

Ortholuge: a tool for precise, high-throughput prediction of orthologs

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Abstract: Accurate ortholog prediction is a critical component of many comparative genomics analyses. Reciprocal best-BLAST hit (RBBH) is a widely used method for identifying orthologs, yet it can generate false predictions when the true ortholog is missing. Ortholuge addresses this failure by evaluating predicted orthologs using ratios of phylogenetic distances for each set of predicted orthologs. Our work shows that predicted orthologs with atypical phylogenetic divergence are much more likely falsely predicted or functionally divergent. We call these orthologs whose phylogenetic divergence reflects the degree of species divergence: supporting-species-divergence orthologs or SSD orthologs. We have recently developed an improved version of Ortholuge that contains a novel statistical approach to fit and model the distribution of Ortholuge phylogenetic distance ratios. This analysis allows the calculation of the expected false discovery rate for SSD orthologs. We are also developing a web-accessible database of pre-computed Ortholuge predictions for all sequenced microbial genomes. This platform will facilitate powerful and accurate cross-species analysis.

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