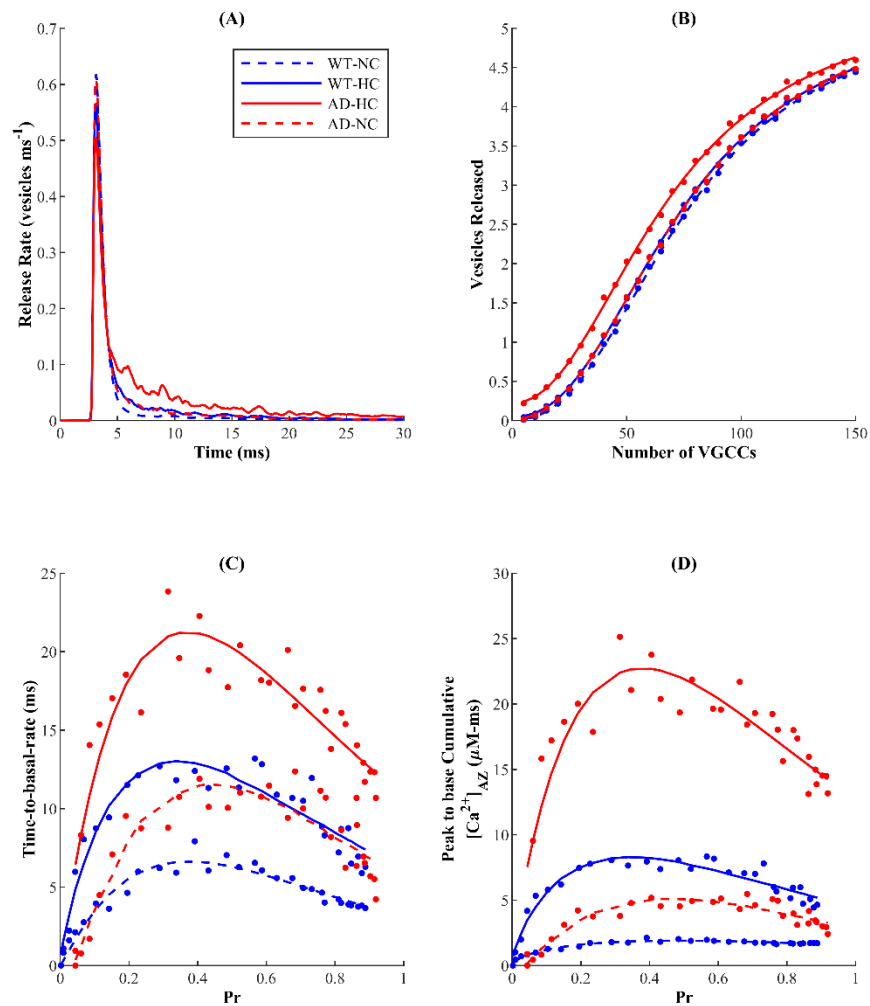
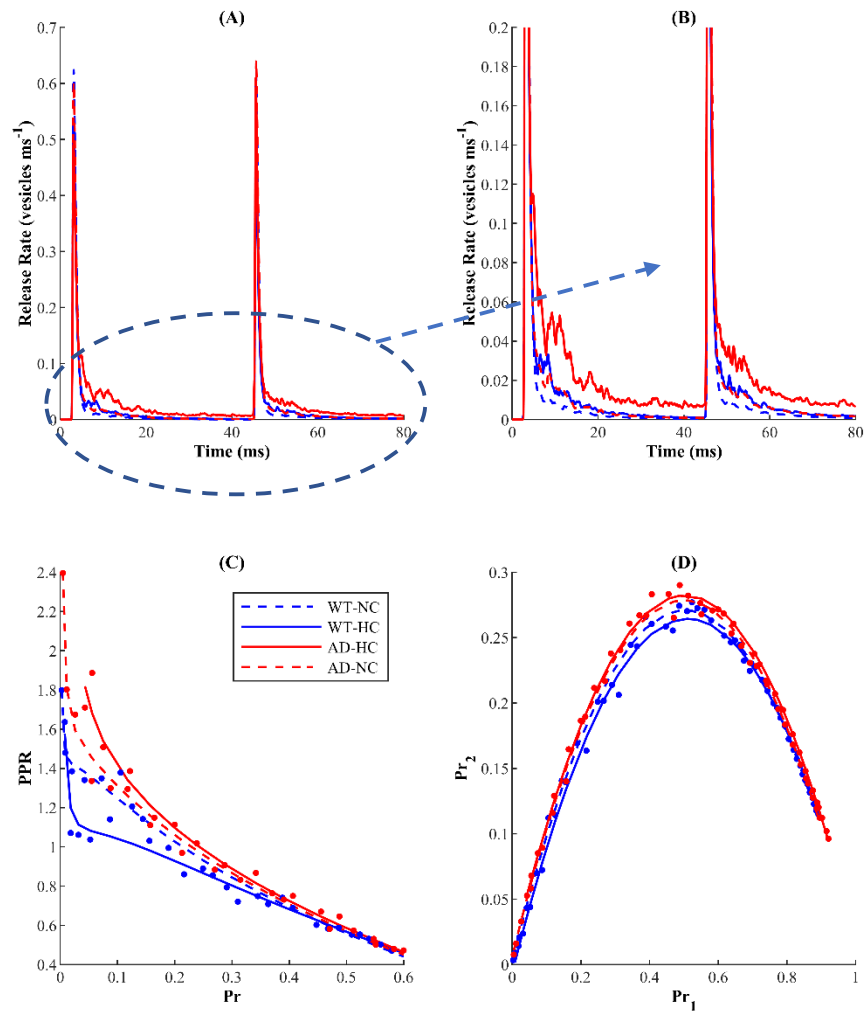


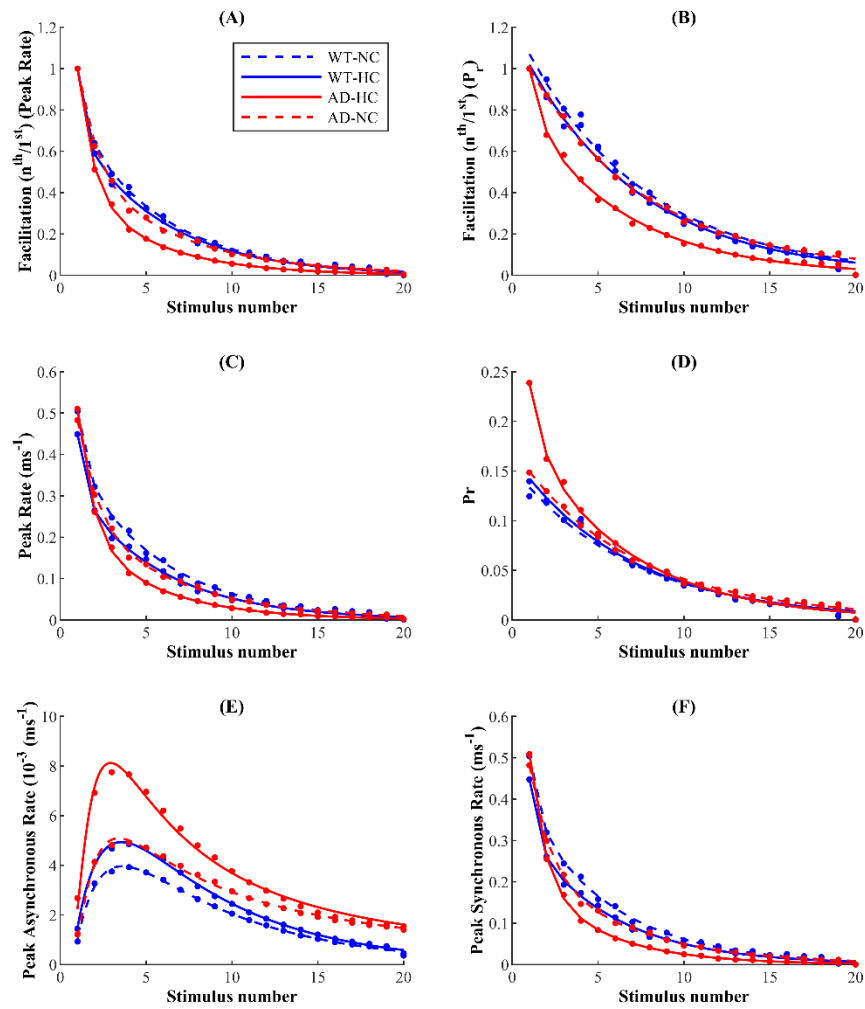
Supplementary Figures



SI Figure 1. Coupling between the microdomains around IP_3Rs and VGCCs influences Ca^{2+} in the AZ and neurotransmission profiles in AD and WT synapses. Transmitter release rates within 30 ms of stimulus (A) and total vesicles released (B) for different coupling configurations. Decay time of peak release rate (C) and cumulative Ca^{2+} concentration from peak to basal rate in the AZ (D) are markedly influenced by coupling.



SI Figure 2. Stronger coupling between the microdomain of IP_3Rs cluster and AZ exacerbate the release rate and enhanced PPR in AD-affected synapses but only marginally affect the bell-shaped behavior of Pr_2 as a function of Pr_1 . Release profile (A) (zoomed-in (B)) following paired-pulse stimulation protocol shows an increase in release rate by stronger coupling in the microdomain of IP_3Rs cluster and AZ in both WT and AD-affected synapses. (C) The enhanced PPR in AD-affected synapses with respect to WT synapses is exacerbated by stronger coupling. (D) Pr in response to the second pulse (Pr_2) as a function of Pr following the first pulse (Pr_1) shows that the bell-shaped response is marginally affected by the coupling strength.



SI Figure 3. Stronger coupling between the microdomain of IP_3Rs cluster and AZ exacerbate the stronger depression in AD-affected synapses. Facilitation obtained from peak rate (A) and P_r (B) shows that HC enhances the synaptic depression in AD-affected synapses. Peak release rate (C) and P_r (D) following each AP in the train under different coupling conditions. (E) Asynchronous and (H) peak synchronous release under different coupling conditions.
