Developing methods for differential mRNA secondary structure analysis

Supervisory team:
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Project description:

RNA is not a simple intermediate molecule between DNA and protein, but can play an important role in regulating cellular processes. Although RNA is a single stranded molecule, it can form stable secondary structure. For example, the UTR of mRNA can often form hairpin like structures which affect how the mRNA is regulated, processed and translated. These secondary structures can be profiled at single-nucleotide resolution using high-throughput sequencing technologies such as DMS-seq or SHAPE-seq. Changes in the UTR structure of a mRNA molecule between experimental conditions or timepoints may play a role in promoting (or repressing) the binding of regulatory proteins or increasing its rate of translation. However, the tools necessary for interrogating this type of data and identifying differences in RNA secondary structure between conditions are underdeveloped.

The aim of this project is design and implement computational approaches to enable the identification of differences in secondary structure between conditions and to understand how these differences play a role in gene regulation. This will include methods for processing and filtering reads calculating the frequency of modified nucleotides and exploiting the correlation between them to better infer changes in secondary structure. Subsequently we will use this information to build contact maps and molecular dynamics of RNA structure and develop methods to both identify and interpret the differences between these. We will assess the performance of these methods using both simulated and real data, and subsequently will apply these approaches to ask questions about the how the structure of the UTR impacts gene regulation in Drosophila.

This project enable you to gain experience in multiple areas; including gene regulation, the processing of high-throughput sequencing data and the design and implementation of novel algorithms to analyse this data. As such it would suit both a student with a life sciences background who has some understanding of programming and statistics or a student with a computational background who is interested in computational biology/gene regulation

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.