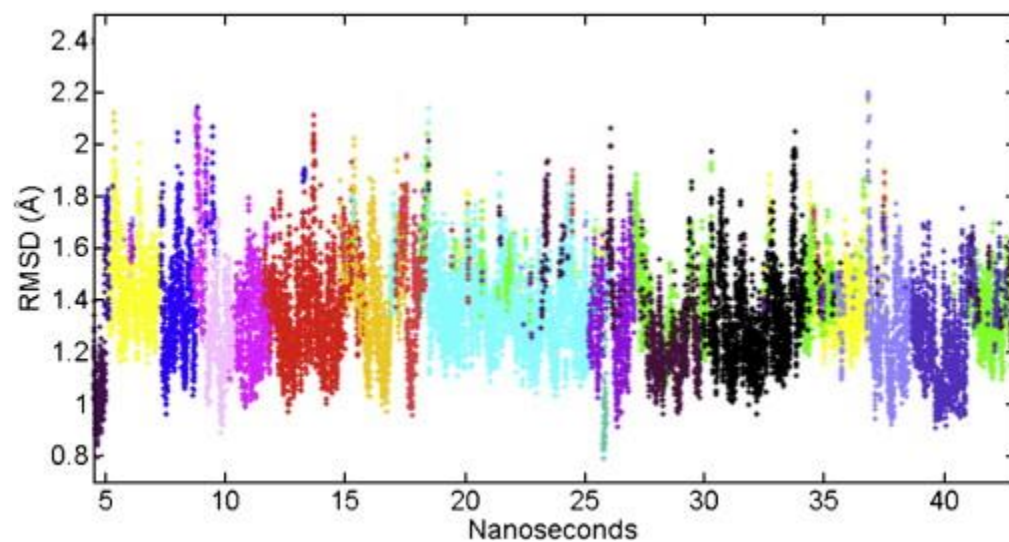
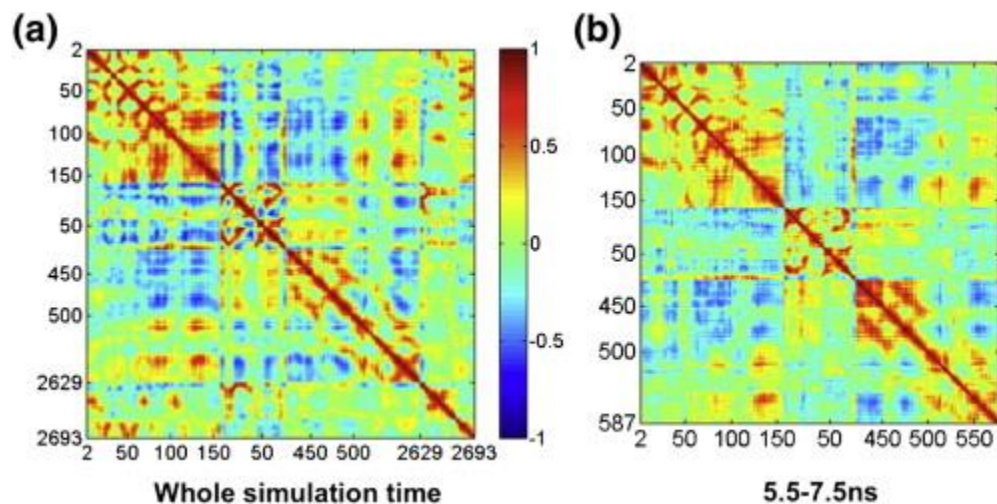


Alternative allosteric mechanisms can regulate the substrate and E2 in SUMO conjugation.

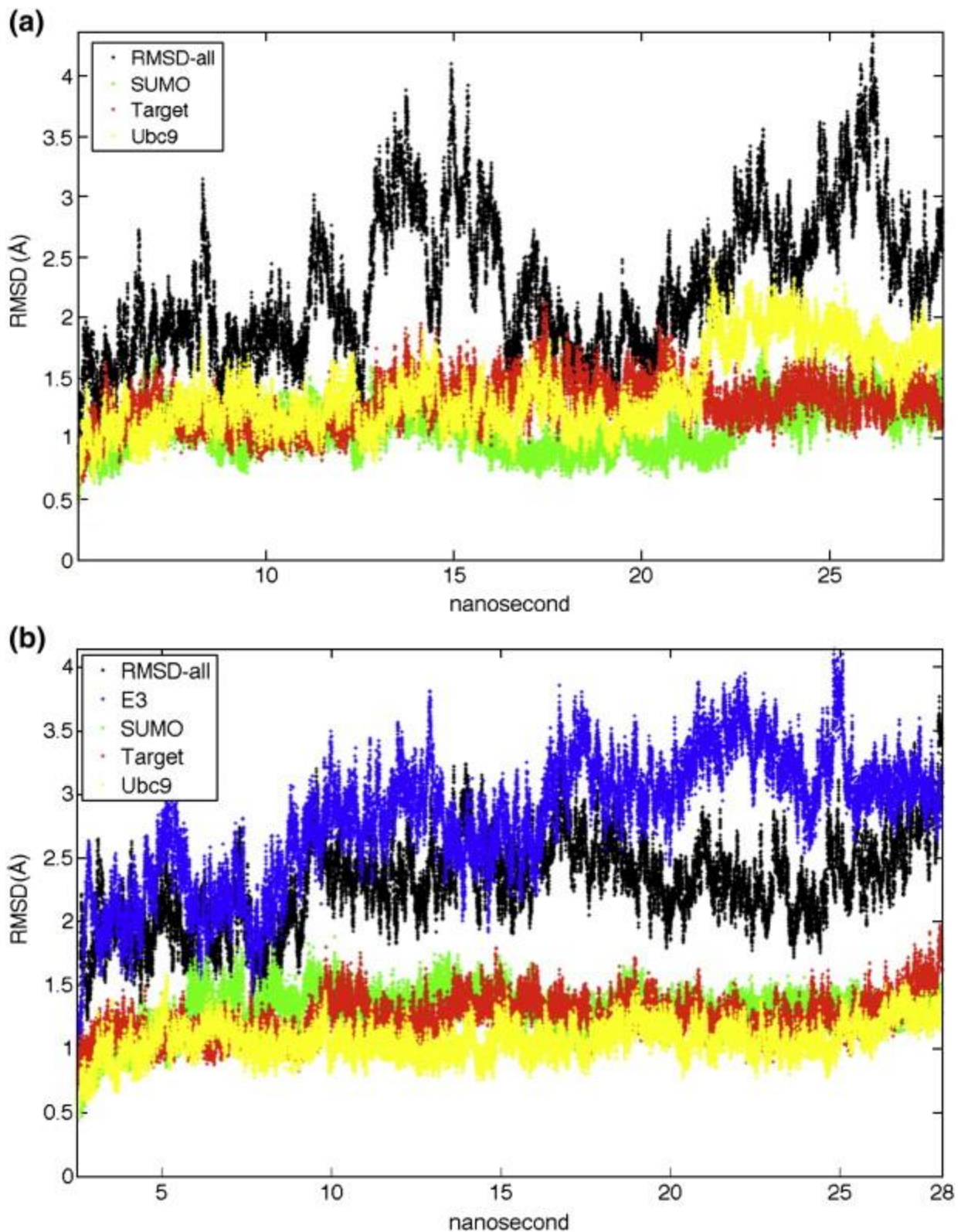
Supplementary Figures 1-6:



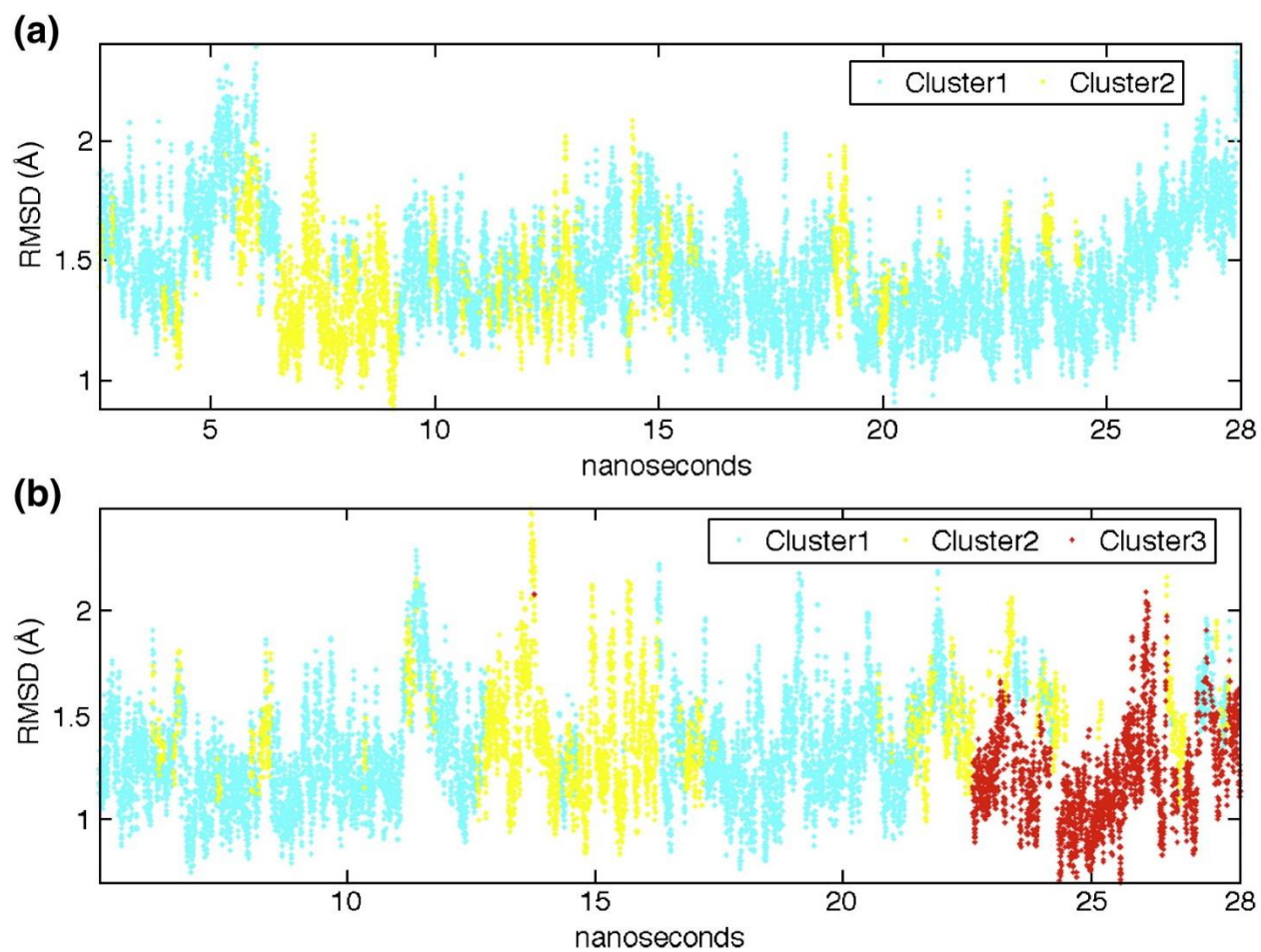
Supplementary Figure 1. RMSD evaluation of the $E2^{Ubc9}-E3^{RanBP2}-SUMO-Target^{RanGAP1}$ complex, after clustering with an RMSD threshold of 2.2 \AA , in the time course of the simulation for 43 ns. The color code of each line represents a different [conformational ensemble](#).



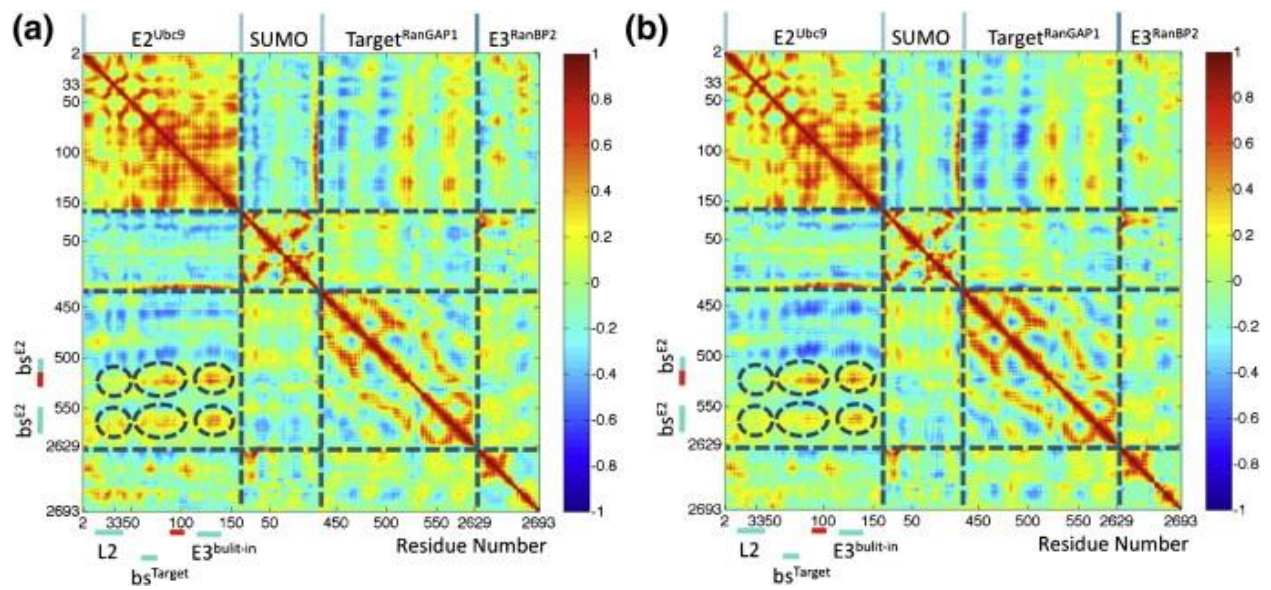
Supplementary Figure 2. A. The correlation plot is derived from the $E2^{Ubc9}-E3^{RanBP2}-SUMO-Target^{RanGAP1}$ complex from the whole trajectory time. The graph indicates that the strong correlation at the $E2^{Ubc9}-Target^{RanGAP1}$ interface is dominant for the whole trajectory. B. The correlation plot is derived from the $E2^{Ubc9}-SUMO-Target^{RanGAP1}$ complex from the time interval of 5.5–7.5 ns. The correlation of the $E2^{Ubc9}-Target^{RanGAP1}$ interface quite differs than the correlation pattern observed for the $E2^{Ubc9}-E3^{RanBP2}-SUMO-Target^{RanGAP1}$ complex trajectory.



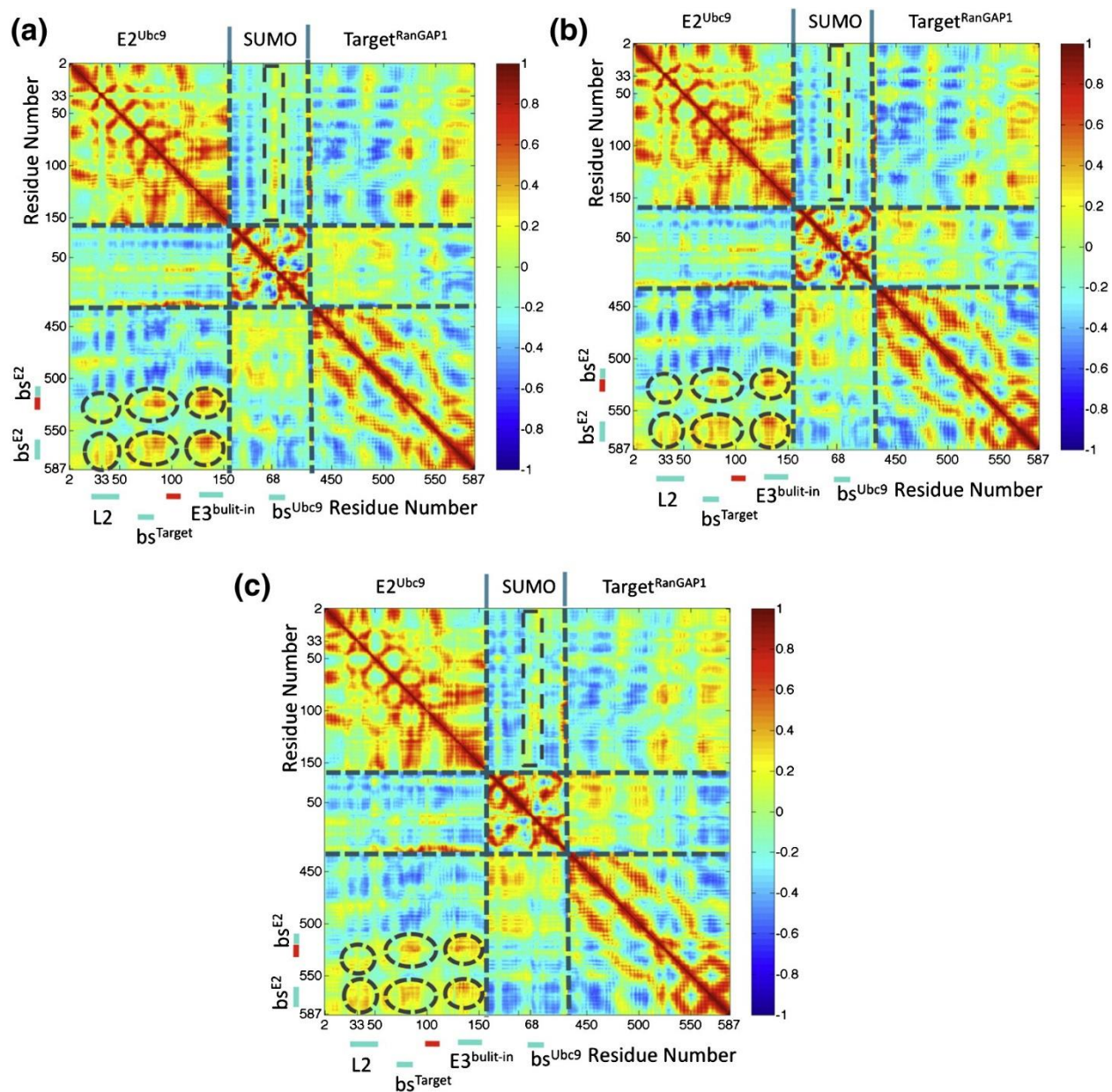
Supplementary Figure 3. A. RMSD evaluation of the $E2^{Ubc9}$ - $E3^{RanBP2}$ -SUMO-Target^{RanGAP1} complex, in the time course of the simulation for 48.5 ns. The color code of each line is indicated in the legend. B. The extent of the conformational change observed by loop 2 of $E2^{Ubc9}$. Loop 2 is represented in transparent surface and cartoon and the rest of $E2^{Ubc9}$ is shown in cartoon. The white snapshot is extracted from 10 ns and the yellow one from 24 ns. C. RMSD evaluation of the $E2^{Ubc9}$ -SUMO-Target^{RanGAP1} complex, in the time course of the simulation for 43 ns. The color code of each line is indicated in the legend.



Supplementary Figure 4. A. RMSD evaluation of the E2^{Ubc9}-E3^{RanBP2}-SUMO-Target^{RanGAP1} complex, after clustering with an RMSD threshold of 2.5 Å, in the time course of the simulation for 48.5 ns. The color code of each line represents a different conformational ensemble. B. RMSD evaluation of the E2^{Ubc9}-SUMO-Target^{RanGAP1} complex, after clustering with an RMSD threshold of 2.5 Å, in the time course of the simulation for 43 ns. The color code of each line represents a different conformational ensemble.



Supplementary Figure 5. Coupled Correlated Fluctuations observed for $E2^{Ubc9}$ - $E3^{RanBP2}$ - $SUMO$ - $Target^{RanGAP1}$ complex implies an [allosteric effect](#). The correlation plots are derived from the control trajectory of $E2^{Ubc9}$ - $E3^{RanBP2}$ - $SUMO$ - $Target^{RanGAP1}$. A. The coupled fluctuations observed during cluster 1. B. The coupled fluctuations observed during cluster 2.



Supplementary Figure 6. Coupled Correlated Fluctuations observed for E2^{Ubc9}-SUMO-Target^{RanGAP1} complex implies an allosteric effect. The correlation plots are derived from the control trajectory of E2^{Ubc9}-SUMO-Target^{RanGAP1}. A. The couple fluctuations observed during cluster 1. B. The coupled fluctuations observed during cluster 2. B. The coupled fluctuations observed during cluster 3.