

FOCUS: ELECTRON TRANSFER DISSOCIATION: EDITORIAL

Focus in Honor of Josh Coon, Recipient of the 2012 Biemann Medal

he 2012 Biemann Medal was awarded to Professor Josh J. Coon at the 60th annual ASMS Conference for his contributions to the discovery and development of electron-transfer dissociation (ETD), a method originating in Professor Don Hunt's lab with primary team members Josh Coon and John Svka. ETD is the ion-ion counterpart to electron-capture dissociation (ECD), and it has proven to be a versatile ion activation method for characterization of peptide and proteins, among other categories of molecules. This special focus issue contains manuscripts authored by scientists who have collaborated with or inspired Josh over the past decade as he embarked on his independent academic career. Josh and his research group continue to explore innovative applications of ETD as well as advance the instrumentation to improve and extend the capabilities of ETD on new mass spectrometer platforms. For example, Josh's group integrated ETD with the high performance Orbitrap mass spectrometer. ETD has become a mainstream ion activation method, in large part because of Josh's early work, and the technology has allowed tremendous inroads in characterization of molecules important in a number of compelling biological applications.

The original roots of ETD were inspired by the development of the landmark electron-capture dissociation method, which emerged from Fred McLafferty's lab in 1998 from efforts of Roman Zubarev and Neil Kelleher (for which Roman Zubarev's contributions were notably honored by a Biemann award in 2007). ECD, which utilized low energy electrons to promote the exothermic capture of an electron by a positively charged ion, was originally implemented on FTICR mass spectrometers and proved to be an exciting alternative to conventional collisional activation MS/MS methods. The radiofrequency voltages associated with quadrupole ion traps prevented the practical implementation of ECD, and this technical hurdle motivated Don Hunt and his group to embrace the challenge of developing a new method suitable for quadrupole ion trap mass spectrometers. Their efforts paid off in 2004 with the first demonstration of electron-transfer dissociation in a quadrupole linear ion trap by using anthracene anions as the electron donating agent.

Josh was born in Mt. Pleasant, a small community in central Michigan. He graduated from Central Michigan University in 1998 with a BS degree in chemistry. Josh moved to Gainesville, Florida, to pursue his Ph.D., graduating in 2002 under the supervision of Willard Harrison. He pursued post-doctoral research in Don Hunt's group at the University of Virginia



from 2002 to 2005, during which time he joined forces with John Syka (Thermo-Fisher Scientific) to develop ETD. In 2005, he began his academic career at the University of Wisconsin and was promoted to Associate Professor in 2010, then Professor in 2012. Josh was previously honored with an American Society for Mass Spectrometry Research Award in 2007, a Pittsburgh Conference Achievement Award, and the Arthur F. Findeis Award from the American Chemical Society in 2011.

Josh has already left a positive mark on many coworkers and colleagues during his past decade in science. John Syka spent a couple of productive years working side-by-side with Josh in the Hunt group during the development of electrontransfer dissociation. The collaborative effort was intense and fraught with urgency arising from ongoing competition from other groups pursuing similar goals, particularly Scott McLuckey's group who were working on ion-ion reactions. John recalls a sense of pride when witnessing Josh deliver the first talk on ETD at the ASMS conference in 2004 (Nashville). John credits Josh's strong presentation with catalyzing a significant buzz that led to a standing room only crowd for John's subsequent talk in a later session. Former graduate student Danielle Swaney confirms Josh's positive influence and exceptional work ethic as a mentor, as exemplified by his patient efforts to teach his group the art of packing capillary LC columns one early Saturday morning. Danielle also notes that Josh encouraged his students to compete for speaker slots at conferences, exuded excitement about new results, and humanized the mass spectrometers in the lab by endowing them with names. As Danielle recounts "one instrument was notorious for breaking down, and in the spirit of Josh's love of "South Park" (an animated TV sitcom), guickly earned the name "Kenny" because it was always dying." Graeme McAlister, another former graduate student, echoes Danielle's sentiments about Josh's abilities as a mentor as well as a master accruer of resources and opportunities that allowed the pursuit of a large number of projects. Graeme recalls the fast pace of research and notes that high-impact projects like the implementation of ETD on an Orbitrap mass spectrometer was achieved in under a year owing to Josh's resourcefulness and enthusiasm. Graeme also remains deeply appreciative of the external internships and collaborations that Josh cultivated, thus ensuring many enrichment opportunities for his group members.

The high intensity in the Coon group is balanced by some creative recreational outlets. Graeme remembers a Halloween pumpkin carving contest that led to the infamous "Orbipumpkin," which was successfully interfaced to an Orbitrap instrument such that the LEDs on the pumpkin were synchronized with the mass spectrometer. In addition to his attributes as a scientist and mentor, Josh has developed other talents outside the lab, including woodworking and fishing. University of Wisconsin colleague Lloyd Smith recalls a salmon-fishing expedition in which Josh not only built the boat but apparently landed most of the fish while also providing encouraging tutelage. Lloyd recounts Josh's expertise in "drifting" a boat down a creek, identifying prime fish hang-outs, tying flies, casting with pinpoint accuracy, and landing fish with barbless hooks. Lloyd remembers the trip with obvious delight and appreciation for the opportunity to engage in sport with his skilled and warm-spirited junior colleague.

Doctoral adviser Will Harrison (University of Florida) perhaps best captures Josh's spirit and drive when he states: "Everyone should have a Josh Coon in the research group at least once. Josh was one of those rare students you tried to keep up with—indeed, hoped not to fall too far behind. I greatly enjoyed Josh, a thoughtful young man with many ideas; what a delight to have as a graduate student. Though graced with a fine sense of humor, Josh was highly focused about chemistry. Early on Josh began planning for his career beyond Florida. He knew what he wanted and pursued it with gusto. I have followed his rise with pride and pleasure, but not surprise. It was clear that Josh would take on analytical chemistry in full-attack mode. And so he has."

This Special Focus Issue on "Electron-Transfer Dissociation and Other Ion Activation Methods" is dedicated to Josh Coon and contains eleven original articles. The issue opens with an article, authored by Josh Coon et al., which reports the implementation and improved performance of electron-transfer dissociation in a modified collision cell of a hybrid linear ion trap/Orbitrap mass spectrometer. The second article, submitted by Julian et al., elucidates some of the factors that modulate the adduction of 18-crown-6 to proteins and the potential implications for charge solvation in the gas phase. Turecek et al. employ electron-transfer dissociation, molecular dynamics calculations, and deuterium labeling in concert to explore conformations of leucine-photolabelled pentapeptide ions in the gas phase. In the fourth article, Williams et al. report that protein/metal complexes arising from nonspecific metal ion adduction have smaller crosssections than those of corresponding protonated species based on ion-mobility measurements, thus demonstrating that crosssection alone should not be used as an indicator of specific metal interactions. The next article, contributed by Heck et al., describes the performance metrics for ETD undertaken in the HCD collision cell of an Orbitrap Velos mass spectrometer. Based on a statistical analysis of the collisional activated dissociation and electron-transfer dissociation of doubly protonated peptides, Zubarev et al. rationalize a trend in the propensity for cleavage of the second peptide bond depending on the identities of the first two amino acids. In the seventh article, McLuckey et al. reveal patterns in the extent of hydrogen atom loss, proton transfer, side-chain cleavages, charge reduction without dissociation, and formation of c/z ions as a function of the length and nature of terminal residues (K, R, H) for a series of peptides subjected to electron-capture or electron-transfer dissociation. A stepped collision energy scheme for HCD in a O Exactive mass spectrometer is used to increase the number of peptides identified and overall protein sequence coverage by Yates et al. in the next article. Kennedy et al. describe the detection of enkephalins based on an in vivo microdialysis sampling method in conjunction with capillary LC-MS in the ninth article. Lloyd Smith and co-authors describe a means to increase charge states of tryptic peptides by derivatization of the carboxyl groups with tertiary or quaternary amines, thus improving ETD performance. In the final article, Marshall et al. simulate the time-domain signal from a truncated isotopic distribution of an antibody in order to evaluate the impact of blanking to increase signal-to-noise ratios in FTICR-MS.

Josh's contributions to the invention of ETD (with Hunt and Syka) and his continuing development and applications in this area have culminated in his selection as the recipient of the 2012 Biemann Medal. The *Journal of the American Society for Mass Spectrometry* is honored to present this focus section to highlight Josh's contributions and the impact of his work.

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