Modeling two-dimensional infrared spectroscopy of hydrogen bonded systems
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3.1 INFRARED SPECTROSCOPY

Spectroscopy is the study of light-matter interactions. It aims at probing the structure of matter. When an infrared laser beam incides on matter it disturbs the nuclear positions and motion (vibrations), and consequently the molecular bond lengths and angles. The magnitude of this perturbation depends on the resonance between the vibrational energy levels and the frequency of the incident light. If the wavelength of the light is resonant with the difference between the vibrational energy levels, the system will go from the ground state to an excited state. The molecule will vibrate with well-defined frequencies, (as long as the vibrations live long enough) which can be related to their structure. The question of how a molecule goes from one state to the other arises. The energy of a molecule is described by a potential energy surface (PES) that relates the structure of a system with its energy. When the atoms of a molecule vibrate they behave as a mass on a spring with an energy depending on the square of the atomic displacement, to the lowest order approximation. This movement can be described by a harmonic oscillator, where the different energy levels are given by values of $E_n = (n + 1/2) \hbar \omega$, where $n$ represents the quantum number, see Figure 3.1 a. This means that the different energy levels are quantized, and only discrete energy levels are allowed. Each frequency is directly related with a normal mode, which is a displacement vector of the atomic movements. A vibration is a molecular finger print that is directly connected with the molecular structure. The number of modes is dependent on the number of atoms (N), and on the structure. A linear molecule has $3N - 5$ normal modes, whereas a non-linear molecule has $3N - 6$ vibrations. In the harmonic approximation these modes are fully independent of each other (orthogonal) behaving as independent harmonic oscillators. For a transition to be infrared active it is a necessary condition that the dipole moment associated to the transition is non-zero. Such is the case of the O-H stretch vibration of water and the C=O stretch vibration in proteins, which strongly absorb and vibrate in different regions of the IR spectrum, such as 3500 cm$^{-1}$ and 1600 cm$^{-1}$, respectively.
3.2 MOLECULAR VIBRATIONS OF SPECIAL INTEREST

As described in the previous section, molecules have many possible vibrational normal modes. This section will focus on the amide I vibration and the O-H stretch vibration. Both modes are present in proteins and at protein water interfaces, and as such, they are a very important subject to study.

3.2.1 The amide I vibration

The amide I vibration is mainly composed of the C=O stretch and the N-H bending, Figure 3.2. It is present in the amide group of aminoacids, peptides, and proteins [67–75]. This vibration is comprised in the spectral range of 1600 cm$^{-1}$ to 1800 cm$^{-1}$, and it has a strong absorption in the IR region [32]. The absorption frequency is strongly dependent on the environment, making the
3.2 Molecular Vibrations of Special Interest

Figure 3.2: Schematic representation of the Amide I vibration. The arrows indicate the vibrational modes, namely the C=O stretch and the N-H bend.

Amide I vibration widely used to probe protein structure and dynamics, since there is a frequency shift induced by the environment.

Let us consider a dimer system composed of two N-methylacetamide molecules, Figure 3.3, where the C=O of one molecule is hydrogen bonded with the N-H group of the neighboring molecule. Here the amide I frequency of the H-bond accepting group will be shifted to the red side of the IR spectrum, as a consequence of the hydrogen bond. A more complex picture arises when accounting for the vibrational coupling between the molecules. This means that the vibrations are close enough to feel each other. Because their electronic structure is changed, the potential energy surface is modified, thereby altering the vibrational energy levels, and thus the vibrational frequencies. When the coupling is strong enough, the infrared lines will split in two and the strength of the coupling is related to the distance between the two infrared peaks. The coupling strength is determined by the distance and the angles between the transition dipoles and this quantity provides information that can be used to disentangle structural conformations. The simplest model to predict the couplings is the transition dipole coupling model [25].

In Chapter 2 the different secondary structures of proteins have been discussed and now an overview of their vibrations in the infrared region will be given. An α-helix exhibits two main absorption peaks in the infrared region with vibrational frequencies centered at \( \sim 1638 \, \text{cm}^{-1} \) [76], due to the degenerate out of phase amide I collective vibration, and at \( \sim 1660 \, \text{cm}^{-1} \), caused by the in-phase collective vibration of the amide I modes, the latter is the most IR intense. Conversely, these frequencies change with the length of the α-helix [77]. The most pronounced shift due to the in phase oscillation of all residues (A_1 mode),
that red shifts to $\sim 1650 \text{ cm}^{-1}$ [76], with the increase of the length [78]. The degenerate mode ($E_1$) does not show a significant shift. Both bands are broad and they overlap in the linear absorption spectra, thus the most characteristic band of $\alpha$-helices is centered at $\sim 1650 \text{ cm}^{-1}$ [76].

The other common secondary structure motif, the $\beta$-sheet, also has pronounced vibrations in the infrared region. Idealized $\beta$-sheets have four possible vibrational modes but only two are infrared active [79], where the most intense one is centered at $\sim 1640 \text{ cm}^{-1}$. A high frequency mode is located at $\sim 1670 \text{ cm}^{-1}$, but due to low intensity it is almost not seen in the linear absorption spectra. $\beta$-turns are the secondary structures with the most blue shifted spectra, $\sim 1680 \text{ cm}^{-1}$, Figure 3.4. These characteristic vibrations enable the identification of the different secondary structures, allowing to understand also the secondary structure composition of a protein. For example, the IR spectrum of a protein that is mainly composed by $\beta$-sheets has a non-symmetric broad peak centered at $\sim 1640 \text{ cm}^{-1}$, whereas in case of a protein with a high percentage of $\alpha$-helices the peak is symmetric and centered at $\sim 1650 \text{ cm}^{-1}$.

Solvent exposure changes the line shapes by broadening the peaks, as a consequence of hydrogen bonding [76]. In this case, the vibrational frequencies of the protein domains are red shifted and the line shapes are broadened when

![Figure 3.3: Vibrationally uncoupled dimer of N-methylacetamide molecules. The amide I unit s of the lower N-methylacetamide molecule is isotope labelled using $^{13}\text{C}$ and $^{18}\text{O}$.](image)
3.2 MOLECULAR VIBRATIONS OF SPECIAL INTEREST

Figure 3.4: Frequency shifts due to different secondary domains of a protein. The residues of an α-helix and β-sheet are in atomistic representation, and the protein is represented in new cartoon. The oxygens are shown in green, the nitrogens in pink, the carbons in blue, and the hydrogens in light grey. An α-helix is colored in purple, and a β-sheet in blue. The hydrogen bonds between different residues are represented in black. Note that, the frequency ranges provided in the picture are the IR intervals where these units are expected. The frequencies may shift significantly due to environment.
compared to the non-solvated counterparts. Because of the broadened line shapes, caused by hydrogen bonding and the coupling between the different units, the spectral lines overlap, making it difficult to clearly distinguish the different structural motifs [24–33,79]. Notwithstanding, the approximated values of the frequencies are the IR ranges that these domains are expected to vibrate. Note that, these frequencies can be largely affected by the environment and structural disorder. Thus, an α-helix in solution has a different frequency than one on a membrane.

Isotope labelling of the different domains makes it possible to distinguish between the individual amide units. In this case, atoms in the amide group are replaced by other isotopes, most commonly $^{13}$C, $^{18}$O, and D. Due to the mass change, the isotope labeled units will vibrate with a different frequency, and therefore the coupling with their non-isotope labeled counterparts is reduced [80]. This method can be applied to define protein motifs enabling to study them independently [28,43,81].

3.3 Non-linear response

Linear infrared spectroscopy is a powerful method to probe structural properties of a system as discussed above. However, it has a low sensitivity to dynamical properties, such as molecular rotations. Two-dimensional infrared spectroscopy is a correlation spectroscopy method, and it is sensitive to fast dynamical fluctuations of a system. In the following sections a general framework for modeling linear absorption and two-dimensional infrared spectroscopy is presented.

3.3.1 Spectral modeling

The two-dimensional spectrum can be modeled theoretically, using molecular dynamics (MD) and response function calculations [24–33,82,83]. In classical molecular dynamics the molecules are described by point charges and bonded potentials, which interact with each other via non-bonded potentials [84–86]. This method enables the simulation of large systems as a function of time. This means that we can understand how a system behaves in time by using classical MD simulations. Here, Newton’s laws of motion are integrated in order to predict the atomic positions as a function of time. This method has been proven to be a useful basis for calculating two-dimensional infrared spectra, as
it allows the extraction of dynamical information. Two-dimensional spectra can be obtained from classical MD simulations by using the time-dependent Hamiltonian for a vibrational mode. This Hamiltonian has the form:

\[ H(t) = \sum_i \omega_i(t) B_i^\dagger B_i - \frac{\Delta}{2}(t) B_i^\dagger B_i^\dagger B_i B_i \]

\[ + \sum_{i,j} J_{ij}(t) B_j^\dagger B_i - \sum_i \vec{\mu}_i(t) \cdot \vec{E}(t)(B_i^\dagger + B_i) \]  

(3.1)

Here, \( B_i^\dagger \) and \( B_i \) are the bosonic creation and annihilation operators and \( \vec{E}(t) \) is the external laser field used to excite the molecules. The site frequencies, \( \omega_i(t) \), the transitions dipoles, \( \vec{\mu}_i(t) \), for each oscillator are calculated with electrostatic maps, which assume dependence of the frequencies and transition dipoles on the electric field [29,30,36]. The latter are based on the Stark effect [87], which relates the shift of spectral lines with the electrostatic environment. Because in classical MD the molecules are represented by point charges, this approach enables the construction of the Hamiltonian from the electrostatic environment generated by these charges. Here the electrostatic potential created by the point charges of the force field is counted on the atoms of interest. For example, in the case of the amide I mode there are maps that take the contribution of the electric field, and its potential, in four atoms of the backbone of a protein while others take only this contribution in two atoms of the protein backbone. The anharmonicity is taken from the difference between the frequencies of the first excited state and the second excited state \( \Delta = 2\omega_{eg} - \omega_{fg} \), whereas the coupling constants \( J_{ij} \) depend on the system that is being studied. The transition dipole coupling model provides a good description of the spatial interaction between oscillators:

\[ J_{ij} = \frac{1}{4\pi\varepsilon_0} \left( \frac{\vec{\mu}_i \cdot \vec{\mu}_j}{r_{ij}^3} - 3 \left( \frac{\vec{\mu}_i \cdot r_{ij}}{r_{ij}} \right) \left( \frac{\vec{\mu}_j \cdot r_{ij}}{r_{ij}} \right) \right) \]  

\[ \frac{r_{ij}^5}{r_{ij}^3} \]  

(3.2)

where \( \vec{\mu} \) is the transition dipole of two involved units, \( i \) and \( j \), where \( r_{ij} \) is the distance between the transition dipoles, as these are mechanically coupled. Here, \( \varepsilon_0 \) (vacuum permitivity) is used since the distances between the neighboring molecules are very small. For short distances it breaks down, making it necessary to employ other models, which is the case for the intramolecular coupling in water, where the mechanical coupling dominates [88]. In summary, there are several maps and coupling models that can be used to extract the necessary information to build the vibrational Hamiltonian, that subsequently will be used to calculate the spectrum. Furthermore, each approach depends on the
3.3.2 Induced light polarization

The aim of optics is to study light-matter interactions, and to provide an explanation for the phenomena arising from the interaction of the electromagnetic spectrum with a molecular system. When an electromagnetic field interacts with a sample, it will cause a perturbation, which can be described by perturbation theory, if the field is not too strong. The induced polarization can be described as an expansion of the different powers of the perturbation:

$$P(t) = \epsilon_0(\chi^{(1)}E^{(1)} + \chi^{(2)}E^{(2)} + \ldots + \chi^{(n)}E^{(n)})$$  \hspace{1cm} (3.3)

where $\chi^{(n)}$ are the different orders of the susceptibility tensors and $E$ is the incident field vector. For a non centrosymmetric medium all susceptibilities may be present, whereas the even ones vanish in case for the centrosymmetric and isotropic cases. Hence, taking the macroscopic polarization as an ensemble average of the expectation value of the transition dipole, using Dirac’s notation, $\bar{P}(t) = \left\langle \langle \psi(t)|\hat{\mu}\psi(t)\rangle \right\rangle_E$, the $n^{th}$ order polarization induced by $n$ interactions with the light field is given by:

$$\bar{P}^{(n)}(t) = \sum_{m=0}^{m=n} \left\langle \langle \psi^{(n-m)}(t)|\hat{\mu}|\psi^{(m)}(t)\rangle \right\rangle_E$$  \hspace{1cm} (3.4)

where $\left\langle \ldots \right\rangle_E$ is the ensemble average, $\hat{\mu}$ is the dipole operator, $\psi^{(m)}$ are the $m^{th}$ order corrections to the wavefunctions. The expressions for the wavefunctions can be simplified by transforming to the interaction picture, in which the time dependence is in the perturbative part of the Hamiltonian operator ($H_{IP}$). This simplifies the expressions, since the time-dependence is passed to the operators. Thus, the wavefunction can be written as:

$$\psi^{(m)}_I(t) = \left(-\frac{i}{\hbar}\right)^m \int_{t_0}^{t} d\tau_m \int_{t_0}^{\tau_m} d\tau_{m-1} \ldots \int_{t_0}^{\tau_2} d\tau_1 \hat{H}_{IP}(\tau_m) \hat{H}_{IP}(\tau_{m-1}) \ldots \hat{H}_{IP}(\tau_1) \psi_I(t_0)$$  \hspace{1cm} (3.5)
This equation can be rewritten in the Schrödinger picture via an unitary transformation:

\[ \psi_I^{(m)}(t) = e^{-i/\hbar \hat{H}_I^P(t-t_0)} \psi_I^{(m)}(t_0) \]  

\[ \psi_I^{(m)}(t) = U(t,t_0) \psi_I^{(m)}(t_0) \]  

where \( U(t,t_0) \) is the time evolution operator, describing the time evolution of the wavefunction and \( \psi_I^{(m)}(t) \) is the wavefunction in the interaction picture. The Hamiltonian can be transformed from the interaction picture to the Schrödinger one via a unitary transformation:

\[ \hat{H}_I^P = U^\dagger(t,t_0) \hat{H}_P(t) U(t,t_0) \]  

where, \( U(t,t_0) \) is the time evolution operator and \( U^\dagger(t,t_0) \) is the hermitian conjugate. This approach is useful to describe the time-dependence of a system upon perturbation [89].

### 3.3.3 Linear infrared spectroscopy

In the beginning of this section the different energy levels that compose the vibrational oscillator have been introduced [89]. For the linear absorption only the two lowest levels corresponding to the fundamental transition need to be considered. Let us consider the following system composed by \( N \) two level systems, Figure 3.5.

![Figure 3.5](image)

**Figure 3.5:** Schematic representation of the collection of states formed by \( N \) two level systems, where \( N \) represents the number of single excited states.

When a short resonant laser pulse interacts with a system, a coherent superposition between the ground state and the excited state is formed, in
which the transition dipole dictates the amplitude of the oscillation between the two states. With time the system goes back to the ground state resulting in the emission of a photon. Using perturbation theory, described in the previous section, it becomes possible to follow the time evolution of the system, and therefore calculate the response of the perturbation created by the laser beam. This can be represented by Feynman diagrams, Figure 3.6, which pictorially show the time evolution of the system.

![Feynman Diagram](image)

**Figure 3.6:** The Feynman diagram represents the linear response function. The arrows represent the interactions with the laser field, in which an arrow pointing towards a vertical line represents an excitation, while the dashed arrow represents deexcitation. The $\tau_1$ and $\tau_2$ are the times when the applied fields interact with the system.

The linear response function is given by:

$$S^{1D}(t_1) = -\left(\frac{i}{\hbar}\right)\langle g|\mu^{ge}(\tau_2)U^{ee}(\tau_{12})\mu^{eg}(\tau_1)|g\rangle. \quad (3.9)$$

where $\mu$ are the transition dipoles and $U^{ee}$ is the time evolution operator in the interaction picture and $\tau_1$ and $\tau_2$ are the times at which the electric field interacts with the system. The response function is converted to the frequency domain by a Fourier transform:

$$I(\omega) = \int_0^{\infty} S^{1D} e^{-i\omega t_1} \Gamma^{1D}(t_1) dt_1 \quad (3.10)$$

where $I(\omega)$ is the linear absorption spectrum, $\Gamma^{1D} = e^{-\frac{t_1}{T_1}}$ is the relaxation factor, which includes a vibrational lifetime $T_1$, and $t_1 = \tau_2 - \tau_1$. 
3.3.4 Two-dimensional infrared spectroscopy

Even though linear infrared spectroscopy can be a useful tool to probe dynamics, the broadened line shapes may hide some transitions that contain information about equilibrium fluctuations. Two-dimensional infrared spectroscopy presents a solution to this problem and as stated before it is sensitive to dynamics. This multipulse optical technique was inspired by correlation NMR [90] and it is very frequently used to probe fast dynamical properties of a system, such as hydrogen bonding dynamics. The main advantage of 2D IR spectroscopy is that the vibrational spectrum is spread over two frequency axes, relating the frequency of an initial excitation of a given vibration with the remaining vibrations, thereby rendering the technique sensitive to vibrational couplings [23,30,37,72,78–80,91–107]. Here, higher excited states are accessible and, due to the short coherent light pulses, the oscillation of the polarization continues after the interaction, and the radiated field can be measured by a weak laser pulse. The laser pulses are separated by time delays.

![Figure 3.7: Schematic representation of the collection of states formed by N three level systems, with N representing the number of single excited states, and N(N + 1)/2 is the number of doubly excited states.](image)

For example, consider a collection of N three level systems each, with a ground state \(g\), a first excited state \(e\), and a second excited state \(f\), shown in Figure 3.7. The system interacts with three laser pulses at three consecutive
time points. The time delay $t_1$ is the delay time between the first two laser pulses, $t_2$ is the delay between the second and third pulse, and $t_3$ is the delay after the third pulse. After interacting with the first laser pulse, the system is brought to a coherent superposition between the ground state and the first excited state and evolves during time $t_1$. The second laser pulse can create a coherent superposition of two single excited states or can de-excite the system back to the ground state, or it can create a single excited state population. The third laser pulse either brings the system to a coherent superposition between the ground state and a single excited state, or between double excited states. Finally, an electric field is generated after time $t_3$. This signal may be subsequently Fourier transformed with respect to the time delay between the two first pulses, $t_1$, and the time between the last pulse and the signal detection, $t_3$, to the frequency domain. The time delay between the second and the third pulses is denoted the waiting time and may be used to study dynamics. The interactions of the system with the applied laser pulses result in three processes: ground state bleach (GB), stimulated emission (SE), and excited state absorption (EA). These are represented by the Feynman diagrams shown in Figure 3.8.
The vertical lines represent the time evolution of the ket and the bra, respectively. The time increases upwards and arrows that point towards the vertical lines represent excitation, while arrows pointing away represent deexcitation [82].

The 2D IR spectra are given by the sum of the signal emitted in two directions $\vec{k}^I = -\vec{k}_1 + \vec{k}_2 + \vec{k}_3$ and $\vec{k}^{II} = \vec{k}_1 - \vec{k}_2 + \vec{k}_3$. Here $\vec{k}_1$, $\vec{k}_2$ and $\vec{k}_3$ are the wave vectors of the incoming fields, and $\vec{k}^I$ is the wave vector of the rephasing signal, while $\vec{k}^{II}$ is wave vector the non-rephasing counterpart. An echo signal is produced in the case of the rephasing diagram, due to the fact that the phase coherent oscillations during $t_1$ and $t_3$ are opposite in phase [89].
The third-order response functions related to the Feynmann diagrams given in Figure 3.8 [83,89,108] are:

\[
S_{GB}^{(k)}(t_3, t_2, t_1) = -\left( \frac{i}{\hbar} \right)^3 \langle \mu^{ge}(\tau_1) \rangle U^{ee}(\tau_1, \tau_2) \mu^{eg}(\tau_2) \mu^{ge}(\tau_4) U^{ee}(\tau_4, \tau_3) \mu^{eg}(\tau_3) E \Gamma(t_3, t_2, t_1)
\]

\[
S_{SE}^{(k)}(t_3, t_2, t_1) = -\left( \frac{i}{\hbar} \right)^3 \langle \mu^{ge}(\tau_1) \rangle U^{ee}(\tau_1, \tau_3) \mu^{eg}(\tau_3) \mu^{ge}(\tau_4) U^{ee}(\tau_4, \tau_2) \mu^{eg}(\tau_2) E \Gamma(t_3, t_2, t_1)
\]

\[
S_{EA}^{(k)}(t_3, t_2, t_1) = \left( \frac{i}{\hbar} \right)^3 \langle \mu^{ge}(\tau_1) \rangle U^{ee}(\tau_1, \tau_4) \mu^{ef}(\tau_4) U^{ff}(\tau_4, \tau_3) \mu^{fe}(\tau_3) U^{ee}(\tau_3, \tau_2) \mu^{eg}(\tau_2) E \Gamma(t_3, t_2, t_1)
\]

\[
S_{GB}^{(k)}(t_3, t_2, t_1) = -\left( \frac{i}{\hbar} \right)^3 \langle \mu^{ge}(\tau_4) \rangle U^{ee}(\tau_4, \tau_3) \mu^{eg}(\tau_3) \mu^{ge}(\tau_2) U^{ee}(\tau_2, \tau_1) \mu^{ge}(\tau_1) E \Gamma(t_3, t_2, t_1)
\]

\[
S_{SE}^{(k)}(t_3, t_2, t_1) = -\left( \frac{i}{\hbar} \right)^3 \langle \mu^{ge}(\tau_2) \rangle U^{ee}(\tau_2, \tau_3) \mu^{eg}(\tau_3) \mu^{ge}(\tau_4) U^{ee}(\tau_4, \tau_1) \mu^{ge}(\tau_1) E \Gamma(t_3, t_2, t_1)
\]

\[
S_{EA}^{(k)}(t_3, t_2, t_1) = \left( \frac{i}{\hbar} \right)^3 \langle \mu^{ge}(\tau_2) \rangle U^{ee}(\tau_2, \tau_4) \mu^{ef}(\tau_4) U^{ff}(\tau_4, \tau_3) \mu^{fe}(\tau_3) U^{ee}(\tau_3, \tau_1) \mu^{eg}(\tau_1) E \Gamma(t_3, t_2, t_1)
\]

(3.11)

where, \( \Gamma(t_3, t_2, t_1) \) is the relaxation factor in which the vibrational lifetime \( T_1 \) is included and has the form:

\[
\Gamma(t_3, t_2, t_1) = e^{-\frac{t_3 + 2t_2 + t_1}{2T_1}}
\]

(3.12)
The signal is then Fourier transformed to the frequency domain and the two-
dimensional spectra are given by the sum of the rephasing and non-rephasing
signals:

\[ S(\vec{k}_I)(\omega_3, t_2, \omega_1) = \int_0^\infty \int_0^\infty \left[ S^{(GB)}_{\vec{k}_I}(t_3, t_2, t_1) \right. \]
\[ + S^{(SE)}_{\vec{k}_I}(t_3, t_2, t_1) + S^{(EA)}_{\vec{k}_I}(t_3, t_2, t_1) \] \[ \left. e^{i(\omega_3 t_3 - \omega_1 t_1)} \right] dt_3 dt_1 \] (3.13)

\[ S(\vec{k}_{II})(\omega_3, t_2, \omega_1) = \int_0^\infty \int_0^\infty \left[ S^{(GB)}_{\vec{k}_{II}}(t_3, t_2, t_1) \right. \]
\[ + S^{(SE)}_{\vec{k}_{II}}(t_3, t_2, t_1) + S^{(EA)}_{\vec{k}_{II}}(t_3, t_2, t_1) \] \[ \left. e^{i(\omega_3 t_3 + \omega_1 t_1)} \right] dt_3 dt_1 \] (3.14)

Thus by summing the equations 3.13 and 3.14, the absorptive part of the two-
dimensional spectra is given, where \( I \) is given by the imaginary part of signal:

\[ I(\omega_3, t_2, \omega_1) = Im\left[ S(\vec{k}_I)(\omega_3, t_2, \omega_1) + S(\vec{k}_{II})(\omega_3, t_2, \omega_1) \right] \] (3.15)

Numerical Integration of the Schrödinger equation, the so-called NISE approach,
is used to calculate both linear and 2D IR spectra [83, 108]. Due to the
instantaneous interaction between the external field and the system and the
short pulse duration, the system evolves during the delay between pulses as if
there is no electric field present. Hence, the coupling between excited states with
different excitation level is zero. Thus, the Hamiltonian is block diagonal with a
ground state block (\( H^{gg} \)), an excited state block (\( H^{ee} \)), and double excited state
block (\( H^{ff} \)). This allows us to treat these blocks separately [83,108]. Therefore,
the time-dependent Schrödinger equation for each individual diagonal block is:

\[ \frac{d\psi(t)}{dt} = -\frac{i}{\hbar} H(t)\psi(t) \] (3.16)

where \( \psi \) is the wavefunction at a given time \( t \) and \( H \) is the Hamiltonian. Thus,
the solutions to this equation can be found using the time evolution operator:

\[ \psi(t) = U(t, t_0)\psi(t_0) \] (3.17)

with \( U(t, t_0) \), the time evolution operator, defined as:

\[ U(t, t_0) = e^{\frac{i}{\hbar} \int_{t_0}^{t} H_0 dt} \] (3.18)
where $H_0$ is the Hamiltonian operator for the unperturbed system and the plus sign on the exponential denotes the time ordered exponential. Therefore, the integration is performed in small time steps during which the Hamiltonian can be considered constant. Thus, the time evolution of the system is given by:

$$
\psi(t) = \left[ \Pi_{n=0}^{(t-t_0)/\Delta t} U((n + 1)\Delta t + t_0, n\Delta t + t_0) \right] \psi(t_0)
$$

(3.19)

where $n$ is the number of steps. In this way time-evolution matrices, $U$, for each excitation manifold are obtained for the delays between the interactions.

3.3.5 Main characteristics of a 2D IR spectrum

A two-dimensional spectrum reveals the correlation between excitation and detection frequencies. The spectrum contains diagonal peaks and off-diagonal ones, which contains structural and dynamical information. The 2D IR spectrum, thus, contain diagonal peaks originating from the ground state bleach and stimulated emission, which both result in decreased absorption, Figure 3.9 (A).

![Illustration of a typical 2D IR spectrum](image.png)

**Figure 3.9:** Illustration of a typical 2D IR spectrum, where blue represents an induced absorption and red bleach and stimulated emission. The different peak types A-D are described in the text.
Below the diagonal peaks, excited state absorption peaks are present (B), which reflects an additional absorption and these peaks have the opposite sign of the diagonal ones. Furthermore, cross peaks arise due to the coupling between different modes, resulting in delocalization of vibrational excitons. The cross peaks originate from bleach/stimulated emission (C) and excited state absorption (D) processes [91,109].

The line shapes of the two-dimensional spectrum portray dynamical information of the system. As written in the previous section a two-dimensional infrared spectrum is a correlation spectrum. Here, the frequency at which a system is excited is correlated with the frequency at which the system is probed, after a time delay.

![Figure 3.10: (a) Illustration of the variation of the line shape of a 2D IR spectrum with the waiting time. (b) Illustration of the center line slope. (c) Illustration of the variation of the diagonal and antidiagonal line widths with the waiting time.](image)

When the system is probed immediately after excitation, time delay $t_2=0$, there is typically a strong correlation between the frequencies, which will give rise to a diagonally elongated peak (elliptic shape) [91,109]. With the increase of the waiting time the system is allowed to relax and the correlation between both the initial and final frequencies is lost. The latter gives rise to a round peak.
with a large anti-diagonal elongation (circular peak), see Figure 3.10. With
the waiting time the peak shapes change from an elliptic peak to a round peak.
Thus, the time scale of this change provides information of how the vibrational
mode is interacting with the bath. For example, a system in which the line
shape is changing from elliptic to circular, is a system in which the dynamics
is fast, and it is said that the system has a short memory (a homogeneous
system). In case the line shape is diagonally elongated during the different time
delays the dynamics of a system is slow and it is said that it has a long lived
memory (an inhomogeneous system). Therefore, by measuring the diagonal and
anti-diagonal elongation it is possible to retrieve quantitative information on
the dynamics from the peak shape.

From the line shape of the spectrum the frequency-frequency correlation
function (FFCF) can be obtained. This is a measure of the frequency fluctuations
of a given oscillator with time [110]. This quantity describes the probability of a
molecule vibrating with a given frequency maintaining the same frequency after
a period of time. Because of structural fluctuations the vibrational frequency
of a molecule will change with time, since the molecule experiences different
environments. This process is called spectral diffusion to which FFCF’s are
often sensitive and can be used to provide more details about the time scale.
The FFCF for an isolated $|0\rangle \rightarrow |1\rangle$ transition is given by:

$$C(t) = \langle \delta \omega_{10}(t) \delta \omega_{10}(0) \rangle$$ (3.20)

where $\delta \omega_{10}(t) = \langle \omega \rangle - \omega(t)$. The FFCF can be approximated by the sum of
two terms [110]:

$$C(t) = \frac{\delta(t)}{T_2} + \sum_i \Delta_i^2 e^{-t/\tau_i}$$ (3.21)

where $\Delta_i$ is the amplitude of the frequency fluctuation, $\tau_i$ is the correlation time
between the $i$th component and $T_2$ is the dephasing time. Furthermore, for a
diagonally elongated peak one can define the axis of an ellipse as:

$$a = \eta \sqrt{1 + M(t_w)} \quad \text{and} \quad b = \eta \sqrt{1 - M(t_w)}$$ (3.22)

where $M(t_w)$ is the correlation function, $\eta$ is a normalization factor. The ellipse
axis are defined by $a$ (on diagonal) and $b$ (antidiagonal). Thus, the eccentricity
of an ellipse is given by:

$$\epsilon = \sqrt{1 - \left( \frac{b}{a} \right)^2}$$ (3.23)
by replacing equation 3.22 into the previous equation:

$$\epsilon = \sqrt{1 - \frac{1 - M(t_w)}{1 + M(t_w)}}$$  \hspace{1cm} (3.24)

this equation can be rewritten in terms of the correlation function:

$$M(t) = \frac{a^2 - b^2}{a^2 + b^2}$$  \hspace{1cm} (3.25)

The above expression shows how one can use the eccentricity of a peak of a 2D spectrum to retrieve the correlation function. Thus, for a diagonally elongated peak (inhomogeneous) the value of the correlation function $M(t)$ is approximately 1 and the eccentricity ($\epsilon$) should be 1. On the other extreme, for a very homogeneous peak (round) the eccentricity ($\epsilon$) is 0 and the correlation function $M(t)$ is approximately 0.

The center line slope (CLS) analysis is a method that allows the extraction of FFCF’s and spectral diffusion. Here, two spectral cuts parallel to the detection frequency axis are chosen and the slope is calculated through the lines that connect these cuts. Furthermore, for a system with only one single vibrational component the cuts are taken within a frequency range around the maximum of the 2D IR spectrum. This procedure is repeated for the spectrum at different waiting times. For short waiting times the center line has a significant slope, but with the increase in the waiting time the spectrum becomes more symmetrical due to spectral diffusion and the center line has slope zero. The central line slope is related with the FFCF and it takes values between 1, in the absence of a homogeneous component, and 0 for a fully homogeneous peak [110].

Fast frequency fluctuations are a reflection of systems with fast dynamics, resulting in antidiagonal broadening already at $t_2 = 0$ as the correlation is lost during $t_1$ and $t_3$. Because of the excitation transfer between oscillators, cross peaks are likely to increase in intensity with the waiting time. A probe for this increase in intensity, caused by the dynamics of an excitation hopping from one site to another, is the population transfer. This quantity measures the probability of an excited unit at time zero to be excited at a given time $t$. Population transfer dynamics can be used to analyze how an excitation flows inside the system, reflecting the strength of the coupling between molecules.

The molecules in which the transition dipole is aligned parallel with the polarization of the electric field are excited preferentially when compared to the case in which the transition dipole has an angle with the applied field. Because
the number of molecules that have their transition dipole perpendicular to the laser pulse is zero, the initial parallel response is larger than the perpendicular one [91, 105, 109].

![Figure 3.11: Illustration of the orientation of the laser pulses in a 2D IR experiment.](image)

Thus, the parallel signal decays faster than the perpendicular one. This difference in decay allows one to extract dynamical information regarding molecular orientational motion. One quantity that is widely used to characterize the orientational motion of the molecules is the anisotropy decay. Here the normalized difference between the signal along the pump and probe polarization directions is taken:

$$R(t) = \frac{\Delta \alpha_{||} - \Delta \alpha_{\perp}}{\Delta \alpha_{||} + 2\Delta \alpha_{\perp}}$$

(3.26)

where $\Delta \alpha_{||}$ is the parallel signal and $\Delta \alpha_{\perp}$ is the perpendicular one. A fast anisotropy decay is characteristic for a system with fast reorientational or population transfer dynamics and it is usually associated with systems with weak hydrogen bonding or with systems in which the excitations are highly delocalized [91, 109]. For an isolated molecule the anisotropy decay reflects its rotational motion.

Two dimensional infrared spectroscopy is also very useful to probe chemical exchange, since it is possible to follow in time the evolution of these processes [111–114]. Considering two molecules A and B that transform into each other during time. Initially, there no interconversion between both species, therefore in the 2D IR spectrum only the peaks corresponding to their initial frequencies will appear, see Figure 3.12.
3.3 Non-linear Response

Figure 3.12: Schematic representation of a 2D IR spectrum of a chemical exchange process. The diagonals peaks (in purple and green) are connected with two different configurations (A and B). The blue cross peaks appearing at later times reveal the chemical exchange of the two species interconverting.

With time the chemical exchange process takes place and can inter-convert into each other. Thus, by probing the system after some time cross peaks resulting from this exchange will appear. By measuring the spectra at different waiting times, one can retrieve information regarding the reaction rates.