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Molecules, nonlinearity, and function in regulatory networks.

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Biological regulatory networks are capable of sophisticated functions, such as integrating chemical signals, storing memories of previous molecular events, and keeping time. These networks often contain feedback loops, which can promote bistability and oscillation. However, feedback alone is not enough. Strong nonlinearities in the network dynamic are also needed. It is known that many regulatory proteins form higher-order complexes and multimers. I will discuss two important sources of nonlinearity in multimerization. First, ample experimental evidence suggests that protein subunits *in vivo* can degrade less rapidly when associated in complexes. For homodimers, this effect leads to a concentration dependence in the protein degradation rate. Theoretical analysis of two model gene circuits in bacteria, i.e. switch and oscillator, demonstrates that this effect can substantially enhance the function of these circuits. Second, active proteins can often be sequestered into inactive complexes. This molecular titration can lead to sharp nonlinearities, and suggests a scenario for the rapid evolution of bistable or oscillatory circuits in nature.