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Quantum combinatorial model of gene expression

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Abstract:
We propose that the DNA within the chromatin behaves as a dynamic combinatorial library capable of forming novel structures by reversible processes. We also hypothesize that states within the library may be linked via quantum tunneling. RNA polymerase then could scan these states and the system decoheres to the "appropriate" state. Two ways of sustaining quantum coherence at relevant time scales could be possible, first, screening: the quantum system can be kept isolated from its decohering environment, second, the existence of decoherence free subspaces .We discuss the role of superconductivity in context of avoiding decoherence in context of our hypothesis.

Keywords: Tautomeric, Decoherence, Superconductivity.

Background:
Combinatorial libraries have been extensively used in the pharmaceutical industry to discover novel drug compounds. In essence a combinatorial library: a library of related chemical compounds is synthesized by chemical methods. The combinatorial library can then be screened for identification of compounds binding to a target protein. A variation on the combinatorial library has been introduced by Ramstrom and Lehn **[1]** which has been termed as dynamic combinatorial library. This chemistry employs continuous interconversion between the library constituents to generate libraries. Novel structures are continuously generated by reversible chemical reactions which are used for spontaneous assembly and interconversion of building modules. The dynamic combinatorial library is thus able to form all variations of building blocks which however are limited by the time and chemical resources. We propose that the DNA within the chromatin behaves as a dynamic combinatorial library capable of forming novel structures by reversible processes. We also propose that states within the library are linked via quantum tunneling. These states are scanned by RNA polymerase and the system decoheres to the "appropriate" state.

Discussion:
Quantum tunneling is a term widely used in chemistry and is also termed as chemical tautomerization. Several compounds such as nucleotide bases exist as mixtures of related chemical structures known as tautomers. In context of nucleic acids tautomeric structures differ with respect to the position of protons with in nucleotides thus resulting in keto and enol forms. The alternative positions of keto and enol forms are linked by proton tunneling **[2]** and each preparation of nucleotides contains a mixture of tautomers. Each molecule of a DNA base exists as superposition of enol or keto form **(Figure 1)** linked by proton tunneling, the composition of the mixture being governed by relative stability of each tautomer. It is noteworthy that there are several molecules in the DNA that exist in such superposition. We propose that the DNA molecule exists in a superposition of all the possible tautomeric states, the search of the DNA space results in selection of most appropriate configuration of DNA for the given environmental condition/developmental stage. It is however critical that the quantum superposition of all possible states in the combinatorial library can be built up and scanned before the onset of decoherence. This is also the principle that forms the

basis of a quantum computer. That is why quantum computation is so fast.

Time scales involved

A two potential model has been proposed by Khalili and MacFadden to give a rough estimate of time scales involved. The authors have proposed a 1-dimensional quantum mechanical model of a double potential well containing a single particle that must exist in a superposition of being in both sides of the well until a measurement is made **(See supplementary material for the following equations).**

Usually a=1Å, m=10^{-27} kg (proton mass) and $\omega = 10^{12}$ Hz (terahertz vibration frequency). Thus the value of t_s comes to about 10^{12} seconds. Horsewill *et al.* **[3]** have experimentally calculated coherent proton tunneling in a hydrogen bonded network as $t_s = 10^{-7}$ seconds. The scanning of DNA molecule to explore all possibilities the quantum mechanical evolution of its wave function will involve a large number of such tunneling processes. These will involve similar timescale t_s as a quantum system isolated from its environment.

Thus decoherence time t_D is very important and is defined as the time that the full quantum superposition of all possible states in the combinatorial library can be scanned by RNA polymerase before the interaction with the environment decoheres it. After collapse the quantum state is reset and the wave function starts to evolve again. If decoherence is rapid, i.e., $t_D < t_s$, then the DNA molecule will never get a chance to scan other configurations before collapsing back to original state. However if $t_D > t_s$, then there is a chance that it will find itself in the "appropriate configuration". This scanning is extremely rapid and much faster than that achieved through chemical reactions and random thermal collisions.

A question has been raised (although in a different context) by Khallili and MacFadden that what would happen if the "appropriate configuration" of the DNA molecule is achieved after decoherence has taken place. Would this mean that the "appropriate configuration" would be lost as the wave function evolves again? The authors posit that this won't be the case. Once the appropriate configuration is selected, the DNA molecule is transcribed. This leads to significant change in the dynamics of the system. In these conditions, the thermal fluctuations are not the only source of decoherence. Here the system is coupled more strongly to environment as more nucleotides enter the transcription complex. Thus once transcription begins, then it will be permanently coupled to its environment and the transcription becomes an irreversible act (a classical measurement). In this case the DNA molecule is irreversibly dragged into the macroscopic world represented by the appropriate state. Thus in essence if the time needed for scanning of all possible structures within the quantum combinatorial library is shorter than decoherence time, quantum mechanics can speed up the process considerably. This is because the scanning time is much shorter than the time required scanning all the structures classically.

Avoiding decoherence

It is important to avoid decoherence in order to obtain the quantum mechanical advantage. Avoiding decoherence in the 'warm and wet' conditions of the cell is not trivial and our knowledge of understanding of decoherence in complex systems is far from complete. Margadonna and Prassides **[4]** have demonstrated superconductivity in doped fullerene molecules. This indicates that certain organic structures may support quantum superpositions. The use of quantum tunneling to transport charges along DNA double helix by whole transfer has been demonstrated by Giese *et al*., **[5]** as also the coherent proton tunneling in hydrogen bonded network by Horsewill *et al.* **[3].** Intramolecular quantum tunneling has been demonstrated to be responsible for room temperature chemical properties of organic chemicals such as benzene. The three π electrons have been shown to tunnel across all bonds in the benzene ring. As mentioned above the tautomeric forms also display quantum tunneling. A number of enzyme reactions **[6, 7, & 8]** have been shown to involve quantum tunneling of electrons and protons. Proton tunneling has also been demonstrated to be dominant reaction mechanism responsible for the rate acceleration performed by aromatic amine dehydrogenase **[9].** It is essential for our hypothesis that there exist some ways of sustaining quantum coherence at relevant time scales. In this context two ways have been hypothesized. The first way is screening: in this method the quantum system can be kept isolated from its decohering environment.

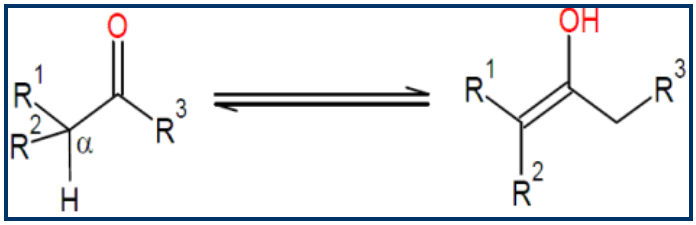

Figure 1: Keto and Enol forms of nucleotides

For instance, an active site is partially screened from van der Waals-mediated thermal interactions from the rest of the cell. In DNA the histone wrapped double helix might shield coding protons in DNA from decoherence. The second way is the existence of decoherence free subspaces. In building a quantum computer attempts have been made to identify degrees of freedom (subspaces of Hilbert space) that are not affected by coupling of the system to its environment. It is notable that when a system couples very strongly to its environment through certain degrees of freedom, it may effectively "freeze" other degrees of freedom by quantum Zeno effect, allowing entanglements and coherent superpositions to persist. Davies provides an example of a double-well one-dimensional potential (similar to the one described above). A particle which is placed in the lowest energy state of one well will shuttle back and forth through the barrier, and will oscillate with a particular frequency. However, if the particle is placed in an excited state of the well this shuttling frequency will be different. Consequently an initial state consisting of superposition of lowest energy and excited states soon evolves into a complex pattern. If the particle is now allowed to interact with external environment, the environment has the effect of forcing the complicated pattern of oscillations into synchrony, thus maintaining a limited form of quantum coherence because of environmental interactions **[10],** present an example demonstrating the above point in the context of neutrino oscillations in a medium. This model can possibly be extended to DNA.

The discovery of high temperature superconductivity has established the existence of large-scale quantum coherence at temperatures close to biological temperatures. DNA molecules act as ohmic conductors and can also superconduct **[11].**

Conclusion:

We have proposed in this paper that the DNA within the chromatin behaves as a dynamic combinatorial library capable of forming novel structures by reversible processes and that states within the library are linked via quantum tunneling. RNA polymerase scans these states and the system decoheres to the "appropriate" state. Two ways of sustaining quantum coherence at relevant time scales could be possible. In the first way, that is screening, the quantum system can be kept isolated from its decohering environment. The second way is the existence of decoherence free subspaces. The role of superconductivity in context of avoiding decoherence has been discussed in context of our hypothesis.

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Supplementry material:

Time scales involved

Such kinds of situations exist in real world such as the inversion resonance in NH_3 or strangeness oscillations in the neutral K-meson. Consider a 1-D double oscillator potential V(x), symmetric about x=0

$$V(x) = \frac{m\omega^2}{2}(|x| - a)^2$$

Where m is the mass of particle, ω is the oscillator parameter and 2α is the distance between the two sites.

If the particle starts from the right hand side of the double well then it can be represented as superposition of the lowest two eigenstates of the full Hamiltonian of the system

$$\psi(x, t = 0) = \frac{1}{\sqrt{2}}(\psi_0 + \psi_1)$$

The shuttling time that is the time taken to shuttle back and forth between the two wells is given by

$$t_s = \frac{h}{2\Delta E}, \qquad \Delta E = E_1 - E_0 \ ,$$

Where E_0 and E_1 are the lowest two energy eigenvalues. T_s is extremely sensitive to the potential parameters since

$$\Delta E = 2h\omega\sqrt{\frac{2V_0}{\pi h\omega}}\exp\left(-\frac{2V_0}{h\varpi}\right) \ ,$$

Where the height of the potential barrier between two wells is

$$V_0 = \frac{1}{2}m\omega^2 a^2 \quad .$$