | -0.00324 | 0.93442 | 0.92979 | 0.06558 | 0.07021 | **0.99473** |
| 10 | 0.00494 | -0.00212 | 0.99967 | 0.99261 | 0.00033 | 0.00739 | **1.00000** |
| 11 | 0.00416 | 0.00072 | 1.00416 | 1.00072 | -0.00416 | -0.00072 | **1.00000** |
| 12 | 0.00157 | 0.00303 | 1.00157 | 1.00302 | -0.00157 | -0.00302 | **1.00000** |
| 13 | -0.00094 | 0.00382 | 0.99906 | 1.00381 | 0.00094 | -0.00381 | **1.00000** |

Figure 4 shows a computer simulation with probability fluctuations around $10^{-6}$ (calculations have been done also with probability fluctuations as small as $10^{-15}$; see legend of Figure 4). After a number of measurements, in all cases, a stable position is obtained in Figure 4:

$$\text{Prob } (success) = 1 \text{ or Prob } (success) = 0 \quad (10)$$

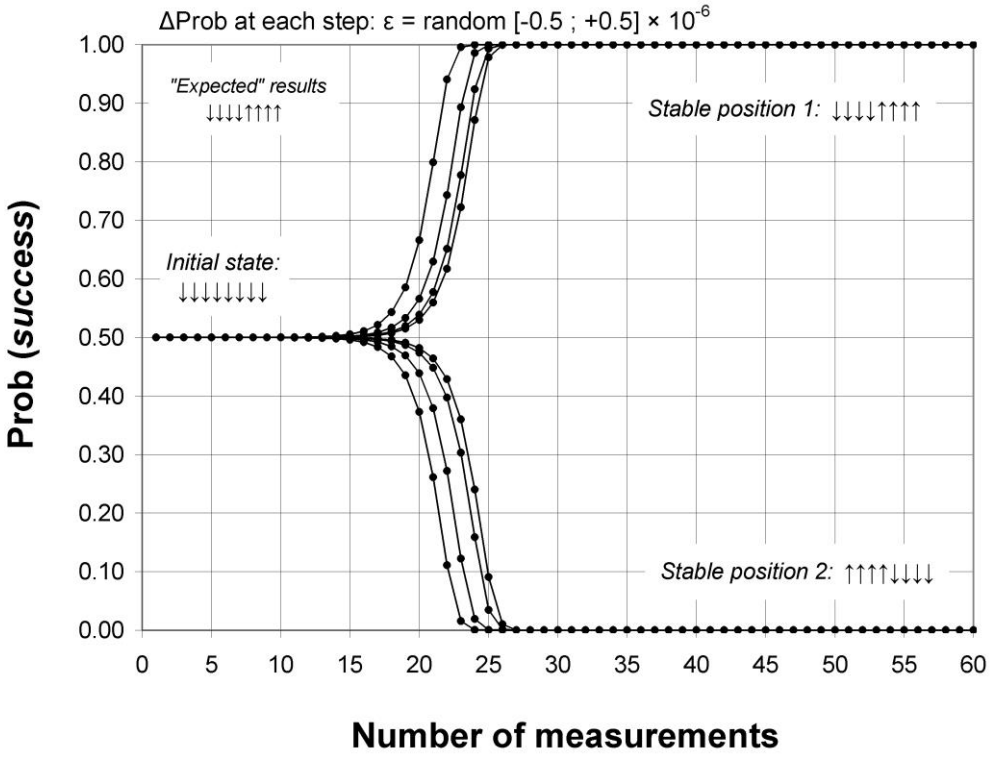



*Figure 4. Evaluation of the probability of "success" by taking into account measurement fluctuations. In this figure, the probability is computed with the formula defined in Figure 3. The probability of success is initially equal to 1/2. The equation* $\mathrm{Prob}_{n+1}(success) = p_{n+1} = (p_n + \delta_n)(p_n + \varepsilon_n)/\Delta$ *with* $p_0 = 1/2$ *(see text for the definition of* $\Delta$*) allows calculating the probability of success after successive measurements subjected to fluctuations. The initial 1/2 probability is replaced with the new calculated value and the joint probability obtained after each random step is used for the next calculation of probability of success and so on. The values of* $\delta$ *and* $\varepsilon$ *at each calculation step are randomly obtained in the interval –0.5 to +0.5 × 10-6. We observe in this computer simulation that the probability of "success" is unstable and after a few calculation steps, one of the two stable positions is achieved: either "success" or "failure". The same calculations have been made with a smaller change of probability of "success"; in this case, the transition occurs after a greater number of calculation steps: 40–50 calculation steps with* $\varepsilon$ *= random [–0.5 to +0.5] × 10-15). Moreover, with a number of observers >2, the transition towards stable positions occurs with fewer calculation steps (not shown). The figure depicts the results obtained after eight computer simulations.*

We conclude that the initial state with probability of "success" equal to 1/2 is *metastable* if we take into account the measurement fluctuations. Comparable results are obtained with a number of observers > 2 (the transition of the probability from 1/2 to 1 is achieved after fewer measurements when the number of observers increases).

Table 3 shows that the transition of Prob (*success*) toward 0 or 1 is possible only with a number of observers ≥ 2 and taking into account measurements fluctuations.

*Table 3. Calculation of Prob (success) according to the number of observers..*

| **Number of observers** | **0** | **1** | **2** | **3** | **…** | **N** |
|---|---|---|---|---|---|---|
| Calculation of Prob (*success*) | $\frac{p^0}{p^0+q^0}=1/2$ | $\frac{p}{p+q}=p$ | $\frac{p^2}{p^2+q^2}$ | $\frac{p^3}{p^3+q^3}$ | … | $\frac{p^N}{p^N+q^N}$ |
| Evolution of Prob (*success*) taking into account measurement fluctuations* | 1/2 | $1/2+\varepsilon_i$ | 0 or 1 | 0 or 1 | … | 0 or 1 |

* Starting with $p_0 = 1/2$.

In Figure 4, only one of the two stable positions, namely the stable position #1, corresponds to the "expected" results; indeed, in the stable position #2, an "inactive" label is always associated with "↑" and an "active" label is always associated with "↓". Note that in both stable positions, the probability to observe "↑" increases from ~0 to 1/2. However, an "experiment" is not limited to sample testing, but begins with the preparation of the experimental device. Thus, we must take into account that the biological systems are prepared in an *asymmetrical* state since the resting state (background noise) is always implicitly associated with the label *IN*. As a consequence, *only the stable position #1 is a possible state* for the observers and therefore:

$$\text{Prob}\,(success) = 1 \tag{11}$$

## 8. WHICH CHARACTERISTICS OF BENVENISTE'S EXPERIMENTS ARE DESCRIBED BY THIS MODELING?

In stable position #1, Prob (*success*) = 1 (Figure 3). This means that "↓" is systematically observed in association with the label *IN* and "↑" in association with the label *AC*. Therefore, the same process describes both the emergence of "↑" from the background and the concordance of the labels with the states of the biological device. Thus, the initial question – "Is Prob $(\uparrow|AC) > (\uparrow|IN)$?" – receives a positive answer.

When Bob participates in in-house blind experiments, Alice and Bob are in the same stable position. Therefore, they both observe that the label *IN* is always associated with the outcome "↓" and that the label *AC* is always associated with the label "↑" and therefore:

$$\text{Prob}(\downarrow) = \text{Prob}(IN) = 1/2 \text{ and } \text{Prob}(\uparrow) = \text{Prob}(AC) = 1/2 \tag{12}$$

When Eve acts as an external supervisor of blind experiments, she associates each label of the list with each outcome (↑ or ↓). We can calculate the probability of "success" and "failure" in this experimental situation:

$$\text{Prob}_E\,(success) = \text{Prob}(IN)\times\text{Prob}(success|\,IN) + \text{Prob}(AC)\times\text{Prob}(success|\,AC) \tag{13}$$

$$= \text{Prob}\,(IN)\times\text{Prob}\,(\downarrow) + \text{Prob}\,(AC)\times\text{Prob}\,(\uparrow) \tag{14}$$

$$= [\text{Prob}(IN)]^2 + [\text{Prob}(AC)]^2 \tag{15}$$

$$= (1/2)^2 + (1/2)^2 = 1/2 \tag{16}$$

$$\text{Prob}_E\,(failure) = \text{Prob}(IN)\times\text{Prob}(failure|\,IN) + \text{Prob}(AC)\times\text{Prob}(failure|\,AC) \tag{17}$$

$$= \text{Prob}\,(IN)\times\text{Prob}\,(\uparrow) + \text{Prob}\,(AC)\times\text{Prob}\,(\downarrow) \tag{18}$$

$$= \text{Prob}\,(IN)\times\text{Prob}\,(AC) + \text{Prob}\,(AC)\times\text{Prob}\,(IN) \tag{19}$$

$$= 2\times\text{Prob}\,(IN)\times\text{Prob}\,(AC) = 1/2 \tag{20}$$

Therefore, the outcomes "↑" and "↓" are associated at random with the labels *IN* and *AC*. This equation explains the mismatches between labels and biological outcomes in blind "public demonstrations" of Benveniste's experiments; the apparent "jumps" of "biological activity" from sample to sample are easily described. Indeed, the probability for the label *AC* to be associated with "↑" decreases from 100% to 50% and the probability for the label *IN* to be associated with "↑" increases from 0% to 50%. It is as if the "biological activity" randomly moved from some samples with the "active" label to samples with the "inactive" label.

In summary, all characteristics of Benveniste's experiments are described in this modeling: "success" of experiments with internal supervisor such as Bob and "failure" with external supervisors such as Eve.

## 9. COMPARISON WITH THE LOGIC OF THE TWO-SLIT INTERFERENCE EXPERIMENT OF YOUNG

We have seen that:

$$\text{Prob}_B\ (success) = 1 \text{ for experiments supervised by Bob} \quad (11)$$

$$\text{Prob}_E\ (success) = [\text{Prob}(IN)]^2 + [\text{Prob}(AC)]^2 \text{ for experiments supervised by Eve.} \quad (15)$$

We can easily calculate that the difference between these two probabilities of "success" is equal to:

$$\text{Prob}_B\ (success) - \text{Prob}_E\ (success) = 2 \times \text{Prob}(IN) \times \text{Prob}(AC) \quad (21)$$

We can do the same calculations with Prob (*failure*). Similarly, we have seen that:

$$\text{Prob}_B\ (failure) = 0 \text{ for blind experiments supervised by Bob} \quad (11)$$

$$\text{Prob}_E\ (failure) = 2 \times \text{Prob}(IN) \times \text{Prob}(AC) \text{ for experiments supervised by Eve.} \quad (20)$$

The difference between these two probabilities of "failure" is equal to:

$$\text{Prob}_B\ (failure) - \text{Prob}_E\ (failure) = -2 \times \text{Prob}(IN) \times \text{Prob}(AC) \quad (22)$$

Therefore, $\text{Prob}_B$ (*success*) and $\text{Prob}_B$ (*failure*) for experiments with Bob can be written as follows:

$$\text{Prob}_B\ (success) = \text{Prob}_E\ (success) + 2 \times \text{Prob}(IN) \times \text{Prob}(AC) \quad (23)$$

$$\text{Prob}_B\ (failure) = \text{Prob}_E\ (failure) - 2 \times \text{Prob}(IN) \times \text{Prob}(AC) \quad (24)$$

The term 2 × Prob (*IN*) × Prob (*AC*) is equivalent to an "*interference*" term. The logical structure of the modeling of Benveniste's experiments is thus reminiscent of the results that are obtained with Young's two-slit experiment (or with an interferometer of Mach-Zehnder). In Young's two-slit experiment, according to non-detection vs. detection of the path of the photon trajectory (slit *A* or slit *B*), interferences are observed on the screen or not, respectively. In the modeling of Benveniste's experiments, the role of the slits *A* and *B* is played by the labels *IN* and *AC*. In a previous article, this analogy with the self-interference of a single photon has been depicted in detail [26].

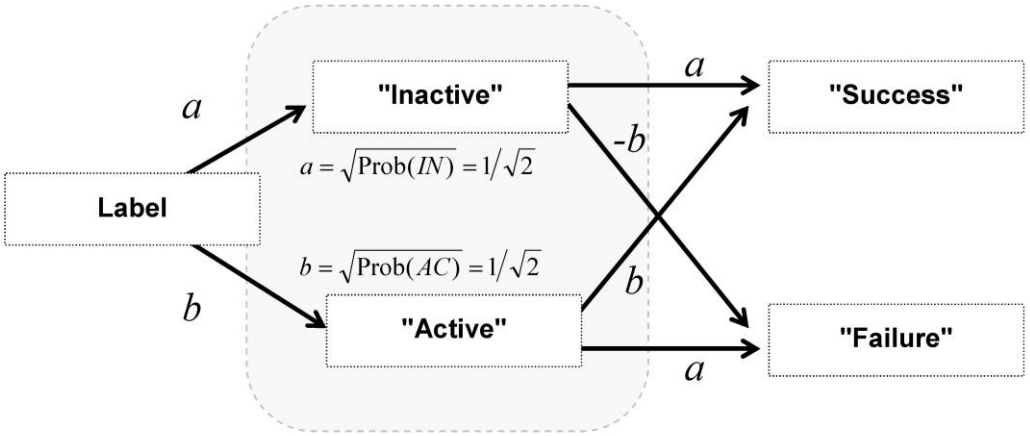
In Young's two-slit experiment, the indistinguishability of the paths of the photon through slit *A* or slit *B* is responsible for the interference patterns (constructive interferences are comparable to "success" and destructive interferences to "failure"). In the present modeling, we observe the following probability transition (Figure 4):

$$\text{Prob}(IN \mid success) = 1 \rightarrow \text{Prob}(IN \mid success) = 1/2 \quad (25)$$

$$\text{Prob}(AC \mid success) = 0 \rightarrow \text{Prob}(AC \mid success) = 1/2 \quad (26)$$

The "paths" *IN* and *AC* are distinguishable in the initial position; indeed, if "success" is observed, then the probability of "path" *IN* is equal to one and the probability of "path" *AC* is equal to zero. In contrast, in a stable position, the "paths" become indistinguishable with probability equal to 1/2 for each label.

It is interesting to note that we find here the notion of probability amplitude. Indeed, in quantum logic, the probability of an event is obtained by squaring its probability amplitude. As described in Figure 5, in experiments supervised by Bob (which give the same results as open-label experiments), the probability of "success" is obtained by making the sum of the probability amplitudes of the two paths that lead to success and then by squaring it. For blind experiments supervised by Eve, the probability of success is obtained by squaring the probability amplitude of each path that leads to "success" and then by making the sum of the probabilities of the two paths.




Square of the sum of the probability amplitude of the paths (with Bob) :

$$\text{Prob}_{\text{B}}(success) = (a \times a + b \times b)^2 = 1$$

$$\text{Prob}_{\text{B}}(failure) = (b \times a - a \times b)^2 = 0$$

Sum of the squares of the probability amplitude of the paths (with Eve) :

$$\text{Prob}_{\text{E}}(success) = (a \times a)^2 + (b \times b)^2 = 1/2$$

$$\text{Prob}_{\text{E}}(failure) = (b \times a)^2 + (a \times b)^2 = 1/2$$

*Figure 5. Classical or quantum-like probability of "success". The probabilities of "success" are different according to quantum-like or classic probability. Indeed, quantum-like probability is calculated as the* square of the sum *of the probability amplitudes of the different possible "paths". Classical probabilities are calculated as the* sum of the squares *of the probability amplitudes of the "paths".*

## 10. CONDITIONS FOR TRANSITION TOWARDS A STABLE POSITION

The achievement of a stable position as depicted in Figure 4 supposes first that the perceptions of the observers are independent and second that there is no physical "barriers" in the macroscopic world that would block the transition of the probability of success from 1/2 to 1. For this purpose, we have to examine the two key macroscopic systems in the modeling, namely the experimental system and the experimenters/observers. Finally, we have to wonder whether they have something special for observing these phenomena. In other words, is any experimental system always appropriate? Are some experimenters more "gifted" than others? As a first step, we examine more deeply the origin and consequences of independent perceptions.

### 10.1. Independence of perceptions

A key condition of the modeling is the *independence of perceptions* of the different observers. The independence of two events, $E_1$ and $E_1$, is written as:

$$\text{Prob}(E_1 \cap E_2) = \text{Prob}(E_1) \times \text{Prob}(E_2) \tag{27}$$

As a consequence, the independence of the two events is only partial if:

$$\text{Prob}(E_1 \cap E_2) = \text{Prob}(E_1) \times \text{Prob}(E_2) + d \quad (\text{with } 0 < d < 1) \tag{28}$$

If, as in Figure 3, the probability to observe the event "success" is the same for the two observers; the joint probability is Prob (*success*) = $p^2 + d$. The probabilities of the other experimental situations can be easily calculated. For example, the situation (not allowed in the macroscopic "reality") where one observer perceives "success" and the other one perceives "failure" is $p - (p^2 + d) = p \times (1 - p) - d = pq - d$ (Figure 6). Equations (8) and (9) for the probability of "success" can be modified:

$$\text{Prob}_{n+1}(success) = p_{n+1} = \frac{(p_n + \delta_{n+1})(p_n + \varepsilon_{n+1}) + d}{\Delta} \tag{29}$$

$$\text{with } p_0 = 1/2 \text{ and } \Delta = (p_n + \delta_{n+1}) \times (p_n + \varepsilon_{n+1}) + (q_n - \delta_{n+1}) \times (q_n - \varepsilon_{n+1}) + 2d \quad (30)$$

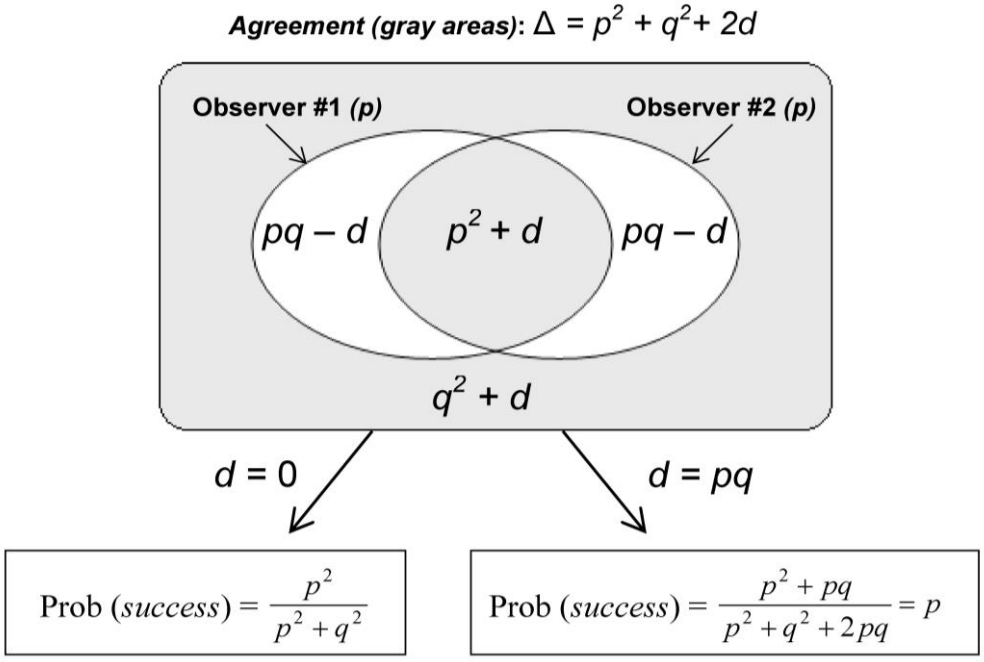



*Figure 6. General case for joint probability of "success" of two observers according to the degree of independence of perception of "success" of each observer. Parameter d varies from 0 to pq according to the more or less independence of perception of "success". When d = 0, perceptions are independent and quantum-like probabilities arise. When d = pq, the probability of perception of "success" is equal to p as in classical probability.*

When the value of $d$ gradually changes from $d = pq = 1/4$ to $d = 0$, one progressively moves from classical to quantum-like probability and Prob(*success*) increases from 1/2 to 1 (Table 3). Parameter $d$ varies according to the distinguishability of the "paths" *IN* and *AC* (as in Young's two-slit experiment). In Figure 4, $d = pq$ in the initial state (paths are distinguishable) and $d = 0$ in the stable state (paths are indistinguishable). With the values of data from Benveniste's experiments reported in Table 1, we can calculate that $d = 0.07$.

*Table 4. From classical to quantum-like probability by varying the value of d = pq.*

| | **Value of *d**** | | | | | |
|---|---|---|---|---|---|---|
| | **0.25** | **0.20** | **0.15** | **0.10** | **0.05** | **0** |
| Prob (*success*) | | | | | | |
| Stable position #1 | **0.5** | 0.72 | 0.82 | 0.89 | 0.95 | **1** |
| Stable position #2 | **0.5** | 0.28 | 0.18 | 0.11 | 0.05 | **0** |
| Classical vs. quantum-like probability | | | | | | |
| Pure classical | × | | | | | |
| Intermediate | | × | × | × | × | |
| Pure quantum-like | | | | | | × |

In Benveniste's experiments, $d = 0.07$ for a stable position ~0.92 according to the results of Table 1.
* See Figure 6.

There is also an important consequence of the coexistence of (1) independence of perceptions and (2) intersubjective agreement. If the perceptions of the two observers are independent, but are nevertheless correlated after measurement, this means that the perceptions do not pre-exist, but are created by measurement (i.e. interaction with the macroscopic environment). This is one of the most counterintuitive features of quantum logic: a measurement of a quantum (-like) system both creates and records a property of the system.

In the stable position, the "paths" *IN* and *AC* are undistinguishable; in quantum logic, these two states are said superposed and quantum (-like) interferences are observed. Talking about what observers *really* perceive has no sense; the only reality is the macroscopic world, that is, after asking observers what they perceive. In other words, we cannot compare perceptions that remain definitely out of reach, but we can compare answers that belong to the macroscopic "reality"; we can thus construct and share a common modeling of the world external to our senses and minds.

### 10.2. Are some experimental systems more frequently associated with an experimenter effect?

We have seen that the experimental systems used by Benveniste's team were asymmetrical (the "resting state" of the system was associated with the "inactive" label). Moreover, the "signal" (i.e. the state of the system associated with the "active" label) was present in the experimental background noise.

Laws of physics must be respected during the transition of probability of "success" from 1/2 to 1. When calculating Prob (*success*) as depicted in Figure 4, we supposed that elementary random fluctuations were possible and accumulated up to a threshold sufficient for the transition. In some devices, the probability fluctuations of outcomes are allowed, but only around a fixed value or up to a maximal value. For the establishment of a relationship as described in the modeling, it must be possible to go freely from an initial point (such as "↓") to a final point (such as "↑") after a series of random fluctuations. A pollen grain which is only submitted to Brownian motion on the surface water is a good picture of such a system. The fact that Benveniste's experiments were performed in the context of a laboratory of biology was perhaps not fortuitous. Indeed, biological systems exhibit many degrees of freedom and consequently, they frequently exhibit a large "flexibility".

### 10.3. Are some experimenters more exposed to an experimenter effect?

The observation of high "success" rates requires maintaining a stable position (Figure 4). A stable position is the consequence of a question which permanently underlies the experimental process, specifically: "Is Prob (↑| *AC*) > (↑| *IN*)?" Moreover, we have seen above that a stable position is characterized by the indistinguishability of the two "paths" *IN* and *AC*. How these requirements could be translated in terms of mental cognitive processes?

If labels (*IN* and *AC*) and biological outcomes (↓ and ↑) are separately perceived by the experimenter, in the absence of any definition of "success", classical probability applies as described in Figure 7A. In contrast, if the experimental situation is perceived in an integrated manner (i.e. as a *relationship* between labels and biological outcomes), the logical structure of the results is comparable with Young's two-slit experiment as described in Figure 7B. In this case, "success" is perceived as a *new "object"* which is *not the simple addition of the separate perceptions* of labels and biological outcomes. This situation is also reminiscent of the Necker cube which does not appear as a simple collection of lines on a 2D surface, but is immediately perceived as a 3D cube by a human observer (Figure 8).

Some experimenters are probably more "talented" than others for performing such a task, namely maintaining expectation/perception of a shape rather than its separate elements. Training is certainly also important in order to structure mental processes for this purpose. Thus, experimenters working with Benveniste were dedicated to a biological system and they have repeated the same experiments day after day for years. Implicit learning – a well-known unconscious process during learning tasks – could also play an important role. Note that only one "gifted" experimenter is sufficient in the modeling; the joint probability with another observer (not particularly "gifted") will nevertheless achieve a stable position since independence of perceptions of the different observers and intersubjective agreement are still present.

The implementation of the experiments on the "memory of water" by teams which were poorly trained, more or less motivated, more or less concentrated and whose daily work was not dedicated to this theme of research could be one of the reasons of the failure of the diffusion of Benveniste's experiments. In contrast, the circumstances were quite different in Benveniste's laboratory. Indeed, the stakes were important, the experimenters were highly trained and committed in these manipulations and the "survival" of the group depended on "successful" experiments. Such situations could be favorable to the development of mental states necessary for maintaining stable position.

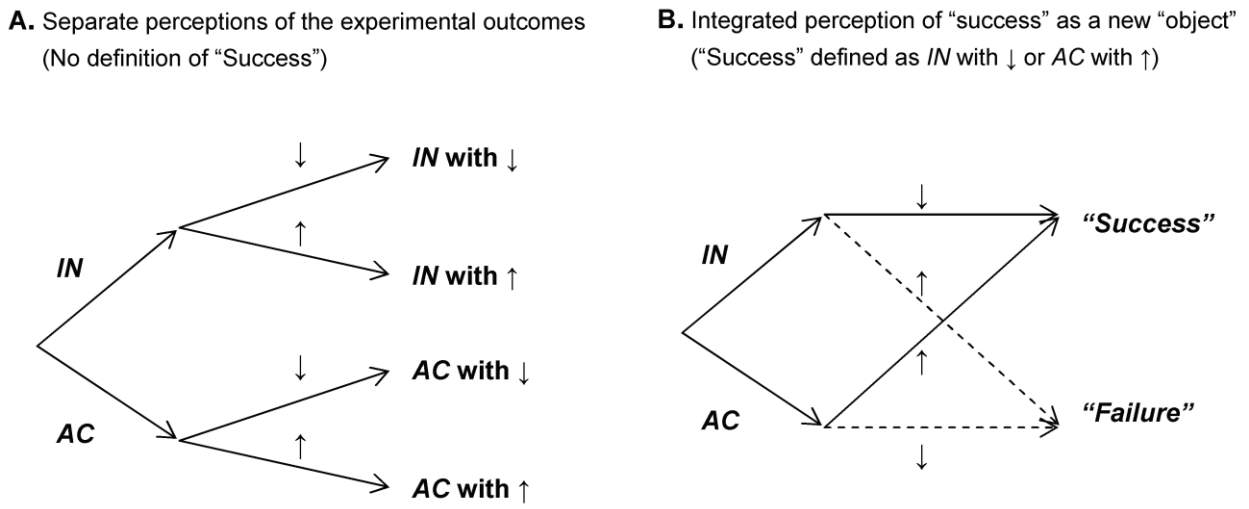



*Figure 7. "Success" as a new "object". If labels (IN and AC) and biological outcomes (↓ and ↑) are separately perceived (i.e. are not connected by any definition of "success"), classical probability applies (A). In contrast, if the experimental situation is perceived in an integrated manner, then the perception of the experimental situation is reminiscent of the logic of Young's two-slit experiment (B). In this latter case, "success" is perceived as a new "object" which is not the simple addition of the separate perceptions of labels and biological outcomes.*

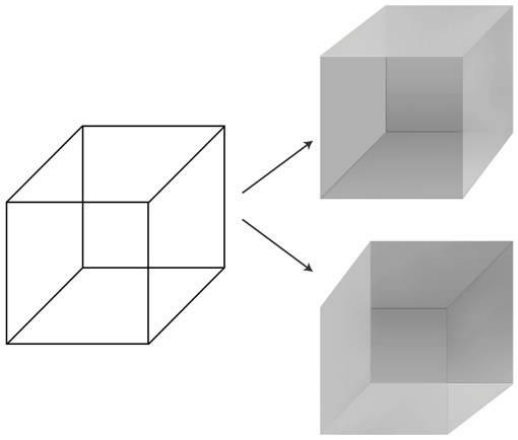


Figure 8. *Analogy with Necker cube [27]. A human observer immediately perceives the lines on the left as a cube (with two possible positions in space as shown on the right). The perception of a 3D cube needs an observer who is committed in the interpretation of the left figure. Thus, the perception of the 3D figure can be considered as a first-person perspective whereas the description of the 2D lines is a third-person perspective. In this last case, a detached observer (i.e. uninvolved in the perception/interpretation process) describes another observer who stares a paper sheet where lines have been printed [28].*

## 11. CONCLUSION

The present modeling benefited from readings of articles on quantum cognition [29-34], quantum Bayesianism (QBism) [35, 36], relational interpretation of quantum physics [37, 38], convivial solipsism [39] and hidden-measurements interpretation of quantum physics [40] (these references are not exhaustive). The modeling of Benveniste's experiments based on an involvement of the observers has two purposes. The first one is an attempt to close the controversy by suggesting that the disputed Benveniste's experiments could have been a misinterpreted epiphenomenon of a more general phenomenon. The experimenters were thought to be impartial observers of the world but, according to this interpretation, they were themselves an essential part of the experimental process that they studied. In other words, they described what they constructed and they constructed what they described.

Therefore, this reappraisal of Benveniste's experiments suggests that these results deserved attention even though the hypothesis of "memory of water" was not supported. The second purpose is to propose to extend this modeling to situations that potentially could involve unnoticed experimenter effect. Indeed, the modeling based on the involvement of the observers in experimental outcomes could give a theoretical framework for some improbable, unexplained or poorly reproducible results. More fundamentally, it could also enlighten the relationship between mental states and macroscopic states.

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