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Saving Science. And beyond

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1. Introduction

We commend Dan Sarewitz, a professor of Science and Society at Arizona State University, for his recent article on the status of science (Sarewitz, 2016). The article sheds light on the complex issue of irreproducibility and lack of progress in certain areas of scientific research, particularly on the sociological determinants of the *status quo*. These are compelling explanations and therefore will not be addressed in our commentary. We will posit, instead, that contrary to Sarewitz' opinion, the notion that progress in fundamental science cannot be managed from "outside" by managers focused on specific practical results, or contrary to the current NIH practice, from "inside" by "study sections" populated by peers that while accepting the current dogma, may be incapable or unwilling to recognize a novel idea and, thus, intent to maintain the status quo (Huang, 2013).

Perplexing statements

Sarewitz's core argument is that science cannot correct itself: Scientists must come back into the real world and save science by being asked and/or directed to achieve a goal (i.e., prevent cancer by means of a "vaccine") by administrators rather than pursuing their own scientific interest. Hence, Science should be managed like engineering missions, similarly to the Manhattan project. However, there is a difference between preventing cancer and making an atomic bomb. In the latter, solid theories to understand nuclear fission were already available, while in the former, mainstream biomedical sciences as well as their root science, organismal biology, lack a global theory of organisms which could provide principles upon which to build a theory of cancer.

It is not by chance that the problems that Sarewitz address regarding lack of progress and irreproducibility of data occur in biomedical sciences and economy. These disciplines lack the solid theoretical foundations of mathematics and physics. Our point here is that general theories provide organizing principles and construct objectivity by framing observations and experiments. There is no fundamental reason why this should not be the case in biological sciences once a proper analysis of the constraints hindering such theorizing is done and dealt with (Longo et al., 2015; Soto et al., 2016). In this regard, the article gets to the roots of the problem when citing Susan Fitzpatrick which identifies the "dogma of reductionism" as a reason for the lack of progress.

Let us examine some of these perplexing statements: *"First, scientific knowledge advances most rapidly, and is of most value to society, not when its course is determined by the "free play of free intellects" but when it is steered to solve problems — especially those related to technological innovation."*

This is a truly 'Baconian' approach to science. Although it can be argued that it has worked in some instances, it is neither the only nor the main road to discovery. For example, a significant number of relevant advancements have been made by chance (penicillin, vaccines), or because of the development of theoretical foundations (DNA studies based on Schrödinger's conjectures). Experimental discoveries need to be included into an organized theoretical framework in order to be 'understood' and extensively appreciated as such. The paradigmatic example of the Mendelian experiment (that had to wait fifty years before it was given its due) showed that even relevant "advancements' *can be overlooked before a new theoretical hypothesis emerges*. This is another example that strengthens the notion that true scientific and/or technological advancement takes place *only when 'raw data' is interpreted within a theoretical context.* Indeed, the role of theories is to provide organizing principles, to determine which are proper observables and to construct objectivity by providing a framework for observations and experiments (Longo et al., 2015; Longo and Soto, 2016).

"Second, when science is not steered to solve such problems, it tends to go off half-cocked in ways that can be highly detrimental to science itself". This statement is challenged by facts. Significant progress in the sciences has been made by scholars who manifested an astonishing *indifference* towards applied and moneymaking aims. For instance, recent advancements in mathematics (see the incredible story of Grigorij Perlman) are truly remarkable, notwithstanding their complete disregard for practical applications. History teaches us that Galileo's approach was the consequence of an insight into nature that matured during the Italian Renaissance, as a consequence of new 'metaphysics' where 'scientific knowledge' was thought to allow Mankind to reach God, then identified with nature (not as 'technology power'). Similarly, the physical-mathematical program of study undertaken by Newton relied mainly on strong religious commitments and the alchemical-esoteric interests in which he was heavily involved, rather than on some specific 'technological' input. These strong religious commitments were eventually replaced when scientists recognized that "reality" is not directly accessible and that theory is thus the appropriate tool for constructing objectivity.

"Third — and this is the hardest and scariest lesson — science will be made more reliable and more valuable for society today not by being protected from societal influences but instead by being brought, carefully and appropriately, into a direct, open, and intimate relationship with those influences". This may become a scary proposition. Societal influences may drive technological commitments; however, as such, they have nothing to do with the search for scientific knowledge. A society may request 'technological commitments'. Shaped by religious or historical contingencies, a society may give up scientific knowledge in order to 'reconcile' the technological outcome with its general beliefs. Those contingencies may widely differ from one society to another. Consequently, societal responses to a similar problem (i.e., food production) may vary widely depending on different economic and cultural premises and constraints. In this regard, the current debate about GMOs offers a good example. And yet, society may not be interested in the ultimate quest for knowledge. Moreover, a "majority vote" does not help in assessing knowledge: instead, knowledge is constructed by the search of new paths, usually explored against mainstream research, and systematically against common sense (Bachelard, 2002; Wolpert, 1994). In this quest, "negative and paradoxical results" are crucial because scientists cannot predict all physical dynamics by equations (Poincaré); neither can they identify Euclid's geometry with space (Riemann). Similarly, we cannot decide and compute all definable propositions and functions (Gödel and Turing). Against the dominating view and against the "technological expectation and demand" of solving all problems, these negative results opened the way to 20th century science and its astonishing accomplishments such as modern dynamical systems, relativity theory, theories of computation and then computers.

"This research lacked the key ingredient that made DOD [US Dept. of Defense] such a successful innovator in other fields: the money and control needed to coordinate all the players in the innovation system and hold them accountable for working toward a common goal". Currently, (grant) money is a 'critical' factor to do science because

the technological tools used are very expensive (mainly in physics and biological sciences). Yet, in several instances, a single person with limited resources can make astounding advancement. A case in point was the discovery of *H. pylori* as the 'causal', ultimate factor in gastric ulcer genesis made by a single medical practitioner, mostly working in isolation. Another example is the case of Dr. You-You in China who discovered the anti-malaria properties of Artemisia extract by relying on the 'traditional' efficiency recorded for this plant, while the 'rest of the World' was searching for a hypothetic 'synthetic magic bullet'. The pharmacological principle was extracted according a truly ancient protocol dating from 300 a.C (according to the *Handbook of Prescriptions for Emergencies*) (Yu, 2011) because the 'modern' purification methods were ineffective. The rationale for extracting this specific principle was suggested by oral medical tradition dating back to the medieval age. The extracted drug introduced into treatment in the '70s was not 'recognized' by the Western world until a few years ago and is still not patentable (only the extraction procedure has been marketed). This is an outstanding example of technological failure not only in achieving the required 'goal', but also demonstrates that *'technology' may delay the discovery of new solutions*.

This result was achieved by working far from current scientific mainstreams, in scientific structures with loose links to the so-called 'Big Science' (namely the US academies), and originally published only in Chinese journals. However, such an 'unconventional' approach led to her being awarded the Nobel Prize!

> "If we think that scientific progress is best pursued by 'the free play of free intellects', we give science a free pass to define progress without reference to the world beyond it. But if there is nothing by which to measure scientific progress outside of science itself, how can we know when our knowledge is advancing, standing still, or moving backwards? It turns out that we cannot".

We find this statement troublesome. Today, We think that 'progress' may be conceived as follows:

- *Advancement in knowledge*: a scientific discovery enables validation and expansion of a previous theory. This refinement will then be useful for making new predictions and/or to pose new questions. This criterion relies on the coherence of any theoretical framework and, as such, is independent from any programmed and explicit external 'constraints'. Diversity of quests and the exploration of totally unexpected paths is at the core of scientific invention.
- *Technological advancement*: may lead to solving a specific problem. Yet, several solutions are oftentimes available. How can one choose the best? Again, the societal/historical context will drive that choice. This criterion is a 'relative' one.

> "The reason that bias seems able to infect research so easily today is that so much of science is detached from the goals and agendas of the military-industrial innovation system, which long gave research its focus and discipline".

The opposite may be true. The endless search for 'results' that could fit within a 'technological agenda' leads scholars to provide data which are consistent only with such framework. Everything out of that perspective is inevitably ignored. This applies to all the 'omics'.

Additional observations

Technological efficiency cannot be considered as a proof of "truth". For about two thousand years, humankind was successfully able to trace the trajectories of stars, and to navigate without technology, and eventually discovered new continents. Yet, these endeavors were performed first by men who trusted a wrong cosmological theory, i.e. the Ptolemaic one. Thus, wrong theoretical assumptions may eventually lead to useful previsions and right performances, until a threshold of accumulating contradictions is reached. Thereby, if Science deals with the search for 'knowledge', then technology can hardly be viewed as a major criterion of 'scientific advancement'.

Broadly speaking, a statement can be demonstrated to be 'correct' by different strategies:

1. Phenomena that can be framed according to the reductionist approach and are ruled by linear dynamics.
2. Yet, an overwhelming body of other events (both in physics and in biology) cannot be 'reduced' to simple rules and the case for achieving a 'true' quantitative description of the phenomenon is a matter of statistical reliance (probability).
3. In the mathematical field, results cannot be submitted to 'technological vindication'. Indeed, in this case, reliability of the mathematical 'performance' is achieved by the invention of radically new concepts and structures. Then, in adherence to a set of basic premises or postulates and rigorous internal rules (logic rules), 'logic' demonstrations help in setting these results on robust grounds.

Yet, even those results can be biased by 'ideological' (metaphysical) premises that shape the experimental methodology. Ultimately, 'free' science cannot exist without an 'a priori' (meaning, philosophical) premise (Bizzarri et al. 2013). The invention of mathematical infinite spaces, a marker of the Western scientific revolution, originated from the invention of perspective in Italian paintings during the Renaissance. This mathematical infinite space was a mystic and symbolic revolution aiming to express the presence and the infinity of God (Longo, 2011). Similarly, well recognizable ideological premises lie behind any technological process.

In this regard, two aspects deserve to be highlighted:

1. The need to reach a 'marketable' technological result (for instance, a therapeutic drug) implies that only those molecules that can be patented are deemed worthy of interest and are chosen for extensive investigation. No room is then left for 'natural' compounds, even if those molecules are as effective as their 'synthetic' counterparts, because they cannot provide an economic benefit. In this case, the 'technological goal' stands against the possibility of achieving a reliable treatment for a given disease. Again, the case of Artemisia for malaria provides an excellent example: the pharmacological principle was extracted according a truly ancient protocol dating from 400 BC because the 'modern' purification methods were ineffective. The rationale for extracting this specific principle was suggested by oral medical tradition dating back to the medieval age. The extracted drug introduced into treatment in the '70s was not 'recognized' by the Western world until a few years ago and is still not patentable (only the extraction procedure has been marketed). This is an outstanding example of technological failure not only in achieving the required 'goal', but also demonstrates that *'technology' may delay the discovery of new solutions*.
2. The availability of technological devices (namely the so-called high-throughput technologies) drives scientific investigation towards those fields in which that technological tool may be financially fruitfully applied. In turn, the experimental design is frequently shaped to fit the specific requirements of the available technology. Indeed, the widespread use of a particular technology is further strengthened by the necessity to increase the financial return of such practice. In summary, the adoption of some technologies inevitably leaves aside potential relevant topics. Today, in the cancer research field, scientists search for mutated "cancer genes", their sequencing and analyze gene expression patterns because this approach is deemed a 'promising' strategy according to the Somatic Mutation Theory of carcinogenesis (SMT). In turn, the availability of analytical gene technologies reinforce the narrative of SMT. In this case, the endless refinement of current 'molecular' technology strengthens the current paradigm and discourages the search for a different perspective.
3. The virtual space of research is significantly 'limited' because only those fields that are supposed to be worthy of study are taken into consideration. Often, a technologically refined device is available in those fields. This means that research programs, based on authentically new perspectives, are seldom funded. Additionally, scientific journals are reluctant to accept any alternative contributions to the dominant interpretation (metaphysics). All this argues against the idea that scientists are kept in a sort of creative freedom; instead, they are rather constrained to think in ways imposed by the scientists recognized as leaders by membership in prestigious entities (scientific academies) or by being recipients of prestigious prices, and by the funding opportunities created by the tax-supported and/or philanthropic agencies. We already know enough about various societal problems like world hunger, infectious and metabolic diseases. In this context, knowledge does not constitute the 'limiting factor'. Probably, what is missing is the political/economic will to solve them. For instance, one may rhetorically ask… why are we ceaselessly searching for a magic bullet to 'eradicate' metabolic diseases (obesity, diabetes) when we already know that such goal may be successfully achieved by proper dietary regimes, physical exercise and elimination of environmental pollutants that increase the propensity to develop these diseases. However, the 'simple' solution (diet, exercise and a clean environment) is conflicting with our technological framework whereby a pharmacological agent is considered as a solution for every situation and with our politico-economical system, prone to hinder regulations that threaten the earnings of the industries that feed this epidemic.

Conclusion

Science – or more specifically the Life Sciences - is experiencing a true crisis. However, we consider unlikely that the solution may be the one envisaged by D. Sarewitz. Technology may support Science. Nevertheless, Science cannot be reduced to Technology. Without a guiding vision there is no road ahead; the science becomes an engineering discipline, concerned with temporal practical problems. Finally, as stated by Carl Woese, "a society that permits biology to become an engineering discipline, that allows that science to slip into the role of changing the living world without trying to understand it, is a danger to itself" (Woese, 2004).

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