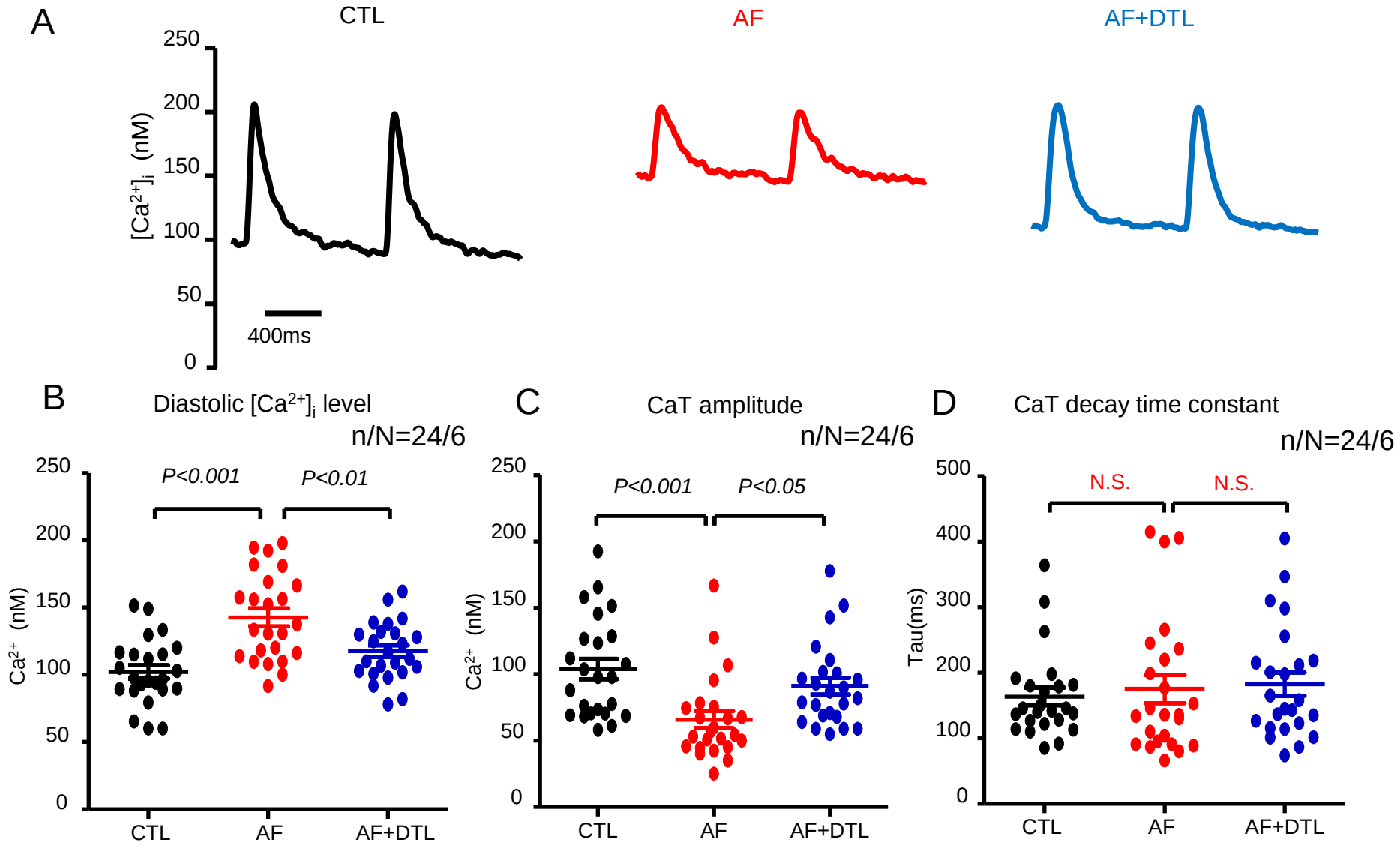
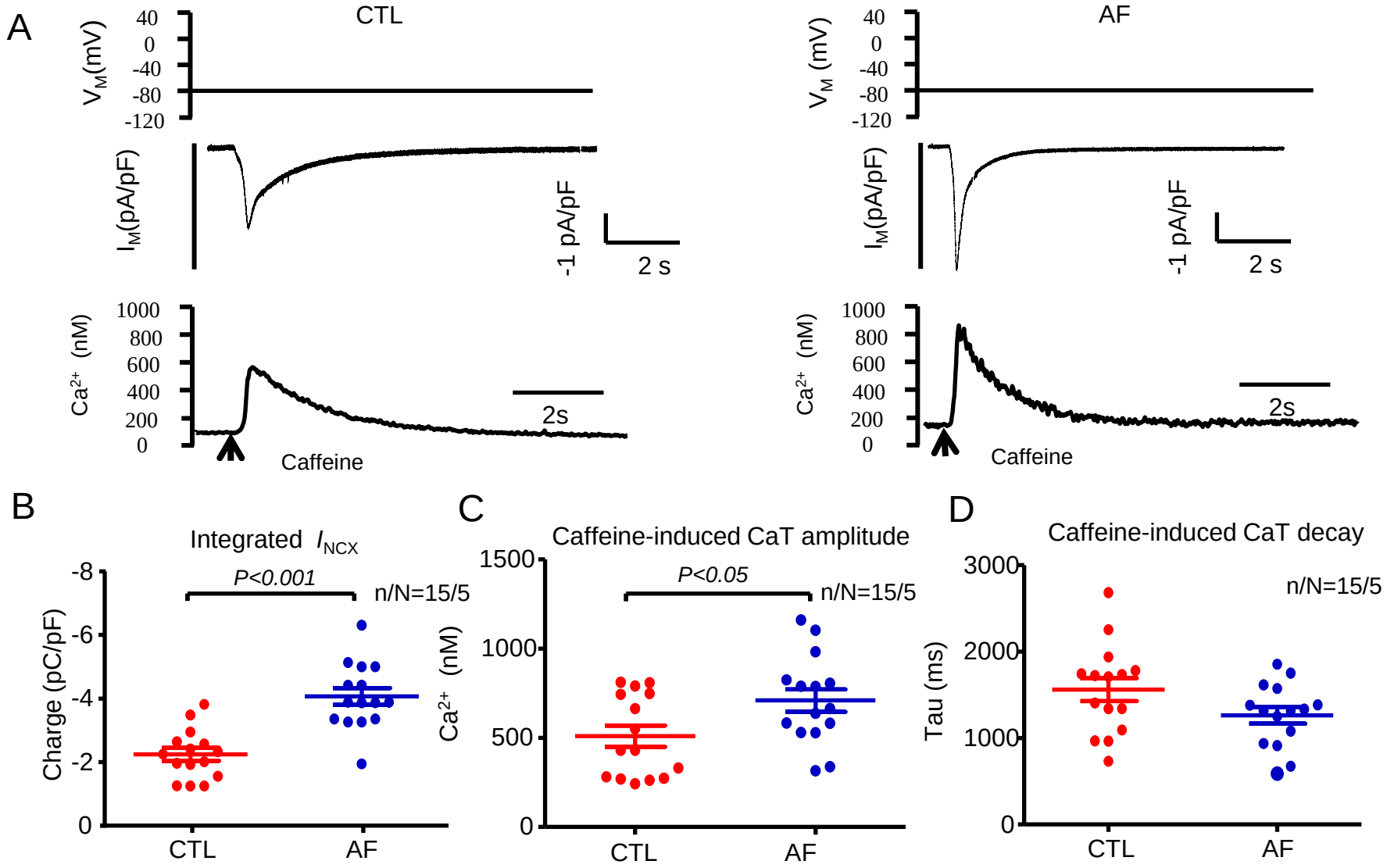
Suppl. Fig. 1



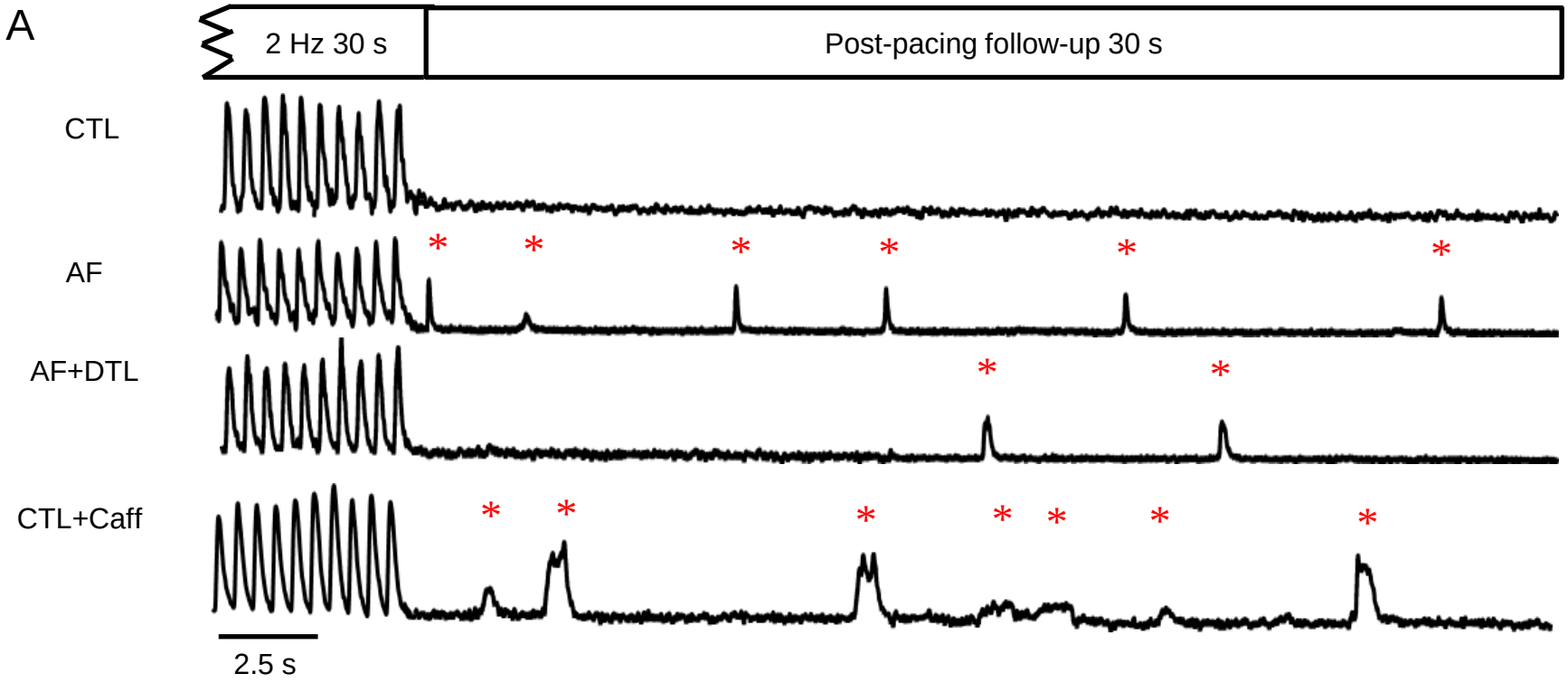
Supplemental Fig. 1. A) Original recordings of Ca2+ transients (CaTs) from single CTL, AF and AF plus DTL treatment cardiomyocytes. Diastolic [Ca2+]i level (B), CaT amplitude (C), and CaT decay time constant (D) in left atrial cardiomyocytes from CTL and AF dogs. Each point represents the result from a single cell. Horizontal lies show mean±SEM. n/N=24/6=cells/dogs per group.(ANOVA followed by Bonferroni post-hoc test)

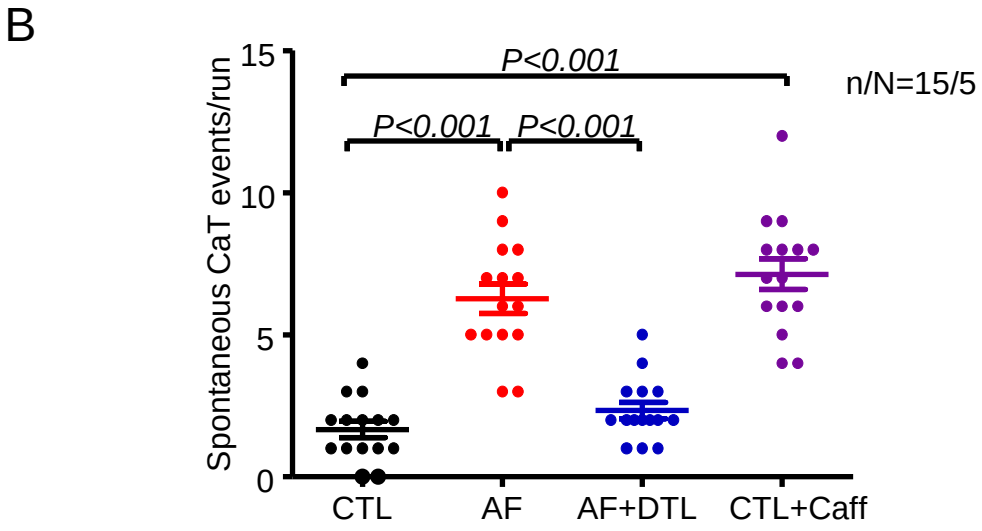
Suppl. Fig. 2



Supplemental Fig. 2. A) Representative recordings of membrane currents (Im) (top) and [Ca2+]i (bottom) respond to caffeine (10 mmol/l) in left atrial cardiomyocyte from CTL (left) and AF dogs (right). B) Integrated membrane current carried by the Na+/Ca2+ exchanger (NCX) in response to caffeine. C) Caffeine-induced CaT amplitude, which is used to estimate total sarcoplasmic reticulum Ca2+ content. D) Decay time constant of CaT induced by caffeine. Each point represents the result from a single cell. Horizontal lies show mean±SEM. n/N=15/5=cells/dogs per group.(t-test)

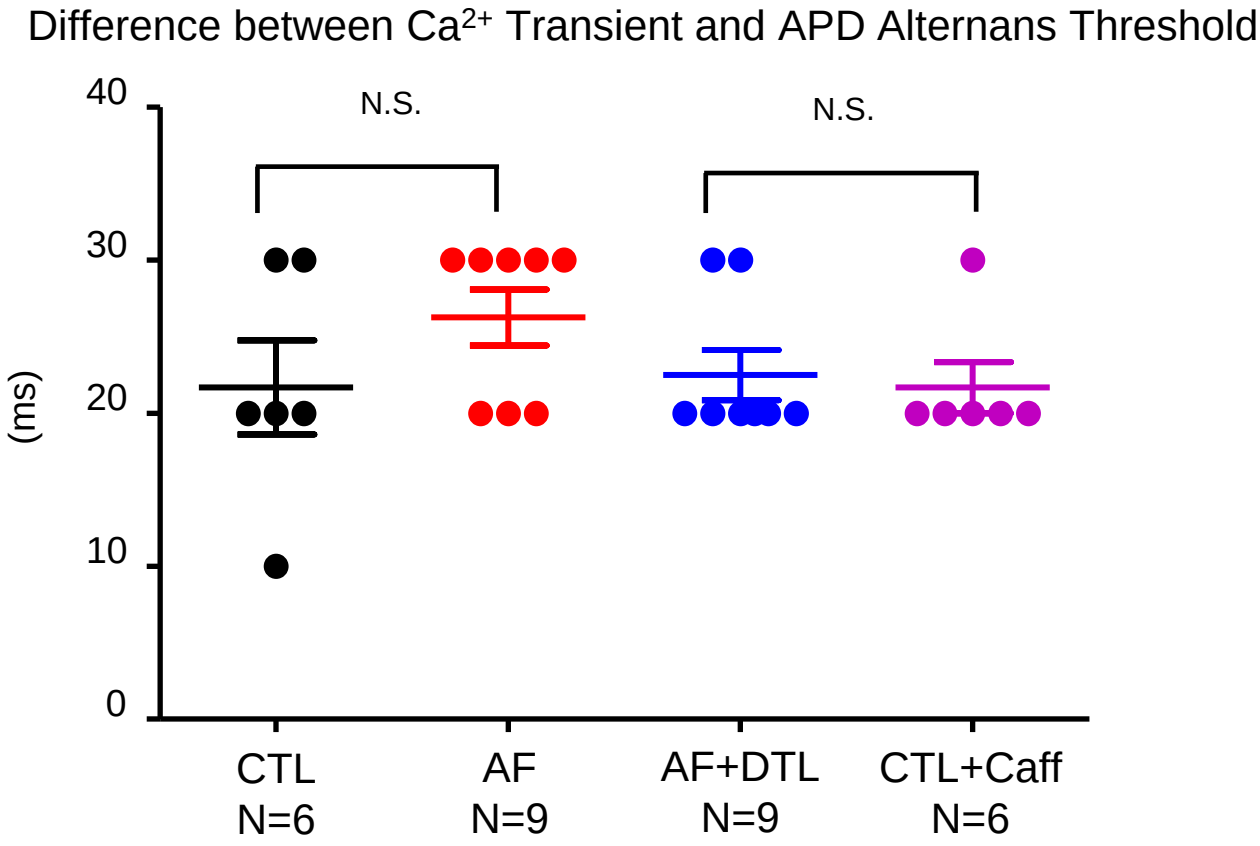
Suppl. Fig. 3





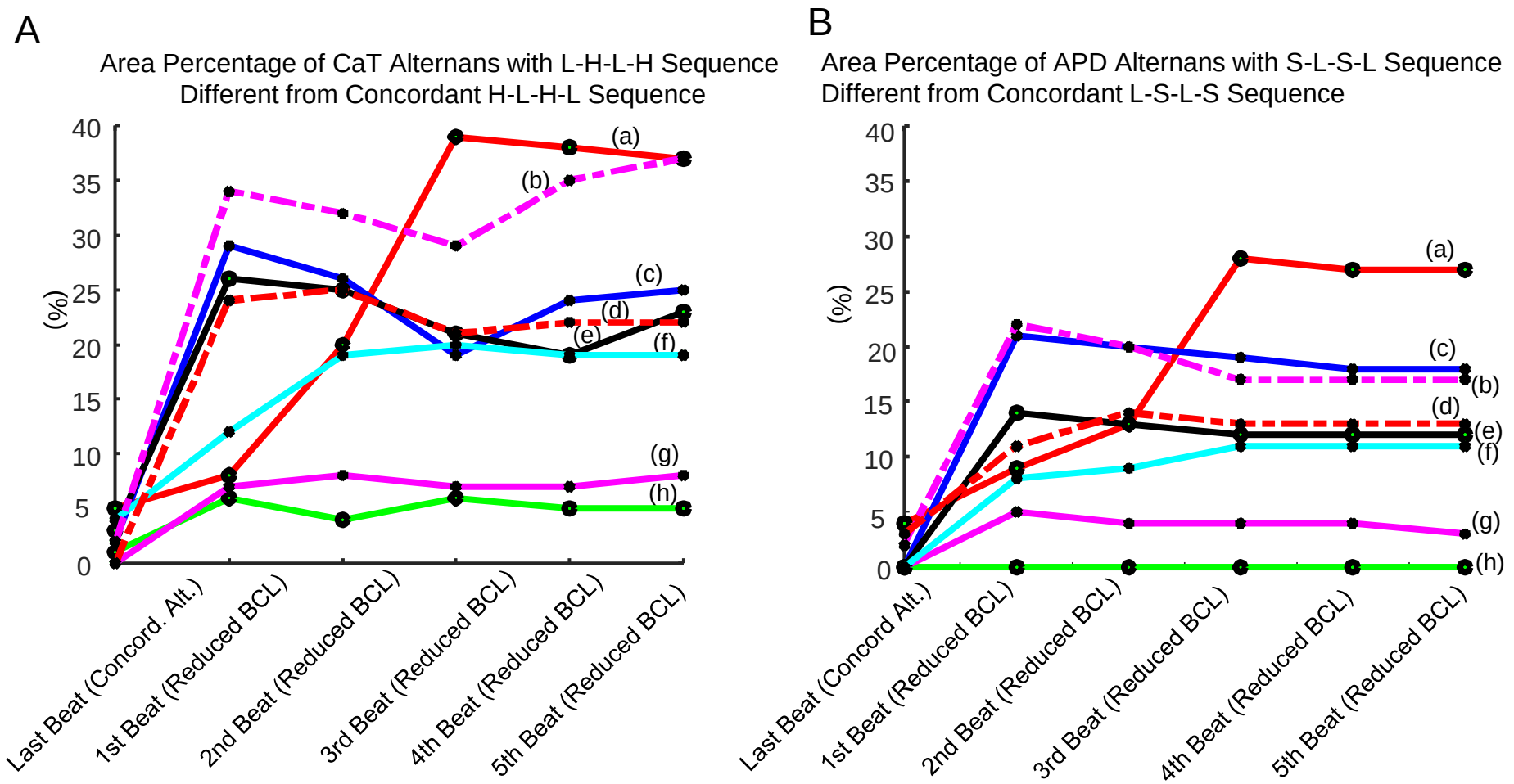
Supplemental Fig. 3. A) Spontaneous Ca2+ events after Ca2+ loading by 30 seconds of 2-Hz pacing. B) Post-pacing spontaneous Ca2+ transient events under each condition. Each point represents the result from a single cell. Horizontal lies show mean±SEM. n/N=15/5=cells/dogs per group.(ANOVA followed by Bonferroni post-hoc test)

Suppl. Fig. 4



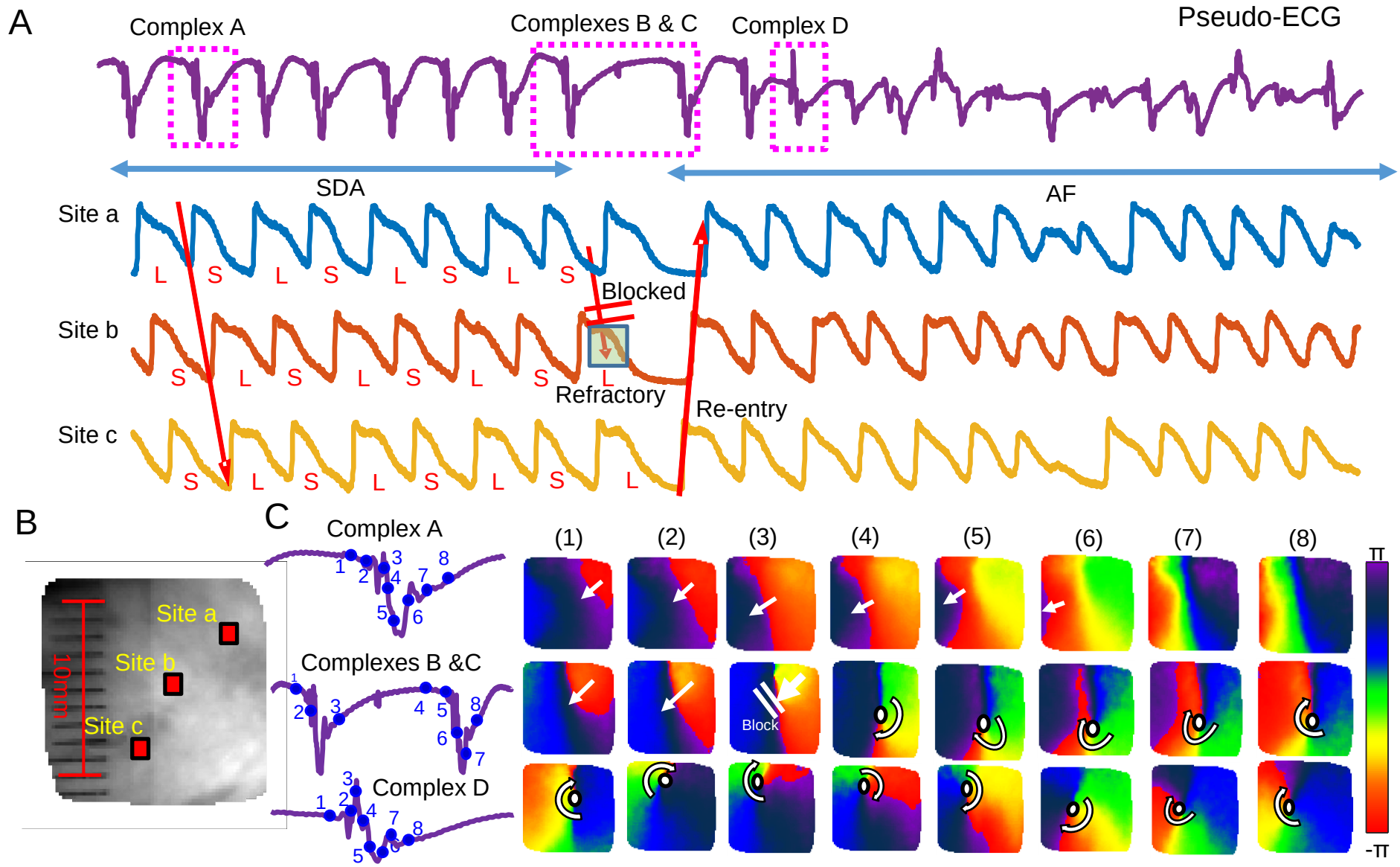
Supplemental Figure 4: Difference between Ca^{2+} transient and APD alternans threshold in each experiment. The CaT and APD alternans threshold difference in optically mapped preparations. In all preparations the threshold was reached at longer cycle lengths for Ca^{2+} than for APD.

Suppl. Fig. 5



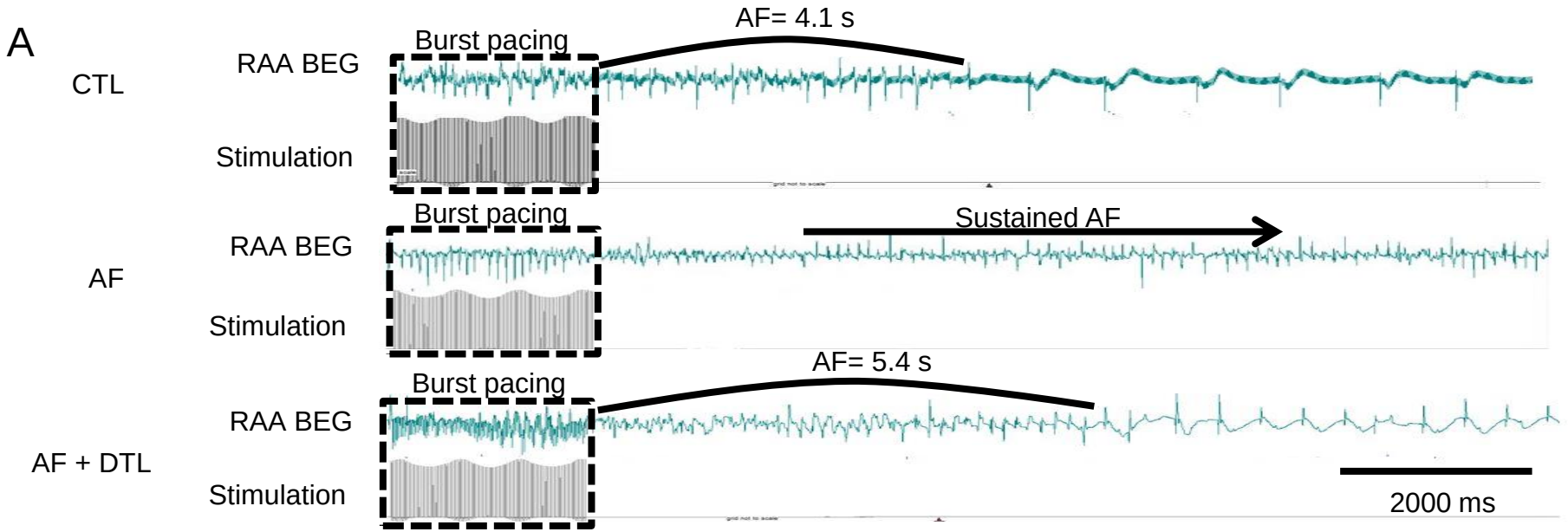
Supplemental Figure 5. The area change of CaT alternans (L-H-L-H sequence) (A) and APD alternans (S-L-S-L) (B) at the transition from concordant alternans to discordant alternans. The beats include the last beat of concordant alternans and the first five consecutive beats of discordant alternans. The line label (a) to (e) in A) is corresponding to the same AF atrium tissue in B) labeled from (a) to (e). The area percentage of L-H-L-H of CaT alternans and S-L-S-L of APD alternans are calculated by the number of pixels showing the alternans sequence different from the concordant alternans as H-L-H-L of CaT and L-S-L-S of APD, divided by the total pixels in the field of view. Two matrices correlation CaT and APD is highly correlated (correlation=0.94).

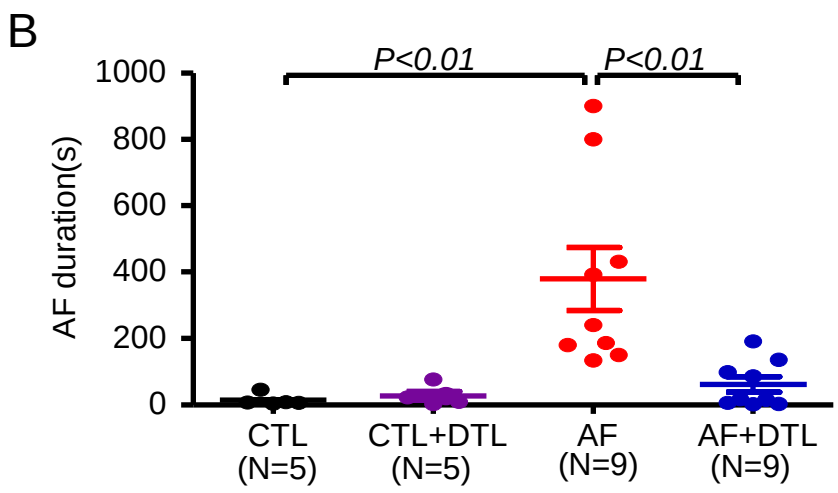
Suppl. Fig. 6

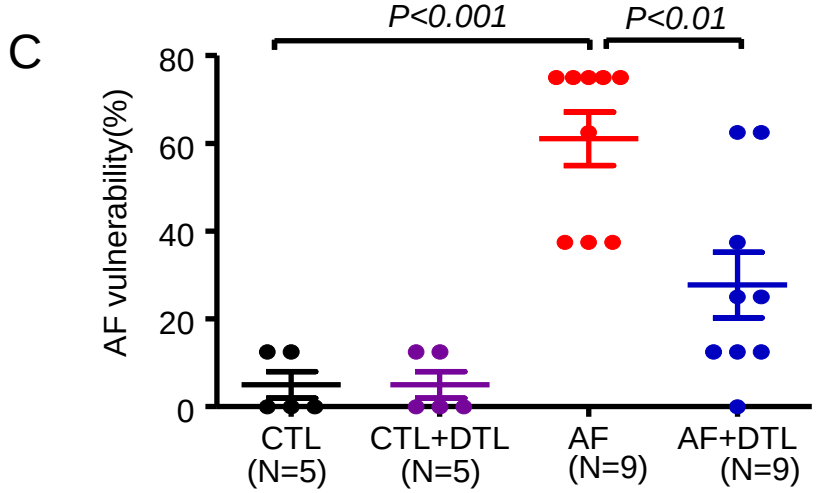


Supplemental Fig. 6. Induction of reentry in an AF atrium with discordant APD alternans. A) Pseudo-ECG and action potential at different sites in tissue, with conduction block initiating reentry indicated by red arrows. B) The three sites in an AF atrium, where AP showed in A. C) The three segments of pseudo-ECG of Complexes A, conduction block and reentry of complexes B, C, and D, and 8 snapshots of phase-maps, corresponding to the time-points indicated in blue color in the amplified Pseudo-ECG episodes . The positions of phase singularities (PSs) are indicated by white circle surrounded by black line.

Suppl. Fig. 7

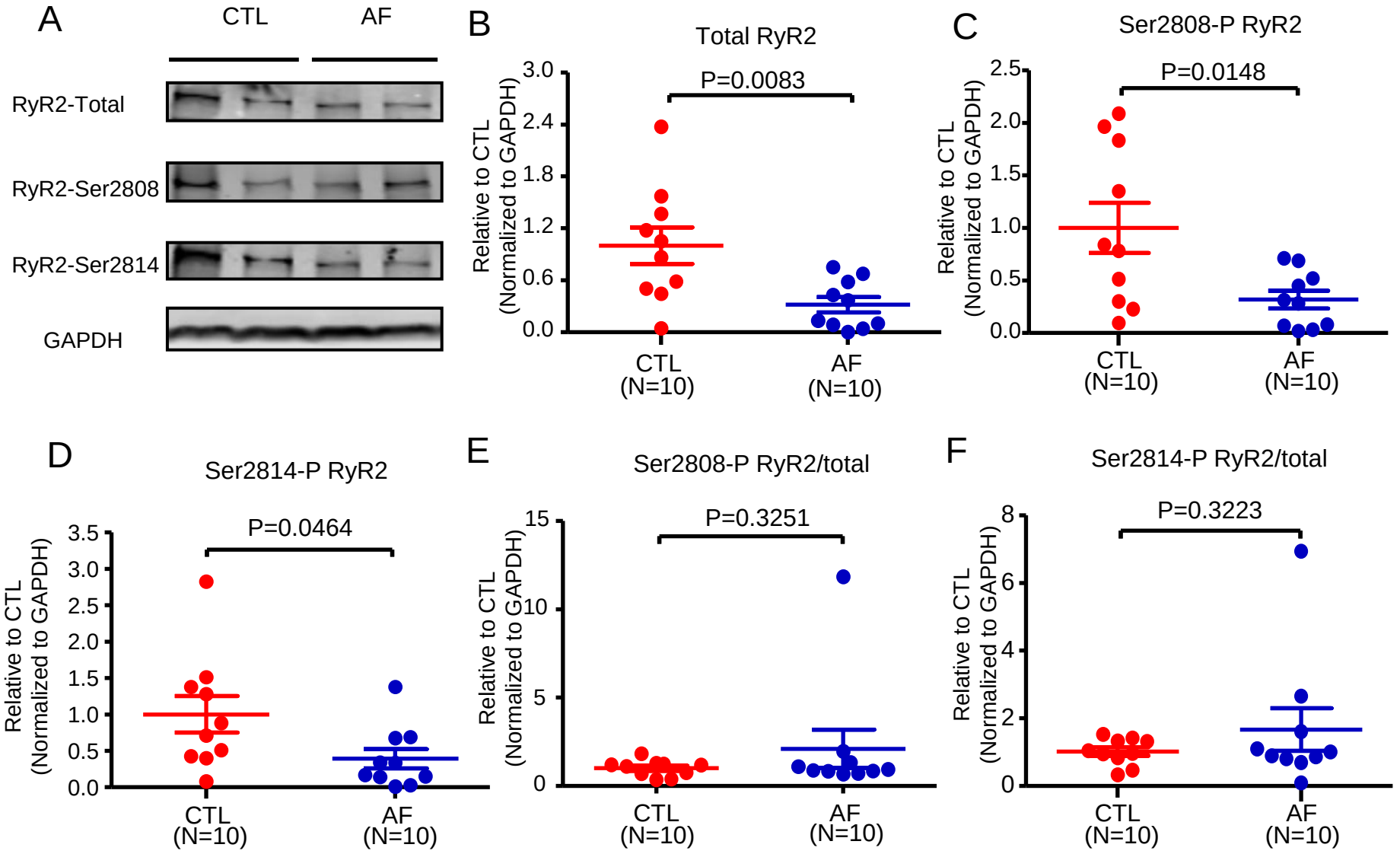






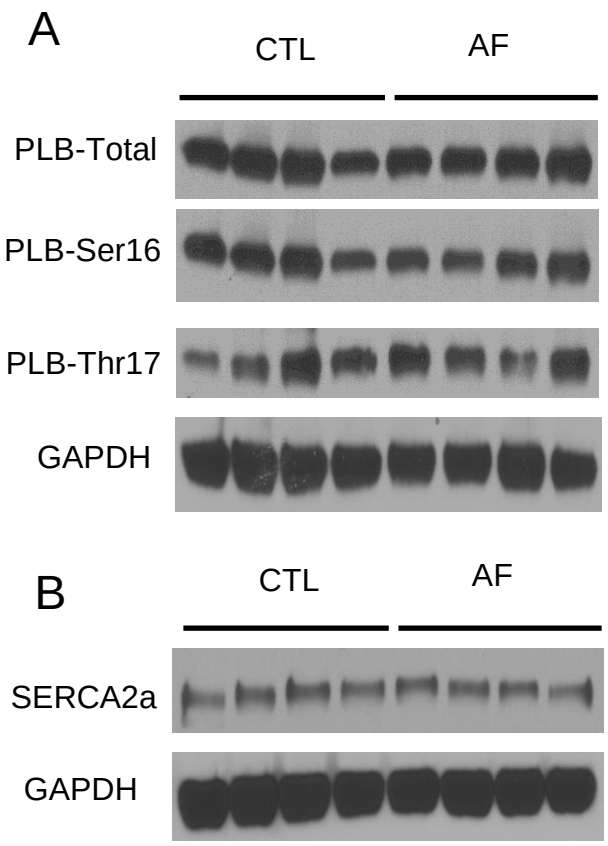
Supplmental Fig. 7. Atrial fibrillation duration and vulnerability in vivo. A) Bipolar epicardial electrogram (BEG) recordings of burst-pacing induced atrial fibrillation (AF), with results from right atrial appendage (RAA) of one CTL dog and an AF dog before and after dantrolene administration. B) Mean±SEM duration of induced AF. (ANOVA test) C) AF vulnerability percent of sites with premature stimuli inducing AF. N=number of dogs per group. (Mean±SEM, ANOVA test)

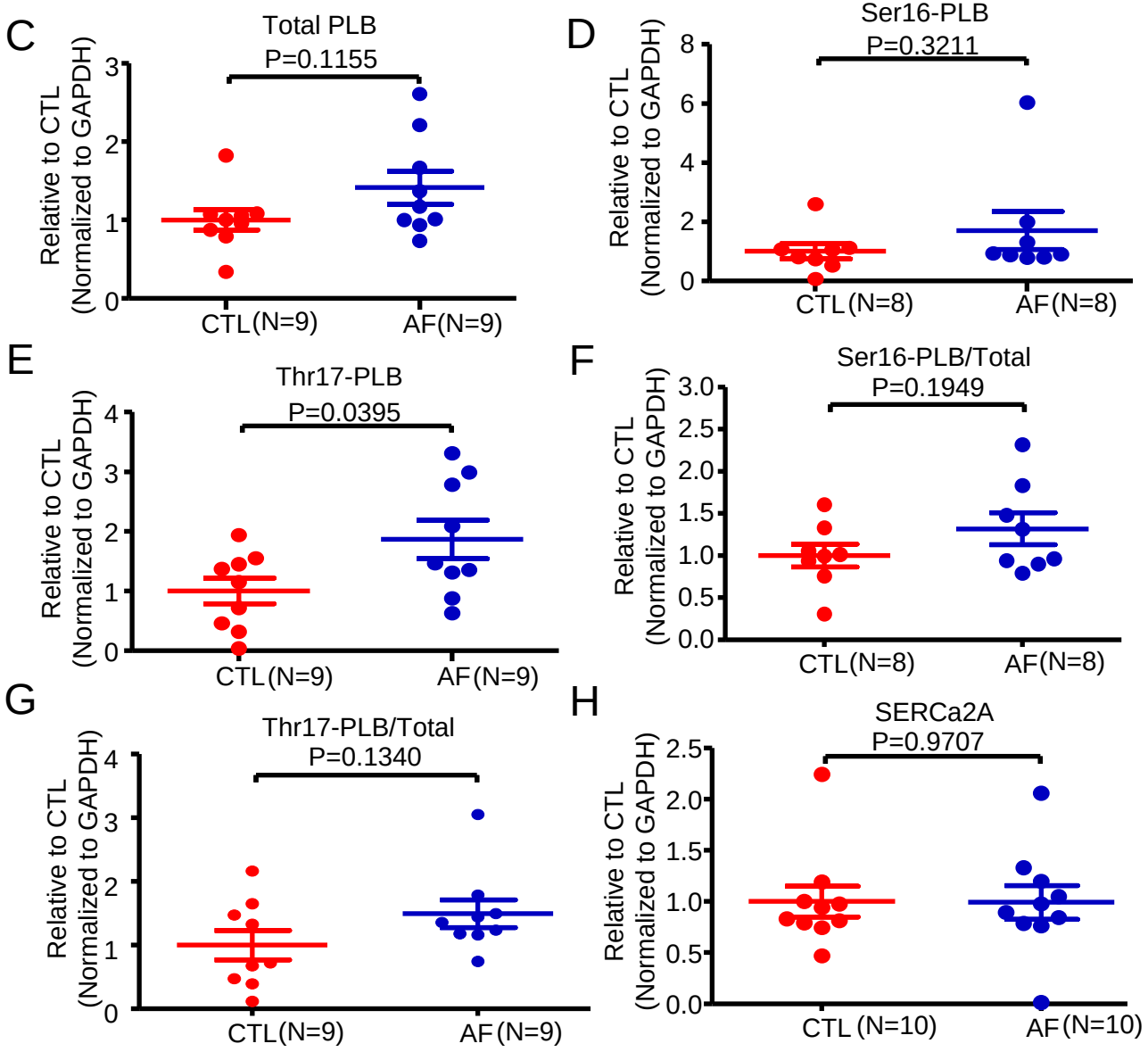
Suppl. Fig. 8



Supplemental Figure 8. Representative immunoblots for RyR2 and p-RyR2 (A), Expression of total RyR2 (B), p2808-RyR2 (C), p2814-RyR2 (D), p2808-RyR2/total RyR2 (E), p2814-RyR2/total RyR2 (F) in left atrial cardiomyocytes freshly isolated from CTL and AF dogs. Each point represents the result from one dog. Horizontal lies show mean ± SEM. (N=dogs per group; t-test)

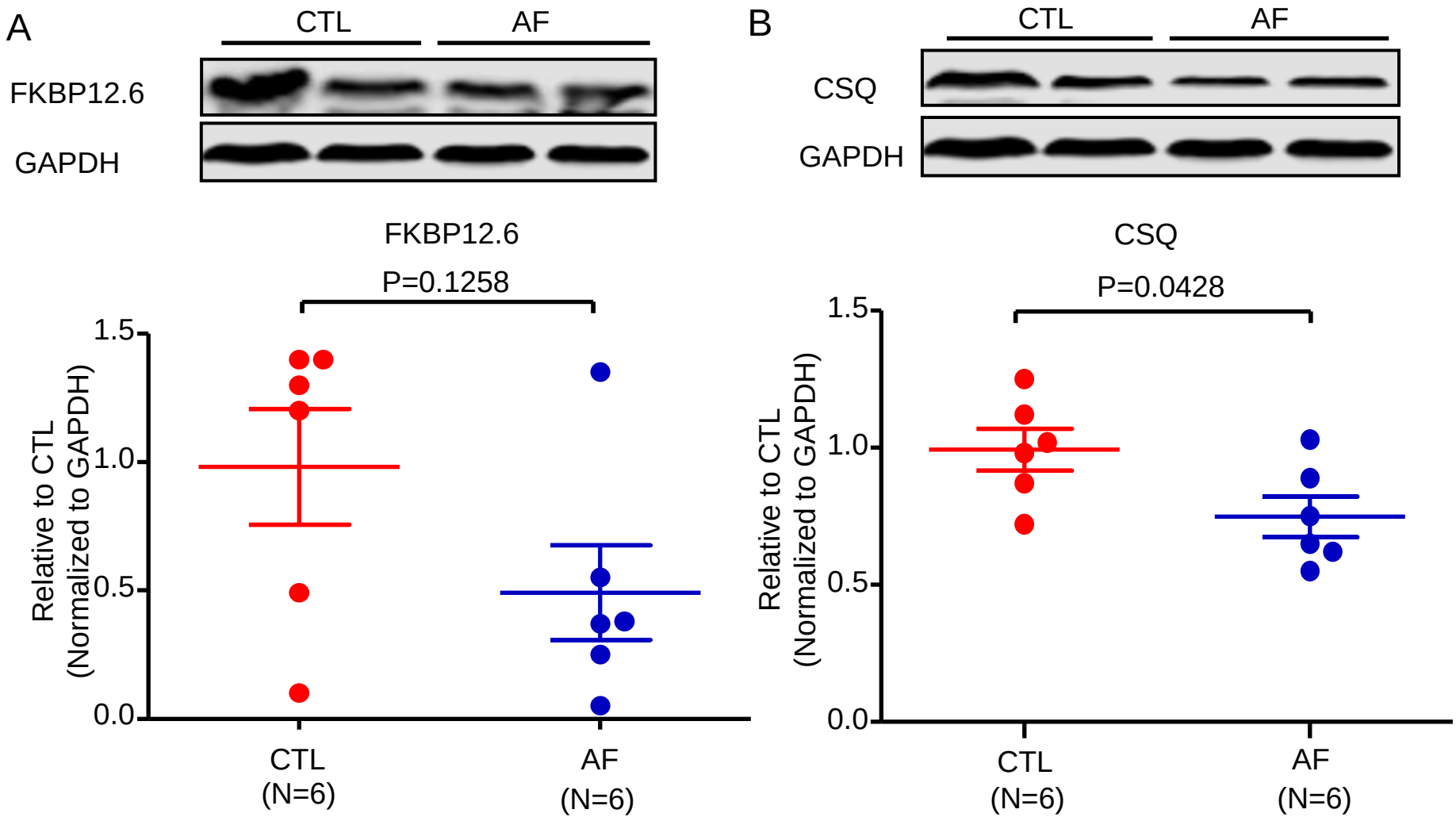
Suppl. Fig. 9





Supplemental Figure 9. Representative immunoblots for PLB and p-PLB (A) and SERCA2a (B). Expression of total PLB (C), Ser16-PLB (D), Thr17-PLB (E), Ser16-PLB /total PLB (F), Thr17- PLB/total PLB (G), and SERCA2a (H) in left atrial cardiomyocytes from CTL and AF dogs. Each point represents the result from one dog. Horizontal lies show mean ± SEM. n=dogs per group.(t-test)

Suppl. Fig. 10



Supplemental Figure 10. A) Representative immunoblots (top) and mean ± SEM FKBP12.6/GAPDH band-intensity (bottom) in left atrial cardiomyocytes from CTL and AF dogs. B) Representative immunoblots (top) and mean ± SEM CSQ/GAPDH (bottom) band-intensity in left atrial cardiomyocytes from CTL and AF dogs. Each point represents the result from one dog. Horizontal lies show mean ± SEM. N=dogs per group.(t-test)