

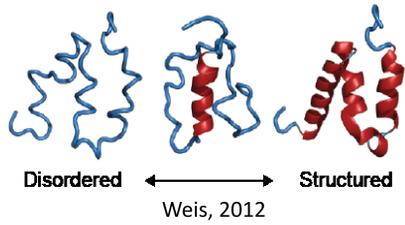
# More Exquisitely Adapted Species Have Higher Structural Disorder in Vertebrate Protein Domains

Catherine Weibel\*, Jennifer James, Sara Willis, Paul Nelson, Joanna Masel

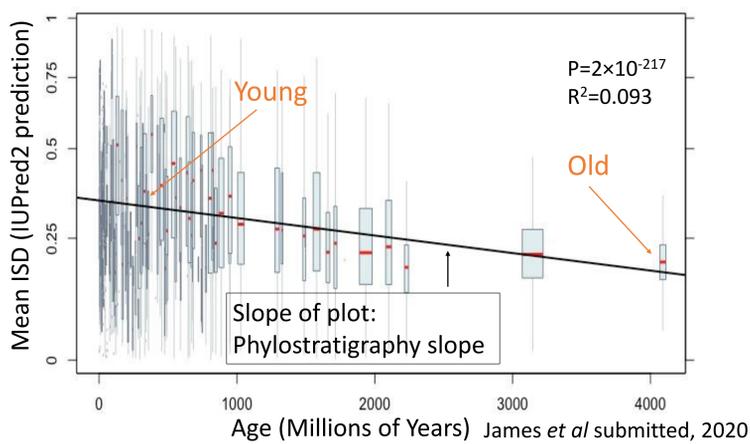
University of Arizona, Departments of Physics and Mathematics



**1** Intrinsic Structural Disorder (ISD) describes the degree of conformational freedom of protein structures; linked with protein folding and aggregation (Foy *et. al*, 2019)



Work done in the Masel lab has found that old protein domains have lower ISD than young protein domains



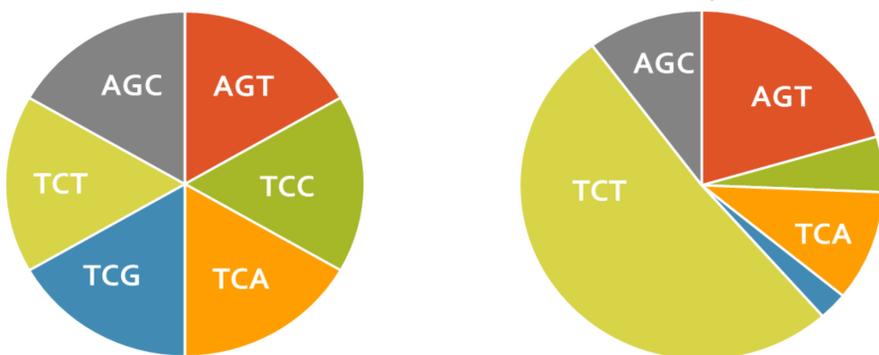
This implies the potential for an **arrow of time** for disorder trends in protein evolution

**Do species with more effective selection prefer protein domains with more or less ISD ?**

**2** Effectiveness of selection is reflected in **synonymous codon usage**

Codon Nonadapted Serine

Codon Adapted Serine



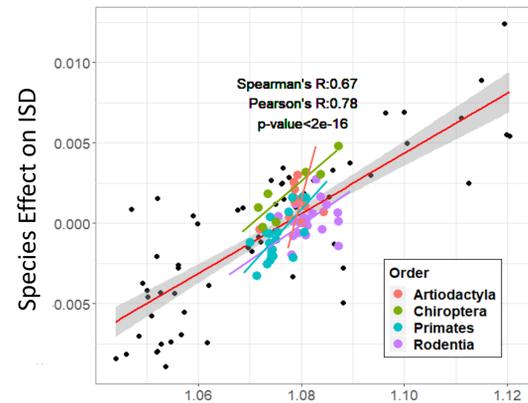
We designed a metric that is comparable between species, Codon Adaptation Index of Species (CAIS). It controls for GC content and amino acid composition.

**3** We extracted how a given protein domain is different depending on which species it is found in



We ran linear models with species as fixed effect and Pfam as random effect to calculate a species-specific disorder metric

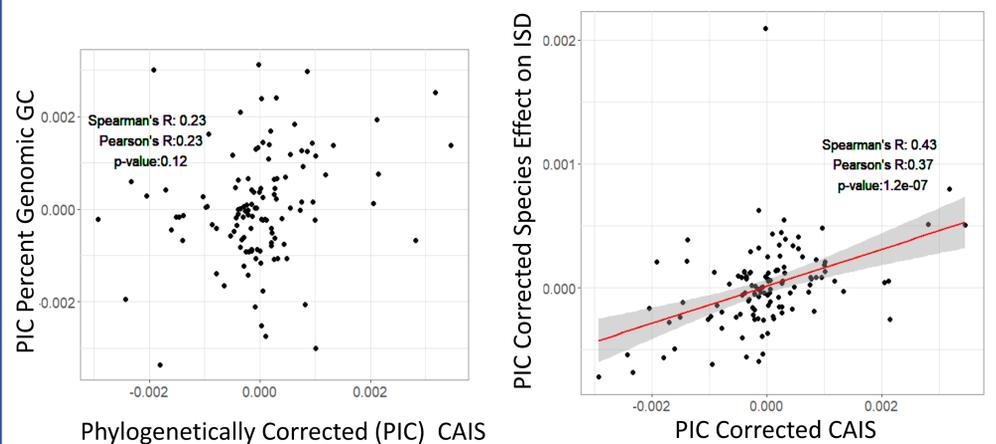
**4** Well-adapted species have higher ISD



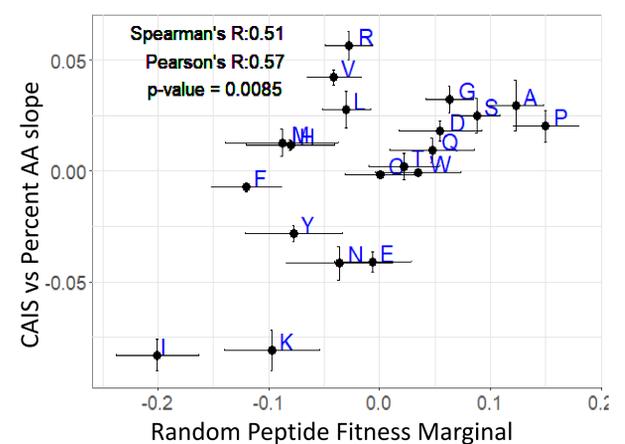
Less Adapted ← → More Adapted  
Codon Adaptation Index of Species (CAIS)

Data vulnerable to Simpson's Paradox, pseudoreplication and phylogenetic confounding; solved by using Phylogenetic Independent Contrasts (PIC)

**PIC analysis confirms: Well-adapted species have higher ISD and CAIS is uncorrelated with genomic GC content**



**5** Species with more effective selection have protein domains that are enriched in less deleterious random peptides in *E. coli* (Marginal Effects from Kosinski *et. al*, in prep.)



Relationships between domain age and amino acid composition found in James *et. al* 2020 **cannot be explained** by variations in effectiveness of selection of species

