The numerous molecular functions of non-coding RNAs are achieved through their complex 3D structures. Understanding these geometries and how they form enables us to create new functional RNA molecules, explain the mechanics of diseases, and study molecular evolution. It is known that RNA structure folds hierarchically. First stems, composed of stacked canonical base pairs, form enclosing loops. The complex architectures of the loops are determinant for the final conformation yet, the free-energy models that accurately capture the stems formation do not take most loop geometries into account.

Nonetheless, the modularity of RNA architecture and how various recurrent sub-structures such as the kink-turn or sarin-ricin motif can be found in a variety of contexts with varied sequences is well established. The distinct secondary structure elements (i.e., hairpins, bulges, interior loops and multi-loops) in known 3D structures have been catalogued and well studied. Those databases are then used to enhance theoretical models. However, known larger structural motifs that can span many loops can not be recovered by automatic methods that become prohibitive in time and resources at their scale.

To overcome these limitations, we recently designed algorithms based on a graph representation of RNA structures. Our new method is able to recover all identical structural motifs, without size limitation, between any pair of RNAs in the non-redundant set of determined RNA 3D structures. My presentation will mainly focus on how this analysis recovers known complex 3D modules, such as the A-minor that anchors in 3D regions distant in sequence, and can propose novel ones that are well conserved and span multiple loops. The biggest module our method uncovers is a large sub-structure spanning hundreds of nucleotides and base pairs shared between the ribosomes of T. Thermophilus, E. Coli, and P. Aeruginosa. Finally, I will present how this information is being leveraged to understand the impact of mutations or chemical modifications on function, and predict accurate 3D structures.