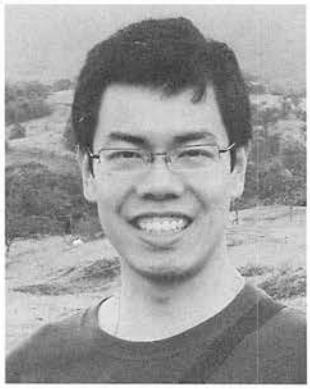
Identification of altered gene regulatory networks in gliomas by using Gene Network Entropy Analysis



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Oligodendrogliomas grade II and astrocytomas grade II may present similar phenotypes, making the diagnosis a difficult task. Thus, a better understanding of the differences between gene regulatory networks underlying both types of cancers may aid in the development of strategies to diagnosis, prognosis and therapy. Despite the massive investments in genome research and the numerous genomic data analysis methods, the knowledge about the abnormalities associated with both cancers is still incomplete. The problem consists not only in identifying molecular interactions, but in verifying if the differences found in networks comparison analyses are due to intrinsic fluctuation of the individual or if they are indeed associated with the disease. Therefore, it is crucial to develop strategies that take into account those fluctuations. Seeking advances in this direction, we developed a method namely, Gene Network Entropy Analysis (GNEA) to compare and statistically identify alterations between two gene regulatory networks. Our method is based on the Jensen-Shannon divergence for networks introduced by Takahashi et al (2012). GNEA was applied on microarray data derived from oligodendroglioma grade II and astrocytoma grade II tissues. A standard method to identify differentially expressed genes namely Gene Set Enrichment Analysis (GSEA) was also applied for a comparative analysis. GNEA and GSEA identified 64 and 24 gene sets associated with both types of cancer, respectively. Eight sets were identified by both analysis, demonstrating that in addition to differentially expressed genes identified by GSEA, differentially connected genes identified by GNEA may also be involved in different cancers.

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EDUCATIONS/TRAINING

2007	Doctor in Sciences (Bioinformatics) University of São Paulo, Brazil.
2003	Bachelor in Computer Science - University of São Paulo, Brazil.

POSITIONS AND HONORS

2011-Present	Assistant Professor, Dept. of Computer Science, Univ. of São Paulo, Brazil
2011-2013	CNPq Research Productivity Fellow Level 2
2009-2011	Foreign Postdoctoral Research Fellow, Computational Science Research Program - RIKEN, Japan
2007-2009	Postdoctoral Researcher - Human Genome Center, Institute of Medical Sciences, the University of Tokyo, Japan
2009	Honorable mention - CAPES Ph.D thesis award in Biological Sciences
2008	Best Ph.D. thesis in Computer Science awarded by the Brazilian Society for Computer Science
2006	Japan International Cooperation Agency (JICA) scholarship
2003-2007	CAPES graduate student scholarship
2002-2003	PIBIC/CNPq undergraduate student scholarship

RECENT PUBLICATIONS (10 most relevant papers in Bioinformatics)

1. Santos SS, Takahashi DY, Nakata A and Fujita A. A comparative study of statistical methods used to identify dependencies between gene expression signals. ***Briefings in Bioinformatics*** (in press)
2. Takahashi DY, Sato JR, Ferreira CE and Fujita A. Discriminating different classes of biological networks by analyzing the graphs spectra distribution. ***PLoS ONE*** 7: e49949, 2012.
3. Fujita A, Severino P, Kojima K, Sato JR, Patriota AG and Miyano S. Functional clustering of time series gene expression data by Granger causality. ***BMC Systems Biology*** 6: 137, 2012.
4. Nagasaki M, Fujita A, Sekiya Y, Saito A, Ikeda E, Li C and Miyano S. XiP: a computational environment to create, extend, and share workflows. ***Bioinformatics*** 29: 137-139, 2012.
5. Kojima K, Seiya I, Yamaguchi R, Fujita A, Yamauchi M, Gotoh N and Miyano S. Identifying regulational alterations in gene regulatory networks by state space representation of vector autoregressive models and variational annealing. ***BMC Genomics*** 13: S6, 2012.
6. Nagasaki M, Saito A, Fujita A, Tremmel G, Ueno K, Ikeda E, Jeong E and Miyano S. Systems biology model repository for macrophage pathway simulation. ***Bioinformatics*** 27:1591-1593, 2011.
7. Fujita A, Kojima K, Patriota A, Sato JR, Severino P and Miyano S. A fast and robust statistical test based on likelihood ratio with Bartlett correction to identify Granger causality between gene sets. ***Bioinformatics*** 26: 2349-51, 2010.
8. Niida A, Imoto S, Yamaguchi R, Nagasaki M, Fujita A, Shimamura T and Miyano S. Model-free unsupervised gene set screening based on information enrichment in expression profiles. ***Bionformatics*** 26: 3090-97, 2010.
9. Fujita A, Sato JR, Garay-Malpartida HM, Morettin PA, Sogayar MC and Ferreira CE. Time-varying modeling of gene expression regulatory networks using the wavelet dynamic vector autoregressive model. ***Bioinformatics*** 23: 1623-30 2007.
10. Fujita A, Sato JR, Garay-Malpartida HM, Yamaguchi R, Miyano S, Sogayar MC and Ferreira CE. Modeling expression regulatory networks with the sparse vector autoregressive model. ***BMC Systems Biology*** 1: 39, 2007.