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Adaptation by Plasticity of Genetic Regulatory Networks

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Genetic regulatory networks have an essential role in adaptation and evolution of cell populations. This role is strongly related to their dynamic properties over intermediate-to-long time scales. We have used the budding yeast as a model Eukaryote to study the long-term dynamics of the genetic regulatory system and its significance in evolution. A continuous cell growth technique (chemostat) allows us to monitor these systems over long times under controlled condition, enabling a quantitative characterization of dynamics: steady states and their stability, transients and relaxation. First, we have demonstrated adaptive dynamics in the *GAL* system, a classic model for a Eukaryotic genetic switch, induced and repressed by different carbon sources in the environment. We found that both induction and repression are only transient responses; over several generations, the system converges to a single robust steady state, independent of external conditions. Second, we explored the functional significance of such plasticity of the genetic regulatory network in evolution. We used genetic engineering to mimic the natural process of gene recruitment, placing the gene *HIS3* under the regulation of the *GAL* system. Such genetic rewiring events are important in the evolution of gene regulation, but little is known about the physiological processes supporting them and the dynamics of their assimilation in a cell population. We have shown that cells carrying the rewired genome adapted to a demanding change of environment and stabilized a population, maintaining the adaptive state for hundreds of generations. Using genome-wide expression arrays we showed that underlying the observed adaptation is a global transcriptional programming that allowed tuning expression of the recruited gene to demands. Our results suggest that non-specific properties reflecting the natural plasticity of the regulatory network support adaptation of cells to novel challenges and enhance their evolvability.