**Supplemental Data** 



**Figure S1** Spine  $[Ca^{2+}]$  (lower figure) during coincident activation given various IP<sub>3</sub> profile magnitudes (as shown in the top figure). Ca<sup>2+</sup> trends in the lower figure are the result of the same-colored IP<sub>3</sub> profile in the top figure. As the magnitude of the IP<sub>3</sub> profile is increased, the delay time (as measured from the small initial peak due to CF activation to the time of significant rise toward the true maximum) decreases. Note the shorter time window in the lower figure as compared to the top figure.



Figure S2 Similar data as Figure S1 but with constant IP<sub>3</sub> profiles. The varying delay is still observed.



**Figure S3** Normalized log sensitivity of spine cytosol  $Ca^{2+}$  with respect to three parameters related to IP<sub>3</sub> calculated during the supralinear calcium spike observed during coincident activation (see Figure 9). Changes in the two parameters that govern the decay rate of IP<sub>3</sub> in the system ( $K_{deg}$  and  $K_s$ ) have a very small effect on [ $Ca^{2+}$ ] As a comparison, the sensitivity of [ $Ca^{2+}$ ] to  $d_{IP3}$  (IP<sub>3</sub>R sensitivity to IP<sub>3</sub>) is also included. Therefore, adjusting  $K_{deg}$  and  $K_s$  to account for other phenomena (e.g., IP<sub>3</sub> degradation due to 3-kinase) will have a minimal role in shaping the system response during coincident activation.