Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

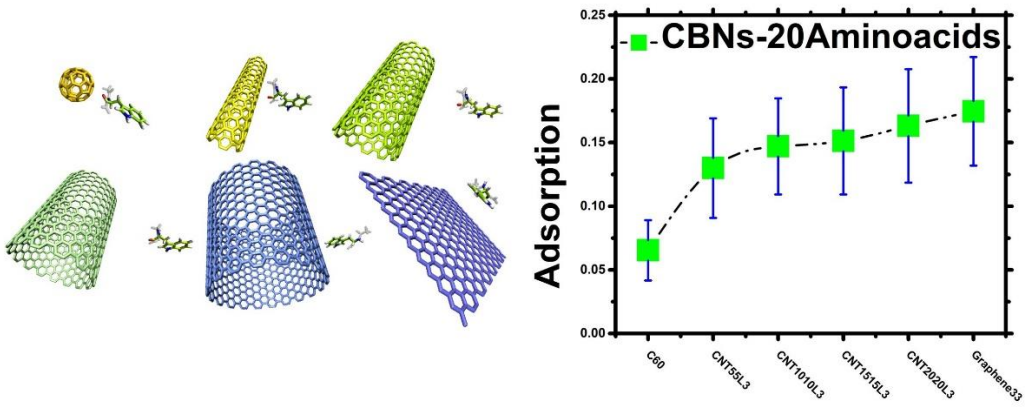
Study on Dynamics and Cluster Analysis between Carbon-based Nanoparticles and Amino Acids

Wanying Huang [1], Haihong Jia [3] and JunYan Luo [2,*]

[1] T-Life Research Center, State Key Laboratory of Surface Physics, Department of Physics, Fudan University, Shanghai 200433, China; huangwanying1128@163.com
[2] Department of Physics, Zhejiang University of Science and Technology, Hangzhou 310023, China; jyluo@zust.edu.cn
[3] Institute of Physics & University of Chinese Academy of Sciences, Chinese Academy of Sciences, Beijing 100190, China; hhjia1217@iphy.ac.cn
* Correspondence: jyluo@zust.edu.cn; Tel.: (Zhejiang University of Science and Technology，Zhejiang 310000, China)

Abstract

We research the interaction between six representative carbon-based nanoparticles (CBNs) and 20 standard amino acids through all-atom molecular dynamics simulations. The six carbon-based nanoparticles are fullerene(C60), CNT55L3, CNT1010L3, CNT1515L3, CNT2020L3, and two-dimensional-graphene(Graphene33). Their curvatures decrease sequentially, and all of CNT are single-walled carbon nanotubes. We have observed that as the curvature of CBNs decreases, the adsorption effect of 20 amino acids with them has an increasing trend. In addition, we also used multi-dimensional clustering to analyze the adsorption effects of 20 amino acids on six carbon-based nanoparticles. We observed that the π-π interaction still plays an extremely important role in the adsorption of amino acids on carbon-based nanoparticles. Individual long-chain amino acids and "Benzene-like" Pro also have a strong adsorption effect with carbon-based nanoparticles.



 doi:10.20944/preprints202111.0406.v1

Keywords:

CBNs, amino acids, Molecular dynamics

Introduction

In recent years, the interaction between nanoparticles and proteins has attracted widespread attention[1; 2]. Experimental and theoretical simulation studies between nanoparticles and proteins[3] have been in continuous progress[4], which is of great significance for the research of biopharmaceuticals, especially targeted drugs[5]. Various gold nanoparticles modified with different peptide chain groups have become important research objects for cancer-targeted drugs[6]. In addition, recent interactions between two-dimensional nanomaterials and individual nucleotides[7] indicate that this two-dimensional screening structure of in-plane graphene and hexagonal boron nitride arrays may inspire the development of laboratory-on-a-chip sequencing in the future. Carbon-based nanoparticles, as the most basic nanoparticles, have been widely concerned about the molecular dynamics research between them and proteins[8-12]. At present, many researchers have used molecular dynamics to study the interaction between carbon-based nanoparticles and proteins[5; 13-17].

The interaction between amino acids and carbon-based nanoparticles or modified carbon-based nanoparticles has attracted wide attention from researchers in the experimental, quantitative calculation, and molecular dynamics[10; 12; 18]. Experimentally, the interaction between carbon-based nanoparticles and amino acids, the unique electronic and optical properties of single-walled carbon nanotubes[23], coupled with their size and mechanical strength, make single-walled carbon nanotubes become the key to the sensing platform[9] to the development of the next generation of biological transmission. Experimental studies have shown that carbon-based nanomaterials can promote neuronal electrical signals[16]. In addition, researchers have

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

developed a variety of electrochemical biosensors based on carbon nanotubes[17]. Moreover, in terms of drug delivery, carbon-based nanoparticles, especially those modified by peptides, have always received extensive attention from biomedical workers[24]; in terms of quantitative calculations, the study of amino acids or amino acids in a vacuum computing environment The interaction between aromatics and carbon nanotubes[4; 10; 11], and this part of the research content is also an important reference for studying the interaction of 20 amino acids and carbon-based nanoparticles in aqueous solutions; For all-atom molecular dynamics, on the one hand, some researchers have studied the interaction between some amino acids and a single carbon nanotube in one system[14].

However, there is still a lack of molecular dynamics research between a single amino acid and a variety of carbon-based nanoparticles of different sizes in an aqueous environment, especially the corresponding research with a long simulation time. The comprehensive all-atom simulation study between carbon-based nanoparticles and 20 representative amino acids is very important: (1) This work is an important preliminary work for multi-scale research between carbon-based nanoparticles and ultra-large proteins; (2) The research is a paradigm for the study of interactions between other nanomaterials and 20 amino acids, and it is also the basis for future research on the relationship between complex nanomaterials and their interactions; (3) The work is also a study on the binding of nanoparticles and amino acid-related small molecules or proteins. It also as an important supporting material for prediction.

Our research has done a detailed studying on the interaction between a single amino acid and six carbon-based nanoparticles at the full-atom level. We tried to explore the relationship between 20 standard amino acids and 6 kinds of carbon-based nanoparticles from two views. For the view of carbon-based nanoparticles, under the premise of excluding the volume limitation, will nanoparticles with different curvatures affect the adsorption effect between them and amino acids; For the another view of 20 amino acids, different groups of amino acids are compared with 6 Will the adsorption effect of a representative carbon-based nanoparticle be affected by its type? Whether it is hydrophilic-hydrophobic interaction, π-π interaction, the positive/negative charged side chain, or simply the length of the side chain, these may affect the adsorption effect between a single amino acid and carbon-based nanoparticles. In addition, we hope that cluster analysis in machine learning can well characterize the adsorption strength between six representative carbon-based nanoparticles (CBNs) and 20 amino acids. Next, let us explore the interactions between six representative carbon-based

 doi:10.20944/preprints202111.0406.v1

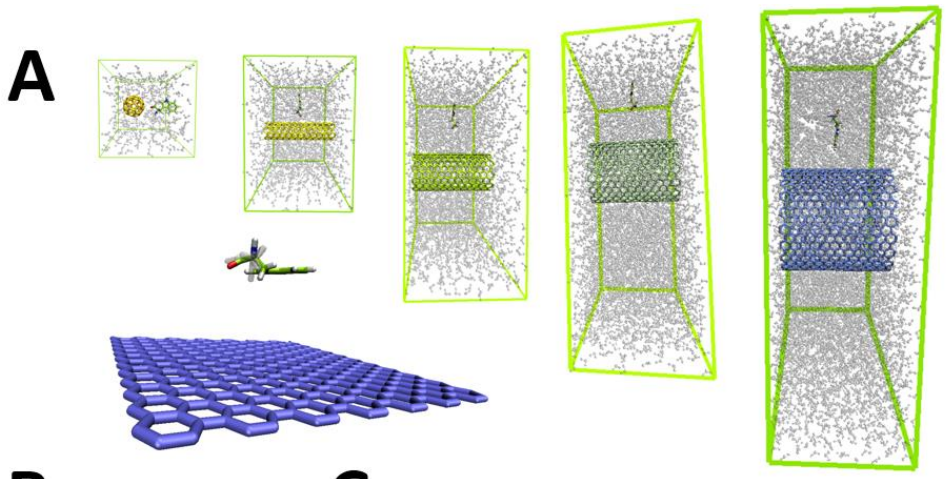
nanoparticles (CBNs) and 20 amino acids from the perspective of all-atom molecular dynamics simulations.

1 System and Method

1.1 Simulation system

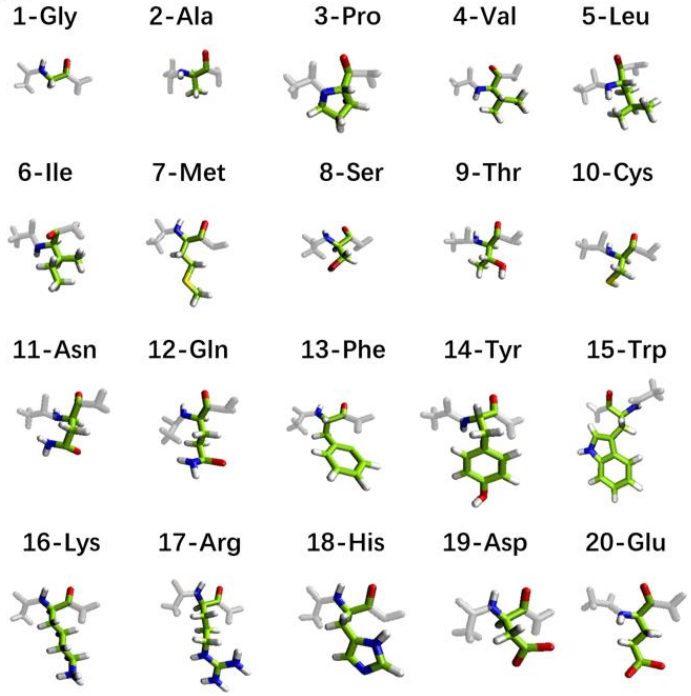
In our research, 120 molecular systems (6CBNs×20Aminoacids×3) were constructed, and the interaction between 6 carbon-based nanoparticles and 20 amino acids (Figure1BC) in an aqueous solution (Figure1A) was studied, and each study The system has done 3 repeated simulation studies, with a total of more than 360 simulation research trajectories, each trajectory 200ns, we try to objectively statistical research from the All-atom level. Among them, the six types of carbon-based nanoparticles are fullerene (C60), single-walled carbon nanotube (CNT55L3, CNT1010L3, CNT1515L3, CNT2020L3), and graphene (graphene33). In our research, the C60 is the carbon-based nanoparticle with the largest curvature (1/r), and the graphene33 with the smallest curvature is close to the planar state.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1



B

Group	Animoacids
Nonpolar	1-Gy
	2-Ala
	3-Pro
	4-Val
	5-Leu
	6-Ile
	7-Met
Polar	8-Ser
	9-Thr
	10-Cys
	11-Asn
	12-Gln
Aromatic	13-Phe
	14-Tyr
	15-Trp
Positively	16-Lys
	17-Arg
	18-His
Negatively	19-Asp
	20-Glu



D

Number	CBNs	Lx(nm)	Ly(nm)	Lz(nm)	diameter	Radius(nm)	Curvature(1/nm)	S/(V-Vcnt)
C1	C60	2.25	2.25	2.25	0.668 nm	0.334	2.99401	0.125
C2	CNT55L3	4.16	4.16	2.93	0.673 nm	0.3365	2.97177	0.125
C3	CNT1010L3	5.94	5.94	2.93	1.346 nm	0.673	1.48588	0.125
C4	CNT1515L3	7.36	7.36	2.93	2.020 nm	1.01	0.99009	0.125
C5	CNT2020L3	8.61	8.61	2.93	2.712 nm	1.356	0.73746	0.125
C6	Graphene33	2.95141	2.982	8.22	3 nm×3nm	$\rightarrow \infty$	$\rightarrow 0$	0.125

Figure1 (A) Schematic diagram of amino acid and carbon-based nanoparticle simulation system (take 15-TRP as an example): orange is C60, yellow is CNT55L3, light green is CNT1010L3, green is CNT1515L3, bright blue is CNT2020L3, and purple is Graphene33. (B) The Group of 20 amino acids: the orange component is the nonpolar amino acid group; the yellow component is the polar uncharged amino acid

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

group; the green component is the aromatic amino acid group; the blue component is the positively charged amino acid group; the purple components is negatively charged amino acids. (C) Schematic diagram of the molecular structure of 20 amino acids. (D) Table: the spatial size list of six representative carbon nanoparticles and amino acid systems

From CNT55L3, CNT1010L3, CNT1515L3 to CNT2020L3, as shown in Figure 1A, the radii of carbon nanotubes with different radii increase, and the curvature decreases. The parameters of each carbon-based nanoparticle are shown in Figure1D-Table. In our research, to exclude the possibility of amino acids entering the carbon nanotubes as the CNT radius increases sequentially, we have used periodic boundary conditions. In other words, we studied the periodic infinitely long carbon tube CNT and the carbon-based plane Graphene, which allows us to focus only on the effect of the curvature of the carbon-based nanoparticle on its adsorption effect.

In addition, in order to eliminate the influence of CBNs volume on the adsorption effect, when constructing the system, we followed the principle of the same surface contact volume ratio of all simulation systems, namely

$$\varphi = \frac{S_{CBNs}}{V - V_{CBNs}}$$

The φ value of all simulation systems is fixed, that is, the surface entropy of the adsorption space of the system is a fixed value. Among them, S_{CBNs} represents the surface area of carbon-based nanoparticles, V represents the volume of the system, and V_{CBNs} represents the volume of carbon-based nanoparticles.

Our research, based on previous studies of molecular dynamics between carbon-based nanoparticles and proteins by other researchers, has grouped 20 amino acids. As shown in Figure 1B, they are (1) Nonpolar amino acids (Nonpolar, aliphatic R group):1-Gly, 2-Ala, 3-Pro, 4-Val, 5-Leu, 6-Ile, 7-Met; (2) Polar amino acids (Polar, uncharged R group): 8-Ser, 9-Thr, 10-Cys, 11-Asn, 12-Gln; (3) Aromatic amino acids (Aromatic R group): 13-Phe, 14-Tyr, 15-Trp; (4) Positively charged amino acids (Positively charged R group): 16-Lys, 17-Arg, 18-His; (5) negatively charged amino acids (Negatively charged R group): 19-Asp, 20-Glu. Such a combination arrangement allows us to study well, which properties of the amino acid side chain affect its adsorption effect with carbon-based nanoparticles. The molecular structures of 20 amino acids are shown in Figure 1C. Among them, the amino acids of the non-polar amino acid group start from amino acids 1-7, and the side chains increase sequentially. The shortest side chain is 1-Gly, and the longest is 7-Met; the amino acids of the polar

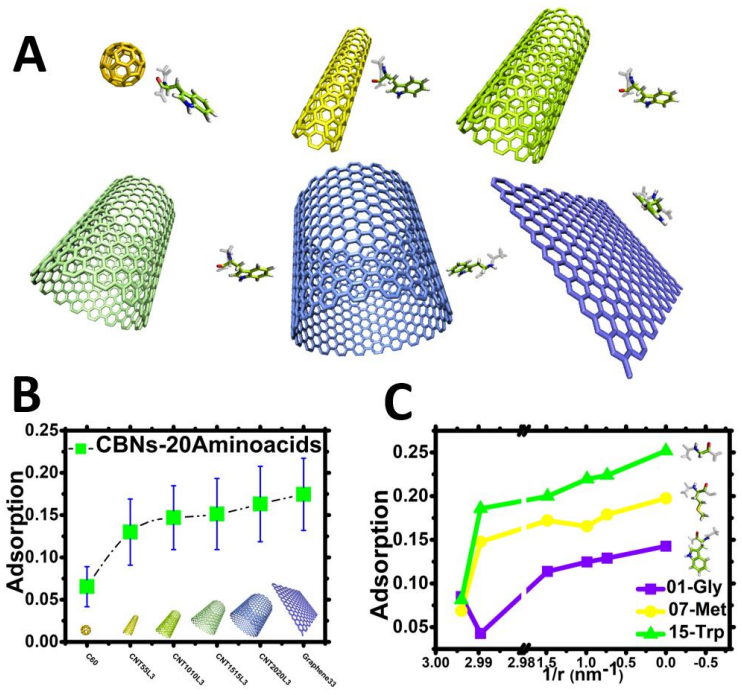
Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

non-charged amino acid group are from 8-12 In the positively charged amino acid group, we put 18-His with a benzene ring at the end, but the 17-Arg in this group is the positively charged amino acid with the longest side chain.

1.2 Simulate system MD parameters

A molecular system of 120 simulation systems (6CBNs×20Aminoacids) in an aqueous solution, among which we selected the most commonly used SPC216 model for water molecules. Among them, the larger carbon-based nanoparticles are the CNT2020L3 system, and we have added 21,245 water molecules. We use Gromacs software[25; 26] throughout our molecular dynamics research. Our study used the frog-leap method simulation, and the simulation integration step as 2fs. To ensure sufficient adsorption time between amino acids and CBNs, the duration of each simulation was 200ns. Ensure that our all-atom simulation time is sufficient to extract sufficient conformational information to prepare for the subsequent multi-scale coarse-grained force field. In the initial stage, the distance between amino acids and CBNs is about 1.5 nm. Our simulation systems are all NVT systems[27]. The simulated temperature of the system is 330K, and we use the Berendsen temperature adjustment method. We used periodic boundary conditions to make our carbon nanotubes periodic infinite length and infinite graphene plane[26].

2 Results and Discussion



Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

Figure2 (A) Six representative carbon-based nanoparticles. (B) The average adsorption strength of 6 CBNs for 20 amino acids: the green square is the average adsorption strength of each carbon-based nanoparticle for 20 amino acids, and the blue bar line is The corresponding error. (C) The adsorption trend of three representative amino acids, the purple dotted line is 01-Gly, the yellow dotted line is 07-Met, and the green dotted line is 15-Trp.

This paper mainly studies the adsorption trend between 6 representative carbon-based nanoparticles and 20 standard amino acids, as shown in Figure 2A. Our research found that as the curvature decreases, the adsorption rate shows an increasing trend, as shown in Figure 2B. Moreover, our research also makes suitable use of multi-dimensional clustering analysis to describe the overall change in its adsorption rate, when 20 amino acids change with the decreasing curvature of carbon-based nanoparticles. As shown in Figure 2C, the purple line is the short-chain amino acid 01-Gly, the yellow line is the hydrophobic amino acid 07-Met with the longest side chain, and the green line is the aromatic amino acid 15-Trp with the longest side chain. We can observe that the adsorption strength of the three amino acids is: 15-Trp>07-Met>01-Gly. In other words, the adsorption strength of aromatic amino acids is much greater than that of amino acids with the longest side chain.

2.1 Kinetics Analysis

In our work, the minimum contact distance Mindist changes with time for each group of amino acids. The change of the minimum contact distance with time is a very important indicator. In many studies of protein and nanoparticles, this indicator is used to describe the change of the distance from the surface of the nanoparticle with time. The reason is that different carbon-based nanoparticles have different radii, and choosing the Mindist indicator can better reflect the adsorption between amino acids and carbon-based nanoparticles. Next, we will discuss the kinetic characteristics of different groups of amino acids Mindist over time.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

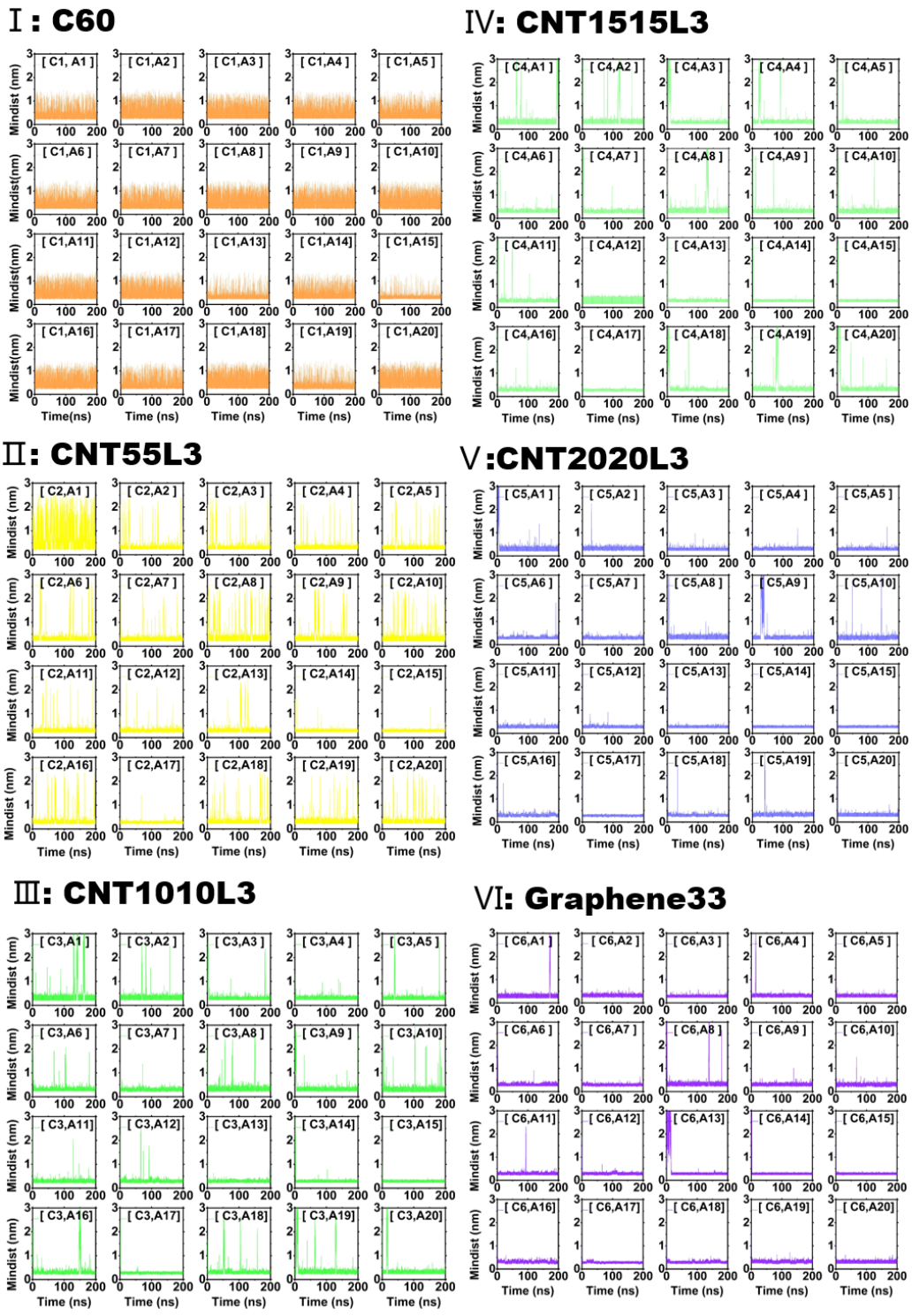


Figure3 The change of the minimum distance between CBNs and amino acids over time, the horizontal axis t (ns), the vertical axis Mindist (nm). From C1-C6 respectively: I group picture C1 orange line C60, group II picture C2 yellow line CNT55L3, group III picture C3 bright green line CNT1010L3, group IV picture C4 green line CNT1515L3, group V picture C5 bright blue line CNT2020L3, VI Group picture C6 purple line Graphene33; each group picture contains 20 kinds of representative amino acids and Mindist changes over time between CBNs, non-polar amino acid group A1-A7 are: 1-

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

Gly, 2-Ala, 3-Pro, 4-Val, 5-Leu, 6-Ile, 7-Met; Polar uncharged amino acid group A8-A12 are: 8-Ser, 9-Thr, 10-Cys, 11-Asn, 12-Gln; Aromatic amino acid group A13-A15 are: 13-Phe, 14-Tyr, 15-Trp; Positively charged amino acid group A16-A18 are: 16-Lys, 17-Arg, 18-His; Negatively charged amino acid group A19-A20 are: 19-Asp, 20-Glu.

We could observe the dynamic changes from the perspective of the curvature of carbon-based nanoparticles from Figure3. Figure3 I group picture C1 orange line C60, the adsorption performance of 20 representative amino acids and C60 is not good, most of them are in the state of pulsating separation in space; Figure3II group picture C2 yellow line CNT55L3, most of the adsorption effect with CNT55L3 is better than that of C60 group There was a short stay; Figure3III group C3 bright green line CNT1010L3, some amino acids showed strong adsorption performance, especially aromatic amino acids; Figure 3 IV group C4 green line CNT1515L3, the overall amino acid adsorption effect is not bad, even 5-Leu and CNT1515L3 both showed good adsorption performance; Figure3V group picture C5 bright blue line CNT2020L3, most of the amino acids have excellent adsorption effects, except for a few amino acids, such as 9-Thr and CNT2020L3, part of the separation occurs; Figure 3 VI Group Graph C6 Purple line Graphene33, this is the group with the best overall adsorption effect, and some short-term "jumping" behaviors can also be ignored. We indeed observe the changes in the adsorption effect of carbon-based nanoparticles with 20 amino acids from the perspective of changes in the curvature of carbon-based nanoparticles, and some trends can be preliminarily drawn, but rigorous analysis and judgment still require statistical research.

2.2 Statistical Analysis

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

（a）Mindist-distribution between CBNs and 20 amino acids

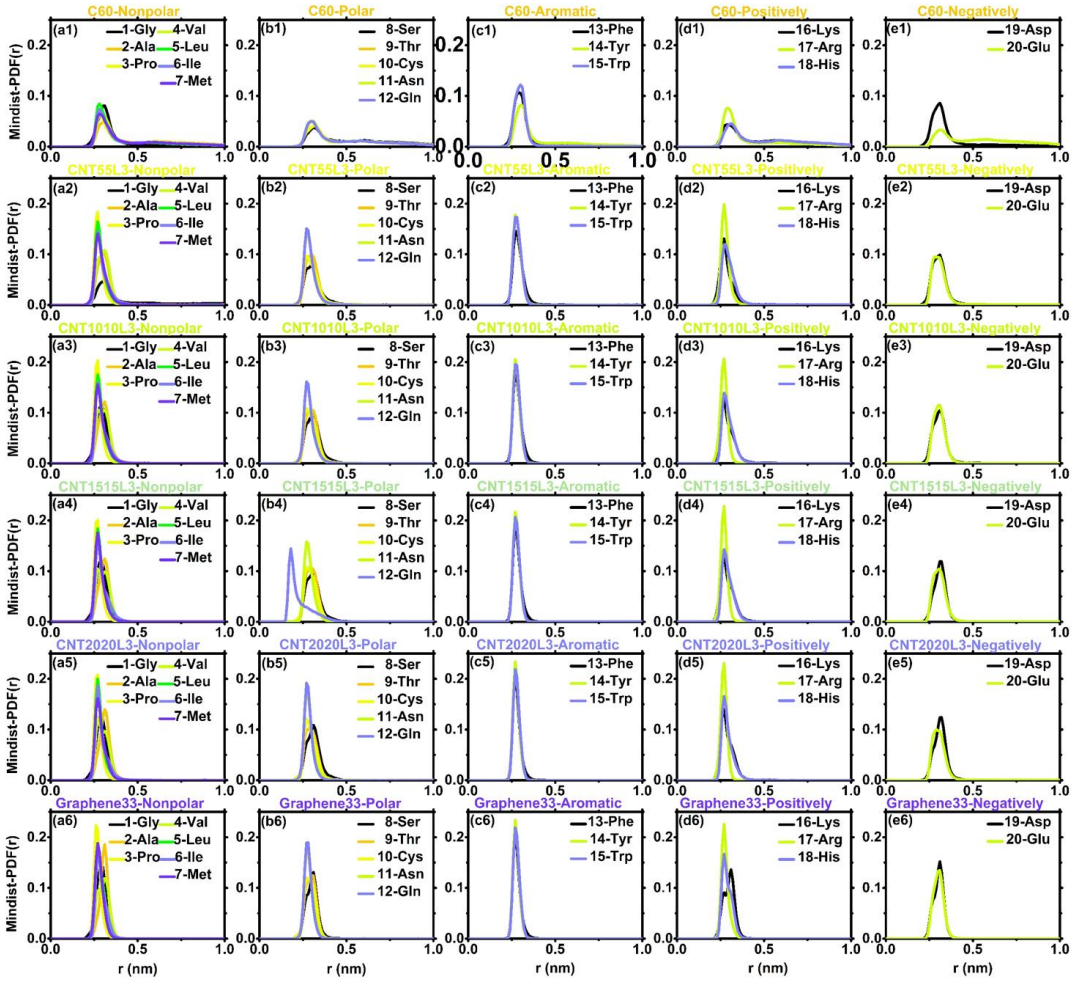


Figure4 The mindist distribution between 20 kinds of amino acids and 6 kinds of carbon-based nanoparticles. Numbers 1-6 are each group of amino acids and 6 kinds of carbon-based nanoparticles 1-C60, 2-CNT55L3, 3 -CNT1010L3, 4-CNT1515L3, 5-CNT2020L3, 6-Graphene33, the amino acid groups are: (a1)-(a6) are non-polar amino acid group, the black line is 1-Gly, the orange line It is 2-Ala, the yellow line is 3-Pro, the light green line is 4-Val, the bright green line is 5-Leu, the blue line is 6-Ile, and the purple line is 7-Met; (b1)-(b6) is Polar amino acid group, the black line is 8-Ser, the orange line is 9-Thr, the yellow line is 10-Cys, the light green line is 11-Asn, and the blue line is 12-Glu; (c1)-(c6) is the Aromatic amino acid group, the black line is 13-Phe, the light green line is 14-Tyr, the blue line is 15-Trp; (d1)-(d6) is the positive Positively charged amino acid group, the black line is 16-Lys, light green line is 17-Arg, the blue line is 18-His; (e1)-(e6) are negatively charged amino acid group, The black line is 19-Asp, and the light green line is 20-Glu.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

We will analyze the statistical distribution from the data that the minimum distance changes over time. This research step is very necessary because, in Mindist data, some data smaller than 0.3 nm are actually in dynamic changes. As shown in Figure4, we can macroscopically observe the adsorption relationship between each group of amino acids and CBNs. Among them, the adsorption effect of aromatic amino acids and CBNs is the best, and their First-peak can be greater than 0.225, while the first-peak of negatively charged amino acids hovers around 0.1, and the overall is less than 0.15. Non-polar amino acids have different adsorption strengths from CBNs according to their side chains and chain lengths; polar non-charged amino acids have different internals, but the overall adsorption strength is lower than non-polar amino acids; The strongest positively charged amino acids is comparable to aromatic amino acids; But the overall adsorption strength of negatively charged amino acids is weak.

（b）The adsorption between CBNs and 20 amino acids

(1) **The average adsorption strength.** Figure 2B shows the average adsorption strength of 20 amino acids for 6 kinds of CBNs. We will calculate the First-peak minimum distance distribution of the CBNs obtained from Figure 4 on the 20 amino acids, that is, the amino acids corresponding to the same CBNs are added and averaged. As a result, we are pleased to observe from Figure 2B that as the curvature of CBNs becomes smaller, the adsorption strength of carbon-based nanoparticles for 20 amino acids has an obvious upward trend. This also shows that Average-mindist-distribution-First-peak can well describe the influence of CBNs curvature changes on the adsorption strength of 20 amino acids. In other words, the surface curvature of carbon-based nanoparticles has an obvious effect on the adsorption between them and amino acids.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

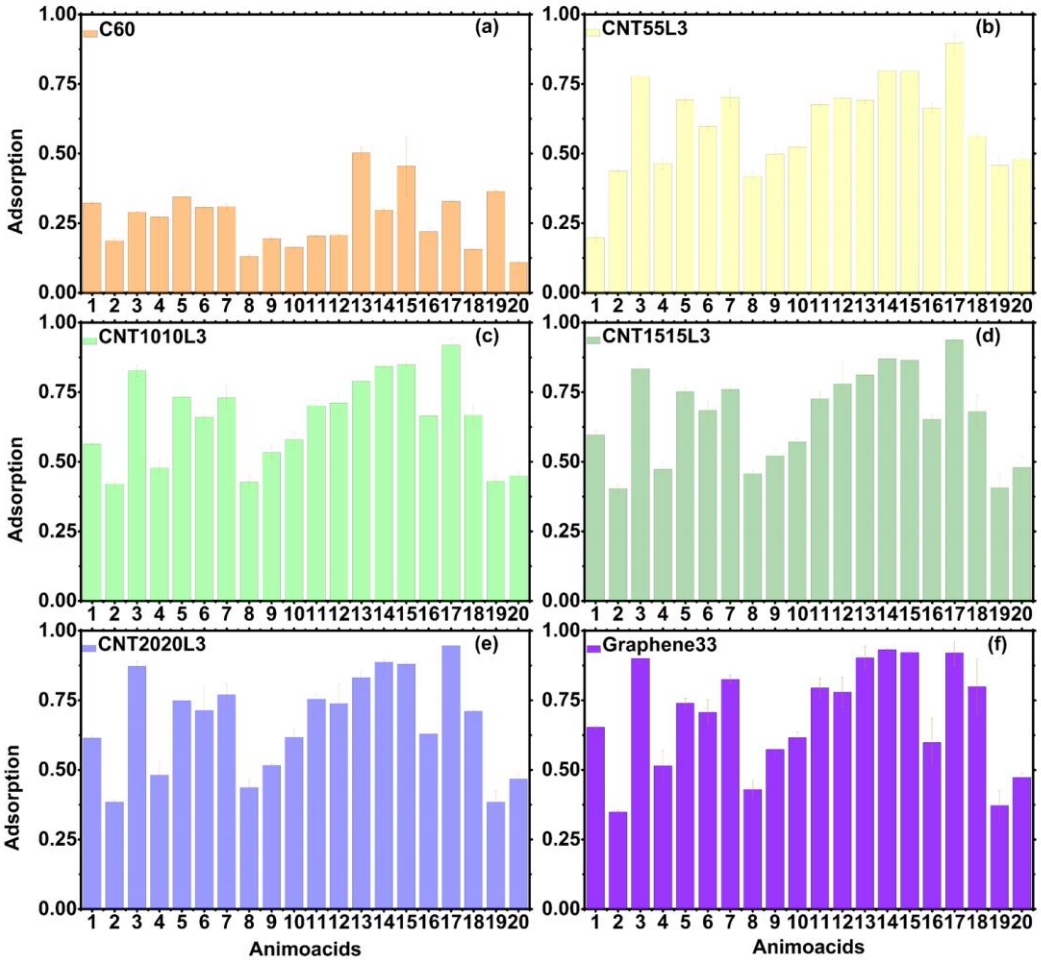


Figure5 The statistics of the adsorption distance of various carbon-based nanoparticles for 20 amino acids less than 0.3nm: (a) the average adsorption statistics of 20 amino acids by C60. (b) the average adsorption statistics of 20 amino acids by CNT55L3, (c) the average adsorption statistics of 20 amino acids by CNT1010L3. (d) the average adsorption statistics of 20 amino acids by CNT1515L3. (e) the average adsorption statistics of 20 amino acids by CNT2020L3, and (f) the average adsorption statistics of 20 amino acids by Graphene33 Adsorption statistics.

(2) **The adsorption strength with 0.3 nm.** In Figure 5, we tried to count the changes in the overall adsorption strength of different amino acids when the minimum distance between CBNs and 20 amino acids was less than 0.3nm. We ranked each group of amino acids. Among them, we set different color settings for the adsorption statistics of different carbon-based nanoparticles. We can see that, as shown in Figure 5, the adsorption strength between the black C60 and each amino acid is the lowest overall, while the other groups have little difference. Among them, the order of the Nonpola part in Figure5-b(c)(d)(e) part is the same, all of which are 2-Ala, 4-Val, 6-Ile, 5-Leu,

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

7-Met, and 3-Pro. But it seems that this classic statistical method does not have too many regular results for the adsorption of individual amino acids to carbon-based nanoparticles. However, it is worth mentioning that 3-Pro, a “benzene-like” amino acid, shows excellent adsorption capacity with CBNs.

（c）The multi-dimensional cluster analysis

We hope to characterize the influence of 20 amino acids on the curvature changes of CBNs through machine learning multi-dimensional cluster analysis. The multi-dimensional cluster analysis is shown in Figure 6, the horizontal axis represents the curvature of CBNs, and the vertical axis represents the Mindist-distribution-first-peak of amino acids.

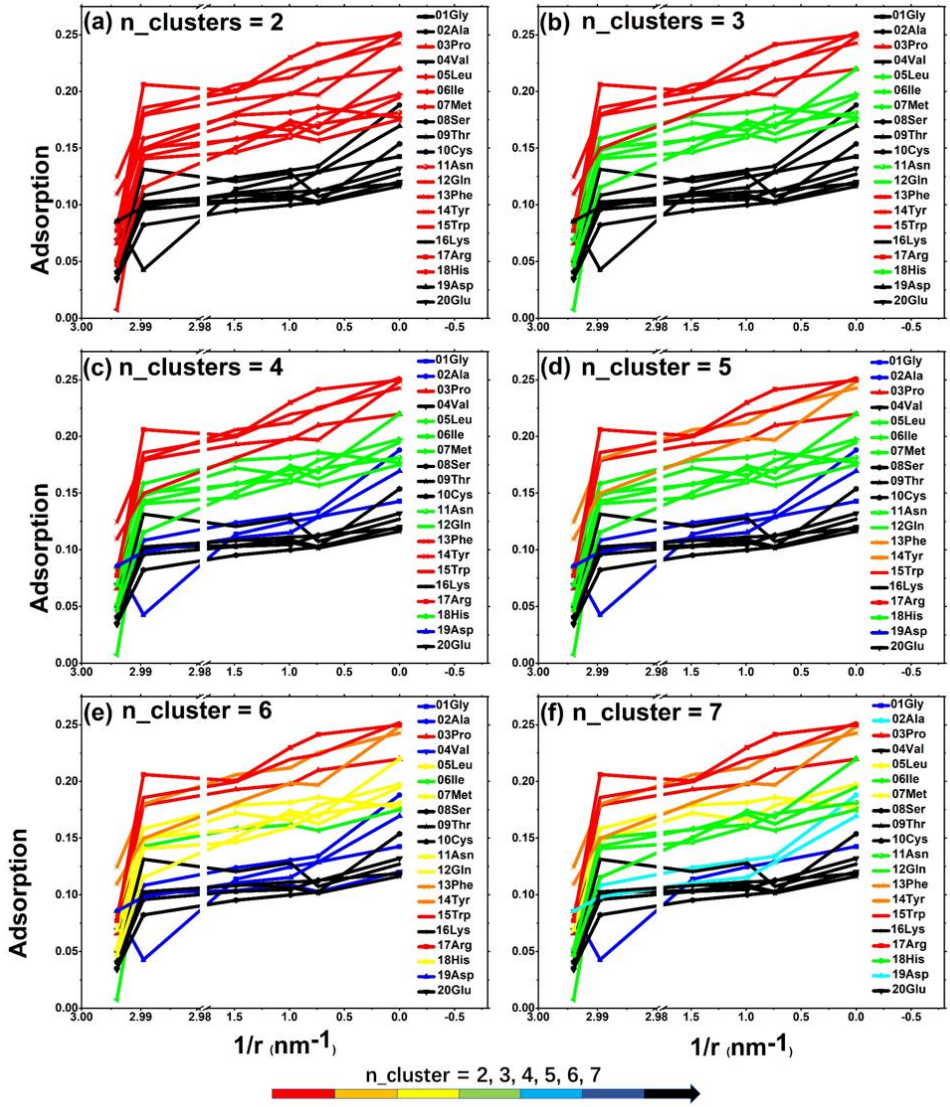


Figure6 Multi-dimensional clustering analysis (the horizontal axis of this group of

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 November 2021 doi:10.20944/preprints202111.0406.v1

graphs is the curvature corresponding to the 6 types of carbon-based nanoparticles), clustering the peak distribution peaks of the 20 amino acids to the nearest distance of the carbon-based nanoparticles: (a) n_cluster=2; (b)) n_cluster=3; (c) n_cluster=4; (d) n_cluster=5; (e) n_cluster=6; (f) n_cluster=7. The colors of the lines with cluster scores from high to low are a red dotted line, orange dotted line, yellow dotted line, green dotted line, bright blue dotted line, dark blue dotted line, and black dotted line.

Our research separately counts the situation when n_cluster=2,3,4,5,6,7. For example, in the process of changing from red to black in Figure 6 (a), the clustering value decreases successively. When n_cluster=2, the amino acids in the upper region include: special hydrophobic amino acid 03-Pro, long-chain hydrophobic amino acid 05-Leu, 06-Ile, 07-Met; long-chain uncharged amino acid 11-Asn, 12-Glu; all aromatic Group of amino acids 13-Phe, 14-Tyr, 15-Trp; partially positively charged amino acids 17-Arg, 18-His. When n_cluster=3, as shown in Figure6(b), long-chain hydrophobic amino acids (05-Leu, 06-Ile, 07-Met) and long-chain uncharged amino acids (11-Asn, 12-Glu) fall out of the first echelon. When n_cluster=4, the first echelon remains unchanged, and the lower zone begins to split. When n_cluster=4, as shown in Figure6(c), the median region begins to change. The first echelon of the upper region is the red special hydrophobic amino acid 03-Pro, the long-chain aromatic amino acid 15-Trp, and the positively charged amino acid 17-Arg. The second echelon of the upper region is the orange aromatic amino acid 13-Phe, 14-Tyr. Next, when n_cluster=5, 6, 7, as shown in Figure6(d)(e)(f), no matter which region the amino acid arrangement is changed, the first and second echelon of the upper region remain unchanged. The first echelon of the upper region is the red special hydrophobic amino acid 03-Pro, the long-chain aromatic amino acid 15-Trp, the positively charged amino acid 17-Arg, and the second echelon of the upper region is the orange aromatic amino acid 13-Phe,14-Tyr.

In other words, the special hydrophobic amino acid 03-Pro, the long-chain aromatic amino acid 15-Trp, and the positively charged amino acid 17-Arg are far ahead of the adsorption capacity of these three amino acids on carbon-based nanoparticles; the remaining two aromatic amino acids The adsorption effect of 13-Phe and 14-Tyr is better than that of other amino acids.

3 Summary and outlook

We studied the interactions between six representative carbon-based nanoparticles

(CBNs) and 20 amino acids through all-atom molecular dynamics simulations. Constructed 120 molecular systems (6CBNs×20Aminoacids), studied the interactions between 6 carbon-based nanoparticles and 20 amino acids in aqueous solutions, and performed 3 repeated simulation studies for each research system, totaling more than 360 Simulate research trajectories, each trajectory 200ns, trying to objectively statistical research from the all-atom level.

We have observed that as the curvature of carbon-based nanoparticles decreases, the adsorption effect of 20 amino acids with them is getting better and better. In addition, we also used multi-dimensional clustering to analyze the adsorption effects of 20 amino acids on six carbon-based nanoparticles. We observed that the π-π interaction plays an extremely important role in the adsorption of amino acids on carbon-based nanoparticles. Individual long-chain amino acids also have a strong adsorption effect with carbon-based nanoparticles. Specifically, the special hydrophobic amino acid 03-Pro, the long-chain aromatic amino acid 15-Trp, and the positively charged amino acid 17-Arg, these three amino acids are far ahead in the adsorption capacity of carbon-based nanoparticles; the remaining two aromatic amino acids The adsorption effect of 13-Phe and 14-Tyr is better than that of other amino acids. The regular adsorption effect between CBNs and amino acids can also bring certain inspiration to the new generation of nano-biocomputers.

In addition, this research work as a full-atom simulation of carbon-based nanoparticles and 20 kinds of amino acids has laid a solid simulation data foundation for further multi-scale coarse-grained force field extraction.

Acknowledgement:

Support from the National Natural Science Foundation of China (Grants No. 11647082 and No. 11774311) is gratefully acknowledged. Wangying Huang would like to thank Professor Guanghong Zuo and Dr. ZhengYu Wang for helpful discussions.

References

[1] D. R. Bell, J. K. Weber, W. Yin, T. Huynh, W. Duan, and R. Zhou, In silico design and validation of high-affinity RNA aptamers targeting epithelial cellular adhesion molecule dimers, PNAS, 117, 8486-8493 (2020).

[2] S. Liu, X.-Y. Meng, J. M. Perez-Aguilar, and R. Zhou, An In Silico study of TiO2 nanoparticles interaction with twenty standard amino acids in aqueous solution, Scientific Reports, 6, 37761 (2016).
[3] Y. Cheng, D. Li, B. Ji, X. Shi, and H. Gao, Structure-based design of carbon nanotubes as HIV-1 protease inhibitors: atomistic and coarse-grained simulations, J Mol Graph Model, 29, 171-7 (2010).
[4] C. Rajesh, C. Majumder, H. Mizuseki, and Y. Kawazoe, A theoretical study on the interaction of aromatic amino acids with graphene and single walled carbon nanotube, J Chem Phys, 130, 124911 (2009).
[5] G. Zuo, S.-G. Kang, P. Xiu, Y. Zhao, and R. Zhou, Interactions Between Proteins and Carbon-Based Nanoparticles: Exploring the Origin of Nanotoxicity at the Molecular Level, small, 9, 1546-1556 (2013).
[6] D. An, J. Su, J. K. Weber, X. Gao, R. Zhou, and J. Li, A Peptide-Coated Gold Nanocluster Exhibits Unique Behavior in Protein Activity Inhibition, J Am Chem Soc, 137, 8412-8 (2015).
[7] Z. He and R. Zhou, Exploring an In-Plane Graphene and Hexagonal Boron Nitride Array for Separation of Single Nucleotides, ACS Nano, 15 (7), 11704-11710(2021).
[8] V. Georgakilas, N. Tagmatarchis, D. Pantarotto, A. Bianco, J.-P. Briand, and M. Prato, Amino acid functionalisation of water soluble carbon nanotubes, Chemical Communications, 3050-3051 (2002).
[9] L. Piao, Q. Liu, and Y. Li, Interaction of Amino Acids and Single-Wall Carbon Nanotubes, The Journal of Physical Chemistry C, 116, 1724-1731 (2012).
[10] T. Roman, W. A. Diño, H. Nakanishi, and H. Kasai, Amino acid adsorption on single-walled carbon nanotubes, The European Physical Journal D, 38, 117-120 (2006).
[11] Z. Yang, Z. Wang, X. Tian, P. Xiu, and R. Zhou, Amino acid analogues bind to carbon nanotube via pi-pi interactions: comparison of molecular mechanical and quantum mechanical calculations, J Chem Phys, 136, 025103 (2012).
[12] K. M. Zhengding Su, Elisabeth Daub, Tong Leung, and John Honek, Single-Walled Carbon Nanotube Binding Peptides: Probing Tryptophan's Importance by Unnatural Amino Acid Substitution, J. Phys. Chem. B, 111, 14411-14417 (2007).
[13] D. Y. a. L. Dai, Self-Assembled Graphene/Carbon Nanotube Hybrid Films for Supercapacitors, J. Phys. Chem. Lett, 1, 467–470 (2010).
[14] Z. He and J. Zhou, Probing carbon nanotube–amino acid interactions in aqueous solution with molecular dynamics simulations, Carbon, 78, 500-509 (2014).
[15] L. S. Nechaeva, E. V. Butyrskaya, and S. A. Zapryagaev, Computer simulation of amino acid sorption on carbon nanotubes, Journal of Structural Chemistry, 58, 217-225 (2017).
[16] D. P. Viviana Lovat, † Laura Lagostena,†,‡ Barbara Cacciari,§ Micaela Grandolfo,| Massimo Righi,| Giampiero Spalluto,†,⊥ Maurizio Prato,*,†,⊥ and Laura Ballerini*,‡,|, Carbon Nanotube Substrates Boost Neuronal Electrical Signaling, Nano Lett, Vol.5, No.6, 1107-1110 (2005).
[17] J. Wang, Carbon-Nanotube Based Electrochemical Biosensors: A Review, Electroanalysis, 17, 7-14 (2005).
[18] C. E. B. Ryan R. Moore, And Richard G. Compton, Basal Plane Pyrolytic Graphite Modified Electrodes: Comparison of Carbon Nanotubes and Graphite Powder as Electrocatalysts, Anal. Chem. 76, 2677-2682 (2004).
[19] W. Li, J. Wang, J. Zhang, S. Takada, and W. Wang, Overcoming the Bottleneck of the Enzymatic

Cycle by Steric Frustration, Physical Review Letters, 122, 238102 (2019).
[20] H. Zorgati, M. Larsson, W. Ren, A. Y. L. Sim, J. Gettemans, J. M. Grimes, W. Li, and R. C. Robinson, The role of gelsolin domain 3 in familial amyloidosis, PNAS, 116, 13958-13963 (2019).
[21] J. Kong, J. Li, J. Lu, W. Li, and W. Wang, Role of substrate-product frustration on enzyme functional dynamics, Physical Review E, 100, 052409 (2019).
[22] R. G. Huber, J. K. Marzinek, D. A. Holdbrook, and P. J. Bond, Multiscale molecular dynamics simulation approaches to the structure and dynamics of viruses, Prog Biophys Mol Biol, 128, 121-132(2017).
[23] R. P. Deo, N. S. Lawrence, and J. Wang, Electrochemical detection of amino acids at carbon nanotube and nickel-carbon nanotube modified electrodes, Analyst, 129, 1076-81 (2004).
[24] A. Bianco, K. Kostarelos, and M. Prato, Applications of carbon nanotubes in drug delivery, Curr Opin Chem Biol, 9, 674-9 (2005).
[25] R. D. Lins and P. H. Hunenberger, A new GROMOS force field for hexopyranose-based carbohydrates, J Comput Chem, 26, 1400-12 (2005).
[26] P. H. H. Walter R. P. Scott and W. F. V. Gunsteren*, The GROMOS Biomolecular Simulation Program Package, J. Phys. Chem. A, 103, 3596-3607 (1999).
[27] D. Chandler, Introduction to Modern Statistical Mechanics, OXFORD UNIVERSITY PRESS, (1944).