BIOGRAPHICAL SKETCH

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NAME: Castellano, Ronald Keith

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POSITION TITLE: Professor of Chemistry

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Gettysburg College	B.S.	05/1995	Chemistry
Massachusetts Institute of Technology (w/Julius Rebek, Jr.)	Ph.D.	08/2000	Organic Chemistry
Swiss Federal Institute of Technology (with the late François Diederich)	Postdoctoral	07/2002	Organic Chemistry

A. Personal Statement

For nearly 18 years research in my laboratory has used organic synthesis, physical organic chemistry, spectroscopic methods, and computation to design, prepare, and study novel organic molecules that show unique and useful behavior. Current research interests include: a) exploiting Nature's "information rich" molecular building blocks or strategies to design next-generation optoelectronic materials and devices (e.g., light-emitting diodes and photovoltaics), b) designing universal molecular scaffolds to aid the rapid and efficient synthesis of complex multifunctional systems (e.g., as therapeutics), c) developing new approaches to accessing functional organic materials through spontaneous self-assembly, d) leveraging the development of therapeutics through molecular design, synthesis, and physical organic studies. My laboratory has hosted 29 graduate students (17 Ph.D.s awarded to date), 22 University of Florida undergraduates, 14 summer researchers (primarily funded through the NSF REU program), and two high school students since 2002. My current cohort of 7 graduate students includes 2 females, 1 of whom is Hispanic. Particularly relevant to the current proposal, a strong training in supramolecular chemistry and the noncovalent interactions relevant to biological systems has allowed my laboratory to productively collaborate with researchers in both the UF Dept. of Physiology and Functional Genomics (Prof. M. Raizada) and the UF Dept. of Pharmacology & Therapeutics (Prof. B. Law). In these efforts we have been principally responsible for molecular synthesis, molecular/pharmacophore modification, and chemical mechanism of action model studies. I am currently Head of the Organic Division, hold a University Term Professorship, and am an Associate Editor (Supramolecular Chemistry) for *Frontiers in Chemistry*.

1. Ferreira, R. B.; Law, M. E.; Jahn, S. C.; Davis, B. J.; Heldermon, C. D.; Reinhard, M. K.; **Castellano, R. K.**; Law, B. K. Novel Agents that Downregulate EGFR, HER2, and HER3 in Parallel. *Oncotarget* **2015**, *6*, 10445–10459.
2. Ferreira, R. B.; Wang, M.; Law, M. E.; Davis, B. J.; Bartley, A. N.; Higgins, P. J.; Kilberg, M. S.; Santostefano, K. E.; Terada, N.; Heldermon, C. D.; **Castellano, R. K.**; Law, B. K. Disulfide Bond Disrupting Agents Activate the Unfolded Protein Response in EGFR- and HER2-Positive Breast Tumor Cells. *Oncotarget* **2017**, *8*, 28971–28989.
3. Wang, M.; Ferreira, R. B.; Law, M. E.; Davis, B. J.; Yaaghubi, E.; Ghilardi, A. F.; Rodriguez, E.; Chiang, C.-W.; Narayan, S.; Heldermon, C.; **Castellano, R. K.**; Law, B. K. A Novel Proteotoxic Combination Therapy for EGFR+ and HER2+ Cancers. *Oncogene* **2019**, *38*, 4264–4282.
4. Wang, M.; Law, M. E.; Davis, B. J.; Yaaghubi, E.; Ghilardi, A. F.; Ferreira, R. B.; Chiang, C.-W.; Guryanova, O. A.; Kopinke, D.; Heldermon, C.; Castellano, R. K.; Law, B. K. Disulfide Bond Disrupting Agents Activate the Tumor Necrosis Family-Related Apoptosis-Inducing Ligand/Death Receptor 5 Pathway. *Cell Death Discov.* **2019**, *5*, 153.

B. Positions and Honors

Positions and Employment

1993–1995	Undergraduate Research Assistant, Gettysburg College, Gettysburg, PA
1995–2000	Graduate Student, Massachusetts Institute of Technology, Cambridge, MA
2000–2002	NSF International Research Scholars Postdoctoral Fellow, Swiss Federal Institute of Technology, Zürich, Switzerland
2002–2009	Assistant Professor of Chemistry, University of Florida, Gainesville, FL
2009–2018	Associate Professor of Chemistry, University of Florida, Gainesville, FL
2012–	Head, Organic Division, Department of Chemistry, University of Florida, Gainesville, FL
2016–2019	University Term Professor, University of Florida, Gainesville, FL
2018–	Professor of Chemistry, University of Florida, Gainesville, FL
2018–2019	Colonel Allen R. and Margaret G. Crow Term Professor, University of Florida, Gainesville, FL
2019–2022	University Term Professor, University of Florida, Gainesville, FL

Other Experience and Professional Memberships

1993–	Member, American Chemical Society
1993–	Member, Division of Organic Chemistry, American Chemical Society
1995–	Member, Phi Beta Kappa National Honor Society
2002–	Member, Center for Heterocyclic Compounds, University of Florida
2002–	Ad hoc Journal Reviewer (~ 450 reviews)
2005	Chair-Elect Designate, Florida Section of the American Chemical Society
2005–	Member, Center for Macromolecular Science and Engineering, University of Florida
2006	Chair-Elect, Florida Section of the American Chemical Society
2007–2008	Chair, Florida Section of the American Chemical Society
2009	Past Chair, Florida Section of the American Chemical Society
2011	Ad-hoc member, NIH SBC-A Study Section
2013, 2017	Review panel, NSF (Macromolecular, Supramolecular and Nanochemistry)
2014	Guest Editor for *Molecules* special issue (“Intramolecular Hydrogen Bonding”)
2014–	University of West Florida *MARC U*STAR Scholars Program*, External Mentor
2015–2019	Regional Editor (USA), *Current Organic Chemistry* (Bentham Science Publishers)
2019–	Associate Editor, *Frontiers in Chemistry*

Honors and Awards

2000	National Science Foundation International Research Scholars Postdoctoral Fellowship
2003	Research Corporation, Research Innovation Award
2004–2018	*8-time* UF Anderson/College of Liberal Arts and Sciences Scholar Faculty Honoree
2006	Invited Speaker, NSF Workshop in Physical Organic Chemistry (one of 16)
2006	National Science Foundation CAREER Award
2007	Invited contributor to the *Journal of Materials Chemistry* “Emerging Investigators” issue
2007	Salutes to Excellence Award, Florida Local Section of the American Chemical Society
2007	Invited Speaker, Young Academic Investigators Symposium sponsored by the Organic Division of the American Chemical Society
2009	Invited Speaker, US–China Workshop for Early Career Chemical Scientists - Supramolecular Chemistry, Beijing, China (one of 12 from the U.S.)
2011	UF-HHMI Science for Life Distinguished Mentor
2011	Research Corporation for Science Advancement Scialog Fellow
2013	IUPAC Young Observer (one of 11 from the U.S.)
2013	ACS Chemistry Ambassador
2016–2019	UF Term Professorship Award
2017	SEC Visiting Faculty Travel Grant
2018–2019	Colonel Allen R. and Margaret G. Crow Term Professorship Award
2019–2022	UF Term Professorship Award

C. Contributions to Science

1. My early independent (and single PI) work, primarily funded through the University of Florida and an NSF CAREER award, explored for the first time how weak but persistent stereoelectronic interactions within small organic molecules could usefully influence their self-assembly, bulk structure, and emergent macromolecular behavior. The body of work: a) developed efficient synthetic strategies to novel donor-σ-acceptor molecules that form robust, networked assemblies in solution (organogels), b) showed that molecular-level structural perturbations that arise from or otherwise influence through-bond (hyperconjugative-type) donor–acceptor interactions have consequences on solid-state and supramolecular assembly structure, c) revealed that intermolecular orbital delocalization is conceivable for self-assembled donor-σ-acceptor molecules where the accompanying electronic structure shows promise for semiconductive organic materials applications. In the broadest sense, the science exposed nontraditional non-covalent interactions and associated molecular architectures as novel candidates for directional supramolecular assembly.

    a. Li, H.; Homan, E. A.; Lampkins, A. J.; Ghiviriga, I.; **Castellano, R. K.** Synthesis and Self-Assembly of Functionalized Donor-σ-Acceptor Molecules. *Org. Lett.* **2005**, *7*, 443–446.
    b. Lampkins, A. J.; Abdul-Rahim, O.; Li, H.; **Castellano, R. K.** Enhanced Small-Molecule Assembly through Directional Intramolecular Forces. *Org. Lett.* **2005**, *7*, 4471–4474.
    c. Lampkins, A. J.; Li, Y.; Al Abbas, A.; Abboud, K. A.; Ghiviriga, I.; **Castellano, R. K.** Assessable Consequences of Donor-σ-Acceptor Interactions in *β*-Aminoketones. *Chem. Eur. J.* **2008**, *14*, 1452– 1463.
    d. Yuan, L.; Sumpter, B. G.; Abboud, K. A.; **Castellano, R. K.** Links Between Through-Bond Interactions and Assembly Structure in Simple Piperidones. *New J. Chem.* **2008**, *32*, 1924–1934.

2. In other single PI work, my lab has made significant synthetic and mechanistic contributions to the design of molecular scaffolds that allow the rapid and efficient preparation of discrete multifunctional architectures. Seminal work involves benzotrifuranone (BTF), a highly symmetric trilactone capable of one-pot sequential aminolysis to afford a trifunctionalized product. It joins only one other molecular reagent capable of useful single-pot trifunctionalization. The underlying basis for the unique reactivity of BTF, stepwise strain release, has yet to be explored in the chemical community and is currently under active investigation in our laboratory.
    a. Baker, M. B.; Ghiviriga, I.; **Castellano, R. K.** Molecular Multifunctionalization via Electronically Coupled Lactones. *Chem. Sci.* **2012**, *3*, 1095–1099.
    b. Baker, M. B.; Ferreira, R. B.; Tasseroul, J.; Lampkins, A. J.; Al Abbas, A.; Abboud, K. A.; **Castellano, R. K.** The Selective and Sequential Aminolysis of Benzotrifuranone: A Synergism of Electronic Effects and a Ring Strain Gradient. *J. Org. Chem.* **2016**, *81*, 9279–9288.
    c. Figg, C. A.; Bartley, A. N.; Kubo, T.; Tucker, B. S.; **Castellano, R. K.**; Sumerlin, B. S. Mild and Efficient Synthesis of *ω*,*ω*-Heterodifunctionalized Polymers and Polymer Bioconjugates. *Polym. Chem.* **2017**, *8*, 2457–2461.
    d. Ferreira, R. B.; Figueroa, J. M.; Fagnani, D. E.; Abboud, K. A.; **Castellano, R. K.** Benzotrifuran (BTFuran): A Building Block for π-Conjugated Systems. *Chem. Commun.* **2017**, *53*, 9590–9593.

3. The structure- and function-serving roles of the nucleobases are well-appreciated from biological systems. Our lab has been alternatively exploring these heterocycles as components of π-conjugated materials where their optical, electronic, molecular recognition, and self-assembly properties might mutually be brought to bear on downstream optoelectronic applications. In our initial work we prepared among the most fluorescent isomorphic nucleobase analogues and subsequently used them, through collaborative work (with Prof. Jiangeng Xue), in UV-violet OLEDs that provide state-of-the-art performance. We have since focused primarily on introducing the canonical nucleobases (i.e., A, C, G, T/U) to extended (e.g., oligomeric) π-constructs. This work has introduced intrinsically functional and "information rich" heterocycles for organic materials design.

    a. Butler, R. S.; Cohn, P.; Tenzel, P. A.; Abboud, K. A.; **Castellano, R. K.** Synthesis, Photophysical Behavior, and Electronic Structure of Push–Pull Purines. *J. Am. Chem. Soc.* **2009**, *131*, 623–633.
    b. Yang, Y.; Cohn, P.; Eom, S.-H.; Abboud, K. A.; **Castellano, R. K.**; Xue, J. Ultraviolet–violet Electroluminescence from Highly Fluorescent Purines. *J. Mater. Chem. C* **2013**, *1*, 2867–

2874.

c. Bou Zerdan, R.; Cohn, P.; Puodziukynaite, E.; Baker, M. B.; Voisin, M.; Sarun, C.; **Castellano, R. K.** Synthesis, Optical Properties, and Electronic Structures of Nucleobase-Containing π-Conjugated Oligomers. *J. Org. Chem.* **2015**, *80*, 1828–1840.

d. Fagnani, D. E.; Bou Zerdan, R.; **Castellano, R. K.** Synthesis, Optoelectronic Properties, Self-Association, and Base Pairing of Nucleobase Functionalized Oligothiophenes. *J. Org. Chem.* **2018**, *83*, 12711–12721.

4. We have been exploring how supramolecular chemistry paradigms borrowed from solution can be used to "program" the arrangement of π-conjugated materials in the solid state to ultimately improve optoelectronic device performance. These studies have recently shown, using a systematic structure-property approach, how hydrogen-bond promoted self-assembly can strengthen π-stacking interactions, improve charge carrier mobility, and lead to favorable optical properties for organic solar cells. Overall, the science is revealing a new "bottom-up" approach to program desirable chromophore structural order in thin film environments.
    a. Schulze, B. M.; Shewmon, N. T.; Zhang, J.; Watkins, D. L.; Mudrick, J. P.; Cao, W.; Bou Zerdan, R.; Quartararo, A. J.; Ghiviriga, I.; Xue, J.; **Castellano, R. K.** Consequences of Hydrogen Bonding on Molecular Organization and Charge Transport in Molecular Organic Photovoltaic Materials. *J. Mater. Chem. A* **2014**, *2*, 1541–1549.
    b. Bou Zerdan, R.; Shewmon, N. T.; Zhu, Y.; Mudrick, J. P.; Chesney, K. J.; Xue, J.; **Castellano, R. K.** The Influence of Solubilizing Chain Stereochemistry on Small Molecule Photovoltaics. *Adv. Funct. Mater.* **2014**, *24*, 5993–6004.
    c. Shewmon, N. T.; Watkins, D. L.; Galindo, J.; Bou Zerdan, R.; Chen, J.; Keum, J.; Roitberg, A. E.; Xue, J.; **Castellano, R. K.** Enhancement in Organic Photovoltaic Efficiency through the Synergistic Interplay of Molecular Donor Hydrogen Bonding and π-Stacking. *Adv. Funct. Mater.* **2015**, *25*, 5166–5177.
    d. Weldeab, A. O.; Li, L.; Cekli, S.; Abboud, K. A.; Schanze, K. S.; **Castellano, R. K.** Pyridine-Terminated Low Gap π-Conjugated Oligomers: Design, Synthesis, and Photophysical Response to Protonation and Metalation. *Org. Chem. Front.* **2018**, *5*, 3170–3177.

5. We have recently introduced a new class of chiral 1-D hydrogen-bonded supramolecular polymers constructed from paracyclophane building blocks. These platforms are proving to be structurally, mechanistically, and functionally distinct from previous systems.
    a. Fagnani, D. E.; Meese, M. J., Jr.; Abboud, K. A.; **Castellano, R. K.** Homochiral [2.2]Paracyclophane Self-Assembly Promoted by Transannular Hydrogen Bonding. *Angew. Chem. Int. Ed.* **2016**, *55*, 10726–10731.
    b. Henderson, W. R.; Fagnani, D. E.; Grolms, J.; Abboud, K. A.; **Castellano, R. K.** Transannular Hydrogen Bonding in Planar-Chiral [2.2]Paracyclophane-bisamides. *Helv. Chim. Acta* **2019**, *102*, e1900047.
    c. Henderson, W. R.; Zhu, Y.; Fagnani, D. E.; Liu, G.; Abboud, K. A.; **Castellano, R. K.** Self-Assembling [n.n]Paracyclophanes: A Structure-Property Relationship Study. *J. Org. Chem.* **2020**, *85*, 1158–1167.
    d. Henderson, W. R.; Kumar, A.; Abboud, K. A.; **Castellano, R. K.** Influence of Amide Connectivity on the Hydrogen Bond Directed Self-Assembly of [n.n]Paracyclophanes. *Chem. Eur. J.* **2020**, *Accepted Article*.