

## **Supplementary Information**

### **Alzheimer's Protective Cross-interaction Between Wild-type and A2T Variants Alters A $\beta$ 42 Dimer Structure**

**PD<sup>1\*</sup>, AC<sup>1</sup>, GB<sup>2</sup>**

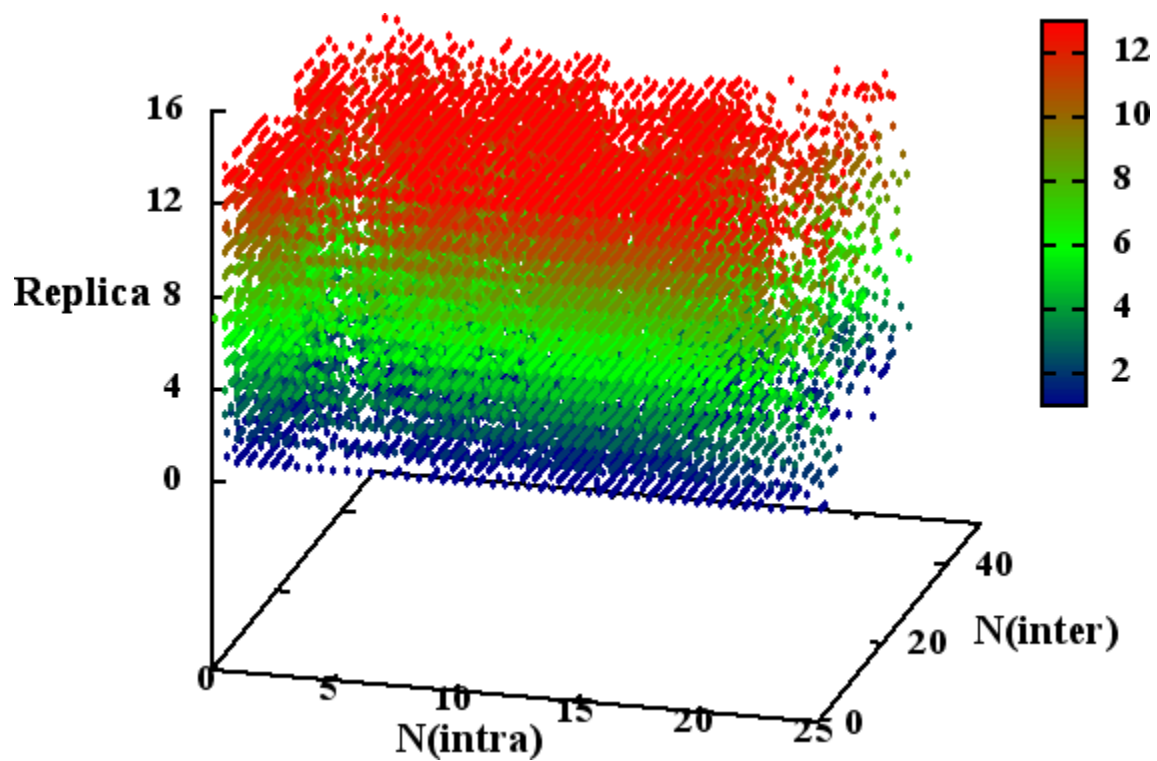
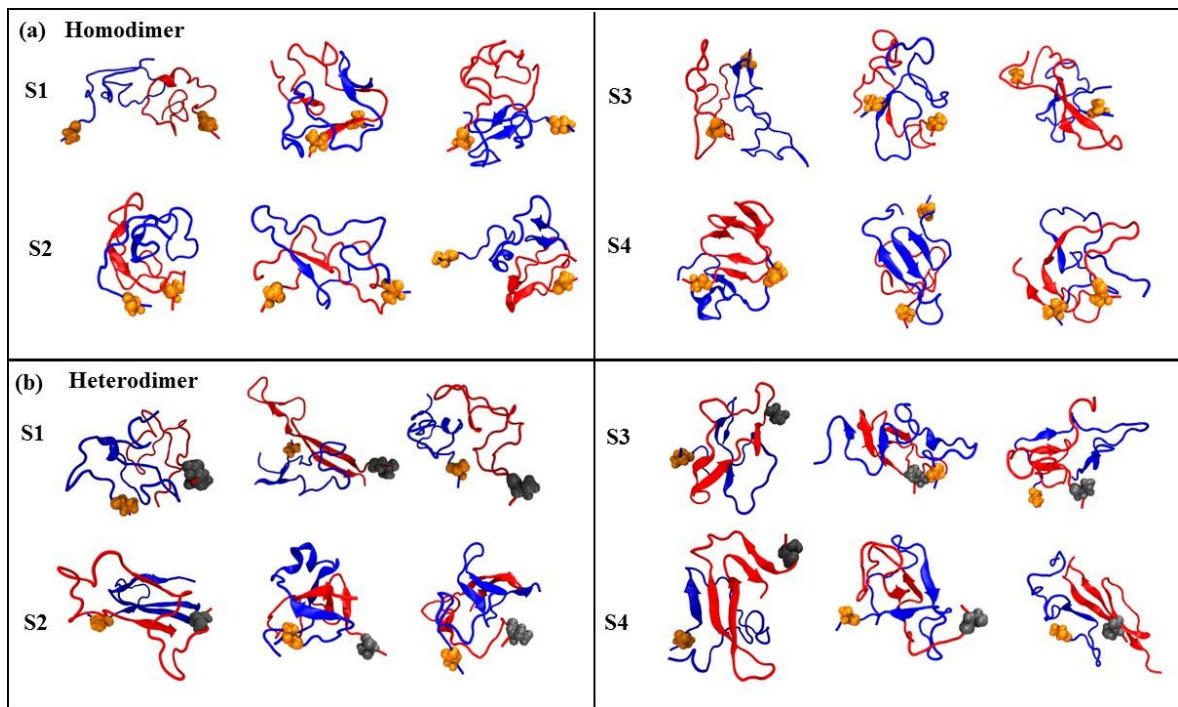


Figure S1. Conformational sampling as a function of intra- and inter-chain contacts, as obtained from the first 13 replicas for the heterodimer system.



**Figure S2: Representative structures of S1-S4 states (top panel: homodimer and bottom panel: heterodimer).**

**Table S1: Probability (in %) of inter-chain salt-bridges.** Those with probability <5% are marked as “-”.

Homodimer		Heterodimer
<b>D7-K28</b>	6.3	-
<b>E11-K28</b>	8.3	-
<b>D23-K28</b>	-	7.8
<b>K16-D23</b>	-	6.0
<b>D7-K16</b>	-	6.8
<b>R5-E11</b>	-	5.7
<b>D3-K28</b>	-	5.2

**Table S2: Average  $\Delta G^{\text{Binding}}_{\text{vdW}}$  and  $\Delta G^{\text{Binding}}_{\text{elec}}$  (in kcal/mol) of S1-S4 dimer structures.**

		<b>S1</b>	<b>S2</b>	<b>S3</b>	<b>S4</b>
WT homodimer	$\Delta G^{\text{Binding}}_{\text{vdW}}$	-111.25	-138.32	-116.31	-95.90
	$\Delta G^{\text{Binding}}_{\text{elec}}$	-21.50	-29.51	-6.01	-19.01
A2T heterodimer	$\Delta G^{\text{Binding}}_{\text{vdW}}$	-102.47	-137.46	-122.55	-122.41
	$\Delta G^{\text{Binding}}_{\text{elec}}$	-25.43	-47.68	-46.70	-44.40

**Table S3: Summary of cluster analysis:** total % of population, number of clusters and size distribution of top 5 clusters for S1-S4 regions of homo- and heterodimer.

<b>Homodimer</b>	<b>S1</b>	<b>S2</b>	<b>S3</b>	<b>S4</b>
% of total population	9.40	22.75	19.75	22.37
# clusters	38	28	60	38
Size of top five clusters (%)	1. 21.64 2. 14.27 3. 11.33 4. 8.22 5. 8.00	1. 20.51 2. 15.17 3. 13.11 4. 12.70 5. 12.05	1. 9.97 2. 9.23 3. 9.14 4. 7.79 5. 7.14	1. 19.09 2. 12.14 3. 10.71 4. 9.31 5. 8.94
<b>Heterodimer</b>	<b>S1</b>	<b>S2</b>	<b>S3</b>	<b>S4</b>
% of total population	22.75	15.82	19.17	13.16
# clusters	42	54	55	31
Size of top five clusters (%)	1. 12.80 2. 10.60 3. 10.53 4. 8.93 5. 8.00	1. 28.41 2. 13.51 3. 9.56 4. 6.59 5. 5.39	1. 17.14 2. 12.47 3. 6.40 4. 6.05 5. 6.05	1. 22.20 2. 13.14 3. 12.99 4. 9.99 5. 9.41