Personal Reflections on Big Science, Small Science, or the Right Mix

Michael S. Lauer

Late June, 1969, at a suburban Philadelphia day camp. There was much to look forward to: color war, soccer, nature hikes, bug juice, barbecues, swimming, softball, and, of course, no school! But I paid little attention, as for me these paled compared with the upcoming big event, the much-anticipated launch of Apollo 11, the rocket that would fulfill President Kennedy’s call to land men on the moon and bring them back home. During the next few weeks, my parents and I spent hours glued to the TV; and my parents quietly endured the smell of glue emanating from model rockets and lunar modules taking form in my room.

Some 20 years later, Bernadine Healy, Director of the National Institutes of Health, called for a moon shot for women’s health. The resulting Women’s Health Initiative (WHI) would be a big science effort that would invest substantial resources, enabling scientists to address questions about hormone replacement therapy, supplementation with Vitamin D and calcium, and diet as interventions that might prevent serious health conditions faced by postmenopausal women. Like the National Institutes of Health’s WHI succeeded; a national team of top-notch scientists enrolled well over 100,000 women into several randomized trials and observational studies. The surprising findings of the relative harms of hormone replacement therapy led to sweeping changes in clinical practice and likely played a role in the past decade’s decline in breast cancer incidence.

Now, 25 years later, American science and engineering face an uncertain future. Although big science projects have always generated controversy, shrinking budgets have invited only more criticism. The United States invests a lower proportion of its Gross Domestic Product into research and development than several other economically developed nations. Of perhaps greater concern, there has been a steady decline in public support of science; whereas in the 1960s the federal government provided two third of research funds, today it only provides 1 of 3. At the National Institutes of Health, there has been a steady decade-long decline of purchasing power. At the National Heart, Lung, and Blood Institute (NHLBI), this has translated into lower pay lines, with the institute awarding 36% fewer new R01 grants than it did 10 years ago.

Some prominent thought leaders have argued that the National Institutes of Health and other funders need to rethink seriously their business models. Instead of funding a smaller number of big science projects, projects like the WHI, government research agencies, they argue, should rediscover small science, science that is based on the work of many scientists working in many settings, each getting relatively small sums of money to do their work. NHLBI Project Officers often hear skeptics of big science initiatives ask questions like, How many R01s will we have to sacrifice in order for your big project to happen?

So what strategy should an agency like the NHLBI take? Should we aim to fund more small projects, meaning low-budget investigator-initiated R01s? Should we trim back on our big science projects, such as relatively expensive clinical trials and epidemiology studies? Should we stop funding trials and epidemiological projects altogether or insist on shifting to low-cost pragmatic alternatives that leverage rapidly evolving information technologies? And what about projects that involve highly innovative, but risky technologies or candidate therapies, where cheap options are few or absent? And if we are to fund a mix of big and small science, to follow the maxim of a diversified portfolio, what’s the right mix? And how do we determine, in advance, which projects constitute the right strategy?

Prominent thought leaders have struggled with these questions. Some, like Gregory Petsko, argue that “the right way to direct science is almost not to direct it all,” but rather allow priorities to set themselves through “the free exchange of ideas in the scientific literature, in meetings, and in review panels.” Others, like Vermeulen et al., counter that they are “less sanguine about [this] belief that the scientific community alone has the capacity to ascertain the practical value of particular lines of inquiry.” Stuart Firestein points out that science by its nature is based on ignorance and that it is nary impossible to predict which technologies and hypotheses will succeed. We recently published a report showing that percentile rankings of NHLBI R01 grants were unable to predict subsequent academic productivity.

The views expressed in this paper are those of the author and do not necessarily reflect those of the National Heart, Lung, and Blood Institute, the National Institutes of Health, or the US Federal Government.

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deeper impact, namely a harmful change in fundamental scientific paradigms. They recently lamented that “individual curiosity-driven science has been replaced by large consortia dedicated to the proposition that gathering vast amounts of correlative data will somehow provide the answer to life’s fundamental questions.” The science economist Paula Stephan summarized the conundrum when she wrote that “we just don’t know” whether it is “better to spend $3 billion on the Human Genome Project or to support 6,000 researchers each to the tune of $500,000?” Megaprojects, like epidemiological cohorts, that “provide inputs for more research down the road” but don’t by themselves provide answers “are especially difficult to evaluate.”

In his AAAS (American Association for the Advancement of Science) Presidential Address, William Press noted that science is heavy tailed, meaning that a small number of efforts will account for most of the impact; Nasim Taleb describes this phenomenon as extremistan, meaning “a process where the total can conceivably be impacted by a single observation … also called ‘fat tailed.’” At the NHLBI, we too observe such a pattern. The Pareto plot in the Figure shows 2-year citation data for 118,070 articles published between 1990 and 2010 and supported by ≥1 NHLBI R01 or R21 grant. More than 75% of the citations were generated by just 30% of the articles, whereas 40% of the articles generated fewer than 2% of the citations.

Despite the unquestionable successes of previous big science investments, I worry that in a time of unprecedented fiscal constraints big science presents an existential threat to the invaluable offerings of small science. As stewards of scarce public monies, we at National Institutes of Health have an even more pressing responsibility than in years past to consider explicitly the opportunity costs of new or renewed large-scale projects that diminish our ability to support individual laboratories. How many paradigm-changing, yet wholly unpredictable, discoveries will be lost? We should also worry about the impact on our ability to nurture science trainees, who
only are aware of decreasing chances for funding, but also
will have fewer opportunities to be exposed to the individual,
curiosity-driven science that Goldstein and Brown credited
with enabling a series Nobel-winning breakthroughs.12

So, what might be the characteristics of worthy big science
projects? As Stephan13 writes, it may be impossible to come
up with definitive answers, given the small sample size—by
definition big science projects are few in number—and the un-
certainties about how to measure outcome. But thinking back
on my experiences, I might offer a few suggestions. There
were some prima facie successes, such as the Apollo moon
shots, the WHI, the Hubble telescope, and the nation’s re-
search attacks on infectious diseases such as AIDS and polio.

So, here are 6 suggested criteria for prospective evaluation of
large-scale projects in our current era of ever shrinking resources:

1. Will it capture the public imagination? The Apollo moon
shots sure captured my 8-year-old boy sense of wonder.
Abraham Lincoln once remarked that anything is possible
but only with the backing of public sentiment. Admittedly, some highly worthwhile projects, like dis-
covering the molecular structure of DNA, may be dif-
ficult to communicate to a lay audience.

2. Is government leadership and financial support critical for
success? Some projects would not happen on their
own because no one private party has the financial in-
centives to embark on them.

3. Is there a clear, measurable, and achievable objective?
In July 1969, we could say unequivocally that we sent
men to the moon and back. Some objectives may be less
clear, but the WHI trials were finished and did lead to
marked changes in practice, and today AIDS, at least in
the United States, is a chronic disease, not the fast-paced
crime of course one was. Some large-scale projects have enabled
the scientific community to better understand where to
shift investments; for example, Mendelian randomization
studies15 that leverage discoveries stemming from the
Human Genome Project may inform worthwhile and
less worthwhile lines of inquiry.

4. Is it—in a timely manner—stretching new technological
and organizational capabilities? The moon shot was possible
because of recently developed rocketry technolo-
gies, the advent of high-power computers, and strong
partnerships between the private and public sectors. In
today’s parlance, we might ask whether a new project
leverages contemporary scientific advances or resources.

5. Is it possible to proceed in measured stages? And to
learn from inevitable stumbles and failures? The manned
space program started with the small Mercury rockets,
then the bigger Gemini missions that sent 2 men up
at once and tested the ability to dock orbiting space-
craft, and only then the giant Apollo rockets. Even so
there were bumps, even tragic disasters, along the way.
Clayton Christensen,16 an expert in innovation, urges
open-minded organizations to discover and exploit dis-
ruptive technologies by planning to fail often, quickly,
and inexpensively.

6. Irrespective of success or failure, will something be
learned and will there be the courage to stop? Or at least
recognize when it is time to scale back so as to allow new
efforts with emerging priorities to get their turn. This
question is particularly important, but difficult, indeed
gut-wrenching, during a time of shrinking resources.

A few weeks ago, National Aeronautics and Space
Administration posted a video that recreated the events, lead-
ing to the famous Apollo 8 photograph of earthrise. I enjoyed
watching it, and even more so, sharing it and my boyhood
collections with my 2 college-age sons who are both plan-
ning careers in science or engineering. I also shared this essay
with them, and I must admit that despite the amazing accom-
plishments of the moon program, I advised for the short term
that they seek training opportunities in the kind of nurturing
individual curiosity-driven laboratories that Goldstein and
Brown12 benefitted from during their formative years. In the
long term, I hope that they will be able to thrive and contribute
to a scientific and technological enterprise that sees its share
of great achievements, whether they come from big science,
small science, or whatever the right mix is.

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