Ancient Egyptians mummified various animals for different reasons, ranging from food for the afterlife through to veneration as a deity. (Photo: Rob Koopman/Flickr (CC BY-SA 2.0))

Richard Losick has been at Harvard University for over half a century, during which time he has devoted himself to undergraduate teaching and investigating cell fate determination in bacteria, principally Bacillus subtilis. This bacterium is remarkable for its rich repertoire of alternative states, which it uses to cope with an unpredictable environment, as explained in the Primer “Bacillus subtilis: A bacterium for all seasons” previously published in this journal (Curr. Biol. [2020] 30, 1146–1150).

Who turned you on to biology in the first place? I was fascinated with science from as early as I can remember, but I did not connect it to academics until high school, when I took Biology with Mr. (Casper) Hill. He was an inspiration. Also, as a Black man, Mr. Hill (and the diverse community in which I attended high school) had a lasting impact on me.

And what drew you to your specific field of research? A happy coincidence. I came to Harvard as a Junior Fellow from MIT, where my friend Linc Sonenshein was completing his PhD in the laboratory of Salvador Luria on a phage of B. subtilis that gets trapped in developing spores. Meanwhile, down the hall from me, Jim Watson’s graduate student Dick Burgess discovered a subunit of RNA polymerase in Escherichia coli that is responsible for promoter recognition. This raised the exciting questions of whether alternative sigma factors exist and whether such factors control phage gene expression and complex developmental processes, such as spore formation (as recounted in Cell [2018] 172, 1146–1152).

If you had to choose a different field of biology, what would it be? If I were young and just starting out now, I would delve into the genetics of behavior in mammals. I greatly admire the work of my Harvard colleagues Catherine Dulac and Hopi Hoekstra, who study the neurological and genetic basis for behavior in rodents, and I would try to join their labs as a graduate student!

Who were your key early influences? After Mr. Hill, my senior thesis mentor at Princeton, Charles Gilvarg, taught me the value of critical feedback in science. He sent me to do my PhD with Phil Robbins at MIT, who inspired me by working side by side with his lab members at the bench. Also, Salvador Luria was an inspiration. He even invited graduate students to his home to discuss great works of literature, fearing that we were too narrowly focused on science. He had a big impact on my career, sending me to Harvard as a Junior Fellow, where Jack Strominger welcomed me into his lab. Also, as explained above, I tackled a problem that was initiated in Luria’s lab.

Do you have any scientific heroes? The founders of molecular biology, including Oswald Avery, Seymour Benzer, Sydney Brenner, Salvador Luria, Matt Meselson, and Jim Watson.

Which historical scientist would you like to meet and what would you ask them? Oswald Avery. His 1943 (the year of my birth) letter to his brother leaves no doubt that he well understood the monumental significance of his discovery that Frederick Griffith’s transforming principle was DNA. I would ask him why he was reticent to make the case more explicitly in his 1944 publication and why he failed to attend key meetings and argue for DNA as the genetic material. In my view, his discovery (with Colin MacLeod and Maclyn McCarty) was the most important in biology over the last century, but it was slow to gain wide acceptance and principal credit went to others.

Do you have a favorite paper or science book? Avery’s publication, of course: ‘Studies on the chemical nature of the substance inducing transformation of pneumococcal types: Induction of transformation by a deoxyribonucleic acid fraction isolated from pneumococcus type III’ (J. Exp. Med. [1944] 79, 137–158). And the breathtakingly elegant and seminal paper of Seymour Benzer entitled ‘Fine structure of a genetic region in bacteriophage’ (Proc. Natl. Acad. Sci. USA [1955] 41, 344–354), which brought genetics to the level of nucleotides and helped define the gene, as well as set the stage for Crick to show that the code is triplet and non-overlapping.

What is the best advice that you’ve been given? I learned how to give a talk and write clearly from my former...
colleagues at Harvard, including Jim Watson, Wally Gilbert, Matt Meselson, and Mark Ptashne. They taught me that less is more. When giving a talk, whether on research or in teaching, use clear slides and spell things out with simple and direct statements. And, in writing, don’t waste words.

Also, and as mentioned above, I learned the value of critical feedback from my undergraduate mentor, Charles Gilvarg. He went through my senior thesis with a fine-tooth comb, and this told me that he deeply cared about my research and reasoning. Also, he explained that I should be pleased by the critical feedback that I received from my first publication based on my senior thesis because it showed that the reviewer had thought deeply about our research.

If you had not made it as a scientist, what would you have become? I hesitate to think!

What’s your favorite experiment? Certainly an early highlight of my laboratory was the discovery of the first alternative sigma factors in phage-infected cells by our team of Tom Fox, Jan Pero, and Robert Tjian. But the big remaining challenge was proving that these factors were in fact the products of known phage regulatory genes. This was perplexing with the limited tools that were available in the mid-1970s. We took advantage of nonsense mutants of the regulatory genes and tRNA suppressors that inserted different amino acids at the same codon. Using two-dimensional gel electrophoresis, we showed that certain suppressors caused a shift in isoelectric point, doing so individually for each of the three regulatory proteins. This could only be true if each protein were the product of the corresponding regulatory gene! We were thrilled!

What has been your biggest mistake…? I have been wrong more than once! The important lesson that I learned was not to stay wedded to ideas and/or findings that prove to be incorrect. Early on, we observed what we thought was a modification of RNA polymerase during spore formation, but it proved to be an artifact of purification. When we realized this, we published a follow-up paper documenting our error.

What are your favorite and least favorite conferences? Without question, the iconic ‘Biological Regulatory Mechanisms’ Gordon Research Conferences are at the top of my list because of their breadth and exciting science. Sadly, they were discontinued over 20 years ago and replaced by many more specialized meetings. ‘Biological Regulatory Mechanisms’ meetings were attended by leading scientists in diverse fields and the talks were breathtaking. At the other end of the spectrum, my least favorite are giant society conferences that have so many attendees that it is always difficult to have meaningful interactions.

In what ways do inclusion and diversity influence your work? As explained above, I attended high school in a diverse community and was greatly influenced by my inspiring biology teacher, Mr. Hill, who was a Black man. All this was in contrast to my subsequent experience in college (Princeton), which back then (1961–1965) was almost exclusively white and male and had a distinct social pecking order. (Princeton is vastly different and better now!) Motivated by these prior experiences, I have sought to promote women and those who are part of underrepresented minorities in science throughout my career at Harvard. I am most proud of a program that I ran with funding from the Howard Hughes Medical Institute (HHMI) in which I identified incoming underrepresented students and students from disadvantaged backgrounds with an interest in science. I helped to place these students in host laboratories for long-term research projects leading to a senior thesis. I made sure that they were well mentored, and we all gathered in person for an annual retreat at which seniors spoke on their theses and past graduates spoke on their current activities. It is my view that programs such as this one can be effective strategies for promoting diversity in science. Having said that, I have to add that, in my opinion, universities need to take a more even-handed and thoughtful approach in our support of the diverse populations of aspiring young STEM students and faculty than is currently the case.

How has education in the sciences changed over the course of your career? Having taught in introductory science courses since the beginning of my career, I have witnessed broad changes in STEM education both at my institution and nationally. Early in my career, teaching in the sciences was often treated as a burden, sometimes (and even still) referred to as a ‘teaching load’. But things have markedly improved over the years, and I like to think that I contributed, at least in a small way, to the improvements in the culture for teaching that I have witnessed. Among the many heroes who have wrought this cultural change are Harvard’s Eric Mazur, who invented wireless polling and flipping the classroom, the HHMI for its Professors Program, which promotes innovations in STEM education, and former National Academy of Sciences President Bruce Alberts for his tireless leadership in promoting science education. What I have learned over the years is not only that I am a better educator for doing research, but that I am a better scientist for being an educator.

Which aspect of science do you wish the general public knew more about? Mistakes are an inevitable feature of discovery. But we celebrate the fact that science is self-correcting. What makes science unique is that conclusions are constantly being tested, investigated, and if need be corrected by both ourselves and others.

What do you think is the biggest problem that science as a whole is facing today? The lack of effective communication to the public of the self-correcting nature of science and the data dependence of its conclusions.

The Biological Laboratories, Harvard University, 16 Divinity Avenue, Cambridge, MA 02138, USA. E-mail: losick@mcb.harvard.edu