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## Molecular Dynamic Simulations of Operator DNA Distortions Made by Transcriptional Regulator MerR

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Many bacteria possess a mercury resistance (*mer*) operon that encodes enzymes and transport proteins that effect protonolysis of organomercurials and reduction of Hg(II) to volatile, elemental Hg(0). Transcription of the *mer* operon is regulated by the Hg(II)-specific regulatory protein MerR. The MerR homodimer binds a palindromic DNA sequence (the MerO operator) that lies within the overlong 19-bp spacer between the -35 and -10 RNA polymerase binding sites of the *mer* promoter. It is well known that metal-free-MerR bends operator DNA  $\sim 40^\circ$  laterally and, upon binding Hg(II), it also underwinds the DNA axially  $\sim 30^\circ$ , correcting the -10 and -35 sites to the orientation seen in promoters with a typical 17-bp spacer. *In vivo* and *in vitro* DNA footprinting have shown that several bases in the central-non-dyadic 4-bp "hyphen" (positions -23 to -26) become distorted upon Hg(II)-activation of MerR. Although there is no 3D structure of MerR yet, we recently used molecular dynamics (MD) to simulate the behavior of a MerR-Hg model based on its small-angle X-ray scattering (SAXS) and crystallographic structures of other MerR family members. In this current work we expanded that model to an activated MerR-DNA complex. Since all 3D MerR family regulator-operator complexes are in the activated form, the initial state of our 23-bp model DNA operator is already bent and underwound and remains so after a 2 ns equilibration. Moreover, two

bases in the activated dyad center remain unpaired over a 60 ns trajectory. In contrast, in a 60 ns simulation of the 23-bp operator alone, the activated conformation instantly collapses into the general form of B-DNA with the dyad center bases forming hydrogen bonds. These and other atomic level details arising from the MD simulations of interactions between MerR and its operator DNA were in good agreement with *in vivo* genetic analysis and protein-DNA footprinting data. Thus, MD will be useful to dissect the energetics and information transduction of the unique activation mode of the widely found MerR family of transcriptional regulators.