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Saving science. A reply

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*Dear Sir***,**

I am pleased that the inaugural issue of *Organisms* included a very thoughtful response to my recent article "Saving Science" (Sarewitz, 2016). Bizzarri et al.'s "Saving Science. And beyond" (2017) expands and enriches the conversation about how to understand and address the current difficulties of the science enterprise, difficulties that Bizzarri et al. and I, along with many others, recognize as undermining the vitality, integrity and social value of science. I take it from their article that Bizzarri et al. also share with me an understanding of some of the key causal elements that lie behind these difficulties, perhaps especially the perverse incentives in the academic science system and in the economy that drive knowledge creation along avenues that fail to contribute meaningfully to the advance of science or to the solution of urgent social challenges.

Nonetheless, in several important respects I believe that Bizzarri et al have misportrayed the thrust of my argument. Debates about science have for nearly a century--at least since the Bernal-Polanyi debates of the 1930s (Brooks, 1996)--been locked into an artificial dualism where the only available positions might be portrayed as "science autonomous" versus "science controlled." As a cultural matter, the "science autonomous" side of the argument has long been in the driver's seat. Even America's notoriously scientifically illiterate public agree by a huge margin that if scientists are left alone to do what they want, great social benefits will eventually accrue (National Science Board, 2016). "Science controlled," on the other hand, is what authoritarian states and faceless bureaucrats and even well-meaning citizens incapable of understanding how science really works would seek to foist on scientists. The results can only be disaster (Polanyi, 1962).

I've never actually met anyone who really believes that science really can or should be fully controlled by the state, but the trope remains an evocative bugbear for fighting off critics of the scientific status quo.

Bizzarri et al. are by no means protectors of the status quo, yet they clearly place me in the "science controlled" camp, saying that I think that science must be "asked and/or directed to achieve a goal (i.e. prevent cancer by means of a 'vaccine') by administrators . . . Hence, Science should be managed like engineering missions, similarly to the Manhattan Project."

I did say that if science is being called upon to address societal problems, it can and should be managed, but I devoted many thousands of words to trying to provide nuance and specificity about what "managing science" might mean—and I did *not* say or imply that science should be managed like engineering projects, or that the Manhattan Project is a good generic model for managing science today. What I had hoped to accomplish, but apparently failed, at least with Bizzarri et al., was to establish a perspective that was independent of the autonomy-versus-control dichotomy, but instead builds from the synergies that occur when scientific creativity and practical problem solving are appropriately brought together—a problem of institutional design and management, but not of control.

The best way to illustrate Bizzarri et al.'s mischaracterization of my position is to revisit one of the main examples that *they* raise in attacking my argument: the discovery and development of the anti-malarial drug artemisinin by the Chinese scientist Youyou Tu (for which she shared the 2015 Nobel Prize for medicine). As Bizzarri et al. note, the drug's discovery occurred well outside the mainstream of scientific and technological efforts to combat malaria in western universities and corporations, but relied instead upon "oral medical tradition dating back to the medieval age" in China. Apparently they offer up this example because they think I am arguing that science must be made subservient to existing "technological commitments" using "very expensive" "technological tools," to achieve a "'marketable' technological result," where "only those molecules that can be patented are deemed worthy of interest."

I don't believe in, nor did I argue for, the necessity of any of those things, but the artemisinin story does perfectly illustrate two of the main points of my article that Bizzarri et al. don't mention. First, the urgent search for a cure for malaria by Chinese scientists was triggered by a request from North Vietnamese leaders during the Vietnam war (McNeil, Jr., 2016). A problem needed solving, and a coordinated and managed effort was quickly ramped up by Chinese authorities to do so. Second, artemisinin was already known in traditional Chinese medicine as efficacious (Tu, 2015). It offered, that is, an empirical performance baseline upon which progress toward solving the problem could be demonstrated and improvement in performance could be assessed (Sarewitz and Nelson, 2008). Problem context provided the motivation: North Vietnamese soldiers needed better malaria therapies. A creative scientist, Youyou Tu, searching the archives of ancient Chinese medicine, unshackled from the standard theoretical, technological, and commercial pathways—but working within a focused problem context, makes the discovery (or, perhaps better said, the re-discovery). This is exactly the type of story that needs to inform our understanding of how great science in the service of urgent social problems so often does its best work.

Bizzarri et al. assert that "Societal influences may drive technological commitments; however, as such they have nothing to do with the search for scientific knowledge," but in offering up the artemisinin story they make just the opposite point: it was precisely the societal imperative to reduce the toll of a disease, pursued through the "technological commitment" of Chinese scientists in a *managed* effort to screen a wide variety of natural compounds, that provided the foundation for Tu's discovery.

Thus, a related important aspect of my argument is that technological performance is a strong validator of scientific findings. If a scientific insight is embodied in a technology and the technology does what it is supposed to do (e.g. prevent or cure malaria), then that suggests the science is right. Major areas of science, ranging from pharmaceutical development to semiconductor physics to aerodynamics, have in this way been guided by technology. Indeed, as I discuss in "Saving Science," the high failure rate of clinical trials for new pharmaceuticals (which are a type of technological demonstration project) was a crucial clue leading toward broad awareness of the "reproducibility crisis." Trials were failing because the underlying science was no good (Begley and Ellis, 2012).

Bizzarri et al. write, however, that "Technological efficiency cannot be considered as a proof of 'truth,'" and they go on to explain how "For about two thousand years, humankind was successfully able to trace the trajectories of stars, and to navigate without technology . . . "even as they "trusted a wrong cosmological theory." I am not sure what aspect of my argument Bizzarri et al. thought they were addressing here. Early navigators didn't need any theory at all; what mattered was their knowledge and charting of the position of the stars, their understanding of wind and currents and bathymetry, and so on. Improvements to navigation came not from theoretical advances, not from Copernicus overthrowing Ptolemy, but from the invention of tools for better observation—the compass, the sextant, the chronometer.

This is the standard story prior to the mid 19th century, up until which point technological advance owed little if anything to scientific theory. (On the other hand, scientific advance owed much to technological development, e.g., telescopes, microscopes, accurate time-keeping devices, and so on). Steam engines preceded thermodynamic theory. Vaccines preceded immunology. In such cases, technologies serving social and economic aims helped guide scientific inquiry by revealing phenomena that were not previously apparent or didn't even exist in nature. If relevant theory can be developed (often motivated by the scientific desire to explain what the technology reveals empirically), strong synergies can be cultivated between scientific and technological advance—thermodynamics became an important input to the design of steam engines;

the invention of transistors catalyzed the search for fundamental knowledge in solid-state physics. These relationships have been well documented for decades by scholars of innovation (e.g., Rosenberg, 1982; Misa, 1985; Stokes, 1997; Ruttan, 2006), and the artemisinin story provides yet another, quite wonderful illustration. From this perspective alone, Bizzarri et al.'s assertion that "societal influences may drive technological commitments; however, as such they have nothing to do with the search for scientific knowledge" is bewildering.

The synergistic links between technological and scientific advance provide a very powerful way to assess the validity of the science. In contrast, as I argue in "Saving Science," today's proliferation of poor quality science is made possible by the ideology of the autonomous scientist, accountable to nothing but her imagination, her peer reviewers, and her tenure committee, rather than to the need to help solve real problems.

Bizzarri et al. disagree, and suggest that "[t]he opposite may be true," that poor quality results may be explained by scientists who are captured by a "technological agenda" such as the "omics." This is an illuminating difference in perspective but one that I think is complementary, not contradictory, to my position. For one thing, my discussion of the relation between technology and science focuses on technology's contribution to solving real-world problems (e.g., a vaccine that prevents a disease), and not on use of various technological tools in the practice of science.

I completely agree (and explicitly make the point in my article) that the availability of powerful technological tools for doing research (Bizzarri et al. mention gene sequencing; I discuss transgenic mice) can often become an end in itself, driving science in unproductive directions. Bizzarri et al. see this as evidence not that scientists "are kept in a sort of creative freedom" but that they are "constrained to think in ways imposed by the scientists recognized as leaders by membership in prestigious entities . . . and by the [available] funding opportunities." I agree with this as well. Scientists simultaneously insist on the sanctity of intellectual autonomy and peer review even as they are captured by intellectual and technological fads and dead ends.

Where we likely differ is in our prescription for reform. Bizzarri et al. seem to say that if scientists could be liberated from the tyranny of perverse incentives and the constraints of convention, hierarchy, and the marketplace, then they would be positioned to be truly free, and thus to achieve the sorts of fundamental discoveries that we might all hope for. Assuming that such an ideal can actually be approached, we must still ask how many such scientists should be funded by taxpayers, and how big a proportion of the total research enterprise they should constitute. These are interesting and perhaps even important political, institutional and epistemological questions—ones that science policy scholars and practitioners have wrestled with at least since the 1960s (e.g., Weinberg, 1963; Toulmin, 1964). But ultimately they are questions for policy makers, not scientists, to answer.

But government mostly funds science to advance the public good and solve problems that face us, and it was explicitly in that context that I sought in "Saving Science" to shed light on the deep problems that beset the science enterprise. Rather than simply insisting that science will get better when scientists are set free, the important need is to understand the context within which that freedom can best be linked to human betterment. We have innumerable examples of institutional arrangements (such as various settings for health care delivery; e.g., Consoli et al., 2016) that can bring creative science and problem solving together to the benefit of both.

It is toward those sorts of models that we will need to move if the science enterprise is to escape from the problems of poor quality and poor public value that now undermine and delegitimate it. A new effort in that regard is the Highly Integrative Basic And Responsive (HIBAR) research initiative, sponsored by the Association of Public and Land Grant Universities (http://www.aplu.org/projects-and-initiatives/research-science-and-technology/hibar/index.html), with its combined focus on research quality and social value.

And finally, I agree wholeheartedly with Bizzarri et al. that enormous progress could be made on many health problems with significant social underpinnings (diabetes, obesity, addiction, some cancers and infectious diseases, etc.), if we could re-align our political and economic priorities. I differ with the notion, however, that we "already know" how to solve such problems. On the contrary, the "knowledge" necessary to catalyze appropriate political action to help solve those problems seems especially hard to come by, and this is in part precisely because it is so difficult to develop predictive and accurate understanding about the consequences of action in complex social and political settings (Nelson, 1977). Fortunately, technological discoveries often allow us to solve such problems in the absence of understanding. Bizzarri et al. end by re-asserting the primacy of scientific understanding over technological action. This seems to me an ideological stance. A more historically and empirically grounded view would acknowledge their mutual interdependence, and recognize it as an opportunity for getting out of the mess that science has gotten itself into.

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ORGANISMS shares Daniel Sarewitz' concerns about the notorious problems currently affecting the biomedical sciences and with his apt characterization that for the sake of science, scientists (not science) ought to get out of "the mess" they have gotten themselves into. Our respective views in this regard differ, however, on who/what has/have been responsible for the sad outcome that we both acknowledge. Both Sarewitz and ORGANISMS have exposed their respective preferences on whether an "autonomous", a "controlled" approach or the third way proposed by Sarewitz may be the most productive strategy to correct the "mess" and then restore the prestige that the biomedical sciences and those who work in it deserve. These desired outcomes will necessarily have to directly and indirectly affect those in need of pragmatic solutions to their health problems as well as those in the society at large who generate the funds required to conduct basic and applied research.

There is, however, a difference in emphasis between our respective views. The comments by ORGANISMS have referred mostly to science as practiced for the sake of knowledge, rather than science applied to solve a health, societal or a utilitarian problem. Einstein did not think of practical applications when positing general relativity. His immense achievement was by no means augmented by making GPS useful. In addition, Quantum Mechanics originally had modest applied ambitions: its practical consequences changed the world, from laser to key components of computer hardware. As currently practiced, biomedical science appears to aim at achieving medical or societal successful ends by adopting an ideology, reductionism, and by adopting a metaphor, namely, the organism as a computer. This now dominant theoretical construct was not made explicit by the biomedical community nor debated in its midst; therefore, the merits and rationale for its adoption and its eventual consequences were not carefully examined. This is likely to have been the main reason that the empirical outcomes of this research have neither improved understanding nor resulted in useful means to cure or prevent diseases and in turn resulted in "the mess" science and scientists are now witnessing.

Sarewitz also makes a relevant point by stating that what he aimed at "was to establish a perspective that was independent of the autonomy-versus-control dichotomy, but instead builds from the synergies that occur when scientific creativity and practical problem solving are appropriately brought together—a problem of institutional design and management, but not of control."

Indeed, the tension between practical issues and theory may sometimes generate important novel scientific theoretical concepts, while also solving practical issues. Indeed, this is how algebra emerged, creating algorithms useful to solve practical matters. However, rather than practical, everyday problems, the main source of inspiration for the development *of new mathematical concepts and structures comes from abstract thinking, such as the Euclidean lines with no thickness, or from the theoretical analysis of physical phenomena. These mathematical innovations, in turn, have helped to arrange physical concepts in new, more meaningful ways. And, this happened by the free, open interaction among scientists, rather than by institutional arrangements bringing "…creative science and problem-solving together to the benefit of both." In fact, the historical record shows that from Galileo to Pasteur and Schrödinger, the solution of many relevant problem required new theoretical inventions.. From this perspective, the success of such institutional arrangements would presuppose that the tacit ideology permeating biomedical sciences today, i.e., reductionism, and the misuse of the mathematical concept of information, program and signal would cease to provide the theoretical framework for research. Moreover, the hard Laplacian determinism central to the idea of program (and the view of the organism as a computer) have also generated nefarious consequences beyond the biomedical sciences, affecting economics, politics and finally threatening democracy. Thus, while disagreeing about how to address the "mess", which to us centers in replacing ideology (reductionism) with explicit theories, we applaud Sarewitz' contribution to the ongoing dialogue. In the end, theories are a better choice to resolve "the mess" because they are subject to analysis, evaluation, and eventual rejection. As allegedly observed by Boltzmann, there is nothing more practical than a good theory.*