

**Table S1.** AChE X-ray structure PDB depositions of native and liganded enzymes used in analysis shown in Tables 1 and 2 and Figs 3 and 4. Ligands are grouped by type of their interaction with AChE (reversible or covalent) and by one or more sites that they interact with when bound within the AChE. Description of site topography on the AChE molecule is given in the Figure S1.

Ligand			<i>Torpedo californica</i> AChE (TcAChE)			mouse AChE (mAChE)			human AChE (hAChE)		
type	Binding site in AChE	name	PDB ID	Resolution (Å)	Space group	PDB ID	Resolution (Å)	Space group	PDB ID	Resolution (Å)	Space group
		<i>none</i>	2ACE	2.5	<b>P 3<sub>1</sub> 2 1</b>	1J06	2.35	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	4EY4	2.16	<b>P 3<sub>1</sub> 2 1</b>
reversible	Choline binding site	Tacrine	1ACJ	2.8	<b>P 3<sub>1</sub> 2 1</b>	--	--	--	--	--	--
		Edrophonium	1AX9	2.8	<b>P 3<sub>1</sub> 2 1</b>	--	--	--	--	--	--
		Huperzine A	1VOT	2.5	<b>P 3<sub>1</sub> 2 1</b>	--	--	--	4EY5	2.3	<b>P 3<sub>1</sub> 2 1</b>
	Choline binding site + Peripheral site	BW284c51	1E3Q	2.85	<b>P 3<sub>1</sub> 2 1</b>	--	--	--	--	--	--
		decamethonium	1ACL	2.8	<b>P 3<sub>1</sub> 2 1</b>	1MAA	2.9	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	--	--	--
	Peripheral site	gallamine		--	--	1N5M	2.2	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	--	--	--
		Fas2	1FSS	3.0	<b>P 2<sub>1</sub> 2<sub>1</sub> 2</b>	1KU6	2.5	<b>P 6<sub>5</sub> 2 2</b>	4EY8	2.6	<b>H 3 2</b>
covalent	Active Ser + Acyl pocket + Choline binding site	TFK+	1AMN	2.8	<b>P 3<sub>1</sub> 2 1</b>	2H9Y	2.4	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	--	--	--
		Rivastigmine	1GQR	2.2	<b>P 3<sub>1</sub> 2 1</b>	--	--	--	--	--	--
		sarin	--	--	--	2Y2V	2.45	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	--	--	--
		VX	--	--	--	2Y2U	2.6	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	--	--	--
		DFP	--	--	--	2JGI	2.9	<b>P 2<sub>1</sub> 2<sub>1</sub> 2<sub>1</sub></b>	--	--	--

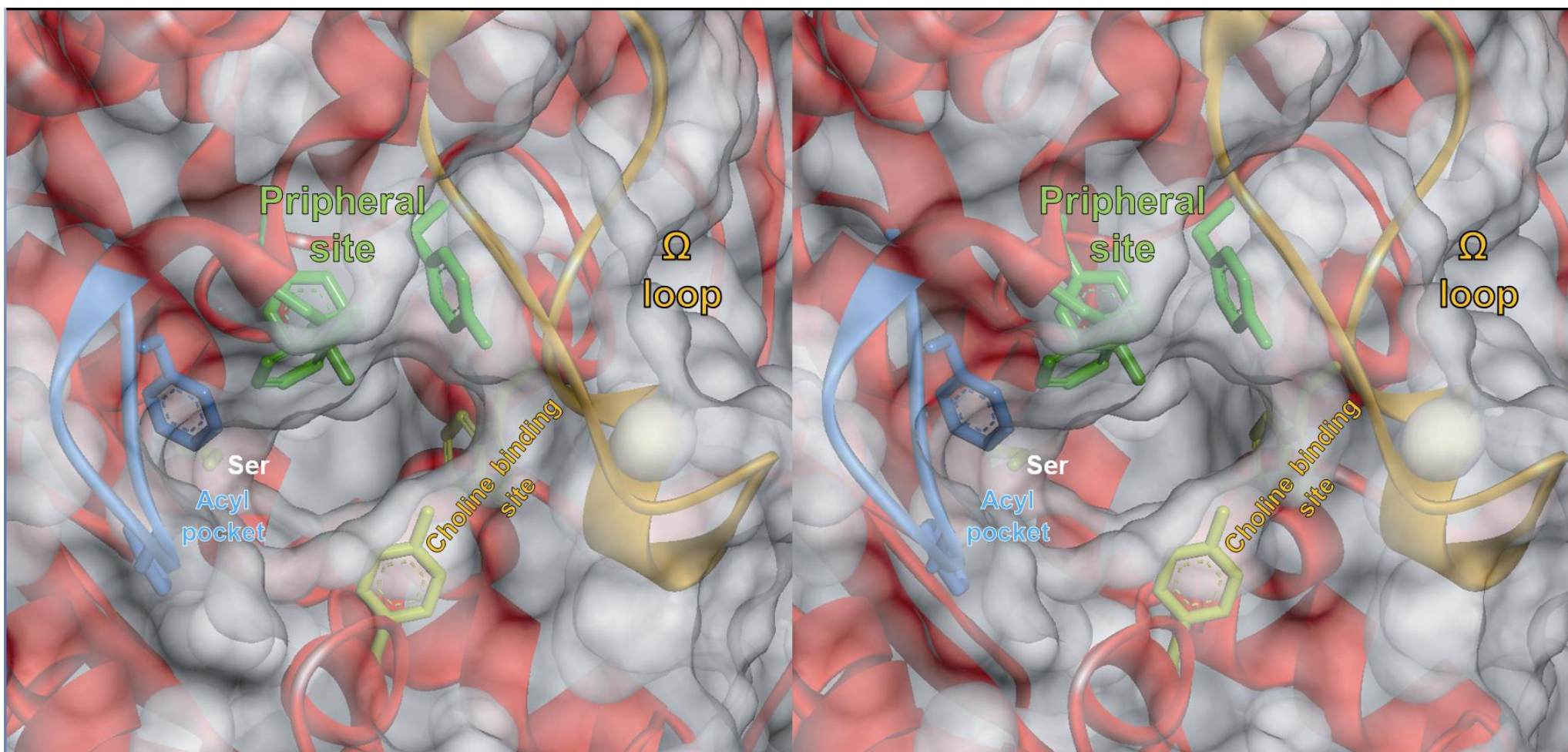


Figure S1. Topography of AChE binding sites for reversible and covalent ligands in the AChE active center gorge. A stereo view. The view of the active center is identical to the one used in Figs 1 and 2. The active serine (203 in mammalian AChE and 200 in TcAChE) is surrounded by the Acyl pocket on the left (defined by Phe 295 and Phe 297; Phe 288 and 290 in TcAChE) and the Choline binding site on the right (defined by Trp 86 and Tyr337; Trp 84 and Tyr 330 in TcAChE). The Peripheral site is located at the opening of the gorge, closest to the viewer, and defined by Trp286, Tyr72 and Tyr124; Trp279, Tyr70 and Tyr121 in TcAChE).