KHANH DAO DUC, University of British Columbia

A study of stochastic dynamics of mRNA translation and their impact across biological scales

The translation of mRNA into protein is a fundamental cellular process, mediated by the flow of ribosomes. As these dynamics can be locally regulated by many molecular mechanisms, analytical tools are needed to find the determinants of translation speed. I will present analytical and computational methods that we recently developed to study translation across different scales, using a wide array of structural, sequencing, and imaging data. These methods importantly rely on a stochastic interacting particle model that generalizes the totally asymmetric simple exclusion process (TASEP). We analytically studied this process to determine its phase diagram and find the key parameters that govern translation efficiency. In the context of recent advances in deep sequencing, we also used the model to infer translation rates for a large set of genes in yeast, and analyzed the contribution of traffic jams, codon specificity, and other biophysical parameters. These results more recently guided our studies of the molecular structure of the ribosome (obtained from cryoEM) and translation kinetics observed in vitro using lysate systems. Overall, these completing approaches emphasize the major role played by the ribosome in gene expression, at both molecular and population levels.