Science Discussion: We are researchers at Caltech working with Professor Frances Arnold, one of the recipients of the 2018 Nobel Prize in Chemistry. We use directed evolution to engineer proteins to do chemistry not found in nature (yet). Let's Discuss!!

ScienceModerator [1] and r/Science AMAs[1]

[1]Affiliation not available

April 17, 2023

Abstract

Hi Reddit, We are graduate students and postdocs in Professor Frances Arnold's research group at Caltech. We use directed evolution, the algorithm for which Frances won the Nobel Prize last week, as a tool to engineer proteins. Directed evolution, like Darwinian evolution, is about "survival of the fittest" by selecting beneficial mutations that enhance a desired function. The key difference is that in directed evolution the person running the experiment chooses which mutations are beneficial – in other words, we choose the definition of "fittest" in "survival of the fittest." Understanding how a protein's sequence connects to its structure is challenging (relevant XKCD), and understanding how that structure confers function is another significant challenge. A strength of directed evolution is that one does not need to know a lot about the protein to use it; all one needs is the genetic information (the DNA that encodes the protein of interest) and a way of testing each variant for the function of interest. We don't need to know exactly how or why the protein is able to catalyze a reaction or understand why a mutation enhances that activity. Proteins have been engineered using directed evolution for myriad uses, from higher stability for use in your laundry detergent to remove stains to producing blockbuster pharmaceutical compounds in place of less environmentally friendly syntheses. Unfortunately Frances is not able to join us for the discussion, but we are happy to answer any questions you have about directed evolution, proteins, Caltech, and beyond! Useful links on directed evolution: "What is directed evolution and why did it win the chemistry Nobel prize?" from Chemistry World C&EN Online explanation of directed evolution and phage display Frances discussing the Nobel Prize on NPR's Science Friday TEDxUSC talk by Frances: "Sex, Evolution, and Innovation" Learn more about the Arnold Group: http://fhalab.caltech.edu/ Follow Dr. Arnold on Twitter: https://twitter.com/francesarnold Our discussion panel guests today are: Anders Knight (/u/AndersKnight): Anders is a fourth-year bioengineering graduate student in the Arnold lab. He works on engineering heme proteins to do carbene transfer reactions not found in nature. An open-access paper on these kinds of reactions is available here. Kari Hernandez (/u/Kari_-Hernandez): Kari is in the 4th year of her Ph.D. and received her B.S. in chemical engineering from the University of Arizona. Her work focuses on making useful molecules by evolving heme proteins to do non-natural reactions. Jennifer Kan (/u/JennyKan): Jenny is a postdoc in Frances Arnold's lab at Caltech. Her favourite thing to do is to teach proteins to make cool bonds. Twitter: @sbjennykan Tina Boville (/u/TinaBoville): Tina is a postdoc in the Arnold lab evolving enzymes to make chemical building blocks called noncanonical amino acids. She is very interested in green chemistry and lab sustainability and is a fellow at the Resnick Institute. Patrick Almhjell (/u/PatrickAlmhjell): Patrick is a second-year graduate student in the Biochemistry and Molecular Biophysics program at Caltech, working on the same project as /u/TinaBoville. Patrick loves chemistry but not the chemistry lab, so he appreciates being able to use enzymes in water instead. An open-access review on noncanonical amino acid synthesis is available here. Kevin Yang (/u/KevinKYang): Kevin is a 5th year PhD student in Frances Arnold's lab. His research focuses on using machine learning to accelerate directed evolution. Read his open-access paper on using machine learning in protein engineering. Zach Wu (/u/zvxywu): Zach is a 4th year graduate student in Chemical Engineering. His research focuses on developing methods for engineering proteins efficiently and understanding the

sequence function relationship. Our guests will begin answering questions starting at 1:00PM PST.

the WINNOWER

REDDIT

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SCIENCEMODERATOR R/SCIENCE

Hi Reddit,

We are graduate students and postdocs in Professor Frances Arnold's research group at Caltech. We use directed evolution, the algorithm for which Frances won the Nobel Prize last week, as a tool to engineer proteins.

Directed evolution, like Darwinian evolution, is about "survival of the fittest" by selecting beneficial mutations that enhance a desired function. The key difference is that in directed evolution the person running the experiment chooses which mutations are beneficial – in other words, we choose the definition of "fittest" in "survival of the fittest."

Understanding how a protein's sequence connects to its structure is challenging (relevant XKCD), and understanding how that structure confers function is another significant challenge. A strength of directed evolution is that one does not need to know a lot about the protein to use it; all one needs is the genetic information (the DNA that encodes the protein of interest) and a way of testing each variant for the function of interest. We don't need to know exactly how or why the protein is able to catalyze a reaction or understand why a mutation enhances that activity.

Proteins have been engineered using directed evolution for myriad uses, from higher stability for use in your laundry detergent to remove stains to producing blockbuster pharmaceutical compounds in place of less environmentally friendly syntheses.

Unfortunately Frances is not able to join us for the discussion, but we are happy to answer any questions you have about directed evolution, proteins, Caltech, and beyond!

Useful links on directed evolution:

"What is directed evolution and why did it win the chemistry Nobel prize?" from Chemistry World

C&EN Online explanation of directed evolution and phage display

Frances discussing the Nobel Prize on NPR's *Science Friday*

TEDxUSC talk by Frances: "Sex, Evolution, and Innovation"

Learn more about the Arnold Group: http://fhalab.caltech.edu/

Follow Dr. Arnold on Twitter: https://twitter.com/francesarnold

OUR DISCUSSION PANEL GUESTS TODAY ARE:

Anders Knight (/u/AndersKnight): Anders is a fourth-year bioengineering graduate student in the Arnold lab. He works on engineering heme proteins to do carbene transfer reactions not found in nature. An open-access paper on these kinds of reactions is available here.

Kari Hernandez (/u/Kari_Hernandez): Kari is in the 4th year of her Ph.D. and received her B.S. in chemical engineering from the University of Arizona. Her work focuses on making useful molecules by evolving heme proteins to do non-natural reactions.

Jennifer Kan (/u/JennyKan): Jenny is a postdoc in Frances Arnold's lab at Caltech. Her favourite thing to do is to teach proteins to make cool bonds. Twitter: @sbjennykan

Tina Boville (/u/TinaBoville): Tina is a postdoc in the Arnold lab evolving enzymes to make chemical building blocks called

noncanonical amino acids. She is very interested in green chemistry and lab sustainability and is a fellow at the Resnick Institute.
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Kevin Yang (/u/KevinKYang): Kevin is a 5th year PhD student in Frances Arnold's lab. His research focuses on using machine learning to accelerate directed evolution. Read his open-access paper on using machine learning in protein engineering.
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