Models for nonlinear optical spectra of coupled oscillators
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Collective oscillations and infrared spectra of inhomogeneous $\beta$-sheets$^1$

In this chapter, we numerically calculate the collective amide I oscillations and the associated linear and two-dimensional infrared (2DIR) spectra for model antiparallel $\beta$-sheets and study the effect of static inhomogeneity. To visualize the collective vibrational states, a new method is introduced, which proves very useful in classifying the optically dominant states with respect to their symmetry properties and phase relations, even in the absence of exact symmetries. We find that energy (diagonal) and interaction (off-diagonal) disorder may have profoundly different effects on the main peaks in the linear spectrum. We also show that in the 2DIR spectra, calculated with the sum over states model, energy disorder leads to horizontally stretched cross peaks. This indicates that energy disorder is one of the origins of the recently observed Z-shape in experimental spectra. Finally, we find that the anharmonic splitting between associated positive and negative features in the 2DIR spectra scales inversely proportional with the vibron delocalization size imposed by the disorder, thus offering a spectroscopic ruler for this size.

4.1 Introduction

The use of infrared spectroscopy in the study of protein conformation relies on the structural information contained in (collective) vibrations. In linear (one-dimensional) infrared spectra of proteins, this information is often hidden under broad line shapes,

resulting from inhomogeneity and the congestion of many vibrational states in a rather narrow spectral region [Krimm and Bandekar 1986; Jackson and Mantsch 1995]. This problem may to some extent be circumvented by performing nonlinear (multi-pulse) experiments, in which the spectral information is spread along two independent frequency axes, revealing correlations and anharmonic couplings between various vibrational modes. Moreover, these experiments allow for the observation of relatively weak transitions as cross-peaks with strong transitions and for the detection of relative polarization angles between transitions [Khalil et al. 2003a]. Also, these multi-dimensional techniques facilitate the distinction between homogeneous and inhomogeneous relaxation [Loring and Mukamel 1985; Tanimura and Mukamel 1993].

In recent years, two-dimensional infrared (2DIR) spectroscopy has successfully been applied to a series of small molecules, such as water and small peptides, confirming the potential of the technique to determine structure and dynamics at the molecular level [Hamm et al. 1998; Woutersen and Hamm 2001a; Woutersen et al. 2001; Golonzka et al. 2001; Zanni et al. 2002; Rubtsov et al. 2003b; Asbury et al. 2003b,a; Bredenbeck et al. 2003]. In addition, several groups have taken up the challenge to study proteins using 2DIR spectroscopy. The most interesting and challenging question is whether this technique may be used to probe the structure of these complex systems and to follow structural changes in real time. To this end, the existence of clear 2DIR markers for structural elements should be investigated. Clear markers for secondary structural elements, which were partially known already from the analysis of linear spectra, have been established in the amide I region of the spectrum (around 1650 cm\(^{-1}\)). In this context, theoretical and experimental model studies have been performed of \(\alpha\)- and \(3_{10}\)-helical structures [Moran et al. 2003; Wang and Hochstrasser 2004; Abramavicius et al. 2004; Fang et al. 2004], as well as \(\beta\)-sheets and hairpins [Cheatum et al. 2004; Demirdöven et al. 2004].

The theoretical study by Cheatum et al. [2004], based on an idealized vibrational exciton (vibron) model for the collective amide I oscillations, suggested that the 2DIR spectrum indeed offers markers for \(\beta\)-sheet structure. In particular, it was found that the cross-peaks in this spectrum may be useful to distinguish antiparallel \(\beta\)-sheets from parallel ones as well as \(\beta\)-hairpins. Experiments by Demirdöven et al. [2004], in which poly-L-lysine and proteins with different \(\beta\)-sheet content were studied, confirmed the existence of structural markers and the potential of 2DIR spectroscopy to assess the relative \(\beta\)-sheet content. Further experimental studies have even demonstrated the first application of 2DIR spectroscopy to detecting the kinetics of thermal denaturing of a protein [Chung et al. 2005]. Finally, large \(\beta\)-sheets form when proteins aggregate into amyloid fibrils [Nelson et al. 2005; Nelson and Eisenberg 2006], and nonlinear infrared spectroscopy is a most useful tool to study their structure [Zhuang et al. 2005; Londergan et al. 2006] and formation kinetics [Strasfeld et al. 2008; Ling et al. 2009].

Of course, the experimentally observed linear and 2DIR spectra of proteins are considerably more complicated and harder to interpret than the ones obtained in idealized model studies. One reason is that in experiment one probes the entire protein, and not an isolated secondary structural element. Moreover, in a real protein those
elements are never ideal. Reproducible as well as random inhomogeneity occurs in
the energies of the individual amide I oscillators (diagonal disorder) and the transfer
interactions between them (off-diagonal disorder) as a result of conformational irreg-
ularity (for instance twisting of the sheet) and random solvent shifts. An important
source of diagonal disorder (of the order of 10’s of cm$^{-1}$) is the effect of hydrogen
bonding with surrounding protic molecules in the solvent [Mirkin and Krimm 1991;
Hamm et al. 1998; Scheurer et al. 2001; Ham et al. 2003b]. Effects of random diagonal
disorder on the linear [Choi et al. 2002] and 2DIR [Hamm et al. 1998] spectra of glob-
ular proteins have been considered, while also the effect of conformational disorder
on the linear spectra of β-sheets have been modeled [Demirdöven et al. 2004].

In this work, we perform a systematic study of the effect of random disorder on
the linear and 2DIR spectra of model antiparallel β-sheets. Deliberately, we focus on
a simple model, in which we still treat the sheet as an idealized plane (finite) lattice
and incorporate the disorder in a phenomenological way, instead of taking coordi-
nates for specific proteins from NMR experiments and generating disorder distribu-
tions from molecular dynamics simulations. We believe our approach is useful to
investigate the existence of generic spectroscopic markers for β-sheet content, which
should not depend too much on the details of the model.

In addition to investigating the one- and two-dimensional spectra, we also pay
considerable attention to the nature of the underlying collective vibrational states.
Cheatum et al. [2004] showed that for homogeneous antiparallel β-hairpins the opti-
ically dominant states can be related in a simple way to the (basic) collective oscil-
lations of a single unit cell, consisting of four oscillators. These four basic states are
distinguished by the relative phases of the four oscillators. For extended β-sheets,
such an identification was argued to be harder, but still was tentatively made for two
optically important states (the $|a^-\rangle$ and the $|a^+\rangle$ states). Hard evidence for this was
not given, however. The question concerning the nature of the states gained interest
with the clear detection of two dominant spectral peaks in experiment (named the
$|a^-\rangle$ and $|a^+\rangle$ states) [Demirdöven et al. 2004]. We introduce a new visualization
method of collective states that facilitates and clarifies their proper assignment.

In Section 4.2 we introduce the model and give the expressions for the spectra
in terms of one- and two-quantum eigenstates. Section 4.3 presents our results and
discussion concerning the nature of the one-quantum eigenstates and the linear spec-
trum. Homogeneous systems are considered in Sections 4.3.1-4.3.3, while the effects
of disorder are the subject of Sections 4.3.4 (diagonal disorder) and 4.3.5 (off-diagonal
disorder). We then switch to a discussion of simulated 2DIR spectra in the pres-
ence of disorder (Section 4.4) and demonstrate that this spectrum may be used as
an experimental ruler for the vibron delocalization size. Section 4.5 contains a short
discussion of the spectrum of parallel β-sheets. Finally, we conclude in Section 4.6.

4.2 Model and expressions for the spectra

Many proteins contain β-sheets as secondary structural elements. They are large, al-
most two-dimensional structures, consisting of long polymerized polypeptide chains,
called strands. The chemical structure of an antiparallel β-sheet is shown in Figure 4.1.
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Figure 4.1: Chemical structure of the anti-parallel $\beta$-sheet. The sheet is built from strands that run in the horizontal direction. In the vertical direction, the strands are bound together by hydrogen bonds (dashed lines). The structure shown is $2 \times 2$ unit cells large, a single unit cell is detailed inside the box. The four dipoles in this unit cell are indicated by arrows. The center of the circle on each arrow gives the position of the dipole. The arrow shows its direction in the $xy$-plane. The dipole component in the $z$-direction is indicated by the symbol inside the circle. A dot (cross) means that the normalized dipole has a positive (negative) $z$-component. The components of the dipoles in the plane of the sheet are antisymmetric with respect to inversion of the unit cell; those perpendicular to the sheet are symmetric.

In our convention in the current chapter, the strands run in the horizontal ($x$) direction. In the vertical ($y$) direction, strands are held together by hydrogen bonds (dotted lines in Figure 4.1). The direction perpendicular to the sheet is the $z$ direction. The geometry of the sheet is determined by the torsion angles of the strands ($\phi, \psi$) and the hydrogen bond length $r$. Our parameters are $(\phi, \psi) = (-160^\circ, 118^\circ)$ and $r = 0.304$ nm. This is the same structural model that was studied by Cheatum et al. [2004]. As argued in the Introduction to this chapter, we will focus on idealized planar sheets; we thus neglect strand turns and incomplete unit cells that may occur at the sides of the sheet, as well as twists of the sheet.

The amide I vibration, which is primarily a stretching of the C=O bond in amide groups [Krimm and Bandekar 1986], has a frequency of about 1675 cm$^{-1}$. It occurs more than 100 cm$^{-1}$ away from other vibrational modes, which is used as the justification for considering it decoupled from other modes. The antiparallel $\beta$-sheet is

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2We will consider the coupling of the amide I mode to the vibrational mode closest in energy, which is
seen to contain four amide I oscillators per unit cell, labeled 1 to 4 in Figure 4.1. For the optical response each amide group in the sheet is treated as an anharmonic vibrational oscillator. The dipole of the oscillator lies on the C=O bond, 86.8 pm from the carbon atom and makes an angle of $20^\circ$ with this bond, towards the nitrogen atom. The directions of the dipoles of the four oscillators within the plane of the $\beta$-sheet are indicated in Figure 4.1 by arrows; the very small tilting out of this plane is indicated by a cross (pointing downward) or a dot (pointing upward). Explicit values for the three vector components of the dipoles follow from the geometry of the sheet and are given by Cheatum et al. [2004, Table 1], who also give the three-dimensional positions of the oscillators.

The oscillators are coupled by interactions that transfer the vibrational excitation energy from one oscillator to another. The whole sheet can then be described by the Hamiltonian

$$H = \sum_{n=1}^{N} b_n^\dagger (\epsilon_0 + \xi_{nn}) - \frac{A}{2} b_n^\dagger b_n b_n + \sum_{n,m=1}^{N} J_{nm} b_n^\dagger b_m,$$

(4.1)

where the $b_n^\dagger$ and $b_n$ are the Bose creation and annihilation operators, respectively, for an excitation quantum on the $n$th oscillator and $N$ denotes the total number of oscillators. The $\epsilon_0 + \xi_{nn}$ in the first term of the Hamiltonian are the transition energies of the $n$th oscillator. In previous work on $\beta$-sheets all these energies have been taken equal, $\xi_{nn} = 0$. However, this assumption is too restrictive for a sound understanding of experimental data. As was explained in the Introduction to this chapter, variations in local structure and solvent exposure affect the site energies. We will model such effects by including energetic disorder, taking the site energies randomly and independently from a Gaussian distribution,

$$P(\xi_{nn}) = \frac{1}{\sigma \sqrt{2\pi}} e^{-\xi_{nn}^2/2\sigma^2},$$

(4.2)

where the standard deviation $\sigma$ determines the magnitude of the disorder. We will study the effects of this disorder on the collective excited states and the spectra. For the average single-oscillator frequency we will use $\epsilon_0 = 1675$ cm$^{-1}$.

The parameter $A$ in the first term of the Hamiltonian, which we take to be 16 cm$^{-1}$ [Hamm et al. 1998], is the strength of the anharmonicity, the energy of a doubly excited oscillator is $2\epsilon_0 + 2\xi_{nn} - A$. Finally, the second term in the Hamiltonian describes interactions between oscillators, where the prime on the summation excludes self-interactions (terms with $n = m$). The interactions are taken from the transition dipole coupling model (TDC) [Krimm and Bandekar 1986; Torii and Tasumi 1992]. Although the validity of this model is disputed and it has been demonstrated that interactions through the peptide backbone may be much stronger than predicted by a TDC calculation [Torii and Tasumi 1998; Ham et al. 2003a; Choi et al. 2003], we prefer to use one consistent interaction model and include TDC interactions only. We will briefly discuss the coupling model in Section 4.5. The array of oscillators coupled by

the amide II mode, in Chapter 5
interactions is shown in Figure 4.2, where the three strongest interactions have been drawn (solid lines: 18.7 cm\(^{-1}\); dotted lines: -7.4 cm\(^{-1}\), and dashed lines: -4.1 cm\(^{-1}\)). Aside from these three interactions, we have accounted in our calculations also for the next five weaker interactions (see caption of Figure 4.2).

Variations in local structure will obviously also lead to disorder in the interactions. Furthermore, the exact form of the nuclear potential is also not necessarily identical for different oscillators, leading to possible disorder in the anharmonicity parameter \(A\). In the present treatment, we will mostly be concerned with energetic disorder. In Section 4.3.5 we will briefly consider interaction disorder, while variations in the anharmonicity, which are known to be of little importance in the optical response of peptides [Jansen and Knoester 2006a], are not included.

With the knowledge of the sheet geometry and Hamiltonian, we can proceed to calculate the collective energy eigenstates, which may be referred to as (delocalized) vibrons. These follow from a simple diagonalization of the Hamiltonian. Because the Hamiltonian (Eq. 4.1) does not change the number of excitations in the system, the eigenstates fall apart into different classes, labeled by this number. We expand the eigenstates in the site representation. A one-quantum state \(|u\rangle\), from the class of eigenstates with one excitation quantum in the system, can then be written as

\[
|u\rangle = \sum_{n=1}^{N} u_n b_n^\dagger |g\rangle.
\]

A two-quantum state \(|w\rangle\) can be decomposed as

\[
|w\rangle = \sum_{n,m \geq n} (1 + \delta_{nm})^{-1/2} w_{nm} b_n^\dagger b_m^\dagger |g\rangle.
\]

Here, \(|g\rangle\) is the ground state, without any excitation quanta, and the coefficients \(u_n\) and \(w_{nm}\) are the components of the eigenstate in the chosen basis. They follow from an \(N \times N\) and an \(N(N + 1)/2 \times N(N + 1)/2\) matrix diagonalization, respectively.
Once the eigenstates and their energies are known, it is straightforward to calculate linear and 2DIR spectra using nonlinear response theory (See Chapter 3). The linear absorption spectrum as a function of frequency $\omega$ is, up to a constant factor, given by

$$A(\omega) = \sum_u \frac{|\vec{\mu}_u|^2 \gamma}{(\omega - E_u)^2 + \gamma^2}. \quad (4.3)$$

The summation runs over all one-quantum states $|u\rangle$, with energy $E_u$ and transition dipole to the ground state $\vec{\mu}_u = \sum_n u_n \vec{\mu}_n$, with $\vec{\mu}_n$ the dipole vector of molecule $n$. The applied Lorentzian line-shape has a homogeneous full width at half maximum (FWHM) of $2\gamma$.

The 2DIR signal is radiated from a system after interaction with three linearly polarized laser pulses with wave vectors $\vec{k}_1$, $\vec{k}_2$, and $\vec{k}_3$, which arrive at times $t - t_3 - t_1$, $t - t_3 - t_2$, and $t - t_3$, respectively. For a fixed time $t_2$ the signal is measured by scanning $t_1$ and $t_3$. The spectrum in the frequency domain is obtained by a double Fourier transform. The variable $\omega_1$ is the Fourier conjugate of $t_1$, $\omega_3$ is the conjugate of $t_3$. The 2DIR spectrum is calculated as the sum of rephasing and non-rephasing contributions. For details concerning the calculation of the signal, we refer to Chapter 3. Like in the work of Cheatum et al. [2004], we will neglect orientational relaxation. As pointed out by Woutersen and Hamm [2001a], even for small peptides molecular rotation is much slower than the time scale of the experiment.

### 4.3 Results and discussion: linear spectra and the one-quantum eigenstates

#### 4.3.1 Homogeneous unit cell

In Figure 4.3, we present the numerically calculated linear spectra for a single unit cell of four oscillators, the $3 \times 1$ β-hairpin (i.e., a system made up of three unit cells in the horizontal direction), and the $3 \times 3$ extended β-sheet (having nine unit cells in a square arrangement). In all cases, the system was chosen homogeneous ($\sigma = 0$) and we used a homogeneous linewidth of $\gamma = 2 \text{ cm}^{-1}$. These spectra (with somewhat different widths) have been given by Cheatum et al. [2004] already. We show them here, because we want to expand on the nature of the states responsible for the various spectral features. In the current subsection, we focus on the unit cell, while the homogeneous hairpin and sheet are discussed in Sections 4.3.2 and 4.3.3, respectively. The effect of disorder in β-sheets is analyzed in Sections 4.3.4 and 4.3.5.

The spectrum of the single unit cell (dotted) is dominated by two peaks, occurring at about 1653 cm$^{-1}$ and 1677 cm$^{-1}$. A very faint peak can still be discerned at 1696 cm$^{-1}$. Using the inversion symmetry of the unit cell’s Hamiltonian with respect to its center (i.e., with respect to interchanging oscillators 1 and 4, and at the same time 2 and 3), the four collective eigenstates underlying these peaks were calculated analytically by Cheatum et al. [2004]. The two strongest peaks in the spectrum arise from the eigenstates that are antisymmetric with respect to the inversion operation.
Figure 4.3: Linear absorption spectra in arbitrary units for a single unit cell of four oscillators (dotted), a $3 \times 1 \beta$-hairpin, existing of a horizontal row of three adjacent unit cells (dashed), and a $3 \times 3$ extended $\beta$-sheet (solid). In all cases a value of $\gamma = 2 \text{ cm}^{-1}$ was used for the homogeneous broadening.

(referred to as $a$ states by Cheatum et al. [2004]). This is a direct consequence of the fact that the large dipole components are the ones in the plane of the sheet, which are antisymmetric with respect to the inversion operation, as is seen in Figure 4.1. The state underlying the main peak at $1653 \text{ cm}^{-1}$ results from the $|a-\rangle$ state, which is the antisymmetric state in which the oscillators 1 and 2 have opposite phase. The second peak (at $1677 \text{ cm}^{-1}$) results from the $|a+\rangle$ state, which is antisymmetric with respect to the inversion, and has oscillators 1 and 2 in phase. The $a$ states are polarized in the plane of the sheet.

The other two eigenstates of the unit cell are symmetric with respect to inversion ($s$ states) and have a very small oscillator strength, caused by the small $z$ components of the oscillator dipoles, which are symmetric with respect to the inversion operation. The faint peak at $1696 \text{ cm}^{-1}$ results from the $|s-\rangle$ state, which is symmetric, with oscillator 1 and 2 having opposite phase. The $|s+\rangle$ state (at $1674 \text{ cm}^{-1}$) is not visible, because its oscillator strength is too small. Obviously, the $s$ states are polarized perpendicular to the plane of the sheet. We note that the current labeling of the $|s+\rangle$ and $|s-\rangle$ states is interchanged with respect to the one originally given by Cheatum et al. [2004], where $+$ and $-$ were used to indicate higher and lower energy, respectively. For the optically dominant $a$ states, this does not affect the labels.

For future assignment of the eigenstates, it is useful to introduce a visualization of their wave functions that emphasizes the symmetry and phase relations. We do this by making color maps on the plane of the system, like is done in Figure 4.4(a) for the four eigenstates of the single unit cell. In this map, each oscillator is represented by a square, whose color indicates the eigenstate’s component ($u_n$) on that
4.3: Results and discussion: linear spectra and the one-quantum eigenstates

Figure 4.4: (a) Color maps of the four one-quantum eigenstates \((a-), |s+\rangle, |a+\rangle, \text{and } |s-\rangle\) of the homogeneous \(\beta\)-sheet unit cell, in order of ascending energy. The colors indicate the value of the wave function on each of the four oscillators of the unit cell, where red stands for positive values and blue for negative components (see legend to the right). Below each state, its energy and the square of its transition dipole to the ground state (in units of the squared dipole of the single oscillator) are given, as well as its symbol. (b)-(f) As in (a) but now for the five states that dominate the dashed spectrum of the homogeneous \(3 \times 1\) hairpin (12 oscillators) given in Figure 4.3.

4.3.2 Homogeneous hairpin

In Figure 4.3 we see that the spectrum of the \(3 \times 1\) hairpin (dashed) has two dominant peaks, which are slightly blue-shifted relative to the main peaks of the unit cell. A third weak peak around \(1695 \text{ cm}^{-1}\) is slightly red-shifted relative to the \(|s-\rangle\) state of the unit cell. Finally, a fourth feature is seen as a shoulder on the red side of the largest peak. All these peaks were explained analytically, even at a quantitative
level, by Cheatum et al. [2004] already. It was argued that in hairpins the interactions between adjacent unit cells are so weak that unit cell eigenstates with different symmetry and phase properties are hardly mixed by them. More explicitly, for the \( N \times 1 \) hairpin the eigenstates are to a good approximation given by four bands of states, denoted as \( |a-\rangle_k, |a+\rangle_k, |s-\rangle_k, \) and \( |s+\rangle_k, \) with [Cheatum et al. 2004]

\[
|a-\rangle_k = \sqrt{\frac{2}{N+1}} \sum_{l=1}^{N} \sin \left( \frac{\pi kl}{N+1} \right) |a-\rangle_l, \tag{4.4}
\]

and similar for the other bands. Here, \( |a-\rangle_l \) denotes the state in which the \( l \)th unit cell is in its basis state \( |a-\rangle, \) and \( k = 1, \ldots, N \) is the wave number of the state. Based on estimating interband coupling coefficients, it was argued by Cheatum et al. [2004] that the hairpin’s eigenstates responsible for the main peaks near 1657 cm\(^{-1} \), 1679 cm\(^{-1} \), and 1695 cm\(^{-1} \) to a good approximation are given by the \( k = 1 \) states of the \( |a-\rangle, \) the \( |a+\rangle, \) and the \( |s-\rangle \) bands, respectively. The state that contributes the shoulder in the largest peak was associated with the \( k = 3 \) state of the \( |a-\rangle \) band.

The above identification of the eigenstates of hairpins can be made more convincingly by giving their color maps. In order of ascending energy, these maps are given in Figure 4.4(b)-(f) for the four states that are responsible for the spectral features discussed above, as well as for a fifth state that gives a small shoulder in the red wing of the peak near 1679 cm\(^{-1} \). We first note that the five states displayed are either symmetric ((b)-(e)) or antisymmetric (f) with respect to inversion relative to the center of the hairpin. The existence of a definite parity with respect to this inversion results from the fact that the Hamiltonian of a homogeneous hairpin (and also a homogeneous extended sheet) has inversion symmetry. The color maps also demonstrate other (approximate) symmetry properties, however. For instance, comparison with Figure 4.4(a) clearly shows that the state displayed in Figure 4.4(c), mainly responsible for the spectral peak at 1657 cm\(^{-1} \), repeats the color pattern of the \( |a-\rangle \) basis state in each of its three unit cells. Thus, inside each unit cell the cell symmetry and phase relations follow those of the \( |a-\rangle \) state, with the same overall sign of the phase for all three unit cells. This confirms that indeed this state to a good approximation is the \( |a-\rangle_{k=1} \) state. Similarly, Figures 4.4(e) and (f) clearly exhibit the symmetries and phase relations appropriate for the \( |a+\rangle_{k=1} \) and the \( |s-\rangle_{k=1} \) states, respectively. The other two states at first sight have less regular color maps. Upon closer inspection, however, Figure 4.4(b) in each of its unit cells has the (approximate) symmetry and phase relations belonging to the \( |a-\rangle \) basis state, with the middle cell having an opposite overall phase relative to the outer two. Thus, this state has the symmetries and phase relations appropriate for \( |a-\rangle_{k=3} \), confirming its assignment made by Cheatum et al. [2004]. Likewise, the remaining state in Figure 4.4(d) has the phase relations that belong to \( |a+\rangle_{k=3} \), although in this case the exact amplitudes on each of the oscillators, while having the correct signs, considerably deviate from the ideal \( |a+\rangle_{k=3} \) state, probably due to mixing with the close lying \( |s+\rangle \) type basis states of the three unit cells.

We have studied the color maps for the four optically dominant eigenstates of hairpins of up to six unit cells long and found that always they have the phase
symmetries and phase relations appropriate to the states $|a^-\rangle_{k=1}$, $|a^+\rangle_{k=1}$, $|a^-\rangle_{k=3}$, and $|s^-\rangle_{k=1}$ (in order of descending oscillator strength). The $|a^-\rangle_{k=3}$-type state was found to shift from 1649 cm$^{-1}$ to 1654 cm$^{-1}$ with increasing hairpin length, consistent with the dispersion of the $|a^-\rangle$ band found by Cheatum et al. [2004]. The three other states vary very little in energy, reflecting the weak intercell interactions.

Owing to the symmetry of the various dipole components on the oscillators, only states that are (anti-)symmetric with respect to both the global symmetry and the cell symmetry will have a large oscillator strength. A state that is perfectly symmetric (anti-symmetric) with respect to the global symmetry and perfectly anti-symmetric (symmetric) with respect to the unit cell symmetry has no oscillator strength at all. Quite generally, the low-wavenumber states, in which no overall phase differences exist between different unit cells, dominate the spectrum. These statements also hold for extended β-sheets (see below). In practice, cell symmetries are not exact, although, as we have seen above, for hairpins they survive the intercell interactions to a very good approximation. Finally, the polarization of the states is governed entirely by the global symmetry. State that are antisymmetric (symmetric) with respect to global inversion, have a transition dipole to the ground state that is oriented parallel (perpendicular) to the plane of the hairpin. In practice this means that, as for the isolated unit cell, all $a$-type ($s$-type) states are polarized parallel (perpendicular) to the plane of the system.

### 4.3.3 Homogeneous sheet

The spectrum of the $3 \times 3$ sheet (solid line in Figure 4.3) shows more structure than the one for hairpins. The main peak is now red-shifted relative to the $|a^-\rangle$ state of the unit cell, the feature around 1680 cm$^{-1}$ appears to consist of two closely spaced peaks, while a new feature (with substructure) has emerged just above 1660 cm$^{-1}$. The weak peak near 1700 cm$^{-1}$ is shifted to the blue relative to the unit cell and the hairpin spectrum. As was noted by Cheatum et al. [2004], assigning the spectral peaks for extended sheets is more complicated than for hairpins. The reason is that in extended sheets strong interactions exist between unit cells (for instance the interaction between oscillators 7 and 10 in Figure 4.2 and the interactions between 3 and 9, and between 4 and 10).

First, these stronger interactions lead to wider vibron bands than in the case of hairpins, as is clear from the separation between highest and lowest peaks in Figure 4.3. Second, and more importantly, as these interactions are not weak relative to the energy differences between the four eigenstates of the isolated unit cell, these states will be mixed in extended sheets. Thus, one expects that in extended sheets the intracell parity and phase properties are mixed, making it more difficult to associate the spectral peaks with unit cell eigenstates, such as $|a\pm\rangle$. In spite of this, Cheatum et al. [2004] tentatively labeled the dominant state at about 1645 cm$^{-1}$ as an $|a^-\rangle$-type state, while the one near 1680 cm$^{-1}$ was associated with $|a^+\rangle$.

The color maps introduced above allow us to asses in more detail to what extent the unit cell symmetries persist for extended sheets. The seven eigenstates of the

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3In the paper by Cheatum et al. [2004] this state appears at 1641 cm$^{-1}$. The discrepancy is due to the fact that in the current calculations, we only account for the 8 strongest interactions $J_{nm}$ (see Figure 4.2)
3 × 3 sheet with the largest oscillator strengths are depicted in Figure 4.5 in order of ascending energy. Since the global inversion symmetry is exact for this system, all eigenstates are either anti-symmetric (the first six) or symmetric (the last one) with respect to inversion in the sheet’s center. As noted above, this means that the first six states are polarized in the plane of the sheet, while the seventh is polarized perpendicular to it. In addition to the global symmetry, several states in Figure 4.5 show rather consistent intracell parity and phase relations. In particular, the second state (energy 1647.2 cm⁻¹) to a good approximation has |a⁻⟩ character: seven unit cells out of nine have a⁻ symmetry. This justifies its identification as an |a⁻⟩-type state. The strong a⁻ character is immediately recognized from the fact that the color map resembles an array of six columns that alternate in color when going from left to right. The fact that no overall phase changes occur between unit cells (i.e., the same cell pattern is repeated) indicates that this resembles the smallest-wavevector state with a⁻ character, with the strongest transition dipole.

Studying more general $N \times N$ sheets, we have found that always by far the
4.3: Results and discussion: linear spectra and the one-quantum eigenstates

The strongest state in the spectrum occurs near 1645 cm\(^{-1}\). It always is antisymmetric with respect to global inversion. Moreover, for \(N\) even, this state to an excellent approximation has \(a^-\) symmetry (with regards to the phases of the oscillators): all unit cells have the required \(a^-\) symmetry for \(N\) up to 14, while for \(N = 16\) only four (out of 256) cells have a symmetry that is not \(a^-\). For \(N\) odd, the cell symmetry is not present in all unit cells, as we already found above for \(N = 3\).

A second strong peak in the sheet spectra is found near 1680 cm\(^{-1}\). As is illustrated in Figure 4.5, it is mainly caused by the transition at 1680.7 cm\(^{-1}\), which to a very good approximation has \(a^+\) symmetry. Note the clear difference between the color map of this state (a stack of rows that alternate in color from top to bottom) and the one at 1647 cm\(^{-1}\) (alternating columns), illustrating the usefulness of these maps. Centered around 1660 cm\(^{-1}\) there are several states with considerable oscillator strength. The one at 1660.1 cm\(^{-1}\) still has a large \(a^-\) character and can be interpreted as a higher-wavevector state in the \(|a^-\rangle\) band; this identification is confirmed by the fact that relative phase changes occur between unit cells in the vertical (\(y\)) direction. By contrast, the state at 1662.7 cm\(^{-1}\) has no consistent intracell parity and phase relation, implying that it arises from strong mixing of unit cell eigenstates. All states dealt with so far have negative parity with respect to the global inversion symmetry, and therefore are polarized within the \(xy\)-plane. Only the very faint state near 1705 cm\(^{-1}\) has positive global parity and is polarized in the \(z\)-direction. Notice that the color map of this state clearly has a checker-board pattern, indicative of the lowest-wave-vector state with a strong \(s^-\) character.

We finally notice that if we would have imposed periodic boundary conditions, the eigenstates would always preserve clear parity labels, both with respect to the global symmetry and with respect to phase relations within cells [Miyazawa 1960; Miyazawa and Blout 1961; Chirgadze and Nevskaya 1976]. The reason is that all unit cells would be equivalent then and for the optically allowed states, no phase differences would occur between unit cells, because of the \(q = 0\) selection rule imposed by the translational symmetry. As was noted by Cheatum et al. [2004], however, the use of periodic boundary conditions on extended sheets leads to significant qualitative errors, especially in the polarization properties of the dominant \((a^+\) and \(a^-\) type) states.

### 4.3.4 Sheet with diagonal disorder

As mentioned in the Introduction to this chapter, disorder plays an important role in understanding experimental spectra. In this subsection, we will discuss the effect of diagonal disorder on the linear spectrum of extended \(\beta\)-sheets. Figure 4.6 shows the linear spectrum for a \(3 \times 3\) sheet in the absence of disorder (solid line) and for two values of the disorder strength: \(\sigma = 5\) cm\(^{-1}\) (dotted) and \(\sigma = 10\) cm\(^{-1}\) (dashed). In all cases the homogeneous width was set to \(\gamma = 2\) cm\(^{-1}\).

The observed changes due to disorder are quite typical. The first obvious effect is a broadening of the spectral lines. This results from the fact that disorder breaks the inversion and approximate translational symmetry in the system; it thus mixes the unperturbed eigenstates and breaks the optical selection rules for the vibrons: more collective states become strongly dipole allowed. We calculated the FWHM \(W\) of
Collective oscillations and infrared spectra of inhomogeneous $\beta$-sheets

Figure 4.6: Linear absorption spectrum, in arbitrary units, of a 3×3 $\beta$-sheet in the absence of disorder (solid) and with diagonal disorder of strength $\sigma = 5 \text{ cm}^{-1}$ (dotted) and $\sigma = 10 \text{ cm}^{-1}$ (dashed). Spectra with disorder were obtained through Monte Carlo simulations, averaging over 10,000 disorder realizations. In all spectra a value of $\gamma = 2 \text{ cm}^{-1}$ was used for the homogeneous broadening of individual vibron transitions. The three spectra have equal area, reflecting the conservation of total oscillator strength. The disorder-induced broadening of spectral lines and red-shift of the dominant $|a-\rangle$ peak are clearly visible.

the strongest peak (the $|a-\rangle$ peak) as a function of the disorder strength $\sigma$ (keeping the system size constant at 3×3 unit cells). For $5 \text{ cm}^{-1} \leq \sigma \leq 30 \text{ cm}^{-1}$, which is significantly larger than the homogeneous half width of 2 cm$^{-1}$, we observe power-law behavior: $W \sim a\sigma^b$ (squares in Figure 4.7). When both $W$ and $\sigma$ are expressed in wavenumbers, a least squares fit yields $a = 1.1$ and $b = 1.2$. Power-law scaling of the optical linewidth of energetically disordered exciton systems has been found previously by Schreiber and Toyozawa [1982a] and Fidder et al. [1991a]. These authors reported $b = 4/3$ for one-dimensional systems and $b = 2$ for two-dimensional systems, in both cases with equal orientation of all oscillator dipoles. Comparing our result for $b$ with the cited values, we observe that line broadening in $\beta$-sheets does not scale as in a two-dimensional system. This is not surprising, since the interactions in the sheet render the system non-isotropic. In addition, the occurrence of four different dipole orientations leads to four interwoven vibron bands, which also leads to a different line broadening.

Apart from line broadening, disorder also causes the energy separation between the two main spectral peaks (the $|a-\rangle$ and the $|a+\rangle$ peaks) to increase. This is visible in Figure 4.6 mainly as a redshift of the $|a-\rangle$ peak. The peak shift, caused by disorder-induced coupling between the homogeneous eigenstates, is well known for J aggregates [Schreiber and Toyozawa 1982a; Fidder et al. 1991a]. The redshift $S$ of the $|a-\rangle$ state in our $\beta$-sheet model (triangles in Figure 4.7) is observed to fol-
4.3: Results and discussion: linear spectra and the one-quantum eigenstates

Figure 4.7: Dependence of the width (squares) and shift (triangles) of the $|a-\rangle$ peak in the linear absorption spectrum of the $3 \times 3$ unit cell $\beta$-sheet on the strength $\sigma$ of the diagonal disorder. The lines indicate power-law fits, for which the parameters are given in the text.

low power-law scaling for $\sigma \leq 17 \text{ cm}^{-1}$: $S \sim \sigma^b$, with $b = 1.5$ from a least-squares fit. Again the result can be compared with linear aggregates, where the exponent is found to be slightly smaller, $b = 1.35$ [Fidder et al. 1991a]. For larger values of the disorder the peak shift does not increase anymore, but even decreases somewhat. This effect can be understood by realizing that for these large values of $\sigma$, the peaks broaden so much that they start to overlap. In particular, the $|a-\rangle$ peak starts to merge with the higher-energy peaks. The growing overlap displaces the weight of the total peak to the high-energy side, causing a blue-shift that compensates for the disorder-induced red-shift. The net effect is a deviation from the power-law behavior which we observed for smaller disorder values.

Finally, we analyze the nature of the eigenstates in the presence of disorder. To this end, we plot in Figure 4.8 the color maps of the state with the largest transition dipole to the ground state that occurs within three randomly chosen disorder realizations for $\sigma = 5, 20,$ and $50 \text{ cm}^{-1}$. For small disorder, we expect these dominant states to be of the $|a-\rangle$ type. Indeed, for the three states found for $\sigma = 5 \text{ cm}^{-1}$, we still see an overall color pattern that resembles the alternating red and blue columns of the state at 1647.2 cm$^{-1}$ in Figure 4.5. The fact that we are still dealing with weak disorder, is clear from the fact that all three states considered are still strongly delocalized over the entire sheet. Even the global inversion symmetry seems not to be broken very strongly, implying that these states are mostly polarized within the plane of the sheet. The disorder of 5 cm$^{-1}$ is too small to cause strong mixing be-
between the lowest-lying $|a-\rangle$ type state and states of different symmetries, and the broadened low-energy absorption peak may still be referred to as $|a-\rangle$ peak.

At $\sigma = 20 \text{ cm}^{-1}$, we see from the many white or very light sites in the color maps that the states tend to get more localized on a part of the sheet. Anderson localization of exciton states is well known in the field of electronic excitons in J aggregates and semiconductors, and in many such systems the exciton localization size is considered an important microscopic quantity whose measurement has attracted much attention [Bakalis and Knoester 1999b,a; Dahlbom et al. 2001]. Also for vibron models of globular proteins, localization has been studied [Hamm et al. 1998; Choi et al. 2002]. Even though at $\sigma = 20 \text{ cm}^{-1}$ the vibron states are localized in our model $\beta$-sheets, and their global symmetry is lost, we see that within their localization area their color maps still bear a marked (though not perfect) resemblance to the alternating red and blue column pattern. This justifies to still refer to these states as $|a-\rangle$-type states and also, in hindsight, justifies to identify the strong $|a-\rangle$ absorption peak defined by Demirdöven et al. [2004] as $|a-\rangle$-type peak.

For $\sigma = 50 \text{ cm}^{-1}$, the states are strongly localized. Even in this case, however, we recognize that locally the strongly dipole allowed states seem to carry a fair $|a-\rangle$ type character. It should be noted, however, that for this large value of $\sigma$ no distinction can be made between different absorption bands anymore, so that we cannot speak of an $|a-\rangle$ peak in the spectrum. The fact that we still only found states that locally

Figure 4.8: Color maps of the one-quantum eigenstate with the largest dipole to the ground state for a disordered $3 \times 3$ unit cell $\beta$-sheet. Three values of the disorder were considered ($\sigma = 5, 20, \text{ and } 50 \text{ cm}^{-1}$ from top to bottom), and for each $\sigma$ value three disorder configurations were generated randomly (left to right). For each of these realizations, the optically strongest state is shown. Color coding is as in Figure 4.5.
4.3: Results and discussion: linear spectra and the one-quantum eigenstates

look like the $|a-\rangle$ states, directly results from the fact that selecting the largest dipole automatically selects phases between neighboring oscillators that also apply to the $|a-\rangle$ type states.

We notice that a more complete study of the nature of the eigenstates in the presence of disorder requires a more systematic investigation of the energy dependence of certain moments of the wave functions. A good choice would be to consider the autocorrelation function of the wave function as a function of energy [Chachisvilis et al. 1997]. This would allow one to distinguish whether states underlying the strongest absorption bands indeed may be referred to in a statistically meaningful way as $|a-\rangle$ or $|a+\rangle$ states. Recently, a similar study was performed to investigate the chiral behavior of exciton states in helical cylinders [Didraga and Knoester 2004].

4.3.5 Off-diagonal disorder

We have seen that for $\sigma \leq 17 \text{ cm}^{-1}$, the $|a-\rangle$ peak shifts to lower energy with increasing disorder strength. While for energetic disorder this is the normal behavior for the lower band edge states, for disorder in the interactions $J_{nm}$ this need not be the case. Such disorder naturally arises from conformational disorder: small random deviations of oscillator positions and dipoles from their regular values lead to random changes in the TDC interactions. This type of disorder was simulated by Demirdöven et al. [2004], who applied random Gaussian shifts of the oscillator positions. They found that the $|a-\rangle$ peak was broadened and shifted to the blue as a result of disorder, while the $|a+\rangle$ peak hardly changed in position and width. No explanation was offered, except that the change in position of the $|a-\rangle$ peak was ascribed mainly to fluctuations in the interstrand distances. Our study shows that this is not correct.

As a simple example, we have considered interaction disorder in a single unit cell by varying the positions of the four oscillators. The displacements are random and uncorrelated. We first look at variations in the $xy$-plane, by taking the absolute value of the displacement from a Gaussian distribution and its direction from a uniform distribution. Figure 4.9 shows the resulting linear spectra for different disorder strengths, where for clarity the spectra have been scaled to equal amplitude of the $|a-\rangle$ peak. From the figure we observe that the $|a-\rangle$ peak shifts to the blue and strongly broadens, while the $|a+\rangle$ peak shifts slightly to the red and hardly broadens. The explanation for the shifts is that the conformational disorder decreases the average TDC strength, thus giving smaller vibron dispersions and keeping the average vibron transitions closer to the single-oscillator frequency. Since for the $|a+\rangle$-type states the various interactions largely cancel each other (which is why this state occurs so close to the single-oscillator energy), the net effect of disorder in these interactions on the line shift is also smaller. For the same reason, the fluctuations in the strengths of the interactions have a much smaller effect on fluctuations in the position of the $|a+\rangle$ state than the $|a-\rangle$ state, leading to the considerably smaller line broadening of the $|a+\rangle$ peak.

To get a better understanding of the origin of the strong blue-shift of the $|a-\rangle$ peak, we also randomly varied the oscillator positions in only one of the spatial directions. In the resulting spectra (not shown), we observe that fluctuations in the
Collective oscillations and infrared spectra of inhomogeneous $\beta$-sheets

Figure 4.9: Spectra of a single unit cell with disorder in the oscillator positions. Oscillators have been randomly displaced in the $xy$-plane with a uniform distribution of the angle of displacement and a Gaussian distribution of standard deviation $s$ in the distance. The four spectra correspond to $s = 0$ (solid), $s = 17.3$ pm (dotted), $s = 50$ pm (dashed), and $s = 100$ pm (dash-dotted). Spectra have been averaged over 50,000 disorder realizations. In all cases a value of $\gamma = 2$ cm$^{-1}$ was used for the homogeneous broadening of individual vibron transitions. We observe that the vibronic band narrows with increasing disorder, resulting from a blue-shift of the $|a-\rangle$ peak.

$x$-direction almost entirely explain the blue-shift of this peak, while variations in the interstrand spacing (i.e., Gaussian disorder in the $y$-direction) have almost no effect on the position of this peak. This conclusion is in marked contrast to the suggestion made by Demirdöven et al. [2004] that the interstrand distances are the crucial quantities. We also found that disorder in the $z$-component of the oscillator positions leads to a small blue-shift of the $|a-\rangle$ peak.

4.4 Results and discussion: 2DIR spectra of extended sheets

Figure 4.10 shows the calculated 2DIR correlation spectrum in the ZZYY-polarization without disorder (panel (a)) and with Gaussian diagonal disorder of strength $\sigma =$
4.4: Results and discussion: 2DIR spectra of extended sheets

Figure 4.10: 2DIR spectra in the ZZYY polarization for a homogeneous 3 × 3 unit cell β-sheet (a) and the same sheet with Gaussian diagonal disorder of standard deviation $\sigma = 10\,\text{cm}^{-1}$ (b). In both spectra we used $\gamma = 2\,\text{cm}^{-1}$ for the homogeneous broadening of the vibron transitions. To generate the spectrum in (b), we averaged over 500 disorder realizations. Contours are drawn at ±0.5, 1, 2, 5, 10 and 20% of the largest amplitude in the spectrum. Solid contours enclose negative (bleaching and stimulated emission) peaks, while positive (induced absorption) peaks are drawn as dotted contours.

10 cm$^{-1}$ (panel (b)). In both plots a homogeneous HWHM of $\gamma = 2\,\text{cm}^{-1}$ has been used. Panel (b) was generated by averaging over 500 disorder realizations. The spectrum for the homogeneous system was discussed at considerable length by Cheatum et al. [2004]. It contains negative peaks (solid lines), resulting from bleaching and stimulated emission contributions, and associated positive peaks (dashed lines), resulting from induced-absorption processes to two-quantum eigenstates. As a result of the anharmonicity of the oscillators, the induced-absorption peaks are red-shifted along the $\omega_3$ direction relative to the associated negative features. The spectrum shows such pairs of positive and negative features both at the diagonal of the ($\omega_1, \omega_3$) plane, where $\omega_1$ and $\omega_3$ basically probe the same vibron, as well as outside the diagonal, where the correlation between two different vibron states is seen as cross-peak. As was argued by Cheatum et al. [2004], in particular the cross peaks seem to be sensitive probes for secondary structure in proteins. In the calculated spectra for the homogeneous sheet, we clearly see the cross peaks between $|a-\rangle$ and $|a+\rangle$, between $|a-\rangle$ and $|s-\rangle$, and between $|a-\rangle$ and the states around 1660 cm$^{-1}$. The fact that all features in the 2DIR spectra are extended in the $\omega_1$ direction, and not in the $\omega_3$ direction, results from the homogeneous broadening, which merges close-lying peaks of the same sign in the spectrum. In the $\omega_3$ direction, the close-lying pairs of positive and associated negative contributions, even after homogeneous broadening, still stay visible as separate peaks of opposite sign (albeit with less amplitude with increasing value of $\gamma$).

As expected from the linear absorption spectrum, we observe that the features in
the 2DIR spectrum broaden when disorder is present. The diagonal peaks strongly stretch along the diagonal, leading to a rather featureless diagonal ridge. As in the case of the linear spectrum, this results from many vibron transitions obtaining a large transition dipole as a consequence of the symmetry breaking by the random disorder. Disorder also has a clear influence on the cross peaks, which are seen to further extend along the \( \omega_1 \) direction than in the homogeneous case. This results from the extra broadening, which, like the homogeneous broadening, leads to merging peaks of the same sign in the two-dimensional spectrum, while preserving the separate positive and negative peaks along the \( \omega_3 \) direction. We observe that the strong cross peak positioned around \((\omega_1, \omega_3) \approx (1685 \text{ cm}^{-1}, 1640 \text{ cm}^{-1})\) is slanted out of the horizontal direction towards the diagonal direction. This results from the fact that within a certain realization of the disorder configuration, a positive correlation exists between the energies of different vibron transitions, for instance of the \(|a-\rangle \) and the \(|a+\rangle \) type transitions. This correlation derives from the fact that in a finite system, the average of the \( N \) randomly chosen \( \xi_{nn} \) values is not exactly zero, but deviates from this mean by an amount that is different for each disorder realization. This deviation in the average transition energy shifts all vibron transitions within a certain disorder realization by the same amount, i.e., creates a positive correlation between the vibron energies within a given disorder realization. We note that this correlation is not perfect, as has been shown explicitly for the case of excitons in linear molecular aggregates by Knoester [1993a], which explains why the cross peak is not oriented exactly along the diagonal direction of the spectrum. Also for the other cross-peaks observed in Figure 4.10(b) this correlation effect is visible, albeit only weakly for the peak around \((\omega_1, \omega_3) = (1640 \text{ cm}^{-1}, 1680 \text{ cm}^{-1})\). Generally speaking, the slanting of cross-peaks in 2DIR spectra away from the \( \omega_1 \) axis is indicative of the presence of static disorder [Rubtsov et al. 2003a]; dynamic fluctuations on time scales short compared to the pulses or \( t_2 \) tends to wash out the correlations necessary for this slanting, as we have also seen in the homogeneous limit, Figure 4.10(a).

The stretching of the cross peaks along the \( \omega_1 \) direction, in combination with the strong broadening of the diagonal peaks, creates an overall 2D spectrum that looks like a ‘Z’. This Z-shape may be taken as spectral signature for the presence of \( \beta \) sheets in a protein. Recently, this shape has indeed been observed experimentally for poly-L-lysine, as well as for \( \beta \)-sheet containing proteins, such as Concanavalin A and Ribonuclease A [Demirdöven et al. 2004]. Our simulations show that energetic disorder offers a natural explanation for the observed Z-shape. The absence of slanting of the cross-peaks in the experimental spectra indicate, however, that the time scale of the frequency fluctuations in these systems is shorter than the pulse durations used.

As was suggested in earlier work [Cheatum et al. 2004], the splitting between positive and associated negative peaks in the 2DIR spectrum is expected to contain information about the number of oscillators that share an excitation, i.e., about the vibron delocalization size \( L \). The reason is that this splitting finds its origin in the anharmonic term of the Hamiltonian, \( H_{anh} = -\frac{A}{2} \sum_{n=1}^{N} b_n^\dagger b_n^\dagger b_n b_n \), which roughly stated adds the squared amplitudes of the vibron states on all oscillators. For a state shared by \( L \) oscillators, this amplitude scales as \( 1/\sqrt{L} \), leading to an expected anharmonic
splitting $\Delta \sim A/L$ between the positive induced-absorption peak and the associated negative bleaching peak (the latter one being higher in energy). Similarly, using simple statistical arguments, Hochstrasser and co-workers arrived at $\Delta = 2A/(L+1)$ for $L$ coupled oscillators [Hamm et al. 1998].

It is useful to derive the expected scaling from perturbative arguments, instead of the above heuristic ones. In the absence of $H_{anh}$, there is no anharmonic shift and the two-quantum eigenstates are just the two-boson states $|u,v\rangle = \sum_{n,m} u_n v_m b_n^+ b_m^+ |g\rangle$. Let us consider the effect of $H_{anh}$ on the vibronic overtone $|2u\rangle = \frac{1}{\sqrt{2}} \sum_{n,m} u_n u_m b_n^+ b_m^+ |g\rangle$, where the prefactor $1/\sqrt{2}$ ensures proper normalization (the one-quantum eigenvector $u_n$ is assumed to be normalized to unity). To first order in $H_{anh}$, the anharmonic shift is then given by

$$
\Delta_1 = -\langle 2u | H_{anh} | 2u \rangle = A \sum_n |u_n|^4 = \frac{A}{L},
$$

where $L \equiv (\sum_n |u_n|^4)^{-1}$ is now the participation ratio, a well-known measure of the one-particle delocalization size in disordered systems [Thouless 1974]. This confirms the scaling postulated by Cheatum et al. [2004]. One may argue, however, that for our system the value of $A$ does not justify a first-order treatment. To estimate higher-order effects, we also consider the second-order shift of the energy of the state $|2u\rangle$, which reads:

$$
\Delta_2 = -2A^2 \sum_{u',u''} \frac{|\sum_n u_n^2 u_n' u_n''|^2}{2E_{u} - E_{u'} - E_{u''}}.
$$

If we consider this shift in particular for states $|u\rangle$ that occur at the bottom of the vibron band, such as the spectrally dominant $|a-\rangle$-type states, we see that $\Delta_2$ is positive, i.e., it increases the energy spacing between the bleaching and the induced-absorption peaks. We can further estimate $\Delta_2$ by approximating the energy denominator in Eq. 4.6 by $B$, where $B$ is of the order of the total vibron band width. The summations over $u'$ and $u''$ can then be performed using the closure relation on these wave functions, leading to $\Delta_2 = 2A^2/(BL)$, where again $L$ is defined as the participation ratio. Since for the system under consideration, $2A = 32 \text{ cm}^{-1}$, while $B$ is of the order of $60 \text{ cm}^{-1}$, we see that $\Delta_2 \approx \Delta_1/2$. It is likely that yet higher-order terms add similar contributions, leaving us with an expected scaling $\Delta = cA/L$ with $c$ of the order of unity.

Using our numerical simulations of the 2D spectrum, we have investigated whether indeed such simple scaling relations exist between the peak splitting $\Delta$ and the delocalization size of the one-quantum states. Because the spectrum is two-dimensional, one may define the splitting between the positive and negative peaks in various ways. We have defined the splitting $\Delta_{a-}$ as the frequency separation between the negative minimum and the positive maximum in a slice through the 2D spectrum at $\omega_1 = \Omega$. Here, $\Omega$ is the position of the maximum of the main $(a-)$ peak in the linear absorption spectrum. Note that, due to the broadening of the vibron band with increasing disorder strength, $\Omega$ is different for each value of the disorder strength $\sigma$. In
Figure 4.11: Splitting between the positive and negative parts of the diagonal $|a-\rangle$ peak in the 2DIR spectrum versus the inverse localization size $1/L$, with $L$ obtained from the average participation ratio. The data (squares) have been obtained for a $3 \times 3$ sheet, using the ZZYY polarization, and taking $\gamma = 2 \text{cm}^{-1}$. For each $\sigma$ value, the spectrum was obtained by averaging over 500 disorder realizations. The solid line is the best linear fit for $L \geq 8$ (see text for slope).

Figure 4.11 the splitting obtained from this procedure over a range of values of the disorder strength ($1 \text{cm}^{-1} \leq \sigma \leq 30 \text{cm}^{-1}$) is plotted against the delocalization size $L$. The latter was calculated as the average participation ratio of the vibron states at energy $\Omega$ [Thouless 1974]:

$$L = \langle \sum_u (\sum_{n=1}^N u_n^4)^{-1} \delta(\Omega - E_u) \rangle / \langle \sum_u \delta(\Omega - E_u) \rangle,$$

where $\langle \ldots \rangle$ indicates the disorder average.

From Figure 4.11 it is clear that, as long as the disorder strength is not too large (i.e., the localization size is not too small), the expected relationship

$$\Delta_{a-} = c A / L$$

holds. For $L \geq 8$, corresponding to $\sigma \leq 10 \text{cm}^{-1}$, we find $c = 3.4$. For larger values of the disorder strength, the peak splitting shows a sharp decrease. This unexpected decrease is entirely due to the behavior of the positive peak and is probably caused by interference effects with other spectral features, similar to the nonmonotonic be-
behavior of the peak shift $S$ as a function of disorder strength observed in Section 4.3.4.

The scaling relation Eq. 4.8 provides a tool to estimate the vibron delocalization size in $\beta$-sheets from the experimentally observed peak splitting, provided that static disorder dominates the spectral broadening. For electronic excitations in linear molecular aggregates, it has been demonstrated that the two-color pump-probe spectrum provides a similar spectroscopic ruler for the exciton delocalization size [Bakalis and Knoester 1999b; Juzeliūnas 1988].

To close this section, we note that in various publications the participation ratio has been used in a slightly different way, defining $L$ as the inverse of the average of $\sum_{n=1}^{N} u_{n}^4$ [Schreiber and Toyozawa 1982a; Fidder et al. 1991a]. Both definitions correctly monitor the localization behavior, though their numerical values differ, in particular for larger disorder strengths, where distribution functions get broader. We have checked that the alternative definition for $L$ still gives the linear scaling Eq. 4.8, with $c = 3.1$.

### 4.5 Discussion: parallel versus anti-parallel sheets

As mentioned in the Introduction to this chapter, large $\beta$-sheets are formed in amyloid fibrils. In this section, we briefly comment on the spectra of parallel $\beta$-sheets, in which all strands are oriented in the same direction. In proteins, these structures are rarely found, because, in order to form them, the peptide chain has to fold back to form each additional strand. Protein aggregates, however, have been speculated to contain parallel sheet structure [Nelson and Eisenberg 2006]. In the spectrum of an ideal parallel sheet, symmetry requirements allow only a single bright peak [Cheatum et al. 2004]. However, the oscillator strength of “forbidden” vibron transitions can be nonzero due to finite size effects. This leads to additional peaks in the spectrum, and, in particular, to cross peaks in the 2D spectrum. The origin of these peaks is entirely analogous to the mixed symmetry cross peak that we have observed in the spectra of anti-parallel sheets around $(1640 \text{ cm}^{-1}, 1680 \text{ cm}^{-1})$. If such cross peaks indeed exist in the spectrum of parallel sheets, they might be mistaken for a cross peak between $|a-\rangle$ and $|a+\rangle$ states. With this invalid assignment, the identification of anti-parallel $\beta$-sheet structure from the presence of a cross peak could be wrong. Before discussing the presence of cross peaks in the spectrum of parallel sheets, we will first assess the role of the TDC coupling model.

The mixed symmetry cross peaks are not seen in experimental spectra of poly-L-lysine, which is thought to form anti-parallel $\beta$-sheets under certain conditions [Demirdöven et al. 2004]. One of the reasons for their appearance in our calculations might be the limited validity of the TDC coupling model, which we have used in this chapter. As we saw in Section 4.3, the nature of the bright states in the spectrum is mainly a result of the symmetry properties of the sheet. However, the locations and intensities of the peaks are a result of the relative strength of the couplings between individual oscillators. In this chapter, we have used the TDC mechanism to calculate these couplings ($J_{nm}$). For closely spaced amide groups, the point dipole approximation in the TDC model might break down, leading to an unphysical prediction of the coupling. In our $\beta$-sheet model, this will primarily affect the coupling between
the closely spaced oscillators 1 and 4 ($J_{14}$) in each unit cell. Furthermore, mechanical coupling between amide groups along the backbone [Torii and T assumi 1998], which is not included in the TDC model, will affect $J_{12}$ and $J_{25}$. To assess the effect of a different coupling model, we have calculated the couplings in the β-sheet geometry from a combination of TCC interactions and the nearest neighbor coupling map map made by [Gorbunov et al. 2005]. The results are summarized in Table 4.1. Comparison with the TDC values shows that the two coupling models yield the same signs for all couplings. The magnitudes of the values for $J_{14}$ and $J_{12}$ are, however, considerably different.

These different values for the couplings do, however, not lead to a drastically different spectrum. The 2DIR spectrum, shown in Figure 4.12 (b), still shows a main $|a-\rangle$ peak, as well as a cross peak between the $|a-\rangle$ and $|a+\rangle$ modes. The nature of these modes, which we have again labeled $|a-\rangle$ and $|a+\rangle$, can be studied by looking at their color maps (not shown). Indeed, we again find vertical stripes for the $|a-\rangle$ state and horizontal bands for the $|a+\rangle$ mode, confirming their identity. The cross peak of the $|a-\rangle$ mode with mixed symmetry states around $(1640$ cm$^{-1}, 1660$ cm$^{-1})$ still appears, although its intensity is smaller than in the TDC model.

Returning to the parallel sheets, we compare the calculated spectra of parallel and anti-parallel β-sheets, built from 6 strands with 6 amide groups each, in Figure 4.12. A cross peak indeed appears in the spectrum of the parallel sheet, but its frequency along $\omega_3$ is considerably lower than the $|a-\rangle$, $|a+\rangle$ cross peak in the anti-parallel sheet. We therefore conclude that, although care has to be taken, the presence of a cross peak between $|a-\rangle$ and $|a+\rangle$ states in the 2D spectrum can be used to distinguish parallel from anti-parallel β-sheets.

4.6 Conclusions

In this chapter, we numerically studied the effects of static disorder on the collective vibrational vibron states of the amide I type in antiparallel β-sheets, and the corresponding linear and two-dimensional infrared spectra. We mostly focused on energetic (diagonal) disorder. To analyze the nature of the vibron states, we introduced
a new visualization technique in which the vibron wave function is represented as a two-dimensional color map. This color map facilitates recognizing symmetries of the wave function and phase relations between various oscillators in the sheet. Using these maps, we confirmed that for homogeneous $\beta$-hairpins the collective states to a very good approximation separate in four different bands that have a one-to-one correspondence to the four eigenstates ($|a-\rangle$, $|a+\rangle$, $|s-\rangle$, $|s+\rangle$) of a single unit cell in the sheet.

For $\beta$-sheets that are extended in both directions, this identification is less ideal, as strong interactions between different unit cells mix the various types of cell eigenstates. Still, using the color maps, we have been able to demonstrate that in the absence of disorder several of the optically dominant states of extended sheets still reflect the symmetries and phase relations of the cell eigenstates. In particular, the strongest state near 1645 cm$^{-1}$ has a clear $|a-\rangle$ character, as recognized from its color map, which closely resembles an array of alternating red and blue columns. A second optically strong state near 1680 cm$^{-1}$ is recognized as an $|a+\rangle$-type state through its representation as a stack of rows that alternate in color. Finally, a checker-board color pattern is typical for the $|s-\rangle$-type state that occurs around near 1705 cm$^{-1}$. A few other visible states are either recognized as higher wave vector states of the above ones or as mixtures of various unit cell states.

Energetic disorder has strong effects on the vibron states, as it destroys the translational symmetry (which is not perfect anyhow, as a consequence of edge effects) and leads to localization of the vibron states. As we demonstrated, however, within their localization area in particular the states underlying the optically strongest peak
in the linear spectrum clearly exhibit the $|a-\rangle$-type color map. In hindsight, this strongly suggests that the experimentally observed $\alpha-\$ peak reported by Demirdöven et al. [2004] for poly-L-lysine and several $\beta$-sheet containing proteins may be associated with the $|a-\rangle$ state. A more rigorous identification should involve an analysis of the color maps for these systems, using their known coordinates as input for constructing the Hamiltonian.

The effects of energetic disorder on the linear spectrum of extended (two-dimensional) sheets reported here are quite generic: broadening and shifts of absorption lines follow power laws as long as the disorder strength is not too large. The powers found differ from those obtained for two-dimensional lattices, as a consequence of the strong anisotropic nature of the interactions in $\beta$-sheets. We have also found that disorder in the interactions, caused by random shifts of the oscillator positions, causes the dominant $|a-\rangle$ peak to shift to the blue, rather than the red. This marked difference with energetic disorder finds its origin in a decrease of the average TDC interactions in the presence of this type of disorder, and is dominated by shifts in the direction of the peptide strands.

For the 2DIR spectrum, energetic disorder leads to stretching of the diagonal peaks in the diagonal direction and stretching of the cross-peaks mainly in the horizontal direction. These two effects together lead to a Z-shape in the two-dimensional spectrum, which may be a useful signature of anti-parallel $\beta$-sheet content in experimentally observed spectra. Indeed, a Z-shape has been observed in the 2DIR spectra of various $\beta$-sheet containing systems [Demirdöven et al. 2004]. As opposed to our model results, the cross-peaks in the experimental spectra do not exhibit a slanting relative to the $\omega_1$ direction, which indicates that in the experiment the disorder has a time scale short compared to the pulse durations. We also found that, for not too large disorder, the splitting between associated positive and negative features in the 2DIR spectrum scales inversely proportional with the delocalization size of vibrons in the $\beta$-sheet. Future studies should address the effects of dynamic disorder [Kwac and Cho 2003a,b] and investigate whether in this case a similar scaling relation exists between the peak splitting and the vibron coherence size. Simulations on a $\beta$-hairpin including dynamic disorder have been reported [Jansen and Knoester 2008], and the application of similar methods to extended sheets would be a useful step towards this goal.