Inherent Size and Complexity Constraints in Prokaryote Gene Regulatory Networks

Michael Gagen

Abstract: There are no fully scalable technologies, including in biology. Whatever the technology – oxygen uptake by lungs rather than through the skin, bones to support weight on land, regulatory technologies within cells or between cells in multicellular organisms – the adoption of any one technology to solve one set of limitations both potentiates novel behaviours and at the same time imposes additional constraints and limitations. The gene regulatory networks of prokaryotes (single-cell life) will also be size and complexity constrained by the adopted regulatory technology. Here, we generalize network growth models in response to recent comparative genomics results showing that the number of prokaryote gene regulators scales quadratically with gene number. Our generalized models then predict an upper limit to the size and complexity of prokaryote genomes which is very close to that observed in the evolutionary record. An immediate implication is that the protein-only regulatory networks of prokaryotes cannot explain the much larger and more complex genomes of multicellular eukaryotes. This conclusion is consistent with recent exciting findings of novel RNA regulatory mechanisms in eukaryotes. We compare these results with two alternate models proposing that regulator numbers scale linearly with gene number (though no plausible physical mechanism underlies such models). To make this comparison as accessible as possible, all three models have been encoded into a JAVA applet showing actual comparative genomics results, simulated statistics on the numbers of inbound and outbound regulatory links, the sizes of the largest fully connected island, the predicted maximum gene count for prokaryotes, and so on.