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Big, small or mezzo?

Lessons from science studies for the ongoing debate about 'big' versus 'little' research projects

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During the past six decades, the importance of scientific research to the developed world and the daily lives of its citizens has led many industrialized countries to rebrand themselves as 'knowledge-based economies'. The increasing role of science as a main driver of innovation and economic growth has also changed the nature of research itself. Starting with the physical sciences, recent decades have seen academic research increasingly conducted in the form of large, expensive and collaborative 'big science' projects that often involve multidisciplinary, multinational teams of scientists, engineers and other experts.

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Although laboratory biology was late to join the big science trend, there has nevertheless been a remarkable increase in the number, scope and complexity of research collaborations and projects involving biologists over the past two decades (Parker *et al*, 2010). The Human Genome Project (HGP) is arguably the most well known of these and attracted serious scientific, public and government attention to 'big biology'. Initial exchanges were polarized and often polemic, as proponents of the HGP applauded the advent of big biology and argued that it would produce results unattainable through other means (Hood, 1990). Critics highlighted the negative consequences of massive-scale research, including the industrialization, bureaucratization and politicization of research (Rechsteiner, 1990). They also suggested that it was not suited to generating knowledge at all; Nobel laureate Sydney Brenner joked that sequencing was so boring it should be done by prisoners: "the more heinous the crime, the bigger the chromosome they would have to decipher" (Roberts, 2001).

A recent Opinion in *EMBO reports* summarized the arguments against "the creeping hegemony" of 'big science' over 'little science' in biomedical research. First, many large research projects are of questionable scientific and practical value. Second, big science transfers the control of research topics and goals to bureaucrats, when decisions about research should be primarily driven by the scientific community (Petsko, 2009). Gregory Petsko makes a valid point in his Opinion about wasteful research projects and raises the important question of how research goals should be set and by whom. Here, we contextualize Petsko's arguments by drawing on the history and sociology of science to expound the drawbacks and benefits of big science. We then advance an alternative to the current antipodes of 'big' and 'little' biology, which offers some of the benefits and avoids some of the adverse consequences.

Big science is not a recent development. Among the first large, collaborative research projects were the Manhattan Project to develop the atomic bomb, and efforts to decipher German codes during the Second World War. The concept itself was put forward in 1961 by physicist Alvin Weinberg, and further developed by historian of science Derek De Solla Price in his pioneering book, *Little Science, Big Science*. "The large-scale character of modern science, new and shining and all powerful, is so apparent that the happy term 'Big Science' has been coined to describe it" (De Solla Price, 1963). Weinberg noted that science had become 'big' in two ways. First, through the development of elaborate research instrumentation, the use of which requires large research teams, and second, through the explosive growth of scientific research in general. More recently, big science has come to refer to a diverse but strongly related set of changes in the organization of scientific research. This includes expensive equipment and large research teams, but also the increasing industrialization of research activities, the escalating frequency of interdisciplinary and international collaborations, and the increasing manpower needed to achieve research goals (Galison & Hevly, 1992). Many areas of biological research have shifted in these directions in recent years and have radically altered the methods by which biologists generate scientific knowledge.

Despite this long history of collaboration, laboratory biology remained 'small-scale' until the rising prominence of molecular biology changed the research landscape

Understanding the implications of this change begins with an appreciation of the history of collaborations in the life sciences—biology has long been a collaborative effort. Natural scientists accompanied the great explorers in the grand alliance between science and exploration during the sixteenth and seventeenth centuries (Capshew & Rader, 1992), which not only served to map uncharted territories, but also contributed enormously to knowledge of the fauna and flora discovered. These early expeditions gradually evolved into coordinated, multidisciplinary research

programmes, which began with the International Polar Years, intended to concentrate international research efforts at the North and South Poles (1882–1883; 1932–1933). The Polar Years became exemplars of large-scale life science collaboration, begetting the International Geophysical Year (1957–1958) and the International Biological Programme (1968–1974).

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Despite this long history of collaboration, laboratory biology remained 'small-scale' until the rising prominence of molecular biology changed the research landscape. During the late 1950s and early 1960s, many research organizations encouraged international collaboration in the life sciences, spurring the creation of, among other things, the European Molecular Biology Organization (1964) and the European Molecular Biology Laboratory (1974). In addition, international mapping and sequencing projects were developed around model organisms such as *Drosophila* and *Caenorhabditis elegans*, and scientists formed research networks, exchanged research materials and information, and divided labour across laboratories. These new ways of working set the stage for the HGP, which is widely acknowledged as the cornerstone of the current 'post-genomics era'. As an editorial on 'post-genomics cultures' put it in the journal *Nature*, "Like it or not, big biology is here to stay" (Anon, 2001).

Just as big science is not new, neither are concerns about its consequences. As early as 1948, the sociologist Max Weber worried that as equipment was becoming more expensive, scientists were losing autonomy and becoming more dependent on external funding (Weber, 1948). Similarly, although Weinberg and De Solla Price expressed wonder at the scope of the changes they were witnessing, they too offered critical evaluations. For Weinberg, the potentially negative consequences associated with big science were "adminstratitis, moneyitis, and journalitis"; meaning the dominance of science administrators over practitioners, the tendency to view funding increases as a panacea for solving scientific problems, and progressively blurry lines between scientific and popular writing in order to woo public support for big research projects (Weinberg, 1961). De Solla Price worried that the bureaucracy associated with big science would fail to entice the intellectual mavericks on which science depends (De Solla Price, 1963). These concerns remain valid and have been voiced time and again.

As big science represents a major investment of time, money and manpower, it tends to determine and channel research in particular directions that afford certain possibilities and preclude others (Cook & Brown, 1999). In the worst case, this can result in entire scientific communities following false leads, as was the case in the 1940s and 1950s for Soviet agronomy. Huge investments were made to demonstrate the superiority of Lamarckian over Mendelian theories of heritability, which held back Russian biology for decades (Soyfer, 1994). Such worst-case scenarios are, however, rare. A more likely consequence is that big science can diminish the diversity of research approaches. For instance, plasma fusion scientists are now under pressure to design projects that are relevant to the large-scale International Thermonuclear Experimental Reactor, despite the potential benefits of a wide array of smaller-scale machines and approaches (Hackett *et al*, 2004). Big science projects can also involve coordination challenges, take substantial time to realize success, and be difficult to evaluate (Neal *et al*, 2008).

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Another danger of big science is that researchers will lose the intrinsic satisfaction that arises from having personal control over their work. Dissatisfaction could lower research productivity (Babu

& Singh, 1998) and might create the concomitant danger of losing talented young researchers to other, more engaging callings. Moreover, the alienation of scientists from their work as a result of big science enterprises can lead to a loss of personal responsibility for research. In turn, this can increase the likelihood of misconduct, as effective social control is eroded and "the satisfactions of science are overshadowed by organizational demands, economic calculations, and career strategies" (Hackett, 1994).

Practicing scientists are aware of these risks. Yet, they remain engaged in large-scale projects because they must, but also because of the real benefits these projects offer. Importantly, big science projects allow for the coordination and activation of diverse forms of expertise across disciplinary, national and professional boundaries to solve otherwise intractable basic and applied problems. Although calling for international and interdisciplinary collaboration is popular, practicing it is notably less popular and much harder (Weingart, 2000). Big science projects can act as a focal point that allows researchers from diverse backgrounds to cooperate, and simultaneously advances different scientific specialties while forging interstitial connections among them. Another major benefit of big science is that it facilitates the development of common research standards and metrics, allowing for the rapid development of nascent research frontiers (Fujimura, 1996). Furthermore, the high profile of big science efforts such as the HGP and CERN draw public attention to science, potentially enhancing scientific literacy and the public's willingness to support research.

Rather than arguing for or against big science, molecular biology would best benefit from strategic investments in a diverse portfolio of big, little and 'mezzo' research projects

Big science can also ease some of the problems associated with scientific management. In terms of training, graduate students and junior researchers involved in big science projects can gain additional skills in problem-solving, communication and team working (Court & Morris, 1994). The bureaucratic structure and well-defined roles of big science projects also make leadership transitions and researcher attrition easier to manage compared with the informal, refractory organization of most small research projects. Big science projects also provide a visible platform for resource acquisition and the recruitment of new scientific talent. Moreover, through their sheer size, diversity and complexity, they can also increase the frequency of serendipitous social interactions and scientific discoveries (Hackett *et al*, 2008). Finally, large-scale research projects can influence scientific and public policy. Big science creates organizational structures in which many scientists share responsibility for, and expectations of, a scientific problem (Van Lente, 1993). This shared ownership and these shared futures help coordinate communication and enable researchers to present a united front when advancing the potential benefits of their projects to funding bodies.

Given these benefits and pitfalls of big science, how might molecular biology best proceed? Petsko's response is that, "[s]cientific priorities must, for the most part, be set by the free exchange of ideas in the scientific literature, at meetings and in review panels. They must be set from the bottom up, from the community of scientists, not by the people who control the purse strings." It is certainly the case, as Petsko also acknowledges, that science has benefited from a combination of generous public support and professional autonomy. However, we are less sanguine about his belief that the scientific community alone has the capacity to ascertain the practical value of particular lines of inquiry, determine the most appropriate scale of research, and bring them to fruition. In fact, current mismatches between the production of scientific knowledge and the information needs of public policymakers strongly suggest that the opposite is true (Sarewitz & Pielke, 2007).

Instead, we maintain that these types of decision should be determined through collective decision-making that involves researchers, governmental funding agencies, science policy experts and the public. In fact, the highly successful HGP involved such collaborations (Lambright, 2002). Taking into account the opinions and attitudes of these stakeholders better links knowledge production to the public good (Cash *et al*, 2003)—a major justification for supporting big biology. We do agree with Petsko, however, that large-scale projects can develop pathological characteristics, and that all programmes should therefore undergo regular assessments to determine their continuing worth.

Rather than arguing for or against big science, molecular biology would best benefit from strategic investments in a diverse portfolio of big, little and 'mezzo' research projects. Their size, duration and organizational structure should be determined by the research question, subject matter and intended goals (Westfall, 2003). Parties involved in making these decisions should, in turn, aim at striking a profitable balance between differently sized research projects to garner the benefits of each and allow practitioners the autonomy to choose among them.

This will require new, innovative methods for supporting and coordinating research. An important first step is ensuring that funding is made available for all kinds of research at a range of scales. For this to happen, the current funding model needs to be modified. The practice of allocating separate funds for individual investigator-driven and collective research projects is a positive step in the right direction, but it does not discriminate between projects of different sizes at a sufficiently fine resolution. Instead, multiple funding pools should be made available for projects of different sizes and scales, allowing for greater accuracy in project planning, funding and evaluation.

It is up to scientists and policymakers to discern how to benefit from the advantages that 'bigness' has to offer, while avoiding the pitfalls inherent in doing so

Second, science policy should consciously facilitate the 'scaling up', 'scaling down' and concatenation of research projects when needed. For instance, special funds might be established for supporting small-scale but potentially transformative research with the capacity to be scaled up in the future. Alternatively, small-scale satellite research projects that are more nimble, exploratory and risky, could complement big science initiatives or be generated by them. This is also in line with Petsko's statement that "the best kind of big science is the kind that supports and generates lots of good little science." Another potentially fruitful strategy we suggest would be to fund

independent, small-scale research projects to work on co-relevant research with the later objective of consolidating them into a single project in a kind of building-block assembly. By using these and other mechanisms for organizing research at different scales, it could help to ameliorate some of the problems associated with big science, while also accruing its most important benefits.

Within the life sciences, the field of ecology perhaps best exemplifies this strategy. Although it encompasses many small-scale laboratory and field studies, ecologists now collaborate in a variety of novel organizations that blend elements of big, little and mezzo science and that are designed to catalyse different forms of research. For example, the US National Center for Ecological Analysis and Synthesis brings together researchers and data from many smaller projects to synthesize their findings. The Long Term Ecological Research Network consists of dozens of mezzo-scale collaborations focused on specific sites, but also leverages big science through cross-site collaborations. While investments are made in classical big science projects, such as the National Ecological Observatory Network, no one project or approach has dominated—nor should it. In these ways, ecologists have been able to reap the benefits of big science whilst maintaining diverse research approaches and individual autonomy and still being able to enjoy the intrinsic satisfaction associated with scientific work.

Big biology is here to stay and is neither a curse nor a blessing. It is up to scientists and policy-makers to discern how to benefit from the advantages that 'bigness' has to offer, while avoiding the pitfalls inherent in so doing. The challenge confronting molecular biology in the coming years is to decide which kind of research projects are best suited to getting the job done. Molecular biology itself arose, in part, from the migration of physicists to biology; as physics research projects and collaborations grew and became more dependent on expensive equipment, appreciating the saliency of one's own work became increasingly difficult, which led some to seek refuge in the comparatively little science of biology (Dev, 1990). The current situation, which Petsko criticizes in his Opinion article, is thus the result of an organizational and intellectual cycle that began more than six decades ago. It would certainly behoove molecular biologists to heed his warnings and consider the best paths forward.

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