Materials Research Express

PAPER

Biocompatibility of 2D silicon nitride: interaction at the nano-bio interface

Ashkan Shekaari and Mahmoud Jafari

Department of Physics, K. N. Toosi University of Technology, Tehran, 15875-4416, Iran

E-mail: shekaari@email.kntu.ac.ir and jafari@kntu.ac.ir

Abstract

Determining potential abilities of nanostructures to induce toxicity to biological molecules is still a convoluted challenge in the realm of nanomedicine. Based on the unprecedented achievements of two-dimensional nanomaterials in nearly all areas of applied sciences particularly medicine, we carried out all-atom molecular dynamics simulations to assess the biologically important, yet unmapped issue of biocompatibility of 2D, hexagonal $\beta$-Si$_3$N$_4$ nanosheet via investigating its possible cross interactions with both human serum albumin (HSA) and p53 tumor suppressor. Examining the conventional MD indicators in presence and absence of the monolayer revealed that hexagonal Si$_3$N$_4$ nanosheet weakly binds to these two proteins without inducing any important, dramatic change to their secondary structures, revealing accordingly the biological compatibility of the monolayer in case it is released as therapeutics or carriers in vivo. This finding was also broadly supported by the related time-dependent behaviors of the protein-monolayer as well as the protein-water interaction energies.

1. Introduction

The stupendous advent of nanoscience and nanotechnology has enabled human being to precisely manipulate matter at one of the deepest levels of reality, the nanoscale, with a pervasive impact on nearly all branches of physical sciences, from materials science, to electronic devices, to biotechnology, leading to the emergence of multifarious interdisciplinary fields at the interface of physics, chemistry, and biology. Among such uncharted territories is nanobiotechnology [1], which has made a categorically great contribution to modern medicine and therefore to the dawn of nanomedicine epoch via adding functionalities to nanomaterials and then by interfacing them with biological structures, aiming at diagnosing, preventing, and treating diseases on molecular scales as well. These nanomaterials, whether as therapeutics or carriers, inevitably interact with biological entities within human body; then one ultimate goal of such so-called nanobiosystems is their in vivo applications [2]. To this end, they must accordingly conquer several intractable challenges, which an important of them is the biocompatibility prerequisite, in the sense that nanobiomaterials should not exhibit any toxic or injurious effect on biological systems (cells, proteins, tissues, etc.). Therefore, in vivo toxicological evaluation of nanomaterials is cardinal for exploiting them in nanomedicine.

As yet, $sp^2$ carbon nanomaterials, particularly fullerenes [3], carbon nanotubes [4], and graphene [5], have excited the ardor of scientists in the area of nanomedicine because they are best suited for drug delivery [6–8], sensing biological targets [9, 10], biomedical imaging [11], and cancer treatment [12]. Novel 2D layered nanomaterials such as MoS$_2$ [13], boron nitride [14], WS$_2$ [15], and graphite-carbon nitride [16] have also captivated many researchers in biosensing and nanomedicine because of their structural similarities to graphene as a paragon of layered nanomaterial. As a result, except silica [17, 18], minimal attention has so far been paid to silicon-based nanomaterials in terms of their potential medicinal applications. Indeed, the macroscopic state of Si$_3$N$_4$ has been proved to be biocompatible and stable in vivo, and such properties, when combined with its phenomenal mechanical features [19–21], make Si$_3$N$_4$ an intriguing ceramic implant material, being truly useful in some healthcare applications, particularly in orthopedic surgery [22].
A recent investigation on Si₃N₄ nanostructures carried out in 2020 [23] has unveiled a new, 2D member of this family, showing the yet-continuing promisingness of silicon nitride materials in the post-graphene age. In the same work, it has been proved that β-Si₃N₄ nanosheets exhibit a semiconducting behavior with a band-gap of about 2 eV. Taking into account the findings that semiconducting MoS₂ [24] or graphene [25] monolayers indeed destabilize amyloid beta fibrils [26], we therefore hypothesized 2D Si₃N₄ may exhibit the same effect based on the structural and electronic similarities. As a result, the present work has been devoted to evaluating the biocompatibility of β-Si₃N₄ monolayers as a first step in testing our hypothesis in case they are released in vivo. We carried out the present investigation via examining possible cross interactions of the monolayer with two specific homo sapiens proteins, namely human serum albumin (HSA)—as the most abundant protein in human blood plasma, constituting about half of the serum protein [27]. We applied all-atom molecular dynamics (MD) simulations, and calculated and examined a number of important conventional MD indicators as described in section 2.

### 2. Computational details

Initial atomic positions of HSA and p53 proteins were taken from RCSB Protein Data Bank (PDB) [28] with entry codes 3B9M and 1TUP, respectively. All the classical MD simulations were carried out by NAMD (version 2.14b2) [29], in parallel, on Debian-style [30] Linux [31] systems using Open MPI v.3.1.6 [32], and with the July 2018 update of CHARMM36 [33, 34] force fields. The VMD program (version 1.9.4a9) [35] was also used for post-processing. The two nanobiosystems including HSA–monolayer and p53–monolayer (abbreviated as HSA-ML-W and p53-ML-W; ML for monolayer and W for water) were then solvated in two boxes of TIP3P [36] water with dimensions 17.8 × 15.5 × 8.7 and 17.8 × 15.5 × 7.5 nm³ respectively, under periodic boundary conditions with a unit-cell padding of about 2 nm to decouple periodic interactions, as illustrated in figure 1.

We also solvated the two proteins in the same water boxes (abbreviated as HSA-W and p53-W) this time without Si₃N₄ monolayer, and accordingly referred to them as the reference (control) trajectories to which the results of HSA-ML-W and p53-ML-W simulations were compared, respectively. Na⁺ and Cl⁻ ions were randomly distributed (replaced by the same number of water molecules) in order for the entire systems to be electrostatically neutral, as tabulated in table 1.

The switching and cutoff distances of 1.0 and 1.2 nm were also used for truncating non-bonded van der Waals interactions, respectively. Particle-mesh Ewald (PME) [37] with grid dimensions 180 × 160 × 88 and

![Figure 1. The simulated nanobiosystems including (a) HSA-ML-W, and (b) p53-ML-W—rendered in VMD using Tachyon parallel/multiprocessor ray tracing system. The α-helices, β-strands, and random coils/turns have been shown in pink, yellow, and cyan/white, respectively.](image)

### Table 1. The number of ions added to the systems for making them electrostatically neutral, as well as the net charge values before and after neutralization. Each ion was replaced by one water molecule.

| System     | Number of ions added | Net charge (e) | Number of water molecules removed |
|------------|----------------------|----------------|----------------------------------|
|            | Na⁺  | Cl⁻  | Before | After                |                                |
| HSA-W      | 14   | 0    | −14    | 8.4 × 10⁻⁶  | 14                              |
| HSA-ML-W   | 14   | 0    | −14    | 4.6 × 10⁻⁴  | 14                              |
| p53-W      | 0    | 3    | +3     | 2.0 × 10⁻⁶  | 3                               |
| p53-ML-W   | 0    | 3    | +3     | 3.7 × 10⁻⁴  | 3                               |

A recent investigation on Si₃N₄ nanostructures carried out in 2020 [23] has unveiled a new, 2D member of this family, showing the yet-continuing promisingness of silicon nitride materials in the post-graphene age. In the same work, it has been proved that β-Si₃N₄ nanosheets exhibit a semiconducting behavior with a band-gap of about 2 eV. Taking into account the findings that semiconducting MoS₂ [24] or graphene [25] monolayers indeed destabilize amyloid beta fibrils [26], we therefore hypothesized 2D Si₃N₄ may exhibit the same effect based on the structural and electronic similarities. As a result, the present work has been devoted to evaluating the biocompatibility of β-Si₃N₄ monolayers as a first step in testing our hypothesis in case they are released in vivo. We carried out the present investigation via examining possible cross interactions of the monolayer with two specific homo sapiens proteins, namely human serum albumin (HSA)—as the most abundant protein in human blood plasma, constituting about half of the serum protein—and the p53 tumor suppressor protein known as the guardian of the genome due to its role in conserving genome stability by preventing mutations [27]. We applied all-atom molecular dynamics (MD) simulations, and calculated and examined a number of important conventional MD indicators as described in section 2.
of a was also calculated using Murnaghan isothermal equation of state to produce the 2D structure, as shown in Figure 2. The purple parallelogram is the associated unit cell, containing six Si and eight N atoms in a hexagonal Bravais lattice.

180 × 160 × 80 were respectively applied to systems containing HSA and p53 for long-range interactions. Four minimization simulations corresponding to HSA-ML-W, p53-ML-W, HSA-W, and p53-W were carried out, each for 400 000 conjugate-gradient steps (0.4 ns). The next four MD simulations were carried out, each for 50 ns, with integration time-step 1 ns within the NPT ensemble at 310 K and 1.013 25 bar using Langevin forces with damping constant of 2.5/ps along with the Nosé-Hoover Langevin piston pressure control. For systems without the silicon nitride monolayer (namely, HSA-W and p53-W), the dielectric constant was set to 1. The hydrogen donor-acceptor distance and the angle cutoff have been respectively set to 3 Å and 20° to identify hydrogen bonds. Solvent-accessible surface area (SASA) was calculated for each system using the rolling-ball algorithm with radius 1.4 Å for probe sphere. To further check whether stable nano–bio complexes are made, the interaction energy between protein–monolayer as well as protein–water in both presence and absence of the monolayer, were also calculated as functions of time for each protein using

\[ E_{\text{int}} = \sum_{i>j} \frac{q_i q_j}{\epsilon r_{ij}} + \sum_{i>j} 4\epsilon q_i \left( \frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left( \frac{\sigma_{ij}}{r_{ij}} \right)^6, \]

where \( q \) is atomic charge, \( \epsilon \) is permittivity, \( r_{ij} \) is the distance between atoms \( i \) and \( j \), and \( \sigma_{ij} \) and \( \epsilon_{ij} \) are also the associated Lennard-Jones parameters.

3. Force field of β-Si3N4 nanosheet

The initial force field describing bulk phase of β-Si3N4 was constructed using the values provided by Wendel et al [40]. The force field associated to 2D Si3N4 was then obtained via calibrating that of the bulk phase in a way that the molecular–mechanical dielectric constant of the monolayer obtained by NAMD was fitted to its quantum-mechanical analogue (namely, \( \kappa \approx 2.37 \) calculated using QUANTUM ESPRESSO [41]). To this end, we adopted a self-consistent [42], plane-wave, pseudopotential approach [43] at PBE-GGA [44] level of density-functional theory (DFT) [45]. Scalar-relativistic ultrasoft pseudopotentials [46, 47] (Si. pbe-n-rrkjus_psl.1.0.0.UPF and N. pbe-n-rrkjus_psl.1.0.0.UPF [48]) generated by Rappe-Rabe-Kaxiras-Joannopoulos (RRKJ) [49] pseudization method with nonlinear core correction [50] were used to model core electrons. The valence shells of N and Si atomic species were also described by 2s2p and 3s3p orbitals, respectively. The pseudo-wavefunctions and charge density were expanded in a plane-wave basis set with kinetic energy cutoff values 90 and 360 Rydberg (Ry) respectively, for which energy convergence was optimally achieved. We started from the β-Si3N4 primitive cell of bulk phase containing 6 silicon and 8 nitrogen atoms in a hexagonal Bravais lattice under periodic boundary conditions with experimental lattice constant \( a_0 = 7.82 \) Å, and then applied a vacuum space of >15 Å along \( z \) to produce the 2D structure, as shown in Figure 2. The equilibrium (zero-pressure) lattice constant of the nanosheet was also calculated using Murnaghan isothermal equation of state [51, 52], leading to theoretical, PBE-GGA value of \( a = 8.262 \) Å, which is about 5.63% larger than that of bulk phase (\( a_0 \)).

We carried out four density-functional molecular dynamics (DFMD) simulations including one minimization and one finite-temperature free-dynamics simulation at 310 K within the Car-Parrinello (CP)
approach for each zero-field \( (E_1 = 0) \) and nonzero-field \( [E_2 = 16 \text{ kcal/(mol.Å.e})] \) setup—the electric field was applied, along +z, to change the dipole moment \( (\rho) \) of the monolayer. Each finite-temperature simulation was preceded by an electronic minimization to bring electronic wavefunctions on their ground states relative to starting atomic configurations. The two setups \( (E_1 \text{ and } E_2) \) were minimized after 100 damped-dynamics steps \( (0.012 \text{ ps}) \) with time-step \( \Delta t = 0.12 \text{ fs} \), and with electron damping value of 0.1 \( (=\text{damping frequency times } \Delta t) \). The fictitious electron mass in CP Lagrangian \[ 54 \] was set to 1000 a.u. \( (1000 \text{ times rest mass of electron}) \) to guarantee the validity of adiabatic approximation \[ 55 \]; the mass cutoff of 2.5 Ry was also chosen for Fourier acceleration effective mass to keep the quality of simulations from being adversely affected, as well as to minimize electron drag effect. These four DFMD simulations were all started from the same minimized structure in terms of ionic degrees of freedom, in that the value of total force exerted on each atom was \( < 10^{-4} \text{ eV/Å} \). The propagation time was chosen about 0.36 ps \( (3000 \text{ Verlet steps}) \). Electronic equations of motion were also accelerated using a preconditioning scheme \[ 56 \]. We ignored at least the first 0.12 ps \( (1000 \text{ steps}) \) of the simulations for thermalization and reliable statistical averaging. Both electronic and ionic contributions were taken into account in estimating the average value of total dipole moment. The dielectric constant was also calculated using

\[
\kappa = 1 + \frac{\Delta \rho}{\epsilon_0 E \Omega}.
\]
where \( \Delta p = | p_{E_1} - p_{E_2} |, \epsilon_0 = 2.398 \times 10^{-4} \text{mol.e}^2/(\text{kcal.Å}) \) is vacuum permittivity, and \( \Omega \) is volume of the monolayer.

4. Results and discussion

Figure 3 illustrates RMSD, gyration radius, per-residue RMSF, number of internal hydrogen bonds, and SASA calculated for HSA in both presence and absence of the Si\(_3\)N\(_4\) monolayer in a contrasting fashion.

From figure 3(a), it is seen that the HSA structure has remained stable during the simulations with all-atom RMSDs of \(<0.5\) and \(0.6\) nm from the reference crystal structure (3B9M) respectively on interaction with the monolayer (HSA-ML-W) and in aqueous solely (HSA-W). The RMSD of HSA-ML-W also takes smaller values compared to the other over the last 35 ns, demonstrating that interaction with Si\(_3\)N\(_4\) nanosheet considerably reduces thermal fluctuations of HSA due to binding to the nanosheet, and accordingly decreases the protein’s conformational change more than that of HSA-W.

Time dependence of radius of gyration illustrated in figure 3(b) also reveals the fact that the overall structural compactness of HSA on interaction with the monolayer is slightly (by \(~1.0\) Å) smaller than those of HSA-W or the initial crystal structure. Per-residue RMSFs (figure 3(c)) averaged over all frames further indicate that interaction with the nanosheet considerably decreases the flexibility of all regions of HSA, and therefore makes its secondary structure resistant to any change raised by thermal fluctuations in aqueous. Consistently, the number of hydrogen bonds within the protein in both HSA-W and HSA-ML-W (figure 3(d)) exhibit no remarkable change over the entire trajectory compared to each other. More precisely, the number of hydrogen bonds averaged over the last 45 ns is about 147 for HSA-W and 139 for HSA-ML-W, indicating a decrease as negligible as 5.5% on interaction with the monolayer. The calculated SASAs (figure 3(e)) over the last 40 ns of the two trajectories also show convergence in a way that HSA-ML-W takes larger values compared to HSA-W on average, in agreement with gyration radius (figure 3(b)). As a result, HSA strongly binds onto the surface of Si\(_3\)N\(_4\) monolayer, forming a stable complex.

The secondary structure of HSA as a function of time has also been presented in figure 4 in both presence and absence of the silicon nitride monolayer.

Consistent with the previous analyses, no dramatic change is accordingly observed, and the \(\alpha\)-helix-rich structure of HSA (figure 1(a)) is clearly preserved on interaction with the monolayer.

Examining the corresponding Ramachandran plots also confirms the preceding observations as illustrated in figure 5.

As is seen, the distributions of dihedral angles (dominantly on the right-handed \(\alpha\)-helix region) over different areas are nearly the same for both HSA-W and HSA-ML-W at \(t = 0\) and 50 ns. The distributions associated to HSA-W and HSA-ML-W at \(t = 50\) ns are also nearly the same, indicating that the secondary structure of HSA remains intact on interaction with 2D Si\(_3\)N\(_4\) nanostructure, in agreement with the previous observations.
Similar findings were obtained for p53. Comparing the associated all-atom RMSD curves in the absence and presence of the silicon nitride nanosheet (figure 6(a)) indicates that the related secondary structure also remains unchanged during the last 40 ns, with values of about 0.25 and 0.3 nm for p53-ML-W and p53-W, respectively.

That the RMSD of p53-ML-W takes smaller values over the entire time-span reveals that interaction with 2D Si$_3$N$_4$ dramatically decreases fluctuations of the protein caused by thermal energy; therefore, abates the tendency toward any conformational change.

Examining the time dependence of radius of gyration (figure 6(b)) further indicates that the overall structural compactness of p53 in both presence and absence of the monolayer are nearly the same over the entire trajectory. The fluctuating RMSF curves, illustrated in figure 6(c), show a considerable decrease in their average values by $\sim 0.7$ nm, and therefore in the overall flexibility of the protein on interaction with the monolayer. The peak in the middle (at residue 209) of the p53-ML-W curve is for arginine residue, which exhibits a high degree of flexibility at this point based on the fact that it is located on a Turn secondary structure with a distance of about 2.8 nm from the monolayer, indicating no effective binding between them as well.

Interaction with Si$_3$N$_4$ nanosheet has also no (significant) impact on the number of hydrogen bonds within p53, and consequently on the secondary structure of p53 as seen in figure 6(d)—average values of number of hydrogen bonds over the last 45 ns are 47 for p53-W and 49 for p53-ML-W, indicating an increase as small as 3.9% on interaction with the monolayer.

The SASA curves (figure 6(e)) in the presence and absence of the monolayer show nearly the same converging patterns over the last 40 ns of the trajectories. Nonetheless, a negligible difference between the two

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure5.png}
\caption{The Ramachandran plots obtained for HSA-W and HSA-ML-W at $t = 0$ ((a) and (c)) and $t = 50$ ns ((b) and (d)), respectively. The white, red, and blue areas are respectively the sterically-disallowed region for amino acids, the allowed regions corresponding to the helix and extended conformations, and the outer limit regions. The cyan points also indicate the distribution of dihedral angle values of each residue in $\phi - \psi$ space.}
\end{figure}
Figure 6. The calculated RMSD (a), radius of gyration (b), per-residue RMSF (c), number of hydrogen bonds (d), and SASA (e) for p53 in absence (p53-W, red) and presence (p53-ML-W, blue) of the monolayer.

Figure 7. Secondary structure of p53 in (a) water (p53-W), and (b) on interaction with the Si₃N₄ monolayer (p53-ML-W), showing no significant discrepancy, consistent with the previous analysis. All the secondary structures, particularly α-helix, Extended, and Turn, have remained relatively intact in absence and presence of the nanosheet.
Figure 8. The Ramachandran plots for p53-W and p53-ML-W at $t=0$ (a) and (c) and $t=50$ ns (b) and (d).

Figure 9. Time dependence of the interaction energy calculated for protein-monolayer as well as protein-water in presence and absence of the Si$_3$N$_4$ monolayer for both HSA and p53.
curves could be observed from 18 ns on, with smaller values for that of p53-ML-W consistent with the related RMSD (figure 6(a)) and gyration radius (figure 6(b)). Indeed, such a discrepancy is not so important as to considerably change the secondary structure of the protein.

The secondary structure of p53 has been illustrated in figure 7 in both presence and absence of the silicon nitride monolayer over the entire trajectory.

Nearly the same β-rich patterns is observed in the two subfigures consistent with the tertiary structure of p53 (figure 1(b)), demonstrating a minimal, insignificant change in the related secondary structure on interaction with the monolayer.

The associated Ramachandran plots illustrated in figure 8 are also in agreement with the previous findings. In the same way as HSA but to a higher extent, the distributions of dihedral angles (dominantly on Extended region) over different areas are very close to each other comparing p53-W and p53-ML-W at both $t = 0$ and 50 ns. As a result, no considerable change in the related secondary structure could be observed in case it is in contact with the monolayer.

We finally estimated the time dependence of interaction energy ($E_{int}$) between protein-monolayer on one hand, and protein-water in both presence and absence of the monolayer on the other, as illustrated in figure 9. The average values of $E_{int}$ for p53- and HSA-monolayer are respectively about $-151$ and $-510$ kcal/mol, which are dramatically larger (therefore, weaker bindings) than those of protein-water interactions, showing that these biological proteins do not make stable complexes on interaction with the monolayer. That HSA has the lower value is also an indication of the fact that it is a considerably larger protein compared to p53, which accordingly led to larger SASA values comparing figures 3(e) and 6(e).

Interaction with Si$_3$N$_4$ nanosheet also decreases p53-water binding by about 16.7% from $-3574$ in p53-W to $-2977.7$ kcal/mol in p53-ML-W. In contrast, the presence of monolayer increases HSA-water binding by 1.85% from $-18201.4$ in HSA-W to $-18537.7$ in HSA-ML-W. However, none of these (percent) values is significant so as to dramatically affect the protein-water bindings.

**5. Conclusions**

All-atom molecular dynamics simulations were applied to investigate the biocompatibility of 2D, hexagonal β-Si$_3$N$_4$ monolayer via examining its possible impacts on both HSA (human serum albumin) and p53 anti-tumor protein. We accordingly calculated and examined a number of important MD indicators including RMSD, radius of gyration, per-residue RMSF, number of hydrogen bonds, solvent-accessible surface area, and secondary structure of each protein in a contrasting fashion in both presence and absence of the monolayer. Results verified that the secondary structures of these proteins remain nearly intact on interaction with Si$_3$N$_4$ nanosheet. Examining the associated protein-monolayer and protein-water interaction energies in presence and absence of the monolayer further revealed that these biological proteins do not make stable complexes with the monolayer. The presence of Si$_3$N$_4$ also affected both HSA- and p53-water bindings very marginally. It was accordingly inferred that hexagonal β-Si$_3$N$_4$ nanosheet is indeed a biocompatible material and could then be used as a therapeutic or carrier for in vivo applications.

**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the results reported in this paper.

**ORCID iDs**

Ashkan Shekaari [https://orcid.org/0000-0002-7434-467X](https://orcid.org/0000-0002-7434-467X)

Mahmoud Jafari [https://orcid.org/0000-0001-9706-6572](https://orcid.org/0000-0001-9706-6572)

**References**

[1] Maine E, Thomas V J, Bliemel M, Muriza A and Utterback J 2014 The emergence of the nanobiotechnology industry *Nat. Nanotechnol.* 9 2–5

[2] Scale-Goldsmith M M and Leary I F 2009 Nanobiosystems *WIREs Nanomol. Nanobi.* 1 553–67

[3] Kroto H W, Heath J R, O’Brien S C, Curl R F and Smalley R E 1985 C$_{60}$: Buckminsterfullerene *Nature* 318 162–3

[4] Iijima S 1991 Helical microtubules of graphitic carbon *Nature* 354 56–8

[5] Novoselov K S, Geim A K, Morozov S V, Jiang D, Zhang Y, Dubonos S V, Grigorieva I V and Firsov A A 2004 Electric field effect in atomically thin carbon films *Science* 306 666–9
Shekaari A and Jafari M 2020 Unveiling the thermodynamic properties of two-dimensional MoS2

Chen C et al 2005 Multihydroxylated [GdiC66(OH)2]n nanoparticles: Antineoplastic activity of high efficiency and low toxicity Nano Lett. 510 2050–7

Liang X et al 2010 Metallofullerene nanoparticles circumvent tumor resistance to cisplatin by reactivating endocytosis Proc. Natl. Acad. Sci. USA 107 7449–54

Zakharian T Y, Seryshev A, Stharaman B, Gilbert B E, Knight V and Wilson J L 2005 A fullerene-paclitaxel chemotherapeutic: synthesis, characterization, and study of biological activity in tissue culture J. Am. Chem. Soc. 127 12508–9

Liu Z, Tabakman S, Welsher K and Dai H 2009 Carbon nanotubes in biology and medicine: In vitro and in vivo detection, imaging and drug delivery Nano Res. 2.85–120

Yang W, Ratina P, Ringer S P, Thordarson P, Gooding J I and Braet F 2010 Carbon nanomaterials in biosensors: should you use nanotubes or graphene? Angew. Chem. Int. Ed. Engl. 49 2114–28

Gong H, Peng R and Liu Z 2013 Carbon nanotubes for biomedical imaging: the recent advances Adv. Drug Deliv. Rev. 65 1951–63

Liu Z, Robinson J T, Tabakman S M, Yang K and Dai H 2011 Carbon materials for drug delivery and cancer therapy Mater. Today 14 316–23

Wang G, Xao W-J, Wang J, Lu Q-Q and Xia X-H 2013 Immunobilization and catalytic activity of horseradish peroxidase on molybdenum disulfide nanosheets modified electrode Electrochem. Commun. 35 1146–8

Merlo A, Minapati V R S S, Pandit S and Mijakovic I 2018 Boron nitride nanomaterials: biocompatibility and bio-applications Biomater. Sci. 6 2298–311

Cheng L et al 2014 PEGylated WS2 nanosheets as a multifunctional theranostic agent for in vivo dual-modal CT/photoacoustic imaging guided photothermal therapy Adv. Mater. 26 1886–93

Yang G, Zhu C, Du D, Zhu J and Lin Y 2015 Graphene-like two-dimensional layered nanomaterials: applications in biosensors and nanomedicine Natl. Sci. Rev. 11427–31

Yang L and Cheng J 2015 Silicon nitride for microfluidic nanochannels Appl. Phys. Lett. 101 173701

Chen F, Habblel G, Zhao F R and Jokster J V 2018 Multifunctional nanomedicine with silica: Role of silica in nanoparticles for therapeutic imaging, and drug monitoring J. Colloid Interface Sci. 521 261–79

Riley F L 2000 Silicon nitride and related materials J. Am. Ceram. Soc. 83 243–65

Klemm H 2010 Silicon nitride for high temperature applications J. Am. Ceram. Soc. 93 1501–22

Bocanegra-Bernal M H and Matovic B 2010 Mechanical properties of silicon nitride-based ceramics and its use in structural applications at high temperatures Mater. Sci. Eng. A 527 1314–38

Rahaman M and Xiao W 2018 Silicon nitride bioceramics in healthcare Int. J. Appl. Ceram. Tec. 15 8611–72

Shekaari A and Jafari M 2020 Unveiling the first post-graphene member of silicon nitrides: A novel 2D material Comput. Mater. Sci. 180 109693

Medulla S K, Murugan N A, Subramanian V and Agher H 2019 Destabilization of amyloid fibrils on interaction with MoS2-based nanomaterials RSC Adv. 9 16133–24

Zhang N, Hu X, Guan P, Zeng K and Cheng Y 2019 Adsorption mechanism of amyloid fibrils to graphene nanosheets and their structural destruction J. Phys. Chem. C 123 897–906

Shekaari A and Jafari M 2020 Non-equilibrium thermodynamic properties and internal dynamics of 32-residue beta amyloid fibrils Physica A 537 124873

Read A P and Strachan T 1999 Human Molecular Genetics 2 (New York: Wiley)

The Protein Data Bank (https://pdb.org/)

Phillips J C, Braun R, Wang W, Gumbart J, Tajkhorshid E, Villa E, Chipot C, Skeel R D, Kale L and Schulten K 2005 Scalable molecular dynamics with NAMD J. Comput. Chem. 26 1781–802

Debian homepage (https://debian.org/)

Torvalds L 1999 The Linux edge Commun. ACM 42 38–9

Open MPI homepage (https://open-mpi.org/)

Vanommeslaeghe K et al 2010 CHARMM general force field: A force field for drug-like molecules compatible with the CHARMM all-atom additive biological force fields J. Comput. Chem. 31 671–90

MacKerell A D Jr et al 1998 All-atom empirical molecular modeling and dynamics studies of proteins J. Phys. Chem. B 102 3586–616

Humphrey W, Dalke A and Schulten K 1996 VMD: visual molecular dynamics J. Mol. Graphics 14 33–8

Jorgensen W L, Chandrasekhar J, Madura J D, Impey R W and Klein M L 1983 Comparison of simple potential functions for simulating liquid water J. Chem. Phys. 79 926–35

Darden T, York D and Pedersen L 1993 Particle mesh Ewald: An N log(N) method for Ewald sums in large systems J. Chem. Phys. 98 10089

Lee B and Richards F M 1971 The interpretation of protein structures: estimation of static accessibility J. Mol. Biol. 55 379–400

Shake A and Rupley J A 1973 Environment and exposure to solvent of protein atoms. Lysozyme and insulin J. Mol. Biol. 79 351–71

Wendel J A and Goddard W A 1992 The Hispanic biased force field for silicon nitride ceramics: Predictions of thermodynamic and mechanical properties for α- and β-Si3N4 J. Phys. Chem. 97 5048

Giannozzi P et al 2009 Quantum ESPRESSO: a modular and open-source software project for quantum simulations of materials J. Phys. Condens. Matter 21 395502

Kohn W and Sham L J 1965 Self-consistent equations including exchange and correlation effects Phys. Rev. 140 A1133–8

Pickett W E 1989 Pseudopotential methods in condensed matter applications Comput. Phys. Rep. 9 115–97

Perdew J P, Burke K and Ernzerhof M 1996 Generalized gradient approximation made simple Phys. Rev. Lett. 77 3865

Parr R G and Yang W 1989 Density-Functional Theory of Atoms and Molecules (Oxford, New York: Oxford University Press)

Vanderbilt D 1990 Soft self-consistent pseudopotentials in a generalized eigenvalue formalism Phys. Rev. B 41 7892

Laasonen K, Pasquarello A, Car R, Lee C and Vanderbilt D 1993 Car–Parrinello molecular dynamics with Vanderbilt ultrasoft pseudopotentials Phys. Rev. B 47 10142

Rappe A M, Rabeh K M, Kaxiras E and Joannopoulos J D 1990 Optimized pseudopotentials Phys. Rev. B 41 1227

Louie S G, Froyen S and Cohen M L 1982 Nonlinear ionic pseudopotentials in spin-density-functional calculations Phys. Rev. B 26 1738

Giannozzi P, de Angelis F and Car R 2004 First-principle molecular dynamics with ultrasoft pseudopotentials: parallel implementation and application to extended bioinorganic systems J. Chem. Phys. 120 5903

Murnaghan F D 1944 The compressibility of media under extreme pressures Proc. Natl. Acad. Sci. USA 30 244–7

Shekaari A and Abolhasami M R 2017 First-principles investigation of the thermodynamic properties of two-dimensional MoSe2 Clin. J. Phys. 55 105–14
[53] Kokalj A 1999 XCrySDen—a new program for displaying crystalline structures and electron densities J. Mol. Graph. Model. 17 176–9
[54] Shekaari A and Abolhassani M R 2017 Car–Parrinello molecular dynamics study of the melting behaviors of n-atom (n=6,10) graphene quantum dots Chem. Phys. Lett. 678 177–85
[55] Kohanoff J 2006 Electronic Structure Calculations for Solids and Molecules: Theory and Computational Methods (Cambridge: Cambridge University Press)
[56] Tassone F, Mauri F and Car R 1994 Acceleration schemes for ab initio molecular-dynamics simulations and electronic-structure calculations Phys. Rev. B 50 10561
[57] Gnuplot homepage (http://gnuplot.info/)