Frances H. Arnold

Dick and Barbara Dickinson Professor of Chemical Engineering
and Biochemistry, California Institute of Technology

"An Artificial Protein Family Created by Structure-Guided Recombination"

Tuesday, April 4, 2006 at 3:30 p.m. in FRNY G140

"Engineering by Evolution"

Wednesday, April 5, 2006 at 11:30 a.m. in FRNY G140

PURDUE UNIVERSITY | **School of Chemical Engineering**

Previous Kelly Lectures in Chemical Engineering

1965 Warren L. McCabe
1966 Arthur B. Metzner
1967 Olaf A. Hougen
1968 R. Byron Bird
1969 C. Judson King
1970 L.E. Scriven
1971 Charles N. Satterfield
1972 Robert L. Pigford
1973 Andreas Acrivos
1974 John M. Prausnitz
1975 Michel Boudart
1976 Arthur E. Humphery
1977 Rutherford Aris
1978 James J. Carberry
1979 Warren E. Stewart
1980 Paul J. Flory
1981 Neal R. Amundson
1982 William R. Schowalter
1983 Thomas J. Hanratty
1984 Wolfgang M.H. Sachtler
1985 Benjamin G. Levich
1986 Alan S. Michaels
1987 Morton M. Denn
1988 Edward L. Cussler
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1990 H. Ted Davis
1991 Reuel Shinnar
1992 Robert S. Langer
1993 Arthur W. Westerberg
1994 W. Harmon Ray
1995 Doulgas A. Lauffenburger
1996 John H. Seinfeld
1997 Lanny D. Schmidt
1998 Matthew Tirrell
1999 George Stephanopoulos
2000 Robert A. Brown
2001 Gerhard Ertl
2002 Mark E. Davis
2003 Gregory Stephanopoulos
2004 William B. Russel
2005 Special symposium celebrating 40 years
Frank S. Bates
Alexis T. Bell
Ignacio E. Grossmann
Michael L. Shuler
James Wei

The Kelly Lecture

Arthur Kelly, an alumnus of the university, established the Kelly Fund at Purdue University in 1956. The income from this fund is used to bring outstanding scientists and engineers to the campus for lectures and discussions in the Department of Chemistry and the School of Chemical Engineering.

2006 KELLY LECTURE

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Frances Arnold is the Dick and Barbara Dickinson Professor of Chemical Engineering and Biochemistry at the California Institute of Technology. Her research group engineers enzymes, biosynthetic pathways, and genetic regulatory circuits by directed evolution.

Dr. Arnold has co-authored more than 200 publications and edited several books on protein engineering and laboratory protein evolution. A member of the National Academy of Engineering and the Institute of Medicine of the National Academies, she has served on the Science Board of the Santa Fe Institute and the Science Advisory Boards of several corporations. Her recent awards include the Olin-Garvan Medal of the American Chemical Society (2005), the Food, Pharmaceuticals and Bioengineering Division Award of the AIChE (2005), the David Perlman Memorial Lectureship of the ACS Biochemical Technology Division (2003), the Carothers Award from the Delaware ACS (2003), and the Professional Progress Award of the AIChE (2000). She has more than 25 patents issued or pending.

After receiving her B.S. in Mechanical and Aerospace Engineering from Princeton University in 1979, she worked at the Solar Energy Research Institute in Golden, Colorado. She completed her Ph.D. in Chemical Engineering at the University of California, Berkeley in 1985. Following post-doctoral research in Chemistry at U. C. Berkeley and the California Institute of Technology, Dr. Arnold joined the faculty of Caltech's Division of Chemistry and Chemical Engineering in 1987. She has three sons, ages 8, 10, and 15.

"An Artificial Protein Family Created by Structure-Guided Recombination"

Tuesday, April 4, 2006

We are investigating ways in which proteins can be recombined to create new proteins with desirable properties. This approach circumvents our profound ignorance of how the amino acid sequence encodes protein function and exploits the ability of biological systems to evolve and adapt. Computational tools assist the experimental search for new proteins by identifying elements of structure that can be swapped among related proteins while minimizing structural disruption. Structure-guided recombination of homologous proteins generates libraries of diverse sequences, a large fraction of which retain the parental fold. We have used this approach to make a library comprising thousands of properly-folded cytochromes P450 which differ from their bacterial parents by up to 101 amino acid substitutions. High throughput sequencing and functional analysis of the resulting proteins has produced a large dataset which, unlike natural sequences, includes unfolded and nonfunctional sequences in addition to sequences with nonnatural functions. Besides providing new insights into what it takes to make a functional cytochrome P450, free from many of the filtering effects of natural selection, these laboratory-generated enzymes exhibit interesting and useful new activities, including the ability to produce the authentic human metabolites of drugs.

"Engineering by Evolution"

Wednesday, April 5, 2006

Biological engineers, or "synthetic biologists," dream of constructing new forms of life that perform tasks according to human specifications. Such life forms might be used to produce fuel or synthesize complex biologically active molecules; engineered cells might some day search out and destroy cancer cells or pathogens inside a human body. The dream, however, is somewhat grander than the reality, mainly because we are profoundly ignorant of the mapping from DNA sequence to biological function. (Re)writing a genome is tough when you don't know what to write. To overcome at least some of the problems, I will argue that we can look to the design algorithm that has produced the biological world: evolution. This simple algorithm works at all scales of biological complexity, from single proteins to ecosystems. Evolution in the laboratory, or "directed" evolution, exploits the unique nature of biological substrates—themselves the products of evolution—for forward engineering. No other engineering substrate lends itself so well to this physical optimization. With current algorithms, however, directed evolution still needs a good starting point. Thus there is a critical role for "rational" design to provide the raw material for evolutionary optimization.