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RNAs are remarkably versatile molecules that function in diverse cellular and viral processes. This versatility stems from RNA's ability to both encode genetic information and form complex, dynamic three-dimensional structures. The Bonilla lab uses a combination of structural biology and biophysical tools to understand the process by which RNAs attain their functional three-dimensional structures and how these structures, in turn, determine important biological activities in cells and viruses.

The Bonilla lab has two primary research focuses. The first centers on understanding the general principles that govern the conformational landscape of RNAs. To achieve this, the lab studies the folding and conformational properties of model system RNAs of varying complexity. By delving into these structures, they aim to uncover the "rules" that guide RNA folding and conformational dynamics.

Although RNA molecules are often portrayed as flexible "strings," many RNAs form well-defined, three-dimensional structures that interact with proteins, small-molecules, and other RNAs to regulate critical biological operations. The ability of RNA to encode genetic information, form functional three-dimensional structures, and undergo dynamic structural rearrangements makes RNA a remarkably versatile polymer. For example, folded RNA three-dimensional structures can act as catalysts of essential chemical reactions; as scaffolds that organize the assembly of complex RNA-protein machines; and as structurally dynamic switches that turn gene expression on or off upon binding to a specific metabolite. Intriguingly, the functional versatility of RNA might have played a pivotal role during the early evolution of life, prior to the emergence of complex proteins.

The second research focus is understanding how RNA three-dimensional structures dictate specific functions, with an emphasis on viral RNAs. The Bonilla lab seeks to elucidate how these structures serve as regulators of essential aspects of the viral life cycle, with the goal of opening avenues for the development of therapeutic strategies.

As scientists delve deeper into RNA biology, they continue to unveil novel structure-based RNA functions in cellular and viral RNAs. Recently, functional RNA structures have sparked great interest as therapeutic agents or drug targets. However, despite their importance, relatively few RNA three-dimensional structures have been solved, and the structural mechanisms of many RNA-based processes remain mysterious. A major experimental challenge has been the dynamic nature of RNA structures, which constantly fluctuate between multiple conformational states, making RNA a difficult target for structural biology techniques.

Cryo-electron microscopy (cryo-EM) has emerged as a premier structural biology tool that can capture macromolecules in distinct conformations and under variable solution conditions. As such, it promises to illuminate RNA dynamic conformational landscapes in a way not previously possible. Bonilla and his colleagues have demonstrated the power of cryo-EM for visualizing small, conformationally dynamic RNA structures that had been elusive for decades, revealing intermediates in the folding pathways of complex, functional RNAs. In addition to cryo-EM, the Bonilla lab uses single-molecule biophysics, functional assays, computational tools, and other structural biology and biophysical tools to understand the RNA folding process and to reveal the mechanisms by which RNA three-dimensional structures dictate important biological functions in cells and viruses.

EDUCATION

B.S. in chemical engineering, 2012
University of Washington

Ph.D. in chemical engineering, 2019
Stanford University

POSTDOC

University of Colorado, 2019–2023

POSITIONS

Assistant Professor, 2023–
The Rockefeller University

AWARDS

NIH Ruth L. Kirschstein National Research Service Award, 2019

HHMI Hanna H. Gray Fellow, 2020

Irma T. Hirschl/Monique Weill-Caulier Trust Research Award, 2024

SELECTED PUBLICATIONS

Bonilla, S.L. et. al. The promise of cryo-EM to explore RNA structural dynamics. *J. Mol. Biol.* 434, 167802 (2022).

Bonilla, S.L. et. al. Cryo-EM reveals an entangled kinetic trap in the folding pathway of a catalytic RNA. *Science Adv.* 8, eabq4144 (2022).

Bonilla, S.L. et. al. Viral RNA hijacks host machinery using conformational changes of a tRNA-like structure. *Science* 374, 955–960 (2021).

Bonilla, S.L. et. al. High-throughput dissection of the thermodynamic and conformational properties of a ubiquitous class of RNA tertiary contact motifs. *Proc. Natl. Acad. Sci. U.S.A.* 118, e2109085118 (2021).

Bonilla, S.L. et al. Single-molecule fluorescence reveals commonalities and distinctions among natural and in vitro-selected RNA tertiary motifs in a multistep folding pathway. *J. Am. Chem. Soc.* 139.51, 18576–18589 (2017).