Entanglement Swapping Model of DNA Replication

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Abstract

Molecular biology explains function of molecules by their geometrical and electronical structures which are mainly determined by utilization of quantum effects in chemistry. However, further quantum effects are not thought to play any significant role in the essential processes of life. On the contrary, consideration of quantum circuits/protocols and organic molecules as software and hardware of living systems that are co-optimized during evolution, may be useful to pass over the difficulties raised by biochemical complexity and to understand the physics of life. In this sense, we model DNA replication with a reliable qubit representation of the nucleotides: 1) molecular recognition of a nucleotide is assumed to trigger an intrabase entanglement corresponding to a superposition of different tautomer forms and 2) pairing of complementary nucleotides is described by swapping intrabase entanglements with interbase entanglements. We examine possible realizations of quantum circuits/protocols to be used to obtain intrabase and interbase entanglements. Lastly, we discuss feasibility of the computational and experimental verification of the model.

Keywords: DNA base pairing, quantum information theory, entanglement swapping, monogamy of entanglement

1. Introduction

According to the central dogma of molecular biology, genetic information stored in double-stranded DNA (dsDNA) is duplicated by replication of two strands independently. At each step of the replication of a single-stranded DNA (ssDNA), enzyme DNA polymerase (DNA*pol*) first recognizes the nucleotide base (N = {A, T, G, C}) of the DNA strand. Then, it finds complementary of this base ($\bar{\text{N}}$ = {$\bar{\text{A}}$=T, $\bar{\text{T}}$=A, $\bar{\text{G}}$=C, $\bar{\text{C}}$=G}) from the surrounding environment to synthetase a new dsDNA by base pairing.

Conformational changes occurring within DNA*pol* at each step of the replication were demonstrated in detail by crystallization experiments (Patel et al., 2001). Also, all possible interactions between amino acid side chains and unpaired nucleotide bases were obtained by quantum chemical calculations (Cheng et al., 2003). However, there are still some unclear points about the high fidelity of replication process (Patel et al., 2001) such as 1) the exact mechanism for the base recognition in free nucleotide and ssDNA cases, 2) searching mechanism for finding the correct nucleotide, and 3) mechanism for the pairing of the bases. Since there are a lot of amino acids in the active site of DNA*pol* that contribute to these mechanisms (Patel et al., 2001), both experiments and quantum chemical calculations are still insufficient to clarify these mysteries. Thus, until the development of more sensitive setups and more complex calculations, information processing models could be useful tools for a better understanding of DNA replication.

During the DNA replication, newly synthesized strands elongate with a rate 3,000 nucleotide per minute in humans (Snustad and Simmons, 2003) and 30,000 nucleotide per minute in bacteria (Nelson and Cox, 2005). Neither DNA binding nor nucleotide binding to the DNA*pol* limits this rate, they are very fast steps (Patel et al., 2001; Goel et al., 2002, 2003). Also, replication without proofreading and repair mechanisms occurs with an error rate of 10^{-4} to 10^{-6} per nucleotide (Nelson and Cox, 2005). These precision and accuracy of DNA*pol* seem to be similar with the fundamental constrains of quantum mechanics and relatively long decoherence time makes quantum information processing models acceptable for DNA replication (Goel et al., 2003; Goel, 2008).

1.1. Quantum Information Models for DNA replication

To understand the underlying mechanisms of DNA replication several quantum information processing models were proposed. For example, Patel (2001) formulated nucleotide selection from surrounding environment as an unsorted database search. He examined the pertinence of Grover's algorithm (Grover, 1997) in explaining the number of different deoxyribonucleotides in the evolutionary context. Although he achieved to model base pairing as oracle of the algorithm, initiation of the model requires the symmetric superposition of four nucleotides which is not quite possible. Wave analogue (Patel, 2006) of this quantum search algorithm in which symmetric superposition state is replaced by the center-of-mass mode is more realistic for enzyme activity. However, if this model

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(Patel, 2006) is adopted for the activity of DNA*pol*, it should begin with the interaction of DNA*pol* and four different free nucleotides, contrary to the knowledge that DNA*pol* first binds to ssDNA in the replication (Patel et al., 2001; Goel et al., 2002, 2003).

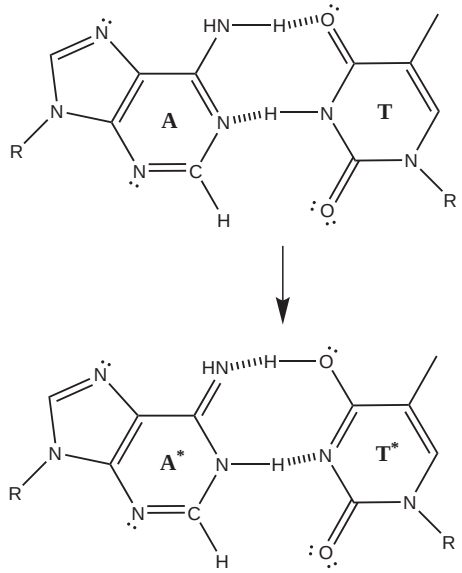

Figure 1: A·T→A*·T* tautomeric transition in dsDNA.

Recently, Cooper (2009a,b) modeled base recognition mechanism in replication (and transcription) to understand time-dependent DNA mutations and A·T richness of DNA. To explain the stability of base pairs, he assumed that interbase hydrogen bonds are rearranged by sequential intermolecular and intramolecular proton tunnelings. In this assumption, interbase tunnelings turn bases into unusual tautomers pair-by-pair (Figures 1, 2). Then, intramolecular tunnelings introduce coherent superposition states in which enol and imine protons of unusual tautomers are shared between two electron lone pairs that belong to a single atom. In the recognition step of the model, enzyme transcriptase (RNA-dependent DNA*pol*) makes quantum measurements on the coherent states of protons that are present on Watson-Crick (*WC*) edge (Figure 3). Although this model is compatible with molecular genetic transcription data of bacteriophage T4, some possible results of the transcriptase measurements, such as the decohered states corresponding to tautomers $G^{\sharp}_{002}$ and $G^{\sharp}_{000}$ (Cooper, 2009a,b) do not generate information about any usual tautomer form. Technically, qubit representation of a nucleotide base was accepted as the tensor product of states corresponding to the *WC* edge protons in the model. Then, Hilbert space should be 8-dimensional, but four bases states, that do not correspond to common tautomers, give no meaningful information to the enzyme. Therefore, in such situations where result of the measurements is one of these additional states, enzyme can not recognize the nucleotide base of DNA. This expresses an efficiency problem in both recognition and searching mechanisms.

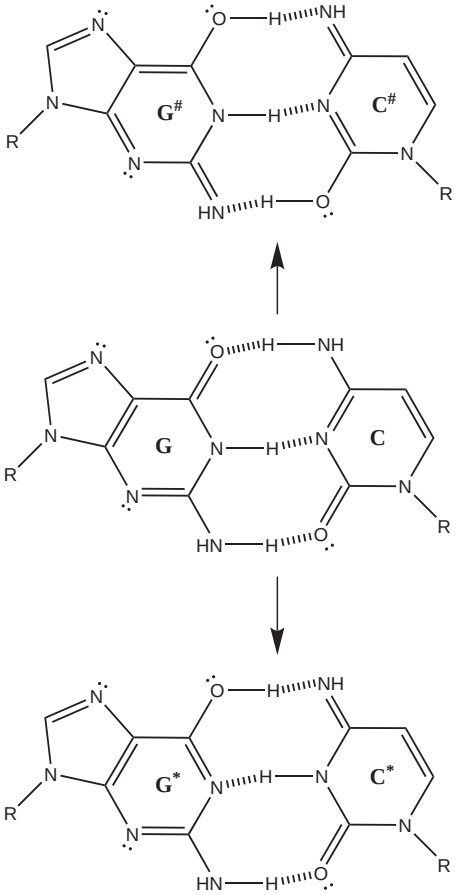

Figure 2: G·C→G$^{\sharp}$·C$^{\sharp}$ and G·C→G*·C* tautomeric transitions in dsDNA.

1.2. Motivation of Entanglement Swapping Model of Replication

The fastest quantum search algorithm (Grover, 1997; Zalka, 1999) is only four times faster than the slowest classical search algorithm in the situation of searching complementary nucleotides of template bases. Therefore, if nontrivial quantum effects are involved in DNA replication, they should be evolved to increase the accuracy instead of the speed. In this sense, our model is motivated to investigate quantum effects increasing accuracy in DNA replication.

Free nucleotide binds to a solvent exposed pocket within DNA*pol* before base pairing, whereas template base is flipped out of the helix axis and into the active site (Patel et al., 2001). However, it is theoretically known that interaction with water molecules can induce transitions to rare tautomer forms (Fogarasi, 2008) which have different hydrogen bonding patterns on the *WC* edge. Such higher energetic states can be also mediated by interactions with carboxylate and sodium ions (Samijlenko et al., 2004). Thus, tautomeric transitions is likely in both incorporated nucleotide and template base after recognition and before base pairing. If they are not prevented, such transitions lower the efficiency of replication.

In this work, molecular recognition of a nucleotide is assumed to trigger an intrabase entanglement corresponding to a superposition of different tautomer forms. Such superpositions

will be invariant in the situations causing tautomeric transitions and so, increase accuracy. Then, pairing of complementary nucleotides via hydrogen bonding is described by swapping intrabase entanglements with interbase entanglements. Although van der Waals bonds between nucleotide bases in ssDNA are modeled by entanglement in a recent study (Rieper et al., 2011), this is the first example of modeling hydrogen bonds by entanglement and using multiparticle entanglement swapping (Bose et al., 1998) in living systems. Following two subsections about proton tunneling between base pairs and covalency of interbase hydrogen bonds elucidate why quantum dynamics are continued by entanglement swapping after increasing accuracy of replication and provide the required conceptual framework for entanglement description of interbase hydrogen bonds.

1.2.1. Proton Tunneling within a Base Pair

Tautomeric shifts on both bases by a double proton tunneling through hydrogen bonds (Figures 1, 2) was firstly introduced in 1963 by Löwdin to model time dependent mutations. Several ab inito quantum chemical calculations with electron correlation (Florián and Leszczyński, 1996; Kryachko, 2001; Kryachko and Sabin, 2003) have been done to support this mutagenesis model. After these correlated ab inito calculations, Villani calculated more reliable potential energy surfaces by density functional theory (DFT) method (2005; 2006; 2007; 2008; 2010) and found possible transitions $A{\cdot}T \rightarrow A^{*}{\cdot}T^{*}$ (Figure 1), $G{\cdot}C \rightarrow G^{\sharp}{\cdot}C^{\sharp}$ and $G{\cdot}C \rightarrow G^{*}{\cdot}C^{*}$ (Figure 2) by concerted or two step double proton-coupled electron transfers (Villani, 2004). Since calculated transition probabilities (Villani, 2005, 2006, 2007, 2008, 2010) are pure quantum mechanical, tautomerization in dsDNA, which is an observational fact, should have a quantum mechanical nature based on quantum mechanical proton transfer (proton tunneling) rather than a classical one. Thus, we can assume that DNA double helix is a decoherence-free subsystem (Lidar et al., 1998; Kempe et al., 2001; Lidar and Whaley, 2003) in which nucleotide base pairs exist in a superposition of the states corresponding to different tautomer pairs. However, cellular environment may cause a decoherence effect on nucleotide base in both free nucleotide and ssDNA cases. Therefore, we have to assume that quantum dynamics continues until the end of the replication and this makes enzyme DNA*pol* another noiseless subsystem (Knill et al., 2000; Lidar and Whaley, 2003) in which basis states evolve into superposition states that are immune to decoherence.

1.2.2. Covalency of the Interbase Hydrogen Bonds

Base pairing occurs via hydrogen bonding and nature of the interbase hydrogen bonds is well understood (Hobza and Šponer, 1999; Šponer et al., 2008). A nonlocal DFT method (Guerra et al., 1999) showed that covalent contribution to hydrogen bonds is 38% in A·T pairing and is 35% in G·C pairing. This conclusion was then supported by subsequent DFT studies (Guerra et al., 2000; van der Wijst et al., 2006) and similar conclusions were reached by semiemprical methods with geometrical and atoms-in-molecules topological parameters, natural bond orbital analysis, and spectroscopic measurements (Wilkens et al., 2002; Mohajeri and Nobandegani, 2008). Furthermore, consideration of some substituents in bases caused a decrease in the total hydrogen bond strength and an increase in covalent contribution up to more than 49% (Guerra et al., 2006).

Such conclusions show that interbase hydrogen bonds are not classical hydrogen bonds based on only electrostatic interactions, but they are quantum mechanical. Covalency of them illustrates the interaction of acceptor orbital and unoccupied antibonding orbital linking donor and hydrogen atoms (Guerra et al., 1999). This can be interpreted as quantum mechanical share of proton by donor and acceptor. Thus, base pairing should be done by a quantum mechanical process and such an implication supports the concluding assumptions of previous subsection. According to these assumptions, the states produced by the recognition interaction between DNA*pol* and nucleotide base should be superposition of the states of usual and unusual tautomer forms found in the allowed transitions (Figures 1, 2). These superposition states will correspond to intrabase entanglements. Whereas, the states produced by the base pairing will correspond to interbase entanglements, since the state of a hydrogen bonded atom pair can be written as an entangled state considering the present knowledge about covalent nature of interbase hydrogen bonds. Intuitively, biomolecules are thought as exactly classical objects since their de Broglie wavelengths are comparatively smaller than their actual size due to their huge complexity and high temperature. However, it is both theoretically and experimentally shown that entanglement can occur in macroscopic and hot non-equilibrium systems, such as living ones (Amico et al., 2008; Vedral, 2008, 2010; Cai et al., 2010).

2. Entanglement Swapping Model of Replication

2.1. Qubit Representation of Input and Output Nucleotide States in Replication

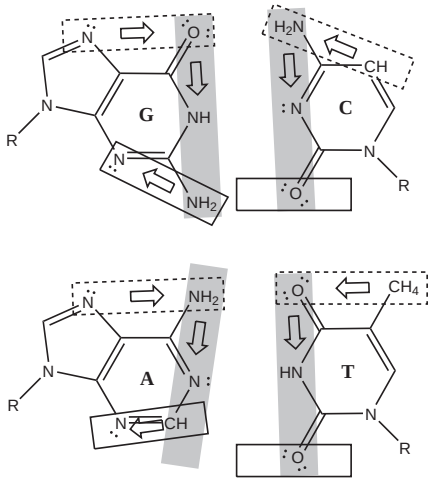

Figure 3: Parts of the nucleotides: atoms can be grouped according to region they will be found in DNA. Hoogsteen (↔major groove), Watson-Crick (↔pairing plane), and Sugar (↔minor grove) edges are indicated respectively by dashed, filled, and plain boxes. Arrows inside the boxes show the order of the qubits used in qubit representation.

Recognition process requires formation of at least two hydrogen bonds between amino acid side-chains of the DNA*pol* and nucleotide base (Seeman et al., 1976; Cheng et al., 2003). Such pairs of hydrogen bonds can occur over one of the three parts of nucleotides (Cheng et al., 2003) shown in Figure 3. In consensus, hydrogen bond donor and acceptor atoms of bases are only O and N atoms. However, there are a small number of computational observations in which C atoms of nucleotide bases have the ability to make blue-shifting hydrogen bonds (Kryachko and Sabin, 2003). In this respect, when electronic configurations of the individual O, N, and C atoms on *H*, *WC*, and *S* edges (Figure 3) are considered, it is found that each atom has two different energy states: a relatively lower energy state for acceptor situation and a relatively higher energy state for donor situation (Figure 4). These lower and higher energy states can be regarded as qubits $|0\rangle$ and $|1\rangle$, respectively (Figure 4). Then, reliable qubit representations can be written down for all the three edges of each nucleotide base (Table 1).

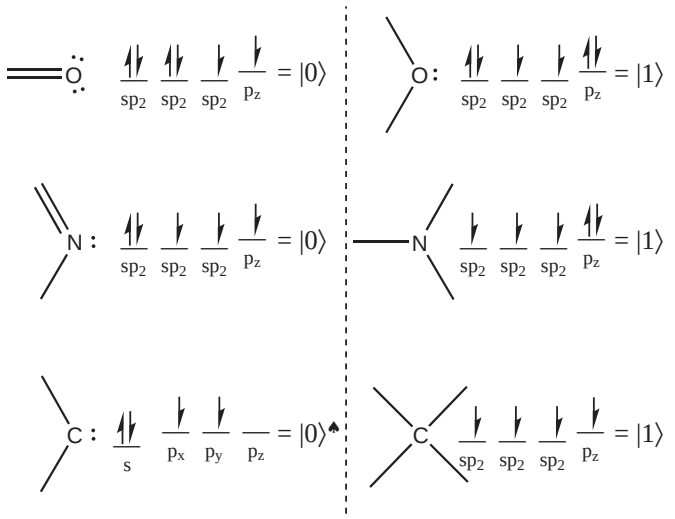

Figure 4: Electronic configurations and qubit representations of the O, N, and C atoms: higher energy state $|1\rangle$ (lower energy state $|0\rangle$) corresponds to the presence (absence) of a proton which is bonded to that atom and participates in interbase hydrogen bonds (Figures 1-2). Configuration indicated by ♠ is not present in any tautomer form. However, it is possible to observe it in blue-shifting hydrogen bonds of DNA.

2.2. Quantum Aspect of the Enzyme Action

To avoid efficiency problems in both recognition and searching mechanisms, states of the nucleotides which are measured by DNA*pol* should live in a 4-dimensional Hilbert space. Also, states corresponding to usual tautomer forms should be orthogonal to each other. Under these conditions, DNA*pol* should recognize bases in both free nucleotide and ssDNA cases only over the *H* edge according to Table 1. It is known that sequence-specific dsDNA binding proteins usually interact with the major groove (Rohs et al., 2010) and so, they recognize nucleotide bases of dsDNA over the *H* edge, too. Such a coincidence is not a surprise, since reading information from dsDNA and ssDNA by different proteins ought to depend on similar principles.

Table 1: Qubit representations of usual and unusual tautomer forms found in the allowed transitions (Figures 1-2): $|0\rangle$ and $|1\rangle$ states are assigned according to the absence and presence of a proton that can be shared in a hydrogen bond and order of the qubits are determined as shown in Figure 3.

Tautomer form	$\|N\rangle_H$	$\|N\rangle_{WC}$	$\|N\rangle_S$
A	$\|01\rangle$	$\|101\rangle$	$\|10\rangle$
A *	$\|00\rangle$	$\|011\rangle$	$\|10\rangle$
T	$\|10\rangle$	$\|010\rangle$	$\|0\rangle$
T *	$\|11\rangle$	$\|100\rangle$	$\|0\rangle$
G	$\|00\rangle$	$\|011\rangle$	$\|10\rangle$
G *	$\|01\rangle$	$\|101\rangle$	$\|10\rangle$
G $^\sharp$	$\|01\rangle$	$\|110\rangle$	$\|00\rangle$
C	$\|11\rangle$	$\|100\rangle$	$\|0\rangle$
C *	$\|10\rangle$	$\|010\rangle$	$\|0\rangle$
C $^\sharp$	$\|10\rangle$	$\|001\rangle$	$\|1\rangle$

If DNA*pol* makes a quantum measurement on the state $|N\rangle_H$ to recognize a nucleotide base, first qubit gives information about purine-pyrimidine distinction, whereas the second one gives information about imino-enol distinction. In this sense, DNA*pol* should pair bases whose qubit representations are complementary to each other (see Table 1). Not only correct base pairings, but also mispairings like A·C* and G*·T pairings can be accounted for by this assumption.

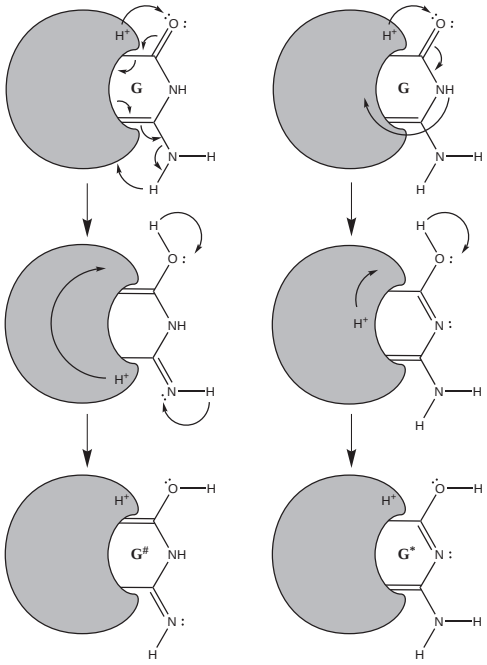

Figure 5: An hypothetical mechanism for the tautomeric transitions of nucleotide base G by proton transfer between enzyme DNA*pol* and nucleotide. Grey structure represents the active site of DNA*pol* and arrows show proton and electron delocalizations.

A quantum measurement requires an entanglement between the measuring device and measured system. In this case, it can be considered as a quantum mechanical hydrogen bonding between the DNA*pol* and the nucleotide base. Also, it is reason-

able to assume that entanglement between the DNA*pol* and the nucleotide should be maximal since an accurate measurement requires strong coupling between measuring device and measured system.

Hypothetically, a proton transfer between the DNA*pol* and the second atom of *H* edge (or equally the first atom of *WC* edge) which occurs during the recognition, can trigger a tautomeric transition (Figure 5). Since such a transfer has a quantum nature in a quantum mechanical hydrogen bonding, recognition can trigger a transition to the superposition of usual and unusual tautomer forms by a unitary transformation **U**. This mechanism is a toy model of enzyme's being a noiseless subsystem in which basis states $|\mathrm{N}\rangle_{WC,I}$ (Table 1) evolve into superposition states $|\mathrm{N}\rangle_{WC,Q} = \sum_t |\mathrm{N}^t\rangle_{WC,I}$ ($t = \{\ , *, \sharp\}$) as follows:

$$
\begin{aligned}
|\mathrm{A}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{A}\rangle_{WC,Q} &= a_1|011\rangle + a_2|101\rangle\,, \qquad (1)\\
|\mathrm{T}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{T}\rangle_{WC,Q} &= t_1|010\rangle + t_2|100\rangle\,,\\
|\mathrm{G}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{G}\rangle_{WC,Q} &= g_1|011\rangle + g_2|101\rangle + g_3|110\rangle\,,\\
|\mathrm{C}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{C}\rangle_{WC,Q} &= c_1|100\rangle + c_2|010\rangle + c_3|001\rangle\,.
\end{aligned}
$$

Indeed, these superpositions of different tautomer forms are nothing else then intrabase entanglements of the atoms on *WC* edge. Nucleotide bases A and T have two different tautomer forms, whereas G and C have three different tautomer forms in allowed transitions (Figures 1, 2). Thus, we observe two two-qubit entanglements in the states of A and T, while there are two three-qubit entanglements in the states of G and C (Figure 6).

Recognition process of complementary nucleotide base $\bar{\mathrm{N}}$ also involves a quantum measurement in which a maximal entanglement is formed between DNA*pol* and $\bar{\mathrm{N}}$. However, DNA*pol* can not bind to $\bar{\mathrm{N}}$ in such a quantum mechanical way until it disentangle itself from N. This is because of the entanglement monogamy (or polygamy) (Coffman et al, 2000; Koashi and Winter, 2004; Cavalcanti et al., 2005) which roughly says that if A and B are maximally entangled, then any one of them can not be simultaneously entangled with C. In the context of monogamy, formation of intrabase entanglement in N breaks the maximal entanglement between DNA*pol* and N. Then, a maximal entanglement between DNA*pol* and $\bar{\mathrm{N}}$ becomes possible.

Similarly, recognition of $\bar{\mathrm{N}}$ induces an intrabase entanglement in $\bar{\mathrm{N}}$ which disentangles DNA*pol* from $\bar{\mathrm{N}}$. This disentanglement allows DNA*pol* to bond N and $\bar{\mathrm{N}}$ together and then to bind to the subsequent N of ssDNA in a quantum mechanical way. Therefore, formation of intrabase entanglements not only prevents the uncontrollable tautomeric transitions caused by cellular environment, but also provides separation of DNA*pol* from one nucleotide and binding of it to another.

After base pairing, nucleotide base pairs should exist in a superposition of states corresponding to different tautomer pairs. Since state of a hydrogen bonded atom pair can be written as the Bell state $|\beta_{01}\rangle = (|01\rangle + |10\rangle)/\sqrt{2}$, these superposition states $|\mathrm{N}_1 \cdot \bar{\mathrm{N}}_2\rangle_{WC,O}$ are actually interbase entanglements. So it can be said that in the case of G·C pair, there are three two-qubit entanglements in $|\beta_{01}\rangle$ state, and in the case of A·T pair, there are two two-qubit entanglements in $|\beta_{01}\rangle$ state. In order to turn intrabase entanglements into interbase entanglements, **U** should be followed by an irreversible transformation **S**. Therefore, in our model, base pairing occurs as a multiparticle entanglement swapping in which DNA*pol* swaps intrabase entanglements with interbase entanglements (Figure 6).

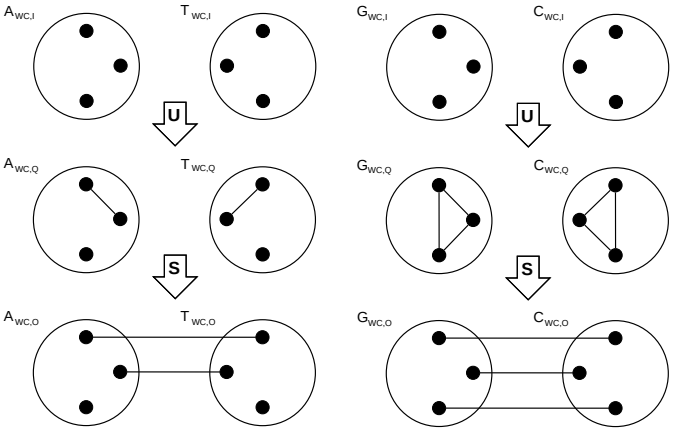

Figure 6: Entanglement swapping model of replication. Each circle represents the *WC* edge of related nucleotide base. Atoms on *WC* edge are shown by small dark points. A line linking two of such points means that there is an entanglement between the atoms shown by these points.

3. Construction of the Model

3.1. Quantum Circuit for Intrabase Entanglement

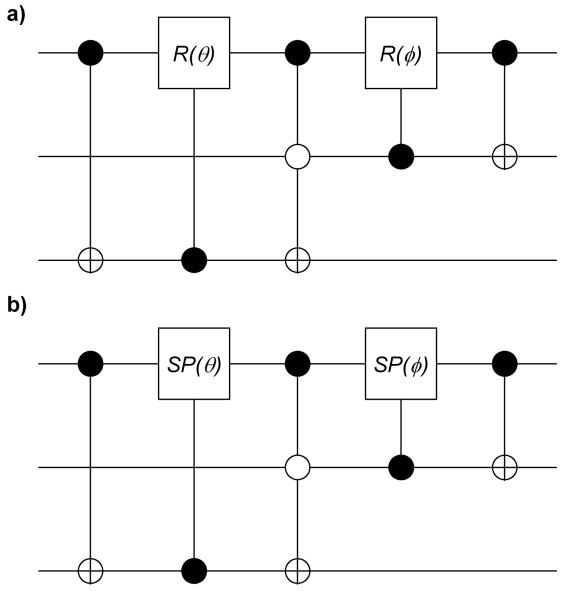

Figure 7: Two of the possible quantum circuits for transformation **U** which turns $|\mathrm{N}\rangle_{WC,I}$ states into the $|\mathrm{N}\rangle_{WC,Q}$ states. *a*) A circuit with only *controlled – NOT* and *controlled – Rotation* gates. *b*) A circuit with only *controlled – NOT* and *controlled – Superposition* gates. Superposition matrix $SP(\theta)$ of *controlled – Superposition* gates equals to the multiplication of rotation matrix $R(\theta)$ and Pauli-*Z* matrix.

Two candidates for the transformation **U** are shown in the Figure 7. To provide an equilibrium between maximal entanglement and robustness, we take the angles θ and ϕ in the second quantum circuit (Figure 7-b) as $\arccos(\sqrt{2}/\sqrt{3})$ and $\arccos(1/\sqrt{2})$, respectively. Then, $|\mathrm{N}\rangle_{WC,Q}$ states are obtained as:

$$\begin{aligned} |\mathrm{A}\rangle_{WC,Q} &= (|01\rangle - |10\rangle)|1\rangle/\sqrt{2}\,, \\ |\mathrm{T}\rangle_{WC,Q} &= (|01\rangle + |10\rangle)|0\rangle/\sqrt{2}\,, \\ |\mathrm{G}\rangle_{WC,Q} &= (|011\rangle + |101\rangle + |110\rangle)/\sqrt{3}\,, \\ |\mathrm{C}\rangle_{WC,Q} &= (|100\rangle - |010\rangle + |001\rangle)/\sqrt{3}\,. \end{aligned} \tag{2}$$

To consider each base pair as an intact system, tensor products of these states should be taken.

$$\begin{aligned} |\mathrm{A}\rangle_{WC,Q} \otimes |\mathrm{T}\rangle_{WC,Q} = \frac{1}{2}(&|011\rangle|010\rangle + |011\rangle|100\rangle \\ &- |101\rangle|010\rangle - |101\rangle|100\rangle)\,, \\ |\mathrm{G}\rangle_{WC,Q} \otimes |\mathrm{C}\rangle_{WC,Q} = \frac{1}{3}(&|011\rangle|100\rangle + |101\rangle|100\rangle + |110\rangle|100\rangle \\ &- |011\rangle|010\rangle - |101\rangle|010\rangle - |110\rangle|010\rangle \\ &+ |011\rangle|001\rangle + |101\rangle|001\rangle + |110\rangle|001\rangle)\,. \end{aligned} \tag{3}$$

We reorder qubits of these product states in such a way that hydrogen bonded atom pairs come next to each other in order to clarify base pairing. Then, we get

$$\begin{aligned} |\mathrm{A}\cdot\mathrm{T}\rangle_{WC,Q} = \frac{1}{2}(&|00\rangle|11\rangle|10\rangle + |01\rangle|10\rangle|10\rangle \\ &- |10\rangle|01\rangle|10\rangle - |11\rangle|00\rangle|10\rangle)\,, \\ |\mathrm{G}\cdot\mathrm{C}\rangle_{WC,Q} = \frac{1}{3}(&|01\rangle|10\rangle|10\rangle + |11\rangle|00\rangle|10\rangle + |11\rangle|10\rangle|00\rangle \\ &- |00\rangle|11\rangle|10\rangle - |10\rangle|01\rangle|10\rangle - |10\rangle|11\rangle|00\rangle \\ &+ |00\rangle|10\rangle|11\rangle + |10\rangle|00\rangle|11\rangle + |10\rangle|10\rangle|01\rangle)\,. \end{aligned} \tag{4}$$

3.2. Swapping Protocol for Interbase Entanglement

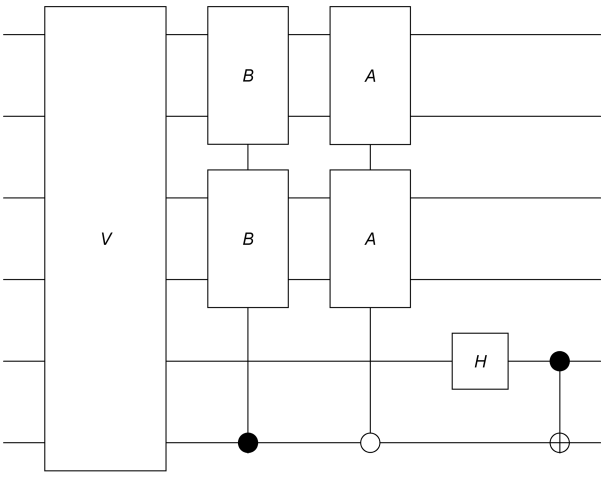

Figure 8: Quantum circuit for **S** which swaps intrabase entanglements to interbase entanglements: H is the *Hadamard* gate which equals to $SP(\pi/4)$ defined in Figure 7. Transformations A and B are shown in the subsequent figure. See Appendix for the details of transformation V.

Swapping intrabase entanglements to interbase entanglements can be achieved by a three-step protocol **S** as follows:

1. Reordered base pair states are subjected to a transformation V as shown in Figure 10. Then, fifth and sixth qubits of the G·C (or C·G) pair become $|01\rangle$, whereas fifth and sixth qubits of the A·T (or T·A) pair become $|11\rangle$. After this transformation, any improper base pair exists in a superposition of states in which third qubit pair is always $|00\rangle$ or $|10\rangle$.

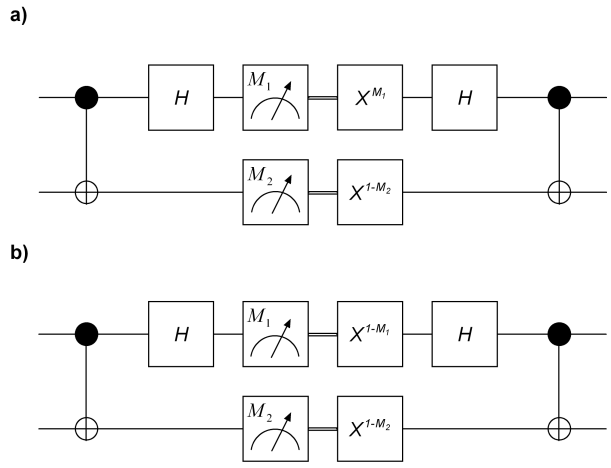

Figure 9: Quantum transformations A and B used in **S**: they are actually modified Bell measurements. Modifications made by X which is the *NOT* gate (or Pauli-X gate) and X's superscript (M_1 or M_2) is the outcome of the measurement which is done immediately before it. *a*) A transforms any Bell state $|\beta_{ij}\rangle$ into the Bell state $|\beta_{11}\rangle$. *b*) B transforms any Bell state $|\beta_{ij}\rangle$ into the Bell state $|\beta_{01}\rangle$.

2. If the sixth qubit is $|0\rangle$, first and second qubit pairs undergo a transformation A as shown in Figure 9-a. Otherwise, these qubit pairs are transformed with transformation B (Figure 9-b). Then, first and second qubit pairs of proper base pairs collapse into Bell state $|\beta_{01}\rangle = (|01\rangle+|10\rangle)/\sqrt{2}$, whereas first and second qubit pairs of improper base pairs collapse into Bell state $|\beta_{11}\rangle = (|01\rangle - |10\rangle)/\sqrt{2}$.

3. Firstly, fifth qubit is passed through a *Hadamard* (H) gate. Then, sixth qubit is converted by *NOT* (X) gate if the fifth qubit is $|1\rangle$. After this step, third qubit pair of the G·C (or C·G) pair becomes $|\beta_{01}\rangle$, whereas third qubit pair of the A·T (or T·A) pair becomes $|\beta_{11}\rangle$. In contrast, fifth and sixth qubits of any improper base pair exists in one of the Bell states $|\beta_{00}\rangle = (|00\rangle + |11\rangle)/\sqrt{2}$ or $|\beta_{10}\rangle = (|00\rangle - |11\rangle)/\sqrt{2}$.

Immediately after **S**, proper $|\mathrm{N}_1\cdot\tilde{\mathrm{N}}_2\rangle_{WC,O}$ states are written in terms of the Bell states as follows.

$$\begin{aligned} |\mathrm{A}\cdot\mathrm{T}\rangle_{WC,O} &= |\mathrm{T}\cdot\mathrm{A}\rangle_{WC,O} = |\beta_{01}\rangle|\beta_{01}\rangle|\beta_{11}\rangle, \\ |\mathrm{G}\cdot\mathrm{C}\rangle_{WC,O} &= |\mathrm{C}\cdot\mathrm{G}\rangle_{WC,O} = |\beta_{01}\rangle|\beta_{01}\rangle|\beta_{01}\rangle. \end{aligned} \tag{5}$$

4. Discussions

NOT gate used in the quantum circuit of **U** (Figure 7-b) converts $|1\rangle_N$ into $|0\rangle_N$. When state of the DNA*pol* is also considered with the subscript E, this transformation should be

$|1\rangle_N|0\rangle_E \rightarrow |0\rangle_N|1\rangle_E$. Since $|0\rangle$ and $|1\rangle$ states of an atom respectively correspond to the absence and presence of a proton bonded to that atom, this transformation can be regarded as a quantum mechanical proton transfer from the nucleotide base to DNA*pol* through the atom on which the gate acts. Vice versa is possible for the action of *NOT* gate on the state $|0\rangle_N$.

Other gate used in the quantum circuit of **U** is *SP*. When its argument θ equals to $\arccos(1/\sqrt{2})$, it transforms $|0\rangle_N$ into $(|0\rangle+|1\rangle)/\sqrt{2}$ and $|1\rangle_N$ into $(|0\rangle-|1\rangle)/\sqrt{2}$. The former transformation should be $|0\rangle_N|1\rangle_E \rightarrow |\beta_{01}\rangle_{NE}$ by taking into account also the state of DNA*pol*, whereas the latter transformation should be $|1\rangle_N|0\rangle_E \rightarrow |\beta_{11}\rangle_{NE}$. So, the action of the *SP(θ)* on the state $|0\rangle_N$ can be considered as formation of a quantum mechanical hydrogen bond between the nucleotide bases and enzyme through the atom on which gate acts. On the contrary, an antibonding should occur by the action of *SP(θ)* on the state $|1\rangle_N$. This is because of the fact that free energy in the state $|\beta_{11}\rangle_{NE}$ is greater than the one in which there is no interaction. Since entanglement measure of the generated state changes when the argument θ is changed, action of *SP* can produce bondings/antibondings with different strengths for different arguments.

Both the proton transfer and hydrogen bonding are the usual tasks done by enzymes and there are some evidences for the unignorable role of quantum effects and dynamics on the enzymatic reactions (Kohen and Klinman, 1999). Therefore producing an intrabase entanglement by transformation **U** is a possible action performed by the enzyme DNA*pol*.

The intact system which is exposed to decoherence is the whole nucleotide base - DNA*pol* complex. Hence, states of the nucleotide bases alone are not sufficient to determine if decoherence has a significant effect on the transformation **U** or does not. To draw a complete picture of interaction, assume that there are q hydrogen bond acceptors and $(k-q)$ hydrogen bond donors in the active site of DNA*pol*. If so, enzyme's active site can be represented by the state $|0\rangle_E^{\otimes q} \otimes |1\rangle_E^{\otimes(k-q)}$ after a proper ordering in which all $|0\rangle$ qubits are put to left of all $|1\rangle$ qubits. Then, we can obtain the initial state of the nucleotide base - DNA*pol* complex as $|s\rangle_I = |\mathrm{N}\rangle_{WC,I} \otimes |0\rangle_E^{\otimes q} \otimes |1\rangle_E^{\otimes(k-q)}$. Cellular decoherence effect can not be assumed as a measurement, because interaction with water can induce transitions to rare tautomer forms (Fogarasi, 2008), instead of stabilizing to one of them. However, cellular effect on the state $|s\rangle$ can be simplified as a weak collective decoherence (Kempe et al., 2001; Lidar and Whaley, 2003) which turns $|1\rangle$ states into $e^{i\phi}|1\rangle$, while $|0\rangle$ states remain unchanged. Since we have already considered $|0\rangle$ and $|1\rangle$ states of an atom respectively as the absence and presence of a proton bonded to that atom, this simplification makes sense: decoherence can not affect an absent proton.

When spacing between the qubits is smaller than the wavelength of the radiation field which acts as a boson bath for the qubit system, collective decoherence dominates among the others (Lidar et al., 1998; Kempe et al., 2001; Lidar and Whaley, 2003). In this sense, weak collective decoherence seems to be relevant not only to long-range electrostatic interactions with the intracellular ions, but also to short-living couplings with the thermal reservoir. Investigation of the effect of thermal reservoir on the internal DNA mobility requires a lattice dynamic approach based on an atomistic description of the molecule (Yakushevich, 2004). According to the appropriate methods given in (Kim and Prohofsky, 1987; Xiao-feng and Yuan-Ping, 2008), maximum frequency of the vibrational modes in DNA is a few hundreds of cm^{-1} at room temperature. Corresponding phonon wavelength is in the order of μm and this is quite longer than the qubit spacing in our model, which is no more than 3 Å. Thus, phonon bath can not distinguish the qubits and collective decoherence is expected to be the dominant decoherence mechanism in the DNA replication.

Defining a variable λ_K which equals to the number of $|0\rangle$ qubits minus the number of $|1\rangle$ qubits in a state over K qubits, Kempe et al. (2001); Lidar and Whaley (2003) showed that subspaces of Hilbert space spanned by the states with constant λ_K are decoherence free during a collective dephasing process as described above. Then, a decoherence free subspace for a specific λ_K is denoted as $DFS_K(\lambda_K)$ (Kempe et al., 2001; Lidar and Whaley, 2003).

In our model, there is no proton exchange between the system and its environment during the transformation **U**. For example, when a $|1\rangle$ qubit of nucleotide base turns into $|0\rangle$ qubit after a *NOT* gate, a $|0\rangle$ qubit of DNA*pol* should also turn into $|1\rangle$ qubit, since *NOT* gate corresponds to a quantum mechanical proton transfer between the nucleotide bases and DNA*pol*. Therefore, value of the $\lambda_{K=3+k}$ remains fixed and transformation **U** does not take any state $|s\rangle$ out of the $DFS_{3+k}(2q-k+1)$ or $DFS_{3+k}(2q-k-1)$. This means that decoherence is avoided during the formation of interbase entanglements.

Moreover, each state that corresponds to an intrabase entanglement (Equations 1, 2) lives in one of the decoherence free subspaces $DFS_3(+1) = \mathrm{Span}\{|001\rangle, |010\rangle, |100\rangle\}$ and $DFS_3(-1) = \mathrm{Span}\{|011\rangle, |101\rangle, |110\rangle\}$. Hence, even if nucleotide bases are exposed to cellular environment as in the actual case (Patel et al., 2001), intrabase entanglements will not be fragile after once they are obtained. This allows DNA*pol* to safely search for the complementary free nucleotide base after the recognition of nucleotide base of ssDNA and to safely continue pairing of bases after finishing the search.

Besides **U**, swapping protocol **S** also includes *NOT* gates and *SP* gates which are regarded as respectively proton transfer and hydrogen bonding/antibonding between a nucleotide base and DNA*pol*. Additionally, **S** contains swap gates (Figure 10) and modified Bell measurements (A and B). Swap gate exchanges the states of two qubits on which it acts: $|10\rangle \rightarrow |01\rangle$ and $|01\rangle \rightarrow |10\rangle$. So, it can be interpreted as a quantum mechanical proton transfer similar to interpretation of *NOT* gate. However, atoms on which swap gate acts can belong either to the same nucleotide or to the different nucleotides in the base pair. Hence, this proton transfer should be considered inside a nucleotide base or between the two different bases.

Outcome of the modified Bell measurement B is the Bell state $|\beta_{01}\rangle$, whereas the outcome of the modified Bell measurement A is the Bell state $|\beta_{11}\rangle$. Thus, these measurements can also be thought as a quantum mechanical hydrogen bonding/antibonding. Contrary to the ones produced by *SP* gates, this bonding/antibonding is between the two nucleotide bases

and its strength is always maximum. Consequently, **S** consists of nothing more than proton transfers and hydrogen bondings/antibondings which are the usual tasks done by enzymes like DNA*pol*.

Conservation of the proton number of nucleotide base - DNA*pol* complex is trivial under the actions of swap gates and modified Bell measurements. Hence, decoherence suppression during and after the swapping protocol **S** can be demonstrated in a similar way as is done for the transformation **U**.

Immediately after the entanglement swapping, states of proper base pairs are found as in Equation 5. According to these states, A·T (or T·A) base pair has two hydrogen bonds and G·C (or C·G) base pair has three hydrogen bonds as in the actual case. However, these hydrogen bonds have a maximum strength since Bell states are maximally entangled. These states should change by the quantum evolution in the presence of the asymmetric double well potentials of the hydrogen bonded atom pairs. Thus, strengths of the hydrogen bonds should gradually decrease to the actual ones. Moreover, there is an antibonding between the last atom pair in A·T (or T·A). These atoms repulse each other because of the higher free energy of antibonding, but strength of this repulsion should also decrease by time. Since one of the atoms in this antibonding is C atom, final strength of the repulsion should be negligible.

On the other hand, both first and second atom pairs of the improper base pairs have an antibonding after the entanglement swapping. Final strength of the repulsions due to these antibonding interactions are not negligible and so, they should destabilize and separate the improper base pairs. However, state of the last atom pair in these base pairs are obtained as $|\beta_{00}\rangle$ or $|\beta_{10}\rangle$. Since total proton number of the base pair does not remain constant after collapsing to these states, atom pair and DNA*pol* can not separate from each other. In fact, these Bell states should be treated as an entanglement between the atom pair and DNA*pol* when state of the enzyme is also under consideration: $|00\rangle_{N\bar{N}} \pm |11\rangle_{N\bar{N}} \rightarrow |00\rangle_{N\bar{N}}|11\rangle_E \pm |11\rangle_{N\bar{N}}|00\rangle_E$. It can be that it is this entanglement which keeps DNA*pol* in place till the correct $\bar{\mathrm{N}}$ comes along. Both of the asymmetric potentials and destabilization of the base pair should weaken this entanglement. When entanglement is weakened enough, DNA*pol* can bind to the correct $\bar{\mathrm{N}}$ because of the converse monogamy (Hayashi and Chen, 2011) which roughly says that if A and B are weakly entangled, then any one of them could be strongly entangled with C. After that, a Pauli-X transformations can fix the total number of protons on the improper base pair and make incorrect $\bar{\mathrm{N}}$ separable from the complex.

Neither **U** nor **S** is unique for the given model. However, this is not a disadvantage since there are several DNA*pol* species and families with different replication fidelities. This diversity in replication fidelity of DNA*pol* can be accomplished by different **U** and **S** pairs.

5. Conclusions

Since all of the steps in both **U** and **S** can be expressed as proton transfer and hydrogen bonding, the scenario proposed in our model could be tested step by step with the help of computational methods of quantum chemistry.

In addition to computational tests, some experimental setups may be designed to explore some of the predictions of the model. For example, states of base pairs immediately after the pairing are obtained as in Equation 5. Indeed, $|\mathrm{N}_1 \cdot \bar{\mathrm{N}}_2\rangle_{WC,O}$ states are superpositions of different tautomer forms with equal probability amplitudes. As discussed before, these amplitudes should change by the quantum evolution in the presence of the asymmetric double well potentials of the hydrogen bonded atom pairs until they reach the actual values. Then, it can be hypothesized that if this evolution can be prevented in a proper way, probability of point mutations due to the formation of rare tautomer forms should be higher than the ones obtained *in vivo*. This may be achieved by sufficiently decreasing the time periods between two successive replications.

However, there are some deficiencies in the description of the present model which should be removed before any computational or experimental test. Most important deficiency is the absence of enzyme's state in the computations. To obtain a more realistic description, a state should be assigned to the enzyme and the whole process including **U** and **S** should leave this state invariant at the end. In 1991, a self-consistency condition for a quantum state was introduced to describe and understand a disparate interaction (Deutsch, 1991). A similar utilization of the self-consisted states in the description of the enzymes seems to be appropriate. This is possible, even though the state of an enzyme is expected to be mixed, and that the purification of a mixed state in Deutsch's formalism is impossible (Pati et al., 2010). We note that proofs given in (Pati et al., 2010) are not valid for the mixed states which are used to describe enzymes under the self-consistency condition. We plan to investigate this further in the near future.

Finally, entanglement swapping may be a basic tool used by enzymes and proteins in the cellular environment. If so, similar models may be developed for amino acid - tRNA, aminoacyl-tRNA - mRNA, and amino acid - amino acid interactions in the protein synthesis. If successful models for these interactions can be developed, then we can achieve a deeper understanding of the role of the quantum effects and dynamics on the cellular information processing. Perhaps, entanglement swapping will join and contribute to the debates on the universal triplet genetic code (Patel, 2001, 2005; Tlusty, 2007) and on the mechanism behind adaptive mutation (Ogryzko, 1997; McFadden and Al-Khalili, 1999; Ogryzko, 2009) after such models.

All in all, quantum effects are used mainly for the determination of molecular shapes, sizes and chemical affinities in molecular biology and biochemistry. Although functions of bio-molecules are explained by structure, such as the complementary geometries of molecules and weak intermolecular hydrogen bonds in nucleotide base pairs, further quantum effects are not thought to play any significant role in the present biochemical complexity. However, they may be more useful tools to understand the physics of life if quantum circuits/protocols and organic molecules are considered as software and hardware of the living systems. Reconsideration of evolution as co-optimization of hardware (structure) and software (function),

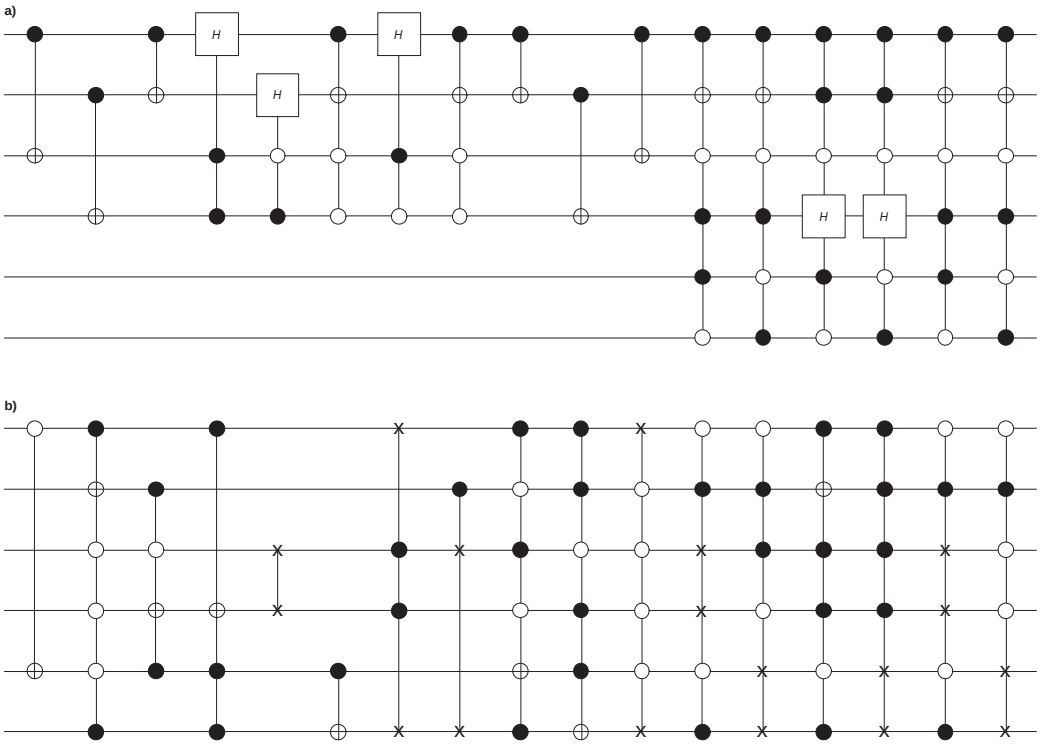

Figure 10: Quantum transformation V used in **S**: quantum gates indicated by a double $\times$ are swap gates. *a*) First part of the transformation V which makes the states of the proper base pairs orthogonal to each other and to the states of the improper base pairs. *b*) Second part of the transformation V which converts the third qubit pair into $|01\rangle$ in G·C (or C·G) pair and into $|11\rangle$ in A·T (or T·A) pair. In the case of an improper base pairing, it produces a superposition of states in which third qubit pair is always $|00\rangle$ or $|10\rangle$.

reconciles two opposite approaches: natural selection and self-organization. Thus, emergence of the life as a biochemical complexity may be demystified in the context of quantum information theory.

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Appendix A. Transformation V used in S

Transformation V used in **S** has thirty four gates as shown in Figure 10. Such a gate number is very high for an efficient replication process. However, this is a general representation and each gate is not effectively used in the all base pair combinations. Effective gate number of each base pair is as shown in Table 2. In fact, average effective gate number is only 12.93. In the case of improper base pairs, there is a little decrease in this number to 12.41. On the contrary, average of the effective gate number increases to 14.50 in the case of proper base pairs. Such a difference in these two cases can interpreted as an evolutionary advantage: enzyme DNA*pol* spends less time for improper base pairs in the pairing process of replication.

Table 2: Effective gate number of transformation V (Figure 10) for each base pair $N_1 \cdot \bar{N}_2$.

N_1 \ $\bar{N}_2$	A	T	G	C
A	09	10	16	14
T	12	09	13	12
G	13	09	18	18
C	10	08	18	18

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