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# THE NAI FELLOW PROFILE: AN INTERVIEW WITH DR. FRANCES ARNOLD

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In an interview with T&I, distinguished inventor and professor Dr. Frances Arnold discusses her most recent work and shares her thoughts on the benefits of her eclectic background, the divide between pure and applied science, and teaching students to innovate.

## INTRODUCTION

As a part of our continuing mission to honor academic invention and inventors, *Technology and Innovation (T&I)* is pleased to present Dr. Frances Arnold, renowned biochemist and chemical engineer, as the subject of this issue's NAI Fellow Profile. Arnold is the Dick and Barbara Dickinson Professor of Chemical Engineering, Bioengineering and Biochemistry and the director of the Donna and Benjamin M. Rosen Bioengineering Center at the California Institute of Technology.

Arnold holds a B.S. in mechanical and aerospace engineering from Princeton University and a Ph.D. in chemical engineering from the University of California, Berkeley. After completing postdoctoral work in chemistry at UC Berkeley and Caltech, she became a faculty member at Caltech, where she remains today. She is the author of over 200 peer-reviewed publications and numerous book chapters, commentaries, and reviews; the editor of three books; and inventor on 49 U.S. patents. She is the recipient of numerous prestigious awards, including the National Medal of Technology and Innovation and the Charles Stark Draper Prize, as well as one of the rare scholars who has achieved the distinction of being elected to

*(photo courtesy of Frances Arnold)*

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the U.S. National Academies of Science, Engineering, and Medicine and elected a fellow of the National Academy of Inventors, the American Association for the Advancement of Science, and the American Academy of Arts and Sciences.

Arnold has been lauded for her pioneering work in directed evolution, which allows for the engineering of proteins through the recombination or mutation of genes, followed by a careful artificial selection process to choose the desired traits. The resulting engineered proteins have the potential to revolutionize how we solve major global issues in health care, agriculture, and sustainable energy, among many other areas. For example, her work with the P450 enzyme has opened new, sustainable routes to pharmaceutical intermediates, safer ways to protect crops, and enhanced neuroimaging. The Arnold research group is a breeding ground for some of the most innovative work in bioengineering being done today, and, a gifted teacher as well as researcher, Arnold is also fostering a new generation of innovators in her laboratory.

*T&I* was honored when Dr. Arnold agreed to discuss her most recent work and to share her thoughts on the benefits of her eclectic background to her success, the divide between pure and applied science, and strategies for teaching students to innovate.

## INTERVIEW

***T&I:*** How would you describe your current work in a nutshell?

**Arnold:** I am interested in the evolution of chemical novelty—specifically, how do new enzyme catalysts arise from old ones. It happened a gazillion times in nature, but it's hard to capture evolution in the act. We can only see the results, usually well after the new and old functions diverged. I 'breed' enzymes in the laboratory, using mutation and recombination (a kind of 'molecular sex'), to better understand how new catalytic activities appear and also to create catalysts that nature never made but are useful to humans. These experiments demonstrate the power of evolution as an innovation machine.

**T&I:** Your original training was in mechanical and aerospace engineering, your Ph.D. was in chemical engineering, and then you moved into biochemical engineering, biochemistry and chemistry. How do you feel about having traversed such a wide intellectual terrain. In terms of invention and innovation, what advantages do your multiple perspectives offer.

**Arnold:** I have no doubt that my unusual training, and even my lack of formal training in biochemistry, contributed to the invention of directed enzyme evolution. I came at the protein engineering problem from an engineering perspective, free from the rigor that biochemical scientists feel the need to use. Rather than try to minimize the complexity of proteins by developing a 'rational' design approach, which would require that I understand the system in detail, I used what has worked well for billions of years: evolution. I use technology to speed it up a bit.

***T&I:*** When you first published work on protein engineering, the divide between pure and applied science was pronounced. From your perspective as a renowned scientist and a holder of 49 patents, to what extent has the relationship between pure and applied science changed?

**Arnold:** I will answer this big and interesting question only from the perspective of protein engineering and directed evolution. I always try to do both pure and applied science, solving an important problem while learning something deeper and more general along

*(photo courtesy of Frances Arnold)*

the way. By making new enzymes in the laboratory, we have the opportunity to observe how molecular problems can be solved. We learn which problems can be solved by evolution—e.g., can a specific new catalytic activity appear through a series of single amino acid changes—and we can study the details of the solutions. With some reverse engineering (biochemistry), we learn new things about these very complicated catalytic systems and the amazing ability of nature to innovate.

***T&I:*** In recent years, there has been a great deal of discussion concerning women and their underrepresentation in STEM fields. You have said that one of your greatest achievements has been your role in teaching and advising the many superb students who have studied under you at Caltech. Have your female students asked for advice on issues related to gender and science. If so, what advice have you offered them?

**Arnold:** Advice is cheap, and I try to avoid offering too much. Each young person has to navigate these issues on his or her own and make choices appropriate for them. Like evolution, many paths are possible, even if they are not direct!

***T&I:*** Keeping with the topic of students and teaching, could you offer an outline of how you engage your students in the invention and innovation process. What strategies or methods do you employ. Why is this an important learning process for them above and beyond their scientific training?

**Arnold:** I have a very simple strategy for promoting invention and innovation: collect really smart, interactive people together, give them space and resources, set the standard for excellence, and then largely leave them alone. Because my students and postdocs come from very different backgrounds in chemistry, engineering, and biology, they look to each other for help and a free exchange of ideas, not competition. This creates a supportive environment where everyone not only succeeds, but they can afford to take risks and do something really new. This is also how Caltech works as an institution—I try to emulate this process in my own laboratory.

***T&I:*** You have said that you were interested in languages when you were a student. Although you have pursued a different career path, anyone who has seen you speak can see that you are a gifted communicator. Because science is so dependent on communication for impact, I'd like to pursue that idea with you. What does being a good communicator mean for you in terms of advancing your scientific agenda. What role do more "popular" communication forums (e.g., TED talks)—as opposed to your scholarly publications and presentations—play in your work?

**Arnold:** I have benefited greatly from giving 'popular' talks to young audiences or broader audiences. These forums force one to think about the larger implications of the work and to identify effective ways to capture the audience's attention and communicate ideas. Because I am too lazy to generate many different talks, I started to use the same tools to communicate ideas in talks to experts as well. Then I learned that even the experts appreciate the emphasis on fundamental ideas and simple analogies—because no one can keep up with newest advances in all fields. Humor is also effective, and I wish I were better at that!

## CONCLUSION

Even with all of her accolades, in many ways, it seems as if her work is just beginning, as Arnold is constantly pushing limits, expanding boundaries, and seeking new opportunities for innovative science. At the end of the interview, Arnold offered some thoughts on future directions. On the research side, she shared that her upcoming work "involves bringing new chemistry into the biological world to access whole new classes of chemicals and materials.. She also commented on her deep engagement on the tech transfer side with her newest venture, Provivi, Inc., where she sees her work as having two main goals: to "1) bring new enzymes to the market, so that they can replace dirtier, unsustainable chemical processes and 2) develop natural and non-toxic ways to combat pests in agriculture, so that we can feed growing populations without ecosystem destruction.. Whether hearing her speak or reading her research, it is clear that, in every aspect, Arnold's work is characterized by a deep and sincere motivation to use innovation to better our lives and the state of our planet. In her final words, "I am always looking for ways to make the products we need in a cleaner, cheaper, and more sustainable fashion, and for where that ability opens new opportunities to combat chemical waste, pollution and harm to the planet."

## FURTHER READING


1. Arnold, F.H. The Library of Maynard-Smith: my search for meaning in the protein universe. Microbe 6(7):316-318; 2011.
2. Arnold, F.H. The nature of chemical innovation: new enzymes by evolution. Q. Rev. Biophys. 48(4)404-410; 2015
3. Flytzanis, N.C.; Bedbrook, C.N.; Chiu, H.; Engqvist, M.K.M.; Xiao, C.; Chan, K.Y.; Sternberg, P.W.; Arnold, F.H.; Gradinaru, V. Archaerhodopsin variants with enhanced voltage-sensitive fluorescence in mammalian and Caenorhabditis elegans neurons. Nat. Commun. 5:4894; 2014.
4. Prier, C.K.; Arnold, F.H. Chemomimetic biocatalysis: exploiting the synthetic potential of cofactor-dependent enzymes to create new catalysts. J. Am. Chem. Soc. 137(44):13992-14006; 2015.
5. Shapiro, M.G.; Westmeyer, G.G.; Romero, P.A.; Szablowski, J.O.; Küster, B.; Shah, A.; Otey, C.R.; Langer, R.; Arnold, F.H.; Jasanoff, A. Directed evolution of a magnetic resonance imaging contrast agent for noninvasive imaging of dopamine. Nat. Biotechnol. 28(3):264-272; 2010.
6. Wang, Z.J.; Renata, H.; Peck, N.E.; Farwell, C.C.; Coelho, P.S.; Arnold, F.H. Improved cyclopropanation activity of histidine-ligated cytochrome P450 enables the enantioselective formal synthesis of levomilnacipran. Agnew. Chem. Int. Ed. Engl. 53(26):6810-6813; 2014.