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# **Supplemental Information**

# Computational Modeling Reveals Frequency Modulation of CalciumcAMP/PKA Pathway in Dendritic Spines

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# Reaction kinetic type selection for PDE1 activation

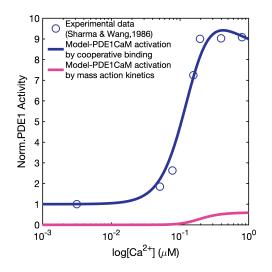
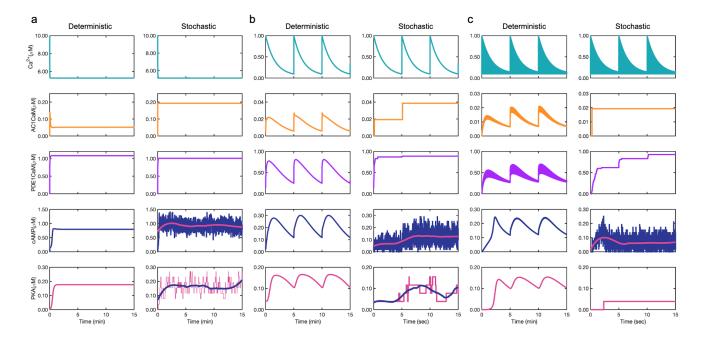


Figure S1: Cooperative binding kinetics shows a better fit for PDE1 activation by  $Ca^{2+}$  in comparison to massaction kinetics.



#### **Stochastic vs Deterministic Simulations**

Figure S2: Comparison of stochastic and deterministic simulations for a) Non-oscillating  $Ca^{2+}$ , b)  $Ca^{2+}$  oscillating in minute scale, and c)  $Ca^{2+}$  oscillating in second scale.

# Effect of AC1 activation by $G_s$ on cAMP production

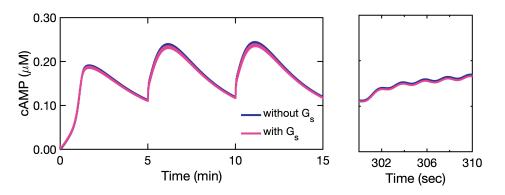
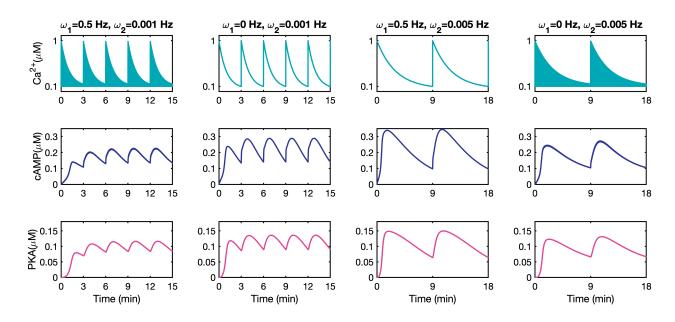


Figure S3: AC1 activation by  $G_s$  does not affect cAMP production.



### **Other oscillation frequencies**

Figure S4: Two other calcium minute-scale frequencies ( $\omega_2=0.001$  and  $\omega_2=0.005$ ) along with second-scale oscillations ( $\omega_1=0.5$ ) were chosen to confirm that cAMP and PKA only pick up minute-scale oscillations of calcium.