

## Controlling the Production of DNA Precursors

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Cellular concentrations of DNA precursors, deoxynucleoside-triphosphates (dNTPs), is tightly regulated to ensure high DNA replication fidelity. dNTP concentrations are maintained primarily through a conserved set of allosteric regulations on ribonucleotide reductase (RNR), an essential enzyme that catalyzes the rate limiting step in the production of dNTPs. The two modes of allosteric regulation, the specificity regulation and activity regulation, have been studied biochemically and structurally to great detail, which led to deep molecular level insights. However, we lack a quantitative framework to analyze the functional consequences of these allosteric effects on the dynamical properties of dNTP metabolism. We used minimal kinetic models and stochastic simulations to show that specificity regulation in RNR ensures low fluctuation levels of dNTPs. Based only on dynamical properties, we propose that a single enzyme such as RNR cannot lower the fluctuation of all 4 dNTPs, which suggests the requirement of an extra enzyme such as dCMP/dCTP deaminase in dNTP metabolism.