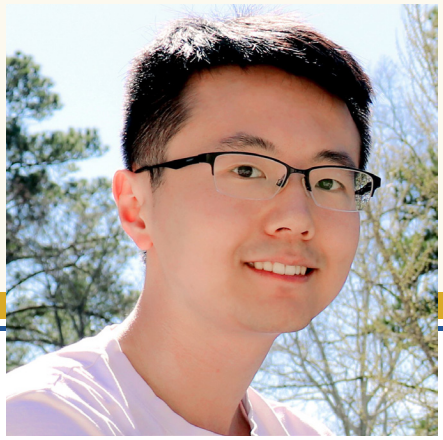

HONGLUE SHI, Ph.D.

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CRISPR-Cas enzymes are versatile tools for gene editing and research applications such as transcriptional regulation and imaging. The speed and accuracy of CRISPR-Cas enzymes are crucial, yet how they identify a unique ~20-base-pair target within billions of base pairs in the genome is still unclear. Dr. Honglue Shi aims to obtain a more quantitative and predictive understanding of how natural and engineered CRISPR-Cas enzymes rapidly and accurately target specific DNA sequences in Dr. Jennifer Doudna's lab at the University of California, Berkeley. Shi will use structure-guided biochemistry to develop a kinetic model for CRISPR-Cas9 search speed and accuracy. He will then test the generality of the model on additional CRISPR enzymes and ancestral RNA-guided TnpB enzymes. This research is fundamental to understanding both the evolutionary history of RNA-guided enzymes and the utility of these systems for genome editing. In the future, these results will enable predictions and design of genome editing functions that are not possible or practical today and will greatly accelerate the field as well as the precision and outcomes of next-generation genome editing tools.

As a Ph.D. student in Dr. Hashim Al-Hashimi's lab at Duke University, Shi focused on the development of biophysical approaches such as NMR spectroscopy to extend the description of nucleic acids from static structures to dynamic ensembles, which results in a deeper and more predictive understanding of how nucleic acids are being recognized by other biomolecules. Having developed this expertise in nucleic acid biophysics and perspectives in dynamic ensembles, Dr. Shi is ready to elucidate the properties that define the best genome editors in Dr. Doudna's lab.

FELLOW