## SEMINAR School of Biological and Health Systems Engineering

## Nanoarchitectural engineering of DNA and RNA for biological discovery

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**Abstract** Nucleic acid molecules, with their well-defined helical features and predictable interactions, are highly programmable materials ideal for creating sophisticated nanoscale objects aimed at biological discovery. In the first part of the seminar, I will discuss our construction of synthetic nucleic acid topological structures, such as knots and links, by linking nodes formed by nucleic acid four-way junctions. These structures enable the study of crucial nucleic acid-processing enzymes, such as topoisomerases. In the second part, I will detail our work on engineering natural RNA molecules to construct self-assembled RNA structures suitable for structural determination. We developed ROCK (RNA oligomerization-enabled cryo-EM via installing kissing-loops), which increases molecular weight and reduces flexibility, thereby facilitating efficient cryo-EM structural determination. This has enabled the first sub-3 Å RNA-only cryo-EM structure. Furthermore, we have applied similar principles to X-ray crystallography for resolving small RNA motifs. Our work has led to the solution of the structure of an artificially designed RNA branched kissing-loop motif, which has been instrumental in constructing complex self-assembled RNA nanostructures.

**Biosketch** Di Liu is an assistant professor in the School of Molecular Sciences at Arizona State University. Liu was born and raised in Zibo, which is an industrial city in China's Shandong province and is known for its delectable barbeque. Liu earned his bachelor's degree in chemistry at Nanjing University, where he worked under the direction of Prof. Zijian Guo to synthesize photoactivatable platinum-based anticancer drugs. In 2011, he embarked on his doctoral studies at the University of Chicago, where he worked with Prof. Yossi Weizmann on synthetic nucleic acid topologies and RNA nanostructures. During his doctoral study, he was supported by the Howard Hughes Medical Institute (HHMI) International Predoctoral Fellowship. In 2017, Liu started his postdoctoral research in Prof. Peng Yin's lab at Harvard University as a Merck Fellow of the Life Sciences Research Foundation (LSRF). His research at Harvard primarily focused on increasing the complexity of self-assembled RNA nanostructures and resolving RNA structures using cryo-EM. In August 2023, Liu joined the School of Molecular Sciences and the Biodesign Center for Molecular Design and Biomimetics. Currently, his research focuses on employing nanoarchitectural approaches based on the programmability of nucleic acid molecules to study DNA topology, solve RNA structures, and enhance the efficacy of RNA-based therapeutics.



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