Gendered Innovations in Science, Health & Medicine, Engineering, and Environment

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It is a great honor to be with you here today. My thanks to the Rector, to Professor Capitolina Diaz, and all of you for welcoming me to your beautiful university.

Today we will explore Gendered Innovations, a project I founded at Stanford University in 2009. Gendered Innovations was produced through a large international collaboration involving the European Commission, the National Science Foundation, and Stanford University. Gendered Innovations has brought together over 100 basic scientists and gender experts in a series of collaborative workshops. And, importantly, new policies have been implemented in the European Union, Canada, and the United States.

Innovations is about integrating sex and gender analysis into the design of research. The operative question is how can we harness the creative power of sex and gender analysis for discovery? Does considering gender add a valuable dimension to research? Does it take research in new directions?

First a bit of background. Governments and universities in the U.S. and Western Europe have taken three strategic approaches to gender equality over the past several decades. I call these the three fixes:
1. "Fix the Numbers of Women" focuses on increasing the numbers of women participating in science and engineering.
2. "Fix the Institutions" promotes gender equality in careers through structural change in research organizations.
3. "Fix the Knowledge" or "gendered innovations" stimulates excellence in science and technology by integrating sex and gender analysis into research.

We have a new study that came out in Nature Human Behavior last December. Analyzing 1.5 million medical papers, we found a link between #1 “Fix the Numbers of Women” and #3 “Fix the Knowledge.” We found that if there are more women on the research team—in the position of first or last author—that articles were more likely to incorporate sex and gender analysis, or vice versa. It could be that including gender analysis in research pulls women into research careers. For policy makers, our findings demonstrate an important empirical link between increasing the numbers of women in academic medicine and enhancing excellence in research by incorporating gender and sex analysis.

My remarks today focus on this third strategic approach—fixing the knowledge. It is the newest area, and the most important for the future of science, engineering, and innovation.

Let's dive in. Doing research wrong costs lives and money. For example, ten drugs were recently withdrawn from the U.S. market because of life-threatening health effects; eight of these posed greater threats for women. Not only did these drugs cost billions of dollars to develop—but when they fail, they cause death and human suffering. We can't afford to get it wrong.

The good news is that doing research right can save lives and money. An analysis of the US Women's Health Initiative Hormone Therapy Trial—a large, government-funded trial done in the 1990s—found that for every $1 spent, $140 were returned to taxpayers in health care savings. The study also saved lives: There were 76,000 fewer cases of cardiovascular disease, 126,000 fewer breast cancers, and 45,000 more quality-adjusted life years. While most of the results were positive, the analysis did find 263,000 more osteoporotic fractures.

These examples show that it is crucially important to get the research right. This is the goal of the Gendered Innovations project. This project: 1) develops state-of-the-art methods of sex and gender analysis for the natural sciences and engineering; and 2) provides case studies to provide concrete examples of how gender analysis leads to discovery and innovation. I will discuss some of these case studies with you today.

Our first example comes from cells and tissues—looking specifically at stem cell research. Let's go back to why ten drugs were withdrawn from the market. There are many reasons why drugs fail—and fail more often for women. One reason is faulty research in the preclinical phase. Let's see how this works in stem cell research.

Why might the sex of the cell be relevant? Research shows that there are sex differences in the therapeutic capacity of stem cells. We know, for example that female cells are more regenerative (or active) than male cells. Yet, very few researchers consider the sex of the cell—which can lead to failed research. An international research team from Norway and Australia worked with stem cells in mice. They appropriately used male and female mice (using both animals in basic research is excellent design). But they used all female stem cells—this was an unconscious and arbitrary decision. It means that in the discovery phase, they did not see anything unique to male stem cells. Nor did they detect important differences in function between male and female cells.

The result of not considering the sex of the stem cells was that their male mice died—and they didn't know why. They thought maybe the postdoc made a mistake. Eventually, through a Gendered Innovations workshop in Norway, the team realized they should also consider the sex of the stem cells. They found that sex-matching of donor and recipient yielded the best results—so, matching male animals with male cells, and matching female animals with female cells worked the best. But, of course, all combinations of donor/recipient interaction should be tested before being ruled out.

But it's never that easy. In addition to analyzing sex in stem cells, we need to analyzing factors intersecting with sex. In the case of stem cells these factors may include cell type, disease being treated and other variables: hormonal, immunological, and environmental.

Let me just interject here: Sex matching ,which may be important for stem cell research, may also be important in human organ transplant. For heart transplant, sex-matching yields the best long-term outcomes. The same is also true for kidney transplant, but lung transplant doesn't follow this pattern. So, we cannot make any assumptions, all possibilities need to be examined. But GENDER can also be an issue! I don't know the exact situation here in Spain, but in the U.S. women donate more organs than men. This means that there are more female hearts available for transplant than male hearts. This means that even though a surgeon may know the best *science*, i.e., that it is best to match sex when attempting a heart transplant, he or she may not have the right heart available.

So far, I have been talking mainly about analyzing sex. The example I gave concerning stem cells had to do with analyzing sex. Now I want to open the discussion to gender—and talk specifically about analyzing gender in animal research. This is important because sex and gender interact in the human bodies. I, for example, have a sex, I'm female. But I also have a gender; I have the various cultural attitudes and behaviors considered appropriate for a woman (or not!—I often must adopt behaviors considered appropriate for a man in order to success in my professional life). Be that as it may, I want to discuss why it is important to look at the larger cultural environment when we do animal research—in this case the environment of the laboratory.

As researchers begin to analyze sex in animal research, it is important that they not see "sex" (or a biological trait), when they are really looking at "gender" (or an environmental condition that may impact male and female animals differently).

Let's look at two quick examples of how gender might influence animal experiments. First example. Importantly, differences in caging practices between male and female animals should not be mistaken for biological sex differences. Ritz et al., a research group in Canada, show that males are often caged alone (because they fight). Females are typically caged 3-4 in a group (because this saves money). When animals are housed alone, they "expend more energy maintaining body temperature, which can cause differences in parameters such as caloric intake, muscle activity, metabolic rate, fat distribution, or body size." Animals housed together, by contrast, tend to sleep clustered together and, as a result, expend less energy to keep warm.

The danger is that if we don't analyze gender or environmental factors, "sex difference" may be identified where, in fact, differences result from housing conditions. Metabolic differences between male and female animals observed in the laboratory may not be related to the innate characteristics of sex but to caging practices. Again, it is important here not to "see" a sex difference when what we are looking at is influenced by caging differences. We all know this, but Prendergast et al., a research group at Berkeley, found that more than half of the studies of mice failed to specify the number of animals per cage. If there is no data, studies are not reproducible.

There is a lot more to say about caging, but you get the point.

Second example. An important study by Sorge et al. discusses the impact of the **sex** of the researcher. This example focuses on pain research. The researchers induce pain in rats and mice. What they found is amazing. They found that rats and mice don't show their pain to men researchers. This is really important because the researchers are studying sex differences in pain response. Animals don't show their pain when a man is in the room, as compared to an empty room, but they do show their pain when a woman is in the room. All sorts of conditions were tried: man in the room, a woman in the room, an empty room, a chair in the room, etc.

The researchers identified this as the “male-observer effect.” What’s going on? It’s not how the researchers act or how they handle the animals. What is it? The animals smell the men, they smell male pheromones. According to Jeff Mogil (whose lab this comes out of), this phenomenon may throw into question all prior results from pain research.

There is much more to say about basic biomedical research, but I want to move on to computer science. My next example comes from machine learning, specifically natural language processing, and focuses on Machine Translation.

I start with a story. A couple of years ago I was in Madrid and interviewed by some Spanish newspapers. Sadly, I don’t read Spanish. When I returned home, I put the articles through Google translate and was shocked that I was referred to repeatedly as “he.” Londa Schiebinger, he said, he wrote, he thought. Google Translate has a male default.

How can such a cool company as Google make such a fundamental error?

Google Translate defaults to the masculine pronoun because “he said” is more commonly found on the web than “she said.” The method or tool of analysis in this case study is analyzing Gender. And here is the interesting part. We know from NGram (another Google product) that the ratio of “he said” to “she said” has fallen dramatically from a peak of 4:1 in the 1960s to 2:1 since 2000. This parallels exactly the women’s movement and, in the U.S., robust governmental funding to increase the numbers of women in science. With one algorithm, Google wiped out forty years of revolution in language, and they didn’t mean to. This is unconscious gender bias.

The fix? A couple of years ago the Gendered Innovations project held a workshop where we invited two natural language processing experts, one from Stanford and one from Google. They listened for about 20 minutes, they got it, and they said, “we can fix that!”

Fixing it is great, but constantly retrofitting for women is not the best road forward. I had to ask myself how is it that Google engineers, many of whom are educated at Stanford, made such a simple mistake? What are we at Stanford doing wrong? For one thing, we don’t teach gender analysis in core engineering courses—something we are now trying to fix.

So, again, some products can be fixed, but what if Apple, Google, and other companies started product development research by incorporating gender analysis? What innovative new technologies, software, and systems could be conceived?

The point I want to make is that this unconscious gender bias from the past amplifies gender inequality in the future. When trained on historical data (as Google Translate is), the system inherits bias (including gender bias). It turns out that even though Google wanted to fix the problem, they have been unable to. It's always harder to fix something once the basic platform is set. Importantly, Google translate is creating the future (technology, i.e., our devices, programs, and processes shape human attitudes, behaviors, and culture). In other words, past bias is perpetuated into the future, even when governments**,** universities, and companies themselves have implemented policies to foster equality. So, the big question is: how can humans intervene in automated processes to create the society we want?

There are many examples like the Google translate, where unintentional bias is built into algorithms or systems software. We at Stanford are holding a workshop next week, where we will identifying exactly where in machine learning bias resides, whether in the input (data), the output (predictive models), or the algorithms. We will map the emerging solutions, and we will discuss who should be involved in the decision making to fixing these problems: Computer scientists? Ethics teams? Government oversight committees?

I could give many more examples of Gendered Innovations. On our website, we have twenty-six case studies, or specific examples, across the areas of natural science, medicine and health, engineering, and environment similar to the case studies I've discussed with you here today. Designing sex and gender analysis into research is one crucial component contributing to world-class science and technology.

Let me conclude with a quick look at policy. Policy is one driver of innovation and can help encourage scientists and engineers to integrate gender analysis into their research.

First, granting agencies can ask applicants to explain how sex and gender analysis is relevant their proposed research. And this is where it gets interesting.

I consider the European Commission the global leader in policy in this area. In December 2013, the European Commission launched Horizson2020, and encouraged PI seeking funding to integrate sex and gender analysis into research design. And the EC identified 137 areas of science and technology where gender analysis could benefit research, including computer hardware and architecture, nanotechnology, oceanography, geosciences, organic chemistry, aeronautics, space medicine, biodiversity, ecology, biophysics, among other.

Second, in the same way that granting agencies can encourage researchers to include sex and gender analysis in their research when seeking funding, editorial boards of peer-reviewed journals can require sophisticated sex and gender analysis when selecting papers for publication. Importantly, *The Lancet* adopted guidelines for authors and reviewers for integrating sex and gender analysis into research in December of 2016. For biomedical and health research it is now clear that sex must be considered as a biological variable.

Third, to support research, it is important for universities to integrate knowledge of sex and gender analysis into the curriculum, as I discussed in the Google translate example.

And fourth, industry can incorporate the smartest aspects of gender into new products. Products that meet the needs of complex and diverse user groups enhance global competitiveness and sustainability.

There is much work to be done! Researchers need to learn sophisticated methods of sex and gender analysis. Universities need to incorporate these methods into their curricula. Corporations need to integrate these insights into product design.

But eyes have been opened—and we cannot return to a world that ignores gender. Innovation is what makes the world tick. As I hope I’ve begun to show, gendered innovations spark creativity by offering new perspectives, posing new questions, and opening new areas to research. Can we afford to ignore such opportunities?