Commencement Address at Macaulay Honors College

City University of New York

June 6, 2014
Avery Fisher Hall

Graduates, faculty, and families: Greetings and congratulations to you all.

I have three simple rules for commencement talks:

- Tell stories and don't pontificate
- Choose only one theme and stick to it
- Don't use more than my allotted time

In my wife's immortal words: "Leave them begging for more."

Today, my one theme is: Good Questions.

So your first question should be: "Why questions?"

There are at least two answers.

First: They are important. They are the pathway to knowledge. They tell others how and why we seek knowledge. And they turn learning into stories.

Second, and more pertinent to this day: Your accomplishments give you the freedom to ask them.

Let me explain: To get your degree today, you need to show that you know things. Now you are equipped to ask the questions that lead to new knowledge.

I have an affinity for this topic because questions were important in the slow development of my own career. As a pre-med student at Amherst College, science never excited me. I was learning the answers without knowing the questions. In fact, I didn't know how many great questions were still unanswered. This may explain my 'Gentleman's C' in Organic Chemistry!

I was more excited by literature, because we were expected to use our own ideas to answer stimulating questions about poems and novels.

Eventually, I did go to medical school. At that time, during the Vietnam War, doctors had to fulfill service obligations. Lacking any scientific credentials, I was lucky to get a position in the Public Health Service that allowed me to do research a the NIH. This time—at the age of 28, late in a prolonged adolescence—science seduced me, with questions, not facts.

I was thrown into a laboratory that had just discovered that a small chemical regulator of mammalian cells could control bacterial genes. I was told to figure out how that worked. In effect, I was allowed to stand at the edge of what was known and look out into the darkness of what we don't know. At that point, science became a compelling quest.

I was reminded of that feeling two weeks ago, reading the New York Times obituary of the adventurous biologist, Gerald Edelman. Edelman received a Nobel Prize in 1972 for discovering the shape and composition of antibodies—the proteins our immune cells make to protect us from foreign substances like infectious agents.

Edelman often said that he was interested in what he called "dark areas", places in science where mystery reigned. But how is mystery rolled back? He said, "Anybody in science, if there are enough anybodies"—[that is, "anybodies," as opposed to antibodies]—"can find the answer. It's an Easter egg hunt. That isn't the idea." He continued, "The idea is, can you ask the question in such a way to facilitate the answer? And I think the great scientists do that."

Let's think about Edelman's statement as it applies to what is arguably the most important—and certainly the best known—discovery in modern biology: the DNA double helix. Eventually someone would have discovered the double helix on some "Easter egg hunt," looking with powerful microscopes and x-ray devices that can define molecular structures.

But Watson and Crick won instant and lasting fame when they discovered the structure of DNA over sixty years ago—in part because they were looking for an answer to a deeper question. If DNA contains genes, a cell's inherited information, how is that information transmitted from a cell to its progeny cells during cell division?

The organization of the double helix revealed the answer: DNA's four building blocks (A, C, G, and T) are specifically paired—A with T, C with G—in the double helix. This means that the information contained in the order of the building blocks will be accurately duplicated and transmitted. A great question produced profound answers—the foundation of heredity, the genetic code, the language that forms all of modern biology.

On a more modest scale, consider how questions influenced my own best known work. Mike Bishop and I discovered some genes that, when mutated, drive normal cells to form cancers. Students hearing about this today wonder why anyone would give us a Nobel Prize for something that should have been found by anyone. Any one of Edelman's "Any Bodies" should have found those "Easter eggs" by determining the sequence of building blocks in DNA from human cancer cells, looking for mutated genes.

But when we did our work, the methods for large scale sequencing of DNA had not yet been invented. So we could not have been on that Easter egg hunt. We didn't have a simple way to see the eggs.

Instead, we were trying to answer a couple of perplexing questions about a virus—a retrovirus—that caused cancers in chickens: Why did that chicken retrovirus carry a cancer-causing gene? And where did that gene come from? We discovered that the viral gene came from a normal chicken gene; that it was mutated; and that it was one of many similar genes, derived from normal cellular genes, that allow retroviruses to cause cancer. At that point, a whole set of new questions arose. Ultimately these led to new ways to diagnose and treat human cancers now widely used in medical practice.

Profiles of people in any field of discovery, not just biology, can teach us how they became engaged with the problems they study. Their stories often give us clues about why some questions produce more success than others.

Consider two recent examples from the New York Times:

The first teaches us why things are important. From the earliest stages of human history—and probably before that—people have asked whether life occurs elsewhere in the vast universe we can see on a dark night. Is there life on the few nearby planets in our very own solar system, circling our own star, the sun? Probably not. But, more intriguingly: Could there be planets likely to support life circling some of the other billions of stars in distant galaxies?

Geoff Marcy, an astrophysicist at UC Berkley is one of the millions who have pondered these questions, but among the few men and women who have come up with answers. He took advantage of two features of his time. One was a prediction made in the 1950's: The gravitational force of a planet, even a planet too small and far away to see, should perturb the movement of the star it circles. His second advantage was the recent development of instruments—including a telescope on the unmanned American spacecraft called Kepler—that could record such perturbations.

Thanks to his work and others, astronomers now estimate that about 20 percent of stars are circled by planets, and often multiple planets. There may even be more planets than stars—over one hundred billion. That raises still more questions. Most obviously: How can we identify those most likely to house some form of life? And how can we test them for unknown forms of life?

Graduates, women and men: Get cracking!

An interview with Sebastian Seung, a neuroscientist at Princeton, unveils an even more fundamental aspect of question-asking in science: the need to simplify a question so that it is answerable.

Seung was trained as a theoretical physicist, working on string theory, then gravitated towards theories of the brain. But he got frustrated by how little was actually known and how little could be directly tested. He told his interviewer, "We've failed to answer simple questions...People want to know, 'What is consciousness?' and they think that neuroscience is up to understanding that. They want us to figure out schizophrenia and we can't even figure out why a neuron (A nerve cell) responds to one (thing) and not another."

In short, he came to find the complexities of brain theory baffling and untestable. They seemed as unsatisfying to him as string theory and its largely untestable ideas had been.

So he became an experimental neuroscientist, and a happy one, working on questions that drastically reduced the complexity of the problem. His new work explains how just one nerve cell responds to multiple signals from other cells. It is a small beginning—but a concrete one—a start to an international effort to ask an enormous question: How and why are billions of cells in a human brain each connected to thousands of others?

Now let’s get back to you.

Whether you end up in the natural or the social sciences, in the arts or the humanities, it is my hope that you will find your questions. I hope that you will conceive and pursue questions that matter to you, matter in general, and are designed to be answerable.

If I were starting out today, I’d ask how to balance the aspirations of an enlarging global population against the fragility of our planet. This means figuring out how to teach the dangers of providing so many people with the energy, food, water, and pleasures they want and deserve. It means learning how to persuade political leaders of the necessity to act. It means finding technological solutions that reduce environmental damage, mitigate climate change, and protect against rising oceans.

Of course, you will need to find your own passion and write your own questions. Your satisfaction in life may depend on it. And given the incredible talen in this room, even our future as a species may depend on it.

Now go forth with my best wishes and congratulations!

Posted: June 12, 2014