

## Towards A Platform for Engineering RNA Regulatory Networks Using High Throughput RNA Structure Characterization

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Non-coding RNAs (ncRNAs) play central roles in maintaining, regulating and defending the genomes of all organisms. In fact, their regulatory versatility and ubiquity have made ncRNAs increasingly important tools for engineering synthetic biological systems. In addition, the increased focus on developing computational methods that can predict RNA structures holds promise for an engineering paradigm based on computational RNA design. Combined with the emergence of experimental RNA characterization techniques based on next-generation sequencing, ncRNAs are beginning to rival proteins as core components of the synthetic biology toolbox.

In this talk, I will describe our work in engineering RNA-based genetic circuitry inside cells, and in developing a high-throughput technique for characterizing RNA structures and interactions called SHAPE-Seq. In particular, I will focus on ncRNA transcription regulation in bacteria, and how trans-acting mechanisms can be used to construct RNA-only genetic networks. I will then describe how our solution to an immediate engineering challenge – namely how to create more ncRNA regulators that can serve as building blocks for these networks – motivates a deeper understanding of the structures of engineered ncRNA regulators. This need drives our development of SHAPE-Seq, a technique that combines chemical probing and next generation sequencing that can characterize RNA structures and interactions in high-throughput. I will then focus on experimental and computational aspects of SHAPE-Seq, and applications of SHAPE-Seq data to understanding RNA folding and design. I will conclude with thoughts on how these tools promise to transform the future of RNA synthetic biology. Throughout the talk I will make connections to emerging challenges that will require computational biology solutions.