AMERICAN UNIVERSITY OF BEIRUT
FACULTY OF ARTS & SCIENCES
Department of Chemistry

2022 Makhlouf Haddadin Symposium

October 6–7, 2022
Jassim Al-Qatami Engineering Lecture Hall (ELH),
Munib and Angela Masri Building

Prof. Makhlouf J. Haddadin

Professor Makhlouf J. Haddadin was born in the beautiful village of Ma'in, Jordan, on March 21, 1935. He went to the Hussein College in Amman for high school, and was later awarded a full scholarship from the Jordanian Ministry of Education to study Chemistry at AUB. He received a B.Sc. in 1957 and continued at AUB as an MS student under the direction of the late Professor Costas Issidorides. He did his Ph.D. in Organic Chemistry with Prof. Alfred Hassner at the University of Colorado, Boulder. After graduating in 1962, Dr. Haddadin went to Harvard University for two years of Postdoctoral research under the direction of the late Professor Louis Fieser.

In 1965, Prof. Haddadin decided to return to his alma mater as an Assistant Professor of Chemistry, where he quickly climbed the academic and administrative ladders. In 1969, he was promoted to Associate Professor with Tenure, and he became a Professor in 1975. He served AUB in numerous important administrative positions, including vice president for academic affairs, acting Dean of Health Sciences, and acting President at some of the most testing times of AUB. Despite his busy time at AUB, Dr. Haddadin found time for distinguished Sabbatical research leaves at many prestigious places including University of Notre Dame, University of North Texas, and University of California at Davis.

Professor Haddadin has been especially celebrated for his achievements in the area of heterocyclic chemistry that resulted in the publication of more than 125 scholarly papers in prestigious international journals. A landmark event in Professor Haddadin's career was his co-discovery of the Beirut Reaction–a reaction that impacted the field of pharmaceutical chemistry and yielded 40 patents in numerous countries. His most recent contributions revolved around the "Davis-Beirut Reaction", co-discovered with Professor Mark J. Kurth of the University of California at Davis. In 2018, Dr. Haddadin was the first faculty to hold the Bonnie and Costantine Issidorides Chair in Organic Chemistry and until his retirement. In addition to Chemistry, Dr. Haddadin is also known for his love and passion for Arabic History. Dr. Haddadin retired from AUB in 2022 after 57 years of outstanding research, extraordinary services, mentoring and inspiring generations of students who currently hold important positions in academia and the chemical industries.

On September 21, 2022, Professor Makhlouf Haddadin sadly passed away in his native Jordan. May he rest in peace.

Makhlouf Haddadin Endowment

The Makhlouf Haddadin Endowment was established by Prof. Bilal R. Kaafarani in February 2011. Since 2011, proceeds from the Endowment have been used to grant the Makhlouf Haddadin Awards to distinguished graduating chemistry undergraduate and graduate students. As of 2015, the Endowment proceeds have been also used to fund an annual Makhlouf Haddadin lectureship/symposium.

For more details: www.aub.edu.lb/haddadin

2022 Makhlouf Haddadin Symposium Schedule

Thursday, Oct 6, 2022	
9:00 am	Professor Bilal Kaafarani *Opening remarks*
9:10 am	FAS Interim Dean Saouma BouJaoude
9:20 am	President Fadlo Khuri
Session 1 | Chair: Professor Tarek Ghaddar	
9:40 am	Professor Teri W. Odom, *Gold Nanostars as Structural Valency Probes*
10:20 am	Professor Kirk S. Schanze, *Conjugated Polyelectrolytes in Biosensing and Disinfection*
11:00 am	Coffee Break
Session 2 | Chair: Professor Kamal Bouhadir	
11:30 am	Professor Prashant V. Kamat, *Perovskite Photocatalysis. Tracking Electron Transfer at $CsPbBr_3$ Nanocrystal Interface*
12:10 pm	Professor Luisa Torsi, *Single-Molecule Reliable Detections with a Large-Area Electronic Interface*
12:50 pm	Lunch
Friday, Oct 7, 2022	
Session 3 | Chair: Professor Bilal Kaafarani	
9:00 am	Professor Hanadi Sleiman, *DNA Nanostructures: From Design to Biological Function*
9:40 am	Professor Thomas E. Mallouk, *Managing Electrons and Protons in the Bio-Inspired Conversion of Renewable Energy*
10:20 am	Professor Denis Liotta, *Novel Therapeutics for Treating Viral Diseases, Cancer and Neurological Disorders*
11:00 am	Coffee Break
Session 4 | Chair: Professor Digambara Patra	
11:30 am	Professor Bruce A. Arndtsen, *Alternative Energetic Drivers for Metal Catalyzed Coupling Reactions*
12:10 pm	Professor Svetlana B. Tsogoeva, *Multi-Step Domino Reactions: Access to Versatile Compounds for Material and Life Sciences*
12:50 pm	Lunch
2:30 pm	*The Art of High Impact Publication: Round Table Discussion About Publishing Science and More!* Professor Prashant V. Kamat, Editor-In-Chief of *ACS Energy Letters* Professor Teri W. Odom, Editor-In-Chief of *Nano Letters* Professor Kirk S. Schanze, Editor-In-Chief of *ACS Applied Materials & Interfaces* Professor Hanadi Sleiman, Associate Editor of the *Journal of the American Chemical Society*

Gold Nanostars as Structural Valency Probes

TERI W. ODOM
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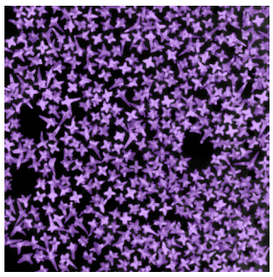
Abstract



Anisotropic gold nanoparticles exhibit shape-dependent optical properties beneficial for optical sensing, biomedical imaging, and photocatalysis. Although different synthetic approaches can result in anisotropic nanoparticles, usually a desired shape requires the use of seed particles, where nucleation is followed by selective faceted growth. In contrast, Good's buffers can act both as nucleating and shape-directing agents for the synthesis of a new class of biocompatible anisotropic nanoparticles: gold nanostars (AuNS). This talk will discuss the fundamentals and applications of AuNS that support positive, negative, and neutral curvature. First, we will describe details of AuNS growth and mechanistic insight gained from unconventional analytical tools. Second, we will discuss the functionalization with biological ligands that can facilitate both nanoparticle assembly and single-particle imaging of their interactions with live cells. Finally, we will show how targeting nanoconstructs based on AuNS show distinct properties from their spherical counterparts when interacting with cancer cells, which opens prospects for a novel type of assay based on real-time dynamics.

Related Readings

1. Choo, P.; Arenas-Estban, D.; Jung, I.; Chang, W. J.; Weiss, E. A.; Bals, S.; Odom, T. W. "Investigating Reaction Intermediates during the Seedless Growth of Gold Nanostars Using Electron Tomography", *ACS Nano* **2022**, *3*, 4408–4414.
2. Choo, P.; Liu, T.; Odom, T. W. "Nanoparticle Shape Determines Dynamics of Targeting Nanoconstructs on Cell Membranes", *J. Am. Chem.* Soc. **2021**, *143*, 4500–4555.
3. Coughlin, E. E.; Hu, J.; Lee, A.; Odom, T. W. "Light-Mediated Directed Placement of Different DNA Sequences on Single Gold Nanoparticles", *J. Am. Chem.* Soc. **2021**, *143*, 3671–3676.

Biography

Teri W. Odom is Joan Husting Madden and William H. Madden, Jr. Professor of Chemistry and Chair of the Chemistry Department at Northwestern University. She is an expert in designing structured nanoscale materials that exhibit extraordinary size and shape-dependent optical and physical properties. Odom is a Member of the American Academy of Arts and Sciences (AAAS) and a Fellow of the American Chemical Society (ACS), the Royal Society of Chemistry (RSC), the Materials Research Society (MRS), the American Institute for Medical and Biological Engineering (AIMBE), the American Physical Society (APS), and Optica. Select honors and awards include: the RSC Centenary Prize; the ACS National Award in Surface Science; a Research Corporation TREE Award; a U.S. Department of Defense Vannevar Bush Faculty Fellowship; a Radcliffe Institute for Advanced Study Fellowship at Harvard University; an NIH Director's Pioneer Award; the MRS Outstanding Young Investigator Award; the National Fresenius Award from Phi Lambda Upsilon and the ACS; an Alfred P. Sloan Research Fellowship; and a David and Lucile Packard Fellowship in Science and Engineering. Odom was founding Chair of the Noble Metal Nanoparticles Gordon Research Conference (GRC) and founding Vice-Chair of the GRC on Lasers in Micro, Nano, Bio Systems. She was an inaugural Associate Editor for *Chemical Science* and founding Executive Editor of *ACS Photonics*. Currently, Odom is Editor-in-Chief of *Nano Letters*.

Conjugated Polyelectrolytes in Biosensing and Disinfection

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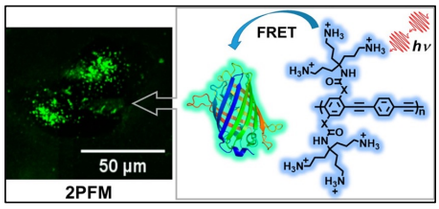
Abstract

Conjugated polyelectrolytes (CPEs) featuring poly(phenylene ethynylene) and poly(thiophene) backbones substituted with ionic solubilizing groups are water soluble. These materials display a variety of interesting properties, including self-assembly into nanoscale aggregates, ability to process into nanostructured layer-by-layer films and optical/stimuli responsive behaviour in the presence of ions, surfactants and biomacromolecules. We have explored the use of cationic CPEs as fluorescent sensors for polyphosphates (pyrophosphate, ATP and ADP). In addition, cationic CPEs exhibit profound light-activated biocidal activity vs. a broad spectrum of bioagents, including bacteria, virus particles and spores. The talk will give a high-level overview work in this area, including recent work concerning the interaction of cationic CPEs with mammalian and bacterial cells.



Related Readings

1. Jiang, H.; Taranekar, P.; Reynolds, J. R.; Schanze, K. S. "Conjugated Polyelectrolytes: Synthesis, Photophysics, and Applications", *Angew. Chem.* **2009**, *48*, 4300–4316.
2. Huang, Y.; Li, Z.; Risinger, A. L.; Enslow, B. T.; Zeman, C. J., IV; Jiang, G.; Yang, Y.; Schanze, K. S. "Fluorescence Spectral Shape Analysis for Nucleotide Identification", *Proc. Nat. Acad. Sci. USA* **2019**, *116*, 15386–15391.
3. Jagadesan, P.; Yu, Z.; Barboza-Ramos, I.; Herman Lara, H.; Vazquez-Munoz, R.; Lopez-Ribot, J. L.; Schanze, K. S. "Light-Activated Antifungal Properties of Imidazolium-Functionalized Cationic Conjugated Polymers", *Chem. Mater.* **2020**, *32*, 6186–6196.

Biography

Kirk Schanze earned his B.S. in Chemistry from Florida State University in 1979 and his Ph.D. in Chemistry from the University of North Carolina at Chapel Hill in 1983. He was appointed a Miller Postdoctoral Fellow at the University of California, Berkeley, from 1984-1986 and began his independent faculty career at the University of Florida in 1986. Schanze was University Distinguished Professor and Prominski Professor of Chemistry at the University of Florida until 2016. He is currently the Robert A Welch Distinguished University Professor at the University of Texas at San Antonio. He has authored or co-authored more than 350 peer-reviewed articles on basic and applied research topics, with a primary focus on organic and organometallic materials chemistry, and is named in 20 patents or disclosures. He was a Senior Editor of the ACS journal *Langmuir* from 2000 - 2008. Since 2008, Schanze is Editor-in-Chief of *ACS Applied Materials & Interfaces*, the ACS journal focused on chemistry and engineering of applications-focused research in materials and interfaces.

Perovskite Photocatalysis. Tracking Electron Transfer of $CsPbBr_3$ Nanocrystal Interface

PRASHANT V. KAMAT

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Abstract

The rise of metal halide perovskite based solar cell with efficiencies exceeding 25% has rejuvenated interest in nanoscale perovskite materials for photocatalysis. The metal halide perovskites are analogous to metal chalcogenides in the sense that they absorb in the visible region, their bandgap can be tuned through anion composition and size and shape can be readily varied using hot injection synthetic approach. However, relatively few mechanistic studies exist on the photocatalytic reduction and oxidation processes. The softness of perovskite materials makes them susceptible to surface transformation or degradation in polar solvents. Capping with CdS shell allowed us to carry out electron transfer reactions in polar medium. Using viologen as a probe we have now succeeded in probing the electron transfer of $CsPbBr_3$ nanocrystals. The nature of binding of viologen molecule with the surface has direct influence on the charge separation. Ways to stabilize electron transfer product and improve the photocatalytic performance of perovskite nanocrystals will be discussed.

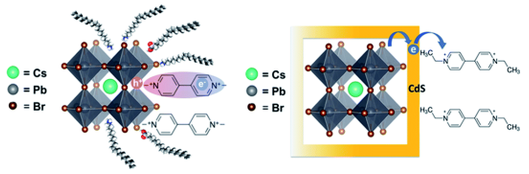

Figure 1. Surface interaction between CsPbBr3 nanocrystal and an electron acceptor (viologen) dictate the charge separation and overall photocatalytic performance.

Related Readings

1. DuBose, J. T.; Kamat, P. V. "Efficacy of Perovskite Photocatalysis: Challenges to Overcome", *ACS Energy Letters* **2022**, *7*, 1994–2011.
2. DuBose, J. T.; Kamat, P. V. "Energy Versus Electron Transfer: Managing Excited State Interactions in Perovskite Nanocrystal-Molecular Hybrid", *Chem. Rev.* **2022**, *122*, 12475–12494.
3. Kipkorir, A.; Cho, J.; DuBose, J. T.; Kamat, P. V. "CsPbBr3–CdS Heterostructure: Stabilizing Perovskite Nanocrystals for Photocatalysis", *Chem. Sci.* **2021**, *12*, 1481–14825.

Biography

Prashant V. Kamat is a Rev. John A. Zahm, C.S.C., Professor of Science in the Department of Chemistry and Biochemistry and Radiation Laboratory at the University of Notre Dame. He is also a Concurrent Professor in the Department of Chemical and Biomolecular Engineering. Professor Kamat has for more than three decades worked to build bridges between physical chemistry and material science to develop advanced nanomaterials that promise cleaner and more efficient light energy conversion. He has published more than 500 scientific papers that have been well recognized by the scientific community. Thomson-Reuters has featured him as one of the most cited researchers each year since 2014 (2014 -2020). He is a Fellow of ACS, MRS, ECS and AAAS. He is also Pravasi Fellow of the Indian National Science Academy. He is currently serving as the Editor-in-Chief of *ACS Energy Letters*.

Single-Molecule Reliable Detections With a Large-Area Electronic Interface

LUISA TORSI

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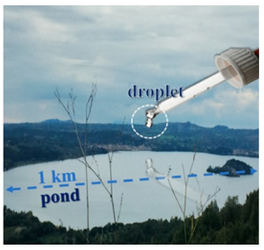
Abstract

A large millimeter-wide electronic interface can detect at a single-molecule/entity limit-of-detection. The technology is called SiMoT - Single-Molecule with a large Transistor. So far, antigens (Immunoglobulins, C-reactive proteins, spike 1, HIV p-24), antibodies (anti-immunoglobulins, anti-spike1), peptides, viruses (SARS-Cov-2), bacteria (Xylella fastidiosa), and even DNA strands (KRAS, miR-182) have been detected. Selectivity is assured by covering the gate electrode with a large number (1011-1012/cm2) of recognition elements to affinity binding the target element. SiMoT detects directly in a droplet (0.1 mL) of a real fluid such as saliva from COVID-19 patients, blood serum, pancreatic cysts juice, and olive saps from infected trees. Relevantly Brownian diffusion enables the entity to statistically hit the millimeter-wide interface in a few minutes. Considering the footprint of a molecule on a millimeter-wide interface, it is like spotting a droplet of water falling on the surface of a 1 Km wide lake as depicted in the graphical abstract. The applications span from a handheld intelligent single-molecule binary bioelectronic system for fast and reliable immunometric point-of-care testing of COVID-19 patients and Xylella fastidiosa single bacterium detected in infected plants sap. The phenomenon enabling such outstanding performance level was discovered in 2018. While still under investigation, it is supposed to involve an amplification that starts from the single affinity binding that triggers a propagating collaborative response. Future actions include the deepening of our understanding of the sensing mechanism and the engagement in a campaign of thousands of clinical trials that will bring SiMoT beyond TRL5.



Related Readings

1. Macchia, E.; Torricelli, F.; Bollella, P.; Sarcina, L.; Tricase, A.; Di Franco, C.; Österbacka, R.; Kovács-Vajna, Z. M.; Scamarcio, G.; Torsi, L. “Large-Area Interfaces for Single-Molecule Label-free Bioelectronic Detection”, *Chem. Rev.* **2022**, *122*, 4636–4699.
2. Macchia, E.; De Caro, L.; Torricelli, F.; Di Franco, C.; Mangiatordi, G. F.; Scamarcio, G.; Torsi, L. “Why a Diffusing Single-Molecule can be Detected in FewMinutes by a Large Capturing Bioelectronic Interface”, *Adv. Sci.* **2022**, 2104381.
3. Macchia, E.; Manoli, K.; Holzer, B.; Di Franco, C.; Ghittorelli, M.; Torricelli, F.; Alberga, D.; Mangiatordi, G. F.; Pallazzo, G.; Scamarcio, G.; Torsi, L. “Single-Molecule Detection with a Millimetre-Sized Transistor”, *Nat. Commun.* **2018**, *9*, 1–10.

Biography

Luisa Torsi is a professor of chemistry at the University of Bari and adjunct professor at Abo Academy University in Finland. From UNIBA she received her laurea degree in Physics and the PhD in Chemistry and was post-doctoral fellow at Bell Labs in USA. In 2010, Torsi was awarded with the H.E. Merck prize being yet the first women to receive this recognition. In 2019, she received the Distinguished Women Award by the International Union of Pure and Applied Chemistry (IUPAC). She has been also the only women president of the European Material Research Society, the largest of its kind in EU. Prof. Luisa Torsi is also the winner of the Wilhelm Exner Medal 2021, a prize awarded since 1921 by the Austrian Industrial Association to celebrate excellence in science. Torsi has authored 220 papers, published also in *Science* and *Nature* journals. Her works gathered almost 15,000 Google scholar citations resulting in an *h*-index of 59. Gathered research funding for over 28 M€, comprises several national and European projects, mostly coordinated by her. Torsi is committed to the role-modeling for younger women scientists. In a recent campaign by Fondazione Bracco, she was featured in a story of TOPOLINO (Italian series of Disney comics), as “Louise Torduck”, a successful female scientist of the Calisota valley.

DNA Nanostructures: From Design to Biological Function

HANADI SLEIMAN

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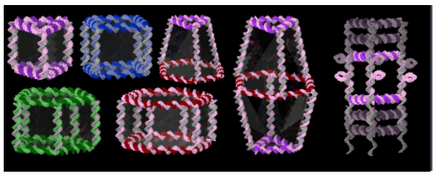
Abstract

DNA is known to us as the molecule of life, the blueprint that defines who we are. But the very properties that make DNA such a reliable molecule for information storage also make it one of the most remarkable building materials.

Over the past few years, our research group has taken DNA out of its biological context and has used this molecule to build nanostructures, for applications in biology and materials science. DNA structures can be precisely controlled in size, shape, and presentation of molecules on their surface. They can load drug cargo and deliver on demand, in response to specific biological triggers. We find that they resist nuclease degradation, silence gene expression, and have a favorable in vivo distribution profile. The applications of these DNA structures as drug delivery vehicles to cancer cells will be described.

We will also describe a method to 'print' DNA patterns onto other materials, thus beginning to address the issue of scalability for DNA nanotechnology. Finally, we will discuss the ability of small molecules to reprogram the assembly of DNA, away from Watson-Crick base-pairing into new motifs.



Related Readings

1. Seeman, N. C.; Sleiman, H. F. "DNA Nanotechnology", *Nat. Rev. Mat.*, **2018**, *3*, 17068.
2. Rizzuto, F. J.; Platnich, C. M.; Luo, X.; Shen, Y.; Dore, M. D.; Lachance-Brais, C.; Guarne, A.; Cosa, G.; Sleiman, H. F. "A Dissipative Pathway for the Structural Evolution of DNA Fibers", *Nat. Chem.* **2021**, *13*, 843–849.
3. Bujold, K. E.; Hsu, J. C. C.; Sleiman H. F. "Optimized DNA "Nanosuitcases" for Encapsulation and Conditional Release of siRNA", *J. Am. Chem. Soc.* **2016**, *138*, 14030–14038.

Biography

Hanadi Sleiman is Professor of Chemistry and Canada Research Chair in DNA Nanoscience at McGill University. She received her Ph.D. from Stanford University and was a CNRS postdoctoral fellow in Prof. Jean-Marie Lehn's laboratory at the Université Louis Pasteur. She joined the faculty at McGill University in 1999, and her research group focuses on using the molecule DNA as a template to assemble nanostructured materials for drug delivery and diagnostics. Sleiman is Fellow of the Royal Society of Canada, Associate Editor of *J. Am. Chem. Soc.*, and Editorial Advisory Board member of *Chem*, *JOC*, and *ChemBioChem*. Among her recognitions are the NSERC John C. Polanyi Award (2021), Research Corporation Cottrell STAR award (2021), Killam Research Fellowship (2018), CSC R. U. Lemieux Award (2018), Netherlands Scholar Award in Supramolecular Chemistry (2018), Izatt-Christensen Award in Supramolecular Chemistry (2016), Swiss Chemical Society Lectureship (2012), CIC E. Gordon Young Award (2011), CSC Strem Award (2009). She received the McGill Principal's Prize and the Leo Yaffe Award for Excellence in Teaching.

Managing Electrons and Protons in the Bio-Inspired Conversion of Renewable Energy

THOMAS E. MALLOUK

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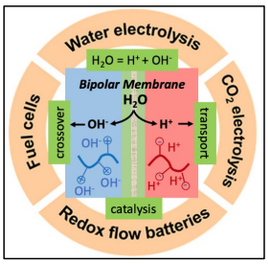
Abstract

Future solar energy conversion systems (both photovoltaic and fuel-producing solar cells) must be efficient, stable, and inexpensive in order to be competitive with fossil energy sources. In biological photosynthesis, the internal quantum efficiency for light-induced charge separation is near unity, and similarly high efficiencies can be achieved in photovoltaic cells based on dye sensitization of semiconductors. However, it remains a challenge to adapt these kinds of molecular photosystems to the efficient production of energy-dense fuels. By coupling the photosensitizers of dye cells to nanoparticulate or molecular oxygen evolution catalysts, we can now make solar cells that split water with visible light. Using related design ideas, we have also made visible light-powered "Z-schemes" in which dye-sensitized hydrogen-evolving particles are coupled to oxygen evolving particles by redox mediators. The low solar conversion efficiency of these systems is a consequence of the kinetics of charge separation and recombination at the dye-sensitizer interface, which in turn are related to the management of protons generated in the water oxidation reaction. This problem of proton management at the anode of water splitting solar cells led us to investigate system-level issues that arise with (photo)electrochemical fuel production near neutral pH. In buffer-based water splitting cells, losses from solution resistance and electrochemically generated pH gradients become substantial in cells that run continuously for periods of hours. This problem can however be addressed by using bipolar membrane-based cells in which the cathode and anode operate at low and high pH, respectively. Bipolar membranes enable efficient water splitting and CO_2 electrolysis, and are also interesting for other membrane-based electrochemical energy conversion devices such as fuel cells and redox flow batteries. The catalytic reaction enabling these applications is water association/dissociation at the bipolar polymer interface, which is still not fully understood.



Related Readings

1. Nishioka, S.; Hojo, K.; Xiao, L.; Gao, T.; Miseki, Y.; Yasuda, S.; Yokoi, T.; Sayama, K.; Mallouk, T. E.; Maeda, K. "Surface-Modified, Dye-Sensitized Niobate Nanosheets Enabling an Efficient Solar-Driven Z-Scheme for Overall Water Splitting", *Sci. Adv.* **2022**, *8*, eadc9115.
2. Yan Z.; Mallouk, T. E. "Bipolar membranes for Ion Management in (Photo-) Electrochemical Energy Conversion", *Acc. Mater. Res.* **2021**, *2*, 1156–1166.
3. Yan, Z.; Hitt, J. L.; Zeng, Z.; Hickner, M. A.; Mallouk, T. E. "Improving the Efficiency of CO2 Electrolysis by Using a Bipolar Membrane with a Weak Acid Cation Exchange Layer", *Nature Chem.* **2021**, *13*, 33–40.

Biography

Thomas E. Mallouk received his bachelor's degree from Brown University, where he did undergraduate research with Aaron Wold, and was a Ph.D. student with Neil Bartlett at the University of California, Berkeley. Prior to moving to Penn in 2019, he held faculty positions at the University of Texas at Austin and at Penn State University. He is currently Vagelos Professor in Energy Research in the Department of Chemistry at the University of Pennsylvania. His research focuses on the synthesis of inorganic materials and their application to solar energy conversion, catalysis and electrocatalysis, nano- and microscale robotics, low dimensional physical phenomena, and critical element separations. He is the author of 400+ publications, including a few good ones, and a member of the U.S. National Academy of Sciences.

Novel Therapeutics for Treating Viral Diseases, Cancer, and Neurological Disorders

DENIS LIOTTA

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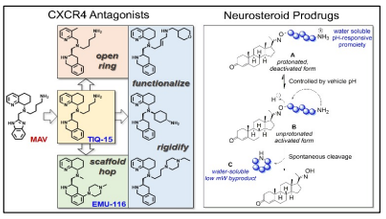
Abstract

Led by Dr. Dennis Liotta, the Liotta Research Group (LRG) is a complex medicinal chemistry organization within Emory University. This talk will start with an overview of the LRG's earlier success in the antiviral arena and transition into LGR's recent endeavors in (1) developing novel CXCR4 antagonists as immunomodulators for treating cancer and (2) designing fast-release neurosteroid prodrugs for treating traumatic brain injury.

Part I. CXCR4 antagonists – Pro-angiogenic and immune cells expressing chemokine receptor CXCR4 traffic along concentration gradients of its chemokine ligand CXCL12, which disseminates from stromal niches in lymph nodes, lung, liver, and bone marrow. The CXCR4/CXCL12 axis is hijacked by numerous cancer types characterized by dramatic CXCR4 and/or CXCL12 upregulation. Consequently, CXCR4 antagonists have significant therapeutic potential against cancer progression. In the past decade, the LRG has designed, synthesized, and evaluated over 350 tetrahydroisoquinoline-containing CXCR4 antagonists. Leading this pipeline is EMU-116, which exhibited enhanced pharmacokinetic properties and superior anti-tumor efficacy compared to mavorixafor, a small molecule CXCR4 antagonist studied in clinical trials. Ultimately, our CXCR4 antagonist pipeline has significant potential to deliver the best-in-class CXCR4 antagonist for treating a variety of cancers.

Part II. Neurosteroid prodrugs – Despite tremendous amount of scientific effort allocated towards the development of pharmacological interventions for reducing the impact of traumatic brain injury (TBI) on public health, none have resulted in an FDA-approved neuroprotective agent. In recent years, neurosteroids, such as progesterone, emerged as promising neuroprotective agents for treating TBI. Unfortunately, previous investigations into the use of neurosteroids for TBI treatment typically required administration in a hospital setting, thus losing valuable time before the treatment could be administered. To address this unmet need, the LRG has developed two generations of progesterone prodrugs having improved aqueous solubility and fast in vivo release rate. Their efficacy was demonstrated in a rat model of acute TBI.



Related Readings

1. Fritzemeier, R.; van der Westhuyzen, A.; D'Erasmo, M.; Sharma, S.; Bartsch, P.; Wali B., Sayeed, I.; Liotta D. "Neurotherapeutic Potential of Water Soluble pH-responsive Prodrugs in Traumatic Brain Injury" *J. Med. Chem.*, under submission.
2. Jecs, E.; Tahirovic, Y.; Wilson, R.; Miller, E.; Kim, M.; Truax, V.; Nguyen, H.; Akins, N.; Saindane, M.; Wang, T.; Sum, C.; Cvijic, M.; Schroeder, G.; Burton, S.; Derdeyn, C.; Xu, L.; Jiang, Y.; Wilson, L.; Liotta, D. "Synthesis and Evaluation of Novel Tetrahydronaphthyridine CXCR4 Antagonists with Improved Drug-like Profiles", *J. Med. Chem.* **2022**, *65*, 4058–4084.
3. Sayeed, I.; Wali, B.; Guthrie, D.; Saindane, M.; Natchus, M.; Liotta, D.; Stein, D. "Development of a Novel Progesterone Analog in the Treatment of Traumatic Brain Injury", *Neuropharmacology* **2019**, *145*, 292–298.

Biography

Dennis Liotta is professor of Chemistry at Emory University. In his decades-long career at Emory University, Dr. Liotta has dramatically improved the longevity and quality of life of millions worldwide. His accomplishments are not limited to just one significant discovery, as he has been directly involved in the discovery and development of multiple lifesaving therapeutics. As a serial entrepreneur and visionary leader, he has also fostered many businesses in the biotech industry and pioneered new approaches to drug development in academia. Dr. Liotta's research focuses on the discovery and development of novel antiviral, anticancer, and anti-inflammatory agents. He has authored over 300 peer-reviewed publications, cited by scientists around the globe tens of thousands of times. These publications fundamentally shaped modern medicinal chemistry and profoundly influenced countless young researchers. An inventor of over 100 US patents, Dr. Liotta contributed to 18 lifesaving, FDA-approved therapies and is recognized as a premier discoverer of novel therapeutics. While his biggest impact came from the HIV/AIDS therapeutics he co-discovered, Dr. Liotta has made important contributions to other therapeutic fronts, such as oncology and neurological diseases, creating many clinical candidates to address unmet medical needs. Dr. Liotta embodies the finest qualities of a scientist dedicated to improving human health through original research in medicinal chemistry.

Alternative Energetic Drivers for Metal Catalyzed Coupling Reactions

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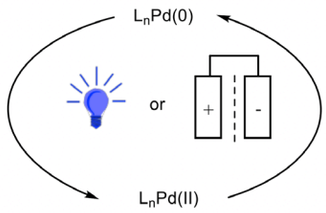
Abstract

The ability of transition metal catalysts to mediate new bond forming reactions has had a dramatic impact on modern molecular synthesis. Nevertheless, a central feature in these reactions is need to balance of often reverse operations on the catalyst so it is regenerated at the end of each cycle of product formation, which can limit catalytic activity and the scope of many transformations. This talk will describe our efforts to address these challenges by introducing alternative, often renewable, energy sources into catalysis, and from this create new bond forming reactions. These include using visible light excitation directly on active palladium catalysts to drive the oxidative addition/reductive elimination cycle in coupling reactions independent of the classical limits in thermal catalysis, or the use of electrochemistry to change the nature of the metal throughout the cycle. Combining these with the favored energetics of carbon monoxide conversion to carboxylic acid derivatives can be used to drive the build-up of reactive products from stable reagents. The use of this chemistry to create ambient temperature and general catalysts for carbonylation reactions, multicomponent transformations, acyl halide or even super-electrophile formation, or new avenues to C-H bond functionalization, will be discussed, as will the mechanistic origins of these influences, and their ability to enable the use of earth abundant catalysts in traditionally precious metal catalyzed reactions.



Related Readings

1. Martin Torres, G; Liu, Y; Arndtsen, B. A. "A Dual Light-Driven Palladium Catalyst: Breaking the Barriers in Carbonylation Reactions", *Science* **2020**, *368*, 318–323.
2. Liu, Y.; Zhou, C.; Jiang, M..; Arndtsen, B. A. "Versatile Palladium-Catalyzed Approach to Acyl Fluorides and Carbonylations by Combining Visible Light- and Ligand-Driven Operations", *J. Am. Chem. Soc.* **2022**, *144*, 9413–9420.
3. Kinney, R. G.; Tjutrins, J.; Torres, G. M.; Liu, N. J.; Kulkarni, O.; Arndtsen, B. A. *Nat. Chem.* **2018**, *10*, 193–199.

Biography

Bruce Arndtsen is a James McGill Professor of Chemistry at McGill University. He obtained his undergraduate chemistry degree from Carleton College in 1988, followed by a Ph.D. in 1993 from Stanford University with Prof. Lisa McElwee-White, and postdoctoral research from 1993-1995 at University of California, Berkeley with Prof. Bob Bergman. In 1995, he began his independent career at McGill University, where he rapidly moved to his current position of full professor. Research in his laboratory is at the intersection of metal catalysis, synthesis, and mechanism. This includes developmental work on using alternative energy sources in metal catalysis, coupling chemistry, chiral anions in asymmetric catalysis, new classes of cycloaddition reactions, and multicomponent synthesis. His has been published many of the impactful journals in chemistry (*Science*, *Nature Chem.* and others), and highlighted in many venues. During his career, he has been named a Canadian Research Chair (Tier I and Tier II equivalents) at McGill, received an NSERC Accelerator Award, two DuPont Research Awards, and in 2021 received the Alfred Bader Award in Organic Chemistry by the Canadian Society for Chemistry.

Multi-Step Domino Reactions: Access to Versatile Compounds for Material and Life Sciences

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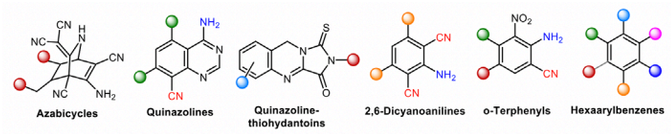
Abstract

The domino process is a powerful tool to economically and sustainably build up complex molecular architectures which drastically reduces the number of work-up and purification steps. Recently we developed new metal-free multi-step domino reactions and one-pot processes for the waste-reducing and cost-effective preparation of versatile frameworks, which otherwise are difficult to access via traditional methods. The developed new methods engage malononitrile and other simple and readily available compounds in a wide range of domino reactions to construct e.g., azabicycles, fluorescent quinazolines, quinazoline-thiohydantoins, 2,6-dicyanoanilines, o-terphenyls and hexaarylbenzenes of interest for medicinal chemistry and materials science. The in vitro tests against multidrug-resistant P. falciparum strains (Dd2 and K1), human cytomegalovirus (HCMV) and multidrug-resistant P glycoprotein-overexpressing CEM/ADR5000 leukemia cells revealed the selected domino products and some corresponding artemisinin-containing hybrid compounds as highly active agents, outperforming the clinical reference drugs. These recent results will be discussed in the talk.



Related Readings

1. Held, F. E.; Guryev, A. A.; Fröhlich, T.; Hampel, F.; Kahnt, A.; Hutterer, C.; Steingruber, M.; Nesterov-Mueller, A.; Marschall, M.; Tsogoeva, S. B.“ Facile access to potent antiviral quinazoline heterocycles with fluorescence properties via merging metal-free domino reactions”, *Nature Commun.* **2017**, *8*, 15071.
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3. Grau, B. W.; Dill, M.; Hampel, F.; Kahnt, A.; Jux, N.; Tsogoeva, S. B. “Four-Step Domino Reaction Enables Fully Controlled Non-Statistical Synthesis of Hexaarylbenzene with Six Different Aryl Groups”, *Angew. Chem. Int. Ed.* **2021**, *60*, 22307–22314.

Biography

Svetlana B. Tsogoeva graduated with Distinction in 1995 from St. Petersburg State University, where she completed her doctoral thesis in 1998 on the “Synthesis of Modified Analogues of Steroid Estrogens” supported by Procter & Gamble. Then, she moved to the Johann Wolfgang Goethe University, Frankfurt am Main, Germany, for postdoctoral research. In July 2000 she joined the Degussa AG Fine Chemicals Division as a research scientist. In January 2002 she was appointed a first junior professor in Germany at the Georg-August-University of Göttingen. Since February 2007, she has been professor of organic chemistry at the Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany. She has published over 140 papers in international peer reviewed journals. Her awards and distinctions include a Thieme Chemistry Journal Award (2007), an Otto-Röhm Research Award (2012), Research Award from the Volkswagen Foundation (2022). Her research is currently focused on multi-step domino reactions & one-pot processes, organocatalysis and medicinal chemistry.

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Professor Mark J. Kurth, University of California-Davis
Professor Seth R. Marder, Georgia Institute of Technology
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Professor George M. Whitesides, Harvard University
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