### Roundup 2.0: Enabling Comparative Genomics for over 1800 Genomes

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Roundup 2.0: enabling comparative genomics for over 1800 genomes

Todd F. DeLuca1,∗, Jike Cui1, Jae-Yoon Jung1, Kristian Che St. Gabriel2 and Dennis P. Wall1,2,∗

1 The Center for Biomedical Informatics, Harvard Medical School and 2 Department of Pathology, Beth Israel Deaconess Medical Center, Boston MA 02115, USA

ABSTRACT

Summary: Roundup is an online database of gene orthologs for over 1800 genomes, including 226 Eukaryota, 1447 Bacteria, 113 Archaea and 21 Viruses. Orthologs are inferred using the Reciprocal Smallest Distance algorithm. Users may query Roundup for single-linkage clusters of orthologous genes based on any group of genomes. Annotated query results may be viewed in a variety of ways including as clusters of orthologs and as phylogenetic profiles. Genomic results may be downloaded in formats suitable for functional as well as phylogenetic analysis, including the recent OrthoXML standard. In addition, gene IDs can be retrieved using FASTA sequence search. All source code and orthologs are freely available.

Availability: http://roundup.hms.harvard.edu

Contact: dpwall@hms.harvard.edu; todd_deluca@hms.harvard.edu

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1 INTRODUCTION

Orthologs are genes from different organisms that descend from a single ancestral gene in the most recent common ancestor (Fitch, 1970). In comparative genomics, they are used to infer the function of novel genes from the function of well-studied ones, to construct phylogenies and explore the evolution of genes and species, and to study sequence conservation and change. They are also valuable in analyzing gene networks, studying gene gain and loss, and finding genes in model organisms that correspond to human disease genes (Altenhoff and Dessimoz, 2009). Also, we replaced ClustalW (Thompson et al., 1994) with WU-BLAST (W.Gish, personal communication) with NCBI BLAST (Altschul et al., 1990). Also, we replaced ChastellW (Thompson et al., 1994) with Kalign (Lassmann and Sonnhammer, 2005). Kalign is faster than ChastellW and produces better alignments for more distantly related sequences. This change resulted in 9% closer maximum likelihood distances between orthologs computed using PAML 4.0 (Yang, 2007), and 0.3% more orthologs on average. Since the Roundup database stores orthology for 12 combinations of divergence and E-value thresholds, RSD was modified to compute orthologs for any number of parameter combinations as quickly as for one parameter combination. This change should be of interest to researchers investigating the effect of different parameter settings and degree of global sequence similarity on ortholog inference. With the addition of other caching and file I/O changes, RSD is over six times faster than the previous version in our performance tests.

In addition to housing the orthologs inferred by RSD, Roundup builds clusters of orthologous genes, i.e. orthogroups, using deterministic single-linkage clustering. It partitions a graph into connected subgraphs by creating a cluster for every gene and then

orthology databases (Chen et al., 2006; Datta et al., 2009; Huerta-Cepas et al., 2011; Kristensen et al., 2011; Li et al., 2006; Linard et al., 2011; Ostlund et al., 2010; Rouard et al., 2011; Schuster et al., 2007; Tatusov et al., 2003). Roundup compares well to other major databases, with recent studies showing similar ortholog composition for model organisms (Altenhoff and Dessimoz, 2009; Chen et al., 2007). The data in Roundup include clusters of orthologs for a wide range of sequence conservation, allowing searches for distant orthologs, and also phylogenetic profiles that enable functional investigation, phylogenetic analysis and prediction of network organization (Cui et al., 2011).
merging two clusters if a gene in one of the clusters is orthologous to a gene in the other one. The result is that every gene in a group is orthologous to at least one other gene in the group and to no genes in any other groups. In contrast to other orthology databases (Chen et al., 2006; Schneider et al., 2007; Tatusov et al., 2003), Roundup orthologous groups are built on the fly using genomes selected by the user. This allows users to include exactly their genomes of interest and to explore the effects of including different genomes in the grouping of orthologs.

3 GENOMES AND ORTHOLOGS

The 1807 genomes in Roundup 2.0 are from UniProtKB (Magrane and Consortium, 2011), including 226 Eukaryota, 1447 Bacteria, 113 Archaea, 21 Viruses and Viroids. The approximately 63 CPU core-years to compute the orthologs took several weeks on our research computing cluster. Roundup used a fault-tolerant computational pipeline to compute orthologs for all 1631721 pairs of genomes across 12 parameter combinations selected to allow researchers access to results for a broad range of divergence and E-value threshold settings. As a result, there are over 11 billion orthologs available in Roundup. The genomes and orthologs are updated 2–4 times per year.

4 WEB INTERFACE

The Roundup website provides two ways to search for orthologs. The approximately 63 CPU core-years to compute the orthologs took several weeks on our research computing cluster. Roundup used a fault-tolerant computational pipeline to compute orthologs for all 1631721 pairs of genomes across 12 parameter combinations selected to allow researchers access to results for a broad range of divergence and E-value threshold settings. As a result, there are over 11 billion orthologs available in Roundup. The genomes and orthologs are updated 2–4 times per year.

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Conflict of Interest: none declared.

## REFERENCES


Cui, J. et al. (2011) Phylogenetically informed logic relationships improve detection of biological network information. BMC Bioinformatics, 12, 476.


