Fraser Paper Discussion

In the paper “Evolutionary Rate in the Protein Interaction Network” by Fraser et al., the evolutionary rate of a protein is thought to rely upon its dispensability to the organism and how compatible these changes are with the protein function. While proteins were previously studied on an individual basis, technological advances have enabled researchers to study proteins at a genome scale. More specifically, among other advantages, it allows the role of protein – protein interaction in rate of evolution to be studied.

Fraser et al. formulated two hypotheses based upon preliminary data showing the rate of evolution to between number of interactors and protein evolutionary rate (seen in figure1). One hypothesis states, “if different interactions depend on different sites, proteins with more interactors could evolve more slowly because a greater proportion of the protein is involved in protein functions. Alternatively, if proteins with many interactors have a greater effect on organism fitness, they could evolve more slowly… because the entire sequence is subjects to stronger selections against slightly deleterious mutations.

Data supporting the first hypothesis showed that reduction of growth rate due to deletion of a gene is positively correlated with that protein’s number of interactors. Their research also showed that although the putative orthologs illustrated a negative correlation between evolutionary rate and fitness effects, highly conserved orthologs showed no relations between protein interaction and evolutionary rate. Figure two shows a diagram of both scenarios. It illustrates that either the number of protein interactions alone, or the number of protein interactions in conjunction with the protein fitness effects contributes to reduction of evolutionary rate with the number interactions. However, hypothesis 2 was rejected since the protein fitness effect does not mediate evolutionary rate.

To further elucidate hypothesis one, Fraser et al. explored the possibility that interacting proteins co-evolve as an alternative to substitutions being removed by selection. Thus, they hypothesized that if co-evolution is a significant means of change in proteins limited by interaction, then they should evolve at similar rates. Thus, they performed a study that showed that “interacting proteins evolve at rates significantly closer than is expected to occur by random chance.

Nevertheless, Fraser et al. developed the alternative hypothesis that the similarity in evolutionary rates of interacting proteins could be due to their participation in the same functional pathway, and thus their similar fitness effects. Their research showed that interacting proteins have similar effects on organism fitness. However, it was found that the correlation between fitness effects and interacting proteins contribute only slightly to their evolutionary rates. Figure 3a shows the distribution of ∆K values, showing the similarity between evolution rates and interacting proteins. Figure 3b shows that interacting proteins also have similar fitness effects. Finally, figure 3c is a causal model to determine whether the similarity in fitness effects explains similar evolutionary rates.

This study found that the co-evolution of interaction proteins plays a significant role in the similarity in rates of evolution.