

## ***Models of Evolution for Disordered Protein***

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**Background and Objective:** Most models of protein evolution are based upon proteins that have fixed three dimensional structures. A significant fraction of protein, so called disordered protein, does not have a fixed 3D structure. Since these disordered proteins are not constrained by the need to maintain short and long range interactions, they might be expected to evolve differently than ordered protein. Our objective was to develop models of disordered protein evolution and compare them with models for ordered protein.

**Methods:** Substitution matrices were constructed based upon homologues of 287 disordered or 290 ordered protein sequences. Separate matrices for each of three levels of similarity (>85%, 85-60%, 60-40%) were constructed for each type of protein.

**Results:** The substitution matrices for disordered and ordered protein differed significantly from each other at each similarity level. The disordered matrices reflected a greater likelihood of evolutionary changes relative to the ordered matrix, and these changes involved non-conservative substitutions. Glutamic acid was an interesting exception to this result.

**Discussion and Conclusions:** The models of evolution indicate that there are important differences between the substitutions that are accepted in disordered protein relative to ordered protein. Whereas ordered proteins are constrained over long term evolution by their need to maintain intra- and intermolecular interactions, disordered proteins appear to have fewer constraints.

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