

on a no less important problem. Namely, that of discovering design principles in biological circuits and understanding why nature adheres to those principles.

From decades of research in molecular biology it is emerging that nature has converged time and again on similar molecular circuits. Such extensive convergent evolution owes to a combination of the following four factors. First, various physical-chemical constraints limit what molecular circuits are feasible. Second, not all feasible circuits are equally likely to be created from an existing biological network by random mutation. Third, only circuits that function very well and whose performance is robust to fluctuations enable the carrying organisms to survive natural selection. Fourth, similar functional properties (*e.g.*, fast responses, robustness to perturbations, high gains of outputs with respect to inputs) are required quite often in different contexts. Because most feasible circuits that could evolve from existing biological networks through a small number of frequent genetic events (mostly point mutations, gene duplications and gene deletions) are rarely found in living organisms, the last two factors are critical for explaining the observed convergence. This convergence and its underlying causes have deep implications. They mean that molecular biology might one day be structured around a number of simple laws or principles whose understanding hinges largely on engineering considerations similar to those applying to human-designed circuits. The major breakthroughs in the exact sciences occurred when the main regularities (laws) were discovered and then explained. From this process ensued the predictive power that earned these sciences the qualifier “exact”, which still sets them apart from biology. If a similar process is nowadays taking place in molecular biology this is largely through the discovery and explanation of design principles.

The focus on discovering and explaining engineering-derived design principles of biological networks was pioneered by Michael Savageau in the early 1970’s. And indeed it is to Michael Savageau’s 1976 classic “Biochemical Systems Analysis: A Study of Function and Design in Molecular Biology” [6] that Uri Alon’s book most directly compares. Both