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Quantum Physics and the Origins of Genetic Change: A Tutorial Approach

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Abstract

This work provides a historical overview of how heredity has been understood and a key problem in quantum biology is shed light on: the role of quantum mechanics in point mutation, a cornerstone of evolution. A foundation in core genetic concepts is provided, including the meaning and location of chromosomes and genes in cells, DNA structure, the replication mechanism, the genetic code, and tautomeric forms, mutation types,natural selection, neo-Darwinism. Finally, how Heisenberg uncertainty and quantum tunneling facilitate mutation is explored.

Keywords: Chromosomes, DNA, Genetics, Mutation, Quantum Biology,Hisenberg Uncertainty, Quantum Tunnelling, RNA.

Introduction

The journey begins with two intriguing questions: how are characteristics passed down from generation to generation, and how do entirely new traits arise in offspring? The earliest scientific theory on this topic dates back to Hippocrates. He believed that information was compiled from a man's semen and a woman's menstrual blood, and then transferred to the uterus. Aristotle, however, challenged this notion. He pointed out that a man losing a hand wouldn't result in his child being born without one. Instead, he proposed that there's an interaction between a woman's blood and a man's sperm [1] .

According to Sanskrit scripture from about 300 BC, the Charaka Samhita argues that a child’s characteristics are determined by four factors: those which are transferred by the mother’s sexual organs, by the father’s sperms, by the mother’s food, and lastly, those characteristics which pass from soul to the child’s body. Furthermore, each of these is in turn composed of four parts, and the overall sixteen factors will contribute to determining a child’s characteristics [2].

The notion of heredity changed profoundly during the nineteenth century. In 1866, Charles Darwin suggested Pangenesis as a hypothetical mechanism to describe heredity. According to this theory, each cell in an organism emits organic particles which are called gemmules. They circulate in the body and are finally collected in the gonads. The particles transfer characteristics to the next generation. Experiments in the nineteenth century did not show any evidence of these particles. But recent experiments show that nucleic acid and the prions perform the same role [3].

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The most interesting and important work on heredity was carried out by Gregor Mendel and published in 1865. The work was neglected by the scientific community until 1901 when Hugo de Vries brought Mendel's work to life. Mendel discovered the mechanism of heredity through experimentation on peas. He considered seven properties of the peas. Mendel observed that the re-appearance of the properties is controlled by certain factors which nowadays we call genes. He saw that in the first generation, some properties would not show up. He divided the properties into two and called them recessive and dominant [4].
In this work, we describe DNA and the transfer of heredity information to the next generation, and finally, we explain the role of quantum mechanics in all of this.

Chromosomes and the DNA Structure

One of the most important discoveries at the end of the nineteenth century was the chromosome. The chromosomes in cells can be seen with a normal microscope. They consist of hereditary genes called Deoxyribonucleic acid or DNA, which carries hereditary commands. The main role of DNA is to save genetic information. Deoxyribonucleic acid has a complex composition and a high molecular weight which plays a role in protein construction. The genes are units of heredity that determine the properties of an organism. Genes hold information about protein structure and are saved in DNA sequences, while in some viruses, they are saved in RNA. For a genetic property to show up, the gene must translate the information into a protein. Various proteins are activated in a cell as a result of different genes' activities. All saved genetic information is called the genome [5](Figure 1).

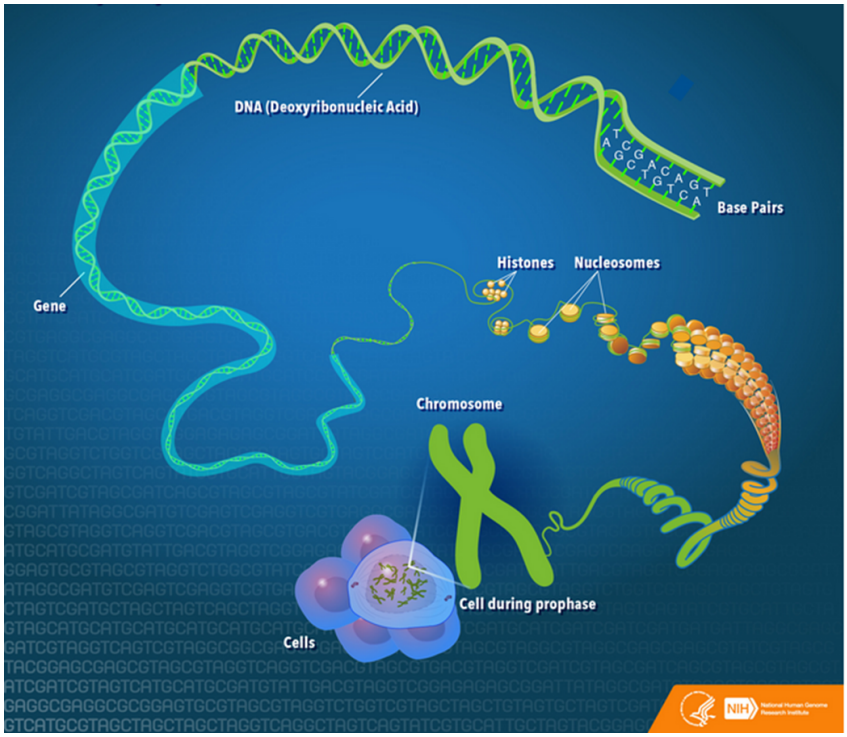

Figure 1. Location of genes and chromosomes in a cell/Source: National Genome Institute.Licensed under a CC-BY-3.0 License

The number of chromosomes in a human cell is 46 (2x23), and the number of genes is approximately 19,000-20,000. Sometimes DNA is called a map, as it holds all the commands that are necessary to make all parts of a cell, including proteins and RNA. Some parts of DNA are the bases for genes, while other parts of DNA build structures or make

arrangements of information. A chimerical view of DNA is a long polymer with some basic blocks as nucleotides. The strands that hold everything together consist of sugar and phosphate groups that are connected via ester linkages (organic acids that make up a composition as esters, having a general formula of R-CO-OH). As we mentioned, DNA exists inside each cell's nucleus. It consists of two strands of sugar and phosphate and pairs of bases: thymine (T), adenine (A), guanine (G), and cytosine (C). Together, sugar, phosphate, and a base form a nucleotide. All the information about a cell's activities is encoded by the arrangement of these four nucleotides. The nucleotides consist of deoxyribose sugar, a phosphate group, and one of the four bases that we mentioned above, which are nitrogen bases. The molecule is like a curled ladder named the double helix. The ladder part of the molecule, composed of sugar-phosphate molecules and their neighbor nucleotides, holds covalent interactions, and there is a hydrogen connection between the phosphates that form the curled DNA strand. Nitrogen bases are tied together. Both nucleotides hold a hydrogen link, and they are DNA units. In a DNA molecule, adenine is always connected to thymine (A-T), while cytosine is connected to guanine (C-G) [6].

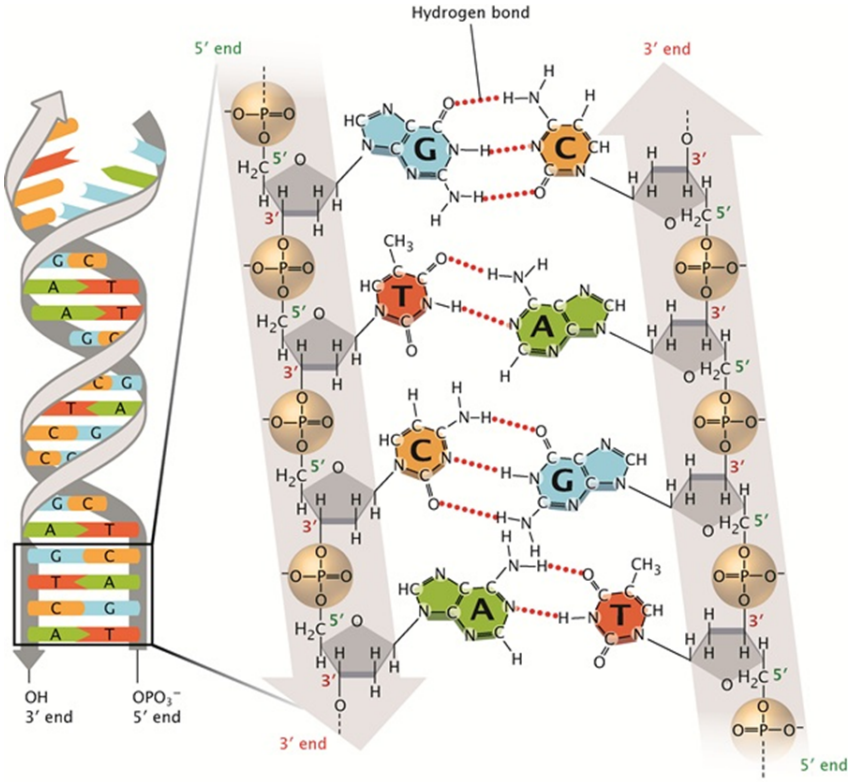

Figure 2. The DNA Structure[6].Licensed under a CC-BY-3.0 License.

The main question in any evolutionary process is what causes or initiates a change. How have changes in a species happened and been saved? At the beginning of the twentieth century, a Danish botanist by the name of Hugo de Vries invented the word "gene" to distinguish an individual's phenotype from its genotype.

He observed in a potato farm a completely new type of Oenothera lamarckiana which was longer than the normal ones and whose petals were oval-shaped rather than the normal heart-shaped ones. He understood the flower should be a mutant, and he showed that the mutant characteristics transferred to the next generation [7].

T. H. Morgan from Columbia University studied Hugo De Vries's mutants. He used the fruit fly as his subject. He exposed them to intense X-rays, used strong acid on them, and gave them poison. It was only in 1909 that he managed to find fruit flies with blue eyes [8].
This approach is known as the Mendelian approach. A combination of this approach with natural selection is also known as Neo-Darwinism, whereby a mutation is caused by a change in the genetics of the parent cell. This process produces, provided that natural selection supports it, a more adaptable new species. If, on the other hand, natural selection is not in favour of the new change, then the new species is discarded. The successful mutations will be saved for the next generations to come, and evolution carries on.
In Neo-Darwinism, the mutation occurs completely at random, i.e., the changes do not occur in response to just one environmental variation. While the environment keeps on changing, it will require a very long stretch of time for an adaptable mutation to happen and persist. This approach is in sharp contrast to the Lamarckian approach of evolution, whereby mutation occurs as a consequence of an environmental challenge and is saved, similar to that of giraffe neck lengthening. The theory of natural selection was discarded then, but it regains its importance nowadays [9].

Mutation process and Types

There an example of a gene is described that allows us to visualize the patterns of sequence variation caused by mutations. We compare the variations we see within human species with those seen between humans and other animals,the gene BRCA1. Women with mutations in this gene have a significantly increased risk of cancer [10]. The BRCA1 protein is involved in oxidative DNA damage repair. If this protein does not function correctly, DNA damage can accumulate in individual somatic cells, and occasionally this leads to cancer [11].
Mutations can disrupt the function of a gene in several different ways: small deletions of one or more nucleotides in the DNA coding region, large deletions and insertions, and several inversions. Genes have evolved through many millions of years of natural selection, so we expect them to usually be quite good at what they do. Therefore, most mutations introduced into a functional gene sequence are deleterious [12] . Of course, not all mutations are harmful. Some will be neutral and there must be occasional useful mutations that increase the fitness of the sequences. If there was no beneficial mutation, the gene sequences could never have evolved in the first place to be functional [13].

The BRCA1 gene has been sequenced in many other species as well as humans, where a significant portion of their loci is identical to each other, which would exhibit a significant degree of conservation in mammals. All of these sequences must have come from a common ancestor at some point in the past. They have gradually diverged from each other due to the fixation of different mutations in different species [14]. The DNA structure allows the contributed enzymes and proteins to come to the loop. Each of the double helix strains is an inverse of the other, which means that the final point of one is the start point of another. The stages of replication can be summarized as follows: an enzyme as DNA Gyrase influences the double helix, another enzyme as Helicase separates into strains, then a massive number of tiny proteins as Single-stranded DNA binding proteins(SSBs) connect to the DNA fibers to hold separation of the two strains; finally, the DNA polymerase enzyme in the length of DNA fiber moves and when finds an A base connects to a T, and if finds a C base connects it to a G then again all the process is tested, and finally two Double Helix is produced (Figure 1Proton Transfer.5). If everything were done perfectly and correctly, no variation would be observed, but, sometimes and rarely, everything is not perfect, and an error occurs. Based on three

parameters: human and chimpanzee nucleotide divergence at each site 0.012, and effective ancestral population size 2 to 3 and species divergence time between six to seven million and generation length 15 to 25 years, mutation rate estimated between $(2.2 - 1.1) \times 10^{-8}$ per position [15] . Here, the important question is: how does that occur?

Tautomerization Process

Watson and Crick, the founders of DNA, suggested in 1953 that a process such as tautomerization is the cause of mutations, which is basically the motion of protons inside a molecule (tautomers are typical isomeric compositions with the same molecular formula, but their connected mutual bonds group to the circle between inside and outside the circle can change) [16]. Every physicist knows that any process that deals with the motion of protons is a quantum mechanical one. Schrödinger, in his book "What is Life," published in 1943, mentioned that mutation should fall in the quantum mechanical realm. Was Schrödinger correct?

In Figure 3, the hydrogen bonds are shown as dashed lines between oxygen and nitrogen. This implies that there is a shared proton. A proton is a quantum entity holding simultaneously both particle and wave properties. According to quantum mechanics, the position of the proton cannot be known exactly. It moves between two bases. The position of the proton (H) is not exactly in the middle of the two bases, but it is closer to one of them. This asymmetry is necessary for an important feature of DNA replication.
Consider a pair (e.g., A-T), where A is on one strand and T is on the other, and together they hold the two hydrogen bonds (protons), where one of the protons is nearer to the nitrogen atom and the other near the oxygen atom in T (Figure 3a). It opens a possibility to make a hydrogen bond at A-T. However, there is a set of possibilities to find the particles in many places. If the two protons that they hold (genetic letters) jump to the other side of the hydrogen bond, then this means that they become close to the other bases [17].

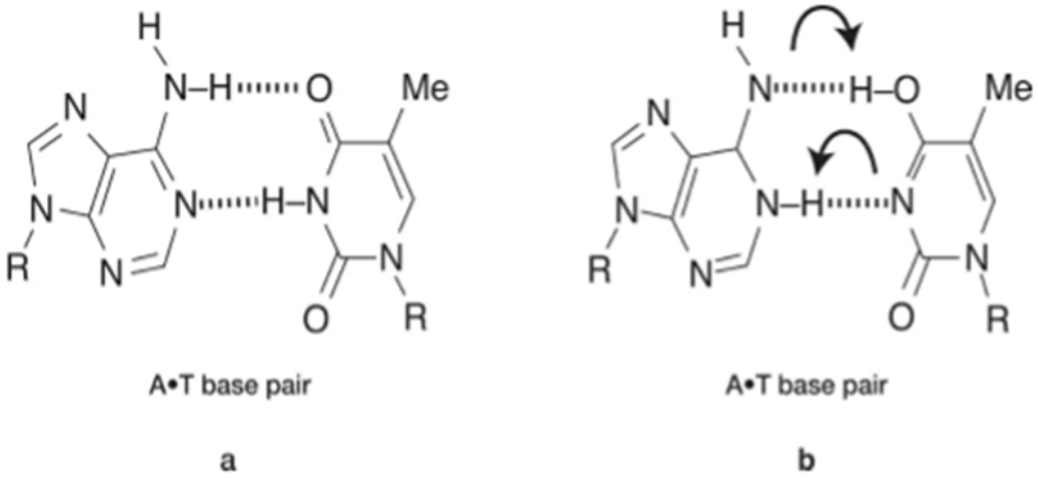

Figure 3. (a) Standard double bases of A-T with their protons in normal positions. (b) The double protons make a mutation in the cross of the double helix to produce a tautomeric form of both A and T [17], p. 223.Licensed under a CC-BY-3.0 License

We know that the protons, which make hydrogen bonds in the DNA, are responsible for determining the double bases that are used in genetic code replication. So if encoded protons move (in the opposite direction), they can alter the genetic code. For example, if a genetic letter on a DNA strand is T, which normally pairs with A, a tautomeric shift can cause both A and T to adopt rare tautomeric forms. These forms can temporarily alter their pairing properties. While protons may jump back to their original positions, if they do so while in their tautomeric forms, errors can occur during DNA replication. The tautomeric forms of guanine and thymine are known as enol or keto depending on the proton positions, while cytosine and adenine can adopt amino or imino forms.

During DNA replication, if a base is in its tautomeric form, it can pair incorrectly. For example, if T is in a rare tautomeric form, it may pair with G instead of A. Consequently, G will be incorporated into the new strand, while A remains in the old strand. Similarly, if A is in a tautomeric form, it may pair with C instead of T, leading to a mismatch in the new strand. Such mismatches during DNA replication can lead to mutations, which are changes in the DNA sequence that can be passed onto future generations.

Of course, it is not easy to provide direct evidence for the above assumption. However, in 2011, a research group at Duke University [18] tried to clear that mistake of coupled bases in DNA with protons in tautomeric form. Actually, it can stay on in the DNA polymerase places. Therefore, it is possible to suddenly change to a new DNA that exhibits mutation. However, it appears that tautomers are the cause of mutations, and evolution proceeds in this way. But the question is, why do the protons move toward the wrong positions? Few classical solutions state that the reason goes back to the molecular vibrations caused by external factors.

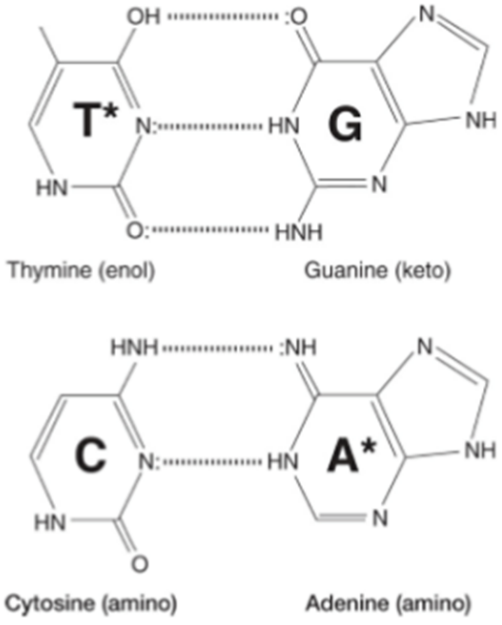

Figure 4. In the tautomeric form (enol), shown as T*, T wrongly connects to G instead of A. Similarly, A can make a mistake and connect to C. If these errors happen during DNA replication, then mutations will occur [17], p225. Licensed under a CC-BY-3.0 License

Entering Quantum Mechanics

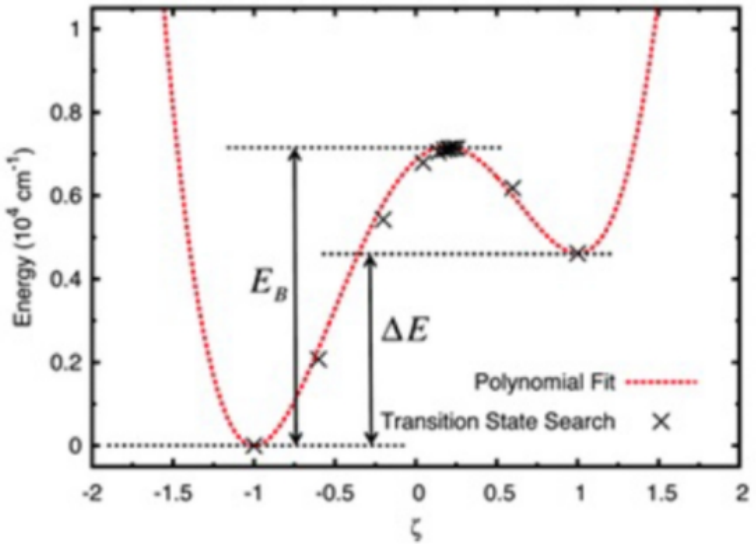

Figure 5. Adenine-Thymine potential. Reused from [19].Licensed under a CC-BY-3.0 License.

Figure 5 shows the potential energy profile of the hydrogen bond between adenine and thymine bases on DNA. The potential represents two asymmetric wells. Protons must overcome the energy barriers to move from right to left. This is possible if influenced by nearby water molecules, of which there are only a few. Another way to achieve the same is quantum tunnelling. It is a phenomenon that allows particles to appear or exist in classically forbidden locations. Quantum tunnelling can pave the way for the protons to overcome hydrogen bonds to create tautomeric forms [5].

Another approach for determining the probability of finding the proton in the right well is the time-energy form of the Hiesenberg uncertainty principle. where $\Delta t\ \Delta E = \hbar$, in this equation Δt represent uncertainty in time, ΔE represent uncertainty in energy and ħ is reduced planck constant (h=6.6×10^{-34} joule/second) over 2π . The energy of the barrier lies in the range of IR and approximately is equal to 6300cm^{-1} or 0.784 ev=$1.256 \times 10^{-19} j$. From this we can obtain$\Delta t \approx 0.83 \times 10^{-15} s$.

This is a quantum mechanical limitation on the measurement of time in the hydrogen bond of DNA.The minimum measured time in biological processes can be on the order of femtoseconds [20], and the above number is a reasonable estimate. We assume that the proton appears automatically, without any specific cause, in the right-side well.

DNA mutations can be formed by different mechanisms, for instance, chemical destruction, ultraviolet rays, radioactive decay, and cosmic rays. All these mechanisms are based on the molecular level, which truly can be regarded as a quantum mechanical process.

If quantum tunneling plays a role in the basic tautomeric forms of DNA, then quantum mechanics will have a vital role in mutations that produce further mutations.

According to McFadden and Al-Khalili [17], the tautomeric forms of DNA bases provide approximately 0.01% of all natural DNA bases, which is able to make the same ratio of errors, namely, much more than 1 in a billion, the ratio of mutations in nature. Therefore, if the tautomer bases are in a double helix shape, then many errors will be corrected, which keeps high fidelity in DNA replication.

By a simple model, it can be shown that quantum tunneling can actually occur in DNA bonds. Figure 6, shows a double asymmetric rectangular well approximation for the potential in the figure 5, where $x \rightarrow \frac{x(position)}{2a} = \varsigma$ and $2a$ is the distance between the two minima and the energies are in $\frac{1}{cm}$. Eq.1 shows the mathematical interpretation of the potential.

$$V(x) = \begin{cases} \infty & \text{if } x < -1.5 \\ 0 & \text{if } -1.5 \leq x < -0.5 \\ 6300 & \text{if } -0.5 \leq x < 0.5 \\ 4000 & \text{if } 0.5 \leq x < 1.5 \\ \infty & \text{if } x \geq 1.5 \end{cases} \quad \text{(eq.1)}$$

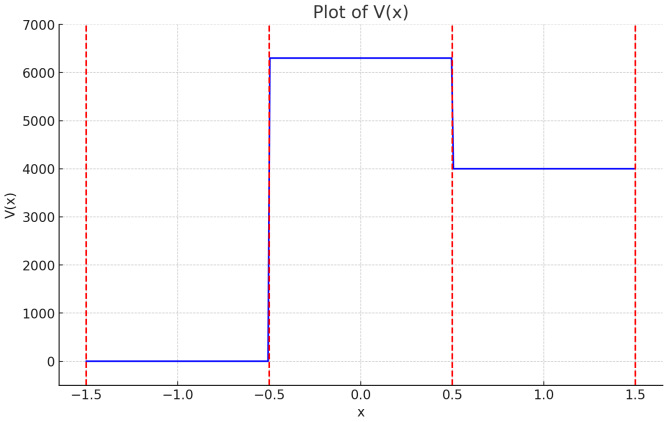

Figure 6. Double asymmetric rectangular well approximation for the potential in the figure 5. by solving the schrodinger equation (eq.2) for the above potential, the normalized wave function for each region can be obtained.

The time-independent Schrödinger equation in one dimension is:

$$-\frac{\hbar^2}{2m}\frac{d^2\psi(x)}{dx^2} + V(x)\psi(x) = E\psi(x) \quad \text{(eq.2)}$$

In the regions $x > 1.5$ and $x < -1.5$ because $V(x) = \infty$ then

$\psi(x) = 0$

In the region $-1.5 < x < -0.5$, $V(x) = 0$, the Schrödinger equation simplifies to:

$$-\frac{\hbar^2}{2m}\frac{d^2\psi(x)}{dx^2} = E\psi(x) \quad \text{(eq.3)}$$

The general solution for (eq.3) is:

$$\psi(x) = A\sin(kx) + B\cos(kx) \quad \text{(eq.4)}$$

where

$$k = \sqrt{\frac{2mE}{\hbar^2}} \qquad \text{(eq.5)}$$

In the region $-0.5 < x < 0.5, V(x) = 6300$,The Schrödinger equation in this region becomes:

$$\frac{d^2\psi(x)}{dx^2} = \frac{2m}{\hbar^2}(6300 - E)\psi(x) \quad \text{(eq.6)}$$

Let

$$k_1 = \sqrt{\frac{2m(6300 - E)}{\hbar^2}} \qquad \text{(eq.7)}$$

The general solution is:

$$\psi(x) = C\sin(k_1 x) + D\cos(k_1 x) \quad \text{(eq.8)}$$

In the region $0.5 < x < 1.5, V(x) = 4000$

The Schrödinger equation becomes:

$$\frac{d^2\psi(x)}{dx^2} = \frac{2m}{\hbar^2}(4000 - E)\psi(x) \qquad \text{(eq.9)}$$

Let

$$k_2 = \sqrt{\frac{2m(4000 - E)}{\hbar^2}} \qquad \text{(eq.10)}$$

To find the coefficients A, B, C, D, F, and G, we need to solve these boundary condition equations simultaneously. This typically involves solving a system of linear equations, which requires numerical methods using Python code and the hosted Jupyter Notebook service Colab. By considering the case where a proton has been localized in the left well, the eigenvalues and eigenfunctions of the Schrödinger equation can be obtained.

The first five energy eigenvalues and their corresponding wave functions are shown in Figure 7.

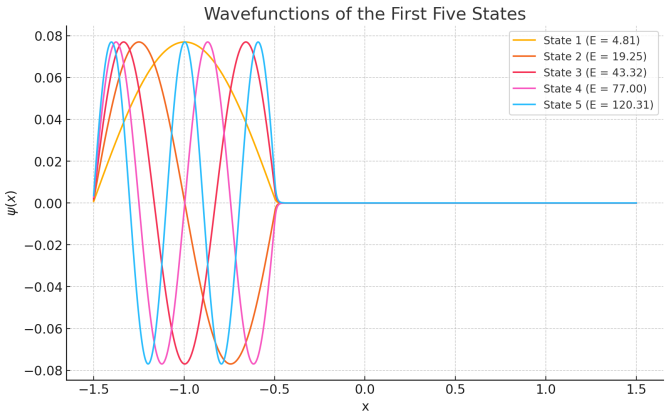

Figure 7. The first five energy levels and their corresponding wave functions.

Figure 8 shows the wave function and eigenvalues for the states 28, 29, and 30. It can be seen that the wave function in the state 29 appears in the well on the right side. This means we have a probability of observing the particle in a classically forbidden region of the potential. In quantum mechanics, this is known as tunneling.

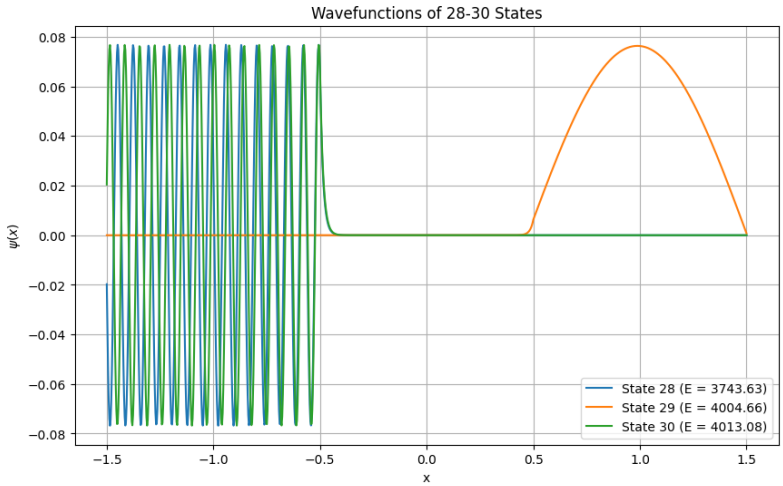

Figure 8. The wave function and eigenvalues for the states 28, 29, and 30 show tunneling in state 29.

The study by A. D. Godbeer, J. S. Al-Khalili, and P. D. Stevenson investigated the potential for quantum tunneling to create adenine-thymine tautomers within DNA. Their findings suggest that quantum tunneling is unlikely to be a significant mechanism for this process, even when considering thermal effects. The probability of tunneling was found to be extremely low, at a maximum of 2×10^{-9} ,which does not change significantly with different initial conditions or potential energy surface geometries [19]. This aligns with the statement that quantum tunneling cannot be easily turned on or off, making it challenging to measure its impact compared to other mutation causes like chemical mutagens and radiation.

There may be a way to show that quantum mechanics is a cause of mutation. This can be done by comparing classical and quantum information. Classical information can be read many times without changing it, while quantum information changes each time by measurement. Hence, when the DNA polymerase enzyme breaks a DNA strand to find the position of a codon proton, it actually performs a quantum measurement. If the proton state

corresponds to a genetic code letter, then the measurement can be regarded as a cause of mutation.

Although all of the genome of the cell is copied at the time of DNA replication, most of the reading of the genes doesn't occur at the time of DNA replication; it occurs at the time of the process wherein genetic information is applied for protein synthesis. The process is divided into two parts: transcription and translation. The copying of information from DNA to RNA and from RNA to protein machinery synthesizes. In the process, it is possible that one gene more than others is read. If the reading of the DNA code during transcription is via quantum measurement, then we should expect the deformation of a gene to be possible. Of course, that increases the probability of mutation. Studies on human genes show that genes that are read in a high state more readily accept mutation. Although the evidence is consistent with quantum measurement, they do not prove they hold quantum mechanics.
Reading of DNA holds chemical interactions that can, via various ways, destroy molecular structures and cause mutations without necessarily invoking quantum mechanics. Yet in biology, we need certain evidence of quantum mechanics' role.

Conclusions

This tutorial article begins with a historical background of mankind's activities from ancient Greece to clarify the causes behind heredity and the evolution of species. In summary, it examines the sources of genetic mutations and the causes behind mutations during DNA replication. The tautomerization process is introduced, and for the adenine and thymine bond, it is shown through two approaches, Heisenberg uncertainty and quantum tunneling, that the proton of the hydrogen bond can appear in a classically forbidden position. This can lead to the formation of a rare tautomeric form for either T or A, which can cause misconnection between bases. If during DNA replication these misconnections are not corrected, they can be passed on to the next generation as mutations.

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