American Chemical Society

National Awards Nomination Packet

James Flack Norris Award in Physical Organic Chemistry:2018
for: Eric Anslyn

Received: 11/01/2016 *Cycle Year: 1*

"For pioneering applications of physical organic chemistry to the development of new chemical sensors"

NOMINATOR:

Dennis Dougherty
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- Have you discussed this award nomination with the nominee? *Yes*

NOMINEE:

Eric Anslyn
Email: anslyn@austin.utexas.eduXXX

UTexas Chem and Biochem
1 University Sta Stop A1590
Austin, TX 78712-0803
UNITED STATES

ACS Current Member: Yes
Years of Service: 34
Date of birth: 01/01/1960
Present Position: University Distinguished Professor, U. of Texas, Austin
Industry: Academia

CODE OF CONDUCT:

- To the best of my knowledge, including past and present circumstances, the nominee:
  1. Employs and requires good safety protocols and practices in his/her laboratory and/or work environment;
  2. Upholds the highest ethical standards in his/her laboratory and/or work environment; and
  3. Otherwise engages in conduct that is consistent with both the objects of the American Chemical Society as stated in Article II Section 1 of its Constitution and the Chemical Professional Code of Conduct.

Code of Conduct Answer: *Yes*

SUPPORTER 1

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Monday, October 31, 2016

Nomination of **Eric Anslyn**
James Flack Norris Award in Physical Organic Chemistry

I have known Eric Anslyn since his time as a graduate student at Caltech, and I have followed his independent career. He is one of the brightest, most creative organic chemists of his generation. He is leading the way with new and innovative applications of macrocyclic/supramolecular chemistry, combining clever design with rigorous analytical skills to produce truly exciting results. He is a clearly superior candidate for the Norris Award.

Anslyn pioneered the field of differential sensing (a term he coined) using supramolecular chemistry. This is a union of receptors – synthetic, natural, or combinatorial - with a variety of signal transduction mechanisms and chemometrics. Physical organic chemistry is key, involving insightful chemical design of molecular recognition interactions, exploitation of photophysical events, and complex mathematical statistical analysis. Since Anslyn started the field, it has exploded with numerous other researchers using supramolecular chemistry in this manner. Ansyln has used deep levels of statistical analysis to demonstrate that concentrations of complex analytes in complex mixtures, such as wine, lipid compositions, and kinases in cellular extracts, can be monitored. For example, Anslyn developed a protocol for citrate sensing that has turned out to be completely practical in a medical setting for the analysis of citrate in dialysis fluids.

Anslyn was also the leader in deciphering the mechanisms by which boronic acids bind and signal sugars. Anslyn showed that the historical notion of a B-N bond in o-aminomethylphenylboronic acids was wrong. Further, Anslyn revealed that, contrary to the conventional wisdom, PET modulation of fluorescence in boronic-acid based receptors does not occur. Instead, sugars simply lead to disaggregation of the receptors, leading to emission turn-on.

Another clever use of mechanistic insight produced a novel approach to signal amplification. The protocol involves a triggering mechanism induced by the analyte that leads to an organometallic catalytic reaction that generates up to 70 fluorophores for each individual analyte.

Using detailed knowledge of reaction mechanisms, Anslyn generated a highly selective, activity-based probe for the important cellular signaling molecule NO. It exploits a cascade of reactions that "sew up" an extended conjugated poly-aromatic structure, leading to a fluorescence turn on of 1500-fold. The probe has been sent to dozens of chemists around the world.

What separates Anslyn from other workers in this field is the fact that not only has he prepared and evaluated novel structures, he has completely reshaped the intellectual foundation of much of the field. After decades of (highly valuable) efforts to maximize affinity and specificity, Anslyn showed that, in many contexts, just the opposite approach can be just as powerful. His indicator displacement assay was a key conceptual advance that opened up many new avenues for sensor development. When combined with rigorous analytical tools such as principal component analysis, artificial neural networks such as the multilayered perceptron, and linear discriminant analysis, the power and range of applicability of molecular recognition studies have been greatly expanded.

Another hallmark of Anslyn's work is that his receptors are not overly exotic molecular structures, but rather are elegant in their simplicity. That is, Anslyn has avoided the error of overly complex, "overdesigned" receptors that could never find practical use. Instead, Anslyn has shown that simpler structures based on sound recognition principles, when combined with combinatorial strategies and sophisticated analysis protocols, can produce sensors that can actually be used in the real world. As a result, Anslyn's work has produced 20 patents related to sensing.

Anslyn is an outstanding educator, having been recognized in numerous ways by UT for his commitment to education. I had the good fortune of collaborating with him on our textbook, *Modern Physical Organic Chemistry*. Not only did Eric initiate the project, his clear pedagogical vision and his constant focus on the student and on how to best communicate complex topics to students were essential to the success of the project.

It is clear that Eric Anslyn possesses a unique combination of skills. He has a deep understanding of fundamental physical organic chemistry, which he applies to all aspects of his work. He is creative and highly innovative, developing beautiful molecular systems that function as designed. And, he is able to appreciate and implement the practical aspects of his work, perhaps ultimately to the significant betterment of society. His nomination for the James Flack Norris Award has my complete and enthusiastic support.

Sincerely,

Biographical Sketch:

Eric V. Anslyn

Welch Regents Chair
University Distinguished Teaching Professor

Education:

Postdoctoral Work: [12/87-9/89]
Columbia University, New York, New York
Research Advisor: Professor Ronald Breslow
Research: Mechanistic studies of Ribonuclease A mimics. Detailed kinetics analyses of imidazole catalyzed 3'-5' UpU hydrolysis and isomerization. Synthesis and kinetics studies of bis-imidazole β-cyclodextrin catalyzed phosphodiester hydrolyses.

Ph.D., Chemistry: [11/87]
California Institute of Technology, Pasadena, California
Research Advisor: Professor Robert Grubbs
Research: Mechanistic and theoretical studies of olefin metathesis and ring opening metathesis polymerizations catalyzed by group IV and VI metals.

B.S., Chemistry: [5/82]
California State University, Northridge; GPA= 3.97/4.00
Research Advisor: Professor Edward Rosenberg
Research: Mechanistic studies of ligand fluxuations on clusters.

Research Awards, Honors, and Honorary Positions:

1st Czarnik Award Winner, International Molecular Sensors and Molecular Logic Gates, 2016
Saul Winstein Lecturer, UCLA, May 2014
Edward Leete Award, for Outstanding Contributions to Teaching and Research in Organic Chemistry, from The Organic Division of the ACS, Awarded on September 10th, 2013.
Comps Class Project Awardee, Carleton College, Northfield MN.
Izatt-Christensen Award in Macrocyclic and Supramolecular Chemistry, awarded at the 8th ISMSC in Washington DC, July 7th to 11th 2013.
Senior Visiting Fellow of the Institute for Advanced Study, Hong Kong University of Science and Technology, 2013-2014
Ta-shue Chou Award, For Outstanding Achievements in Physical Organic Chemistry, Feb. 21st 2012, Academia Sinica, Taiwan.
Gassman Lecturer, University Minnesota, Oct. 2011
Ramshorn Mark of Excellence, From Dean of the Cockrell School of Engineering, Oct. 29th 2009
Visiting Professor, Institute of Chemical and Engineering Sciences, Singapore, Dec. 15th-19th 2008
Faculty Service Award from the College of Natural Sciences, 2008
Visiting Professor, Hong Kong Baptist University, May 9th -11th 2007
Honorary Professor, East China University of Science and Technology, Induction May 2007
Adjunct Professor, Department of Biochemistry and Molecular Biology, The University of Texas Medical Branch, Galveston
American Association for the Advancement of Science, Election as a Fellow, 2006
Hamilton Textbook Award, from the University Coop. 2006
Cope Scholar Award. Granted from the ACS in Spring 2006.
Dreyfus Teacher-Scholar Award: 1994-1996
Alfred P. Sloan Research Fellow: 1994-1996
Proctor and Gamble University Research Initiative: 1993-1996
Searle Scholar: 1991-1994
Presidential Young Investigator: 1990-1995
Camille and Henry Dreyfus Young Faculty Award: 1989
National Science Foundation Post-Doctoral Fellowship: 1988
Union Carbide Fellow in Catalysis: Academic Year 86-87
Graduated with B.S. Summa Cum Laude: 1982
Analytical Chemistry Award, C.S.U., Northridge: 1980

20 Significant Outcomes:

"Physical Organic Chemistry by Any Other Name Would Smell as Sweet" Chapin, B.M.; Anslyn, E.V., *Isr. J. Chem*., **2016**, 56, 38-45.

"Click and chemically triggered declick reactions through reversible amine and thiol coupling via a conjugate acceptor" Diehl, K.L.; Kolesnicheko, I.V.; Robotham, S.A.; Bachman, L.; Zhong, Y.; Brodbelt, J.S.; Anslyn, E.V. *Nature Chem*. **2016**, XX XX, DO1: 10.1038/NCHEM 2601

"Differential sensing for the regio- and stereoselective identification and quantitation of glycerides" Diehl, K.L.; Ivy, M.A.; Rabidoux, S.; Petry, S.M; Muller, G.; Anslyn, E.V. *Proc. Natl. Acac. Sci*, **2015**, E3977-E3986. PMID: 26175025

"Chromogenic/Fluorogenic Ensemble Chemosensing Systems" Wu, J.; Kwon, B.; Liu, W. Anslyn, E.V.; Wang, P.; Kim, J.S., Chem. Rev., **2015**, 115, 7893-7943. PMID: 25965103

"Differential Sensing of MAP Kinases Using SOX-Peptides" Zamora-Olivares, D.; Kaoud, T.S.; Jose, J.; Ellington, A.; Dalby, K.N.; Anslyn, E.V., *Angew. Chem. Int. Ed.* **2014**, *53*, 14064 –14068. PMID: 25319433.

"Rapid Optical Methods for Enantiomeric Excess Analysis: From Enantioselective Indicator Displacement Assays to Exciton Coupled Circular Dichroism" Jo, H.H.; Lin, C.-Y.; Anslyn, E.V. Acc. Chem. Res. 2014, 47, 2212-2221. PMID: 24892802.

"On the Rate of Boronate Ester Formation in Ortho-Aminomethyl-functionalized Phenyl Boronic Acids", Collins, B.E.; Metola, P.; Anslyn, E.V. *Supramolecular Chemistry*, **2013**, *25*, 79-86. PMID: 23441105.

"Discimination of Flavonoids and Red Wine Varietals by Arrays of Differential Peptidic Sensors" Umali, A. LeBoeuf, S.E.; Newberry, R.W.; Kim, S.; Tran, L.; Rome, W.A.; Tian, T.; Taing, D.; Hong, J.; Kwan, M.; Heymann, H.; Anslyn, E.V. *Chem. Sci.* **2011**, *2*, 439-445.

"Dynamic multi-component covalent assembly for the reversible binding of secondary alcohols and chirality sensing" You,Lei; Berman, Jeffrey S.; Anslyn, E.V. Nature Chemistry 2011, 3, 943-948. PMID: 22109274.

"A Highly Selective Low-Background Fluorescent Imaging Agent for Nitric Oxide" Yang, Y.; Seidlits, S.; Adams, M.M.; Lynch, V.M.; Schmidt, C.E.; Anslyn, E.V.; Shear, J.B. *J. Am. Chem. Soc*. **2010**, 132, 13114-13116. PMID: 20672823.

"Electrophilic coordination catalysis: a summary of previous thought and a new angle of analysis," Houk, R. J.; Monzingo, A.; Anslyn, E. V., Acc Chem Res., **2008**, 41(3), 401-10. PMID: 18229891.

"Signal amplification by allosteric catalysis" Zhu, Lei; Anslyn, Eric V *Angew. Chem., Int. Ed,* **2006**, *45*, 1190-1196. PMID: 16432908.

"A Structural Investigation of the N-B Interaction in an o-(N,N-Dialkylaminomethyl)arylboronate System" Zhu, Lei; Shabbir, Shagufta H.; Gray, Mark; Lynch, Vincent M.; Sorey, Steven; Anslyn, Eric V J*. Am. Chem. Soc.* **2006**, *128*, 1222-1232. PMID: 16433539.

"Guanidinium Groups Act as General-Acid Catalysts in Phosphoryl Transfer Reactions: A Two-Proton Inventory on a Model System" Piatek, Anna M.; Gray, Mark; Anslyn, Eric V. *J. Am. Chem. Soc*. **2004**, *126*, 9878-9879. PMID: 15303835.

"Rate of Enolate Formation is Not very Sensitive to the Hydrogen Bonding Ability of Donors to Carbonyl Oxygen Lone Pair Acceptors; A Ramification of the Principle of Non-Perfect Synchromization for General-Acid-Catalyzed Enolate Formation", Z. Zhenlin, T. S. Snowden, M.D. Best, E.V. Anslyn, J. Am. Chem. Soc. 2004, 126, 3488-3495. PMID: 15025476

"Sensing a Paradigm Shift in the Field of Molecular Recognition: From Selective to Differential Receptors," J.J. Lavigne, E.V. Anslyn, *Angew. Chemie,* **2001**, *40*, 3118-3130.

"Teaching Old Indicators New Tricks," S.L. Wiskur, H. Ait-Haddou, J.J. Lavigne, E.V. Anslyn, A*ccounts of Chemical Research*, **2001**, *34*, 963-972. PMID: 11747414

"A Chemosensor for Citrate in Beverages", A. Metzger, E.V. Anslyn, *Angew. Chem., Int. Ed. Eng.* **1998**, *37*, 649-652.

Eric V. Anslyn, Youjun Yang, Michelle M. Adams, "Fluorescent Nitric Oxide Probes and Associated Methods", U.S. Patent No. 8637323, Issued January 28, 2014

John McDevitt, Eric Anslyn, Jason Shear, Dean Neikirk and Nick Christodoulides, "Method and System for The Analysis of Saliva Using a Sensor Array", U.S. Patent No. 7651868, Issue January 26, 2010

On Oct 27, 2016, at 5:04 PM, J Fraser Stoddart <jfstoddart@gmail.com> wrote:
Dear Dennis

Attached is my attempt to a 400-word supporting reference. Please let me know in the next 24 hours if this document is up to your expectations officer

Best regards

Fraser

Eric Anslyn Recommendation Letter

In his groundbreaking research, stretching back over a quarter of a century, Eric Anslyn has revolutionized the science of Physical Organic Chemistry through the merging of fundamental investigations of the mechanism of organic reactions, molecular recognition and photophysical techniques with his own highly distinctive approach to supramolecular analytical chemistry. A combination of insightful chemical design of molecular recognition processes involving receptors and their analytes, the exploitation of photophysical effects revealed on account of interactions between receptors and their analytes, and the application of complex mathematical statistical analysis to these phenomena has positioned Anslyn at the forefront of taking Physical Organic Chemistry from its humblest of origins into a new era characterized by high complexity that addresses functions or performs tasks. It is for this sea change in the discipline that I support with unfettered enthusiasm the nomination of Eric Anslyn for the 2018 James Flack Norris Award in Physical Organic Chemistry.

Anslyn has positioned himself at the forefront of contemporary advances in Physical Organic Chemistry by his development of a now much-used method of optical signaling in molecular recognition events that he has called the indicator display assay. Add to this new methodology his differential sensing techniques for the identification and quantification of analytes and his signal amplification of fluorescent signals by allosteric catalysis, not to mention his fundamental mechanistic investigations on the binding of sugars by boronic acid, his activation of carbonyl groups for nucleophilic attack, and his declick chemistry, and you have a proliferation of creativity of awesome proportions.

No single organic chemist has done more than Anslyn to transfer the traditional Physical Organic Chemistry of the Winstein era into new territory relying on the use of different commodities and contemporary concepts. Chemists, organic and otherwise, will probably look back on these times and refer to it as the Anslyn era. Eric has been daring enough to go where no one in organic chemistry has gone before and, to this extent, has not only created his own field but has also revitalized a discipline. If anyone should want to challenge this evaluation of his remarkable accomplishments, let them reflect on the fact that Anslyn, in collaboration with Dennis Dougherty, has left as a legacy to the rejuvenated field the world's most widely used text on Physical Organic Chemistry, appropriately entitled, *Modern Physical Organic Chemistry*.