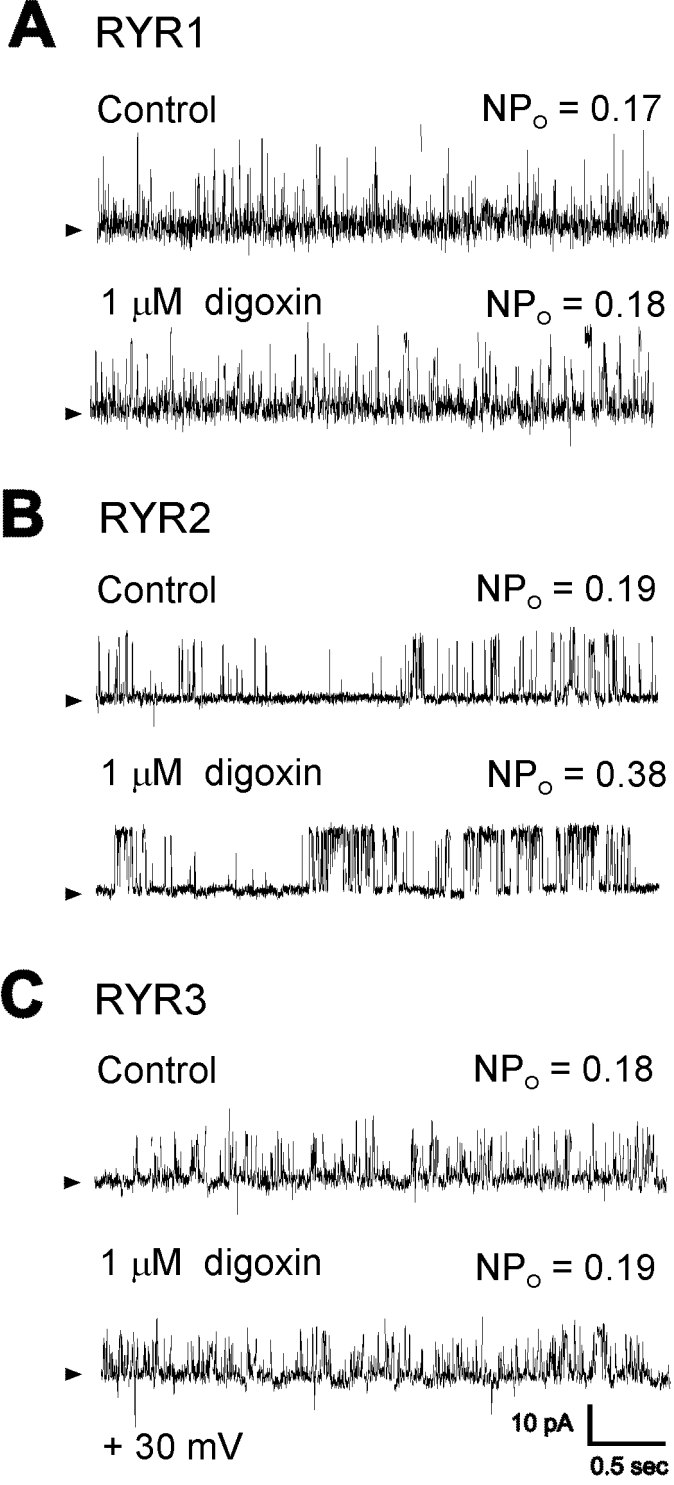
A
RYR1
Control
NP$_o$ = 0.17
1 μM digoxin
NP$_o$ = 0.18
B
RYR2
Control
NP$_o$ = 0.19
1 μM digoxin
NP$_o$ = 0.38
C
RYR3
Control
NP$_o$ = 0.18
1 μM digoxin
NP$_o$ = 0.19
+ 30 mV
10 pA
0.5 sec

Figure S1

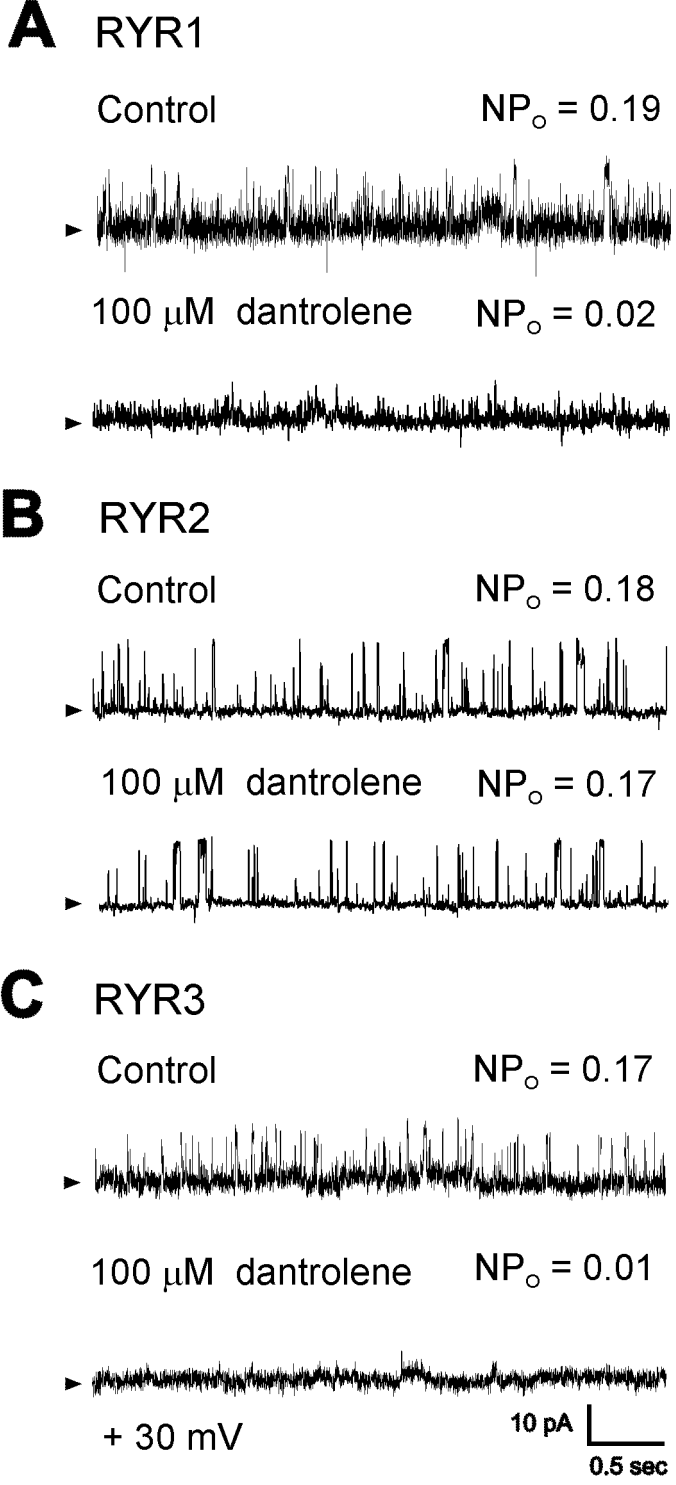
A
RYR1
Control
NPo = 0.19
100 μM dantrolene
NPo = 0.02
B
RYR2
Control
NPo = 0.18
100 μM dantrolene
NPo = 0.17
C
RYR3
Control
NPo = 0.17
100 μM dantrolene
NPo = 0.01
+ 30 mV
10 pA
0.5 sec

Figure S2

Online Supplementary Material: captions for figures S1 and S2.

Fig. S1. Digoxin potentiates recombinant homomeric RyR2 steady-state (NP_o) activity while failing to do potentiate homomeric RyR1 and RyR3 after channel reconstitution into lipid bilayers. Application of 1 μM digoxin to the bilayer *cis* side increased homomeric RyR2 NP_o, which reached 200% of control (***B***) while failing to increase the activity of RyR1 (***A***) and RyR3 (***C***) homomeric channels. Recombinant channel proteins were expressed and reconstituted as described in Materials and Methods. Arrowheads on the left of each trace point to the baseline (nonconducting channel states).

Fig. S2. Dantrolene drastically reduces the activity (NP_o) of recombinant homomeric RyR1 or RyR3 channels while failing to reduce homomeric RyR2 NP_o following channel reconstitution into lipid bilayers. Application of 100 μM dantrolene to the bilayer *cis* side almost totally blunts the activity of homomeric RyR1 (***A***) and RyR3 (***C***) NP_o, but failed to blunt homomeric RyR2 activity (***B***). Recombinant channel proteins were expressed and reconstituted as described in Materials and Methods. Arrowheads on the left of each trace point to the baseline (nonconducting channel states).