FURMAN

Chemistry Department
2021 Summer Research Program

George Shields Research Group

As a computational chemistry group, our research focuses on the application of efficient and accurate computational methods to understand the structure and dynamics of systems ranging from water clusters, to sulfate aerosols in the atmosphere, to biological systems. Computational chemistry is highly visual, with daily use of molecular graphics. No previous computer experience is necessary to work in our group. We must read and understand many experimental techniques in order to make sure our computational predictions are grounded in reality. So students in the group learn a tremendous amount about a variety of different experimental and computational techniques for understanding nature.

I. Atmospheric Aerosols in Prebiotic Chemistry and the Origin of Life

Recent research suggests that atmospheric aerosol particles may have played a catalytic role in the synthesis of biological molecules in the absence of enzymes. The Miller experiment of 1953 demonstrated the abiotic synthesis of amino acids from a gaseous mixture and electricity. Since then, many possible catalytic pathways have been shown to lead to the abiotic polymerization of such biological monomers, including mineral surfaces, deep sea thermal vents, etc. Our group is interested in exploring the catalytic role of atmospheric aerosols in the formation of polypeptides without the need for ribosomes. Our work is highly relevant to prebiotic chemistry and chemical evolution because current experimental techniques cannot access the relevant size regime for aerosols. We have published two papers this year on the reaction of the amino acid Glycine to form diglycine in a small water cluster, showing that this reaction is thermodynamically favorable and kinetically enhanced by a handful of water molecules.[1,2]

II. Thermodynamics of Aerosol Formation

Aerosol particles in the atmosphere serve as seeds for cloud formation and have a net cooling effect on the global climate, in contrast to greenhouse gases that warm the climate. Sulfate aerosols in particular have a large cooling effect, but their formation pathways in the presence of different component vapors, temperature and pressure conditions as well as their size and distribution in the atmosphere remains unclear. To answer some of these questions, we model the formation of sulfate and other aerosols at a molecular level. The end goal is to explain the growth of nanoscale small gas phase clusters to large aerosols and cloud droplets in the micrometer range. That will minimize the large uncertainty associated

with the role of aerosols in the global climate and refine models used to understand the severity of global warming and aerosols' possible role in mitigating it.[3]

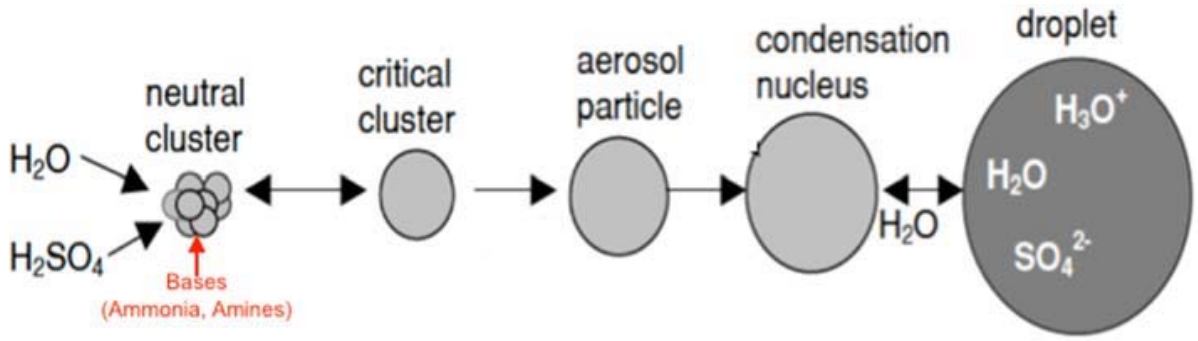

Figure: The formation and growth of aerosols in the atmosphere

In atmospheric aerosols, the molecular clusters are held together by weak and dynamic hydrogen bonds. That makes the kinds of structures they can form and their relative stability very hard to determine. We develop and apply different tools to 1) sample the large number of configurations these clusters can adapt efficiently[4] and 2) determine which ones are important, and why.[5]

III. Development of a Pharmacophore Model and Identification of Neutral Antagonist Molecules to Inhibit the μ Opioid Receptor Protein

Approximately 50% of marketed drugs target G-Protein Coupled Receptors (GPCRs). Because the μ opioid receptor (MOR) is a GPCR and is known to be involved in therapeutically relevant pathways that lead to pain and addiction, we are currently studying the specific structural characteristics that promote functional antagonism at the MOR. The goal of this project is to apply computational chemistry methods to predict molecules that will inhibit the μ opioid receptor protein (MOR). The MOR is the molecular target of morphine, heroin, and other opioid drugs. A pharmacophore model illustrates the regions of space where specific steric and electronic features must be present in order to bind to a target and block its biological response, in this case the MOR. Neutral antagonism means that a neutral antagonist molecule (NA) that fits the pharmacophore model will prevent opioid drugs from activating the MOR, thus inhibiting the action of opioids. A molecule that is a NA can thus be used to prevent or treat opioid addiction. The overall idea is to use computational tools to help find a non-opioid molecule that would be useful for the treatment of opioid addiction. The big picture is that opioid addiction is a compelling problem, and there are few molecules that can be used to treat opioid addition that don't have the chemical structure of opioids. Thus, the available treatments are themselves addictive. We aim to invent molecules based on non-opioid chemical frameworks that can treat opioid addiction and are not addictive themselves.

IV. Collaborations with Tim Hanks and Paul Wagenknecht

In addition to the above projects, we have started collaborations with these two Furman groups, using computational tools to help them with their projects.

References (undergraduates underlined)

1. "Water-Mediated Peptide Bond Formation in the Gas Phase: A Model Prebiotic Reaction" Ariel G. Gale, Tuguldur T. Odbadrakh, Benjamin T. Ball, and George C. Shields* **J. Phys. Chem. A. 124** (2020) 4150-4159. DOI: 10.1021/acs.jpca.0c02906

2. "Transition States of Gas Phase Glycine Dimerization Driven by Water Molecules" Ariel G. Gale, Tuguldur T. Odbadrakh, and George C. Shields* **Int. J. Quantum Chem. 120** (2020) e26469. DOI 10.1002/qua.26469

3. "Particle formation and surface processes on atmospheric aerosols: a review of applied quantum chemical calculations" Angelina Leonardi, Heather M. Ricker, Ariel G. Gale, Benjamin T. Ball, Tuguldur T. Odbadrakh, George Shields*, and Juan G. Navea* **Int. J. Quantum Chem. 120** (2020) e26350. DOI: 10.1002/qua.26350

4. "Computation of Atmospheric Concentrations of Molecular Clusters from *ab initio* Thermochemistry" Tuguldur T. Odbadrakh, Ariel G. Gale, Benjamin T. Ball, Berhane Temelso, and George C. Shields* **J. Vis. Exp. 158** (2020) e60964. DOI: 10.3791/60964 URL: https://www.jove.com/video/60964

5. "Effect of Mixing Ammonia and Alkylamines on Sulfate Aerosol Formation" Berhane Temelso*, Elizabeth F. Morrison, David L. Speer, Bobby C. Cao, Nana Appiah-Padi, Grace Kim, and George C. Shields* **J. Phys. Chem. A 122** (2018) 1612-1622. DOI: 10.1021/acs.jpca.7b11236 ACS Editor's Choice, open access article. Selected for 2019 Virtual Issue on Research in Physical Chemistry at Primarily Undergraduate Institutions, **J. Phys. Chem. B 123** (2019). DOI: 10.1021/acs.jpcb.9b02336