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Rigor – The essence of scientific work

Some months ago, I read a new biography of Leonardo da Vinci and one of the facts that interested me most about this Renaissance giant was that one of his favourite mottos was "Ostinato Rigore".

Undoubtedly, that idea of unrelenting rigor marked the life of this brilliant artist, scientist, hydraulic and military engineer. Leonardo looked for perfection and beauty with such obstinacy that it caused him great suffering and limited the number of his incredible works.

We could propose a definition for rigor saying that it consists in the disciplined application of reason to subjects related to knowledge and or communication.

Rigor is many things. It is dissatisfaction with uncertainty, with inaccurate answers, with unprecise measurements, with the spread between the plus and the minus.

Rigor is also being methodical commitment to experimental procedure, to the need of controlling all parameters that can affect the results of our tests.

But rigor is also strict adherence to the truth, it is to disrobe ourselves of our prejudices and enthusiasm when we interpret our results, it is to search for all possible explanations of what we observe, it is accepting a result that demonstrates the fallacy of our most precious hypothesis

Rigor is an attitude that contrasts with the weaknesses of human nature, does not allow laziness, the lack of attention, the acceptance of inexact methods, the adoption of groundless conclusions, accepting the predominant opinion despite the lack of data which sustain it. A famous biochemist, Dr. Efraim Racker, once said “there’s nothing sadder that an ugly fact destroying a beautiful idea”. Rigor demands us to accept the destruction of that beautiful idea by facts.

Rigor is in the essence of scientific work, in each one of the stages of the research work. Rigor implies a structured and controlled way of planning, developing, analyzing and

evaluating our research and a special care in adapting the presentation of the results to the demands of the audience we communicate the results of our investigations.

Let's review step by step the stages of research and how rigor influences them.

Investigations start with questions that we ask ourselves about the universe, human beings, and nature that surrounds us. Scientific questions are different from the ones that philosophers or theologians ask themselves due to the fact that the scientific questions can and should have experimental answers.

In the formulation of question(s), the rigor is precisely in achieving precision in formulating the questions thus allowing us to imagine experiments able to answer them. It is not enough to ask ourselves 'What causes cancer ?' All the available information should be used to break down that big question into a series of other related questions that enable to obtain clear answers. For example 'Why a serine 45 mutation of the beta catenine protein is frequently found in many tumours?'

When making this question, the rigorous scientist will have one hypothesis, a possible answer that can be experimentally checked and that will answer the question. For example: 'Serine 45 of beta catenine is phosphorylated by a protein kinase". When this phosphorylation is prevented by mutation, cellular division is stimulated and cancer results. This would be our hypothesis.

Thoroughness demands us to propose a project with all the necessary experiments to answer the question using our hypothesis as a focus in order to prove it right or to demonstrate it wrong.

Being rigorous in the formulation of a scientific research project implies many aspects. A key component is choosing questions and hypothesis that can be answered experimentally in the time and with the means proposed in the project. Another main aspect is the rigor in the bibliographic analysis of existing knowledge, mentioning the reports that favour our hypothesis as well as those not supporting our ideas.

In the methodological part, the selection of appropriate methods to carry out experiments require great thoroughness and rigor. If a biological model is adopted for our studies on cancer, we have to ask ourselves how valid is this model 'could the results be extrapolated to human cancers?' The methods that measure what we want to measure must be chosen with utmost precision.

It is always good and rigorous to use alternative methods to have independent verifications and eliminate artefacts that can result from the use of one method or technique. In the formulation of a project different approaches are to be proposed and adapted to the different alternatives of eventual results. A 3-4 years work project cannot be built totally depending on whether the first experiment gives us a positive result.

Another aspect that requires great honesty and thoroughness is precisely the evaluation of research projects presented by our peers. We are judges deciding on the financing of projects from which the careers of academics and students depend and that may generate important advances to knowledge.

In evaluating projects, we must forget who are our friends and enemies, the competitions between Faculties and Universities and rigorously analyse the project within its scientific context, in its relevance and in the thoroughness in the approach of the authors. Every praise and criticism we include in these evaluations should be validly supported.

Once the project is approved and entering into execution, we again need rigor.

The most creative and personal exercise of a scientific researcher is the design of the experimental protocols. As a painter chooses his or her paintbrushes and colours, researchers choose the number of samples, the variation in the components, the tests that serve as negative controls, those that act as positive controls demonstrating that everything works as expected during the assay.

As in art, there are protocols that are rustic, baroque, surreal or impressionistic. It is magnificent that personality can find expression. Luis Federico Leloir, the great Argentinian Nobel Prize winner told us that all his experiments had only 3 test-tubes: one control and two experimental samples and in this manner he discovered the mechanism of synthesis of glycogen and won the Chemistry Nobel Prize. Young thesis students generally want to answer all their questions at once in one experiment with hundreds of tubes. In any case the adequacy of protocols will be reflected by the fact that the whole design should pursue the ideal of a straight answer. A clear and sound answer that says yes or no to our question. The same as with the beauty pursued by artists, this ideal of a clear and unambiguous answer is elusive and slips out of our hands. We always find that the protocol left a small door open or a control that was missing and we have to try it all

over again more rigorously until little by little we extract the small pieces of the truth we are seeking for.

The analysis of the results is another point that calls for rigor. How credible are they? How general or specific? How statistically significant? Which eventual interpretations are sustained by those results? Are there other experiments that allow us to discriminate between those interpretations?

We reach the critical stage in which we must communicate the new discoveries we have learned from our researches. Until that moment, it has been a personal exercise, a secret fight to extract a jewel, a new and unknown truth from the womb of Nature.

However, in order to be true research it must be communicated and put in a show window, visible to our scientific peers for them to examine, to analyze, to test.

Generally, before publishing it, before putting it on the global show window, it is useful and rigorous to show our results more privately to other colleagues and friends. This may have several forms, for example, a Department Seminar in which we orally present, a private consultation to a friend that is in the same field of knowledge. Something much more advanced, although yet preliminary, could be a free communication in a National or International Congress.

To make these presentations, where a very good review can be received, it is however strategic to be ready to send a paper since many people will know of our results and some unethical colleagues will try to publish similar results.

The final destiny of scientific research is publication and by the nature this workshop, I imagine, the matter of rigor in publications is what you are most interested in.

In science, communication is essential since it is the interface between the research authors and the rest of the world. Before they are communicated, the results of the investigation are nonexistent, there is no contribution to human culture, the answers to our questions that rose from our experiments are only anecdotic.

This communication has to be rigorous in order to comply with the main purpose of publications: to present our results to the critical analysis of our scientific peers, allowing our experiences be checked and expanded by other researchers working on similar projects. This objective defines the terms of the rigor in a scientific communication and, at

the same time, defines what scientific work is. Some time ago we discussed the inclusion of publications of 1 page or less, or the summaries of scientific meetings as valid publications in the CV's of academics.

In general, very brief publications, even though they are in journals with qualified Editorial Committees cannot be considered as such since they do not comply with the indispensable pre-requisite of offering enough details on the methods and materials used to allow other people with adequate training, to be able to repeat our experiences. This alerts us against the current trend of many scientific journals of minimizing the section on 'materials and methods'.

Obviously, in the case of 'Abstracts' of Congresses, they do not fulfil another indispensable requirement: revision and approval by a Committee of Peers of the Editorial Committee. Even though the Congress may have had this Committee, a 200 word 'Abstract' cannot be seriously evaluated regarding the scientific rigor of the research process and of the analysis of the results.

Let us see once again how each one of the components of a scientific publication is influenced by rigor.

The title must briefly reflect the essence of the results of the work. Rigor restricts the amount of 'merchandising' in the titles. In science there are words and areas that are fashionable, that call the attention, that 'sell' better than others that are no longer attractive. Obviously we want to attract many readers, but we cannot fool them.

Often a title offers us that we think we will find in the paper the solution to many of our questions. Upon reading the full work, however, we notice that the real contributions are much more modest and that the title 'oversells' the work done. Rigor is clearly missing.

In the first page we also find a list of the authors. Ethics and rigor require that all those that significantly contributed intellectually to the work be included. The authors are co-responsible of everything included in a publication and should share an adequate knowledge of its content.

A general rule establishes that any of the authors should be able to present a half-hour seminar on the content of the publication. If one of the authors is unable to do so, it is fair to ask oneself if he should really be included among the authors. Clearly, technical staff, that play a fundamental role in the execution of experiments should not be included if

they did not make an intellectual contribution to the design of the protocols and to the interpretation of the results.

The ‘introduction’ should provide the reader a summary vision of what was known in the field previous to its publication, recognizing the significant contribution of other groups through the corresponding bibliographical citations. In this part of the manuscript it is also necessary to establish the question we made ourselves and briefly announce the results we are going to be presenting.

The section on ‘materials and methods’, as already expressed, has to be rigorous in offering the necessary full experimental detail to allow other scientists, with the necessary infrastructure and knowledge, to repeat our experiments.

The section ‘results’ is clearly the most important one in the work. Rigor in its presentation requires the information of the number of times the experiment was repeated and the variability obtained in the results achieved. It is easy to mislead the inexperienced reader, playing with the scales of the figures but these games clearly sin against rigor.

Once again, the text of the figures and tables require the inclusion of every detail of the variables used, of the concentration of the components and that these be expressed in values that are independent in the special conditions in which our experiments are made (for example the calculation of radioactivity in counts per minute depends on the efficiency of our counter, etc.).

In the section ‘discussion’, rigor implies presenting clearly an objective interpretation of the results, saying in what measure progress has been made in knowledge, including the different interpretations our results have. It is licit to speculate on the possible meanings of such results but we must clearly separate what we consider solidly demonstrated from what is mere speculation on our part.

If our results differ from others reported by other authors it is our duty to point it out and be very careful and respectful while looking for possible explanations for discrepancies.

In the ‘bibliographical references’ it is once again essential that quotes of papers of those works that are relevant to the field of our publication be made correctly. It is necessary to moderate the natural tendency of ‘self-quoting’ used to magnify the contributions our group has made to the field. Some authors include in their quotes all the works that they

have ever previously published although they have little to do with the subject of the manuscript.

But scientific rigor in publications is not only on the side of the authors of the papers but it also requires equal effort from the editorial committees where they are presented.

A paper is the result of an arduous work and a lot of sacrifices by a group of people. Most scientific papers include invisibly years of work and the efforts of thesis students and researchers, many hours of thought and reflection, many funds spent on materials, equipment and reagents. Along with the sheets or the bytes that reach a magazine's editorial office, comes the hope and ambitions of that group of authors of obtaining a degree, of winning a fellowship or a project, or of being promoted in their academic career and, of course, also of having made a contribution to knowledge of that field.

It is a great responsibility for the editors to provide that paper a fair and exact evaluation, while on the other hand, it is their duty to keep up the seriousness of science and its credibility. The whole magnificent building of science and its extraordinary conquests require that the knowledge published in well-known journals be reliable and serious.

All of us who have been in the business for many years, have frequently lost much time and effort trying to repeat without success some experiments published in good journals.

There is no better way to evaluate papers than sending them to expert peers in the field. Fortunately most of them make a tremendous effort to provide a balanced and constructive opinion of the papers revised. In my experience, in almost all my publications, evaluators that have critically examined my work have been right and contributed to the improvement of those works. However, obviously, peers are human beings and as such they have their prejudices and limitations.

I am convinced that the papers that come from Chile or from another country from the third world are revised by most of the editors with a different attitude than those presented from Harvard, Cambridge or the University of Paris. This hurts us, but we understand since we also review with a different degree of credibility the papers that come from Africa, Asia or another Latin American country compared to those coming from more developed countries.

In general, my experience as an editor is that those prejudices are balanced out when one asks opinions from several evaluators. Obviously there are cases in which the reviewers of

papers do not do their job well and deliver judgment without even having read the paper. All journals should have black lists of this type of referees that don't keep up to the most elemental scientific rigor and seriously damage people.

While reading some papers on scientific rigor I was surprised that there is a certain debate on the relationship between rigor and relevance. Some have even expressed that a dichotomy exists between those two words that would define that if the work is relevant less rigor should be expected. Others believe that both components are indispensable to make the products of the investigation be useful or usable.

Frankly I understood little of the debate and I think that it is simply a matter of semantics on the meaning of the word 'relevance'.

Likewise there is in this debate a confusion on what is the execution of a research project and what its communication implies.

If we understand the word relevance as an adaptation to the interests of the addressees of the communication of a scientific paper, we can recognize there can be different levels of rigor in the communication of a scientific work.

Clearly a scientific work, for example on cancer and some molecular mechanisms that underlie them, must be executed with the maximum scientific rigor. However, the rigor of communication is going to be very different when that same work is sent to a specialized journal (i.e.: Cancer Research) than when it is presented as part of a symposium on cancer or when it is delivered as a lecture to the general public. The strictness of the details of methodology, controls and all the rest will be very different. This is an important point we have to have in mind in defining the editorial line of our journals.

If they are highly specialized journals, the editors that are their gate keepers, must establish a high grade of rigorousness as a requisite in the papers since their readers are people from the field that want to know all the details of the work . Journals focusing on review articles on more general topics, will be less demanding on techniques and methodology, emphasizing the more integrative ideas of the field.

We must be conscious that even rigor in science can be exaggerated and lead to paralyzing extremes. Some years ago, I met a person with excellent training, already elderly, who paid so much attention to detail that when weighing something he left the reagent on the analytical balance for two hours until it reached the temperature of the

balance. Then his failing sight did not allow him to see correctly the numbers on the scale. In the years I knew him, he never completed an experiment.

But the best story on the extremes where the rigor in science can reach is by Jorge Luis Borges in one of his extraordinary tales called precisely ‘Rigor in Science’ and I quote:

..In that Empire, the Art of Cartography reached such Perfection that the map of one Province alone took up the whole of a City, and the map of the empire, the whole of a Province. In time, those Unconscionable Maps did not satisfy, and the Colleges of Cartographers set up a Map of the Empire which had the size of the Empire itself and coincided with it point by point. Less Addicted to the Study of Cartography, Succeeding Generations understood that this Widespread Map was Useless and not without Impiety they abandoned it to the Inclemencies of the Sun and of the Winters. In the deserts of the West some mangled Ruins of the Map lasted on, inhabited by animals and Beggars; in the whole Country there are no other relics of the Disciplines of Geography.

Suárez Miranda - Viajes de Varones Prudentes

Libro Cuarto, Capitulo XLV, LZrida, 1658

I do not want to finish without mentioning a fundamental aspect on the rigor in science. Rigor is one of the most important formative values that science can give to Society.

We are at a time when there is an open debate on the relationship between science and society. This debate tries to define a new contract between science and society at the time science and its product, knowledge, has a huge impact on the social and economical development of people.

In this new contract, society grants science and scientists freedom to research in the fields established by their curiosity with the only limitation of the ethics of their culture. Additionally, society grants us financial and human resources to carry out these investigations and gives us a certain degree of recognition.

What do we give in exchange?

Obviously we provide the knowledge our investigations generate. Part of that knowledge is quickly applicable and generates new technologies, better and more competitive products. Another fraction of knowledge is not yet applicable and is useful to increase the scientific and cultural heritage of the world.

But there is another contribution that science can give to Society that has, by no means, less valuable. That contribution is given through science education to children and young people in schools and high-schools.

A high-quality science education, an education not centred in the teaching of equations, formulas or definitions, but that makes students rediscover the main principles of science through their own inquiries and experiments, can make an enormous contribution to society. This contribution consists in transmitting to children, the future citizens, a new rational way to face the world and its problems with the values of science.

These values, the search for truth, the rigor in their questions and in the demonstrations and disrespect for dogmas and for authority for the sake of authority, will contribute to make our citizens and our societies more free, more progressive, more capable of solving their problems.

Scientific rigor is a value that should penetrate our daily thoughts, our media, the discourse of our politicians, and our complete culture.

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