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Title: A Phylogenetic Model for the Detection of Epistatic Interactions Author(s): Nasrallah, CA (Nasrallah, Chris A.); Huelsenbeck, JP (Huelsenbeck, John P.) Source: MOLECULAR BIOLOGY AND EVOLUTION Volume: 30 Issue: 9 Pages: 2197-2208 DOI: 10.1093/molbev/mst108 Published: SEP 2013 Times Cited in Web of Science Core Collection: 6 Total Times Cited: 6 Usage Count (Last 180 days): 1 Usage Count (Since 2013): 13 Cited Reference Count: 51 Abstract: Paired epistatic interactions, such as those in the stem regions of RNA, play an important role in many biological processes. However, unlike protein-coding regions paired epistatic interactions have lacked the appropriate statistical tools for the detection of departures from selective neutrality. Here, a model is presented for the analysis of paired epistatic regions that draws upon the population genetics of the compensatory substitution process to detect the relative strength of natural selection acting against deleterious combinations of alleles. The method is based upon the relative rates of double and single substitution, and can differentiate between nonindependent interactions and negatively epistatic ones. The model is implemented in a fully Bayesian framework for parameter estimation and is demonstrated using a 5S rRNA data set. In addition to the detection of selection, modeling the double and single substitution processes in this manner inherently accounts for a substantial proportion of rate variation among stem positions Accession Number: WOS:000323616600018 PubMed ID: 23748181 Language: English Document Type: Article Author Keywords: epistasis; compensatory mutation; RNA; phylogenetics KeyWords Plus: COMPENSATORY FITNESS INTERACTIONS; RNA SECONDARY STRUCTURES; MAXIMUM-LIKELIHOOD; DNA-SEQUENCES; RIBOSOMAL-RNA; SUBSTITUTION RATES; BAYES FACTORS; EVOLUTION; SITES; SELECTION Addresses: [Nasrallah, Chris A.] N Carolina State Univ, Dept Genet, Raleigh, NC 27695 USA. [Nasrallah, Chris A.; Huelsenbeck, John P.] Univ Calif Berkeley, Dept Integrat Biol, Berkeley, CA 94720 USA. [Huelsenbeck, John P.] King Abdulaziz Univ, Dept Biol Sci, Jeddah 21413, Saudi Arabia. Reprint Address: Nasrallah, CA (reprint author), N Carolina State Univ, Dept Genet, Raleigh, NC 27695 USA E-mail Addresses: nasrallah@statgen.ncsu.edu **Author Identifiers:** Author **ResearcherID** Number **ORCID** Number Fac Sci, KAU, Biol Sci Dept L-4228-2013 Publisher: OXFORD UNIV PRESS Publisher Address: GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND Web of Science Categories: Biochemistry & Molecular Biology; Evolutionary Biology; Genetics & Heredity Research Areas: Biochemistry & Molecular Biology; Evolutionary Biology; Genetics & Heredity **IDS Number: 2070E** ISSN: 0737-4038 eISSN: 1537-1719 29-char Source Abbrev.: MOL BIOL EVOL ISO Source Abbrev .: Mol. Biol. Evol. Source Item Page Count: 12 Funding: Funding Agency Grant Number National Institutes of Health GM-069801 National Science Foundation DBI1202884 The authors thank Tracy Heath for helpful discussions and Jeff Thorne, Nicolas Galtier, and two anonymous reviewers for comments on the manuscript. This work was supported by National Institutes of Health grant GM-069801 to J.P.H. and National Science Foundation postdoctoral fellowship DBI1202884 to C.A.N. **Open Access:** No Output Date: 2017-07-26

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