

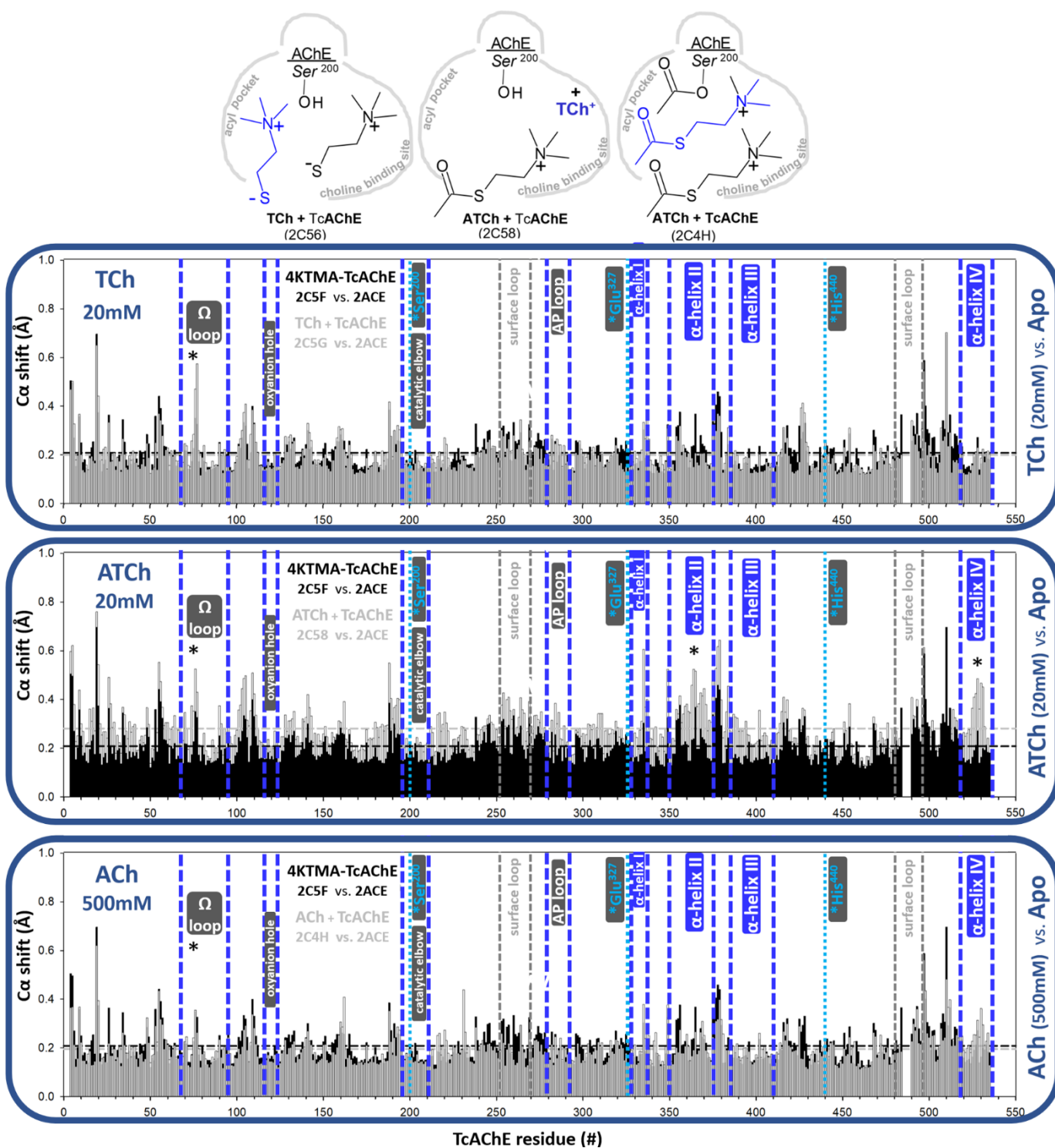
## **Supporting information**

# **Shifts in Backbone Conformation of Acetylcholinesterases Upon Binding of Covalent Inhibitors, Reversible Ligands and Substrates**

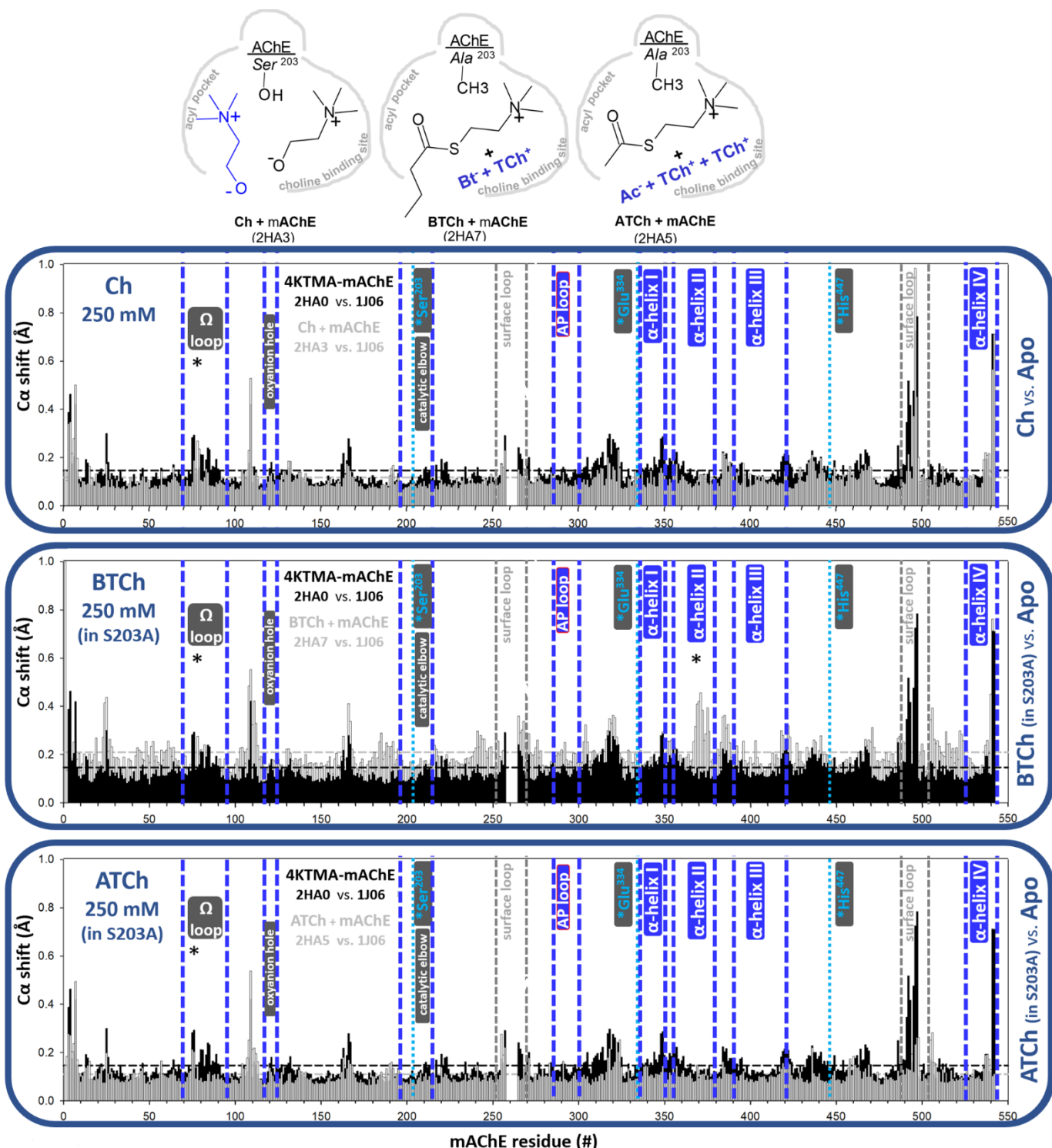
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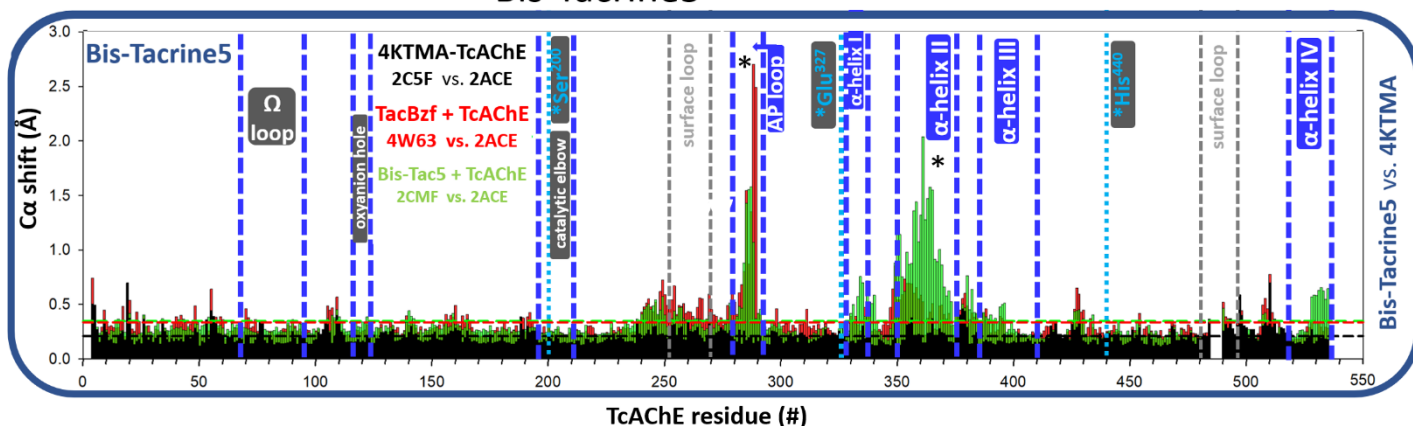
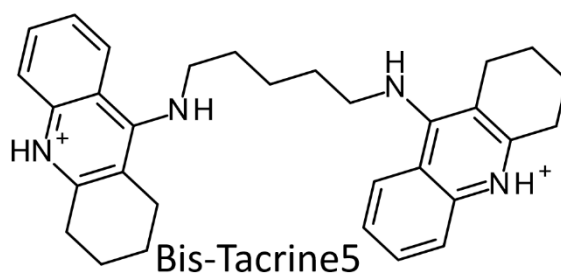
Figures S1 – S3



**Figure S1.** Structure of substrates ACh and ATCh and product TCh in reversible complexes with TcAChE. Schematics are based on X-ray structures with PDB codes given in parentheses. Bar charts from PACCT3 analyses of each of three structures compared to the apo AChE (2ACE). Alpha carbon shifts (in Å) of conjugated backbones are represented as vertical bars for each amino acid in the linear AChE sequence. Horizontal dashed lines indicate an average backbone atom shift while stars indicate shifts considered as significant. Functionally important structural elements of hAChE bracketed between vertical, dashed, blue lines and labelled.



**Figure S2.** Structure of substrates ATCh and BTCh and product Ch in reversible complexes with mAChE. Schematics are based on X-ray structures with PDB codes given in parentheses. Bar charts from PACCT3 analyses of each of three structures compared to the apo AChE (1J06). Alpha carbon shifts (in Å) of conjugated backbones are represented as vertical bars for each amino acid in the linear AChE sequence. Horizontal dashed lines indicate an average backbone atom shift while stars indicate shifts considered as significant. Functionally important structural elements of hAChE bracketed between vertical, dashed, blue lines and labelled, are mapped within the 3D structure of the hAChE in the Figure 2.



**Figure S3.** Structure of Bis-Tacrine5 reversible inhibitor of TcAChE. Bar charts from PACCT3 analyses of the reversible complex X-ray structure compared to the apo AChE (green bars). Parallel comparisons of Tacrine-benzofuran\*TchAChE complex vs. apo TcAChE (red bars) and 4KTMA-TcAChE conjugate vs. apo TcAChE (black bars) are given for comparison. Alpha carbon shifts (in Å) of conjugated backbones are represented as vertical bars for each amino acid in the linear AChE sequence. Horizontal dashed lines indicate an average backbone atom shift while stars indicate shifts considered as significant. Functionally important structural elements of hAChE are bracketed between vertical, dashed, blue lines and labelled.