Quantum Computing and Drug Discovery

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1 Introduction and Background

Most of the resources dedicated to quantum computing research focus on either the mechanics behind building quantum computers or applications in STEM fields. Such STEM topics range from cybersecurity, to general engineering application, and medicine. Within medicine, drug discovery is subtopic abounding in promise for quantum computing use. Some problems to be solved include molecular comparison and design, protein folding, and quantum annealing (which is less of a problem and more of a utility).

Before exploring these applications of quantum computing, some background may be necessary. Generally speaking, when a person takes medication, certain molecules enter the body and bind to receptor proteins in the cytoplasm of a cell or to nerves. The structure of these proteins or the receptor sites of nerves are highly specific and will only accept a molecule with the correct configuration to complete a task.

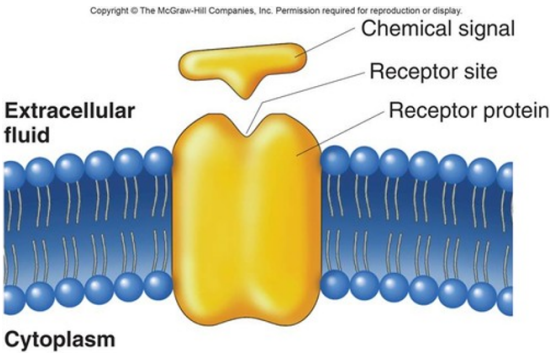

Figure 1: A receptor protein with a signal about to bind to it.

From Figure 1 we can see that the structure of the chemical signal is complimentary to the receptor site on the protein. This plays an integral role in our first application: molecular comparison and design.

2 Molecular Comparison and Design

If we know how the mechanism of receptor site binding works, could we then engineer a fake molecule to fit the receptor site on its appropriate protein? Yes, and no. We could do this and in fact many drugs operate in this way, but the issue is that for most receptor proteins, we do not know the structure of the receptor site and we cannot easily get it either. Some approaches we can take to get around this are that we can replicate the molecule that is supposed to bind to the protein or we can use drugs that we already know the effects and uses of and tweak them to fit our needs.

Two such drugs that use this first method of replication are 5-MeO-aMT and Methyldopa. 5-MeO-aMT replicates serotonin, the neurotransmitter that stabilizes mood. The only change in structure between 5-MeO-aMT and serotonin is the addition of an NH_2 bond and an extra hydrogen molecule. This is enough to elevate mood to euphoria rather than stabilize it, and so 5-MeO-aMT is banned in most countries[2]. Methyldopa, on the other hand, replicates norepinephrine and is used in medications to lower blood pressure[1].

Selective Serotonin Reuptake Inhibitors (SSRIs) were developed by the method of molecule comparison. These medications are commonly used to treat depression and psychosis. The most common of these drugs is Zoloft, taken by over 37 million Americans. In the 1990s, researchers knew that zimelidine, which is a molecule in antihistamines, exhibited inhibition of the reuptake of serotonin in the synaptic gaps (the space between nerves where neurotransmitters inhabit) but not norepinephrine[10].

The process that goes into figuring out how we can find molecules that work similarly to others is molecule comparison. This happens by find places where two molecules line up or are similar to each other and superimposing them[8].

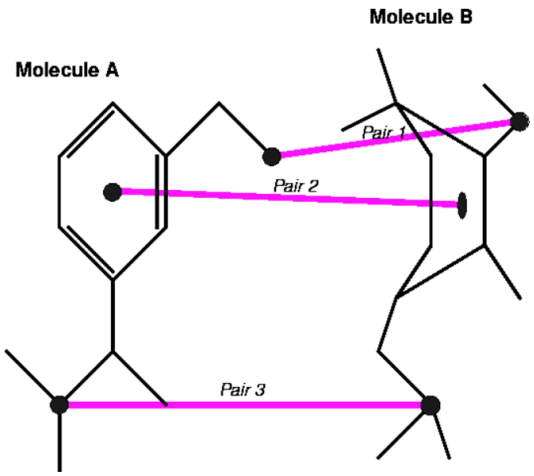

Figure 2: The similarities of molecules A and B

Figure 2 shows two molecules and demonstrates how they appear similar. When

dealing with big molecules, it can be difficult to find the best comparison as there can be many possibilities for alignment and many databases to search through. Currently, classical algorithms (of which there are many) accomplish this just fine, but quantum computing may be able to accomplish this with more accuracy and quicker, too.

While there is not much literature to be found exactly explaining these quantum algorithms (which could be due to matters of intellectual property rights since the technology is so young), the general goal seems to remain the same across the board: turn the comparisons into large, multivariate equations and solve them. There are many factors that can change the structure of a molecule such as pressure and temperature, making complex equations necessary. Classical computers have been able to handle the workload, as evidenced by the many drugs currently available, but quantum computers – in whatever capacity and methodology they are using to work – can provide deeper insights into the properties of molecules.

Along with comparing to known molecules, quantum computing may provide hope for creating new molecules. Quantum molecular design is a complex, multi-step process, but here we will look at it in three main steps[5]:

Step 1: Extract binding information from a target. At the beginning, the quantum computer has some idea of what the final molecule needs to be like. For example, if the goal is to create a molecule in the Janus family of kinases, then the algorithm searches for an example of a kinase in that family.

Step 2: Search in a larger database. Here the algorithm searches that target against a database of scaffolds published in literature, theoretical scaffolds created combinatorically, and even combines some of them together. The result is a list of matches that have the same binding pattern at their most basic level.

Step 3: Create a novel chemical space by varying functional groups.

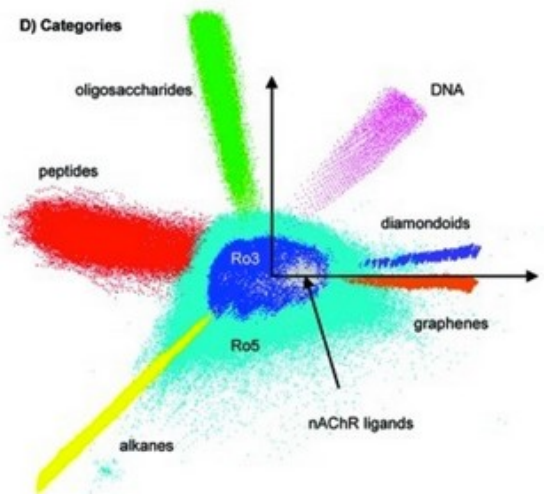

Figure 3: The PubChem chemical space

A chemical space is defined as the property space spanned by all possible molecules and chemical compounds adhering to a given set of construction principles and boundary conditions. The most well-known and widely used chemical space if pictured above in Figure 3. The quantum algorithm will create a new chemical space containing 10 million to a billion molecules of similar properties by looking at the variations that can occur on each of the matches produced in step 2.

Perhaps the most useful and relevant quantum approach here is the use of Grover's Search Algorithm. In step 1, we are essentially searching for a single file (an example of a Janus kinase) in the larger database of kinases. That is, the example that we find has to satisfy a certain set of conditions, which are those conditions that make it a Janus kinase. In step 2, we are searching again, but instead of searching for a single file, we are searching for multiple or giving a list of results that most closely represent our query. By using Grover's search algorithm, we can cut down the time needed to search for similar molecules from $O(N)$ to $O(\sqrt{N})$, which not only saves time, but saves money and resources as well.

3 Protein Folding

As mentioned earlier, a major problem to overcome in drug discovery is the inability to predict what the receptor sites of proteins look like. A tandem to molecular comparison and design, one of the innovations in quantum computing is using quantum algorithms and techniques to try and solve this issue.

Proteins, at their most basic definition, are conglomerations of many amino acid chains all bundled up and folded in a very specific way. According to the funnel hypothesis of protein folding, the native structure of a protein is believed to be the global minimum of its free energy. Figure 4 below shows a graphical representation of this hypothesis.

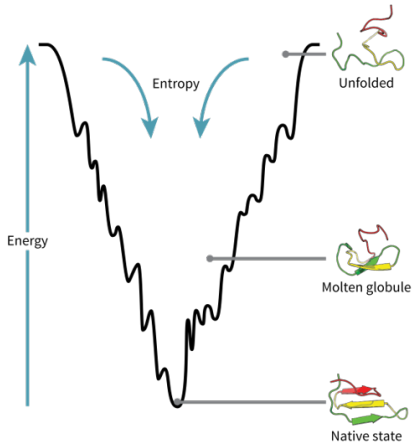

Figure 4: The funnel hypothesis

In summary, the implication of this hypothesis is that there is a vast and broad range of possible configurations of a protein that classical computation just cannot parse through all the possibilities. Literature on quantum computation utility has focused on the protein lattice model, which aims to describe a protein's structure as the folding of amino acids at a series of right angles that do not cross over each other[6]. Such relevant literature uses adiabatic quantum computing.

For reference, diabatic quantum computing is constructed from the following three assumptions[7]:

1. Rapidly changing conditions prevent the system from adapting its configuration during the process, hence the spatial probability density remains unchanged.

2. Typically, there is no eigenstate of the final Hamiltonian with the same functional form of the initial state.

3. The system ends in a linear combination of states that sum to reproduce the initial probability density.

Contrarily, the adiabatic process states:

1. Gradually changing conditions allow the system to adapt its configuration, hence the probability density is modified by the process.

2. If the system starts in an eigenstate of the initial Hamiltonian, it will end in the corresponding eigenstate of the final Hamiltonian.

The computational goal is to find the configuration of amino acids into a lattice model that uses the least amount of energy. However, this problem is *NP-hard*, which means that there is no polynomial-time classical algorithm that can solve it. Thus, we turn to quantum computing. It is true that we be able to find such an algorithm, but we may not be able to solve the problem in any significantly faster way. To aid in finding an algorithm, we consider quantum annealing.

4 Quantum Annealing

Quantum annealing aims to find the absolute minimum from withing a set of very large, but nonetheless, finite set of possible solutions using quantum mechanics rather than classical[6]. In mathematical terms:

$$x \in \{x_i : i \geq 0\} \text{ such that } x \leq x_i \text{ for all } x_i$$

Quantum annealing is most often accomplished using D-Wave, an adiabatic quantum computer in Burnaby, British Columbia, Canada. The algorithm in the D-Wave system begins by setting up a qubit in superposition. The qubit is measured, resulting in roughly equal probability of 0 or 1. Then, a magnetic field is applied to the qubit,

resulting in a tilt to the energy well. The qubit has a higher probability being in the lower well. The figure below from D-Wave shows this phenomena[11].

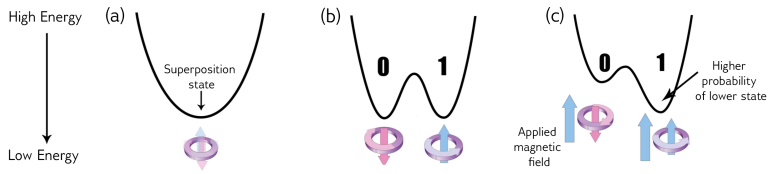

Figure 5: Energy diagram over time during the annealing process

Quantum annealing can help us to discover organic materials, which are most often used in medicines because of they are biodegradable[3]. In tandem, we could use quantum annealing and computation to find a molecule's structure and properties jointly. Many chemical properties can be discovered by trying to discover another. For example, one could tell a chemical's toxicity by trying to find if it is corrosive. One could discover the explosiveness of a material by trying to see how flammable it is. However, we do not necessarily want to corrode somebody's skin to figure out if something is corrosive or blow up a building to find out the heat of combustion. So, we must find these things computationally, in which case it could be ideal to find out multiple properties at once. Finding these things simultaneously means that quantum annealing can also increase cost efficiency and time efficiency of discovering drugs. However, this matter of time decrease depends highly on the refinement and advancement of quantum technology to a sufficiently better state than we have now. All of this means that it could be a while before we see these technologies manifest in drug discovery.

5 Criticism and Conclusions

It should be acknowledged that this discussion of quantum utility in drug discovery may subliminally imply that these possibilities are entirely advantageous and should be invested in. But there is a humbling perspective to investigate here. It is this: A useful quantum computer needs to process a set of continuous parameters that is larger than the number of subatomic particles in the universe.

To comprehend this, we begin by understanding that in a two-qubit system, there are 2^2 or 4 basic states: $|00\rangle$, $|01\rangle$, $|10\rangle$, $|11\rangle$. So, for an N qubit system, there are 2^N basic states. Experts say that the number of qubits needed for a useful quantum computer is between 1,000 and 10,000[4]. Thus, the number of continuous parameters describing the state of a useful quantum computer is at the very minimum $2^1,000$, which is about $10^3$00. The number of subatomic particles in the observable universe is $3.28 \times 10^8$0, which is obviously a vast amount smaller than the minimum needed. All of this is just to make a quantum computer able to compete with a current, normal laptop.

Mikhail Dyakonov, a theoretical physics researcher at the University of Montpellier

in France who theorized Dyakonov surface waves, is a pessimist in the sense that he believes we could never harness systems of that size[4]. This criticism is misleading. We do not need the number of subatomic particles to do quantum computation. Following from the assertions above, we only need N photons to get 2^N vectors in superposition, which we can then measure and potentially get different outcomes. We are not using all continuous parameters at once. The cardinality of the real numbers $\mathbb{R}$ is uncountable, and yet we use $\mathbb{R}$ to do calculus and solve many real-world problems. The cardinality of the set of subatomic particles is countable and finite. If we can use an uncountable set in a practical way, then size should not be a barrier for the use of quantum computing.

In a sociological sense, if the human race limited itself to solving only the problems we could wrap our heads around, then we surely would not have progressed to the level of technological advancement we have today. A person from the Middle Ages could likely not even fathom the concept of a cell phone, and yet here we are: we all have one and the assumption when you meet someone is that they have one, too.

In conclusion, drug discovery is a highly sought after application of quantum computation and mechanics. It promises the ability to cut time and costs in the drug discovery process by capitalizing on chemical properties and protein formation. Research into drug applications is being invested in by many big pharma companies and technology agencies like IBM and Google[9]. However, it is not without its criticism. We must ask ourselves, though, if the ends justify the means.

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