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On the definition and evolution of the quantum states of biological systems at cellular level

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"Quello che voglio dire è che Dio mi ha offerto di amare e di servire un determinato luogo, e che mi ha fatto fare, per onorare questo luogo, un sacco di cose… diciamo così… bizzarre, in modo che io potessi testimoniare, contro tutti gli infiniti e contro tutti i sofismi, che il Paradiso è in un certo luogo e non dovunque, e che è qualcosa di preciso e non qualsiasi cosa. E io, dopo tutto questo, non sarei affatto sorpreso di scoprire che, se dovesse esserci una casa in cielo per me, questa dovrebbe avere davvero un lampione verde."

Chesterton, Uomo Vivo

A Via Celoria 16. Alla comunità del Clu di fisica, la mia patria; perchè ora posso andare via consapevole di avere trovato un lampione verde e una cassetta postale rossa. Per cui non perdo niente, ma riguadagno sempre di più tutto.

Summary

Chapter 1

Introduction

In this first chapter, I will look at the origin of quantum biology. How and why physicists in the second half of the 20th century had to introduce a new way of studying living organisms and physiological processes on mesoscopic scales by trying to bring together the studies of theoretical chemistry with quantum mechanics. I will therefore try to explain the motivations and studies that led to the emergence of this new branch of physics.

Quantum biology is the study concerning the application of principles of quantum mechanics and theoretical chemistry to biology.

It uses computer models to analyse and reveal the nature of biological processes that are fundamental to living organisms. This science deals with the influence of non-trivial quantum phenomena, which can be explained by reducing the biological process to fundamental physics, although these effects are difficult to study and may be speculative in nature.

In addition, I will describe three applications that have brought fame to this new branch of physics, which have been attracting the interest of many scientists worldwide over the past ten years.

Although quantum effects are difficult to observe at the macroscopic level (long timescales and large distances) with time it has been discovered that the processes necessary for the overall function and thus survival of the organism appear to be based on quantum mechanical dynamical effects, even at the molecular level [1].

1.1 The Origins of Quantum Biology

The origins of the topic go back to the pioneers of quantum mechanics at the beginning of the 20th century. Indeed, some of the insights provided by some of these physicists are still relevant to our understanding of quantum biology today.

Quantum biology's origins are often traced back to **1944** with the publication of Erwin Schrödinger's famous book, *What is Life?* [2]. Even before this, several other quantum physicists had already made inroads into biology. For example, the German physicist Pascual Jordan published a book a year before Schrödinger's, entitled "Physics and the Secret of Organic Life" [3] , in which he had posed if the laws of atomic and quantum physics were important for life. In fact, Jordan thought about this question for over a decade and used the term Quantenbiologie since the late 1930s. The murky origins that motivated and sustained his interest in quantum biology are inextricably linked to his political sympathies with Nazi Germany and play an important role in explaining why the field did not flourish further after the war ended.

Quantum biology was in fact born shortly after the development of quantum mechanics itself. By 1927, the mathematical framework of the new quantum mechanics was in place, thanks to the efforts of Bohr, Heisenberg, Pauli, Schrödinger, Dirac, Born, Jordan, Fermi and others. Flushed with their success at taming the atomic world, and with the arrogance of youth on their side, many quantum pioneers strode out of their physics laboratories and away from their blackboards to seek new areas of science to conquer.

It was only natural therefore for many to ask whether the new atomic physics might also have something to say about the building blocks of life. Advances in experimental physics around this time were also posing new questions. Just as Robert Hooke's microscope had opened up a new world of the very small in the mid-seventeenth century, new techniques and key experiments in the decades between the two world wars helped lay the foundations of

an even smaller, molecular biology. These included the discovery of X-ray mutagenesis by H.J. Muller in 1927, Theodor Svedberg's measurement of the atomic weights of proteins by using his famous ultra centrifuge in the mid-1920s and, later, the crystallization of a virus by W.M. Stanley in 1935. These and other breakthroughs promoted a feeling of optimism that, with the tools of quantum mechanics, the secrets of life could finally be laid bare.

However, not everyone was so confident that the principles of physics and chemistry would be sufficient to explain biology. One such critic was Niels Bohr himself; and yet, as we shall see, it was Bohr's pessimism regarding the importance of quantum mechanics in unlocking the secrets of life that would, paradoxically, influence and inspire the men who would lay the foundations of quantum biology.

At the same time as the quantum revolution was taking place in physics, enormous strides were being made in biology through neo-Darwinian synthesis, which brought together the rediscovered principles of Mendelian heredity with the mutations identified by Hugo de Vries and Thomas Hunt Morgan [4].

However, many mysteries remained, specially surrounding the nature of the heritable material. Microscopic studies at the end of the nineteenth century associated visible chromosome fibres with Mendel's heritable factors, called at the time "genes". Biochemical studies established that chromosomes consisted of proteins and nucleic acids; but the intrinsic mechanisms of how the genetic information is written into ordinary chemicals and then inherited remained a complete mystery.

The idea of **vitalism** held that that there is a "life force" that gives organisms a special quality, absent in inanimate matter, and these scientists and philosophers were convinced that certain aspects of life required principles outside of classical science. For example, in 1907, the French philosopher Henri Bergson first published his Creative Evolution, in which he argued that heredity and evolution were driven by an 'élan vital' peculiar to the living [5].

Many scientists remained similarly unconvinced that the extraordinary dynamics of life and heredity could be accounted for by classical sciences such as thermodynamics, organic chemistry and physics.

1.1.1   The Organicists

Another factor influencing the birth of quantum biology is more subtle and has to do with the philosophical movement of **organicism** that was popular with many of the leading scientists of the time. Organicism was a reaction to two opposing schools of thought in biology.

The first was mechanism, whose origins go at least as far back as the French Philosopher René Descartes, who maintained that all living organisms are essentially machines, differing in complexity but not in principle from those machines that had driven the Industrial Revolution. The movement tended to be reductionist in the sense that it maintained that in biology, just as in all inorganic phenomena, the whole is no more than the sum of its parts. According to the mechanists, all life should ultimately be explainable in terms of the fundamental building blocks of matter and the forces that connect them, each obeying deterministic physical and chemical laws.

The opposing position to this is that of vitalism, which has deep roots in the religions and mythologies of the ancient world.

The organicists sought a middle ground. They accepted that there was something mysterious about life but claimed that the mystery could in principle be explained by the laws of physics and chemistry, only that these had to be new laws, yet undiscovered. One of the early proponents of organicism was Ludwig von Bertalanffy, generally accepted as the founder of the interdisciplinary field called "general systems theory", which has since been applied to everything from biology to cybernetics. His work is considered to be among the forerunners of systems biology. In his 1928 book Kritische Theorie der Formbildung (Critical Theory of Morphogenesis) [6], he claimed that there

was a need for new organizational principles to describe life. His ideas influenced many other scientists, including the German physicist Pascual Jordan, who was one of the authors of the famous 1925 Dreimännerwerk (Three-man paper), together with Max Born and Werner Heisenberg. This classic paper introduced the world to matrix mechanics, the mathematical framework on which quantum mechanics is built. The following year, Jordan moved to Copenhagen to work with Niels Bohr.

In 1929, Bohr gave a lecture to the Scandinavian Meeting of Natural Scientists entitled "The atomic theory and the fundamental principles underlying the description of nature" [7]. After mainly focusing on the successes of quantum mechanics in describing the nature of the atomic and subatomic world, he moved on to consider whether it might have something to say in biology:

"Before I conclude, it would be natural at such a joint meeting of natural scientists to touch upon the question as to what light can be thrown upon the problems regarding living organisms by the latest developments of our knowledge of atomic phenomena which I have here described."[7]

It was not clear what Bohr was hinting at with his remark about "the problems of living organisms". He continue attempting to clarify his philosophical views, particularly on the measurement problem in quantum mechanics, as well as his ideas on "complementarity", which will be discussed further below. Indeed, in his 1929 lecture, he emphasized in his typically vague way that

"... the development of the atomic theory has... first of all given us a recognition of laws which cannot be included within the frame formed by our accustomed modes of perception; the lessons we have learned by the discovery of the quantum of action open up to us new prospects which may perhaps be of decisive importance, particularly in the discussion of the position of living organisms in our picture of the world."
[7]

But, despite the ambiguity of these words, Bohr was nevertheless a hugely charismatic and inspiring figure and his interest in the link between quantum mechanics and life encouraged Pascual Jordan further to develop his own ideas. After returning to Germany, as professor at the University of Rostock, Jordan maintained over the next couple of years a regular correspondence with Bohr regarding the relationship between physics and biology over the next couple of years. Their ideas culminated in what is arguably the first scientific paper on quantum biology. The papaer was written by Jordan in 1932 and appeared in the German journal with the title "Quantum mechanics and the fundamental problems of biology and psychology" [3].

Jordan incorporated the organicism approach into his thinking by claiming that life's missing laws were the rules of chance and probability (the indeterminism) of the quantum world that were somehow scaled up inside living organisms. Jordan was convinced he could extend quantum indeterminism from the subatomic world to macroscopic biology. He even made a connection with free will by suggesting a link between quantum mechanics and psychology.

Jordan's belief that living organisms have a unique ability to amplify the quantum into the macroscopic world does have a lot of resonance with modern views of quantum biology. However, he went much further and, in doing so, ultimately discredited the entire field by attempting to link his theories to Nazi philosophy in a mutual legitimization. Indeed, his biological speculations became increasingly politicized and aligned with Nazi ideology, due to his genuine sympathy to fascism. He even claimed that the concept of a single dictatorial leader (Führer), or guide, was a central principle of life:

"We know that there are in a bacterium, among the enormous number of molecules constituting this creature a very small number of special molecules endowed with dictatorial authority over the total organism, they form a steering centre of living cell. Absorption of light quantum anywhere outside of this centre can kill the cell just as little as a great nation can be annihilated by the killing of a single soldier.

But absorption of a light quantum in the steering centre of the cell can bring the entire organism to death and dissolution similar to the way a successfully executed assault against a leading statesman can set an entire nature into a profound process of dissolution." [3]

Despite his politicized biological speculations, he correctly pointed out that inanimate objects were governed by the average random motion of millions of particles, such that the motion of a single molecule has no influence whatsoever on the whole object. This insight, as we will see, is usually credited to Erwin Schrödinger, who later claimed that life was different from inorganic chemistry because of its dependence on the dynamics of a small number of molecules. Jordan similarly argued that the few molecules that control the dynamics of living cells within the "Steuerungszentrum" have a dictatorial influence, such that quantum-level events that govern their motion, such as Heisenberg's uncertainty principle, are amplified to influence the entire organism.

In August 1932, the same year that Jordan published his Naturwissenschaften paper, Niels Bohr delivered another key lecture, at the International Congress on Light Therapy in Copenhagen, Denmark [8]. Like Jordan, he was influenced by the organicists' view that the mysterious ingredient of life was yet to be discovered; but, rather than opting for quantum indeterminacy, Bohr claimed that the mystery ingredient was a quantum concept he had helped to conceive: complementarity. Often referred to as waveparticle duality, seen as the central tenet of quantum mechanics.

Indeed, for Bohr, the notion of complementarity went deeper than merely describing the dual nature of quantum entities, which later he attempted on expanding it into a broader philosophical notion. But, in its simplest form, it can be applied, for example, to the nature of light, which can exhibit both wave-like and particle-like properties, but never both at the same time: the properties are complementary. Bohr attempted to extend this notion into biology by arguing that there was an analogous complementarity between

the functionality of life and our ability to study it. On a fishing trip in the Baltic around 1932, Werner Heisenberg reports a conversation on Darwinian theory in which Bohr suggests the following:

Through the process of heredity, nature tests rejecting the great majority and preserving a few suitable ones. But there is the second assertion: that the new forms originate through purely accidental disturbances of the gene structure. This claim is much more questionable [9].

Several decades and a world war later, in the early 1960s, Heisenberg was considering the same question when, at a meeting on the banks of Lake Starnberg in Germany and listening to a lecture about mutation and selection, he pondered whether,

"Something like intention were associated with Darwinian mutation... We could ask whether the aim to be reached, the possibility to be realised, may not influence the course of events. If we do that, we are almost back with quantum theory. For the wave function represents a possibility and not an actual event. In other words, the kind of accident that plays so important a role in Darwinian theory may be something very much subtler than we think, and this precisely because it agrees with the laws of quantum mechanics" [9].

1.1.2 The Cambridge Theoretical Biology Lab

The interest in the physical basis of life was not limited to mainland Europe. In the summer of 1932, an interdisciplinary group of scientists at the University of Cambridge set up the Theoretical Biology Club with the ambitious aim of solving "the great problem" of whether life could be explained by the actions of atoms and molecules. The group's aim, like its counterparts in Germany and Austria, was to explore whether the "new physics" (i.e. quantum mechanics) could provide novel laws in biology.

Members of the group included some of the most influential scientists in early twentieth century biology, including biochemist Frederick Gowland Hopkins, who was awarded the Nobel Prize in Physiology or Medicine in 1929 (with Christiaan Eijkman for the discovery of vitamins), Joseph Woodger, who had translated Bertalanffy's 1928 book into English, developmental biologist Conrad Waddington, and the great evolutionary biologist and geneticist J.B.S. Haldane.

In 1934, Haldane wrote a paper entitled "Quantum mechanics as a basis for philosophy" [10], where he clarifies his position by arguing that, at the molecular level, life differs from inanimate matter in that it can be influenced on the macroscale by single events at the quantum level, If bacteria are heated or poisoned with certain reagents, the number of survivors falls off exponentially. This is taken to mean that the life of the cell depends on a single unstable molecule, whose change involves its death. As the transformation of such a molecule involves the uncertainty principle, this principle plays a large part in the life of bacteria. But higher organisms, even protozoa, behave as if their life depended on a number of similar molecules. The uncertainty principle in this form plays a less important part in their lives. They are protected from it by the laws of statistics, just as are large material particles consisting of many molecules.

By the end of the 1930s, a number of highly influential scientists on both sides of the Atlantic were examining the implications of the "new physics" for biology, driven by a growing mechanistic picture of biology at the smallest scales, but under the umbrella of organicism.

However, the Second World intervened to curtail any further progress. Meanwhile, Pascual Jordan became increasingly politicized and evermore determined to link his ideas in quantum biology with Nazi ideology, with the conviction that, "after the victory, it could stand as a symbol and representation of the unbounded means of power of the new Reich" [11]. In 1941, he published the book Die Physik und das Geheimnis des organischen Lebens

(Physics and the Secret of Life) [12], in which he continued to pose the question "Are the laws of atomic and quantum physics of essential importance for life?" However, after Germany's defeat, Jordan's highly politicized ideas became anathema. The other matchmakers of the proposed marriage between biology and fundamental physics were scattered in the aftermath of the Second World War; and physics, shaken to its core by the atomic bomb, turned its attention to more traditional problems.

1.2 Order from Order

In this section I describe one of the most important ideas developed by Erwin Schrodinger in his book "What is life?"[2].

By 1940s, it was known that genes governed heredity, but nobody knew what genes were made of. Schrödinger was impressed by the extraordinary high fidelity of genetic inheritance, which had been shown to be associated with mutation rates of less than 10^{-8} per gene per generation. He claimed that high fidelity of heredity could not be accounted for by the classical laws, because genes were too small.

Schrödinger's argument starts from a consideration of the laws of classical physics and chemistry, such as those of thermodynamics or the gas laws. He called these "order from disorder" laws to reflect the fact that their orderliness is a product of underlying disorderly molecular dynamics. He pointed out that their accuracy is limited by $\frac{1}{\sqrt{N}}$, where N is the number of particles involved.

So, a balloon filled with a trillion particles deviates from the strict behaviour of the gas laws by only one part in 1 million, thereby providing relatively accurate gas laws for such macroscopic systems. However, a balloon filled with only 100 particles will deviate from orderly behaviour by one part in 10, or 10%, and will thereby experience significant deviations from the gas

laws. For example, all the molecules in the balloon will sometimes, randomly, move towards its centre, causing the balloon to contract while at a constant temperature, thereby violating Boyle's law.

This, he argued, created a problem in understanding the physical basis for the fidelity of heredity because genes were known to be too small to be subject to the order from disorder laws. Using target theory, he estimated the size of a gene as no bigger than a cube of sides 300 Angstrom containing a maximum of about 1 million atoms, so the level of noise in heredity if based on the order from disorder principle should be about one in 1000, or 0.1% clearly much higher than the observed mutation rates.

Schrödinger concluded that the accurate laws of heredity could not be founded on these order from disorder classical laws. He argued that genetic information had to be encoded at the molecular level as "an unusually large molecule which has to be a masterpiece of highly differentiated order, safeguarded by the conjuring rod of quantum theory" [2].

Schrödinger called this principle on which he claimed life depended "order from order", arguing that "incredibly small groups of atoms, much too small to display exact statistical laws, do play a dominating role in the very orderly and lawful events within a living organism" [2].

On the nature of genes, he claimed that genetic information must be encoded by a "more complicated organic molecule in which every atom, and every group of atoms, plays an individual role, not entirely equivalent to that of many others " (as is the case in a periodic structure).

"We might quite properly call that an aperiodic crystal or solid" [2]. Schrödinger claimed that life was sensitive to the dynamics of small numbers of particles, and indeed, its structure and dynamics were encoded at the atomic level. He even suggested that "mutations are actually due to quantum jumps in the gene molecule" [2], note that what Schrödinger meant by "quantum jumps" is quantum tunnelling through a finite potential barrier, rather than the old notion of quantum jumps of electrons between energy levels.

Schrödinger's book influenced both James Watson and Francis Crick, the co-discoverers of the DNA double helix, and was a factor in their decision to investigate the nature of genes. According to Watson, "this book very elegantly propounded the belief that genes were the key components of living cells and that, to understand what life is, we must know how genes act" [13]. The years following the publication of Schrödinger's book a large development of the molecular biology without any reference to quantum phenomena, i.e. the discover of DNA double helix and the meteoric rise of molecular biology, a discipline which developed largely without reference to quantum phenomena.

Physicists similarly dismissed the possibility that quantum effects could play a role in biology, particularly due to the extraordinary level of control (vacuum, temperature) that would be needed to show case them in organic physical systems. Quantum phenomena such as tunnelling or quantum interference effects depend on a system being well isolated from its surroundings. This was considered to be unsustainable for biologically relevant time scales within a hot, wet and complex system such as a living cell.

There were, however, occasional forays into the borderland between biology and quantum mechanics. When Watson and Crick published their structure of DNA they speculated that mutations could be caused by tautomerization of DNA bases from their common imino forms to the rare enol forms, which could produce incorrect base pairs during DNA replication. The idea received a quantum twist from the Swedish physicist Per-Olov Löwdin, who proposed [11] that quantum tunnelling of protons could generate the tautomeric bases, thereby providing a physical mechanism for Schrödinger's speculation that random point mutations might have a quantum origin. But few geneticists knew of or were influenced by Löwdin's work. Thus, the prevailing view in the 1960s not needed among biologists, biophysics and biochemists was broadly dismissive of the notion that quantum mechanics played any kind of special role in living systems.

For example, the writings of Christopher Longuet Higgins, a British theoretical chemist who made major contributions to molecular chemistry using mathematical modelling and analysis. In 1962, Longuet-Higgins wrote a paper entitled "Quantum mechanics and biology" [14], in which he was scathing of attempts to justify the importance of quantum mechanics in biology.

Let us then summarize the role of the early quantum pioneers. The organicists, such as Von Bertalanffy, were convinced that the deterministic classical laws of physics and chemistry were insufficient to account for the phenomena of life and that there was a missing ingredient yet to be discovered. Quantum physicists, such as Bohr, Schrödinger and Jordan, took this as a cue and suggested that quantum physics was that missing ingredient. They seized on the notions of complementarity and the uncertainty principle to claim that measurement and quantum randomness may play a role in evolution, perhaps even providing some directional control to the evolutionary process. However, this claim was largely discredited and nearly all biologists remain wedded to the notion that there is no directionality in the mutational driver of evolution. The remaining ideas were vague such as the central role that some physicists such as Eugene Wigner ascribed to life, or rather to consciousness, as the magical ingredient necessary to solve the measurement problem [15].

On the other hand, both Jordan and Schrödinger identified a real point of contact between quantum and biological processes that is highly relevant to today's work in quantum biology: macroscopic biological phenomena may be triggered by the dynamics of relatively small numbers of particles whose behaviour is ruled or at least influenced by the non-trivial quantum phenomena such as uncertainty. Jordan referred to a "very small number of special molecules endowed with dictatorial authority over the total organism" [12]; whereas Schrödinger insisted that "incredibly small groups of atoms play a

dominating role in the very orderly and lawful events within a living organism" [2].

Schrödinger went on to point out that this reliance on the dynamics of small numbers of particles separates biological systems with their order from order principle from macroscopic inanimate systems dominated by laws obeying the order from disorder principle. These ideas were picked up by some biologists, such as Haldane, who similarly insisted that "higher organisms, even protozoa, behave as if their life depended on a number of similar molecules" [10]. Although, reflecting the interests of their times, these quantum pioneers were particularly interested in the role of the uncertainty principle in life, their insights are transferable to the non-trivial quantum mechanical phenomena, such as coherence, tunnelling and entanglement, which are the focus of most modern quantum biology.

Also significant is Schrödinger's claim that "The living organism seems to be a macroscopic system which in part of its behaviour approaches purely mechanical (as contrasted to thermodynamical) behaviour to which all systems tend, as the temperature approaches the absolute zero and the molecular disorder is removed" [2]. In this, Schrödinger was essentially pinpointing the role of the randomizing influence of thermal motion,what we refer to today as "environmental decoherence" [16], which no need separates the quantum from the classical world, and is often traced back to the work of Dieter Zeh [17].

Schrödinger is essentially claiming that living systems somehow circumvent decoherence, an idea that resonates with modern work on the role that environmental noise may play a role in maintaining coherence in living cells, as I will show in the next chapter.[1]

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[1]Frolich's Case: During the 1960s and 1970s, there remained, however, a few physicists who entertained the possibility that quantum mechanics played a key role in biology. For example, the German-born British physicist Herbert Fröhlich proposed a theory in which quantum mechanical coherence, now known as Fröhlich coherence, plays an important role in biological systems [18], [19], [20]. A biological system that attains such a state of coherence is known as a Fröhlich condensate. He argued that biological organization was facilitated by coherent excited states at the molecular level, driven by the flow of energy provided by metabolic processes that generate molecular vibrations in terahertz range. While highly controversial, there is a current interest in testing this hypothesis experimentally using available sources of intense terahertz radiation [21].

Chapter 2

First results of Quantum Biology

In this chapter, I will describe three applications that have brought fame to this new branch of physics, and attracted the interest of many scientists worldwide over the past ten years. Quantum effects are subtle, with the fundamental unit of $\approx 10^{34} \frac{J}{s}$ (that is a very small value). In addition, quantum effects, like superposition and entanglement, are easily destroyed by the interaction with the environment. This explains why we usually do not observe quantum effects in the macroscopic world. A rule of thumb is the famous $k_B T$ argument, stating that whenever the interacting energies are smaller than room temperature, quantum effects cannot persist. However, as quantum mechanical laws are fundamental, in special situations the consequences of quantum mechanics can be macroscopic. The explanation of the photoelectric effect revealed the quantised nature of energy carriers (photons) and the importance of energy levels. But, what about quantum effects in biology? For a long time the prevailing view was that in "warm and wet" biological systems quantum effects cannot survive beyond the trivial, i.e. explaining the stability of molecules. In the first part of this introduction I will explain why the $k_B T$ argument fails, later I will briefly outline how quantum effects can be harnessed in biological systems (i.e. ion channels, photosynthesis and the olfactory sense, which are not covered in this thesis).

2.1 The $K_B T$ argument

The $k_B T$ argument is a mean-field argument that is very useful for many systems to estimate the possible impact of quantum mechanics on a given physical system. The most simplistic argument against quantum effects in biological systems is that life usually operates at $300 - 310K$, which is by far too hot to allow for quantum effects. Let me explain the argument in more detail to show where it breaks down when dealing with living systems. A physical system with a given Hamiltonian $\hat{H}$ in thermal equilibrium is described by the density operator

$$\rho_{Thermal} = \frac{e^{-\beta \hat{H}}}{Z} = \sum_{i=0}^{N} p_i |i\rangle \langle i| \tag{2.1.1}$$

where $\beta = \frac{1}{k_B T}$ denotes the inverse temperature, $|i\rangle$ the orthonormal basis of the Hamiltonian, $Z = Tr(e^{-\beta \hat{H}})$ and $p_i = \frac{e^{-\beta E_i}}{Z}$ the probability to be in state $|i\rangle$ with corresponding energy E_i. If the energies E_i are small compared to the temperature, then all probabilities are roughly equal, $p_i \approx \frac{1}{Z}$. Due to thermal fluctuations, it is impossible to predict which state $|i\rangle$ the system occupies, and thus the thermal state is the totally mixed state $\rho_{Thermal} = \frac{1}{d}$ with d the dimension of the Hilbert space. It is impossible to process any information with the maximally mixed state, as any unitary operation will leave the maximally mixed state unchanged. On the other hand, if the energies are very small compared to the temperature, then the $k_B T$ argument presumes the system to be in its ground state. However, there are many situations where this line of argument fails, among them non-equilibrium dynamics, entanglement and effective temperatures in complex systems.

2.2 Non Equilibrium

Some quantum effects are sensitive to temperature. For example in quantum computing, to use ion traps or quantum dots the systems have to be cooled to few Kelvin [22]. But the thermal argument is only true for equilibrium states.

Let us consider spin systems in more detail. Electron spins have two possible states, and for typical organic molecules, the energy difference between these two states is much smaller than thermal energy. At room temperature the spin is in a fully mixed state, thus, spins cannot be entangled at room temperature. However, dynamical systems avoid the equilibrium state. It was shown theoretically that two spins, given a suitable cycling drive, can maintain their entanglement even at finite temperature and coupled to the environment [23] . This is a good example to show how our intuition fails in non equilibrium situations. Even though, every thermal state in the parameter regime is separable, the non-thermal state passing along the parameter curve is not! Another possibility is to use quantum effects before the system had time to equilibrate with the environment. In spin chemistry, a weak magnetic field, on the order of $1 - 10mT$ is shown to influence the rate of chemical reactions [24]. This fields are incredibly weak compared to thermal noise, the ratio is around $\mu_{B}B/k_{B}T \approx 10^{-5}$. The only explanation of how such weak fields can alter the outcome of chemical reactions is by manipulating the spins of the involved molecules. This is of fundamental importance for animal magneto reception, i.e. a species of bird (European Robin), is believed to use this sort of electron entanglement to measure earth magnetic field [25] for navigation. I will briefly discuss this result later.

2.3 Entanglement

An other example that shows the break of the $K_{B}T$ is presented by the Van der Waals forces in DNA. Van der Waals bonding is one of the weakest chemical bonds. As will be explained in chapter 4 DNA consists of a sequence of the four nucleic acids. The electron clouds of neighbouring sites have dipole-dipole interaction, resulting in an attractive van der Waals bonding. The coupling between nucleic acids leads to phonons with frequencies ω in the optical range, with large interaction energies compared to thermal energy, $\frac{k_{B}T}{\omega} << 1$. The simple $k_{B}T$ argument states that as the first excited state has

so much more energy than thermally available, the DNA has to be in its electronic ground state. For each single uncoupled nucleic acids this is true, but the situation changes in a strand of DNA due to the coupling. The attractive part of the dipole dipole interaction reduces energy, and also creates entanglement between the π electron clouds of the bases. The electronic system is globally in the ground state. As a consequence of the global entanglement, the system has to be locally in a mixed state. It is impossible to distinguish with local measurements whether a local state is mixed due to temperature or due to entanglement. In chapter 4 it will be shown that entanglement creates local mixtures that correspond to more than $2000K$ of thermal energy.

2.4 Quantum enhanced processing of classical information

In the above paragraph I argued why quantum effects can exist in biological systems, here I will show how they can be advantageous. The first two examples of biological systems, photosynthesis and ion channels, use coherence for transport problems. The other examples, avian compass, olfactory sense and DNA, deal with the determination of classical information using quantum channels. Spin correlations enable European robins to measure the earth magnetic field, in which the interacting spins constitute quantum channels, which lead to the classical knowledge needed for navigation. In the olfactory sense a quantum channel, phonon assisted electron tunnelling, is employed to identify different molecules.

2.5 Single particle - Coherence

Coherence effects play a fundamental role in transport problems, which is of importance for systems like ion channels or photosynthetic complexes (transferring electronic excitations). Describing coherence keeps track of more information than just the probabilities of being in a certain state. Consider the

most simple quantum state, a qubit:

$$\rho = \begin{pmatrix} p_0 & c_{01} \\ c_{02} & p_1 \end{pmatrix}$$
(2.5.1)

where p_i are the probabilities to be in state $|i\rangle$ and $c_{01} = c_{10}^*$ quantify the coherence $|0\rangle\langle 1|$ between the two states. While the p_i's can be directly measured, the coherences are more subtle. The state ρ will have a different time evolution for different values of c_{01}. This is known as interference effects. If $c_{01} = 0$, then the particle is in a mixture of states (either $|0\rangle\langle 0|$ or $|1\rangle\langle 1|$), which is unknown to the observer. If $c_{01} \neq 0$, then the particle can be in superposition of both states. While it is always possible to find a basis in which the state ρ is diagonal, some bases are intuitively preferred.

In the case of the double slit experiment, see fig. 2.1, this basis is the left ($|L\rangle$) and right ($|R\rangle$) path. In this experiment the key question is whether a single particle passes through either the left or right slit (no coherence), or both slits simultaneously (requires $|L\rangle\langle R|$ coherence terms).

If there is no path coherence, the particle will go through either of the slits, and give rise to a classical pattern on the screen. With path coherence, the particle goes through both slits simultaneously and will interfere with itself giving rise to an interference pattern on the detector screen.

Coherence describes a particle's ability to exist in several distinct states simultaneously. These states can represent, for example, position, energy or spin in the case of a superposition of positions, a particle can gather non-local information.

2.5.1 Ion channel

Coherence can be utilised in transport problems, because interference patterns are very sensitive to a couple of parameters, e.g. the mass of the particle. It is a standing conjecture ([26]) that interference effects might explain the efficiency of ion channels in cells.
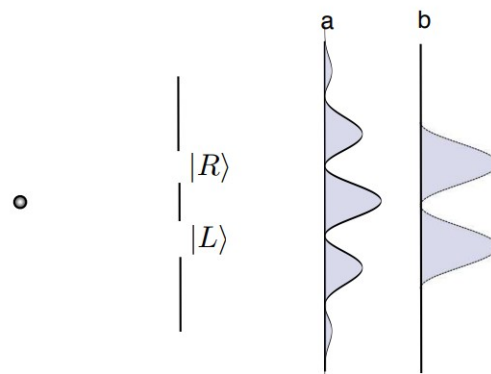
FIGURE 2.1: *This graphic shows a typical double slit experiment. Photons are sent through the double slit, leading to either pattern a or b on the detection screen. If it can be known through which slit a photon passed, there exists no path coherence and the detection screen shows a classical pattern (b), with highest arrival probability directly behind the open slits. However, if no path information leaves the system, the photons fly through both slits simultaneously. This path coherence leads to the typical interference pattern (a). With coherence the photons can arrive at positions on the detector screen which are classically forbidden, i.e. in the centre of the screen. Because of this ability to change arrival destinations, interference effects are important for transport problems.*
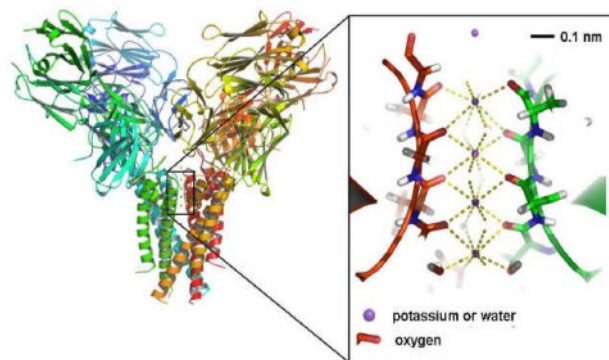

FIGURE 2.2: *Schematic illustration of the KcsA postassium channel taken from ([26]) . This protein complex is composed by four transmembrane subunits (left) and selects with four axial trapping sites formed by the carbonyl oxygen atoms in which a potassium ion or a water molecule can be trapped. Path coherence along the trapping sites can lead to ion species selected transport*

For a cell or bacterium to function properly it needs to maintain a delicate balance of different ions inside and outside the cell. This non-equilibrium steady state is achieved with the use of ion pumps and channels, see fig. 2.2. The problem for an ion channel is to be highly permeable for one species of ions, but tight for other ions. The potassium channel for example transmits around 10^8 potassium ions per second through the membrane, while only 10^4 transmitted sodium ions. As both sodium and potassium ions carry the same charge, the key difference between the ions is their **mass, thus, it is thus postulated that the ion channels use interference for ion selected transport**.

2.5.2 Photosynthesis

The transport problem that received the most scientific attention is photosynthesis. After photon absorption the electron excitation needs to be transported to the reaction centre, where a chemical reaction converts the energy into sugar. It was shown experimentally, that at low temperatures the photosynthetic complex FMO supports coherent transport over a short period ([27]). There are a number of papers investigating the details of the transport and the importance of coherence in the system. Further, there is a good amount of evidence that suggests that the existence of coherence speeds up the transport in the first part of the time evolution (see ([28]) and references therein). The second part, interaction with the environment, decoheres the system. It turns out that this decoherence further speeds up the excitation transfer, as it keeps the system from being trapped in dark states.

2.6 Entanglement of two Particles

When discussing the behaviour of two particles, the most interesting point is the correlations between them. Quantum information typically distinguishes two kinds of correlations: classical correlations and entanglement.

Entanglement is a strange quantum mechanical property that allows two or more particles to be stronger correlated, that they would be classically correlated. This also means that while the global state is perfectly known, the local state is fully mixed. Let us consider a spin singlet state in more detail. Note, that I ignored the thermal influence for now and focus on the properties of the ground state of the two particle system at zero temperature. The wave function is given by $|\psi\rangle = \frac{1}{\sqrt{2}}(|\uparrow\downarrow\rangle - |\downarrow\uparrow\rangle)$, or as a density operator

$$\rho = |\psi\rangle\langle\psi| = \frac{1}{2}\begin{pmatrix} 1 & 0 & 0 & -1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ -1 & 0 & 0 & 1 \end{pmatrix} \tag{2.6.1}$$

While this state looks somewhat similar to the above coherence example, there are distinct differences. The coherence terms in the corner show that the spins of two spatially separated electrons simultaneously are anti-correlated. That means that each individual electron has not a defined spin. Mathematically this is more clear when taking the partial trace of the state, i.e. write down the individual state (density operator) of a single electron

$$\rho_A = Tr_B |\psi\rangle\langle\psi| = \frac{1}{2}\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{2.6.2}$$

which is the fully mixed state. As previously mentioned, the simple $k_B T$ fails in the presence of entanglement. How can a single particle be in a fully mixed state at zero temperature? Also note, that when a single particle is entangled with another one, it cannot have the above described self-coherence. **Thus, entanglement creates non-local correlations and non-thermal excitations**.
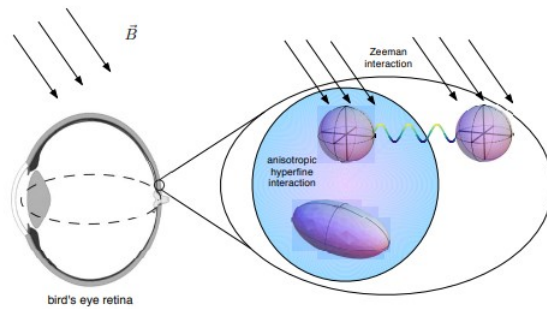
FIGURE 2.3: *According to the RP model, the back of the bird's eye contains numerous molecules for magnetoreception ([32]). These molecules give rise to a pattern, discernible to the bird, which indicates the orientation of the field. In the simplest variant, each such molecule involves three crucial components (see inset): there are two electrons, initially photo-excited to a singlet state, and a nuclear spin that couples to one of the electrons. This coupling is anisotropic, so that the molecule has a directionality to it*

2.6.1 Avian compass

The field of spin chemistry investigates the influence of spin correlations between two spatially separated electrons on chemical reactions. There is experimental evidence ([29],[30],[31]) that a migrating species of birds, the European Robin, exploits this feature to navigate in Earth magnetic field.

The ratio of Earth magnetic field energy to thermal energy is about $\frac{\mu_B 60 \mu T}{k_B 310 K} \approx 10^{-8}$. It is still puzzling for the scientific community how birds are able to detect this minuscule signal. For the avian compass to work, the spins of the two electrons need to be correlated. The easiest way to create the correlations is by using Pauli exclusion principle to initialise the two electrons in a singlet state. Coherent single electron photoexcitation and subsequent electron translocation leads to an entangled state, which provides the necessary spin correlations. While both electron spins interact with the earth magnetic field, one of them additionally interacts with a nuclear spin, which causes the state of the electrons to oscillate between singlets and triplets. After some time the excited states relax either in a singlet or triplet state, leading to different chemical end products. The required information about the earth magnetic field is encoded in the oscillation frequency and can be recovered by detecting the relative amount of singlet or triplet chemicals.

2.7 Vibrations of many particles

For many particle systems, vibrations are a common phenomenon. Vibrations, or phonons, describe the collective movement of many particles. The dynamics of vibration can either be quantum or classical. One characteristic parameter of vibrations is their frequency. Molecules have a unique spatial arrangement of atoms, linked by chemical bonds acting as springs, thus, each molecule has an individual set of characteristic vibrations. In the olfactory sense, experimental evidence supports the hypothesis that these vibrations are measured using phonon assisted electron transport ([33], [34]). Even though molecular vibrations can be described efficiently using classical methods, this mechanism still has a remarkable sensitivity to the quantum details of a molecule. It has been demonstrated that fruit flies can distinguish between normal fragrant molecules and deuterium enriched molecules, although the molecules have a very similar shape.

Chapter 3

A quantum Model for DNA

In this chapter I analyze a quantum model for the information processed and stored in DNA. It has been shown that the electronic degree of freedom is delocalized and maintains coherence even at room temperature [35]. Than I will try to develop a simpler model to understand if it is possible to arrive at a minimal theory that will characterize in the same way the results that quantum biologists have already reached. In the first model [35], the electron cloud of DNA nucleic acids is a chain of coupled quantum harmonic oscillators with a dipole-dipole interaction at the nearest neighbors modeling the Van Der Walls bond. The coupling and distance between amino acids, crucial parameters of the model are tabulated in the literature and are estimated by numerical simulations [36].

It will be shown that for realistic parameters nearest neighbour entanglement is present even at room temperature and I will quantify the amount of entanglement in terms of negativity and single base Von Neumann Entropy. The strength of the single base Von Neumann Entropy will depend on the neighbouring sites, thus questioning the notion of treating single bases as logically independent units. An expression for the binding energy of the coupled chain in therms of entanglement will be derived and I will show **the connection between entanglement and correlation energy, a quantity commonly used in quantum chemistry**.

3.1 The molecular biology about DNA interactions

Many numerical studies explain the importance of dispersion energies in DNA [36]. Dispersion energies describe attractive van der Waals forces between non-permanent dipoles, which has recently been discovered as an important factor for stabilizing macromolecules [37], [38]. Modelling macromolecules, such as DNA, is a tedious and complex task. It is currently nearly impossible to fully quantum mechanically simulate the DNA. Quantum chemistry has developed several techniques that allow the simulation of DNA with simplified dynamics. In [36] the authors first quantum mechanically optimise a small fragment of DNA in the water environment. Then, using molecular dynamics, they described the potential energy which is divided into the electrostatic and Lennard-Jones terms. The former term is modelled by the Coulomb interaction of atomic point-charges, whereas the latter describes repulsion and dispersion energies,

$$V(r) = \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}} + 4\epsilon \left[\left(\frac{\sigma}{r_{ij}} \right)^{12} - \left(\frac{\sigma}{r_{ij}} \right)^{6} \right] \qquad (3.1.1)$$

where the strength of the dispersion energy is scaled with the parameter ϵ. For $\epsilon = 1$ the dynamics of the DNA strand is normal. For a weaker dispersion, $\epsilon = 0.01$, there is in increase of 27% in energy in the DNA. This increase of energy induces the unravelling of the double helix to a flat, ladder-like DNA. Many factors contribute to the spatial geometry of DNA, e.g. water interaction, the phosphate backbone, etc. However, one of the strongest contributions is the energy of the electronic degree of freedom inside a DNA strand, which is well shielded from interactions with water. Stronger interaction ($\epsilon = 1$) allows the electrons clouds to achieve spatial configurations that require less structural energy. This allows a denser packing of the electron charges inside the double helix.

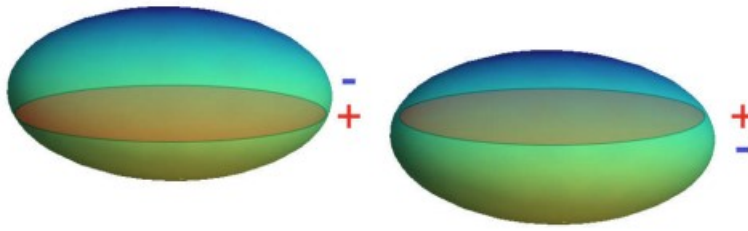Here I investigate with a simple model of DNA whether continuous variable

FIGURE 3.1: *This graphic shows a sketch of a DNA nucleic acid. The mostly planar molecules are divided into the positively charged molecule core (red) and the negatively charged outer π electron cloud (blue-yellow). In equilibrium the centre of both parts coincide, thus there is no permanent dipole. If the electron cloud oscillates around the core, a non permanent dipole is created. The deviation out of equilibrium is denoted by (x, y, z). The corresponding dipole is $\bar{\mu} = Q(x, y, z)$. This oscillation might be caused by an external field, or induced by quantum fluctuations, as it is given in a DNA strand.*

entanglement can be present at room temperature, and how this entanglement is connected to the energy of the molecule. There are many technically advanced quantum chemically calculations for van der Waals type interaction, i.e. [39]. The aim of this work is to understand underlying quantum mechanical features and their role in this biological system. It will be shown that chemical bonds are described by entanglement.

3.2 Dispersion energies between nucleic acids

The nucleic bases adenine, guanine, cytosine and thymine are planar molecules surrounded by π electron clouds. I model each base as an immobile positively charged centre while the electron cloud is free to move around its equilibrium position, see 3.1.

There is no permanent dipole moment, while any displacement of the electron cloud creates a non-permanent dipole moment. Denoting the displacement of two centres by (x, y, z), I assume the deviation out of equilibrium $|(x, y, z)|$ to be small compared to the distance r between neighboring bases
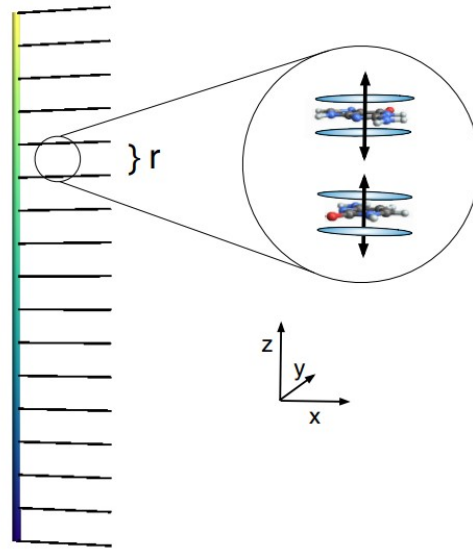
FIGURE 3.2: *This graphic shows a sketch of a single DNA strand. The chain is along z direction. Each bar in the single strand DNA represents one nucleic acid: adenine, thymine, guanine or cytosine. Around the core of atoms is the blue outer electron cloud. The oscillation of these electron clouds is modelled here as non-permanent harmonic dipoles, depicted by the arrows, with trapping potential Ω_d in dimension $d = x, y, z$.*

in chain. The displacement of each electron cloud is approximated to a second order process and described by a harmonic oscillator with trapping potential Ω that quantifies the Coulomb attraction of the cloud to the positively charged centre.

A single DNA strand resembles a chain of harmonic oscillators 3.2, where each two neighboring bases with distance r have dipole-dipole interaction. The Hamiltonian for the DNA strand of N bases if given by

$$H = \sum_{j, d=x,y,z}^{N} \left(\frac{p_{j,d}^2}{2m} + \frac{m\Omega_d^2}{2} d_j^2 + V_{j,dip-dip} \right) \tag{3.2.1}$$

where d denotes the dimensional degree of freedom, and the dipole potential

$$V_{j,dip-dip} = \sqrt{\epsilon} \frac{1}{4\pi\epsilon_0 r^3} \left(3(\bar{\mu}_j \cdot \bar{r}_N)(\bar{\mu}_{j+1} \cdot \bar{r}_N) - \bar{\mu}_j \cdot \bar{\mu}_{j+1} \right) \tag{3.2.2}$$

with $\bar{\mu}_j = Q(x_j, y_j, z_j)$ dipole vector of site j and $\bar{r}_N$ normalised distance vector between site j and $j+1$. Due to symmetry $\bar{r}_N$ is independent of j. I choose

periodic boundary conditions, i.e. $\bar{\mu}_{N+j} = \bar{\mu}_j$. The dimensionless scaling factor ϵ is varied to study the effects on entanglement and energy identical as in [37]. In order to compare this model with [37], I consider 'normal' interaction, where the dipole dipole interaction has full strength modelled by $\epsilon = 1$ and 'scaled' interaction, where the dipole-dipole interaction is reduced to a hundredth of the original strength modelled by $\epsilon = 0.01$. The distance between neighbouring bases in DNA is approximately $r_0 = 4.5$. For generality I will not fix the distance. In general the single strand of DNA will not be perfectly linear and thus the dipole potential has coupling terms of the form xz etc. Detailed analysis following [40] shows that the energy contribution from the cross coupling terms is small, and they will be ignored here. This leads to the interaction term

$$V_{j,dip-dip} = \frac{Q^2}{4\pi\epsilon_0 r^3}(x_j x_{j+1} + y_j y_{j+1} - 2z_j z_{j+1}) \qquad (3.2.3)$$

The different signs for x, y and z reflect the orientation of the chain along z direction. A discrete Fourier transformation of the form

$$d_j = \frac{1}{\sqrt{N}} \sum_{l=1}^{N} e^{i\frac{2\pi}{N}jl} \hat{d}_l \qquad (3.2.4)$$

$$p_{j,d} = \frac{1}{\sqrt{N}} \sum_{l=1}^{N} e^{-i\frac{2\pi}{N}jl} \hat{p}_{l,d} \qquad (3.2.5)$$

decouples the system into independent phonon modes. These modes can be diagonalized by introducing creation operator $a_{d,l} = \sqrt{\frac{m\Omega_d}{2\hbar}}(\tilde{d} + \frac{i}{m\Omega_d}\tilde{p}_{p,l})$ and annihilation operator $a_{d,l}^\dagger$.

It can be computed the dispersion relation

$$\omega_{xl}^2 = \Omega_x^2 + 2\left(2cos^2\left(\frac{\pi l}{N}\right) - 1\right)\frac{Q^2}{4\pi\epsilon_0 r^3 m} \qquad (3.2.6)$$

$$\omega_{yl}^2 = \Omega_y^2 + 2\left(2cos^2\left(\frac{\pi l}{N}\right) - 1\right)\frac{Q^2}{4\pi\epsilon_0 r^3 m} \qquad (3.2.7)$$

Nucleid Acid	α_x	α_y	α_z	Ω_x	Ω_y	Ω_z
Adenina	102.5	114.0	49.6	4.1	3.9	6.0
Cytosine	78.8	107.1	44.2	4.7	4.1	6.3
Guanine	108.7	124.8	51.2	4.0	3.8	5.9
Timine	80.7	101.7	45.9	4.7	4.2	6.2

TABLE 3.1: *Numerical values for polarizability of different nucleid acid bases [41] in units of* $1au = 0.164 \cdot 10^{-40} \, Fm^2$. *The trapping frequencies are calculated using the formula* $\Omega = \sqrt{\frac{Q^2}{m_e \alpha}}$ *and are given in units of* $10^{15} Hz$.

$$\omega_{zl}^2 = \Omega_z^2 + 2\left(2sin^2\left(\frac{\pi l}{N}\right) - 1\right)\frac{Q^2}{4\pi\epsilon_0 r^3 m} \tag{3.2.8}$$

and the Hamiltonian in diagonal form

$$H = \sum_{l=1, d=x,y,z}^{N} \hbar\omega_{dl}\left(n_{d,l} + \frac{1}{2}\right) \tag{3.2.9}$$

where $n_{d,l} = a_{d,l}^\dagger a_{dl}$ is the number operator of normal mode l in direction d. The trapping potentials Ω_d can be found in letterature (see table 3.1) throught the relation $\Omega_d = \sqrt{\frac{Q^2}{m_e \alpha_d}}$, where α_d is the polarizability of nucleid base. The number of electrons in the cloud, will not be discussed [1]. In Table 3.1 it is assumed the number of interacting electrons to be one, but the final results are independent of this special choice.

Although the values for the four bases differ, all show similar $\Omega_x \approx \Omega_y$ (transverse), while there is an increase of 50% in the longitudinal direction, $\Omega_z \approx \frac{2}{3}\Omega_{x,y}$. In the following the chain will be approximated to have the same value of trapping potential at each base. In x,y direction I will use $\Omega_{x,y} = 4 \cdot 10^{15} Hz$, and in z direction $\Omega_{x,y} = 6 \cdot 10^{15} Hz$.

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[1]Both the trapping potential Ω_d^2 and the interaction term $\frac{Q^2}{m}$ depend linearly on the number of electrons, and thus the dispersion frequencies $\omega_{d,l}^2$ have the same dependence. The quantities of interest in this chapter are entanglement and energy ratios, which are both given by ratios of different dispersion frequencies and are thus invariant of the number of electrons involved

3.3 Entanglement and Energy

I now investigate the influence of entanglement on energy. I will also derive an analytic expression for the change in binding energy depending on entanglement witnesses.

An entanglement witness W is an operator that is positive on all separable (biseparable) states. Thus, $Tr(W\rho) < 0$ signals entanglement [42].

The chain of coupled harmonic oscillators is entangled at zero temperature, but is it possible to have entanglement at room temperature?

There is a convenient way to calculate a criterion for nearest neighbour entanglement for harmonic chains [43], which compares the temperature T with the coupling strength ω between neighbouring sites. In general, for $\frac{2k_B T}{\hbar\omega} < 1$ one can expect entanglement to exist. Here the coupling between neighbouring clouds is given by $\omega = \sqrt{\sqrt{\epsilon}\frac{Q^2}{4\pi\epsilon_0 mr^3}} \approx \epsilon^{\frac{1}{4}} 1.6 \cdot 10^{15} Hz$ for $r = 4.5$ Å, which leads to $\frac{2k_B 300K}{\hbar\omega} = 0.05$ for $\epsilon = 1$, and 0.16 for $\epsilon = 0.01$. This means that the coupling between electron clouds is dominant compared to the temperature, and thus implies the existence of entanglement even at biological temperatures. An exact method to quantify the amount of entanglement in harmonic states is the violation of one of the two inequalities, related to the covariance matrix the state [44].

$$0 \leq S_1 = \frac{1}{\hbar}\langle(d_j + d_{j+1})^2\rangle\langle(p_{d,j} - p_{d,j+1})^2\rangle - 1 \tag{3.3.1}$$

$$0 \leq S_2 = \frac{1}{\hbar}\langle(d_j - d_{j+1})^2\rangle\langle(p_{d,j} + p_{d,j+1})^2\rangle - 1 \tag{3.3.2}$$

with d_j the position operator of site j in direction d and $p_{d,j}$ the corresponding momentum operator. If one of the inequalities is violated, the sites j and $j+1$ are entangled.

The negativity, a widely used measure for entanglement, is calculated using the formula $Neg = \sum_{k=1}^{2} max[0, -ln\sqrt{S_k + 1}]$. The negativity measures the

amount of entanglement between two subsystems. It can be directly calculated from space and momentum operator expectation values, namely the above defined $S_{1,2}$ criteria. The amount of negativity between neighbouring bases for room temperature is shown in 3.3.
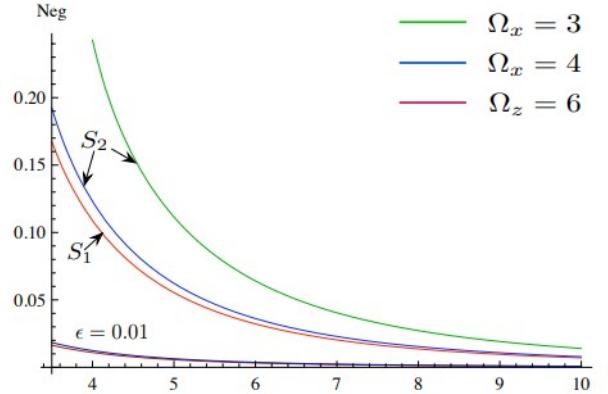

FIGURE 3.3: *This graphic shows the nearest neighbour negativity as a function of distance between sites in Å at T = 300K. The three upper curves are for scaling factor $\epsilon = 1$, the lower two curves are for scaling factor $\epsilon = 0.01$. The red curve is for z direction and $\Omega_z = 6 \cdot 10^{15} Hz$. The blue and green curve are for x direction and $\Omega_x = 4 \cdot 10^{15} Hz$ and $\Omega_x = 3 \cdot 10^{15} Hz$. The negativity for $\epsilon = 0.01$ is much smaller than in the unscaled case. The amount of negativity strongly depends on the distance r between sites and the value of trapping potential Ω. The lower the potential, the higher the negativity. A typical distance between neighbouring base pairs in DNA is approximately $r = 4.5$. Along the chain (z direction) the S_1 criterion is violated, whereas transversal to the chain S_2 (x direction) is violated. This reflects the geometry of the chain. Along the main axes of the chain energy is reduced by correlated movement. Transversal to the chain it is energetically better to be anticorrelated.*

For the normal coupling there is substantially more entanglement present than for the scaled interaction. This correlates with the amount of binding energy found in [37], where the DNA with normal coupling has a lower energy than the DNA with scaled coupling.

The above result motivates the question whether the binding energy can be expressed in terms of entanglement measures. In the limit of long distances, an analytical expression connects the amount of binding energy in the chain of oscillators with the values of $S_{1,2}$. Due to the strong coupling the chain

of oscillators is effectively in its ground state, which I will assume in the following analysis.

The dispersion relations of the electron cloud oscillations can be expanded for large distances, i.e. $r^3 \to \infty$

$$\omega_{zl} \approx \Omega_z - 4\frac{Q^2}{4\pi\epsilon_0 m}\frac{1}{2\Omega_z}\cos\left(\frac{2\pi l}{N}\right)\frac{1}{r^3} + O\left(\frac{1}{r^6}\right) \qquad (3.3.3)$$

and similarly $\frac{1}{\omega_{zl}}$

$$\frac{1}{\omega_{zl}} \approx \frac{1}{\Omega_z} + 4\frac{Q^2}{4\pi\epsilon_0 m}\frac{1}{2\Omega_z^3}\cos\left(\frac{2\pi l}{N}\right)\frac{1}{r^3} + O\left(\frac{1}{r^6}\right) \qquad (3.3.4)$$

Inserting this expansion into the entanglement criterion S_2 gives:

$$S_{z,2} \approx -\frac{Q^2}{\pi\epsilon_0 m}\frac{1}{2\Omega_z^2}\frac{1}{r^3} \qquad (3.3.5)$$

while the corresponding expression for $S_{z,1}$ has a positive value. A similar expansion of the dispersion relation in the x direction leads to:

$$S_{x,1} \approx -\frac{Q^2}{2\pi\epsilon_0 m}\frac{1}{2\Omega_x^2}\frac{1}{r^3} \qquad (3.3.6)$$

This implies that nearest neighbor (n.n.) electronic clouds are entangled even at large distances. However the amount of entanglement decays very fast. I will now compare this result with the binding energy in the ground state. The binding energy is defined as the difference of energy of the entangled ground state and any hypothetical separable configuration

$$E_{z,bind} = \langle \hat{H}_z \rangle - \sum_{I=1}^{N}\langle \hat{H}_{zI} \rangle = \frac{\hbar}{2}\left(\sum_{l=1}^{N}\omega_{zl} - N\Omega_z\right) \qquad (3.3.7)$$

This definition is analogous to the definition of correlation energy in chemistry [45]. The first approximation to the full Schrodinger equation is the Hartree-Fock equation and assumes that each electron moves independent of the others. Each of the electrons feels the presence of an average field made up by the other electrons. Then the electron orbitals are antisymmetrised.

This mean field approach gives rise to a separable state, as antisymmetrisation does not create entanglement. The Hartree-Fock energy is larger than the energy of the exact solution of the Schrodinger equation. The difference between the exact energy and the Hartree-Fock energy is called the correlation energy

$$E_{corr} = E_{exact} - E_{HF} \tag{3.3.8}$$

This definition of binding energy is a special case of the correlation energy, This model describes the motional degree of freedom of electrons, namely the displacement of electron clouds out of equilibrium. I show for this special case that the amount of correlation energy is identical to entanglement measures. Expanding the binding energy for $r^3 \to \infty$, the leading term is of order $\frac{1}{r^6}$

$$E_{z,bind} \approx \frac{\hbar}{2} \left[-\left(\frac{Q^2}{\pi \epsilon_0 m} \right)^2 \frac{N}{16 \Omega_z^3} \frac{1}{r^6} \right] = -\frac{N \hbar \Omega_z}{8} S_2^2 \tag{3.3.9}$$

since the first order vanishes due to symmetry and similarly for x direction:

$$E_{x,bind} \approx -\frac{N \hbar \Omega_x}{8} S_1^2 \tag{3.3.10}$$

Eqs. 3.3.9 and 3.3.10 show a simple relation between the entanglement witnesses $S_{1,2}$ and the binding energy of the chain of coupled harmonic oscillators. The stronger the entanglement, the more binding energy the molecule has. Interestingly, along the chain the S_1 criterion is violated, whereas transversal to the chain S_2 is violated. This reflects the geometry of the chain. Along the main axes of the chain energy is reduced by correlated movement. Transversal to the chain it is energetically better to be anti-correlated. This means that the entanglement witnesses $S_{1,2}$ not only measure the amount of binding energy, but also the nature of correlation which gives rise to the energy reduction. This relation motivates the search for entanglement measures describing the binding energies of complex molecules. While the binding energy just measures energy differences the corresponding entanglement measures reflect more information. Without correlations between subsystems there

would not be a chemical bond. It is precisely the purpose of entanglement measures not only to quantify, but also to characterise these correlations.

3.4 Aperiodic potentials and information processing in DNA

In the calculations above, a periodic potential energy was assumed, from which analytical solutions could be deduced. The effect of a non-periodic potential energy will now be studied. Since there are, as we have already seen, no significant differences in the potentials of the different nucleic acids (look at the table 3.1), one could intuitively assume that there will be a local change of potentials without a total entanglement break. To verify this more intuitively, one can simulate a system of 50 randomly chosen bases and numerically solve the coupling matrix, a result is given in the literature [35]. The smallest dispersion frequency determines the thermal robustness; the smaller the frequencies ω_l the larger the probability that the thermal heat bath can excite the system. Sampling over 1000 randomly chosen sequences yielded $min(\omega_l) = 3.210^{15}Hz$ as the smallest dispersion frequency. Comparising this with the thermal energy gives $\frac{2k_B 300k}{\hbar \omega_l} \approx 0.03$, which is still small. This means that the thermal energy is more than 20 times smaller than the smallest phonon. One can therefore continue to work in the fundamental state. Different sequences will lead to variations in the degree of entanglement of the base chain. For each string, the average Von Neumann entropy of the individual sites was determined and compared with the classical information set as measured by the Shannon entropy of each string. The Von Neumann entropy of a single site j is obtained following [44] with the formula

$$S_V(r_j) = \frac{r_j + 1}{2} ln\left(\frac{r_j + 1}{2}\right) - \frac{r_j - 1}{2} ln\left(\frac{r_j - 1}{2}\right) \tag{3.4.1}$$

where $r_j = \frac{1}{\hbar}\sqrt{\langle x_j^2 \rangle \langle p_{x_j}^2 \rangle}$ is the symplectic eigenvalue of the covariance matrix of the reduced state.
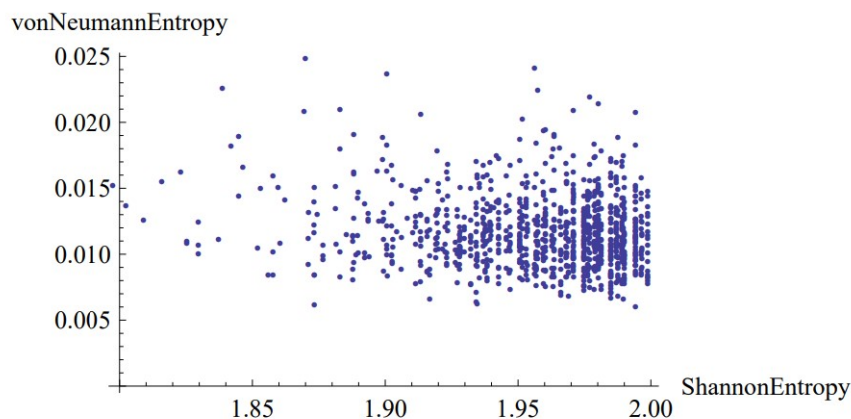
FIGURE 3.4: *This graphic shows the average single site Von Neumann entropy of a chain of nucleic acids dependant on the classical Shannon entropy of the string. Each string contains 50 bases with a random sequence of A,C,G, or T. The distribution of nucleic acids determines the classical Shannon entropy. For each nucleic acid the value of polarizability of Table 3.1 in x direction is used. There is no direct correlation between quantum and classical information. The average amount of Von Neumann entropy varies strongly for different sequences.*

To check whether the relative frequencies of A, C, G, and T affect the degree of entanglement within a chain of coupled oscillators, It also has been calculated the classical Shannon Entropy of each string. Fig. 3.4 shows the average amount of quantum entropy and classical entropy at a single point. In this model, there is no direct correlation between the two Classical and Quantum Entropy. Indeed for the same amount of Shannon entropy, i.e. same relative frequencies of A,C,G and T, the value of quantum correlations (Von Neumann Entropy) varies strongly between around 0.007 and 0.025. One could note that for achieving a comparable amount of local disorder by thermal mixing a temperature is needed more than 2000*K*. This is a quantum effect without classical counterpart.

Any uncoupled base to a neighbor will be in the ground state because the thermal energy is low compared to the energy gap of the oscillator. As the coupling increases, the chain bases evolve from a separable ground state to an entangled one. Due to the global entanglement, each base mixes locally.

This feature cannot be represented by classical vibrational descriptions. In a classic view if the system is in the ground state, each individual unit will be in the respective ground state. Although the fact that globally entangled states mix locally is well known, little is known regarding possible consequences to biological systems. In the following paragraphs I will discuss this quantum effect on the flow of information in DNA.

How much information about the neighbouring sites is contained in the quantum degree of freedom of a single base? Is it accurate to describe the electronic degree of freedom of a single nucleic acid as an individual unit or do the quantum correlations between bases require a combined approach of sequences of nucleic acids?

This will be important in the following paragraph, which deals with the flow of information in biological systems, where I will describe a model that describes mutations in the DNA. A crucial component of this model is energy quanta that come from the electronic degrees of freedom of nucleic acids. If the amount of energy available is sequence dependent, i.e., it changes with changing neighbours, then there could be non-random mutations. In the previous sections, It has been shown that there is a correspondence between the amount of entanglement available and the binding energy of nucleic acids. Therefore, instead of examining the available energy levels, It will be considered the Von Neumann entropy. It will be shown that the quantum state of an aperiodic chain of coupled harmonic oscillators in principle encodes information about its neighbours and is therefore sequence dependent. Results are follow: the quantum state of a single base should not be treated as an individual unit.

In summary, the results achieved by this model are as follows.

- The entanglement contained in the chain coincides with the binding energy of the molecule.

- As the interaction energy given by $\hbar\omega$ is roughly 20 times larger than the thermal energy $k_B 300K$ the motional electronic degree of freedom is effectively in the ground state. Thus the entanglement persists even at room temperature.

- For randomly chosen sequences of A,C,G,T or in aperiodic potentials there exists no direct correlation between the classical information of the sequence and its average quantum information. Indeed the average amount of Von Neumann entropy varies strongly, even among sequences having the same Shannon entropy.

- The quantum state of a single base contains information about its neighbour, so it is reasonable to question the idea of dealing with the individual basis of DNA as independent bits of information.

In this chapter, I have studied and analyzed a first approach with which quantum effects can be studied at the biological level. Indeed, I have traced and verified how far and in what way the principles of quantum physics, which govern the dynamics of objects on atomic scales, have survived on a mesoscopic scale in forming the fundamental building blocks of life.

Now I want to generalise the attempt to highlight this type of behaviour with another approach. In fact, quantum mechanics introduces and expounds a formalism that can be applied a priori even to abstract objects, which do not have to do with an actual physical system. And this is the study that led me to define and develop models that take the whole cell into account, introducing the concept of the quantum biological state. Which I will describe in the next chapter. Armed with this new tool, which is precisely the formalism brought by quantum mechanics, and having outlined the importance that this tool assumes in the study of biology, I will try to apply it both to the DNA model and to a system composed of a finite number of cells.

Chapter 4

Quantum Biology at cellular level

4.1 Two views of quantum Biology

In accordance with the article [46] I can apply quantum theory to the study of biological phenomena on two distinct views or scales. They were born this way the Quantum biology at the macro molecular level (*QBML*) and the Quantum Biology at cellular level (*QBCL*). The main topic of this article is a more ambitious way of incorporating quantum physics into biology. It is to assume that this discipline can serve as a general language to predict and describe the results of measurements on natural systems. And precisely because of this generality, quantum theory deserves a broader field of application than is currently the case. Indeed, the quantum formalism provides a universal set of rules for dealing with probabilities that takes into account the context of a particular experimental setup (i.e., the sample space depends on the property being measured). Importantly, it covers cases where different measurement set-ups are incompatible with each other, a situation that often occurs when experiments are conducted on an individual basis. These rules can and should be expanded and enhanced as there are many cases in other sciences where different measurement set-ups are incompatible (and/or the sample space depends on the conditions of the experiment). Consequently, the application of quantum formalism should be extended to the entire natural world, including living systems.

4.1.1 QBML

One application of quantum theory is to study possible quantum mechanical effects at the level of biological macromolecules (typically proteins or nucleic acids), like I did in Chapter 3. This approach extends the reach of quantum chemistry to objects larger than ordinary molecules. Quantum effects such as tunneling and entanglement are known from studies of inanimate nature and small molecules, especially their electronic structure, the kinetics of electron/energy transfer, and the analysis of non classical forces in chemical reactions and bonding.

4.1.2 QBCL

At the cellular level, quantum formalism can describe the relationships between the numerous properties and events that individual cells undergo, changes that alter the entire cell (e.g. reproduction, death, differentiation and other instances of cellular decision-making). A priori, these events can be divided into two classes: measurements performed by a researcher in the laboratory on biological objects, or the responses of biological systems to various environmental conditions in their natural habitat. It is important to note that events of the second type can also be considered measurements despite the absence of a human observer, since the environment itself can be considered an observer. Consequently, QBCL implies from a formal point of view that the properties of biological systems (e.g. cells) are represented by linear operators that act on the states of the system and correspond to different "measurement" scenarios (i.e., experimental and/or environmental contexts) and, above all, that these operators are not necessarily commutative.

4.2 A Decoherence argument

Instead of defending quantum coherence in a specific biological system, we will propose a much more general counter-argument against decoherence, highlighting the limitations of this concept and its relative nature. This is a

crucial point. To illustrate it at the simplest and most elementary level possible, we must discuss the notions of density operator and preferred states, which play an important role later on.

The density operator formalism was introduced by Von Neumann in 1932. He wanted to deal with situations in which the quantum state cannot be represented by a vector in a Hilbert space. This ambiguity may arise from the fact that we only know incompletely how the system under investigation was prepared (e.g. due to uncontrollable influences from the system's environment). It is easy to prepare simple systems (such as an electron or an atom) in a well-defined state, but, complex systems are hard to prepare, partially because it is virtually impossible to isolate them from their environment. It is therefore necessary to include this additional uncertainty in the description of these systems. The formalism of the density matrix is a more general method than the wave function (an element of Hilbert space) for describing the state of the physical system. Therefore, in quantum biology, the description using the density operator is more appropriate because biological systems are so large than their environment, unlike individual electrons or molecules, thus they can not be precisely controlled.

However, the additional uncertainty in our description is not sufficient to destroy all quantum effects, i.e. taking the environment into account does not necessarily lead to the appearance of truly classical behaviour. To explain this crucial point, I need to talk about the basis of a density matrix. Indeed, the presence of off-diagonal terms is another way of saying that the system is in a state of superposition relative to the chosen basis.

Now, three crucial points regarding density operators must be noted:

- The state of the system can be described using different bases. Furthermore, an important property of a density operator is that, for any state, one can always find a basis in which there will be no off-diagonal terms. The representation of the state in such a special basis is called

"diagonalisation", as only the elements diagonal elements remain, see Fig. 4.1.

$$\begin{bmatrix} 1/\sqrt{2} & 1/\sqrt{2} \\ -1/\sqrt{2} & 1/\sqrt{2} \end{bmatrix} \begin{bmatrix} 1 & 2 \\ 2 & 1 \end{bmatrix} \begin{bmatrix} 1/\sqrt{2} & -1/\sqrt{2} \\ 1/\sqrt{2} & 1/\sqrt{2} \end{bmatrix} = \begin{bmatrix} 3 & 0 \\ 0 & -1 \end{bmatrix}$$

$$\rho_1 \longrightarrow T^{-1}\rho_1 T$$

$$\begin{bmatrix} 1/\sqrt{2} & 1/\sqrt{2} \\ -1/\sqrt{2} & 1/\sqrt{2} \end{bmatrix} \begin{bmatrix} 1 & 1 \\ 1 & 1 \end{bmatrix} \begin{bmatrix} 1/\sqrt{2} & -1/\sqrt{2} \\ 1/\sqrt{2} & 1/\sqrt{2} \end{bmatrix} = \begin{bmatrix} 2 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\rho_2 \longrightarrow T^{-1}\rho_2 T$$

FIGURE 4.1: *A symmetric density matrix ρ_1 can be converted to a diagonal one by the action of a unitary matrix T. In this figure there are two examples of diagonalization. Top: the resulting matrix has two diagonal terms. Bottom: the resulting matrix has only one diagonal term.*

Since there is no interference between the elements of the base, the state of our system state in this representation can be thought of as a classical "mixture" of these states in a special base. It could also happen that, after diagonalisation, only one base state. In this case, the state of the system is called pure, as opposed to the more general mixed states, which contain more than one element in their diagonalised representation, and thus could be thought of as a statistical set of these states.

- Given a density matrix describing a state of a complex system $(A + B)$, one can obtain a description of one part of the system (say, A), by a procedure of "tracing out" the information about B. This procedure is somewhat similar in spirit to coarse-graining, where certain degrees of freedom are deemed non-relevant and averaged out.

In this approach, the physical system is described by a reduced density matrix ρ_S obtained from the density matrix ρ of the total system $(S + E)$ (including system S coupled to its environment E):

$$\rho = |\psi_{ES}\rangle \langle\psi_{ES}| \tag{4.2.1}$$

further, the density matrix is manipulated to obtain the reduced density matrix:

$$\rho_S = Tr_E \left| \psi_{ES} \right\rangle \left\langle \psi_{ES} \right| \tag{4.2.2}$$

Starting from an arbitrary state of the joint system $(S + E)$, and choosing some basis for a description, the reduced density matrix of S:

$$\rho_S = \sum_{i,j=1}^{N,M} \alpha_i \alpha_j^* \left\langle \epsilon_i | \epsilon_j \right\rangle \left| S_i \right\rangle \left\langle S_j \right| \tag{4.2.3}$$

will in general contain off-diagonal terms $\left| S_i \right\rangle \left\langle S_j \right|$.

Decoherence refers to the fact that these off-diagonal terms will quickly vanish with time, because the dynamic evolution of the joint system $(S + E)$ will generally lead to states of the environment corresponding to the different basis states of the system, rapidly becoming orthogonal, so that $\left\langle \epsilon_i | \epsilon_j \right\rangle \rightarrow 0$. As the ρ_S becomes effectively diagonal, the resulting absence of interference between different basis states is proposed to explain why macroscopic superposition states (such as Schrodinger's cat) are never observed, or, in other words, why typical macroscopic systems, which are only rarely isolated from their environment, behave classically. The states of the system that survive the action of decoherence are called "*preferred states*".

Another crucial aspect of decoherence is that it is a base-dependent term. That is, if one were to take a reduced density operator rho that was diagonal because it was represented in the base of preferred states, and now write it in a different base, some non-diagonal terms will reappear. In this alternative base, there will be interference between the elements of the states of the new base and the notion of superposition will still apply.

This dependence of the decoherence process becomes a significant factor when moving from physics to biology. Due to the very diverse and nuanced role of the environment, the question of what the preferred states of a system should be is far from obvious and trivial in biology. For a biologist, there are many bases for representing the state of a cell that are interesting and become relevant in different experimental contexts.

The "biologically significant bases" do not necessarily correspond to the bases of the "preferred states" in a given environment. Consequently, if a preferred state of a cell (in a given environment) resembles an overlap in some biologically significant base, it will, by definition, be resistant to decoherence[1].

4.3   Biological adaptation

Now let's consider a cell in a given environment E_1. For simplicity, let us take a starving cell that has no exchange with the environment.

$$E_1 \qquad\qquad E_2$$

$$\begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \Leftrightarrow \begin{bmatrix} \alpha_{11} & \alpha_{12} & \alpha_{13} \\ \alpha_{21} & \alpha_{22} & \alpha_{23} \\ \alpha_{31} & \alpha_{32} & \alpha_{33} \end{bmatrix} \longrightarrow \begin{bmatrix} \alpha_{11} & 0 & 0 \\ 0 & \alpha_{22} & 0 \\ 0 & 0 & \alpha_{33} \end{bmatrix}$$

$$\rho_1 \Leftrightarrow T^{-1}\rho_1 T \xrightarrow{\text{Decoherence}} \rho_2$$

FIGURE 4.2: *Diagonalisation should not be confused with decoherence. Left: diagonalisation does not affect the state of the system, since it is a change of base to describe the same state (i.e. a passive transformation). In fact, an alternative basis is always possible. After changing the environment, the effects of the environment lead to the disappearance of the off-diagonal terms, so that the reduced density matrix of the system changes to ρ_2. This matrix describes a different state of the system (i.e. decoherence corresponds to an active transformation). Note that in this case we have chosen T so that it transforms the basis of the density matrix into the preferred states that are einselected in the new environment E_2, otherwise we would not obtain a description of the new state with a diagonalised matrix (ρ_2).*

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[1]For example, consider a chemical reaction describing the transition of a chiral molecule from one enantiomer to another. Naively, the preferred basis for describing this reaction should correspond to the alternative molecular structures (e.g. *A* and *B* two enantiomers). This is an acceptable assumption for describing chemical reactions in vitro (i.e. in homogeneous cell-free solutions). However, it is not obvious that the same assumption is equally valid in vivo when the whole cell is described with a density matrix. In vivo, one cannot overlook the fact that enzymes convert one molecular structure into another. If one describes the state of the whole cell with the density matrix rho, the state transitions of the cell between the alternative molecular structures A and B correspond to the off-diagonal terms in rho. Diagonalizing rho, one obtains another set of preferred states described as superpositions of states of the cell with these alternative molecular structures *A* and *B*

Due to decoherence, the state of this cell is described by a diagonal density matrix ρ_1 based on the preferred states Fig. 4.2. Now suppose we change E_1 to a different environment, E_2. In general, this new environment will select a different set of preferred states. The old density matrix ρ_1 will not be diagonal in the basis composed of the new preferred states, i.e., the old preferred states must be represented as superpositions of the new preferred states. This means that the description of the old state with a density matrix written in the new basis will contain terms that are not diagonal Fig. 4.2.

By decoherence, these off-diagonal terms disappear, describing a transition from one preferred basis to another (Fig. 4.2 right panel) and from ρ_1 to ρ_2. However, from the biological point of view, it is the process of adaptation of the cell to its new environment. This suggests that changing the preferred base could be a simple and inexpensive way to describe biological adaptation.

The interaction of a system with its environment is not sufficient to make its behaviour classical. Thus, I can conclude that the assumption of decoherence as a general argument against nontrivial quantum effects in biology is not justified, because the environment that we have to consider when searching for the preferred states of a given biological system is often very diverse and complex.

Consequently, the preferred states of a biological-molecular system might appear as superpositions in a more naive basis (e.g., molecular structure) or in another biologically significant basis. On the other hand, an active change in the environment affects the density operator of a system, since the sets of preferred states differ in different environments. Our message is that the notion of preferred state is fundamental in biology and must be treated with great care.

It believed that the decoherence approach to the problem of the quantum to

classical transition opens the door to biology by including the environment in the description of the system under study, thus giving it a central role.

4.4 A particular state of Superposition

It is commonly believed that cells are irredeemably classical objects and therefore cannot be in a state of superposition. In the cited article [46] it is argued that the notion of a living cell in superposition is neither unreasonable nor paradoxical.

From this point forward, I will propose to consider the notion of "formal superposition" and distinguish it from Schrodinger's cat.

Consider, for example, a human hand that can be either left $|L\rangle$ or right $|R\rangle$. Further, now we consider an exotic base, with two states represented as: $|+\rangle = \frac{|L\rangle + |R\rangle}{\sqrt{2}}$ and $|-\rangle = \frac{|L\rangle - |R\rangle}{\sqrt{2}}$. Then it is not formally wrong to represent state $|L\rangle$ as a superposition of these states: $|L\rangle = \frac{|+\rangle + |-\rangle}{\sqrt{2}}$.

Therefore, the question whether a system X is superposed or not is an invalid question that has no meaning without the choice of a basis. The really relevant question is whether there is any practical need to use a basis that represents our system X in superposition to the elements of this (perhaps exotic) basis.

In physics, one is usually limited to a class of environments in which the preferred basis usually does not change. However, biology is much more complicated and complex. One reason for this practical necessity is whether the elements of this hypothetical A base can be distinguished in another environment that might become relevant to the description of our experiment. This may happen, for example, if the environment changes and the states of this new basis A become the preferred states of our system. The main

result is that these seemingly exotic bases (and the associated nature of superposition) are serious, because changes in the environment that affect the distinguishability of states are actually a common phenomenon in biology.

The formalism of quantum mechanics provides us with the extra baggage of seemingly paradoxical superposition states of macroscopic objects. However, it is important to note the difference between illegitimate superposition states (e.g. Schrodinger's cat states, which are macroscopically distinct) that we certainly have to get rid of from a theoretical point of view, and the more benign notion of a superposition state that results from the choice of a particular (perhaps "exotic") basis, with the components being indistinguishable in a given environment.

4.5   Do we really need this language in biology?

A first trend in biology is "nanobiology" which deals with the analysis of individual biological objects rather than their assemblies. The second trend is "systems biology" which examines all relevant properties of biological systems in a single experimental study, with the goal of mathematically modelling the dynamics of an entire system. The question now is whether it is possible to know all relevant properties of a single cell at once? It is assumed that in order to answer these questions, one must return to the "first principles" of physics and consider quantum theory. Is it possible, then, to study what is known as systems nanobiology?

From a formal point of view, it is reasonable to expect that quantum theory is the appropriate language to explain the limitations of single cell experiments. This is because the crucial innovation of quantum formalism is the mathematical notion of an operator acting in the space of states of the system to be described. Such operators could represent the properties of the system under study in a particular measurement setup (be it a human observer or

an "environment as observer"). The most important feature of the operator formalism is that some operators (corresponding to different "measurement situations") cannot be interchanged.

This non-commutativity directly implies the notion of superposition, since a system that is in an eigenstate of a particular operator is in general not in an eigenstate of a non-commutative operator, but can only be represented as a linear combination of such states. Consequently, one can see that the notion of superposition arises naturally as a general way to formalise **the limits of what can be known about the system under study, and thus gains importance after the merger of systems biology with nanobiology**.

In summary, the emerging discipline of systems nanobiology necessarily requires a formalism that captures the non-commutative properties of a single biological object (e.g. a single cell). This formalism will naturally require the notion of superposition.

Let's consider a system in the state P, in a particular environment E_0. For a new environment E_1 it can be introduced a basis A, whose elements represent the potential outcomes of the system's interaction with the new environment E_1. The basis A corresponds to a spectrum of different alternative states that the system can assume in the new environment E_1 potentially, but which coexist as mere potentials before the environment actually changes (i.e., from E_0 to E_1). Only the elements of the base A can be stable under the new conditions; the state P is stable in the old environment E_0 before the environment is changed and can be represented as a superposition of these alternative elements of the base A; and for each new environment E_i, this formalism must have operators A_i acting on the space of states of the system and representing this environment, such that the results of the interaction with the environment E_i correspond to the eigenstates of the operator A_i.

We have reached a very profound point in the study of the cell and physiological processes. We are able to have many variables in mind and we realise

more and more that we need a new language. A new study that can quantify even the inevitable ignorance we have about the system we want to study.

In the next chapter, I will analyse a biological model that I created to simulate the dynamics of mutations contained within DNA. I will elaborate it on the concept of a biological state and how this can be studied under quantum biology at cellular level, which has been extensively analysed in this chapter.

Chapter 5

Theoretical biological model for epigenetic mutations

Recent studies over the last ten years have shown that quantum effects can cause mutations in DNA, leading to changes in the genetic information that is passed on to future generations ([47] and [48]). In this chapter I will analyse what it means that the information coded in DNA must necessarily be quantum in nature and not just classical.

The quantum mechanical properties of DNA can cause its structure to change, leading to mutations. This can lead to the expression of new traits or the development of diseases. Understanding the quantum effects that contribute to genetic mutations is a very active area of research and has great potential to greatly improve our understanding of genetics and evolution. Further studies in this area could lead to the development of new techniques for controlling and manipulating genetic mutations, with implications for the treatment of genetic diseases and the improvement of crops and livestock.

I will clarify the concept of information and how this concept can be applied to the physiological model I am considering. Through the quantum model I provide, I will measure the entanglement entropy and quantum capacity of the system, of which I will write a brief theoretical presentation found extensively in the literature. By comparing with the results achieved in the article [49] I will conclude that my model is not only simpler from a theoretical point of view, but also reflects in a very acceptable way the results arrived at by the scientists in the above article.

5.1 The shape of DNA

5.1.1 The Tautomeric form of the nucleotide bases

DNA (deoxyribonucleic acid) is the molecule that encodes all the necessary genetic information in living organisms -just as the atom is considered the building block of the universe, indeed DNA can be considered the building block of life. In DNA, genetic information is encoded as a sequence of nucleotides: Adenine (A), Thymine (T), Guanine (G), and Cytosine (C). These nucleotide bases are paired by hydrogen bonds (A-T, G-C) and attached to sugar-phosphate chains that form the two backbone strands of the double helix, see Fig. 5.1. DNA is well suited for storing biological information because the double-stranded helix structure gives the molecule a built-in duplicate of the encoded information.
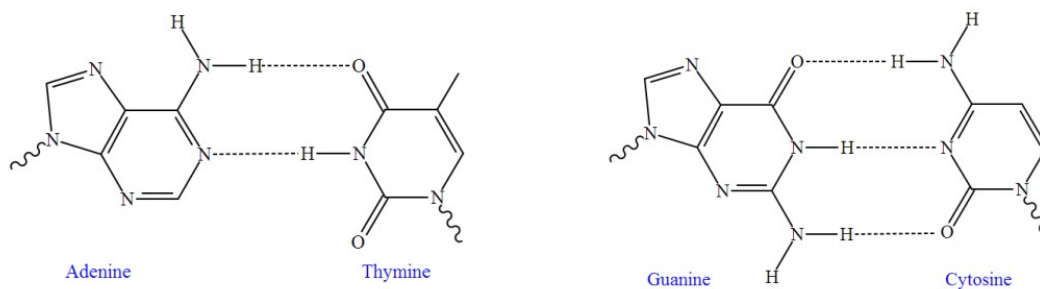
FIGURE 5.1: *Left, an A-T base pair with two hydrogen bonds. Right, a G-C base pair with three hydrogen bonds.*

This means that if one strand of the double helix has a specific base sequence (for example ATGACTG) then the other strand must have the complimentary sequence (TACTGAC). The reason why A pairs with T and G pairs with C comes down to matching electron lone pairs. In essence the hydrogen bond is a single proton shared between two lone electrons (two separate atoms,each containing an extra unpaired electron in their outer orbital shell compete for possession of the single proton). In addition to the normal forms, the tautomeric forms of the nucleotide base pairs must also be considered. Tautomeric forms are obtained by moving a proton from its original (or normal)

alone pair into another position. This changes the inherent complementarity between the bases and as such the tautomeric bases pair differently, see Fig. 5.2. The diagram below gives a direct comparison between the normal forms and the tautomeric forms with their complementary bases:
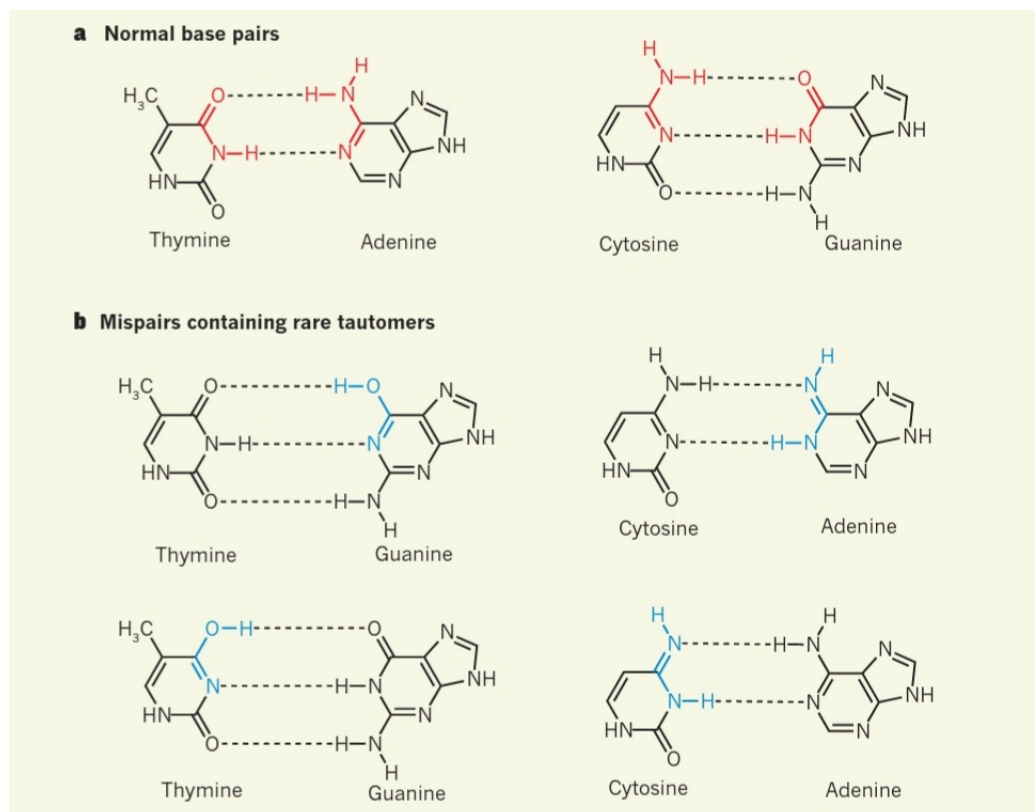

FIGURE 5.2: ***a**: normal pairing between nitrogenous bases without any mutation due to tunnelling effect. **b**: rare pairing due to the tautomeric form of the nitrogenous bases.*

These changes from the normal to the tautomeric forms introduce errors into the DNA replication process–creating point mutations–and can irreparably effect the genetic code (the mutation rate in human cells varies, depending on age and other physiological factors, between 10^{-9} and 10^{-6} mutations per year per base pair, see [50]). These point mutations, if not checked after initial replication, can be amplified through continued replications, ultimately leading to severe mutations in the cell. It is not unreasonable to suggest that these changes from normal to tautomeric forms correspond to a sort of "quantum jump" where the proton transfer within the hydrogen bond parallels jumping between various stationary states [51].

5.1.2 Quantum Theory of the Hydrogen Bond

In order to investigate the properties of the hydrogen bond the electronic structure of the atoms involved must first be understood. In DNA there are several molecules that have multiple electron lone pairs, all jostling in competition to catch the protons in the surrounding environment, and this is what leads to the formation of the hydrogen bonds.

The attraction of an individual electron lone pair on a proton can be modeled by a single-well potential. However, since there are two electron lone pairs competing for a single proton in a hydrogen bond, the hydrogen bond can be represented as a superposition of two such potentials, i.e. a double-well potential. In the double-well potential there is a bump, or potential barrier, separating the two equilibrium positions, see Fig. 5.3.

$$N : H - -- : N \qquad N : - - -H : N$$

FIGURE 5.3: *Equilibrium states in which hydrogen bonding can be found, this transition changes the nature of the nucleic acid.*

Above is a representation of the two equilibrium positions. Assuming that the probability of being in either state is the same, one can predict that under certain circumstances the proton may jump from one position to another. In a quantum mechanical system the proton can be represented by a wave packet, which allows for the proton to penetrate into areas that were forbidden before in the classical system. It is then possible for the proton to travel from one equilibrium state to another by means of tunneling through the potential barrier, achieving this "quantum jump" from one state to another like in Fig. 5.4.

5.1.3 Proton Tunneling in DNA

When looking specifically at proton tunneling in DNA the scope of the problem must be expanded slightly. Due to the nature of the nucleotide there will always be at least two hydrogen bonds involved in any calculations and thus
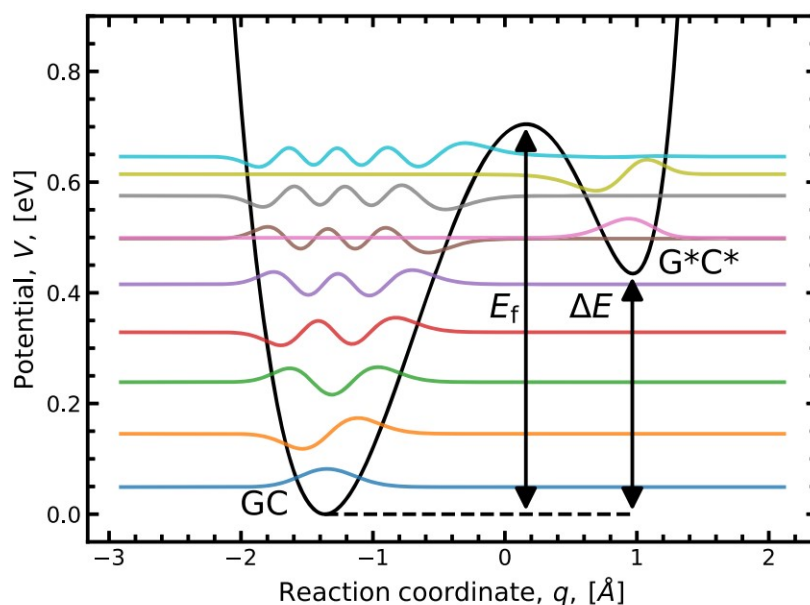
FIGURE 5.4: *Proton transfer potential energy landscape. The coloured horizontal lines denote the first ten eigenstates. The first eigenstate energy is $E_0 = 0.049$ eV, the forward reaction barrier $E_f = 0.704$ eV, reaction asymmetry between the canonical and tautomeric form $\Delta E = 0.435$ eV. All these informations are taken from the article [52].*

the question becomes one of motion and stability of two protons. In other words this becomes a quantum mechanical two body problem.

This problem has been studied many times, and in very different ways. As can be seen from the article [52]. I can however conclude that the quantum tunnelling contribution to the proton transfer rate is several orders of magnitude larger than the classical over the barrier hopping. Furthermore, I find a large tautomeric occupation probability of 10^{-4}, suggesting that such proton transfer may well play a far more important role in DNA mutation than has hither to been suggested. These results could have far reaching consequences for current models of genetic mutations.

5.2 The content of life: genetic information

5.2.1 Information flow in biological systems

DNA contains all the information necessary for physiological processes to be performed correctly. In this part of my thesis, we will talk about the information encoded, stored and decoded in DNA, one of the most complex and important biological systems in biology.

The functionality of cells or bacteria depends on a delicate balance between the concentrations of different molecules. Therefore, most of the information in a cell consists of classical information which can be easily memorized. Quantum aspects come into play when information is processed at the atomic level. Any interaction in a cell is based on chemical reactions, which are dominated by the quantum aspects of electron shells. I can say that there will certainly be a degree of information flow that is controlled by quantum mechanics.

I take the case of the Born-Oppenheimer theory, in which the use of its approximation showed to be successful for many problems in atomic and molecular physics. Since the nuclei of molecules are about 1000 times heavier than electrons, they can be considered as classical particles. Given a configuration of nuclei, I can then contract the resolution of the Schrodinger equation for electrons, obtaining the dynamics of the quantum part of the system. The idea of the Born Oppenheimer approximation will be examined in this section under the aspect of information processing in living systems, see Fig. 5.5
.

I will first take up some concepts about the quantum information and the Von Neumann entropy, which will be the two quantities that I will measure in the simulations of the systems I have devised. One problem in quantifying information in biological systems is that we usually know neither the coding nor the decoding part of a molecule. The channel capacity formalism is able to circumvent this problem and will be introduced in the first part of the next section.
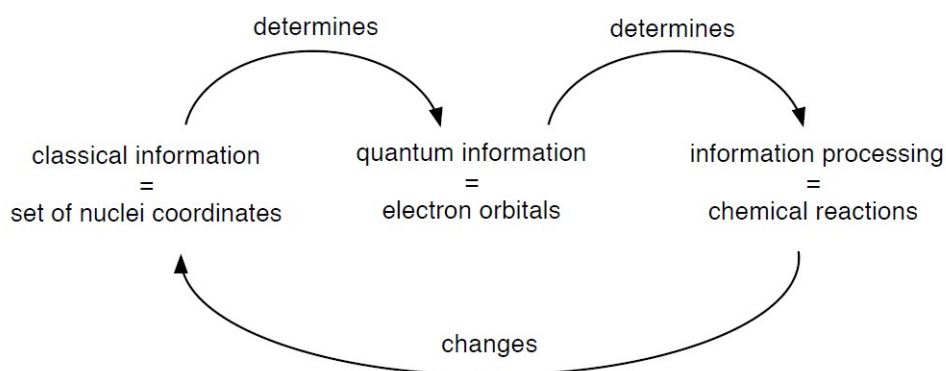
FIGURE 5.5: *In the Born-Oppenheimer approximation, complex molecules are separated by the set of coordinates of the heavy nuclei, treated as classical particles, and the light electrons, treated in a fully quantum-mechanical manner. Every interaction in the cell uses chemical reactions, which are determined by the electronic states of the molecules. A chemical reaction can transform a given molecule into a different one, thus changing the information carried by that molecule.*

5.2.2 Information theory

The mathematical definition of information was first given by Shannon [53]. The amount of information is defined from a communication process between a source that produces a message to be transmitted, chosen from a set of possible messages, and a receiver that receives the message through a communication channel; in order to transmit the messages, the source encodes them through an appropriate code, thus the possible messages of the source are the elements that must be encoded. The amount of information associated with each message that can be transmitted by a source is related to the probability of the message being transmitted: the lower the probability of the message, the greater the amount of information associated with the message.

If P is the probability of a message, the information associated with the message is defined as:

$$I(m) = log_2 \frac{1}{P} = -log_2 P \tag{5.2.1}$$

If the source always emits the same message (which therefore has probability

1) the associated information is 0, in fact the emission of the message carries no information, since it is already known.

If the messages that can be transmitted are N and are equiprobable the probability of each is $1/N$ and therefore the information of each message is:

$$I(m) = log_2 \frac{1}{P} = log_2 \frac{1}{N} = -log_2 N \qquad (5.2.2)$$

Entropy is defined as the total amount of information related to all messages that the source can emit, calculated as a weighted average (with respect to probabilities) of the information quantities of the messages.

$$H(S) = \sum_{k=1}^{N} P_k I(k) = \sum_{k=1}^{N} P_k log_2 \frac{1}{P_k} \qquad (5.2.3)$$

That is the Shannon's formula. The entropy is maximum when all messages are equiprobable. For N equiprobable messages, the entropy is $log_2 N$ ($\sum_{i=1}^{N} \frac{1}{N} log_2 N$). Thus we have that:

$$H(S) \leq log_2 N \qquad (5.2.4)$$

This just introduced is classical information theory. In the quantum models I have simulated, I have calculated another type of quantity, which is derived from the Von Neumann Entropy: the Entropy of Entanglement. Von Neumann Entropy is Shannon's analogue for quantum systems. A lot has been described in the literature about this magnitude [54]. Here I will briefly outline the characteristics and how this quantity is calculated given a quantum system.

The Von Neumann entropy is an extension of the concept of Gibbs entropy from classical statistical mechanics to quantum statistical mechanics. For a quantum-mechanical system described by a density matrix ρ, the Von Neumann entropy is

$$S = -Tr(\rho ln \rho) \qquad (5.2.5)$$

where *Tr* denotes the trace and *ln* denotes the (natural) matrix logarithm. If the density matrix ρ is written in a basis of its eigenvectors $|1\rangle , |2\rangle , |3\rangle$... as:

$$\rho = \sum_{j}^{N} \eta_j |j\rangle \langle j| \tag{5.2.6}$$

then the Von Neumann entropy is merely

$$S = \sum_{j}^{N} \eta_j ln \eta_j \tag{5.2.7}$$

The Von Neumann entropy is also used in different forms (conditional entropies, relative entropies, etc.) in the framework of quantum information theory to characterize the entropy of entanglement, that is the exactly the measurement that I did in my simulations.

The entropy of entanglement (or entanglement entropy) is a measure of the degree of quantum entanglement between two subsystems constituting a two-part composite quantum system. Given a pure bipartite quantum state of the composite system, it is possible to obtain a reduced density matrix describing knowledge of the state of a subsystem. The entropy of entanglement is the Von Neumann entropy of the reduced density matrix for any of the subsystems. If it is non-zero, i.e. the subsystem is in a mixed state, it indicates the two subsystems are entangled. If it is one, the entropy is maximized. More mathematically; if a state describing two subsystems *A* and *B*

$$|\Psi_{AB}\rangle = |\phi_A\rangle |\phi_B\rangle \tag{5.2.8}$$

is a separable state, then the reduced density matrix

$$\rho_A = Tr_B |\Psi_{AB}\rangle \langle \Psi_{AB}| = |\phi_A\rangle \langle \phi_A| \tag{5.2.9}$$

is a pure state. Thus, the entropy of the state is zero. Similarly, the density matrix of *B* would also have 0 entropy. A reduced density matrix having a non-zero entropy is therefore a signal of the existence of entanglement in the system.

Let us assume that a quantum system consists of N particles. A bipartition of the system is a partition that divides the system into two parts A and B, containing k and l particles respectively, with $k + l = N$. The bipartite entanglement entropy is defined with respect to this bipartition.

The bipartite Von Neumann entanglement entropy S is defined as the Von Neumann entropy of any of its reduced states, since they have the same value (can be proved by Schmidt's decomposition of the state with respect to the bipartition); the result is independent of which one we choose. For a pure state $\rho_{AB} = |\Psi\rangle \langle\Psi|$, it is given by:

$$S(\rho_A) = -Tr(\rho_A log \rho_A) = -Tr(\rho_B log \rho_B) = S(\rho_B) \qquad (5.2.10)$$

where $\rho_A = Tr_B(\rho_{AB})$ and $\rho_B = Tr_A(\rho_{AB})$ are the reduced density matrices for each subdivision.

The entanglement entropy can be expressed using the singular values of the Schmidt decomposition of the state. Any pure state can be written as $|\Psi\rangle = \sum_{i=1}^{m} \alpha_i |u_i\rangle_A \otimes |v_i\rangle_B$ where $|u_i\rangle_A$ and $|v_i\rangle_B$ are orthonormal states in subsystem A and subsystem B respectively. The entanglement entropy is simply:

$$-\sum_{i}^{m} |\alpha_i|^2 log(|\alpha_i|^2) \qquad (5.2.11)$$

This form of entropy writing makes it explicit that the entanglement entropy is the same, regardless of whether the partial trace is calculated on subsystem A or B.

In summary, the main difference between Von Neumann entropy and entanglement entropy concerns the properties of the system whose entropy is measured. The Von Neumann entropy is defined for a single-state quantum system. It measures the amount of information contained in the system, i.e. the amount of uncertainty that remains about its configuration after a measurement has been made. In other words, Von Neumann entropy describes

the inhomogeneity of the quantum system, which only reduces to zero when the system is in a pure state. Entanglement entropy, on the other hand, is defined for a system consisting of two or more parts that are strongly correlated with each other, i.e. are in an entangled state. It measures the amount of uncertainty about the configuration of the individual parts, which cannot be reduced by any measurement made on only one part of the system. In other words, entanglement entropy describes the inhomogeneity of the distribution of correlations within the compound system, and can be different from zero even if each individual part of the system is in a pure state.

5.2.3   Quantum Channels, sending and storing

See [55] for a general introduction to channels, which provide the most general formalism for how information can be transmitted from one party to another. The fact that the channel picture of information does not make any assumptions about how information is encoded by a physical system is one advantage of using it. The channel capacities for a specific physical system determine the theoretical maximum amount of information that can be transmitted. Due to the system's complexity, little is known for sure when dealing with biological systems. The physically-possible information processing capacity, which is an upper bound on the actual information processing that takes place, can be estimated using channel capacities for a suitable approximation of the system. In the following sections, I'll go over some of the fundamentals of quantum channels.

In quantum information theory, a quantum channel is a communication channel that can transmit quantum information and classical information. An example of quantum information is the state of a qubit. An example of classical information is a text document transmitted via the Internet. More formally, quantum channels are completely positive (CP) maps that preserve the trace between operator spaces. In other words, a quantum channel is nothing more than a quantum operation seen not only as the reduced dynamics of a system, but as a pipeline designed to carry quantum information (some

authors use the term "quantum operation" to also include decreasing trace maps, while reserving the term "quantum channel" for strictly conservative trace maps). For the time being, it will be assumed that all state spaces of the systems considered, classical or quantum, are of finite dimension and that all the quantum channels involved were memoryless, so the output of a channel at a given time depends only on the corresponding input and not on the previous ones.

In mathematical terms this is described as:

$$\rho_{out} = G(\rho_{in}) = \sum_{i=1}^{M} E_i \rho_{in} E_i^{\dagger} \tag{5.2.12}$$

where E_i are the Kraus operators fulfilling $\sum_{i=1}^{M} E_i^{\dagger} E_i = 1$, ρ_{in} is the input state, ρ_{out} the corresponding output state of the channel. Suppose the alphabet consists of the letters $(\rho_i, i \in \{1,2\})$ and there exists decodings that can perfectly distinguish the two states. The initial state is, for example, $\rho_{in} = \rho_1$. After passing through the noisy channel, the output state is $\rho_{out} = (1-p)\rho_1 + p\rho_2$, i.e. with probability $1-p$ the state is sent correctly as ρ_1 and with probability. p a different state, here ρ_2, exits the channel. An important question is how many bits k of information can be sent reliably through the channel G with n uses of the channel. In other words, what is the maximal rate $Rn = k$ of sending reliably information? The maximal rate is also known as the channel capacity. In the following paragraph, to fix the ideas, I will calculate the channel capacity for the simplest channel, the identity channel.

5.2.4 Identity Channel

Here I will consider the ideal scenario, namely the channel transmits the message correctly, without changing anything, i.e. $G(\rho) = \rho$, $\forall \rho \in H$. The aim is to transmit k bits of information without error. It is possible to use the channel G n times, which leads to a rate of transmission of $R = k/n$. A state ρ_x is chosen to encode the message x, $x \in \{0,1\}^{\otimes nR}$. After passing through the channel the output state is given by $\rho_{out} = G^{\otimes nR}(\rho_x)$. For the

decoding, a measurement POVM [1] D_x is applied on the state ρ_{out} such that $\text{Tr}(D_x(\rho_x)) = 1$ while $\text{Tr}(D_x(\rho_{y \neq x})) = 0$. The probability of decoding the state correctly is given by

$$P_{\text{succ}}(Rn = k) = \max_{\{D_x\}x, \{\rho_x\}x} \frac{1}{2^{nR}} \sum_{x \in \{0,1\}^{\otimes nR}} \text{Tr}\left[D_x(G^{\otimes nR}(\rho_x))\right] \qquad (5.2.13)$$

Note that for any channel G, the maximization is performed over all possible encodings (states ρ_x) and decodings (measurements D_x). For the identity channel, the maximal rate, i.e., the channel capacity, can be determined analytically. Eq. (5.2.13) simplifies to

$$P_{succ}(Rn = k) = \max_{D_x x} \frac{1}{2^{nR}} \sum_{x \in 0,1^{\otimes nR}} \text{Tr}\left[D_x(\rho_x)\right] \qquad (5.2.14)$$

$$\leq \frac{1}{2^{nR}} \sum_{x \in 0,1^{\otimes nR}} \max_{D_x x} \text{Tr}\left[D_x\right] \qquad (5.2.15)$$

$$\leq 2^{-nR}\text{Tr}(1) \qquad (5.2.16)$$

$$= 2^{-n(1-R)} \qquad (5.2.17)$$

where in the second line, the Cauchy-Schwarz inequality was used, and the dimension of the measurement POVM is $d = 2^n$. If the rate is chosen to be larger than one, i.e., $k > n$, the probability of decoding the message correctly drops exponentially. The best achievable rate is $R = 1$.

The above scenario is valid both for classical and quantum channels. How is it possible to calculate channel capacities for more interesting cases than the identity channel? There is a useful theorem by Schumacher [55] which quantifies how much information can be sent through a noisy quantum channel

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[1]In functional analysis and quantum measurement theory, a positive operator-valued measure (POVM) is a measure whose values are positive semi-definite operators on a Hilbert space. POVMs are a generalisation of projection-valued measures (PVM) and, correspondingly, quantum measurements described by POVMs are a generalisation of quantum measurement described by PVMs (called projective measurements). In rough analogy, a POVM is to a PVM what a mixed state is to a pure state. Mixed states are needed to specify the state of a subsystem of a larger system (see purification of quantum state); analogously, POVMs are necessary to describe the effect on a subsystem of a projective measurement performed on a larger system.

with one use of the channel. And it is precisely this measurement and result that I studied and analysed in the model I devised.

5.2.5 Schumacher Theorem

Theorem: Classical capacity in a single use for noisy channels. Let G be a quantum operation that preserves the trace. The classical capacity in a single use can be calculated as:

$$C^1(G) = \max_{\{p_j, \rho_j\}} \left[S\left(\sum_j p_j G(\rho_j)\right) - \sum_j p_j S(G(\rho_j)) \right] \tag{5.2.18}$$
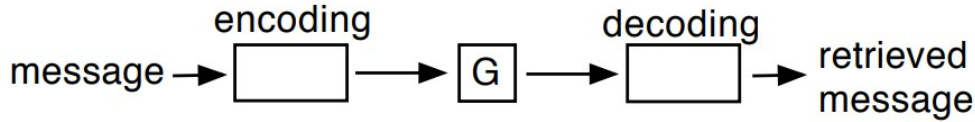

FIGURE 5.6: *The capacity of a classical communication channel, when it can be used only once, is measured by the one-shot classical capacity, which determines the amount of information that can be transmitted reliably.*

where S denotes the Von Neumann entropy. It can be shown that the maximisation of Eq. 5.2.18 can be obtained using a set of at most d^2 pure states, where d is the size of the input channel. It is easy to generalise the classical 1-use channel, as shown in Fig.5.6, to an n-use quantum channel:

$$C_n(G) = \max_{\{p_j, \rho_j \in H^{\otimes n}\}} \left[S\left(\sum_j p_j G^{\otimes n}(\rho_j)\right) - \sum_j p_j S(G^{\otimes n}(\rho_j)) \right] \tag{5.2.19}$$

If sender and receiver also share an infinite amount of entanglement, they can use this entanglement to enhance the transmission of classical information ([56], [57], [58]), as shown in Fig. 5.7. The maximum transmission rate is now referred to as "entanglement-assisted classical capacity" and can be calculated as follows:

$$C_E = \max_{\rho \in H} \left(S(\rho) + S(G(\rho)) - S\left((G \otimes \mathbb{I}_{\text{anc}})(\Phi)\right) \right) \tag{5.2.20}$$
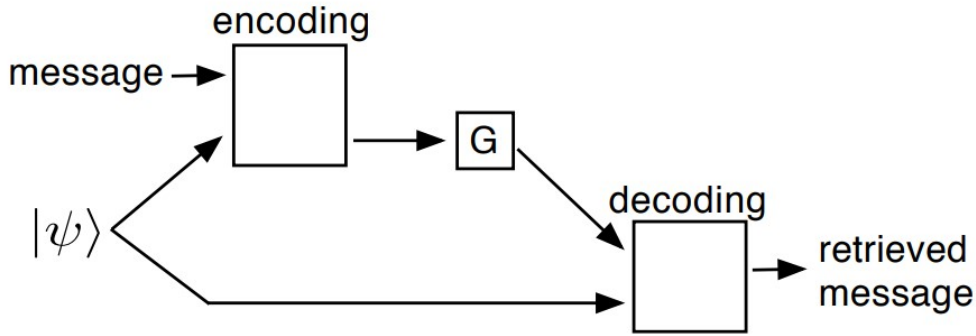
FIGURE 5.7: *The capacity of both classical and quantum channels can be increased if the sender and receiver of a message have a pre-existing entangled state represented by $|\psi\rangle$.*

where S is the Von Neumann entropy, G the genetic channel and Φ the purification of ρ on the largest Hilbert space [2].

Similar channel capacities exist for the transmission of quantum information. The channel capacities ([59],[60])

---

[2]Let $\mathcal{H}_S$ be a finite-dimensional Hilbert space, and consider a generic (possibly mixed) quantum state ρ defined on $\mathcal{H}_S$, and admitting a decomposition of the form

$$\rho = \sum_i p_i |\phi_i\rangle\langle\phi_i|,$$

for a collection of (not necessarily mutually orthogonal) states $|\phi_i\rangle \in \mathcal{H}_S$, and coefficients $p_i \geq 0$ such that $\sum_i p_i = 1$. Note that any quantum state can be written in such a way for some $\{|\phi_i\rangle\}_i$ and $\{p_i\}_i$.

Any such ρ can be purified, that is, represented as the partial trace of a pure state defined in a larger Hilbert space. More precisely, it is always possible to find a (finite-dimensional) Hilbert space $\mathcal{H}_A$ and a pure state $|\Psi_{SA}\rangle \in \mathcal{H}_S \otimes \mathcal{H}_A$ such that

$$\rho = \mathrm{Tr}_A(|\Psi_{SA}\rangle\langle\Psi_{SA}|)$$

Furthermore, the states $|\Psi_{SA}\rangle$ satisfying this are all and only those of the form

$$|\Psi_{SA}\rangle = \sum_i \sqrt{p_i}|\phi_i\rangle \otimes |a_i\rangle,$$

for some orthonormal basis $\{|a_i\rangle\}_i \subset \mathcal{H}_A$. The state $|\Psi_{SA}\rangle$ is then referred to as the "purification of ρ". Since the auxiliary space and the basis can be chosen arbitrarily, the purification of a mixed state is not unique; in fact, there are infinitely many purifications of a given mixed state. Because all of them admit a decomposition in the form given above, given any pair of purifications $|\Psi\rangle, |\Psi'\rangle \in \mathcal{H}_S \otimes \mathcal{H}_A$, there is always some unitary operation $U : \mathcal{H}_A \to \mathcal{H}_A$ such that

$$|\Psi'\rangle = (I \otimes U)|\Psi\rangle.$$

$$Q_1 = \max_{\{\rho \in H\}} \left(S(G(\rho)) - S\left((G \otimes \mathbb{I}_{\text{anc}})(\Phi) \right) \right) \qquad (5.2.21)$$

$$Q_E = \frac{C_E}{2} \qquad (5.2.22)$$

where Q_1 is the quantum capacity in a single use and Q_E denotes the entanglement-assisted quantum capacity.

5.3   The Biological Quantum Models

Based on the previous sections, I wanted to go and analyse a quantum model describing the dynamics in time and space of genetic mutations in DNA. I wanted to find the simplest possible model. I therefore chose to analyse both one dimensional Heisenberg and Ising quantum model, whose description is amply shown in the literature.

Both models present a coupling term with an external field and a term describing the interaction of each site with adjacent ones. These two fields are the two minimum and necessary ingredients that allow the physic-chemical interactions of the amino acid chain to be described. The first neighbour interaction is intended to represent the electrostatic interaction between the electronic clouds of base bonds and the external field is intended to represent the stabilisation of the chain of bonds between phosphate groups and sugars.

In quantum mechanics, the collapse operator is a mathematical operator that describes the process of wave function collapse. The wave function collapse is a fundamental aspect of quantum mechanics that occurs when a quantum system interacts with its environment, resulting in the reduction of the system's wave function to a single eigenstate.

The collapse operator, denoted by the symbol $\hat{C}$, has the form of a Hermitian operator. In general, the collapse operator can be written as:

$$\hat{C} = \sum_k c_k \hat{A}_k \tag{5.3.1}$$

where c_k are complex coefficients and $\hat{A}_k$ are Hermitian operators. The specific form of the collapse operator depends on the particular physical system being considered.

The collapse operator is used in the formalism of quantum mechanics to describe the process of quantum measurement, which is the process of obtaining information about a quantum system by interacting with it. When a measurement is made on a quantum system, the wave function collapses into one of its eigenstates, corresponding to the result of the measurement.

The collapse operator plays an important role in the theory of quantum measurement, as it describes the way in which the wave function of a quantum system is collapsed during the measurement process. The form of the collapse operator reflects the specific interaction between the quantum system and its environment, which is responsible for the wave function collapse.

In the context of spin chains, the collapse operator is a mathematical operator that describes the process of measurement-induced decoherence, which causes the wave function of the spin chain to collapse into an eigenstate due to the interaction with the environment. The specific form of the collapse operator depends on the type of measurement being made on the spin chain. For example, if the measurement is a local projective measurement on a single spin in the spin chain, the collapse operator can be written as:

$$\hat{C}_j = |\uparrow_j\rangle\langle\uparrow_j| + |\downarrow_j\rangle\langle\downarrow_j| \tag{5.3.2}$$

where $|\uparrow_j\rangle$ and $|\downarrow_j\rangle$ are the two eigenstates of the spin operator at site j of the chain.

In general, the collapse operator for a measurement on a spin chain can be written as a linear combination of projectors onto the eigenstates of the measured quantity. The specific form of the collapse operator depends on the

type of measurement being made, as well as the interaction between the spin chain and the environment.

In my case the collapse operator will be the same type of operator that appears in the Hamiltonian to represent the coupling with the external field, which is precisely the interaction of the spin chain with the environment. That is, the Pauli z-matrix.

Both models operate on an SU(2) space. Where the spin up and spin down states represent the mutated or unmutated gene, respectively. And the probability of transiting I will see is closely linked to the value of the external fields that I can freely set. Evidently, a mutation excites the system and provides it with an energy gap. In my simulations I analyse how the mutation of each site varies along the spin chain, i.e. along the ideal amino acid chain and over time.

I also measured the entanglement entropy, which is a quantity that measures the amount of information required to describe the quantum state of a system composed of two or more entangled subsystems, which I have already discussed in the previous section.

In particular, the entanglement entropy between two subsystems A and B of a quantum system is defined as the Von Neumann entropy of the partial density operator of A, i.e. the trace of the square of the density operator of subsystem A. In other words, entanglement entropy measures the amount of information that is lost when subsystem B is "ignored" and only subsystem A is observed.

Entanglement entropy is a very important concept in quantum physics, as it is closely related to the concept of decoherence, which is the process of loss of quantum coherence of a system interacting with the external environment. Furthermore, entanglement entropy has been used to study the nature of the quantum phase transition and the quantification of the complexity of quantum systems.

Decoherence is a physical process that causes a system to lose quantum coherence. Specifically, when a quantum system interacts with its external environment, the quantum properties of the system leak into the environment and are replaced by classical properties. This process of loss of coherence is the well-known concept of decoherence.

Entanglement entropy is closely related to decoherence because quantum entanglement is a property that disappears when the system decoheres. When two particles (or two subsystems) are entangled, the properties of one particle are related to the properties of the other, even if the particles are far apart in space. However, when these particles interact with the external environment, the quantum coherence between them is destroyed and the entanglement dissolves. When a system decoheres, the entanglement entropy between its subsystems decreases and the system becomes more and more classical. In other words, entanglement entropy is a measure of quantum entanglement, and its evolution over time is related to the decoherence of the system. Studying entanglement entropy in a quantum system can therefore provide important information on the nature of decoherence and the transition from quantum to classical behaviour.

5.3.1 The Qutip library

The `mesolve` function of QuTiP (Quantum Toolbox in Python) is a function to solve the Schrödinger equation or master equation for an open quantum system. This function is very useful for simulating the evolution of a quantum system under the influence of a Hamiltonian and collapse operators representing the effect of noise or interaction with the environment.

The basic syntax of the mesolve function is as follows:

```
mesolve(H, rho0, tlist, c_ops, e_ops, args=None, options=None)
```

where:

- `H` is the Hamiltonian of the system;

- `rho0` is the initial state of the system;

- `tlist` is the list of times at which the evolution of the system is to be calculated;

- `c_ops` is a list of collapse operators describing the effect of noise or interaction with the environment;

- `e_ops` is a list of operators of observables that we wish to calculate during the evolution of the system;

- `options` is an object that allows us to specify some additional options, such as the numerical method to be used for solving the equation.

QuTiP's `mesolve` function solves the master equation for an open quantum system using the fourth-order Runge-Kutta numerical integration method (RK4). The RK4 method is a popular algorithm for solving ordinary differential equations (ODEs), such as the master equation.

The master equation is a first-order differential equation for the density matrix of the open quantum system, which describes the time evolution of the system in the presence of collapse operators representing the effect of noise or interaction with the environment. Specifically, the master equation has the following form:

$$\frac{d\rho}{dt} = -i[H, \rho] + \sum_n \gamma_n \left(L_n \rho L_n^\dagger - \frac{1}{2}\{L_n^\dagger L_n, \rho\} \right), \tag{5.3.3}$$

where H is the Hamiltonian of the system, ρ is the density matrix of the system, L_n are the collapse operators representing the effect of noise or interaction with the environment, and γ_n are the decoherence rates associated with the L_n operators.

The main idea of the RK4 method is to divide the time interval $[0, t_f]$ into a set of subintervals of amplitude h, and to approximate the solution of the master equation in each subinterval by a series of linear approximations. In particular, the RK4 method uses four linear approximations to calculate the solution in each subinterval, and combines these approximations to obtain a global solution of the master equation.

The RK4 method is one of the most accurate and stable numerical methods for solving ordinary differential equations, and is particularly suitable for solving the master equation for open quantum systems. QuTiP's `mesolve` function uses an optimised version of the RK4 method that is able to handle large density matrices and calculate the system's observables efficiently.

The mesolve function returns a Result object that contains information on the evolution of the system. In particular, it is possible to access the density matrix of the system at each instant of time, the observables calculated during the evolution and the average values of the observables. To solve the master equation instead of the Schrödinger equation, simply specify the `solver="me"` option in the call to the mesolve function.

5.3.2   The Biological Heisenberg model

Idealized mutation

Let us analyse the first model. The Hamiltonian can be written in the following form [3]:

$$\hat{H} = -J \sum_{j=1}^{N} \hat{\boldsymbol{\sigma}}_j \cdot \hat{\boldsymbol{\sigma}}_{j+1} - h \sum_{j=1}^{N} \hat{\sigma}_j^z, \tag{5.3.4}$$

where J is the coupling constant and h is the external field. The spin operators act upon the tensor product $(\mathbb{C}^2)^{\otimes N}$, of dimension 2^N. To define it, recall the Pauli spin-1/2 matrices:

$$\hat{\sigma}^x = \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}, \quad \hat{\sigma}^y = \begin{pmatrix} 0 & -i \\ i & 0 \end{pmatrix}, \quad \hat{\sigma}^z = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}, \tag{5.3.5}$$

and for $1 \leq j \leq N$ and $a \in x, y, z$ denote

$$\hat{\sigma}_j^a = I^{\otimes j-1} \otimes \hat{\sigma}^a \otimes I^{\otimes N-j}, \tag{5.3.6}$$

---

[3]The σ Pauli are quantum operators.

where I is the 2×2 identity matrix. Given a choice of real-valued coupling constants J_x, J_y, J_z, and h, the Hamiltonian is given by:

$$\hat{H} = -\frac{1}{2} \sum_{j=1}^{N} (J_x \hat{\sigma}_j^x \hat{\sigma}_{j+1}^x + J_y \hat{\sigma}_j^y \hat{\sigma}_{j+1}^y + J_z \hat{\sigma}_j^z \hat{\sigma}_{j+1}^z + h \hat{\sigma}_j^z), \qquad (5.3.7)$$

where the h on the right-hand side indicates the external magnetic field, with periodic boundary conditions. It is common to name the model depending on the values of J_x, J_y, and J_z: if $J_x \neq J_y \neq J_z$, the model is called the Heisenberg XYZ model; in the case of $J_x = J_y \neq J_z$, it is the Heisenberg XXZ model; if $J_x = J_y = J_z = J$, it is the Heisenberg XXX model.

In these first simulations, I studied the average magnetisation value over time for each site, which from a biological point of view identifies the degree of mutation of the gene.

The degrees of freedom I can set are the initial state of the simulation and the values of spin number and the strength of the external fields and coupling between first neighbours and the environment.

I start by assuming a particular initial state. The first spin up (mutated gene) and the others in the down state (non-mutated gene).
In the Fig. 5.8 I compute the magnetisation of each spin varied the number of spins, the intensity of the external field and the interaction between first neighborhood fields. By setting $\gamma = 0$, I cancel the system's interaction with the environment and the spin chain becomes a closed system (since the collapse operator in this case is zero).

There is no general phenomenon worth mentioning, only the marginal delay of the spin following the initial mutation that is affected by the fact that the first spin has been changed. The value of the magnetisation fluctuates in a non-constant manner, see Fig. 5.9.

The addition of a possible interaction of the chain with the environment can be seen in figure 5.10. There are no more complete oscillations in any case.
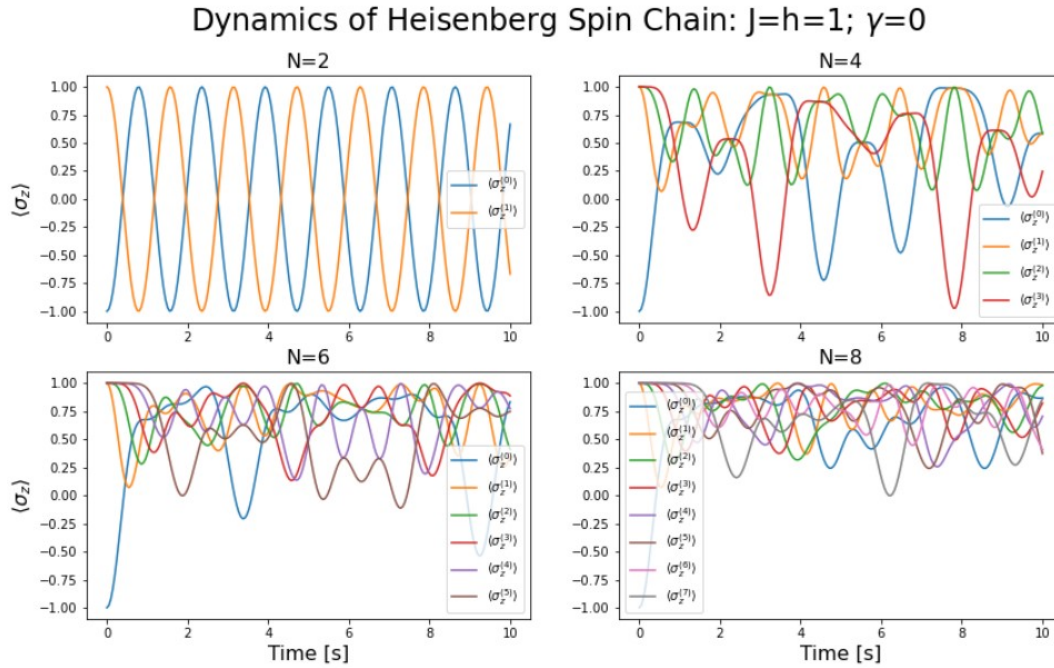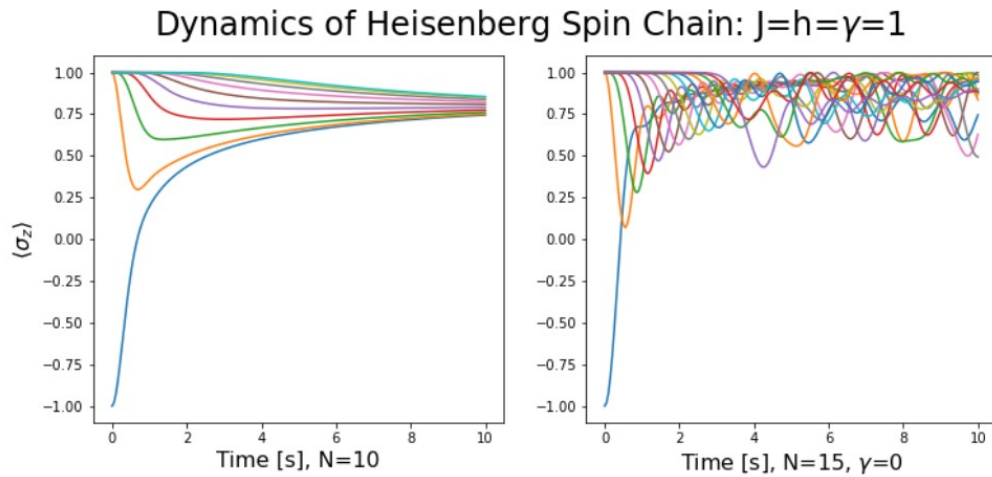
FIGURE 5.8: *Average value of the component along z of the spin of each site as time varies. In the case of zero interaction with the environment ($\gamma = 0$), and external field strength and coupling field between first neighborhood $J = h = 1$ in the Heisenberg model.*
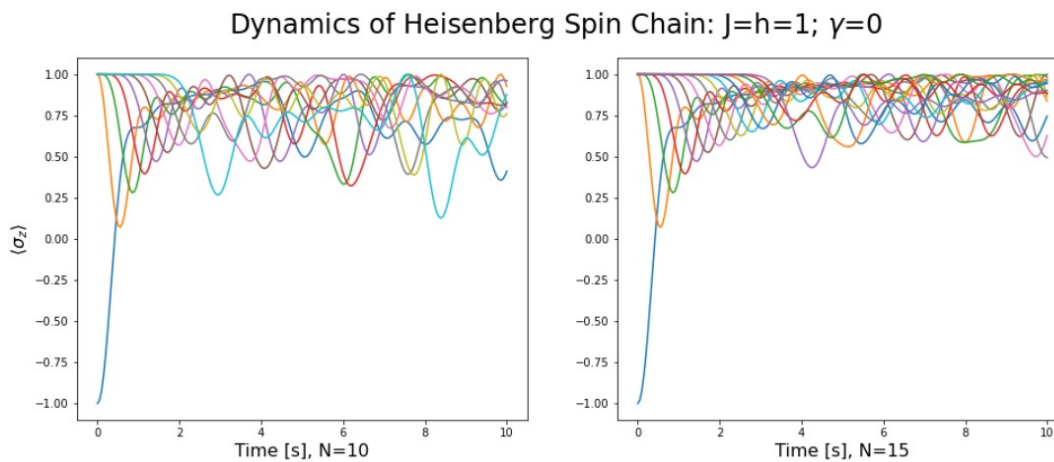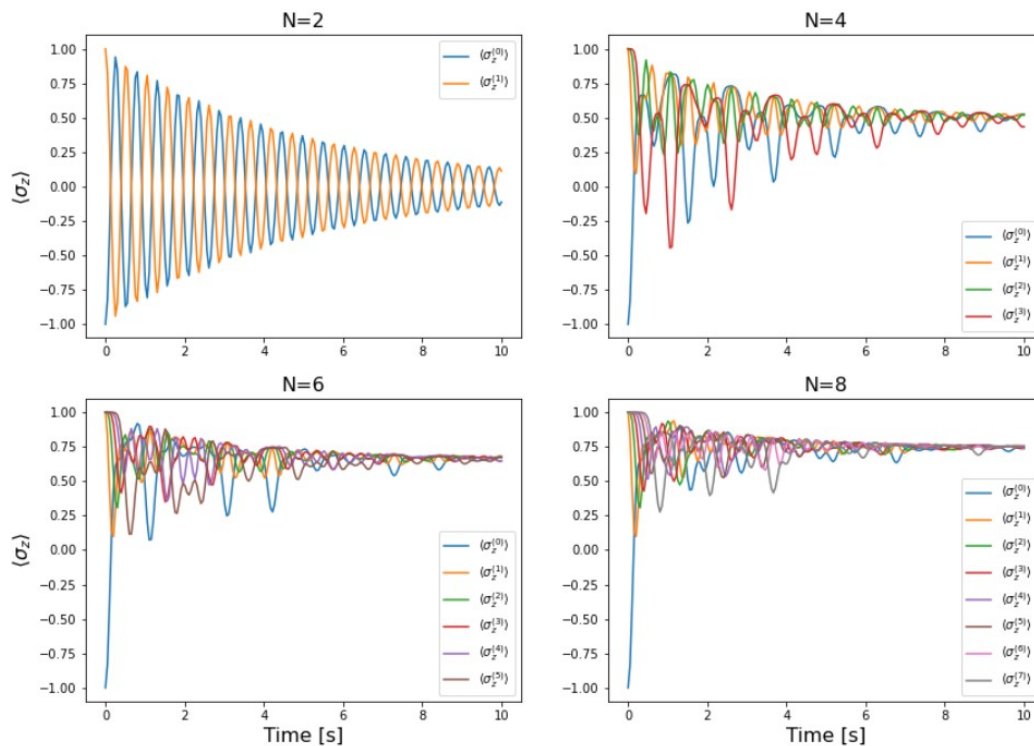

FIGURE 5.9: *Average value of the component along z of the spin of each site as time varies. In the case of zero interaction with the environment ($\gamma = 0$), and external field strength and coupling field between primes $J = h = 1$ in the Heisenberg model. Case of 10 spin (left) and case of 15 spin (right). The legend is not shown in order to show more clearly the trend of magnetisation in the first moments of the simulation.*

However, one can again see the delayed response of the spin sensing the delayed presence of the flipped spin at the first place in the chain.
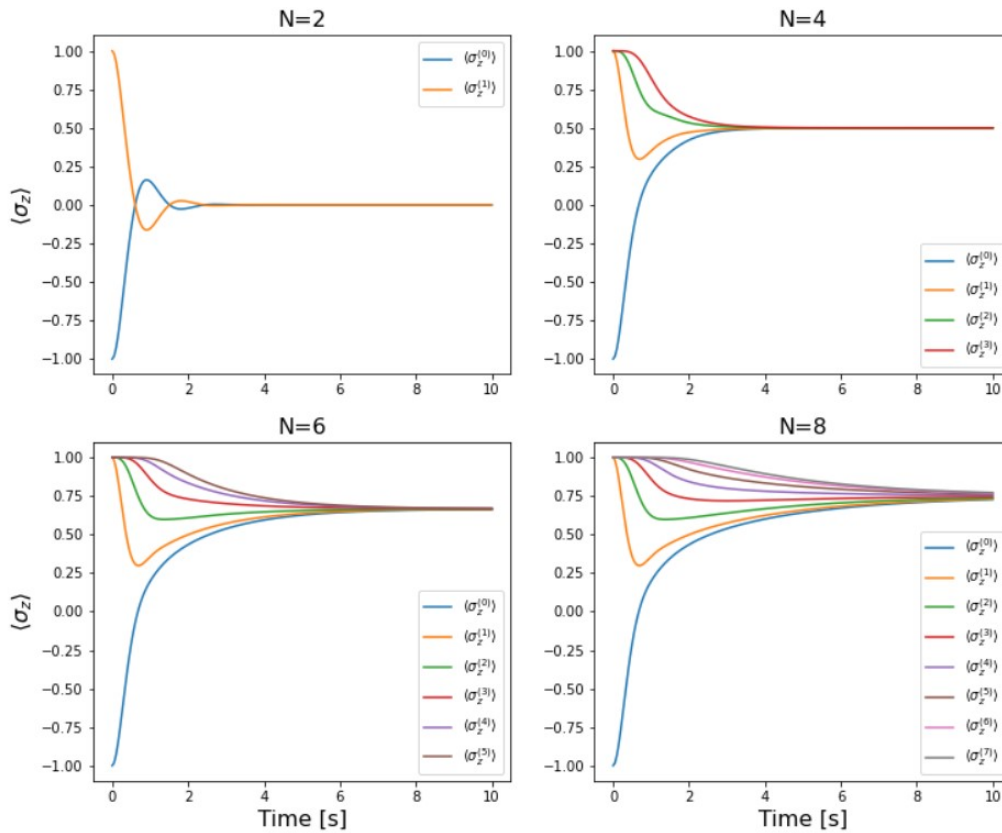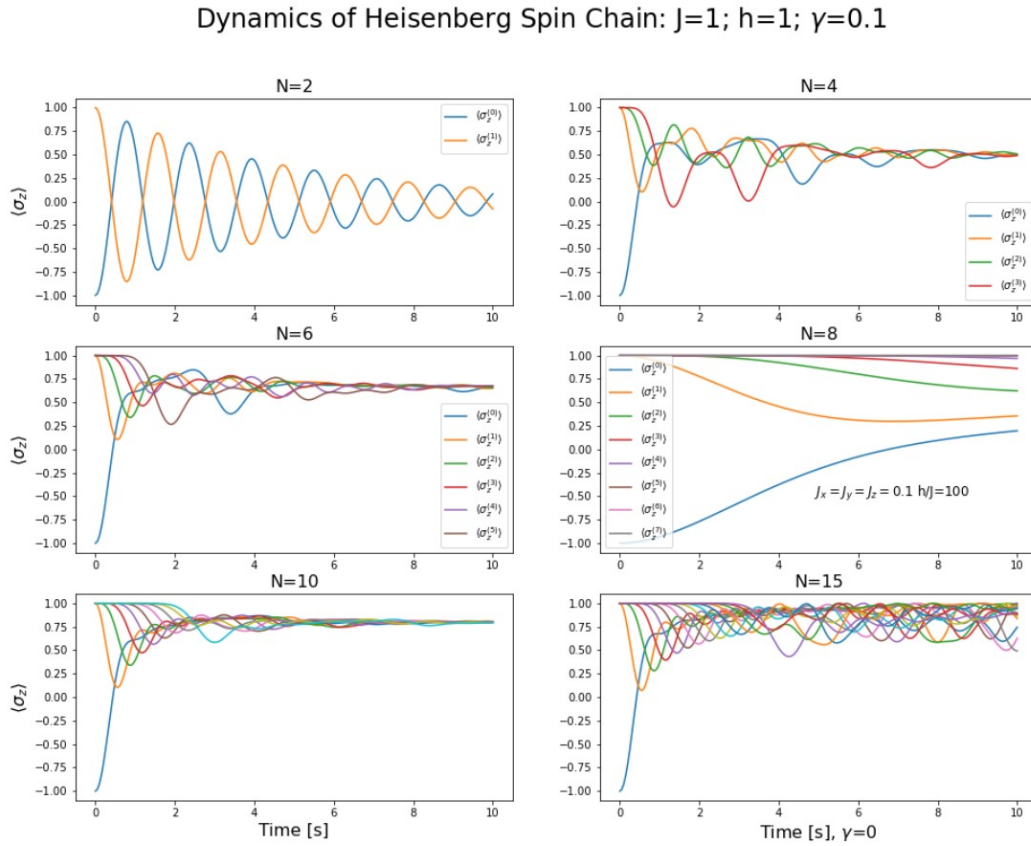
FIGURE 5.10: *Average value of the component along z of the spin of each site as time varies. In the case of unit interaction with the environment ($\gamma = 1$), and external field strength and coupling field between primes $J = h = 1$ in the Heisenberg model. From left to right, from top to bottom the spin number increases.*

For $N = 15$ the system is too complicated to solve from a computational point of view, and the simulation would have taken too long when it decides to include the factor γ as well, so I set it to zero. In Fig. 5.11, the simulations refer to a number of different spins. I see again that the oscillation due to the absence of interaction with the environment is very prevalent and makes the system very chaotic.

By increasing the value of the coupling field J, an increase in the number of oscillations of the mean spin values can be observed, see Fig. 5.12. The slight interaction with the environment causes the amplitude of the oscillations to decrease, destroying quantum coherence.

FIGURE 5.11: *Average value of the component along z of the spin of each site as time varies. In the case of unit interaction with the environment ($\gamma = 1$), and external field strength and coupling field between primes $J = h = 1$ in the Heisenberg model. Case of 10 spin (left), case of 15 spin (right) set with $\gamma = 0$ as it was too computationally demanding to calculate.*

FIGURE 5.12: *Average value of the component along z of the spin of each site as time varies. In the case of interaction with the environment equal to ($\gamma = 0.1$), and external field strength and coupling field strength respectively $J = 3$ and $h = 1$ in the Heisenberg model. From left to right, from top veros bottom the number of spins increases.*

FIGURE 5.13: *Average value of the component along z of the spin of each site as time varies. In the case of interaction with the environment equal to ($\gamma = 0.1$), and external field strength and coupling field equal $J = h = 1$ in the Heisenberg model. From left to right, from top to bottom the number of spins increases. In the case of $N = 8$ I show the case of a coupling field one order of magnitude smaller than the external field.*

Given the large level of chaos due to a large value of the spin-coupling constant I place $J = 1$, see Fig. 5.13. And given the large damping due to interaction with the environment I set $\gamma = 0.1$. In particular in this figure I have also shown the case of very different coupling and external fields ($h/J = 100$). The delay effect is always present. One spin after another in the chain lowers its magnetisation influenced by the presence of the flip in the spin of the first site. And their degree of mutation changes and fluctuates depending on how large the coupling constant between first neighbours is.

To clarify the physical meaning of these simulations, I measure the probability of spin-up occupancy of sites in the chain. I can then quantify how the epigenetic mutation localises or disperses in the chain as a function of time.
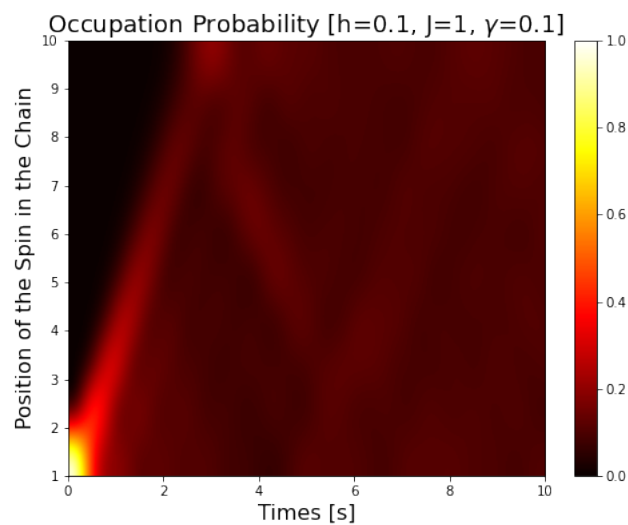
FIGURE 5.14: *Probability of flipping along the spin chain (indexed on the y-axis) over time (indexed on the x-axis). The closer the colour is to white, the greater the probability of a mutation occurring. The Heisenberg model is set to the value of the fields $h = 0.1$, $J = 1$, $\gamma = 0.1$.*
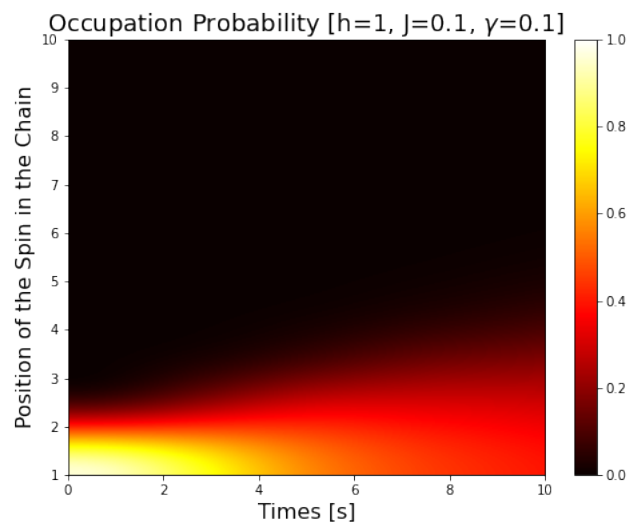

FIGURE 5.15: *Probability of flipping along the spin chain (indexed on the y-axis) over time (indexed on the x-axis). The closer the colour is to white, the greater the probability of a mutation occurring. The Heisenberg model is set to the value of the fields $h = 1$, $J = 0.1$, $\gamma = 0.1$.*

In Fig. 5.14 and Fig. 5.15 I see two very different mutation behaviours. In fact, in the first case (Fig. 5.14) the mutation evolves and reaches all the DNA sites, dissolving more and more in function of time. In the second case (Fig.

5.15), when the coupling field is much smaller than the external field, the mutation is localised and remains at the level of the first and second DNA genes.

Subsequently setting the values of the fields appropriately, the emerging result is that no matter how large h is, if J is not greater than or equal to one the mutated gene cannot expand.

Looking closely at the symmetries of DNA, I can assume that everything can be described by a model in two dimensions. So let us set the coupling along the y-axis equal to zero and refine the Heisenberg model. By redoing the simulations with this value of the coupling field. I note that now a value of $J_x = J_z = 1$ is no longer sufficient for the mutation process on the whole chain. But a higher value greater than one is required.

Realistic mutation

I now use the same type of simulations but starting from a much more truthful initial state. In fact, two types of mutations can occur due to the tunnelling effect in the nitrogenous bases. Those relating to purine bases and those relating to pyrimidine bases. To each type of mutation I associate a rate a and b. Each gene will incur an a priori supposedly random mutation type. I use the following code to implement the initial state:

```
psi_list=[]
for n in range(N):
    a=random.random()
    b=random.random()
    c=1
    numbers=[a,b,c]
    d= random.choice(numbers)
    psi_list.append(d*basis(2,0)+math.sqrt(1-d**2)*basis(2,1))
psi0 = tensor(psi_list)
```

What I get in the end is an initial macrostate where each gene is in a mutated-unmutated overlap with two different probability rates of mutation respectively caused by a mutation supported by the tunnelling effect. These are the main results.
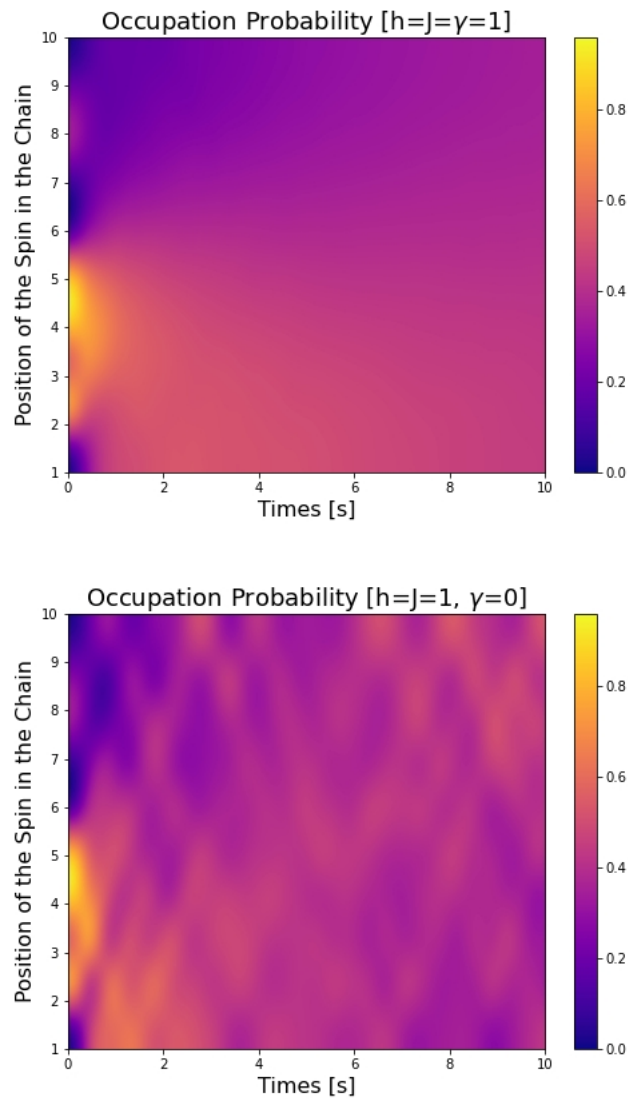

FIGURE 5.16: *Probability of flipping along the spin chain (indexed on the y-axis) over time (indexed on the x-axis). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour approaches blue the lower the probability that a mutation occurs. The Heisenberg model is set to the value of the fields $h = 1$, $J = 1$, $\gamma = 1$ (top) and $h = 1$, $J = 1$, $\gamma = 0$ (bottom).*

Fig. 5.16 shows the case where unit coupling and external field influence the location of the mutation in the case of net interaction with the environment

and null interaction with the environment by setting the parameter γ. As could already be assumed, the mutation is strongly localised in the case $\gamma = 1$ and strongly dispersed in the case $\gamma = 0$. For the above considerations we can therefore set the parameter $\gamma = 0.1$. The graph does not distinguish the type of mutation only if it is present in the initial state.
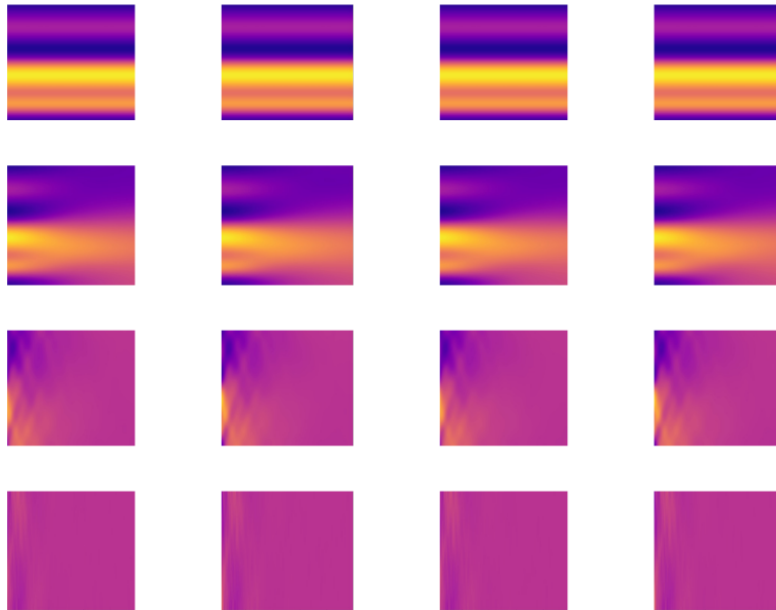
FIGURE 5.17: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour approaches blue the lower the probability that a mutation occurs. From left to right the value of the external field h, takes on larger and larger values* $[0, 0.1, 1, 10]$. *From top to bottom, the value of the coupling field J between neighbouring primes takes on larger and larger values* $[0, 0.1, 1, 10]$.

By varying the fields appropriately, I am also able to identify a phase transition when the field J goes from being less than unity to when it becomes larger. The mutation in fact only intercepts the whole chain in the case where the coupling field exceeds this value, regardless of the value of the field h, see Fig. 5.17. In particular, when the mutation intercepts the whole DNA chain we arrive at a large overlapping macro-state of mutated-unmutated gene.

I wanted to eventually compare the effect of the fields when they are of the same order of magnitude. And as could be imagined when $J > h$ (Fig. 5.18
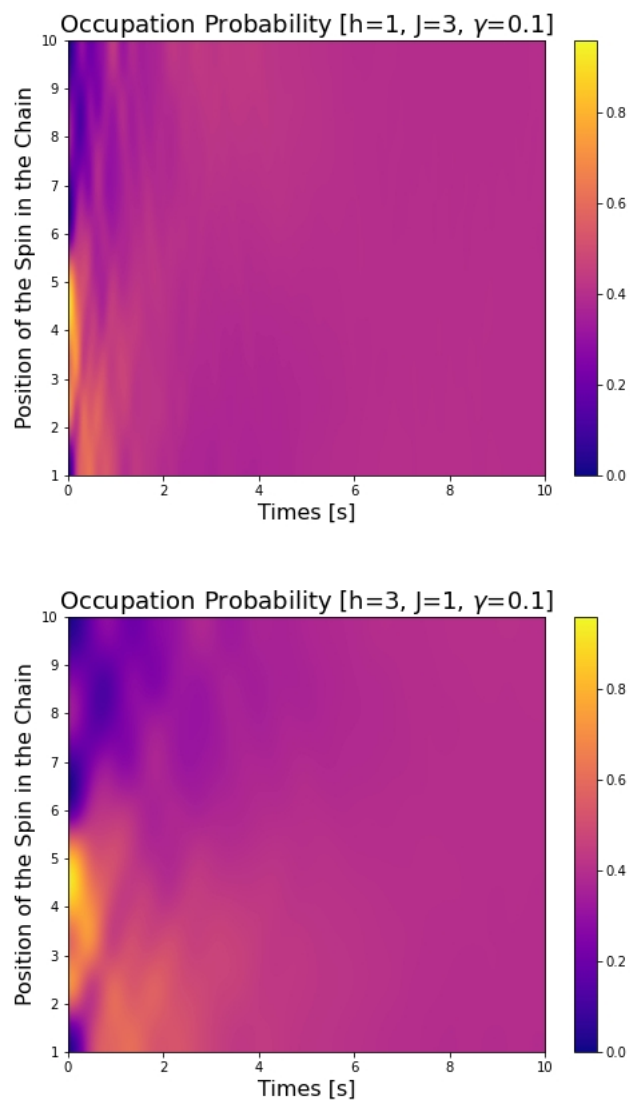
FIGURE 5.18: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour approaches blue the lower the probability that a mutation occurs. The field J and the field h are of the same order of magnitude. Case J > h (top), case J < h (bottom).*

) the oscillation of the mutation is larger and the overlapping macrostate is established earlier.

5.3.3 The Biological Ising model

Idealized mutation

For the second model, I performed the same type of simulations as in the previous section. However, I change the operator describing the dynamics of the problem. In fact, in this case, I model the genetic chain with the following Hamiltonian:

$$\hat{H} = -J \sum_{j=1}^{N} \sigma_j^z \sigma_{j+1}^z - h \sum_{j=1}^{N} \sigma_j^x, \tag{5.3.8}$$

where J is the coupling constant and h is the external field. The main difference between the two models lies in the way the spins interact with each other. In the Heisenberg model, the spins are allowed to interact with each other in all three spatial dimensions. This means that the interaction between two neighboring spins can be in any direction, which gives rise to a more complex and rich set of behaviors. In contrast, the Ising model only allows for interactions between neighboring spins in one dimension, typically along a lattice. This makes the Ising model simpler and easier to analyze than the Heisenberg model.

Another difference between the two models is the way they are formulated mathematically. The Heisenberg model is described using a vector operator, known as the spin operator, which acts on each individual spin. The Ising model, on the other hand, is described using a scalar variable, which represents the orientation of each spin.

Overall, the Heisenberg model and the Ising model are both important quantum models used to study the behavior of interacting spins in a lattice. While the Heisenberg model is more complex and allows for richer behaviors, the Ising model is simpler and easier to analyze, making it a popular choice for many applications.

For this model, I have focused on the representation of the occupancy probability of a mutation in the chain as time varies. Since this is the physical quantity that best clarifies the behaviour of the mutation.

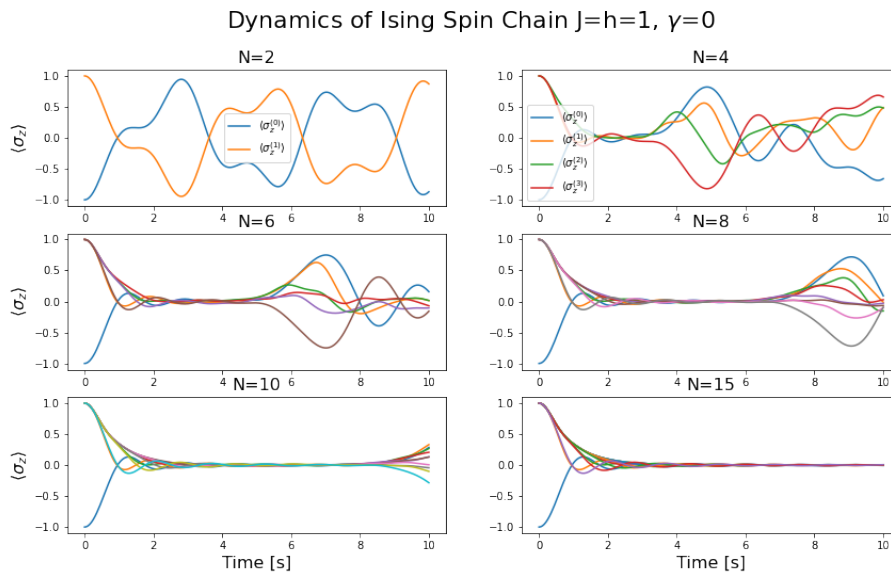I again started from the same initial state investigated in the previous section.

FIGURE 5.19: *Average value of the component along z of the spin of each site as time varies. In the case of zero interaction with the environment ($\gamma = 0$), and external field strength and coupling field between first neighborhood $J = h = 1$ in the Ising model.*

In Fig. 5.19 I see the results of the first simulation on the new system. First of all, one can see a big difference from Heisenberg's model, in particular one can see that the average value for each spin settles to zero quickly at the beginning and then after a few seconds takes on a non-zero value oscillating around zero. By increasing the number of spins in the chain, the area where there is non-zero magnetisation shifts along the positive direction of the time axis. Until it disappears altogether in the case of 15 spin.

If I add the factor $\gamma = 1$, the system interacts with its surroundings, I have no fluctuation of the magnetization but a rapid decrease towards zero, look at Fig. 5.20. From the following simulations I will set $\gamma = 0.1$ given the rapid decrease to the null value of the magnetisation.
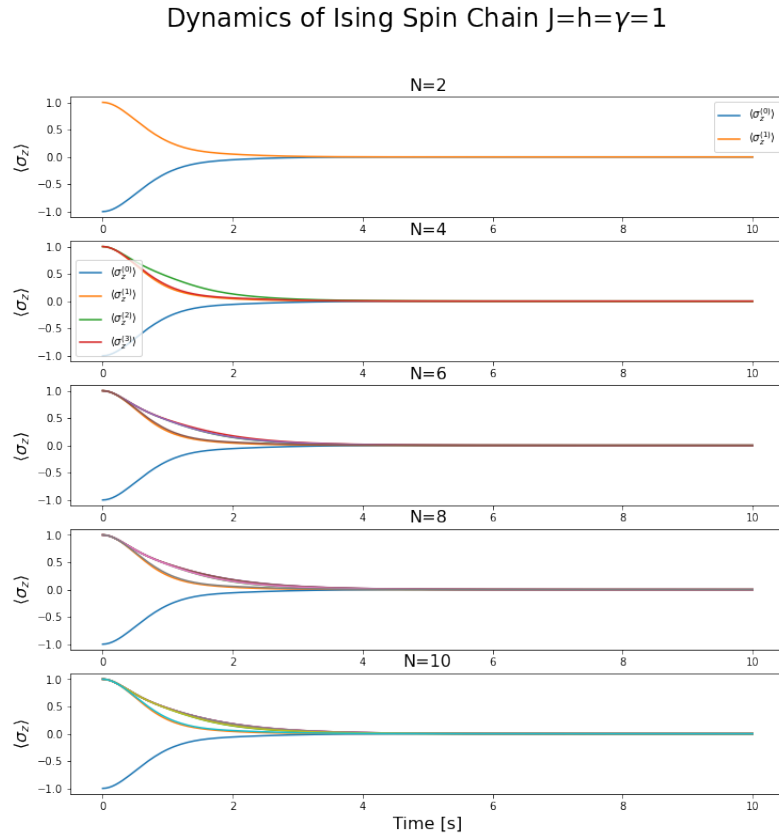
FIGURE 5.20: *Average value of the component along z of the spin of each site as time varies. In the case of unit interaction with the environment ($\gamma = 1$), and external field strength and coupling field between first neighborhood $J = h = 1$ in the Ising model.*

I now analyse the dynamics of the mutation as the coupling and external fields vary. I focused on measurements of the mutation as a function of time and the position of the chain spin.

As can be seen in Fig. 5.21, once the external and coupling fields are fixed to the unit, the mutation pattern varies considerably as the system's intensity changes with the environment. In the case of $\gamma = 0$ the mutation succeeds in expanding along the entire chain, and there also emerges an instant in which the mutation is only localised to the last spin while all the others are unmutated, thus reflecting a situation mirroring the initial one. While setting $\gamma = 1$. There is no oscillation whatsoever, and after a few seconds the whole system is in a state of superposition with equal probability of having a mutated and an unmutated gene. With $\gamma = 0.1$ the transition period from localised mutation to overlapping macrostate, in the sense described above,
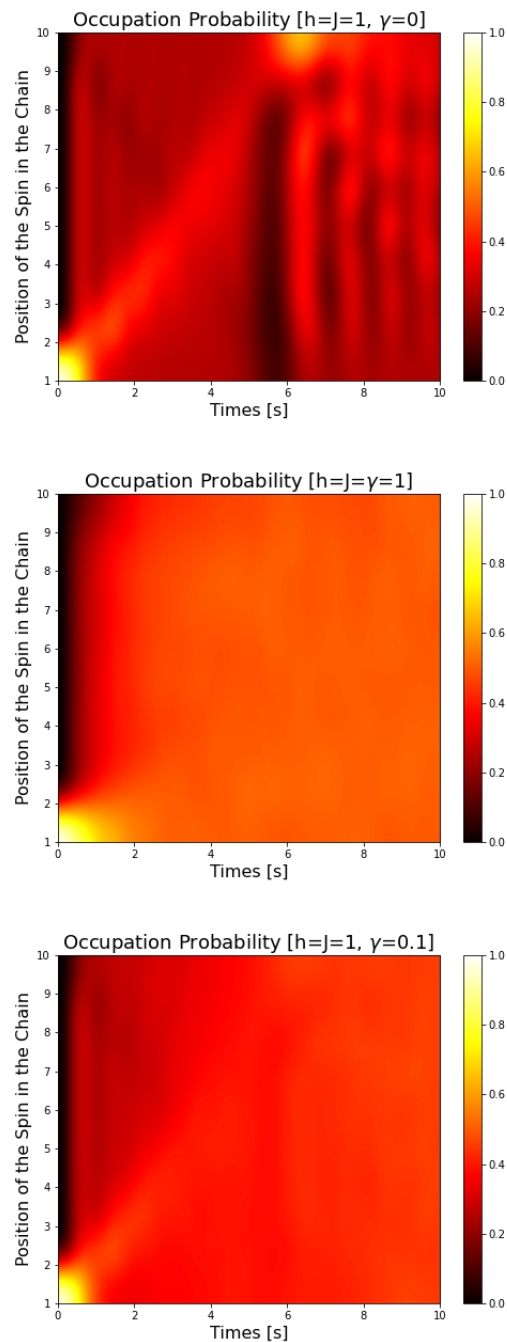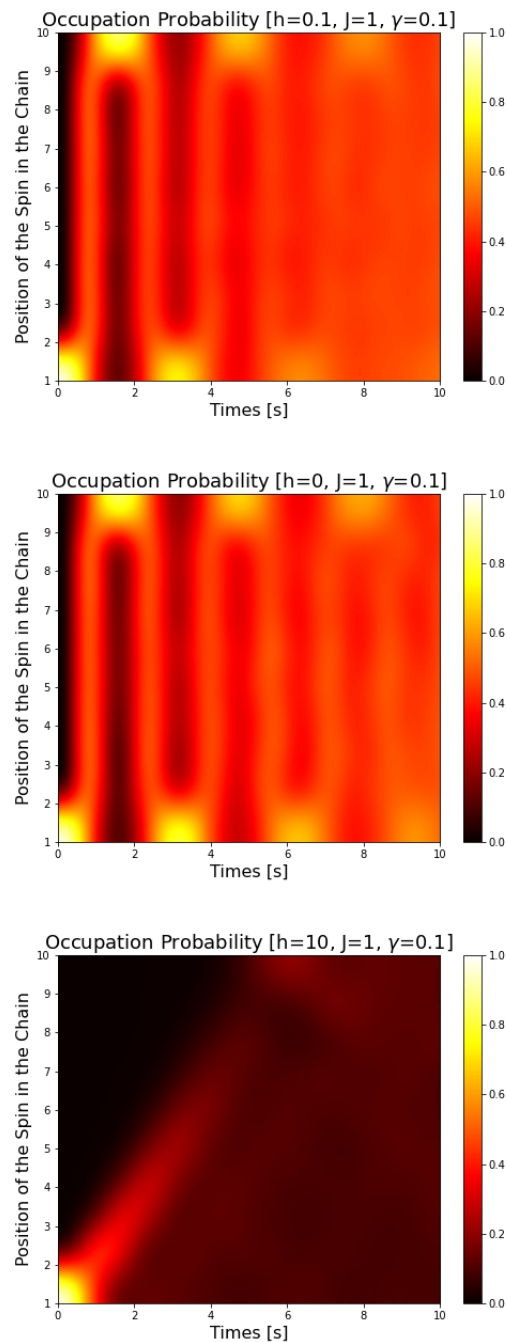
FIGURE 5.21: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour is to black the lower the probability that a mutation occurs. The range J and the range h are equal to one. Case $\gamma = 0$ (top), case $\gamma = 1$ (middle) and case $\gamma = 0.1$ (bottom).*

is somewhat longer but still emergent. I make the assumption of minimal but nevertheless preset interaction of the DNA with the environment, for which

I set $\gamma = 0.1$, for the next simulations.

FIGURE 5.22: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour is to black the lower the probability that a mutation occurs. The field $\gamma = 0.1$, the field $J = 1$ and the external field take on different values. Case $h = 0.1$ (top), case $h = 0$ (middle) and case $h = 10$ (bottom).*

Instead, I analyse the case of the coupling field between first neighbours fixed $J = 1$ and the external field. The field h goes from values much lower than unity to values much higher than unity, going from a null value, see Fig. 5.22. It can be seen that the net effect of the external field on the dynamics of the mutation is to accelerate or decrease the time in which the mutation propagates from the first gene to the last and then back again. Indeed, at the bottom of the same figure, it can be seen that the mutation expands at a constant rate throughout the DNA, never reaching the last gene with sufficiently high probability.

At this point I make a similar study for the coupling field J, which varies with a fixed external field h. A clear phase separation can also be seen here. For values zero or less than unity for J, the mutation is strongly localised to the point where it was prepared, see Fig. 5.23. For J of order of magnitude greater than h, when it is fixed to one, the mutation not only manages to propagate along the entire chain, but is reflected numerous times, as great as the value of J is.

In the last case I analyse h and J of the same order of magnitude but different value. In the case $h > J$ (Fig. 5.24) the mutation is reflected only once and reaches the last gene with a probability not too high. In contrast, in the case $h < J$ (Fig. 5.25) the mutation succeed in expanding and being reflected with a high degree of certainty.

By resuming, I fixed the initial state to an ideal situation in which only one gene is mutated, and I wanted to go and quantify how and under what conditions this mutation localises or expands throughout the chain: no matter how big h is, if J is not greater than and or equal to one the mutated gene cannot expand.

Realistic mutation

In this section I have adopted the initial state of the previous section, in order to refine the model and make it more realistic.
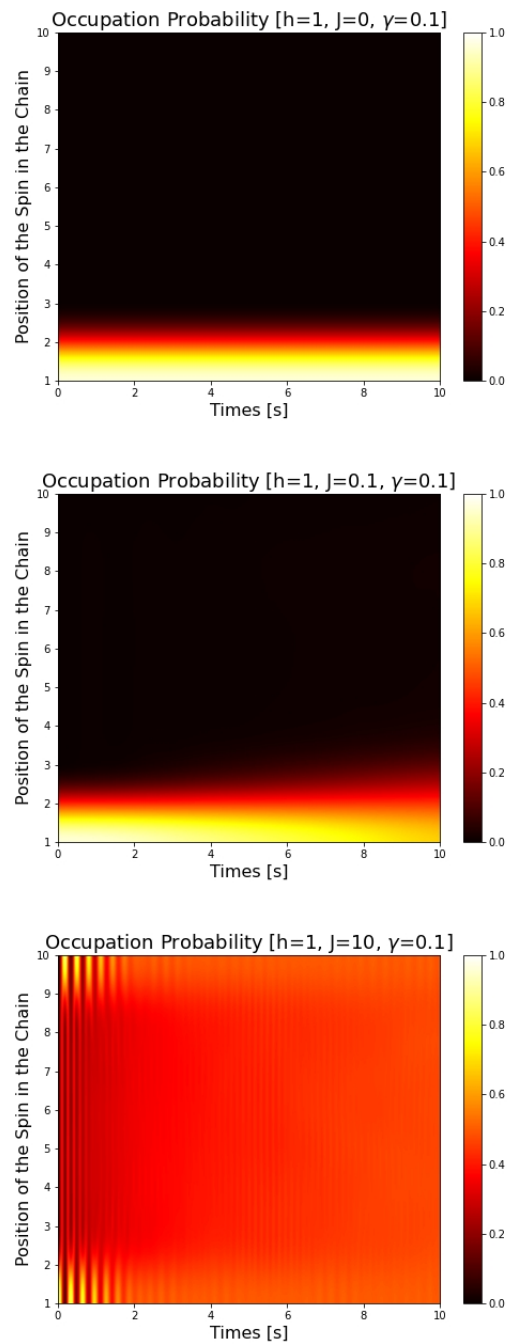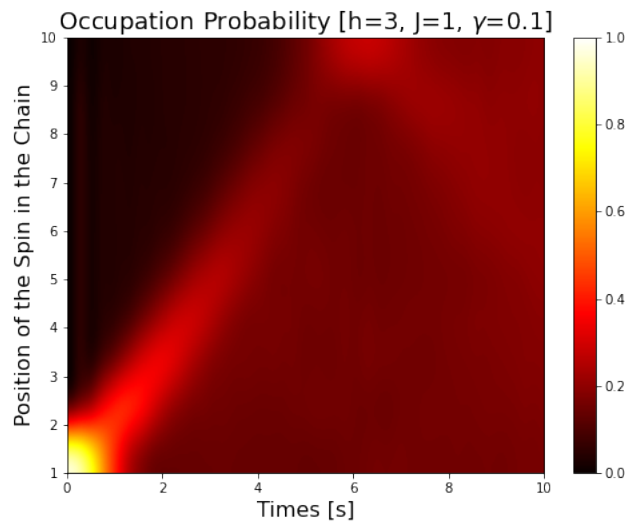
FIGURE 5.23: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour is to black the lower the probability that a mutation occurs. The field $\gamma = 0.1$, the field $h = 1$ and the external field take on different values. Case $J = 0$ (top), case $J = 0.1$ (middle) and case $J = 10$ (bottom).*

FIGURE 5.24: *The box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour is to black the lower the probability that a mutation occurs. The field $\gamma = 0.1$. The outer field and the first-neighbour interaction field take on two different values but of the same order of magnitude ($h = 3$ and $J = 1$).*

Compared to the Heisenberg model, the mutation amplification rate along the chain is non-linear and much more chaotic when $\gamma = 0$. And no preferential direction of mutation diffusion seems to emerge, see Fig. 5.26. In fact, in Heisenberg's model one could see straight lines on the propagation of the mutation, in this case it is more of a spatio-temporal pattern of spots. Again, if $\gamma = 1$ the mutation is well localised and then disperses in the known overlapping macrostate. Once again a parameter $\gamma = 0.1$ was chosen.

Here again, I wanted to sample the dynamics of mutation by varying both fields J and h, see Fig. 5.27. I see a sharp phase transition, from a mutation localised in time and space to an oscillation and subsequent dispersion due to interaction with the environment, ($\gamma = 0.1$ in all these simulations as in the previous section). The critical parameter also in this case is given by the J field, which from a value of 1 allows the mutation to expand along the chain. In contrast to the Heisenberg model, the oscillation is more evident, regular and sharp, especially in the case of fields $J > 1$.
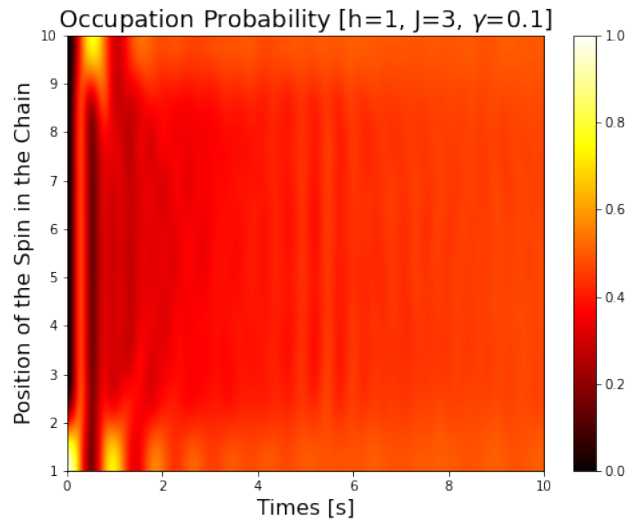
FIGURE 5.25: *The box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour is to black the lower the probability that a mutation occurs. The field $\gamma = 0.1$. The outer field and the first neighbour interaction field take on two different values but of the same order of magnitude ($h = 1$ and $J = 3$).*

Finally, look at Fig. 5.28, I wanted to compare the situation of coupling and external fields of the same order of magnitude. In this case I can differentiate two behaviours that I had already observed in the previous section, in fact when $J > h$, the emerging behaviour is the oscillation of the mutation probability, when one is in the case $J < h$ one has the expansion at a constant rate along the whole chain.

5.3.4 The dispersion of information in the DNA

The quantum capacity of a quantum channel is related to the entropy of the system because it is a measure of how much quantum information can be transmitted through the channel. The entropy of a quantum system is a measure of its uncertainty or randomness, and the quantum capacity of a channel is a measure of how much of the uncertainty of the input state is preserved in the output state.
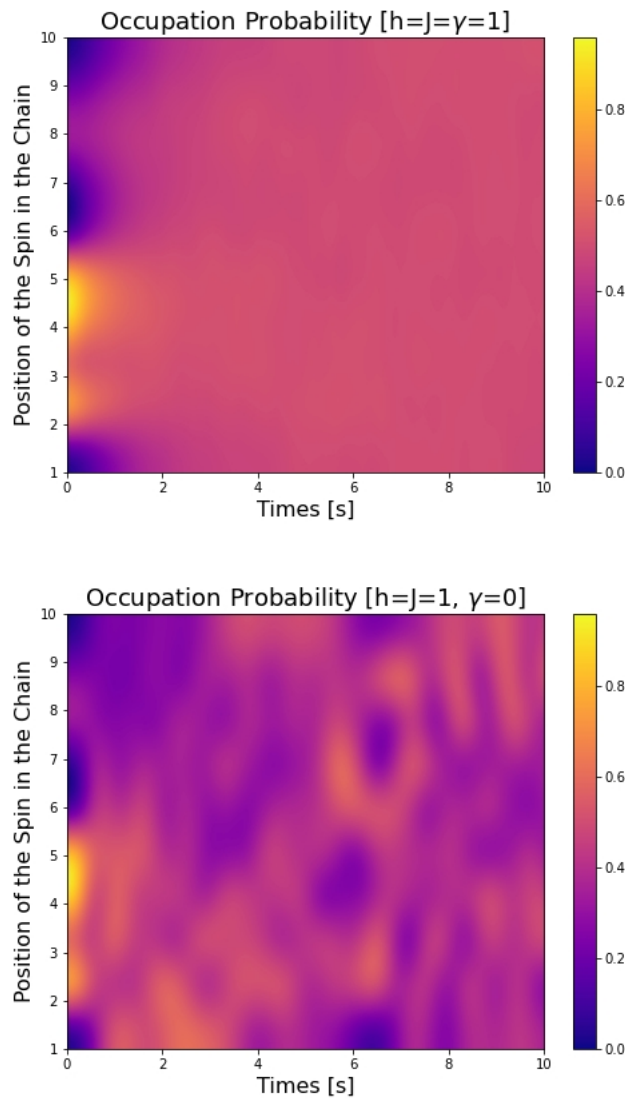
FIGURE 5.26: *Probability of flipping along the spin chain (indexed on the y-axis) over time (indexed on the x-axis). The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour approaches blue the lower the probability that a mutation occurs. The Ising model is set to the value of the fields $h = 1$, $J = 1$, $\gamma = 1$ (top) and $h = 1$, $J = 1$, $\gamma = 0$ (bottom).*

In other words, if a quantum channel preserves the entropy of the input state, it means that it is preserving the quantum information, and the channel has a large quantum capacity. On the other hand, if a channel increases the entropy of the input state, it means that the channel is destroying the quantum information, and the channel has a small quantum capacity [61].
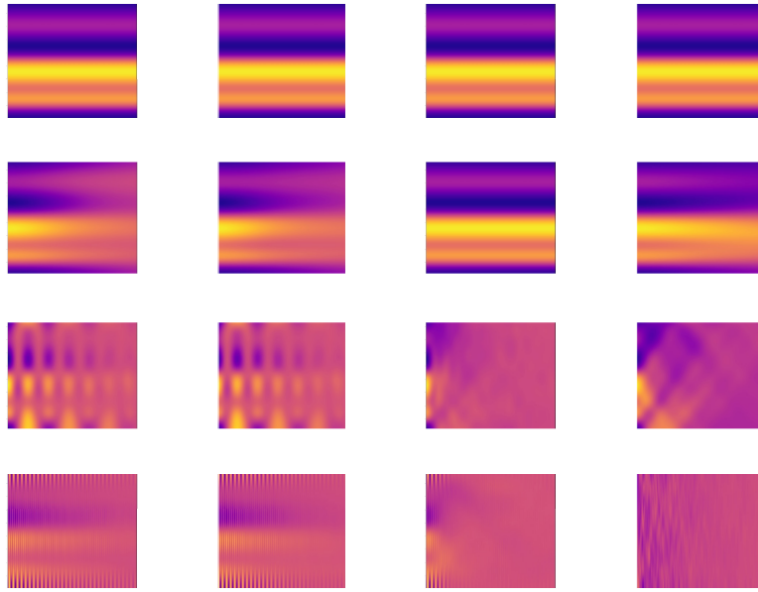
FIGURE 5.27: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side) in Ising model. The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour approaches blue the lower the probability that a mutation occurs. From left to right the value of the external field h, takes on larger and larger values* $[0, 0.1, 1, 10]$. *From top to bottom, the value of the coupling field J between neighbouring primes takes on larger and larger values* $[0, 0.1, 1, 10]$

In this sense, the entropy of the output state is a good indicator of the quantum capacity of the channel, because it reflects the amount of quantum information that has been transmitted through the channel. The Von Neumann entropy is a commonly used measure of entropy for quantum systems, and it is often used to calculate the quantum capacity of a quantum channel.

If the Von Neumann entropy of a subsystem is zero, then that subsystem is in a pure state and is not entangled with any other subsystems. However, if the Von Neumann entropy of a subsystem is nonzero, then that subsystem is in a mixed state and may be entangled with one or more other subsystems. In particular, if the Von Neumann entropy of a bipartite quantum system is nonzero, then the two subsystems of that system are entangled. This is because the Von Neumann entropy of a subsystem measures the amount of information that is missing about the state of the other subsystem, and entanglement is precisely the kind of correlation that can cause information to
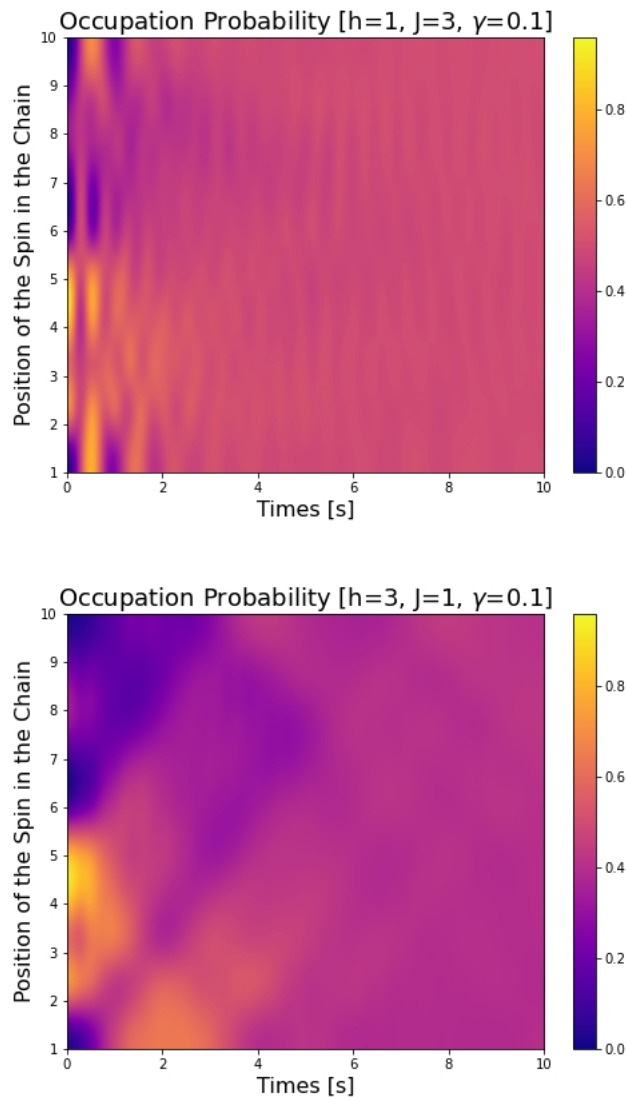
FIGURE 5.28: *Each box represents the probability of flipping along the spin chain (indexed on the y-axis, vertical side) and over time (indexed on the x-axis, horizontal side) in Ising model. The closer the colour is to yellow, the greater the probability of a mutation occurring. The closer the colour approaches blue the lower the probability that a mutation occurs. The field J and the field h are of the same order of magnitude. Case J > h (top), case J < h (bottom).*

be missing about one subsystem when the other subsystem is measured.

In literature, it is amply shown and demonstrated that the greater the entanglement of the system, the more effective the quantum capacity of the channel acting on the same system will be, see [62], [63]. Finally I am going to track down entanglement-maximising configurations in my models.

For both models implemented, I calculate the Von Neumann entropy. And I go to identify which values of the outer and coupling fields between first neighbours maximise entanglement. J and h vary in the interval $[0,2]$ for both models.

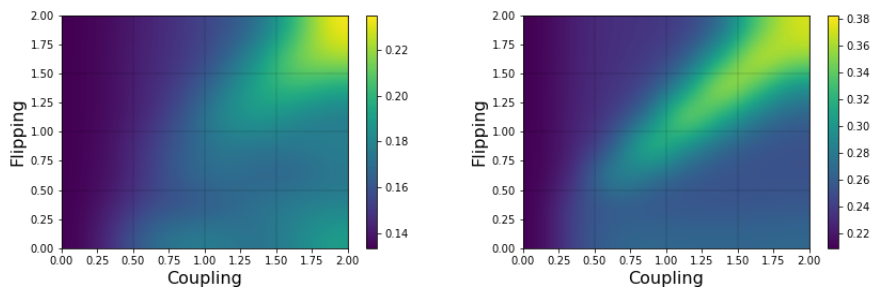I start by analysing the Heisenberg model. I set the $N = 5$ in order to have faster simulations.

FIGURE 5.29: *Each box represents the Von Neumann Entropy of the first spin as a function of h and J (along the x-axis and along the y-axis, respectively) in the Heisenberg model. The flipping and coupling fields take on values within the range [0,2]. The closer the colour approaches yellow the greater the Von Neumann Entropy and the greater the entanglement shared by the spins. The closer the colour approaches black the greater the entanglement entropy decreases. The field $\gamma = 0.1$ is fixed. Initial instant case (left), final instant case (right).*

In Fig. 5.29, it is shown how the Von Neumann Entropy varies as a function of time, at the beginning of the simulation (figure on the left) and at the end (figure on the right). The behaviour for each site of the system is the same: entanglement is maximised along a straight line and reaches its maximum when both fields are equal and greater than one.

This result does not change along the chain, in fact in Fig. 5.30 the same behaviour is found for the last spin of the chain.

Analysing the Ising model, the area in which entanglement is maximised is quite different. In Fig. 5.31 it is indeed shown for the first site of the chain that the Von Neumann entropy increases with time and is maximal along the horizontal line $h = 0.5$, and $J > 1$. This behaviour does not depend on the
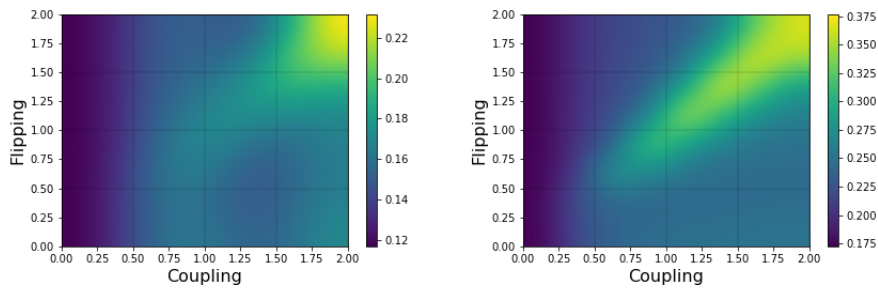
FIGURE 5.30: *Each box represents the Von Neumann Entropy of the last spin spin as a function of h and J (along the x-axis and along the y-axis, respectively) in the Heisenberg model. The flipping and coupling fields take on values within the range [0,2]. The closer the colour approaches yellow the greater the Von Neumann Entropy and the greater the entanglement shared by the spins. The closer the colour approaches black the greater the entanglement entropy decreases. The field $\gamma = 0.1$ is fixed. Initial instant case (left), final instant case (right).*

site I am considering, in fact in Fig. 5.32 the same kind of phenomenon is shown for the last spin.
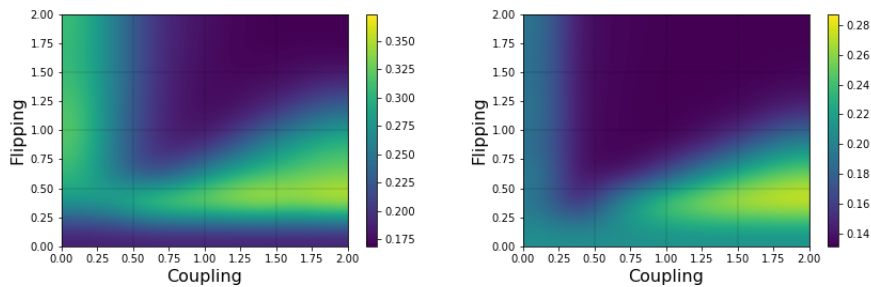

FIGURE 5.31: *Each box represents the Von Neumann Entropy of the first spin as a function of h and J (along the x-axis and along the y-axis, respectively) in the Ising model. The flipping and coupling fields take on values within the range [0,2]. The closer the colour approaches yellow the greater the Von Neumann Entropy and the greater the entanglement shared by the spins. The closer the colour approaches black the greater the entanglement entropy decreases. The field $\gamma = 0.1$ is fixed. Initial instant case (left), final instant case (right).*

I can now calculate for both models the quantum capacity of the system. I maximise the entanglement using the previous results and since I assume that there is no information leakage I use the identity channel to calculate this quantity. Many models on the evolution of mutations in DNA have been discussed in the literature. All of these models aim to understand how the
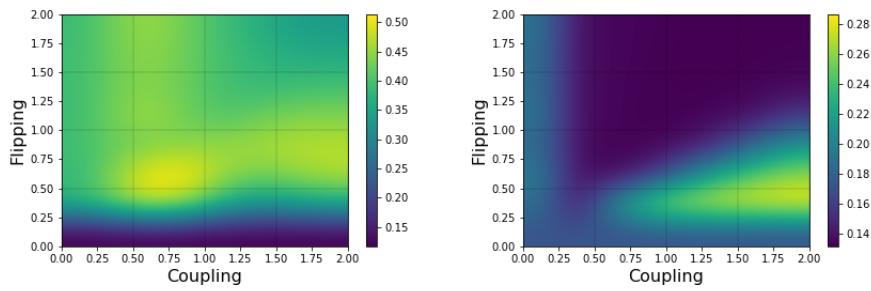
FIGURE 5.32: *Each box represents the Von Neumann Entropy of the last spin as a function of h and J (along the x-axis and along the y-axis, respectively) in the Ising model. The flipping and coupling fields take on values within the range [0,2]. The closer the colour approaches yellow the greater the Von Neumann Entropy and the greater the entanglement shared by the spins. The closer the colour approaches black the greater the entanglement entropy decreases. The field $\gamma = 0.1$ is fixed. Initial instant case (left), final instant case (right).*

information contained in DNA can be stored and passed on to future generations.

In particular, in the work of Ivan B. Djordjevic [64], it has derived many representations to describe a quantum biological channel. He has proposed new quantum mechanical models to accurately describe the process of creation spontaneous, induced, and adaptive mutations and their propagation in time. This article not only shows that the information contained in DNA is quantum (it has a higher capacity), but also shows that there is a threshold value of mutation probability that if it is too high there can no longer be any transmission of information, see Fig. 5.33. In this figure after a single base error probability $p = 10^{-3}$ the capacity has an abrupt decrease. I check if there is a similar behaviour for my models.

Fig. 5.34 shows the quantum capacity of the spin chain under the conditions that maximise entanglement (found in the previous section) in Heisenberg's model. After some simulations I have seen that the capacity does not change fixed the position of the spin. In time, however, the behaviour is very peculiar. For $p < 10^{-1}$ the capacity is constant and over time takes on a larger and larger value. As the system evolves over time the peak that the capacity takes on for higher values of p disappears and allows there to be a sharp decrease as very low values. If the quantum capacity of a channel decreases, it
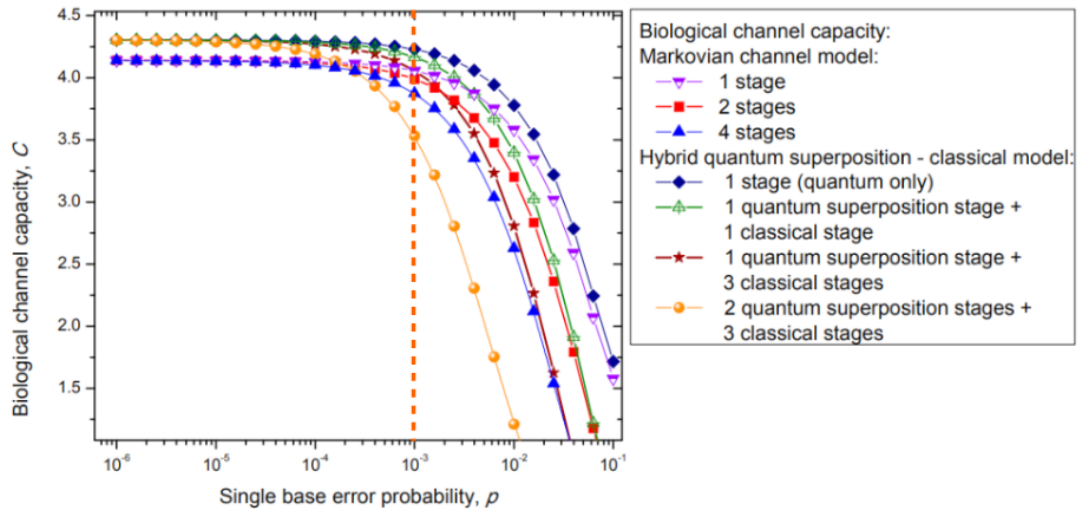
FIGURE 5.33: *Biological channel capacity as a function of epigenetic mutation probability. The vertical dashed orange line represents the threshold mutation probability rate value after which the information contained in the DNA stops being correctly transmitted.*

means that the maximum rate at which quantum information can be transmitted over the channel has reduced. It may also mean that the quantum information transmitted over the channel is more susceptible to errors and distortion, making it more difficult to retrieve the original information at the receiving end.

In Ising model, the behaviour is very different, see Fig. 5.35. As before, we do not have a very particular dependence, fixed time, on the spin I am considering. As time varies for lower values of $p < 10^{-1}$ we still have a constant trend which however decreases over time and does not increase as in the previous model. Furthermore, for higher values of p we can clearly see that the capacity varies chaotically until it stabilises at the final time with a peak and a faster decrease.

There is a substantial difference between the capacities found and those proposed in the literature. The decrease is found for much lower probabilities. By a factor of 100 to be exact. The hypothesis I would like to put forward is as follows. In the literature [50] it is shown that with the onset of cancer the mutation rate increases 100-fold. And that is exactly what happens in this case. It may therefore appear that the models implemented can represent the evolution of epigenetic mutations in the case of a cancer cell.
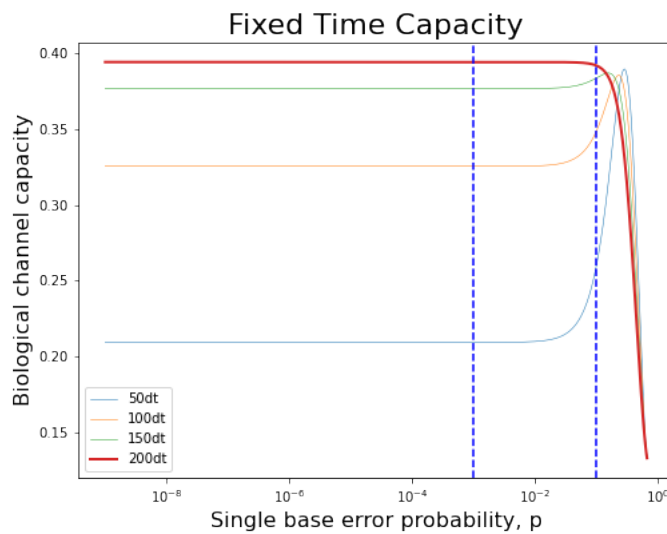
FIGURE 5.34: *Capacity of the biological channel as a function of flipping probability in the Heisenberg model. Each curve represents the capacity at a fixed time, as described by the legend in the figure. The two vertically dashed blue lines represent the threshold mutation probability rate value after which the information contained in the DNA stops being transmitted correctly in this case and in the case of Fig. 5.33*

FIGURE 5.35: *Capacity of the biological channel as a function of flipping probability in the Ising model. Each curve represents the capacity at a fixed time, as described by the legend in the figure. The two vertically dashed blue lines represent the threshold mutation probability rate value after which the information contained in the DNA stops being transmitted correctly in this case and in the case of Fig. 5.33*
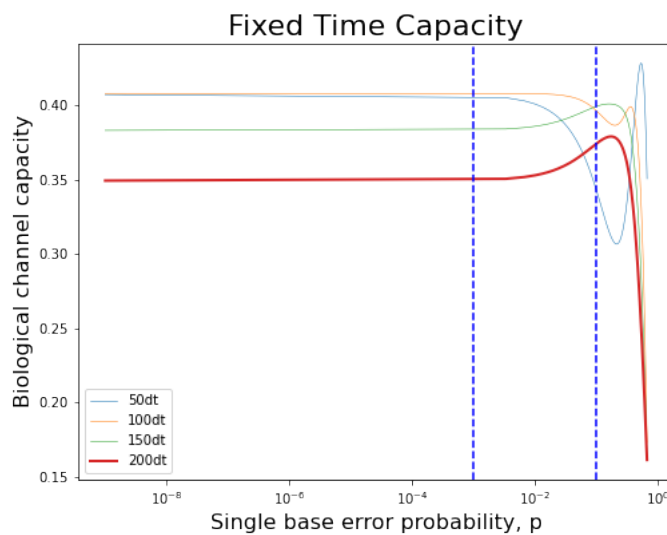
Chapter 6

Conclusion and outlooks

In this work, I focused on a new branch of physics called Quantum Biology. After a brief historical overview, see Chapter 1, I investigated the conditions and requirements for its introduction. Attempting to unify the complexity of living organisms and the depth of quantum mechanics into a single discipline is a very challenging task. In Chapter 2, I highlighted the first results of Quantum Biology, which have been extensively studied and documented in the literature I collected.

In Chapter 3, I presented a quantum model for DNA molecules developed by Dr. Elisabeth Rieper. The results achieved by this model showed that the entanglement contained in the chain corresponds to the binding energy of the molecule, and thus the entanglement persists even at room temperature. For randomly chosen sequences of A, C, G, T, or in aperiodic potentials, there is no direct correlation between the classical information of the sequence and its average quantum information. The average amount of Von Neumann entropy varies strongly, even among sequences having the same Shannon entropy.

In Chapter 4, I delved into another area of application of Quantum Biology: Quantum Biology at the Cellular Level (QBCL), which uses the formalism of quantum mechanics to study the states that a biological system can assume. This topic assumes that there are many variables within the cell that a measuring instrument cannot consider all together with the same experiment, so operators can be constructed that represent formally incompatible quantities.

In Chapter 5, I simulated an open quantum Heisenberg and Ising system. The objective was to try to find an analogy with the physiological environment described by the DNA macromolecule and attempt to explain its meaning. First, I sampled different values of coupling fields between first neighborhood, external fields, and interaction with the environment, calculating the probability of flipping along the spin chain in time and space. I thus began to become familiar with the code. Then I studied one of the properties taken into account when studying a physiological phenomenon, namely the Capacity of the Channel of the system, which is the capacity of the system to store and transmit the information it receives. By maximizing the entanglement of the open system and calculating the quantum capacity of the channel, I found that the trend is plausible for the same trend that some scientists have conducted on the same system. With one difference, a factor of 100 that is the same rate found in the cancerous phase of cells.

6.1 Outlooks

My work stands only at the beginning of the study of DNA as a quantum open system. There are so many questions and modifications that can be made to the code. First of all, one can give different shapes to the coupling fields and the external field. And one can study the relationship that exists between the number of spins investigated and the γ factor that couples to the operator representing the environment. These models represent the first, fundamental and necessary step in paving the way towards this field.

6.2 Improvement of QM for living systems

Biology refers to the study of living systems, but this shifts the problem to defining what life is. Let me compare the movement of a bird and a kite. Both fly in the sky under appropriate conditions, yet there are distinct differences between the two systems. The kite simply follows the laws of physics in the sense that if the wind changes direction, so will the kite; if the wind

blows harder or weaker, the kite will rise or fall. Birds are different. While both birds and kites must obey the same laws of physics, birds have learned to react. Given variations in the wind, the bird will decide to change, for example, the position of its wings to counteract the wind change. Or it may simply fly elsewhere where the wind conditions are better for flying. The ability to react to one's environment is a characteristic that all living systems share. If it were possible to design a robot that looks like a bird and makes the same decisions given some environmental information, like a bird, then most people would not be able to distinguish the robot from the living bird. How does a bird, or any other living system, achieve this goal? I will not try to answer the question of how aware a bird is of its own flight. But it is clear that some sort of information processing and future prediction occurs within the bird. This requires a lot of computation within the bird. More specifically, the bird needs a predictive model of itself and its environment. The bird must be able to predict, for example, "If the wind slows down, I will lose altitude." If losing altitude is not advantageous for the bird, it must decide which counteraction to take. The more information stored about its environment, the better the reaction. If the future state of the environment is predicted correctly, it can adapt to changes or exploit resources. Although little is known about how exactly the brain stores information or how decisions are made, living organisms must still obey the fundamental laws of physics and computation.

Although it is difficult to determine how many bits of information an organism can store, it is easy to say that total memory is finite. The more information an organism wants to store and process, the more energy must be expended. On the other hand, spending more energy on information processing does not necessarily improve predictions, as the computational models used may be inefficient. Is there a way to determine the minimum amount of resources needed to simulate an individual's environment and classify the efficiency of the computational model? Computer science has developed theoretical models to precisely measure this. It has been shown [65] that using

quantum mechanics it is possible to predict the future more efficiently, i.e., using fewer resources. The key idea is this: the state of the environment is divided into equivalence classes. If two states lead to the same future statistics, there is no need to distinguish them and they represent the same equivalence class. If two states lead to different futures, they are distinguished and stored as different states. Sometimes, however, the future statistics of two states are very similar but not completely identical. If information is stored classically, the two states that lead to similar futures must be completely distinguishable. Storing the same information in a quantum way requires fewer resources. Maximizing the predictive capacity of the brain therefore requires the use of quantum mechanical effects. Although it is very difficult to determine whether living systems actually use quantum mechanics to maximize their predictive capacity with the available resources, the most efficient physically possible predictive "black box" uses quantum effects.

6.3   The levers as the fundamental principle of life

Elisabeth Rieper, referring to the intuition that quantum mechanics could be used to explore models to explain the physiology of certain processes, see the article [35], refers to the concept of lever. Life involves controlled reactions to environmental stimuli and can be broken down into three steps: detecting the stimulus, processing the data, and amplifying the small-energy decision into a large-scale reaction. The energy scale difference between the decision-making process and the amplification of that decision is necessary for behavior to occur. Biological phenomena are difficult to explain using traditional physics formulas because they do not adequately account for amplification processes. This is one of the reasons that levers are so important for life. Shapes, for example, can act as levers that control the outcome of chemical reactions. Other levers, such as the use of quantum mechanics to control chemical reactions, are also likely to be present in living systems. The potential benefits of these quantum effects make it probable that nature has learned

to exploit them over billions of years of research and development. An example of a bio-quantum lever could be the occurrence of adaptive mutations. As discussed in Chapter 5, quantum mechanics allows for the selective excitation of a specific base pair in a gene into its tautomeric form, which resembles an option for mutation. Detecting the tautomer quickly enough can lead to a permanent mutation through the action of DNA polymerase. The frequency of gene readouts and the likelihood of optional mutations becoming actual mutations are controlled by other processes in the cell. The creation of tautomers requires only a small amount of energy, approximately 20 times that of thermal energy, but the energetic consequences of mutations on gene expression can be significant, potentially determining the life or death of an organism. Therefore, the optional mutations created by tautomers would constitute a powerful lever.

Quantum effects are present in biological systems. Although the why and how is still a subject of research, there is no doubt about the fact itself. Scientists will increasingly realise that life and life processes are strongly linked to the physics of open quantum systems. Without the laws of quantum mechanics, we cannot understand life and life processes. The challenge is to understand how in a moist and noisy environment (such as a protein, a membrane, a cell and a whole organism) the 'perfect' laws of quantum physics survive. The near future will see new experiments studying, for example, the effects of strong magnetic fields, the analysis of single molecules/systems and femtosecond coherent microscopy. One challenge is to understand how quantum effects, clearly present at a certain level of functional description, translate into observations at a higher level of complexity.

New systems will be studied, such as neurons, neural networks and perhaps the whole brain. We will see a closer connection between our further understanding of life and our understanding of quantum computing, artificial intelligence and various other technologies.

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