168. Protonic Quantum Correlations in the H-Bond Dynamics of Nucleic Acids

Part 1

Conformational Comparison of G-C with *Benner*'s κ-π

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A new base pair (called κ-π) of *Watson-Crick* type, with an H-bond pattern different from that in A-T and G-C base pairs, has been recently synthesized by *Benner* and coworkers and shown to be stable and incorporable into duplex DNA and RNA by polymerases. This new base pair, which contains three H-bonds, is compared with G-C, in the framework of modern dynamical theory of quantum nonlocality and quantum correlations (also called *Einstein-Podolsky-Rosen* correlations). Connection with the traditional treatment of proton transfer in DNA base pairs, which uses the adiabatic approximation (thus considering the protons as classical particles), is explicitly made. As a result, the dynamics of the H-bond pattern of G-C is shown to exhibit a specific quantum-mechanical phase stability (or: rigidity, stiffness), which is clearly missing in the case of κ-π. This finding is discussed and illustrated, also in connection with recent quantum chemical calculations of proton transfers in DNA base pairs. Additionally, certain speculations concerning a probable 'evolutionary advantage' of G-C with respect to κ-π are shortly considered.

1. Introduction. – It is well-known that H-bond is of prime importance for structure and functioning of biological systems. *E.g.*, the discovery of the structure of DNA [1] made also clear that life without H-bond were impossible, since H-bonds between base pairs hold the two strands of DNA together. Very recently, *Benner* and coworkers [2] extended the genetic alphabet with a new base pair of *Watson-Crick* type, called κ-π. They also showed that this base pair is stable and can be enzymatically incorporated into duplex DNA and RNA [2]. This novel work motivated the present quantum dynamical analysis of protonic quantum correlations in the H-bonds of the base pairs, in connection with our current investigations concerning quantum correlations and dynamics of proton transfer in H_2O [3–5].

An important role in the present work play also *Löwdin*'s quantum chemical calculations of the potential energy surfaces (or curves) of the protons by their movement along the H-bond directions in DNA base pairs [6] [7]. These calculations indicate the existence of a double-well potential energy profile related with the considered protonic motions, which also means that the protonic quantum states participating to H-bonds of DNA have finite lifetimes. The possible biological significance of this fact with respect to mutagenesis has been extensively discussed [6] [7].

Since the discovery of *Bell*'s inequalities (see [8a] for an introduction) and, in particular, during the last decade it has been recognized that modern quantum theory accounts for striking *delocalization* effects which have no classical analogue. In other terms, one speaks of quantum or *Einstein-Podolsky-Rosen* (EPR) correlations [8–10]. (For readers being interested in a mathematical definition of EPR correlations, we recommend the presentation of *Primas* in [10], pp. 136–146.) Their existence – and the corresponding violation of *Bell*'s inequalities – has been verified through a large number of experiments (see references cited [8–10]). Two very recent (and really impressive) experiments demonstrate, for the first time, quantum delocalization of whole atoms, namely He [11a] and Na [11b], over distances of the order of 1 μm. Thus, also atomic nuclei appear to be quantum objects, which furthermore implies that the nuclear coordinates – in the physical context of time-dependent processes – have to be treated as dynamical variables rather than parameters (*i.e.* classical quantities). Apparently, these [11] (and other [3–5]) quantum delocalization effects are in 'conceptual conflict' with the classical treatment of the nuclear degrees of freedom in the framework of standard quantum chemical calculations.

The importance of EPR correlations for the dynamics of 'heavy' particles (like protons, deuterons, alkali atoms, *etc.*) in *condensed* matter was recently recognized [5] and demonstrated through novel predictions of the theory to five different experimental topics (*cf.* [3–5]).

The present paper applies for the first time the modern theory of quantum correlations to the dynamics of protons participating to H-bonds in DNA base pairs. These correlations are due to the quantum, nonlocal character of the protons of base pair H-bonds. In particular, we are dealing with the 'stabilities' of the G-C and κ-π base pairs. Both pairs have three H-bonds. Moreover, melting experiments of oligomers containing these base pairs showed that they have comparable stability, in the standard thermodynamic sense [2]. Our investigations, however, show that the H-bond pattern of G-C has a specific quantal stability (being due to quantum correlations between the protonic motions of its H-bonds), which is clearly missing in the κ-π base pair. This is shown to imply a specific kind of 'phase stability', or 'quantum rigidity' for G-C, which could also be considered to be associated with an 'evolutionary advantage' of G-C with respect to κ-π.

The present paper is organized as follows: *Sect. 2* and *3* deal with *Benner*'s and *Löwdin*'s investigations. *Sect. 4* and *5* present the quantum mechanical prerequisites and our main theoretical result. *Sect. 6* is mainly of 'technical' character and contains the proof of the main theoretical result. *Sect. 7* deals with the concrete application of the theoretical results to the cases of G-C and κ-π; here, an increased quantum mechanical 'phase rigidity' or 'stiffness' of the former with respect to the latter base pair is revealed. At last, *Sect. 8* contains some speculations related to the biological significance of the natural and new base pairs, in the light of the present quantum dynamical theory. Some mathematical details of *Jordan* blocks are presented in the *Appendix*.

2. On *Benner*'s Extension of the Genetic Alphabet. – The geometry of a *Watson-Crick*-type base pair can accomodate several mutually exclusive hydrogen bonding schemes (for some examples, see *Fig. 1*). Each of them is defined by the distribution of H-bonds (proton-donor or -acceptor) on the purine and pyrimidine rings. Nature, however, uses only two of these schemes (the well known G-C and A-T) and, in particular, one 'incompletely', as adenine (instead of diaminopurine) is used as the complement for uracil or thymine in natural nucleic acids.

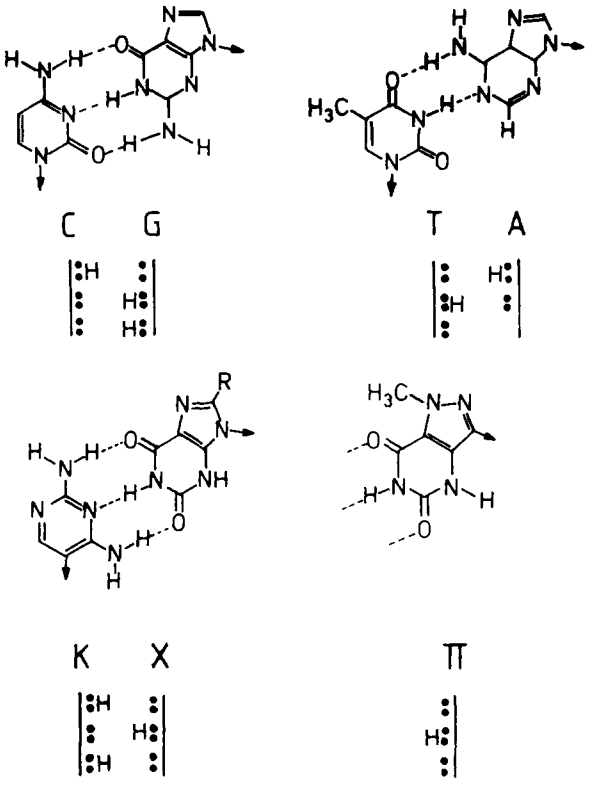

Fig. 1. *The base pairs G-C, T-A, κ-χ, and the base π, which forms with κ the base pair κ-π.* (The arrows indicate the bonds of the bases with the sugar-phosphate backbones of the DNA double helix.) κ-π has the same H-bond pattern with κ-χ, which differs from that of G-C. Below the structural formulas are shown *Löwdin*'s schematic representations of the corresponding H-bond patterns. Compare the more 'symmetric' H-bond pattern of κ-π (or κ-χ) to that of G-C (for details, see the text).

Very recently, a novel *Watson-Crick*-type base pair (called κ-π, see *Fig. 1*) exhibiting a different H-bond pattern from that in A-T and G-C base pairs, was designed and synthesized [2] [12]. Furthermore, this base pair was successfully incorporated into duplex DNA and RNA by adequate polymerases. Additional melting experiments with several oligonucleotides showed that duplexes containing a κ-π base pair are only slightly less stable than duplexes containing only A-T and G-C. Moreover, duplexes containing the new base pair appear to be considerably more stable than those containing mismatches involving the new bases, which in turn have melting temperatures similar to duplexes containing mismatches of natural bases [2].

Thus, this pioneering biochemical work demonstrated the feasibility of expanding the genetic alphabet by increasing the number of letters that enzymatically can be incorporated into nucleotides by template-directed polymerization. Among other consequences, also the possibility of synthesizing new RNA molecules with the potential for greatly increased catalytic power (even RNA that may catalyse its own replication) has been pointed out [2].

3. Proton Tunneling in DNA Base Pairs and Its Biological Significance. – Since the discovery of the structure of DNA, it has been conjectured that tautomeric forms of the bases A, C, G, and T might cause 'errors' by DNA replication and associated processes. For instance, as *Watson* and *Crick* already 1953 wrote: 'Our model suggests possible explanations for a number of other phenomena. For example, spontaneous mutation may be due to a base occasionally occurring in one of its less likely tautomeric forms.' (See [1], p. 966.)

Tautomeric forms of DNA bases are crucial for *Löwdin*'s 'double proton transfer' model of mutagenesis, which has been studied for many years [6] [7]. A (*coupled*) *double proton transfer* in a A-T of G-C base pair corresponds to the following: if one proton of the two H-bonds in A-T or the three H-bonds in G-C moves from its equilibrium position near its N-atom, along the line of the H-bond (see the broken lines in *Fig. 1*), to the lone electron pair of its 'opposite' O-atom, then this is likely to induce the reversal motion of a second proton in another H-bond of the same base pair, the later being in order to maintain the gross electric neutrality of the base pair [6]. In G-C, of course, there are two H-atoms 'belonging' to G, which, together with the H-atom of C, may undergo the coupled proton transfer under consideration. In this case, therefore, two different double-well potentials for the considered double proton transfer were calculated (see below).

First calculations on this topic (on the MO-LCAO-SCF level [6]) showed that the specific double proton transfer in DNA base paires indicated above may lead to double-well potential energy profiles (in short: potentials) for the two protons involved. The derived potentials support the formation of some short-lived tautomeric forms of the bases. As *Löwdin* pointed out, the protons are not classical particles but 'wave packets' obeying the laws of quantum theory, and thus they may be subject to the well-known tunnel effect in the double-well potentials mentioned above. This effect implies that the genetic code cannot be 100% stable, which furthermore means that this proton transfer over a distance of *ca.* 1 Å may be one of the driving forces in the evolution of living organisms on the earth [6].

In this context, it should be mentioned that *Clementi et al.* carried out an *ab initio* SCF calculation for the (possible) tunneling of one proton in the G-C base pair. They found that a single proton transfer (which formed an ion pair) gave a single-well energy profile characterized by a monotonically increasing energy function [13].

More recent calculations (on the *ab initio* SCF level) on the coupled double proton transfer in DNA base pairs, however, do support the existence of the aforementioned double-well potentials [7]. It is also interesting to note that these recent calculations exhibit far more asymmetric double-well potentials than the previously reported work [6]. This means that the structure of the base pairs in DNA appears to be more stable than previously believed. As a consequence, the experimentally determined spontaneous mutation rates in DNA, as cited in [6], cannot be explained any more in a quantitative way, with the aid of the numerical results of reference [7].

Nevertheless, the above results support qualitatively *Löwdin*'s hypothesis that certain tautomeric forms of the bases may result from double proton tunneling in the *Watson-Crick* base paires in DNA double helix. Additionally, the results of *Kong et al.* [7] indicate that the possibility of error in the genetic code replication in G-C base pair occurs more easily than that in A-T base pair, because the barrier hight of the double proton transfers in G-C base pair (48.85 and 64.02 kcal/mol) is lower than that in A-T base pair (70.24

kcal/mol). In other words, the equilibrium concentrations of the tautomers is expected to be greater in the case of G-C than in the case of A-T. It has been speculated that this observation might offer a possible explanation for the larger A-T to G-C content in higher organisms [6]. For another speculation about this point, see *Sect. 8*.

4. Couplings in Proton-Transfer Dynamics of G-C and κ-π. – Schematic representations of base pairs (like those shown in *Fig. 1*), DNA fragments, proteins, molecular water clusters, *etc.* overemphasize a *static* (or 'frozen') point of view for these molecular systems, and in a sense one can speak of the 'crystallographer's viewpoint'. In realistic situations (like DNA in living organisms at room temperature), however, the geometric form of these systems fluctuates with time, due to *i*) the well-known thermal motion and *ii*) the relative weakness of the H-bond (*ca.* 3 kcal/mol). This is one crucial reason stressing the fact that the standard quantum chemical calculations (as those mentioned above) are often of crude approximative character. In general, as a matter of fact, even the most modern quantum chemical computer calculations of molecular systems consider the nuclei – and even the protons – as classical mass points and treat only the electrons – and in most cases only some of them – quantum mechanically. In the scientific literature, one finds a huge number of different calculatory approaches, called approximations, methods, or techniques; *cf.* [14–20].

The most popular of these methods has been the adiabatic (*Born-Oppenheimer*) approximation, with its various specific forms. However, in the context of *time-dependent*, *i.e.* dynamical processes (like a chemical reaction or fluctuations in the H-bonding pattern of DNA), this approximation has been recently shown to be unphysical and sometimes even to yield incorrect results [20]. Thus, in these cases, it must be replaced by the so-called *diabatic* representation (or by a more suitable one). For a pedagogical overview, which also contains some experimental examples, see the excellent review article by *O'Malley* [20].

In the following, let us consider (some aspects of) the dynamics of the aforementioned coupled double proton transfer in G-C, and – in principle – also in κ-π. In the light of the diabatic representation, one can write the effective second-order *Hamiltonian* matrix (using standard notation for the matrix elements) as

$$H(R_1,R_2) = \begin{pmatrix} H_{11}(R_1) & V(R_1,R_2) \\ V(R_1,R_2) & H_{22}(R_2) \end{pmatrix} \tag{1}$$

cf. [20]. As an example, the diagonal matrix elements H_{11} and H_{22} (where $H_{ii} = T_{ii} + V_{ii}$, in standard notation) will be considered to represent the matrix elements of the *Hamiltonians* of the aforementioned two double proton transfer in G-C (and κ-π), and the dynamical variables R_i represent the corresponding positions of two protons, as described in *Sect. 3*. Of particular importance, however, is here the nondiagonal element $V(R_1,R_2)$ which represents the quantum mechanical coupling between the two protonic dynamical processes being described by $H_{11}(R_1)$ and $H_{22}(R_2)$.

It is now important to realize that, due to physical reasons, the coupling $V(R_1,R_2)$ cannot vanish for all positions of the moving protons. This can be shown at least in the following two ways. *i*) An illustrative way (using the language of quantum chemistry) is given by noting that every proton drags with it a significant electron cloud, as it moves from one end of the H-bond to the other. In the coupled motion of two protons, as

considered above, the repulsion between these clouds, as the protons pass each other, results in a interaction (coupling) between them. *ii*) A more subtle reason for this coupling is given by the fact that protons are also quantum objects, thus exhibiting an intrinsic delocalization which has to be of the order of the *de Broglie* wavelengths λ_{dB} of a proton. A short calculation of λ_{dB} of a (quasi-free) proton with kinetic energy being equal to the thermal energy k_BT (k_B: *Boltzmann* constant) gives at room temperature $\lambda_{dB} \approx 1.5$ Å. This numerical estimate of the protonic delocalization (which could appear to some readers to be surprisingly large) implies that the wave functions of the delocalized protons partially overlap so that they can interfere, thus creating intrinsic quantum correlations between them.

5. Quantum Correlations in G-C and Its Increased Stability. – It is well-known that the G-C base pair in DNA, having three H-bonds, is more stable against breaking than A-T, which has only two of them. In a crude approximation, one has to expect that the stability of the κ-π (or κ-χ) base pair, which exhibits three H-bonds, may be comparable with the stability of G-C. Indeed, the corresponding melting experiments in oligomers [2] mentioned in *Sect. 2* support this expectation.

Omiting here mathematical technicalities (which will be given in the next section) let us present the following surprising finding of our quantum dynamical investigations:

> The base pair G-C is expected to exhibit a higher specific quantal stability than the κ-π, this being due to specific time-dependent quantum correlations between the protons during their motions (around their equilibrium positions).

Some explanations and illustrative remarks may now be helpful: *1*) The term 'more stable state' is usually considered to mean nothing other than 'state with lower (free) energy'. This is trivially true in classical mechanics and thermodynamics. But in quantum mechanics, where the phase relations between identical particles must be taken into account, the above two terms do not have always the same meaning. (In this context, one usually refers to the case of superconductivity, as an example, where the perfect phase 'matching' (or coherence) of the quantum states of the individual electron pairs causes a dramatic increase in the stability of the electric supercurrent against thermal disturbances.) *2*) The quantum (or EPR) correlations mentioned above are intrinsically connected with the phase coherence of quantum systems. This coherence is well-known to cause a specific 'rigidity' or 'stiffness' of the corresponding quantum state. As a consequence, it costs energy to change the phase of this quantum state in space or time – thus making the system more 'stable', say, against thermal disturbance through its environment. It should be emphasized that EPR correlations have no classical analogue, and thus they cannot be illustrated through some example refering to 'common sense' [8] [9]. *3*) With the aid of quantum mechanics (of dynamical processes), it can be shown that, in the case of G-C, an increased phase stability concerning the two coupled proton transfers (see *Sect. 3*) may appear, and that this is not probable for κ-π. We can namely prove that – under specific conditions, see *Sect. 6* below – the effective 2×2 *Hamiltonian* matrix, *Eqn. 1*, for G-C does not have two eigenstates (as one usually expects), but *only one*; *cf.* also the *Appendix*. This restriction of the space of states functions corresponds to – or represents – the aforementioned increased phase rigidity or stiffness. *4*) This fact can be verbally described by saying that the protons in G-C move 'cooperatively' or 'coherently', or that their motions are 'EPR-correlated', or that the protonic system became 'more

rigid', *etc.* As a consequence, it is now more difficult to disturb the motion of one of the protons, since any applied disturbance acts 'at the same time' on all protons (H-atoms), due to the quantum (or EPR) correlations 'connecting' them. Apparently, this corresponds to an effective 'weakening' of the disturbance, as concerns its action on one specific proton, and equivalently to an increased 'stability' of the H-bonds against disturbances. (Remember, however, that quantum correlations do not have any classical analogue.) *5*) Due to the facts that, in real systems, *i*) DNA is not in gas phase but is surrounded by H_2O, ions, proteins *etc.*, and *ii*) the temperature of interest is finite, one recognizes that the thermal motion may affect the coupling operator $V(R_1,R_2)$, which then – at least in certain cases – should be assumed to be time-dependent.

6. Theoretical Details and Proof. – This topic, which is mainly of technical character, considers the proof of the quantum theoretical result discussed in *Sect. 5*. Therefore, readers with less interest in quantum mechanics of dynamical processes may skip it and proceed to the next *Sect. 7*.

Almost 30 years ago, it was recognized that the well-known adiabatic approximation (and its standard variations) of the *Schrödinger* equation cannot describe correctly many dynamical processes even in small atomic and molecular systems; *cf.* [20]. (For condensed-matter dynamics the adiabatic approximation is irrelevant.) Some simple examples of such processes are: atomic and molecular inelastic collisions, elementary chemical reactions, charge and/or energy transfer between atoms and/or molecules.

The conventional adiabatic approximation has been meanwhile considerably improved and/or replaced by: *a*) its extension to complex adiabatic parameters and complex energy surfaces, *cf.* [14] [15] [17]; *b*) the different diabatic approximations, *cf.* [18–20]; *c*) the method of optical potentials, *cf.* [21]; *etc.* The most powerful and well-founded approach, however, which at the same time 'unifies' the aforementioned improvements and clarifies their limitations, seems to be the recently discovered 'theory of dilation analytic operators', also called Complex Scaling Method (CSM): *cf.* [22] for a recent overview and an extended list of references, and [23] for a pedagogical introduction.

These improvements establish also a crucial extension of the well-known basic quantum mechanical formalism: The *Hamiltonian* matrices become *non-Hermitian*, and especially *complex symmetric* [22] [23]; *cf.* also [24]. Thus the matrix elements H_{11}, H_{22} and V of H in *Eqn. 1* are in general complex quantities, which also implies that the effective *Hamiltonian* $H(R)$ is non-*Hermitian*. An important consequence is that now H may have *complex* eigenvalues, which also implies that the corresponding eigenstates are non-stationary.

In the present context, it should also be mentioned that already 1927 *Dirac* had pointed out the necessity of using non-*Hermitian Hamiltonians* for the treatment of decaying states, *cf.* [25]. Similarly, in *Prigogine*'s novel theory of microscopic irreversibility, *cf.* [26], the aforementioned hermiticity and, moreover, the unitarity of the evolution operator, are lost.

Having in mind certain general results of the CSM [22] [23], let us now assume the effective *Hamiltonian* matrix $H(R_1,R_2)$, *Eqn. 1*, to be complex symmetric. Then we can prove the following theorem [17]:

> The 2×2 matrix $H(R_1,R_2)$ has in general two complex eigenvalues and two linearly independent complex eigenvectors. Under a specific condition (*Eqn. 3*, below), how-

ever, H becomes non-diagonalizable (*i.e.* it becomes a *Jordan* block of order 2), and it has only one eigenvector.

We now proceed to the proof of the theorem. As is well-known, the eigenvalues E_+ and E_- following from the time-independent *Schrödinger* equation $H\Psi_\pm = E_\pm\Psi_\pm$ are given by

$$E_\pm = \frac{1}{2}(H_{11} + H_{22}) \pm \frac{1}{2}\sqrt{(H_{11} - H_{22})^2 + 4V^2} \tag{2}$$

(compare *e.g.* [14] [15] or any textbook of quantum chemistry). Here and in the following, the arguments R_i are often omitted for simplicity. These two quantities 'cross' another (or: intersect) for R values making the square root expression equal to zero, *i.e.*

$$H_{11} = H_{22} \pm i\,2V, \tag{3}$$

which then also implies that $E_+ = E_-$. (Parenthetically, it should also be noted that the condition $E_+ = E_-$ is the starting point of different discussions of the so-called 'non-crossing rule' of the adiabatic approximation; *e.g. cf.* [14–17] [20].)

As mentioned in *Sect. 3*, we are interested in cases where V does not vanish identically (*i.e.* for all values of R_i). For these cases, it has been proved [17] that the *Hamiltonian* matrix H, under the *Condition 3*, exhibits a *Jordan block* structure [27], *i.e.* it is similar to the matrix

$$J(E) = \begin{pmatrix} E & 1 \\ 0 & E \end{pmatrix} \tag{4}$$

This means that no similarity (nonsingular) transformation is able to diagonalize H. Furthermore, H has *only one* eigenvector [27], which in the present case has the explicit form [17].

$$\Psi_J = \begin{pmatrix} 2V \\ H_{22} - H_{11} \end{pmatrix} \tag{5}$$

For more details, see the *Appendix*. Of course, for *Hermitian* matrices this never can happen.

7. Consequences for the G-C and κ-π Phase Stability. – In this section, the previous formal results and discussions are explicitly applied to the dynamics of the coupled double proton transfers (see *Sect. 3*) in these base pairs. As discussed in *Sect. 4*, the diagonal elements H_{11} and H_{22} may be assumed to describe the two possible double proton transfers under consideration, and V may represent the quantum mechanical coupling (or 'interaction') between them. Furthermore, and to simplify the following remarks, let us restrict our considerations to the 'equidistant' (or 'cooperatively coupled') double proton transfers being defined by the requirement:

$$R_1 = R_2 \equiv R.$$

By considering the pattern of the H-bonds in the base pairs (see *Fig. 1*), the following point may be observed: *The triple H-bond pattern in κ-π (and κ-χ) exhibits a specific symmetry that is missing in G-C.* This is easily seen with the aid of *Löwdin*'s schematic representations of the H-bond patterns as shown in *Fig. 1*. Namely, the H-atom of the base contributing only one H-atom in the H-bond pattern (*i.e.*, π or χ) is situated in the 'central' position, and the other two H-atoms 'belonging' to κ are situated symmetrically

in the two 'outer' positions of the pattern. This symmetric distribution of the H-bonds of κ-π is clearly not present in the G-C base pair.

This observation, however, appears to be crucial for the quantum dynamics of the protonic motions in the considered base pairs. Namely, the aforementioned 'symmetry' in κ-π also implies that the two double proton transfers (as discussed in *Sect. 3*) are expected to have similar potential energy curves V_{ii}, for a significant part of the numercial range of R. Thus, we can assume in first approximation that

$$H_{11}(R) = H_{22}(R) \quad \text{for } \kappa\text{-}\pi \tag{6}$$

Remember that in the presently considered case of a complex symmetric effective *Hamiltonian,* the quantities H_{11} and H_{22} may be complex.

The same considerations suggest also that the corresponding 'asymmetry' of the H-bond pattern of G-C gives rise to the inequality (for a significant part of the range of R)

$$H_{11}(R) \neq H_{22}(R) \quad \text{for G-C} \tag{7}$$

This result is in line with the different numerical values of the two potential barriers mentioned in *Sect. 3*, where only the real parts of (the generally complex quantities) $H_{11}(R)$ and $H_{22}(R)$ were considered.

Some further reasoning leads now straightforward to the envisaged result. *i*) κ-π: *Equality 6* and the *Condition 3* can be fulfilled simultaneously in the trivial case $V = 0$ only, which also makes the *Hamiltonian H* diagonal. But the latter point also implies that the two quantities H_{11} and H_{22} are uncoupled, in the approximation under consideration. Thus, we may conclude that there do not exist quantum correlations and phase stability of the aforementioned character between the two double proton transfers in κ-π. *ii*) *G-C*: *Inequality 7* and the necessary *Condition 3* for the occurrence of *Jordan* blocks in the *Hamiltonian H* can be fulfilled simultaneously, for some value(s) of R, with nonvanishing coupling V. Thus, the quantum correlations between the two double proton transfers and the aforementioned increased phase stability (see *Sect. 5* above) may become effective in the G-C base pair.

To illustrate furthermore these findings, let us continue these investigations concerning the G-C base pair by taking into account the calculated forms of the potential energy curves of *Kong et al.* [7]. To be specific, let us consider, in particular, the following special case of the C-G dynamics, *Eqn. 7*:

$$H_{11}(R) \text{ and } H_{22}(R): \quad \text{real} \tag{8}$$

$$V(R,R) \equiv i\bar{V}(R) \quad \text{with real } \bar{V}(R) \tag{9}$$

Due to the considered validity of the restriction $R_1 = R_2 \equiv R$, see above, we also may assume for the kinetic energies $T_{11} = T_{22}$. The *Condition 3* for the appearance of a *Jordan* block, for some 'position(s)' R_c, in the effective *Hamiltonian* matrix (by choosing the minus sign in it) reads now:

$$V_{11}(R_c) = V_{22}(R_c) + 2\bar{V}(R_c) \tag{10}$$

Let now $V_{22}(R)$ represent the potential energy of the coupled transfer of the C-hydrogen with the 'central' G-hydrogen of the H-bond pattern; $V_{11}(R)$ then represents the corresponding potential energy of the transfer of the two 'outer' protons in this bonding,

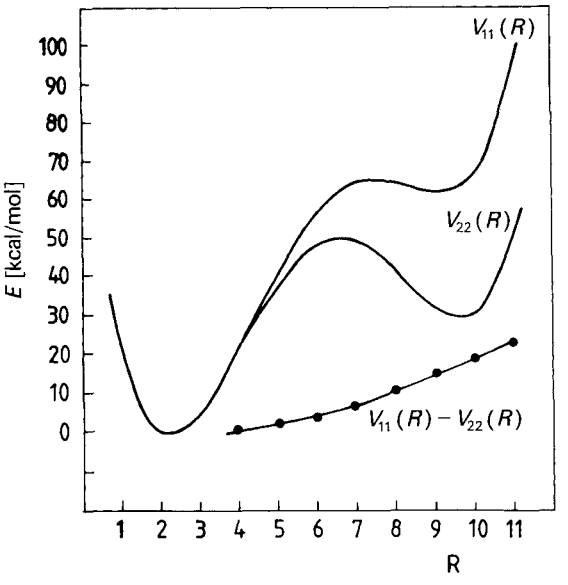

Fig. 2. *Schematic representation of the double-well potentials of the coupled double proton transfers in the C-G base pair* [7] *and their difference.* The 'reaction' coordinate R for the double proton transfers under consideration is given in units of 0.1 Å. $V_{22}(R)$ represents the considered potential energy of the coupled transfer of the single C-hydrogen with the 'central' G-hydrogen of the H-bond pattern; $V_{11}(R)$ represents the corresponding potential energy of the transfer of the two 'outer' protons in this bonding, *cf. Fig. 1.* Note the remarkable approximative linearity of the difference $V_{11}(R)$-$V_{22}(R)$ with respect to the 'reaction' coordinate R, for a large part of R values. The physical meaning of this observation is a specific 'enhanced' phase stability (or rigidity) of the considered system (paper in preparation).

cf. Fig. 1. For this special choice, the recent results of *Kong et al.* [7] for the double-well potentials of these transfer processes are represented schematically in *Fig. 2*, together with their difference. These data reveal the following surprising feature: as one sees in *Fig. 2*, the function $V_{11}(R) - V_{22}(R)$ is *almost* (but not exactly) *linear* in the 'reaction' coordinate R. This is by no means trivial, since this quasi-linearity holds for (almost) all R values between the two potential-energy minima. (This linear relationship is subject of current investigations.)

Since the coupling V may fluctuate in the course of time (*e.g.* due to thermal disturbances), the possible value(s) of R_c may 'fluctuate', too.

By taking into account the specific form of the single eigenvector $\Psi_J(R_c)$, *Eqn.* 5, in the case of a *Jordan*-block *Hamiltonian*, we immediately conclude the following: the *direction* of $\Psi_J(R_c)$ is almost *independent* of the specific value of R_c, *i.e.*

$$\Psi_J(R_c) \sim \begin{pmatrix} i \\ 1 \end{pmatrix}. \tag{11}$$

In other words, it follows that all the possible *Jordan*-block eigenvectors $\Psi_J(R_c)$ are related to (approximately) the same physical state, despite of the fact that the effective *Hamiltonian*, *Eqn. 1*, is strongly R-dependent – an unexpected result indeed. Thus, this striking finding physically means that the considered quantum mechanical phase stability

(or rigidity) of the C-G system is higher than the previous general derivations may have indicated.

At this stage, it is instructive to mention a possible 'constructive role' that thermal motion (or: disturbance) may play by the stabilisation of the DNA base pairs. This remark is certainly not expected, since usually one assumes that the thermal motion disturbs (or even destroys) quantum effects. However, the situation is here more subtle. Due to the thermal motion, namely, the distance between individual bases in base pairs does fluctuate in time; *cf. Sect. 5*, point 5. This implies a time dependence in the functional form and the strength of the quantities $H_{11}(R)$, $H_{22}(R)$ and $V(R,R)$. Therefore, *Condition 3*, being necessary for the occurrence of the specific quantum 'cooperativity' under consideration, can now be fulfilled easier, during many time instants (or short time intervals), as time goes on. This qualitative consideration also illustrates the aforementioned dynamical character of the effect being revealed by the theory, and it is conceptually in line with the novel work of *Prigogine* and coworkers concerning the 'constructive role' of irreversibility in self-organisation processes; *cf.* [26].

8. Some Speculations on the Biological Role of Phase Rigidity. – The extension of the genetic alphabet through the novel experimental work of *Benner* and coworkers [2] appears to be of 'practical' importance for biochemistry of living organisms, and at the same time, it stimulates further investigations concerning the prebiotic evolution of biological macromolecules (*cf.* [28–32]) and, more generally, the self-organisation of living matter. Here let us shortly consider some related speculative points.

As mentioned above, G-C and κ-π have similar thermodynamic stability as well as stability against the spontaneous occurrence of tautomeric forms of the bases involved; *cf.* in particular [12]. Thus the question arises, why Nature has not incorporated the new base pair in DNA or RNA. In this context, *Benner* notices that the C–C bond between base and sugar is more difficult to synthesize than the corresponding N–C bond appearing in the natural nucleosides [12]. Furthermore, our present investigations reveal that the G-C base pair exhibits an additional 'quantum-correlation stability' of its triple H-bonding pattern, which is clearly missing in the κ-π (or κ-χ) base pair. From this specific point of view, G-C might have an additional 'evolutionary advantage' as compared to κ-π.

A further extension of these considerations is based on the fact that the A-T base pair has only two H-bonds, as the complement of thymine (or uracil) is adenine and not a diaminopurine, as mentioned in by *Piccirilli et al.* [2] and *Löwdin* ([6a], pp. 297–298). Thus, a NH_2 group seems to be 'missing' here. In this context, one usually points out that the A-T base pair is extensively used in higher organisms, because it can be opened 'more easily' during replication, which might also represent a specific evolutionary advantage. In the light of the present quantum mechanical investigations, however, one immediately recognizes that an additional NH_2 group on adenine (to create a diaminopurine having a triple H-bond with thymine) would result to the *same symmetric* H-bond pattern as in κ-π (*cf. Fig. 1*), thus creating a base pair *without* the quantum-correlation stability being characteristic for G-C. In this sense, one could speculate that Nature has 'removed a NH_2 group from A-T, and not from G-C, not just by accident'.

It would be interesting to extend the preceding investigations by considering possible quantum correlations between protons (or H-atoms) belonging to adjacent base pairs along the DNA helical axis. If namely the aforementioned quantum-correlation stability

(or: rigidity, stiffness) does really cause some kind of evolutionary advantage (or disadvantage), then one would expect that Nature may make already some 'use' of it. But then this ought to be manifested in specific features (or patterns) of DNA nucleotide sequences of living organsims. Further work along these lines is in progress.

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Appendix. – Some additional remarks on eigenvectors and eigenvalues of *Jordan* blocks may be helpful here. As mentioned previously, there exist special cases where the *effective* (or: relevant, reduced) *Hamiltonian* matrix H exhibits a *Jordan block* structure, *i.e.* it is similar to the matrix

$$J(E) = \begin{pmatrix} E & 1 \\ 0 & E \end{pmatrix} \tag{A.1}$$

It holds that no similarity (*i.e.* arbitrary nonsingular) transformation is able to diagonalize $J(E)$, *cf.* [27]. Furthermore, every *Jordan* block, like $J(E)$, has *only one* eigenvector.

Due to the revealed physical importance of *Jordan* blocks in the presently considered proton transfer processes and, more generally, in the framework of dynamics in condensed matter [5], let us outline here the proof of the last statement. Let $J(E)$ be the above *Hamiltonian* in the corresponding representation. The time-independent *Schrödinger* equation reads then

$$\begin{pmatrix} E & 1 \\ 0 & E \end{pmatrix} \cdot \begin{pmatrix} c_1 \\ c_2 \end{pmatrix} = \lambda \begin{pmatrix} c_1 \\ c_2 \end{pmatrix} \tag{A.2}$$

Matrix multiplication on the left-hand side leads explicitly to the linear system of equations:

$$E \cdot c_1 + c_2 = \lambda \cdot c_1 \tag{A.3a}$$

$$0 + E \cdot c_2 = \lambda \cdot c_2 \tag{A.3b}$$

Eqn. A.3b gives

$$\lambda = \mathrm{E} \tag{A.4b}$$

and putting this result into *Eqn. A.3a*, we obtain

$$E \cdot c_1 + c_2 = E \cdot c_1 \tag{A.4a}$$

But this equation implies necessarily that it must hold

$$c_2 = 0 \tag{A.5}$$

Thus, we conclude that *all* eigenfunctions (or: eigenvectors) of a *Hamiltonian* matrix of the type $J(E)$ associated with the eigenvalue *Eqn. A.2* have the form

$$\Psi_J = c_1 \cdot \begin{pmatrix} 1 \\ 0 \end{pmatrix} \quad (c_1\text{: arbitrary complex number}) \tag{A.6}$$

In other words, all eigenfunctions of the *Hamiltonian* constitute a one-dimensional subspace (or: ray) of the two-dimensional space being in general spanned by the eigenfunctions of a 2×2 matrix. This restriction represents the aforementioned increased phase rigidity of the quantum mechanical state of the system.

Note Added in Proof. – Recent investigations showed that the main results (*6*) and (*7*) can be proved also under more general conditions, *i.e.* without using the restrictive condition $\mathrm{R}_1 = \mathrm{R}_2 \equiv \mathrm{R}$ of *Sect. 7*.

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