“Topological Motifs in Cellular Networks”

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Transcriptional regulation of cellular functions is carried out through a complex network of interactions among transcription factors and the promoter regions of genes and operons regulated by them. To better understand the system-level function of such networks, simplification of their architecture was previously achieved by identifying the motifs present in the network, which are small, repeated, topologically distinct regulatory interaction patterns (subgraphs). However, the interaction of such motifs with each other, and their form of integration into the full network has not been previously examined. By studying the transcriptional regulatory network of the bacterium, Escherichia coli, we demonstrate that the two previously identified motif types in the network (i.e., feed-forward and bi-fan motifs) do not exist in isolation, but rather aggregate into homologous motif clusters that largely overlap with known biological functions. Moreover, these clusters further coalesce into one giant supercluster, thus establishing distinct topological hierarchies that show similar global statistical properties that the whole network does. Knowledge of only two global statistical parameters allows us to correctly predict the density of all subgraphs in five well-characterized cellular networks, and to show that the highly abundant subgraphs (motifs) cannot exist in isolation, but undergo a percolation transition and aggregate into predictable motif clusters. These results have important implications on the evolutionary origin and function of subgraphs and motifs in all biological networks.

REFRESHMENTS AT 4:15 P.M.

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