Robust estimation of isoform expression with RNA-Seq data

Abstract

Qualifying gene and isoform expression is one of the primary tasks for RNA-Seq experiments. Given a sequence of counts representing numbers of reads mapped to different positions (exons and junctions) of isoforms, methods based on Poisson generalized linear models (GLM) with the identity link function have been proposed to estimate isoform expression levels from these counts. These Poisson based models have very limited ability in handling the overdispersion in the counts brought by various sources, and some of them are not robust to outliers. We propose a negative binomial based GLM with identity link, and use a set of robustified quasi-likelihood equations to make it resistant to outliers. An efficient and reliable numeric algorithm has been identified to solve these equations. In simulations, we find that our approach seems to outperform existing approaches. We also find evidence supporting this conclusion in real RNA-Seq data.