A Non-Interconnected Feedback (Autogenous Control)

B Interconnected Feedback Loop

Figure S5. Protocol for interconnected feedback loops. Evolution of the DEG-FB loop is used as an example. For robust operation, a heat shock system lacking regulated degradation of σ^{32} by a member of its own regulon could evolve an independent controller that stabilizes the levels of FtsH tightly around its desired value (**A**). A more straightforward solution to the problem is to employ the protocol of an interconnected loop whereby the FtsH module is evolved just by fusing a promoter for binding of σ^{32} to the FtsH gene (**B**). In both cases, the red symbols must be added for a robust modular system.