

## Publication

Quantification of pre-mRNA escape rate and synergy in splicing

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Splicing reactions generally combine high speed with accuracy. However, some of the pre-mRNAs escape the nucleus with a retained intron. Intron retention can control gene expression and increase proteome diversity. We calculated the escape rate for the yeast PTC7 intron and pre-mRNA. This prediction was facilitated by the observation that splicing is a linear process and by deriving simple algebraic expressions from a model of co- and post-transcriptional splicing and RNA surveillance that determines the rate of the nonsense-mediated decay (NMD) of the pre-mRNAs with the retained intron. The escape rate was consistent with the observed threshold of splicing rate below which the mature mRNA level declined. When an mRNA contains multiple introns, the outcome of splicing becomes more difficult to predict since not only the escape rate of the pre-mRNA has to be considered, but also the possibility that the splicing of each intron is influenced by the others. We showed that the two adjacent introns in the SUS1 mRNA are spliced cooperatively, but this does not counteract the escape of the partially spliced mRNA. These findings will help to infer promoter activity and to predict the behavior of and to control splicing regulatory networks.

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