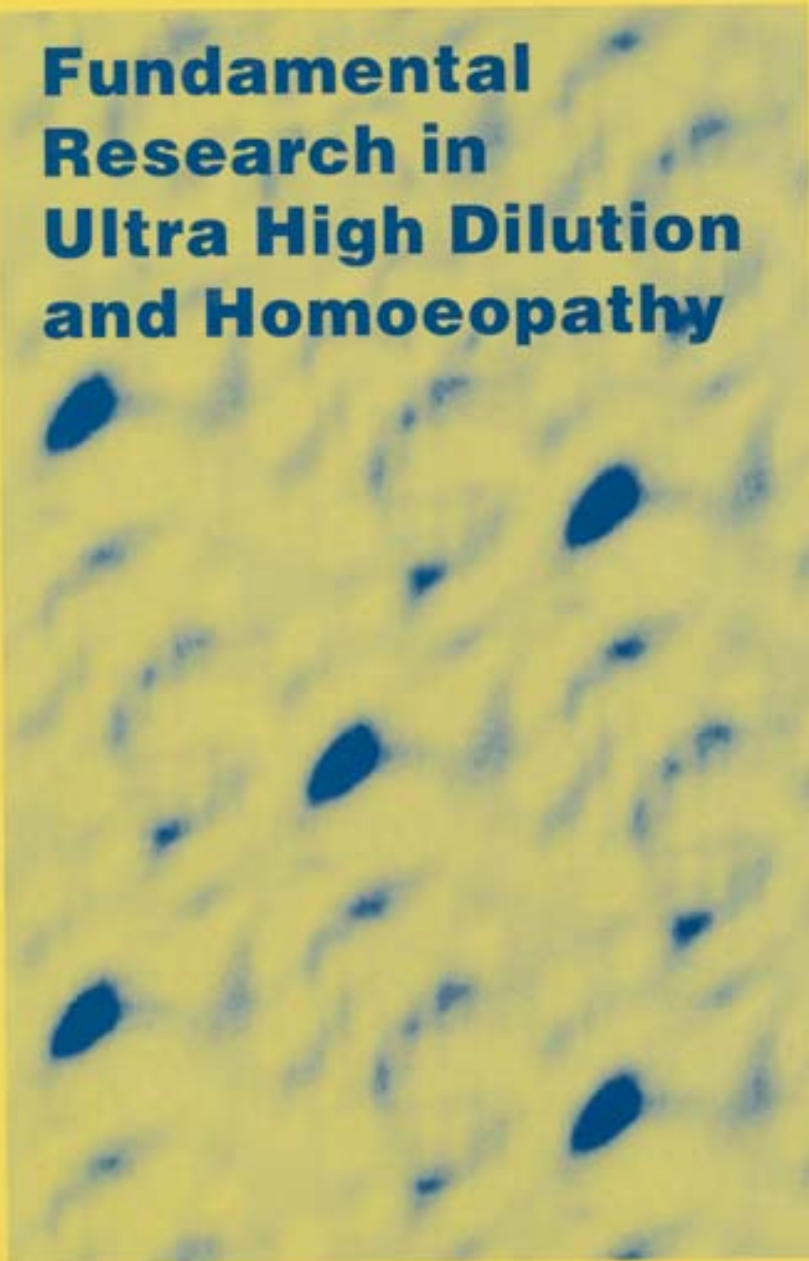


**Fundamental
Research in
Ultra High Dilution
and Homoeopathy**



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INFORMATION AND COMMUNICATION IN LIVING ORGANISMS

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1- Introduction

In many experiments, we could demonstrate the effectiveness of high dilutions prepared according to the homeopathic process. Our experiments were performed by using serially diluted homeopathic solutions of endogenous molecules active on the immune system. The results indicated that homeopathic high dilutions of endogenous substances containing theoretically no molecule ($> 10^{-24}$) had an immunomodulatory and endocrine activities (Doucet-Jaboeuf *et al.*, 1982; Bastide *et al.*, 1985, 1987, 1995; Youbicier-Simo *et al.*, 1993, 1996a, 1996b, 1997). These activities were specific and the higher the dilution, the greater the capacity of the test substances to act on the organism. As a working hypothesis concerning the mechanisms underlying the observed effects of highly diluted endogenous compounds, we propose that non-molecular specific information corresponding to the original molecule is conveyed to the recipient organism which deals with this special cue to restore normal immune and endocrine functions.

We hypothesis that this information is likely transferred by electromagnetic waves. Information can be inhibited by strong electromagnetic fields as well as it can be transferred by an electronic device (Hadji *et al.*, 1992, Endler *et al.*, 1994a, 1994b, 1997). Furthermore, this information is totally dependent on the receiver's state. In the endogenous molecule models, the organism recognizes self information automatically. These models are completely independent of the law of identity or the similia law which concern exogenous molecules and are helpful for the recognition of information by the organism.

As such, a new paradigm is necessary to attempt understanding the physical information of living organisms : just as the mechanistic paradigm seizes the material interactions between objects and the symbolic paradigm assumes linguistic facts, we introduce the paradigm of signifiers discovered by A. Lagache (Lagache 1988, 1997; Bastide & Lagache 1992, 1995, 1997).

2- Effectiveness of high dilutions of endogenous molecule according to the receiver's state.

We first tested the effectiveness of high dilutions in mice. Classical immunopharmacological *ex vivo* models were used to evaluate the effect of diluted immunomodulators. Healthy mice pretreated with thymulin (a thymic hormone) 4C, 7C, 9C or 11C respectively, showed a significantly depressed specific humoral and cellular immune response with the highest dilutions. The effect on immunocompromised mice was a significantly stimulation of specific humoral and cellular immune responses (Doucet-Jaboeuf *et al.*, 1982; Bastide 1985, 1987, 1995). We always observed an opposite effect when we compared the results obtained in healthy mice with those obtained in immunocompromised mice (Bastide, 1994).

We also tested the effect of bursin on the humoral immune response of bursectomized chickens (Youbicier-Simo 1993, 1996a, 1996b, 1997). Chicken embryos were surgically deprived of the Bursa of Fabricius at 80h of incubation and then treated *in ovo* with saline or bursin, (a tripeptide isolated from the bursa of Fabricius : Lys-His-Gly-NH₂), on days 6 and 9 of embryonic life. Four groups of chickens were tested : one untreated sham-operated control group ; one saline-treated bursectomized group ; one 7C bursin-treated group ; one 15C-20C (a pool of 15C to 20C dilutions) bursin-treated group. The four groups were repeatedly immunized with porcine thyroglobulin (Tg). Plasma corticosterone levels and serum titers of antibodies against thyroglobulin were evaluated. The immunized normal control group exhibited high concentrations of corticosterone and ACTH on day 38 while their bursectomized counterpart remained at baseline values. Normal hormonal levels were restored in the two high dilution-treated groups. Specific antibodies to Tg remained at background levels in the bursectomized group in spite of repeated stimulations, whereas the normal control group produced a strong and specific antibody response. *In ovo* administration of high dilutions of bursin induced high antibody production similar to that observed in normal chickens. These results were replicated successfully in other experiments including a randomized control tripeptide (Trp-Leu-Leu-NH₂) at the concentration of 100 fg . The latter tripeptide yielded no noticeable effect, therefore warranting the specificity of highly diluted bursin (fig 1) . These results were emphasized by a study on the circadian rhythms of these hormones. The animals underwent a 12L-12D light-dark schedule for 12 weeks. Then, we measured the circadian rhythms of plasma ACTH, corticosterone (CORT), melatonin (MLT) and the pineal enzymatic activities of N-

acetyl-transferase (NAT) and hydroxy-indole-o-methyl-transferase (HIOMT). The data showed that intact and bursin-supplied bursaless chickens exhibited pronounced diurnal rhythms of plasma ACTH and CORT, with low light-time levels and significantly higher night-time values reaching a sharp peak at midscotophase.

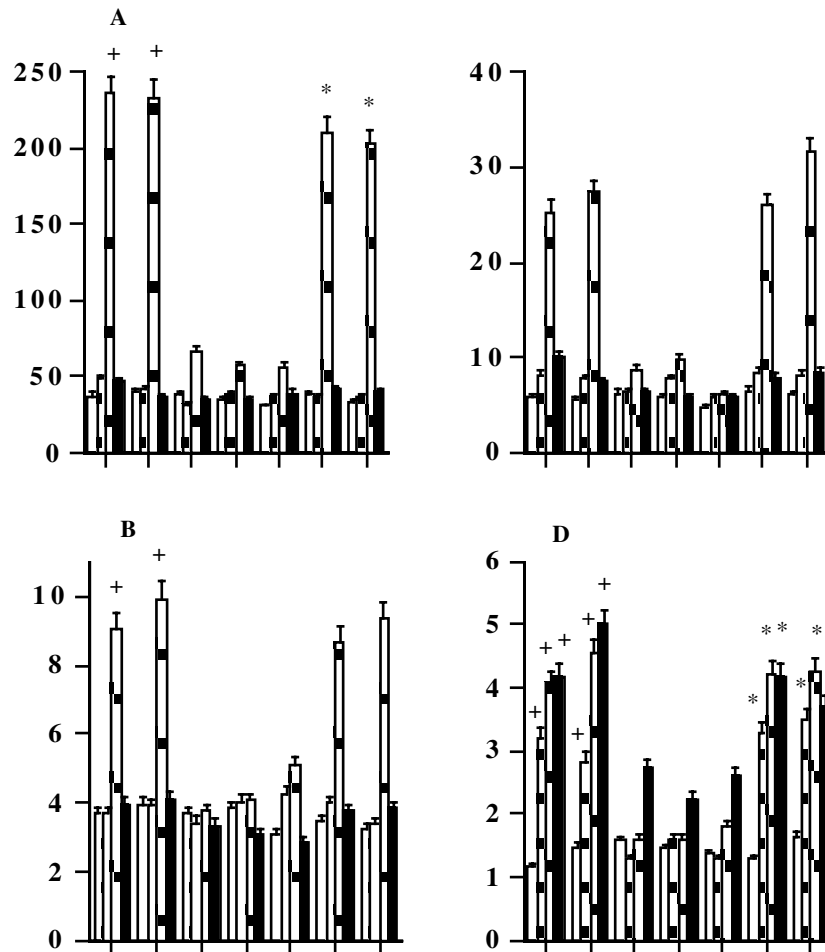


Figure 5: ACTH (A), corticosterone (B), melatonin (C) and anti-Tg IgG (D) responses to immunization against porcine Tg. Seven experimental groups were used (N, N+S, Bx, Bx+S, Bx+Pf, Bx+Bf, Bx+B⁻²⁷). The animals were immunized at the age of 21, 30 and 38 days. Blood samples were collected the day before the first immunization (d20: white columns) and at the age of 29 (dotted columns), 38 (hatched columns) and 47 (dark columns) to check the plasma levels of hormonal (ACTH, corticosterone, melatonin) and specific antibody (IgG) responses.

+P<0.01 vs Bx; *P<0.01 vs Bx+S.

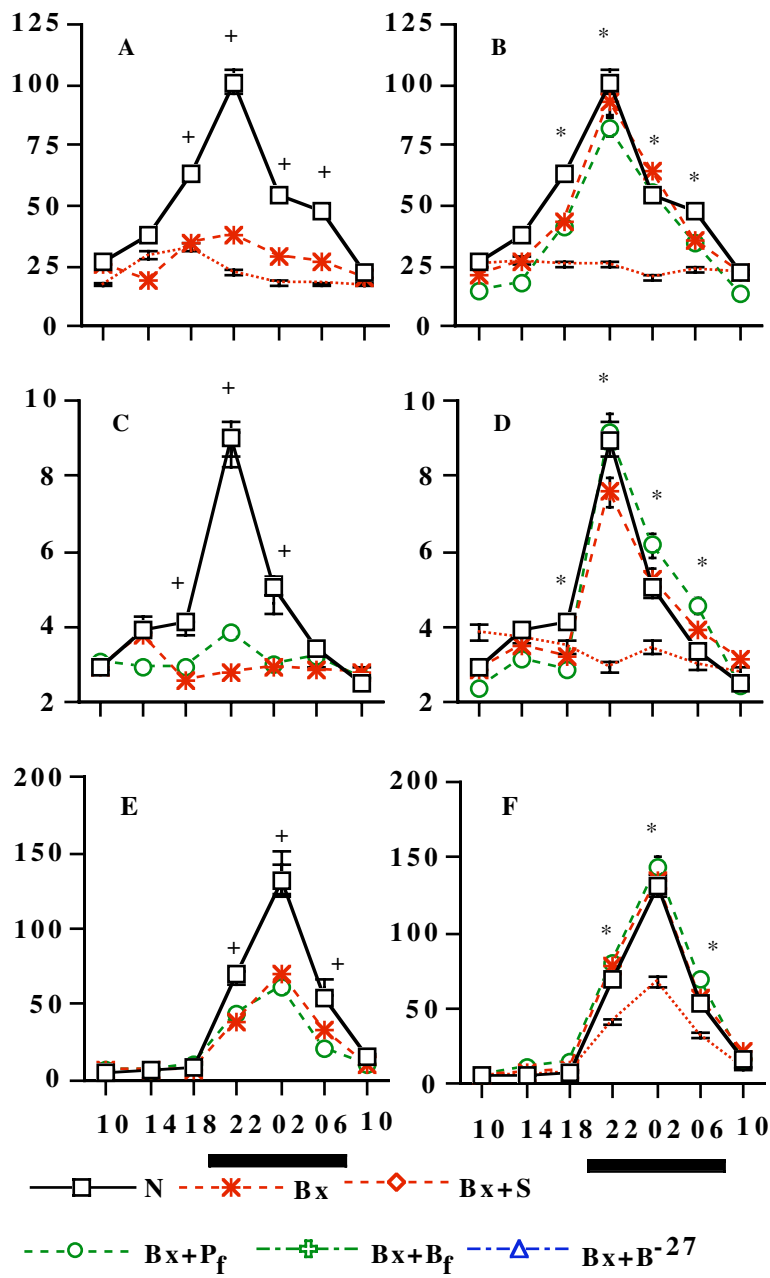


Figure 7. Circadian rhythms of the pituitary (A, B), adrenal (C, D) and pineal (E, F) hormones. The 7 groups of animals listed above were submitted to a 12L-12D alternating light-dark cycle, with lights off from 0700 to 1900 (black bar below the figures). The plasma samples were assayed for ACTH (A, B), corticosterone (C, D) and melatonin (E, F). +P<0.01 vs Bx; *P<0.01 vs Bx+S.

The waveform rhythms of both hormones were severed after bursectomy. In all groups and regardless of the treatment, a daily rhythm of MLT with middark crest was recorded

and persisted in Bx birds despite 50% reduction in height. This waveform profile was in keeping with the rhythm of NAT, but HIOMT remained arrhythmic. Neither the saline nor the control compound (Trp-Leu-Leu-NH₂) could reverse the effects of bursectomy.

The effect of administration of high dilutions of bursin / interleukin 3 / thymulin in total body irradiated mice gave us very precious indications on the activity of high dilutions (Guennoun *et al.*, 1996, 1997). The immunodepression model was a strong single total body irradiation of inbred BALB/c mice treated before and after irradiation in drinking water by high dilutions of a mixture of thymulin, bursin and IL-3. Our purpose was to evaluate the modifications in mortality rate of high dilution treated mice compared with irradiated untreated control mice. The evaluation of the recovery of lymphocyte status was also performed in some cases. The animals underwent total body irradiation (TBI) by ⁶⁰Cobalt γ - rays. The dose of irradiation was 6.3 ± 0.2 Gy (0.12 Gy/min); it was measured by PTW Unidos 0.125 cm³ dosimeter. The beam covered the whole surface of the cage (20 cm x 20 cm) containing the mice. Mice were treated "per os" by drinking water. Before each experiment, all the solutions were blinded. When used, the solutions were succussed for 2min 30; then 2.5 ml were added to 250 ml of "Contrexeville" water (trade mark of a mineral water for consumers instead of tap water). The final solution was poured into the feeding bottle which was covered with a metallic paper (3 layers) and covered again with adhesive plastic (to avoid mice eating the metal). Mice were treated *ad libitum* starting 48 h before irradiation and throughout the experimentation. The different solutions were renewed every 7 days in the same bottles without any further sterilization. The following groups have been tested:

Control group: irradiated mice receiving only 2.5 ml of MilliQ pure water in the drinking water (USW).

Succussed solvent group: irradiated mice receiving 2.5 ml of succussed solvent diluted according to the remedies (SW pool 15-20C).

Succussed remedies: irradiated mice receiving the ternary highly diluted solution bursin-IL3-thymulin (BIT) (pool 15-20 C) in the drinking water (11 experiments throughout the year). When the mortality rate was expressed according to circannual variations, we observed that the radioprotective index ((Index = % mortality unsuccussed water group - % mortality Bursin/IL 3/THymulin) was higher in the cold season than in the warm season. These variations in sensitivity may be related to the circannual variations of the immune response. It was demonstrated that the cellular immune response was greater in the warm season while the humoral immune response had its acrophase in November-December (Mac Murray *et al.*, 1983). The defence against immunodepression caused by irradiation is much more due to the cellular

immune response than to the humoral response as in all acquired immune deficit. Taking this into account, it is evident that the irradiated mice were protected better in summer by high dilutions. Oppositely, they were not protected at all or died more than the untreated controls in winter as shown in Fig.3.

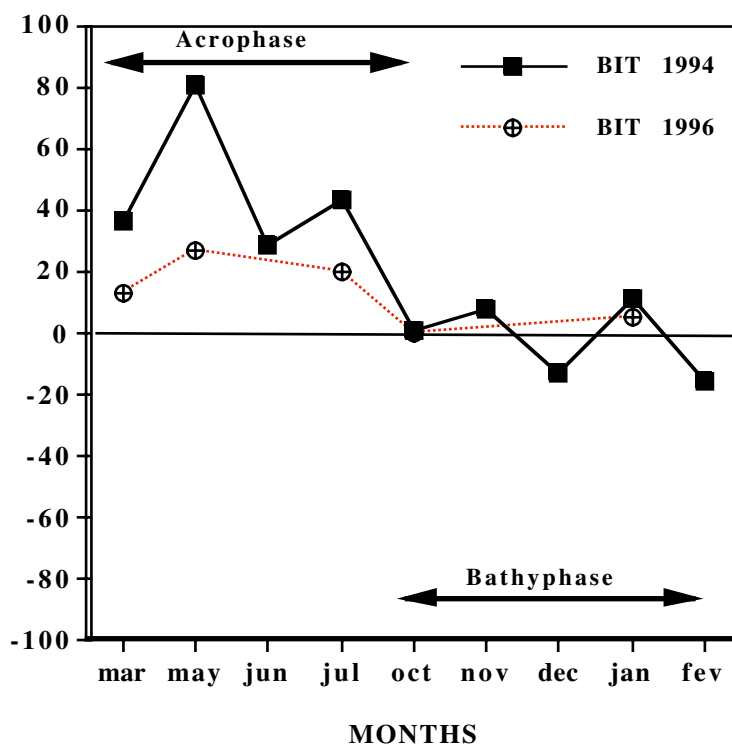


Figure 3: Highly diluted BIT radioprotective index according to the season (Guenoun *et al.*, 1996, 1997).
(Index= % mortality unsuccessful water group - % mortality Bursin/IL 3/THymulin)

3 - An endogenous molecule information received and treated by a living organism is either corrective as a physiological response or pathogenic when it goes beyond the receiver's capability.

The experimental results reported here demonstrate the efficiency of highly diluted homeopathic solutions of hormones or peptides in biological systems. Of course, all these experiments have nothing to do with the similia principle which is a communication system about symptoms. They raise the question of the nature of the thymulin-derived

signal, for example at a concentration below 10^{-23} M, or bursin used at the theoretical concentration of 10^{-27} g (15-20 CH pool). These solutions are theoretically devoid of active molecules. We propose, therefore, that the succussed preparations obtained by successive 100-fold dilutions of immunomodulators transmitted "information" specific to the molecules used to prepare the solution, even though no active substance was present in the solution. This "information" has to be defined: this approach was permitted thanks to the new paradigm proposed by Lagache (1988).

The paradigm of signifiers takes place within the framework of the logic of analogy. The communication will be mediated by "*semantic objects*" as physical signifiers : their application can be used to interpret the therapeutic effects of homeopathic high dilutions. In fact, the living organism cannot be considered as an object: it functions as a whole and cannot be separated into its different elements; it is different before and after the events that it comes across; it is continuously modified as a function of time; it has a psychological memory and a physical one ; it is in a continual and irreversible learning process. The living organism (body and mind) is a complex structure able to exchange information with the external world; information also circulates in the internal world allowing exchanges at every level : *the living organism is an informed-informing structure. Living beings communicate with their world in a non verbal way, whether on a somatic or psychological level.*

The *semantic object* makes sense for the living organism at the body level : the circulation of this type of signifier has its own original laws.

- Each piece of information is not an object even if it has a *carrier*: for example, the information of the remedy is carried by the potentized dilution (the transmission of the information being due to the electromagnetic carrier obtained by the succussion of the solvent of the remedy as shown by Endler and colleagues (1995, 1997).

- The sense is non-local; it concerns the whole organism designated as the receiver. This receiver then creates the meaning and is able to modify its behaviour.

- The simplest mode of representation for living structures is a *mimetic representation*. When the living organism receives this information brought by the semantic object (i.e. the potentized endogenous molecule) , it receives it not as a material object but as information about this object which calls for a processing and active regulation by the whole organism: this is an operation of *active mimesis* and the effect is compared to a physiological function. The bursectomized chickens treated by high dilutions of bursin is the best model: no residual information exist and a strong

questioning of the embryos allows a good reception and treatment of the information which acts in a physiological manner.

However, when the mimetic representation is received but either too strong, or in such a way that the organism cannot react positively, the opposite effect is observed and designated as a *passive mimesis*: a pathological effect appears or increases. The model of the irradiated mice is helpful for understanding. It is a break-point model in which the slightest variation of the mice health state can induce either an active mimesis which gives a protective effect (acrophase of the cellular immune response during the warm season) or a passive mimesis which increases the pathogenic effect (lowest level of the cellular immune response in winter).

The same observation has been done by Endler et al. in the metamorphosis of the frogs modified by high dilutions of another endogenous molecule, thyroxine (1997a, 1997b). As the frogs are normal and not deficient, the thyroxine information will be understood in different ways according to the capacity of the normal frog to treat this information. When the normal frog receives strong material dosis (i.e. 10^{-9}M), the authors observe an acceleration of the metamorphosis of the normal frogs which can be considered as passive mimesis as a pathogenesis which would collect toxic effects. When a 1 to 100 dilution occurs, the active mimesis is observed and the metamorphosis is slowed down. When low potencies are used, the authors observe a slowing down effect; the treatment with high potencies shows a slowing down effect or an acceleration of the metamorphosis according to initial or experimental conditions: as we could demonstrate with the irradiated mice model, it is very easy to change the direction of the effect by using endogenous molecules: the information is treated but sometimes, it will produce the physiological effect (active mimesis) or the opposite effect (passive mimesis). The information received is an addition to the normal thyroxine information just at the period of the metamorphosis: this supplement of information can be misunderstood (as in our irradiated mice) and the opposite effect is observed.

These variations did not exist in the model of the bursectomized chickens: no bursin information was remaining as the chickens were surgically deprived at day 3 of the embryonic life. The highly diluted bursin was always acting in an active mimesis as the physiological effect because it was *replacing the normal information* of the molecule.

4 - The simila law model

All these examples of the informative effect of high dilutions of endogenous substances are helpful to approach the functioning of information in living organisms. However, the effects of endogenous molecules is totally independent of the

similia law or the identity law even though their interpretation can be done in the same paradigm. However, when high dilutions of an exogenous substance are administered to a patient, the framework of information which has to be used is the *similia law which consider only the symptoms*. In a patient, the pathological symptoms may be considered as an attempt at communication by the patient's body: the symptoms become the process of communication about the pathology, the organism being unable to find itself the mechanisms of regulation necessary to find again the normal state. These symptoms are read by the physician to identify the remedy able to give the whole symptoms in a healthy subject (similia law): the homeopathic remedy will act as a semantic object and will transmit an artificial and alleviated information on the whole symptoms. Then, the body is able to recognize and treat this information which allows the negation of the symptoms recognized as an erroneous adaptation. The more similar the symptoms of the patient and the remedy, the more effective the remedy. The medical device has to re-inform the patient and makes his symptoms move on towards a higher level of integration. The action of the homeopathic remedies consists of a dynamic analogy between pieces of information as proposed by A. Lagache in the paradigm of signifiers.

The observation of the biological effects of high dilutions of endogenous molecules such as hormones (thymulin, bursin, thyroxin) or cytokins have been of help for understanding the information process of a living organism: since these self-informations were naturally and automatically recognized, no framework of lecture such as identity law or similia law were necessary. As such, we could demonstrate the organism's capacity to increase a pathology or to correct it according to its capacity to treat the endogenous molecule information transmitted by potentized high dilutions.

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