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"How Economics Shapes Science?"

TRANSCRIPTION

Thank you very much for the kind introduction, and thank you very much for inviting me to give this seminar at OST today. I think perhaps it's the fourth or fifth time I've come to OST, and it's always a pleasure to be here.

What I'm going to talk about today is funding for scientific research, and how getting incentives right is important. The presentation is based on my book, which I will shamelessly show you, and which has just come out.

Just by way of setting the stage for our discussion, there's considerable evidence that research contributes to economic growth. Let me just give you two examples. One is that life expectancy, in the last 70 years, has increased by 14 years. Why has this happened? Well, a considerable part of this happened as a result of research that has brought new drugs for the treatment of certain diseases, such as infection, but more recently has brought new drugs for the treatment of cardiovascular problems and diabetes, which has contributed to some increased life expectancy. But research also has contributed to increased life expectancy by linking certain kinds of behaviors to bad outcomes – such as information used by the anti-smoking campaigns, that comes from very serious research.

Look at what has happened to advances in information technology: a considerable amount of research shows how information technology has contributed to economic growth. This was done through fundamental research that created many new products and innovations, such as integrated circuits, the Web, the modern capacity hard-drives, etc.

It is important to realize that the public sector has played a very important role in a lot of the research that affects growth. Much of the research that eventually – and the "eventually" is pretty important – contributes to economic growth takes place in the public sector and is supported through public funds. Of course, it is important to point out that this research is not sufficient for growth: industry plays an absolutely crucial role, here. But today I'm going to focus primarily on public research funds.
Given this important role that public research plays and the really long lags that often exist between research and its economic impact on growth, policies that are affecting public research today will have an impact for many years to come on the economy.

So it is crucial to get the most out of public R&D budgets – or if not the most, to get more – and that is going to be my focus today. This is always important – and even more so in times of austerity. *Nature*'s editorial this week concerns exactly this and how, in the United States, there is an interest on the part of the administration of trying to use research funding more efficiently.

My book explores how public research organizations and scientists respond to incentives. I think of it as a "good news / bad news" story. If you get the incentives right, we can enhance productivity, but if you get them wrong, there are severe consequences for productivity.

In most of my examples today, I am going to focus on R&D at universities in the United States. I'm going to do this for two reasons: one, it is the system I know the best. I have considerable experience on serving on a number of government committees and advisory boards in the United States, I have been on National Science Foundation Advisory Boards, and I recently completed a three-year term at the National Institutes of Health (NIH), on the advisory board for General Medicine. I also serve on the Board of Higher Education and Workforce at the National Research Council. But what I know is not the only reason for the U.S. focus. The other reason is that the US system is often held up as an example and other countries have been interested in emulating this.

Today I will focus on five outcomes or problems that have been related to incentives created by the way we fund research. First, I'm going to talk about the strong risk aversion that seems to have developed among researchers in the US, because of the way grants have been structured and the consequences of that. Second, I'm going to talk about the way the incentives system has ended up funding much older researchers, and has had a very difficult time getting funding to younger researchers. Third, I'm going to talk about how we've ended up having a very, very expensive review system, and the amount of resources that consumes. Fourth, I'm going to talk about human resource issues that have evolved because of these incentives. Then I'll close by what may be for many people the most controversial thing, since I'm going to argue that, at least in the United States, we have underinvested in certain areas of science, such as the physical sciences and engineering.

There will be additional themes here that I will briefly note, which is that scientific research can be expensive and that costs affect the practice of science. I'll provide some background regarding how public research funds are distributed and I'll give you a little bit of detail, particularly about how NIH distributes its funds, because NIH distributes over half of all federal research funds in the United States, so it is a very important component.

Let me talk just very briefly about the very high cost of research. In the United States, even a very small lab at a university can easily spend half a million dollars for personnel – that is post-docs and graduate students, probably one staff scientist, sometimes more. Equipment is also expensive: Even a very basic sequencer costs $500,000, and when you get to the large scale devices, such as colliders – we spent eight billion dollars on a collider, as you know – and the price tags of telescopes have grown considerably. Countries have had to scale back the size of the telescopes they can build because the costs got so high. Facilities are expensive: research space is exceptionally expensive to build because of all its special requirements, particularly if one is working with dangerous materials or one's research requires very clean labs. And materials are expensive, even mice.

Of course I have to talk about mice because there is a mouse on the cover of my book. Mice are king when it comes to research: 90% of all animal models used in research are mice, and it's estimated that there are over 30 million mice in use, some people say it's closer to 80 million, and this estimate is a few years old. That tells you a little bit about why there's a mouse on the cover of the book. In case you didn't notice, it is made out of hundred-dollar bills…

As I said, a lot of mice are used, but these mice are not cheap. Your basic mouse costs $40, but most researchers are now working with what we would think of as "designer mice" that have been genetically modified or had a gene knocked out or whatever, to be particularly susceptible to a disease – such as cancer, obesity, alcoholism, Alzheimer's. To create one of these mice costs approximately $3,500. Keeping them is also very expensive. I have a neighbor here in Paris who runs a "mouse facility", and her estimate is that it costs about 40 cents per week per mouse, that is if you have 20,000 mice, it quickly adds up to 400,000€ a year!

I became interested in this when I joined the first meeting I went to at the National Institutes of General Medicine. I opened a budget – and you know, for an economist, getting to look at a budget is the most fun thing – and I wanted to see how much the equipment cost, etc., and the first entry was per diems for this man's mice. First of all the fact that you talk about a per diem for a mouse intrigued me, and then for these genetically modified mice that have to be kept in their own cage – because you don't want them to get sick, you can't put them with other mice – it costs about 65 to 75 cents a day to keep them. He was changing labs, and it was going to cost something like $50,000 to move his mice, because they have to be handled very specially, etc.

It is not unknown in the United States that if one institution wants to hire a researcher who has a lot of mice, they make him an offer that they can keep his mice cheaper, because the researcher has to pay for the mice and their upkeep out of his lab funding. There is a famous researcher in Stanford who was spending a million dollars a year taking care of his mice, and he was given a very good offer where he could move, and it would cost about 40% less to take care of his mice in another institution. Mice play an incredibly important role right now in discovery: two weeks ago there was a major article about Alzheimer's and the role the "tau" protein plays in that disease; all of this research is coming out of a mouse model that has been designed to have Alzheimer's. Nobel prizes have been awarded to people who have designed or created these new mice.

I think this is very interesting: the cost of mouse upkeep has been a big factor in Fudan University being able to recruit Tian Xu, from Yale University. He goes to work there for three months every year. He’s a Howard Hughes’ Investigator in the United States, which is the most elite kind of funding one can have from a private foundation in the United States. Fudan is providing facilities for 45,000 mouse cages (there are usually five mice to a cage)… That is no less than a quarter of a million mice. I estimate it could easily cost him $12,000,000 a year to keep these mice in the United States, but as another friend said: what University in the United States has the land and space to be able to build the huge facilities that are needed to house that many mice? I mean, it’s an incredible number of mice!

Let me just give you, by way of background and since I want to talk about the kind of perverse incentives that have occurred, a three-minute lesson on the US funding system. In the United States, universities receive approximately 55 billion dollars a year for research and development, and 60% of this comes from the Federal Government. Over one half of what comes from the government comes from the National Institutes of Health funding (NIH). The National Science Foundation (NSF) plays a much smaller role, with 10%, and then there is Defense, Energy, and other agencies such as NASA.

This chart shows you the support for academic R&D by sector, between 1953 and 2008. The blue bars are in constant dollars, the money that comes from the government, the little red bars are money that comes from industry, The red line is the percent coming from the industry and the blue line the percent coming from the federal government. It’s fun to see what happened when the United States reacted to Sputnik: you see that huge increase in the late 1950’s in the percent the federal government was giving to research. That other increase that you see is the doubling of the National Institutes of Health budget, which was proposed by President Clinton in 1998, and passed. In a five-year period the NIH budget doubled in nominal terms, from 14 billion dollars to 28 million dollars a year, as this chart shows you, in nominal and constant dollars.

So, universities get those funds, and what do they do with them? Universities and medical schools perform about 75% of research that is published in the United States, so most of our research occurs at universities, as opposed to research institutes as in many countries in Europe. Research in universities is organized around a faculty member’s lab. Faulty members think of these as being their labs. When you are hired at a university, the dean gives you what is called a “startup package”, due to last three years: it gives you money for graduate students and post-docs, for equipment and for supplies, and then, after three years, you are on your own to find money for your lab, and you are expected to get this funding from external agencies.

Labs are so much the property, at least in name, of researchers that on any researcher’s webpage you’ll find pictures like this – this is the AMON Lab at the Whitehead Institute affiliated with MIT – that shows people who work in their lab, and they always call the lab by the name of the researcher. Most of these pictures are very basic, like this one; however, some labs really like to display humorous pictures on their website: this is Christine White’ group at the University of Illinois, and two years ago *Science* voted a research paper of hers as one of the ten most important research papers of the year, but there's clearly a sense of humor there, because they also put Arnold Schwarzenegger in their picture.

As I said, at most universities you have to find funds to run the lab after three years, but in most universities you'll also have to find some support for your salary. So most universities in the United States expect faculty to teach, but not to teach all the time, and they can buy out some of their time on research grants. Also, faculty salaries are for nine months, and if you want to earn more, you can have a grant that pays you for research in the summer, and of course everybody assumes they are going to be able to do that. But at medical schools in the United States, it's even more important for faculty to find funding, and I'm going to talk more about that later, and that's because many people at medical schools, even if they have a position that says they are tenured and provides job continuity, do not have a salary guarantee. So, unless you bring in money at these institutions, you will not, in a couple of years, receive a full salary, and you will be in a financial crisis.

Six out of ten federal dollars are distributed through peer review – and if you ask any scientist in the United States about peer review they'll just tell you it's the Gold standard; scientists are really committed to peer review. The pluses are that it encourages freedom of intellectual inquiry, it promotes the sharing of information (because of course one of the incentives for serving on a peer review committee is that you get to read proposals and learn about others' research); it provides incentives to remain productive throughout your career (because you have to stay productive to get these funds); It's open in the sense that if you don't get funding in one year, you can still apply the next year, and it has often been argued that it has encouraged entrepreneurship among US scientists, because when you meet a venture capitalist and you want to say: "Here is what's great about my research, here is why you should invest money in our ideas", it's not that much different than what you tell the NIH as to why *they* should invest money in your research. You become specialized at "selling" your research to other people.

The majority of grants in the United States are for 3 to 5 years, very short-term grants, which means faculty are almost always in the process of getting or renewing grants. As I said, your salary is part of the grants, but it also has funds for graduate students, post-docs, equipment and materials and "indirect recovery". If everything you're asking for is a million dollars, the university will have to say: "You will have to add 50% to that" – indirect varies slightly from university to university – so the university will ask for a million and a half dollars, and take half a million dollars to supposedly pay for the heat, the electricity, running administration, etc. We could spend a long time talking about that, it's a very controversial issue in the United States. Faculty on "soft money" positions must support themselves entirely off the grants. Increasingly, an "innovation" has been that universities, and particularly medical schools, hire somebody, and then they say: "You have absolutely no salary coming from us after a year or two years, and you are completely on your own to raise this money."

Let me just briefly talk about how peer review functions. Both NIH and NFS, in somewhat similar ways, evaluate submitted proposals for a specific project, and one of the things I should point out is that all of this money comes through project proposals; you're not proposing yourself as a researcher, you are proposing a project. Another words, the emphasis is on the project instead of the person. This is worth noting because at the Howard Hughes Medical Institute, you do not propose a project, you present why Howard Hughes should support you. We could get into a big discussion about the pluses of that, and the Wellcome Trust has become so interested in the Hughes model that they have just adopted a system of supporting people rather than projects.

So, it is important to realize that all of these funds are project-based. You write a proposal for a specific piece of research, it is reviewed by a panel that scores it, and then the funding decisions are made, but there is considerable agency differences regarding what is paid for (for example NFS, that has a much smaller budget, says it would only pay for two months of faculty salary, while NIH would pay for all of your salary); the size of budgets varies considerably, who reviews them varies somewhat, and who has the final say and grants the ability to formally resubmit also varies…

I am just going to briefly tell you a little bit more about NIH. NIH has 27 institutes. The largest is the National Cancer Institute, which has a budget of about 6,5 billion dollars annually. It is followed by Allergy and Infectious Disease (NIAID), and Heart, Lung and Blood (NHLBI); then comes General Medicine (NIGMS), that has a two billion dollar budget and really supports the most basic research that come out of NIH, and this is the Institute I was on the advisory board for three years and know the most about. Some institutes at NIH run internal labs and by law – this is something that Congress likes to do – they have to put 5% of their budget into awards given to small businesses for innovation (SBIRs).

These NIH funds represent a huge budget; it is really the bread and butter, the way academic researchers live. The budget includes funds for staff, graduate students, post-docs, faculty salary, equipment, material and indirect costs. The most common of these grants is called an RO1. How does it work? You submit a proposal (there are three distinct times during the year when you can submit), which is assigned to a "study section", which is a group of reviewers; these reviewers get them beforehand, they score them, evaluate them and triage them. Historically, they decided that they would not even waste their time talking about 50% of the proposals. When they physically meet, they discuss the remaining half, they comment and score them. It's like golf: the lower the score the better. Then, NIH will decide what the payline is – how much money they have, basically – and which ones will be funded, but they also have to be reviewed by groups called the General Council, as to whether they can be funded. Each general council meets three times a year. Historically, you could resubmit two more times if turned down. What happened at NIH is when money got tight, nobody was funded the first time, nobody was funded the second time, they only got funded the third time, and this meant that there was at least a three-year lag in reviewing your initial proposal, because it took a long time to get the comments to you, it took a long time to reply.

What counts, what do the reviewers care about? There is an incredible weight on what we call "preliminary data". While I was at General Medicine, we put 875 million dollars into something called the Protein Structure Initiative (PSI), because it is widely believed that understanding protein structures and determining them can lead to tremendous insights. Crystallography is one of the basic ways to determine protein structure; it is very hard to get a crystal, and so the saying around NIH at this time was: “no crystal, no grant”. If you couldn’t document that you already had the crystal, you weren’t going to get the grant.

Results from previous research carry tremendous weight. Now I’ve read through probably 2400 summaries of reviews, and it’s always: “they published a paper in *Science*, a paper in *Nature*, a paper in *Proceedings of the National Academy* and so on. They’ve done this, they’ve done that, it is very important, and what is also very interesting is, particularly for younger researchers, their lineage: they trained with David Baltimore, or they did this and they did that… It is formally mentioned in the review, which is, I think, quite interesting.

The success rates have been from 10% to 40%, depending on how much money the government had, and it varies by time and by institute. I think you have to look at this green line to see that success rates haven’t been constant over time: they went up considerably to about 35% soon after the doubling of public funding, and at the time of this chart they were around 22%. In this more recent one, you’ll see that for RO1’s they are 21.8% right now, but they got as low as about 20%.

Can you apply to renew a project that was funded? Yes you can, and most people do. There are incredible incentives, once again, to do so, and you have to wonder if this is rational. Your renewed application for a grant has a much higher probability of being funded, and it’s not uncommon to be supported on the same grant for forty years. So it’s the same line of research that changes and evolves. There is one investigator at NIH who has been on the same grant number for 52 years; he is at Cornell University and he is in his mid-eighties at this time. As you know, the United States doesn’t have a mandatory retirement for academics.

There are a huge number of pluses, as scientists perceive them, and there have been some huge successes from NIH funding. In the interest of time I won’t go through these, but NIH is very good at reminding you of all the things that they’ve contributed to.

What I really want to focus on now, for the rest of my time, are some problems that I think that this system has engendered. The first one, that I think is a real problem, is that it has really created a strong bias towards risk aversion, on the part of both the scientists and the people who review. Scientists avoid risk by only submitting proposals that they see as “sure bets”. Even if it is a sure bet they know they only have a 20% chance to get funded.

Why is the system risk averse? Number one: if the only way you’re going to eat is by getting funding it encourages risk aversion. Stephen Quake, a physicist at Stanford, says: “It is funding or famine these days for scientists in the U.S.”. It’s not so much ego, it’s feeding yourself. It has become especially important for faculty on soft money – it is estimated that 35% of all the investigators NIH funds are on soft money. This is a big problem.

Another reason the system is risk averse is that there are these strong incentives I talked about to continue a line of research, not to start totally afresh with a whole new line of research. Another factor is that the very low probability of success (17 to 20% at NIH), encourages reviewers to prefer sure bets. Once again, I've read through many of these reviews where you could read things like: "This looks very interesting, this is exciting, but there is no preliminary data, we simply can't put money into this". Roger Kornberg, a Nobel laureate, says: "If the work that you propose to do isn't virtually certain of success, then it won't be funded".

Risk aversion is a huge concern for economic growth. It is pretty clear that if most scientists are risk averse, there is little chance that transformative research is going to be done, which can lead to significant returns. Incremental research of course yields results, but in order to realize substantial gains, at least some people need to do very risky research. So you really have to be concerned that portfolios of what is funded have really become very, very loaded towards risk aversion.

NIH is aware of this, and so they said: "Oh, we will create some incentives for risky research". So they created two programs, which are very similar: one is called the Eureka program, and the other one is called the Pioneer Awards. They award a lot of money to people for five to ten years, something like 5 million dollars, but what are the chances of getting funded? They had 2300 applications for Pioneer Awards that could take you three to four months to write, and 18 were awarded. That's a risky proposition in and of itself.

Another problem with the way the incentives system has been created is that the age at the time you get your first award has really changed. The number of newly funded investigators hardly changed at all at the time of the doubling; we increased by two-fold the amount of funding, and it went to established investigators. So what happened is that experienced researchers who had one grant got two grants. Universities said: "Oh, you are so good we will give you more floor-space, we'll give you more of this," and that's where it went.

Success came later in careers: the average age for an investigator getting his first grant went from 37.2 in 1985 to 42.4 years in 2006, a fairly short period of time. The reasons: if you need to have preliminary results, it will take you a long time to be ready to submit your first proposal. As I said, historically you didn't get funded the first time, you didn't get funded the second time, so if you spent three years getting your preliminary data, and then three years in resubmission success came later. Institutions are hiring later-stage researchers.

I think it is a concern, both because there is some relationship, I believe, between age and productivity, but I also think it is a concern because we need to be investing in some new investigators to carry on for the future.

What you need to look at on this chart here is these red bars representing the new investigators; the blue bars representing the grants going to established investigators. Look at how, during the doubling, blue bars increased and the red bars stayed fairly constant. This also shows you the percent of new investigators getting funding, and you just see that it really went down. This is during a period when the size of the biomedical workforce in the United States is growing tremendously, primarily because of new people being trained.

The second chart I think is just incredible. It tells you who is getting these grants, in terms of the age distribution, and look at this: in 1995, only 14.5% were over 55 years of age, who were getting grants, and 25% were 36 or younger. By the end of this period, in 2003, 15% were 36 or younger, while 27.6% were more than 55 years old. This system of being risk averse, of wanting preliminary data, etc. really shifted this age distribution considerably.

Elias Zerhouni, who was the head of NIH until recently, perceived this as a huge problem. The director of the NIH is a presidential appointee, and he was a Bush appointee, so when he left in 2008, his parting shot was to make it formal NIH policy to "support new investigators at success rates comparable to those for established investigators submitting new applications." And so things really began to change. The number of new investigators went from 1261 in 2006 to 1798 in 2009. But how did they do this? I told you they had a payline, so what they had to do is reach way above, to higher golf scores basically, to fund these people, so now there is a lot of criticism that they are funding lower quality research. Once again there are some tradeoffs here.

A second problem I want to talk about is the cost of this kind of review. If you are talking about using resources efficiently, one of the things one wants to think about is if it is an overly expensive way to do peer review. It has been estimated that researchers who are supported on federal grants spend 42% of their research time on administrative tasks: filling out forms, attending meetings, going through submissions. Most principal investigators have really become like heads of small firms, and spend a great deal of a time on paperwork. How about the reviewer's point of view: it has been argued that a 25-page proposal to the NIH took 30 hours to evaluate, including seven hours for each of three assigned reviewers. That comes to about 1700$ per proposal in terms of opportunity cost, given how much these people earn, on average.

NIH (and NSF) – I don't know if this is a problem in France, but it's really been a problem in the U.S. – reported that the number of scientists declining an invitation to review has been increasing over time. People say they don't have time to review, and it's been particularly a problem getting senior reviewers. One of the things that we did when I was on Council was that we reviewed all the appeals – you very seldom win but you have a right to appeal – and most of the appeals were based on the argument, basically, that the reviewer was stupid, or at least that he didn't know what he was saying, and actually some of them make a very strong case that the proposal was really reviewed by somebody who simply was ignorant of a specific field.

What did NIH do in response to such criticisms and problems? First of all they said "Oh, we can save time if proposals are shorter", so they streamlined the proposal format and procedure, and cut the proposal from 25 to 12 pages. Then they said: "It's a waste of time resubmitting two times, you can only resubmit once". It had been a concern that after triage, if you were part of the 50% (and most of these were younger people) you didn't even get a score and you didn't have a clue about how well your proposal did, so now everything gets scored, so at least you get some signal. Then they made it easier on reviewers. They said: "You have to attend twelve meetings, but you can do them over six years rather than four. And if you come to 18 meetings, we are going to give you a 250,000$ automatic grant extension. If you have three or more grants (this is quite telling, there are a number of people who do), then you have to serve as a reviewer, you cannot say "No, thank you".

Let me talk about some of the human resource problems that I think these incentives have created. A big concern of mine, and something I have spent a great deal of time working on, is the way the United States, much more than any other country in the world, staffs its labs. In most university labs, the people actually doing the research – and I can show you this using bibliometric data also – are graduate students and post-docs. There are a lot of good reasons for this: they have fresh ideas, they are flexible, they are temporary (if you don't get your grant renewed you can say "Good Bye"), and they are cheap. And cheap is definitely part of this.

You can think of this as a pyramid system, or, as I often refer to it, as a pyramid scheme, in which you have the principal investigator at the top, and a few staff-scientists, and then a lot of post-docs, graduate students, and some undergraduate students. The system works as long as the funding environment is growing very quickly. If you completely staff all your research positions with new recruits the system will rapidly become unable to absorb all of them. This is what has happened: It has become increasingly difficult for young researchers to find independent research positions in academe or in government, and this is particularly true in the biomedical sciences, which are dominant in the United States. It is also becoming increasingly difficult to get jobs in industry. Companies in pharma had a lot of consolidation, and are not hiring as much now as in the past. So what has happened is we've got a very large group of disenchanted young researchers in the United States, many of whom are international, who simply cannot find good job-matches for themselves. They are very disenchanted, quite vocal. I would argue that this is something that is socially very inefficient.

This chart just gives you an example in the biological sciences: in 1973, five to six years after you came out you had a 50% chance of being in a tenure track position; in 2006 you had a 12.5% chance of being in a tenure-track position. What has happened is that the probability that an individual continues as a postdoc, works in industry or government or is out of the labor force (which about 10% of them have experienced) or working part-time has grown.

What I find really interesting here is that there is evidence that while this has gotten much worse lately, it's been going on for a while, and even the very best have had problems finding independent research positions. NIH funds a program called the

Kirschstein Postdoctoral Fellows. It is a very elite program; they choose only a hundred post-docs a year. You can go to virtually anyone's lab and they'll take you; you have your own funding. It is a period where you could supposedly be very creative and do very good research. There is an interesting piece of research by David Levitt, who is a biomedical professor at the University of Minnesota. He got the names of all the Kirschstein Fellows from 1992 to 1994. It is not only the best and the brightest, but if you were a post-doc in 1992 to 1994, you finished your post-doc about four years later, just when the NIH budget doubled. You were trained well, and you came out just when the resources were really growing. You should have had the best world of all. So two years ago David Levitt spent a lot of time trying to find these people, to see what had happened to them. He found that 25%of them had tenure-track positions, 30% were working in industry, and 20% were researchers working in someone else's lab. He couldn't even find 14% of them, which is a fairly high dropout rate for people in whom such large investments in training have been made.

Every five years, the NIH is required to have an outside committee evaluate how its training programs are working, and whether there are problems with this way of staffing labs. In my way of thinking, almost all the committee members are very established researchers who have a huge commitment to maintaining the status quo. The most recent report was issued a year ago, exactly this month. Here is a quote from it: "The body of graduate students and postdoctoral fellows supported on NIH funds provides the dynamism, the creativity and the sheer numbers that drive the biomedical research endeavor". The system has been "incredibly successful in pushing the boundaries of scientific discovery". I argue in the end this is rather doubtful. The committee rationalizes, in the report that the system is fair, that students know outcomes and they continue to do it regardless. I should tell you as an aside that absolutely none of these programs list student outcomes on their webpage. You can find out, but you don't find out from the programs. What was their recommendation? If they can't find a job, let them be high-school teachers! I swear it was one of the major recommendations. So you're supposed to spend seven years getting a PHD, that's the medium amount of time, three to five years as a post-doc, so twelve years of training to become a high-school teacher, even if you may not have the personality to actually be a good high-school teacher.

The second human resource problem is soft money positions. As I said, NIH supports salary with no limit on the number of months, and what it has really encouraged universities to do is to hire researchers on soft money positions. I also point out that it's not only those without tenure, but medical schools have had an "innovation" that they can give a faculty member tenure without really giving the faculty member a salary guarantee. As I said, this has extreme incentives for being risk averse. If it is "Funding or famine", you're going to submit a very sure proposal.

I won't take time going through this, it just shows you data saying that at 62 out of 119 medical schools in the United States, tenure is equated with a specific salary guarantee, that only 8 of these present "total institutional support" and that in all other 54, there is some form of limit on guarantee. At 42 of them, tenure comes with absolutely "no financial guarantee". I was in a taxi after a conference with tenured faculty from the Stanford medical school, a great medical school, right? None of their tenured positions are backed by salary guarantees. They said Stanford would go absolutely broke if all of their grants went out. They just couldn't pay their salaries.

I think the fact that we have so many people on soft money positions has become a real issue. The final human resource issue I want to talk about is the way the salary structure has evolved in the United States. I think it has a lot to do with funding.
As you know, the United States is known for having strong research universities, and one of the ways the U.S. has built these strong research universities is having the resources to attract and reward highly productive scientists; another way is by paying very high salaries and rewarding productive people with high salaries, and by also creating very interesting lab packages for people. One thing that this has done is to create wide salary differentials in departments and between universities.

There is a very, very large salary differential now between private and public Universities. As you know, we have public universities such as the University of Wisconsin, the University of Michigan, or the University of Minnesota, all the California systems are public, and then we have private universities such as the universities of Chicago, Yale, Stanford, Harvard, etc. What has evolved is that private universities have the resources, in part because of their large endowments, to pay significantly higher salaries. So right now if you list the Top-20 institutions in terms of the salary they offer, Harvard is at the top and the only public institution on this list is UCLA, it's in 20th position, $40,000 below Harvard. (UCLA is the University of California in Los Angeles, and the cost of living in LA, before the housing meltdown, was so extraordinarily high that they really were forced to pay above what most public institutions pay.)

Then there are big differences across and within institutions, and within rank across institutions, so it's very easy to find out that somebody who has the same rank, and oftentimes approximately the same research productivity as you, can earn three times more in another institution. There are also very wide differences within departments for the same rank, and that depends upon when you were hired rather than upon productivity. In my department, in the 1990s, we had growing budgets, and when we hired people we hired them at top salaries, and there could be people who had been there two or three years before who got considerably less.

One of the things I do in my book is I show that salary inequality is considerably on the rise in academe in the United States. The gap between the haves and have-nots has become, as you may be aware, a huge issue in the United States; the "Occupy Wall Street" movement, and then the "We are the 99%" slogan, were very dominant in the news this fall, and so there's been lots of reports on what income inequality is in the U.S.. What is interesting is that within academe, inequality has grown at almost three times the rate of growth of inequality in the larger society. It's not as big as in society at large, but the rate of growth in inequalities is much greater in academe.

I'm a believer in that inequality contributes to research productivity by attracting and rewarding productive people, but I really think there becomes an issue at what point one draws the line here. I think this has really become a problem for the United States. I think there are at least two concerns with this right now. One is the divide between rich and poor universities. This divide is almost exclusively between public and private universities. Very recently, we watched the University of Wisconsin lose a number of very strong researchers who were hired by universities such as Harvard and Stanford, which can offer them significantly larger packages. There is a big concern that a lot of the very strong public universities in the United States are at risk of losing a lot of the human resources that made them great, and that there will be much more of a sorting, a stronger concentration of really great universities, leaving everything else to be much more mediocre.

Then, I think there is a problem of substantial income inequality within a university, and a department, that at some point threatens the fabric of the university. Strong universities are clearly built by faculty working together to build new programs and curricula and by providing excellence in the classroom. If the only thing that is rewarded, and is rewarded with huge amounts of pay differentials, is research productivity, then I think it becomes increasingly hard to get a faculty to work together on curricula changes, etc. Given all countries seem to want researchers to collaborate more, and there are huge moves in all the funding system to promote collaboration, one has to really think about what these huge income gaps do towards collaboration. Whenever you collaborate on a grant with somebody, you know exactly how much he or she is getting. At some point, if you are of the same rank, you may want to ask yourself if you want to work hard helping someone else get research funded, or published, when he or she earns three times what you are earning, and may be involved in other things and won't have the time to really work on the research?

Finally, I want to conclude by talking about the mix of what the United States fund. How are we spending our resources? This graph shows the share of University federal R&D obligations by field. What you really need to look at here is the life sciences, primarily the biomedical sciences. They get 67% of all federal funding in the United States. Down here we have psychology, social sciences, math, environmental engineering and physical sciences. Their curves are quite flat, and you can particularly look at what has happened to the physical sciences: it is at a 35-year low. You can of course see how the percent going to life sciences was benefited by the doubling, etc.

Why does the U.S. have this incredibly heavy focus on biomedical sciences, much heavier, presumably, than in Europe? I think there are a couple of reasons. These are just primary hypothesis on my part, but there is an extremely well organized disease-focused health and research lobby in the United States. Just to tell you a story: the current director of the National Institutes of Health who replaced Zerhouni is Francis Collins. The very first thing he did the first week he was director was to have an open meeting with the public, with stakeholders, in Washington. I went because I was there for General Medicine, and as you went in the room – it was in a auditorium that held 400 people at NIH – they had a list of participants, and when you started flipping through it, you noticed all the participant organizations started with an A, because almost every organization was the American Association of… lung problems, dermatological problems, of certain kinds of cancer, etc. They became very, very, very specific organizations, and what really astonished me – it tells you how naïve I was – is that when he had a one-hour question period, unabashedly, at least twenty people stood up, introduced themselves, and they would say: “We would like to know what you’re going to do for our disease! Specifically. Our disease, we followed it, got 500 million dollars last year, and we need more; we have this many people dying from this, this many young children living with it”, etc. It was all: “What are you going to do for our organization?”

Now what you have to understand is that these organizations are there to go to Congress and to lobby, and there’s some really interesting research by David Mallory and some of his students that shows that this lobbying seems to pay off in terms of getting the NIH’s attention regarding what they may focus on. But more generally, it convinces Congress that the public really wants research in health, and I think it doesn’t hurt that Congress is “older”: the average age of members of the House of Representatives in 2009 was 56, and the average age of senators was almost 62, and both chambers are considerably older than they have been at their “youngest”, in 1981, when average age was 48.4 in House, and 52.5 in the Senate. Senator Arlen Specter was NIH’s key person in the Senate and facilitated bringing considerable extra resources to NIH. He actually lost his seat recently – it’s a long story – but he’s a three-times survivor of cancer, and he spoke very eloquently about the importance of biomedical research.

So you have all this funding going to biomedical researchers, and what has happened is it led to a building boom at universities. This graph shows the net assignable square feet for research space at universities and medical schools in the United States, by field and year. Once again, you only need to look at one thing: all the new research space has been given to biological, biomedical and health sciences. Look at how pretty flat the curves for other fields are. These are the labs these people are doing their research in.

Incentives played a big role here, of course. Universities said: “There’s all this NIH money, we can hire people on soft money, but if we want to attract people, we need better labs”, etc. And the rules allow interest on debt to be included in calculating this indirect rate, so how do you pay for these buildings? You borrow. And then you can deduct the interest, or you can use the interest payments to raise the indirect rate that you charge on your grants. Universities built all this new space, they try to fill it with many researchers working on soft money, because there’s not much risk to universities in terms of salary commitment: if it doesn’t work, they don’t have to pay them.

The consequences of this, now that the NIH budget is flat, have become huge. There’s a concern that universities may have trouble paying the interest on theses bonds or servicing the bonds. Given that the NIH’s budget is not growing, and unless they default (which, of course, is a possibility), somebody is going to have to pay, and who could pay here? Well, you know we charge tuition in our universities, and they have been raising tuitions, so students could definitely pay; faculty could also pay by getting lower salary increases or even decreases (as it has happened in some places recently), or other disciplines could pay, and I think a lot of it is coming from other disciplines, with universities saying: “We simply don’t have the resources to expand this other department, so we're going to cut other departments. Because we have this space, we need to do something with it."

Somewhat more generally, I think we can argue that this mix may be inefficient, and that it may be time for the United States to rethink what our federal R&D portfolio is, what we are investing in.

Biomedical research has clearly had what we can think of as a great run. It has created a lot of very strong breakthroughs, but in the book I make the case that one could argue that the marginal product of another dollar spent in biomedical research right now is not as high as it once was. We can see diminishing returns, suggested by the very slowed rate at which new drugs are being brought to market, and there's been a remarkable number of failures, of research that looked like it was going to pay off in terms of new drugs, and there has been a lot of concern that the basic research behind it has just, in some sense, been lacking, in part, let me once again say, because of incentives. I know people at the medical school of Stanford who will say that they have trained their students (you know all the students in the pyramid scheme?) to be overly specialized to such an extent that they don't have any understanding of human physiology, and so, research that can look really promising when you look at it in the very narrow sense, fails as you get anywhere near a human model.

Then there have been some very interesting studies showing what happened to U.S. publications associated with the doubling of NIH budget. You would at least think they would grow, that you would get something more out of it, but there is very little evidence that the publications in the U.S. biomedical field increased. It is important to realize that a lot of the breakthroughs that have contributed to better health outcomes have not been developed by people in the biomedical fields. The laser, for instance, certainly had a huge impact in surgery, but it wasn't developed by people in the biomedical field, it came straight out of physics. The MRI (Magnetic Resonance Imaging) is also something that came from physics.

I think one needs to remind the public that funds for the physical sciences in the United States (in terms of the percentage of federal research funding) are at an all-time 35% low and yet that a number of things that have added to our health outcomes come out of these kinds of fields.
Going forward, it seems hard for me to make the argument that we should continue to support the biomedical sciences at this large rate.

To sum up, I think the U.S. system has produced some great science, and much of this is attributed to opportunities that have been available for researchers in the United States, and the incentives underlying this. But incentives can also have a downside. Sometimes you can think there are some tipping points in these incentives, and I'm concerned that we have gone over the tipping point. In that sense, I think there are lessons here for any country or group of countries that they should attend to when they think of emulating what we have done in the United States. I particularly think that you need to be aware of what you allow funding for. I think the “innovation” of soft-money positions has really caused us problems in the United States. And the response of universities to it has also really caused problems. Bruce Alberts even had an editorial in *Science* about this. He is the current editor of *Science*, and a past president of the National Academy of Sciences, and he is concerned that we have gone overboard with regard to soft-money positions, etc.

Also, the huge commitment beginning in the early 1990s to support university labs off of grants by funding postdoctoral appointments and graduate students has been a problem.

Let me just close by saying I don’t think more money is always the answer. People in science always just say: “Well if you gave us more, it would solve our problems”. One of the very interesting things is that the doubling of the NIH budget between 1998 and 2002 really didn’t have all the good outcomes people had predicted would come out of it.

I’ll stop there.