Figure S1

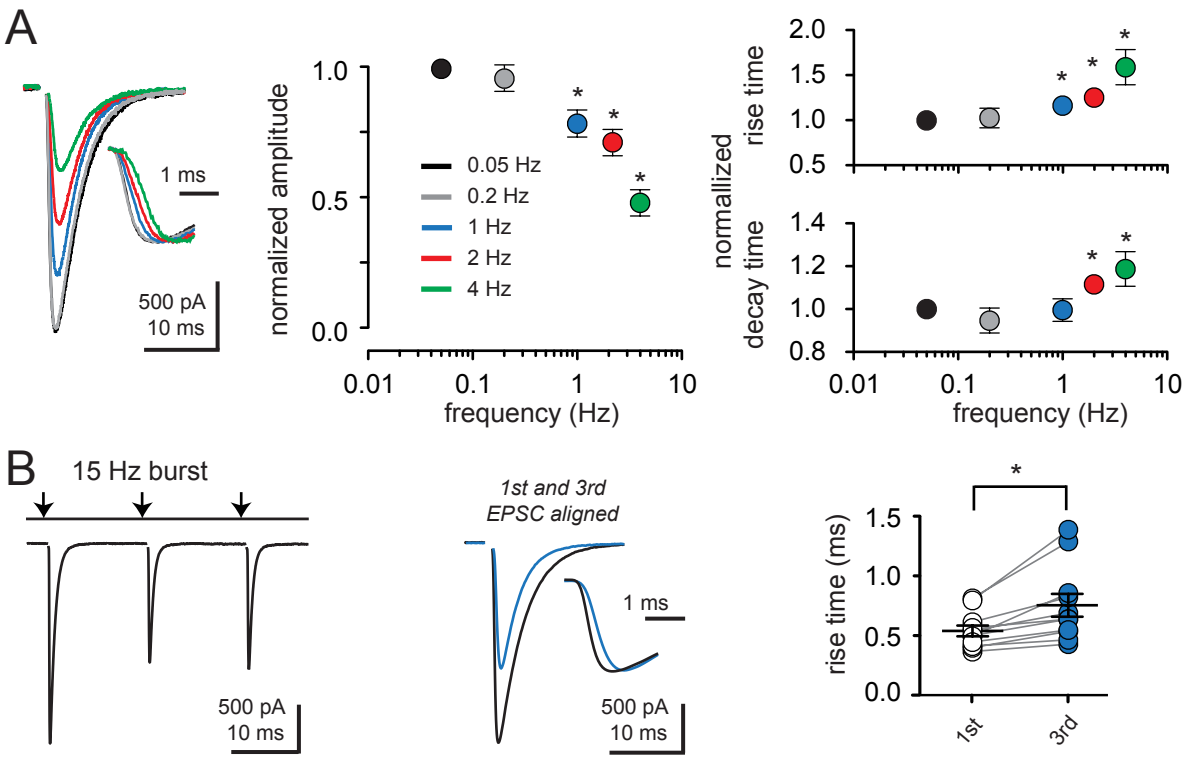

Figure S1

Figure S2

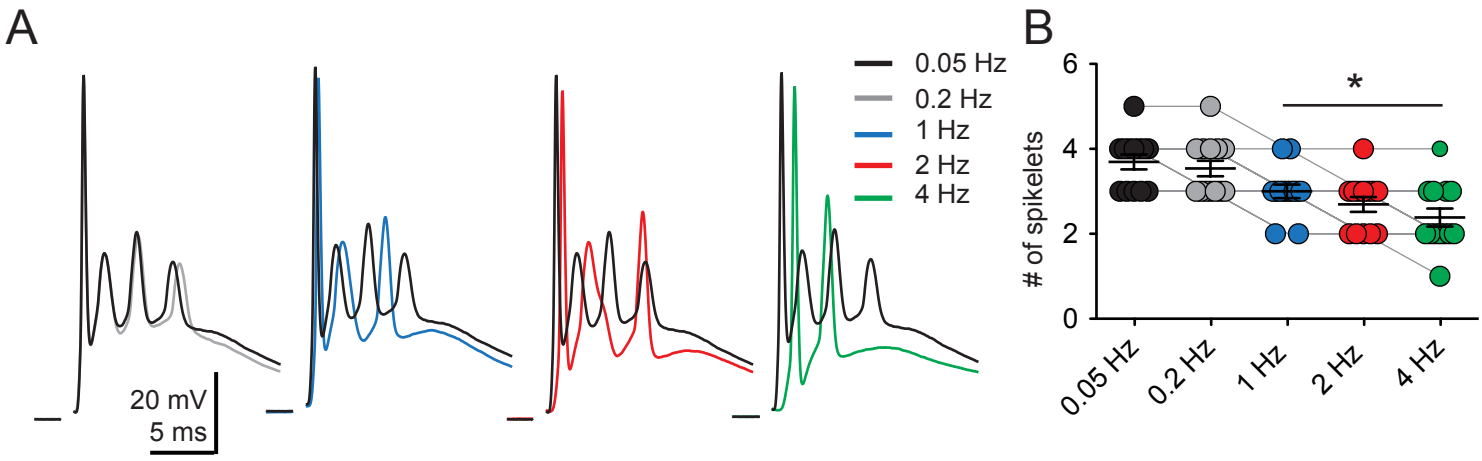

Figure S2

Figure S3

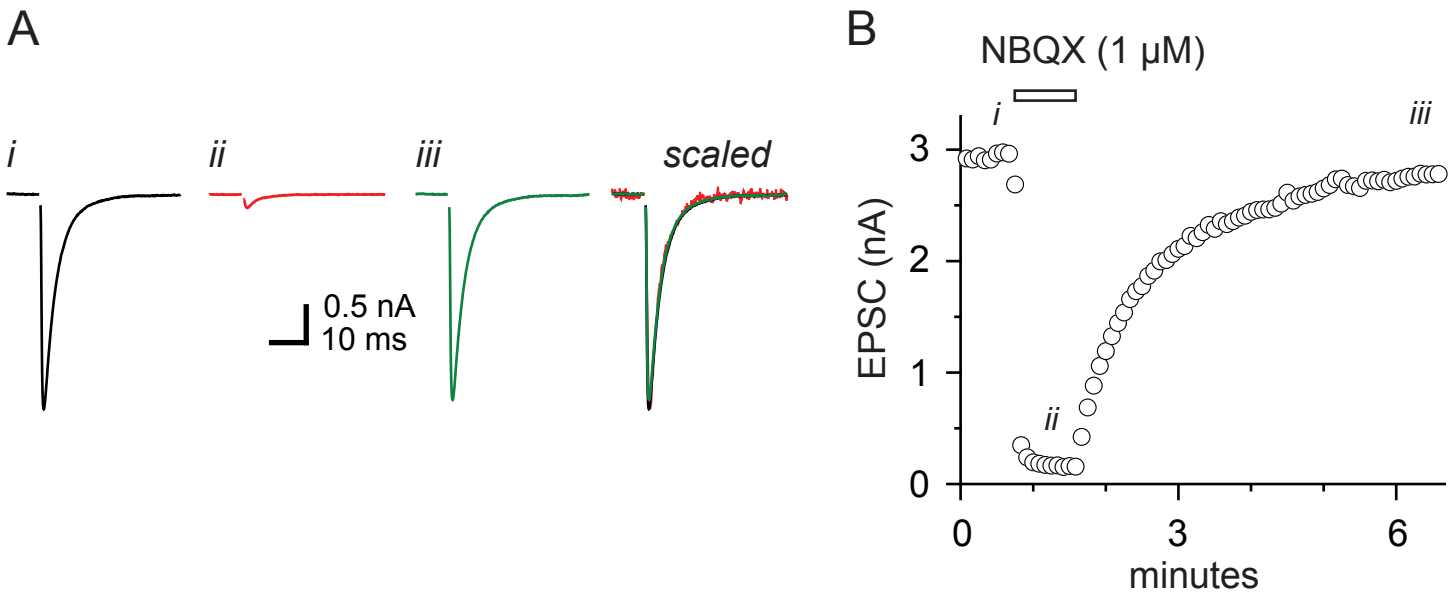

Figure S3

Figure S4

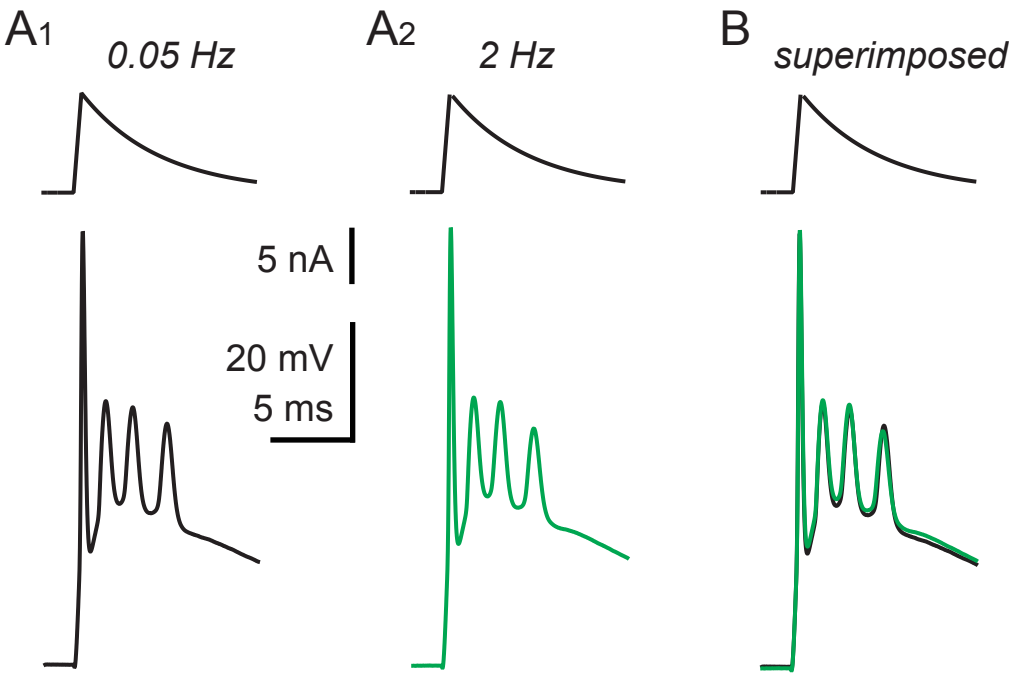

Figure S4

Figure S5

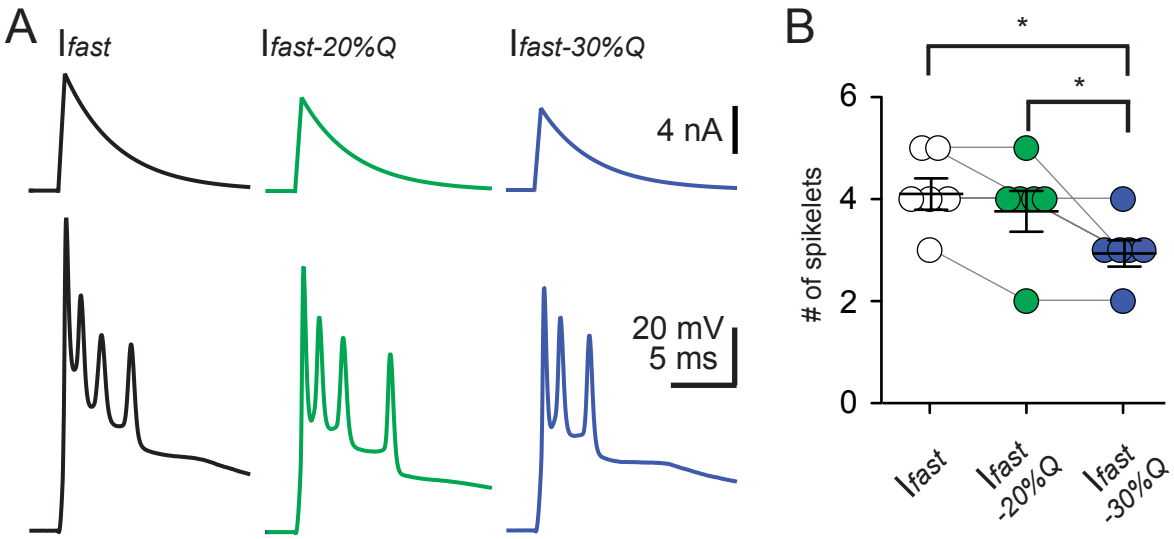

Figure S5

Supplementary Information

Desynchronization of multivesicular release enhances Purkinje cell output

Stephanie Rudolph, Linda Overstreet-Wadiche, and Jacques I. Wadiche

Figure S1 - The amplitude and kinetics of CF-PC EPSCs during repetitive and burst stimulation.

(A) Left: Superimposed CF-PC EPSCs during persistent 0.05 Hz (black), 0.2 Hz (grey), 1 Hz (blue), 2 Hz (red), and 4 Hz (green) stimulation in the same cell. Inset depicts peak-scaled EPSCs showing the slowing of the rise time. Summary of EPSC peak amplitude depression (middle) and kinetics (right) during repetitive stimulation across physiologically-relevant frequencies ($n = 4 - 9$; asterisks denote $p < 0.05$).
(B) EPSCs following a stimulus train of three pulses at 15 Hz (left). Superimposed 1^{st} and 3^{rd} EPSCs, with inset depicting peak-scaled EPSCs in an expanded time scale. Summary of the EPSC rise-time of the 1^{st} (0.41 ± 0.05 ms) and 3^{rd} EPSC (0.62 ± 0.09 ms) during a three pulse 15 Hz stimulus train ($n = 11$; $p < 0.01$).

Figure S2 - The CpS waveform during repetitive stimulation.

(A) Left: Superimposed CpSs following persistent stimulation at 0.05 Hz (black), 0.2 Hz (grey), 1 Hz (blue), 2 Hz (red), and 4 Hz (green). (B) Summary data shows the total number of spikelets during repetitive stimulation at various frequencies ($n = 13$; asterisks denote $p < 0.05$; ANOVA). Each data point represents individual experiments and black horizontal traces are the mean values ± SEM.

Figure S3 - Lack of NBQX effect on the CF-PC EPSC time course.

(A) Representative example of CF-PC EPSCs before (i), during (ii) and following (iii) NBQX (1 µM) application. (B) CF-PC EPSC peak amplitude time course.

Figure S4 - Kinetics of complex-like-spikes do not depend on the frequency of current injection.

Repetitive somatic current injections (top traces) of an EPSC-like waveform at 0.05 Hz (A1) and 2 Hz (A2) evokes complex-like-spikes (bottom traces). (B) Superimposed traces from A1 and A2 show that the frequency of current injection has no effect on the number or kinetics of complex-like-spikes.

Figure S5 - The amplitude of EPSC-like current injections can alter the number of CpS spikelets.

(A) Complex-like-spikes (bottom traces) evoked by somatic current injections (top traces) of an EPSC-like waveform (0.4 ms rise and 4 ms decay) scaled so that the quantity of charge is reduced by 20% (green; $I_{fast\ -20\%Q}$) or 30% (blue; $I_{fast-30\%Q}$) relative to control (black; I_{fast}). (B) Summary data shows a reduction in the total number of spikelets as a result of $I_{fast-30\%Q}$ (blue) current injection but not $I_{fast-20\%Q}$ (green) compared to I_{fast} (open circles; $p < 0.05$; ANOVA). Each data point represents individual experiments and black horizontal traces are the mean values ± SEM.

Supplemental Experimental Procedures for Figure 9.

AMPAR model is similar to the scheme used in Wadiche and Jahr (2001) with rates adjusted for inhibition by KYN. Rates were as follows (units are $M^{-1}s^{-1}$ for rates denoted by * or s^{-1}) k_{c0c1}* = 6 x 10^6, k_{c1c0} = 2.0 x 10^3, k_{c1c2}* = 3 x 10^6, k_{c2c1} = 4.7 x 10^3, β = 1.7 x 10^3, α = 4.7 x 10^3, k_{oc7} = 1.1 x 10^2 , k_{c7o} = 2.5 x 10^2, k_{c1c3} = 4.2 x 10^2, k_{c3c1} = 1 x 10^2, k_{c2c4} = 2 x 10^3, k_{c4c2} = 4.7 x 10^1, k_{oc5} = 3.1, k_{c5o} = 4.0, k_{c7c6} = 3.0, k_{c6c7} = 3.2 x 10^{-1}, k_{c3c4}* = 6 x 10^6, k_{c4c3} = 1 x 10^3, k_{c4c5} = 4.7 x 10^2, k_{c5c4} = 9.8 x 10^2, k_{c5c6} = 1.0 x 10^4, k_{c6c5} = 4 x 10^3, k_{c0cd}* = 1 x 10^6, k_{cdc0} = 1 x 10^3, k_{cdcdd}* = 5 x 10^6, k_{cddcd} = 5 x 10^3, k_{cdc1d}* = 1 x 10^4, k_{c1dcd} = 4.9 x 10^3, k_{c1c1d}* = 2.3 x 10^3, k_{c1dc1} = 1 x 10^6. Rates k_{c0c1}, k_{c1c2}, k_{c3c4}, and k_{cdc1d} are dependent on [glutamate], whereas k_{c0cd}, k_{cdcdd}, and k_{c1c1d} are dependent on [KYN].

Supplemental References

Wadiche, J.I., and Jahr, C.E. (2001). Multivesicular release at climbing fiber-Purkinje cell synapses. Neuron *32*, 301-313.