Approaches to building spatio-temporal models of splicing regulation that include RNA structure

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Artificial intelligence has been used widely to learn biological outcomes from molecular data which are often surveyed by next-generation sequencing. Famous examples include so called splicing code approaches that predict condition-specific exon inclusion at high accuracy. Despite that, machine learning does not provide any insight into the molecular mechanisms underlying the biological process. We developed a method that combined machine learning with convoluted NGS signals which reflect spatio-temporal aspects of RNA processing to predict splicing outcomes in two human cell lines. We show that convolutions of epigenetic signals with long-range RNA-RNA interactions enhance the significance of features represented by splicing factors and that RNA structure overall brings epigenetic signals to the place of action. These effects are also affected by the transcription rate implying that co-transcriptional and post-transcriptional splicing are also sensitive to the local epigenetic context shaped by RNA structure. In sum, our results imply that spatio-temporal organization of RNA processing is strongly affected by long-range RNA-RNA interactions.