DNA Replication via Entanglement Swapping

Onur Pusuluk 1 and Cemsinan Deliduman 2,3

1 Istanbul Technical University, Faculty of Science and Letters, Physics Department, Maslak 34469, Istanbul, Turkey
2 Mimar Sinan Fine Arts University, Department of Physics, Beşiktaş 34349, Istanbul, Turkey and
3 Feza Gürsey Institute, Çengelköy 34684, Istanbul, Turkey

Quantum effects are mainly used for the determination of molecular shapes in molecular biology, but quantum information theory may be a more useful tool to understand the physics of life. Organic molecules and quantum circuits/protocols can be considered as hardware and software of living systems that are co-optimized during evolution. We try to model DNA replication in this sense as a multi-body entanglement swapping with a reliable qubit representation of the nucleotides. In our model molecular recognition of a nucleotide triggers an intrabase entanglement corresponding to a superposition state of different tautomer forms. Then, base pairing occurs by swapping intrabase entanglements with interbase entanglements. We examine possible realizations of quantum circuits to be used to obtain intrabase entanglement and swapping protocols to be employed to obtain interbase entanglement. Finally, we discuss possible ways for computational and experimental verification of the model.

PACS numbers: 03.67.Ac, 82.39.Jn, 87.14.gf, 87.14.gk

According to the central dogma of molecular biology, genetic information stored in DNA is duplicated by replication and is used by successive transcription and translation. During replication, enzyme DNA polymerase (DNApol) recognizes the nucleotide bases N = {A, T, G, C} of template DNA strand and finds their complementaries {A=T, T=A, G=C, C=G} from the surrounding environment for base pairings. Recognition interaction between this single-stranded DNA (ssDNA) and polymerase enzyme is one of the several unknown aspects of replication. Also, mechanism used for finding the correct nucleotide from the surrounding environment is a mystery. Since a lot of amino acids exist in the active site of DNApol 1, both experiments and quantum chemical calculations are insufficient to clarify these mysteries. However, there are some quantum information processing models proposed for replication mechanism.

In 2001, Patel 2 formulated nucleotide selection from surrounding environment as an unsorted database search and examined the possibility of the use of Grover’s algorithm 3 in the evolutionary context. Although he achieved to model base pairing as oracle in the algorithm, initiation of the algorithm requires the superposition of four nucleotides which is not quite possible. In the wave analogue of the algorithm 4 replication should begin with the interaction of DNApol and all of four nucleotides, but it is known that DNApol first binds to DNA template in this process 1. Recently, Cooper 5 showed that molecular genetic transcription data of bacteriophage T4 is compatible with a quantum treatment in which enzyme makes a measurement on coherent protons that causes an entanglement between enzyme and protons. According to this model, enzyme-nucleotide interaction takes place on the protons and electron lone pairs that contribute to the base pairing. However, Watson-Crick (WC) edge of the nucleotides (Figure 1) can not be represented as four orthogonal states by such a treatment. In this paper, we try to model DNA replication as a multiparticle entanglement swapping 6 with a reliable qubit representation of nucleotides. In the model, molecular recognition of a nucleotide takes place on the protons and electron lone pairs that are present on the Hoogsteen (H) edge.

Meanwhile, covalent structure of the nucleotide bases is not static. Random, reversible and infrequent proton-coupled electron delocalizations convert bases into rare tautomer forms (N*, G*, C*). In 1963, Löwdin 7 claimed that tautomeric shifts on both paired DNA bases by a double proton tunneling through hydrogen bonds can be responsible for mutations. After some correlated ab inito calculations 8, 9 that support Löwdin’s claim, Villani 10, 11 calculated more reliable potential energy surfaces by density functional theory (DFT) method and found possible A-T→A*-T*, G-C→G*-C’ and G-C→G*-C* transitions by concerted or two step double proton-coupled electron transfers. Since calculated transition probabilities are pure quantum mechanical ones, tautomerization in double-stranded DNA should have a quantum mechanical nature. However, cellular environment may cause a decoherence effect on nucleotide base in both free nucleotide and ssDNA cases. Therefore, we assume that enzyme-nucleotide base interaction can suppress the decoherence effect and bring the state of nucleotide base to a superposition of all tautomer forms. Indeed, superposition of all tautomer forms is nothing else then intrabase entanglement of the atoms on WC edge.

Base pairing occurs via hydrogen bonding, but nature of the interbase hydrogen bonds is not well understood because of the insensitivity of experiments. A nonlocal DFT method 12 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 and similar conclusions were reached by semiempirical methods with geometrical and atoms-in-molecules topological parameters, natural bond orbital analysis, and spectroscopic measurements. Covalency of hydrogen bonds means that electron lone pair of the acceptor orbital is quantum mechanically shared between its own orbital and unoccupied antibonding orbital linking donor and hydrogen atoms. Thus, we can interpret the state of a hydrogen bonded atom pair as an entangled state. Hence, in our model, bases are paired by swapping intrabase entanglements with interbase entanglements.

The first qubit carries information about purine-pyrimidine distinction, whereas the second one carries information about imino-enol distinction. In this sense, DNApol should pair bases whose qubit representations are complementary to each other. Not only correct base pairings, but also mispairings like A·C* and G*·T pairings can be accounted for by this assumption.

We assume that base recognition by DNApol should occur over the $H$ edges of the nucleotides via a quantum measurement. 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. In this respect, when electronic configurations of the individual O, N, and C atoms in $H$, WC, and S edges 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. Surprisingly, only $H$ of the nucleotides can be represented as four orthogonal states if lower energy states are regarded as $|0\rangle$ qubit and higher energy states are regarded as $|1\rangle$ qubit:

\begin{align}
|A\rangle_H &= |01\rangle, & |T\rangle_H &= |10\rangle, \\
|G\rangle_H &= |00\rangle, & |C\rangle_H &= |11\rangle.
\end{align}

The first qubit carries information about purine-pyrimidine distinction, whereas the second one carries information about imino-enol distinction. In this sense, DNApol should pair bases whose qubit representations are complementary to each other. Not only correct base pairings, but also mispairings like A·C* and G*·T pairings can be accounted for by this assumption.

FIG. 2: Electronic configurations and qubit representations of the O, N, and C atoms: configuration indicated by ♠ is not present in any tautomer form. However, it is possible to observe it in blue-shifting hydrogen bonds of DNA.

However, since pairing occurs between WC edges of nucleotides, information processing starting with recognition over $H$ edges should continue over the WC edges. Equality of the second qubit of $H$ edge and the first qubit of WC edge makes such a transition in interaction region reasonable. Qubit representation of WC edges of nucleotides before replication are as follows:

\begin{align}
|A\rangle_{WC,I} &= |101\rangle, & |T\rangle_{WC,I} &= |010\rangle, \\
|G\rangle_{WC,I} &= |011\rangle, & |C\rangle_{WC,I} &= |100\rangle.
\end{align}

A double proton transfer between the DNApol and the first atom of WC edge which occurs immediately after the recognition, can trigger a tautomeric transition (Figure 3). If such a transfer has a quantum nature, recognition interaction can trigger an unitary transition to the superposition of all tautomer forms. A candidate for such a transformation $U$ is shown in the Figure 4. Since $|0\rangle$ and $|1\rangle$ states of an atom respectively correspond to the absence and presence of a proton bonded to that atom, NOT gate can be regarded as a quantum mechanical proton transfer. Due to the same reason, $SP$ gates can be considered as formation of a quantum mechanical hydrogen bond between the enzyme and the particular atom. 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
obtained as:

FIG. 4: A possible quantum circuit for $U$. This means that intrabase entanglement by transformation $U$ is a possible action for the enzyme DNApol.

To provide an equilibrium between maximal entanglement and robustness, we take the angles $\theta$ and $\phi$ in the quantum circuit for $U$ as $\arccos(\sqrt{2}/\sqrt{3})$ and $\arccos(1/\sqrt{2})$, respectively. Then, $|N\rangle_{WC,Q}$ states are obtained as:

$$|A\rangle_{WC,Q} = (|01\rangle - |10\rangle)/\sqrt{2},$$

$$|T\rangle_{WC,Q} = (|01\rangle + |10\rangle)/\sqrt{2},$$

$$|G\rangle_{WC,Q} = (|011\rangle + |101\rangle + |110\rangle)/\sqrt{3},$$

$$|C\rangle_{WC,Q} = (|100\rangle - |010\rangle + |001\rangle)/\sqrt{3}.$$

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

$$|A \cdot T\rangle_{WC,Q} = \frac{1}{2}(|00\rangle|11\rangle|10\rangle + |01\rangle|10\rangle|10\rangle,$$

$$|G \cdot C\rangle_{WC,Q} = \frac{1}{3}(|01\rangle|10\rangle|10\rangle + |10\rangle|01\rangle|01\rangle + |11\rangle|00\rangle|00\rangle + |00\rangle|11\rangle|11\rangle + |10\rangle|01\rangle|01\rangle + |10\rangle|11\rangle|00\rangle + |00\rangle|10\rangle|10\rangle + |10\rangle|00\rangle|10\rangle + |10\rangle|10\rangle|01\rangle).$$

If intrabase hydrogen bonds have a quantum nature as discussed, each hydrogen bonded atom pair of two paired nucleotides $(N_1 \cdot N_2)_{WC,Q}$ can be considered to be in an entangled state. Then, in order to turn intrabase entanglements into interbase entanglements, $U$ should be followed by an irreversible transformation, $S: |N_1 \cdot N_2\rangle_{WC,Q} \rightarrow |N_1 \cdot N_2\rangle_{WC,O}$, which is an entanglement swapping (Figure 5). We observe that, in the case of G-C pair, before $S$ there are two three-qubit (intrabase) entanglements and after $S$ there are three two-qubit (interbase) entanglements. Similarly, in the case of A-T pair, before $S$ there are two two-qubit entanglements and after $S$ there are two two-qubit entanglements.

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

1. Third and fifth qubits of the reordered base pair states (second and third qubits of the nucleotide base in template DNA) are subjected to a transformation $V$ as shown in Figure 6.
2. A Bell measurement is performed on the third and fourth qubits of the reordered states.
3. If the result of the measurement is one of the two Bell states $|\beta_{00}\rangle$ and $|\beta_{11}\rangle (|00\rangle \pm |11\rangle)/\sqrt{2}$, fourth and fifth qubits of the reordered states are subjected to the Pauli-X transformation.
4. A Bell measurement is performed on the first and second qubits of the reordered states.

FIG. 3: Tautomeric transition by proton transfer between enzyme and nucleotide.

FIG. 4: A possible quantum circuit for $U$ which transforms $|N\rangle_{WC,I}$ states to the $|N\rangle_{WC,Q}$ states: superposition matrix $SP(\theta)$ of controlled – Superposition gates equals to the multiplication of rotation matrix $R(\theta)$ and Pauli-Z matrix.

FIG. 5: Entanglement swapping model of replication.
5. If the result of the measurement is one of the two Bell states $|\beta_{00}\rangle$ and $|\beta_{10}\rangle$, second and fifth qubits of the reordered states are subjected to the Pauli-$X$ transformation.

![Diagram](image)

FIG. 6: Transformation $V$ in the protocol which swaps intra-base entanglements to interbase entanglements: this transformation entangles the qubits on the condition of their equality. Hadamard matrix $H$ equals to $SP(\pi/4)$.

If possible $|N_1 \cdot N_2\rangle_{WC,O}$ states are written in terms of the Bell states $|\beta_{01}\rangle$ and $|\beta_{11}\rangle (|00\rangle \pm |11\rangle)/\sqrt{2}$, then state ensembles of base pairs after $S$ are found to be

$$|A \cdot T\rangle_{WC,O} = \{0.43, |\beta_{01}\rangle|\beta_{01}\rangle|10\rangle; 0.07, |\beta_{11}\rangle|\beta_{01}\rangle|10\rangle; 0.07, |\beta_{01}\rangle|\beta_{11}\rangle|10\rangle; 0.43, |\beta_{11}\rangle|\beta_{11}\rangle|10\rangle\},$$

$$|G \cdot C\rangle_{WC,O} = \{P_{jm}^{1}|\beta_{jk}\rangle|\beta_{mn}\rangle(a_{jm}|01\rangle + b_{jm}|10\rangle)\}.$$

|TABLE I: Probabilities and probability amplitudes in state ensemble of G-C pair |
|---|---|---|---|---|
|l| $a_{00}$ | $b_{00}$ | $P_{00}^{1}$ | $a_{10}$ | $b_{10}$ | $P_{10}^{1}$ |
|1| +0.51 | -0.86 | 0.11 | +0.51 | +0.86 | 0.11 |
|2| +0.38 | +0.92 | 0.09 | -0.38 | -0.92 | 0.09 |
|3| +0.96 | -0.28 | 0.03 | -0.96 | +0.28 | 0.03 |
|4| -0.92 | +0.38 | 0.02 | +0.92 | -0.38 | 0.02 |
|l| $a_{01}$ | $b_{01}$ | $P_{01}^{1}$ | $a_{11}$ | $b_{11}$ | $P_{11}^{1}$ |
|1| +0.51 | +0.86 | 0.11 | +0.51 | +0.86 | 0.11 |
|2| +0.38 | -0.92 | 0.09 | +0.38 | -0.92 | 0.09 |
|3| -0.96 | -0.28 | 0.03 | -0.96 | -0.28 | 0.03 |
|4| +0.92 | -0.38 | 0.02 | +0.92 | -0.38 | 0.02 |

We note that, besides $U$, $S$ also consists of only proton transfer and hydrogen bonding processes, excluding Bell measurements. Bell measurements can be thought as formation of a quantum mechanical hydrogen bond between measured atom pair if the outcome state is $|\beta_{01}\rangle$ or $|\beta_{11}\rangle$. However, when the state of an atom pair collapses to $|\beta_{00}\rangle$ or $|\beta_{10}\rangle$, atom pair and DNApol can not separate from each other since total proton number of base pair does not remain constant after the measurement. Thus, Bell measurements should be treated as formation of quantum mechanical hydrogen bonds between the enzyme and measured atom pair if the outcome state is $|\beta_{00}\rangle$ or $|\beta_{10}\rangle$. In such circumstances, conditional Pauli-$X$ transformations can fix the total number of protons on base pair and make atom pair - enzyme complex separable.

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

Since all of the states in both $U$ and $S$ can be expressed as proton transfer and hydrogen bonding, our model could be tested by repeating the scenario with quantum chemical computations. Experimental verification is also possible. Evolution of the $|N_1 \cdot N_2\rangle_{WC,O}$ states in the presence of double well potentials can be prevented by sufficiently decreasing the time period between two successive pairings. Then, probability of point mutations due to the formation of rare tautomer forms may increase according to Equation 5 and Table I.

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.

Onur Pusuluk acknowledges support from TÜBİTAK National Scholarship Program for Ph.D. Students.

[1] Patel, P. H., et al., J. Mol. Biol. 308, 823 (2001).
[2] Patel, A. D., Pramana - J. Phys. 56, 367 (2001).
[3] Grover, L. K., Phys. Rev. Lett. 79, 325 (1997).
[4] Patel, A. D., Int. J. Quantum Inf. 4, 815 (2006).
[5] Cooper, W. G., Biochem. Gen. 47, 892 (2009); Biosystems 97, 73 (2009).
[6] Bose, S., et al., Phys. Rev. A 57, 822 (1998).
[7] Löwdin, P. O., Rev. Mod. Phys. 35, 724 (1963).
[8] Florián, J. and Leszczyński, J., J. Am. Chem. Soc. 118, 3010 (1996).
[9] Kryachko, E. S., Int. J. Quantum Chem. 90, 910 (2001); Kryachko, E. S. and Sabin, J. R., Int. J. Quantum Chem. 91, 695 (2003).
[10] Villani, G., Chem. Phys. 316, 1 (2005); 324, 438 (2006); Phys. Chem. Chem. Phys. 12, 2664 (2010).
[11] Villani, G., Chem. Phys. 336, 143 (2007); J. Chem. Phys. 128, 114306 (2008).
[12] Guerra, C. F., et al., Chem. Eur. J. 5, 3581 (1999).
[13] Guerra, C. F., et al., J. Am. Chem. Soc. 122, 4117 (2000); van der Wijst, T., et al., Chem. Phys. Lett. 426, 415 (2006); Guerra, C. F., et al., Chem. Eur. J. 12, 3032 (2006).
[14] Wilkens, S. J., et al., J. Am. Chem. Soc. 124, 1190 (2002); Mohajeri, A. and Nobandegani, F. F., J. Phys. Chem. A 112, 281 (2008).
[15] Kohen, A. and Kliman, J. P., Chem. Biol. 6, R191 (1999); Liang, Z., X. and Kliman, J. F., Curr. Opin. Struct. Biol. 14, 648 (2004); Sen, A. and Kohen, A., J. Phys. Org. Chem. 23, 613 (2010).