

Suitable materials for efficient detection of colorectal cancer biomarkers: acumen from DFT

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ABSTRACT

Early diagnosis of Colorectal Cancer (CRC) is crucially important for prognosis planning, curing, and saving human lives. The novel technique, which detects volatile organic compounds (VOCs) associated with CRC biomarkers in patients' exhaled breath, has proven to be non-invasive and cost-effective. In this context, finding suitable materials to be used as a platform in nano-biosensors to detect CRC fingerprints with high sensitivity at the order of parts per billion (ppb) under ambient conditions is of great importance. In the present investigation, we explore the functionalization of boron monoxide (BO) monolayer using density-functional theory (DFT) to selectively detect CRC-related VOCs biomarkers. Four VOCs (Benzaldehyde "C₇H₆O", Butanol "C₄H₁₀O", Indole "C₈H₇N", Isopropanol "C₃H₈O") have been experimentally identified as key CRC biomarkers and are considered in this study. To improve the sensing mechanism, light metal (LM) atoms (Li, Na, K, Ca) have been selected for embedment in the pores of BO in a single-atom catalyst (SAC) fashion. The stability of the LM functionalized BO monolayer was confirmed by binding energies that exceeded the corresponding bulk cohesive energies and was further validated through ab initio molecular dynamics (AIMD) simulations at 300 K. Functionalization with LM atoms enhanced the adsorption energies of the studied VOCs compared to interfering air molecules (N₂, O₂, H₂O, CO₂). The selectivity toward VOCs was further supported by evidence of high adsorption energy, charge transfer, variations in magnetization, and changes in work function. The calculated sensor responses for the four VOCs were 2.5, 5.8, 4.0, and 6.3, respectively. Collectively, these findings highlight LM-doped BO as a promising candidate material for nano-biosensors enabling early detection of CRC biomarkers.

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Introduction

Colorectal cancer (CRC) is one of the most common cancers worldwide, ranking third in occurrence and second in leading cause of cancer-related deaths globally [1]. Over the past several decades, slow progress has been made in the arena of early diagnosis, especially for instance, CRC continues to be frequently detected at an advanced stage when the prognosis becomes challenging [1]. Each year, CRC accounts for approximately 1.9 million new cases and 935,000 deaths, with an estimated projection of an increase to around 3.2 million new cases and 1.6 million deaths by 2040 [1].

The routine diagnostic methods for CRC, such as colonoscopy and tissue biopsy, are highly invasive and often inconvenient for patients [2]. Breathomics (breath analysis) is a rapidly advancing field in

diagnostic science and has increasingly been utilized in the detection of various diseases, including different types of cancers. It is well established that distinct volatile organic compounds (VOCs) are produced in different types of cancer due to specific metabolic and biochemical processes [3]. These VOCs can serve as biomarkers for disease identification. Therefore, efficient detection of CRC-related VOCs offers a non-invasive and cost-effective method contributing to the early diagnosis of cancer diseases [3–7].

Single-atom catalysis (SAC) yields optimal catalytic efficiency and is proven to be a powerful method in tuning the properties of 2D systems towards specific applications ranging from electro-catalysis in energy conversion [8–14] to gas sensing [15–17] to energy storage [18–21] and biosensing applications [22–25]. A recent review by Humayun et al. summarized the design and diverse utilization of metal SACs in electro-

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catalysis [12]. The embedment of metal SACs into the pores of carbon nitrides (e.g., C_3N_4) has been reported and shown to achieve a great selectivity towards detecting toxic gases such as NO_x [26]. In the case of ferromagnetic transition metal SAC, the change in magnetization after the capture of toxic gases was explored in the reduction reaction of toxic gases [27] and selective gas sensing of VOCs related to cancer diseases [28–30]. Very recently, Hussain et al. employed DFT calculations to study the sensing properties of SAC systems based on tungsten diselenide (WSe_2) and tungsten ditelluride (WTe_2) monolayers toward specific VOCs related to CRC [31]. Enhanced adsorption energies of the CRC-related VOCs were found with the incorporation of selected foreign elements, such as Fe, Mn, and Zn, into the WSe_2 and WTe_2 monolayer.

Amongst the porous 2D materials with multifunctionality aspect, boron oxide (BO) has recently been revived and attracted research interest. Namely, in 2023, Perras et al. [32] employed advanced multi-dimensional nuclear magnetic resonance methods to reveal the atomic structure of boron monoxide (BO). This material was first reported in 1940 [33] and synthesized in 1955 [34]. Recent characterization demonstrated that BO consists of B_3O_3 hexagons connecting B_8O_8 and B_8O_4 rings to form two-dimensional nanosheets with relatively large pores [35]. These structural features make BO highly suitable for multifunctional applications, as the uniformly distributed large pores serve as effective adsorption sites for various molecules, enhancing its potential for VOC detection [36]. Based upon the mentioned characteristics, BO monolayer possesses properties to make it a good candidate with great potential for the detection of VOCs linked to CRC, as will be further elaborated below.

The enhancement of local polarity can be explored in the selective adsorption of VOCs related to cancer diseases [28,29]. The principle is that the surface dipole induces dipole moments in various locations within the VOC molecule, and that would trigger the van der Waals (vdW) interactions between the surface and VOCs, much stronger than those between the surface and interfering air molecules. This is the intrinsic mechanism behind enhanced selectivity. For instance, the TM-doping of $Ti_3C_2O_2$ MXenes is shown to be relevant for the selective detection of VOCs related to Alzheimer's disease [28] and lung cancer [29]. Furthermore, the TM doping anion sites in TMD MoS_2 are shown to be relevant for selective adsorption and detection of lung cancer [30]. Currently, we are exploring the same idea in searching for reusable biosensors working under ambient conditions to detect several kinds of cancer diseases based upon light metal atoms (Li, Na, K, Ca) embedded in recently synthesized porous carbon nitride 2D structures [37] and other porous 2D systems such as BO [38] and BN [39]. Promising results have been achieved.

Although significant progress has been made in applying 2D materials and SACs for gas sensing and disease-related VOCs detection, systematic investigations targeting CRC biomarkers remain scarce. In particular, the recently characterized BO monolayers, with their distinctive porous architecture, have not yet been explored for selective CRC-VOC detection via light metal functionalization. Addressing this gap, the present study investigates LM-functionalized BO monolayers as a potential platform for sensitive and selective CRC diagnosis through breath analysis. In doing so, this work not only contributes to the development of advanced functional materials for non-invasive biosensors but also highlights new opportunities for the early detection of colorectal cancer.

To pursue this goal, we focus on four VOCs that have been experimentally identified as CRC biomarkers in prior clinical and analytical investigations [32,40–43]: isopropanol (C_3H_8O), butanol ($C_4H_{10}O$), indole (C_8H_7N), and benzaldehyde (C_7H_6O). These compounds span chemically diverse classes, reflecting the metabolic heterogeneity that underlies CRC. Specifically, C_3H_8O , a secondary alcohol associated with disrupted metabolic pathways linked to gut microbiota imbalance and cancer progression; $C_4H_{10}O$, a primary alcohol produced through microbial fermentation in the colon and consistently detected in exhaled breath and fecal samples of CRC patients; C_8H_7N , a nitrogen-containing heteroaromatic compound derived from bacterial tryptophan metabolism, implicated in host-microbiome interactions and carcinogenic processes; and C_7H_6O , an aromatic aldehyde arising from amino acid and lipid degradation pathways, with elevated concentrations observed in biological headspace samples from CRC patients. Collectively, these VOCs represent a spectrum of alcohols, nitrogen-containing aromatics, and aldehydes that hold promise as non-invasive molecular signatures for CRC detection.

To enhance the selectivity towards the detection of VOCs, the functionalization of BO with light metal atoms is explored (e.g., Li, Na, K, Ca). By exploring the CRC-VOCs interactions with LM-functionalized BO monolayers using spin-polarized density functional theory (DFT) implemented in the Vienna Ab initio Simulation Package (VASP), this study establishes both the sensitivity and selectivity of the material platform. Through rigorous computational analysis, we aim to clarify methodology, provide comparative insights, and emphasize practical relevance that ultimately advances computational materials design for biomedical sensing applications.

Computational model and method

Boron monoxide (BO) monolayer crystallizes into a 2D Bravais square lattice with a primitive cell (PC), shown in Fig. 1a, having the lattice parameter $a = b = 7.826 \text{ \AA}$. The primitive cell contains basis

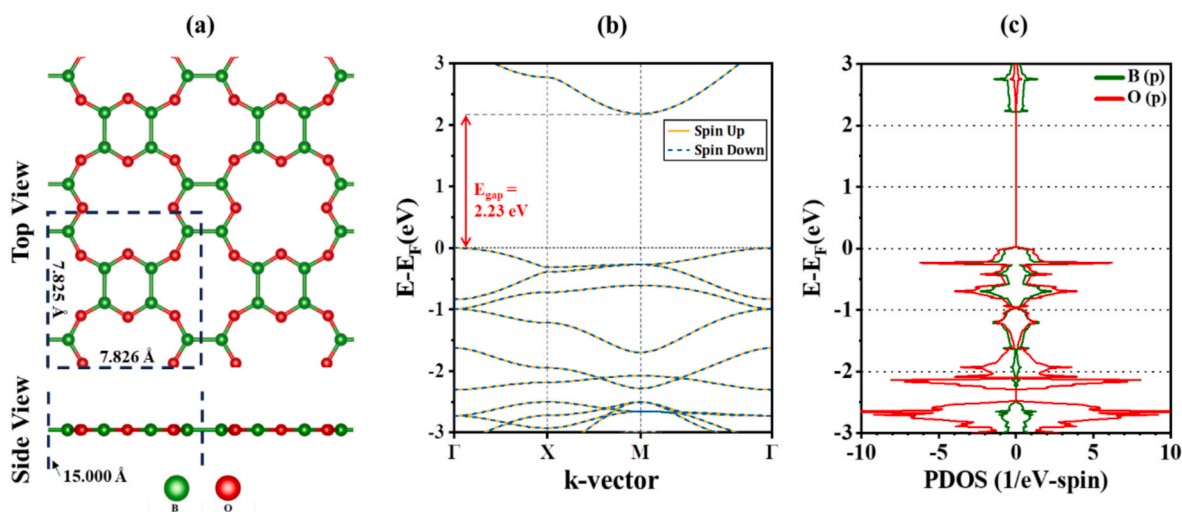


Fig. 1. Pristine Boron Oxide (BO) monolayer. (a) Optimized atomic structure (top and side views), (b) band structure, and (c) projected density of states (PDOS) of pristine BO monolayer. The Fermi level is taken as an energy reference denoted by the horizontal dashed line ($E_F = 0$).

atoms of eight B and eight O atoms. The modeled structures through this study were based on a computational supercell of size 2×2 PCs (i.e., $32\text{B} + 32\text{O} = 64$ atoms) with periodic boundary conditions along xy-directions (see Fig. 1a). The supercell's meant to be moderately large enough ($A = B = 15.652 \text{ \AA}$) to accommodate the atomic relaxations of large molecules such as VOCs related to CRC. A vacuum space of $C = 20 \text{ \AA}$ along the z-direction is supplied to ensure the isolation of the BO ML from its mirror images produced by the periodic boundary conditions.

To analyze the adsorption properties, we conducted spin-polarized DFT calculations involving atomic structure optimization, adsorption mechanism, charge transfer, magnetization, work function, and sensor response assessments. The calculations were performed using the VASP within the frameworks of DFT and the projected augmented plane wave (PAW) method [44]. The Perdew-Burke-Ernzerhof (PBE) functional form within the generalized gradient approximation (GGA) framework was used to address the exchange–correlation potential [45]. To improve the prediction of bandgap energy, such as in case of semi-conducting materials, more sophisticated hybrid functionals can be used such as Heyd-Scuseria-Ernzerhof (HSE) [46]. In our present work we explore PBE functionals as being suitable for ground-states problems such as adsorption properties and no need to use HSE as our samples exhibit metallization after the embedment of LM atoms. Furthermore, for reliable adsorption energy accuracy, the vdW interactions are taken care of by the incorporation of the DFT-D3 dispersion correction due to Grimme et al. [47]. In our DFT calculations, some essential parameters were optimized to reproduce reliable results such as bulk total density of states (TDOS). Among these essential parameters, the cut-off energy, which was set to $E_{\text{cut}} = 500 \text{ eV}$, and the k-grid of the Brillouin zone. In sampling the Brillouin zone, we utilized the Monkhorst-Pack technique [48] with grids of $5 \times 5 \times 1$ for geometry optimization and $8 \times 8 \times 1$ for density of states (DOS) calculations. In the structure relaxation, we applied the convergence tolerances for the total energy of 10^{-6} eV and for the Hellmann-Feynman atomic force of $0.01 \text{ eV/\AA}$. Bader charge analysis within the framework of VASP was utilized to estimate the charge exchange between molecules and the host substrate [49].

Based upon total energy calculation, the average binding energy (E_{bind}) of metal atoms (M) embedded in the pores of the BO monolayer can be calculated using the formula:

$$E_{\text{bind}} = \frac{E_{\text{BO-nM}} - (E_{\text{BO}} + nE_{\text{M}})}{n} \quad (1)$$

where $E_{\text{BO-nM}}$, E_{BO} , and E_{M} stand for the total energies of BO embedded with n metal atom(s), pristine BO, and isolated metal atom, respectively. To validate the thermodynamic stability of the functionalized substrate, ab-initio molecular dynamics (AIMD) was performed at 300 K. The study comprises the two samples (i) 1 K@BO and (ii) 2 K@BO. The Nose-Hoover thermostat was used to control the temperature with a time step of 1.0 fs for a duration of 5.0 ps.

The adsorption energy (E_{ads}) of VOC or air molecule on top of the substrate is defined as:

$$E_{\text{ads}} = E_{\text{Sub-Mol}} - E_{\text{Sub}} - E_{\text{Mol}} \quad (2)$$

where $E_{\text{Sub-Mol}}$, E_{Sub} and E_{Mol} are the total energies of the substrate with and without molecules and the free molecule, respectively.

To assess whether the sensor is reusable or disposable, it is necessary to estimate the recovery time [50], which is defined as follows:

$$\tau = v_0^{-1} \exp \left[-\frac{E_{\text{ads}}}{k_B T} \right] \quad (3)$$

where $v_0 = 10^{13} \text{ s}^{-1}$ is the attempt frequency [51], E_{ads} is the adsorption energy, k_B and T are the Boltzmann constant and the absolute temperature, respectively.

The selectivity based on work function is defined [52] as follows:

$$S = \frac{|\Phi - \Phi_0|}{\Phi_0} \quad (4)$$

where Φ_0 and Φ are the work functions of the substrate before and after the adsorption of the molecule.

Results and discussion

Adsorption on pristine BO

Fig. 1a shows the relaxed atomic structures of a supercell composed of 2×2 PCs of pristine BO. The primitive cell is a Bravais square lattice, containing eight B and eight O atoms, with lattice parameters $a = b = 7.826 \text{ \AA}$ consistent with the both the original experimental work of Perras et al. [35] and ab-initio calculations of Mortazavi et al. [53]. The obtained B-O bond lengths are $1.37\text{--}1.39 \text{ \AA}$, consistent with the DFT results of Mortazavi et al. [53]. Fig. 1b displays the band structure of one primitive cell showing the existence of an indirect bandgap energy of $E_g = 2.23 \text{ eV}$, where the valence-band maximum (VBM) is located at the center of the Brillouin zone (Γ -point) and the conduction-band minimum (CBM) is located at the M-point. The latter value of E_g is obtained using the PBE functional and is consistent with $E_g = 2.18 \text{ eV}$ reported by Mortazavi et al. [53] using DFT-PBE. It is a well-known trend that the DFT underestimates the bandgap energy. Corrections can be made by the inclusion of the hybrid functional of Heyd, Scuseria, and Ernzerhof (HSE06) [46], whose inclusion improves the bandgap energy to 3.78 eV [53]. Fig. 1c displays the spin-polarized partial density of states (TDOS) for pristine BO using DFT-PBE. The contributions from B and O atoms are shown in green and red curves, respectively. Both atoms contribute equally to VBM, revealing the covalent character of the B-O bonds. However, B atoms contribute more to the CBM revealing the fact of their being less electronegative than B atoms (i.e., more electropositive).

Regarding the calculations of the adsorption activity on the surface of BO, we tested the adsorption of N_2 molecules on seven different sites, as shown in Fig. 2a. The N_2 molecule was brought close to the BO surface at about $1.5 \text{ \AA}$ above each of the seven sites shown, then the atomic relaxation was performed. The obtained absolute values of the adsorption energies corresponding to these seven sites are shown in Fig. 2b. We concluded that the three sites 1–3 are favorable, with a bit of superiority towards site 2 (i.e., the center of the largest pore “ B_8O_8 ring”) with an adsorption energy of $E_{\text{ads}} = -0.165 \text{ eV}$.

After determining the favorable binding site for molecular adsorption (i.e., to be site #2, on top of center of the biggest pore “BO ring”), we performed the calculations of atomic relaxations of free four VOCs molecules, namely: (i) Benzaldehyde “ $\text{C}_7\text{H}_6\text{O}$ ”, (ii) Butanol “ $\text{C}_4\text{H}_{10}\text{O}$ ”, (iii) Indole “ $\text{C}_8\text{H}_7\text{N}$ ”, and (iv) Isopropanol “ $\text{C}_3\text{H}_8\text{O}$ ”, with results presented in Fig. S1 (Supplementary Information). The atomic structures of these latter four VOCs are consistent with the experimental findings of reference [32,40–43]. Testing of adsorption of VOCs, such as Benzaldehyde, was carried out on site #2 (Fig. 2a) versus adsorption distance and molecule orientation revealed that the molecule stabilizes in physisorption state at about $1.85 \text{ \AA}$. Thereafter, the adsorptions of a total of four VOCs and four interfering air molecules H_2O , CO_2 , N_2 and O_2 were carried out. The obtained results of absolute adsorption energies $|E_{\text{ads}}|$ are shown in Fig. 3. It is apparent that pristine BO does not yield any selective adsorption towards the VOCs, and this is attributed to the fact that pristine BO is a polar material but with a uniform distribution of electric dipole moments. One should consider the BO functionalization with light metal atoms (e.g., Li, Na, K, Ca) to bargain for stable embedment in the intermediate-sized pores of BO and creation of stronger local dipoles to enhance the vdW interactions as well as the physisorption energies of the VOCs.

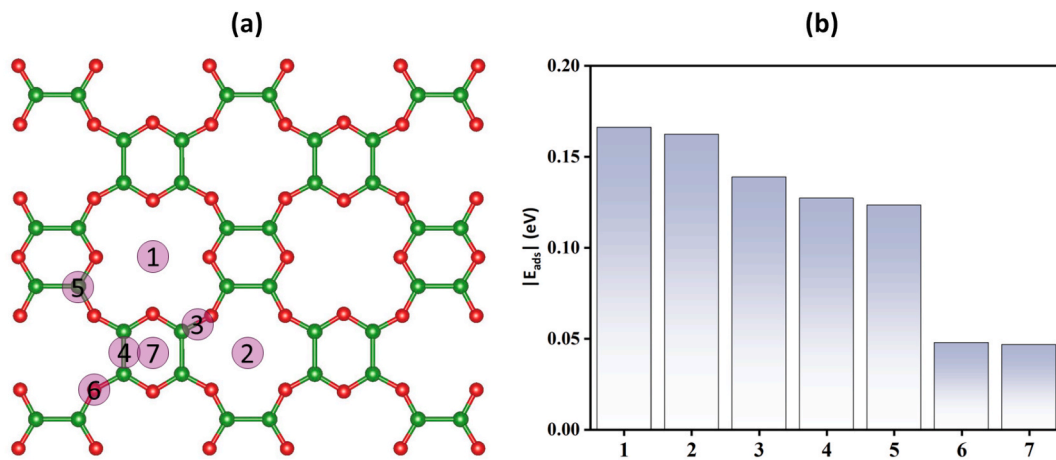


Fig. 2. (a) Testing sites for active adsorption of N_2 gas molecule on pristine BO monolayer and (b) the corresponding adsorption energy (E_{ads}) at each site.

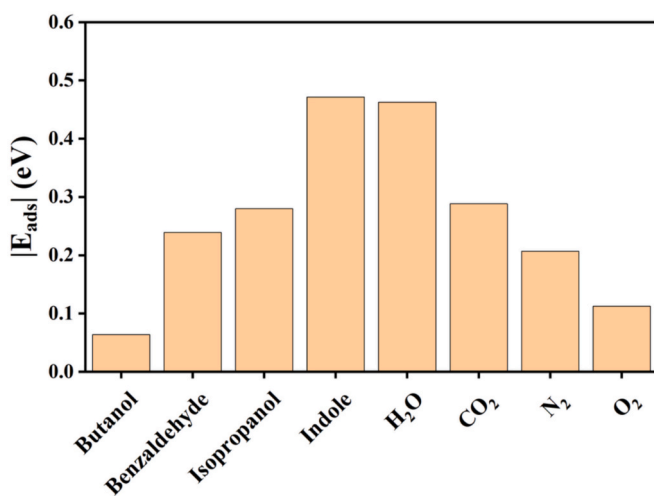


Fig. 3. Absolute values of adsorption energies of 4 VOCs, related to colorectal cancer biomarkers, and four interfering air molecules on pristine BO monolayer.

Functionalization of BO

Based on our recent work [38], we selected the same four light metal atoms (Li, Na, K, Ca) were successfully embedded in the two pores of the

primitive cell of BO with an average $|E_{ads}|$ larger than the corresponding cohesive energies of 1.63 (Li), 1.11 (Na), 0.93 (K) and 1.84 (Ca) eV/atom [54], respectively. The stabilities of the structures were confirmed by the AIMD simulations performed at 400 K for a time interval of 8 ps [38].

In the present work, the aim is to investigate VOCs associated with CRC. One should be more concerned with a comparative study of the adsorption of the selected VOCs and the air molecules (CO_2 , H_2O , O_2 , N_2) existing in the exhaled breath of patients. In contrast to the previous project, the computational supercell is relatively larger and consists of 2×2 PCs, and the number of LM atoms varies between 1–2 atoms (see Fig. 4a). Mainly, the LM atoms are embedded in BO pores in single-atom catalyst (SAC) fashion to enhance the local dipole moments to trigger stronger interactions with VOCs than those with interfering air molecules. The embedment of LM atoms was tested on two different sites existing in the two intermediate-sized pores of BO as shown in Fig. 4a. The results of absolute values of binding energies $|E_{bind}|$ are shown in Fig. 4b and compared to the cohesive energies $|E_{coh}|$. All binding energies of the four LM atoms are greater than their corresponding $|E_{coh}|$ values in the locations of embedment, except in case of double SAC of potassium “K”. This latter trend might have occurred because of K being monovalent but larger to be accommodated in the intermediate-sized pore. Vice versa, being small, Li atom favors the embedment in the intermediate pore.

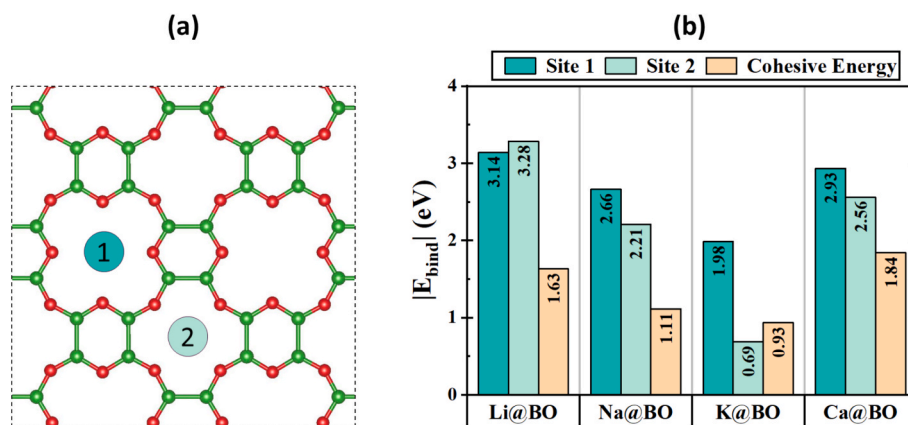


Fig. 4. (a) Testing sites for binding light-metal atoms (Li, Na, K, and Ca) on pristine BO monolayer, and (b) their corresponding absolute values of binding energies are compared to the cohesive energy of each metal.

Adsorption of VOCs on functionalized BO

Fig. 5a and Fig. 5b show the relaxed BO samples after the embedment of single and double LM atoms (Li, Na, K, Ca) in SAC fashion in the respective two pores to yield the minimum energy configurations. We have carried on with the adsorption of the four VOCs, on the above eight samples as well as pristine BO ML and the obtained relaxed structures are shown in Fig. S2. The average $|E_{ads}|$ of the studied four VOCs on pristine and LM-embedded BO are shown in Fig. 6. One may notice that the double LM-SAC induces more enhancement in $|E_{ads}|$. Moreover, the $|E_{ads}|$ is larger than 1.0 eV in two cases of K and Ca catalysts. Such values ensure the achievement of selective adsorptions compared to interfering air molecules. So, we have decided to select K and Ca for further investigation as being the promising functionalization for BO to ensure the candidature of the doped BO as a biosensor to detect the VOCs related to colorectal cancer.

It is very important to validate the thermal stability of the LM-doped BO at room temperature (RT). Ab-initio molecular dynamics (AIMD) simulations have been performed on the two samples, 1 K@BO and 2 K@BO, for a period of 5 ps in time step of 1 fs. The results of relaxed atomic structures at RT are compared to those obtained at 0 K in Fig. 7a (side view perspective). In contrast to the flat structure at 0 K, the

potassium atom(s) stabilize in a buckled fashion at RT. The results of total energy versus simulation time (up to 5 ps) for both 1 K@BO and 2 K@BO samples at RT (i.e., $T = 300$ K) are shown in Fig. 7b. The results show that energy fluctuations do not exceed 1.0 eV in amplitude, which is about 0.2 %. This should be taken as evidence for the thermal stability of the LM-doped BO systems.

Electronic structures of LM@BO

Fig. 8 shows the relaxed atomic structure of 1 K@BO, using 2×2 PC sample, their corresponding band structures and spin-polarized PDOS. The Fermi level is taken as an energy reference ($E_F = 0$). The embedment of a 1 K atom in the pore of BO results in the metallization of the sample, yet it remains paramagnetic as the DOSs of spin-up and spin-down states are shown to stay symmetric. After the adsorptions of the VOCs, the results of $|E_{ads}|$, magnetization (M) and change of magnetization (ΔM) for pristine BO and 1LM@BO and 2LM@BO (with LM = Li, Na, K, and Ca) are summarized in Table 1 and Table 2, respectively. The results can reveal the $|E_{ads}| > 1.0$ eV just in cases of Benzaldehyde and Indole on 1 K@BO and 1Ca@BO samples, as well as all VOCs on 2 K@BO and Benzaldehyde on 2Ca@BO samples. Further, the magnetization is zero except in one case of 2Ca@BO with $\Delta M \neq 0$, as well.

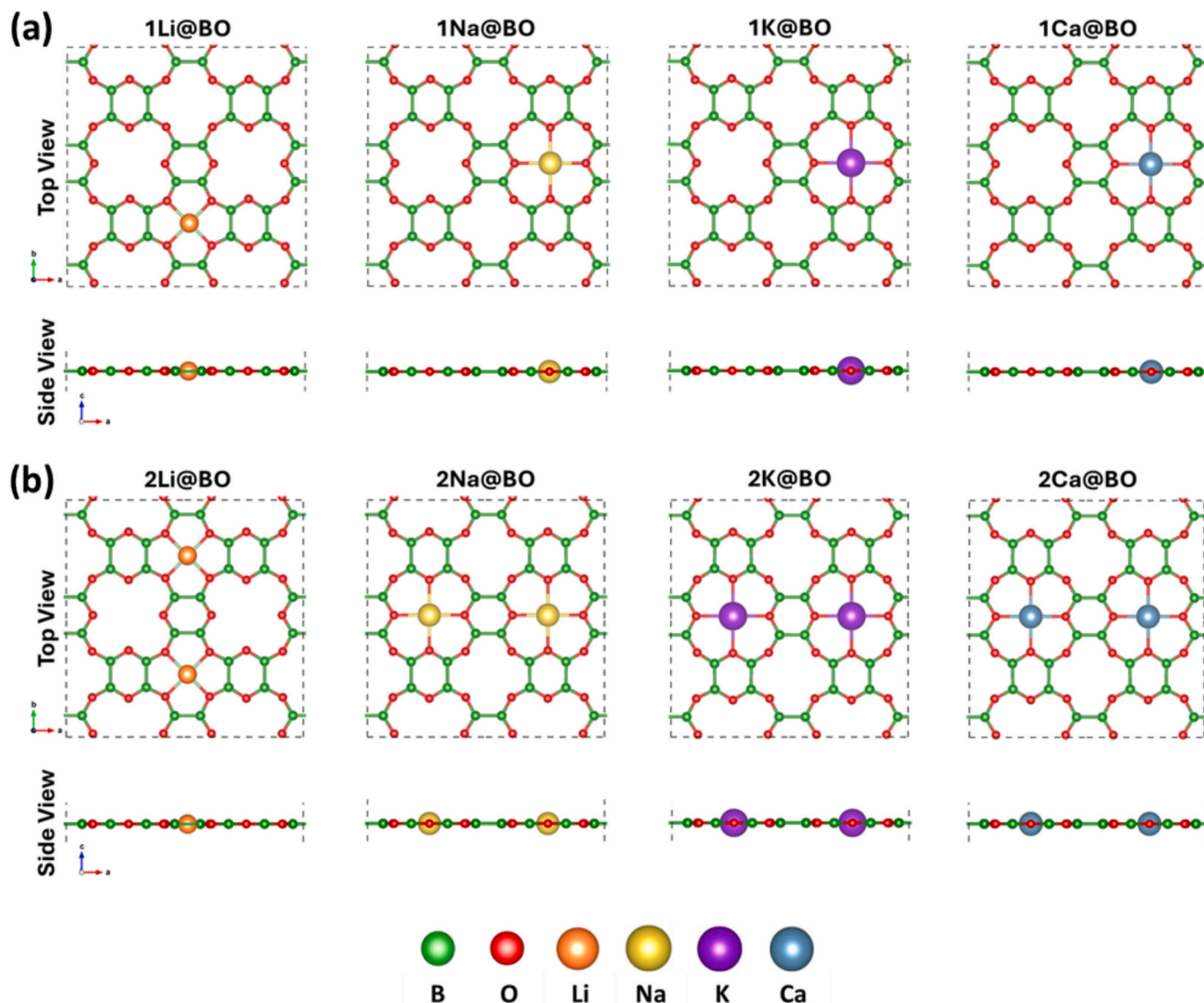


Fig. 5. Relaxed atomic structures of (a) 1 SAC light-metal (LM) atom and (b) 2 SAC-LM atoms embedded in BO pores. (LMs: Li, Na, K, and Ca).

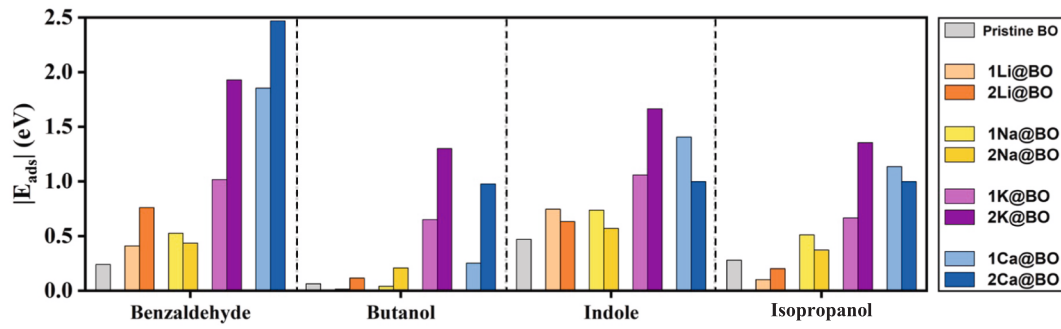


Fig. 6. Absolute values of adsorption energies of four VOCs, related to colorectal cancer biomarkers, independently deposited on pristine BO (gray), 1 SAC-LM atom (light color), and 2 SAC-LM atoms (dark color) embedded in BO. (LMs: Li, Na, K, and Ca).

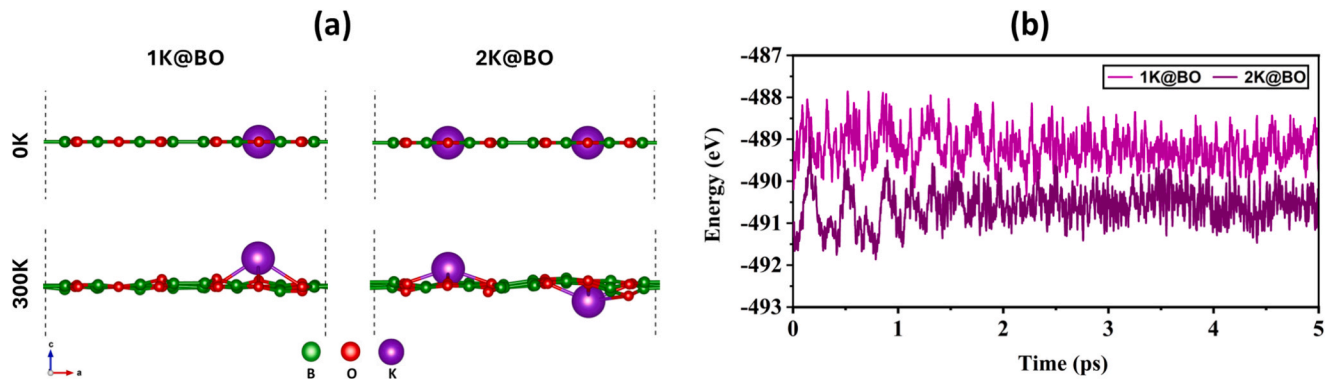


Fig. 7. (a) Optimized atomic structures of 1 K@BO and 2 K@BO at 0 K and 300 K. (b) Ab-initio Molecular Dynamics (AIMD) simulations showing total energy as a function of time at 300 K over a 5 ps interval for both 1 K@BO and 2 K@BO, represented by dark purple and light purple lines, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

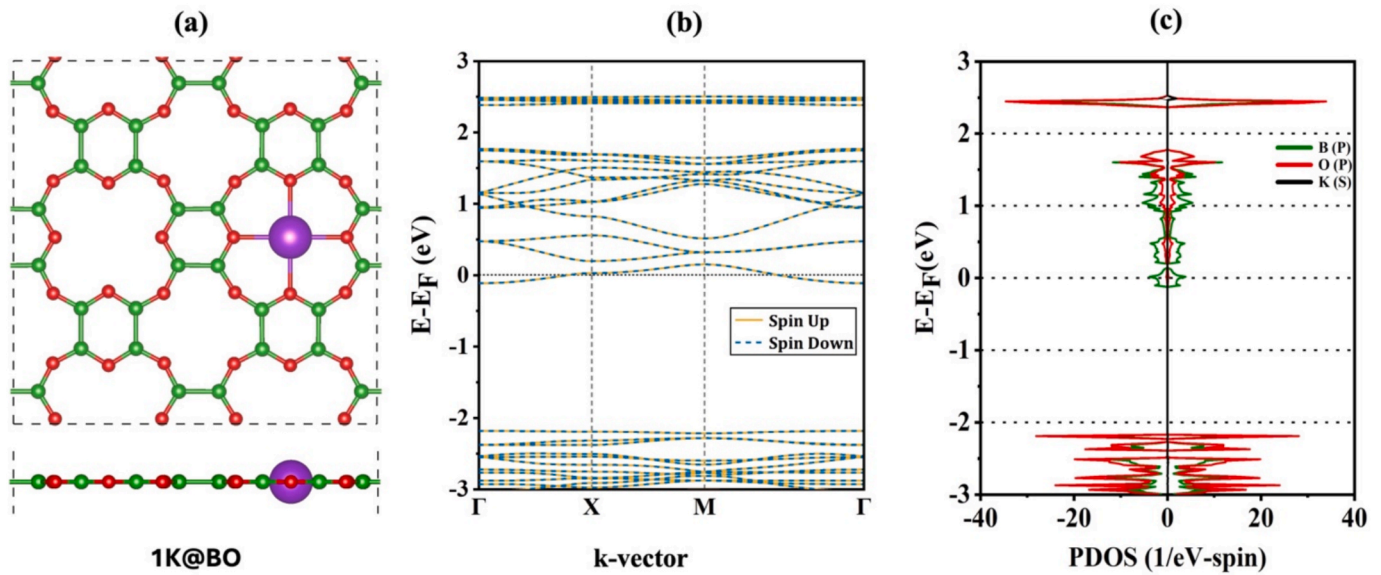


Fig. 8. Potassium SAC doped BO (K@BO). (a) Optimized atomic structure (top and side views), (b) band structure, (c) and projected density of states of K@BO. The Fermi level is taken as an energy reference, denoted by the horizontal dashed line ($E_F = 0$).

Table 1

Adsorption data comprising adsorption energy and magnetization and its change after the adsorption of four VOCs, related to colorectal cancer biomarkers on pristine and SAC LM-embedded BO ML (with LM = Li, Na, K, Ca).

VOCs	Pristine BO ($M_0 = 0.00 \mu_B$)		1Li-doped ($M_0 = 0.00 \mu_B$)		1Na-doped ($M_0 = 0.00 \mu_B$)		1 K-doped ($M_0 = 0.00 \mu_B$)		1Ca-doped ($M_0 = 0.00 \mu_B$)	
	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)
Benzaldehyde (C_7H_6O)	-0.239	0	-0.409	0	-0.526	0	-1.017	0	-1.853	0
Butanol ($C_4H_{10}O$)	-0.064	0	-0.013	0	-0.040	0	-0.651	0	-0.252	0
Indole (C_8H_7N)	-0.471	0	-0.746	0	-0.737	0	-1.057	0	-1.406	0
Isopropanol (C_3H_8O)	-0.280	0	-0.102	0	-0.512	0	-0.666	0	-1.135	0

Table 2

Adsorption data like in Table-1 but using DAC LM-embedded BO ML.

VOCs	2Li-doped ($M_0 = 0.00 \mu_B$)		2Na-doped ($M_0 = 0.00 \mu_B$)		2 K-doped ($M_0 = 0.00 \mu_B$)		2Ca-doped ($M_0 = 1.18 \mu_B$)	
	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)	E_{ads} (eV)	ΔM (μ_B)
Benzaldehyde (C_7H_6O)	-0.782	0	-0.435	0	-1.928	0	-2.469	1.08
Butanol ($C_4H_{10}O$)	-0.384	0	-0.207	0	-1.300	0	-0.975	0.7
Indole (C_8H_7N)	-0.634	0	-0.571	0	-1.665	0	-0.998	1.18
Isopropanol (C_3H_8O)	-0.146	0	-0.372	0	-1.354	0	-0.998	0.58

Table 3

Adsorption data of four VOCs, related to colorectal cancer biomarkers, and four interfering air molecules on 1 K@BO ML.

	E_{ads} (eV)	d (Å)	$E_g \uparrow$ (eV)	$E_g \downarrow$ (eV)	Δq (e)	τ (sec)
Substrate = K@BO	N/A	N/A	0.004	0.004	N/A	N/A
Benzaldehyde (C_7H_6O)	-1.017	1.85	0.010	0.010	-0.129	1.114×10^5
Butanol ($C_4H_{10}O$)	-0.651	1.62	0.006	0.006	0.004	0.081
Indole (C_8H_7N)	-1.057	2.73	0.007	0.007	0.036	5.361×10^5
Isopropanol (C_3H_8O)	-0.666	1.80	0.007	0.007	0.001	0.147
Water vapor (H_2O)	-0.841	2.79	0.006	0.006	-0.012	127.104
Oxygen (O_2)	-0.228	3.16	0.007	0.007	-0.037	6.631×10^{-9}
Carbon dioxide (CO_2)	-0.787	1.49	0.007	0.007	-0.014	15.723
Nitrogen (N_2)	-0.701	3.07	0.011	0.011	-0.027	0.566

Table 3 summarizes the results of $|E_{ads}|$, distance (d) of the VOCs and interfering air molecules to the LM@BO ML, bandgap energies of spin-up ($E_g \uparrow$) and spin-down states ($E_g \downarrow$), charge exchange (Δq), and desorption relaxation time (τ) for the adsorption processes.

Charge exchange

The assessment of charge exchange between the molecules and the LM-@BO is done through the Bader charge analysis, and charge density difference (CDD). Fig. 9 shows the results of CDD due to the adsorption of the VOCs on 1 K@BO ML. The charge density is colored in yellow (cyan) to reveal accumulation (deficit) of charge. It seems that all the

VOCs are donors, so the charge is shown to be displaced more toward the substrate. The largest charge transfer should correspond to Benzaldehyde and Indole. This is consistent with the strong $|E_{ads}|$ obtained for these respective molecules as displayed in Fig. 6 and Table 3.

Work function and sensor response

Fig. 10 displays the $|E_{ads}|$ and charge exchanges $|\Delta q|$ for the studied VOCs, and the interfering air molecules. The results are shown in the case of 1 K@BO. The comparison reveals some weak selectivity. Nevertheless, it is worth noting that the selectivity should be more pronounced and further enhanced on the 2 K@BO substrate as displayed

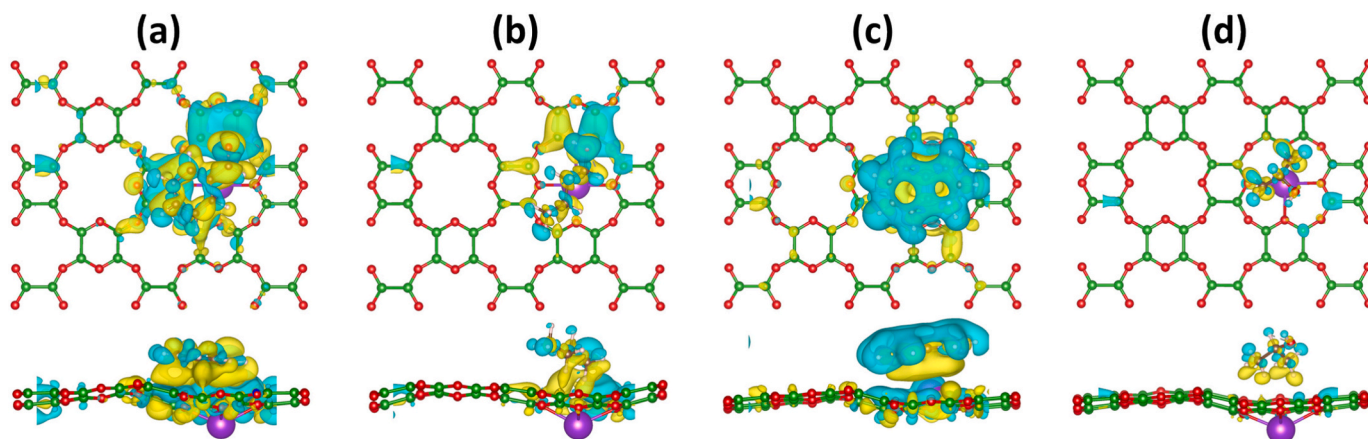


Fig. 9. Charge Density Difference (CDD) showing the bond characteristics of maximally localized Wannier functions (MLWFs) of four VOCs: (a) Benzaldehyde, (b) Butanol, (c) Indole, and (d) Isopropanol, related to colorectal cancer biomarker, on 1 K@BO. Yellow and Cyan iso-surfaces indicate charge aggregation and depletion, respectively. The iso surfaces' level is 0.0002 e/Bohr³. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

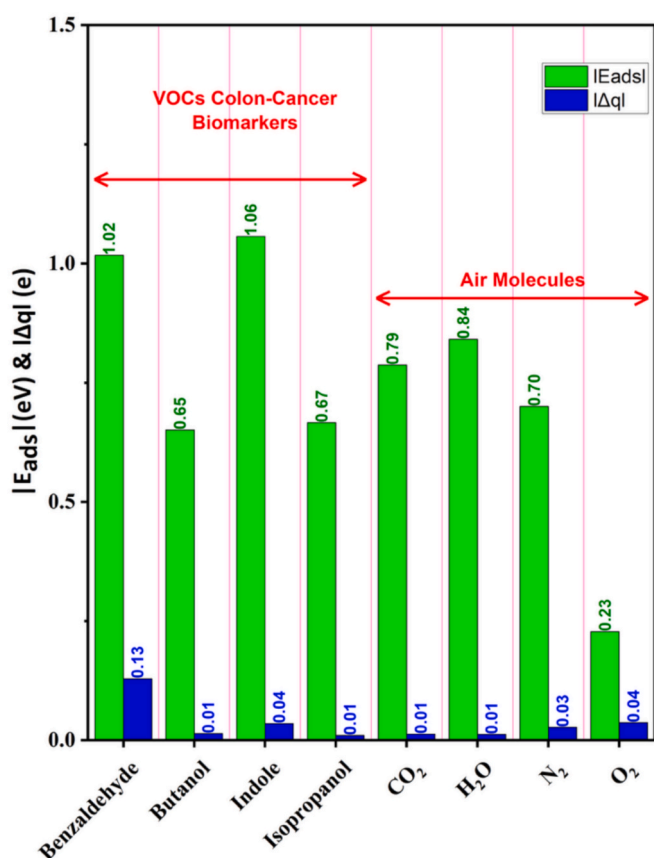


Fig. 10. The absolute values of adsorption energies and charge transfers of four VOCs, related to colorectal cancer biomarker, and four interfering air molecules on 1 K@BO monolayer.

in Table 2, where $|E_{ads}| = 1.928$ eV, 1.300 eV, 1.665 eV and 1.354 eV for the respective four VOCs. These latter adsorption energies $|E_{ads}| \gg 1.0$ eV while in case of air molecules $|E_{ads}| < 1.0$ eV.

Fig. 11a shows the results of work function (Φ), upon the adsorptions of the VOCs, and the interfering air molecules on 1 K@BO sample in blue bars. The $\Phi_0 = 3.57$ eV of the 1 K@BO before the adsorption of the VOCs is shown in a horizontal dotted line. As can be noticed, the change in $\Delta\Phi = |\Phi - \Phi_0|$ is larger in the cases of adsorption of VOC compared to air

molecules. This trend should be an indication for the selective adsorption of VOCs to yield enhanced sensor response. The sensor response is evaluated based on equation (4) and the results are displayed in Fig. 11b. The latter Figure displays the clear selectivity of the 1 K@BO sample toward the detection of VOCs compared to the interfering air molecules (i.e., the sensor responses for VOCs exceeded ratio 2.0 (i.e., 200 % in percentage) while the air molecules do not exceed ratio 1.0 (i.e., 100 % in percentage). It is further noticeable that the work function gets reduced after the adsorption of VOCs. This means that the substrate becomes more conductive as attributed to the donated charge by the VOCs. This trend strongly alters the deviation of IV characteristics and consequently the sensor response.

Finally, it is worth mentioning that although the present study is computational in nature, the synthesis of light-metal-doped BO monolayers is possible given advances in 2D material fabrication. Methods such as CVD, ALD, and MBE have been used for doped boron-based and oxide monolayers. However, the key challenges include achieving uniform dopant incorporation, preventing clustering, and ensuring structural stability, with surface defects and oxygen vacancies requiring careful control.

Conclusion

Efficient detection of volatile organic compounds (VOCs) related to CRC, which is one of the leading causes of cancer-related deaths, offers a promising strategy for accurate patient identification and timely intervention, potentially reducing mortality rates. This study explored the detection of selected VOCs linked to CRC, such as benzaldehyde, butanol, indole, and isopropanol on pristine and light metal functionalized BO monolayers using spin-polarized DFT method. It was found that pristine BO barely can distinguish among the specific VOCs and interfering air molecules (N₂, O₂, CO₂, H₂O) based on adsorption energies. However, the incorporation of light metals (Li, Na, K, Ca) in BO at low doping concentrations improved the adsorption mechanism and enhanced the selectivity. Among the studied systems, K@BO stands out with ideal adsorption energies of -1.017 – -0.651 – -1.057 and -0.666 eV for benzaldehyde, butanol, indole, and isopropanol, respectively. To gain insight into the VOC detection mechanism, we performed calculations of the electronic density of states, band structures, charge transfer, magnetism, and work function. It was found that the VOCs are found to play the role of charging donors (i.e., reducing molecules) and thus enhance the transport properties of the substrate. The work-function-based calculations of sensitivity have revealed clear selectivity towards VOCs, especially in cases of K and Ca embedment/decoration. We

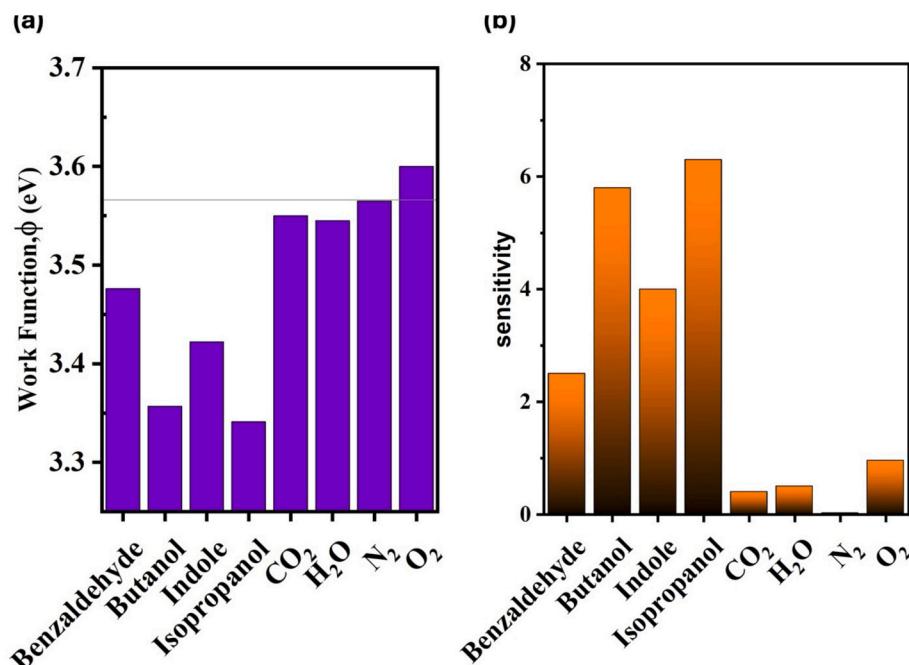


Fig. 11. (a) Work Function, Φ , before (horizontal dashed line) and after (blue colour bars) the adsorptions of four VOCs, related to colorectal cancer biomarkers, and four interfering air molecules on 1 K@BO ML. (b) The corresponding sensor response “sensitivity”, calculated based on the work function. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

concluded that 1 K@BO and 1Ca@BO should be good candidate materials for promising biosensor for the detection of CRC biomarkers. These findings highlight the promising potential of LM@BO-based nano-sensors for the highly sensitive detection of CRC-related VOCs.

CRediT authorship contribution statement

Ibrahim Alghoul: Writing – review & editing, Investigation, Formal analysis, Data curation. **Wael Othman:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Ibrahim Abdi:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Tanveer Hussain:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Nacir Tit:** Writing – original draft, Validation, Supervision, Resources, Project administration, Investigation, Conceptualization.

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 work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rinp.2025.108493>.

Data availability

Data will be made available on request.

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