Chapter 1. A “telephone for molecules”

A scene of science fiction where one teleports “ghosts of molecules”

On July 9th, 1992, at Clamart, there was a public demonstration, which if conclusive would be a strong argument for supporting the new research of J. Benveniste. These new experiments, which J. Benveniste set up a few months ago, generated more incredulity than high-dilution experiments themselves. J. Benveniste indeed claimed that he was now capable of transferring, through an original device, the “activity” of biological molecules to water which thus acquired the “biological properties” of the original molecule.

Four visitors foreign to the laboratory participated to this demonstration.[1] The experiment, called a “transmission experiment”, was performed with an electronic device which, to tell the truth, did not look much. It was reminiscent of these devices that handymen who are passionate with electronics build with components bought in specialized stores. Nevertheless, without seeming put off by the rustic character of the equipment, the visitors placed at the “output” of the device a vial of water that was called “naive”. At the “input” of the device, a tube containing a solution having a biological effect was also placed. Then the device was switched on. After fifteen minutes, the tube at the “output” of the device was considered to be “impregnated”; water was supposed to have acquired the “biological properties” of the solution contained in the tube placed at the “input”.

Irresistibly, we cannot refrain from thinking about the numerous scientists – crazy, of course – who populated the imagination of writers, film-makers or comic strip writers and who, through complex electric equipments, transfered the soul of a human being into a robot. The best-known example is the robot of *Metropolis*. At Clamart, however, one just transfered the “soul” of dissolved molecules… Moreover, the experiment was performed in full light, on a beautiful day of July and the various protagonists had nothing frightening. One was thus far from the nights full of lightning which usually illuminate the mad experiments of these fictional scientists.

Meanwhile, the visitors changed the labels of the waer tubes that received various “imprints” during “transmission”. Thanks to this coding, the results of the experiment and its interpretation could not be influenced – whathever the reason and the mechansism –- by the experimenter. However, these new experiments are not subjective. It is one of the main reasons for which the test of basophil degranulation has been abandoned and replaced by this new method. As a general rule, results obtained after blind process are always more

convincing, if one can exclude of course a complicity between those who code and the experimenter.

When the operation of coding is ended, the tubes were given to Jamal Aïssa and Hédi Litime, two collaborators of J. Benveniste who were in charge of the biological model used for these experiments. Thus let us successively describe the new device for "electromagnetic transmission" and the biological system which was coupled with it.

How did the "telephone for molecules" work?

The device which allowed these unexpected experiments was a radio-electronic device built from a kit sold in specialized shops. This kit allowed building a phone amplifier at little cost with electronic components, a printed circuit board and a few weld points. In 1992, this type of device was used as a sound amplifier for a telephone. The loudspeaker, normally connected to the output of the amplifier, was replaced here by an electric coil (also known as solenoid). The input of the device was connected to another coil (Figure 1.1). The complete device was placed into a plastic box with a switch outside and input and output coils. This is a brief description of this device which was supposed to revolutionize biology. We are far from high technology and from sophisticated equipment. But, after all, important discoveries have been sometimes performed with limited equipment.

A tube containing the solution with "biological activity" to be transmitted was placed on the coil at the input and a tube or a vial containing water that one wished to "imprint" was placed on the coil at the output of the amplifier. The idea behind this device was that the variations of the electromagnetic field supposed to be emitted from the solution containing "real molecules" induced an electric current in the coil at input. This current was thought to be amplified by the low-frequency amplifier and then injected in the coil at the output therefore creating an electromagnetic field in the neighborhood of the latter. The electromagnetic field that was generated by the coil at output was supposed to structure water. Water was thus supposed to behave like a magnetic tape. The technical aspect of this device should not frighten the reader. It is sufficient to consider this electronic device as a simple "black box" with an input and an output.

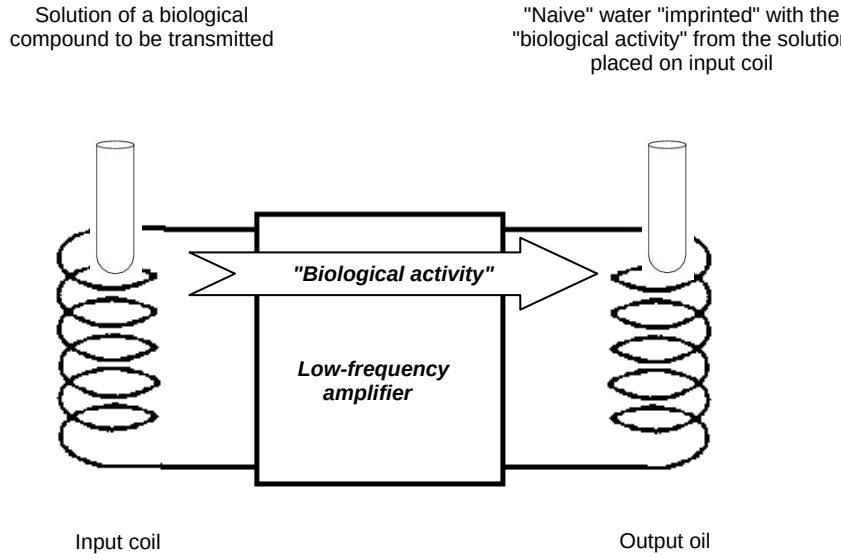


Figure 1.1. First version of the device for "electromagnetic transmission". The first version of the transmission device included an amplifier which was placed between two electric coils (solenoids). On the coil wired at the input of the amplifier, a tube containing the compound with an "activity" to be "transmitted" was placed; on the coild wired at the output, one placed a tube or a vial containing "naive" water to be "imprinted" thanks to the electromagnetic field supposed to be emitted from the output coil.

How to listen to information transmitted by the "telephone for molecules"?

In other words, how to know that the "ghosts of molecules" have been transmitted and have correctly "structured" water? For this purpose, a biological model which is known to react in "classical conditions" to the compound to be transmitted is used. The device of physiology used by J. Benveniste for these experiments is called "Langendorff preparation" or isolated infused heart. It allows physiologists to maintain the functions of a heart of rat or guinea pig during several hours. The effects of pharmacological agents on heart functioning can thus be studied.

Here again, we will simplify the technical descriptions so as not to dilute the main subject. The model of Langendorff is a very classic experimental device in heart physiology. It allows measuring various parameters of the heart functioning: frequency, tension of the cardiac muscle or coronary flow. We will talk only about coronary flow because the team of Clamart quickly focused on it.[2] It is indeed with the changes of this parameter that the effects of high dilutions and electromagnetic transmissions were best evidenced.

The understanding of these experiments requires simply remembering that one studies the flow of a liquid which – by construction – goes necessarily through the coronary arteries. The coronary arteries play the role of flow regulator according to their state of contraction. To vizualise the coronary flow and it variations, the reader can imagine a flexible rubber pipe enclosed in a fist. As the fist tightens more or less the pipe, the flow of water varies accordingly. When the muscles of the wall of the coronary arteries contract, the flow through the artery decreases. On the contrary, if the muscle fibers of the wall relax, the flow increases. This is what is sketched on Figure 1.2.

How was the coronary flow measured? Simply by using an automatic sampler, which collected the liquid that flowed under the device (one minute per tube) (Figure 1.3).

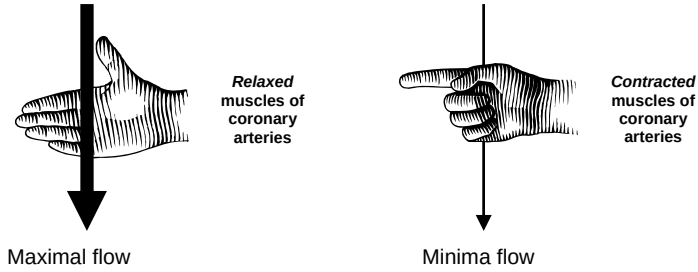


Figure 1.2. Flow changes of coronary arteries. The flow of liquid through coronary arteries is like the flow through a flexible pipe. The flow depends on the state of contraction of the muscle fibers in the wall of the coronary arteries. These muscle fibers are pictured here by a hand. When the muscle fibers are relaxed, the coronary flow increases; on the contrary, when they contract the coronary flow decreases. Various biological or pharmacological substances (mediators of inflammation, acetylcholine, bacterial endotoxins, etc.) modify the contraction state of these muscles. The consequences are variations of coronary flow.

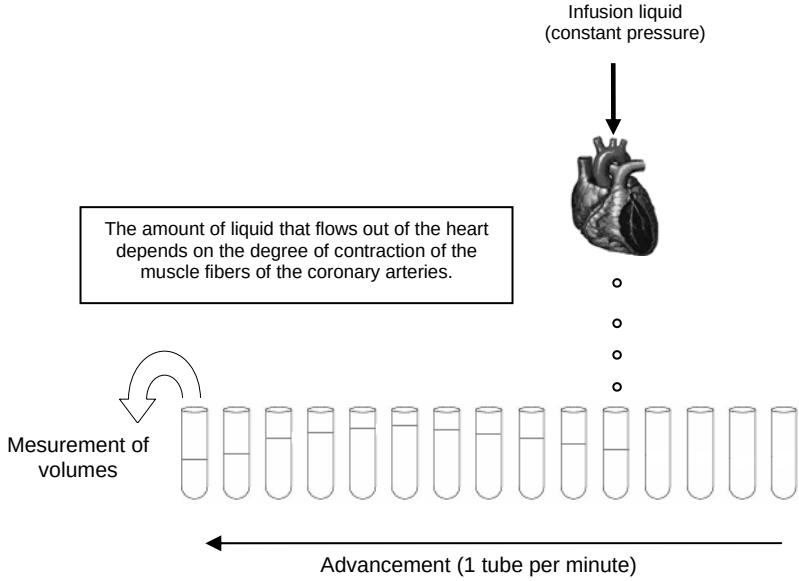


Figure 1.3. Measurement of coronary flow of isolated heart of guinea pig or rat.
The heart is continuously infused by a physiological liquid. The amount of liquid which flows outside the heart varies according to the state of contraction of the muscles in the wall of the coronary arteries. The liquid is collected in tubes which circulate below (one per minute). The volume of liquid in each tube is measured through a graded tube with a precision of 0.1 mL.

To understand how the changes of coronary flow are interpreted, here is how the results appeared for the blind samples n°3 and n°4 of the experiment of July 9th on the worksheet of the experimenter (Figure 1.4). Each minute, the volume collected during this duration is recorded. The injection of the sample is performed when the coronary flow is stable (during at least 3 minutes).

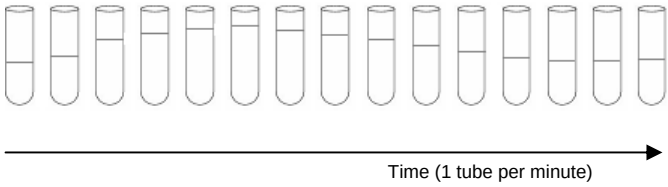
Figure 1.4. Measurement of the coronary flow of the isolated heart of guinea pig or rat. Here is a data sheet in an experiment intended to assess variations of the coronary flow with the Langendorff device. After checking the stability of the flow for 3 minutes, the sample to be tested was injected (arrow). Every minute, the physiological liquid was measured with a precision of 0.1 mL and the result was recorded in the corresponding column and line. On this example we note that the sample n°3 induced a change of the coronary flow ("active" sample) whereas the sample n°4 did not induce significant variations ("inactive" sample).

	Volumes (mL)	
Time (min)	n°3	n°4
-3	4.0	4.1
-2	4.0	4.1
-1	4.0	4.1
1	4.0	4.1
2	4.5	4.0
3	5.8	4.1
4	6.5	4.1
5	6.8	4.0
6	7.0	4.1
7	6.9	4.1
8	6.2	4.0
9	6.0	4.0
10	5.5	4.1
11	5.0	4.1
12	4.5	4.1
13	4.2	4.1
14	4.2	4.1
15	4.2	4.1

With the sample n°3, we observe that the flow which was 4.0 mL/min at the baseline increased from the second minute and reached a maximum of 7.0 mL/min at the 6th minute and then gradually decreased. There were only few changes with the sample n°4: the values oscillated between 4.0 and 4.1 mL/min. Even without cutting-edge knowledge in biology or in statistics, it is easy to understand that these two samples were associated with very different profiles of flow variations with time (Figure 1.5). Let us recall that these two samples were initially the same. The only difference *a priori* could be only in a property acquired during the process of transmission.

Experiment of July 9th, 1992

Effect of sample n°3 on coronary flow (active sample)



Effect of sample n°4 on coronary flow (inactive sample)

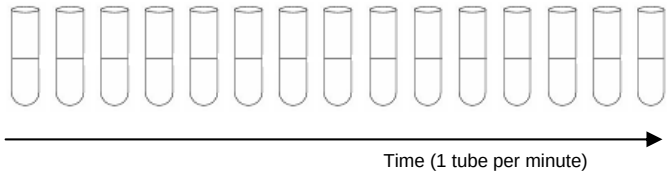


Figure 1.5. Effects of samples n°3 and n°4. This figure illustrates the "direct" demonstration of the effects of high dilutions or electromagnetic transmissions with the Langendorff device. The samples n°3 and n°4 were tested on July 9th, 1992 in a blind experiment (cf. Figure 1.4). One notes on these pictures where the volumes of liquid from the 1st to the 15th minute are represented to scale that the variations of flow for the sample n°3 are immediately visible; on the other hand, concerning the sample n°4, one notes that there was no change of the flow.

On the isolated heart, a pharmacological agent is all the more "active" that the change of coronary flow which it induces is more important. Since the basal value can varies with different preparations, one generally gives the maximal variation of the coronary flow as a percent of the basal value measured during the minutes which preceded the injection:

$$\% \text{ of maximal change of coronary flow} = 100 \times (\text{maximal flow} - \text{minimal flow})/\text{basal flow}$$

Thus for sample n°3, one calculates a maximal change of coronary flow equal to $(7 - 4)/4 = 75\%$. For sample n°4, one finds, $(4.1 - 4)/4.1 = 2\%$.

This calculation always gives positive values. We could distinguish the overall decreases or increases of the coronary flow but we will not do it for reasons of simplification and especially because it has no impact on the understanding and the interpretation of the experiments that we describe here. Unless expressly

indicated, what is reported is always a percentage of absolute change of coronary flow. To put it simply, we try to know if something "moves" but we are not interested in the direction of this change. However, on graphs, we can distinguish the increases and the decreases of the coronary flow with time because in this case the formula applied for every experimental point is:

% of change of coronary flow at time t = 100 × (flow at time t – minimal flow)/basal flow

In practice, one considers that below 10% the change of flow is not significant. We can thus conclude that sample n°3 was "active" and that sample n°4 was "inactive".

Two hearts which beat in unison

The above description allows understanding the interest of J. Benveniste for this experimental device in his quest for the "crucial" experiment which would convince skeptics. On one hand, the effect (or the absence of effect) can be seen first hand within a few minutes after the administration of the content of the "imprinted" vial. On the other hand, "transmission" was made in a sealed vial while the preparation of high dilutions required the decreasing passage of molecules from tube to tube with consequently a non-zero risk of contamination. Even if we reported arguments against contamination as an explanation of the high dilution results in the first part of this book (Chapter 15), the fact that this question was discarded, was obviously more satisfactory.

Furthermore, during several years, from 1992 to 1996, Benveniste used two Langendorff devices that worked in parallel. The purpose was not to increase the pace of the measurements, but rather to consolidate the results with two measurements for the same sample on two different hearts. Besides, a series of samples was sometimes tested in ascending order on device A and in descending order on device B. This allowed making sure that there was no persistence or contamination due to a previous sample. Useless to say that this kind of precaution – that is the use of dual equipment – is rare for "classic" researches.

If we come back to the samples of the experiment of July 9th, we notice that, tested in parallel *on the second device*, the samples n°3 and n°4 confirmed the previous results (Figure 1.6) with 93% of maximal variation for n°3 and only 3% for n°4. We consequently feel more assured for these results. We must admit that we chose these samples for didactic reasons because the change or absence of change was obvious. On average, as we will see, the changes of the coronary flow were rather around 20%.

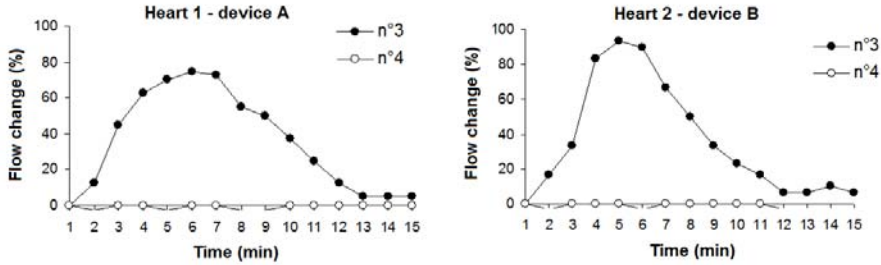


Figure 1.6. At each time point (in minutes), the change of the coronary flow is calculated as a percentage by dividing every change of volume in mL with the basal value of the flow. These percentages are shown on these figures. They correspond to the changes of coronary flow reported for samples n°3 and 4 coming from the experiment of July 9th, 1992. It must be noted that each of the samples was tested on two Langendorff devices which worked in parallel in order to confirm the results.

With some compounds or in some experimental situations, the profiles of the coronary flow over time can be much more complex than in these examples where a simple increase of the coronary flow was observed. Thus, a decrease of the coronary flow, then an increase and finally a return at the basal level were sometimes noticed. This could be due to the large number of mediators released by the heart during this type of reaction. Some substances dilate coronary arteries and consequently increase coronary flow. It is the case for example with nitrovasodilators which are used in patients with coronary insufficiency. Other pharmacological substances such as caffeine contract coronary arteries and thus decrease coronary flow. Rats become allergic to proteins such as ovalbumin (albumin of white egg) after injection of this protein. A few weeks later, the heart of the animal is placed in the device of Langendorff and an allergic reaction is induced by the injection of a small quantity of this protein in the liquid of infusion of the heart. This allergic (or anaphylactic) shock is accompanied with an upheaval of the functioning of the heart. Indeed, diverse mediators of inflammation are then released by heart tissues and various profiles of coronary flow – combining increase and/or decrease – can be observed according to the sequences of release of the mediators.

Generally, after the last "imprinted" sample had been tested during a working session on an isolated heart, a sample of the the compound at "classic" concentration" was tested (for example, ovalbumin at 0.1 µmol/L) to assess the reactivity of the heart (calibration) and to demonstrate that the biological preparation had a normal behavior in "classic" conditions.

Another compound – known as lipopolysaccharide (LPS) – was often used in transmission experiments. LPS is an endotoxin, which is a substance from the bacterial wall also inducing a variation of the coronary flow.

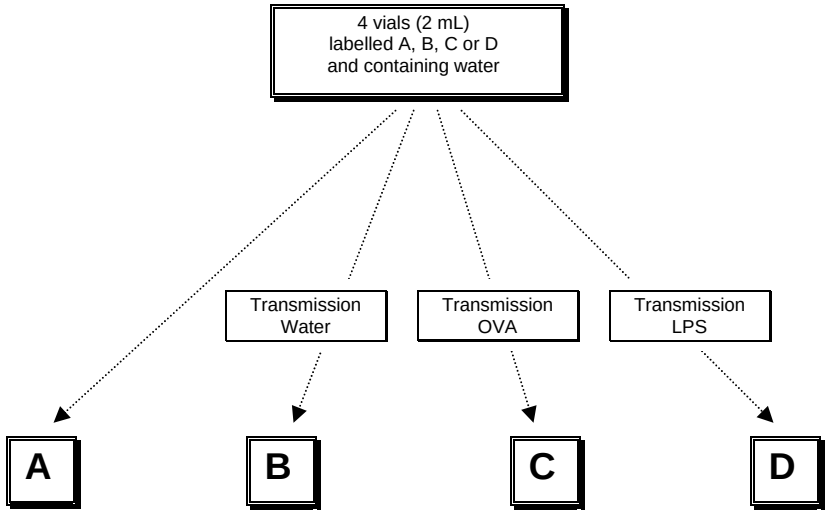
Which "messages" were transmitted on July 9th through the "telephone for molecules"?

As indicated on the technical sheet on the next page, several molecules underwent the process of "transmission" during this experiment of July 9th, 1992. First, ovalbumin (sample C) and LPS (sample D) were transmitted from samples containing solutions of these substances. Then, as a control, a vial of water (without dissolved compound) underwent the same process of transmission (sample B). Finally, a vial of water which did not undergo transmission was also included in the experiment as an additional control (sample A).

Overall, 12 tubes were prepared and one expected to find 5 active samples (4 "ovalbumin-transmitted" samples and 1 "LPS-tranmsitted" sample) and 7 inactive samples. It is necessary to note that one did not try to discriminate LPS and ovalbumin in this experiment. One "simply" wished to discriminate "active" and "inactive" samples. In order to understand the stake of this experiment, it is necessary to remember that, in the current state of knowledge, there is no physical, chemical or biological means to discriminate these various samples.

Technical sheet of the experiment of July 9th, 1992

Type of experiment: electromagnetic transmission on July 9th, 1992
Place of the experiment: Clamart (for transmission and assessment of samples)
Blinding: on July 9th by 4 participants not belonging to l'U200; unblinding on July 13th.
Number of recordings to be tested: 12 tubes tested on July 10th on 4 hearts (measurements on the two Langendorff devices in parallel).
Additional in-house blinding: no.



Blinding of 12 tubes* numbered from 1 to 12 (*blind tests*):

4 tubes « **A** »; 3 tubes « **B** »; 3 tubes « **C** »; 2 tubes « **D** »

+

3 tubes not blinded (*open-label tests*):

1 tube « **A** »; 1 tube « **B** »; 1 tube « **C** »

*The content of each tube was obtained after 1/1000 dilution of "informed" water in physiological saline for heart infusion.

Consistent results

On July 10th, a small volume of each of the 12 tubes was injected in the infusion circuitry of the two devices of Langendorff. We have already anticipated the results obtained with samples n°3 and n°4. Four hearts of guinea pig allowed the testing of all samples (2 successive hearts for each device). The results are described in Table 1.1.

Test samples	Maximal changes of coronary flow	
	Apparatus A	Apparatus B
Blind tests		
n°1	55%	15%
n°2	58%	24%
n°3	75%	93%
n°4	2%	3%
n°5	93%	53%
n°6	3%	2%
n°7	5%	5%
n°8	8%	8%
n°9	3%	5%
n°10	3%	5%
n°11	13%	14%
n°12	42%	37%
Open-label tests		
Water	2%	3%
Transmitted water	2%	3%
Transmitted ovalbumin	35%	37%
Ova 0.1 µmol/L	55%	45%

Table 1.1. Results of the experiment of July 9th, 1992 before unblinding. One expected to find 5 active tubes (transmitted ovalbumin) and 7 inactive tubes (water or transmitted water). One indeed notices that 5 samples induced large changes of coronary flow: samples 1, 2, 3, 5 and 12 (there was however a doubt on sample 11 which had values superior to 10%). Expected results were obtained with open-label samples.

The results of the experiment therefore seemed consistent. We indeed notice that 5 samples (n°1, 2, 3, 5 and 12) were very active during two independent

measurements.[3] Furthermore, the open-label controls were correct. It would be astonishing if the experiment was not a success. But it is necessary to wait for the unblinding which took place next Monday.

Notes of end of chapter

[1] The participants in this experience were Raphaël Douady (CNRS, Ecole Normale Supérieure, Paris), Alexandre Fiebig (Ecole Normale Supérieure Cachan), Anne Jullien (medical student) and Michel Schiff (CNRS, Paris).

[2] For the interested readers, let us remind that the coronary arteries irrigate the heart muscle. Their entry is situated on the aorta, where the latter leaves the heart. In the Langendorff preparation, the circulation of the liquid is against the normal flow. Indeed the physiological liquid at constant pressure is administered by a cannula introduced into the aorta by taking care of not going too far and to block the entry of the coronary arteries. The valves of the aorta prevent from penetration into the left ventricle. The liquid is then forced into the coronary arteries. Having irrigated the heart, the liquid is collected by the coronary sinus and conducted into the right auricle. The liquid thus goes out of the heart by the right vessels.

[3] One could consider that sample n°11 being above 10% is significant. It was moreover considered inactive but doubtful ("negative?" was reported on the data sheet before unblinding). One could also point out that given the important reactivity of the heart on this day for this series of samples, the background noise could be higher.