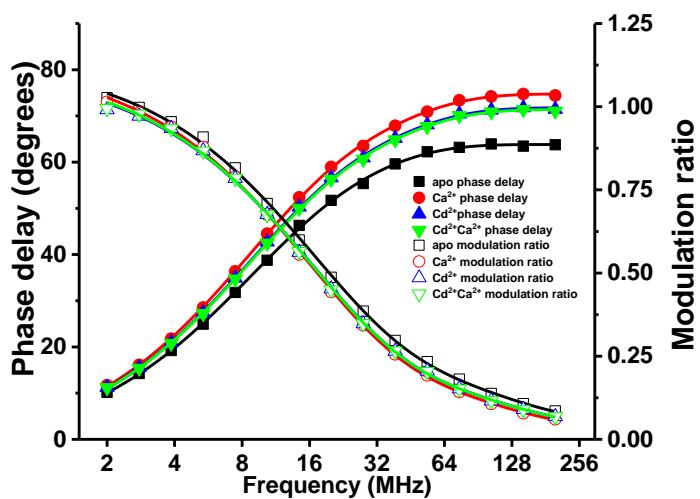
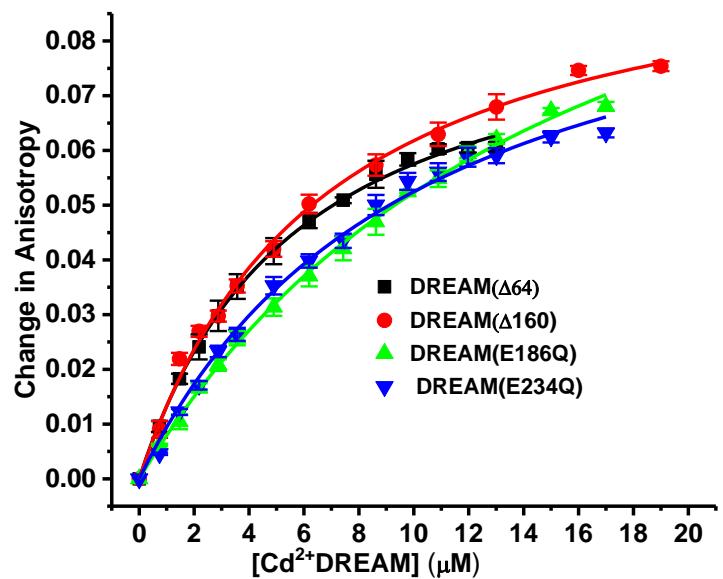


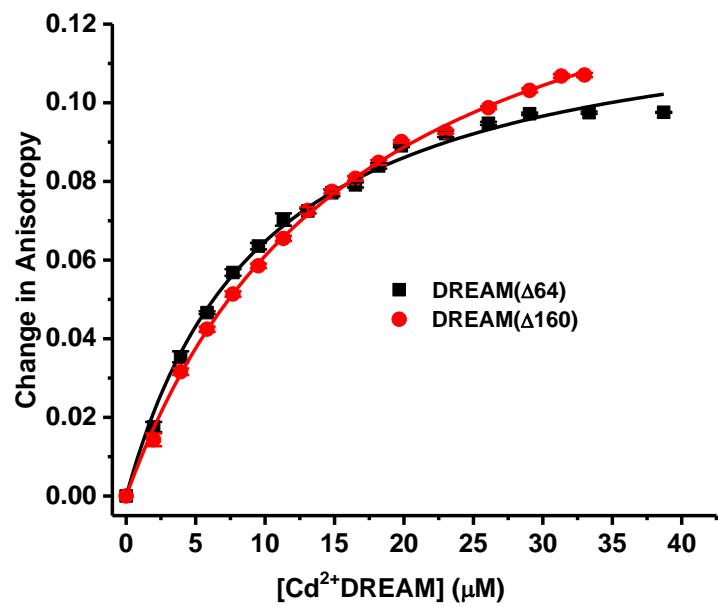
**Figure S1.** Frequency-domain intensity decay of 20  $\mu$ M apoDREAM( $\Delta$ 64) (square),  $\text{Ca}^{2+}$ DREAM( $\Delta$ 64) (circle),  $\text{Cd}^{2+}$ DREAM( $\Delta$ 64) (up triangle), and  $\text{Cd}^{2+}\text{Ca}^{2+}$ DREAM ( $\Delta$ 64) (down triangle). Solid symbols represent phase delay, whereas empty symbols represent modulation ratio. Solid lines correspond to the fitting of the data using the sum of one Gaussian distribution and one single exponential decay model.



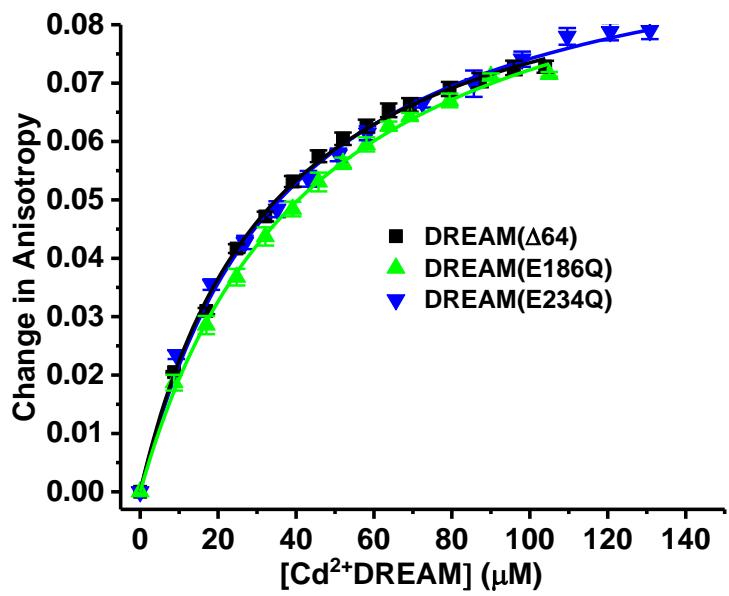
**Figure S2.** Frequency-domain intensity decay of 40 μM 1,8-ANS:54 μM DREAM(Δ64) complexes in the presence of EDTA (squares), Ca<sup>2+</sup> (circle), Cd<sup>2+</sup> (up triangle), and Cd<sup>2+</sup>Ca<sup>2+</sup> (down triangle). Solid symbols represent phase delay, whereas empty symbols represent modulation ratio. Solid lines represent the fitting of the data using three-exponential decay model.



**Figure S3.** Titration of 0.5 μM PS1HL9 against Cd<sup>2+</sup>-bound DREAM constructs. The solid lines represent the fits of the experimental data using Equation 1; standard deviations are shown as error bars.



**Figure S4.** Titration of 0.5 μM Kv4.3 (2–22) “site-1” against Cd<sup>2+</sup>-bound DREAM constructs. The solid lines represent the fits of the experimental data using Equation 1; standard deviations are shown as error bars.



**Figure S5.** Titration of 0.5 μM Kv4.3 (70–90) “site-2” against Cd<sup>2+</sup>-bound DREAM constructs. The solid lines represent the fits of the experimental data using Equation 1; standard deviations are shown as error bars.