



Rational design of core functionalized N-alkylated corroles for controlled film gas sensing and methanol detection

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ABSTRACT

Porphyrinoid macrocycles have long been employed as active materials in chemical sensing, relying on molecular engineering of peripheral functionalization to direct the formation of ordered, supramolecular architectures. In contrast, modifications at the macrocyclic core have predominantly involved metal insertion into the inner cavity, whereas the introduction of organic functional groups directly at the core has been comparatively less explored. In contrast, this study investigates an alternative N-alkylation strategy to modulate molecular organization and fine-tune sensitivity and selectivity in gas-sensing devices. Transferring the alkyl chains from the periphery to the corrole core inverts the conventional design paradigm for porphyrinoid-based sensing materials, enabling a more direct control over molecular packing and analyte diffusion. We synthesized 11 compounds, differing in alkyl chain length, branching, and substitution pattern, and integrated them into quartz microbalance (QMB) transducers to construct an innovative corrole-based electronic nose. Systematic exposure to Volatile Organic Compounds (VOCs) revealed that N-alkylation effectively tunes the sensitivity and selectivity profiles according to the alkylated groups, their position, and, ultimately, the molecule charge. Unlike classical approaches, correlation analyses and multivariate data treatment confirmed that alkylation preserves selective interactions while reducing the contribution of non-specific dispersion forces. As a proof-of-concept, the optimized sensor array successfully discriminated methanol adulteration in both real and synthetic wine samples, achieving a near-perfect classification with low estimation error for methanol concentration. This approach establishes N-alkylation as a promising alternative to metallation for the rational design of porphyrinoid-based e-noses, offering a versatile and scalable strategy for detecting methanol and other contaminants in complex matrices.

1. Introduction

The deposition of the sensing layer onto the desired transducer surface is a critical step in developing reliable chemical sensors based on organic materials. This passage aims to preserve the binding properties of receptor functional groups through supramolecular organization in the solid state. For this reason, achieving high selectivity and stability in chemical sensing platforms requires a multiscale engineering strategy in which molecular structure, supramolecular organization, and film microstructure are meticulously co-designed [1,2]. The sensing

performance of organic sensing layers is governed not only by the intrinsic reactivity toward target analytes but also by the ability to assemble macrocycles into ordered, porous architectures that modulate the strength, directionality, and specificity of host-guest interactions. These concepts align with emerging film-engineering methodologies where structural confinement and controlled molecular packing enhance, for example, gas reactivity [3].

Porphyrinoids (porphyrins, corroles, and related macrocycles) exemplify this concept well, offering several tools for systematically modulating their supramolecular assembly, including peripheral

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substitutions, core metalation, and skeletal modification [4]. It is well known that a proper molecular design enables the formation of thin films, nanosheets, and porous networks with application-specific porosity and packing [4,5].

Although this approach has proven effective in many fields, it faces a potential drawback in gas sensing. Often, these supramolecular organizations are achieved through the presence of long or complex peripheral groups, which may introduce competing selective and non-selective interactions or limit the structural freedom of receptors used as building blocks [6–8]. In addition, this approach places the interaction-driven groups at the periphery of the macrocycle, whereas selective binding events are mainly addressed in the core or at the macrocyclic aromatic system, further reducing the selectivity of the resulting sensor. This outcome has been particularly evident in the case of cavitands [9], but the same effect has also been observed with alkoxy-substituted tetraphenylporphyrins [7].

Alternative sensing strategies often employ the electronic nose (e-nose) concept to detect target analytes in complex matrices. This methodology is based on a combinatorial approach, using a set of broadly selective sensors designed to interact with wide classes of chemical compounds. Rather than relying on a single lock-and-key mechanism, the e-nose mimics the human olfactory system by using sensors with complementary and partially correlated response patterns. In this framework, the molecular architecture of corroles provides an ideal platform owing to multiple potential interaction sites, including the inner-core NH groups, the extended aromatic π -system, and the meso-substituents. This structural and synthetic versatility enables systematic tuning of sensor responses through specific molecular modifications.

Conventionally, the selectivity of corroles, and, more generally, of porphyrinoids, for e-nose platforms is modulated by the inclusion of various metal centers, leveraging the Hard-Soft Acid-Base (HSAB) theory to guide coordination. [10,11] However, this approach often offers a relatively narrow range of functional modification and is limited by the axial coordination chemistry of the metal-analyte bond. On the other hand, peripheral spacers may improve film formation and increase porosity by introducing alkylic chains. As a drawback, this modification often leads to indiscriminate increases in non-specific interactions, which can increase correlations among different sensors and thereby reduce model performance [8].

This work explores a novel functionalization approach that introduces functional groups at or close to the macrocyclic core. To the best of our knowledge, this approach has not yet been investigated for sensing purposes. Corrole, a porphyrinoid that is assuming an important role among the plethora of porphyrin analogs [12], can offer this opportunity by modifying the inner core of the macrocycle—through targeted N-alkylation—that provides a powerful yet underexplored mechanism for controlling intermolecular spacing, supramolecular packing, and analyte diffusion within the solid-state film. Such internal modifications enable more predictable sensing responses, fine-grained control over film morphology, and complementary sensing behaviors, depending on the number, position, and length of substituents.

For this purpose, we exploited eleven N-alkylated corroles differing in the position of substitution (N21 and N22), the number of substituents (mono-, di-, and tri-alkylated), and the length or branching of the alkyl chains (methyl, ethyl, butyl, octyl, and methylbutyl) that we have recently synthesized to study their coordination chemistry [13–15]. It is worth noting that N-alkylation is a relatively underexplored functionalization of corrole, and very few examples of synthesized compounds are reported in the literature. The sensing properties were first characterized by exposure to vapors of various chemical probes, judiciously selected to sample different Linear Solvation Energy Relationship (LSER) parameters [16]. We then correlated the molecular stacking and packing within thin films, assessed by simple UV–vis spectroscopy, with the packing and stacking of molecules in the sensing layers, estimated from the film sensitivities toward hydrocarbons. Indeed, steric

hindrance from N-substituents modulates the accessible free volume, thereby directly influencing the sensor sensitivity toward non-polar analytes. At the same time, this behavior does not diminish the overall sensing capability of the films toward other classes of compounds; instead, it highlights a desirable contrast in the interaction profiles of receptors based on their structural differences. As a result, the structural tunability of the films translates into an improved sensitivity–selectivity balance, with potential impact on analyte discrimination in complex vapor mixtures.

In this context, the aforementioned sensor array was optimized and employed as an electronic nose platform to detect methanol adulteration in real wine samples, which is essential for regulatory compliance and product quality assurance. Methanol is a naturally occurring component of wine, formed during fermentation as a result of the enzymatic hydrolysis of pectins [17]. Although low concentrations, typically below 150 mg/L in table wines, are generally well tolerated physiologically, higher levels may pose significant health risks [18,19]. As a toxic alcohol, methanol has been implicated in severe poisoning events, especially in cases of intentional adulteration, where it is illicitly added to increase alcoholic strength at minimal cost. In addition, some grape varieties, particularly those belonging to *Vitis labrusca* (such as Isabella or Uva Fragola), naturally yield higher methanol concentrations due to their elevated pectin content [20]. Consequently, distinguishing methanol produced naturally during fermentation from methanol introduced through adulteration is essential for oenological quality control and food safety. Traditional analytical techniques for methanol determination—e.g., gas chromatography with flame ionization detection (GC-FID)—offer high accuracy but are time-consuming, require specialized expertise, and are unsuitable for rapid or on-site screening [21–23]. Notably, while corroles and porphyrinoids are widely utilized as gas-sensing materials, their application for the quantification of methanol within the complex matrix of wine headspace remains, to the best of the authors' knowledge, currently unreported. For this reason, we conducted tests on six samples of Italian wines and artificial wine solutions to assess the potential of our platform for methanol detection. The results demonstrated a satisfactory ability to identify methanol even within real wine matrices.

2. Results and discussion

2.1. Sensor characterization

We synthesized a non-alkylated corrole as a reference (TTC) and eleven N-alkylated corroles, each involving different numbers and N-positions of alkyl chains (methyl, ethyl, butyl, octyl) or ramifications (methyl butyl), as previously published by our group [13–15]. General synthetic and purification procedures are reported in the Supporting Information. These sensing materials were deposited on Quartz Microbalances (QMBs) by drop casting to form a novel e-nose platform (see Fig. 1).

An initial study aimed to explore if and how the presence, length, position, ramification, and number of alkyl chains can influence the responses toward a set of probe chemicals, which include three series of linear alkanes, alcohols, and amines of different lengths, four gases, and other compounds of interest (e.g., water, acids, and aromatic compounds). This set of compounds was chosen to probe the different non-covalent interaction mechanisms involved during the absorption process. To quantitatively rationalize these interactions within the solid-state sensing films, the Linear Solvation Energy Relationship (LSER) model was employed. This semi-empirical approach represents a well-established alternative in literature for characterizing sensing mechanisms, as it synthesizes the primary non-covalent forces into five fundamental parameters: polarity (II), polarizability (R^2), Lewis acidity and H-bond donating behavior (α), Lewis basicity and H-bond accepting behavior (β), and a solute descriptor related to the cavity formation and dispersion interactions ($\log L^{16}$). Table S1 and Fig. S1 report the LSER

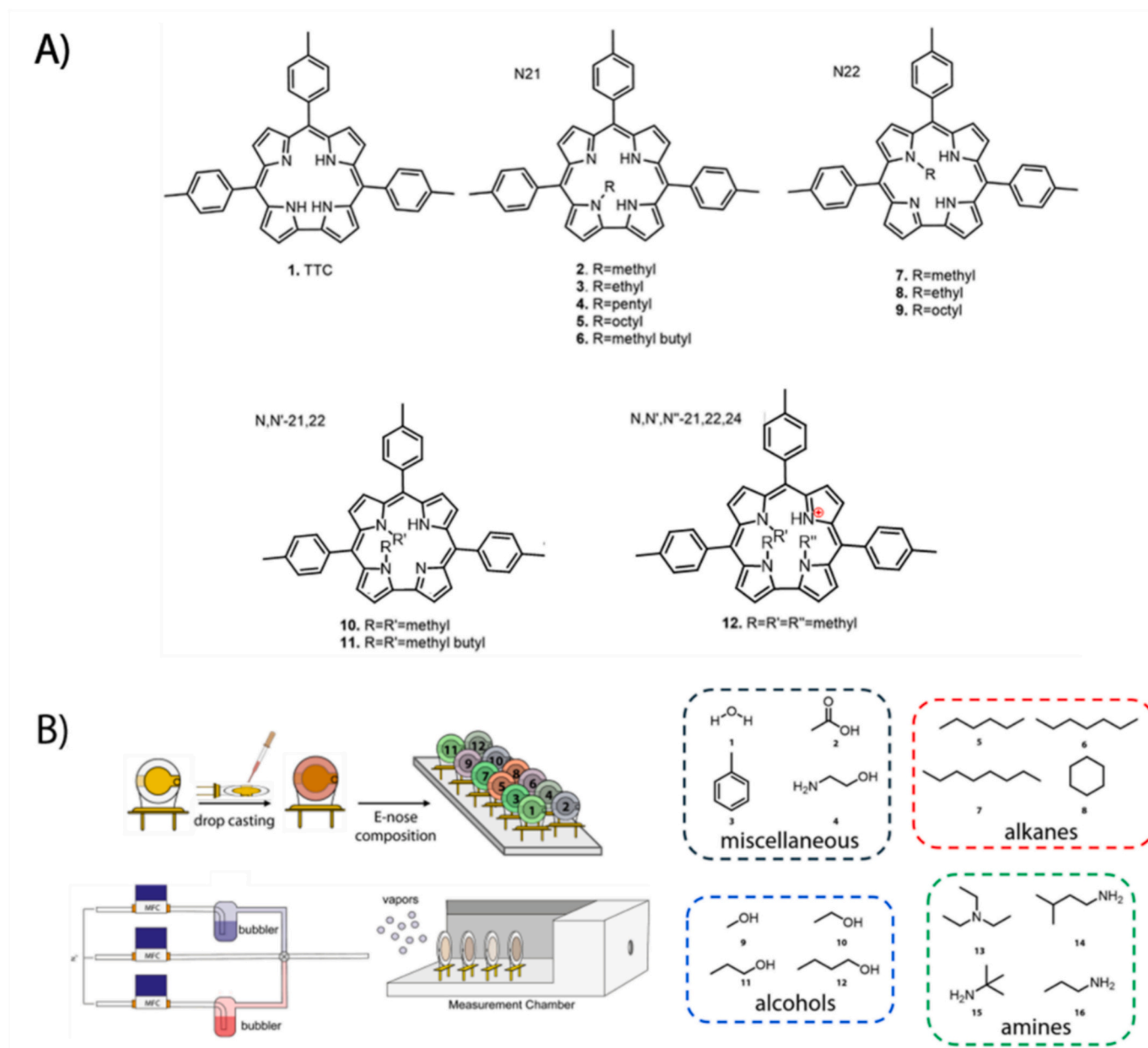


Fig. 1. A) Compounds utilized in the studies. B) Experimental setup for vapor measurements.

parameters for the analytes tested.

Since Quartz Microbalances (QMBs) are mass-sensitive transducers, the observed signal is proportional to the cumulative sum of these supramolecular interactions, as mediated by the affinity of the receptor layer. Consequently, the application of the LSER model allows for estimating the relative weight of each interaction type for each element in the array by correlating sensor sensitivity with the analyte's LSER parameters. This approach provides an integrated view of the sensing mechanisms, elucidating how specific structural modifications of corroles modulate the fundamental interactions that drive the overall sensor responses.

For each compound, we tested five concentrations with four replicates, yielding a total of 320 samples, equally divided among the 16 analytes. The samples tested, along with their concentrations, are reported in Table S2.

The sensor array comprises 12 elements (hereinafter, QMB1 to QMB12) that differ in position, number, length, and ramification of alkylic substituents. In particular, QMB1 is a pristine corrole with no

substitution groups. QMB2 to QMB6 present a single alkylic chain on the nitrogen in position 21, linear in four cases (QMB2:methyl, QMB3:ethyl, QMB4:butyl, QMB5:octyl) and branched in one case (QMB6:methyl butyl). N22-alkyl corroles have been used in QMB7 to QMB9 (QMB7: methyl, QMB8:ethyl, QMB9:octyl). NN'-21,22-dimethyl and NN'-21,22-butyl methyl corroles have been deposited onto QMB10 and QMB11, respectively. Finally, the tris-(N-methyl) corrole was utilized in the QMB12. Interestingly, this latter compound is positively charged due to the presence of four substituents at the macrocycle core (three N-methylated groups and an NH). A full characterization of these compounds and an evaluation of changes associated with the position of substituents are reported in Ref. 15.

For each measurement, the frequency shift due to gas/vapor absorption is extrapolated and used to describe the sensor response as reported in the experimental section. The characteristic curves, reporting concentration versus response data with the corresponding relative linear fits, are presented in Figs. S2-S5.

Fig. S6 reports the sensitivity patterns toward the tested VOCs.

Considering the comparison with non-substituted corrole, the presence of alkyl groups attenuates the sensitivity toward polar molecules (short-chained alcohols and water, for example) in all the cases except for QMB12. This latter outcome is expected as N-alkylation reduces the occurrence of hydrogen bonding by substituting one or more NH groups and increases hindrance at the macrocycle center. In the case of Tris-(*N*-methyl)⁺, the presence of a stable positive charge significantly influences selectivity, shifting the affinity toward water and polar compounds.

A more detailed and rational comparison of the influence of substituent number and position has been obtained by reporting the normalized sensitivities of the different VOCs. Normalization involves dividing the sensitivities for the deposited mass reported in Table S3. Fig. 2A reports the sensitivities obtained for alkanes, alcohols, and amines, considering only the methyl-substituted macrocycles. As a general outcome, the presence of a methyl group reduces the sensitivity

toward polar species, except for the case of the charged Tris-(*N*-methyl)⁺ corrole. Considering the position of substitution, N21-methyl shows higher sensitivity toward short-chain alcohols (methanol and ethanol), while N22-methyl shows higher affinity for alkanes, long-chain alcohols, and amines. With respect to mono-substituted, dimethyl corrole shows a generally higher sensitivity than mono-substituted toward all the analytes considered, as if it combines both QMB2 and QMB3 sensing properties.

Fig. 2B compares methyl, ethyl, and octyl-alkyl corroles (N21 and N22). The trend previously described between the N21 and N22 positions is generally preserved over the length of the N-alkyl chain, even if, as expected, the sensitivity toward alkanes increases when the length of the substituent group increases.

Finally, we compare TTC with all the N21 corroles (Fig. 2C). It is immediately evident that alkylation lowers the sensitivity toward alcohols and amines with respect to TTC. At the same time, it appears to

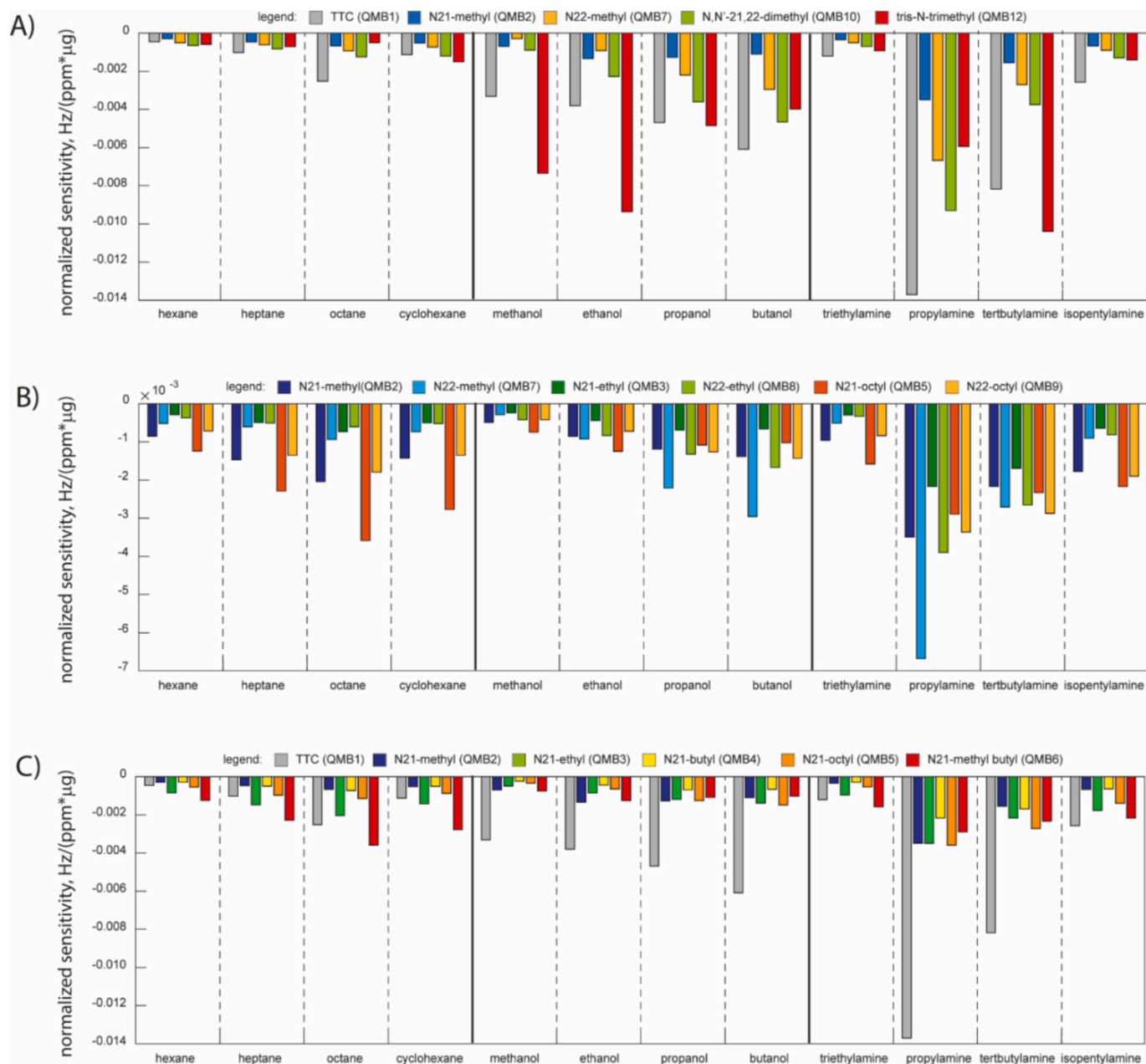


Fig. 2. Sensitivity patterns normalized by mass deposited in the case of (A) mono-, di-, and trimethyl corrole series, (B) N21 and N22 mono-substituted alkyl corrole series, and (C) N21-alkyl corrole series.

reduce the influence of the response pattern due to steric hindrance and analyte dispersion interactions. For example, while TTC sensitivity increases linearly with alcohol chain length (from methanol to butanol), the N21 alkyl corrole sensitivities exhibit a peculiar pattern, as previously described. This outcome is a remarkable result, as the relative variation now appears less correlated with non-selective interactions, represented, for example, by the $\log L^{16}$ parameter previously mentioned.

We further analyzed the correlation between the sensitivity of each sensor, considering only the VOCs (Fig. S7). In particular, a nonparametric estimator, such as Spearman's correlation, can better capture trends due to the general non-linear behavior and the wide range of sensitivities.

From the correlation analysis, QMB1 (non-alkylated) appears to be more closely correlated with short-chained N-alkyl corroles, such as the mono- and dimethyl-substituted ones (QMB2, QMB7, QMB10). The trimethyl corrole is generally poorly correlated with other sensors because its positive charge makes its sensing properties quite peculiar. If we fix the position of the alkyl group, the increase in chain length tends to reduce the correlation in all the cases (QMB2 to QMB5 for N21, QMB7 to QMB9 for N22, and QMB10–11 for N,N'-21,22). Finally, the presence of a non-linear substituent group appears to significantly alter the pattern of responses, as illustrated by N21-methyl butyl corrole, where the correlation with all other sensors is generally low. This outcome demonstrates that N-alkylation is an efficient synthetic procedure for producing sensors with a distinct, peculiar pattern of sensitivity and could be a valid alternative to metalation. At the same time, we want to ensure that the N-alkylation process preserves the more selective interactions and does not increase the influence of non-selective ones, such as dispersion forces.

Thus, we investigated whether there is a correlation between the previously introduced LSER parameters and the sensitivities of the QMBs in the array. Absolute values of sensitivities were used to ensure

positive correlation when parameters increase the characteristic curve slope, and vice versa. In this framework, the correlation coefficients serve as indicators of the relative weight of each interaction type, providing a quantitative measure of the importance of the different mechanisms involved in the analyte-corrole interaction. Specifically, a null correlation indicates that a particular mechanism is negligible for that receptor; a positive value suggests that the interaction favors analyte partitioning into the film; a negative correlation implies that the specific mechanism tends to inhibit the interaction, acting as a repulsive contribution. Understanding how structural modifications alter these relative contributions can help drive selectivity toward target compounds and facilitate the design of complementary receptors for e-nose platforms.

As a first outcome, Fig. 3 confirms the similarities between TTC and alkyl corroles with short chains (QMB1, QMB2, QMB7, QMB8, QMB10, and QMB12). The sensitivities of these sensors are primarily correlated with acid-base interactions (α and β), polarizability (R^2), and dispersion forces ($\log L^{16}$), while the polarity parameter (Π) appears to have a marginal impact across the array. A slight increase in its contribution is observed only in some N-methylated derivatives, attributed to the out-of-plane distortion induced by the N-substitution, which strengthens dipole-dipole interactions. The $\log L^{16}$ parameter represents dispersive interactions, which are typically minimized in sensing applications to enhance the selective binding properties of molecular receptors. For example, $\log L^{16}$ is negatively correlated with the sensitivities of TTC and alkyl corroles with short chains. Remarkably, as chain length increases, N-alkylation tends to reduce or eliminate the correlation with this term. This behavior contrasts with conventional peripheral alkyl substitution, where longer chains typically lead to responses dominated by dispersion forces. [8] In the case of long-chain substituents (e.g., QMB5 and QMB9), the drastic reduction in α and β correlations suggests a steric shielding effect, where the alkyl groups obstruct the accessibility of the macrocycle core. Consequently, the sensing mechanism for these

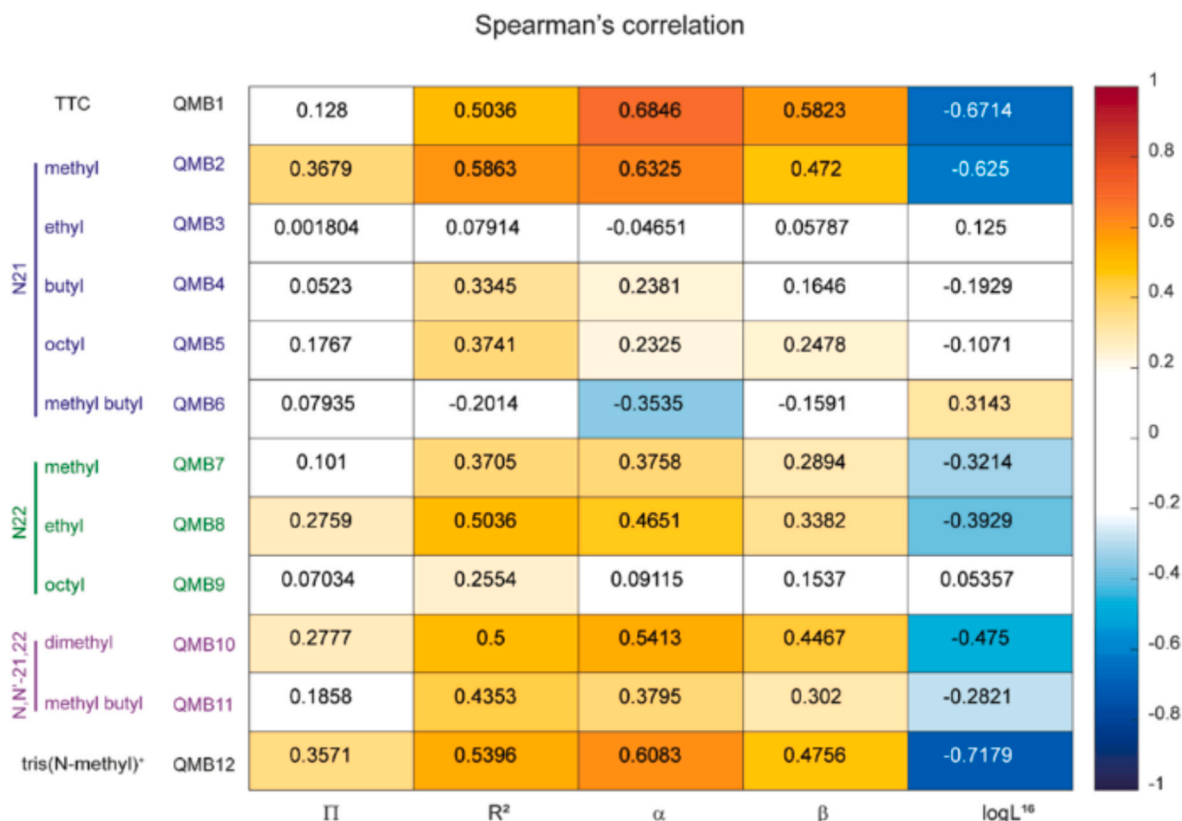


Fig. 3. Correlation matrix between sensors (based on sensitivities) and LSER parameters of VOCs.

derivatives is simplified, relying primarily on polarization interactions involving the aromatic π -system (R^2).

Whereas shorter chains decrease the negative influence of steric hindrance, preserving polarization and hydrogen bonding with the center of the tetrapyrrolic ring (e.g., because of an increase of distortion). These outcomes corroborate the viability of N-alkylation as an alternative synthetic strategy to peripheral substitution or metallation for tailoring and directing sensing performance.

2.2. Optical and morphological characterization with gas sensing correlation

Here, we propose the normalized ratio between the Soret-band maximum and the Q-band maximum in thin films (divided by the same ratio measured in solution) as a spectroscopic proxy for the degree of intermolecular aggregation in N-alkyl corroles. A normalized value approaching unity indicates that the macrocycles retain a more solvated-like optical response, consistent with limited π - π coupling and increased intermolecular spacing, an effect plausibly governed by steric factors associated with N-alkyl substituents, both their position on the macrocycle, the length and rigidity of the alkyl chains. Conversely, significant deviations from unity, accompanied by a redistribution of Soret/Q-bands intensities, suggest stronger electronic coupling and more compact molecular organization within the film. This interpretation is consistent with the broader literature on porphyrinoid thin films, where variations in Soret-band position, width, and relative intensity have long been associated with differences in molecular packing, aggregate formation (H- or J-type), and excitonic interactions, providing indirect insight into supramolecular arrangements [24,25]. Fig. 4A reports the experimental values, and Fig. S8 shows full spectra. Thus, films exhibiting higher normalized Soret/Q-bands ratios are expected to possess a larger effective free volume or intermolecular voids, which, in turn, are expected to drive interactions in accordance with analyte size. Experimental evidence of this behavior involves the use of non-polar analytes, such as alkanes, which interact predominantly through dispersive (London) forces and therefore require accessible, weakly confining environments to be effectively accommodated. Fig. 4B reports the correlation plots for the N21 and N22 homologous series. Accordingly, films characterized by low aggregation, as reflected by a higher normalized ratio, tend to exhibit higher sensitivities to alkane vapors. This outcome is consistent with the general understanding that porphyrinoid packing, porosity, and available free volume of sensing films

are key determinants of the uptake of non-polar guest molecules. Furthermore, optical spectral features can serve as robust, non-destructive indicators of these structural properties. It is worth noting that the N21 and N22 substituents generated two distinct correlation curves. In particular, N22 curves have a higher slope, meaning that they can more easily interact with the alkanes, in accordance with crystallographic evidence of a higher distortion of the aromatic ring in these macrocycles.

The AFM characterization was then performed on both ultra-flat glass and QMB gold surfaces, providing a direct link between molecular structure and supramolecular organization, to further investigate the sensing mechanisms of films. The non-alkylated TTC film exhibits a predominantly smooth surface with shallow, sub-nanometric undulations (Fig. 5e), consistent with a densely packed lamellar arrangement driven by π - π stacking interactions in a typical J-type configuration. Conversely, N-alkylation significantly alters the film morphology across all derivatives examined (Fig. 5a–d), leading to a transition toward textured, heterogeneous surfaces with porous and globular features. This morphological change is likely triggered by the intrinsic out-of-plane distortion of the N-substituted macrocycle, which disrupts the coherent stacking required for lamellar growth and promotes a more open, porous arrangement.

The UV–Vis spectra of the films (Fig. S8) provide further spectroscopic evidence of this reorganization. While the TTC film exhibits a predominantly red-shifted Soret band indicative of the aforementioned J-type lamellar stacking, the N-alkylated derivatives show broader bands and a more complex excitonic profile. The emergence of a blue-shifted component (around 400–410 nm) alongside a red-shifted shoulder suggests a coexistence of H-type cofacial aggregation and J-type interactions. This spectral complexity is entirely consistent with the distorted conformation of the N-substituted core, which prevents the formation of uniform lamellar structures. The AFM investigation further reveals that the film morphology depends on both the length and position of the N-alkyl substituent. N-methylated corroles promote a fine, granular topography with sub-micrometric aggregates (Fig. 5a, c), whereas N-octyl derivatives display a markedly coarser landscape characterized by globular clusters and crater-like formations (Fig. 5b, d). This chain-length-dependent evolution is driven by the increased steric hindrance and conformational flexibility of the octyl chains, which more effectively obstruct close π - π stacking. The resulting ‘hill-and-valley’ topography is consistent with a cofacial aggregation mode, in which face-to-face stacking generates compact columnar domains (hills)

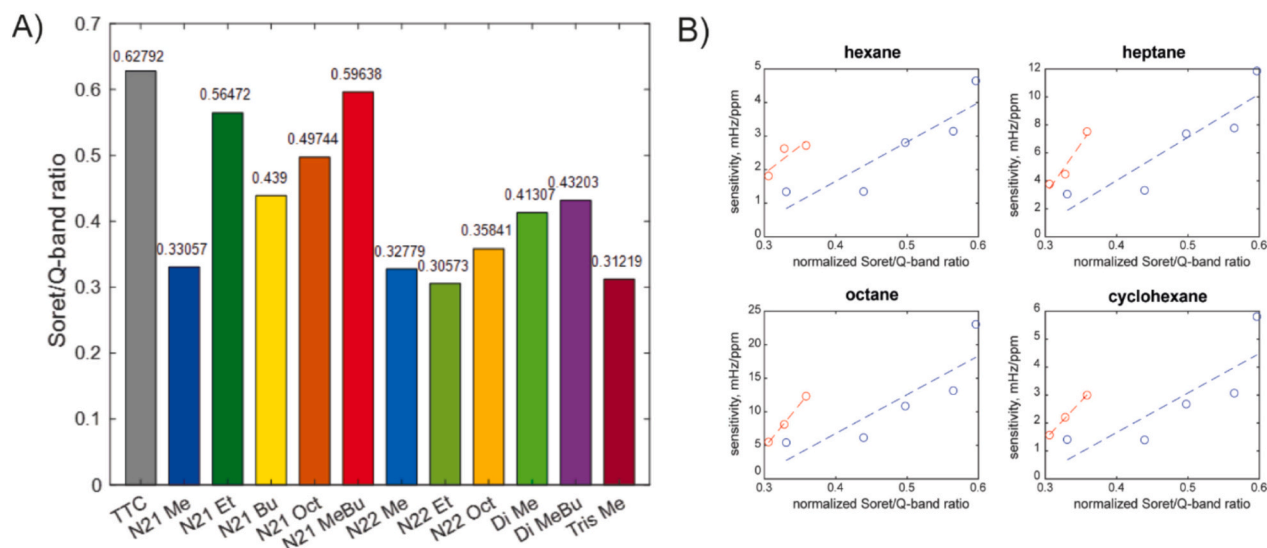


Fig. 4. Soret/Q-band ratio calculated from solid films spectra (left). On the right, the correlation between this optical parameter and sensitivities to the four different alkanes tested.

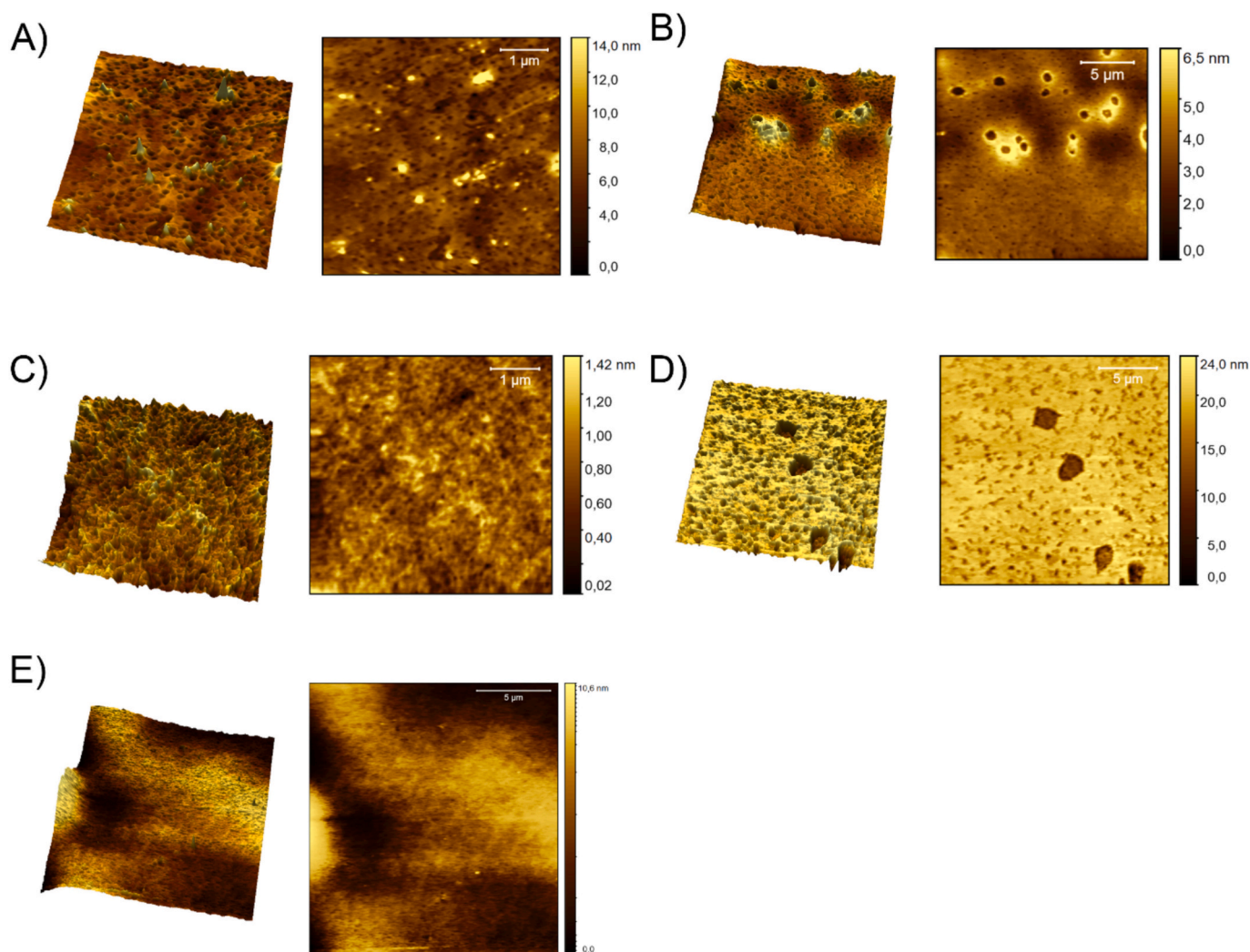


Fig. 5. AFM topographic images (2D and 3D views) of corrole films deposited on ultra-flat glass: (a) N21-methyl, (b) N21-octyl, (c) N22-methyl, (d) N22-octyl, and (e) TTC. Please note that (b) scale is 5 μm .

separated by interstitial regions (valleys). Crystallographic structures further evidence that the alkylic chain tends to orient the corroles face-to-face, promoting cofacial stacking (see Fig. S9, which shows lattices of N21-methyl and N21-ethyl, reproduced from CIF files in the Cambridge Crystallographic Data Centre, CCDC 2269991 and CCDC 2344465, respectively).

Finally, AFM analysis of the films deposited on QMB gold electrodes (Fig. S10) confirmed the preservation of these porous, globular morphologies on the actual transducer surface, despite the intrinsic roughness of the polycrystalline gold, which attenuated the morphological contrast between methyl and octyl derivatives.

2.3. Multivariate data analysis

After rationalizing the single sensor properties according to the structural properties of corroles, we decided to utilize an unsupervised multivariate approach, such as t-SNE [26], to evaluate the possibility of clustering the analytes of interest with the sensor array developed. The experimental dataset comprises a 320×12 matrix, containing 20 samples for each of 16 compounds at five different concentrations. It is worth noting that this can be considered a quite complex clustering problem due to the similarities between most compounds and the wide range of VOC concentrations. Indeed, the role of concentration is often underestimated, yet it is likely the most common factor contributing to

sample overlap in non-well-designed sensor arrays. Fig. 6A shows the sample plot in the two components obtained from the algorithm, using the Mahalanobis distance and linearly normalized input data. The plot indicates that almost all the 16 compounds are well clustered in the plane. It is possible to distinguish different groups in distinct regions: water (blue), alcohols (red), hydrocarbons (gray), and amines (green). This outcome stems from the sensor array design and well illustrates the working principle of e-nose platforms, where, albeit using broad, selective sensing, complementary sensitivity patterns enable separation of compounds based on their interaction mechanisms. At the same time, homologous series within these classes are still well separated based on the length of their chains (e.g., ethanol, methanol, propanol, and butanol). Amines are also ordered from left to right when considering the hindrance of chains connected to the NH_2 group. Although t-SNE is an unsupervised algorithm, we obtained an almost perfect clustering, despite the similarities among the selected compounds and the extended concentration range considered, confirming the possibility of using N-alkylation as a valid alternative to metalation or peripheral substitutions for developing e-nose platforms. To further investigate the influence of sensor choice on clustering, we mapped the local Mahalanobis distances of individual features to the overall distance used in the t-SNE algorithm (Fig. 6B). Indeed, the Mahalanobis distance uses the covariance matrix as weights, thereby reflecting both the correlations between sensors and between sensors and compounds.

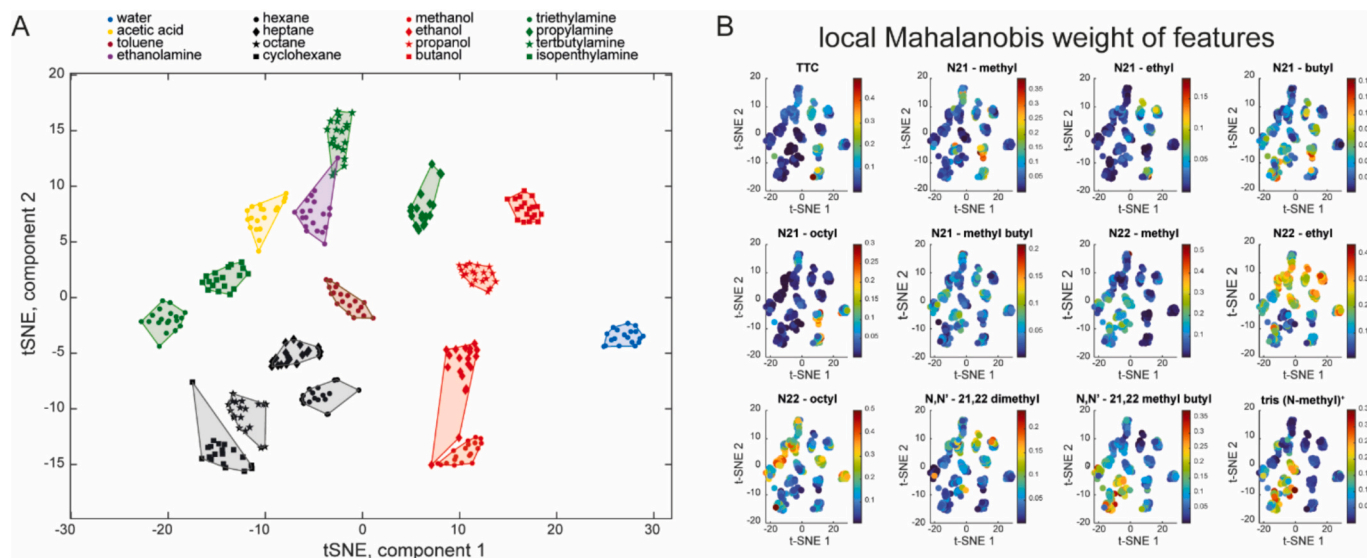


Fig. 6. A) t-SNE plot of the overall dataset. B) The local Mahalanobis weight of the 16 single features/sensors. The contribution to the overall weight for each sample is shown as a color map from blue to red.

For this reason, the outcome partially reflects the analogies found in the correlation matrix reported in Fig. 3, even though it provides a more detailed picture of the clustering regions of individual receptors. In particular, each feature provides a weight represented by a color on the map; thus, samples with similar colors have similar weights from the descriptor. This means that regions with similar colors can be seen as clusters for the single feature. On the contrary, when a color change is present, the samples are differentiated by that sensor. In Fig. 6B, the color maps illustrate that the influence of substitution positions (N21 and N22) and substituent length is more effective at separating samples within the same homologous series (e.g., alcohols, amines, and hydrocarbons). For example, N21-methyl clusters methanol and ethanol; N21-ethyl shows a higher contribution to methanol and butanol, while N21-butyl shows a higher contribution to ethanol and propanol.

Although in the case of non-linear mapping, it is not possible to define a direction for features in the clustering space, this local mapping of features can provide further insight into mapping mechanisms and help optimize the array for specific tasks.

2.4. Case studies with real samples

Based on these outcomes, we used this array in a potential case study to detect methanol in wine. A preliminary experiment on different white and red wines identified the optimal sensor subset (see Table S4 and Fig. S11). In this phase, eight sensors were ultimately selected by balancing the complementarity of their sensitivity patterns, repeatability, and stability of response to wine headspace compounds. While analyzing pure compounds under low-humidity conditions allowed characterization of the interaction mechanisms in the different sensing films, the use of real wine samples provides a direct approach to identify a subset of sensors optimized for this specific application, accounting for the concomitant presence of variable amounts of ethanol at high relative humidity content.

Apart from cross-selectivity interferences, high humidity levels may cause, in some sensors, an excess of absorbed water molecules. This massive uptake can lead the sensing layer to deviate from the rigid-film regime (Sauerbrey behavior) by increasing the film viscosity or altering its adhesion to the transducer. Such changes induce significant viscoelastic damping, enhancing dissipative phenomena and altering the resonance frequency. These effects can ultimately destabilize the oscillation signals from the QMB, making it essential to select sensors that maintain a stable, gravimetric response in complex matrices for reliable

quantification. According to these latter aspects, QMB1 and QMB12 have been excluded, even though they showed promising sensing performance in a dry atmosphere.

The first case study simulates artificial wine adulteration by measuring samples containing a fixed alcohol concentration of 15% with varying proportions of ethanol and methanol. PCA in Fig. 7A shows the data visualization in the PC1-PC2 plane. It is possible to observe a non-linear pathway of scores from 0% to 15% ethanol and from 15% to 0% ethanol-methanol percentages. The two principal components account for a substantial portion of the total variance, underscoring the array's ability to represent the problem's complexity in a minimal number of dimensions.

Then, a more complex scenario has been investigated by adding an aliquot of alcohol (ethanol or methanol) to real white wine samples. The addition of ethanol ensures that clustering does not arise from increased alcohol content but rather from intrinsic differences in responses to ethanol and methanol. Furthermore, it also confirms the possibility of detecting methanol presence regardless of the wine's alcoholic grade. The PC1-PC2 plane projection of scores indicates that the different samples appear clustered, both in terms of ethanol content and in methanol adulteration, suggesting potential classification capability.

To prove the classification capabilities, we run a classification task comprising the 55 samples among those reported in Fig. 7B, which include five repetitions of pure white wine, ethanol addition in white wine (0.15%, 0.30%, 0.45%, 0.60%, 1%) and methanol addition in white wine (0.15%, 0.30%, 0.45%, 0.60%, 1%). We run 100 experiments, in which the overall dataset is randomly split into training and test sets (25 and 30 samples, respectively). We then used a hierarchical classification strategy: an SVM model classifies the samples, and a Gaussian process regression (GPR) model estimates the methanol concentration for samples identified as adulterated. These models were built at each iteration, using 25 samples from the training data. Considering the SVM model, we achieved a mean accuracy of 0.994, with a perfect classification score in 93 of 100 cases (across quartiles, $Q1 = Q2 = Q3 = 1$). Curiously, all misclassified samples are pristine wine samples. This first outcome demonstrates that this simple system can recognize methanol contamination in a complex matrix, such as white wine, and across different alcoholic grades. Considering the regression task, the average RMSE of GPR models over the 100 test sets was 0.063% (std = 0.015%). Distributions of accuracies and RMSE obtained over 100 runs are reported in Fig. S12. In this case, the results confirm the feasibility of estimating methanol adulteration with good accuracy, even in a real-

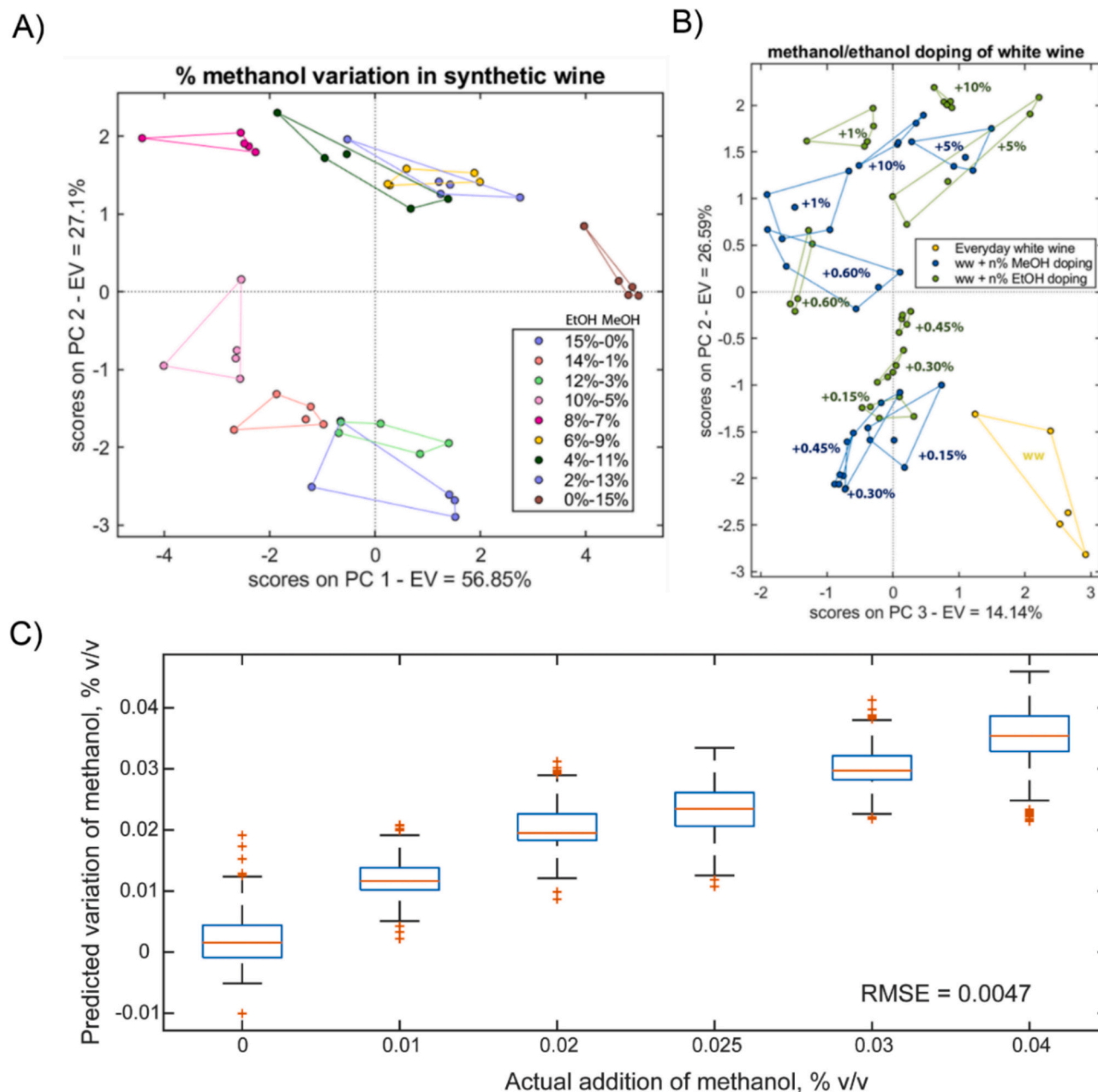


Fig. 7. A) Scores plot in PC1-PC2 projection considering different ethanol/methanol mixtures in water. B) Scores plot reporting the samples of pristine white wine, and methanol or ethanol doped samples at different percentages. C) Performance validation of the multivariate classification model for methanol detection. The data illustrate the system's ability to discriminate between concentrations within the 0.01%–0.04% v/v range, including the 0.032% v/v OIV regulatory limit. The results represent the average performance across 100 cross-validation iterations, with error bars indicating the stability of the sensor response across random 50/50 training/test splits.

world setting.

Additionally, to assess the robustness of the e-nose against variations within the wine matrix, we evaluated the impact of volatile acidity, the second most significant source of variability after ethanol. This was achieved by spiking wine samples already adulterated with 0.05% methanol with acetic acid (0.01% to 0.06% v/v), covering the typical range of volatile acidity (0.04% - 0.08%). Remarkably, the relative variation in sensor response remained extremely limited (within 5%), with no significant fluctuations observed except for a single sensor (see Fig. S13).

Finally, the array was validated by adulterating wine samples up to 0.04% methanol to determine if the system could accurately detect concentrations near the legal limit (ca. 0.032% v/v) defined by the

International Organization of Vine and Wine (OIV). In this experiment, the ethanol concentration was kept constant to establish a stable blank reference and minimize baseline variability. As with the previous regression model, dataset has been randomly and equally divided into training and test to evaluate the performance in validation. In order to reduce the dependance on a specific training/test selection, the validation procedure was iterated 100 times. The resulting regression model yielded a prediction error (RMSE) of 0.004% v/v, which is significantly lower than the OIV threshold (Fig. 7C). These results confirm the feasibility of detecting methanol levels below the legal limit within the proposed case study.

3. Conclusions

Here, we reported the use of N-alkylation in corroles as an effective and versatile synthetic strategy for engineering the sensing properties of porphyrinoid-based materials. By relocating alkyl substituents from the periphery to the macrocyclic core, the resulting compounds exhibit controlled molecular packing, enhanced analyte diffusion, and tunable selectivity.

The investigation of eleven N-alkylated corroles revealed that both the number and position of alkyl chains peculiarly affect sensitivity toward volatile organic compounds, while maintaining selective interactions over non-specific ones. In particular, N21-methylated derivatives exhibited improved responses to short-chain alcohols, whereas N22-substituted analogues showed higher affinities for less polar species. The distinctive behavior of the positively charged tris-(N-methyl) corrole further highlights the structural versatility of this class.

The deposition of these materials onto quartz microbalance transducers enabled the development of a new e-nose platform capable of detecting methanol adulteration in wine with high reproducibility and near-perfect classification accuracy. These findings corroborate the possibility of applying this novel class of sensing materials in practical applications, such as those in the agrifood sector. Beyond this particular case study, N-alkylation may serve as a potential tool for the rational design of supramolecular sensors, in which molecular distortion and internal functionalization act as key parameters for fine-tuning sensing performance.

4. Experimental section

4.1. Reagents

All reagents were purchased from Merck and used without further purification. Compounds **1** and N-alkyl corroles **2–12** were synthesized and purified according to the literature [14–16].

Regarding wine samples, six Italian wines were selected, comprising three red and three white wines with varying alcohol content levels. They are respectively: everyday red (blend, Emilia Romagna 10.5%), Donnafugata (blend, Sicily, 13%), Virica (Shiraz, Lazio, 14%) for the reds, everyday white (blend, Emilia Romagna, 10.5%), Casa Divina Provvidenza (Sauvignon, Lazio, 13%), and Cantina Produttori Bolzano (Sauvignon, Südtirol, 14%) for the whites. All of them were purchased from Italian supermarkets.

4.2. Experimental setup

The Quartz Microbalances (QMBs) are made of AT-cut quartz with a fundamental oscillation frequency of 20 MHz and an estimated sensitivity of 7.20 Hz/ng, determined using the Sauerbrey equation and experimental results [27]. QMB sensors were deposited by drop casting, utilizing a solution containing 1 mg/mL of corrole in CH₂Cl₂. Each sensor was covered with ca. 20 kHz of sensing material for each side (Table S3 reports the exact deposited masses). Fig. 1A lists the twelve corroles utilized.

Sensors were placed in an airtight chamber provided with a gas inlet and outlet, and an electronic board that measures the fundamental frequency of each sensor at 1 sample/s with a resolution of 0.1 Hz. The array was exposed to 16 different chemical probes selected from the principal classes of compounds (such as alcohols, hydrocarbons, amines, etc).

Analytes were delivered using a digitally controlled three-channel mass flowmeter system. Organic vapors of the different analytes were generated by bubbling pure nitrogen through the liquid sample of each compound. The saturated vapor concentration of the volatile organic compound was calculated using Antoine's law. The desired concentrations have been obtained by diluting the saturated vapor concentration with an additional nitrogen flow. Each analyte was measured at five

concentrations, with four repetitions per concentration, for a total of 320 measurements (see Table S1 for the complete list of compounds and concentrations). The total flow rate was kept constant at 200 sccm for the whole experiment. The temperature of the entire system (liquid sample, gas, and sensors) and the environmental humidity were maintained at 20 °C and 8%, respectively, throughout the entire experiment.

The measurement protocol consists of three phases: measuring the baseline, exposing the sample to the desired analyte concentration, and recovering under a nitrogen flow. The response descriptor has been chosen as the frequency change between the end of the adsorption phase and the baseline before the exposure. Characteristic curves were obtained by plotting responses vs. concentration and fitting data with a first-order polynomial equation. Sensitivities have been estimated as the first derivative of the fitting curves, obtaining constant values. Correlations have been calculated using Spearman's rank correlation coefficients to reduce the effect of non-linearities, while also accounting for the different response ranges. Multivariate analysis, t-SNE, and PCA have been performed using an ad hoc algorithm developed in MATLAB with Python code.

AFM measurements were performed in air at room temperature with an home made microscope working in the weak repulsive regime of non-contact mode with an exerted force of less than a nN. BudgetSensors TAP150-GD-10 Gold Coated Soft Tapping cantilevers with a spring constant of 5 N/m and an expected statistical apical radius of 10 nm were used with a typical scan rate of 1–2 s/row (400/500 points/row). Data were background-subtracted and then analyzed using Gwyddion, free and Open Source software, <https://gwyddion.net/>.

Classification has been performed using a radial basis function Support Vector Machine (SVM), and regression has been performed using a Gaussian process regression (GPR) model with constant basis functions and an exponential kernel. In the case of a classification dataset, it has been randomly split into training and test sets of 25 and 30 samples, respectively. Tests have been run 100 times to minimize bias introduced by the specific choice of training and test subsets. For low methanol concentrations, we use a Gaussian process regression (GPR) model with constant basis functions and an exponential kernel. Results report classification outcomes across 100 runs, where each time the 50-sample dataset is randomly split into training and test sets of 25 samples each.

4.3. Real samples

The preliminary experiment was performed on real samples (70 mL) from six different varieties of Italian wines. Measurements were performed considering 5 repetitions in random order.

The second experiment used synthetic wine samples prepared with different ethanol/methanol ratios in water (15%–0%, 14%–1%, 12%–3%, 10%–5%, 8%–7%, 6%–9%, 4%–11%, 2%–13%, 0%–15%). A total of 9 samples were prepared by mixing different percentages of water and ethanol/methanol (70 mL).

The third experiment involved testing wine samples (70 mL) spiked with increasing concentrations of methanol and ethanol (0.15%, 0.30%, 0.45%, 0.60%, 1%, 5%, 10%). All samples were measured five times.

The fourth experiment involved testing wine samples (70 mL) adulterated with 0.05% methanol, spiked with increasing concentrations of acetic acid (0.01%, 0.02%, 0.03%, 0.04%, 0.05%, 0.06%). All samples were measured five times.

The fifth experiment involved testing wine samples (70 mL) spiked with increasing concentrations of methanol (0.010%, 0.020%, 0.025%, 0.030%, 0.040%), up to the legal limit (ca. 0.032% v/v). All samples were measured five times.

CRedit authorship contribution statement

Francesco Pizzoli: Writing – original draft, Investigation, Formal analysis. **Gabriele Magna:** Writing – review & editing, Writing –

original draft, Supervision, Software, Data curation, Conceptualization. **Marco Luce:** Data curation, Investigation, Visualization. **Antonio Criscenti:** Data curation, Investigation, Visualization. **Sara Nardis:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Corrado Di Natale:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Roberto Paolesse:** Writing – review & editing, Supervision, Methodology, Funding acquisition, 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.

Appendix A. Supplementary data

LSER parameters, compounds and concentrations tested, sensor characteristic curves, sensor sensitivities, QMB frequency changes upon deposition, correlation matrix, spectra in solution and films of receptors, wine samples, and optimized array configuration. Supplementary data to this article can be found online at [<https://doi.org/10.1016/j.cej.2026.178800>].

Data availability

Data will be made available on request.

References

- [1] P.M. Bulemo, D.H. Kim, H. Shin, H.J. Cho, W.T. Koo, S.J. Choi, C. Park, J. Ahn, A. T. Güntner, R.M. Penner, I.D. Kim, Selectivity in chemiresistive gas sensors: strategies and challenges, *Chem. Rev.* 125 (2025) 4111–4183, <https://doi.org/10.1021/acs.chemrev.4c00592>.
- [2] P. Najafi, A. Ghaemi, Chemiresistor gas sensors: design, challenges, and strategies: a comprehensive review, *Chem. Eng. J.* 498 (2024) 154999, <https://doi.org/10.1016/j.cej.2024.154999>.
- [3] K. Lee, Y.M. Jo, M.S. Sohn, M. Jeon, C. Kim, O. Gul, S.J. Park, B.K. Kim, K.S. Chang, C.B. Jeong, J. Kim, Y.C. Kang, I. Park, Photoactivated conductive MOF thin film arrays on micro-LEDs for chemiresistive gas sensing, *Nat. Commun.* 16 (2025) 9612, <https://doi.org/10.1038/s41467-025-64602-9>.
- [4] C.M. Drain, A. Varotto, I. Radivojevic, Self-organized porphyrinic materials, *Chem. Rev.* 109 (2009) 1630–1658, <https://doi.org/10.1021/cr8002483>.
- [5] R.D. Mukhopadhyay, Y. Kim, J. Koo, K. Kim, Porphyrin boxes, *Acc. Chem. Res.* 51 (2018) 2730–2738, <https://doi.org/10.1021/acs.accounts.8b00302>.
- [6] R. Paolesse, S. Nardis, D. Monti, M. Stefanelli, C. Di Natale, Porphyrinoids for chemical sensor applications, *Chem. Rev.* 117 (2017) 2517–2583, <https://doi.org/10.1021/acs.chemrev.6b00361>.
- [7] C. Di Natale, D. Salimbeni, R. Paolesse, A. Macagnano, A. D'Amico, Porphyrins-based opto-electronic nose for volatile compounds detection, *Sensors Actuators B Chem.* 65 (2000) 220–226, [https://doi.org/10.1016/S0925-4005\(99\)00316-0](https://doi.org/10.1016/S0925-4005(99)00316-0).
- [8] C. Di Natale, R. Paolesse, A. Macagnano, S. Nardis, E. Martinelli, E. Dalcanele, M. Costa, A. D'Amico, Sensitivity-selectivity balance in mass sensors: the case of metalloporphyrins, *J. Mater. Chem.* 14 (2004) 1281, <https://doi.org/10.1039/B313250A>.
- [9] M. Suman, M. Freddi, C. Massera, F. Ugozzoli, E. Dalcanele, Rational design of cavitand receptors for mass sensors, *J. Am. Chem. Soc.* 125 (2003) 12068–12069, <https://doi.org/10.1021/ja0355271>.
- [10] C. Di Natale, R. Paolesse, A. Macagnano, A. Mantini, P. Mari, A. D'Amico, Qualitative structure-sensitivity relationship in porphyrins based QMB chemical sensors, *Sensors Actuators B Chem.* 68 (2000) 319–323, [https://doi.org/10.1016/S0925-4005\(00\)00451-2](https://doi.org/10.1016/S0925-4005(00)00451-2).
- [11] A. Catini, R. Kumar, R. Capuano, E. Martinelli, R. Paolesse, C. Di Natale, An exploration of the metal dependent selectivity of a metalloporphyrins coated quartz microbalances array, *Sensors* 16 (2016) 1640, <https://doi.org/10.3390/s16101640>.
- [12] C. Di Natale, C.P. Gros, R. Paolesse, Corroles at work: a small macrocycle for great applications, *Chem. Soc. Rev.* 51 (2022) 1277–1335, <https://doi.org/10.1039/D1CS00662B>.
- [13] R. Paolesse, A. Marini, S. Nardis, A. Froio, F. Mandoj, D.J. Nurco, L. Prodi, M. Montalti, K.M. Smith, Novel routes to substituted 5, 10, 15-triarylcroles, *J. Porphyrins Phthalocyanines* 7 (2003) 25–36, <https://doi.org/10.1142/S1088424603000057>.
- [14] F. Pizzoli, A. Mita, F. Caroleo, S. Nardis, U. Calice, M. Caporale, S. Belviso, S. Superchi, A. Marconi, M. Calvaresi, Palladium complexes of N-methylcorroles, *Chem. Eur. J.* 29 (2023) e202302517, <https://doi.org/10.1002/chem.202302517>.
- [15] F. Pizzoli, S. Nardis, A. Fata, M. Marsotto, G. Petrella, F.R. Fronczek, K.M. Smith, R. Paolesse, N-Alkylcorroles, *J. Porphyrins Phthalocyanines* 28 (2024) 358–369, <https://doi.org/10.1142/S1088424624500196>.
- [16] R.W. Taft, J.L.M. Abboud, M.J. Kamlet, M.H. Abraham, Linear solvation energy relations, *J. Solut. Chem.* 14 (1985) 153–186, <https://doi.org/10.1007/BF00647061>.
- [17] Y. Han, J. Du, Relationship of the methanol production, pectin and pectinase activity during apple wine fermentation and aging, *Food Res. Int.* 159 (2022) 111645, <https://doi.org/10.1016/j.foodres.2022.111645>.
- [18] A. Paine, A.D. Davan, Defining a tolerable concentration of methanol in alcoholic drinks, *Hum. Exp. Toxicol.* 20 (2001) 563–568, <https://doi.org/10.1191/096032701718620864>.
- [19] G. Botelho, O. Anjos, L.M. Estevinho, I. Caldeira, Methanol in grape derived, fruit and honey spirits: a critical review on source, quality control, and legal limits, *Processes* 8 (2020) 1609, <https://doi.org/10.3390/pr8121609>.
- [20] C.Y. Lee, W.B. Robinson, J.P. Van Buren, T.E. Acree, G.S. Stoewsand, Methanol in wines in relation to processing and variety, *Am. J. Enol. Vitic.* 26 (1975) 184–187, <https://doi.org/10.5344/ajev.1975.26.4.184>.
- [21] R. Caruso, G.L. Gambino, M. Scordino, L. Sabatino, P. Traulo, G. Gagliano, Gas chromatographic quantitative analysis of methanol in wine: operative conditions, optimization and calibration model choice, *Nat. Prod. Commun.* 6 (2011) 1939, <https://doi.org/10.1177/1934578X1100601237>.
- [22] M. Paolini, L. Tonidandel, R. Larcher, Development, validation and application of a fast GC-FID method for the analysis of volatile compounds in spirit drinks and wine, *Food Control* 136 (2022) 108873, <https://doi.org/10.1016/j.foodcont.2022.108873>.
- [23] B. Lin, X. Wang, L. Tang, S. Wang, Y. Shi, L. Zhao, H. Jiang, Comparative study of headspace and headspace single drop microextraction combined with GC for the determination of methanol in wine, *J. Chromatogr. A* 1673 (2022) 463079, <https://doi.org/10.1016/j.chroma.2022.463079>.
- [24] N.J. Hestand, F.C. Spano, Expanded theory of H-and J-molecular aggregates: the effects of vibronic coupling and intermolecular charge transfer, *Chem. Rev.* 118 (2018) 7069–7163, <https://doi.org/10.1021/acs.chemrev.7b00581>.
- [25] R. Giovannetti, The use of spectrophotometry UV-vis for the study of porphyrins, *macro Nano Spectrosc.* 6 (2012) 87–108.
- [26] L. van der Maaten, G. Hinton, Visualizing data using t-SNE, *J. Mach. Learn. Res.* 9 (2008) 2579–2605.
- [27] G. Magna, R. Belugina, F. Mandoj, A. Catini, A.V. Legin, R. Paolesse, C. Di Natale, Experimental determination of the mass sensitivity of quartz microbalances coated by an optical dye, *Sensors Actuators B Chem.* 320 (2020) 128373, <https://doi.org/10.1016/j.snb.2020.128373>.