Scale-free Meta-Analysis Of Microarrays And The Relationship Between Gene Expression And DNA Sequence Evolution

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Motivation

It is currently anticipated that much of the phenotypic divergence between biological species is due to changes in gene expression patterns. Little is known about the relationship between changes in gene expression and the evolution of non-protein coding DNA sequence within and around genes, where a substantial fraction of regulatory elements are thought to reside. Over 100000 gene expression datasets from microarray experiments are presently available in public databases, but early studies on the evolution of gene expression patterns have reported conflicting results. We believe this situation resulted from comparisons of absolute expression levels measured on different scales.

Methods

We present a methodology to i) compute the divergence of gene expression profiles between pairs of orthologous genes in different genomes, and ii) test for correlations between expression divergence and DNA sequence divergence in UTRs, introns, and gene flanking regions. We extract scale-free information from gene expression profiles that may have been obtained with different microarray platforms, and use correlation-based distances to measure expression divergence. The resulting measure of orthologous gene expression divergence can then be tested for a correlation with different types of DNA sequence evolution such as point substitutions, indels, and differential content of transposable elements.

Results

We apply this methodology to 3,700 pairs of orthologous genes mapped from a rat (rgu34a) onto a mouse (gnf1m) microarray platform; these platforms have been used to measure expression levels in 17 different tissues in common between both species. We show that lineage-specific transposable element insertions in non-protein coding regions in or near genes generally contribute to gene expression divergence.

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