## Short review for

"Patterns of selection across gene regulatory networks"

A large question in organismal development studies: why do some genes seem to be more likely to facilitate the morphological evolution than others. This paper discusses why and how gene regulatory networks (GRNs) play an important role to answer this question, from the perspective of genetics and evolution studies.

The interest in GRNs comes from the hypothesis: a few genes occupy unique positions within developmental networks such that they integrate many inputs and regulate many outputs seem to be more critical in the development. Section 2 argues the existence of such input-output genes, which has more interactions than the other genes. The bow-tie structure, two layers with many nodes while an intermediate layer with a few nodes connect these two layers, is a useful structure to describe the variation in GRNs.

Section 3 shows two cases to illustrate the usage of bow-tie structure in real applications. Several predictions between the gene positive selection and the relative positions compared with input-output genes have been proposed to guide the modelling of GRNs. Three possible GRNs models with different selection strength variations along with the positions have also been proposed with supportive examples in real applications.

However, current GRNs studies concentrate on the rapidly-evolving, adaptive morphological traits while GRNs can be considered at many spatial and temporal scales during the development. The generalization of current GRNs predictions are unclear.

## Comments by me:

- 1. A key step in GRNs study is to establish the GRNs networks from the data. Though coexpression networks may describes the gene correlations, the true gene regulatory interactions may not be fulled revealed by the correlations. Extracting the true regulatory from experimental results, and incorporating other gene functional information when establish the networks would be helpful.
- 2. How to identify the input-output genes and the positive selection may be the next critical problems. From the perspective of statistics, it would be interesting to apply some statistical methods to determine GRNs patterns, detect the significant selection strengths, and find network hubs from the data.

## References