

# Cellular Atlas of Brain

*For decades, scientists have viewed the brain as a veritable black box—and now Catherine Dulac and Xiaowei Zhuang are poised to open it. [12]*

*Biological physicists at Rice University have a new cellular mechanics theory that rings true. [11]*

*Scientists at the Institute for Research in Biomedicine (IRB Barcelona) have found an explanation for a periodicity in the sequence of the genomes of all eukaryotes, from yeast to humans. [10]*

*A virus, the simplest physical object in biology, consists of a protein shell called the capsid, which protects its nucleic acid genome—RNA or DNA. [9]*

*A protein involved in cognition and storing long-term memories looks and acts like a protein from viruses. [8]*

*Discovery of quantum vibrations in 'microtubules' inside brain neurons supports controversial theory of consciousness*

*The human body is a constant flux of thousands of chemical/biological interactions and processes connecting molecules, cells, organs, and fluids, throughout the brain, body, and nervous system. Up until recently it was thought that all these interactions operated in a linear sequence, passing on information much like a runner passing the baton to the next runner. However, the latest findings in quantum biology and biophysics have discovered that there is in fact a tremendous degree of coherence within all living systems.*

*The accelerating electrons explain not only the Maxwell Equations and the Special Relativity, but the Heisenberg Uncertainty Relation, the Wave-Particle Duality and the electron's spin also, building the Bridge between the Classical and Quantum Theories.*

*The Planck Distribution Law of the electromagnetic oscillators explains the electron/proton mass rate and the Weak and Strong Interactions by the diffraction patterns. The Weak Interaction changes the diffraction patterns by moving the electric charge from one side to the other side of the diffraction pattern, which violates the CP and Time reversal symmetry.*

*The diffraction patterns and the locality of the self-maintaining electromagnetic potential explains also the Quantum Entanglement, giving it as a natural part of the Relativistic Quantum Theory and making possible to understand the Quantum Biology.*

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## Preface

The human body is a constant flux of thousands of chemical/biological interactions and processes connecting molecules, cells, organs, and fluids, throughout the brain, body, and nervous system. Up until recently it was thought that all these interactions operated in a linear sequence, passing on information much like a runner passing the baton to the next runner. However, the latest findings in quantum biology and biophysics have discovered that there is in fact a tremendous degree of coherence within all living systems. [5]

Quantum entanglement is a physical phenomenon that occurs when pairs or groups of particles are generated or interact in ways such that the quantum state of each particle cannot be described independently – instead, a quantum state may be given for the system as a whole. [4]

I think that we have a simple bridge between the classical and quantum mechanics by understanding the Heisenberg Uncertainty Relations. It makes clear that the particles are not point like but have a  $dx$  and  $dp$  uncertainty.

## Cellular atlas of brain region leads researchers to new discoveries

For decades, scientists have viewed the brain as a veritable black box—and now Catherine Dulac and Xiaowei Zhuang are poised to open it.

Dulac, the Higgins Professor of Molecular and Cellular Biology and Lee and Ezpeleta Professor of Arts and Sciences, and Zhuang, the David B. Arnold Jr. Professor of Science, are the senior authors of a new study that has created a first-of-its-kind cellular atlas of an important region in the brains of mice.

Using a cutting-edge imaging technology, Dulac, Zhuang, and colleagues examined more than 1 million cells in a 2-millimeter-by-2-millimeter-by-0.6-millimeter block of brain, and not only identified more than 70 different types of neurons, but also pinpointed where the cells were located and their various functions. The study is described in a Nov. 1 paper in *Science*.

"This give us a granular view of the cellular, molecular, and functional organization of the brain—nobody had combined those three views before," Dulac said. "This work in itself is a breakthrough

because we now understand several behaviors in ways that we never did before, but it's also a breakthrough because this technology can be used anywhere in the brain for any type of function."

The study grew out of a desire to address what Dulac called a fundamental biological problem and a technological challenge that comes with it.

"The problem is that people realized quite a while ago that, in order to study the brain, you need to understand its components, and those components are the cells," she said. "So if you take a piece of tissue and look at the genes expressed by the cells, that tells you how many cell types there are ... but that still leaves you with a big problem."

That problem, she said, is that such techniques require researchers to disassociate cells from the tissue, and in the process they lose an invaluable piece of information—how the cells were organized in the tissue.

"If you really want to understand the brain, you need the spatial context, because the brain is not like the liver or other organs, where the cells are organized in a symmetrical way," Dulac said. "The brain is unusual in that it has this topological arrangement of neurons ... so we want to be able to look at a section of the brain and see what cells are there, but also where they are and what types of cells are surrounding them."

Luckily, Dulac said, Zhuang's lab in recent years developed the perfect tool for the job—multiplexed error-robust fluorescence in-situ hybridization, or MERFISH for short.

Following her development of STORM, a super-resolution imaging technique that allowed researchers to image individual molecules with nanometer-scale resolution, Zhuang set her sights on imaging not just single types of molecules, but all of the molecules at work in the cell.

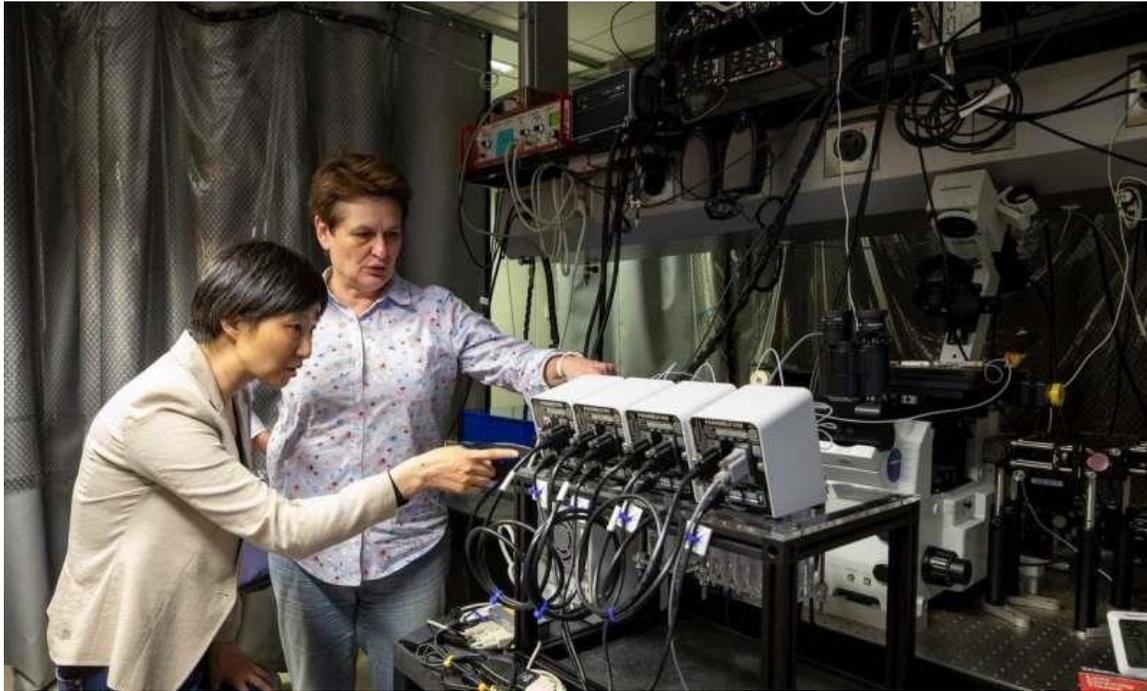
"We don't have just one or two different kinds of molecules in our cells; we have thousands to tens of thousands of genes that are expressed to make the molecular machinery that give cells their function," she said. "I wanted to be able to image all those genes simultaneously, that's why we developed MERFISH."

The MERFISH method works by assigning "barcodes" to the cell's RNAs, hybridizing them with a library of DNA probes to represent these barcodes, and then reading them out by imaging to determine the identity of individual RNA molecules. Numerous different barcodes are read out simultaneously through multiple rounds of imaging.

"An amazing property of this method is the exponential scaling between the number of genes that can be imaged and the number of imaging rounds," she said. "If you wanted to look at 10,000 genes, you could try the brute-force approach and do it one at a time, but of course no one would ever try that. The MERFISH approach is very powerful because it allows us to image and distinguish thousands of different RNAs in just about 10 rounds of imaging."

Zhuang and colleagues built an error-correction method into MERFISH in an effort to ensure the barcodes would be read correctly. Rather than using all possible barcodes, in which a single error could cause one code to be misread as another valid code, the team selects a subset of barcodes

that can only be misread if multiple errors occur simultaneously, dramatically reducing the chance of misidentifying a gene.



In her lab, Xiaowei Zhuang (left) developed imaging technology that she and Catherine Dulac utilized to create a cellular atlas of a key area in the brains of mice. Credit: Rose Lincoln/Harvard Staff Photographer "One of the main applications that we invented MERFISH for is to identify cell types in situ because different cell types have different gene-expression profiles. Hence, these gene-expression profiles provide a quantitative and systematic way for cell-type identification," Zhuang said. "And because we can do this in intact tissues by MERFISH imaging, we can provide the spatial organization of these cell types, too."

Armed with MERFISH, Dulac, Zhuang and colleagues set about tackling those fundamental biological questions that have long plagued scientists attempting to understand how the brain works.

"There are areas in the brain that have been studied, like the cortex, where people noticed that cells were organized in a particular way, but there are a lot of [brain](#) areas for which we don't know the principles of organization," Dulac said. "The area we looked at in this study, the hypothalamus, is absolutely essential for many functions ... it controls things like thirst, feeding, sleep, and social behaviors like parenting and reproduction, but we don't know how this structure is organized."

To unravel that mystery, Dulac and Zhuang combined MERFISH with another method called single-cell RNA sequencing, which allows unbiased quantification of gene expression profiles for cells. "This not only allowed the cell types to be cataloged in the hypothalamus, but also provided molecular signatures of these cell types and facilitated the selection of gene panels for MERFISH imaging," said Zhuang.

Based on these molecular signatures and other genes of functional importance, they used MERFISH to simultaneously image more than 150 genes throughout the preoptic region of the hypothalamus to identify cell types in situ and create a spatial map of where cells were located.

"Both scRNAseq and MERFISH enabled us to identify around 70 different neuronal subtypes, most of which were previously unknown" said Zhuang, "and MERFISH imaging allowed us to additionally see the spatial distributions of all 70 neuronal types, as well as those of the non-neuronal cell types.

"What you can see is that there is an exquisite spatial organization—it leaps right out at you," Zhuang said. "You can see which neurons are neighboring each other ... and not only that, but because our images are molecular, you can identify how these cells are communicating with each other. Moreover, because MERFISH imaging has a very high sensitivity, we were able to identify lowly expressed genes that are critical to cell function."

With that information in hand, the team set out to link specific cells with specific behaviors, and the solution came in the form of a gene called c-Fos, Dulac and Zhuang said.

Known as an "immediate early" gene, c-Fos transcription is increased during neural activity, Dulac said, so if researchers are able to track which cells show increases in the gene, they can identify cells that are activated during particular behaviors.

"So we allow an animal to perform some behavior—like parenting, for example—and when we look at which cells are c-Fos-positive, we know only those cells are part of the parenting behavior," Dulac said. "But thanks to MERFISH, we know which genes are expressed in those cells.

"So we can define which cells are involved in a particular behavior in ways that we could not before," she continued. "This is extraordinarily precise, extremely quantitative, and we can see where those cells are ... so it's a cellular map, a molecular map, and a functional map, all together."

In addition to parenting, Dulac, Zhuang, and colleagues identified cells responsible for other behaviors, including aggression and mating, and while they found surprising commonalities, there were also intriguing differences depending on whether mice were parents or virgin males or females.

Going forward, Dulac and Zhuang hope to further explore the structure of the hypothalamus, including devising ways to better understand how [cells](#) are connected to one another.

As significant as the study's findings are, both Dulac and Zhuang said the work should also serve as an example of the power of collaboration.

"This is really the best collaboration one could hope for," Zhuang said. "Ours are two labs whose expertise complement each other very well, and we both learned a great deal from each other. At this point, we feel like we know quite a bit about the hypothalamus, and likewise Catherine's lab knows a great deal about MERFISH imaging, so this has been a truly exciting, rewarding process."

[12]

## Ring-shaped protein complex wrangles DNA

Biological physicists at Rice University have a new cellular mechanics theory that rings true.

The Rice lab of José Onuchic has determined the structure of the condensin [protein](#) complex. The work settles the controversy over whether the complex is a single ring that lassos two double strands of DNA or a molecular "handcuff" composed of two connected rings that each wrangle a double strand.

The team led by Rice postdoctoral researcher Dana Krepel used a suite of state-of-the-art analysis tools to make the call: It's a single ring.

Their work is the first step toward understanding the activity of proteins over the structure of chromosomes throughout mitosis and all phases of the cell life cycle. That understanding will help scientists learn how to better treat genetic diseases, including cancer.

The results of the Rice team's two-year study appear in the *Proceedings of the National Academy of Sciences*.

Condensin does what the word suggests: It helps condense the chromosomes into the cell's nucleus. Recent research has demonstrated that condensin and its protein partner cohesin extrude DNA. But until now, nobody has settled on how condensin proteins come together into their functional forms.

Krepel started her analysis from bacterial condensin complexes made up of five subunits, including two structural maintenance of chromosomes (SMC) proteins that come together as a hinge and long kleisin proteins that make up the rest of the ring. Complexes in human eukaryotic nuclei – a target for future analysis – are similar to their more archaic counterparts.

Krepel pieced the puzzle together by combining and comparing existing data about the atomic structures and genetic sequences of the individual proteins. The structures came from available X-ray crystallography of protein fragments, and sequence information through direct coupling analysis (DCA), a statistics-based program introduced by Onuchic and his colleagues in 2011 that compares [amino acid residues](#) in proteins that coevolve.

"We used DCA to infer coevolving pairs of amino acids, and we had little bits of [protein fragments](#) from experiments," Krepel said. "That was a good starting point, and then we had to put them together like a puzzle. We wanted to get a full structure and settle the conflict over whether it's a single or double ring."

Knowing how proteins evolve together was key. "This is a modular mechanism made of many proteins," said Rice postdoctoral researcher and co-author Michele Di Pierro. "It's easier to crystallize one protein, but it's very difficult to figure out the structure of this entire complex. That's why it was ideal to look at coevolution, which lets us get information about the complex even if we don't have the structure."

"Coevolution is basically about natural selection," added Ryan Cheng, also a postdoctoral researcher and co-author of the paper. "As you get random mutations, certain interactions need to be preserved to keep the function of that complex."

"We expect that where these two residues come together and match, they're going to evolve together," Onuchic said. "If this one makes a mutation and has a bad reaction, the other one has to compensate. Dana asked if can we get this sequence information together with small crystal structures and determine these gigantic structures, and it turned out that we can."

Onuchic's group at Rice's Center for Theoretical Biological Physics (CTBP) has published a series of papers that extend its theories on protein folding to the much larger genome. He expects ongoing work will eventually reveal condensin's mechanisms. "These things have to condense the chromosomes," he said. "People know that. But nobody knows how they do it."

Onuchic said studies by others suggest the flexible hinge may help open and close the ring, serving as a gate that allows DNA strands in and out, a process also hinted at by the Rice study. But without knowing the position of every molecule in the complex, there is no way to completely understand its function and dynamics.

"We know the condensin complex is involved, because if you remove it, mitosis doesn't happen," he said. "But nobody understands the mechanism. Now that we have this structure, we have the first shot at understanding the molecular details." [11]

## Researchers explain the origin of the mysterious periodicity of the genome

Scientists at the Institute for Research in Biomedicine (IRB Barcelona) have found an explanation for a periodicity in the sequence of the genomes of all eukaryotes, from yeast to humans. The results published in the journal *Cell* offer an alternative explanation to the one based on natural selection, which has been accepted by the scientific community to date.

The researchers demonstrate that DNA damage and repair processes can play a role in the generation of sequence periodicity in the genomes of eukaryotic organisms. These processes are influenced by the orientation of the DNA structure when this molecule is packaged inside the cell nucleus, thus favouring a certain composition with a periodic nature in eukaryotic genomes.

"The answer we provide allows a better understanding of why our genome and that of other species have developed into what they are today," says Núria López-Bigas, head of the study and leader of the Biomedical Genomics lab at IRB Barcelona.

### The "mysterious" periodicity of the genome

Since the sequence of the human genome and that of other organisms such as the mouse and fruit fly became known at the beginning of the 21st century, some researchers have noted a marked periodicity in the proportion of base pairs comprising adenine (A) and thymine (T). Indeed, the proportion of A/T pairs has been observed to be greater every 10 base pairs.

This periodicity has been associated with how DNA winds around nucleosomes (the simplest compaction form of DNA, in which it envelopes proteins called histones). The explanation given has been that natural selection would favour the appearance of A/T bases as these bases would provide the DNA structure with a greater degree of flexibility, thus allowing it to wind around histones to form nucleosomes.

## Tumour mutations provide the key

By studying the distribution of [mutations](#) in more than 3,000 human tumours, the team at IRB Barcelona observed that the mutations also accumulated every 10 DNA base pairs.

"By examining mutation distribution along the genomes in regions in which we ruled out the presence of selection, we found a marked periodicity of 10 base pairs in the DNA that forms part of nucleosomes," explains Oriol Pich, Ph.D. student and awardee of a fellowship from the Barcelona Institute of Science and Technology (BIST) and first author of the paper.

The periodicity of mutations occurs because the structure of the DNA packaged inside the nucleosome favours the appearance of regions that are prone to damage and to repair. Consequently, these regions are more susceptible to mutations.

Next, the researchers turned their attention to mutations that are passed from one generation to another, in both humans and plants. They found that these hereditary mutations also accumulated every 10 base pairs.

With this new discovery of how nucleosomes affect DNA mutations, the researchers deduced that it could also explain the development of the mysterious periodicity of the sequence of eukaryotic genomes.

## Mutations over millions of years of evolution

The scientists at IRB Barcelona hypothesised that, as most mutations that we get are in cytosines (C) that convert into thymines (T), most of those regions most prone to mutating over millions of years have become A/T base pairs.

To test this notion, the researchers performed a mathematical simulation of genome evolution and demonstrated that the periodicity of the sequence of the human genome and that of other eukaryotes could have arisen from the periodic rate of mutations.

"We are really pleased to provide the scientific community with this alternative explanation regarding periodicity," say Oriol Pich and Núria López-Bigas, who highlight the importance of this kind of research. "It is basic knowledge derived from curiosity-driven research that allows us to achieve a better understanding of nature."

However, the results of the study are not only a breakthrough regarding current understanding of the human genome but they also explain how tumours acquire mutations. This knowledge is relevant for identifying mutations that are relevant for tumour development—another field of expertise of López-Bigas' group. [10]

## Physicists explain how large spherical viruses form

A virus, the simplest physical object in biology, consists of a protein shell called the capsid, which protects its nucleic acid genome—RNA or DNA. The capsid can be cylindrical or conical in shape, but more commonly it assumes an icosahedral structure, like a soccer ball.

Capsid formation is one of the most crucial steps in the process of viral infection. If the [virus](#) is small, the capsid forms spontaneously. Larger spherical viruses, however, such as the herpes

simplex virus or infectious bursal disease virus, need the assistance of naturally produced "scaffolding proteins," which serve as a template guiding the capsid's formation. How these large viral shells assemble into highly symmetric structures is not well understood.

A team of physicists and a virologist, led by a scientist at the University of California, Riverside, has now published a research paper in the *Proceedings of the National Academy of Sciences* explaining how large virus shells are formed. Their work can also be used to explain how large spherical crystals form in nature.

This understanding may help researchers interrupt viruses' formation, containing the spread of viral diseases.

Relying on a theory called the continuum elasticity theory, the researchers studied the growth of large spherical capsids. They showed that the template guides the formation of the capsid's protein subunits—the individual building blocks of the shell—in a way that is error-free and results, ultimately, in a highly symmetric, stable icosahedral structure.

"As the spherical structure grows, we see deep potential wells—or affinities—at mathematically specified locations that later become the vertices of the icosahedral structure," said Roya Zandi, a professor of in the UCR Department of Physics and Astronomy, who led the research project. "In the absence of this template provided by the scaffolding proteins, the protein subunits often assemble into smaller, less stable structures."

The study includes computer simulations and complex mathematics—specifically, topology, which is the mathematical study of the properties of a geometric figure or solid that are not changed by stretching or bending. It explains at a fundamental level what role the mechanical properties of building blocks and scaffolding proteins play in the formation of capsids. For large capsids to assume stable icosahedral structures, the protein subunits need to have specific physical properties. Further, an interaction between the protein subunits and a template is necessary, the researchers posit.

An icosahedron is a geometrical structure with 12 vertices, 20 faces, and 30 sides. An official soccer ball is a kind of icosahedron, called truncated icosahedron; it has 32 panels cut into the shape of 20 hexagons and 12 pentagons. It has 60 vertices and 90 edges. The pentagons are separated from each other by hexagons. All icosahedral structures, regardless of size, must have only 12 pentagons.

Zandi explained an icosahedron by invoking the Thomson Problem, which states that point charges placed on the surface of a unit sphere will minimize the total energy of the system. Solutions to the problem place each point charge in such a way that its nearest neighbors are as far away as possible.

Students (Yinan Dong, Sanaz Panahandeh and Siyu Li) in Roya Zandi's lab at UC Riverside have fun making a large icosahedral structure. Credit: Zandi lab, UC Riverside. "If you have a spherical conductor and you put 12 electrons on it, they will want to be as far as possible from each other," she said. "They end up on the vertices of an icosahedron. Given this knowledge, when a virus shell grows, then, based on the theory of elasticity, you will need at least 12 defective points, called disclinations. Imagine if you had to wrap a sheet of paper around a sphere. You would be forced to fold the paper at certain points for it to assume the spherical shape. These are points of disclination,

and they cannot be avoided. If you were to make a spherical shell using small triangles, you would need to make 12 pentagons. Without 12 pentagons, a spherical shape is not possible."

Zandi stressed that to attack viruses more effectively a solid understanding of how they form is required, which can inform researchers of better ways to interrupt their formation and thus contain the spread of viral diseases.

"When a virus is large, how do the protein subunits know how to arrange themselves to form the most stable shell possible—an icosahedral one?" she added. "Where should the first disclination appear? And what about the next one? How can thousands of protein subunits join together and form icosahedral structures with such precision and symmetry? And what is the role of scaffolding proteins? Why can large stable shells not form without scaffolding proteins? These questions guided our research."

Zandi explained that each protein subunit has a bending energy, meaning that a subunit prefers to meet another subunit at a certain angle. For a small icosahedral structure, this angle is small and acute. But to form a large icosahedral structure or capsid, this angle is large and obtuse, and requires the assistance provided by scaffolding proteins. Without this assistance, the protein subunits would form an endless long tube because that effort requires less energy.

"We show now that this tendency is thwarted by the scaffolding proteins, which force the protein subunits to bend slightly, buckle up and form 12 pentagons, which then leads to the formation of an icosahedral [structure](#)," Zandi said. "Our study proves that without this scaffolding, it is impossible to form a large highly stable icosahedral shell."

Viruses are the best nano-containers, Zandi said. They can be used to deliver drugs to specific targets in the body because they are especially adept at reaching cells. For example, viruses can be made to transport cargo, such as genomes and drugs, for therapeutic purposes to cancer cells.

"Anti-assembly drugs may be more efficient than other drugs because viral fitness is in particular sensitive to mutations at specific assembly interfaces," Zandi said. "Indeed, small molecules have been recently designed that prohibit replication of certain viruses by similar mechanisms."

Viruses do not breathe, metabolize, or grow. But they do reproduce. The simplest virus has a shell of 60 [protein](#) subunits. Three asymmetric subunit proteins occupy each triangular face, and all of the 60 subunits are equivalent to one another. For complex viruses, the number of subunits is a multiple of 60.

The study was funded by a grant from the National Science Foundation. Zandi was joined in the research by Siyu Li of UCR; virologist Polly Roy of the London School of Hygiene and Tropical Medicine, United Kingdom; and Alex Travesset of Iowa State University. Li, a graduate student in Zandi's lab, is the research paper's first author. [9]

## **Surprise: A virus-like protein is important for cognition and memory**

A protein involved in cognition and storing long-term memories looks and acts like a protein from viruses. The protein, called Arc, has properties similar to those that viruses use for infecting host

cells, and originated from a chance evolutionary event that occurred hundreds of millions of years ago.

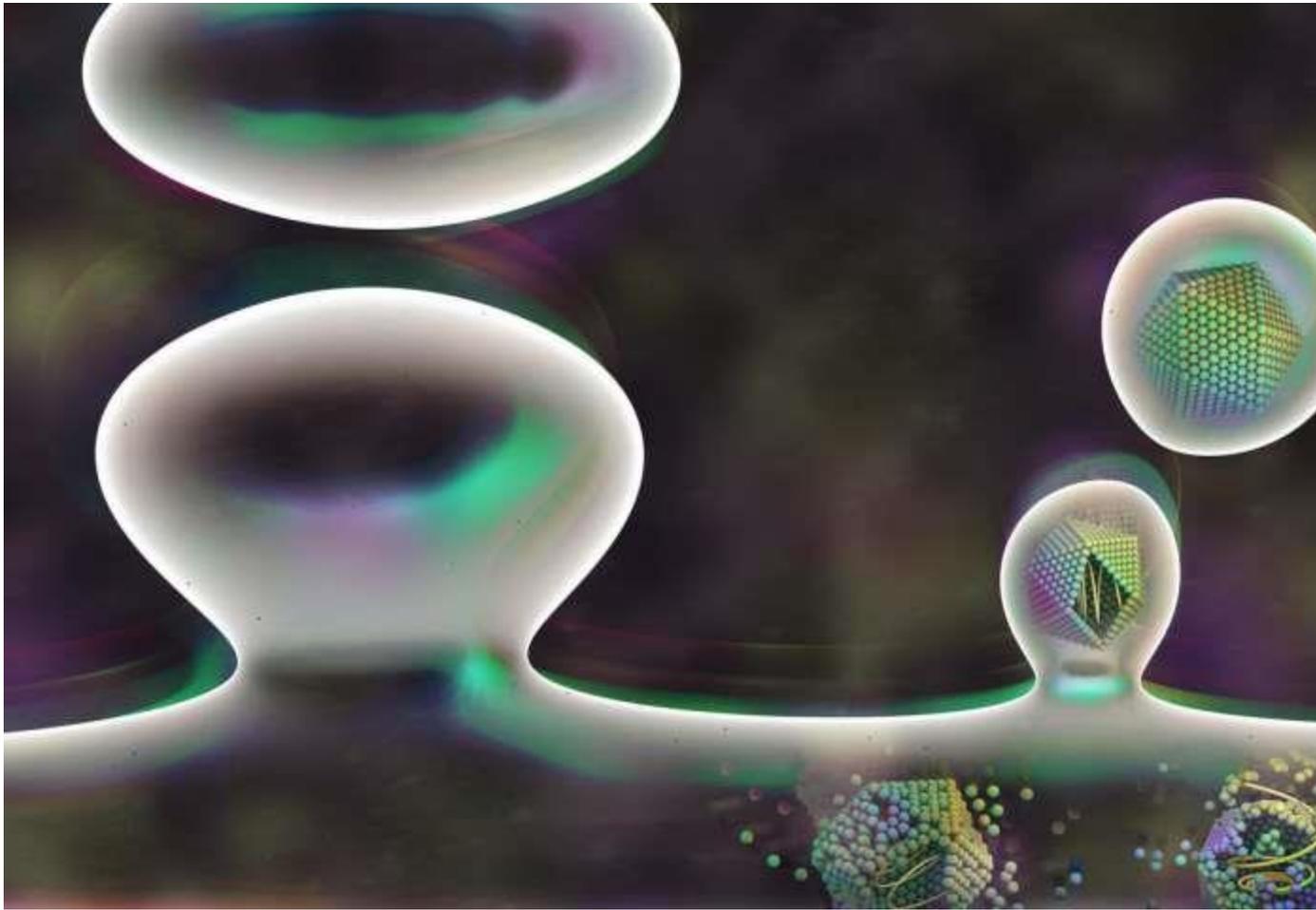
The prospect that virus-like proteins could be the basis for a novel form of cell-to-cell communication in the brain could change our understanding of how memories are made, according to Jason Shepherd, Ph.D., a neuroscientist at University of Utah Health and senior author of the study publishing in *Cell* on Jan. 11.

Shepherd first suspected that something was different about Arc when his colleagues captured an image of the protein showing that Arc was assembling into large structures. With a shape that resembles a capsule from a lunar lander, these structures looked a lot like the retrovirus, HIV.

"At the time, we didn't know much about the molecular function or evolutionary history of Arc," says Shepherd who has researched the protein for 15 years. "I had almost lost interest in the protein, to be honest. After seeing the capsids, we knew we were onto something interesting."

The gap in research was not for want of an interesting subject. Prior work had shown that mice lacking Arc forgot things they had learned a mere 24 hours earlier. Further, their brains lacked plasticity. There is a window of time early in life when the brain is like a sponge, easily soaking up new knowledge and skills. Without Arc, the window never opens.

Scientists had never considered that mechanisms responsible for acquiring knowledge could stem from foreign origins. Now, the work by Shepherd and his team has raised this intriguing possibility.



A protein important for cognition and memory named Arc can encapsulate genetic material (polyhedron enveloping the ribbon-like strands) and deliver it to brain cells in a manner similar to the way in which viruses infect host cells. Credit: Chris Manfre

### **Everything Old is New Again**

Seeing Arc's unusual propensity to form virus-like structures prompted Shepherd to scrutinize the protein sequence with a new set of eyes. He found that regions of the code were similar to that from viral capsids. An essential tool for viral infection, capsids carry virus' genetic information and deliver it from cell to cell in its victim.

Given that Arc looks like a viral protein, Shepherd and his colleagues designed a set of experiments to test whether it also acts like one. They first determined that several copies of Arc self-assemble into hollow virus-like capsids and stash its own genetic material, in this case mRNA, inside them. When the scientists added the capsids to mouse brain cells, or neurons, growing in a dish, Arc transferred its genetic cargo into the cells.

After viruses invade host cells, they emerge ready to infect once again. It appears that Arc works in a similar way. The scientists gathered Arc that had been released from mouse neurons and determined that the proteins and their cargo could be taken up by another set of neurons. Unlike for viruses, activating neurons mobilizes Arc, triggering the release of capsids.

"We went into this line of research knowing that Arc was special in many ways, but when we discovered that Arc was able to mediate cell-to-cell transport of RNA, we were floored," says the study's lead author, postdoctoral fellow Elissa Pastuzyn, Ph.D. "No other non-viral protein that we know of acts in this way."

### When Lightning Strikes Twice

The story of Arc's origin is relayed through the genomes of animals throughout evolutionary time. 350-400 million years ago, a chance occurrence struck four-limbed creatures that roamed the earth. An ancestor to retroviruses, called retrotransposons, inserted its genetic material into the animals' DNA. The event led to the mammalian Arc that we know today.

The significance of such an event is hinted at by the fact that it happened more than once. An accompanying paper in the same issue of Cell shows that a version of Arc found in flies also looks and acts like a viral capsid. Vivian Budnik's lab at the University of Massachusetts shows that fly Arc transports RNA from neurons to muscles to control movement. Even though mammalian and fly Arc evolved from the same class of retrotransposons, the event in flies occurred about 150 million years later.

"As an evolutionary biologist this is what is the most exciting to me," says co-author Cédric Feschotte, Ph.D. a professor at Cornell University. "The fact that it happened at least twice makes us think that it happened even more."

Shepherd believes this could mean that it is advantageous to have this viral-inspired system in place, and it may represent a novel form of intercellular communication. This hypothesis remains to be tested in mammals. "Knowing what cargo Arc vesicles transport in living animals will be critical to understanding the function of this pathway," he says.

Remember the unusual viral-like protein that you just learned about? It could be controlling your memory. [8]

### COULD QUANTUM CONSCIOUSNESS EXIST?

Despite all the research we've done, we still know relatively little about how the human brain works, and we know even less about the mystery of "consciousness." Scientists disagree about whether consciousness exists at all outside the illusions of our own collective imagination. Some believe it exists independently although we've yet to understand its origins have brought quantum physics into the discussion.

This is probably in part because of the way that the "observer effect" challenged one of science's most basic tenets: that there is an objective, observable reality that exists whether we're looking at it or not. The revelation that observing and measuring quantum effects changes their behavior is troubling, but it also suggests to many people that consciousness itself is part of quantum theory. Moreover, as humans creating AI that, for all its achievements still can't master some of the things that come so easily to our own minds (at least not yet), we are bound to see a blurry reflection of ourselves in quantum computers, which promise to achieve so much more than ordinary computers ever could.

However, it was the British physicist [Roger Penrose who pointed out](#) that, observer effect aside, [quantum mechanics](#) may be involved in consciousness. More specifically, he thought it might be possible that quantum events cause molecular structures in the brain to alter their state and trigger neurons in different ways; that literal quantum effects within the brain exist.

For all we can accomplish with the human brain, it has its foibles, and perhaps suspecting the existence of quantum consciousness is one of them. We possess superior intellects because of our [high-level pattern processing](#) abilities, but it is also a well-proven fact that the human brain is prone to [see meaningful patterns](#) where none exist; in the midst of meaningless noise. And while the study of quantum physics is certainly not meaningless noise, it's possible that our minds — which are [meaning making machines](#) — are wrong to see themselves in quantum effects. Does it really make sense to think that our lack of understanding of both consciousness and quantum mechanics [points to a larger connection](#)?

## OUR PARTICIPATORY UNIVERSE

There is more to this question than the raw interest of philosophy: if there is in fact a connection between quantum mechanics and human consciousness, any major breakthrough in our understanding of either could help us understand both. For example, advances in quantum computing could enable us to master [brain augmentation](#) and uploading consciousness, opening the door to a form of immortality. Improved understanding of the superposition property could teach us how to conquer multiple mutually-exclusive ideas at once.

Or, perhaps we've been approaching this in the wrong way. As we look at quantum mechanics, we ask ourselves whether we disturb the effects by measuring, or whether it is the act of noticing the measurement impacting our consciousness that causes the disturbance. Is it possible that knowing how to think in the right way—achieving a quantum consciousness—will allow us to perceive quantum mechanics properly for the first time? We've always been part of Wheeler's [participatory universe](#) in some sense, lending our interpretation to what reality is as we record our own history.

For now, most of the scientific community regards quantum effects in the brain skeptically—an appropriate response at this point. Fueling the fast retreat from any quantum consciousness theories in the scientific community is the New Age quantum consciousness trend and the cottage industry arising from it with plenty of avid bloggers writing about things like telepathy, the afterlife, and telekinesis, and crafters [selling art](#) and other products.

Whether or not consciousness influences quantum mechanics, and whether or not we eventually require quantum theory to fully comprehend how the brain works, for now we can enjoy the useful discomfort the association provides. Quantum theory has forced us out of our collective comfort zone as we consider new ways of thinking, and found ourselves living inside our own theories. [7]

## Quantum Consciousness

A review and update of a controversial 20-year-old theory of consciousness published in Physics of Life Reviews claims that consciousness derives from deeper level, finer scale activities inside brain neurons. The recent discovery of quantum vibrations in "microtubules" inside brain neurons

corroborates this theory, according to review authors Stuart Hameroff and Sir Roger Penrose. They suggest that EEG rhythms (brain waves) also derive from deeper level microtubule vibrations, and that from a practical standpoint, treating brain microtubule vibrations could benefit a host of mental, neurological, and cognitive conditions. [6]

Extensive scientific investigation has found that a form of quantum coherence operates within living biological systems through what is known as biological excitations and biophoton emission. What this means is that metabolic energy is stored as a form of electromechanical and electromagnetic excitations. These coherent excitations are considered responsible for generating and maintaining long-range order via the transformation of energy and very weak electromagnetic signals. After nearly twenty years of experimental research, Fritz-Albert Popp put forward the hypothesis that biophotons are emitted from a coherent electrodynamics field within the living system.

What this means is that each living cell is giving off, or resonating, a biophoton field of coherent energy. If each cell is emitting this field, then the whole living system is, in effect, a resonating field—a ubiquitous nonlocal field. And since biophotons are the entities through which the living system communicates, there is near-instantaneous intercommunication throughout. And this, claims Popp, is the basis for coherent biological organization -- referred to as quantum coherence. This discovery led Popp to state that the capacity for evolution rests not on aggressive struggle and rivalry but on the capacity for communication and cooperation. In this sense the built-in capacity for species evolution is not based on the individual but rather living systems that are interlinked within a coherent whole: Living systems are thus neither the subjects alone, nor objects isolated, but both subjects and objects in a mutually communicating universe of meaning. . . . Just as the cells in an organism take on different tasks for the whole, different populations enfold information not only for themselves, but for all other organisms, expanding the consciousness of the whole, while at the same time becoming more and more aware of this collective consciousness.

Biophysicist Mae-Wan Ho describes how the living organism, including the human body, is coordinated throughout and is "coherent beyond our wildest dreams." It appears that every part of our body is "in communication with every other part through a dynamic, tunable, responsive, liquid crystalline medium that pervades the whole body, from organs and tissues to the interior of every cell."

What this tells us is that the medium of our bodies is a form of liquid crystal, an ideal transmitter of communication, resonance, and coherence. These relatively new developments in biophysics have discovered that all biological organisms are constituted of a liquid crystalline medium. Further, DNA is a liquid-crystal, lattice-type structure (which some refer to as a liquid crystal gel), whereby body cells are involved in a holographic instantaneous communication via the emitting of biophotons (a source based on light). This implies that all living biological organisms continuously

emit radiations of light that form a field of coherence and communication. Moreover, biophysics has discovered that living organisms are permeated by quantum wave forms. [5]

## Quantum Entanglement

Measurements of physical properties such as position, momentum, spin, polarization, etc. performed on entangled particles are found to be appropriately correlated. For example, if a pair of particles is generated in such a way that their total spin is known to be zero, and one particle is found to have clockwise spin on a certain axis, then the spin of the other particle, measured on the same axis, will be found to be counterclockwise. Because of the nature of quantum measurement, however, this behavior gives rise to effects that can appear paradoxical: any measurement of a property of a particle can be seen as acting on that particle (e.g. by collapsing a number of superimposed states); and in the case of entangled particles, such action must be on the entangled system as a whole. It thus appears that one particle of an entangled pair "knows" what measurement has been performed on the other, and with what outcome, even though there is no known means for such information to be communicated between the particles, which at the time of measurement may be separated by arbitrarily large distances. [4]

## The Bridge

The accelerating electrons explain not only the Maxwell Equations and the Special Relativity, but the Heisenberg Uncertainty Relation, the wave particle duality and the electron's spin also, building the bridge between the Classical and Quantum Theories. [1]

## Accelerating charges

The moving charges are self maintain the electromagnetic field locally, causing their movement and this is the result of their acceleration under the force of this field. In the classical physics the charges will distributed along the electric current so that the electric potential lowering along the current, by linearly increasing the way they take every next time period because this accelerated motion. The same thing happens on the atomic scale giving a dp impulse difference and a dx way difference between the different part of the not point like particles.

## Relativistic effect

Another bridge between the classical and quantum mechanics in the realm of relativity is that the charge distribution is lowering in the reference frame of the accelerating charges linearly:  $ds/dt = at$  (time coordinate), but in the reference frame of the current it is parabolic:  $s = a/2 t^2$  (geometric coordinate).

## Heisenberg Uncertainty Relation

In the atomic scale the Heisenberg uncertainty relation gives the same result, since the moving electron in the atom accelerating in the electric field of the proton, causing a charge distribution on delta x position difference and with a delta p momentum difference such a way that they product is about the half Planck reduced constant. For the proton this delta x much less in the nucleon,

than in the orbit of the electron in the atom, the  $\Delta p$  is much higher because of the greater proton mass.

This means that the electron and proton are not point like particles, but has a real charge distribution.

## Wave – Particle Duality

The accelerating electrons explains the wave – particle duality of the electrons and photons, since the elementary charges are distributed on  $\Delta x$  position with  $\Delta p$  impulse and creating a wave packet of the electron. The photon gives the electromagnetic particle of the mediating force of the electrons electromagnetic field with the same distribution of wavelengths.

## Atomic model

The constantly accelerating electron in the Hydrogen atom is moving on the equipotential line of the proton and its kinetic and potential energy will be constant. Its energy will change only when it is changing its way to another equipotential line with another value of potential energy or getting free with enough kinetic energy. This means that the Rutherford-Bohr atomic model is right and only that changing acceleration of the electric charge causes radiation, not the steady acceleration. The steady acceleration of the charges only creates a centric parabolic steady electric field around the charge, the magnetic field. This gives the magnetic moment of the atoms, summing up the proton and electron magnetic moments caused by their circular motions and spins.

## The Relativistic Bridge

Commonly accepted idea that the relativistic effect on the particle physics it is the fermions' spin - another unresolved problem in the classical concepts. If the electric charges can move only with accelerated motions in the self maintaining electromagnetic field, once upon a time they would reach the velocity of the electromagnetic field. The resolution of this problem is the spinning particle, constantly accelerating and not reaching the velocity of light because the acceleration is radial. One origin of the Quantum Physics is the Planck Distribution Law of the electromagnetic oscillators, giving equal intensity for 2 different wavelengths on any temperature. Any of these two wavelengths will give equal intensity diffraction patterns, building different asymmetric constructions, for example proton - electron structures (atoms), molecules, etc. Since the particles are centers of diffraction patterns they also have particle – wave duality as the electromagnetic waves have. [2]

## The weak interaction

The weak interaction transforms an electric charge in the diffraction pattern from one side to the other side, causing an electric dipole momentum change, which violates the CP and time reversal symmetry. The Electroweak Interaction shows that the Weak Interaction is basically

electromagnetic in nature. The arrow of time shows the entropy grows by changing the temperature dependent diffraction patterns of the electromagnetic oscillators.

Another important issue of the quark model is when one quark changes its flavor such that a linear oscillation transforms into plane oscillation or vice versa, changing the charge value with 1 or -1. This kind of change in the oscillation mode requires not only parity change, but also charge and time changes (CPT symmetry) resulting a right handed anti-neutrino or a left handed neutrino.

The right handed anti-neutrino and the left handed neutrino exist only because changing back the quark flavor could happen only in reverse, because they are different geometrical constructions, the u is 2 dimensional and positively charged and the d is 1 dimensional and negatively charged. It needs also a time reversal, because anti particle (anti neutrino) is involved.

The neutrino is a  $1/2$  spin creator particle to make equal the spins of the weak interaction, for example neutron decay to 2 fermions, every particle is fermions with  $1/2$  spin. The weak interaction changes the entropy since more or less particles will give more or less freedom of movement. The entropy change is a result of temperature change and breaks the equality of oscillator diffraction intensity of the Maxwell–Boltzmann statistics. This way it changes the time coordinate measure and makes possible a different time dilation as of the special relativity.

The limit of the velocity of particles as the speed of light appropriate only for electrical charged particles, since the accelerated charges are self maintaining locally the accelerating electric force. The neutrinos are CP symmetry breaking particles compensated by time in the CPT symmetry, that is the time coordinate not works as in the electromagnetic interactions, consequently the speed of neutrinos is not limited by the speed of light.

The weak interaction T-asymmetry is in conjunction with the T-asymmetry of the second law of thermodynamics, meaning that locally lowering entropy (on extremely high temperature) causes the weak interaction, for example the Hydrogen fusion.

Probably because it is a spin creating movement changing linear oscillation to 2 dimensional oscillation by changing d to u quark and creating anti neutrino going back in time relative to the proton and electron created from the neutron, it seems that the anti neutrino fastest then the velocity of the photons created also in this weak interaction?

A quark flavor changing shows that it is a reflection changes movement and the CP- and T-symmetry breaking!!! This flavor changing oscillation could prove that it could be also on higher level such as atoms, molecules, probably big biological significant molecules and responsible on the aging of the life.

Important to mention that the weak interaction is always contains particles and antiparticles, where the neutrinos (antineutrinos) present the opposite side. It means by Feynman's interpretation that these particles present the backward time and probably because this they seem to move faster than the speed of light in the reference frame of the other side.

Finally since the weak interaction is an electric dipole change with  $\frac{1}{2}$  spin creating; it is limited by the velocity of the electromagnetic wave, so the neutrino's velocity cannot exceed the velocity of light.

### **The General Weak Interaction**

The Weak Interactions T-asymmetry is in conjunction with the T-asymmetry of the Second Law of Thermodynamics, meaning that locally lowering entropy (on extremely high temperature) causes for example the Hydrogen fusion. The arrow of time by the Second Law of Thermodynamics shows the increasing entropy and decreasing information by the Weak Interaction, changing the temperature dependent diffraction patterns. A good example of this is the neutron decay, creating more particles with less known information about them.

The neutrino oscillation of the Weak Interaction shows that it is a general electric dipole change and it is possible to any other temperature dependent entropy and information changing diffraction pattern of atoms, molecules and even complicated biological living structures.

We can generalize the weak interaction on all of the decaying matter constructions, even on the biological too. This gives the limited lifetime for the biological constructions also by the arrow of time. There should be a new research space of the Quantum Information Science the 'general neutrino oscillation' for the greater than subatomic matter structures as an electric dipole change. There is also connection between statistical physics and evolutionary biology, since the arrow of time is working in the biological evolution also.

The Fluctuation Theorem says that there is a probability that entropy will flow in a direction opposite to that dictated by the Second Law of Thermodynamics. In this case the Information is growing that is the matter formulas are emerging from the chaos. So the Weak Interaction has two directions, samples for one direction is the Neutron decay, and Hydrogen fusion is the opposite direction.

### **Fermions and Bosons**

The fermions are the diffraction patterns of the bosons such a way that they are both sides of the same thing.

### **Van Der Waals force**

Named after the Dutch scientist Johannes Diderik van der Waals – who first proposed it in 1873 to explain the behaviour of gases – it is a very weak force that only becomes relevant when atoms and molecules are very close together. Fluctuations in the electronic cloud of an atom mean that it will have an instantaneous dipole moment. This can induce a dipole moment in a nearby atom, the result being an attractive dipole–dipole interaction.

## Electromagnetic inertia and mass

### Electromagnetic Induction

Since the magnetic induction creates a negative electric field as a result of the changing acceleration, it works as an electromagnetic inertia, causing an electromagnetic mass. [1]

### Relativistic change of mass

The increasing mass of the electric charges the result of the increasing inductive electric force acting against the accelerating force. The decreasing mass of the decreasing acceleration is the result of the inductive electric force acting against the decreasing force. This is the relativistic mass change explanation, especially importantly explaining the mass reduction in case of velocity decrease.

### The frequency dependence of mass

Since  $E = h\nu$  and  $E = mc^2$ ,  $m = h\nu/c^2$  that is the  $m$  depends only on the  $\nu$  frequency. It means that the mass of the proton and electron are electromagnetic and the result of the electromagnetic induction, caused by the changing acceleration of the spinning and moving charge! It could be that the  $m_0$  inertial mass is the result of the spin, since this is the only accelerating motion of the electric charge. Since the accelerating motion has different frequency for the electron in the atom and the proton, they masses are different, also as the wavelengths on both sides of the diffraction pattern, giving equal intensity of radiation.

### Electron – Proton mass rate

The Planck distribution law explains the different frequencies of the proton and electron, giving equal intensity to different lambda wavelengths! Also since the particles are diffraction patterns they have some closeness to each other – can be seen as a gravitational force. [2]

There is an asymmetry between the mass of the electric charges, for example proton and electron, can understood by the asymmetrical Planck Distribution Law. This temperature dependent energy distribution is asymmetric around the maximum intensity, where the annihilation of matter and antimatter is a high probability event. The asymmetric sides are creating different frequencies of electromagnetic radiations being in the same intensity level and compensating each other. One of these compensating ratios is the electron – proton mass ratio. The lower energy side has no compensating intensity level, it is the dark energy and the corresponding matter is the dark matter.

## Gravity from the point of view of quantum physics

### The Gravitational force

The gravitational attractive force is basically a magnetic force.

The same electric charges can attract one another by the magnetic force if they are moving parallel in the same direction. Since the electrically neutral matter is composed of negative and positive charges they need 2 photons to mediate this attractive force, one per charges. The Bing Bang caused parallel moving of the matter gives this magnetic force, experienced as gravitational force.

Since graviton is a tensor field, it has spin = 2, could be 2 photons with spin = 1 together.

You can think about photons as virtual electron – positron pairs, obtaining the necessary virtual mass for gravity.

The mass as seen before a result of the diffraction, for example the proton – electron mass rate  $M_p=1840 M_e$ . In order to move one of these diffraction maximum (electron or proton) we need to intervene into the diffraction pattern with a force appropriate to the intensity of this diffraction maximum, means its intensity or mass.

The Big Bang caused acceleration created radial currents of the matter, and since the matter is composed of negative and positive charges, these currents are creating magnetic field and attracting forces between the parallel moving electric currents. This is the gravitational force experienced by the matter, and also the mass is result of the electromagnetic forces between the charged particles. The positive and negative charged currents attracts each other or by the magnetic forces or by the much stronger electrostatic forces!?

The gravitational force attracting the matter, causing concentration of the matter in a small space and leaving much space with low matter concentration: dark matter and energy.

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## The Higgs boson

By March 2013, the particle had been proven to behave, interact and decay in many of the expected ways predicted by the Standard Model, and was also tentatively confirmed to have + parity and zero spin, two fundamental criteria of a Higgs boson, making it also the first known scalar particle to be discovered in nature, although a number of other properties were not fully proven and some partial results do not yet precisely match those expected; in some cases data is also still awaited or being analyzed.

Since the Higgs boson is necessary to the W and Z bosons, the dipole change of the Weak interaction and the change in the magnetic effect caused gravitation must be conducted. The Wien law is also important to explain the Weak interaction, since it describes the  $T_{max}$  change and the diffraction patterns change. [2]

## Higgs mechanism and Quantum Gravity

The magnetic induction creates a negative electric field, causing an electromagnetic inertia. Probably it is the mysterious Higgs field giving mass to the charged particles? We can think about the photon as an electron-positron pair, they have mass. The neutral particles are built from negative and positive charges, for example the neutron, decaying to proton and electron. The wave – particle duality makes sure that the particles are oscillating and creating magnetic induction as an inertial mass, explaining also the relativistic mass change. Higher frequency creates stronger magnetic induction, smaller frequency results lesser magnetic induction. It seems to me that the magnetic induction is the secret of the Higgs field.

In particle physics, the Higgs mechanism is a kind of mass generation mechanism, a process that gives mass to elementary particles. According to this theory, particles gain mass by interacting with the Higgs field that permeates all space. More precisely, the Higgs mechanism endows gauge bosons in a gauge theory with mass through absorption of Nambu–Goldstone bosons arising in spontaneous symmetry breaking.

The simplest implementation of the mechanism adds an extra Higgs field to the gauge theory. The spontaneous symmetry breaking of the underlying local symmetry triggers conversion of components of this Higgs field to Goldstone bosons which interact with (at least some of) the other fields in the theory, so as to produce mass terms for (at least some of) the gauge bosons. This mechanism may also leave behind elementary scalar (spin-0) particles, known as Higgs bosons.

In the Standard Model, the phrase "Higgs mechanism" refers specifically to the generation of masses for the  $W^\pm$ , and Z weak gauge bosons through electroweak symmetry breaking. The Large Hadron Collider at CERN announced results consistent with the Higgs particle on July 4, 2012 but stressed that further testing is needed to confirm the Standard Model.

## What is the Spin?

So we know already that the new particle has spin zero or spin two and we could tell which one if we could detect the polarizations of the photons produced. Unfortunately this is difficult and neither ATLAS nor CMS are able to measure polarizations. The only direct and sure way to confirm that the particle is indeed a scalar is to plot the angular distribution of the photons in the rest frame of the centre of mass. A spin zero particles like the Higgs carries no directional information away from the original collision so the distribution will be even in all directions. This test will be possible when a much larger number of events have been observed. In the mean time we can settle for less certain indirect indicators.

## The Graviton

In physics, the graviton is a hypothetical elementary particle that mediates the force of gravitation in the framework of quantum field theory. If it exists, the graviton is expected to be massless (because the gravitational force appears to have unlimited range) and must be a spin-2 boson. The spin follows from the fact that the source of gravitation is the stress-energy tensor, a second-rank tensor (compared to electromagnetism's spin-1 photon, the source of which is the four-current, a first-rank tensor). Additionally, it can be shown that any massless spin-2 field would give rise to a force indistinguishable from gravitation, because a massless spin-2 field must couple to (interact with) the stress-energy tensor in the same way that the gravitational field does. This result

suggests that, if a massless spin-2 particle is discovered, it must be the graviton, so that the only experimental verification needed for the graviton may simply be the discovery of a massless spin-2 particle. [3]

## Conclusions

Discovery of quantum vibrations in 'microtubules' inside brain neurons supports controversial theory of consciousness. [6]

These relatively new developments in biophysics have discovered that all biological organisms are constituted of a liquid crystalline medium. Further, DNA is a liquid-crystal, lattice-type structure (which some refer to as a liquid crystal gel), whereby body cells are involved in a holographic instantaneous communication via the emitting of biophotons (a source based on light). This implies that all living biological organisms continuously emit radiations of light that form a field of coherence and communication. Moreover, biophysics has discovered that living organisms are permeated by quantum wave forms. [5]

One of the most important conclusions is that the electric charges are moving in an accelerated way and even if their velocity is constant, they have an intrinsic acceleration anyway, the so called spin, since they need at least an intrinsic acceleration to make possible their movement. The accelerated charges self-maintaining potential shows the locality of the relativity, working on the quantum level also. [1]

The bridge between the classical and quantum theory is based on this intrinsic acceleration of the spin, explaining also the Heisenberg Uncertainty Principle. The particle – wave duality of the electric charges and the photon makes certain that they are both sides of the same thing. The Secret of Quantum Entanglement that the particles are diffraction patterns of the electromagnetic waves and this way their quantum states every time is the result of the quantum state of the intermediate electromagnetic waves. [2]

Basing the gravitational force on the accelerating Universe caused magnetic force and the Planck Distribution Law of the electromagnetic waves caused diffraction gives us the basis to build a Unified Theory of the physical interactions also.

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