New Mechanism for Facile Charge Transport in Polypeptides

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An electronic hole migration accross a polypeptide chain is discussed with special reference to new *ab initio* computational results and to the experimental observations of Weinkauf et al. on the charge photoinjection into the polypeptide backbone. New mechanistic details for this efficient charge transport process are proposed. The process is viewed as a vibronically induced hole hopping between local aminoacid sites driven by large amplitude torsional motions of the floppy backbone.

Key words: Protein; Polypeptide; Charge Transfer; Hopping.

I. Introduction

Charge migration in biomolecules and other large polymeric structures is a fundamental process. It is often only explained in very global terms. Charge migration in protein-like environments is known to be highly efficient even though the mechanistic origin of this process is still much debated and largely unknown. Various global models were advanced, such as variants of radiationless processes using the Fermi Golden Rule or superexchange processes going over longer distances with a pseudo tunneling mechanism.

In 1995 we felt that a hopping mechanism was indicated by our experiments [1]. In particular this relates to an intermediate type coupling scheme which we felt to be required, rather than a molecular wire of strong coupling. In this article we will discuss a further variant of this intermediate coupling scheme where the coupling is driven by the near zero frequency, large amplitude torsions inherent in all peptide motions and visualized in the famous Ramachandran plots. The major question of interest in this article is why this mechanism of turned-on hopping leads to charge flowing so efficiently.

In order to understand the innate features of such processes it was decided to study first the native polypeptide in the absence of any solvent environment, even though it must be recognized that any large molecule also provides its own solvent. Extensive experimental studies of polypeptide cations carried out by us in the gas phase have lead to a proposal and experimental verification of some key elements suggesting now a unique and detailed mechanism for such charge migration at least for these systems [1 - 5]. We significantly extend our previous hopping model and now develop details of this unusual propagation mechanism based on *ab initio* calculations as well as a combined analysis of the experimental data and the physical model that is now indicated for such a transport.

In earlier work we have demonstrated that the photoinjection of positive charge at a specific chromophore in a series of *de novo* polypeptides can lead to facile migration of this charge over long peptide chains [1 - 3]. The distance and direction of this migration is controlled by a unique local energy landscape determined with astonishing predictability to a first order by the ionization energies of the individual aminoacids, rather than the ionization potential (IP) of the entire supramolecular radical cation [1, 2]. In particular, the flow in a "downhill" direction is very efficient and virtually insensitive to the distance (at least up to 5 aminoacids) between the chromophore and the final site of the lowest local IP (the so called N-terminus, located at the opposite end of the chain) [1 - 3].

Alternatively, the charge flow can be blocked by as small a local barrier as 0.2 - 0.3 eV (difference in IPs between different neighboring aminoacids) [2]. This is a direct evidence for the through-bond, as opposed

to through space, mechanism. It was further concluded [1, 2] that these observations are not consistent with a superexchange model of tunneling through an inert spacer-bridge between donor and acceptor. Rather, in these experiments the charge is really injected into the chain where it spends for a time in real, not virtual states. Thus, the mechanism has been shown to be a hopping between local sites [1, 2, 4].

One more concept, "reactivity follows charge" was advanced as a result of observation of highly specific fragmentation patterns following photoabsorption of one UV or two green photons by an ion [1 - 3]. When ion photofragmentation occurs, the charge is carried by a smaller fragment corresponding to a C – C bond breaking either adjacent to the terminal amino-group or to the chromophore. The bond softening in the presence of charge and stabilizing orbital interactions can result in amazingly low barriers to the bond cleavage down to 0.5 eV. The efficient "transport" of reactivity by charge over a long distance in a large molecule is a fascinating problem and has far reaching consequences. Now, recent femtosecond experiments [5] have revealed that efficiency of hopping does not necessarily imply an ultrafast rate for this process, which was observed now to be slower than 200 - 300 fs per jump. The important conclusion here is high efficiency – not necessarily high speed. Our mechanism clearly makes use of this fact.

In this work we outline a model compatible with experiments and further supported by *ab initio* calculations. We consider charge transfer as a vibronically induced hole hopping between local sites of lowest IP in the chain which happen to be special HOMO orbitals of amide groups, –CONH– (otherwise called peptide groups).

The charge is initially localized at the chromophore in the form of an electronic hole in it's ground electronic state. Following photoabsorption by a cation, the hole is promoted into an excited state lying above the chain localized states and eventually hops to the chain (the charge injection into the chain). As a last step of the charge migration, the hole hops from the chain to the lower energy state localized at the terminal amino group. Both initial and final steps deserve separate discussion in view of the larger electronic energy changes involved in these processes as well as larger differences between the sites of charge localization. Here we focus on the charge migration along the chain which is the main and longest segment of the total charge migration path.

Some major features of our model are worth mentioning here. Typically the HOMOs of the amino acids are some 0.2 - 0.3 eV apart, leading to quasi isolation of sites. The femtosecond experiments indicate an elementary hopping time scale of some 200 - 300 fsec. Nevertheless we propose that the coupling between local charge states, which is responsible for charge transfer between sites, is of intermediate strength, something on the order of 0.1 eV at a point of transition. No less importantly, the coupling is not a fixed value, but rather varies strongly with torsional motion which is the result of the floppy peptide backbone. Hence mostly the site is stationary unless there is a special critical twist in the conformation of the chain. We refer to this as a "ratcheting" (one way) process. These are extremely low frequency motions involving the dihedral angles around the single bonds adjoining the central carbon atom reflecting the substitution that identify the various amino acids (Ramachandran diagram [6, 7]). These operate over large angles in an extremely flat portion of the potential surface and as such constitute special near zero-phonon modes which are operative in propagating the charge through the peptide.

This intermediate strength coupling is strong enough to insure high probability of charge transfer between two adjacent aminoacids when the wiggling molecule attains a favorable conformation, i. e. in the ratchet position. On the other hand, it is important that the coupling is weak enough to allow for local energy differences (of the order of 0.2 eV) between different aminoacids. In a stronger coupling case, such as in charge transfer in a few femtoseconds, all these differences would be washed out and we would instead have a globally delocalized charge state. The charge has to wait until the molecular subunits find a conformation appropriate for the transfer, and thus most of the time it remains well localized at a single location. This is an important property if local effects are to be operative, particularly so for chemical reactivity to be operative. A strongly coupled molecular wire would wash out all such local effects, and as such may often not be desirable. Thus, the torsional motion control of the ratchet reconciles apparent opposites: high efficiency with the relatively slow (compared to pure electronic processes) rate of this process.

The question at hand now is: as desirable as this ratchet mechanism might be, is there any evidence for a special ratchet position which turns on this unique coupling to provide for charge migration of

the otherwise isolated site? In fact the local IP's are up to some 0.2 - 0.3 eV apart – so how do they couple?

In Sect. II we start with examining peculiarities of the electronic structure of peptide groups. and proceed to the potential surfaces of a model compound containing two peptide groups connected through a $-CH_2-$ bridge or, more generally, a $-CHR-$ bridge where R is the unique key for the various amino acids. We discuss the role of weak interactions which result in the flat character of this surface. In Sect. III we discuss variations of relative energies of the ionized states associated with different charge localizations. In Sect IV we consider estimates of the reorganization barriers which occur on the way towards a nuclear configuration favorable for the efficient coupling. Estimates of the coupling strength at the transition are the subject of Section V.

II. Electronic Structure of Isolated Amide Groups

In this work we focus on a mechanism that provides real hole hopping across the peptide chain, not a tunneling. We are primarily concerned with these processes at threshold which means a minimal excess of electronic excitation, just enough for injecting charge into the chain. With this in mind, we start by examining the lowest energy electronic states of the ionized peptide chain excluding, as an initial simplification, the higher excitation as well as charge states at the chromophore and the terminal amino group which are typically at least 0.5 eV apart from the chain.

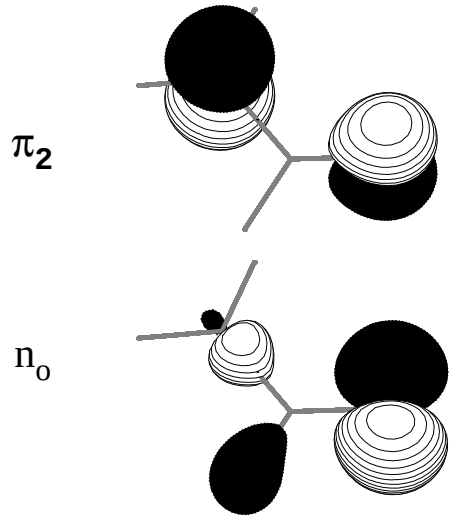

Fig. 1. HOMO (π_2) and HOMO-1 (n_o) orbitals in formamide, $HCONH_2$.

In accordance with Koopmans' theorem, these states result from the electron being removed from the Highest Occupied Molecular Orbital (HOMO) of the neutral molecule. In a peptide chain, the HOMO is typically localized at a peptide group. Two highest OMO's, the HOMO and HOMO-1 are shown on Fig. 1 and usually labelled as π_2 and n_o respectively [8].

These orbitals correspond to a different hole distribution within a peptide group. n_o is mostly a lone pair of oxygen, while π_2 is more uniformly shared by nitrogen and oxygen as a result of conjugation between the lone pair orbital of N, n_N, and the π-system of the carbonyl group, CO. Furthermore these two orbitals have different nodal planes, thus different local symmetry. Hence they have different conditions for orbital overlap with adjacent molecular bonds as is usually required for an efficient through-bond charge transfer [9].

The above conjugation [10] has the well known other manifestation in that it preserves the sp^2 hybridization at N and hence the planarity of the peptide group, $-CONH-$ (the barrier to planarity breaking is 0.7 - 0.8 eV [11]).

The reason why we do not limit the discussion to the HOMO only, but include the HOMO-1 as well, is that these two orbitals are very close to degeneracy, while the rest of OMO's are at least 3 - 4 eV apart from these two.

A word of precaution is warranted concerning the use of Koopmans' theorem as well as the use of certain *ab initio* methods to deduce the character and relative energies of the ion states in these systems. If the energy difference is judged on the basis of orbital energies in the neutral state of the molecule, then the HOMO = π_2 and the $\pi_2 - n_o$ gap is 0.4 - 0.6 eV, this value depending on the nearest chemical environment and on the basis set.

An appropriate simplest non-empirical level of describing an open shell radical cation is the so called Unrestricted Hartree Fock method of Self Consistent Field (UHF-SCF), which properly takes care of the orbital relaxation effect. Now, different from the RHF level appropriate for neutral (R is for restricted), there are two sets of orbitals, for α and β-spins correspondingly, each exibiting somewhat different orbital relaxation. The relaxation compared to the neutral is considerable, but not so large as to prevent correlation between these orbitals in the neutral and ionized

states. The orbital from which the electron was ionized is now a LUMO(β) – the Lowest Unoccupied in the β-set (conventionally, when number of α and β-electrons is different, the unpaired spins are of α type).

The calculation shows that LUMO(β) = n_o . Hence, in this case, the orbital relaxation effects can violate Koopmans' theorem even on the qualitative level. As is known, the orbital relaxation effects can not be described in a completely realistic fashion if treated sparately from the electronic correlation effects which are beyond the SCF level. The two effects are comparable in magnitude, and correlation effects here become quite important. For this reason we also carried out ROVGF(FC) calculations as well to do at least partial justice to these correlations (ROVGF(FC) stands for Restricted Outer Valence Green Functions [12 - 14] with Frozen Core orbitals). This method approximates both effects in a balanced manner. Interestingly enough, now the energy splitting between two ion states drops dramatically down to 0.065 eV in formamide, $HCONH_2$, at ROVGF(FC)/6-31G** level. The use of extended polarized valence-split basis 6-31G** is also essential.

With splittings as small as this, we realize that an accurate value is perhaps still not reached and may require still further sophistication at the *ab initio* level. Nevertheless, what is already evident is, that the two lowest ionic states are so close as to be nearly degenerate, even within a single peptide group. When imbedded into a peptide chain, these two orbitals can change their ordering and, more importantly, they can easily mix and resplit, or in conventional language they can be considered to "rehybridize". Notice also, that this orbital switching / rehybridization can be induced not only by changing the chemical environment of the peptide, but also by changing the molecular conformation, because various weak intramolecular interactions (discussed below) can have an effect on the orbital energies comparable to this splitting.

To conclude this section, we believe that the near degeneracy of π_2 and n_o, which is a special feature of peptide bond $-$CO$-$NH$-$, plays an important role in the mechanism of efficient hole transfer in peptides. The facile rehybridization at every local site renders the local HOMOs more flexible with respect to finding an orbital shape which is optimal for the overlapp with the mediating orbitals of the $-$CHR$-$ bridge. In this way, the charge transfer coupling between two neighboring aminoacids is maximized in certain favorable molecular conformations which are the ratcheting positions mentioned above. The hopping process thus is driven by the ratchet.

III. Model Dipeptide Cation – Potential Surfaces in the Vicinity of Equilibrium Structures

The bulk of the peptide chain consists of peptide groups linked to each other through $-$CHR$-$ bridges. R can be hydrogen, as in glycine, or a $-CH_2-R'$ group as in other natural aminoacids [15]. The bridging carbon atom is labelled C_α in (bio)chemical literature. By virtue of hyperconjugation between π-system of peptide and $C_\alpha-R$ bonds, the ionization energies (IPs) vary slightly in different natural aminoacids, within some 0.2 - 0.3 eV, depending on R (these orbital interactions are also known under names electromeric, gauche or anomeric stereoelectronic effects [16]).

For illustrative purposes below we use *ab initio* calculations of a model system $CH_3(CONH)CH_2$-$(CONH)CH_3$. This is a minimal finite model fragment of a peptide chain. It contains two peptide groups, CONH, thus it is suitable for studying charge transfer between these sites. The model system is chosen such as to ensure maximal possible equivalence in the nearest chemical environment of both sites. Neglecting differences in next nearest neighbours, each peptide group has nearly the same surrounding, $-CH_2-(CONH)-CH_2-$. In spite of this approximate "translational symmetry", the two peptide groups are not equivalent with respect to coupling within the given pair – one group is connected to the $-CH_2-$ bridge through a carbon atom, while the other is connected through nitrogen. Below we shall distinguish between the two counterparts of the pair

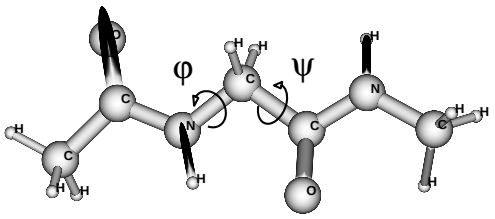

Fig. 2. Model dipeptide, $CH_3(CONH)CH_2(CONH)CH_3$. Torsional angles $\phi(C_\alpha-N)$ and $\psi(C_\alpha-C)$ are defined as dihedral angles $C-N-C_\alpha-C$ and $N-C_\alpha-C-N$, respectively. $\phi, \psi \in (-180, 180]$. On this figure, "N-" and "C-side" are the left and right halves, correspodnigly.

by refering to them as "C-side" and "N-side", respectively, Figure 2.

One important difference between C-side and N-side is that the π_2-orbital of the former has a negligible amplitude at the C atom of carbonyl, hence it cannot hyperconjugate efficiently to the $C_\alpha - R$ and $C_\alpha - H$ σ-bonds of th $-CHR-$ bridge. This explains in particular why the local IPs of peptide groups in the chain correlate with those of parent aminoacids. In this way, every R "knows" which of the two peptide groups (on C- or on N-side) is to be influenced. The R-substituent at C_α is more strongly coupled to the peptide group on the N-side, while the C-side of the same pair is far less sensitive to the nature of R in the bridge between these two sides. In calculations, one clearly sees this mixing of π_2 with the $C_\alpha - R$ bonds of that C_α atom which is connected to the N of the peptide group.

The equilibrium structures of neutral and ion (local minima on the ground state potential energy surface, PES) were found by full geometry optimization at RHF/6-31G* and UHF/6-31G* levels, respectively, using Gaussian94 package [17]. In discussions of the polypeptide structures it is common to describe the conformations in terms of torsional angles $\phi(C_\alpha - N)$ and $\psi(C_\alpha - C)$ (see Fig. 2 and the legend).

The lowest energy structure of the neutral is a planar all-trans conformation, $\phi = \psi = \pm 180^\circ$, shown in Figure 2. Evidently, the energetic preference of this conformation over other ones is dictated by the hydrogenic bonding between the hydrogen atom of amide group on the N-side and the oxigen atom of carbonyl group on the C-side. The $H - O$ distance is 2.14 Å.

Two equilibrium structures (not shown here) were found in the ground ionic state. One corresponds to the charge localization on the C-side (LUMO(β) = n_o(C)), the other on that of the N-side (LUMO(β) = n_o(N)). The two structures are nearly degenerate in energy, that of the second being 0.05 eV higher. As expected, one difference between these structures is that the charge localization undergoes geometry relaxation as compared to the equilibrium geometry of the neutral, while the other peptide group remains intact. The $C - O$ and $C - N$ bonds within the peptide group elongate by 0.09 Å and shorten by some 0.05 Å, respectively, as a result of ionization.

More interestingly, the conformations of the two charge states are very different. The first conformation ($\phi = 58^\circ, \psi = -138^\circ$) has a "scorpion"-like structure with the negatively charged oxygen atom pointing from N-side to the center of the peptide group on the C-side, which binds the positive charge. The two oxygen atoms are clearly inequivalent in this configuration in that one of these two oxygens is closer to the other peptide group, while the second oxygen is more separated form the first peptide bond. In the second conformation (charge on N-side, $\phi = 70^\circ, \psi = 166^\circ$)), the two peptide groups exchange their roles, but this structure exibits the same pattern – the oxygen atom from the neutral side is oriented as much as possible towards the positively charged group.

The above results indicate the special role of weak intramolecular interactions in the charge transfer accross polypeptide backbone. The potential surface of the neutral has large areas where it is very flat, within some 0.05 - 0.1 eV [7]. The minima are shallow and loose. This flatness is a result of the delicate balance between various interactions. Thus weak intramolecular interactions, such as Van der Waals, hydrogenic bonding and dipole-dipole will largely balance over a large range of conformations in the neutral. In the ion, the additional dipole-charge forces will play an important role in maintaining the balance. All above interactions strongly depend on the molecular conformation through the torsional angles ϕ and ψ. When charge arrives at a previously neutral location, this adds a new dipole-charge interaction absent in the neutral. This now changes the location of the shallow minimum on the potential surface of the ion as compared to the neutral.

Similarly, when charge jumps from the C-side to the N-side or vise versa, the two peptide groups exchange their roles in that one is the charge binding site while the other is a dipole which "solvates" the charge. Hence, each of the above processes is associated with considerable conformational changes, $\Delta\phi$, $\Delta\psi$, in the backbone as a result of electronic transitions. Therefore the torsions enter into the set of "accepting modes" (those which change their state upon electronic transition) along with more obvious $C - O$ and $C - N$ bond stretches within the peptide groups. All this also implies strong involvement of the flexible backbone in the charge transfer in peptides. This interaction is firstly local in the pair, but also has important long range conformational consequences.

Influenced by the weak interactions is not only the lowest potential surface of the ion but are also the "resonance" conditions between ionic states (splitting) and the character of these states (localized or delocalized). Near to the equilibrium ion structures,

the "solvation" of the charge acts so as to increase the splitting by virtue of charge-site specific geometry relaxation, thus rendering the charge states with a well localized character typical of isolated local sites. Somewhere midway between the two conformations, the change in the weak interactions contributes to the orbital degeneracy between "left" and "right", hence assisting in the charge delocalization (see Sect. IV).

Notice also that our example includes only two peptide groups interacting with each other, while in real protein environment further additional long range weak interactions with other parts of the folded backbone will undergo a long range control of this process.

There is a certain similarity between the picture described here and that of the charge exchange between two ions in a dipolar solvent. In both cases the solvation is contributing to the charge localization by creating appropriate "reorganization" barriers. An important difference however, is that in the peptide chain there are only two dipolar groups (peptide bonds) in the immediate vicinity of the localized charge that is responsible for this effect. In addition these two dipoles have only limited mobility to form a strongly bound solvation shell. Hence, in a "dry" peptide, the reorganization barrier is lower than in a real solvent. The charge migration is less impeded here.

IV. Reorganization Barrier to Hole Transfer

We now want to focus on certain new mechanistic details which may result in fairly unusual (and favorable) values of the parameters controlling the hole hopping in peptides.

Our analysis of charge transfer coupling and charge distribution in the ion (see Sect. V) indicates that for most of the molecular geometries the adiabatic charge states are well localized on individual sites, and states of different localization are well separated in energy, so that they don't mix. The charge exchange occurs as a result of reaching a particular molecular geometry that leads to a mixing of states, localized on two neighboring peptide groups. These are seen to be near degenerate within an energy tolerance determined by the coupling matrix element (the "transfer integral") between the two local charge states. However, reaching a "resonance" is a necessary but not sufficient condition for an efficient charge flow. Two extra conditions should be met.

Firstly, the coupling should be strong enough to ensure a high probability of charge transition during the time in which the molecule passes ratcheting configuration. This is the region in the configuration space where the two diabatic (localized) states cross. The change of charge localization may occur as an adiabatic passage across one and the same adiabatic potential surface, which means high efficiency of charge transfer. Alternatively, and most typically for many familiar molecular systems, this happens as a non-adiabatic process, or, even more accurately, weakly non-diabatic passage where the change of the diabatic state (hence, of charge localization) is described by a small probability per crossing. This probability, much lesser than unity, is then effective for the rate of charge transfer in the form of the square of the coupling matrix element. We address the question of the coupling strength in the next section.

The second of the above conditions, which is examined in this section, requires that the reorganization barrier is low enough. Reaching the geometry where localized states are in resonance and can mix due to appreciable coupling, implies to climb a top of the barrier on the adiabatic potential surface.

Our *ab initio* calculations in the model degenerate system (two near identical sites) indicate that the barriers are very low. How low is difficult to say with certainty, but they are for sure less than 0.4 eV at the UHF/6-31G* level, and probably much less. Hence we can conclude that we have a model with appreciable mixing under almost barrierlesss conditions in the ratcheting position.

The reasons for the above uncertainty are mostly technical, but are to be sought in the nature of this mixed state. The automatic algorithms for the saddle point searches on a potential surface are highly prone to failures, as was not surprizing in our fairly difficult case. For this reason we performed just a one dimensional scan along the so called Synchronous Transit Path (STP), which is a procedure provided by the Gaussian94 package [17]. In practice this means a linear interpolation between two equilibrium structures (the charge is on the N- or on C-side) in a space of internal coordinates (bond lengths, bond- and dihedral angles). The highest point along this potential surface cut was 0.4 eV above the fully optimized equilibrium structures (energy minima). Any maximum energy point we found here can only be an upper bound of the saddle point energy, since we did not optimize the remaining coordinates. Our path just connected the two minima. To be sure, this optimization, when carried out in total

detail, will further reduce the energy at the highest point.

A more fundamental reason to expect that the actual barrier should be well below the cited value of 0.4 eV, is that the present calculations do not incorporate correlation effects which are generally known to decrease the energy of a transition state more than the energy of an equilibrium structure. Such correlation effects clearly must become very important in our mixed state.

In an attempt to estimate the correlation effects in the ion indirectly, we also performed ROVGF(FC)/6-31G* calculations on 3 points (the two minimal energy structures and the approximate "transition state" in between). The energy of the ion is estimated then as the energy of the neutral plus the ionization potential at this geometry. The result was that the mid point, which was a well defined maximum within the UHF model description of the ion, has now become the lowest energy point within this type of ROVGF approximation.

We should emphasize once again that, while accurate values of these really small potential barriers should wait until highly sophisticated *ab initio* approaches are available, it is quite clear already that the barriers are fairly low indeed, most likely not higher than some 0.1 - 0.2 eV. Indirect physical evidence to that is further provided by the fact that the small local IP differences on the order of 0.2 eV do matter in experiments. If the barriers were appreciably higher than that, the small local IP differences would be virtually unimportant, while overcoming the reorganization barriers would be the real bottleneck to charge flow.

To conclude this section, we believe that this surprizingly low reorganization barrier is an important and uniqie feature of peptides. This is the reason why hole hopping along the protein chain can be so efficient, even if not ultrafast. Clearly, what is demanded here is high efficiency but only moderate speed.

It should be noted as well that even at an effective temperature of the peptide as low as room temperature, the condition is sufficient for a sub-ns frequency of hopping given that the barriers are on the order of 0.2 eV or less. Furthermore, in the torsionally floppy chain, most of the frequency spectrum is well above kT at the room temperature. Hence all vibrations are "frozen out" and do not participate in the total energy redistribution at a thermal equilibrium, save for the near zero frequency torsions. This means in particular, that even in the gas phase experiments with relatively "large" polypeptides (up to 5 aminoacids) and with relatively "small" excess energies (just some 1 eV above the threshold for the charge injection into the chain), the required effective temperature for ratcheting is reached. Indeed, the excess energy, even if thermalized, is now distributed mostly between the torsional modes of the chain. Additionally, these are just those modes which are necessary for the vibronically induced charge transfer. The remaining phonons are not yet active in the chain, a very important property of this special process.

Hence we conclude that we have a near barrierless transition for the charge to jump from one aminoacid site to the next in the ratchet configuration.

V. Hole Transfer Coupling between Peptide Groups

Ab initio computation of the coupling strength for such a mixed state is a most difficult problem. The UHF model for the ion is reasonably satisfactory as far as one is interested in the potential surface calculations, especially in the vicinity of an equilibrium structure. However, the charge delocalization never occurs in our computations at the UHF level, even at the geometric configuration of the approximate transition state. This has to do with the following flaw of the UHF approximation for an ion. This model properly accounts for the orbital relaxation effects, which are charge site specific. The orbital relaxation pattern depends on where the charge is localized. But just as the charge site specific geometry relaxation acts such as to localize the charge, so does orbital relaxation. Even if one takes a symmetric configuration of two totally identical sites for the charge, the UHF typically tends to produce the localized charge, which is a symmetry broken solution, even though it is clear that any physical solution must have symmetry and be delocalized. This is known as one of the forms of Hartree-Fock instabilities [18, 19]. The actual physical state can be reasonably approximated as a linear combination of these symmetry broken and orbitally relaxed HF states, but the HF method as it is can not reproduce such a linear combination as long as this combination is not reducible to a single determinant wave function.

Only when the coupling is so strong that it is stronger than the (relatively large) relaxation effects, the delocalization will take over even within UHF,

because the energy gain due to delocalization is larger than the charge site specific orbital relaxation.

The electronic hole distribution in the ion can be analysed either by comparison of Mulliken populations in the ion and neutral or by examinimg the character of LUMO(β) in the ion. Both approaches lead to the same conclusion: the hole delocalization never occurs in our calculations at the UHF level. In view of the above mentioned deficiency of the UHF approximation, related to the non-linearity of the functional space, this result does not mean that the delocalization does not exist in the physical system. Still, this indirectly indicates that the charge transfer coupling is not very strong.

It is sometimes tacitly assumed that homogeneity of a polypeptide chain (identical aminoacids) automatically implies a band-like model with a globally delocalized character of electronic states irrespective of nuclear configuration. This assumption results in a description of the charge transfer in these systems as a predominantly electronic process driven by the tendency of an initially localized (hence, nonstationary) electronic state to delocalization. The nuclear motions are only important in this picture as far as they produce an ohmic resistance through the electron-phonon scattering or an electronic relaxation through internal conversion. Based on our *ab initio* results, we feel that quite a different model applies to polypeptides. The charge in adiabatic ion states is mostly well localized, while delocalization is a rather exceptional event which requires both the "resonance" between ionic states (controlled by accepting modes) and the special twist in the backbone conformation to produce appreciable coupling.

In order to obtain an estimate of the actual coupling in polypeptides, an alternative to UHF is required. One way to overcome the above shortcoming of UHF calculations in the ion would be to use Koopmans Theorem (KT) based on orbital energies of the neutral. Generally KT tends to another extreme – it can grossly exagerate the strength of the coupling and the tendency for charge delocalization. Still, after finding a configuration with a charge delocalized HOMO and HOMO-1, one can obtain a rough estimate of the coupling strength at this geometry as half of the splitting between the two HOMO's. In calculations, even at the RHF level for neutrals, the HOMO is mostly well localized either on the N- or C-side. It is only at the highest energy point along the STP computed at the UHF level for the ion that we find HOMO being evenly delocalized between the π_2 orbitals of the N- and C-side. The splitting between HOMO and HOMO-1 is 0.5 eV at the RHF/6-31G* level.

Further refinement over the KT can be obtained by using the difference between the first and second IP calculated with the ROVGF method at the transition state geometry. We did so and obtained 0.35 eV splitting at our approximate transition state. This translates into a coupling of 0.18 eV. ROVGF method is a perturbative treatment based on the RHF single determinant nonrelaxed state of the neutral as a reference. As such, this method does not yet fully account for orbital relaxation effects, therefore a somewhat lesser value can be expected for the actual physical coupling.

On the other hand, the actual coupling is unlikely to be considerably less than 0.1 eV, as this is a feasible range for a coupling even between sites separated by several σ bonds. In peptides, the adjacent amide groups are separated by a single carbon bridge. So, we believe that some 0.1 eV coupling strength at a point of transition is a reasonable estimate, which is now in agreement both with the *ab initio* calculation results and the tentative interpretation of experimental results mentioned before. This now reconciles the preservation of the chemically specific local IPs of the aminoacids in the chain with an efficient charge hopping process.

Several interesting possibilities associated with this coupling strength are worth further discussion. If the estimated crossing point between two diabatic (localized) states is as low as expected, say some 0.1 - 0.2 eV in the ratchet position, then the actual adiabatic barrier can be suppressed nearly completely. Hence, the charge transfer in homogenious peptide chains (identical aminoacids) may turn out to be nearly barrierless. Furthermore, there may occur structures of the potential surface, similar to the bottom of the "mexican hat" around a conical intersection. In this case, the barrier does not disappear completely, but now there is a path "around the mountain" which does not require an energy activation.

The interesting conclusion here is that the dependence of the optimal coupling on the backbone conformation came out as a result of calculations. The calculations predict very facile coupling for a certain torsion angle between the two peptide groups of neighboring amino acids. This ratchet position is uniquely capable of the coupling required for charge transport. This model does not yield to conventional simple rationalizations in terms of overlap of the local

HOMOs and the bridge orbitals. This is not surprising in terms of the strong mixing of the ionic states in the transition state at the ratcheting configuration. The strong dependence of the delocalization on the conformation is a result here and appears quite real in calculations. Hence, the torsions are not only accepting modes but the coupling modes as well.

In light of the coupling strength of up to 0.2 eV proposed here, the Golden Rule approximation for the transition rate is questionable, because the slow passage by torsional motion through the region of charge delocalization can become close to the adiabatic one, hence an efficiency close to unity.

At last, it is interesting to compare our findings here with those presented by Serrano-Andres and Fülscher [20]. These authors studied a different though related question of electronic excitations in the *neutral* polypeptide backbone using by CASSCF / CASPT2 level of the theory. They proposed assignment of the characteristic band at 7.3 - 7.5 eV as a charge transfer excitation which shifts an electron between two neighboring peptide units. The coupling between peptide groups was found highly sensitive to the backbone conformation. This is manifested by the energy and especially intensity dependence of CT transitions on the torsional angles. The $\pi_2 - n_o$ mixing in CT states was clearly evident in those calculations at typical non-planar geometries. In the nylon-like polypeptides, where amide groups are separated by longer alkyl chains, these authors find that similar CT excitations are higher in energy and much weaker in intensity. This indicates that the interpeptide coupling dramatically decreases in these polymers, but it is quite appreciable in natural polypeptides with a single carbon bridge. All these findings indirectly support our similar conclusions concerning electronic hole transfer in the polypeptide *radical cations*.

VI. Summary

In summary, we present a new model for highly efficient charge transport in peptide structures. We propose that the process is one of successive ratcheting of the peptide groups of each amino acid, until the critical configuration is attained for strongly coupled charge transfer. In the remainder of this torsional motion the state is localized. Hence hopping between sites is here presented as a ratcheting between amino acids in the chain. The torsional motion is due to near zero phonon modes which are associated with the two extreme low torsion frequencies next to the hinging CHR group of the amino acid. Hence this model has features of both strong and weak coupling depending on the ratchet position. This represents a very important mechanistic aspect of this new charge transfer mechanism. It will even have far reaching effects in the motion of the overall chain. Such long range chain deformations in proteins are well known.

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