

"Home depot" model of evolution of prokaryotic metabolic networks and their regulation

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Abstract:

It has been reported [1] that in prokaryotes the number of transcription factors scales approximately quadratically with the total number of genes. As a consequence the fraction of transcriptional regulators among all genes in small bacterial genomes (< 500 genes) is less than 0.5%, while in large genomes (~10,000 genes) it reaches as high as 10%.

We recently proposed [2] a general explanation of this empirical scaling law and illustrated it using a simple model in which metabolic and regulatory networks co-evolve together. In this model prokaryotic organisms acquire new metabolic functions by the virtue of horizontal gene transfer of entire co-regulated metabolic pathways from a shared gene pool (the "universal metabolic network" [3]) followed by removal of redundant enzymes. This process can be compared to a homeowner buying a tool set from a hardware store (hence our "Home Depot" metaphor) and later returning duplicate or unnecessary items.

We view the full repertoire of metabolic enzymes (or more generally any non-regulatory proteins) encoded in the genome of an organism as its collection of tools. Adapting to a new environmental condition (e.g. learning to use a new nutrient source) involves acquiring new enzymes as well as reusing some of the enzymes/tools that are already encoded in the genome. As the toolbox of an organism grows larger, it can reuse its existing tools more often, and thus needs to acquire fewer new enzymes to master each new regulated task. From this analogy it follows that, in general, the number of regulators in an organism should scale faster than linearly with its total number of proteins.

Our model faithfully reproduces the empirically observed [1] quadratic scaling between these two numbers. Furthermore, the distribution of lengths of co-regulated pathways in our model approximately agrees with that in real-life metabolic network of E coli. Thus, the toolbox analogy provides a conceptual explanation for the empirically observed broad distribution of regulon sizes. I will describe several possible regulatory architectures ensuring proper coordination of activity of metabolic pathways with each other. It remains to be determined which of them (if any) are realized in real-life prokaryotes.

References:

- [1] E van Nimwegen, "Scaling laws in the functional content of genomes", Trends Genet 19:479-84 2003.
- [2] S Maslov, S Krishna, T Y Pang, K Sneppen, "Toolbox model of evolution of prokaryotic metabolic networks and their regulation", accepted for publication PNAS 2009.
- [3] T. Handorf, O. Ebenhoh, R. Heinrich, "Expanding Metabolic Networks: Scopes of Compounds, Robustness, and Evolution", J Mol Evol 61:498–512 2005.