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CHEMPHYSCHEM

Supporting Information

Insight into the Interactions of Amyloid β-Sheets with Graphene Flakes: Scrutinizing the Role of Aromatic Residues in Amyloids that Interact with Graphene

Dragana M. Božinovski,[b] Predrag V. Petrović,[b] Milivoj R. Belić,[b] and Snežana D. Zarić*[a, b]

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Supplementary information

Calculations were performed using four model systems for the graphene flake (Figure S1). The size of graphene model systems was systematically increased, to determine the largest graphene flake that had to be used for the amyloid-graphene interacting system without significant changes in the interaction energy. Model systems $C_{216}H_{36}$ and $C_{294}H_{42}$ were too small to take into consideration, due to the unwanted interactions of the edge of graphene flakes with the β-sheet of amyloid fragment. This was especially evident for the structure 2Y29 (Figure S1). The graphene model system $C_{384}H_{48}$ was found to be the most suitable for our study. The interaction energies for the largest graphene model system $C_{486}H_{54}$ tried did not differ significantly from the energies for the chosen model system $C_{384}H_{48}$ (Table S1).

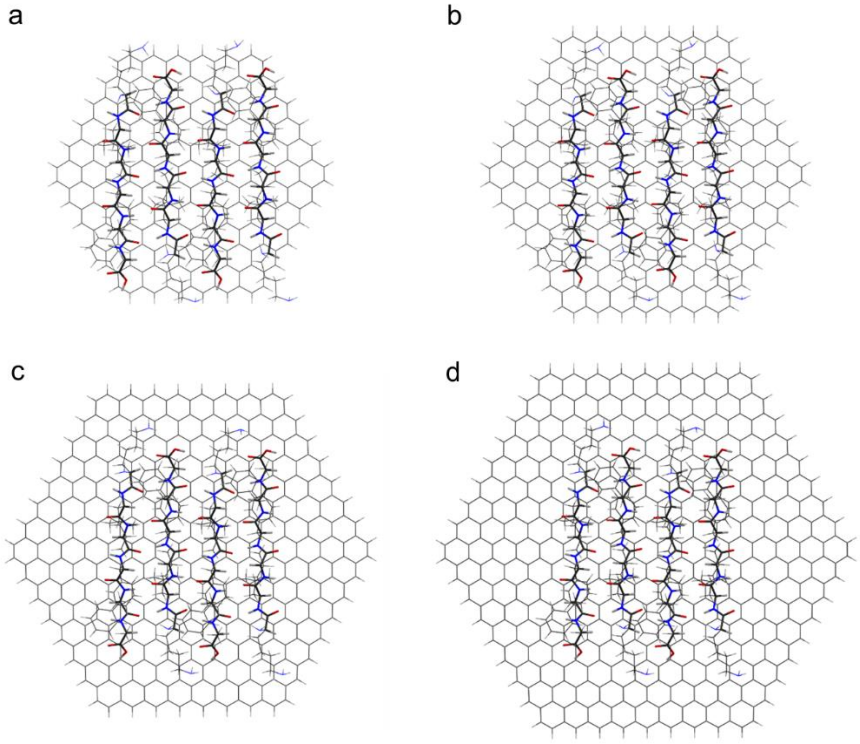

Figure S1. Model systems of 2Y29 amyloid aggregating with graphene a) $C_{216}H_{36}$, b) $C_{294}H_{42}$, c) $C_{384}H_{48}$, and d) $C_{486}H_{54}$ flakes.

Interaction energies were calculated on model systems constructed by aligning the center of mass of graphene flake - C_g with the center of mass of the β-sheet segment containing one tetramer of polypeptide chains - C_a (Figure 1). The plane of the amyloid β-sheet tetramer (the mean plane of all backbone atoms) is kept parallel to the plane of the graphene flake. For each amyloid structure, the aggregates of graphene flake and of both sides, the top (A) and the bottom (B), (Figure S2) of tetramer β-sheet amyloid were

constructed. The strongest interaction energy for each structure was found by varying the normal distance R (Figure 1) between the mean plane of backbone atoms of the amyloid β-sheet and the plane of the graphene flake, in increments of 0.1 Å.

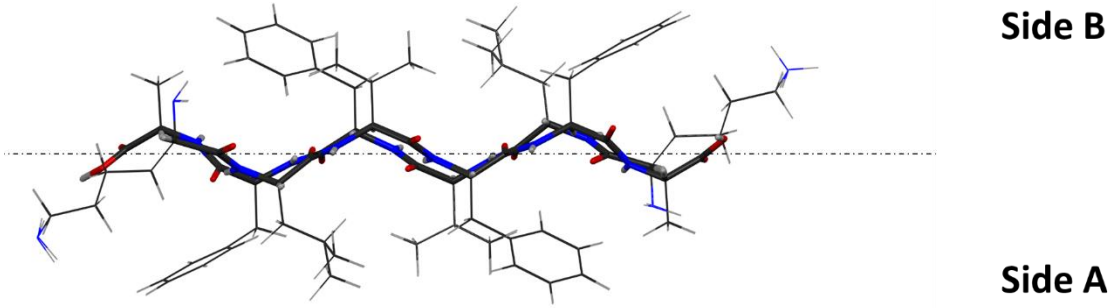

Figure S2. Two sides of the amyloid tetramer β-sheet (an example of 2Y29 structure) that can aggregate with the graphene flake.

Table S1. Interaction energies calculated using B3LYP-D3/6-31G* method (in kcal/mol) for the interaction between two tetramer β-sheet of 2Y29, 2Y2A, 3OW9, 2Y3J, 2Y3L, and 3Q2X/3Q2X$_{mod}$ amyloid structures,[a] and for the interaction between one tetramer β-sheet and graphene $C_{216}H_{36}$, $C_{294}H_{42}$, $C_{384}H_{48}$, and $C_{486}H_{54}$ flakes (examples of the interacting system shown in Figure 1). Values for normal distance R between amyloid β-sheet and graphene flake (as shown in Figure 1) for each calculated interaction energy is given in brackets.

Structure	Interaction between β-sheets	Interaction between β-sheet and $C_{216}H_{36}$	Interaction between β-sheet and $C_{294}H_{42}$	Interaction between β-sheet and $C_{384}H_{48}$	Interaction between β-sheet and $C_{486}H_{54}$
A-2Y29[b]	-40.18	-52.65 [7.5 Å]	-47.64 [7.8 Å]	**-62.39** [7.5 Å]	-59.66 [7.6 Å]
B-2Y29			-47.11 [7.8 Å]	**-61.95** [7.5 Å]	-59.16 [7.6 Å]
A-2Y2A	-40.04		-37.40 [8.6 Å]	**-38.56** [8.6 Å]	
B-2Y2A			-36.70 [8.6 Å]	**-37.79** [8.6 Å]	
A-3OW9	-52.92		-62.29 [7.7 Å]	**-63.22** [7.7 Å]	
B-3OW9			-45.30 [8.3 Å]	**-46.35** [8.2 Å]	
A-2Y3J	-51.53		-42.45 [7.9 Å]	**-43.17** [7.9 Å]	
B-2Y3J			-31.61 [8.7 Å]	**-33.72** [8.6 Å]	
A-2Y3L	-42.62		-21.18 [9.2 Å]	**-22.15** [9.2 Å]	-22.83 [9.2 Å]
B-2Y3L			-59.38 [7.3 Å]	**-61.42** [7.3 Å]	
A-3Q2X	-125.58		-32.20 [9.1 Å]	**-26.48** [9.2 Å]	
B-3Q2X			-37.16 [8.7 Å]	**-37.14** [8.7 Å]	
A-3Q2X$_{mod}$[c]	-75.12			**-36.73** [8.1 Å]	

[a] data from the reference [41]

[b] A and B designate the side of the amyloid β-sheet (Figures 2 and 3, Figure S2 ESI) involved in the interaction with the graphene flake

[c] a model system modified to remove the influence of the hydrogen bonds (Figure S4), additionally explained in reference [41]

Since there is the possibility that interaction energy would change depending on the orientation of the graphene flake, the amyloid segment was rotated by 30 degrees relative to the axis shown in Figure S3. The orientation dependence was explored for two model systems: 2Y2A with graphene $C_{384}H_{48}$, and 2Y29 with graphene $C_{486}H_{54}$. However, there was no significant change in the interaction energy (Table S2).

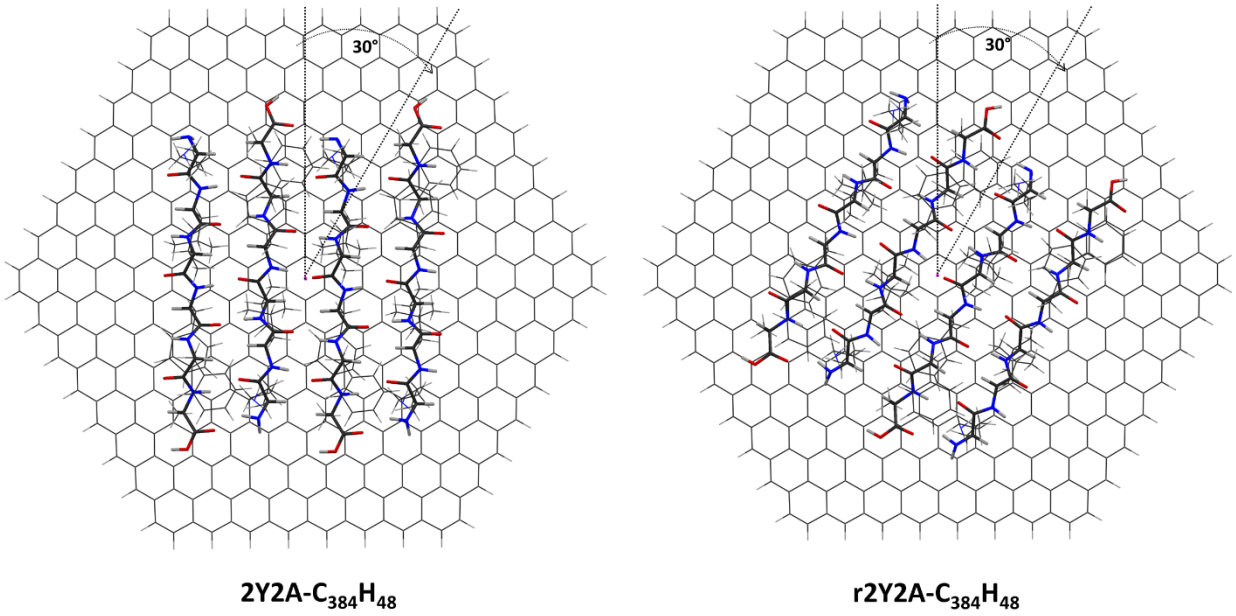

Figure S3. Graphene $C_{384}H_{48}$ flake and 2Y2A aggregate. Amyloid fragment was rotated by 30° around the axis perpendicular to the plane of the graphene flake in the direction of the arrow**.**

Table S2. Interaction energies calculated using B3LYP-D3/6-31G* method (in kcal/mol) for the interaction between the model system 2Y2A and the graphene $C_{384}H_{48}$ flake, and between 2Y29 and $C_{486}H_{54}$, before and after rotation by 30^0about the axis perpendicular to the plane of graphene sheet (as shown in Figure S3).

Structure	Graphene $C_{384}H_{48}$	Graphene $C_{486}H_{54}$
2Y29	-	-59.66
r2Y29	-	-60.14
2Y2A	-38.56	-
r2Y2A	-38.66	-

Structure of the 3Q2X amyloid was modified in order to remove the influence of the hydrogen bonds by replacing all amino groups of Lys with hydrogen atoms as shown in Figure S4.

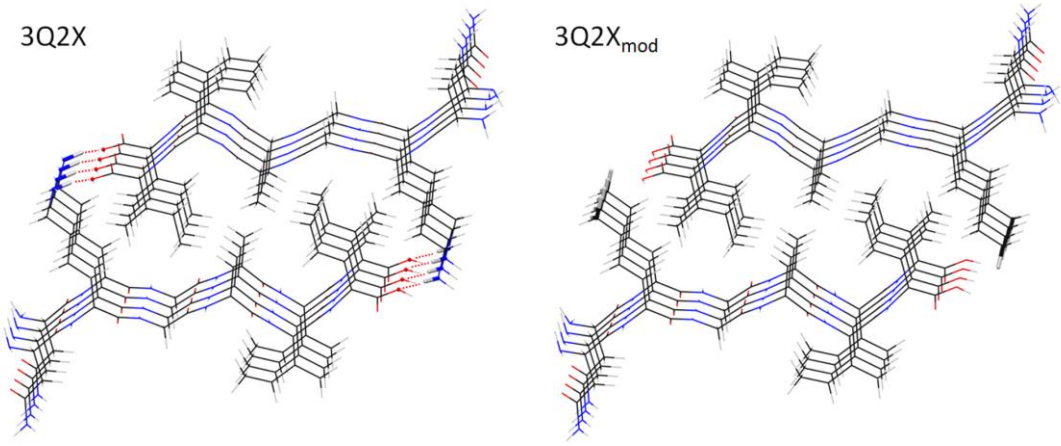

Figure S4. Left - 3Q2X model system with H-bonds between two β-sheets highlighted; right - 3Q2X$_{mod}$ model system with hydrogen atom that replaced amino group from Lys in order to remove the H-bonds between two β-sheets highlighted.

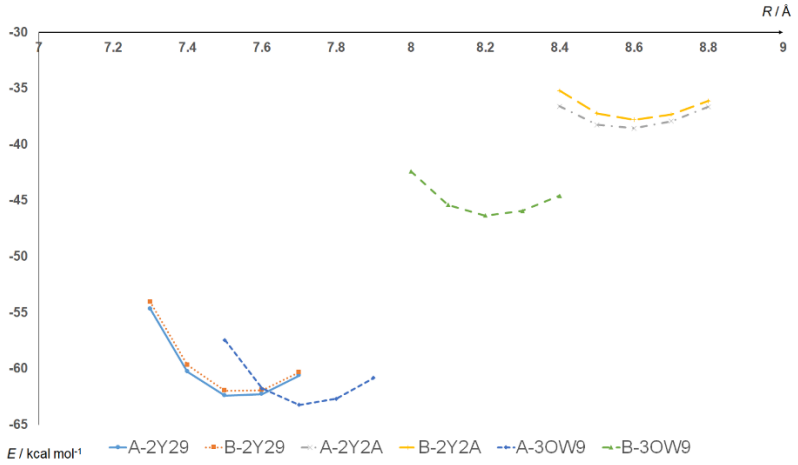

Figure S5. Interaction energies at various distances R for the interaction of aromatic amyloid β-sheets with the graphene $C_{384}H_{48}$ flake.

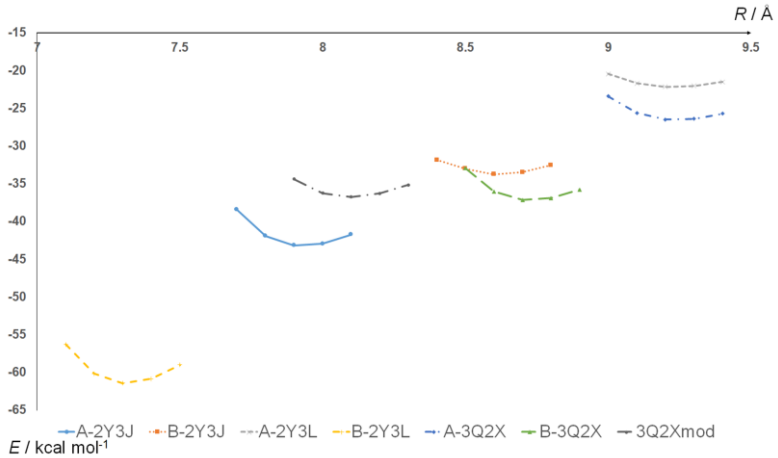

Figure S6. Interaction energies at various distances R for the interaction of non-aromatic amyloid β-sheets with the graphene $C_{384}H_{48}$ flake.