We employ single-molecule techniques to study DNA- and RNA-protein interactions, and have focused on processes related to topology, transcription, and replication. For example, we have examined the mechanisms of Type I Topoisomerases (Koster et al., Nature 2005), their interaction with chemotherapeutic drugs and concomitant implications for the replication fork (Koster et al., Nature 2007), and the mechanisms employed by RNA-dependent RNA polymerases (RdRPs).

I will illustrate the power of these single-molecule techniques by two examples indicating unexpected or rare behavior, in the context of topoisomerases and of RdRPs. In the case of the RdRPs, we have recently studied the polymerization kinetics of the model RdRP from Bacteriophage Φ6 during its replication and transcription modes. We observe a phenomenon that is consistent with strand-switching of the RdRP, which has implications for RNA recombination.