The Governance of Research

Third Munich Lecture

November 2007

General questions

(Why) are academics needed?

What distinguishes academic research from industrial research?

(Why) do we need both?

Are there downsides to using patents to reward research?

In particular

- Why do we have freedom and openness in Academia?

Two alternative views on openness

Appropriability view

Control rights view

Appropriability view

- Two research stages: basic and applied
- Research line pays out only when applied stage is completed
- Applied researcher can hold up basic researcher…
- ….unless patent system protects basic researcher
- Thus here openness benefits more applied research, and it discourages innovations!!

Alternative view: ADS

Openness helps move idea from one stage to the next as it reduces search costs by next stage researchers….

…..this is more valuable in academia than in private sector as academic research is less focused and more diverse

Outline of the lecture

- Part 1: a theoretical framework
- Part 2: a natural experiment

Part 1: Modeling the role for academic freedom and openness

(Aghion-Dewatripont-Stein (2006))

Motivation

- What are the respective roles of *academia* and *private research* in developing innovative products*?*

  1. Traditional story:

     $\longrightarrow$ because of spillovers and insufficient protection of intellectual property rights (IPR), private sector underinvests in ”basic” research

     $\longrightarrow$ however, if spillovers and appropriability is the main problem, second-best solution is to simply subsidize R&D

     $\longrightarrow$ why do we need separate institutions called universities to solve appropriability problem, and is there still a role for academia even with full IPR protection at all stages of research process?

Motivation

2. Incentives story:

   $\longrightarrow$ academia and private sector firms use different incentive schemes which fit different types of research

   $\longrightarrow$ why can't we introduce the desired incentive schemes while remaining within firms' boundaries?

Our Approach

- Focus on *control rights* and on the simple trade-off between *creative control* in academia and *directedness* in private sector research

  $\longrightarrow$ we view academia as a commitment device that leaves control in hands of scientists

- Innovation process modeled as a *multi-stage research line*

  $\longrightarrow$an economically viable product (e.g a new drug) starts with an idea I_0 that can be built upon by researchers. If stage 1 succeeds, get refined idea I_1, leading to ideas I_2, ..., until idea I_k that generates economic value V

  $\longrightarrow$ in a multi-stage research line, creative freedom and therefore academia have a comparative advantage in earlier stages, directedness and therefore private sector research have a comparative advantage in later stages

Our Approach

- *Normative content*:

  $\longrightarrow$ concerns have been expressed about excessive IPR protection, ideas being patented too early

  $\longrightarrow$ e.g, is Bayh-Dole a good idea?

  $\longrightarrow$ Heller-Eisenberg (1998): "anti-commons" hypothesis

- Our model clarifies the social costs associated with early privatization

  $\longrightarrow$ probability of innovation may decline

  $\longrightarrow$ reducing IPR protection for early stage ideas can raise innovation rate and welfare

Related Literature

1. Emphasize the appropriability problem (certain kinds of ideas cannot be fully appropriated by those who develop them)
   $\longrightarrow$ Nelson (1959), Arrow (1962)
2. Emphasize differences in objective functions and incentives systems between academia and private sector
   $\longrightarrow$ Dasgupta-David (1994), Carmichael (1988)
3. Analyze the effects of Bayh-Dole on flow and importance of university patents, and question the existence of an "anti-commons effect" of IPR protection
   $\longrightarrow$ Henderson-Jaffe-Trajtenberg (1998), Murray-Stern (2004), Lach-Schankerman (2004)
4. Multi-stage process
   $\longrightarrow$ Hellman-Perotti (2004)

Basic Framework

- *Modeling strategy*: keep at a minimum the differences between academia and private sector, profit maximizing firms
- Multi-stage research line, where probability of success at any stage depends upon:

  1. number of active scientists
  2. research strategy they pursue

  $\longrightarrow$ with n scientists at stage j who begin with idea I_{j-1} and follow "practical" strategy, probability $\phi(n)$ of getting new idea I_j

Basic Framework

$\longrightarrow$ we consider two specifications:

perfectly correlated draws, with $\phi(n) = p$ for all $n \geq 1$

independent draws, with $\phi(n) = (1-(1-p)^n)$; here, n is meaningfully endogenous

Basic Framework

- Instead of practical strategy, scientist may follow "alternative" strategy, which yields zero probability of success

  $\longrightarrow$ though later consider case where alternative strategy may spawn new lines

- Each scientist has outside option R, will work for this wage if free to follow preferred strategy

- But if scientist works on less-favored strategy, suffers disutility of z

Basic Framework

- Scientists don't know preferences ex ante until they have been exposed to prior idea, and with their employer they cannot write contracts contingent on these or on choice of strategy ex post
- Ex ante probability that a scientist prefers practical strategy is α

  $\longrightarrow$ for simplicity, perfect correlation in preferences across all scientists at a given stage

Basic Framework

- In **academia**, the scientist has control rights over choice of strategy

  $\longrightarrow$ academic wage will be

$$w_a = R;$$

  $\longrightarrow$ with probability α all n scientists work on practical strategy, with probability $(1-\alpha)$ all n work on alternative strategy

  $\Longrightarrow$ probability of advancing to next stage is

$$\alpha\phi(n)$$

Basic Framework

- In the **private sector,** the entrepreneur buys an idea, hires scientists to work on it

  $\longrightarrow$ once it becomes clear which strategy is practical, entrepreneur forces scientists to work on it (e.g through choice of lab equipment)

  $\longrightarrow$ cannot commit to do otherwise

  $\longrightarrow$ private-sector research wages will be:

$$w_p = R + (1 - \alpha)z.$$

  $\Longrightarrow$ probability of advancing to next stage is

$$\phi(n)$$

Analysis of Basic Model

$\longrightarrow$ start with perfectly correlated draws, so $n = 1$ at all stages

- Last stage k :

  $\longrightarrow$ private sector generates payoff:

  $$P_k = pV - w_p = pV - (R + (1 - \alpha)z)$$

  $\longrightarrow$ academia generates payoff:

  $$A_k = \alpha pV - w_a = \alpha pV - R$$

  $\Longrightarrow$ private sector research dominates academic research whenever:

  $$P_k > A_k \Longleftrightarrow pV > z.$$

  $\longrightarrow$ let

  $$\Pi_k = \max\{P_k, A_k\}$$

Analysis of Basic Model

- Stage $(k-1)$:

  $\longrightarrow$ private sector generates payoff:

$$P_{k-1} = p\Pi_k - w_p$$

  $\longrightarrow$ academia generates payoff:

$$A_k = \alpha p\Pi_k - w_a,$$

  where $\Longrightarrow$ private sector dominates academia whenever:

$$P_{k-1} > A_{k-1} \Longleftrightarrow p\Pi_k > z.$$

Analysis of Basic Model

- Stage i :

  $\longrightarrow$ private sector generates payoff:

$$P_i = p\Pi_{i+1} - w_p$$

  $\longrightarrow$ academia generates payoff:

$$A_i = \alpha p\Pi_{i+1} - w_a,$$

  where

$$\Pi_{i+1} = \max\{P_{i+1}, A_{i+1}\}$$

  $\Longrightarrow$ private sector dominates academia whenever:

$$P_i > A_i \Longleftrightarrow p\Pi_{i+1} > z.$$

Results

1. Academia tends to dominate private sector research in earlier stages since Π_{i+1} increases in i; thus it cannot be optimal to have academia operate at later stages than private sector.
2. For k sufficiently large, the line is not viable if entirely managed by the private sector:

   $\longrightarrow$ by contradiction, if it was entirely managed in the private sector:

   $$\Pi_1 = p^k V - (1 + p + ... + p^{k-1}) w_p$$

   $\longrightarrow$ but the above expression is negative if $z > 0$.

Results

3. Academia is viable at earlier stage than private sector if for some i:

$$p\Pi_i - w_p < \alpha p\Pi_i - w_a = 0$$

that is

$$w_a = R < \alpha z.$$

4. More generally: there exists a unique cut-off point i^* such that it is socially optimal:

that research be done in academia if $i < i^*$

that research be done by private sector if $i > i^*$

the cut-off stage i^* is: (i) decreasing in V; (ii) increasing in α; (iii) increasing in z.

Results

- Given optimal transition policy, project satisfies ex ante feasibility (EAF) if $\Omega(i^*) > 0$, where $\Omega(i^*)$ is the ex ante value of project if managed optimally
- Can contrast optimal policy with "early privatization" whereby project moves to private sector as soon as private-sector value is positive

  $\longrightarrow$ e.g, revenue-maximizing TTO facing competition.

Results

- Two costs of early privatization with $n = 1$

  (i) inefficiently high labor costs

  (ii) possible violation of EAF constraint, so that project may not get started in the first place

  $\longrightarrow$ but note that if project gets started, early privatization always raises odds of success. This no longer holds when n varies, as in independent-draws case.

Complementarity beteen openness and freedom (1)

- Suppose two parallel research lines, 1 and 2.
- With positive probability ϕ, if researcher on line 1 does not want to pursue practical strategy on that line, yet if informed about line 2 he will prefer to work on practical strategy for line 2 (and vice versa)
- Openness increases the probability $[\alpha+(1-\alpha)\phi]$ that relevant project is undertaken in academia
- In private sector, practical project is always pursued anyway

Complementarity between Openness and Freedom

- Assume that, if an idea is successful in stage i, there is a probability γ of being able to match up with somebody able to try stage $i+1$ (so far we had $\gamma = 1$).

  $\longrightarrow$ what openness does is to increase γ.

- But there is an alternative to ex-post matching: while completing stage i, one can spend K in training costs, which in turn allows for a sure try on stage $i+1$.

Complementarity between Openness and Freedom

- In the private sector, the payoff at stage i is

$$p\Pi_{i+1} - w_p - K$$

with training, and

$$p\gamma\Pi_{i+1} - w_p$$

without training.

- In academia, the payoff at stage i is

$$\alpha p\Pi_{i+1} - w_p - K$$

with training, and

$$\alpha p\gamma\Pi_{i+1} - w_p$$

without training.

Complementarity between Openness and Freedom

- Results:

  1. Openness is optimal earlier on the line and training is optimal later
  2. Training starts becoming optimal earlier for private sector than it is for academia
  3. A necessary and sufficient condition for it to be optimal to switch directly from freedom and openness to private sector and training, is:

$$K \in [\alpha z(1-\gamma), \frac{z(1-\gamma)}{\gamma}].$$

- Note that the size of the above interval increases with z and also with γ for $\gamma \geq \frac{1}{\sqrt{\alpha}}$.

In words……

- From a control rights perspective, academic researchers will be more sensitive to shifts in openness, for at least two reasons
  - Researchers who are choosing their own research direction are less willing (and arguably less able) to negotiate for access to proprietary knowledge or tools – higher costs, lower direct benefits
  - A more open environment induces the investigation of a greater variety and number of research paths, which will be at first reflected in an increase in more basic research
- Thus, openness and freedom complement each other!!

Openness and basicness of research

- Let us abstract from distinction between academia and private sector research and assume a two-stage line entirely managed by private sector
- Openness facilitates transition to next stage in research line….
- Then one can show that openness encourages stage-1 (basic) research more than stage-2 (applied) research

Thus increasing openness..

- Enhances academic research more than private sector research
- Enhances more early stage research
- May increases overall flow (and diversity!) of research lines

Part 2: Mice

joint with F.Murray and S. Stern


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Phenomenon

Harvard Oncomouse

- Leder & Stewart, Harvard 1984 develop the "Oncomouse"
  - First mouse with genes inserted to predispose mouse to cancer
  - A significant advance along two dimensions:
    - Advancing *basic research* into the role of genes in cancer
    - An input into *applied research* focused on cancer therapies
- Oncomouse is a "dual" discovery & serves as foundation for
  - On-going scientific discovery AND
  - Translation, innovation & economic growth
- Harvard is granted US patent in 1988 & signs an *exclusive* license with DuPont
  - DuPont severely limits licensing, and imposes onerous licensing restrictions (e.g., reach-through rights and article review)
  - Key scientists claim that, in order to build on the Oncomouse discovery, need for higher level of openness and accessibility
  - Not simply a matter of a licensing "fee" but concerns about academic "freedom"
- Ultimately, through direct intervention by NIH (Harold Varmus), low-cost independent access to Oncomice through the Jackson Laboratory

Empirical Predictions

- A shift in the commitment to openness of key scientific inputs (research mice) should influence the rate and nature of follow-on scientific progress
  - The rate of follow-on publications
  - Academic versus Industry
  - Basic versus Applied
  - High versus Low “quality” publications
- However, testing these ideas requires disentangling the impact of “openness” from the fact that more “open” inputs may tend to be more applicable to academic, basic, high-quality research projects

The Mouse Revolution as a Research Setting

- Scientific research mice – a rich setting in which to study how institutions & incentives interact to facilitate scientific openness
- Over the past twenty years, a "revolution" in the use of genetically engineered research mice as a tool for life sciences progress
  - Mice could now be "engineered" to have a particular gene inserted or removed to mimic a disease e.g. cancer or diabetes
  - Over 13,000 specialized mice published in scientific literature
- The 2007 Nobel Prize in Medicine to Mario R. Capecchi, Martin J. Evans and Oliver Smithies for "gene modification in mice"

Why does openness matter?

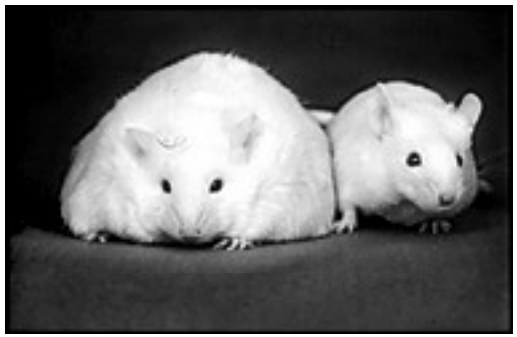
- While the development of genetically modified mice has tremendous for potential application in both basic and applied research, the ability to initiate research “lines” based on new mice require gaining access to those specific mice
  - Mice are costly to make & require specialized techniques including embryo manipulation, stem cell adaptation & molecular biology
  - Many mice are also covered by intellectual property rights and so require a license contract with up-stream researchers

The Jackson Laboratories (JAX): An Open Access Institution for research mice

Jackson Laboratory Mission

- Our mission is to improve the quality of human life through discoveries arising from our own genetic research and by enabling the research and education of others.
- Large not-for-profit research facility in its own right with leading researchers, directed by renowned scientists

• 2.3 million JAX® Mice distributed.
• JAX® Mice shipped to ~ 12,000 laboratories in the United States and 63 other countries.
• More than 2,800 varieties available as breeding mice, frozen embryos, or DNA samples.
• More than 800 varieties of “diseased” mice available including obesity, cancer, heart disease, Alzheimer's disease, & Huntington's disease



A mouse genetically engineered to be obese, with a normal mouse.

Identification strategy

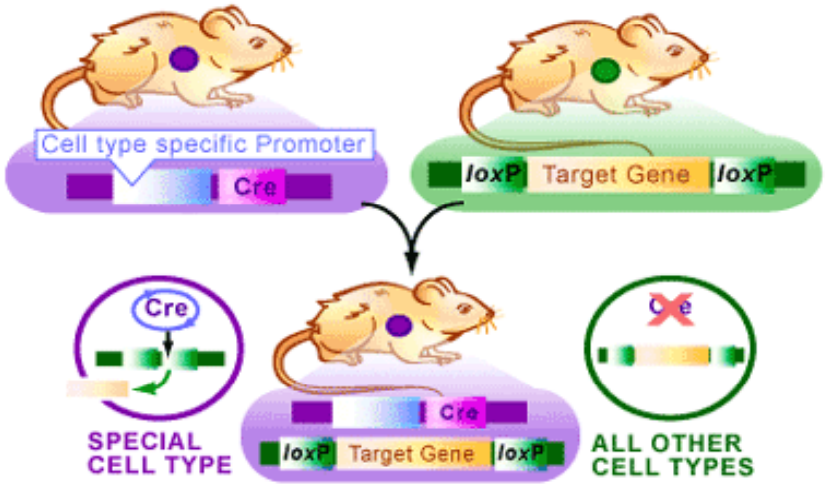
- Scientific research mice are linked with specific scientific research articles – so-called “mouse-articles”
- Citations to mouse-articles in other scientific publications observed over time
  - Citations in these research areas are specific – it is unlikely that one would cite a mouse article unless one was directly using that mouse or providing an explicit comparison with the results from a particular mouse model
- We identify arguably exogenous institutional “shocks” – natural experiments - to the openness of research mice.
  - These provide a source of variation by shifting the degree of openness associated with a mouse article, after the article has been published
- We also observe “control mice” who experience no change in openness subsequent to their initial disclosure through publication

Identification strategy

- *This set-up allows us to observe the use of research mice in "step-by-step" research in both the pre- and post- shock period, and compare the use of a "treatment" and "control" group*
- *We can evaluate the impact of the degree of openness on the rate and direction of follow-on research by examining how the pattern of citations to each individual mouse-article **changes** after the policy intervention*.

The Cre-lox-JAX agreement: A natural experiment in openness

- Cre-lox tool developed by DuPont to create genetically engineered mice in which a target gene can be “turned on or off” in a specific tissue in the body
- DuPont’s IPR (#4,959,317) covered any mouse made using Cre-lox technology & they used it to control Cre-lox mice distribution & follow-on use



THE SHOCK

July 1st, 1998: A Memorandum of Understanding between DuPont, JAX & the National Institutes of Health allowing JAX to distribute Cre-lox mice with a simple license

THE EXPERIMENT

Pre 1998 mice made using Cre-lox could not be shared without a costly license from DuPont which included arduous terms & conditions

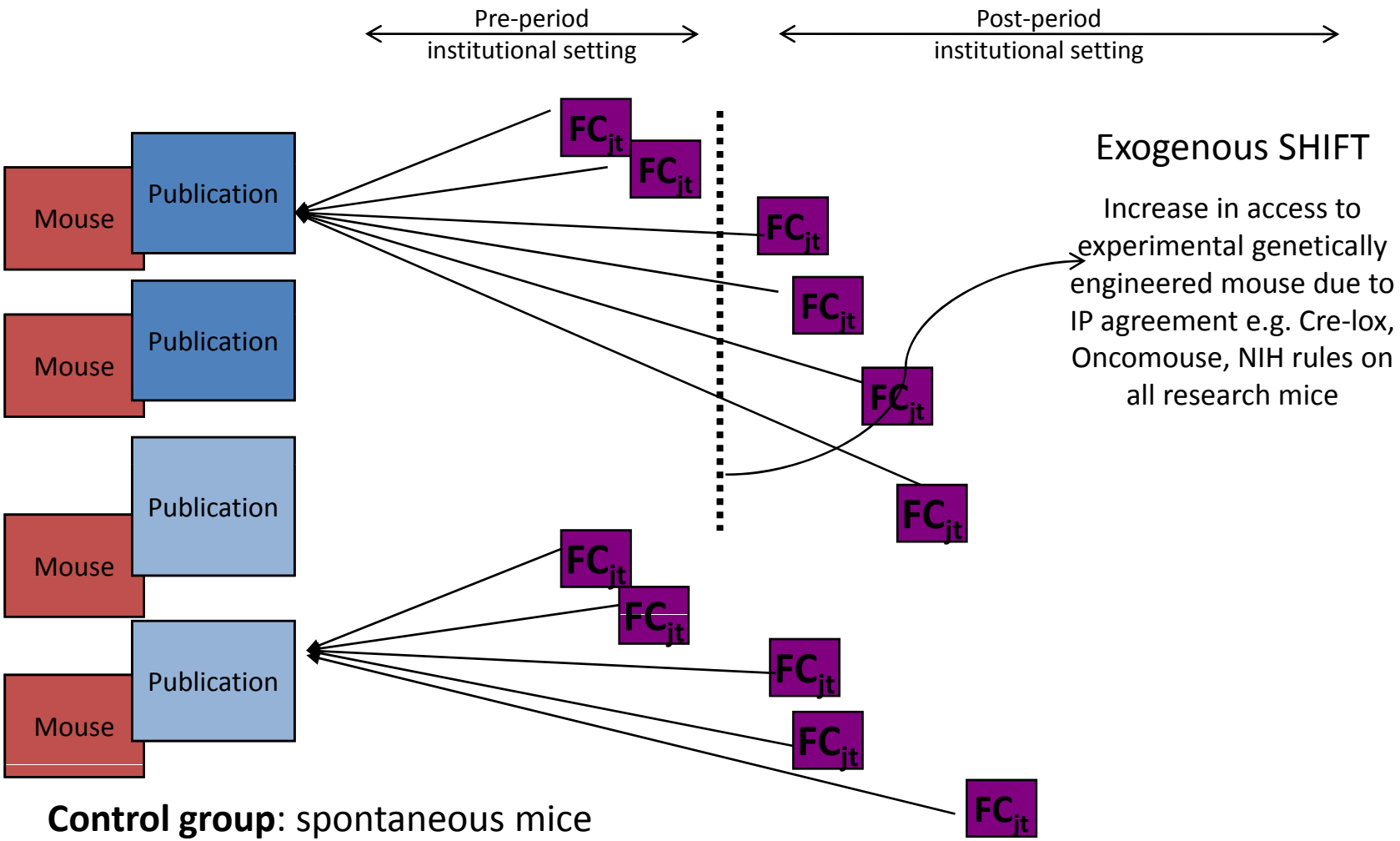
Post 1998 Cre-lox mice available for all researchers at non-profit institutions for internal research via JAX who make the mice readily available & manage the simple licenses

Natural experiments in the openness of scientific research mice

- **The JAX Shock**
  - Two similar JAX shocks impacting Cre-lox mice & Onco-mice both developed using technology controlled by DuPont Corporation
    - Cre-lox Memorandum of Understanding July 1st, 1998
    - Oncomice Memorandum of Understanding July 1st, 1999

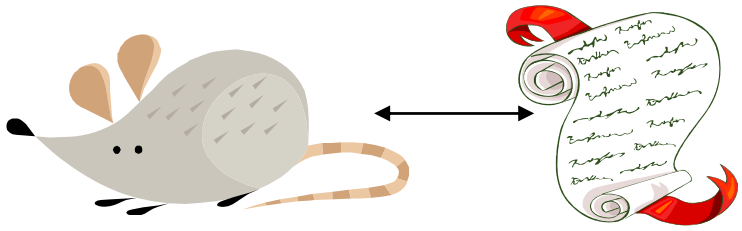
- **The NIH Shock**
  - NIH instigates a formal rule requiring that research mice generated with public sector funding be made available to all researchers but provide no formal oversight or mechanism
    - **July 1st 2001**: "Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources" (64 Federal Register 72090, December 23, 1999) incorporated into grant policies in 2001.

The Identification Strategy



Control group: spontaneous mice not subject to IP

Data



- Data Sources:
  - Mouse Genome Informatics (MGI) database catalogs over 13,000 mice & links each mouse to an original publication in a scientific journal
  - PubMed includes detailed information about each publication
  - ISI Web of Science Science Citation Index is used to gather citation information, including detailed characteristics for each cites
- Sampling Strategy
  - Focus on articles published between 1992 and 1998 (the year of the JAX Shock)
  - Three types of mouse articles
    - “JAX Shock” mouse articles
    - “NIH Shock” mouse articles
    - “control” mouse articles (spontaneous mutation)

Data

- Current Analysis: 138 Mouse Articles (key findings are robust with a greatly expanded dataset of 2638 mouse articles)
  - For each mouse in the sample, we collect detailed information about each of the forward citations to the original mouse article
  - Code key article / author characteristics
    - Public versus Private Sector Authors (by lead author or *any* author)
    - Basic or Applied Journal
    - Paper "quality" as reflected in the journal "impact factor"

Key Citation Measures

- *Forward Citations*$_{jt}$*:* # of Articles Citing *j* in year *t*
- *Public (Private) Citations:* # of Articles where the *lead* author lists a public (private) sector institution as an affiliation
- *Basic (Applied) Citations:* # of Articles published in a journal with a basic (applied) orientation
- *Top-Tier (Non-Top-Tier) Citations:* # of Articles published in a top-tier (non-top-tier) journal

Estimation

- Our differences-in-differences approach to the identification of openness relies on observing variation in openness over time
  - POST-SHOCK = 1 for citation after "exogenous" shock
- To account for count data and over-dispersion, consider a negative binomial (conditional) fixed effects estimator:

$$FORWARD\ CITES_{i,t} = f(\varepsilon_{i,t}; \gamma_i + \beta_t + \delta_{t-pubyear_i} + \psi POST-SHOCK_{i,t})$$

- We also incorporate a "window" period to account for the "transition" years between the time of the shock and its impact on observed publications (two or three years)
- Finally, our analysis is primarily interested in comparing the impact of the shock on different citation margins (e.g., public versus private citations)

$$\psi_{POST}^{PUB} > \psi_{POST}^{PRIV}$$

$$PUBLIC\ CITES_{i,t} = f(\varepsilon_{i,t}^{PUB}; \gamma_i + \beta_t + \delta_{t-pubyear_i}^{PUBLIC} + \psi_{WIN}^{PUBLIC} OPENNESS\ WINDOW + \psi_{POST}^{PUBLIC} POST-OPENNESS_{i,t})$$

$$PRIV\ CITES_{i,t} = f(\varepsilon_{i,t}^{PRIV}; \gamma_i + \beta_t + \delta_{t-pubyear_i}^{PRIV} + \psi_{WIN}^{PRIV} OPENNESS\ WINDOW + \psi_{POST}^{PRIV} POST-OPENNESS_{i,t})$$

Endogeneity issues

- To which extent are JAX shocks truly exogenous?
- Isn’t there something particular with Cre-lox or Onco mice?

The Impact of Openness: The Level of Follow-on Scientific Research

Negative Binomial Models	**Forward Citations**		
Post-Openness Shock	**1.357**	*1.174*	
Post-JAX			**1.709**
Post-NIH			1.132
Article Effects	**Random**	**Fixed**	**Fixed**
Age FE, Calendar Year FE, Transition Window Effects	**X**	**X**	**X**

- Coefficients are reported as incident rate ratios (percentage impact relative to 1.0)
- With article FE, the Overall Openness shock is modest (and marginally significant). The JAX shock is large and highly significant while the NIH shock is smaller and noisy.

The Impact of Openness: Public versus Private Research Output

Two-Equation Negative Binomial Model	**Public Forward Citations**	**Private Forward Citations**
POST-JAX	**1.698**	1.542
POST-NIH	1.144	*1.532*
Article Effects	**Conditional Fixed Effects**	
Age FE, Calendar Year FE, Transition Window Effects	**Y**	**Y**

- Coefficients are reported as incident rate ratios (percentage impact relative to 1.0)
- Post-JAX, Public is quantitatively large and highly significant. The impact of a shock to openness seems to be concentrated in a response by public sector researchers.

The Impact of Openness: Basic versus Applied Research

Two-Equation Negative Binomial Models	**Basic Forward Citations**	**Applied Forward Citations**
POST-JAX	**2.260**	**1.500**
POST-NIH	1.055	**1.490**
Article Effects	**Conditional Fixed Effects**	
Age FE, Calendar Year FE, Transition Window Effects	**Y**	**Y**

- Coefficients are reported as incident rate ratios (percentage impact relative to 1.0)
- While the overall effect is positive and significant, the impact of Post-JAX on Basic research is particularly salient.

The Impact of Openness: Top-Tier versus Non-Top-Tier Citations

Negative Binomial Models	**Top-Tier Forward Citations**	**Non-Top-Tier Forward Citations**
POST-JAX	**2.422**	*1.278*
POST-NIH	**1.331**	1.151
Article Effects	**Conditional Fixed Effects**	
Age FE, Calendar Year FE, Transition Window Effects	**Y**	**Y**

- Coefficients are reported as incident rate ratios (percentage impact relative to 1.0)
- The impact of openness seems to be concentrated in a dramatic increase in top-tier publications.

Interpretations

- Greater openness increases the rate of follow-on research permanently by at least 15-20%, and more than 60% for materials that are provided through an open-access institution such as the Jackson Laboratories
- The effect seems to be concentrated among those researchers and for research outputs which are more closely tied to the norms of “Open Science”:
  - Public Sector Research Outputs
  - Journals with a “Basic” Orientation
  - Higher-quality journals in terms of subsequent impact
- Novel direct evidence for the causal impact of openness on the *direction* of scientific research

Some Concluding Thoughts…

- This experiment supports the ADS approach against a pure appropriability approach…
- ….as it hints at a complementarity between freedom and openness.
- DuPont might have benefited from the Cre-lox shock after all….