Abstract Submitted
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Enhancing Functional Robustness of Gene Regulatory Networks Based on Fitness Landscape Design[1] KYUNG KIM, University of Washington — We aim to develop design principles for enhancing functional robustness of engineered cells using gene-network topology. We observed the effect of genetic regulation types (inhibition and activation) on robustness. Inhibition was much more stable than activation in E. coli. In the case of activation, if the upstream activator expression is shutdown by mutation, then its downstream expression is shut down as well. Without activation, the activator shutdown due to mutation will make its downstream expression remains“ turned off. Thus, the change in the metabolic load is higher in the activation case. Therefore, the stronger activation, the less robust the circuits are. In the inhibition case, we found that the story becomes opposite. When an inhibitor expression is shut down by mutation, the downstream expression turns on because the inhibitor is not expressed. This compensates changes in the metabolic load that might have been decreased without the inhibition. This result presents potential significant roles of network topology on the robustness of engineered cellular networks. This also emphasizes that the concept of fitness landscape, where the local slope corresponds to the fitness difference between different genotypes, can be useful to design robust gene circuits.

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Kyung Kim
University of Washington

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