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VISTA TOOLS FOR INTERACTIVE VISUALIZATION AND ANALYSIS OF MULTIPLE ALIGNMENTS OF DNA SEQUENCES AND WHOLE GENOMES

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Recent studies in the field of comparative genomics demonstrate that multi-species DNA comparison presents a powerful method for discovering functional genomic sequences. Similarity across large evolutionary distances usually reveals conserved, and, by inference, important biological features. Expanding the capabilities of computational tools designed for pair wise DNA comparisons to multiple species requires the development of new algorithms for alignment, analysis of conservation, and visualization of results.

We have developed Phylo-VISTA [1], interactive software with associated Web server that presents a novel method for the visualization and analysis of conservation in multiple sequence alignments by providing several significant extensions to VISTA tools. The tool visualizes a similarity measure for DNA sequences of multiple species. The complexity of visual presentation is effectively organized using a framework based upon inter-species phylogenetic relationships. The phylogenetic organization supports rapid, user-guided inter-species comparison. To aid in navigation through large sequence datasets, Phylo-VISTA provides a user with the ability to select and view data at varying resolutions. The combination of multi-resolution data visualization and analysis, combined with the phylogenetic framework for inter-species comparison, provides a highly flexible and powerful framework for visual data analysis of multiple sequence alignments.

To visualize the results of comparative sequence analysis of multiple genomes we have developed the Multiple VISTA Browser, a new Java tool that presents a logical extension of the VISTA browser [2]. The multiple alignment of genomes, accessible through the browser, was generated by an automatic computational scheme, which originally was applied to the comparative study of the human and mouse genomes [2] and then expanded to the comparison of the human, mouse and rat genomes [3]. Our method uses local alignment for anchoring contigs, followed by a post-processing step to identify regions of possible homology on the base genome, and global alignment. The Multi-VISTA Browser displays human-mouse-rat multiple alignments on the scale of whole chromosomes along with annotations. The user may select any of the three genomes as the reference, and display the level of conservation between this reference and the sequences of the other two species in a particular interval. The user also has the option of browsing and retrieving alignments, annotation, and pattern of conservation for a specific region of interest.

All VISTA tools are available through the portal at <http://www-gsd.lbl.gov/vista/>.

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2. Couronne, O., Poliakov, A., Bray, N., Ishkhanov, T., Ryaboy, D., Rubin, E.M., Pachter, L. and Dubchak, I. (2002), Strategies and Tools for Whole Genome Alignments. *Genome Res.* **13**: 73-80.

3. Brudno, M., Poliakov, A., Salamov, A., Cooper, G.M., Sidow, A., Rubin, E.M., Solovyev, V., Batzoglou, S. and Dubchak, I. (2004), Automated Whole-Genome Multiple Alignment of Rat, Mouse, and Human, *Genome Res.*, in press.