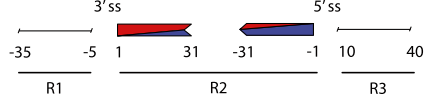
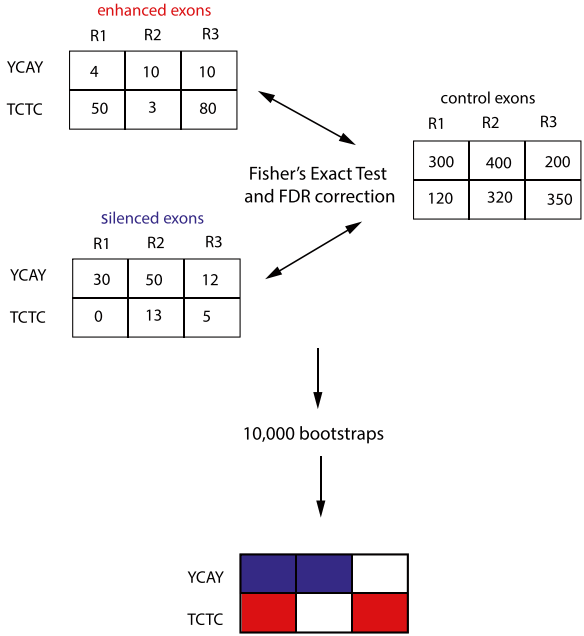
Define 3 regions of interest around the alternative exons
R1 = [-35 : -5] nts from 3'ss
R2 = [1 : 31] nts from 3'ss and [-31 : -1] nts from 5'ss
R3 = [10 : 40] nts from 5'ss



Evaluate the cluster instance of a tetramer in all enhanced, silenced and control exons.

Evaluate statistic significance of region-specific enrichment of each tetramer in alternative exons versus controls using a Fisher's Exact test. Correct p-values with Benjamini-Hochberg FDR correction (p_{fdr})



Calculate the p-values ($p_{bootstrap}$) of each tetramer using the same procedure as described above in 10,000 bootstrap samples of our data, and then estimate empirical p-values of tetramer enrichments

$$p_{empirical}(r,t) = \frac{1 + \#(p_{bootstrap}(r,t) < p_{fdr}(r,t))}{1 + \#\,bootstrap}$$

Retain tetramers with $p_{fdr} \le 0.1$ and $p_{empirical} \le 0.0005$ in R1, R2 or R3 and draw the RNA splicing maps on the basis of the *enrichment score (ES)*.