Transformative research: definitions, approaches and consequences

J. T. Trevors · Gerald H. Pollack · Milton H. Saier Jr. ·
Luke Masson

Received: 11 January 2012 / Accepted: 5 May 2012 / Published online: 25 May 2012
© Springer-Verlag 2012

Abstract In this perspective a definition of transformative research (TR) is proposed and discussed. We define TR as that which “transforms” or causes a major change in thought patterns concerning an area of scientific endeavor. This type of research is often elusive, requires different approaches and sometimes depends on a bit of luck. TR concerns intangibles such as human intuition, serendipity, unpredictable events, implausible hypotheses, a well-prepared mind and often interpersonal communications. Examples are provided to illustrate how TR may unfold. Contributions it makes to basic and applied humanistic knowledge are highlighted.

Keywords Biosciences · Transformative research · Future science · Humanistic knowledge · Intuitive thought · Implementation · Scholarship · Scientific method · Profound discoveries

J. T. Trevors (✉)
School of Environmental Sciences, University of Guelph,
50 Stone Road, East, Guelph, ON N1G 2W1, Canada
e-mail: jtrevors@uoguelph.ca

G. H. Pollack (✉)
University of Washington, Seattle, WA 98195, Box 355061,
USA
e-mail: ghp@u.washington.edu

M. H. Saier Jr. (✉)
Division of Biological Sciences, University of California at San
Diego, 4254 Muir Biology Bldg., La Jolla, CA 92093-0116,
USA
e-mail: msasier@ucsd.edu

L. Masson (✉)
Biotechnology Research Institute, National Research Council of
Canada, 6100 Royalmount Ave, Montreal, QC H4P 2R2,
Canada
e-mail: luke.masson@nrc-cnrc.gc.ca

“We all agree that your theory is crazy, but is it crazy enough?”—Niels Bohr.

“A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it”—Max Planck.

“No amount of experimentation can ever prove me right; a single experiment can prove me wrong.”—Albert Einstein.

Introduction

In this perspective, we advance a definition of transformative research (TR) and provide details and examples as to how this type of research can be implemented. We also address how original scholarship can be assessed. There are those who are comfortable with the status quo, those who are indifferent, and others who will embrace a transformative approach. Profound discoveries through research are the objectives. It should also be noted that for every transformative idea there must be hundreds of misconceptions that lead nowhere. Referring to the quote by Niels Bohr above, then, only a few “crazy theories” in hundreds will prove to be transformative. The challenge will be in how to provide an appropriate incubator to foster the production of such TR.

Some of the most profound transformative advances have been made in the biological sciences. Some examples include, the cell as the basic unit of life, the invention of the microscope, the theory of evolution, a classification system, anatomy, brain functions, the discovery of the structure and function of DNA, the genetic code, reproduction in diverse species, photosynthesis, antibiotics, vaccines, restriction enzymes, genetic engineering, genome sequencing, site-directed mutagenesis and the polymerase chain reaction (PCR). These bioscience discoveries were also moved ahead by the use of mathematics (which is used

in all sciences), computing, advanced microscopes, fluorescent methods and a better understanding of how light interacts with matter. As the distinctions between biosciences and other disciplines are removed, our knowledge becomes less fragmented and knowledge gaps start to be filled. Problems associated with transferring and linking knowledge and methods from one discipline to another still exist, however, these can be addressed by team collaborations, improved instrumentation, new technologies and better communications via on-line journals, texts and e-mail. Profound, new transformative discoveries will be made that encompass many disciplines.

This article is applicable to many, if not all areas of research. We view it as a conduit to a wider debate on TR that will benefit both basic and applied scholarship. More importantly, we hope it will benefit humanity through the alteration of conventional thought patterns. The ideas presented may help scientists distinguish between insightful theories reflecting reality from those that have no useful function.

Our proposed definition of TR is similar to that found in the National Science Board report *Enhancing Support of Transformative Research at the National Science Foundation* in 2007. It describes research that restructures and revolutionizes our means of inquiry, and thereby enhances our knowledge base. It has the capacity to promote paradigm shifts, produce technological cascades, improve existing technologies, and provide a more complete understanding of the universe. It leads to novel hypotheses and research approaches (see Tables 1 and 2).

The nature of TR

TR is usually not planned, although it depends on a receptive mind. It takes advantage of unpredictable events leading to novel hypotheses, some that seem implausible. It begins with learning, development of imagination, visualization of problems and exploration of problem solving techniques. Communication and debate often prove beneficial in allowing the development of transformative ideas.

Anyone who discovers something genuinely new, or comes to appreciate information that was not previously recognized by the same person, experiences a personal revelation, often accompanied by feelings of elation. That knowledge or idea may depend on optimism and hope, but development of the concept usually relies on persistence and mental discipline. New knowledge leaves the person permanently changed. Such individuals will never again be the same. They have intellectually evolved. Personal

Table 1 Examples of past transformative discoveries (and inventions) that have revolutionized scientific inquiry and expanded our understanding of the world we live in

1	Planetary elliptical orbits
2	General and specific relativity
3	An expanding universe
4	Background cosmic radiation
5	The cellular basis of life
6	The theory of evolution
7	Structure and function of DNA
8	Genome sequencing
9	DNA manipulation (restriction endonucleases, polymerase chain reaction)
10	The periodic table
11	Atomic theory
12	Electromagnetism
13	Atomic fission and fusion
14	Continental drift and plate tectonics
15	Radiometric dating
16	Fossil records
17	Organismal and macromolecular classification systems
18	DNA transposition
19	The genetic code
20	RNA splicing and gene regulation by noncoding RNA (ncRNA)
21	Germ theory of disease
22	The laws of thermodynamics
23	$E = mc^2$
24	Prions
25	Quantum mechanics
26	Microscopes and telescopes
27	Four known forces
28	Stem cell research
29	Dark matter
30	Radioactivity
31	Gravity
32	Laws of motion
33	Dual nature of light
34	Photosynthesis
35	Krebs cycle
36	Mitochondria
37	Blood groups
38	X-rays
39	Hormone insulin
40	Oncogenes
41	Human retrovirus (HIV)
42	Mathematical principles

The list is by no means complete

Table 2 Characteristics of TR

1	Novel, innovative and creative
2	Causes controversies
3	Allows insights to be gained into complex problems and opportunities
4	Discovers new and unforeseen solutions
5	Achieves value
6	Reduces problems to the basic cause
7	Exposes the best ways to solve problems
8	Challenges assumptions
9	Examines current and past assumptions
10	Identifies the main problem and related problems
11	Encompasses the big picture
12	Idea generating
13	Requires planning and rigor
14	Asks the right questions
15	Uses the correct experiments

Note TR may include combinations of the characteristics listed below but not necessarily all of these characteristics

change may be essential to trigger expression of novel concepts.

Transformative discoveries leading to paradigm shifts can transform at many levels including scientific, personal and sociological. They may change cultural values and transform a society. When this occurs, there are sociological “stages” of resistance preceding transformation: first denial, then anger, and finally acceptance. Arthur Schopenhauer summarized this progression as follows: “All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident.” On the other hand, Winston Churchill noted: “Men occasionally stumble over the truth, but most of them pick themselves up and hurry off as if nothing ever happened.” Thus, a prepared mind that can recognize an important observation is essential.

What is required to perform transformative science? One needs to diligently work at not rushing off or ignoring ideas when one stumbles over a potential truth. One must not be dissuaded if it does not conform to accepted dogma. Thus one must have the ability to focus and ponder without deviating from the cause. It cannot be required that a researcher consumes excessive time preparing reports under the umbrella of accountability and progress. Unfortunately, this is precisely what is required by the most present-day funding agencies.

From a policy point of view, one should attempt to create the most favorable scholarly conditions, usually dependent on a congenial, peaceful atmosphere with minimal distractions. In some cases, but not others, equipment infrastructure will be important. The agency cannot be too selective about the type of research supported, because no

one can predict how the next breakthrough will occur. If TR is a human matter, then most agencies, institutions, and by extension, researchers, must not overemphasize detailed definition and design.

There is an increasing awareness that in many currently published data sets, observations and findings are only approximations (Ioannidis 2005). In fact, inaccuracies are a part of the scientific process: trial and error, the empirical approach following theorization. Propagation of false information can cloud the truth and mislead scientific directions, delaying crucial discoveries. Dogmatism can lead to such incorrect concepts.

Errors in research are eventually revealed, but they may hinder progress. Thus, TR needs to be followed by more pedantic confirmatory work to insure accuracy—to remove the “bugs or mistakes”. It is therefore incorrect to think that all science should be about brilliant, novel, groundbreaking advances. Any scientist who boldly publishes results will to some degree make mistakes. The progression of scientific discovery of necessity involves a step forward followed by reflection and testing. There is room in science for many different approaches.

Simulations suggest that it is more likely for a research claim to be false than true. Why is this true? Some of the answers presented by Ioannidis (2005) are (1) high rates of non-replicated experiments reduces confirmation of the first discovery or data set; (2) the probability that a research observation is correct depends on previously performed accuracy; (3) The results could have been subject to bias; (4) bias could result from ignoring or not reporting all of the observations; (5) the smaller the number of studies conducted (i.e., the smaller the sample sizes) the more likely the observations will not be reflect the truth; (6) the smaller the effects, the less likely the observations will be accurate; (7) an insufficient number of relationships examined will lead to inaccurate generalizations because the full picture was not viewed. The aim of research must be to approximate correct answers and then progress to the correct answers. To stimulate novel research it may be necessary to paint novel pictures.

TR often begins with a substantial degree of confusion about a topic, question, or ongoing experiment. Data sets may be conflicting or incomplete, leading to inaccurate hypotheses. Hypotheses are sometimes difficult to formulate and test, thought experiments difficult to integrate, and data sets difficult to interpret. New hypotheses may eventually develop, but the progress is usually slow, particularly if the hypotheses are not fully understood by the researchers testing its validity.

Scientific transformation is equated with innovative, cutting edge research. Such proposals appear liberally in seminars, grant applications and research papers; they accompany promises of significant advances, depending on additional funding and research. These imaginative

proposals may yield breakthroughs, but more often, they lead nowhere. It is therefore the responsibility of the funding agencies to try to distinguish in advance the difference. This can be a primary source of error. After all, mistakes, when recognized, can lead to the next important discovery.

Agency-funded public research programs are generally not designed to evaluate and fund TR. Bureaucrats and functionaries are often more concerned with following the rules they themselves have designed. To the administrators, the rules may be all-important, even when discouraging the advancements of scientific discovery. These administrators may not be researchers or may have knowledge outside of the areas being considered. The outcome is often more of the same with minor incremental advances and only rare occasional transformative advances.

How can transformative science be implemented?

Science is the only systematic reliable means of discovery that we have. As stated by McKnight, the balance in science is between (1) depth and breath of education and training, and (2) hypothesis-driven and random inquiry research (McKnight 2009). These principles apply to many areas of teaching and research. The following ideas are presented as possible means to implement TR at the national and international levels.

1. NIH transformative R01 (USA) relies mainly on reviewers outside the field of the proposed research in order to achieve objectivity. The USA—Israel Binational Science Foundation also has a transformative program that operates on similar principles.
2. It will be necessary to refine the definition of TR until it is broadly acceptable. This will hopefully stimulate international debate and promote the evolution of research to more innovative approaches.
3. It will provide examples of where TR is needed and the rationale. However, by its very nature, uncertainties will require flexibility.
4. Granting agencies and politicians must allow researchers to conduct research without hindrance by conservative opinion reviews.
5. It is necessary to convince the public that without TR, dollars spent will be minimally beneficial. We face significant globally interconnected challenges where current solutions are not available, and implementation is not immediately possible. Global climate change, unmanaged human population growth and declining world food reserves are examples.
6. The main impediment to TR may be convincing the scientific establishment to listen and participate and to be attentive to alternatives.

7. The establishment must encourage and support researchers who challenge orthodoxy, especially if the existing knowledge is fragmented and incomplete.
8. Impact factors, citation numbers and the number of students supervised are not the best metrics for assessing TR. Profound discoveries are ultimately the best index.
9. It is known that some researchers maintain their focus on the unknown and remain true to the possibility of original discovery. They generally visualize problems and implement novel approaches. They have foresight and successful track records. Publication numbers and quality, often used as an index of scholarship, are important, but insufficient as a means of evaluation. Novelty and originality must be more highly valued.

Here are some examples of questions that could lead to TR:

1. Why is the speed of light the value it is?
2. How did life originate, and where in the universe did it arise?
3. Is there a quantum basis to the origin of life and if so, what might it be?
4. How did an organic genetic code originate with instructions for the first cell?
5. Is entropy the forward arrow of time?
6. What would be required to engineer a completely artificial cell capable of growth and division?

Industrialized countries have spent money and time on research and development that has led to significant advances (as well as unforeseen setbacks for individuals and humanity). Not only is research published, patented and implemented as technologies, it is too often locked up the minds of individuals and is not shared with other researchers for the better good. Too often, research is confounded with political issues. This is confusing for the public who fund research, and to the researcher whose primary interest is original discovery.

Research infrastructure is improving but can be expensive. New equipment must often be purchased to allow certain types of advanced experimentation. Examples include advanced microscopes, computing facilities, particle colliders, PCR equipment, and imaging facilities. However, TR requires critical reflective thinking, a well-prepared mind, freedom from trivial distractions and minimization of artificially imposed reports and management deadlines. Reflection and collaboration with other researchers will promote major advances.

Transformative advances are promoted by dedication and the capacity for long-term independent thought. The development of independent thought depends on the educational system. Our students must be taught to think for themselves

rather than to accept dogma of any type, religious, political, or scientific. For transformative science to succeed, the assumptions of any hypothesis must be clearly recognized and tested. New ideas must not be killed but embraced, scrutinized and debated. Mistakes must be corrected and data should not deliberately be suppressed. Transparency is important. Experiments need to be conducted that retest the fundamental assumptions and provide the essential controls. To this end, perhaps more philosophy should be integrated into our current educational system to enable students to synthesize their own thoughts from conflicting ideas. In the modern classroom, students are generally taught using the scientific or “Inductive” method that basically combines observation and experimentation. In other words, one assembles a number of observations to formulate a hypothesis and then combines some element of experimentation to verify the hypothesis, which may then develop into a theory. Students rarely question the accepted or how these hypotheses were derived. The deductive method is the opposite of the inductive approach in that one starts with selecting various basic scientific axioms or laws and creates a theory built up by these laws in a logical and deductive manner and then tests that theory empirically. Many of the greatest transformative advances have occurred in this manner. Einstein was able to develop his special theory of relativity by first ignoring Maxwell’s accepted laws of electromagnetism and consequently Newtonian mechanics, and finally by rejecting the idea that light was an ether wave. He simply accepted the fact that the speed of light is invariable, in violation of accepted laws, and since no observation could distinguish the ether, it was no longer needed. Thus he did not support his argument with experimental evidence but rather he supported it with theoretical evidence (Einstein 1919) which was later confirmed by astronomical observations. Indeed questioning of accepted theories and the openness to accept all different interpretations of reality, no matter how bizarre and contrary to current thinking, formed the basis of one of the most transformative examples of scientific work in history, the development of quantum mechanics.

How to conduct TR is difficult to teach to students, research teams, the public and bureaucrats. Research is ultimately about thinking, focusing, dreaming, and writing. It is also about undoing erroneous concepts and replacing them with more reliable or correct knowledge. Most important is to emphasize the need for independent thinking by a questioning, doubting mind.

Benefits of TR

TR is central to the maintenance and advancement of our common humanity (Kariukstis and Hensel 2010; Trevors and Saier 2010). We are becoming increasingly aware of

the fragile nature of our biosphere and the interdependent global economy. As our population and global temperatures increase, we can expect increased incidences of pandemics, extreme weather conditions, hurricanes, and lack of basic security needs, including energy, food, potable water and clean air. World food reserves are currently sufficient to last the world population only about 2 months and are declining as our population passes seven billion. Increasing food production is only one part of the challenge. These interconnected components of human activities depend on existing knowledge and future TR for solutions.

The lack of funding and an exodus of top scholars from research, innovation, and teaching compound the challenge. Funding agencies need to support, encourage and reward TR as such research is interlinked with the needs of societies and humanity. Researchers need to visualize important questions and answers, conduct thought experiments and attend scholarly meetings. Global collaborations may accelerate progress. Researchers must communicate to be grounded in reality in order to avoid illusions and denial. The illusion of success is not the same as actual success. High-risk research may often fail but because the advances are likely to be highly significant, it still needs to be encouraged and supported. Many agencies operate under the illusion that they are funding TR and the brightest researchers, but the proof is in the pudding. What are the resultant advances? Are they truly revolutionary, or do they represent pedantic, minimal advances? Do they help alleviate the tremendous personal, social, environmental, and economic problems that currently face humans? If these problems cannot be solved, there is little hope for continuing human civilizations.

Why would researchers be interested in diverting their reliable approaches to embrace a more transformative approach? Profound discoveries may result from the efforts of a researcher with no established record—an unknown to the self-professed experts. Galileo Galilei described this wisely. “In questions of science, the authority of a thousand is not worth the humble reasoning of a single individual”. In other words, mythology and lies, no matter how widely accepted by an ignorant populous is of no value compared to the knowledge of an educated honest scientist.

The question can be posed—how is TR evaluated from the onset? Two examples were provided in this perspective article. The NIH transformative R01 (USA) relies mostly on reviewers outside the field of the proposed research. This review mechanism attempts to achieve objectivity. The USA—Israel Binational Science Foundation also has a transformative program that operates on similar principles. These are starting points for the assessment and subsequent funding of TR programs. If and when more TR is funded and completed, assessments of the outcomes will likely be

available both as peer reviewed articles and agency reports. This will be revealing, as the international science community will be able to access the success of the programs.

TR is very much the subject of Nobel Prizes. The awards are made for profound discoveries that often bring forth paradigm shifts and knowledge cascades. In recent decades genome sequencing based on rapidly evolving technologies and computing power have made immense advances in biosciences possible. Very much related to these advances are the PCR and site-directed mutagenesis to study specific mutations in the genetic code and the encoded protein. However, as emphasized in this article, TR is often elusive, requires different approaches and sometimes depends on luck. TR concerns intangibles such as human intuition, curiosity, serendipity, unpredictable events, correcting previous knowledge, implausible hypotheses, a well-prepared mind and often interpersonal communication.

A central point is that funding is required for academic salaries, infrastructure, designing, and building new equipment. Researchers need time to think, rethink, deviate from the known knowledge base, develop new profound hypotheses and test them. They may fail many times and perhaps never achieve profound success. These approaches will require public support of TR and may involve academic-industry-government collaborations, local, national and international collaborations (e.g., such as in the preparation of this article). It is known that some collaborations require immense amounts of time and funding. Recent examples, include the International Space Station (ISS) where numerous experiments, including those on human physiology, have been conducted, and the Large Hadron Collider (particle accelerator) near Geneva. Under the supervision of international collaborators, the Hadron collider has several experiments in progress using unique particle detectors. A network cluster involving thousands of computers in the international collaboration will be employed for data analyses which is estimated to take more than a decade. A profound and correct understanding of elementary particles will be of immense value in understanding how these particles, atoms, and molecules behave in mechanisms in living organisms, and maybe even the origin of life. Political leaders will be required to make decisions on the amount of funding governments will provide for TR as opposed to more conventional and applied research. In fact, the two are interconnected and should not be seen as distinctly different. Applied research requires fundamental new knowledge to move ahead. TR is the driving engine of new applied research. These distinctions are not useful in the modern world of scholarship as they are simply obstacles—a form of mental stagnation.

In past eras, transformative discoveries followed a more meandering path, being made by scholars simply exploring

where their intellect and curiosity led them. This is different than the top-down managed bureaucracy employed today where projects are assigned to categories with strict timetables and objectives that produce reports, and some publications, but generally only of incremental value. It should be no surprise that TR breakthroughs are rare, even though there are more researchers employed today than at any other time in human history. Some unknown percentage of present-day research is simply recycling of known knowledge, with only a marginal increase in new knowledge. That being said, it is noteworthy that this type of research still has value. It can independently explore previous research and either validate or disprove the conclusions emanating from that work. This additive research approach is part of the collective international use of the scientific method. However, TR is also urgently needed.

Summary and future perspective

Transformative science should be natural, fun, and free-thinking. Big discoveries come from such activities. It is the gap between expectation and reality that gives us the thrills of transformative discovery. A few researchers manage to breakthrough the wall of minimal expectation. Freethinking is something that most talented people have and it should be developed, and then rewarded.

Research policies that require industrial-academic collaborations and micromanagement of activities trivialize research to a management model. Contempt for unusual science, possibly an international problem, must be counteracted. Individuals and agencies that are under the illusion they can manage profound discoveries need to produce a list of those discoveries to prove their point. These discoveries can then be judged against the definition of TR. There of course will be some outstanding discoveries, but the list will likely not be immense.

Funding agencies need to designate a portion (e.g., up to 10 %) of their total funding to TR opportunities. Simply provide researchers with the opportunity to conduct research, ask profound questions and visualize answers. They should not be judged by metrics that trivialize their approaches. It is more about an intellectual, profound, creative, maybe even chaotic, artistic approach than a regimented, easily rationalized, managed approach. Progress requires profound discoveries, and we must encourage all scientists to reach for the stars. Indeed some progress is being made in this area, through programs to fund high-risk TR, for example in the US by the National Science foundation, the NIH Director's Transformative Research Projects Program (R01), the Grand Challenges Explorations (through the Bill and Melinda Gates Foundation) or by the European FET proactive initiatives.

Test yourself by asking the following question. What is the single, most significant, profound, or transformative thing you know? Is your answer—all things are made of atoms, $E = mc^2$, the cell is the basic unit of life, the estimated age of the Earth and the universe, the theory of evolution, the four known forces or the genetic code? The first answer is arguably the most profound and correct, because we need to know all things are made of atoms (and then we discover protons, neutrons and electrons) to understand the other answers. You are in excellent company if you provided the first answer. Dr. R. Feynman (N. L.) also provided this answer. By knowing that all things are made of atoms, an immense amount of information is known about the universe. With some human imagination, intellect, luck, hard work, and research, a cascade of knowledge from atomic theory was forthcoming in past decades. Cascading effects and paradigm shifts are an immense component of transformative knowledge.

Wisdom and humor to reflect upon

“A person who never made a mistake never tried anything new”—Einstein.

“I never see what has been done; I only see what remains to be done”—Buddha.

“Science knows no country, because knowledge belongs to humanity, and is the torch which illuminates the world.”—Pasteur.

“All my life through, the new sights of Nature made me rejoice like a child.”—M. Curie.

“Time is nature’s way of keeping everything from happening at once”—W. Allen.

Humor, fun and luck are important components of TR.

Acknowledgments JTT is supported by the NSERC (Canada) Discovery Program. MHS is supported by U.S. NIH Grant GMO77402.

References

- Einstein A (1919) Induktion und Deduktion in der Physik, Berliner Tageblatt und Handelszeitung, 25 Dezember 1919 Supl 4
- Ioannidis JPA (2005) Why most published research findings are false. *PLoS Med* 2(8):e124 (0696–0701)
- Kariukstis KK, Hensel N (2010) Transformative research at predominately undergraduate institutions. Council on Undergraduate Research, Washington, DC, p 128
- McKnight SL (2009) Unconventional wisdom. *Cell* 138:817–819
- Trevors JT, Saier MH Jr (2010) Education for humanity. *Water Air Soil Pollut* 206:1–2