The issue of depression and the a-quantum consciousness
Remembering a fabulous day - Letter to Psychiatrists

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ABSTRACT
This letter is not a classic scientific work, but a cavalcade of memories that recall the long road of a research pathway on the relationship between psychopathology, brain and consciousness.

Extraordinary things happened during this journey. Discussions with Kary Mullis, meetings with world-renowned scientists such as Stuart Hameroff, Mark Rasenick, Mario Tiengo and others.

With them, a field of comparison has opened on the fascinating theme of consciousness in its relations with molecular aspects. The state of consciousness in a biochemical reading that, based on acquired experimental data, seems to intersect with the quantum dynamics that try to explain it. This letter is addressed to all psychiatrists who face a difficult contact with the human mind every day.

Dear Psychiatrists
Perhaps expression never more appropriate has been that of Kary Mullis when it conceived the title of its autobiographic book: dancing naked in the field of the mind.

What was for him to be naked in the field of the mind I have never asked him, I believe to have understood, instead, what it means for me and for the friends Fabio and Lucio that I have involved in a problem as old as the world, and still without a solution. Everything is born from a damned day when I thought to face one of the thorniest problems that can torment the human being: the depression.

The depression, in the bread of the psychiatry, has represented a bitter salt. The man tries to enter the mind of another to understand him and to snatch one of his greatest secrets, a game that lasts since many decades and that today it has not still found solutions worthy of such word. There is still a sort of refusal to think that the phenomenon depression is tied up to “spray of molecules” that get lost in the cerebral flow completing inadequate paths that hesitate in those that are defined as “encumbrance” of the behaviour.

It is certainly easy to think of the brain as to a mystery and to invoke as many mysterious links with the affections of the past and the shades that in the daily life they grow on some cerebral convolution. The majority of the psychiatrists is still prone in attempts of interpretation (the depression is not a pathology but a disorder, as the psychiatrists say) which are based on observation, on the experience, on questionnaires that attribute you some points, as if this kind of illness could resemble to a sort of game of the lottery. Even more, they try to administer substances that are in complete antithesis with the diagnosis. They administer substances that move those famous molecules of which, practically they refuse the complexity of the existence.

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All of this induces and indulges to the error, always more often and more and more in dramatic way. One of them, certainly illuminated by a tear of truth, has written that around the forty percent of the major depression diagnoses is wrong, it was the 2001, his name is Bowden and is a psychiatrist in the University of the Texas (Bowden, 2011). More recently, during the tenth World Day on suicide, it has been stated that the diagnostic error is around 70% (Tenth World Day for the Prevention of Suicide, Rome, 2012).

During an interview, our friend Kary Mullis defined our work as a discovery that will revolutionize the world of the medicine, of the philosophy and of the religion.

Why does it revolutionize medicine?
Having identified, through the analysis of platelet fatty acids and the use of an artificial neural network, the possibility of recognizing subjects with Major Depression and Bipolar Disorder, as well as subjects with coronary artery plaque, certainly represents a revolution, because it is the first time that this happens through a blood test.

A revolution because on the psychiatric side, research expresses a result that enters the intimacy of human thought, which enters the most intimate folds of consciousness, and this is a problem in the Society and for traditional diagnostic methods.

It leaves no space, the result obtained, to probabilistic hypotheses, to the possibility of getting lost in the meanders of the so-called risk factors, which, as shown in a letter to the Editor of the British Medical Journal do not always correspond to the determinism of a pathological state.

Many of these risk factors, in both cases (Psychiatry and Cardiology) grant mitigating circumstances or, too often, prove to be inconsistent.

Why does it revolutionize philosophy?
In this long experimental journey an enlightened philosopher, Fabio Gabrielli, our conscience and the consciousness of research, has joined us.

Fabio Gabrielli is the interpreter of four scientific result, in word and in thought. He is the one who has placed in the foreground the concept that we must start from the awareness that man is a synthesis of biological phenomena that must be interpreted in the soul and in the foreground spirit of his action and in the expression of his feelings.

The man must be interpreted in the molecular dynamics that accompany and determine being a “thinking mind”.

Why does it revolutionize religion?
In the same path and within the results obtained, in the light of an argument that arose from essential evidences, we have produced two works, perhaps the least technical and therefore most fascinating, which are in our heart. We had the opportunity to combine medicine, mathematics and philosophy, discussing and interpenetrating concepts and thoughts.

The aforementioned works speak of the biological implication of two magical moments of humanity:

- Of why the passage of the Creation could not have been written if not in the sequence that shows the Genesis.
- Of why, in the human alternation of feelings, emotions, fears, Christ the man, in the Garden of Gethsemane, shows a bipolar profile.

These works are today in the archive of the University of Latvia and in the archive of the PhilPapers.

Perhaps, right now, we begin to understand what Kary Mullis had guessed.

Naked in the field of the mind for us it means to be prone to free us from the tinsels of the mystery and to go to the search of the truth. God, when has created the man, he also has endowed him with tools to understand the human things and if God has created such a complicated man it is because, probably, that truth must be looked for in this complexity and that it is not always easy to find it.

Also, Kary Mullis has found his truth investigating in one of the biological phenomena more complexes that there is, he has reconstructed the DNA going, more than any other man, next to the origin of the terrestrial life.

Let me go back to that famous day and, jumping the preliminary of the meeting, reach the substance of the facts. In that fusion between mathematics and biology, that so much was an obsession for Lucio and me. We seemed to have violated a secret considered impenetrable and, for different roads, always in that year 2008, also others touched with hand that mind that was becoming naked was about to discover great part of her secrets.
That 2008 have certainly been one thrilling year, one of those moments in which the things put on in line themselves and they seem not only true but also clear in the mind.

A small group of researchers, in different parts of the world and under completely different experimental conditions one from the other, had somehow understood that those famous biomolecular traces that so much they frighten, they could have rebuilt that marvellous unknown that is “the consciousness”.

When around a table we found us with the characters of that clear fame that it is such only if we live it in the humility of the silence of a laboratory, we understood that we could be near to anything of very important. Those people had flown through the Atlantic Ocean to discuss of a difficult “scientific question”, not of the economic bargain of the century.

Besides me and Lucio in our incredulity, Mark Rasenick, Stuart Hameroff and Kary Mullis they sat around the same table. We start to discuss of a puzzle of which we thought, and we think that it can be composed among millions of dowels in a well precise sequence and, in conclusion, not difficult to realize. It certainly seemed unbelievable being a step away from to understand how ultra-microscopic biomolecular movements could condition the self in the changes of consciousness.

It is worth to explain, in concise way, what was the fruit of a discussion about the evidences that, if real, they really could have the responsibility to change, substantially, a century of scientific belief: the conscience as answer to a molecular fall, therefore, the depression as possible point of arrival of the fall. I do not even know if, in reality, all have perceived the importance of what we were discussing.

When all friends went back to their laboratories, it perhaps started for me a period among the more difficult that I have scientifically faced. I had to understand how to give body to the hypotheses, to find the biological and scientific justification of the various passages and of the manifold involved substances. I had to assume the responsibility of the conclusions, to which I would have arrived.

I spoke, at that time, of it to the friend Mario Tiengo (famous pain scientist) of whom I do not know how to say if it is because everything that that I do, for him, is right or if really, he was convinced that this was the correct road.

Probably I exaggerate always in not to believe until after all to what I do when it seems me impossible and, for the depth respect that I had for the brain of Mario, I must believe that he was absolutely convinced that the road was correct. He was so convinced that in a letter he wrote me he thought indeed that Lucio and I would have been worthy of the Nobel Prize, his goodness.

In reality, Lucio and me, we are out of the lobby of the scientific power and we are resistant to entering it because, we have perhaps understood, that also in the science big part of the world stirs also for economic interest and inside rules that they don't often bring from any part if not to show what mostly interests.

Now it seems appropriate to explain, to whom will have the patience to read, how we arrived to formulate that famous bio molecular circuit and how one arrives at looking for a philosophical interpretation when the research faces the eternal problem of the brain and the mind.

Three essential points constituted the moment of departure of the reasoning and that we will explain:

1. The viscosity of the platelet and neuronal membrane (Tonello & Cocchi 2010)
2. The protein Gs alpha (Donati et al. 2008)
3. The relationship Tubulin-Consciousness (Hameroff & Penrose 1996)

About the first point, it was ours the discovery that the platelet membrane substantially differentiated from the chemical point of view in the indexes of saturation between depressed, bipolar and normal population.

About the second point, the Gsα protein modified its structure according to the degree of viscosity of the neuronal membrane, in the suicides for psychiatric reasons in comparison to the deads for other causes (Donati et al. 2008).

Speaking of the third point the Tubulin, for the deep bond of connection that it has with the protein Gsα and of its position into the cellular cytoskeleton, it determines those changes that have been valued with the quantum computation in the state of vigil in comparison to the condition of anaesthesia. (Hameroff & Penrose 1996).

We dealt with coordinate this knowledge and to understand how the route could work. I have
realized the possible route, then simplified, for a more comprehensible mathematic evaluation from Lucio. The route is shown in the Fig. 1.

I will try to explain it in the simplest possible way.

In the experimentation (Cocchi and Tonello 2010a,b) on the depression in its relationship with the platelet fatty acids, we have identified that three of them, selected by a particular artificial neural network, the Self Organizing Map (SOM), they had a different degree of saturation, one saturated (palmitic acid) and two unsaturated (linoleic and arachidonic acid).

This situation clearly determined the existence of a relationship among them and a friend, Gianni Lercker, recommended us to use a particular formula that connects each fatty acid with the molecular weight and the melting point in the following way:

\[ B_2 = \sum_{i=1}^{3} \left( A_i \frac{m_{pi}}{mw_i} \right) \]

Where:

- \( mw_i \) = molecular weight of i Fatty Acid
- \( mpi \) = melting point of i Fatty Acid

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<td>1</td>
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<td>Arachidonic A.</td>
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We drew a map of it, mono-dimensional that spread the indexes respectively gotten in coherent way by the smallest to the greatest in agreement to the cases of depression and presumed normalcy.

This was in agreement with the hypothesis of Mark Rasenick because such index was indirect expression of a chemical-physics condition that corresponded to the finding and to the hypothesis of Mark on the relationship between Gsα and the lipid raft membrane.

Because of the possible similarity of the platelets to the neurons, as it is broadly documented, the viscosity of the membrane can modify the state of the Gsα protein. The Gsα protein is connected to the Tubulin.

The Tubulin, depending from the concentration of the lipidic phase of the membrane can be useful as positive or negative regulator of the hydrolysis of the phosphatidylinositol bisphosphate (PIP2) as the protein Gsα does.

It is known that the Tubulin forms complexes of elevated affinity with certain proteins G. The formation of such complexes allows the Tubulin to activate the protein Gsα which, in turn, activates the Protein Kinase C, and it conditions a system for which elements of the cytoskeleton can influence the signal of the Proteins G.

Rapid changes of the lipidic composition in the membrane or in the cytoskeleton can modify the neuronal signal and Hameroff has hypothesized that through this mechanism is possible to modify the state of consciousness.
According to Hameroff the cognitive cerebral functions, included the sensory functions and the control of the behaviour, they are included, as neurocomputation, inside the synaptic net (axons and dendrytes) of integrated neurons.

Despite the understanding of this phenomenon, an explanation of the conscious awareness eludes the modern science.

The problem, difficult to explain, is how the brain produces the aware control and the experience, that is the fenomenologic awareness with the subjective feeling that is realized with what the philosophers call “Qualia.”

Besides the distinction among the state of unconsciousness and the conscious experience, the distinction should be inside the cognitive neurocomputation that, in every moment, it is not accompanied by situations, which drive the conscious experience and the choices.

In the animals and in the surgical patients, submitted to general anaesthesia, the gamma synchrony (between frontal and back brain cortex) is the specific marker that disappears with the loss of conscience and returns to the awakening.

Many scientists, otherwise, face the problem of the origin of the consciousness (from the axons as output of the neuro-computation complexity) or they place the consciousness in the dendrites and in the soma of the neuronal cells.

It is probable that the integration between dendrites and soma is the sub correlated of the consciousness and that the dendritic-somatic integration is the origin of the gamma synchrony.

The best correlation measure with the consciousness seems to be the “gamma synchrony” measured by electroencephalography, among 30 and 90 Hertz, which quickly moves and is redistributed through the brain.

Said this, as reflex of the wise considerations of Hameroff, the group kept on developing the biomolecular hypothesis of the depression setting, beside the biomolecular cascade, with the possibility to measure the gamma synchrony modifications in the different psychiatric expression of the behaviour and of the mood.

For the truth, some have already worked in this sense showing that there are different frequencies of gamma synchrony in different psychotic pathologies.

What has not yet been done and that could open a window on the neuroscientific interpretation of the origin of the depression in its neuronal correlations, it is the sequential study of the whole biomolecular cascade in coherence with the gamma synchrony.

It is, perhaps, possible with the use of the neural nets to classify the different oscillations of the gamma synchrony and identify the ranges of the mood disorders delivering a new, not invasive, tool of objective evaluation to the psychiatrist to set it close to that subjective.

Taken awareness of what springs from the meeting with the friends, we have the impression of something that still escapes the biomolecular circuit hypothesized.

Won’t it be, perhaps, that external variable that, taking back the words of Hameroff “the difficult problem to explain is as the brain produces the aware control and the experience, that is the phenomenological awareness with the subjective feeling, that realizes what the philosophers call Qualia”?

Are we facing the indeterminable? An intense exchange of ideas starts with Fabio, it seems impossible but it is always true that when you approach to the indeterminable one you recourse to the knowledge of the philosopher, it deals with defining the concept, to find the correct words to say it.

Just because we have approached to one of the most intimate secrets of the human consciousness in the perception of the being, it seems us obvious an observation that starts from the biology and mathematics and that is melted in an harmonious and reasonable process that sees involved the quantum computation, the artificial neural nets and the biology.

How to show that the simple and the complex can cohabit with equal dignity, and that they cannot only cohabit, but one is essential to the other in the interpretation of the phenomenon, that is the infinitesimally small? A phenomenon that in everyday demonstrations, is still unclear to the science and to the understanding of the common people.

We leave again with the usual enthusiasm to the search of a “sacred graal” that, for us, it means to show that, not through the unprovable, that what we have demonstrated, it can be true.
We redesign the biomolecular circuit in a way even more elementary setting to the center the impalpability of the gamma wave and we try to understand what it can happen and how much is possible to find a reasonable explanation is.

The new circuit, reinterpreted and redrawn, shows itself as it follows in its extreme simplification but with inherent the essence of the possible explanation that could bring to the “sacred graal”, “the fatty acids” (Fig. 2).

*Do we, so, close the story?*

We hold of no and we try to understand as is possible to explain that external variable which we call by instinct “other consciousness”.

A new graphic attempt of synthesis that seems to have found in the philosophical approach the correct words and definitions, is born. We look for, therefore, to explain the external variable (Fig. 3).

A feeling that translates into physical manifestation and that is usually accomplished with functional and organic changes, measurable.

There is a biomolecular time. This could be the quantum calculation that Hameroff and Penrose developed in relation to the bio-molecular path that leads to the modification of consciousness, understood as the perception of being (in this case the anaesthesia-wakefulness circuit).

There is a time, however, that elapses between what determines the sensation and awareness of sensation, which then follows the physical time of the response.

**Figure 2. Hypothesis of the molecular circuit of consciousness in the expression of gamma synchrony mediated by the membrane fatty acids (not published).**

**Figure 3. The biomolecular Conscience and the abyss of conscience: hypothesis of an “a-quantum” reading of the perception (Cocchi et al. 2009).**

At least for now, apparently not corresponds to the occurrence of a biomolecular phenomenon, so not measurable, such as the relationship tubulin-consciousness, that goes further of the quantum calculation to escape perception.

With Kary we have discussed of it and him, also setting the problem of the measurability of the pre-perception, is in agreement with the theory.

Compared to consciousness as perception of the self, the other event would be dominated by the other consciousness.

“The boundaries of your soul you will not ever find, as you walk through its streets, so deep is its logos.” (Eraclito, fr. 45)

The powerful Heraclitean fragment could serve as a warning to those who normally refer to human biology, quantitative determinations of neural nature, to mere biomolecular temporality (Cocchi et al. 2009).

In this context it would be interesting to consider the possibility of a pre-sensitive phase, we might call original intuition, or a not measurable dimension, not affected by psychic correlations, on whose mysterious nature (root mu, greek muein: “putting a finger in front of the mouth and be silent”), at least for now, the philosophy is requested in person.

From the impossibility to calculate, to give quantum substance to the time that intervenes among what determines the feeling and the awareness of it, a scenery of fertile routes of search may be open up within which entrench also the possibility of an abyss of conscience not quantifiable.
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