Motivation:

The aim of our study was to investigate whether our m6A modification sites prediction model, equipped with a self-attention mechanism, is capable of detecting the well-established pattern of m6A modification enrichment at the stop codon of mRNA. The self-attention mechanism in our model is designed to identify the most informative and relevant features of mRNA sequences that may harbor m6A modifications, which enhances our understanding of the post-transcriptional regulation of gene expression.

Method:

We extracted known positive samples of m6A modification sites from 3'UTR and plotted them into a density plot to analyze their distribution(f\_1). Since all sequences with various lengths of 3'UTR start immediately after the stop codon, we defined the relative distance of a modification site as the number of nucleotides from the stop codon to the site divided by the total number of nucleotides in the sequence. We then filtered out the sites with relatively high attention, denoted as f\_2. To eliminate the impact of the distribution of the original data, we divided f\_2 by f\_1 to obtain the relative percentage of sites recognized by our model in actual positive points at different relative distance, denoted as f\_3.

Result:

Our analysis of the density plot indicated that our model was able to identify the pattern of m6A modification enrichment at the stop codon of mRNA. Specifically, our model recognized more modification sites near the stop codon area, which is consistent with previous research demonstrating that more m6A modification sites cluster near the stop codon area. Thus, our study provides further evidence that m6A modification at the stop codon plays a critical role in post-transcriptional regulation of gene expression.

Analysis and discussion:

Recent research has suggested that m6A modification at the stop codon regulates the efficiency of translation termination by promoting the interaction between the mRNA and release factors. Additionally, m6A modification can affect mRNA stability by regulating the binding of RNA-binding proteins (RBPs) to the mRNA. RBPs are responsible for regulating mRNA metabolism, including stability and translation. The m6A modification at the stop codon may regulate the binding of RBPs, thus influencing mRNA stability. Furthermore, studies have shown that the m6A modification at the stop codon is involved in the regulation of alternative polyadenylation (APA), which generates multiple mRNA isoforms with different 3' UTRs by altering the site of polyadenylation. The 3' UTR plays a critical role in the regulation of gene expression, and APA can affect mRNA stability and translation efficiency. The m6A modification at the stop codon may influence APA by regulating the binding of RBPs to the mRNA.

Our investigation into the self-attention mechanism of our model provides valuable insights into the regulation of gene expression via m6A modification at the stop codon. In conclusion, our findings underscore the importance of m6A modification at the stop codon in post-transcriptional regulation of gene expression, which may lead to a better understanding of the molecular mechanisms underlying gene expression regulation.