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# An optical visualization of free virions for revealing the first public enemy

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## ABSTRACT

Viruses are unseen enemies which tend to disarmingly spread from person-to-person, therefore causing health damages and weakens the immunity system. Their invisibility give rise to various representations, projections and imaginations that allow laypeople to tame the unseen and intangible nature of viruses. For the first time to our knowledge, we are proposing a novel and uncommon scientific approach resting on the synergy between two scientific field: Technical Sciences & Medicine (TSM) with Social Sciences and Humanities (SSH). Therefore, we present the results of our investigations concerning the evaluation of the social impact of the scientific image of free virions on a specific population, particularly affected by the Covid-19 pandemic: people over 60 years old. For this research, we have implemented two scientific imaging solutions to visualize the free viral particles of SARS-CoV-2. The first one is a standard solution of electron microscopy and the second one is an optical and computational solution of microscopy. The scientific representations of SARS-CoV-2 that we have proposed is in fact highly different from the mass media image that we can see everywhere. Concerning the targeted population, we have demonstrated that the scientific image has a negative impact on the population. Thus, the socially constructed representations of these invisible enemies have a preponderant role in driving laypeople's emotional reactions and health-related behaviors. Therefore, imaging viruses remains a critical scientific effort that contributes irrevocably to alleviate laypeople's misrepresentations of these invisible enemies.

**Keywords:** Multiphoton microscopy, COVID-19, SARS-CoV-2, virions, social representations, public health policies

## 1. INTRODUCTION

Viruses are unseen enemies that tend to infect humans and other living organisms quickly, silently, and efficiently. Although, viruses are the simplest and the smallest infectious organisms: their genetic material counts solely between 3 and 400 genes and their size ranges from 20 to 300 nm [1]. A virus vitally requires a living cell that allows its survival. Therefore, viruses deploy various ingenious strategies to infect and to reproduce within living cells which make from them an important threat to humans. Viruses have fearful reputation because they are dangerous for health, they are invisible invaders of living cells that mutate frequently, and disarmingly spread from animals to humans or by man-made

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spread from person-to-person [2]. In virology, the pace of research has accelerated considerably since the COVID-19 crisis. Thus, many scientific teams have focused their work on new treatments for viral infections, but also on new instrumental solutions resting on physics or computer sciences, in order to discover the biological modes of action that occur during a viral infection. Viruses that elicit various viral diseases and are currently at the origin of pandemic outbreaks represent an important challenge to fundamental research, that is faced with innovative solutions to surpass the tread.

In the face of a global health crisis, **the trust between the society and the scientific community** (medical doctors and researchers) **has been severely challenged**. In that context, the synergy between two distinct research areas, the social sciences and humanities (SSH) on the one hand, and the technical sciences & medicine (TSM) on the other, is a path we have chosen to follow in order to explore new interdisciplinary and innovative strategies for **evaluating the trust link between science and society** on the one hand, and to **evaluate the impact of the scientific image of the SARS-CoV-2** that we can propose with our original instrumental solutions.

Viruses are invisible and dangerous enemies which cause more or less serious health damages and affects the immunity system. Their invisibility is the key point between STM & SSH that we have chosen to address in the present works. This invisibility gives rise to a difficult technical solution for observation on the one hand, and produces various representations, projections and imaginations on the other hand that allow laypeople to tame the invisible and intangible nature of viruses. The perception of the biological image and the impact of this image on the social representations of the virus are underpinned by complex cognitive, emotional, social, and cultural processes that impact the trust between science and society in times of crisis.

The multidisciplinary CoviZion research program: “Storytelling of a Virus: Representations, Images and Imaginations. Represent and Understand in Order to Act Better and Live with it”, conducted currently in France aims to construct an innovative collaboration between life sciences, sciences and techniques, and social sciences and humanities that aims to build a holistic overview of the COVID-19 pandemic [3]. Indeed, the SARS-CoV-2 virus which is at the origin of the COVID-19 Coronavirus disease is studied by researchers in life sciences by methods from the field of virology, physics, computational sciences and solutions of nanoscale microscopy that allows imaging of the biological representation of the new virus by innovative methods. Furthermore, researchers from the field of social sciences and humanities implement innovative research protocols adapted to the unprecedented situation, based on mixed methods research design (quantitative and qualitative methods). These research protocols aim to investigate the specificities of socially constructed representations that populations have of the invisible virus SARS-CoV-2, as well as the cognitive, emotional, social and behavioral consequences of the COVID-19 pandemic on lay population. The global methodological approach of CoviZion, inspired by the approaches of collective intelligence and co-design, is not only innovative, but also focused on the population in order to obtain applicable and concrete results that might serve people and public instances to deal more efficiently with current and future pandemic breakdowns. Therefore, the co-design-based research approach strives for transdisciplinary methodologies that are centered on the human and at the service of the global population. Additionally, the scientific and methodological approach of the CoviZion research program allows for crossing interdisciplinary boundaries by applying the co-design tools that by their subsequent integration strive for a thorough transdisciplinary investigation of the unprecedented sanitary crisis [4].

In the current publication, we propose the initial results of the research program CoviZion, resulting in a new scientific positioning, atypical in photonics, in the unprecedented situation of the global health, trust and politic crisis. Indeed, we have chosen to **evaluate the psychological and societal impacts of the scientific image of free virions on a population particularly affected by the Covid-19 pandemic: people over 60 years old**. By consequence, our first experimental step concerns the **photonics part and the production of the scientific image of the virus**. Two scientific imaging solutions were involved which generated two scientific representations: a standard solution of electron microscopy and an optical solution of microscopy which have delivered two kinds of scientific images of the free viral particle of Sars-CoV-2. Thanks to both methods, we have obtained two kinds of scientific images that we have been then provided to the targeted population. The resulting **representations of the virions, very different from the mass media image that we can see everywhere**, have been assigned to the people over 60 years old. Three questions were precisely asked to these persons. First question: what perceptions the current image elicits to them. Second question: what the concrete emotions are they feel while looking at this scientific image. Third question: what they think about the possible societal impact of the current SARS-CoV-2 scientific image on lay population. Thus, the societal and the scientific portraits of SARS-CoV-2 virus have been investigated jointly for the first time.

The first part of this manuscript reminds the protocols involved in each area: TSM on the one hand and SSH on the other. The technical solution proposed for revealing visually the image of virions, the difficulties and the tricks proposed to overcome the technical limitations are presented. Then, the experimental protocol involved for studying the social modes of action of the virus is exposed. In the second part, the results proposing a new scientific image of Sars-CoV-2 for TSM and SSH are proposed independently. Individuals' subjective representations of the SARS-CoV-2 virus were investigated by an innovative research protocol from the field of SSH that aims to combine approaches and methodologies in order to investigate thoroughly individuals' representations and emotions elicited by the invisible SARS-CoV-2 virus. Social representations are common theories that carry cognitive and emotional components which are shared among laypeople in order to express a common knowledge about an object [5]. Thus, individuals' social representations of the invisible and intangible SARS-CoV-2 virus were investigated by social representations approach based on qualitative and quantitative analyses of written and oral narratives of a sample of French laypeople. With such an objective, the SSH approach rests on the conduction of a questionnaire administered to the participants in order to seize specifically the socially constructed representations of SARS-CoV-2 and its societal impacts on lay population. Further, qualitative investigation by research interviews has been conducted in order to seize the specificities, emotional reactions and the societal impacts of SARS-CoV-2 scientific image, such as proposed by our TSM team. Therefore, finally, we propose a conclusion about the perception of the scientific image of the SARS-Cov-2 by a population particularly impacted by the crises. We conclude by the interest of merging the two drastically different scientific fields which are social sciences and humanities and technical sciences & medicine.

## **2. EXPERIMENTAL PROTOCOLS IN TECHNICAL SCIENCES & MEDICINE AND IN HUMANITIES**

### **2.1 Experimental protocol for the investigating the biological image of viruses (TSM)**

All the experiments concerning SARS-CoV-2 virions were conducted in the NSB3 RESINFIT laboratory (University of Limoges, France), with authorized staff. Free SARS-CoV-2 virions were collected from infected cell (university hospital center of Limoges, France) and placed in culture media. Solutions containing viral particles were stored at  $-80^{\circ}\text{C}$ . The supernatant was clarified to remove cell debris and then passed under UV from 30 seconds to a minute to remove their infectious potential by breaking the RNA strands of their genetic material. The medium was filtered by centrifugation in 4 mL Amicon tubes for 10 min at 5000 g. The filtrate was collected (200  $\mu\text{L}$ ) and transferred into 2 mL tubes and diluted by half in PBS. The viral particles were filtered by magnetic spheres on a magnetic rack to remove completely cell debris and medium traces. 40  $\mu\text{L}$  of magnetic spheres were added to the virion solution for incubation for 10 min at room temperature and 30 min on a magnetic rack at room temperature. Then, the magnetic spheres were washed twice with PBS for optical microscopy observations or with  $\text{H}_2\text{O}$  for environmental scanning electron microscopy observation on a rack and then suspended in 100  $\mu\text{L}$  of PBS or  $\text{H}_2\text{O}$ . 10  $\mu\text{L}$  of solution were deposited between slide and coverslip for observation under an optical microscope. Drops of solution were placed in the ESEM chamber for observation.

The dimensions of SARS-Cov-2 free viral particles are between 80 and 120 nm, a range at least three times smaller than the optical resolution of standard imaging systems [6, 7]. Revealing their image from an optical solution is thus a complex problematic. Scanning electron microscopy is a powerful solution which allows to visualize object dimensions in the same ranges as those of the free viral particles. This solution is a first step to reveal the scientific visualization of the free viral particle. Thus, we have used our environmental scanning electron microscope (ESEM), FEI ESEM Quanta 450 FEG, to propose a specific view of the surface of the viral particles at higher magnification [8].

It is crucial to note that the experimental conditions associated with measurements made by electron microscopy are extreme, even with the environmental mode. Indeed, temperature and pressure conditions are still not compatible with an in live observation of the biological modes of actions of the free viral particles. Thus, the life expectancy of biological objects such as virions or cells is a few seconds, leaving no more than a few seconds to record an image before they disappear. No real-time visualization of the viral infection process in a living cell is therefore possible by electron microscopy. Only optical solutions could allow it, provided that a solution adapted to the endogenous fluorescence and a trick allowing to cross the diffraction limit is found. We have recently developed an optical and computational pipeline

named FAMOUS for “fast algorithm for three-dimensional (3D) multiphoton microscopy of biomedical structures”. This tricky solution rests on the consideration that the produced image is resulting from a convolution between the “true image” with the contribution of the system, named the point-spread-function (PSF). Our pipeline FAMOUS proposes to record and to estimate mathematically the specific instrumental contribution contained into the image. The whole technical description of FAMOUS is proposed in [9]. Figure 1 represents the instrumental solution proposed for delivering an optical visualization of the free viral particles of SARS-CoV-2.

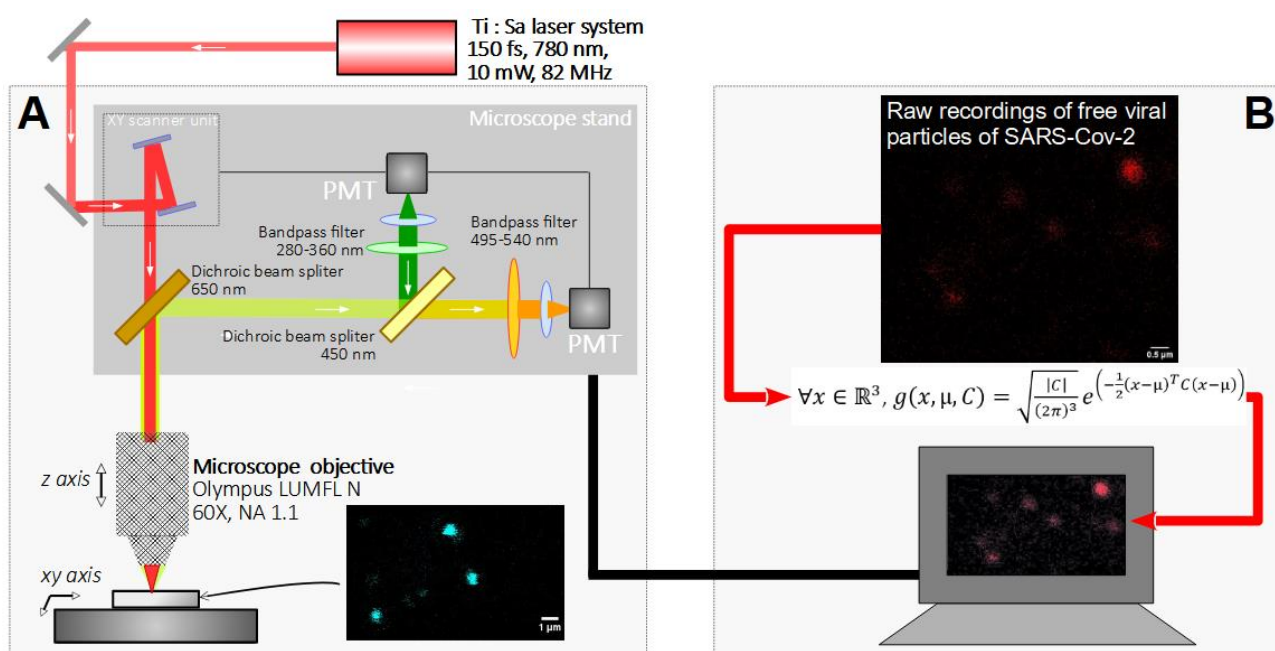


Figure 1. The instrumental and computational pipeline FAMOUS involved for revealing the scientific image of a free viral particle of SARS-CoV-2. The part A concerns the optical microscope constituted by a standard solution of multiphoton microscope. The part B concerns the numerical solution resting on the mathematical fitting of the PSF of the instrument. This solution is made possible thanks to the detection module composed by two detection channels used in the optical microscope.

## 2.2 Mixed-methods research protocol for the investigating social representations of viruses (SSH)

### General presentation of the experimental protocol

The aim of the current research was to investigate the specificities of social representations and emotional reactions related to the invisible SARS-CoV-2 virus. Participants on the current study were older adults, aged 60 years and older, from the ex-Limousin region (actually Nouvelle-Aquitaine region) in France. These older adults were recruited during the COVID-19 sanitary crisis by the snowball sampling procedure during the first semester 2021. Mixed-data based research was led, resting on two specific set of research protocol. Firstly, an online research questionnaire has been administrated to the participants in order to investigate the specificities of participants’ socially constructed representations of SARS-CoV-2 virus, at the origin of the COVID-19 Coronavirus disease and the degree of confidence toward actors directly involved in sanitary crisis management. Further, an additional investigation has been conducted by research interviews in order to refine the quantitative results and to investigate more thoroughly the particular representations elicited specifically by the novel scientific image of SARS-CoV-2 virus, such as proposed with our homemade protocol of imaging (part 2.1), related emotional reactions, and its societal impacts.

### Detailed presentation of the experimental protocol

#### *Online questionnaire*

Firstly, participants ( $N = 144$ ), aged from 60 to 84 years ( $M = 70.22$ ,  $SD = 5.63$ ), completed an **online questionnaire** where they were asked to report spontaneously and without any constraints their most important ideas and feelings related to the new virus. Additionally, research interviews were led. Participants were asked to indicate to what extent



they have confidence in their family doctor, the degree of confidence toward their hospital doctors that intervene during the COVID-19 Coronavirus pandemic, the degree of confidence towards mass media experts and scientists that are researching means to fight against the COVID-19 Coronavirus disease. In order to report the degree of confidence toward actors that are directly involved in sanitary management of the COVID-19 pandemic, participants were asked to indicate their responses on Likert scales that ranged from 0 (*Not at all confidence*) to 10 (*Maximal confidence*). The sample of older adults was composed of 50.00 % of females and 50.00 % of males. Additional instructions specified that participants' responses are confidential and anonymous and that there are no constraints with regard to their answers.

The written responses of older participants were analyzed by IRaMuTeQ software, version 0.7 alpha 2, which is an interface of quantitative software R, version 4.1.0. for Windows [10, 11]. The automatized qualitative data analyses of participants' written responses were conducted in order to obtain multidimensional analyses of the text dataset and to quantify and demonstrate semantic relationships between different concepts.

#### *Research interviews*

In order to investigate more thoroughly older participants' representations of SARS-Cov-2 virus, related emotional reactions, and its societal impacts, **research interviews** were conducted with a sample of 26 older participants. These participants that were aged from 63 to 84 years, from ex-Limousin region (actually Nouvelle-Aquitaine region) in France, were recruited by snowball sampling procedure and interviewed during face-to-face semi-directive interviews in **July 2021, following the COVID-19 pandemic sanitary lockdown in France**. The interviews were conducted by three interviewers trained in research interviews techniques and the totality of interviews were recorder with participants' consent and analyzed afterwards. In particular, the current research aims to investigate participants' social representations, emotional reactions, and societal impacts associated precisely with scientific image of SARS-CoV-2 virus.

During the interviews, the scientific image of SARS-CoV-2 virus produced by ESEM in black and white color (cf., Figure 2) was presented to participants and they were asked by interviewers to elaborate about this scientific image. Three questions were asked individually to the participants:

- 1<sup>st</sup> question: what representations the current target stimulus image elicits to them?
- 2<sup>nd</sup> question: what are the concrete emotions they feel while looking at this scientific image?
- 3<sup>rd</sup> question: what they think about the possible societal impact of the current scientific image on lay population?

Additionally, participants were asked to evaluate their level of stress related to the COVID-19 pandemic on a scale ranging from 0 (*Not at all stressed*) to 10 (*Extremely stressed*) and to describe their subjective living experience of the COVID-19 pandemic at moment of the interview. Moreover, the degree of confidence participants has in actors that are directly involved in sanitary management of the COVID-19 pandemic, such as their family doctors, their hospital doctors that intervene during the COVID-19 Coronavirus pandemic, mass media experts and scientists that are researching means to fight against the COVID-19 Coronavirus disease have been measured.

### **3. EXPERIMENTAL RESULTS OF SIENTIFIC VISUALIZATION OF FREE VIRAL PARTICLES**

In this part, we are presenting the experimental results of images generated thanks to the scientific protocol described in previous part. The two kinds of images produced by each protocol: environmental scanning electron microscope (ESEM), and multiphoton microscopy with our instrumental and computational pipeline FAMOUS.

#### **3.1 Scientific images of SARS-Cov-2 produced by ESEM**

Figure 2 illustrates the image revealed thanks to the solution of ESEM. This technique permits visualizing sample that are in the nanometer scale and provides direct images of viruses used for research purpose. The viral sample analysis by this method was a premier for IRCER laboratory.

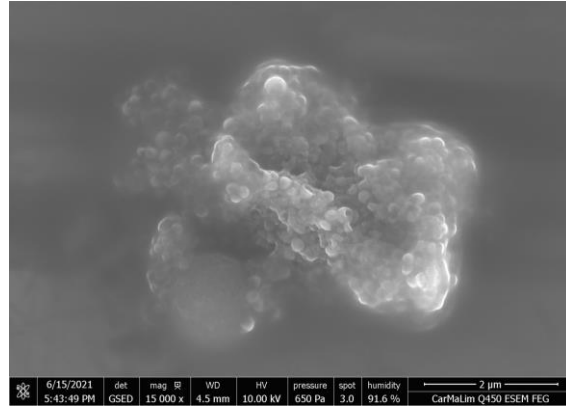


Figure 2. Scientific image of SARS-Cov-2 produced by ESEM. This image was used as target stimulus that represents scientific image of SARS-CoV-2 virus presented to participants during research interviews.

Imagining viruses without inducing shrinkage, ice crystal formation and distortion of the biological sample and keep this sample in normal hydrated state was possible to be realized at IRCER by ESEM just few minutes after the biological sample was introduced into the analyzing chamber. During the acquisition, presented in Figure 2, we faced some technical difficulties related to the fragility of the observed object. We have particularly considered (i) the thermodynamic and kinetic stability of the biological sample and (ii) the pressure and temperature inside the analyzing chamber, keeping the biological sample temperature to just above freezing. Variable pressure can be modified to object sensitivity. In order to visualize the SAR-CoV-2 virus, homogenized biological samples were introduced inside the analyzing chamber. To get adequate contrast and to reduce charging for viral particles at magnifications greater than 15000 x, we used magnetic particles. The pressure inside the analyzing chamber was maintained at 650 Pa and an environmental temperature of 2°C, maintaining a humidity of around 92% while the image was carried out. These parameters help us disperse the build-up of charge induced by the incident electron beam. Electron beam energies was around 10 kV.

### 3.2 Scientific images of SARS-Cov-2 produced by FAMOUS

Figure 3. illustrates the resulting image of SARS-CoV-2 free viral particles produced thanks to our instrumental and computational pipeline FAMOUS.



Figure 3. Scientific image of SARS-Cov-2 produced by our instrumental and computational pipeline FAMOUS. A. A 3D representation of the raw acquisitions of the free viral particles. B. The reconstructed representation of the raw acquisition, thanks to the computational strategy contained into FAMOUS.

Many trials were necessary to obtain the images of free viral particles of SARS-CoV-2. The results of the initial tests were useful in order to defined the correct central wavelength of excitation. Simultaneously, the detection ranges were identified. Then, many complementary tests were necessary to produce the 3D image proposed in Figure 3A. The main difficulty was the recording of 2D stacks all along the depth of the sample. The lifetime of the viral particles was highly reduced in contact with the laser light. This has induced the disappearance of the object at the image.

## 4. QUANTIFIED RESULTS OF THE SOCIETAL IMPACT OF THE SCIENTIFIC IMAGE OF THE SARS-COV-2 FREE VIRAL PARTICLE

### 4.1 Raw results of the quantitative evaluation: online questionnaire<sup>1</sup>

The main results of multidimensional analysis of older participants' written responses obtained by an online questionnaire are represented graphically in Figure 4. The main results demonstrated that the initial 2089 text forms produced by the participants are structured in 7 principal discourse clusters represented with specific color per semantic cluster in Figure 4. The graph of similarity analysis demonstrates existing relationships between participants' verbatims with the size of vertices proportional to the co-occurrence of verbatims in the text dataset. Therefore, the main quantitative results related to the three primary research questions are the following:

- 1<sup>st</sup> question: what representations SARS-CoV-2 virus elicits to them?

Specifically, the multivariate technique of factorial correspondence analyses demonstrated that older participants' representations of SARS-CoV-2 virus elicit the **duality of life (*vie*) and death (*mort*)** represented in the light green cluster and sanitary policies that allow older participants to protect themselves against the COVID-19 Coronavirus disease are represented in **associated clusters** (i.e., mask, vaccination, barrier gestures) are related to 34.55 % of participants' text dataset,  $\chi^2(7, N = 7) = 15.20, p < .0001$ .

- 2<sup>nd</sup> question: what are the concrete emotions they feel while thinking about the SARS-CoV-2 virus?

Further, SARS-CoV-2 virus elicits primarily the **emotion of fear** related to the **risk of serious disease** that represents 34.55 % of participants' text dataset,  $\chi^2(9, N = 10) = 16.62, p < .0001$ .

- 3<sup>rd</sup> question: what is the societal impact of the current scientific image SARS-CoV-2 virus on lay population?

Moreover, older participants expressed their concerns related to the **restricted social life**, and **values of freedom and solidarity** during the COVID-19 pandemic lockdown in France, represented in the red cluster, that represent 30.91 % of the total participants' text dataset,  $\chi^2(7, N = 7) = 17.93, p < .0001$ .

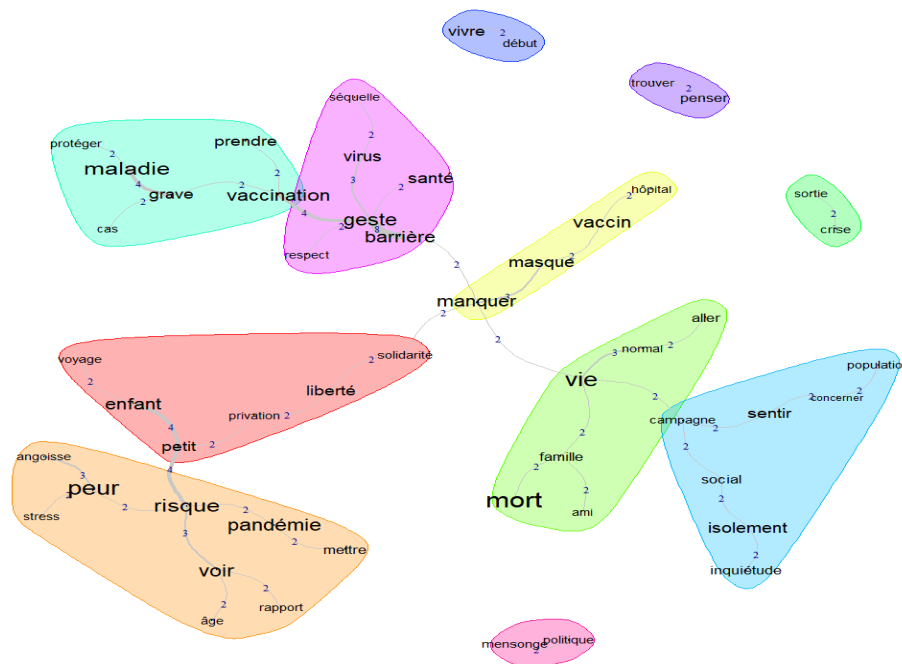


Figure 4. Graph of Similarity Analysis Represented with the Size of Words Proportional to their Frequency in Text Dataset and Specific Color per Semantic Cluster



## 4.2 Raw results of the qualitative evaluation: research interviews

### *General results produced by the research interviews*

The main results of semi-directive research interviews indicated that participants declared below average level of stress reaching the value of 4 over 10, and they declared that their level of stress is lower compared to the beginning of the pandemic, primarily due to the vaccine availability, taking a step back from the mass media, resumption of social life and usual daily activities, and better adaptation to the pandemic situation. Thus, participants declared a less dramatic living experience of the COVID-19 pandemic at the current moment but in the disillusion of a return to normal life, related primarily to the barrier gestures imposed by sanitary policies and the obligation to present their vaccine pass in public spaces. The virus that elicits the COVID-19 Coronavirus disease remains perceived as still present and threatening which calls for safety precautions. Further, participants declared that the vaccination does not offer total protection against the virus, therefore it is primordial to learn to live with the new virus.

### *Answers of the three questions about the scientific image of SARS-Cov-2 virus*

- 1<sup>st</sup> question: what representations the current target stimulus image elicits to them?

In particular, the target stimulus that represents microscopic and photonic visualization of SARS-CoV-2 virus that has been presented to participants during research interviews has been perceived by the participants as a **particularly anxiety-provoking image** that **portends imminent danger**. Participants compared the virus by analogy to a cloud charged with matter, like hailstones, approaching, volatile, ready to explode (examples of participants' verbatims are reported below).

“It can fall at any time, we don't know where” (Male, 78 years)

“It's the unknown, we don't know what we have inside” (Female, 67 years)

“We have the impression that it will do more, that it will grow” (Female, 67 years)

The microscopic and photonic visualization of SARS-CoV-2 virions carries the most agonizing representations of COVID-19. Specifically, participants described the confrontation with the unknown, with the mysterious that encourages the greatest vigilance; lack of control of the virus; its unpredictability; lack of knowledge about this virus; airborne spread and proliferation; viral load linked to the compactness of the cloud; ability to mutate, to transform; unknown origin of the virus and its high pathogenic power (examples of participants' verbatims are reported below).

“I think it's the virus, there are several stuck to each other when we are used to being shown only one. Looks like a thickening uterus, kind of scary, it's spread. It looks like the virus attacked the cells, it's the disease that developed”  
(Female, 78 years)

“Looks like lichen in a vagina” (Female, 84 years)

“This image is like a damaged organ” (Female, 63 years)

- 2<sup>nd</sup> question: what are the concrete emotions they feel while looking at this scientific image?

The microscopic and photonic image of SARS-CoV-2 virus elicits negative emotional reactions, in particular participants declared to feel emotions that are situated between fear, anxiety and disgust that is related to the impalpable, invisible, omnipresent, and uncontrollable virus that overcomes people.

“The image is anxiety-provoking because it is fuzzy, it has no precise shape” (Female, 67 years)

“It's even worse than disgusting, it's diabolical” (Female, 84 years)

“Threatening clouds, the storm is not far” ... “Weird cloud, when it will fall, you will see” (Male, 74 years)

“It's grim, jelly, gelatinous, bally. it's soft. It is disgusting, I don't want to touch it” (Female, 84 years)

“Chernobyl. It is the Corona cloud propagated in the air, without being seen because it is very high. If that's it, it's worse, in transmission and contagion” (Female, 67 years)

“It's more the representation I have of it with little undulating things, but here it's an amalgam of cells, it's denser. It's more impressive by the monstrous, black amalgam, it's more threatening like a storm cloud” (Female, 78 years)

- 3<sup>rd</sup> question: what they think about the possible societal impact of the current scientific image on lay population?

The majority of participants on research interviews declared that the fact to show the target stimulus that represents microscopic and photonic visualization of SARS-CoV-2 virus to lay population might increase the risk of anxieties within the population, a broadcast that would come too late, and a risk of confusion between the common mass media image representing a ball with spikes and the current scientific image of SARS-CoV-2 virus. Indeed, the mass media image representing a ball with spikes became a familiar symbol for people at this advanced stage of the COVID-19 sanitary crisis (cf., July 2021). Moreover, showing the scientific image to the lay population might fuel people’s distrust of the mass media and scientific spheres, and even a distrust towards the COVID-19 vaccine.

“I think that it would worry people even more because they would understand that it is not a real image that is shown in the mass media” (Male, 73 years)

“It can be more anxiety-provoking than the mass media image of the ball with spikes ” (Female, 63 years)

“The image of the real virus which gives the impression of developing cells and has no precise outlines is scarier than the mass media image” (Male, 65 years)

“The scientific image of the virus is scarier than the mass media image, it's more threatening, it is smelling death, a danger, it is elusive” (Female, 84 years)

### 4.3 Degree of confident between the participants and the actors of the fight against the SARS-CoV-2

The degree of confidence between the participant and the scientific community (medical doctors and scientists) is an essential parameter to consider for estimating the impact of the scientific image onto the targeted population. Figure 5 gathers the estimations of the degree of confidence between the participant and Family doctors, Hospital doctors, Mass media experts and scientists. One sample t-test conducted against the midpoint of the scale demonstrated that participants’ degree of confidence is significantly high in their family doctors ( $M = 8.21, SD = 1.81, t(143) = 21.26, p < .001$ ), in their hospital doctors that intervene during the COVID-19 pandemic ( $M = 8.41, SD = 1.82, t(143) = 22.55, p < .001$ ), and in scientists that are researching means to fight against the COVID-19 Coronavirus disease ( $M = 7.65, SD = 2.15, t(143) = 14.81, p < .001$ ). Although, participants declared that their confidence in mass media experts is situated around mean scale value ( $M = 5.05, SD = 2.32, t(143) = 0.25, p = .801$ ).

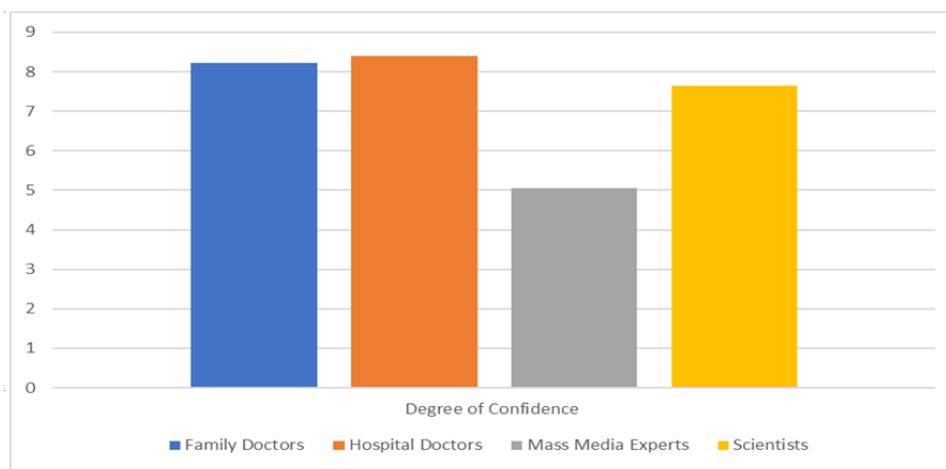


Figure 5. Mean values of the degree of participants’ confidence in actors directly involved in COVID-19 sanitary crisis management

## 5. DISCUSSION ABOUT THE SOCIETAL IMPACT OF SCIENTIFIC IMAGES OF SARS-COV-2 FREE VIRAL PARTICLES

The main results of the current research presented in this publication demonstrated that the scientific image of SARS-CoV-2 virus tends to be compared by analogy primarily to a dangerous and unpredictable cloud that elicits a range of exacerbated negative emotional reactions. At that stage, it is fundamental to remind the preliminary results obtained previously in the initial part of CoviZion program, depicting the general state of mind of the population in this period of sanitary crisis. Indeed, our previous mixed-data based research conducted recently as a part of CoviZion research program within French context demonstrated that the SARS-CoV-2 virus is perceived by the French lay population, aged from 18 to 84 years, primarily as a dangerous and worldwide killing virus that can be transmitted such as a flu [12]. Furthermore, these preliminary results had revealed that the awareness of SARS-CoV-2 transmissibility elicits specific negative emotions (i.e., fear, anxiety, sadness, anger) and aversive reactions (i.e., stress, uncertainty, worries). In particular, the role of mass media and political communications have been identified as the main social construction processes that underpin currently the social representation of SARS-CoV-2 virus within French population [13]. Indeed, in the context of sanitary crisis, lay population is overwhelmed by contradictory news, advices, and simplified scientific explanations that might lead to important misrepresentations of the virus itself and related sanitary situation, exacerbated emotional reactions and irrational individuals' behaviors that might contribute to amplify the global pandemic and make the overall crisis management even more challenging. This initial study depicts the state of mind of the participant included into this program of research devoted that time specifically to the evaluation of the social impact of the scientific image of free viral particle of SARS-CoV-2.

The current study designed by SSH approach, based on mixed-data research design, highlighted the common subjectivity of socially constructed representations of SARS-CoV-2 virus that represents a particularly anxiety-eliciting image, compared by analogy to a dangerous and unpredictable cloud, within lay population. The scientific image of SARS-CoV-2 virus, such as illustrated with our homemade experimental protocol of CoviZion from the culture of free virions until the production of the image proposing a representation of the free viral particle, elicits a range of **exacerbated negative emotional reactions** that drive lay people's behavior. Furthermore, on the one hand, lay people tend to make confidence to family doctors, hospital doctors and scientists that are researching means to fight against the COVID-19 Coronavirus disease. Paradoxically, on the other hand, the scientific image of SARS-CoV-2 virus is perceived as scarier than the common mass media image of the ball with spikes. Indeed, the mass media image tends to be perceived as "generic" because the mass media image embodies the very idea of a virus. Moreover, the mass media image of the SARS-CoV-2 (the ball with spikes) has a scientific reality. Indeed, coronaviruses are spherical viruses enveloped by a lipid layer inside which proteins are inserted, including the famous spike protein ("S protein"), thus giving this structure a shape compatible with the mediatic image shown everywhere [14]. But the attributed color of this object is a pure media invention. Indeed, the object of dimension lower than the resolution does not possess any color in itself. The signal emitted by the virions is found in wavelength ranges corresponding either to the fluorophore used or to the endogenous fluorescence responses produced by the genetic material (nucleic acid assembly).

Thus, the mass media image offers a clear visual information that is concrete and circumscribed, more easily "targetable" by people, and therefore less anxiety-eliciting. While, the scientific image is perceived as "specific", it refers to something unknown, abstract, not very circumscribed, and therefore uncontrollable that is a vector of anxiety. Although, any image is a representation that reflects a given cultural background. This representation is anchored within a common cultural base that provides a means of translation to render the perceived image intelligible. These cultural bases, whether they are societal, biological or physical, must dialogue in order to construct the coherence of this image. Moreover, the mass media, as the etymology of the word indicates, provide a means of dissemination that serve the large-scale construction of a socially shared reality.

## 6. CONCLUSIONS

The overall aim of the current investigation was to construct a relevant study combining for the first time hard and soft sciences, meaning Technical Science & Medicine with Social Sciences and Humanities, in readiness for modify the trust between scientists and lay population. Viruses are invisible enemies that need to be rigorously investigated with the scientific image to understand the biological action of virus and the social representation induced. Thus, we have first proposed a technical solution for visualizing the free viral particles, relying on a two-sided strategy: with scanning electron microscopy on the one hand, and with multiphoton microscopy on the other hand. For this last one, our instrumental and computational pipeline FAMOUS was involved, thus revealing the scientific image of a free viral particle of SARS-Cov-2. After the obtaining of these two scientific images, whose representation was in fact far from the mediatic representation of SARS-Cov-2 virions visualized through mass media, we have shown them to the people over 60 years old, a population particularly affected by the Covid-19 pandemic. Thanks to a mixed-data based research, resting on the implementation of an online questionnaire followed by a protocol of research interviews, the societal impact of the scientific image has been assessed. In particular, three research questions were specifically devoted to the measurement of the societal impact of the scientific image of SARS-CoV-2 virus. The main results demonstrated that the scientific image of SARS-CoV-2 virus tends to be compared by analogy primarily to a dangerous and unpredictable cloud that elicits a range of exacerbated negative emotional reactions, situated between fear, anxiety and disgust. Although, lay people tend to make confidence to family doctors, hospital doctors and scientists that are researching means to fight against the COVID-19 Coronavirus disease. Thus, the scientific image of SARS-CoV-2 virus that has been perceived as scarier than the common mass media image of the ball with spikes, which is already usual for the population, could increase negative emotional reactions of the population and erode public trust at the advanced stage of the sanitary crisis. Therefore, in case when SARS-CoV-2 scientific images are broadcast to the population, they must be irrevocably accompanied by an adequate educational device in order not to amplify the existing sanitary crisis.

The invisible and intangible viruses give rise to various representations and imaginations tainted by a range of fears and fantasies. What is the role of the scientific representation of the virus for the population? Indeed, viruses as invisible invaders of living cells elicit various socially constructed images and representations that allow lay population to tame the invisible, intangible, and often dangerous nature of viruses. Therefore, social representations of viruses that remain a threat to humans and other living organisms are primordial to investigate because they drive laypeople's cognition, emotions and behavioral reactions. The social representations theory posits that "social representations" refer to aggregations of laypeople's beliefs and values that are shared within a given social context. Thus, social representations are common theories that are shared among laypeople in order to express a common knowledge about an object. Further, social representations carry cognitive and emotional components that allow people to share meaning and alleviate negative emotions related also to new objects, such as SARS-CoV-2 virus that is at the origin of COVID-19 Coronavirus disease. Moreover, social representations that are shared via interpersonal communication processes and mass media are primary drivers that allow people to interpret reality and direct health-related behaviors. Social representations are constructed mostly by language that allow to share the socially constructed reality with other individuals. Furthermore, individuals' representations of the SARS-CoV-2 virus tend to be enriched by information provided by mass media and interpersonal conversations that shape the construction of social representations of this new and invisible object. Therefore, public health policies should irrevocably consider the integration and dissemination of proper scientific information by mass media and transparent public consultations at the early stage of the sanitary crisis. Considering the timeline of the sanitary crisis is essential because these early policies might avoid various misrepresentations of the population and related harmful consequences for sanitary crisis management at different levels. In particular, the sanitary policies, such as social distancing and lockdown have been perceived as particularly restrictive and eliciting individuals' ill-being. Therefore, there is a need for further rigorous investigation, based on innovative research methods and scientific technologies, that contribute to effectively investigate viruses and related infectious processes in order to establish and guide related public health policies that might reduce the cumulative negative impacts of restrictive public health policies on the population during future pandemic breakdowns.

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### <sup>i</sup> International Statistical Indicators:

*N*: Sample size

*M*: Mean

*SD*: Standard Deviation

*p*: p-value that determines the significance of results in relation to the null hypothesis

*t*: Student’s T-Test, a method of statistical hypotheses testing of mean values of the sample

$\chi^2$ : Chi-Square Test, a method of statistical hypotheses testing of relationships between variables