



**FIGURE S1** Singular value decomposition (SVD) analyses of RDC data ( $^1\text{H}$ - $^{15}\text{N}$ ) for PEA-15 DED in ERK2-bound form measured from two distinct media as labeled. The free-form NMR structure of PEA-15 DED, PDB 2LS7, was used in all analyses. The secondary  $\alpha$ -helical structures are indicated on top of the plot. Experimental RDC values are shown in red and simulated values in blue. Error bars in simulated data indicate the standard deviation among all NMR models. (A) and (B) SVD analyses of RDC data for all DED residues (1-90); (C) and (D) SVD analyses of RDC data for helices  $\alpha 1$ ,  $\alpha 5$ , and  $\alpha 6$ . A reasonable match between the predicted and experimental RDC values could be obtained in both media, and the order tensor matrix generated by the SVD was used in the back calculations of predicted RDC values as shown in the main manuscript. (E) and (F) SVD analyses of RDC data for helices  $\alpha 2$ ,  $\alpha 3$ , and  $\alpha 4$ . The predicted and experimental RDCs do not match in this region, indicating a substantial rearrangement of  $\alpha 2$ ,  $\alpha 3$ , and  $\alpha 4$  relative to  $\alpha 1$ ,  $\alpha 5$ , and  $\alpha 6$ .