E2EDNA: Automated Simulation Protocol for DNA Aptamers with Small Analytes

Michael Kilgour[1], Tao Liu[1], Brandon D. Walker[2], Pengyu Ren[2] and Lena Simine[1]

[1]Department of Chemistry, McGill University, QC, Email: mjakilgour@gmail.com
[2]Biomedical Engineering, University of Texas at Austin, USA

We present the E2EDNA protocol for DNA aptamer design and analysis. E2EDNA combines off-the-shelf software and novel analysis to enable automated and efficient simulation of single-stranded (ss)DNA, and complexes of ssDNA with small molecule analytes. Existing computational tools used for DNA aptamer design focus on cost-effective secondary structure prediction and motif analysis in the large datasets produced by SELEX experiments. However, practical aptamer optimization often requires more detailed and/or higher accuracy predictions for promising sequences suggested e.g., by SELEX experiments or machine learning algorithms. In the absence of a streamlined procedure, this task is extremely time and expertise intensive. We address this gap by introducing E2EDNA, a computational framework that accepts a DNA sequence in the FASTA format, and the structure of the desired ligand, and performs approximate folding followed by a refining step, analyte complexation, and molecular dynamics sampling at the desired level of accuracy.

In this talk, we will outline the algorithms we use to automate this complex and multi-faceted task, and share preliminary results for a series of aptamer-peptide complexes. We will further briefly outline how such a fully-automated protocol may be used to power machine learning approaches for rapid in-silico aptamer design, potentially shortening the turnaround time for new aptasensors from years to months or weeks.