# Colocalized Raman and IR Spectroscopies via Vibrational-Encoded Fluorescence for Comprehensive Vibrational Analysis

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tion, facilitating diverse applications, such as interfacial sensing, chemical analysis, and biomedical diagnostics. The complementary selection rules of Raman and IR spectroscopies offer distinct, yet mutually reinforcing, insights into molecular structure and dynamics. However, in dynamic or complex chemical environments, either technique alone is not capable of providing a complete and nuanced picture of molecular vibrations. Simultaneous detection of complementary vibrational modes within the same molecular group remains challenging due to wavelength discrepancies and sensitivity mismatches between Raman and IR spectroscopies. In this work, to address the gap between these spectroscopies, we developed an integrated approach based on vibrational-encoded fluorescence (VEF), in which the complementary vibrational information is respectively encoded into the different



parts of fluorescence radiation: Stokes fluorescence carrying Raman information and anti-Stokes fluorescence reflecting IR information. This method employs a dual-resonant microsphere-on-mirror plasmonic structure to bridge the waveband gap, enabling the simultaneous detection of complete vibrational modes in the visible spectrum with ultrahigh sensitivity down to  $\sim$ 100 molecules. Hyperspectral colocalization imaging demonstrates spatial correlations between the complementary vibrations. By careful calibration, the detection efficiency is improved by 8 orders of magnitude compared to unenhanced IR spectroscopy. This approach creates new opportunities for the precise identification of molecular vibrational information in complex chemical environments.

## INTRODUCTION

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Raman and IR spectroscopy are two of the most fundamental techniques for identifying the chemical "fingerprint" information on molecules,<sup>1-3</sup> each sensitive to specific vibrational modes governed by distinct selection rules. Raman spectroscopy is sensitive to symmetric vibrations that alter polarizability, while IR absorption spectroscopy detects antisymmetric modes that change the dipole moment of molecules. Together, these spectroscopies compose complementary vibrational spectroscopy (CVS), enabling the comprehensive interpretation of molecular vibrations. Effectively, these two techniques provide projections of molecular vibrational profiles onto different analytical planes. While one technique can reveal certain chemical features, similar profiles between different molecules may lead to ambiguous interpretations. This issue becomes particularly significant in complex or dynamic chemical environments, such as electrochemical cells,<sup>4</sup> catalytic surfaces,<sup>5–7</sup> security check,<sup>8</sup> physiological tissue,<sup>9</sup> or characterization of art works.<sup>10</sup> In these scenarios, there is a demand for complete identification of vibrational modes<sup>4,11,12</sup> to probe the intrinsic fingerprint information at the chemical bond level. The long-standing challenge of integrating CVSs (Raman and

IR) has attracted significant research attention nearly two decades ago. By employing dual-resonant plasmonic nanostructures, both complementary vibrational signals are concurrently enhanced, yet the vibrational spectra still have to be performed on separate instruments and encounter spatial discrepancies of "hotspots" between visible and MIR spectral regimes.<sup>11,13–15</sup> Hence, integrating Raman and IR spectros-copies presents a significant challenge due to their fundamentally different physical mechanisms and energy scales.<sup>3,16,17</sup>

The core challenge stems from the vast difference in photon energies involved:<sup>18</sup> Raman spectra are obtained from the inelastic scattering of incident visible or near-IR photons, while IR spectra primarily involve the absorption of mid-IR (MIR) photons by specific chemical bonds (Figure 1a). This energy

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Figure 1. (a) Working wavebands of Raman and IR absorption spectroscopy, illustrating a significant waveband gap between the Raman spectrum and the IR absorption spectrum. (b) Schematic of acquiring complementary vibrational information within the same waveband: Raman-active modes are detected in the Stokes region, while IR-active modes are excited by MIR radiation and observed in the aS region. (c,d) Detection of Raman-active and IR-active modes, respectively, within the spectrum. The IR-active modes are encoded to the enhanced-fluorescence in panel (c), and Raman-active modes are detected by the surface-enhanced Raman scattering in panel (d).

mismatch has been considered an insurmountable barrier to simultaneous detection for a long time, as it necessitates two separate detection systems with vastly different sensitivities and noise characteristics.<sup>18–20</sup> Additionally, MIR detectors, which are generally more sensitive to thermal noise, exhibit 2–4 orders of magnitude lower detectivity than visible-light detectors,<sup>21,22</sup> exacerbating the disparities in signal-to-noise ratio (SNR) and sensitivity between the two techniques.<sup>11,13,14,23,24</sup>

Recent efforts to overcome this limitation have focused on indirect methods, such as photothermal expansion, to probe the molecular IR absorption.<sup>24–26</sup> IR photons absorbed by molecules are converted to heat, resulting in localized thermal expansion and subtle changes in refractive index, which can be detected by optoelectronic devices operating in the visible range and overlapped with Raman spectroscopy.<sup>25,27–29</sup> While these techniques offer the potential for integration, they often require high-intensity and short-pulse IR excitation.<sup>30,31</sup> The photothermal process induced by high-power IR laser would significantly contribute to the local temperature increment.<sup>24</sup> Consequently, the heat relaxes and contributes to an intensity variation of photoluminescence (PL).<sup>25</sup>

Some approaches involve engineering the electronic states of molecules to enhance the sensitivity of Raman scattering or IR absorption detection.<sup>29,32–35</sup> These approaches transduce the IR-sensitive vibrations into the anti-Stokes Raman or fluorescence peaks,<sup>29,32–34,36</sup> thus achieving significantly higher detectivity. These techniques merge the gap between the fluorescence spectroscopy and vibrational spectroscopy, which is termed as "VEF".<sup>37</sup> Such advancements enable IR spectroscopy to achieve even single-molecule-level sensitivity, paving the way for more precise and sensitive molecular detection in complex environments. However, the simultaneous acquisition of complementary vibrational modes has not been correlatively

obtained within a unified experimental framework among state-of-the-art spectroscopic platforms. A fundamental challenge persists in achieving concurrent signal acquisition across Raman-active and IR-active vibrational information, particularly on analyzing colocalized molecules.

In this work, we developed a VEF-based method that fundamentally resolves the energy and spatial mismatches using a dual-resonant plasmonic cavity. The molecules residing in the cavity are populated in the vibrational excited states by a single-wavelength MIR laser. Under this "preresonant" condition at the IR-active vibrational state, the molecules are then pumped to the electronic excited states by a continuouswave visible beam. The photon energy of the visible beam is a bit lower than the energy gap of the electronic transition, leading to a low quantum yield of fluorescence without MIR induced. By scanning the MIR excitation wavelength, the subsequent fluorescence intensity is modulated, which is the "vibrational-encoded" procedure of IR-active vibrational modes (Figure 1c). Simultaneously, Raman-active modes are directly obtained from the energy difference between the visible pump and Stokes Raman scattering light. Thus, IR-active and Ramanactive modes are independently deciphered, respectively, from the anti-Stokes and Stokes wavebands of the PL spectrum. By leveraging the nonlinear conversion of molecular IR absorption into anti-Stokes (aS), the VEF method effectively overcomes the inefficiency of direct MIR photon detection. Furthermore, it guarantees that complementary vibrational signals are derived precisely from the same spatial location, since both the converted fluorescence and Raman scattering signals are amplified via the near-field enhancement induced by the visible laser. Our experimental setup integrates VEF-CVS detection with conventional surface-enhanced IR absorption (SEIRA) measurement for comparison. After careful calibration, VEF demonstrates an efficiency increase of 8 orders of magnitude over unenhanced IR reflection spectroscopies and larger detection efficiency than SEIRA, offering a powerful new tool for comprehensive vibrational spectroscopy in complex chemical environments.

#### RESULTS AND DISCUSSIONS

VEF in the Dual-Resonant Plasmonic Cavity. The method is rationally designed for simultaneously acquiring VEF-based Raman and IR spectra (Figure 2a). In our integrated system, the pump and probe beams are precisely aligned and focused on the dual-band resonance cavity (Figure S1a,b). This cavity is constructed by drop-casting silver microspheres (AgMSs) on the pretreated gold film (see sample preparation section in Methods). With a diameter of 4  $\mu$ m, AgMS is tuned to efficiently couple the incident beams and significantly enhance the electric fields in the nanogap of microparticles on the mirror (MSoM), as shown in Figure S1c, up to a 10<sup>4</sup> enhancement factor  $(|E/E_0|^2)$  for visible excitation at 633 nm and  $10^5$  for MIR excitation wavelengths at 6  $\mu$ m  $(\sim 1667 \text{ cm}^{-1})$ . The enhanced areas generated by two beams overlap well, with the full width at half-maximum (fwhm) of the two fields firmly confined to less than 94 nm in this cavity. The overlapping region is determined by the visible-light field, which is more confined to the cavity. Moreover, since both IR absorption and surface-enhanced Raman scattering (SERS) occur within the visible electromagnetic field, this configuration ensures that the enhanced CVS are obtained from the exact overlapping region in the nanocavity. Such a carefully



**Figure 2.** (a) Experimental setup for CVS. The system can operate as a VEF-based CVS (VEF-CVS) setup or detect the IR absorption of molecules in reflection mode. The inset illustrates the working mode of the cavity: blue and red arrows represent the incident visible pump beam and MIR probe beam, respectively; the green arrow denotes the fluorescence-encoded IR signal, and the yellow arrow indicates the scattered Raman signal. (b) PL spectra modulated by the MIR probe beam. The lower graph compares PL spectra with and without MIR laser excitation, showing an enhanced PL intensity. The upper graph presents the molecular PL intensity, which increases by up to 100% with a 1590 cm<sup>-1</sup> MIR excitation. (c) Integrated aS-PL signal as the MIR wavenumber is scanned over time.

designed configuration addresses the concern that the CVS originate from the same group of molecules.

The significant enhancement factor  $(|E/E_0|^2)$  and the small mode volume can efficiently promote the optical nonlinear process, as mentioned, IR-converted fluorescence emission, and Raman scattering. By utilizing a self-assembly method,<sup>38</sup> Rhodamine B (RhB) molecules are embedded within the nanocavity. When the plasmonic microsphere is irradiated by single-wavelength MIR waves, RhB molecules residing in the cavity are populated to a specific IR-active state. The molecules are prepared to be sufficiently activated, or "preresonant state" as previous work employed,<sup>35</sup> for the consequent transition to the electronic excited state, pumped by the visible photons. Only with this preactivation of IR modes, the PL of molecules would be improved and yield a comparatively high quantum efficiency because the energy of visible pump photons is insufficient to leap over the gap between the electronic excited state and the ground state. Therefore, the technique in this manuscript does not require the molecular vibrations to be both Raman- and IR-active, which distinguishes the technique distinctly different from the sum-frequency generation (SFG) spectroscopy.<sup>29,32</sup> Based on this mechanism, the IR absorption of molecules, namely, IR-active vibrations, are addressed from

the aS photoluminescent (aS-PL) intensity increment while switching on and off MIR excitation. Compared to the PL spectrum without the 1595 cm<sup>-1</sup> MIR illuminations, an increase in aS part ( $\Delta$ aS-PL) reaches over 100% due to the activation of IR-active modes. Meanwhile, the inelastic Raman scattering signal is also amplified by the surface-enhanced structure when the visible laser excites the cavity. Eventually, both IR and Raman vibrations are encoded and then radiated as propagating light, which is able to be acquired by the spectrometer in the far field (Figure 2b).

To verify that the  $\Delta$ aS-PL signal in Figure 2b correlates with the IR absorption of molecules, we tune the MIR excitation wavenumber and employ the integral of aS-PL to determine the IR absorption. As the MIR wavenumber sweeping scans at the speed of 25 cm<sup>-1</sup> per minute, the integral of aS-PL would respond to the MIR and interpret the IR absorption band of molecules. In the spectra, the integral of aS-PL keeps a trend to slowly decrease without MIR involved (black line in Figure 2c), which is attributed to the intrinsic bleaching process of fluorescence because of the long-time exposure to the incident visible beam. Once the MIR excitation is on, the intensity shows a close dependency on the wavenumber of MIR photons and the VEF-IR spectrum is the integral difference by MIR on and off (green line in Figure 2c).

The vibrational-encoded process generates aS fluorescent photons through the interaction of incident visible and MIR photons, which bears some resemblance to SFG, particularly vibrational SFG (vSFG). Yet, these techniques differ fundamentally in their selectivity and enhancement mechanisms. vSFG detects molecular vibrational modes via their intrinsic second-order nonlinear susceptibility, requiring these modes to be both Raman- and IR-active to break inversion symmetry. In contrast, the VEF can identify complementary vibrational modes without exclusions. Regarding mechanisms, the nonlinear vSFG process typically depends on the temporal and spatial overlap of two pulsed laser beams on the interfaces, with electric field enhancement derived from the pulses themselves. VEF, however, employs a dual-resonant plasmonic cavity to amplify fields for subsequent photon conversion. We have rigorously investigated whether SFG contributes to aS-PL (Figure S2). Our findings reveal that the enhancedfluorescence induced by 1590 cm<sup>-1</sup> MIR emits at 590 nm rather than at the expected SFG signal wavelength of 575 nm. Furthermore, by modulating MIR photon energy and analyzing the resulting differential aS-PL ( $\Delta aS$ -PL) heatmap, we have conclusively demonstrated the absence of any relationship with either SFG or differential frequency generation (DFG) photon energies.

To further confirm that the variation of aS-PL is strictly due to the vibrational-encoded process rather than the thermal effect, we modulate the pulse frequency of MIR sources. The IR-converted peak at 1595 cm<sup>-1</sup> exhibits a strong dependence on the MIR pulse frequency, even with the same 15% duty cycle (Figure S3a). The aS-PL signal is amplified by over 200% with 200-kHz MIR pulses, compared to that of ~10% with 2kHz IR pulses. The aS-PL intensity features a transient rather than thermally boosted process since the heat is inferred to fluctuate less than 10% based on the MIR power measured (Figure S3b). To investigate the impact of thermal effects on PL signal, we employed a temperature-controlled chamber to measure the PL intensity of RhB molecules across a range of temperatures (from room temperature 25 to 95 °C). We detected a fluorescent peak for RhB at 590 nm, which



**Figure 3.** (a) Heatmap of the PL of an MSoM with sweeping MIR wavenumber. The visible pump wavelength is 633 nm. (b) VEF-CVS spectrum. The Stokes and aS regions are decoded into Raman and IR absorption spectra, respectively, producing a CVS. A comparative analysis is provided among the results from this work, Raman spectroscopy, IR spectra obtained via DFT calculations, and commercial instruments (Bruker FTIR spectrometer and HORIBA Xplora Raman spectrometer). Colored boxes highlight vibrational modes, with colors corresponding to the colored regions on the left and arrows indicating the displacement vectors in molecules. (c) Line width of VEF-IR modes. (d) Line width of VEF-Raman modes. (e) Intensity profiles of the colocalization images in panels (f–h), along the white arrow in panel (f). The images are normalized for clarity, and the intensity curves show an fwhm of 4  $\mu$ m. (f–h) Simultaneous imaging of an MSoM at specific vibrational modes: (f) Raman mode at 1643 cm<sup>-1</sup>, (g) IR mode at 1595 cm<sup>-1</sup>, and (h) aS-PL intensity. The inset shows an optical image captured by the top-view camera (scale bar: 4  $\mu$ m).

exhibited a decrease in intensity with increasing temperature. Our findings indicate that the thermal effect exerts a negative influence on PL intensity, contrary to a potential enhancement we observed via the VEF technique (Figure S4). The PL spectra are acquired by Raman spectroscopy (HORIBA Xplora), and the temperature of the sample is controlled by a closed-loop temperature-controlled chamber (Instec HCS601G-IRM).

**Complementary Vibrational Mode Detection.** The VEF technique transduces molecular IR-active modes into the fluorescence intensity, which can be transformed into MIR absorption spectra through a sweeping scan of the MIR photon energy. The PL heatmap of tuning MIR energy provides a detailed mapping of intrinsic IR absorption bands and Raman vibrational modes. The experimental PL heatmap delineates the intrinsic IR absorption bands and Raman vibrations. The heatmap's darker red regions signify increased PL intensity, corresponding to MIR absorption at a

specific wavenumber. Raman peaks manifest as horizontal red lines traversing the PL heatmap (Figure 3a), which are annotated by the dark blue arrows on the right-y-axis with Raman shift. The comprehensive vibrational modes are extracted from both the aS and Stokes (S) segments of the heatmap. These modes are corroborated by comparing them with theoretical calculations based on density functional theory (DFT) and experimental IR and Raman spectra obtained using an ATR-FTIR spectrometer and Raman microscopy (Figure 3b). Notably, the VEF method outperforms commercial instruments in terms of spectral resolution. The VEF-IR spectrum achieves a fwhm of approximately 8  $cm^{-1}$  at the 1595 cm<sup>-1</sup> peak, while the VEF-Raman peak exhibits a line width of around 20 cm<sup>-1</sup>, which can be decreased by employing a grating with finer gratings. The spectral range of VEF-IR spans 1450-1670 cm<sup>-1</sup>, which is limited by the available wavelengths of our quantum cascade laser (QCL) module. To expand this spectral coverage, multi-QCL chip integration



Figure 4. (a) Visible and (b) MIR power dependence of the aS-PL signal in the VEF-IR spectra. (c) Relationship between the converted-IR intensity and MIR beam power. The slopes of the lines are steeper for absorbable MIR photons, such as those at 1507 and 1595 cm<sup>-1</sup>. (d) Stokes and aS Raman peak intensities as a function of increasing MIR power. (e) VEF-IR spectra for a gradient concentration of the assembly solution. Colored shadows represent the error range for multiacquisitions (n > 8). (f) Dependence of the  $\Delta aS$ -PL integral on the concentration of the assembly solution. (g) VEF-IR spectrum. (h) Surface-enhanced IR absorption spectra obtained in the reflection mode using our experimental setup. Reflection spectra are shown for a single MSoM (green line) and several MSoMs (brown line).

could facilitate the acquisition of broader molecular vibrational bands. Alternatively, nonlinear frequency conversion presents an effective strategy, as demonstrated in recent studies that couple optical parametric oscillators (OPOs) with difference frequency generation (DFG).

A key advantage of our technique is its ability to simultaneously detect both IR-active and Raman-active

modes within the same spectrum. For instance, the backbone of the RhB molecule exhibits two distinct vibrational modes: the asymmetric and the symmetric stretching modes. These two stretching modes are altered, respectively, by the dipole moment and the polarizability of molecules. The asymmetric one at peak 1584 cm<sup>-1</sup> is sensitive to IR but hard to capture in Raman spectrum (indicated by the red region and vibration in

the red box, Figure 3b). On the contrary, the symmetric stretching mode appears prominent at 1643 cm<sup>-1</sup> in the Raman spectrum but inconspicuous in the IR spectrum (see the yellow region and vibrational mode in the yellow box in Figure 3b). These characteristic IR and Raman peaks of RhB molecules are consistently observed by the VEF-CVS method, across different samples, as demonstrated in Figure S5. For vibrational modes both IR- and Raman-active at ~1507 cm<sup>-1</sup>, the VEF-CVS spectrum reveals characteristic peaks consistent with DFT calculations. Notably, the asymmetric stretching mode exhibits a narrower line width and a blue shift in frequency, appearing at 1595 cm<sup>-1</sup> in the VEF-IR spectrum compared to 1584 cm<sup>-1</sup> in the FTIR spectrum. The reduced line width and vibrational frequency shift suggest a specific orientation of RhB molecules adsorbed onto the substrate. In contrast to the randomly dispersed arrangement in solid powder, as indicated by the broad absorption peak measured by FTIR, the collective RhB molecules tend to adsorb onto the Au substrate in a uniform orientation, which contributes to a narrower line width on the VEF-IR spectrum. To confirm this, we performed DFT calculations, which reveal that molecular orientation alone, by adjusting the angle of RhB molecule relative to the substrate, can cause vibrational frequency shifting up to  $3 \text{ cm}^{-1}$  in the spectrum. A detailed analysis of the eigen vibrational mode is provided in the Supporting Information (Figure S6). The calculations show that the vibrational frequency of VEF-IR aligns most closely with the DFT results when the RhB molecule is oriented at a 90-degree angle to the substrate.

Furthermore, the other vibrational modes calculated by DFT are also strongly correlated to the spectra acquired by the VEF method (Figure S7), validating the accuracy of the calculations. A new Raman peak appears at 1560 cm<sup>-1</sup> when using VEF-Raman (orange line in Figure 3b), which is absent in the SERS spectrum. To determine the origin of the peak, we performed DFT calculations, tuning the molecular energy difference corresponding to the electronic excitation state. The 1560 cm<sup>-1</sup> peak emerges as the molecular energy increases (Figure S8). This result indicates that the RhB molecule is activated to a higher energy state by the combined effect of both visible and IR laser beams rather than by either laser alone.

To further confirm the generality of the VEF method, we applied this technique to detect the CVS of cyanine 3.5 (CY3.5), a widely used dye for labeling proteins, nucleic acids, or antibodies.<sup>39-41</sup> The VEF method successfully captured both Raman and IR-active vibrational modes of CY3.5, demonstrating its ability to probe complementary spectral signatures within the same molecular system. The results obtained using the VEF method showed a high degree of correlation with Raman and IR absorption spectra acquired from commercial scientific instruments (Figure S9), validating its accuracy and reliability. Moreover, the hyperspectral imaging capability of the VEF technique allows for precise spatial colocalization of Raman and IR signals, highlighting its utility in complex environments. These findings underline the versatility of the VEF method and suggest its potential for broad applications in chemical analysis, biomedical research, and materials science.

Furthermore, the VEF method excels in the spatial colocalization of complementary vibrations due to the overlapping enhanced fields in both the visible and MIR wavebands, as illustrated in Figure S1. To demonstrate it, we performed hyperspectral imaging of a single MSoM and

achieved spatial colocalization of the Raman signal with the IRactive mode and aS-PL (Figure 3e), as depicted in Figure 3f-h (with the optical image inset in Figure 3h). The bright regions, representing the Raman-active mode, IR-active mode, and aS-PL emission intensity, overlap on the sample surface. The strong correlation between IR-active mode and aS-PL images spatially elucidates that the VEF-IR spectrum rigorously originates from the nonlinear conversion process mediated by a molecular fluorescence behavior. In addition, the spectrally complementary vibrational modes (Raman-active mode in Figure 3f and IR-active mode in Figure 3g) further corroborate the alignment of the enhanced fields for visible and IR excitation, as designed in the VEF configuration. After normalizing these spectral images, the intensity cross-section profiles (Figure 3h) have the same peak center and reveal an fwhm of approximately 4  $\mu$ m, apparently with finer resolution of the diffraction limit of IR laser apparently with finer resolution than the diffraction limit of IR lasers.

In principle, the VEF method addresses the concern that complementary vibration modes are simultaneously obtained at identical spatial position. By conventional methods, <sup>11,13,14,18,42</sup> it would be challenged to identify the vibration information originates rigorously from the same group of molecules in the near-field or unable to attain the same optical spatial resolution in both IR and Raman spectra as shown in Figure 3h.

Sensitivity Performance of VEF. The VEF-IR casts the spotlight on the efficiency of detecting the IR absorption, compared to the FTIR method. A further investigation is demonstrated for the incident power dependency of the aS-PL, by increasing the power of the pump and probe beams. As is shown by the linearity in Figure 4a,b, the intensity of VEF-IR would be proportional to the excitation pump and probe power. By increasing the power of MIR, IR-converted peaks tend to repeatedly appear at the same position (Figure S10). Notably, the nonlinear deviations at an 8 mW pump power, observed in Figure 4a, indicate that at high pump power densities, phenomena such as fluorescence saturation (due to thermal or photochemical effects) could occur during the testing process. Moreover, the VEF-IR peaks show the selectivity on the dependency of MIR wavenumber. For example, the converted-IR intensities have steeper slopes at excitation energies of 1507 and 1695 cm<sup>-1</sup>, because these vibration modes are more IR-sensitive. On the contrary, the Raman-active mode (labeled with dark blue arrows on the right y-axis in Figure 4c) remains inconspicuous even with much higher MIR power, obviously hard to activate by the IR excitation. The trends of curves reveal that the VEF method integrates the Raman with IR but the detection of two type modes is independent from each other. The Raman-active modes are not activated by the IR laser. To evaluate the temperature variation, we measured the aS/S ratio  $(I_{aS}/I_S)$  of Raman peaks and fit the MIR power with the ratio via the toolbox in MATLAB. Based on fitting results,  $I_{aS}/I_S$  exhibit a slight increment with MIR power increasing and fitting results indicate that the average temperature fluctuates less than 10 K (Figure S11). Referring to the data (Figure S4), the fluorescence emission behavior is influenced by competing thermal effects and vibrational-encoded pathways. With excitation visible laser power under 2 mW (Figure S12), the aS-PL intensity stays still with the rising visible power. Upon exceeding this power threshold, the fluorescence signal from vibrational excitation distinctly increases with the visible

power. The inconspicuous response under 2 mW visible laser can be attributed to fluorescence quenching by thermal effect, which is the background of VEF.

The VEF method demonstrates exceptional sensitivity for both Raman and IR spectroscopy. By manipulating the concentration of the assembly solution, we establish a linear relationship between the integral intensity of aS-PL and the solution concentration, confirming that the aS-PL signal originates from the RhB sample molecules (Figure 4e,f). After assembly in the 5  $\mu$ M RhB-CB[7] solution, the average number of molecules can be reduced to about 100, which confirms the high sensitivity of the VEF method (see Table S2).<sup>38</sup> To further push the detection sensitivity of VEF, a series of feasible improvements can be found in section 10, Supporting Information document (Figure S13).

We also compare the IR absorption spectrum acquired using VEF and SEIRA. The nonlinear process in VEF converts the IR absorption signal into visible fluorescence photons, resulting in higher detection efficiency and reduced interference from molecules like  $H_2O$  and  $CO_2$  compared to MCT detectors. The results (Figure 4g,h) show that the upconverted IR spectra obtained via VEF maintain pronounced intensity at 1595 cm<sup>-1</sup>, while the SEIRA spectra exhibit significantly lower IR reflectivity, even when detected on multiple MSoM structures. These findings confirm that the VEF method achieves much higher SNR and sensitivity on a single MSoM structure due to its efficient nonlinear conversion process and photon-detection capabilities.

To quantify the efficiency improvement of our VEF method, we compared it with conventional reflection-mode IR (Refl.-IR) absorption spectroscopy. Using identical samples (an MSoM structure and an ~225 nm-thick RhB film, Figure S14), we detected IR absorption spectra via both VEF and Refl.-IR methods (Figure 2a). After calibrating the responsivity and noise equivalent power (NEP) of the CCD spectrometer and MCT detector (Figure S15), we calculated the efficiency for each technique. With the same incident MIR power, MCT detects about 50% absorption of the RhB film on the gold mirror. Taking the number of molecules and incident 4 mW power account, we derive an efficiency  $\eta$  equaling 5.89 × 10<sup>-18</sup> for each molecule, which means that one molecule can convert  $\sim 10^{18}$  MIR photon to only one detectable photon. On the contrary, if we employ the VEF method for detecting the efficiency, the aS-PL would increase by 139 pW at the wavelength of 600 nm. Considering the number of molecules under the MS, an efficiency of  $2.3 \times 10^{-9}$  can be calculated (details found in Figure S16 in section 12 in the Supporting Information). The VEF method needs fewer MIR photons and converts to visible photons with higher detectivity, which makes the VEF of higher sensitivity.

## CONCLUSIONS

In this work, we developed a CVS technique based on VEF, which elaborately leverages the nonlinear conversion in the dual-resonant plasmonic cavity, to obtain both IR absorption and Raman spectra in the visible waveband. The detection of complementary vibrational modes provides the comprehensive chemical information about molecules, distinguishing this work from the other VEF spectroscopies (Table S3 in Supporting Information). The VEF technique not only overcomes the inefficiency of MIR photon detection but also cospatially locates the complementary groups of vibrational modes. By utilizing the plasmonic cavity, this technique converts

molecular IR absorption into aS fluorescence, enabling the interpretation of IR vibrational modes through the intensity of the aS-PL signals. Simultaneously, VEF integrates IR detection with Stokes Raman scattering spectroscopy, presenting double modalities within a single spectral frame.

We rigorously compared VEF spectra to those obtained from commercial scientific instruments and validated our results using first-principles DFT calculations. These analyses confirmed that the VEF-Raman and VEF-IR modes originate from intrinsic molecular vibrations, demonstrating the technique's accuracy and reliability. Furthermore, the VEF-IR intensity can be enhanced by modulating the repetition frequency and the power of MIR pulses. Hyperspectral imaging of VEF proves its capability for simultaneous and cospatial detection of complete molecular vibrational modes, highlighting its potential for subdiffractional resolution, complementary chemical imaging.

In summary, VEF addresses the challenge of simultaneously detecting IR and Raman spectra while spatially colocalizing complementary vibrational modes from the same molecular groups. The technique is expected to achieve enhanced sensitivity, finer spatial resolution, and refined spectral resolution through the utilization of an objective lens with a higher numerical aperture and the implementation of photoncounting detectors, which significantly boost photon detectivity. With its ability to provide abundant complementary vibrational information, the approach offers detailed insights into chemical bonds' vibrations and underlying molecular structures. This makes it a promising tool for probing the subtleties of molecular interactions and dynamics, particularly within cavity-confined environments.

#### METHODS

**Sample Preparation.** Utilizing a bottom-up nanoassembly approach, we engineered small nanocavities exhibiting dual resonances at both visible (633 nm) and MIR wavelengths. First, we prepared RhB-cucurbit [7] uril (CB [7]) solutions with varying molar concentrations, and the concentration gradient is presented in Table S1.

To fabricate the thin mirror, we deposited a 50 nm layer of Au onto polished silicon substrates, employing a deposition rate of 0.1 Å/s. By immersing the Au-coated silicon substrate in RhB-CB [7] solutions of diverse molar concentrations for 12 h, we achieved the self-assembly of a supramolecular layer of RhB-CB[7] on the gold surface.

For the Ag MSoF optical cavities, AgMSs (4  $\mu$ m in diameter) dispersed in ethanol were precisely deposited onto the RhB-CB[7]-assembled Au-coated silicon substrates with a deposition period lasting less than 60 s. Finally, the samples were thoroughly rinsed with ethanol to remove the unbonded AgMSs.

A quantum-cascading laser (QCL) module, MIRcat Daylight, is equipped as the MIR source in our setup. The laser module available with 1450-1670 cm<sup>-1</sup> emits pulsed or CW waves with the power up to 300 mW. The laser control program is developed with LabVIEW based on the manufacturer's SDK.

**Electromagnetic Field Numerical Simulation.** The electric field of dual-resonant MSoM is solved by the finite element method (FEM), via COMSOL Multiphysics. We employ the 2.5D method<sup>43</sup> to alleviate the computation loading. The diameter of the background field is large enough to be  $\sim 3\lambda_{exc}$ . PML's thickness is set as  $\sim 0.8\lambda$  with five layers of sweep mesh. The local mesh size is about 0.01 nm in the nanogap for a smooth field. Material parameters are referred to Yang's data for Ag<sup>44</sup> and Olmon's data for Au.<sup>45</sup>

**Experimental Setup.** The setup in Figure 2 is self-built based on the components of the s-SNOM apparatus (Neaspec/Attocube, Germany). A detailed description about the optical components can be found in Figure S13, Supporting Information. With the auxiliary

camera and objective, the system is capable of locating the position of the single microsphere and precisely align the laser beams to the plasmonic structure on the sample stage. The PL signal (the green and orange signals in Figure 2a) corresponding to complete vibrations is collected by a parabolic mirror and directed to the CCD of the visible spectrometer.

The parabolic mirror in the system has a numerical aperture (N.A.) of 0.24 and excites the dual-resonant plasmonic cavity in sideillumination mode. Considering the diffraction limit *d* equals  $\lambda_{IR}/2$ N.A., we obtain a theoretically spatial resolution limit of 12.6  $\mu$ m by conventional IR microscopy ( $\lambda_{IR} = 6.08 \ \mu$ m at 1643 cm<sup>-1</sup>).

The spectrometer used in this work is an iHR550 (HORIBA) with a grating of 300 g/mm. The visible laser (633 nm, CW) was purchased from CNI (China). The control and data-process programs are self-developed in LabVIEW and Python.

**DFT Calculation.** DFT calculations were performed using the Gaussian 16 program.<sup>46</sup> The structural optimization, vibration frequency, IR activity, and Raman activity were obtained using  $B3LYP^{47,48}$  functional and 6-311+g (d,p) basis set and consider D3 correction.<sup>49</sup> GaussView 6.0 is used for visualization processing. Multiwfn 3.8 (dev)<sup>50</sup> is used to plot IR and Raman spectra, with a frequency correction factor set to  $0.9688^{51}$  and a fwhm set to  $10 \text{ cm}^{-1}$ .

# ASSOCIATED CONTENT

## **③** Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.5c01957.

Numerical simulation of electromagnetic field, VEF-IR intensity modulated by IR pulses, thermal sensitivity and complementary vibrational modes of rhodamine B molecules, DFT calculation of RhB vibrational spectra, complementary vibrational modes of cyanine 3.5, power dependency of VEF-IR, temperature increment calculated by Raman peaks, optical system of this technique, approximation of efficiency of RhB molecules, comparison between this work and other vibrational-encoded techniques (PDF)

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#### Notes

The authors declare no competing financial interest.

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