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Layer-by-layer assembled MoS₂ thin film as an efficient platform for laser desorption/ionization mass spectrometry analysis of small molecules

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Abstract

A chip-based platform for laser desorption/ionization mass spectrometry (LDI-MS) analysis of small molecules was developed by utilizing layer-by-layer (LBL) assembly of MoS₂ nanoflake and polyallylamine on an arbitrary substrate. The LDI-MS efficiency of small molecules on MoS₂ films increased as a function of LBL assembly cycles until reaching a saturation point. The optimized MoS₂ film exhibit high LDI-MS efficiency, salt tolerance, reusability and uniform ionic signal distributions, and its performance was further enhanced by surface modification with perfluoroalkanes mimicking a clathrate nanostructure.

Graphical Abstract

LBL assembly of liquid phase exfoliated MoS₂ nanoflakes for the fabrication of a chip-based LDI-MS platform.

Introduction

The precise analysis of metabolites with molecular weights less than ~2 kDa is an important goal in chemical biology¹ and pharmaceutical research.² Profiling of metabolites is a direct indicator of the health and phenotypic diversity of living organisms.³ Matrix assisted laser desorption/ionization mass spectrometry (MALDI-MS) is one of the most efficient analytical tools for profiling biomolecules, providing high-throughput analysis of analytes with both high sensitivity and resolution.⁴ However, conventional organic matrices have

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challenges arising from significant interference in the low mass region required for analysis of metabolites such as amino acids, saccharides and fatty acids.⁵

Multiple strategies have been used to create matrix-free laser desorption/ionization mass spectrometry (LDI-MS) platforms that avoid low mass-to-charge (m/z) ratio interferences. Many of the promising systems use metal⁶/semiconductor nanoparticles (NPs)⁷ and carbon nanomaterials.⁸ Use of these nanomaterials overcomes low m/z interferences, but there are several issues that complicate their widespread use, such as the colloidal stability in biological media,^{9,10} formation of ‘sweet spots’ by the coffee ring effect¹¹ and laser-induced decomposition that can lead to the contamination of the mass spectrometer.¹² In this regard, chip-based LDI-MS platforms provide an important alternative to colloidal nanomaterials, with nanostructured silicon,¹³ titanium dioxide,¹⁴ layer-by-layer (LBL) assembled films of NPs^{15,16} and carbon nanomaterials^{17,18} investigated as LDI-MS platforms. Of particular interest, LBL assembly techniques can provide precise fabrication of nanomaterial-based thin films with controllable density, thickness and laser energy absorption capacity that are important parameters to determine the LDI-MS efficiency.^{15–18}

MoS₂, a two-dimensionally layered transition metal dichalcogenides, has been widely employed in material science because of its excellent physicochemical properties, with applications in opto-electronics,¹⁹ catalysis,²⁰ energy storage,²¹ biosensing,²² fluorescence imaging²³ and photothermal therapeutic applications.²⁴ The photothermal conversion properties of MoS₂ directly correspond to one of the requirements of a matrix for the LDI-MS analysis of small molecules. Recently, Xu et al. reported that MoS₂ nanoflakes, prepared by Li intercalation/exfoliation, and the resulting nanocomposites are highly efficient for the LDI-MS analysis of small molecules.²⁵ However, the previous preparation method is challenging and sensitive to environmental conditions, making simplified chip creation problematic for the widespread applications in LDI-MS analyses.

Here, we present the creation and use of MoS₂ thin films as chip-based LDI-MS platforms for the analysis of small molecules. The MoS₂ nanoflakes are prepared by the Na-assisted liquid phase exfoliation in N-methyl-2-pyrrolidone (NMP),²⁶ transferred into water, and then directly used for LDI-MS analysis (Fig. 1). Compared to the previous report,²⁵ this process is simple, safe and less sensitive to environmental conditions. The prepared colloidal MoS₂ nanoflakes exhibited high efficiency for the LDI-MS analysis of small molecules. The MoS₂ nanoflakes were then immobilized on a chemically-functionalized substrate to materialize a chip-based LDI-MS platform.²⁷ The LDI-MS efficiency of [MoS₂ nanoflake]_{*n*} films, where *n* indicates the number of LBL assembly cycles, was optimized with LBL assembly of MoS₂ and polyallylamine hydrochloride (PAAH) by controlling the laser energy absorption capacity of the MoS₂ films (Fig. 1).²⁷ Using this assembly approach, we find that liquid phase exfoliated MoS₂ nanoflakes are highly efficient for LDI-MS analysis of small molecules and can be used to develop a chip-based LDI-MS platform based on LBL assembled [MoS₂ nanoflake]_{*n*} films. In addition, the films provide the potential to further enhancement of LDI efficiency via surface functionalization with perfluorodecanethiol, moderate salt tolerance, uniform ion signals with no sweet-spots, and reusability with almost no contamination of the mass spectrometer.

Experimental

Materials

MoS₂ (<2 μm in the lateral dimension of bare flakes), (3-aminopropyl)triethoxysilane (3-APTES), sodium hydroxide, 1H,1H,2H,2H-Perfluorodecanethiol, PAAH (MW = 15,000), asparagine, cysteine, histidine, glutamic acid, phenylalanine, glutathione, behenic acid, palmitic acid, oleic acid and stearic acid were purchased from Sigma Aldrich and used without purification. Glucose, sorbitol, maltose, sucrose and NMP were purchased from Fisher Scientific.

NaOH-assisted liquid phase exfoliation of MoS₂ nanoflake

5 mg of NaOH was dissolved in 20 mL of NMP. 200 mg of MoS₂ powder was dispersed in NMP solution of NaOH and sonicated by using Auqasnoic 150T (VWR, USA) with 135 W power and 35 kHz frequency for 2 h in an ice bath. The MoS₂ suspension was centrifuged at 4000 RPM to remove large chunks of MoS₂. The supernatant was collected and centrifuged at 14000 RPM to separate the exfoliated MoS₂ nanoflakes. The MoS₂ nanoflakes were washed with NMP 3 times and water 3 times, respectively, and then dispersed in water.

LDI-MS analysis of small molecules with MoS₂ nanoflake

1 μL of 1 mM aqueous solutions of amino acids (asparagine, glutamic acid, histidine and phenylalanine), saccharides (glucose, sorbitol, maltose and sucrose) and fatty acids (behenic acid, palmitic acid, oleic acid and stearic acid) were spotted on the target plate, mixed with 1 μL of the MoS₂ nanoflake suspension (0.5 mg mL⁻¹), and subjected to LDI-MS analysis under both positive and negative ionization modes. For examination of the detectable concentration of each category of small molecules, 1 μL of differently concentrated histidine, sorbitol and stearic acid solutions from 1 mM to 10 nM were spotted on the target plate, mixed with 1 μL of MoS₂ nanoflake suspension, and subjected to LDI-MS analysis under their preferable ionization modes. To obtain survival yield and desorption efficiency, 1 μL of 1 mM methanolic solution of benzylpyridinium salt (BP) was mixed with 1 μL of MoS₂ nanoflake suspension. 1 μL of the mixture was spotted on target plate and subjected to LDI-MS analysis.

Preparation of [MoS₂ nanoflake]₁₋₄ films

The glass substrates were treated in piranha solution (3:1 mixture of concentrated sulfuric acid and 30% hydrogen peroxide, WARNING: Piranha solution is highly corrosive and reactive. Handle with caution) for 30 min at 115 °C, washed with water and ethanol, and dried under a stream of nitrogen. The substrates were immediately immersed in 10 mM toluene solution of 3-APTES for 30 min, sonicated for 2 min in toluene, washed with water and ethanol, and dried under a stream of nitrogen. 3-APTES treated glass substrates were immersed in an MoS₂ nanoflake suspension (1 mg mL⁻¹) for 1 h, washed with water and ethanol and dried under a stream of nitrogen. These [MoS₂ nanoflake]₁ films were used as a starting substrate for LBL assembly process. [MoS₂ nanoflake]₁ films were immersed into PAAH solution (1 mg mL⁻¹, pH 7.4 adjusted by NaOH) for 30 min, washed with water and ethanol and dried under a stream of nitrogen. The PAAH treated MoS₂ nanoflake films were

immersed into the MoS₂ nanoflake suspension. These processes were repeated up to 4 cycles.

LDI-MS analysis of small molecules on [MoS₂ nanoflake]₁₋₄ films

1 nmol of amino acids, saccharides and fatty acids was spotted on [MoS₂ nanoflake]₁₋₄ films and dried under ambient conditions. For examination of the detectable concentration of each category of small molecules, histidine, sorbitol and stearic acid were spotted on the optimized [MoS₂/PAAH]₂ films and dried under ambient conditions. The films were immobilized on a target plate by using conductive double-sided tape and subjected to LDI-MS analysis.

Functionalization of [MoS₂ nanoflake]₃ films and their applications for LDI-MS analysis

[MoS₂ nanoflake]₃ films were immersed in 1 mM ethanolic solution of 1H,1H,2H,2H-Perfluorodecanethiol for 12 h, washed with ethanol and water and dried under a stream of nitrogen. LDI-MS analysis of small molecules on the functionalized and pristine [MoS₂ nanoflake]₃ films was carried out by the same procedure.

Characterization

The size and morphology of MoS₂ nanoflakes were observed using a JEOL 200FX transmission electron microscopy (TEM). The thickness of MoS₂ nanoflake was examined using a DI dimension 3100 atomic force microscopy (AFM). The surface morphology of [MoS₂ nanoflake]₁₋₄ films was analyzed with a FEI Magellan 400 field emission scanning electron microscopy (FE-SEM). UV-vis spectra of MoS₂ nanoflake and [MoS₂ nanoflake]₁₋₄ films were recorded with SpectraMax M2 (Molecular Devices, USA). Contact angle measurements of water on 3-APTES treated substrates and [MoS₂ nanoflake]₁₋₄ films were performed by Phoenix300 (S.E.O., Korea). X-ray photoelectron spectroscopy (XPS) analysis of MoS₂ nanoflake was carried out by using a Quantum 2000 scanning ESCA microprobe (Physical Electronics, USA). All LDI-MS analyses of small molecules with MoS₂ nanoflake and [MoS₂ nanoflake]₁₋₄ films were performed by using a Bruker Autoflex III (Bruker Daltonics, Germany) equipped with a Smartbeam laser (Nd:YAG, 355 nm, 120 μJ, 100 Hz, 50 μm of spot diameter at target plate) in both positive and negative reflection mode. The accelerating voltage was 19 kV, and all spectra were obtained by averaging 500 laser shots with 48 μJ laser power unless otherwise indicated.

Results and discussion

MoS₂ nanoflakes were prepared by liquid-phase exfoliation of MoS₂ powder by 2 h sonication in NMP with assistance of NaOH. This liquid exfoliation process is simple and efficient for producing colloidal MoS₂ nanoflakes on a large scale.²⁵ The exfoliated MoS₂ nanoflakes in NMP were then directly transferred into water by a solvent exchange process, with this suspension stable in water for five months without aggregation. The size and thickness of MoS₂ nanoflakes were around 120 ± 30 nm (Fig. 2a) and 1 – 12 nm, respectively, which corresponds to 1 – 14 layers of MoS₂ sheets (Fig. 2b).²⁵ The average hydrodynamic radius of the MoS₂ nanoflakes was 87 ± 30 nm (Fig. 1c) The zeta potential value of the MoS₂ nanoflakes was -43.0 ± 1 eV. This negative value indicates that the

surface of MoS₂ nanoflakes was oxidized during the liquid phase exfoliation process (For XPS analysis, see Fig. S1 in ESI). The UV-Vis spectrum of MoS₂ nanoflakes exhibited the characteristic absorption peaks of liquid-phase exfoliated MoS₂ sheets at 380 and 445 nm from the deep valence band to conduction band, and 604 and 670 nm from the K point of Brillouin zone (Fig. 1d).²⁸ The absorption in the near UV region (<300 nm) can be attributed to the presence of MoS₂ quantum dots in the MoS₂ nanoflake suspension (Fig. 1d).²⁹ The characterization results clearly indicated the successful exfoliation of bulk MoS₂ into MoS₂ nanoflakes.

The MoS₂ nanoflakes were then used for LDI-MS analysis of three categories of small molecules: amino acids (asparagine, glutamic acid, histidine, phenylalanine), saccharides (glucose, sorbitol, sucrose and maltose), and fatty acids (behenic acid, oleic acid, palmitic acid and stearic acid). In practice, 1 nmol of small molecules dissolved in deionized water (DI water) were subjected to LDI-MS analysis with MoS₂ nanoflakes under positive-ionization mode. All the small molecules were clearly detected as sodium and/or potassium cationic adducts (Fig. S2). The cation adducts were presumably formed from impurities and residual sodium on the surface of MoS₂ nanoflakes that are adsorbed during the NaOH-assisted liquid phase exfoliation process. The amino acids and fatty acids were successfully detected with MoS₂ nanoflakes as the deprotonated form ([M-H]⁻) using negative ionization mode (Fig. S3). Each small molecule in their mixtures was separately detectable in water and phosphate buffered saline (PBS) (Fig. S4). The detectable concentration of small molecules with MoS₂ nanoflakes was determined to be 250 fmol for histidine, 100 fmol for stearic acid and 10 pmol for sorbitol under their preferred ionization mode (Fig. S5). The limit of detection (LOD) of histidine with MoS nanoflakes is slightly higher than that with Au NPs (25 fmol)¹¹ but lower than multi-walled carbon nanotubes (MWCNT, 1 pmol).³⁰ The LOD of steric acid with MoS₂ nanoflakes is also lower than that with graphene (11 pmol) and graphene oxide (GO, 3 pmol).³¹ On the other hand, the LOD of saccharides with MoS₂ nanoflakes was comparable to that with Pd NPs (7 pmol)³² but slight higher than carbon nanomaterials such as graphite (2 pmol), MWCNT (0.2 pmol), Fullerene (4 pmol), graphene (0.3 pmol) and carbon dots (0.01 pmol).³³ These results reveal the potential of MoS₂ nanoflakes as a versatile matrix for LDI-MS analysis of small molecules.

MoS₂ nanoflakes were also used for the LDI-MS analysis of benzyl pyridinium (BP), a standard thermometer molecule, to determine the nature of the energy transfer during ionization. The desorption efficiency (DE) and survival yield (SY) were estimated by summing the absolute intensity of the precursor and product BP ions, and dividing the precursor BP ion intensity by the total ion intensity of precursor and product BP ions (Fig. S6a, b).³⁴ The high DE and SY values indicate that MoS₂ nanoflakes provide efficient LDI-MS analysis with a low extent of fragmentation.³⁵ The DE and SY of MoS₂ nanoflake were calculated as $49,000 \pm 500$ and $58 \pm 4\%$, respectively (Fig. S6c for the comparison of DE and SY obtained from various nanomaterials such as Au and Fe₃O₄ NPs, GO and MWCNT and see Fig. S7 for characterization of those nanomaterials).

[MoS₂ nanoflake]₁ films were fabricated by immobilization of MoS₂ nanoflakes on the functionalized substrate with 3-APTES by electrostatic interactions between primary amine groups of the substrate and the oxidized surface of MoS₂ nanoflakes.²⁷ The UV-Vis

spectrum of the $[\text{MoS}_2 \text{ nanoflake}]_1$ film exhibited characteristic absorption peaks of MoS_2 nanoflakes at 604 and 670 nm, with the intensity of these peaks increasing with the number of LBL assembly cycles up to 4 (Fig. 3a, b). The scanning electron microscopy (SEM) images of $[\text{MoS}_2 \text{ nanoflake}]_{1-4}$ films further confirmed that MoS_2 nanoflakes were coated on the APTES-treated substrates, and the immobilized features and surface coverage successively increased as a function of LBL assembly cycles (Fig. 3c). With LBL assembly cycles, the water contact angle of $[\text{MoS}_2 \text{ nanoflake}]_{1-3}$ films $\sim 77.5^\circ$ and slightly decreased to 73.3° on $[\text{MoS}_2 \text{ nanoflake}]_4$ films (Fig. S8). This slight decrease can be attributed to the increased size and density of MoS_2 nanoflakes.

The $[\text{MoS}_2 \text{ nanoflake}]_{1-4}$ films were used for the LDI-MS analysis of small molecules dissolved in DI water. All small molecules were detected on the $[\text{MoS}_2 \text{ nanoflake}]_1$ film (Fig. 4), but the ion intensities were considerably lower than that observed with MoS_2 nanoflake suspensions (Fig. S2 and S3). With each additional layer, the ion intensities increased and reached a plateau with $[\text{MoS}_2 \text{ nanoflake}]_3$ films for most molecules (Fig. 5 and Fig. S9 for mass spectra of small molecules obtained on $[\text{MoS}_2 \text{ nanoflake}]_3$ films). This saturation tendency is in agreement with water contact angle changes of $[\text{MoS}_2 \text{ nanoflake}]_{1-4}$ films and analogous to the saturation levels previously seen with LBL assembled GO/MWCNT films due to the thermal energy dissipation through the assembled nanomaterials and their fragmentation.¹⁷ To further examine the effect of number of layers on efficiency, the LDI-MS analysis was carried out on $[\text{MoS}_2 \text{ nanoflake}]_{14}$ film, but its LDI-MS efficiency was considerable lower than $[\text{MoS}_2 \text{ nanoflake}]_3$ film (Fig. S10). This result clearly confirmed that the LDI-MS efficiency of $[\text{MoS}_2 \text{ nanoflake}]_n$ films is not linearly enhanced with LBL assembly cycles. Therefore, $[\text{MoS}_2 \text{ nanoflake}]_3$ film was selected as an optimized platform and utilized for the following experiments. Each small molecule dissolved in PBS was also detectable on the $[\text{MoS}_2 \text{ nanoflake}]_3$ with decreased intensity and emergence of $[\text{MoO}]^+$ ion derivatives signal (Fig. S11). The emergence of $[\text{MoO}_n]^+$ ions after exposure to PBS is likely due to the oxidation of MoS_2 nanoflakes in buffer solutions containing concentrated salts,³⁶ but this hypothesis requires further work to study the aging effects of MoS_2 nanoflakes in buffered solutions. The detectable concentration range of histidine, sorbitol and stearic acid was 10 pmol, 10 pmol and 100 pmol, respectively, are slightly lower than those obtained with MoS_2 nanoflakes (Fig. S12). The lower detectable concentration ranges on the $[\text{MoS}_2 \text{ nanoflake}]_3$ film than MoS_2 nanoflake might result from the low interfacing area of the analytes with the surface of MoS_2 nanoflakes.

The ionization efficiency and energetics of the LDI process on the $[\text{MoS}_2 \text{ nanoflake}]_{1-4}$ films were studied using BP as a thermometer molecule.³⁷ The DE value of $[\text{MoS}_2 \text{ nanoflake}]_1$ film was 29 ± 10 (Fig. 6c). This value is quite lower than that of MoS_2 nanoflake ($50,000 \pm 500$) and was consistent with the low mass peak intensity of small molecules on $[\text{MoS}_2 \text{ nanoflake}]_1$ film. However, the DE value significantly increased to $29,600 \pm 325$ for $[\text{MoS}_2 \text{ nanoflake}]_2$ films and reached at $46,000 \pm 500$ for $[\text{MoS}_2 \text{ nanoflake}]_3$ films, comparable to the suspended MoS_2 nanoflakes (Fig. 6c). This increasing tendency of DE is in accordance with that of absorption and ion intensities of small molecules on $[\text{MoS}_2 \text{ nanoflake}]_{1-4}$ films as a function of layer numbers. By contrast, the SY of $[\text{MoS}_2 \text{ nanoflake}]_1$ film was $32 \pm 7\%$ which is lower than that of MoS_2 nanoflake ($58 \pm 4\%$). Considering the low DE on $[\text{MoS}_2 \text{ nanoflake}]_1$ films, this low SY implies that BP

tends to be fragmented rather desorbed off the surface of [MoS₂ nanoflake]₁ films. However, the SY increased to $53 \pm 1\%$ on [MoS₂ nanoflake]₂ films (Fig. 6c), indicating that the successive LBL assembly of MoS₂ nanoflakes not only enhanced energy transfer during the LDI process but also controlled the amount of energy deposited into the analytes during the LDI-MS analysis. The origin of the positive influence of LBL assembly on LDI-MS process can perhaps be attributed to the formation of a percolation network of individual MoS₂ nanoflakes, resulting in increased laser energy absorption capacity and rapid dissipation of locally generated excess thermal energy.

Surface modification of chip-based LDI-MS platforms is an efficient way to improve their efficiency and selectivity.^{38–40} As an example, AuNPs functionalized with perfluoroalkane thiol provided higher LDI-MS efficiency than citrate-stabilized AuNPs.⁴¹ The surface of MoS₂ nanoflakes can be also modified with thiol derivatives through the coordination of thiol group to their defect sites or physisorption.^{42,43} This surface modification strategy has been extensively employed for the cancer therapy and antibacterial application by using MoS₂ nanoflakes.^{44–46} The surface modification strategy was also applied to [MoS₂ nanoflake]₃ films by using 1H,1H,2H,2H-perfluorodecanethiol as a modifier and resulted in slight increase of water contact angle from 77.5 to 78.0° (Fig. S13). This change can be attributed to the functionalization of [MoS₂ nanoflake]₃ films with hydrophobic 1H,1H,2H, 2H-perfluorodecanethiols and could partially contribute the enhancement of LDI-MS analysis efficiency. The functionalized [MoS₂ nanoflake]₃ films were then utilized for LDI-MS analysis of small molecules, with all of them successfully detected with higher ion intensities on the functionalized [MoS₂ nanoflake]₃ films than pristine [MoS₂ nanoflake]₃ films (Fig. 7).

To verify even ion signal distribution in mixtures, 1 μL each of histidine, glucose, glutathione and sorbitol (1 nmol) were spotted on the functionalized [MoS₂ nanoflake]₃ film, dried and subjected to LDI-MS imaging with 100 μm raster width. Although the LDI efficiency of each analyte varied,¹⁸ each analyte spot was clearly observed with a homogeneous ion intensity distribution (Fig. 8). The functionalized [MoS₂ nanoflake]₃ film was repeatedly (n = 6) used for LDI-MS analysis of glucose using the same analysis conditions. The ion intensity decreased ~twofold after the first analysis but then stabilized during 6 cycles of repeated analysis (Fig. S14). This result suggests that the functionalized [MoS₂ nanoflake]₃ film could be part of a reusable chip-based platform for LDI-MS analysis of small molecules.

Conclusions

In summary, we have demonstrated the applicability of liquid phase exfoliated MoS₂ nanoflakes as a matrix for LDI-MS analysis of small molecules including amino acids, saccharides and fatty acids. The MoS₂ nanoflakes provide high LDI-MS efficiency for the analysis of small molecules by efficient photothermal energy transfer. The LDI-MS efficiency of MoS₂ nanoflakes are considerably higher than conventional nanomaterials such as GO, MWCNT, Au and Fe₃O₄ NPs. Furthermore, the MoS₂ nanoflakes are readily immobilized on chemically-functionalized substrates to provide a chip-based LDI-MS platform. The LDI-MS efficiency of MoS₂ films was enhanced by subsequent LBL

assembly process with PAAH. With the optimized number of layers, the [MoS₂ nanoflake]₃ films provided even ion intensity distributions, robustness, and high LDI-MS efficiencies that are comparable to colloidal MoS₂ nanoflakes. The ionization efficiency of the films was further improved by surface functionalization using fluorothiols. Taken together, we show that liquid phase exfoliated MoS₂ nanoflakes and LBL assembly of these materials offer an efficient LDI-MS platform for the analysis of small molecule, providing simple preparation, high LDI-MS efficiency and compatibility for chip-based analysis. Furthermore, we believe that the present [MoS₂ nanoflake]_n films can be utilized as a support to synthesize a multifunctional nanohybrid structures with dielectric⁴⁷ and metallic nanostructures⁴⁸ for multi-modal analysis with surface plasmon resonance (SPR) and surface enhanced Raman scattering (SERS), respectively. From this point of view, the surface chemistry with thiol derivatives and high LDI-MS efficiency will play an important role for the development of a multi-modal analysis platform combining LDI-MS with other sensing technique such as SPR and SERS.^{47–49}

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.
Scheme of LBL assembly of liquid phase exfoliated MoS₂ nanoflakes for the fabrication of a chip-based LDI-MS platform.

Fig. 2.
a) TEM image, b) AFM image with line profile, c) hydrodynamic radius, and d) UV-vis spectrum of MoS₂ nanoflake prepared by NaOH-assisted liquid exfoliation in NMP.

Fig. 3.

a) UV-Vis spectra, (b) the absorbance at 670 nm, and (c) SEM images of [MoS₂ nanoflake]₁₋₄ films.

Fig. 4.

Mass spectra of 1 nmol of amino acids, saccharides and fatty acids obtained on the $[\text{MoS}_2 \text{ nanoflake}]_1$ films under their preferable ionization mode.

Fig. 5. The changes of mass peak intensities of amino acids, saccharides and fatty acids obtained on $[\text{MoS}_2 \text{ nanoflake}]_{1-4}$ films were plotted as a function of the number of assembled layers.

Fig. 6.

a) Mass spectra of BP, (b) fragmentation process of BP, and (c) DE and SY values obtained on [MoS₂ nanoflake]₁₋₄ films.

Fig. 7. Ion intensities of small molecules obtained on the bare or functionalized [MoS₂ nanoflake]₃ films.

Fig. 8.

a) LDI-MS image of histidine, glucose, glutathione and sorbitol obtained on the functionalized [MoS₂ nanoflake]₃ film. b) Accumulated mass spectrum of small molecules from the LDI-MS image. The scale bar is 2 mm.