

Supporting Information

Gorge Motions of Acetylcholinesterase Revealed by Microsecond Molecular Dynamics Simulations

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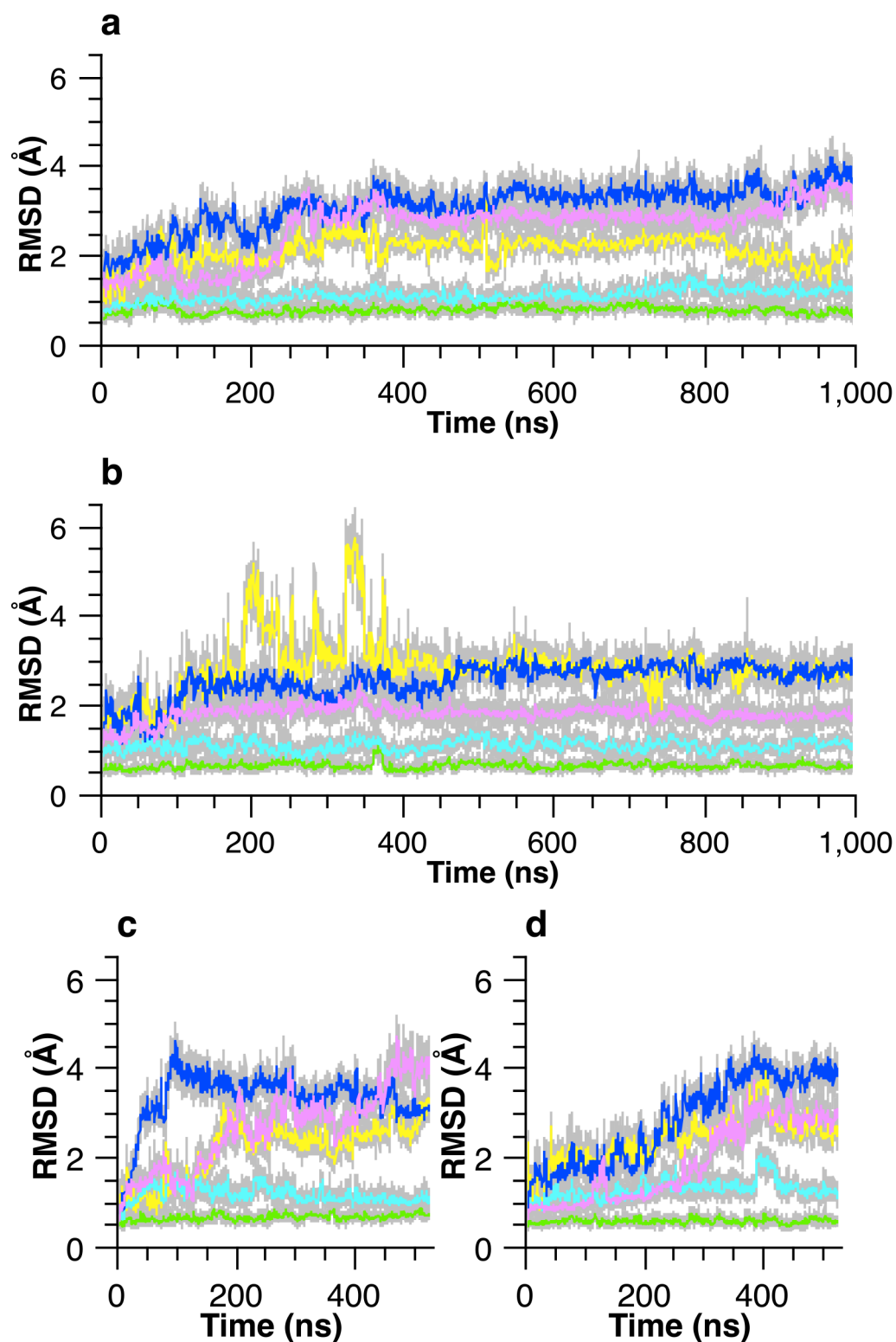


Figure S1. Movements of five subdomains surrounding the active-site gorge. Backbone RMSDs of the Ω -Loop (yellow), S1 (green), S2 (cyan), S3 (blue), and S4 (magenta) versus time in simulations of the monomer (a), complex (b) and apo dimer (c, d).

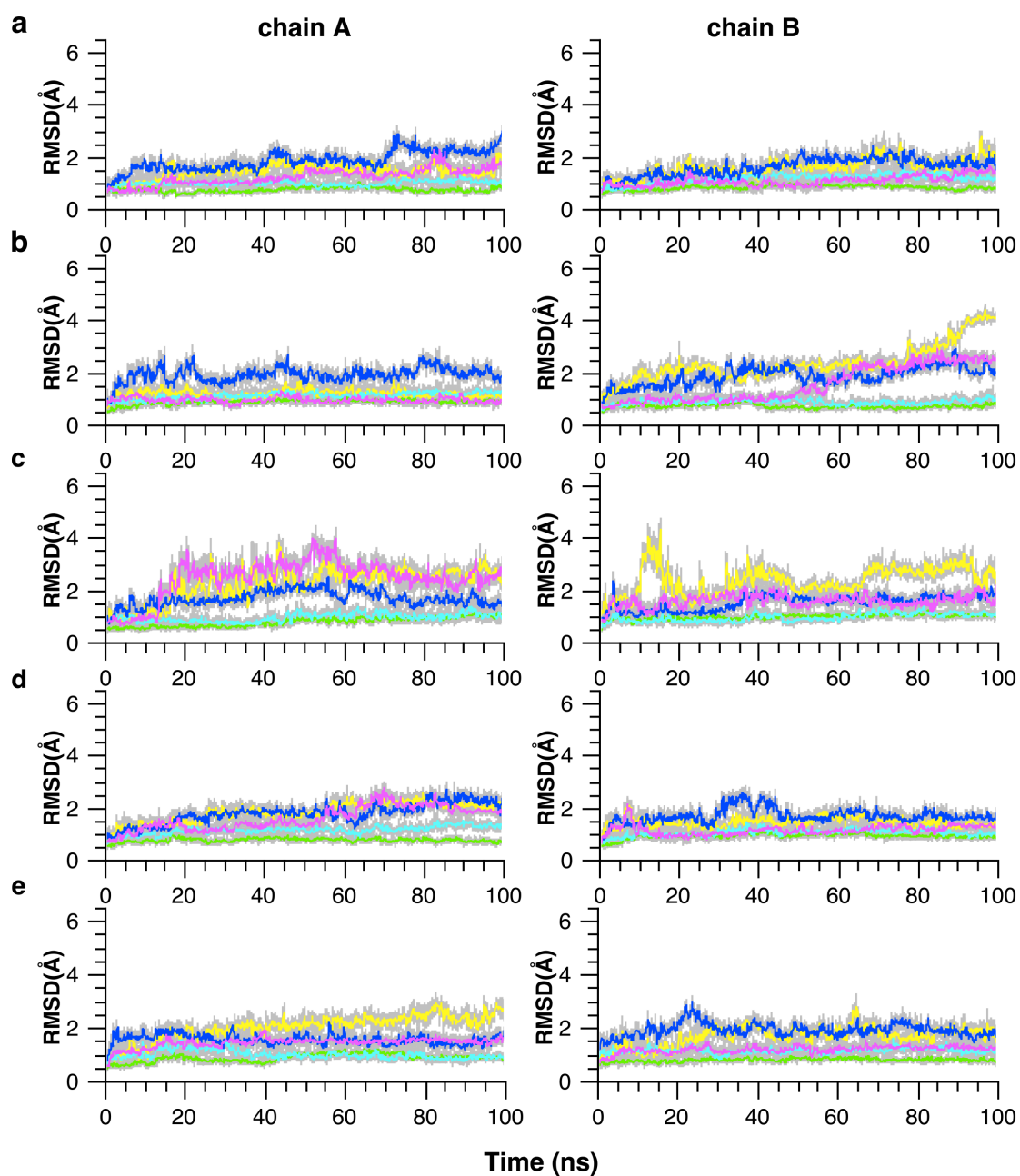


Figure S2. Movements of five subdomains surrounding the active-site gorge in five 100-ns simulations of *TcAChE* dimer in complex with E2020. (a-e) Backbone RMSDs of the Ω -Loop (yellow), S1 (green), S2 (cyan), S3 (blue), and S4 (magenta) versus time of the simulations.

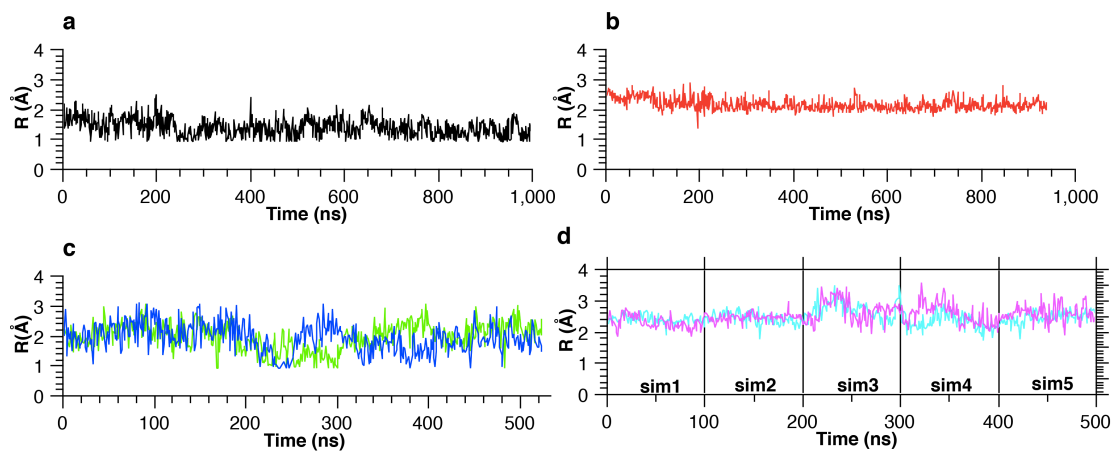


Figure S3. Time-dependent minimal gorge radius (R) in simulations of the *TcAChE* monomer (a), the *TcAChE*-E2020 Complex (b), the apo dimer (c), and the complex dimer (d).

Table S1 Gorge residues with low $|d|$ values and non-gorge residues with high $|d|$ values.

	Gorge Residues ($d < 0.1 \text{ \AA}$)	Non-gorge residues ($d > 0.4 \text{ \AA}$)
Monomer	E82, N280	R216, L321, G322, N364-V371, T376, G390-D393, L420, Y421, A427, P433-W435, G437, V438, F523, W524, F527-A534
Complex	S226, S286, I287, R289, V400, E443	N65, N87, I347-R349, D351, N364-L366, L368, D369, Y375, D380, D381, N424, H425, V438, D504-T507, W524-N533
Chain A of the Dimer	Y116, Y130, R244, V277, E278, N280-L282, G441	R88, I223, G322, V323, S340-S343, N416, Y421, V438, W473, A474, P482, N483, N488, E489, W492, P493, F523, A534
Chain B of the Dimer	L282, S286, N399, V400	R47, P76, G77, E92, D93, G160, P337-K341, S343, E344, K346, D380-I385, N387, N429, L430, G437, V438
Chain A of the Complex Dimer	V71, S79, I115, G117-Y121, S124, Y130, Y148, V150, G198, A201-G203	R216, S340-S345, R349, S359, V360, L373, Q374, D380, D381, I385, K386, R426, L430, V438
Chain B of the Complex Dimer	W114-Y116, I275-E278, P283	R88, G322, V323, K341, S345, D365, L366, D369, A370, T372-D381, N383, I385, K386, R388, G390, D392, D393, G396-H398, I401, 410, N416, L420-H425, A427-L430, F446, P451, L452, Y458-A460, E463-I469, H471, W473, F502, I503, L505-T507, V512, R517, Q519, M520, V522, F523, Q526-T535

Table S2. Residues included in communities resulted from the dynamic correlation analysis of the monomer (I), the complex (II), two chains of the apo (III-IV) and complex (V-VI) dimer. Residues located at five subdomains are labeled with the same color as those shown in Fig. 1.

I

#Community	Residues	Subdomains
C ₀	N65, N66, C67-Q74, P76, G77, G80-M83, N85-C94, L95-N98, W114-L127, S145-S147, K269-W279	Ω-loop+S1+S2
C ₁	Y130-V144	S1
C ₂	P38-E49, Y148-V150, G151-V168, V236-G249, D259, I263-E268, V293-I296, D297-E299, F301	S1+S2
C ₃	L333-M353, S359, D365, G367-R388, L391, D392, I394, V395, W435, Q519-M520	S3+S4
C ₄	F75, F78, S79, W84, D128, V129, F197-S200, L224, N225-C231, L320-V323, N324-L332, D389, D393, I401-V408, L420-A427, S428-E434, M436-F446, E461, R468-W473, K491, W492, K498-V518	Ω-loop+S1+S2+S3+S4
C ₅	E484-S490	/
C ₆	S108-V113, N183-I196, A474-G480	/
C ₇	S4-V8, V15-F30, N59-P64, I99-K107	/
C ₈	G169-D182, G207-R220, F300, N313-K315	/
C ₉	A201-V206	/
C ₁₀	R221-I223, K316-I319, N409-Y419, N481-N483, P493-T497	/
C ₁₁	P232-S235	S2
C ₁₂	R250, N251, N280-F292	S2
C ₁₃	C254-S258, E260-L262	S2
C ₁₄	S304-G312	/
C ₁₅	N9-K14, L31-E37, P50-W58	/
C ₁₆	S354-L366, C521-A534	S3
C ₁₇	G396-V400	S3
C ₁₈	V447-L450, P451-A460, E462-R467	S4

II

#Community	Residues	Subdomains
C ₀	N65, N66, C67-M90, G119-D128, Y130, S147, I275, S329-A336, K341	Ω-loop+S1+S2+S3
C ₁	L95-V101, L135-V150, G151	S1
C ₂	E37-R46, S91-C94, A152-A164, V238, E240-L274, D276-L282, V295	Ω-loop+ S2
C ₃	L332, P337-S340, D342-F352, L373-D392, L394-D397, E434-G437	S3+S4
C ₄	W114, V129, F197-S200, Q225-G227, L320-V323, N324-G328, D393, L404, Y419-A427, V438-L450, P451, L452, R467-W473, N483-P493, I503-H513, R517, Q519-C521	S1+S2+S3+S4
C ₅	R47-K52, I296, D297-S304, E306-M308	S2
C ₆	D2-L6, R19-S28, P102-R105, N131-Y134	S1
C ₇	L7-T18, P53-P64	/
C ₈	P106-V111, D182-I196	/
C ₉	M112, V113, R221-L224, S228-C231, L309-I319, M405-T418, A474-P482, L494-T497	S2
C ₁₀	A29-A36	/
C ₁₁	I115-G118	S1
C ₁₂	P165-H181	/
C ₁₃	A201-S205	/
C ₁₄	V206-H209, T210-R220	/
C ₁₅	P232-S237	S2
C ₁₆	A239	S2
C ₁₇	P283-I287, M353-T372, V522-A534	S2+S3
C ₁₈	F288-P294	S2
C ₁₉	L305	/
C ₂₀	K498-F502, Q514-V518	/
C ₂₁	H398-V400, I401-P403	S3
C ₂₂	S428-W432, V453-S466	S4
C ₂₃	P433	S4

III

#Community	Residues	Subdomains
C ₀	Chain A: T62-N66, C67, Q69-E73, E82, N85-M90, D93, Y96-N98, W114, Y121-D128, S145-S147, Q272, E278, W279	Chain A: Ω -loop+S1+S2
C ₁	Chain A: I99, W100, K133-V144	Chain A: S1
C ₂	Chain A: P38-R46, Q68, S91, E92, C94, L95, G119, F120, Y148-V150, G151-V168, V236, R242-V277, N280-P283, S291, F292, I296	Chain A: Ω -loop+S1+S2
C ₃	Chain A: Q74-S81, M83, W84, I115-G118, V129-G132, F197-S200, L224, Q225-N230, F284-F290, L320-V323, N324-M353, K357-D369, Q374-D377, N382-V400, I401-F407, L420-A427, S428-F448, Y458-E462, R468-W473, N483-P493, K498-V522, W524-P529, L531, L532, A534; Chain B: D365, L373, M379, D380, K530	Chain A: Ω -loop+S1+S2+S3+S4 Chain B: S3
C ₄	Chain A: G449-L450, P451-N457, E463-R467	Chain A: S4
C ₅	Chain A: S4-E37, E49-S61, V101-P106	/
C ₆	Chain A: R47, G169-R174, S237-G241, V293-V295, D297-M308	Chain A: S2
C ₇	Chain A: P48, K107-V113, M175-I196, R221-I223, A474-P482	/
C ₈	Chain A: A201-S205	/
C ₉	Chain A: V206-R220	/
C ₁₀	Chain A: C231-S235	Chain A: S2
C ₁₁	Chain A: L309-I319, V408-Y419, L494-T497	/
C ₁₂	Chain A: A370-L373; Chain B: V522	Chain A: S3
C ₁₃	Chain A: S354-V356;	Chain A: S3
C _{0'}	Chain B: N66, Y70-R88, Y116-G118, S122-Y134, S145, E199, S200, L224, Q225-G227, L321-V323, N324-E327, F330, L420-A427, S428-W432, G437-L450, Y458-E462, R468, S490-F492, F502-H513, R515	Chain B: Ω -loop+S1+S2+S3+S4
C _{1'}	Chain B: I99-V101, P106-V113, W114, I115, A136-V144, W179-G198	Chain B: S1
C _{2'}	Chain B: F35-K51, T62-N65, C67-Q69, E89-C94, L95-N98, L146-V150, G151-Q178, M208-R220, S237-F284, S291-I296, D297-F301, S311, N313,	Chain B: Ω -loop+ S1+S2

	K315	
C₃	Chain A: F523 Chain B: D285-F288, G328, S329, F331-V360, H362, A363, G367, L368, T372, Q374-W378, D381-V395, P433-M436, M520, W524	Chain B: S2+S3+ S4
C₄	Chain A: W378-D381 Chain B: S228-C231, G396-V400, I401-H406, V408, K498-K501, Q514, L516-Q519	Chain A: S3 Chain B: S2+S3
C₅	Chain B: S4-P34, K52-S61, P102-R105	/
C₆	Chain B: S24, L135, P451-N457, E463-R467, I469-Y472	/
C₇	Chain B: G119-Y121, R289, F290	Chain B: S1+S2
C₈	Chain B: A201-G207	/
C₉	Chain B: R221-I223, F314, K316-L320, F407, N409-Y419, W473-E489, P493-T497	/
C₁₀	Chain B: P232-V236	Chain B: S2
C₁₁	Chain B: P302-N310, G312	/
C₁₂	Chain A: K530, N533 Chain B: P361, N364, L366, D369-V371, C521, F523, N525-P529, L531-A534	Chain B: S3

IV

#Community	Residues	Subdomains
C₀	Chain A: T62-N66, C67-M90, Y116, G118-V129, N131-L135, S145-Y148, E199, R243, K270-L282, F290-F292	Chain A: Ω-loop+S1+S2
C₁	Chain A: A136-V144	Chain A: S1
C₂	Chain A: G154-Q162, P232-R242, R244-L266, E268, K269	Chain A: S2
C₃	Chain A: G117, Y130, S200, Q225, S226, P283-R289, G322, V323, N324-M353, K357-A363, L368, V371, T372, Q374-D377, D380-V400, I401-H406, Y421-A427, S428-L450, P451-M470, S490, F502-Q514, L516-V522, N525 Chain B: L373	Chain A: S1+S2+S3+S4 Chain B: S3
C₅	Chain A: P106-I115, N183-G198, D217-R220, H471-T479	/
C₆	Chain A: D2-V8, V15-S28, W58-S61, P104, R105	/

C₇	Chain A: A29-K52, S91-C94, L95-S103, R149, V150, G151-F153, E163-A176, R267	ChainA: Ω -loop+ S1+ S2
C₈	Chain A: S354-V356	Chain A: S3
C₉	Chain A: L177, R216, R221-L224, V293-I296, D297-L321, F407-L420, L494-K501, R515	Chain A: S3
C₁₀	Chain A: A201-S215	/
C₁₁	Chain A: G227-C231	Chain A: S2
C₁₂	Chain A: N364, L366, G367, F523, W524, Q526-N533 Chain B: D369, A370	Chain A: S3 Chain B: S3
C₁₃	Chain A: N9-K14, P53-V57, Q178-D182	/
C₁₄	Chain A: G480-P493	/
C_{0'}	Chain B: T62-N66, C67-M90, L97, G117-V129, S145-Y148, E199, L224, R244, Q272-W279, P283, F284, F290-F292	Chain B: Ω -loop+ S1+ S2
C_{1'}	Chain B: A136-V144	Chain B: S1
C_{2'}	Chain B: P34-K51, S91-C94, L95, Y96, R149, V150, G151-L177, C231-R243, A245-P271, N280-L282, V293-I296, D297-E299	Chain B: Ω -loop+ S1+ S2
C_{3'}	Chain A: L373, W378, M379 Chain B: Y116, S200, A201, Q225-N230, D285-R289, L321-V323, N324-H362, N364, G367, L368, V371, T372, Q374-V400, I401-H406, L420-A427, S428-L450, P451, L452, E462-W473, K498-N525	Chain A: S3 Chain B: S2+S3+S4
C_{5'}	Chain B: P106-I115, Q178-G198	/
C_{6'}	Chain B: D2-S61, N98-R105, Y130-L135	Chain B: S1
C_{7'}	Chain B: G202-R220, G312-K315	/
C_{8'}	Chain B: R221-I223, K316-L320, V408-Y419, L494-T497	/
C_{9'}	Chain B: F300-S311, F407	/
C_{10'}	Chain B: V453-E461	/
C_{11'}	Chain B: A474-K478	/
C_{12'}	Chain A: D365, D369, A370, A534 Chain B: A363, D365, L366, Q526-A534	Chain A: S3 Chain B: S3
C_{13'}	Chain B: T479-P493	/