



Fig S1: Changing the value of ΔG_{ca}° changes the $\mu_{Ca^{2+}}$ value at which ensemble epistasis is maximized Each panel shows the magnitude of epistasis on the y-axis and $\mu_{Ca^{2+}}$ (in $kcal \cdot mol^{-1}$) on the x-axis. Each colored curve represents ensemble epistasis observed with a different G_{ca}° value: $5 kcal \cdot mol^{-1}$ (blue), $10 kcal \cdot mol^{-1}$ (black), and $15 kcal \cdot mol^{-1}$ (green). A) $\mu_{Ca^{2+}}$ -dependent epistasis for the L109I/F145R mutation pair, B) the F78A/F145R mutation pair, and C) M85K/F145R mutation pair.