Funding for Scientific Research: Getting Incentives Right is Important

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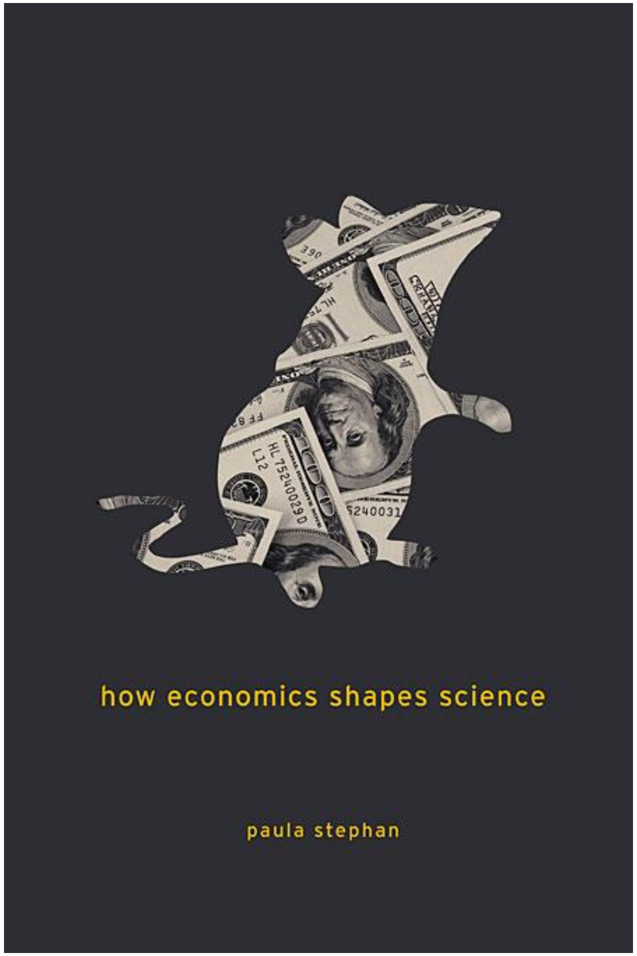
Presentation Based on book



Considerable Evidence that Research Contributes to Economic Growth

- Two Examples should suffice
  - Life expectancy: increased by 14 years since 1940
    - Research which led to the development of antibiotics and treatments for cardiovascular disease has played a role;
    - Research which leads to changes in behavior—anti- smoking campaign —also plays a role
  - Advances in Information Technology have contributed to economic growth. Advances come from research that has led to new products, such as
    - Integrated Circuit
    - World Wide Web
    - Modern capacity hard drives

Public Sector Plays Important Role

- Much of research that (eventually) contributes to economic growth takes place in public sector and is supported by public funds
- This research is not sufficient for growth: Industry plays an absolutely crucial role
- Given important role that public research plays and long lags between research and economic growth, policies that affect public research today will have an impact for many years to come

Crucial to Get More Out of Public R&D Budgets: Focus Today

- Always important—but more important in times of austerity
- Book explores how public research organizations and scientists respond to incentives
- It's a good news/bad news story
  - Get incentives right, and one can enhance productivity
  - Get incentives wrong, and there are severe consequences for productivity

Focus is on R&D at Universities in the United States

- System I know the best
  - Served on National Science Foundation Advisory Boards
  - Served on Advisory Board for large institute at NIH (National Institutes of Health)
  - Serve on Board on Higher Education, National Research Council
- U.S. system is often held up as an example for other countries

Discussion Focuses on Five Outcomes/Problems Related to Incentives in Funding System

- Risk Aversion
- Funding researchers who are increasingly older
- High cost of review/submission
- Human resource issues (3)
- Overinvestment in certain areas of science

Additional Themes

- Scientific research can be expensive; costs affect research practices
- Provide some background regarding how U.S. public research funds are distributed

Research Is Expensive

- Researchers—can easily spend $500,000 for personnel in a small lab
- Equipment
  - Small scale—sequencers--$500,000
  - Large scale—telescopes, colliders—billions of dollars
- Facilities
- Materials
  - Even mice!

Mice

Material

- Mice are king when it comes to research
- 90% of all animal models used in research are mice
- Over 30 million in use

Why a Mouse on Cover of Book?

- Mice are perfect example of expense and how costs affect practice of science
  - At least 30 million mice currently being used in research
  - Expensive—off the shelf costs around $40, but designer mice, such as onco mice, can easily cost $3,500 to create
  - Keeping mice is expensive—in France, costs about .40 € per week per mouse. If you have 20,000 mice quickly adds up to 400,000 € a year.
  - Mouse "packages" used to recruit researchers
  - Mice play an important role in discovery: recent example of "tau" protein and Alzheimer's disease
  - Nobel prizes have been awarded in recent years to individuals who have "designed" innovative mice

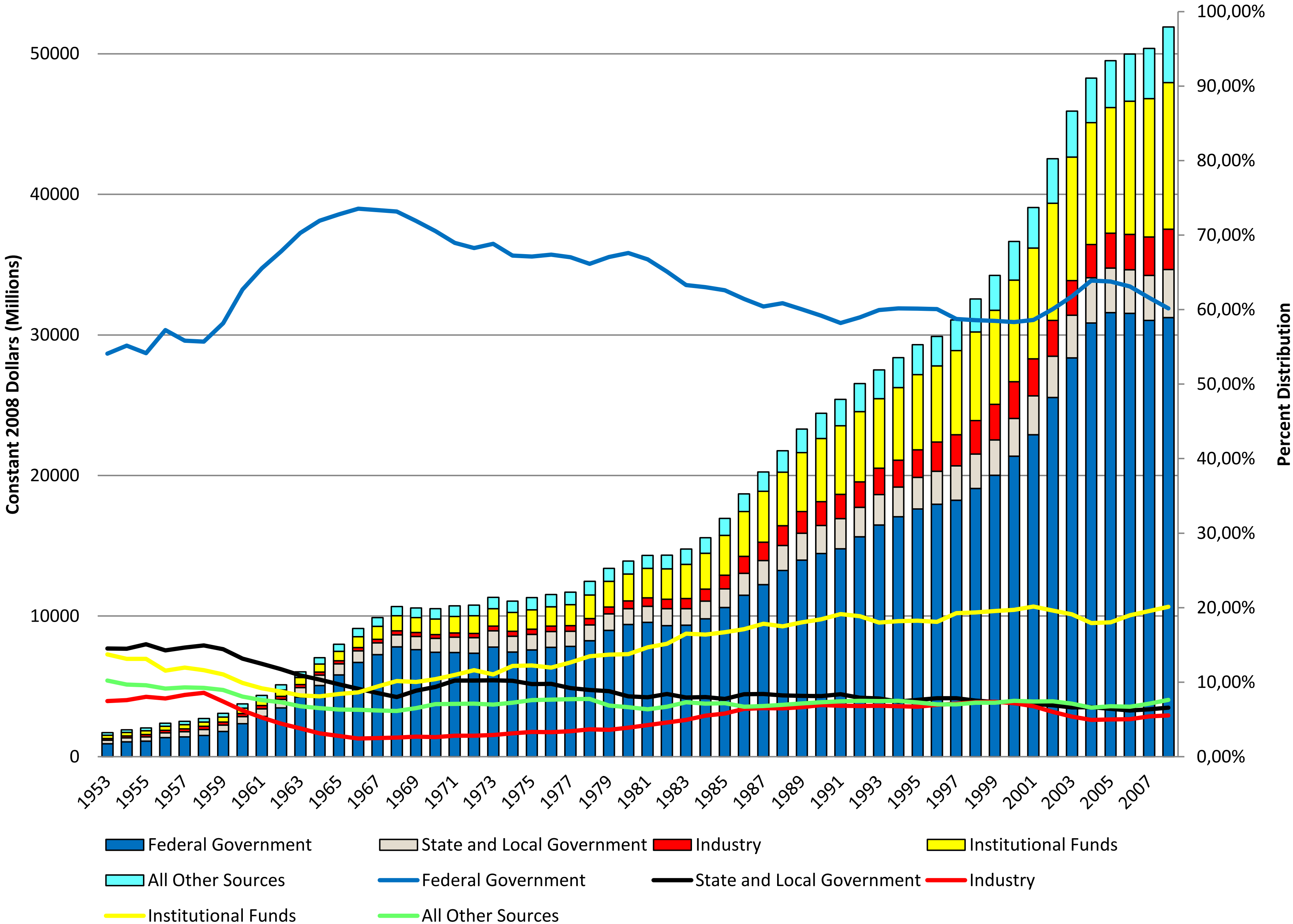
Mice continued

- Cost of mouse upkeep factor encouraging Tian Xu of Yale University to work at Fudan University for 3 months each year
  - Fudan provides facilities for 45,000 mouse cages (usually 5 to a cage)
  - Could cost over $12,000,000 annually in U.S. to keep.
  - Also issue of where one could keep that many mice in US—more mice than all the mice at Johns Hopkins

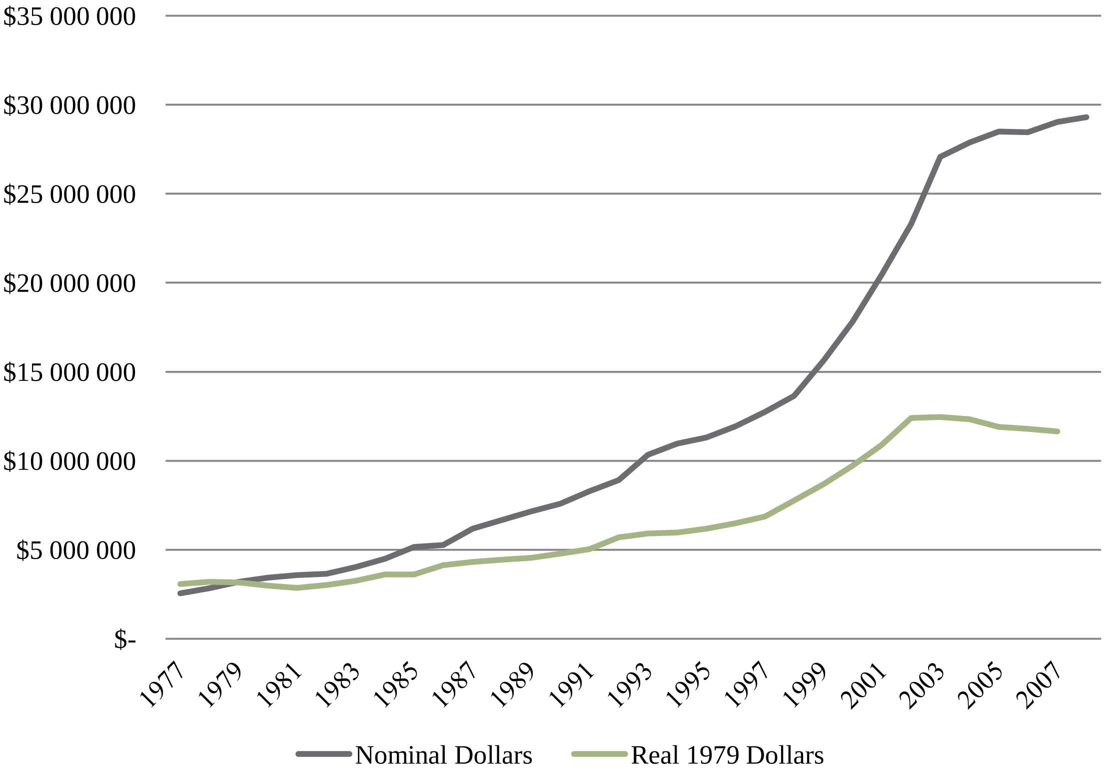
Three Minute Lesson on U.S. System

- Universities receive approximately $55 billion for R&D annually
- 60% comes from the Federal Government
- Over half of that is National Institutes of Health funding (NIH)
- National Science Foundation (NSF) is about 10%; Department of Defense, Department of Energy also support university research

Support for academic R&D, by sector: 1953–2008



NIH Budget 1977-2007



University Research in U.S.

- U.S. universities and medical schools perform 75% of research that is published in the U.S.
- Research in universities organized around a faculty member’s lab.
  - Labs “belong” to faculty
  - Faculty receive startup packages from university when hired that provide funds for equipment, postdoctoral students and graduate students.

Amon Lab: Whitehead Institute

- Amon works on cell division, focusing on how "cells make sure their chromosomes separate in the right way."

And Sometimes

Christine White and Group: U. of Illinois, chemistry

Faculty Labs

- Faculty on their own after 3 years to find funding for their lab
- Must also in most universities find funds to support part of their own salary
- Particularly true in medical schools where faculty must find outside funds to pay themselves as well as support their lab

Peer Review

- Seen as gold standard for distributing funding
  - Encourages freedom of intellectual inquiry
  - Promotes sharing of information
  - Provides incentives to remain producte throughout one's career
  - Open in sense that last year's "loser" can be this year's winner
  - Encourages entrepreneurship—getting money from a venture capitalist is much like getting money from a federal agency—one has to "sell" one's research
- 6 out of 10 federal dollars distributed by peer review to university researchers in United States
- Majority of grants are for 3-5 years
- Faculty salary is part of the grant; also funds for graduate students, postdocs, equipment and materials and "indirect recovery."
- Faculty in "soft money" positions must support themselves entirely off grants.

How Peer Review Functions

- NIH and NSF use somewhat similar systems
- Researcher submits a proposal for a specific project
- Reviewed by a panel that scores it
- Funding decisions then made
- But considerable agency differences regarding
  - What is paid for
  - Size of budgets
  - Who reviews
  - Who has final say on grant
  - Ability to formally resubmit

NIH

- 27 institutes and centers
- Largest is NCI—National Cancer Institute
- Followed by NIAID—Allergy and Infectious Disease; NHLBI—Heart, Lung and Blood
- NIGMS—General Medicine—is 4th and supports most basic research--$2 billion
- Some institutes at NIH run internal labs
- By law, 5% of NIH funds must support SBIRs.

Research Grants at NIH

- Bread and butter for university biomedical researchers
- Budget includes funds for staff, graduate students, postdocs, faculty salary, equipment, materials.
- Indirect cost is charged on top of this—about 50%
- R01 is most common grant; it lasts for 3-5 years.

Peer Review at NIH

- Faculty submit (3 submission rounds a year)
- Proposal assigned to a "study section"
- Triage occurs—half the proposals not formally discussed
- Comments and scores provided on non-triaged
- Scores standardized by pooling them with others from recent meetings
- Like golf: low score is a good score
- A payline is determined; proposals falling within the payline are funded; vast majority of those outside the payline are not although exceptions are made
- Reviewed by General Council of each institute 3 times a year
- Historically could resubmit 2 more times if turned down.

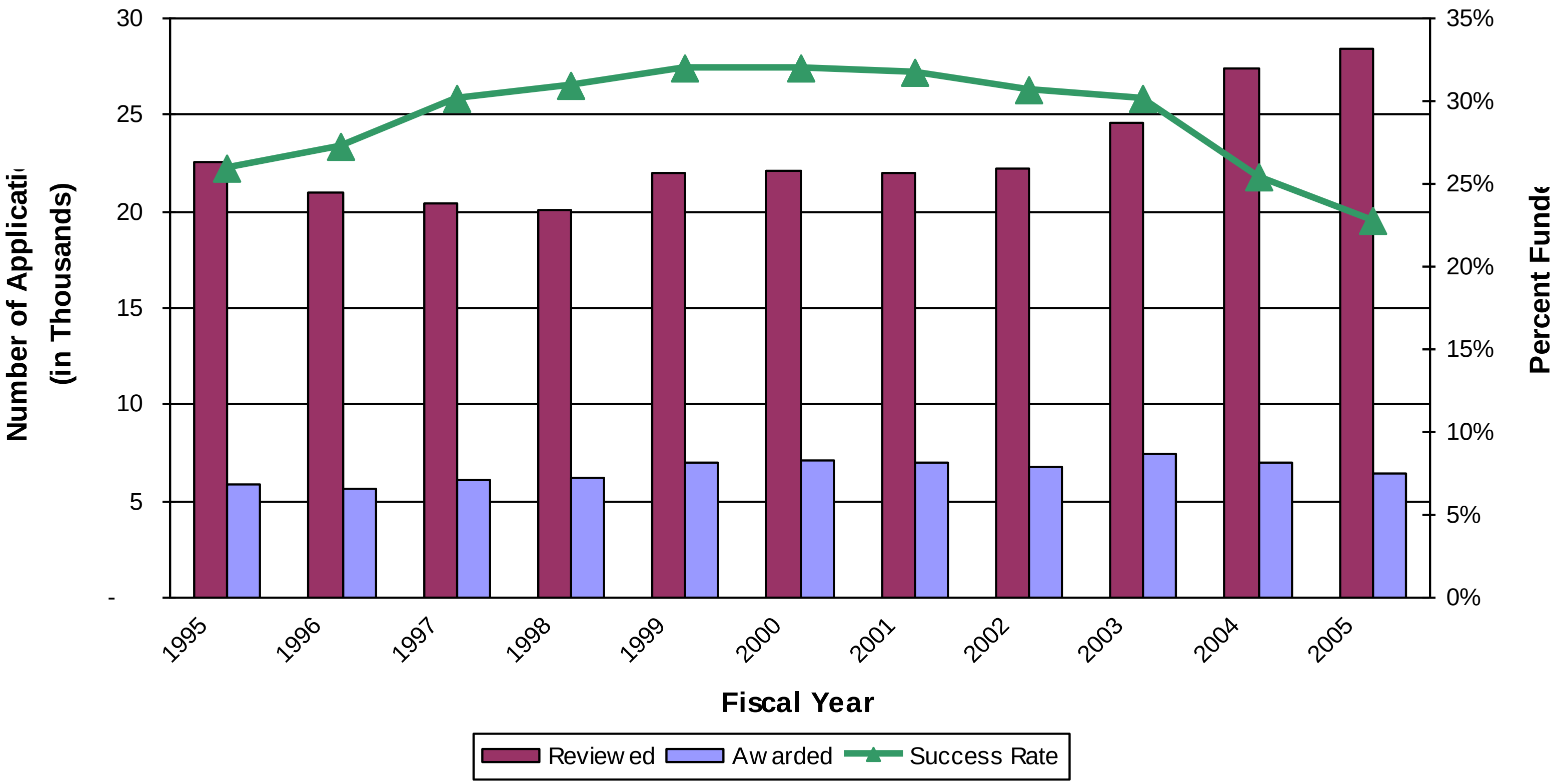
What Counts?

- Considerable weight on strong preliminary data: “no crystal, no grant.”
- Results from previous grant carry considerable weight. Publications are important
- Lineage counts indirectly…comments concerning who one trained with, etc.

Success Rates

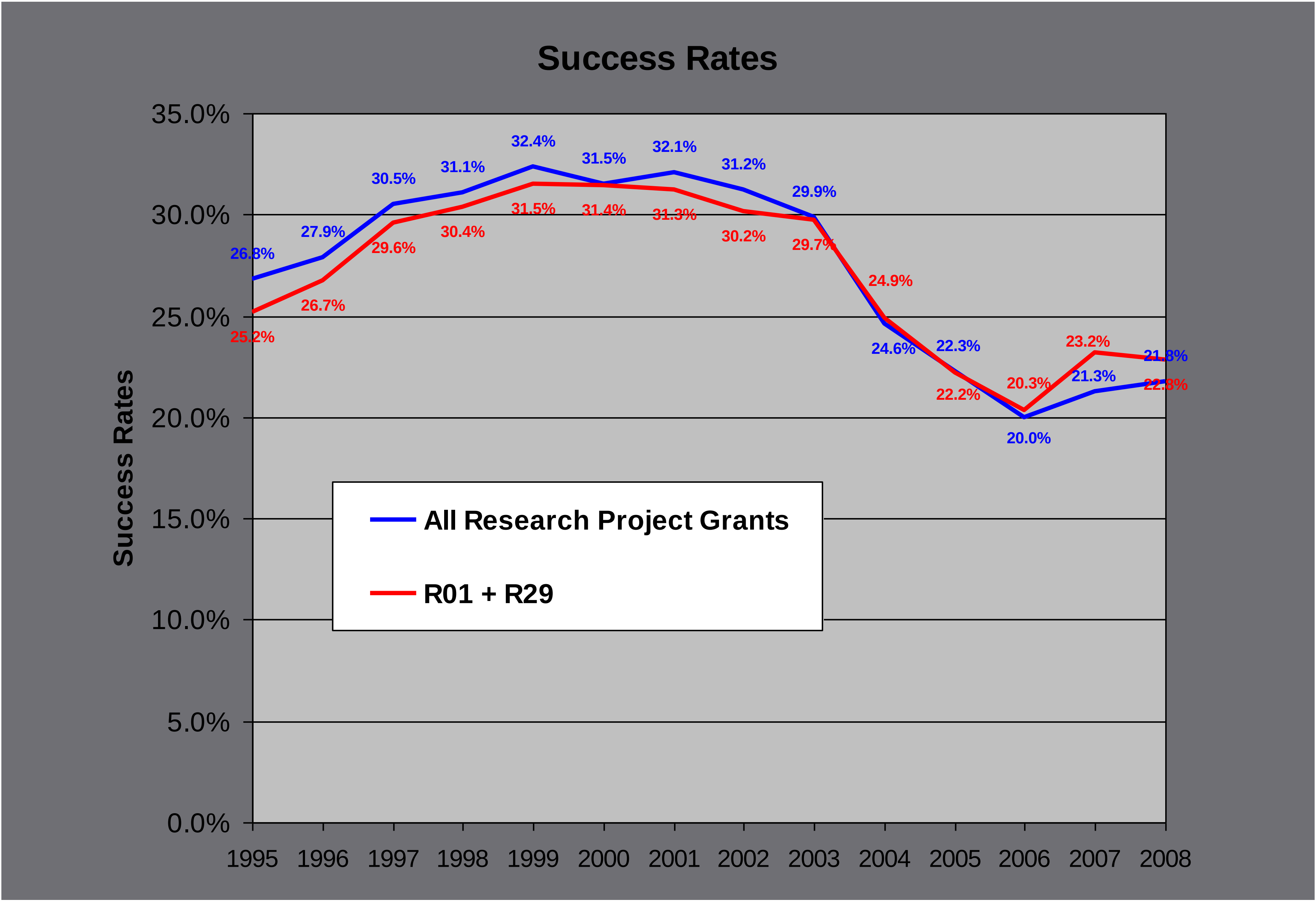
- Historically between 10% to 40%
- Varies by time and by institute.

Number of NIH Competing R01 Equivalent* Applications, Awards and Percent Funded (Success Rate)



NIH, OER: "Investment…"

R01 Equivalent* Includes R01, R23, R29 and R37


Success Rates
Success Rates
35.0%
30.0%
25.0%
20.0%
15.0%
10.0%
5.0%
0.0%
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
All Research Project Grants
R01 + R29
26.8%
27.9%
30.5%
31.1%
32.4%
31.5%
32.1%
31.2%
29.9%
24.6%
22.3%
20.0%
21.3%
21.8%
25.2%
26.7%
29.6%
30.4%
31.5%
31.4%
31.3%
30.2%
29.7%
24.9%
22.2%
20.3%
23.2%
22.8%

FASEB

Grant Renewals

- Researchers can apply to renew a grant
- Most do
- Incentive to do so: renewals do better than new proposals
- Not uncommon to be supported on same grant for 40+ years. One instance of 52 years.

Pluses of System

- Investigator initiated; freedom of intellectual inquiry;
- Open in sense that new submissions are accepted; losers can become winners
- Encourages scientists to be productive throughout career
- Encourages entrepreneurship: getting money from a venture capitalist similar to getting money from a funding agency.

And World Class Research

- 2009 Nobel Prize in physiology awarded to individuals with long tradition of NIH support for their work regarding telomerase. Basis for a number of clinical trials
- 2001 Nobel Prize in physiology awarded for work that shows that protein kinases controls cell division. More than 10 drugs have FDA approval based on this finding for treatment of various cancers
- Progress in pharmacogenomics

Warfarin

- Widely prescribed (20 million plus prescriptions a year in US)
- Dose must be carefully controlled
- Adjusted correct dose can vary by 20-fold across individuals
- Pharmacogenomics consortium (21 groups, 9 countries) combined genomic data for 5000 individuals with known warfarin dose
- Consortium benefits from participation of multiple groups and countries given that adverse drug events are rare
- Found inclusion of genomic information can increase accuracy of predicted dose
- May improve outcomes, decrease costs

Modern Pharma Has Benefited from NIH

- Considerable research that shows that Pharma industry has benefited from academic research supported by NIH
  - Cockburn and Henderson 1997
  - Gambardella 1995
  - Mansfield 1991

Problems: Risk Aversion

- Scientists avoid risk by only submitting proposals they see as “sure bets.”
- Why?
  - Need for faculty to obtain grants to support their salary—especially important for faculty on soft money—perhaps 35% of NIH investigators –no funding, no job!
  - Incentives to continue a line of research
  - Low probability of success (17 to 20 percent at NIH)—reviewers prefer proposals with convincing preliminary data—”no crystal, no grant”
  - Roger Kornberg: To quote the Nobel laureate Roger Kornberg, “If the work that you propose to do isn’t virtually certain of success, then it won’t be funded.”

Concern for Economic Growth

- Pretty clear that if most scientists are risk averse little chance that transformative research will occur, leading to significant returns from investments in research and development.
- Incremental research yields results, but in order to realize substantial gains need more people doing transformative work.

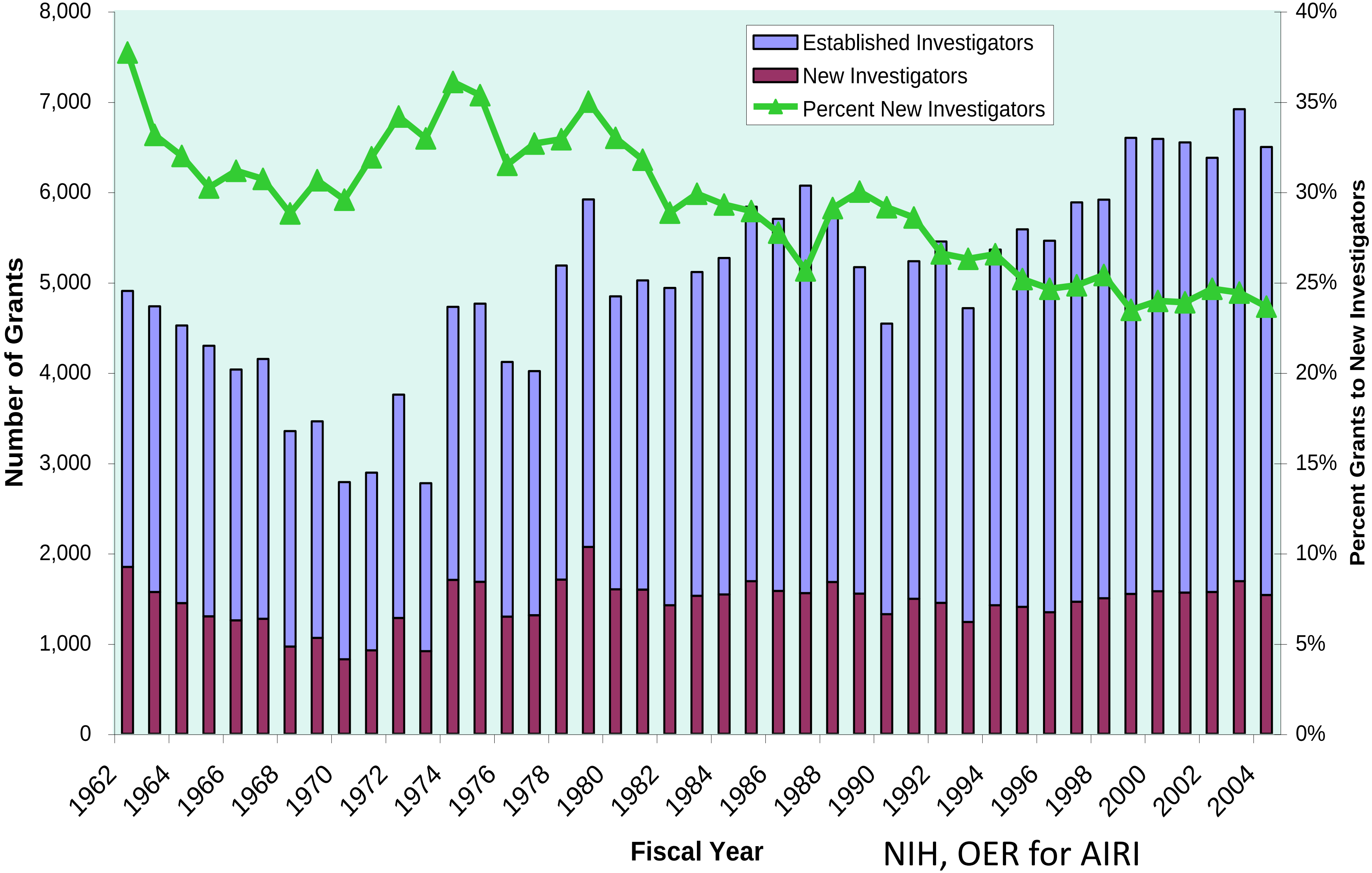
NIH Response

- Eureka and Pioneer awards
- Extremely low success rate
  - Pioneer had 2300 applicants—awarded 18

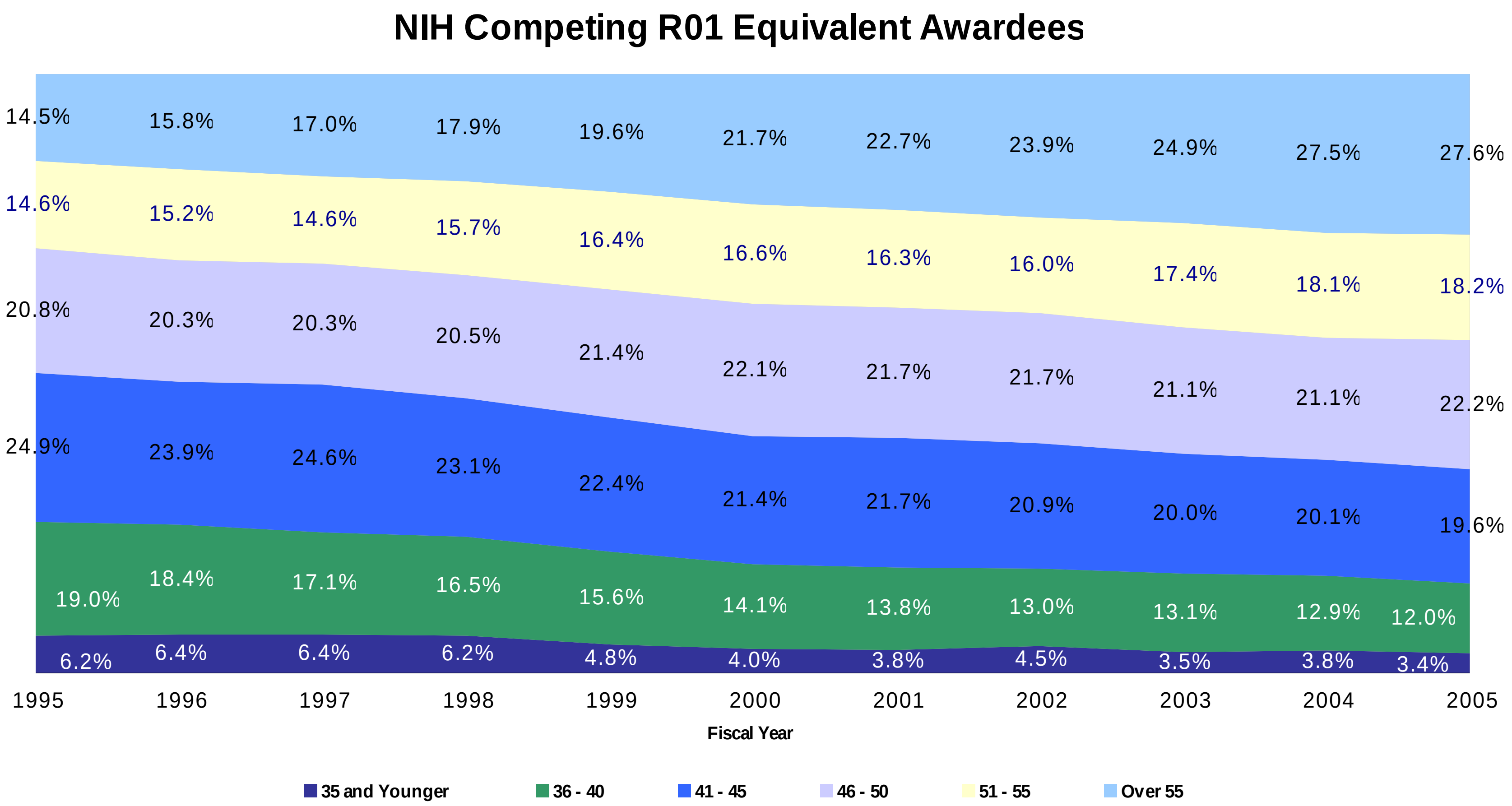
Problems: Age at Time of Award

- Number of new investigators funded remained almost constant during doubling; number of experienced investigators increased
- Success comes later:
  - 37.2 average age of new investigator in 1985
  - 42.4 average age of new investigator in 2006
  - Reasons: need for preliminary results; first time success low; institutions hiring later stage researchers
- Age distribution of concern because
  - Relationship between age and productivity
  - Need as a country to create a new generation of investigators

Number of New and Established Investigators Receiving Competing and R01 and R01 Equivalent Grants to 1962 to 2004



NIH, OER for AIRI



NIH, OER for AIRI

Zerhouni Response

- Just before stepping down as director in fall of 2008, Zerhouni declared it formal NIH policy to "support new investigators at success rates comparable to those for established investigators submitting new applications"
  - Things changed—in 2009 NIH supported 1798 new investigators, up from 1261 in 2006.
  - Quality concerns? Substantial increase in number of grants funded below the payline

Problems: Cost of PI Time; Cost of Review

- For researcher:
  - 42% of research time spent filling out forms, meetings, submission
- For reviewer and agency:
  - NIH 25-page proposal took 30 hours to evaluate, including seven hours for each of 3 assigned reviewers
  - Comes to about $1700 per proposal in terms of opportunity cost
  - NIH (and NSF) reported increased trouble getting scientists to agree to review—especially senior scientists; concern among investigators that their proposals are not properly reviewed by experts

NIH Response

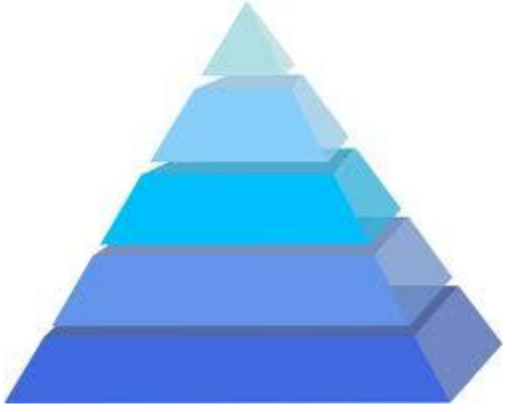
- Streamlined proposal format and procedure
  - Cut proposal from 25 to 12 pages
  - Can only resubmit once
  - All proposals get scored
  - Changed reviewer requirements:
    - Twelve meeting commitment now served out over six years rather than four.
    - Incentives: after 18 meetings—if reviewer chooses to do so—get an automatic grant extension of up to $250,00
    - Incentives: Must serve if one has three or more grants

Problem: Human Resource Issues

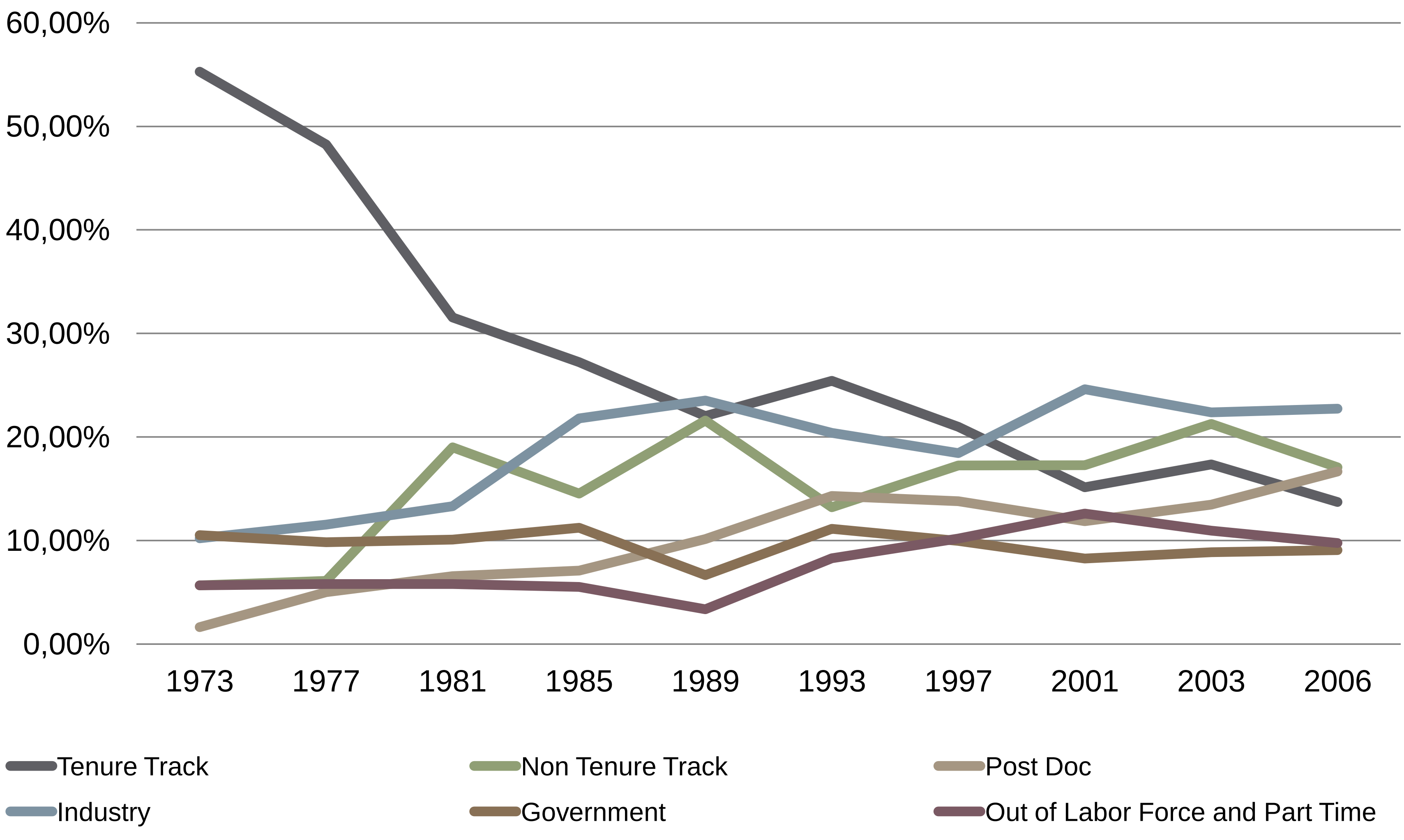
- Incentives to staff labs with graduate students and postdocs
- Many pluses
  - Fresh ideas
  - Flexible
  - Temporary
  - Cheap

Pyramid System (Scheme?)

- Works only if funding grows
- Increasingly difficult for young researchers to find independent research positions in academe or government. Increasingly difficult in industry as well
- Results in large group of disenchanted young researchers; socially inefficient



Biological Sciences: 5-6 Year Cohort



Even Best Have Problems

- 400 NIH Kirschstein postdoctoral fellows receiving awards 1992-1994.
- Not only best and brightest but also have advantage of entering market at or about the time of NIH doubling
- Career outcomes 2010:
  - 25% tenure track
  - 30% industry
  - 20% researcher in someone else's lab
  - 14% cannot be located
  - Remainder at colleges, institutes

Established Researchers' Response

- System works: "body of graduates students and postdoctoral fellows [supported on NIH funds] provides the dynamism, the creativity and the sheer numbers that drive the biomedical research endeavor." (NRC 2011)
- System has been "incredibly successful in pushing the boundaries of scientific discovery." (NRC 2011)
- Rationalize that the system is fair—students know outcomes and continue to come despite this
- "Let them be teachers."

Human Resources: Soft Money Positions

- NIH system that supports salary with no limit on number of months encourages universities to hire in soft money position
  - Estimate that 35% of NIH funding goes to people on soft money
  - Not just those without tenure—many individuals in medical schools who are tenured to no have "money" behind their position
  - Discourages risk taking— "funding or famine"

Meaning of Tenure at Medical School

- “Out of fashion to link tenure to salary”
- At 62 of 119 medical schools in the United States tenure is equated with a specific salary guarantee
  - at only 8 of these does this represent “total institutional support.”
  - at other 54 some form of limit on guarantee
- At 42 of 119 tenure comes with absolutely “no financial guarantee”

Hiring and Rewards

- United States known for strong research universities
- Having resources to attract and reward highly productive scientists is important component of this
- Creates wide salary differentials in departments and between universities

Salary Differentials

- Private-vs. public
  - Only one public institution (UCLA) in top 20 salary list. Pays over $40,000 less than top-paying Harvard
- Differences across and within Institutions
  - Differences within rank across institutions—faculty of same rank can earn three times as much as faculty of that rank at another institution
  - Wide differences within departments for same rank—in some instances faculty can earn twice as much as colleagues with same rank.

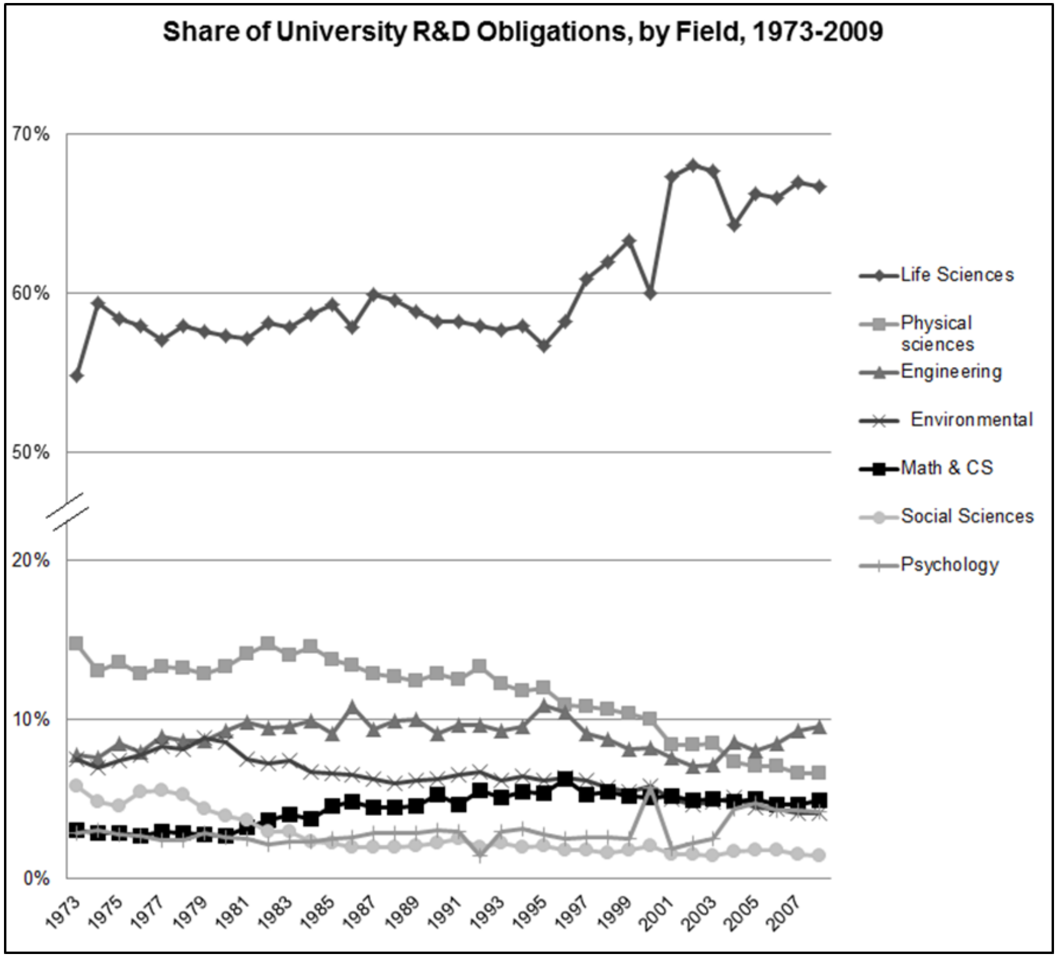
Inequality on the Rise in Academe

- Gap between the haves and have-nots is not as big as that in US society at large, but within academe inequality has grown at almost three times the rate of growth of inequality in the larger society.
- Inequality contributes to research productivity by attracting and rewarding productive people
- But where does one draw the line?

Two Concerns with Inequality

- The divide between rich and poor universities threatens to make more and more universities non-competitive when it comes to hiring and retaining top researchers. U.S. risks losing some of our great research universities—many of which are "public"
- Substantial income inequality within a university—and a department—threatens fabric of the university
  - Strong universities are built by faculty working together to build new programmes and curricula and by providing excellence in the classroom.
  - An over-emphasis on research productivity when it comes to rewards, with associated increase in income inequality, can significantly dull incentives to contribute to other objectives of the university.
  - Also reduces incentive for scientists to work together on research projects—yet we know that collaboration is extremely important in research.

Problem: Mix of What is Funded



Focus on Biomedical Sciences

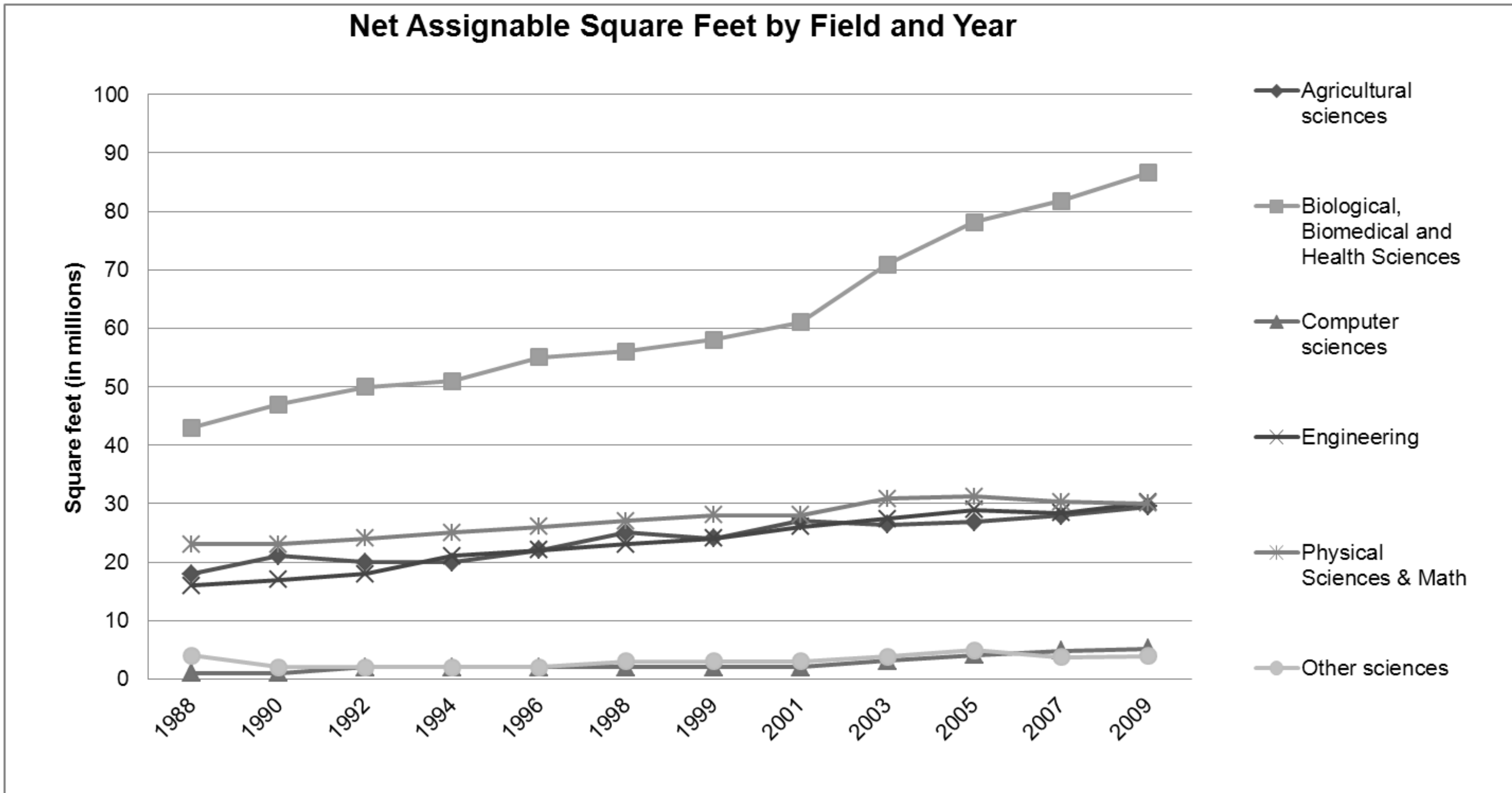
- Two-thirds
- Why?
  - Extremely organized disease-focused lobby in United States for biomedical research
  - Public is supportive
  - Congress is “old”

Age of Congress

- Average age of members of the House of Representatives in 2009 was 56.0;
- Average age of senators was 61.7
- Both chambers considerably older than at their “youngest” in 1981, when average age in House was 48.4 and the average age in the Senate was 52.5

Arlen Spector—3 time cancer survivor

Focus on Biomedical Sciences Led to a Building Boom at Universities



Incentives Played a Big Role

- Rules allow interest on debt to be included in calculating indirect rate
- Universities sought to fill new buildings with many researchers on soft money—no risk to universities in terms of salary commitment

Consequences

- Universities may have trouble servicing the bonds given that NIH budget is not growing
- Unless they default, “others” will pay
  - Students
  - Faculty
  - Other disciplines

Mix May Be Inefficient

- May be time to readjust the U.S. federal R&D portfolio
- Biomedical research has had a great run
- But unclear that marginal product of another dollar spent in biomedical research is as high as it once was.
  - Diminishing returns are likely present--suggested by slowed rate at which new drugs are being brought to market and less than stellar increase in U.S. publications associated with the doubling of NIH budget.
  - Many of breakthroughs that have contributed to better health outcomes have come from other fields of science—the laser and the MRI, for example.
  - Funds for the physical sciences in the United States (in terms of the percentage of federal research funding) are close to a 35-year low. of diminishing marginal productivity

Summing Up

- US system has produced great science.
- Much of this can be attributed to opportunities that have been available for researchers in the US, and the incentives underlying these opportunities.
- But incentives can have a downside as well as an upside.
- There are lessons that any country or group of countries should attend to when they think of emulating the US system.

A Word of Caution

- Beware of what funding is allowed for: consequences can easily become imbedded in the system
  - Soft money positions for faculty
  - Postdoctoral appointments and graduate students

More Money Not Always Answer

- Doubling of NIH budget between 1998-2002 showed that “money” alone is not the answer to many of the problems with the NIH system.
- Success rates at end were same as at the beginning
- Percent of proposals funded on first round declined from 60% to 30%. People were spending more time trying to get their grants.
- Little evidence doubling stimulated the market for university faculty. Few new hires
- Young researchers put at a particular disadvantage
- Some evidence that productivity (publications) has low correlation with amount of funding
- Little evidence that U.S. article output increased substantially during doubling

Questions/Comments

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