1

Introduction

Scientific questions encompassing both the structure and dynamics of molecular systems are difficult to address. Take the case of a folding protein, a fluctuating solvent environment or a transferring electron. In each case, one wants to know the reaction pathway, which requires time-resolving the structure. But the range of time-scales can easily span from femtoseconds to hours, depending on the system. If time-scales are slow, then exquisite structural information can be obtained with nuclear magnetic resonance (NMR) spectroscopy. If time-scales are fast, then fluorescence or absorption spectroscopy can be used to probe the dynamics with a corresponding tradeoff in structural resolution. In between, there is an experimental gap in time- and structure-resolution. The gap is even broader when the dynamics takes place in a confined environment like a membrane, which makes it especially difficult to apply many standard structural techniques.

2D IR spectroscopy is being used to fill this gap because it provides bond-specific structural resolution and can be applied to all relevant time-scales (see these Special Issues [96, 143, 144] and review articles [19, 26, 27, 56, 63, 67, 80, 87, 103, 108, 142, 165, 191, 200, 208]). It has the fast time-resolution to follow electron transfer and solvent dynamics, for instance, or can be applied in a "snapshot" mode to study kinetics to arbitrarily long time-scales. Moreover, it can be applied to any type of sample, including dilute solutions, solid-state systems, or membranes. Its structural sensitivity stems from couplings between vibrational modes that give rise to characteristic infrared bands and cross-peaks. Structures can also be probed through hydrogen bonding and electric field effects that generate dynamic 2D lineshapes. Moreover, 2D IR spectra can be quantitatively computed from molecular dynamics simulations, which provides a direct comparison to all-atom models.

Constructing a 2D IR spectrometer, collecting the data, and interpreting the spectra requires a very broad skill set. Of course, one can qualitatively use 2D IR spectroscopy as an analytical tool, but a little bit of knowledge about

nonlinear optics, vibrational potentials and lineshape theory, enables a much deeper interpretation of 2D IR spectra and a broader range of applications. These topics are explained in various textbooks (see Appendix E) and research articles, but there is no single source that contains all of the fundamental concepts that pertain to 2D IR spectroscopy from which students and researchers new to the field can easily draw upon. This book is intended to foster the ease at which new graduate students and experienced researchers that are moving into the field can learn about the mathematical formalism and technical challenges of 2D IR spectroscopy. Many of the topics also pertain to 2D visible spectroscopy that probes electronic transitions.

But the interpretation of 2D IR spectroscopy is not the sole motivating force for writing this book. Rather, it is our belief that 2D IR spectroscopy will evolve into 3D and higher dimensions. If 2D was the highest-order spectroscopy possible, then one could just memorize the relatively few types of possible 2D pulse sequences (there are really only three) and apply the best one to the problem at hand without intimate knowledge of the chemistry or physics. But with 3D IR spectroscopy there is the potential to develop more sophisticated pulse sequences that are specifically tailored to the problem at hand. Since most of these pulse sequences are yet to be developed, their design and application will require a deeper understanding of the technique, which this book is intended to facilitate.

Only two types of 3D IR experiments have been explored so far, examples of which are shown in Fig. 1.1. The first example is a 3D IR spectrum of a metal carbonyl compound. This spectrum and the accompanying work demonstrated the feasibility of collecting 3D IR spectra, outlined a novel two-quantum pulse sequence, and showed that cascading processes that are major problems in other

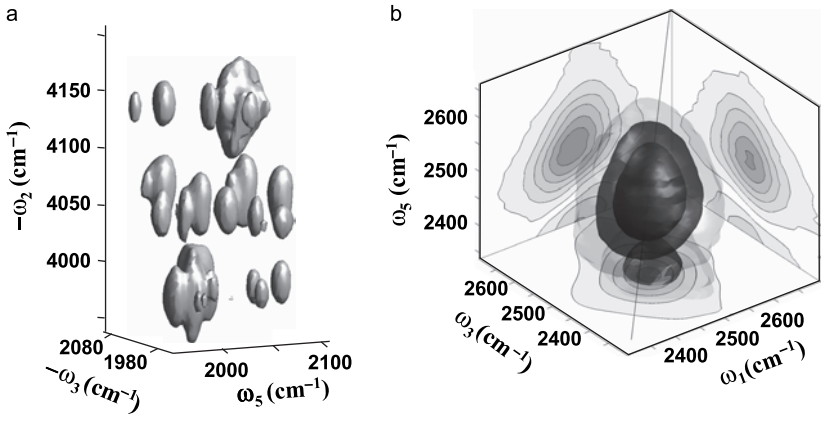

Figure 1.1 3D IR spectra. (a) 3D IR spectrum of a metal dicarbonyl using a two-quantum pulse sequence (adapted from Ref. [43] with permission). (b) Absorptive 3D IR spectrum of the OD stretch of HOD in H_2O [64].

nonlinear spectroscopies are not an issue in multidimensional IR spectroscopy [43–45, 59, 61]. The second experiment is the 3D IR spectrum of water (more precisely, it is the OD stretch of HOD in H_2O) [64]. This spectrum is of interest not only because of what it reveals about the structural dynamics of water, but also because it demonstrates the feasibility of collecting 3D IR spectra even on weakly absorbing chromophores (as compared to the metal carbonyls). These two experiments suggest that many new and exciting 3D and higher-order spectroscopies are possible for a wide range of samples. Designing the pulse sequences to extract the interesting information in these experiments requires the methods contained in this book. We return to 3D IR spectroscopy in the final chapter.

1.1 Studying molecular structure with 2D IR spectroscopy

When one thinks of 2D IR spectroscopy, cross-peaks usually come to mind. Cross-peaks are the hallmark of multidimensional spectroscopy. They are a measure of the coupling between molecular vibrations and thus contain information on the molecular structure. To illustrate the concept, consider two carbonyl stretches, such as from two acetone molecules shown in Fig. 1.2(a). The molecules are made of negative electrons and positive nuclei, which together create the electronic structure of the molecules. The electronic structure, that is the molecular orbitals, dictate the bond lengths and thus the vibrational frequencies [125]. Moreover, the charge distributions of the electrons and nuclei create an electrostatic potential that surrounds the molecule. If the two acetone molecules are close enough, they will feel one another's potentials, which will slightly alter their molecular orbitals, thereby leading to a shift in the vibrational frequencies. When this perturbation occurs, we say that the vibrational modes are *coupled*. Thus, if we can measure the vibrational coupling and understand its distance and angular dependence, we can determine the distances and orientations of the two molecules with respect to one another. 2D IR spectroscopy provides the measurement, through the cross-peaks, and models provide the structure dependence of the coupling.

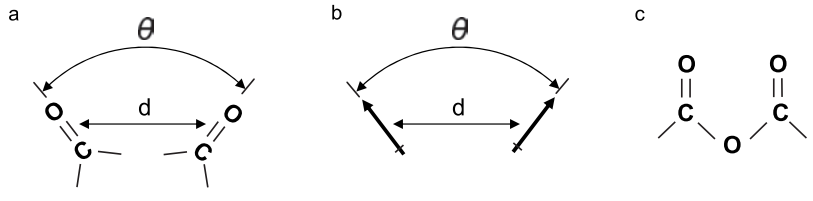

Figure 1.2 Two coupled acetone molecules. (a) The coupling strength will depend on the distance and orientations. (b) Representing the carbonyl stretches with transition dipoles. (c) A molecule in which both mechanical and electrostatic couplings are probably important.

Let us give an example of a coupling model and what it would predict for a 2D IR spectrum. The electrostatic potential around each molecule has a complex distance and angular dependence, at least at short radii, but at distances larger than the carbonyl length, the electrostatic potential can be described by the potential of a dipole [74, 99]. It is actually the *transition dipole* that we are interested in, not the dipole itself, since it is the transition dipole that couples the modes. The transition dipole is the change in the charge distribution of a molecule when it is vibrationally excited [131, 174]. Since acetone is a symmetric molecule, its transition dipole for the carbonyl stretch lies along the carbonyl bond. Thus, when the two acetone molecules are sufficiently far apart, they can each be represented as a transition dipole, which is shown in Fig. 1.2(b). The coupling between two dipoles is given by

$$\beta_{ij} = \frac{1}{4\pi\epsilon_0}\left[\frac{\vec{\mu}_i \cdot \vec{\mu}_j}{r_{ij}^3} - 3\frac{(\vec{r}_{ij} \cdot \vec{\mu}_i)(\vec{r}_{ij} \cdot \vec{\mu}_j)}{r_{ij}^5}\right] \tag{1.1}$$

where $\vec{\mu}_i$ are the directions of the transition dipoles and $\vec{r}_{ij}$ are the vectors connecting the two sites. The coupling β_{ij} scales as $1/r^3$ and depends on the orientation. Of course this formula for transition dipole–dipole coupling breaks down at close distances and for complicated molecular vibrations. Moreover, if the two vibrational modes share common atoms, like two carbonyl stretches located on the same molecule, then the carbonyl modes may be mechanically coupled as well (i.e. one stretch influences the other because of the intervening molecular bonds, see Fig. 1.2c), in which case a more sophisticated relationship between coupling and structure is needed [179]. Nonetheless, if it is understood how the molecular potential depends on the structure, then one can quantitatively interpret 2D IR spectra.

Shown in Fig. 1.3 are simulated 2D IR spectra for two coupled acetone molecules oriented at 45° with respect to one another. In the first spectrum (Fig. 1.3a), the acetone molecules are only separated by a few angstroms so that they are strongly coupled (10 cm^{-1}, see Eq. 1.1). In the second spectrum (Fig. 1.3b) they are farther apart so that the coupling is smaller (4 cm^{-1}). The frequency of one acetone molecule is simulated as if it were an isotope labeled with ^{13}C so that the two molecules have different vibrational frequencies even if they are not coupled. We label the two axes as ω_{pump} and ω_{probe}, for reasons that will become apparent soon. Each acetone molecule creates a pair of peaks near the diagonal of the spectrum, which we collectively refer to as the *diagonal peaks*. One peak lies exactly on the diagonal and the other is shifted off the diagonal to a different ω_{probe} frequency. The on-diagonal peak lies at the fundamental frequency, ω_{01}, along both axes (i.e. $\omega_{pump} = \omega_{probe} = \omega_{01}$). In the convention of this book, this peak is negative. The other peak is shifted because of the anharmonicity of the carbonyl stretch so that

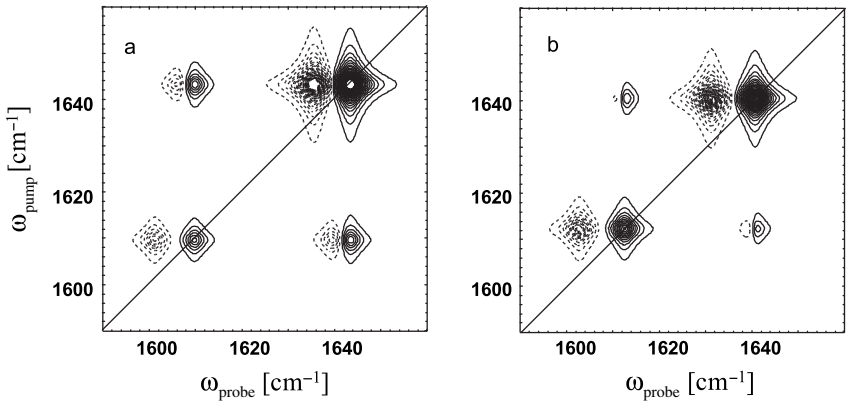

Figure 1.3 Simulated 2D IR spectra of two acetone molecules with a relative orientation of 45° and a transition dipole coupling of (a) 10 cm^{-1} and (b) 4 cm^{-1}, respectively.

the difference in frequency between the two peaks is what is known as the *diagonal anharmonic shift*. Since the two acetone molecules are coupled to one another, cross-peaks appear. The cross-peaks also appear in 180° phase-shifted pairs. On the upper half of the spectrum, one cross-peak will appear at $\omega_{\text{pump}} = \omega_{01}^{\text{CO}_2}$ and $\omega_{\text{probe}} = \omega_{01}^{\text{CO}_1}$ where the superscripts are labels for the two acetone carbonyl groups. This cross-peak most often has a negative intensity but some polarized 2D IR pulse sequences will generate a positive peak instead, depending on the orientation of the carbonyl transition dipoles, which gives additional structural information. The other cross-peak in the pair has the opposite sign and a different ω_{probe} frequency. The frequency difference between the two is the *off-diagonal* anharmonic shift, which is related to the coupling. Another pair of cross-peaks lies on the bottom half of the 2D IR spectrum. Notice that the anharmonic shifts make 2D IR spectra intrinsically nonsymmetric. As a result, in congested spectra with broad lineshapes and/or cross-peaks that are partially obscured by the diagonal peaks, the cross-peaks in the upper and lower halves of the spectrum may appear different, but in well-resolved spectra they should be identical.

In Fig. 1.3(b), where the coupling is weak, the off-diagonal anharmonic shift is smaller, leading to smaller cross-peak separation. In the limit that there is no coupling, the negative cross-peak will sit on top of the positive cross-peak so that they entirely cancel. One may notice upon careful inspection that the coupling not only creates cross-peaks but also changes the diagonal peaks. The diagonal peak frequencies, anharmonic shifts and intensities change because the coupling creates a multidimensional potential energy surface that has a slightly different curvature than each isolated molecule. In fact, one can extract the coupling strength and orientation of the molecules without using 2D spectroscopy by measuring the

frequency shifts and intensity change of each fundamental transitions with standard linear (FTIR) spectroscopy and isotope labeling. However, in practice, 2D IR spectroscopy does a much better job of measuring the coupling with much less work (although isotope labeling is still very useful in 2D IR spectroscopy).

These simulations are intended to provide a qualitative understanding of how coupling alters the curvature of the molecular potential energy surface which results in cross-peaks. In the following section, we expand on how 2D IR spectroscopy probes the molecular potential energy surface.

1.1.1 2D IR spectrum of a single vibrational mode

Before we explain the origin of the cross-peaks, let us describe a simple way of collecting a 2D IR spectrum and what it will look like for a single vibrational mode, such as the carbonyl stretch of an acetone molecule. All we need to construct a 2D IR spectrum are the eigenstates and transition dipoles for the vibrational modes of the molecule that we are interested in. We represent the potential energy curve of the carbonyl stretch by a Morse oscillator (Fig. 1.4a):

$$V(r) = D(1 - e^{-ar})^2 \tag{1.2}$$

where r is the carbonyl bond length, D is the well depth, and a gives the curvature of the potential. The vibrational eigenstates generated from the Hamiltonian with this potential are

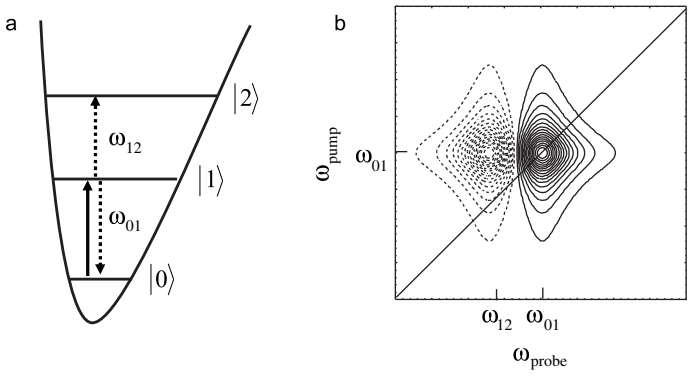

Figure 1.4 (a) Level scheme of an anharmonic oscillator with the dipole-allowed transitions depicted. The solid arrow represents the pump process, the dotted arrow the probe process. (b) Resulting 2D IR spectrum. Solid contour lines represent negative response (bleach and stimulated emission), dotted contour lines positive response (excited state absorption).

$$E_n = \hbar\omega\left(n+\frac{1}{2}\right) - x\left(n+\frac{1}{2}\right)^2 \tag{1.3}$$

where ω is the harmonic frequency of the oscillator, x is the *anharmonicity*, and n is the quantum number [93, 131, 132, 174]. This potential will produce the 2D IR spectrum simulated in Fig. 1.4(b).

The 2D IR spectrum can be measured in either the time or frequency domain. We begin our discussion in the frequency domain in which the 2D IR spectrum can be generated by a simple pump–probe experiment. Imagine that we scan the frequency of a pump pulse across the resonance frequency of the vibrator and plot its absorption as the y-axis of a 2D graph.[1] Whenever resonance with a dipole-allowed 0–1 transition is achieved, $\omega_{\text{pump}} = \hbar\omega - 2x \equiv \omega_{01}$, a certain fraction of molecules in the laser focus will be excited from their ground state $|0\rangle$ into their first vibrationally excited state $|1\rangle$ (solid arrow in Fig. 1.4a). Following the pump pulse, we scan the frequency of a probe pulse for the x-axis. The probe pulse will now measure two possible transitions from the excited state, i.e. the stimulated emission back into the ground state and the excited state absorption into the second excited state $|2\rangle$ (dotted arrows in Fig. 1.4a). In addition, since there are now fewer molecules in the ground state, the probe pulse will not be absorbed as much as it is when there is no pump pulse. Since we typically measure difference spectra (i.e. the difference of absorption between pump pulse switched on minus pump pulse switched off), the difference spectrum will be negative, which is an effect that is called a *bleach*. Both bleach and stimulated emission occur at the original ω_{01} with identical signs. The two contributions result in less absorption or gain, respectively, and by convention we give the signal a negative sign. In contrast, the excited state absorption will be positive because it is a new absorption induced by the pump and its frequency, $\omega_{12} = \hbar\omega - 4x$ is red-shifted from ω_{01} because of the anharmonicity of the potential. The shift is equal to $\omega_{12} - \omega_{01} = 2x \equiv \Delta$, which is the diagonal anharmonic shift.

Thus, by plotting the absorption as a function of the pump and probe frequencies, we will see a doublet of peaks in the 2D IR spectrum with opposite signs. There will be an on-diagonal peak at $\omega_{\text{pump}} = \omega_{\text{probe}} = \omega_{01}$ due to the bleach and stimulated emission signals, whereas the excited state absorption signal appears at $\omega_{\text{pump}} = \omega_{01}$ and $\omega_{\text{probe}} = \omega_{12}$. Even though there are two signals contributing to the on-diagonal peak and only one to the off-diagonal peak, both peaks will have roughly the same intensities because the 1–2 excited state absorption is twice as strong as a 0–1 transition (the 1–2 transition dipoles for a close-to

[1] There is currently no agreement in the community as to whether the x-axis should be the pump or the probe frequency axis. We use the convention of NMR spectroscopy with the probe frequency axis being the x-axis. Moreover, not all research groups follow the same convention for positive and negative signals.

harmonic oscillator scale as $\mu_{12}^2 = 2\mu_{01}^2$). If both peaks are well separated, then the anharmonic shift of the oscillator can be directly read off from a 2D IR spectrum. This condition is true only if the anharmonic shift is larger than the bandwidth of the transition. If it does not hold, then the 0–1 and 1–2 transitions overlap and partially cancel, as in Fig. 1.4(b), in which case the anharmonic shift has to be determined by deconvolution or peak fitting.

1.1.2 2D IR spectrum of two coupled vibrational modes

Using the same procedure as above, we can construct the 2D IR spectrum of two coupled oscillators from their vibrational energy levels and transition dipoles. For two oscillators, we have a 2D potential, which we write as

$$V(r_1, r_2) = V_1(r_1) + V_2(r_2) + \beta_{12} r_1 r_2 \tag{1.4}$$

where $V_n(r_n)$ are the 1D potentials of each carbonyl stretch given by Eq. 1.2 and β_{12} is the coupling given by Eq. 1.1 if transition dipole–dipole coupling is adequate. We refer to the individual carbonyl groups and their parameters as *local modes* (e.g. local mode frequency). To get the eigenstates of the 2D potential, one must diagonalize $H(r_1, r_2)$ generated from $V(r_1, r_2)$. In Chapter 6, we solve this Hamiltonian explicitly, but even without doing so here, one can see that the coupling will shift the observed frequencies because they are no longer pure local modes. Moreover, it will also shift the ω_{12} transitions (the sequence transitions) and create a combination band.[2] Now, we need anharmonic shifts not only for the diagonal peaks, which we call Δ_{ii} for oscillator i, but we also need to describe the shift of the combination band, which we call Δ_{ij} and is the off-diagonal anharmonic shift. The eigenstates before and after diagonalization are shown in Fig. 1.5(a). The anharmonic constants Δ_{ij} describe the deviation of the energy of overtones and combination modes from just being a simple sum of the harmonic energies. That is, if there is no coupling, then $\omega_{0i} + \omega_{0j} = \omega_{0,i+j}$ and $\Delta_{ij} = 0$.

Figure 1.5(a) gives our nomenclature for labeling the eigenstates of two coupled oscillators. $|kl\rangle$ represents a state with k quanta of excitation in the first mode and l quanta of excitation in the second mode. If anharmonicity is small, which typically is the case, then the selection rules of harmonic oscillators still apply, i.e. only one oscillator can be changed by one quantum at a time. And the strength of the transition is determined by the transition dipole of that oscillator. For example,

[2] Oftentimes in the 2D IR literature, ω_{12} is referred to as the overtone transition, which is incorrect. It is actually a sequence band. An overtone transition would give the frequency ω_{02}. Nonetheless, we use these terms interchangeably in this book.

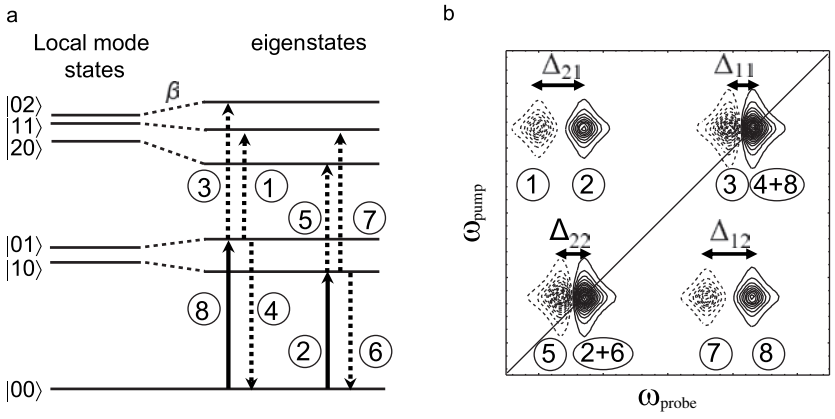

Figure 1.5 (a) Level scheme of two coupled oscillators before coupling (local modes) and after coupling (eigenstates). The dipole-allowed transitions are depicted. The solid arrows represent the pump process, the dotted arrows the probe process. (b) Resulting 2D IR spectrum. Solid contour lines represent negative response (bleach and stimulated emission), dotted contour lines positive response (excited state absorption). The labels (1)–(8) relate each peak in the 2D IR spectrum to the corresponding transition in the level scheme.

transitions $|10\rangle \rightarrow |20\rangle$ and $|10\rangle \rightarrow |11\rangle$ are *dipole allowed*, whereas $|10\rangle \rightarrow |02\rangle$ is *forbidden*. The arrows in Fig. 1.5(a) show all possible allowed transitions for two coupled oscillators.

With these rules in mind, we can now construct the 2D IR spectrum by imagining a pump–probe experiment. That is, we scan the pump frequency across the resonances of the two oscillators. When the pump frequency comes into resonance with an eigenstate, we mark that frequency along the y-axis. For example, when the pump is resonant with the higher-frequency oscillator, we will excite state $|01\rangle$. The subsequent probe pulse now has three possible transitions labeled (1), (3) and (4) in Fig. 1.5(a). In addition, the probe pulse will observe a bleach of *both* oscillators, giving rise to transitions (8) and (2), since the number of molecules in the common ground state $|00\rangle$ is diminished. Transitions (8), (4) and (3) are the same as for a single oscillator (Fig. 1.4), i.e. bleach, stimulated emission and excited state absorption, respectively, of the higher-frequency oscillator, whereas transitions (1) and (2) are new. Transition (1) excites the lower oscillator by one quantum from its ground state to its first excited state when there is already one quantum of excitation in the higher-frequency oscillator: $|01\rangle \rightarrow |11\rangle$. If the two oscillators were not coupled, then the excitation frequency of the second oscillator would not depend on the number of quanta of the first oscillator, and we would have exactly the same frequency for the $|00\rangle \rightarrow |10\rangle$ and the $|01\rangle \rightarrow |11\rangle$ transitions. In that case, peaks (1) and (2) would exactly coincide and cancel each other

due to their identical transition strength but opposite sign. On the other hand, if the off-diagonal anharmonicity Δ_{12} is nonzero, then the two peaks do not cancel, and we obtain a doublet in the off-diagonal region, which we call a *cross-peak*. The existence of a cross-peak in a 2D IR spectrum is a direct manifestation of the coupling between both oscillators. In this context coupling means that the transition frequency of the one oscillator depends on the excitation level of the other oscillator. The off-diagonal anharmonicity Δ_{12} can directly be read off from a 2D IR spectrum, as depicted in Fig. 1.5(b). We will discuss in Chapter 6 how such cross-peaks are related to molecular structure.

1.2 Structural distributions and inhomogeneous broadening

The above sections pertain to an ensemble of identical molecules, but usually there are differences in the structure, hydrogen bonding, and environments of the molecules in the ensemble. Consider, for instance, the OH stretch vibration of a water molecule in liquid water. Each water molecule will sit in a different hydrogen bond environment (Fig. 1.6). Hydrogen bonding deforms the stretch potential such that the vibrational frequency is lowered. Hence, at each instant of time, each water molecule will have a different stretch frequency so that all the molecules together create a distribution of frequencies. If the molecules do not move on the time-scale of the 2D IR pulse sequence, then we say that there is an *inhomogeneous* distribution of frequencies. Each molecule also has an intrinsic linewidth that cannot be narrower than dictated by its vibrational lifetime, which we call the *homogeneous* linewidth. The overall 2D IR spectrum is a superposition of the 2D IR spectra for each individual molecule (Fig. 1.7a). The overall 2D IR spectrum will be broader than the homogeneous linewidths of the individual molecules, especially if the inhomogeneous distribution of the center frequencies is larger than the homogeneous linewidth.

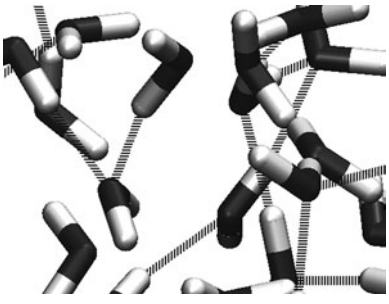

Figure 1.6 Snapshot from a molecular dynamics (MD) simulation of water with the hydrogen bonds indicated.