

# The Direction of Biomedical Science

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## 1 Introduction

Scientists typically have a large degree of control over the type of work they pursue - the direction of science. This is particularly true for those based at academic or non-profit institutions where the majority of “basic” biomedical research is conducted. Policymakers overseeing these institutions, be they university deans or political officials, who wish to influence the direction of research must often do so indirectly. Instead of assigning each scientist to a specific research topic, policymakers change the incentives associated with different types of science and allow scientists to respond; hopefully choosing to pursue the science most valuable to society. Because scientists retain a large degree of control over this direction, it is important to understand the major choices facing (potential) scientists and how different factors might influence the supply of scientists, the research topics they pursue and the rate at which new knowledge is converted into valuable innovations<sup>1</sup>.

This issue of allocative efficiency in science will only increase in importance over time. Compared to 150 years ago, the most pressing problems in medicine are no longer immediately obvious and are less likely to have broad implications for the health of society. Instead of proving the fundamentals of germ theory, biomedical scientists are now tasked with understanding extremely complex facets of human biology and the determinants of diseases that can range from genetic to environmental factors. And as science progresses, the complexities at the frontier of our knowledge will only continue to grow. As example, in the initial version of the International Classification of Diseases (ICD) released in 1900, 3 of the 191 total codes listed to classify causes of death were related to cancer: “carcinoma”, “sarcoma”, and “cancer, malignant disease (not otherwise defined)” (WHO 1900). The most recent version of the ICD has 96 unique diagnoses for malignant neoplasms alone, amongst thousands of other specific diseases (WHO 2012). This continued growth in the specificity with which biomedical research is pursued has important implications for the training and management of the scientific workforce (Jones 2009).

The importance of not just the rate, but the direction of invention has been appreciated by economists for some time (Nelson et al. 1962). This initial work highlighted many difficulties of

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<sup>1</sup>The focus of this overview is on these individual scientists, be they academics or for-profit researchers. The majority of work discussed is based on studies of biomedical scientists, but for answers to some relevant questions, findings from other studies of other scientific disciplines or with broader definitions of “scientists” will be highlighted.

empirically investigating these issues. However, increased access to large, detailed data sets and improved measurement and statistical techniques are opening up new avenues for evaluating the rate and direction of science and the determinants of scientists' behaviors.

## 2 Managing the allocation of science

Economists have long argued that because the product of basic research - information - cannot be fully appropriated by its creators, private markets will underinvest in these activities relative to the socially optimal level (Nelson 1959; Arrow 1962). In order to address this distortion, governments play a significant role as funders of biomedical research. In 2012, public institutions in the U.S. spent nearly \$49 billion on biomedical R&D, with the worldwide total of public support reaching \$100 billion annually (Chakma et al. 2014). For comparison, private expenditures on biomedical R&D (e.g. by pharmaceutical firms) amounted to roughly \$168 billion that same year (Chakma et al. 2014).

Importantly, addressing the problems raised by Nelson and Arrow implies that not only should the government provide funds for these activities, but they must ensure that they are directed towards the particular types of R&D that are most valuable to society, but underinvested in by firms. If the \$49 billion awarded by public organizations were investments that private firms would have made otherwise *or* there were valuable research ideas that remained unfunded, then intervention by policymakers may be necessary.

### 2.1 Allocating Science: In Theory

Put simply, the allocation of biomedical research should be one where investments are made to the areas of science deemed most productive, or in other words, where the supply and demand for that science are the largest. A number of theoretical models have been developed to show formally how the efficient allocation considers both the supply of scientific inputs (e.g. individuals and existing ideas) and the demand for scientific outputs (e.g. new ideas and products) (Garber and Romer 1996, Lichtenberg 2001, Cutler et al. 2012). Garber and Romer (1996) emphasize the importance of considering the incentives of the healthcare delivery system when evaluating what areas of biomedical science will have the greatest demand. Cutler et al. (2012) introduce an important consideration whereby meeting growing demand for medical innovations can potentially increase disparities in health outcomes. Thus, even if policy makers were perfectly informed as to the most "productive" areas of science - put purely in terms of supply and demand sans preferences for equity - the socially optimal portfolio of research investments would still be debatable.

## 2.2 Allocating Science: In Practice

In order to determine how these funds are allocated, most institutions utilize peer review panels. This is often an efficient arrangement as scientists themselves are most informed as to their own abilities as well as the specific lines of research most fruitful for pursuit (Aghion et al. 2008). However, it is also possible that scientists face strategic incentives to be biased towards certain types of research in these settings. They may face cognitive constraints when evaluating new research ideas, or try to exclude funding for research outside of their own field of expertise.

A recent experiment investigated scientists' ability to judge the quality of research ideas as a function of their own expertise in relation to those ideas (Boudreau et al. 2016). The authors found that when evaluating ideas that are randomly selected, the scientists tended to give lower appraisals to topics more similar to their own expertise and more "novel" in nature. They argue that this pattern is in line with the notion of bounded rationality where scientists are more likely to find problems or limitations within certain types of research proposals (Boudreau et al. 2016).

Investigations of the peer review panels at the National Institutes of Health have found that strategic biases (e.g. where scientists attempt to keep funding within their own fields) are typically overwhelmed by the fact that scientists are more informed as to the quality of research ideas within their own fields (Li 2014). And on average, it does appear that NIH review panels can identify the research ideas most likely to result in high-quality outcomes (Li and Agha 2015). Lichtenberg (2001) provides some evidence that to at least a first order approximation, the allocation of biomedical research funding aligns with demand.

However, when left to their own devices there is good reason to think that in this setting, scientists may not choose the most optimal set of research ideas from society's perspective. Just as firms cannot fully appropriate the rents from these activities, so to are there limitations in rewarding scientists for their work. Certainly, incentives such as prizes (e.g. the Nobel awards) and the system of priority, where notoriety is given to the initial discovery, do act to steer scientists towards valuable pursuits. But frictions are likely to remain. To quote Partha Dasgupta and Paul David from their essay on the incentive structure of science:

*"The fundamental point is that society does not care who is successful in solving a given scientific problem, it cares that the problem is solved [...] Yet for the individual scientists (or the scientific team), the identity of the problem-solver and the precise time at which his/her solution can be announced are matters of great concern; the priority-based reward system imparts great significance to differences in timing that are inconsequential from a societal standpoint. This sort of non-congruence between private and social rankings of final outcomes creates fundamental grounds for suspecting that the research portfolio that would be, in effect, selected, for society by the self-governing community of scientists will be an inefficient one."* (Dasgupta and David 1994, pp. 506)

Recent theoretical work on the direction of innovation has begun to formalize why this “non-congruence” can arise (Bryan and Lemus 2016). Namely, mechanisms such as prizes (as opposed to laissez-faire) can incentivize the pursuit of the easiest problems eligible for their award. For example, if it was somehow known that finding the cure to either of two diseases would surely garner a Nobel prize in medicine, but the likelihood of curing one of the diseases was substantially larger, we would expect scientists to commit more effort and resources to this “easier” problem even if curing the “harder” disease would be more valuable to society as a whole. Obviously this example abstracts away a number of other rewards in the market for science, but it exemplifies the difficult task of influencing scientists’ choices without distorting the overall direction of science.

But solving this problem is not straightforward. The main motivation for the public support of basic research (limited appropriation) is precisely the reason why laissez-faire competition is not feasible in this setting. There is no market for the results of most science. This fact, combined with the uncertainties and large fixed costs of basic research imply that funding agencies should utilize prizes in order to distribute resources (Wright 1983; Stephan 1996). Thus, policymakers face a difficult tradeoff when choosing the mechanisms that allocate and incentivize basic research.

Sampat (2012) provides an overview of these tensions at the National Institutes of Health, emphasizing how the NIH has been able to balance competing interests over its history. He highlights three forces: the NIH has (1) developed “safety-valve” mechanisms by which specific areas of science can receive targeted investments; (2) emphasized “serendipity” whereby the uncertainties of basic science should be met with *less* intervention from interested advocates; and (3) integrated itself into a diverse set of constituents both in terms of geography and types of organizations such as academic medical centers, universities, and disease interest groups. Looking more closely at the phenomenon of disease-specific advocacy, Best (2012) documents the ability of interest groups to shape not only the allocation of funding, but also the sociological perceptions, across diseases. Hegde and Sampat (2015) pursue this question of political influence at the NIH even more specifically. The authors exploit a change in lobbying regulations and trace contributions to politicians from disease-specific interest groups. Hegde and Sampat (2015) show that increased lobbying is associated with “soft-earmark” requests in Congressional appropriation bills for the NIH, as well as eventually funded research grants. Whether this ability to influence the NIH’s allocations is socially optimal remains an open question

### 3 Scientific choices

Given the large degree of control afforded to scientists over the direction of science, it is important to have an understanding of the forces that shape individuals’ decisions and how these choices aggregate to shape the rate of innovation. Broadly speaking, there are three major types of decisions facing scientists: (1) whether or not to pursue science as a career; (2) which fields of science to specialize

in and which specific scientific subjects to pursue; and (3) when to translate knowledge generated in “basic” research into commercializable or “applied” research opportunities (e.g. a product). Thus, policymakers have three main margins which they might choose to act on in order to manage the rate and direction of science.

### 3.1 Science as a career: How many scientists are there?

With an interesting regularity over the past sixty years, economists have given attention to the supply of scientists in the U.S. workforce. Studies in the 1950s (Blank et al. 1957; Arrow and Capron 1959), 1970s (Freeman 1975) 1990s (Ehrenberg 1992; Goolsbee 1998) and 2000s (Romer 2001; Freeman and Van Reenen 2009) continued to investigate the extent to which the supply of scientists may be hampered by certain frictions unique to this line of work.

As noted by Arrow and Capron (1959), it is important first to clarify what exactly is meant by a “shortage” (or surplus) of scientists. In the traditional economic sense, a shortage in the supply of scientists implies that at the given wages, an increase in the demand for scientists (e.g. number of individuals) will be met by a less than proportional increase in the supply of scientists. To contrast, Arrow and Capron note that policymakers often imply a shortage in the *demand for scientists*, where they are concerned that the economy has somehow undervalued the contributions made possible by these individuals. While this latter issue is exceptionally difficult to test empirically, the former - whether the supply of scientists can perfectly adjust in response to demand - has largely been the focus of prior work. Understanding the difference in magnitudes between the two is essential when designing national policies.

The most recent empirical studies of the supply of scientists in the U.S. have documented significant rigidity in the supply of scientists. Goolsbee (1998) examines the large federal investments in R&D of the early 1980s and finds that as government spending grew, so too did the wages of scientists. In fact, he finds that each 10% increase in government spending was associated with a 4-5% increase in the wages of scientists who specialized in the areas of R&D targeted by this spending. If there was no shortage and the market for scientists was perfectly competitive, than an increase in demand should not have affected wages. These findings speak to the contrary.

More specific to biomedical research, Freeman and Van Reenen (2009) study Congress’ decision to double the budget of the NIH over the course of six years beginning in 1998. Most notably, they highlight the potential issues with abrupt changes to budgets in the presence of adjustment costs. When large increases and decreases in the NIH’s budget occur, it may inefficiently induce more individuals into the scientific fields at times of budget growth who cannot obtain a sustainable amount of resources once the budget declines. To address this problem, the authors suggest mechanisms be put in place to “bridge” the funding of scientists during budgetary fluctuations.

Why might these rigidities arise? The lengthy training necessary to become a “scientist” - namely, receive a Ph.D. after 5 to 15 years of training beyond undergraduate school - is typically billed as the main culprit. Because individuals cannot quickly move into this sector, career decisions are made many years in advance. Furthermore, we should only expect these fixed costs to increase over time as the amount of knowledge to learn continues to grow. Jones (2009) highlights this “burden mechanism” through which individuals compensate the need for an increased *depth* of knowledge by reducing the *scope* of their knowledge. Jones finds strong empirical support for this model of innovation where educational attainment has increased significantly over time, as has the formation of teams in response to each individual having a narrower skill-sets. These results have negative implications for long-run growth where increased R&D activity may be required to merely sustain the rate of technological progress.

Despite this evidence of large supply-side frictions, it has been suggested that prior federal policies have largely ignored them and instead focused on subsidizing the demand for scientists, which will obviously be limited in impact if these supply-side frictions remain (Romer 2001).

### 3.1.1 Internationalization of Science

Freeman and Van Reenen (2009) also document important changes to the composition of the scientific workforce, where the surge in postdocs in the past two decades appears to be largely driven by foreign-born temporary residents. This introduces another complex set of issues - how should public institutions evaluate the supply of domestic and international scientists? The authors point out that in addition to solving the public good problem of basic research, public investments in R&D are an important determinant of international comparative advantage.

The internationalization of US doctorates and its positive and normative implications remain one of the more understudied aspects of the scientific workforce. Bound et al. (2009) provide a comprehensive examination of this pattern and the forces underlying this shift. Their findings indicate that some of this growth is due to newly-developed countries where undergraduate infrastructure has grown (e.g. South Korea), while some is due to larger, developed countries who have undergone major policy changes in the past three decades (e.g. China and Russia). Bound et al. (2009) also find that the sorts of wage responses to federal spending identified by Goolsbee (1998) are not apparent with more detailed and recent data on the earnings of academic faculty in the sciences. The authors suggest that Goolsbee’s results cannot disentangle the underlying growth in wages for the college-educated during this period, which themselves were also correlated with the growth in science funding. Importantly, both of these studies focus mainly on the level of scientists active in the economy as opposed to the topics of interest amongst these scientists.

### 3.1.2 Supply-side Policies

While clarifying the supply elasticity of the scientific workforce is still an important avenue for future research, a growing body of work has begun to explore the factors that influence what these scientists pursue (Section 3.2 below). Which is the more important policy question? This depends on where in the distribution of scientists the most important advancements are generated. If the majority of scientific discoveries are due to inframarginal individuals (those with strong preferences for science), then perhaps significant concern over the elasticity of this workforce is not of first order. While this is an intuitive notion, sociologists who have studied science (e.g. Thomas Kuhn) have long held theories that significant advancements are more likely to come from marginal “outsiders”. In this case, individuals indifferent between pursuing science or other careers may indeed come to provide important contributions to science. Still, these claims are often rooted in anecdotes or case studies - a systemic analysis of these phenomena would have important implications for the funding behaviors of policymakers. To the extent discoveries are clustered amongst inframarginal scientists (who never considered alternative careers), this would imply that policymakers should be less concerned growing the workforce and more concerned with the projects pursued within the workforce.

## 3.2 Types of Science: What questions do scientists pursue?

### 3.2.1 Research Topics

What determines the specific topics of inquiry (eg. diseases, chemicals, organisms) that scientists pursue? Answering this question is essential for designing policies intent on guiding the choices of researchers - the size and duration of research grants, or the structure of prizes for new discoveries, or whether it is more efficient to fund specific research projects or the more general infrastructure that supports them.

**Aggregate Directions:** Taking a macroeconomic perspective, work by Bhattacharya and Packalen (2011) examines how the aggregate flow of biomedical science responds to shifts in the supply and demand for different types. They identify responses to demand conditions by linking the rate of scientific publications on specific diseases to future changes the prevalence of those diseases. A structural model of supply and demand is then used to also identify scientists’ responsiveness to supply conditions - growth in the publication rates across diseases. Bhattacharya and Packalen’s (2011) results indicate that, much like for-profit firms, scientists appear to respond positively to increases in the expected patient population for different medical conditions. This finding has normative implications, providing initial evidence that, perhaps to a first-order, the incentive structures of science are able to align scientists’ and society’s objectives.

**Public Policy:** National policies intended to influence the specific direction of research are rela-

tively uncommon - most policies, such as the budget of the NIH, are about funding large diverse efforts. And even those policies that do intend to specifically influence the direction of work often lack a clear counterfactual with which to compare. For example, President Obama's BRAIN Initiative<sup>2</sup> involves six federal agencies, more than twenty non-federal organizations and firms, and has long-term objectives of developing treatments for disorders such as Alzheimer's, schizophrenia, autism, epilepsy, and traumatic brain injury. Thus, if one wanted to estimate the effect of these efforts, it is unclear how to even define the many scientific fields and sub-fields likely affected by BRAIN, and how these areas of science would have progressed otherwise. For these reasons, studies of the causal effects of public policies on the direction of science are quite uncommon. One important study by Furman et al. (2012) examined the restrictions of funding for Human Embryonic Stem Cell (hESC) research under President Bush in 2001. The authors compared the rate at which U.S.-based scientists published work on hESC relative to non-U.S. scientists both before and after the policy change. The estimates indicate that U.S. scientists lagged behind their foreign counterparts following the ban, on the order of 30-40%, but were able to recover their rate of work in later years largely through international collaborations. Furman et al.'s (2012) approach of comparing the rate of hESC publications both within and across countries provides a robust research design that could be extended to other settings, but relies on a policy shock that is relatively well-defined.

**Prizes:** The usefulness of prizes as incentives in scientific communities is due to their ability to balance information asymmetries between skilled scientists and the policymakers who fund the rewards (Wright 1983). For example, the Nobel Prize in Physiology of Medicine rewards outstanding contributions that improve the health of humankind, regardless of how those contributions might result in health improvements<sup>3</sup>. The prestige of the Nobel's, in addition to the \$1,200,000 prize, thereby incentivizes scientists to pursue the most "important" problems without specifying what exactly is important to society. Recent years have seen a growth in the prevalence of large pecuniary prizes for advances in science: for example, the Breakthrough Prize in Life Sciences (\$3 million), the Fundamental Physics Prize (\$3 million), the Tang Prize (\$1.7 million) and the Queen Elizabeth Prize for Engineering (\$1.5 million)<sup>4</sup>. Murray (2013) highlights the important role of philanthropies, who are increasingly reliant on these prize mechanisms, in the science funding landscape.

However, creating additional prizes with the prestige of the Nobel's, for example, is difficult because part of the value of these awards is explicitly tied to their uniqueness. Furthermore, there is the risk that prize structures, in general, can incentivize over-investments in pursuit of the award (Dasgupta and Stiglitz 1980, Wright 1983)<sup>5</sup>. Khan (2015) surveys many classic examples of private and public institutions using prizes to solicit innovations - the Longitude Prize, the Daguerreotype "buyout" - and argues that, in fact, the usefulness of these prizes is often overstated. Unlike popular retellings,

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<sup>2</sup>[www.braininitiative.nih.gov](http://www.braininitiative.nih.gov)

<sup>3</sup>In other words, they reward science associated with the largest gains in social welfare.

<sup>4</sup>For more commentary on this trend, see [www.nature.com/news/science-prizes-the-new-nobels-1.13168](http://www.nature.com/news/science-prizes-the-new-nobels-1.13168) .

<sup>5</sup>These concerns are analogous to the "common pool" problem of public resources highlighted by Gordon (1954).

these prizes were plagued by large lobbying efforts on behalf of innovators and judges, alongside difficulties in defining the bounds of the contest (i.e. what submissions are eligible?) and ultimate results (i.e. which eligible submission is the best?). Importantly, the Khan focuses largely on “product” prizes - rewards for new, marketable technologies. As far as the usefulness of prizes in biomedical research, Khan’s arguments may be more relevant for science closer to the “applied” end of the basic-applied spectrum. On the other hand, Brunt et al. (2012) provide a more optimistic view of the usefulness of inducement prizes. The authors examine a series of contests held by the Royal Agricultural Society of England during the turn of the 20th century. The contests utilized both monetary and prestige awards - “gold medals” - in hopes of spurring new technologies. Brunt et al. (2012) find significant increases in the fields of agricultural science targeted, with their most convincing estimates indicating the largest effects were due to the prestigious gold medals.

Khan’s and Brunt et al.’s studies offer examples from grand contest settings, but on a smaller scale organizations, including life science firms, have begun using prizes to crowd source solutions to specific problems (Jeppesen and Lakhani (2010)). Aggregators such as Innocentive<sup>6</sup> now provide platforms for businesses to solicit ideas from individual scientists. Likewise, the 2011 America COMPETES Act gave federal organizations the authority to utilize prize competitions to “spur innovation”, with the [Challenge.gov](http://www.challenge.gov) website detailing all ongoing prizes made available by these agencies. The causal effects of these policies, particularly within the biomedical sciences, remains unclear.

**Intellectual Property and Follow-on Science:** The role of intellectual property rights (IPR) as innovation incentives has received a large amount of attention. For the most part, these investigations have focused on whether patents inhibit or stimulate product development amongst for-profit firms - see Budish et al. (2016) for a recent review of the evidence. A portion of these studies have examined how IPR affect basic science - for example, how a patent covering science on topic  $A$  at time  $t = 0$  effects the rate at which topic  $A$  is pursued at times  $t > 0$ . Two recent papers of note examine biomedical science outcomes - publications - following the receipt (Williams 2013) or loss of non-patent intellectual property rights (Murray et al. 2016). Both investigations find that the use of IPR on a scientific topic (mice strains in Murray et al. (2016) and genes in Williams (2013)) is associated with an approximately 20-40% decline in follow-on science. That the two studies together examined the effects of losing or gaining IPR and arrived at similar results lends further credence to their research designs.

Murray and Stern (2007) examine the effect of patents explicitly by comparing the rate at which publications disclosing patented science are cited by future publications. The authors exploit the fact that there is often a multi-year lag between a discovery’s publication and patent, and compare the focal article’s citation rate before and after the patent is awarded. This approach indicates that post-patent, a publication is cited roughly 10-20% less often. These results also support the

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<sup>6</sup>[www.innocentive.com](http://www.innocentive.com)

“anti-commons” results identified by Murray et al. (2016) and Williams (2013). However, the small sample size and types of discoveries needed for Murray and Stern’s (2007) research design may not be representative of most science. More generally speaking, studies of the affect of patents on follow-on science must overcome concerns of selection where the most valuable science is more likely to be patented. Recent work by Sampat and Williams (2015) utilizes the random assignment of patents to examiners as a way of addressing the selection issue, and trace gene citations over time, pre- and post-patent. The authors do not find any significant changes in the rate of follow-on science for the genes treated with these “random” patents. Although these results seem to somewhat contrast Williams’ earlier findings, this result that patents themselves may not be substantial barriers to follow-on work, but other forms of IPR are fits neatly with initial evidence from Walsh et al. (2007) that patents are not associated limitations to accessing purely knowledge-based inputs, but non-patent restrictions on more tangible inputs such as data and materials may be prohibitive.

**Institutions:** Scientists do not operate in a vacuum, but are rather surrounded by a large number of organizations such as Universities, funding agencies and other supporting organizations. These institutions can have important effects on the willingness of scientists to pursue certain topics. One major institution within the life sciences are biological resource centers (BRCs), which certify and maintain large amounts of biological materials such as cell lines, bacteria and viruses. Furman and Stern (2011) estimate the ability of a major BRC<sup>7</sup> to increase cumulative research that utilizes the resources made available. To do so, the authors investigate the use of materials as they become exogenously available at the BRC following scientist retirements or relocations. Furman and Stern (2011) find that once made available, BRC resources are used 50-130% more often, indicating that institutions that make scientific resources more easily available can have meaningful impacts on the rate of cumulative discoveries that build on one another. This result is especially important given the aforementioned barriers to accessing scientific materials that IPR regimes can create (Walsh et al. 2007).

### 3.2.2 Risk, Creativity & Incentives

Science is often modeled as the recombination of existing ideas in order to generate new ideas (Weitzman 1998). One of the major tradeoffs when designing these recombinations is whether or not to “explore” potentially novel, but uncertain combinations versus “exploiting” more certain, but potentially less novel combinations. How can incentives influence the risks scientists might take when designing these research projects? Manso (2011) provides a useful framework for understanding how different reward structures can influence this explore-exploit tradeoff. In short, incentivizing exploration requires tolerance for failures, and larger rewards in the future relative to the present. Azoulay et al. (2011) empirically test this line of predictions by evaluating the scientific production of

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<sup>7</sup>The American Type Culture Collection; see more: [atcc.org](http://atcc.org).

biomedical researchers funded by “exploit” mechanisms at the NIH compared to individuals funded by “explore” mechanisms at the Howard Hughes Medical Institute (HHMI). In line with the theory, scientists funded by the HHMI produce more on average, and are more likely to produce a very high or low impact publication, which indicates they are more willing to take on risky projects. Furthermore, the HHMI-funded scientists are more likely to investigate areas of science they had not explored previously.

Turning to more intrinsic incentives, Sauermann and Cohen (2010) highlight the important role of motivations in scientists’ decisions. The authors utilize data from the Survey of Doctoral Recipients, conducted by the National Science Foundation<sup>8</sup>, to relate individual’s preferences to innovative outcomes, here, captured by patents. Their results indicate a positive relationships between patenting and individuals’ preferences for income, intellectual challenge and independence in their work. However, it appears that individuals with a strong preference for responsibility within their firm are less likely to patent - suggesting that efforts may be substituted from innovating to managing innovators. Interestingly, the affect of these preferences on patent rates appears to be moderated via the “character” of efforts (e.g. project selection, information sharing), rather than the level of effort (e.g. hours worked). Still, Sauermann and Cohen (2010) are limited in their ability to account for unobservable scientist-level differences or the endogenous matching of individuals to firms. Thus, even with data on preferences in hand, more robust analyses of these forces will face the difficult task of exploiting exogenous matchings of individuals, and their preferences, to specific innovative tasks.

### 3.2.3 Generating vs. Verifying

When attempting to create knowledge, scientists face an important choice of either generating “new” ideas or confirming the validity of “existing” ideas. Understanding the incentives underlying this decision is important for predicting whether optimal levels of verification activities occur in the market for science, and whether or not any underinvestment would warrant public support. This is especially true in the case of biomedical research, where the health and wellbeing of individuals is often directly affected by the acceptance or rejection of scientific findings. Kiri et al. (2015) provide a theoretical model of the scientific community that highlights this decision between generating and verifying. The authors extend initial work on this topic, by Mirowski and Skivas (1991) and Wible (1998), in order to predict the effects of policies that might influence the quality and reliability of scientific findings. They highlight a number of important results, most notably, that the absence of low-quality “generating” activities can in fact be a signal that “verification” activities are not being performed. Furthermore, the authors’ model predicts that the strength of publication incentives (e.g. “publish or perish”) does not affect the share of low-quality generating activities that occur,

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<sup>8</sup>See more here: [www.nsf.gov/statistics/srvydoctoratework](http://www.nsf.gov/statistics/srvydoctoratework).

but rather the share of them that are “caught” by verification activities (Kiri et al. 2015).

A number of studies have investigated the implications of conducting fraudulent science or publishing results with egregious errors. This literature relies predominately on retractions in scientific journals as a focal event, tracing out the consequences of these events for the individuals (Lu et al. 2013, Azoulay et al. 2015b, Azoulay et al. 2015a). In line with a Bayesian model of uncertainty and continuously updating beliefs, this work finds significant declines in the value of the papers and individuals implicated. However, as pointed out by Kiri et al. (2015), these cases do not necessarily imply inefficiencies or frictions in the market of science.

### **3.3 Commercialization: How is science translated into products?**

Science is often depicted as existing along a spectrum ranging from “basic” to “commercial” efforts. More basic science is concerned with generating knowledge about the fundamental forces at play in our universe - the composition of atoms, how chemicals interact or why humans make certain decisions. More commercial science is concerned with applying knowledge about these fundamental forces to create goods or services for consumption. Policymakers have long been interested in influencing the rate at which this commercialization process occurs. Indeed, the NIH has made large investments with the National Center for Advancing Translational Sciences (NCATS) with hopes of easing the commercialization process for scientists<sup>9</sup>. In for institutions such as NCATS to be effective and to design efficient policies, we must understand how scientists choose to “translate” ideas into products and whether or not any frictions impede this process of translation.

#### **3.3.1 Where to work: Industry or Academia**

One of the major decisions scientists make with respect to the commercialization process is their employer, namely, whether they are based in either in industry or academia, or somewhere “in between”. Stern (2004) formalizes the major equilibrium forces that influence how individuals sort between these types of organizations and, importantly, the implications for the ultimate wages received by these individuals. Using data from job offers to biologists, he finds that new Ph.D. graduates are willing to take a 25% wage discount, on average, in exchange for the right to publish their research. These results hold true for both all job offers, and amongst non-academic job offers as well (Stern 2004). Detailed work in this space by Henry Sauermann and Michael Roach have explored heterogeneity across scientists with respect to these preferences for academic-oriented work have identified substantial differences in individuals’ preferences, and suggest that pro-publication policies at private firms may be mostly due to productivity and absorptive capacity considerations (Roach and Sauermann 2010, Sauermann and Roach 2012, Sauermann and Roach 2014). Still, as

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<sup>9</sup>Visit NCATS at [ncats.nih.gov](http://ncats.nih.gov).

a whole this literature typically reinforces the notion that many scientists, in general, resist the commercialization process. These preferences have important policy implications, as this “repugnance problem” may be a first-order barrier to generating a thick market for ideas (Gans and Stern 2010).

Looking across the U.S., Stephan et al. (2004) and Sumell et al. (2009) utilize the Survey of Earned Doctorates to trace the flow of new Ph.D. scientists to their industry employers. The authors find significant disparities between many states training inputs (i.e. University R&D expenditures) and flows of Ph.D.s going to industry. For example, relative to their inputs, Midwest-trained PhDs are more likely to enter industry positions; however, these positions are likely to be *outside* of the Midwest. This movement of high-skilled workers poses difficulties for states hoping to capture returns to their investments, and suggests that national-level policies must take these forces into account. These migration concerns mimic the issues highlighted in Section 3.1.1 with respect to the internationalization of science.

### 3.3.2 When to commercialize: Antecedents and Outcomes

Although it is typically not their primary objective, scientists at academic or non-profit institutions are important sources of commercial developments. What motivates these translations and under what circumstances are these translations most successful?

**Individuals’ Antecedents:** It has been well documented that the rate of scientists pursuing commercial developments with their more basic discoveries has dramatically increased over the past three to four decades (Thursby and Thursby (2002)). This growth, and the underlying characteristics associated with these translations, have been highlighted by numerous studies. Thursby and Thursby (2002) suggest that the growth in commercial activities amongst scientists was due less to major changes in the direction of their work, but rather due to managers - be they faculty or administrators - being more likely to facilitate licensing activities. An investigation by Lach and Schankerman (2008) reveals that, during this timeframe, managers increased the use of royalty agreements with scientists, which on net were more profitable for Universities. By examining the rate and quality of patents, they find that the growth in commercial activities was likely due to higher quality science and not necessarily an increase in the rate at which commercial opportunities are pursued.

This growth in commercialization may also have been due to feedback processes, whereby more translation spawns more translation. For example, Stuart and Ding (2006) find that scientists are more likely to start a new firm or join the board of a new venture if their colleagues had previous experience in the commercial sector. However, Ding et al. (2006) highlight large differences in the propensity for genders to patent their science: women scientists patent at roughly 40% the rate of men on average. This gap appears to be driven by women having networks with fewer commercially-

based scientists, as well as less of a preference for pursuing this type of science. Before drawing policy implications, it is important to understand how much these individual-level factors may be mediated by other forces such as the presence of scientific opportunities. For example, subsidizing particular scientists to pursue a patent will only be valuable insofar as the individuals have ideas to patent. Azoulay et al. (2007) test for the presence of these science-supply-side forces and document large spikes in individuals' publication rates prior to patenting. These spikes are indicative of "discoveries", and the frequency with which they occur prior to patenting suggests that influencing scientists' commercial orientations in their absence may entail significant costs

**Individuals' Outcomes:** The impact of taking on more commercial-based research are not clear a priori. On one hand, efforts to develop patents and products might crowd out efforts to generate or disseminate socially useful research findings. Conversely, scientists' commercial pursuits may spur new ideas and research projects that would otherwise have not occurred. Furthermore, developing new products can generate large welfare gains, particularly in the biomedical sciences where health-related products can generate large spillovers. On net, the econometric evidence has largely found a scientist's commercial activities - namely, patenting - to be associated with increases in the rate and quality of their basic research activities - namely, publications - suggesting that these efforts are likely complements (Agrawal and Henderson 2002, Fabrizio and Di Minin 2008, Azoulay et al. 2009, Magerman et al. 2015). However, for the most part these studies have focused on changes to the *rate* of outcomes following commercialization and less so the nature or *direction* of the science. One exception, Azoulay et al. (2009), find that biomedical scientists who patent also in turn publish with more firm-based coauthors, in journals with a higher share of firm-based authors while working on topics that appear more "patentable".

By and large, these studies use measurable covariates to control for each individual's unobservable, and potentially time-varying, likelihood of pursuing a commercial strategy. However, it remains unclear to what extent these control approaches are empirically effective. New research designs, such as the Michael Bikard's "twin discovery" approach outlined below, are an important step in this direction. But even these approaches must often sacrifice generalizability for more rigorous identification of causal effects. Thus, developing more structural models of the supply and demand for commercial science may provide empirically testable, and generalizable, predictions.

**Institutional Factors:** Di Gregorio and Shane (2003) and Sine et al. (2003) highlight the role of prestige amongst institutions (e.g. Universities) in fostering license deals and spinoff venture formations. Importantly these theories and supporting data suggest that with each success, an Institution's prestige is reinforced, generating a feedback mechanism. This has important implications for the distribution of commercial activities across different institutions and geographies, namely, that organizations should continue to become increasingly specialized in certain aspects of science commercialization, and that the concentration of commercial activities in certain areas will also increase. Whether this upward trend in specialization and commercialization is the most efficient

outcome, or may warrant policy interventions - for example, that maintain a more even distribution of these activities - remains to be examined.

The role of one particular institution - technology transfer organizations - in converting knowledge to products has received a tremendous amount of attention. Indeed, the *Journal of Technology Transfer* is a peer-reviewed publication focusing solely on these matters. Bozeman's (2000) literature review and Thursby et al.'s (2001) survey provide a useful starting point that highlight the many streams and important questions of this literature.

A major difficulty in studying translation events and how organizations and policies can affect them, is that they do not occur at random - comparing the outcomes for individuals at different types of institutions will only be useful insofar as the underlying ideas are equally commercializable. In order to overcome the fact that so much surrounding each idea is unobservable, Mikael Bikard devised a unique method of studying translation events by comparing discovery "twins", where two or more individuals or teams of scientists discover, essentially, the same piece of new knowledge<sup>10</sup>. Thus, by comparing different institutional characteristics *within* discovery twins, Bikard can control for these unobservable differences in discoveries that are problematic in traditional analyses. Initial results from this approach indicates that relative to their firm-based counterparts, academic-based discoveries are much less likely to be sourced for cumulative innovations in general, and frictions in academia may be mediated by their geographical proximity to relevant industries (Bikard 2012, Bikard and Marx 2015).

### 3.3.3 Bayh-Dole Act

One of the most significant public policies designed to influence the commercialization process is the Bayh-Dole Act of 1980<sup>11</sup>. The key provision of this Act was that research institutions could pursue ownership of inventions made possible with federal research funds. The intuition was that if scientists were given rights to these discoveries, they would be more likely to pursue commercialization. Jensen and Thursby (2001) provide a useful theoretical framework that highlights the moral hazard problem in this setting of inventors (scientists) and licensees (e.g. private firms).

An initial empirical examination of the Act indicated that these new incentives may have simply caused scientists to pursue lower quality commercial ventures, as indicated by a decline in the citation-based quality of University-based patents (Henderson et al. 1998). However, using a longer period of patent citation data, Sampat et al. (2003) find that the decline in citations identified by Henderson et al. (1998) could be explained by an intertemporal shift in patent citations, whereby University-based patents post-Bayh-Dole were equally likely to be cited by future patents, but the average time from patent to citation increased significantly. Similar results from Mowery and

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<sup>10</sup>The frequency of these twins in the scientific process has long been noted by, for example, Robert Merton.

<sup>11</sup>Also known as the Patent and Trademark Law Amendments Act, Pub. L. 96-517.

Ziedonis (2002) and Mowery et al. (2002) support the notions that (1) the affected institutions and individuals took time to adjust their processes in response to the Act, and (2) the effects of Bayh-Dole were perhaps larger for the *direction* of University-based commercialization rather than the rate at which it occurred. Whether this change in the nature of University-based science was optimal is still an open question. For example, the later-stage citations that Sampat et al. (2003) identify have been associated both with lower (Lanjouw and Schankerman 2004) and higher (Hall et al. 2005) measures of patent value.

### 3.3.4 National Laboratories and Publicly Employed Scientists

The vast majority of the aforementioned studies have utilized data on what could generally be referred to as “academic” scientists. These individuals are often recipients of federal and commercial research grants, but they are employees of independent non-profit organizations such as Universities, hospitals, “think-tanks” or policy institutes. However, a significant portion of biomedical research is conducted directly at public organization by public employees.

At the NIH, for example, roughly 11% of the annual budget (\$3.4 billion in 2015) is currently allocated to “intramural” research. In fact, the Ransdell Act of 1930 that formed the NIH initially authorized only intramural research to be conducted by staff scientists. It was not until the 1946 that an extramural grant program was adopted across the Institutes. Currently, the NIH has intramural research locations at campuses across Maryland, North Carolina, Montana and Arizona house basic and clinical researchers.

To date, publicly employed biomedical scientists remain relatively understudied, despite discussions that managers of these intramural activities may be in a unique position to facilitate translational efforts that are so often emphasized (Emmert-Buck 2011). Part of the difficulty in evaluating these efforts lies in acquiring the necessary data to study the production and outcomes of intramural “projects”, which may be much less defined relative to their extramural counterparts. Part also lies in identifying variation in the use of intramural research resources that is uncorrelated with shifts in the supply and demand of science. For example, if the goal of the NIH’s intramural program is to fill gaps in our knowledge base that would otherwise have not been pursued, then observing lower productivity amongst these research efforts may simply be a function of lower fertility in those topics pursued.

Looking at federally funded R&D center (FFRDC) more generally, work by Jaffe and Lerner (2001) found that after the 1980’s the commercial output of these institutions grew significantly, while maintaining prior levels of quality. They attribute these successes to particular institutional features. Namely, they find that the most productive FFRDCs are those that maintain a relatively narrow technological focus in their pursuits. These results indicate *returns to scale within* scientific areas at these particular R&D efforts are likely much stronger than any *returns to scope across* scientific

areas. Adams et al. (2003) focus on how FFRDCs can interact with and stimulate industrial R&D by studying cooperative research and development agreements (CRADAs) introduced by the Stevenson-Wydler Act in the 1980s. Their findings suggest that relative to when CRADAs are not in place, industry-laboratory interactions with CRADAs are more productive and are associated with increased investments from both FFRDCs and firms. The authors develop theoretical arguments for why private-public partnerships in R&D should ideally focus on targeting complementary outputs, and that features such as cost-sharing may be necessary to generate efficient levels of investment from both parties. Still, because the formation of these ties is by no means random, further analyses are still necessary to identify the causal forces that moderate successes.

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