A Quantum Approach to the Discretizable Molecular Distance Geometry Problem

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Abstract The Discretizable Molecular Distance Geometry Problem (DMDGP) aims to determine the three-dimensional protein structure using distance information from nuclear magnetic resonance experiments. The DMDGP has a finite number of candidate solutions and can be solved by combinatorial methods. We describe a quantum approach to the DMDGP by using Grover’s algorithm with an appropriate oracle function, which is more efficient than classical methods that use brute force. We show computational results by implementing our scheme on IBM quantum computers with a small number of noisy qubits.

Keywords Distance Geometry · Quantum Computing · Grover’s Algorithm

1 Introduction

The calculation of the 3D structure of a molecule is a fundamental problem for understanding the molecule function, which is particularly true for proteins [1]. X-ray crystallography was the first method applied to this problem, considering crystallized proteins. For cases where the crystallization is not possible, there is another technique, called Nuclear Magnetic Resonance (NMR) [2], where (short) Euclidean distances between atoms in a protein are measured. The 3D protein structure determination using this partial distance information [3] can be modelled
as the DMDGP, which has been addressed from a combinatorial approach in [4, 5, 6, 7, 8, 9, 10].

Quantum computing promises to speed up many important computational tasks, such as searching unsorted databases [11]. Recently, the quantum supremacy has been established by Google [12] and Chinese experiments [13], which means that programmable quantum computers can already execute tasks that classical computers cannot reproduce in a feasible amount of time. The main problem to deliver practical results is the accumulation of noise during the computation and the term NISQ computers [14] has been used to classify the quantum computers that we are going to use in the near future.

An attempt to apply quantum computing to the DMDGP was presented in [15] by exploring the fact that the DMDGP has a finite number of candidate solutions. Grover’s algorithm is used to find the solution among the candidates by exhaustive search.

In this paper, we present a new way of applying Grover’s algorithm to the DMDGP by improving the definition of the oracle function. We implement small instances of our algorithm on IBM Quantum with the goal of showing that the procedure works and can be used in practical applications when quantum computers with reasonable size and small error rates are available.

The structure of the paper is as follows. Section 2 defines the DMDGP and presents the combinatorial approach to this problem. Section 3 describes how Grover’s algorithm can be used in the DMDGP, which is the main contribution of this paper. Section 4 presents the computational experiments that were implemented on IBM Quantum. Section 5 provides the conclusions and final comments.

2 The Discretizable Molecular Distance Geometry Problem

To model our problem, we use a weighted simple undirected graph $G = (V, E, d)$, where $V$ represents the set of atoms and $E$ represents the set of atom pairs for which a distance is available, given by the function $d : E \rightarrow [0, \infty)$.

The problem is then to find a function $x : V \rightarrow \mathbb{R}^3$ that associates each element of $V$ with a point in $\mathbb{R}^3$ in such a way that the Euclidean distances between the points correspond to the values given by $d$. This is called a Distance Geometry Problem (DGP) in $\mathbb{R}^3$ [4, 5, 6, 7, 8, 9, 10], formally given as follows:

**Problem 1 (DGP)** Given a simple undirected graph $G = (V, E, d)$ whose edges are weighted by a function $d : E \rightarrow [0, \infty)$, find a function $x : V \rightarrow \mathbb{R}^3$ such that

$$\|x_u - x_v\| = d_{uv}, \quad \forall\{u, v\} \in E,$$

where $x_u = x(u)$, $x_v = x(v)$, $d_{uv} = d(\{u, v\})$, and $\|x_u - x_v\|$ is the Euclidean distance between $x_u$ and $x_v$.

There is evidence that a closed-form solution for solving (1) is not possible [17] and a common approach is to formulate the DGP as a nonlinear global minimization problem [18],

$$\min_{x_1, \ldots, x_n \in \mathbb{R}^3} \sum_{\{u, v\} \in E} \left( \|x_u - x_v\|^2 - d_{uv}^2 \right)^2,$$

1 The origin of the word graph is related to representation of molecules and this relationship is probably the deepest existing between chemistry and discrete mathematics [16].
where $|V| = n$. In [19], some global optimization algorithms have been tested but none of them scale well to medium or large instances. A survey on different methods to the DGP is given in [20].

The information provided by NMR experiments and geometric properties of proteins allow us to define a DGP class, called the Discretizable Molecular Distance Geometry Problem (DMDGP) [21], defined below, where a combinatorial approach can be applied to the problem [22,23,24].

**Problem 2 (DMDGP)** Given a DGP graph $G = (V,E,d)$ and a vertex order $v_1,\ldots,v_n$ such that

1. $v_1, v_2, v_3$ can be fixed in $\mathbb{R}^3$ satisfying (1);
2. $\forall i > 3$, the set $\{v_{i-3}, v_{i-2}, v_{i-1}, v_i\}$ is a clique with $d_{i-3,i-2} + d_{i-2,i-1} > d_{i-3,i-1}$,

find a function $x: V \rightarrow \mathbb{R}^3$ such that

$$\|x_u - x_v\| = d_{uv}, \ \forall \{u,v\} \in E.$$

We list some important observations about this problem: (1) the DMDGP vertex order is the main idea behind the discrete version of the DGP (for instance, see [25,26,27,28]); (2) the positions for $v_1, v_2, v_3$ guarantee that the solution set will contain just incongruent solutions (aside from a single reflection) and the strictness of the triangular inequality prevents an uncountable quantity of solutions [21]; (3) an exact solution method, called Branch-and-Prune (BP), was presented in [29,30] for finding all incongruent solutions (that is, solutions obtained modulo rotations and translations). The BP algorithm can be exponential in the worst case, which is consistent with the fact that the DMDGP is an NP-hard problem [21].

The DMDGP order “organizes” the search space in a binary tree and the additional distance information (related to the pairs $(v_j, v_i)$, $j < i-3$, $i = 5,\ldots,n$) can be used to reduce the search space by pruning infeasible positions in the tree, which begins with the fixed positions for $v_1, v_2, v_3$. The search ends when a path from the root of the tree to a leaf node is found by the BP algorithm, such that the positions relative to vertices in the path satisfy the DGP equations (1).

There are symmetries in the BP tree [31,32,33,34], related to the cardinality of the DMDGP solution set, which can be computed even before applying BP algorithm. These symmetric properties are based on the set

$$S = \{ v \in V : \exists \{u,w\} \in E \text{ such that } u + 3 < v \leq w \},$$

for a given DMDGP instance $G = (V,E,d)$ [33] (we denote by $u + 3$ the third vertex after $u$).

To illustrate the importance of these symmetries, let us consider a small DMDGP instance given by

$$V = \{v_1, v_2, v_3, v_4, v_5, v_6, v_7\},$$
$$E = \{\{v_1, v_2\}, \{v_1, v_3\}, \{v_1, v_4\}, \{v_1, v_6\},$$
$$\{v_2, v_3\}, \{v_2, v_4\}, \{v_2, v_5\}, \{v_3, v_4\}, \{v_3, v_5\}, \{v_3, v_6\},$$
$$\{v_4, v_5\}, \{v_4, v_6\}, \{v_4, v_7\}, \{v_5, v_6\}, \{v_5, v_7\}, \{v_6, v_7\}\}.$$

It is easy to check that, for this example,

\[ S = \{v_4, v_7\}. \]

To simplify the notation, let us represent the first solution found by BP by a sequence of zeros and ones (remember that the positions for \( v_1, v_2, v_3 \) are fixed):

\[ s_1 = (0, 1, 0, 1). \]

The fact that \( v_7 \in S \) implies that another solution is given by

\[ s_2 = (0, 1, 0, 0), \]

and from the fact that \( v_4 \in S \), more two solutions are given by

\[ s_3 = (1, 0, 1, 0) \]

and

\[ s_4 = (1, 0, 1, 1). \]

In addition to be possible to generate all the other solutions from just one, the set \( S \) also informs us that the cardinality of the solution set is given by \( 2^{|S|} \) \cite{35}. Thus, we can use Grover’s algorithm to find just one solution.

3 Solving the DMDGP by Grover’s algorithm

This section briefly describes the Grover’s algorithm and shows how it can be used to solve the DMDGP.

3.1 Grover’s algorithm

Grover’s algorithm \cite{11} searches a list of elements labeled by integers from 0 to \( N-1 \), where \( N = 2^n \) for some integer \( n \geq 2 \), for a particular element \( i_0 \). The algorithm uses two registers whose number of qubits are \( n \) and 1, respectively. The first step creates a superposition of all \( 2^n \) computational basis states \( \{|0\rangle, \ldots, |2^n-1\rangle\} \) in the first register, which is achieved by applying the Hadamard operator \( H \),

\[ H = \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & 1 \\ 1 & -1 \end{bmatrix}, \]

on each qubit in state \( |0\rangle \), resulting in

\[ |\psi\rangle = \frac{1}{\sqrt{2^n}} \sum_{i=0}^{2^n-1} |i\rangle. \]  \hspace{1cm} (2)

The second register is initialized in state \( |1\rangle \) and, after applying again the Hadamard operator, it changes to the state

\[ |\rangle = H|1\rangle = \frac{|0\rangle - |1\rangle}{\sqrt{2}}. \]
Grover’s algorithm uses two unitary operators. The first is
\[ U_f |i\rangle |j\rangle = |i\rangle |j \oplus f(i)\rangle, \]
where \( i \in \{0, \ldots, N-1\} \), \( j \in \{0,1\} \), \( \oplus \) is the sum modulo 2, and \( f : \{0, \ldots, N-1\} \to \{0,1\} \) is a function, called oracle, that recognizes the searched element \( i_0 \) \( (f(i) = 1 \text{ if and only if } i = i_0) \). Using that \( 1 \oplus f(i_0) = 0 \) and \( 1 \oplus f(i) = 1 \), for all \( i \neq i_0 \), we obtain
\[ U_f |i\rangle |\rangle = (-1)^{f(i)} |i\rangle |\rangle, \]
implying that the state of the first register \( |\psi_1\rangle \) after applying \( U_f \) is
\[ |\psi_1\rangle = \frac{1}{\sqrt{N}} \sum_{i=0}^{N-1} (-1)^{f(i)} |i\rangle. \]

The state of the searched element \( i_0 \) is different from the remaining ones because it is the only one with negative amplitude, but this piece of information is not useful—the probability of finding \( i_0 \) after a measurement is equal to any other wrong element.

The second unitary operator increases the amplitude of \( i_0 \) and at the same time uniformly decreases the amplitude of the other elements. Its definition is
\[ G = 2 |\psi\rangle \langle \psi| - I, \]
where \( |\psi\rangle \) is given by (2) and \( I \) is the identity operator. By applying \( G \) on the incumbent state \( |\psi_1\rangle \), we obtain
\[ |\psi_G\rangle = \sum_{i=0}^{N-1} \frac{N-4}{N\sqrt{N}} |i\rangle + \frac{3N-4}{N\sqrt{N}} |i_0\rangle. \]

The composition of the two operators is the evolution operator \( U = (G \otimes I_{2^k})U_f \). The action of \( U^k \) \( (k \in \mathbb{N}) \) rotates \( |\psi\rangle|\rangle \) towards \( |i_0\rangle|\rangle \) by \( k\theta \) degrees, in the subspace spanned by \( |\psi\rangle|\rangle \) and \( |i_0\rangle|\rangle \), where \( \theta \) is the angle between \( |\psi\rangle \) and \( U|\psi\rangle \) [36]. The number of times \( k \) that \( U \) must be applied so that the angle between \( |i_0\rangle|\rangle \) and \( U^k|\psi\rangle|\rangle \) becomes zero is given by
\[ k = \frac{\arccos \left( \frac{1}{\sqrt{N}} \right)}{\arccos \left( \frac{N-2}{2\sqrt{N}} \right)}. \]

When \( N \) is large, we have
\[ \lim_{N \to \infty} \frac{k}{\sqrt{N}} = \frac{\pi}{4}. \]
Thus, applying \( U \) exactly \( \lfloor k \rfloor \) times and measuring the first register, we obtain \( i_0 \) with probability \( O(1) \) in \( O(\sqrt{N}) \) steps [37,38]. Grover’s algorithm can be extended to query databases with repeated elements [39].

When we apply Grover’s algorithm to practical problems, we have to deal with the problem of defining an efficient oracle function. It is not a trivial task to find an efficient oracle function for the DMDGP.
3.2 The oracle function for the DMDGP

From the DMDGP definition, all distance values between vertices in the set \(\{v_1, v_2, ..., v_n\}\), for \(i = 4, ..., n\), allow us to acquire the following pieces of information:

1. \(d_1, d_2, ..., d_{n-1}\) (distances associated to consecutive vertices);
2. \(\theta_1, \theta_2, ..., \theta_{n-2}\) (angles in \((0, \pi)\) defined by three consecutive vertices); and
3. \(\cos(\omega_{1,4}), ..., \cos(\omega_{n-3,n})\) (cosines of torsion angles in \([0, 2\pi]\) defined by four consecutive vertices [40]), given by

\[
\cos(\omega_{i-3,i}) = \frac{2d_{i-2,i-1}^2 + d_{i-3,i-2}^2 - d_{i-2,i-1}^2}{\sqrt{d_{i-2,i-1}^2 d_{i-3,i-2}^2} - (d_{i-2,i-1}^2)^2},
\]

where

\[
d_{i-3,i-2,i-1} = d_{i-3,i-2}^2 + d_{i-2,i-1}^2 - d_{i-3,i-1}^2,
d_{i-2,i-1,i} = d_{i-2,i-1}^2 + d_{i-2,i}^2 - d_{i-1,i}^2.
\]

From \(\cos(\omega_{i-3,i})\), for \(i = 4, ..., n\), we obtain two possible values for each torsion angle \(\omega_{i-3,i}\); and considering that the DMDGP order \(v_1, ..., v_n\) represents bonded atoms of a molecule, the values \(d_{i-1,i}, \theta_{i-2,i}\) and \(\omega_{i-3,i}\) are exactly the internal coordinates of the molecule that can also be used to describe its structure [21]. This means that the 3D molecular structure is defined by choosing + or -- from \(\sin(\omega_{i-3,i}) = \pm \sqrt{1 - \cos^2(\omega_{i-3,i})}\), for \(i = 4, ..., n\) (the signs + and - are associated to the branches of the BP tree).

The atomic Cartesian coordinates \(x_i = (x_{i1}, x_{i2}, x_{i3})^T \in \mathbb{R}^3\) can be obtained from the internal coordinates using the following matrix multiplications [21]:

\[
\begin{bmatrix}
  x_{i1} \\
  x_{i2} \\
  x_{i3}
\end{bmatrix} = B_1 B_2 \cdots B_{i} \begin{bmatrix}
  0 \\
  0 \\
  1
\end{bmatrix}, \quad \forall i = 1, ..., n,
\]

where

\[
B_1 = \begin{bmatrix}
  0 & 0 & 0 \\
  0 & 0 & 1 \\
  0 & 1 & 0
\end{bmatrix}, \quad B_2 = \begin{bmatrix}
  -1 & 0 & -d_{1,2} \\
  0 & 1 & 0 \\
  0 & 0 & 1
\end{bmatrix},
\]

\[
B_3 = \begin{bmatrix}
  -\cos \theta_{1,3} & -\sin \theta_{1,3} & 0 & -d_{2,3} \cos \theta_{1,3} \\
  \sin \theta_{1,3} & -\cos \theta_{1,3} & 0 & d_{2,3} \sin \theta_{1,3} \\
  0 & 0 & 1 & 0 \\
  0 & 0 & 0 & 1
\end{bmatrix},
\]

and

\[
B_i = \begin{bmatrix}
  -\cos \theta_{i-2,i} & -\sin \theta_{i-2,i} & 0 & -d_{i-1,i} \cos \theta_{i-2,i} \\
  \sin \theta_{i-2,i} \cos \omega_{i-3,i} & \cos \theta_{i-2,i} \cos \omega_{i-3,i} - \sin \omega_{i-3,i} d_{i-1,i} \sin \theta_{i-2,i} \cos \omega_{i-3,i} & 0 & -d_{i-1,i} \cos \theta_{i-2,i} \\
  \sin \theta_{i-2,i} \sin \omega_{i-3,i} & -\cos \theta_{i-2,i} \sin \omega_{i-3,i} + \cos \omega_{i-3,i} d_{i-1,i} \sin \theta_{i-2,i} \sin \omega_{i-3,i} & 0 & 0 \\
  0 & 0 & 0 & 1
\end{bmatrix},
\]

for \(i = 4, ..., n\).
From these matrices, the first three atoms of the molecule can be fixed at positions

\[
x_1 = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}, \quad x_2 = \begin{bmatrix} -d_{1,2} \\ 0 \\ 0 \end{bmatrix}, \quad x_3 = \begin{bmatrix} -d_{1,2} + d_{2,3} \cos \theta_{1,3} \\ d_{2,3} \sin \theta_{1,3} \\ 0 \end{bmatrix},
\]

implying that there are \( N = 2^{n-3} \) possible configurations for a molecule with \( n \) atoms related to the states \( |0\rangle, \ldots, |N - 1\rangle \) of the first register of Grover’s algorithm.

For each qubit of the first register of Grover’s algorithm, states \(|0\rangle\) and \(|1\rangle\) are associated to \( +\sqrt{1 - \cos^2(\omega_{i-3,i})} \) and \( -\sqrt{1 - \cos^2(\omega_{i-3,i})} \), respectively, for \( i = 4, \ldots, n \).

For \( n = 6 \), the possible states are

\[
|0\rangle = |000\rangle, \quad |1\rangle = |001\rangle, \quad |2\rangle = |010\rangle, \quad |3\rangle = |011\rangle, \\
|4\rangle = |100\rangle, \quad |5\rangle = |101\rangle, \quad |6\rangle = |110\rangle, \quad |7\rangle = |111\rangle,
\]

where \(|5\rangle = |101\rangle\), for example, is represented by

\[
-\sqrt{1 - \cos^2(\omega_{1,4})}, \quad +\sqrt{1 - \cos^2(\omega_{2,5})}, \quad -\sqrt{1 - \cos^2(\omega_{3,6})}.
\]

Given a candidate solution \( |k\rangle, k = 0, \ldots, 2^{n-3} - 1 \), we define a function

\[
h: \{0, \ldots, 2^{n-3} - 1\} \rightarrow \mathbb{R}^{3n}
\]

by

\[
h(k) = \left( x_1^k, \ldots, x_n^k \right), \quad (6)
\]

with \( x_i^k \) given by (5), for \( i = 1, \ldots, n \).

For checking if \( h(k) \), for \( k = 0, \ldots, 2^{n-3} - 1 \), is a DMDGP solution, we define another function

\[
g: \mathbb{R}^{3n} \rightarrow \mathbb{R}
\]

by

\[
g \left( x_1^k, \ldots, x_n^k \right) = \sum_{\{u,v\} \in E} \left( \|x_u^k - x_v^k\|^2 - d_{uv}^2 \right)^2, \quad (7)
\]

where \( G = (V, E, d) \) is a DMDGP instance. A DMDGP solution is obtained if, and only if, \( g(x_1^k, \ldots, x_n^k) = 0 \).

In order to define an oracle function \( f \) for the Grover’s algorithm, we first prove that it is possible to define a parameter \( p_1 \), in terms of \( n \), such that

\[
\frac{g(h(k))}{p_1} \in [0, 1],
\]

for all \( k = 0, \ldots, 2^{n-3} - 1 \).

**Proposition 1** Given the function \( g \circ h : \{0, \ldots, 2^{n-3} - 1\} \rightarrow \mathbb{R} \), where \( h \) and \( g \) are defined by (6) and (7), respectively, we have that

\[
\frac{g(h(k))}{6^2(n^5 + n^2)} \in [0, 1].
\]
Let us define candidate solutions of a DMDGP instance $G = (V, E, d)$ by $x_k = (x_{k1}, \ldots, x_{kn}) \in \mathbb{R}^3n$, for $k = 0, \ldots, 2^{n-3} - 1$, which implies that $g(h(k)) = \sum_{\{u,v\} \in E} \left( \|x_k^u - x_k^v\|^2 - d_{uv}^2 \right)^2$.

We want to define $p_1$ such that, for $k = 0, \ldots, 2^{n-3} - 1$, 

$$0 \leq \sum_{\{u,v\} \in E} \left( \|x_k^u - x_k^v\|^2 - d_{uv}^2 \right)^2 \leq p_1.$$ 

Since there are $O(n^2)$ terms in this sum, if we find a value $s$ such that 

$$\max_{k=0,\ldots,2^{n-3}-1} \left\{ \left( \|x_k^u - x_k^v\|^2 - d_{uv}^2 \right)^2 \right\} \leq s,$$

we could define $p_1 = n^2 s$.

For $k = 0, \ldots, 2^{n-3} - 1$, we have 

$$\max_{\{u,v\} \in E} \left\{ \left( \|x_k^u - x_k^v\|^2 - d_{uv}^2 \right)^2 \right\} = \max_{\{u,v\} \in E} \left\{ \left( \|x_k^u - x_k^v\|^4 + d_{uv}^4 - 2\|x_k^u - x_k^v\|^2 d_{uv}^2 \right) \right\} \leq \max_{\{u,v\} \in E} \left\{ \|x_k^u - x_k^v\|^4 \right\} + \max_{\{u,v\} \in E} \left\{ d_{uv}^4 \right\}.$$ 

The maximum value for $d_{uv}$ is related to the maximum value detected by NMR experiments (given by 6 Å [1]), and the maximum value for $\|x_k^u - x_k^v\|$ is obtained when $\theta_{i-2,i} = \pi$, for $i = 3, \ldots, n$, and $\omega_{i-3,i} = 0$, for for $i = 4, \ldots, n$. Considering also 6 Å for $d_{i-1,i}$, for $i = 2, \ldots, n$ (which is greater than the maximum value for a covalent bond in proteins [1]), we obtain 

$$\max_{k=0,\ldots,2^{n-3}-1} \left\{ \left( \|x_k^u - x_k^v\|^2 - d_{uv}^2 \right)^2 \right\} \leq (6n)^4 + 6^4 = 6^4(n^4 + 1).$$

Hence, for $s = 6^4(n^4 + 1)$ and $p_1 = n^2 s$, we obtain 

$$g(h(k)) \in [0, 1].$$

Now, we show that it is also possible to define another parameter $p_2$ such that, for all $k = 0, \ldots, 2^{n-3} - 1$ and a given $\epsilon > 0$, 

$$\left( \frac{g(h(k))}{p_1} \right)^{\frac{1}{2\epsilon}} \in [0, 1 - \epsilon),$$

when $k$ is associated to a DMDGP solution, and 

$$\left( \frac{g(h(k))}{p_1} \right)^{\frac{1}{2\epsilon}} \in [1 - \epsilon, 1].$$
in the other cases.

From (7), a DMDGP solution \( x^k_1, \ldots, x^k_n \) is identified when \( g(x^k_1, \ldots, x^k_n) = 0 \). However, due to rounding errors in fixed-point arithmetics, we define a DMDGP solution \( x^k_1, \ldots, x^k_n \) if, and only if,

\[
g \left( x^k_1, \ldots, x^k_n \right) < \delta,
\]

for a given small value \( \delta > 0 \).

**Theorem 1** Given \( \delta > 0 \), the function \( g \circ h : \{0, \ldots, 2^{n-3} - 1\} \to \mathbb{R} \), where \( h \) and \( g \) are defined by (6) and (7), respectively, and a value \( \epsilon > 0 \) such that \( \delta < 1 - \epsilon \), we have that

\[
\left( \frac{g(h(k))}{6^4(n^6 + n^2)} \right)^{\log_{1-\epsilon}(\frac{1}{64(n^6 + n^2)})} \in [0, 1 - \epsilon),
\]

when \( k \) is associated to a DMDGP solution \( (g(h(k)) < \delta) \), and

\[
\left( \frac{g(h(k))}{6^4(n^6 + n^2)} \right)^{\log_{1-\epsilon}(\frac{1}{64(n^6 + n^2)})} \in [1 - \epsilon, 1],
\]

when \( k \) is not associated to a DMDGP solution \( (g(h(k)) \geq \delta) \).

**Proof** First, note that, for \( p_1 = 6^4(n^6 + n^2) \),

\[
\frac{\delta}{p_1} < \delta < 1 - \epsilon \Rightarrow \ln \left( \frac{\delta}{p_1} \right) < 0 \text{ and } \ln(1 - \epsilon) < 0
\]

\[
\Rightarrow \frac{\ln \left( \frac{\delta}{p_1} \right)}{\ln(1 - \epsilon)} = \log_{1-\epsilon} \left( \frac{\delta}{p_1} \right) > 0.
\]

Defining

\[
p_2 = \log_{1-\epsilon} \left( \frac{\delta}{p_1} \right)
\]

and considering a DMDGP solution \( k \) \( (g(h(k)) < \delta) \), we obtain

\[
0 \leq g(h(k)) \leq \delta \Rightarrow 0 \leq \frac{g(h(i_0))}{p_1} < \frac{\delta}{p_1} < \left( \frac{\delta}{p_1} \right)^{\frac{1}{p_2}}
\]

\[
\Rightarrow 0 \leq \left( \frac{g(h(k))}{p_1} \right)^{\frac{1}{p_2}} < \left( \frac{\delta}{p_1} \right)^{\frac{1}{p_2}}
\]

\[
\Rightarrow 0 \leq \left( \frac{g(h(i_0))}{p_1} \right)^{\frac{1}{p_2}} < 1 - \epsilon
\]

\[
\Rightarrow \left( \frac{g(h(k))}{p_1} \right)^{\frac{1}{p_2}} \in [0, 1 - \epsilon).
\]
When $k$ is not a DMDGP solution ($g(h(k)) \geq \delta$), we get, from Proposition 1,

$$\delta \leq g(h(k)) \Rightarrow \frac{\delta}{p_1} \leq \frac{g(h(k))}{p_1} \leq 1$$
$$\Rightarrow \left(\frac{\delta}{p_1}\right)^{\frac{1}{p_2}} \leq \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} \leq 1$$
$$\Rightarrow \left(\frac{\delta}{p_1}\right)^{\frac{1}{p_2} - (\frac{1}{p_2})} \leq \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} \leq 1$$
$$\Rightarrow 1 - \epsilon \leq \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} \leq 1$$
$$\Rightarrow \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} \in [1 - \epsilon, 1]$$

\[ \square \]

**Corollary 1** For a given $\delta > 0$ and $\epsilon > 0$ such that $\delta + \epsilon < 1$, the function

$$f : \{0, \ldots, 2^{n^3} - 1\} \rightarrow \{0, 1\},$$

defined by

$$f(k) = 1 - \left\lfloor \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} + \epsilon \right\rfloor,$$

where

$$p_1 = 6^4(n^6 + n^2)$$

and

$$p_2 = \log_{1 - \epsilon}\left(\frac{\delta}{p_1}\right),$$

satisfies the following property:

$$f(k) = 1 \iff k \text{ is associated to a DMDGP solution } (g(h(k)) < \delta).$$

**Proof** From Theorem 1, when $k \in \{0, \ldots, 2^{n^3} - 1\}$ is not a DMDGP solution ($g(h(k)) \geq \delta$),

$$\left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} \in [1 - \epsilon, 1] \Rightarrow f(k) = 1 - \left\lfloor \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} + \epsilon \right\rfloor = 0.$$

For a DMDGP solution $k$ ($g(h(k)) < \delta$),

$$\left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} \in [0, 1 - \epsilon] \Rightarrow f(k) = 1 - \left\lfloor \left(\frac{g(h(k))}{p_1}\right)^{\frac{1}{p_2}} + \epsilon \right\rfloor = 1.$$

\[ \square \]
4 Computational results

In this section, we describe the implementation of some instances of the oracle function for the DMDGP on IBM quantum computers. Since the quantum computers that are available nowadays have a high error rate, we restrict to 3-qubit oracles to show that our procedure works and can be extended to meaningful applications when error rates are improved or error correcting codes are implemented.

In our experiments, we have used IBM Qiskit to implement Grover’s algorithm. We hard coded oracle circuits for objective functions corresponding to each possible instance of the DMDGP for molecules with 7 atoms. We ran the experiments on IBM Santiago, IBM Lagos, IBM Bogota, and on IBM QASM Simulator.

In Fig. 1, we have a summary of the results obtained from the search algorithm running on IBM Santiago—which was the best device for most of our experiments—when the searched element was $|010\rangle$. The horizontal axis depicts the possible outcomes, and the vertical axis depicts the probability of each outcome based on 8196 independent runs performed on the device. We compare the results obtained using the standard set of gates and the improved decomposition of multi-controlled $Z$ gates. The results for an ideal noiseless device was obtained by simulations and is also shown in the figure for reference. The left panel shows the results for one oracle call, and the right panel shows the results for two oracle calls. See also Table 1 for the numerical data used to generate the plots. The searched element was successfully marked with either set of gates, even though the multi-controlled $Z$ gates improved the results as expected. The simulated results confirm that we should apply two oracle calls in an ideal noiseless set-up. However, the experiments on real quantum devices clearly show that the second oracle call introduces noise and makes the results worse. Therefore, when executing Grover’s algorithm on noisy quantum devices we must stop before the full number of iterations prescribed by theory, even though the success probability is not yet as high as we could expect from error-corrected devices.

In Fig. 2, we have a summary of the results obtained from the search algorithm running on IBM Lagos, IBM Santiago, and IBM Bogota when the searched element was $|010\rangle$. The horizontal axis depicts the possible outcomes, and the vertical axis...
Table 1 Numerical data used to generate Fig. 1.

| Ket   | One call | Two calls |
|-------|----------|-----------|
|       | IBM Santiago | Simulator | IBM Santiago | Simulator |
|       | std impr | std impr | std impr | std impr |
| 000   | 0.070   | 0.043    | 0.030   | 0.029    |
| 001   | 0.058   | 0.031    | 0.030   | 0.031    |
| 010   | 0.644   | 0.679    | 0.783   | 0.785    |
| 011   | 0.053   | 0.069    | 0.032   | 0.031    |
| 100   | 0.032   | 0.032    | 0.037   | 0.031    |
| 101   | 0.036   | 0.041    | 0.030   | 0.030    |
| 110   | 0.053   | 0.049    | 0.030   | 0.030    |
| 111   | 0.054   | 0.056    | 0.028   | 0.032    |

depicts the probability of each outcome based on 8196 independent runs performed on the device. We also compare the results obtained using the standard set of gates and the improved decomposition of multi-controlled $Z$ gates. The left panel shows the results for one oracle call, and the right panel shows the results for two oracle calls. See also Tables 2 and 3 for the numerical data used to generate the plots—the former corresponding to one oracle call, and the latter corresponding to two oracle calls. Notice that all quantum devices were successful in finding the searched element, even though some of them performed much better than others. When choosing a NISQ computer [14] to solve a real-world problem, it is important to analyse each device in depth, since the quality of the results strongly depends on that choice. It is also important to notice that the second oracle call decreased the success probability on all quantum devices. When programming a NISQ computer, one must keep in mind that adaptations on the algorithms are often necessary in order to reduce the size and depth of the final circuit and compensate the effects of noise and decoherence.

In order to assess the quality of the results it is important to measure the fidelity between the actual probability distribution obtained by the real quantum device and the ideal distribution obtained by the simulator. If $\{p_x\}$ and $\{q_x\}$ are
two probability distributions, then the total variation distance \( d \) is given by [41]

\[
d = \frac{1}{2} \sum_x |p_x - q_x|,
\]

and the Hellinger distance \( h \) is given by [41]

\[
h^2 = \frac{1}{2} \sum_x (\sqrt{p_x} - \sqrt{q_x})^2.
\]

In this work, we used two different definitions of fidelity, both \( 1 - d \) and \( 1 - h \).

It is also useful to consider the selectivity, which is a parameter introduced by Wang et al. [42] to measure how strong is the result of a quantum computation when compared to the second most probable outcome. In this work, we adopt the simplified definition from Zhang et al. [43], given by the ratio

\[
S = \frac{P_s}{P_{ns}},
\]

where \( P_s \) is the success probability, i.e., the probability of measuring the searched element, and \( P_{ns} \) is the maximum probability of measuring a non-searched element.

In Table 4, we summarize the quality of the results obtained with one oracle call on the quantum computers IBM Lagos, IBM Santiago, and IBM Bogota. The parameters used to assess the quality of the results were the fidelity, the selectivity, and the success probability. The values on the tables are averages taken from all experiments. This analysis is important because the quality of the results
vary according to the marked element. Notice that the improved decomposition of multi-controlled \( Z \) gates really helped us to achieve better results.

|                  | Lagos   | Santiago | Bogota   |
|------------------|---------|----------|----------|
| Fidelity \((1 - d)\) | 0.789   | 0.810    | 0.815    |
| Fidelity \((1 - h)\) | 0.825   | 0.838    | 0.849    |
| Selectivity      | 6.432   | 6.776    | 7.599    |
| Success probability | 0.578   | 0.599    | 0.598    |

Table 4 Quality of the results obtained with one oracle call assessed according to different metrics.

|                  | Lagos   | Santiago | Bogota   |
|------------------|---------|----------|----------|
| Fidelity \((1 - d)\) | 0.527   | 0.553    | 0.580    |
| Fidelity \((1 - h)\) | 0.593   | 0.610    | 0.632    |
| Selectivity      | 3.952   | 4.197    | 5.644    |
| Success probability | 0.473   | 0.498    | 0.526    |

Table 5 Quality of the results obtained with two oracle calls assessed according to different metrics.

5 Final comments

We have described implementations of a quantum algorithm that solves small instances of the Discretizable Molecular Distance Geometry Problem (DMDGP). The strategy is to use Grover’s algorithm to search the domain of an oracle function for a point that satisfies all the information required to solve the DMDGP. It is not trivial to build the oracle and this is one of the main contributions of this work. The implementation of our algorithm on small-scale quantum computers shows the consistency of the procedure, which is more efficient than classical methods that employ brute force, because the number of steps of the Grover algorithm is quadratically smaller. We have shown probability distributions of actual implementations on IBM quantum computers and have compared with correct results simulated on classical computers. We remark that it is better to take fewer steps than the number prescribed by Grover’s algorithm because the accumulation of errors would degrade the quality of the results.

Due to uncertainties in NMR data, the natural extension of this work is the development of a quantum approach to the DMDGP with interval distances, which
is one of the important open problems in Distance Geometry [44]. There is an active research on this topic, like the interval BP algorithm [45,46,47,48,49,50] and other approaches based on Clifford algebra [51,52,53].

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