Abstract Submitted
for the MAR14 Meeting of
The American Physical Society

Bioinformatic prediction and in vivo validation of residue-residue interactions in human proteins DANIEL JORDAN, Harvard University, Cambridge, MA, USA, ERICA DAVIS, NICHOLAS KATSANIS, Duke University, Durham, NC, USA, SHAMIL SUNYAEV, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA — Identifying residue-residue interactions in protein molecules is important for understanding both protein structure and function in the context of evolutionary dynamics and medical genetics. Such interactions can be difficult to predict using existing empirical or physical potentials, especially when residues are far from each other in sequence space. Using a multiple sequence alignment of 46 diverse vertebrate species we explore the space of allowed sequences for orthologous protein families. Amino acid changes that are known to damage protein function allow us to identify specific changes that are likely to have interacting partners. We fit the parameters of the continuous-time Markov process used in the alignment to conclude that these interactions are primarily pairwise, rather than higher order. Candidates for sites under pairwise epistasis are predicted, which can then be tested by experiment. We report the results of an initial round of *in vivo* experiments in a zebrafish model that verify the presence of multiple pairwise interactions predicted by our model. These experimentally validated interactions are novel, distant in sequence, and are not readily explained by known biochemical or biophysical features.

Daniel Jordan
Harvard University, Cambridge, MA, USA

Date submitted: 15 Nov 2013 Electronic form version 1.4