# But what does science say?

### By Mariano Rocchi

Please note that this lecture was originally given to an Italian audience and therefore often refers to Italian examples and literature, including Dante.

Right now, disoriented by the coronavirus pandemic, many people are asking themselves this very question. This article is intended to help you navigate a world in which the news is suddenly full of science, or at least information sold as 'science'.

After a few introductory paragraphs, I will use examples to explain how science works. Let us start with a very simple, almost simplistic statement: news can be considered scientific if it has been published in a scientific journal. Of course, that in itself is not enough, and we'll see why, but it helps a lot.

# Procedure for a scientific publication

A researcher, or more often a group of researchers, writes an article on the results of his or her research and submits it to a scientific journal. A first reading of the summary is useful for the editors of the journal to decide if the article is suitable for their journal and whether it contains important innovations compared to what is already known on the subject. If this first judgment is positive, the article is sent to anonymous referees who evaluate it. Referees are usually experts on the subject of the article. They formulate their judgments and send them to the editor who, depending on their recommendations, decides whether or not to accept the article and publish it. That it is a 'scientific journal" does not to say everything. Some journals are very prestigious, for example Nature and Science. These journals only feature articles of major importance. This, however, does not mean that they only publish on topics with important implications for applied science, as in the medical field. Science is above all curiosity. For example, you can find an article on how geckos walk with ease on walls and ceilings thanks to the management of the weak forces of van der Waals that are created on the very thin and numerous bristles of their feet (*Autumn et al., 2000*).

There are many scientific journals, now more than ever, for the following reason. The career success of a researcher, in universities in particular, is often linked to the number of publications. For some years now there has been an explosion of scientific journals, also because publishers can make money from it. Some of these journals, however, are defined as 'predatory'; ones that publish everything as long as the writer pays, without a serious verification of the validity of the results (Brainard, 2020). My mailbox, as that of many of my colleagues, is often full of invitations to publish in journals that have nothing to do with my skills. Any topic for them is fine as long as I pay. Invitations to publish are matched by the countless invitations to speak at conferences of all kinds, on any topic, as long as one attends, at one's own expense, of course. A serious congress that invites you to speak also provides you with economic support for the trip and for the hotel. Back to the journals: how does one evaluate if a journal is serious and reliable? For that there is a sort of ranking of importance, a hit parade of journals. Every year Web of Science calculates exactly how many times articles in a particular journal have been cited by other scientific articles. The more a journal is cited, the higher its impact in the scientific field. This index is called Impact Factor (IF). Scimago, based on Scopus (an abstract and citation data base) has a similar ranking criteria. There are many discussions about this type of journal ranking, but no algorithm would be immune to discussion.

So, if a journal is not in the ranking, it means that it is out of the strictly scientific circuit. In other words, if there are two conflicting articles, the first published in Nature and the second in the "Journal of rejected papers"<sup>(C)</sup>, the difference is obvious! The difference is also clear if the second is in a journal that has an extremely low rating (IF), say, less than 0.5 (an arbitrary value), as compared to Nature which had an IF of 43.070 in 2018. You can check the IF of a journal by typing the name of the journal followed by "Impact Factor" in Google. It usually works.

Another way of making your scientific results known is by presenting a poster of your work at a conference in your field. A poster is usually vetted only to ensure that it does not contain nonsense or gross stupidities. It is, therefore, not a valid argument to say "But these results were presented at

international scientific congresses!" as some people said about the Di Bella cure (<u>Wikipedia</u>). Acceptance at a conference does not necessarily imply endorsement by the scientific community. Many of the results, not all, presented at conferences are later published in a scientific journal. Only when they are published do they begin to have a value, but that is not absolute. The results must be reproducible and need to be confirmed (see below).

For some years now it has been possible to immediately make the results of your research public. Archives have been created to store them. There is no peer review as such, but only a very superficial screening to avoid jokes, offensive content, plagiarism etc. The most well-known, in the biological field, is Biorxiv (pronounced bioarchive), organized by the Cold Spring Harbor Laboratory (Wikipedia). In simple terms, the articles are parked in these archives open to all, but, sooner or later, if they are valid, they will end up in a scientific journal (the secret hope of the authors is that some good journal will offer to review their article). I would like to point out that the above mentioned information about IF is fairly homogeneously valid in the medical field, which is very large and has a large number of scientific journals with publications submitted not only by universities and biomedical research institutions but also by hospitals around the world. For other disciplines the specialized journals are far fewer and therefore the Impact Factor is on average lower.

#### Language problem

Almost all of the scientific journals are in English, which is currently the common language of science. Somewhat like Latin once was: Newton wrote in Latin and Galileo's *Sidereus nuncius* was in Latin. Leonardo da Vinci, "a man without letters", as he said of himself (remember that he was an illegitimate son), could draw the Vitruvian man only when the treatise of architecture of Vitruvius was translated into Italian, in 1490.

The language is a problem and its consequences are not trivial. Many scientists cannot draw on the sources of information. And even if one knows English, not all journals are freely available. Article summaries (abstracts) can be viewed for free, but in order to read the whole article one must either purchase it, or have a subscription, usually through a library or an institution. Some journals can be accessed for free; others make articles accessible only a few months after publication. Alternatively, you can request the article directly from the author. When you do manage to get hold of the article, it is in English!

For many topics Wikipedia, the public encyclopedia that has almost obscured all other encyclopedias, offers a partial solution to the language problem. Wikipedia has a high reputation in the scientific field and the most important topics are also available in several languages (<u>Wikipedia</u>). That is why you are referred every now and then in this article to Wikipedia for further information. However, even with a good knowledge of English and availability of the full article, articles in journals can be difficult to understand without sufficient background in a specific field. This is where science journalism comes into play.

#### Journalism, scientific and non-scientific

There are many popular science magazines that one can buy at newsstands or read on the internet (here are examples of some <u>Italian ones</u>). The fact is that most science news comes to us from the internet and newspapers. That is where the problems start, especially in the headlines. Even in cases where the article consists of an interview with one of the authors of a scientific article, the title is usually written by the editor-in-chief. As it has to attract clicks and the attention of readers, it can sometimes misrepresent the content of the article itself, which is paradoxical, but true. The article itself can also be a problem – the journalist or the researcher may oversell the significance or the possible applications of the work in order to impress readers or, even, for the researcher, to attract funds for his research program. One area in which this often occurs is the field of cancer research, which is popular with readers. If an astute journalist were to look for the promised results a year later, he would probably not find a follow-up to what was recklessly announced. And the credibility of science is once again battered! A little bit like crying wolf.

Speaking of tumors, those who want to follow the tormented path of science in this field can read the Pulitzer Prize winning book '*The Emperor of All Maladies: A Biography of Cancer*' by Siddhartha Mukherjee (reviewed on <u>Wikipedia</u>). It's a story from within because the author is a researcher engaged in the field of cancer.

#### Radiography of a researcher

This article was born out of an attempt to make sense of the information on the coronavirus pandemic that is out there. There are many people talking about it on TV, in newspapers, and on the internet. But with what authority? Are there parameters to evaluate it? In science, references count. If I'm looking for an engineer to build a house, I certainly would not rely on someone who has never built one.

A researcher's references are the number and above all the quality of their publications. The position they hold can be a good indicator of how reliable they are, but it's not the most important criterion; what matters most is their work. How can we find and evaluate a researcher's publications?

For this purpose, there are various databases with very powerful search engines. <u>PubMed</u>, which will soon be active in an <u>updated form</u>, is well known in the biomedical field (for details see <u>Wikipedia</u>). If you click 'advanced' (advanced search) in the updated version, with a little practice you can set up very efficient searches. By adding the 'Affiliation' of the researcher, you can avoid homonyms. <u>Google Scholar</u>, which embraces all knowledge, provides another powerful search engine. Once you have the list of publications, you can then check if they are published in important journals, with high Impact Factor (see above).

There are also sites, similar to those for the IF for journals, that give you the ranking of a researcher, for example the H-Index (see <u>Wikipedia</u>, which also gives its limitations).

These days every TV channel, newspaper or magazine seeks out an expert in virology or epidemiology for interviews and opinions. I was curious about one that appeared to be very popular and looked up his publications. I found very few and, strictly speaking, only one on virology.

#### Dogmas in science do not exist

Einstein's greatest contributions to physics go under the name of general 'theory' of relativity. Theory is an equivocal word. In common language it has come to mean an imaginative hypothesis that has just occurred to someone. In science, 'theory' has a very different meaning: a theory is in fact a well-established scientific explanation based on a collection of facts and experiments.

In science there are many consolidated theories, but there are no dogmas. As Karl Popper said, a scientific theory is only such if it is 'falsifiable', that is, a theory is scientific only if you can conceive and do experiments that can confirm or disprove it, i.e. show it is false. Moreover, a theory must be able to produce verifiable predictions. The general theory of relativity predicted, among other things, the curvature of light and, in some circumstances, gravitational waves. The first prediction was confirmed with the photos of the eclipse of the sun in 1919 (Einstein's second stint in the newspapers; for the first see below). The prediction of gravitational waves has been confirmed much more recently, in 2016 (Wikipedia).

I now turn to a series of examples, each of which illustrates one of the concepts mentioned so far.

### Theories and no dogmas. The problem of the orbit of Mercury.

Newton's universal law of gravitation, published in 1687, perfectly explained the orbits of all celestial bodies. But then scientists realized that the orbit of Uranus had unexplained anomalies. Le Verrier speculated that there was an unknown planet which disturbed its orbit. He made his calculations and wrote to various astronomers (who were skeptical, given that Le Verrier was a mathematician, not an astronomer), telling them where to find the planet. Within a short time, after the letter from Le Verrier, Galle, a German astronomer, found the prophesied planet: Neptune (23-24 night /09/1846). The law of gravitation was safe (see <u>Wikipedia</u>). But then it turned out that the orbit of Mercury, the closest planet to the sun, also had anomalies. Le Verrier, on the back of Neptune's discovery, hypothesized the existence of another planet, and certain of its imminent discovery, gave it the name, Vulcan (because of its proximity to the sun). But Vulcan was never found (*The Hunt for Vulcan: How* Albert Einstein Destroyed a Planet and Deciphered the Universe by Thomas Levenson, is a great book on the topic). The universal law of gravitation was therefore out of balance, because it was unable to explain Mercury's orbit. The deviation was minimal, but sufficient to undermine the foundation of the theory of universal gravitation. In reality, the word 'theory' had never been used for the law of universal gravitation, which was precisely a *law*, and most beautifully efficient in its simplicity. Halley's comet appeared in 1682. Astronomers calculated that it should return in 1758, and, how

wonderful! It was on time! It was at a time when it seemed that science should never be questioned. Instead, it would have been better to use the word *theory*, because in 1915 Einstein (Einstein was on every newspaper for the first time) explained the anomaly of Mercury with the theory of general relativity. It was the end of the law of universal gravitation in its strictest sense (though for the macrocosm it remains fundamentally valid, because it is relatively precise, but no longer valid in the absolute sense) (Wikipedia).

# GPS

Einstein's theory of relativity lends itself well to other considerations. The twin paradox is a famous concept in this context: one of two twins remains on earth and the other leaves for a journey with speed close to that of light. After 20 years (calculated by the twin who remained on earth) the brother returns but only 12 years have passed on his watch. They are no longer the same age! Time is not absolute as Newton thought (and so did we). The example could inspire distrust rather than trust in science in general and in the theory of relativity in particular, which in fact sometimes seems to us to be a challenge to common sense and to our imaginative capacity. Instead, it affects our everyday lives. When we are in a car and we do not know how to get to a place, we simply set the satellite navigator and the problem is solved; it guides us smoothly to the destination. In fact, the navigator uses the Global Positioning System (GPS) which is based on various, very complex parameters. Here we are talking about a comparison in microseconds (millionth of a second) between the atomic clock of the satellites of the GPS system and that of their analogues on the ground. The velocity and, above all, the force of gravity present on the satellites (~20.000 km high; radius of the earth 6.000 km) is very different from that of the system on the ground (the force of gravity is inversely proportional to the square of the distance between two objects). Speed tends to shorten the time while less gravity tends to lengthen it. The offset difference is that the clock on the ground is about 38 microseconds per day ahead for the satellite clock. This imperceptible difference would, in just 24 hours, turn into an error of the order of some kilometers if the relativistic difference of time were not corrected by the algorithms of the GPS (Wikipedia). The GPS example shows how an apparently abstruse science such as relativity has to do with our everyday life.

# The memory of water

In spite of what I have said above one cannot conclude that anything published in a journal, even a prestigious one, cannot be false. However, science always finds in itself the resources to correct itself. The so-called "memory of water" is a curious example. In 1988 Nature published, it seems provocatively, an article by the group of Jaques Benveniste that went down in history as the article on the memory of water (*Davenas et al, 1988*). A solution containing an antibody was diluted so much that at the end practically not even a molecule of antibody was left in the water. And yet, the water behaved as if the antibody was still there. 'It kept its memory' was the conclusion of Benveniste. You can just imagine the implications for homeopathy. It suddenly got a solid and unexpected scientific support. But there had to have been a mistake. And indeed, it was found. Some results were wrongly discarded a priori (in good faith?) thus completely invalidating the statistical analysis, that had led to the abovementioned 'homeopathic' conclusions (Wikipedia) For Italians: Marco Malvaldi (famed for the *Barlume* TV series) speaks extensively and competently about it in his book "*L'infinito tra parentesi. Storia sentimentale della scienza da Omero a Borges*" (2016).

As I said, science always finds in itself the resources to correct itself. In fact, the reproducibility of a result is crucial. Each article always reports the methods and materials that researchers have used so that others can reproduce the experiment, and in that way either validate or contradict the results. In Benveniste's case, no one had been able to reproduce the results of his experiments.

Speaking of reproducibility, lately this has become an acute problem in the field of psychological science. At the end of each year, the journal Science lists the 10 publications which, in the opinion of its readers, have been 'breakthrough of the year'. In 2015 one of these (the third in the Science movie that is on <u>Youtube</u>) was the relatively low reproducibility of the work in the field of psychology <sup>(C)</sup>. The human psyche is complex and difficult to decipher! <sup>(C)</sup>

One of the aims of the recently launched journal "<u>Experimental Results</u>" is to publish the outcome of attempts to reproduce previously published experiments.

### SIRT1 and aging

Here is another glaring example of an error with important economic consequences.

A publication by <u>Cohen et al. (2004)</u> identified some genes, in particular the *SIRT1* gene, as strongly implicated in ageing phenomena. Anti-aging products obviously have a huge market, so the authors from Harvard immediately founded Sirtris, a biotechnology company for the application of this knowledge. GlaxoSmithKline purchased Sirtris for \$720 million. However, it was later found that the fluorochrome used in some experiments had altered the results (<u>Wikipedia</u>). Here too we can see science making mistakes, but then correcting itself (shame about the wasted millions, though!).

# Curious note: coronavirus and social isolation

Social isolation of sick and contagious individuals may seem typical human behavior, as it appears to stem from rational thinking. But *Homo sapiens* was not the first to arrive at this behavior. It had already been noted that infected bees isolate themselves and go to die away from the hive (*Shakar et al., 2015*). Some researchers have recently done experimental work that comes to the same conclusions (*Stroeymeyt et al., 2018*). A (micro) barcode, which was readable by a computer and could follow movements, was placed on the back of several ants. Some ants were then infected with a fungus. Infected ants went to the nest significantly less frequently. This behavior was not developed through reasoning. It had probably arisen by chance and favored by natural selection as it produced an obvious advantage for the survival of the colony. This curious note allows me to introduce a concept that has proved to be central to the understanding of life on earth: the 'theory' of evolution through natural selection, by Darwin.

#### Darwin

Darwin's theory is probably the most controversial scientific theory due to its non-trivial implications, such as the origin of man. On the other hand, we can certainly consider it among the most consolidated. The first documented case of natural selection was that of the *Biston betularia* in the English industrial areas of 1800s. This moth had a light color which camouflaged very well on the trunks of birches. With the industrial revolution, and with very little attention to the pollution caused by the massive use of coal, the tree trunks (and much more) turned black in these areas. The moth therefore became easy to detect against a dark background by predators, usually birds. In the population of this lepidopteran, however, there were rare individuals with dark wings, which was not an advantage in a normal situation. In the industrial areas, however, they became better camouflaged due to their dark wings and had a selective advantage over the light colored ones; they became much more frequent with time (Wikipedia; Youtube). This video (*Betularia*), taken from a BBC documentary on Darwin (Darwin's dangerous idea, 2009), tells in detail the story of *B. betularia*.

Earlier we saw the predictions of the theory of relativity. Darwin's theory can also make predictions. An amusing verification was carried out on the occasion of the 200th anniversary of Darwin's birth and the 150th anniversary of the publication of *On the Origin of Species* (1859). The fact that almost all mammals have teeth suggests that their ancestors had teeth. However, there are mammals without teeth (baleen whales, anteaters, pangolins...). Evolution by natural selection predicts that even if they don't have teeth, they must still have a gene for the production of enamel, even if it is inactive. The genome analysis of these toothless mammals has confirmed this prediction: the gene does not work due to various mutations, but it is there. See <u>Meredit et al, 2009</u>.

#### Coronavirus

One, and first, of Darwin's formidable intuitions was the unity of life on earth (see the <u>tree of life</u>). All life on earth is subject to the same rules, and the rule of fitness (natural selection) also applies to the coronavirus. If a mutation that increases the efficiency of the infectivity (greater fitness) occurs in one virus, it has an advantage over its colleagues and will propagate. You have to see things from the point of view of the virus (as general relativity teaches us <sup>(i)</sup>). There is another concept related to mutations. If there are too few, an organism evolves too slowly; if there are too many the organism is in danger of perishing. In this context it is useful to remember that 99.99% of the species that existed on earth have become extinct! This also applies to bacteria and viruses but only up to a certain point, because of their huge numbers, which are very high compared to multicellular organisms. HIV is the best example. It has a very high mutation rate. Many can be lethal (for the virus) but the chance that the right mutation

(for it B) occurs is very high, and we can't keep up with the virus. The same thing happens, but to a lesser extent, to the flu virus.

# An unusual demonstration of natural selection through an optical illusion: Adelson's chess board

There are many optical illusions. First a premise: the eyes do a relatively simple job; they record an image and transmit it to the brain. It is here that the elaborations begin: the images of the two eyes are merged and straightened, the colors are born, the faces are recognized... and optical illusions arise. There are various books on neurobiology that illustrate how our brains are creative. The directions that creativity has taken over the millions of years of evolution depend not on the greater or lesser objectivity that a process can provide, but on its contribution to fitness, that is, how good an organism is at producing offspring. Before continuing with optical illusions, I'll take a detour to give you another example of how natural selection works in a different physiological process. During the Neolithic period, in a region between Germany, Denmark and the Scandinavian peninsula, people developed cattle breeding, thus making milk widely available. But adults could not digest it, as is still the case even now in various parts of the world. This is because the lactase enzyme, which is responsible for the digestion of lactose, ceases to be produced after weaning. It is a matter of parsimony, as, before cattle breeding, adults simply did not need that enzyme. Undigested lactose is thus used by intestinal bacteria to celebrate, with unpleasant consequences ③. About 10,000 years ago, in the abovementioned region, an individual appeared with a mutation that allowed him to digest milk as an adult. As a result of the mutation the production of the enzyme lactase persisted in adult life. This was a great advantage where hunger, especially in winter, was the rule. This advantage meant a greater probability, compared to others, of reaching reproductive age and of having children. This mutation ensured greater fitness. In fact this is the most striking example of how a favorable mutation can spread very quickly in a population (see Schlebusch et al., 2012; Wikipedia).

Let us now go back to the eye and the brain. Being able to see things with more contrast than the image provided by the eye, would help, for example, to notice in a timely manner a predator hidden among the shrubs. However, it is an advantage that goes at the expense of objectivity, since it alters the original image. In other words, we have an embedded Photoshop. This process of increasing contrast has become innate, automatic and unconscious. A nice demonstration of this is provided by the chess board designed by Edward H. Adelson in 1995. Two squares of the chessboard objectively have the same shade of gray, but we see them as different due to our brain's automatic increase in contrast triggered by the comparison to the neighboring squares. Our brain has a bug, like an apple with a worm B. But the bug is for a good cause: it's for fitness D. For details on the Adelson board see <u>Wikipedia</u> and/or <u>Youtube</u>.

Fitness, therefore, is the touchstone, the polar star, the final judge of evolution. And, to guarantee it, natural selection has provided us with a set of crucial behaviors, common to all species: sexuality and parental care in the first place. However, the survival of the species depends on the survival of the individual up to the reproductive age. Another set of very strong stimuli such as hunger, thirst, physical pain, to name a few, keep us on the right path. Given their importance for fitness, it is no wonder that all these stimuli are so powerfully efficient.

#### **Evolution and tumors**

Another paradigmatic example of the unity of life on earth is given by the study of the evolution of tumors. In population genetics the evolution of a population is studied through the analysis of the individuals composing the population.

A few years ago, technology made it possible to study many biomolecular features at the level of a single cell. This triggered the study of the evolution of tumors through the analysis of the individual cells that compose it. The results showed that evolution of tumors follows the same Darwinian rules as the evolution of species. One just needs to replace the word "fitness" by the conceptually equivalent words "cell proliferation". In the <u>first review</u> on this topic, the authors make the point by a showing the original drawing of Darwin's tree of life next to their illustration of the evolution of a tumor.

# Ancient... conspiracy

Humans have always tried to explain the phenomena that surround them. For many of these phenomena, especially in the distant past, there were no suitable instruments to study them, and perhaps not even the appropriate mentality. So, there had to be someone, behind these phenomena causing them; Jupiter was behind lightning, for example. Modern experimental science was born with Galileo. Each natural phenomenon has a scientific explanation and it is up to us to find it. And even if we cannot find the explanation for some things, it does not mean that the explanation does not exist. We know many things about the evolutionary history of humans, especially now that we are able to perform ancient DNA sequencing. But if we want to trace the history of the last million years of the chimpanzee, we must surrender, because the climatic conditions of the equatorial forest where it lives do not allow the conservation of anything, not even of bones. Therefore, an evolutionary history of these animals, qualitatively comparable to that of humans, can never be written. But this does not mean that this history does not exist.

# **Final consideration**

#### From Dante's Inferno XXVI

Ulysses tells Dante that after his return to Ithaca from Troy, after a while

...nor fondness for my son,

nor pious reverence for my agèd father, nor ev'n the bounden love which should have cheered Penelope, could overcome within me the eagerness I had to gain experience both of the world, and of the vice and worth of men; but forth I put upon the deep and open sea...

And the greatest curiosity was to know what was beyond the columns of Hercules (Gibraltar). Gods had placed boundaries on human knowledge; they had forbidden man to cross Gibraltar.

...we attained that narrow passage-way,

where Hercules set up those signs of his,

which warned men not to sail beyond their bounds.

But Ulysses passes

...we with our oars made wings for our mad flight.

As revenge, gods hit the ship with a storm which three times it made her whirl with all the waters; then at the fourth it made her stern go up, and prow go down, even as Another pleased, (Gods) till over us the ocean's waves had closed.

Ulysses represents the urge of *Homo sapiens* to know. Even though he is in hell, I would propose to raise Ulysses as a patron saint of researchers <sup>(C)</sup>. Well, science is just that, it is a journey of discovery without ideological prejudices, with an open mind ready to question. But this mental attitude is not innate. It is an achievement. The brain of the cub of *Homo sapiens* develops absorbing like a sponge, uncritically, the cultural context in which it is born. And this, especially in closed social contexts, has led to terrible disasters, like religious wars.

The internet has now opened up the cultural context potentially beyond measure. However, I quote an emblematic phrase that I found in a book by David P. Barash (<u>Through a glass brightly, 2018</u>). He writes that the internet is "a self-reinforcing echo chamber, whereby people arrange to encounter ideas and perspectives that accord with their own, reinforcing the illusion that their ideas and perspectives are central to public discourse such that alternative views hardly exist". Anti-vaxxers, flat earthers, etc. are typical examples. It is possible that those of you who got to the end of this article, already agreed with it in some ways. Those who did not, probably stopped after the first few lines, perhaps outraged by the usual arrogance of science.

What is to be done? Sudden conversions like the one of Saint Paul, are very rare. Maybe this article can benefit those on the fence. What else can we do? I think the only place where intervention works are schools. That's where kids can learn what the scientific method is. And the University is responsible for preparing teachers who, aware of the problem, are up to the task.

Mariano Rocchi Emeritus Professor of Genetics President of the European Cytogenetics Association Dept. of Biology Università degli Studi Aldo Moro di Bari mariano.rocchi@uniba.it Bari, May 14, 2020 Mensis IV ab coronaviro condito (Ab Urbe condita - in the year since Rome's founding)