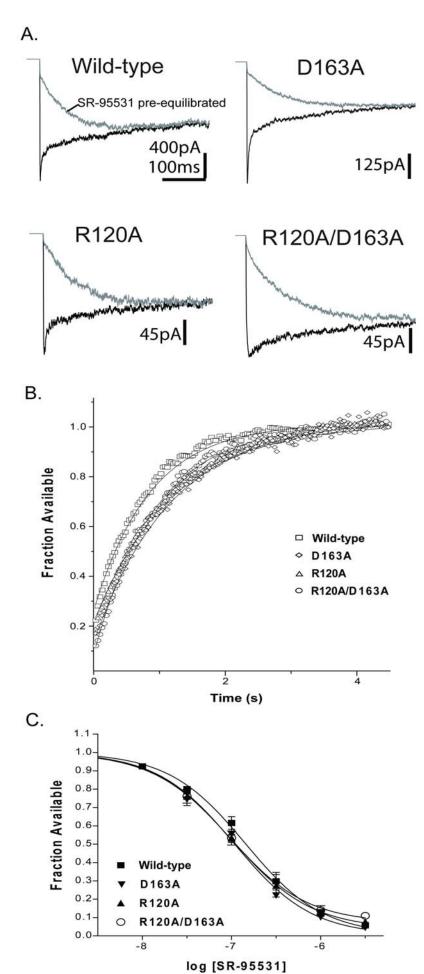
A state-dependent salt-bridge interaction exists across the  $\beta/\alpha$  inter-subunit interface of the GABA<sub>A</sub> receptor.

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Molecular Pharmacology

Supplemental Figure 1



Supplemental Figure 1. Microscopic kinetics for the antagonist SR-95531. A) The K<sub>D</sub>, k<sub>off</sub>, and k<sub>on</sub> for SR-95531 was determined for each receptor type by examining the current response to 30 mM GABA following a pre-incubation in a series of concentrations of SR-95531 (1μM shown above). B) Deconvolution of GABA-evoked currents after SR-95531pre-equilibration from control currents (no pre-equilibration) reveals the time course of SR-95531 unbinding. Deconvolved traces were fit to the equation A(t) =  $[P_{\infty} - (P_{\infty} - P_0) \exp(t/\tau_u)]^N$ , where A(t) is the fraction of available receptors (antagonist not bound at any site),  $P_0$  and  $P_{\infty}$  are the probabilities that a single binding site is available initially at t=0 and at steady state as t $\rightarrow \infty$ ,  $\tau_u$  is the time constant of antagonist unbinding from each site ( $k_{off-SR} = 1/\tau_u$ ), and N is the number of binding sites (Jones et al., 2001). C) Dose response curves for the equilibrium antagonist occupancy in the absence of GABA A(t=0) were fit to the normalized hill equation  $I/I_{max} = 1$  - $1/[(K_{D-SR}/[SR-95531])^{N}+1].$