BIOGRAPHICAL SKETCH

NAME: Christopher J. Ackerson

eRA COMMONS USER NAME (credential, e.g., agency login): ACKERSON.CHRIS

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
The University of Texas at Austin	B.S.	08/1998	Biochemistry
Stanford University	Ph.D.	01/2005	Biophysics
Stanford University	Postdoc	10/2006	Structural Biology
University of Colorado – Boulder	Postdoc	06/2009	Chemistry

A. Personal Statement

This proposal is for NCCAT assistance in determining the structure of a ~100kDa enzyme—the Glutathione Reductase-like Metalloid Reductase. I have some cryo-EM / single-particle analysis experience from graduate school, but have not actively worked in this area since 2006. The field and methods are very different now than they were in 2006!

As a PhD student in Prof. Roger Kornberg's lab, I sought to improve resolution in cyro-electron microscopy single particle reconstructions of proteins. At the start of my PhD (year 2000), we hypothesized that the ~10Å resolution barrier in single-particle cryo-EM reconstruction arose from errors in protein particle selection, alignment, and defocus determination. To address those errors, I developed syntheses of water-soluble gold clusters such as $Au_{144}(SR)_{60}$, followed by method development for their rigid attachment to proteins. We postulated that high electron contrast from gold clusters would facilitate accurate protein particle selection, alignment, and defocus determination. Critical to the approach was rigidity of the cluster-protein linkage, as flexibility in this linkage would lead to uncertainty in computational particle alignment. Overall, my PhD work resulted in methods for making rigid protein-cluster conjugates and a groundbreaking single-crystal structure of one of the gold clusters for which I had pioneered synthesis. That crystal structure revealed the structure of the previously unknown bulk gold-thiol interface, at atomic resolution. Unfortunately, the approach pursued in my PhD did not improve cryo-EM single particle analysis resolution; the "resolution revolution" in this field came with the direct-electron-detectors that became available in 2013.

As a postdoc, I turned my attention to the contrast problem in electron microscopy of whole cells. Beginning as a postdoc and throughout my independent career, I've pursued approaches for intracellular nanoparticle synthesis. I've evaluated library isolated particle binding peptides, metallothioneins, ferritins, mini-ferritins, and metal reducing enzymes.

Ongoing and recently completed projects that I would like to highlight include:

R01 GM137139
Ackerson (PI)
04/01/2020 – 3/31/2024
Clonable Nanoparticles

National Science Foundation (MPS, MSN) Award 2204110
Ackerson (PI)
08/1/2022 - 7/31/2025
Ligand Regiochemistry on Gold Nanoclusters
Role: PI

National Science Foundation 1905179
Ackerson (PI)
08/1/2019 - 7/31/2023
Collaborative Research: Excited State Dynamics of Structurally Precise Metal Nanoclusters.

Colorado Office of Economic Development
Ackerson (PI)
4/1/2021 - 3/31/2024
Anti-Fungal Coatings for Potato Tubers

National Science Foundation 1455099
Ackerson (PI)
08/01/2015 - 07/31/2020
CAREER: Structure of Inorganic Nanoparticle Surface Interfaces Plus Multidisciplinary Nanochemistry Undergraduate Teaching Lab.
Role: PI

Citations:

1. Armstrong J., Shea, P., Cornell, C.C., Bryson, T., Mason, H.E., Morrison, K.D., Tofanelli, M.A., Lewicki, J.P., Wood, B.C., Guilliams, B.F., Compel, W.S., **Ackerson, C.J.** Surpassing the strength of metallogels with a rigid amorphous metal-rich formulation. *Cell Reports Physical Science*, in press (2023)
2. Staicu, L.C., van Hullebusch, E.D., **Ackerson, C.** Microbial Biominerals: Toward New Functions and Resource Recovery. *Frontiers in Microbiology*, 3667 (2021)
3. Riskowski, R.A., Nemeth, R.S., Borgognoni, K., **Ackerson, C.J.** Enzyme-Catalyzed *in Situ* Synthesis of Temporally and Spatially Distinct CdSe Quantum Dots in Biological Backgrounds. *The Journal of Physical Chemistry C*, **123**, 27187-27195 (2019)
4. Anderson, I.D., Riskowski, R.A., **Ackerson, C.J.** Observable but Not Isolable: The $RhAu_{24}(PET)_{18}^{1+}$ Nanocluster. *Small* **17**, 2004078 (2021)

B. Positions and Honors

2021 - Professor, Department of Chemistry, Colorado State University
2015 - 2021 Associate Professor, Department of Chemistry, Colorado State University
2009 – 2015 Assistant Professor, Department of Chemistry, Colorado State University

Other Experience and Professional Memberships

2023 NSF / MPS Workshop, “Challenges and Prospects for the Next 10 Years of Nanochemistry”
2023 NIH Ad hoc proposal reviews
2022 NSF Ad hoc proposal reviews
2019 NIH DT Study Section
2018 NSF / MPS Macromolecular Supramolecular and Nanoscience Review Panel
2018 NIH NIDDK P20 Special Emphasis Panel
2018 NIH DT Study Section (February, June)
2016 NSF / MPS Macromolecular Supramolecular and Nanoscience Review Panel
2009 Ad hoc mail in reviews, NIH RC1 special emphasis panels
2008 - Member, American Association for the Advancement of Science
2003 - Member, American Chemical Society

Honors

2019	Keynote Speaker, ISMPC19, Xiamen, China
2017	Keynote Speaker, ISMPC17, Ascona, Switzerland
2016	Keynote Speaker, Gold, Cardiff, UK
2015	NSF CAREER
2012	Runyon-Rachleff New Innovator Award Finalist
2010	Gilbert Fellow, American Federation for Aging Research
2006	American Cancer Society Postdoctoral Fellowship
1998	Phi Beta Kappa

C. Contributions to Science

1. **"Clonable Contrast" for electron microscopy of cells.** Key accomplishments in development of cloneable EM contrast: (1) Tomographic reconstruction of FtsZ-cSeNP expressing cells, showing SeNPs localizing to FtsZ filaments, providing strong evidence for desired cSeNP function. (2) Developed and defined the 'cloneable nanoparticle paradigm' for intracellular nanoparticle synthesis. (3) Showed that metallothionein can function for cloneable EM contrast in some specialized cases. (4) Showed that peptide mediated inorganic nanoparticle formation is incompatible with physiological conditions. Representative papers are:

    (a) Borgognoni, K.M., Guilliams, B.F., Cohen, R.S., **Ackerson, C.J.** Cloneable Selenium Nanoparticles Enable Multi-Modal, Multi-Scale Bio-imaging contrast. (Give ChemRxiv citation)
    (b) Hendricks, A.R., Guilliams, B.F., Cohen, R.S., Tien, T., McEwen, G.A., Borgognoni, K.M., **Ackerson, C.J.** Cloneable inorganic nanoparticles. *Chem Comm, in press*. doi.org/10.1039DeCC-130G
    (c) Ni, T. W. Staciu, L., Schwartz, C., Crawford, D., Nemeth, R.S., Seligman, J.D., Hunter, W.J., Pilon-Smits, E., **Ackerson, C.J.** Progress toward clonable inorganic nanoparticles. *Nanoscale* **7,** 17320 (2015).
    (d) Morphew, M. K., O'Toole, E.T., Page, C.L., Pagratis, M., Meehl, J. Giddings, T., Gardner, J.M., **Ackerson, C**., Jasperson, S.L., Winey, M., Hoenger, A., McIntosh, J.R. Metallothionein as a clonable tag for protein localization by electron microscopy of cells. *Journal of microscopy* **260,** 20–29 (2015)

2. **Isolation, evolution and engineering of metal(loid) reductases.** At the heart of the cNP paradigm are metal(loid) reducing enzymes. My work has identified 2 novel metal(loid) reductases from environmental isolates. Directed evolution methods to alter the substrates used by one of those enzymes. Library selections have identified peptides that when concatenated to these enzymes exert strong influence over the resulting inorganic nanoparticle size, shape, and surface associations. Representative papers are:

    (a) Hendricks, A.R., Cohen, R.S., McEwen, G.A., Tien, T., Guilliams, B.F., Alspach, A., Snow, C.D., **Ackerson, C.J.** Laboratory Evolution of Metalloid Reductase Substrate Recognition and Nanoparticle Product Size. Submitted to *ACS Chemical Biology*. Preprint available *ChemRxiv* doi.org/10.26434/chemrxiv-2023-w2swm (2023)
    (b) Butz, Z.J., Hendricks, A., Borgognoni, K., **Ackerson, C.J.** Identification of a TeO_3^{2-} reductase/mycothione reductase from *Rhodococcus erythropolis* PR4. *FEMS Microbiology Ecology,* **93,** fiaa220, (2021)
    (c) Butz, Z.J., Borgognoni, J., Nemeth, R., Nilsson, Z.N., **Ackerson, C.J.** Metalloid Reductase Activity Modified by a Fused Se^0 Binding Peptide. *ACS Chem. Bio., **15**, p. 1987 – 1995, (2020)*
    (d) Staicu, L.C., **Ackerson, C.J**., Cornelis, P., Ye, L., Berendsen, R.L., Hunter, W.J., Noblitt, S.D., Henry, C.S., Cappa, J.J., Montenieri, R.L. and Wong, A.O., Musilova, L., Sura-de Jong, M., van Hullebusch, E.D., Lens, P.N.L., Reynolds, R.J.B., Pilon-Smites, E.A.H. Pseudomonas moraviensis subsp. stanleyae, a bacterial endophyte of hyperaccumulator Stanleya pinnata, is capable of efficient selenite reduction to elemental selenium under aerobic conditions. *Journal of Applied Microbiology*, **119**, 400-410. (2015)

3. **"Magic number" metal clusters as contrast agents in biology.** Contrast in 'unenhanced' images of biological specimens is poor. Contrast agents such as dyes, stains, fluorescent proteins, nanoparticles, quantum dots, flurophores, and metals impart a fantastic amount of contrast information in imaging modalities that depend on illumination from light, x-rays or electrons. My earliest contributions to science involve the development of 'magic number' thiol protected gold nanoclusters as contrast agents for enhancing the information in single particle cryo-EM, in whole cells, and in whole organisms. Representative papers are:

    (a) Wong, O. A. *et al.* Structure-activity relationships for biodistribution, pharmacokinetics, and excretion of atomically precise nanoclusters in a murine model. *Nanoscale* **5,** 10525–10533 (2013).
    (b) Sousa, A. A. *et al.* Synthesis, Characterization, and Direct Intracellular Imaging of Ultrasmall and Uniform Glutathione-Coated Gold Nanoparticles. *Small* **8,** 2277–2286 (2012).
    (c) Sexton, J. Z. & **Ackerson, C. J.** Determination of Rigidity of Protein Bound Au (144) Clusters by Electron Cryomicroscopy. *J Phys Chem C Nanomater Interfaces* **114,** 16037–16042 (2010).
    (d) **Ackerson, C. J.**, Jadzinsky, P. D., Jensen, G. J. & Kornberg, R. D. Rigid, Specific, and Discrete Gold Nanoparticle/Antibody Conjugates. *J Am Chem Soc* **128,** 2635–2640 (2006).

4. **Synthesis, structure and electronic properties of gold nanoclusters.** My most influential papers have to do with the synthesis and x-ray crystallography of thiol protected gold clusters. This includes the very first report of a single crystal x-ray structure of a thiol protected gold nanoparticle, the first report of the structural basis for ligand exchange, and the foundation for current understanding of the electronic nature of gold nanoparticles.

    (a) Jadzinsky, P. D., Calero, G., **Ackerson, C. J**., Bushnell, D. A. & Kornberg, R. D. Structure of a thiol monolayer-protected gold nanoparticle at 1.1 A resolution. *Science* **318,** 430–433 (2007).
    (b) Heinecke, C.L; Ni, T.W; Malola, S; Makinen, V; Wong, O.A; Hakkinen, H; **Ackerson, C.J.** Structural and theoretical basis for ligand exchange on thiolate monolayer protected gold nanoclusters. *J Am Chem Soc* **134,** 13316–13322 (2012).
    (c) Hosier, C.A., **Ackerson, C.J.** Regiochemistry of Thiolate for Selenolate Ligand Exchange on Gold Clusters. *J Am Chem Soc* **141**, 309-314 (2019)
    (d) Walter, M., Akola, J., Lopez-Acevedo, O., Jadzinsky, P., Calero G., **Ackerson, C**., Whetten, R., Grönbeck, H., Häkkinen, H. A unified view of ligand-protected gold clusters as superatom complexes. *Proceedings of the National Academy of Sciences*, 105 (27), 9157-9162. (2008).

5. **RF Heating of Metal and Metal-Oxide Nanoparticles.** Nanoparticles that convert external radiation to heat are of biomedical interest. Proposed applications are in hyperthermal cancer therapy and in thermal activation of cells, receptors and enzymes. The mechanisms of heating of gold nanoparticles were unclear, and may include magnetic, inductive and electrophoretic components. We have found that magnetic mechanisms may be important for heating of gold nanoparticles, and have mathematically parsed and compared mechanisms.

    (a) Collins, C. B., Tofanelli, M. A., Noblitt, S. D. & **Ackerson, C. J.** Electrophoretic Mechanism of $Au_{25}(SR)_{18}$ Heating in Radiofrequency Fields. *J Phys Chem Lett* **9,** 1516–1521 (2018).
    (b) Collins, C. Riskowski, R.A., & **Ackerson, C.J.** Radiofrequency remote control of thermolysin activity. *Scientific Reports,* **11**, 6070 (2021)
    (c) Collins, C. B., McCoy, R. S., Ackerson, B. J., Collins, G. J. & Ackerson, C. J. Radiofrequency heating pathways for gold nanoparticles. *Nanoscale* **6,** 8459–8472 (2014).
    (d) McCoy, R. S., Choi, S., Collins, G., Ackerson, B. J. & Ackerson, C. J. Superatom Paramagnetism Enables Gold Nanocluster Heating in Applied Radiofrequency Fields. *Acs Nano* **7,** 2610–2616 (2013).

Complete List of Published Work in Google Scholar (70 peer reviewed publications, 7800+ citations, *h-index*: 32, i10-index: 51) https://scholar.google.com/citations?user=8gqknwoAAAAJ&hl=en&oi=ao

BIOGRAPHICAL SKETCH

NAME: Bradley Forrest Guilliams

eRA COMMONS USER NAME (credential, e.g., agency login): B_GUILLIAMS

POSITION TITLE: PhD Candidate, Chemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Western Carolina University, Cullowhee, NC	BS	05/2019	Chemistry
Western Carolina University, Cullowhee, NC	BS	05/2019	Biology
Western Carolina University, Cullowhee, NC	MS	05/2020	Chemistry
Colorado State University, Fort Collins, CO	PhD	Current	BioAnalytical Chemistry

A. Personal Statement

The common theme in my scientific career is integrating chemistry and instrumentation to address complex biological problems. During my MS research, I worked closely with Drs. Scott Huffman (analytical chemist) and Brian Byrd (vector biologist) to leverage infrared microscopy techniques and chemometrics for the characterization of mosquitos. More specifically, I developed artificial intelligence models to predict the age of a species of mosquitos—information that is epidemiologically relevant and otherwise difficult to obtain.

I am currently a PhD Candidate in the Department of Chemistry at Colorado State University in the lab of Chris Ackerson. Here, my research centers around the development of next generation cloneable contrast tools chiefly for electron microscopy. In this realm, I marry knowledge of inorganic nanoparticle synthesis with protein function and cryo-electron microscopy. Cryo-electron microscopy has really stolen my heart and I will spend the next phase of my career learning the many different aspects of this powerful technique. Thus far, I have experience with cryo-transmission electron microscopy and cryo-electron tomography of biological and aqueous inorganic materials. Over the next several years, I foresee the growing application of biological cryo-electron microscopy techniques (notably single particle analysis and sub-tomogram averaging) in inorganic nanomaterial characterization. Many of the current nanomaterial characterization techniques remove the material from its native context—something which cryo-electron microscopy solves for biologists. It is in this area—the intersection of nanomaterials and biology—where I hope to continue applying and integrating cryo-electron microscopy.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 – Present Graduate Research Assistant, Analytical Resources Core, Colorado State University, Fort Collins, CO

2021 – Present Graduate Research Assistant, Department of Chemistry, Colorado State University, Fort Collins, CO

2020 – 2021 Graduate Teaching Assistant, Department of Chemistry, Colorado State University, Fort Collins, CO

2019 – 2020 Graduate Research Assistant, Department of Chemistry, Western Carolina University, Cullowhee, NC

2019 – 2020	Graduate Teaching Assistant, Department of Chemistry, Western Carolina University, Cullowhee, NC
2018 – 2019	Vector Biologist, College of Health & Human Sciences, Western Carolina University, Cullowhee, NC
2018 – 2019	Chemical Stockroom Employee, Department of Chemistry, Western Carolina University, Cullowhee, NC

Honors

2023	Invited speaker, NIH Common Fund Annual CryoEM Centers Meeting, Pacific Northwest CryoEM Center, Portland, OR
2022	Invited speaker, Three-Dimensional Electron Microscopy, Gordon Research Seminar, Castelldefels, Spain
2019	*Magna cum laude*, Bachelor of Science, Chemistry, Western Carolina University, Cullowhee, NC
2019	*Magna cum laude*, Bachelor of Science, Biology, Western Carolina University, Cullowhee, NC

C. Contributions to Science

1. Mosquito chronological age determination using mid-infrared spectroscopy and chemometrics.

My master's thesis details much of my work applying analytical chemistry in the form of infrared micro-spectroscopy and advanced statistical analysis to problems faced by vector biologists. The chronological age of a mosquito is directly related to its potential threat as a vector for disease. Accurately determining the chronological age of a mosquito is currently both (1) labor & resource intensive and (2) grossly inaccurate. The uncertainty in current chronological age predictive methods is on the order of magnitude that makes it impractical for assessing the demographics of a mosquito population in addition to requiring expensive components and highly-skilled labor. Infrared micro-spectroscopy, coupled with artificial intelligence-based predictive models is a quick and conceptually cost-effective method for *accurately* determining the age of a mosquito population and ultimately determining human-health risk.

Guilliams, B. F., Byrd, B. D., Huffman, S. W. Mosquito chronological age determination using mid-infrared spectroscopy and chemometrics. *Published on 01-Apr-2020*
http://libres.uncg.edu/ir/uncg/listing.aspx?styp=ti&id=32864

2. Cryo-electron microscopy of a Rigid Amorphous Metal-Rich Material (RAMETRIC).

I conducted some cryo-electron microscopy imaging of a new aqueous material developed in the Ackerson Lab at the Molecular Foundry at Lawrence Berkeley National Lab as a part of an instrument-use proposal. Prior to my involvement in the project, our hypothesis about the molecular structure and arrangement of the RAMETRIC material still needed additional supporting data. By treating the RAMETRIC material as one would treat a biological material for cryo-electron microscopy, our primary hypothesis was directly supported. Furthermore, the cryo-electron microscopy images provided a much clearer picture describing changes in the RAMETRIC material as a function of hydration. The corresponding publication for this work is currently accepted awaiting publishing:

Armstrong, J., Shea, P., Cameron, C. C., Bryson, T., Mason, H. E., Morrison, K. D., Tofanelli, M., Lewicki, J. P., Wood, B. C., **Guilliams, B. F.**, Compel. W. S., Ackerson, C. J. Surpassing the Strength of Metallogels with a Rigid Amorphous Metal-Rich Material Formulation. *Accepted for publication in Cell Reports Physical Science, 16-Feb-2023.*

3. Characterization of selenium-based quantum dots formed by disproportionation reaction.

In this research project, I have conducted materials synthesis and characterization via high-resolution transmission electron microscopy, electron diffraction, and fluorescence experiments. Prior to my involvement in this project, additional characterization was needed to support a new hypothesis for one of the interesting discoveries made while working on the project. Furthermore, more support was needed for the proposed mechanism. Ultimately, we have found support for both the proposed mechanism and for our new hypothesis about why selenium quantum dots formed with some metal salts and not with others. The manuscript for this work is in preparation:

Borgognoni, K., Nilsson, Z. N., **Guilliams, B. F.**, McEwen, G. A., Walker. M. M., Ackerson, C. J. In situ Synthesis of Metal Selenide Nanoparticles by Selenium Nanoparticle Disproportionation. *Manuscript in Preparation.*

4. Electron microscopy, synthesis, and development of cloneable nanoparticles.

Most of my PhD work has been conducted in the research area of “cloneable nanoparticles.” Cloneable nanoparticles are nanoparticles where the synthesis is controlled and mediated by an enzyme and/or peptide. In this area, chiefly on electron microscopy, cryo-electron microscopy, electron tomography, and cryo-electron tomography of synthesized cloneable nanoparticles in a variety of contexts. Additionally, I have worked on imaging cloneable nanoparticle quantum dots in correlative light and electron microscopy and helped implement cloneable nanoparticles in a new model system. In this area, several works have been accepted for publication or are submitted for publication:

Hendricks, A. R., **Guilliams, B. F.**, Cohen, R. S., Tien, T., McEwen, G. A., Borgognoni, K., Ackerson, C. J. Cloneable Inorganic Nanoparticles. *Chemical Communications*, 2023, *Accepted Manuscript 02-Jun-2023*, https://doi.org/10.1039/D3CC01319G.

Hendricks, A. R., Cohen, R. S., McEwen, G. A., Tien, T., **Guilliams, B. F.**, Alspach, A., Snow, C. D., Ackerson, C. J. Laboratory Evolution of Metalloid Reductase Substrate Recognition and Nanoparticle Product Size. *Submitted to ACS Chemical Biology, 30-Jun-2023*. *Published on ChemRxiv 13-Jun-2023,* https://doi.org/10.26434/chemrxiv-2023-w2swm.

Borgognoni, K., **Guilliams, B. F.**, Cohen, R. S., Ackerson, C. J., A Cloneable Selenium Nanoparticle as a Multi-modal, Multi-scale cloneable contrast agent. *Submitted for publication in Nature Nanotechnology, 30-Jun-2023.*