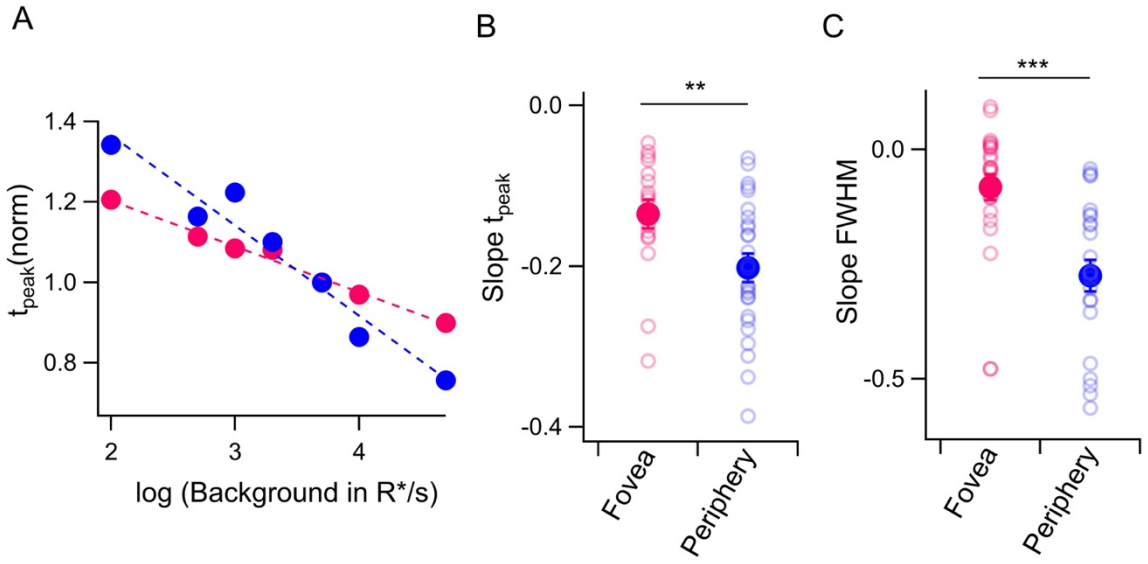
Supplementary Material:

Supplementary Figures:

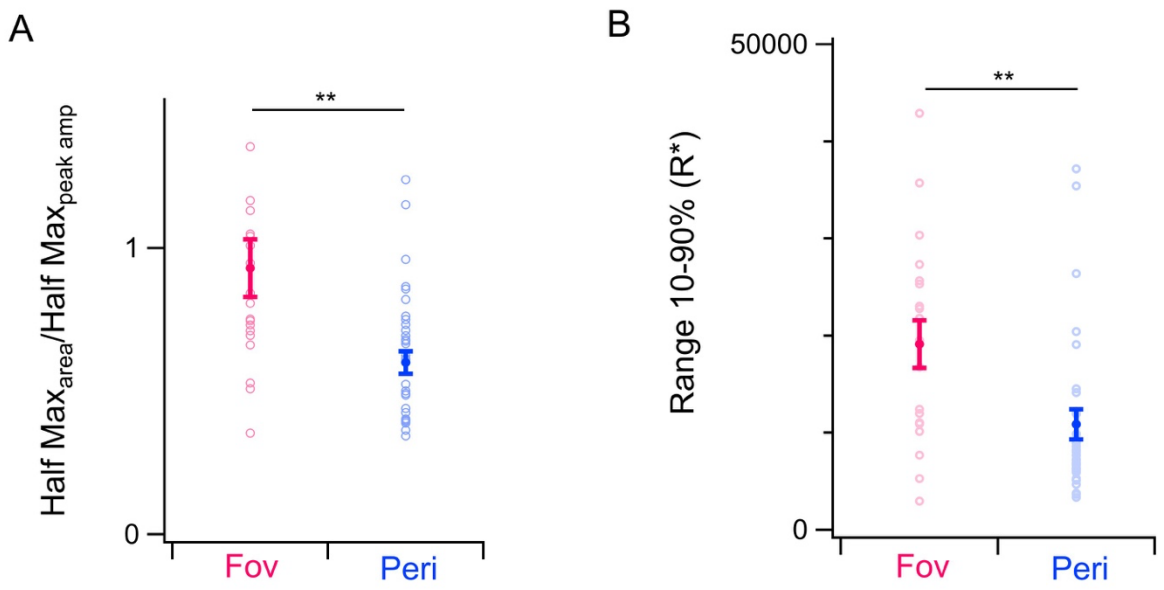


Supplementary Figure 1: Peripheral cones exhibit a stronger luminance dependent acceleration of response kinetics compared to foveal cones.

(A) Relative times to peak plotted across logarithms of their respective backgrounds in an example foveal and peripheral cone. In each cell, the time to peak at each background was normalized by the time to peak at 5000 R*/s in that cell. The relative time to peak was fit with a straight line (dotted line) and the slope was calculated. Slope of the line fit for example foveal cone was -0.1137 and peripheral cone was -0.2248.

(B) Mean ± sem of slopes for straight line fits to relative time to peak (Fig 1D) for foveal cones was -0.1351 ± 0.018 (n=17) and for peripheral cones was -0.202 ± 0.018 (n=27).

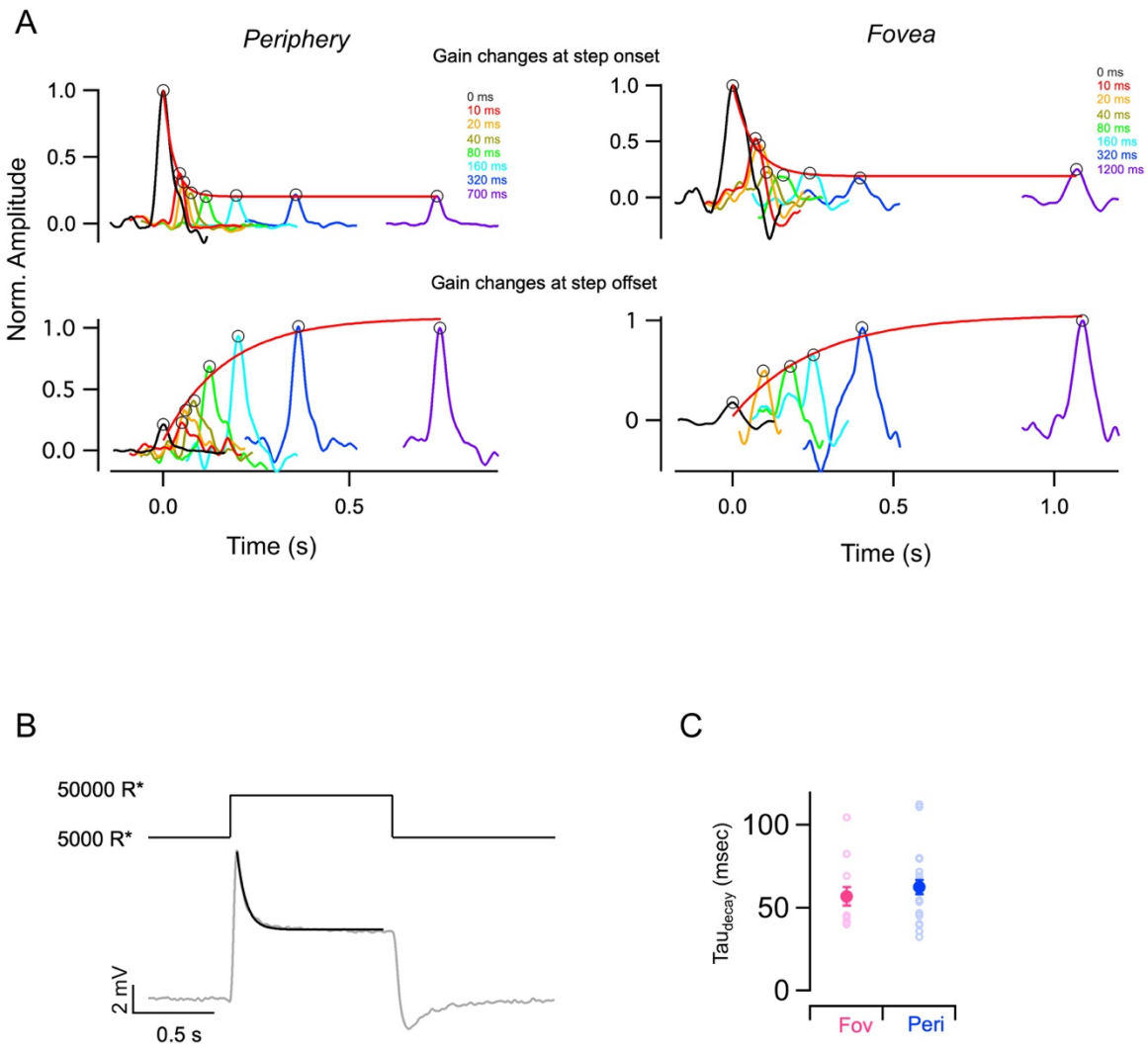
(C) Mean ± sem of slopes for straight line fits to relative FWHM (Fig 1F) for foveal cones was -0.082 ± 0.028 (n=25) and for peripheral cones was -0.275 ± 0.03 (n=27). We used unpaired two tailed t-test for comparison. The significance threshold was placed at α = 0.05 (n.s., $p > 0.05$; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).



Supplementary Fig 2: Peripheral cones exhibit stronger light adaptation than foveal cones.

(A) Ratio of half-maximum backgrounds from Weber fits to integrated response gain (Fig 2H) to amplitude gain (Fig 2D) in foveal and peripheral cones. The ratios were 0.93 ± 0.1 (n=19) for foveal cones and 0.64 ± 0.04 (n=30) for peripheral cones.

(B) Dynamic range defined as the background luminance between 10 - 90% decay of the Weber curve estimated from the fits in foveal and peripheral cones (19 foveal cones, 31 peripheral cones). Dynamic range values are 19142.95 ± 2447.26 R* for foveal cones and 10880.03 ± 1533.19 R* for peripheral cones and significantly different. We used unpaired two tailed t-test for comparison. We used unpaired two tailed t-test for comparison. The significance threshold was placed at α = 0.05 (n.s., $p > 0.05$; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).



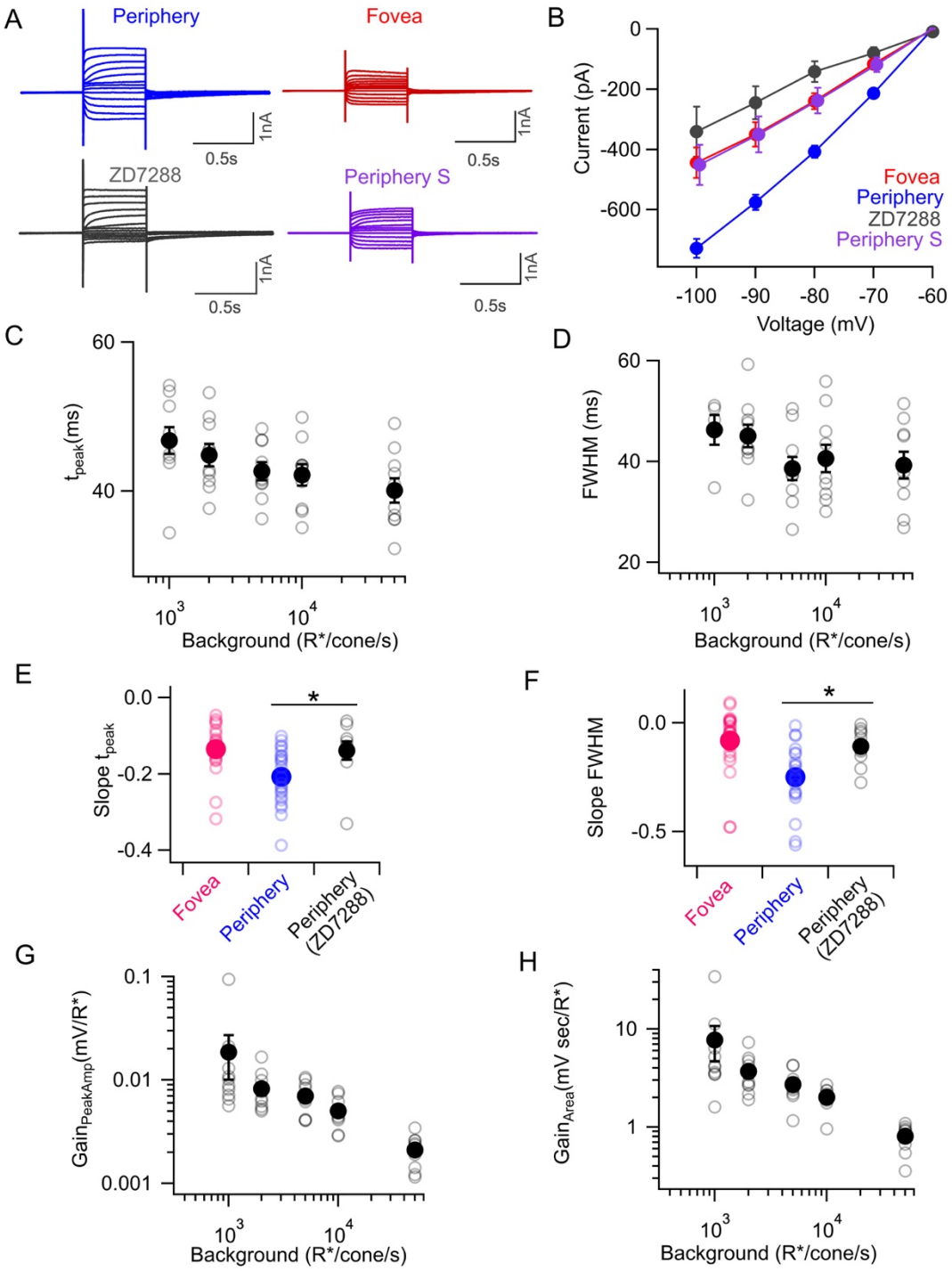
Supplementary Figure 3: Foveal cones have a slower timescale of adaptation compared to peripheral cones.

(A) Top panel shows rapid gain changes of the peripheral cone (left) and foveal cone (right) at light onset (step from 1000R*/s to 10000R*/s). Response gain for each of the flashes were obtained by dividing the response by the flash strength and normalizing to the gain in darkness; black traces correspond to gain in darkness (far left black trace) and to steady-state adapted gain (far right purple trace). Colored traces in between correspond to flashes with a variable delay from the step onset. The kinetics of the gain changes was tracked by identifying the peaks and fitting their time course with a single exponential function. The time constant of the best fit exponential was t_{On} = 27.15 ms for peripheral cone and 62.18 ms for foveal cone. Bottom panel shows the time course of gain changes at light offset for peripheral (left) and foveal (right) cone (step from 10000R*/s to 1000R*/s). Black trace corresponds to steady-state adapted gain (far left trace) and gain in darkness (far right purple trace). Colored traces correspond to flashes with a variable delay from the step offset (same delays as in top panel). The time constant of the best fit exponential for

this exemplar cone was t_{Off} = 168.84 ms for peripheral cone and 260.06 ms for foveal cone (red smooth line).

(B) Exemplar peripheral cone response to a light step as shown in Fig 3. Smooth black line is a fit to a mono exponential function (tau = 51.8 msec)

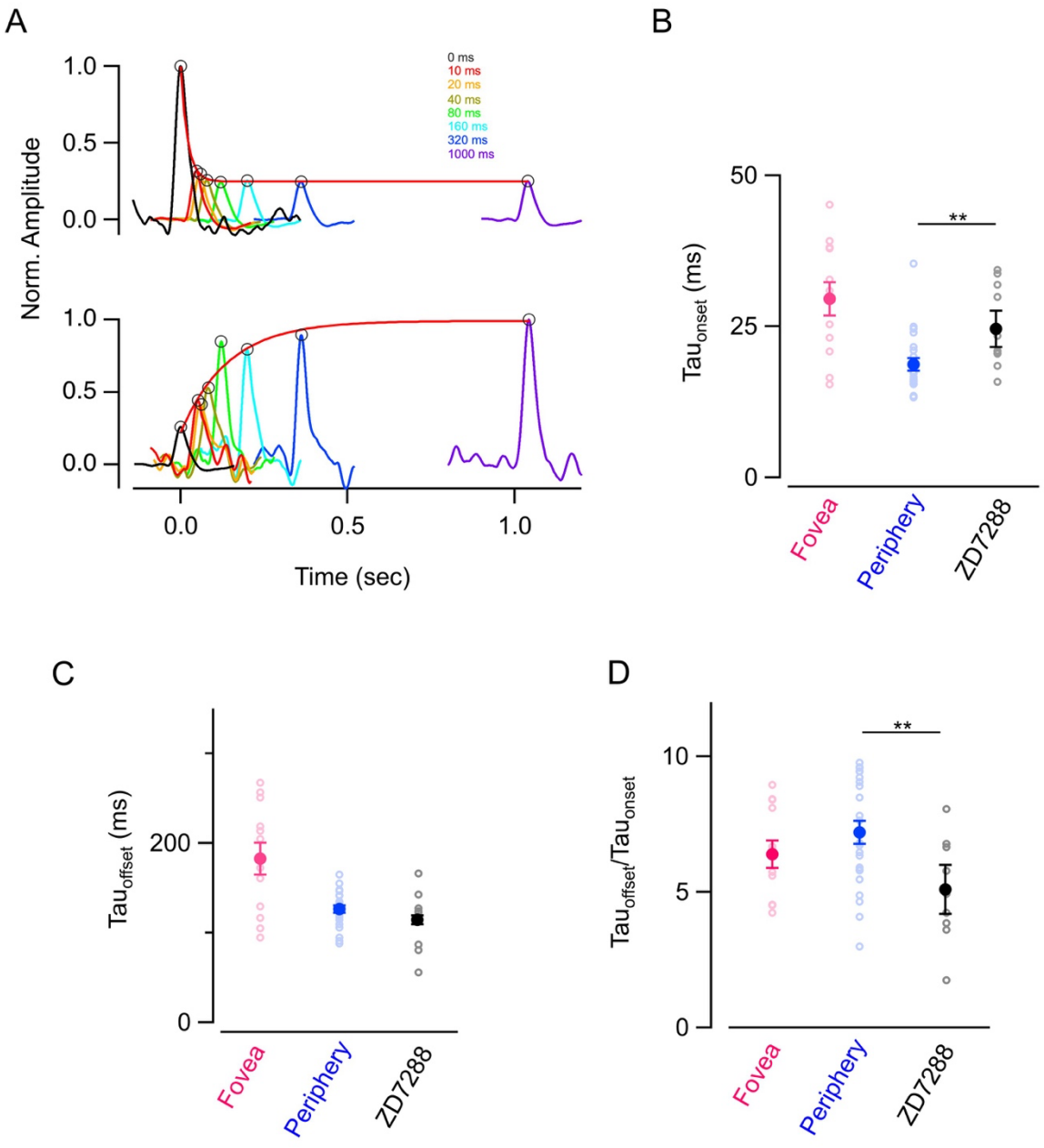
(C) Similar decay constants of foveal (56.9 ± 5.7 msec) and peripheral (62.4 ± 4.2 msec) cone steady-state response.



Supplementary Figure 4: Role of HCN channels in cone function across region and type

(A) Exemplar current responses for peripheral M/L cones before and after bath application of an HCN channel blocker, ZD7288; foveal M/L cones and peripheral S cones.

(B) Current voltage relationship for foveal (n=9), peripheral (n=18), peripheral S (n=4) and peripheral (in presence of ZD7288) (n=8) cones at different hyperpolarizing potentials.
(C) Times to peak of cone flash responses in peripheral cones in presence of ZD7288 across background light levels (n=10).
(D) Full width at half max of cone flash responses in peripheral cones in presence of ZD7288 across background light levels (n=5 at 1000R*/s background and n=10 for all other backgrounds).
(E) Slope of log-normal straight line fit of normalized time to peak in peripheral cones in presence of ZD7288 was -0.14 ± 0.02 (n=10) compared to that in foveal and peripheral cones (foveal and peripheral cone data in this and next panel replotted from Supplementary Figure 1).
(F) Slope of log-normal straight line fit of normalized FWHM in peripheral cones in presence of ZD7288 was -0.11 ± 0.03 (n=10) compared to that in foveal and peripheral cones.
(G) Adaptation of peak response amplitude in peripheral cones in presence of ZD7288 (n=10).
(H) Adaptation of integrated response (area under the curve) in peripheral cones in presence of ZD7288 (n=10). For panels E and F, we performed one-way ANOVA. The significance threshold was placed at $\alpha = 0.05$ (n.s., $p > 0.05$; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).



Supplementary Figure 5: Peripheral cones exhibit slower dynamics of adaptation in presence of HCN channel blocker, ZD7288.

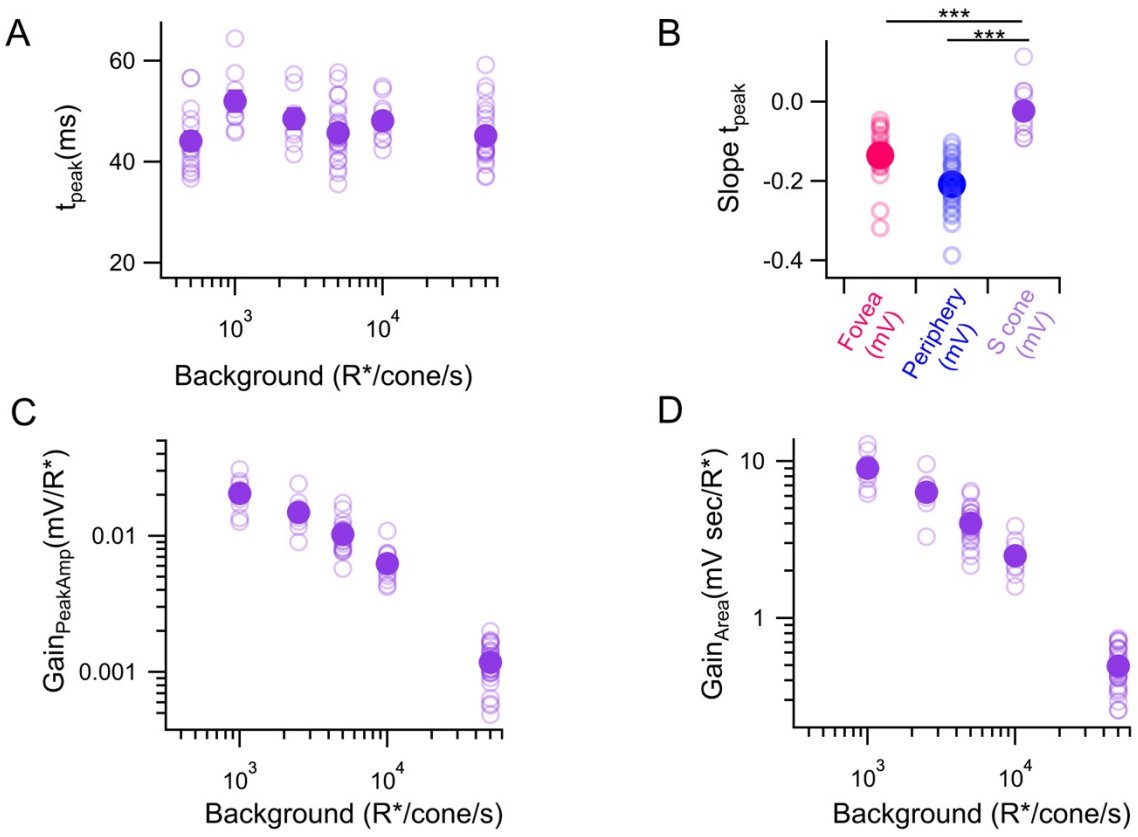
(A) Top panel shows rapid gain changes of the peripheral cone in presence of HCN channel blocker ZD7288 at light onset (step from 5000R*/s to 50000R*/s). Response gain for each of the flashes were obtained by dividing the response by the flash strength and normalizing to the gain in darkness; black traces correspond to gain in darkness (far left black trace) and to steady-state adapted gain (far right purple trace). Colored traces in between correspond to flashes with a variable delay from the step onset. The kinetics of the gain changes was tracked by identifying the peaks and fitting their time course with a single exponential function. The time constant of the best fit exponential was t_{On} = 21.01 ms.

Bottom panel shows the time course of gain changes at light offset. Black trace corresponds to steady-state adapted gain (far left trace) and gain in darkness (far right purple trace). Colored traces correspond to flashes with a variable delay from the step offset (same delays as in top panel). The time constant of the best fit exponential for this exemplar cone was t_{Off} = 142.42 ms (red smooth line).

(B) Time course of gain changes at step onset of peripheral cones with HCN channel blocker ZD7288 (n=11) for light steps (5,000 -> 50,000 R*/s) compared to that in foveal and peripheral cones.

(C) The time constants at step offset for peripheral cones in presence of ZD7288 (n=10) compared to that in foveal and peripheral cones.

(D) The ratio of tau_{onset} over tau_{offset} for the 5,000 -> 50,000 R*/s light steps for peripheral cones in presence of ZD7288 (n=10) compared to that in foveal and peripheral cones. Foveal and peripheral cone data in this figure is replotted from Figure 3). For panels C and D, we performed one-way ANOVA. The significance threshold was placed at α = 0.05 (n.s., $p > 0.05$; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).



Supplementary Figure 6: Luminance dependent changes in kinetics and response gain of peripheral S cones.

(A) Times to peak of S-cone flash responses in the peripheral retina across background light levels. At 500 R*/s, mean ± sem time to peak was 44.1 ± 1.8 ms (n=14). At 1000 R*/s, it was 52.0 ± 2.0 ms (n=9). At 2,500 R*/s, it was 48.5 ± 2.0 ms (n=8). At 5,000 R*/s, it was 45.7 ± 1.1 ms (n=25). At 10,000 R*/s, it was 48.2 ± 1.3 ms (n=10). At 50,000 R*/s, it was 45.2 ± 1.1 ms (n=25).

(B) Mean ± sem of slope of log-normal straight line fit of normalized time to peak in peripheral S cones is -0.023 ± 0.021 ms (n=10) compared to foveal and peripheral M/L cones replotted from Supplementary figure 1B.

(C) Peak response amplitude in peripheral S cones plotted versus background luminance. At 1000 R*/s, mean ± sem peak response gains were 0.02 ± 0.002 mV/R* (n=9). At 2500 R*/s, it was 0.015 ± 0.002 mV/R* (n=8). At 5000 R*/s, it was 0.01 ± 0.0005 mV/R* (n=25). At 10000 R*/s, it was 0.006 ± 0.0006 mV/R* (n=10). At 50,000 R*/s, it was 0.001 ± 0.0001 mV/R* (n=25).

(D) Response integral (area under the curve) of peripheral S cones plotted across background luminance. At 1000 R*/s, mean ± sem peak response gains were 9.05 ± 0.74 mV-s/R* (n=9). At 2500 R*/s, it was 6.33 ± 0.63 mV-s/R* (n=8). At 5000 R*/s, it was 4.03 ± 0.21 mV/R* (n=25). At 10000 R*/s, it was 2.49 ± 0.21 mV/R* (n=10). At 50,000 R*/s, it was 0.49

± 0.03 mV/R* (n=25). For panel B, we performed one-way ANOVA. The significance threshold was placed at $\alpha = 0.05$ (n.s., $p > 0.05$; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).