conformation. In previous work, it was found that MthK channels in which two of the three Ca^{2+} binding sites in the RCK domain have been mutated can diminish Ca^{2+} activation, suggesting that MthK channels can be weakly activated through single Ca^{2+} binding sites (Pau et al. 2011). Thus it is possible that Ba^{2+} activates MthK channels through binding to the C1 site (Figures 4-1, 4-5, and 4-8), and hence that the Ba^{2+}-bound gating ring represents an intermediate, singly liganded conformation in the domain's activation pathway.

To further explore whether the Ba^{2+}-bound gating ring might represent an intermediate, singly liganded conformation, we compared the conformation of a dimeric unit from the Ba^{2+}-bound gating ring with other previously determined MthK RCK domain structures by aligning the structures to yield the minimal rmsd. We reasoned that comparisons yielding low rmsd values might indicate structures in the same conformation, and higher rmsd values would indicate conformational differences.

Through these comparisons, a physical picture of conformational transitions that may underlie MthK gating emerges (Figure 4-9; Table 4-2). We first noted that the structure of the unliganded MthK gating ring (with the D184N mutation; PDB accession number 2FY8; (Ye et al. 2006)) showed that the unliganded ring can exist in two different overall conformations (Figure 4-A, 1 and 2). Unliganded ring (1) contains component RCK domains in two different conformations, indicated in Figure 4-9A by "***a***" (red box) and "***b***," whereas unliganded ring (2) contains all RCK domains in the ***b*** form (Figure 4-9A, blue