ABSTRACT
DNA-binding proteins (DBPs) play critical roles in biology and biotechnology, and there has been considerable interest in the engineering of DBPs with new functions or altered specificities. While there has been success in reprogramming and the specificity of naturally occurring DBPs using selection methods, the computational design of new DBPs that engage with DNA remains an outstanding challenge. Addressing this challenge would lead to new solutions for programmable recognition and manipulation of DNA sequence and structure; and ultimately enable new possibilities for synthetic gene regulation, DNA-modifying enzymes, and many other applications. In this talk, I will describe the development and experimental validation of a computational method for the design of small DBPs that recognize specific target sequences through interactions with bases in the major groove. I will then describe progress towards a generalizable framework for deep-learning enabled design of custom DNA-binding proteins. I will conclude by summarizing my view of the future prospects for this new framework.

BIO
Dr. Cameron Glasscock is a WRF Postdoctoral Fellow in David Baker’s lab at the University of Washington. His postdoctoral research focused on computational approaches for structure-based design of sequence-specific DNA-binding proteins. Prior to his postdoc, Dr. Glasscock was an NSF graduate research fellow with Julius Lucks and Matthew DeLisa at Cornell University and a visiting scholar at Northwestern University’s Center for Synthetic Biology. At that time, he focused on applying novel synthetic biology tools for optimizing gene expression in microbial biomanufacturing hosts, leading to his interest in design of de novo proteins for application in gene regulation and gene editing.