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### **NMR investigations of molecular dynamics**

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NMR spectroscopy is a powerful experimental approach for characterizing protein conformational dynamics on multiple time scales. The insights obtained from NMR studies are complemented and by molecular dynamics (MD) simulations, which provide full atomistic details of protein dynamics. Homologous mesophilic (*E. coli*) and thermophilic (*T. thermophilus*) ribonuclease H (RNase H) enzymes serve to illustrate how changes in protein sequence and structure that affect conformational dynamic processes can be monitored and characterized by joint analysis of NMR spectroscopy and MD simulations. A Gly residue inserted within a putative hinge between helices B and C is conserved among thermophilic RNases H, but absent in mesophilic RNases H. Experimental spin relaxation measurements show that the dynamic properties of *T. thermophilus* RNase H are recapitulated in *E. coli* RNase H by insertion of a Gly residue between helices B and C. Additional specific intramolecular interactions that modulate backbone and sidechain dynamical properties of the Gly-rich loop and of the conserved Trp residue flanking the Gly insertion site have been identified using MD simulations and subsequently confirmed by NMR spin relaxation measurements. These results emphasize the importance of hydrogen bonds and local steric interactions in restricting conformational fluctuations, and the absence of such interactions in allowing conformational adaptation to substrate binding.