

Quantum Annealing Research at CMU: Algorithms, Hardware, Applications

Sridhar Tayur *, Ananth Tenneti

Quantum Technologies Group, Carnegie Mellon University, Pittsburgh, PA 15213

Correspondence*:

Sridhar Tayur

stayur@andrew.cmu.edu

2 ABSTRACT

3 In this mini-review, we introduce and summarize research - at Quantum Technologies Group
4 (QTG) at Carnegie Mellon University, in collaboration with several other institutions, including
5 IIT-Madras and NASA (QuAIL) - related to computational experience with quantum annealing. We
6 present a novel hybrid quantum-classical heuristic algorithm (GAMA, Graver Augmented Multi-
7 seed Algorithm) for non-linear, integer optimization, and illustrate it on an application (in cancer
8 genomics). We then present an algebraic geometry based algorithm for embedding a problem
9 onto a hardware that is not fully connected, along with a companion Integer Programming (IP)
10 approach. Next, we discuss the performance of two photonic devices - the Temporal Multiplexed
11 Ising Machine (TMIM) and the Spatial Photonic Ising Machine (SPIM)- on Max-Cut and Number
12 Partitioning instances. We close with an outline of current work.

1 INTRODUCTION

13 Quantum annealing has emerged as a promising approach because a variety of Combinatorial Optimization
14 (CO) problems that arise in practical situations (Tanahashi et al., 2019; Smelyanskiy et al., 2012; Hauke
15 et al., 2020) can be formulated as a Quadratic Unconstrained Binary Optimization (QUBO) problem, which
16 maps naturally to an Ising model, and solved on specially constructed quantum and semi-classical hardware
17 (Glover et al., 2018; Lucas, 2014; Mohseni et al., 2022; King et al., 2018; Harris et al., 2018; Wang and
18 Roychowdhury, 2019; Chou et al., 2019; McMahan et al., 2016; Wang et al., 2013). A lucid introduction
19 on quantum annealing can be found in (McGeoch, 2014).

		Application
Algorithm for Non-Linear Integer Optimization	Graver Augmented Multiseed Algorithm (GAMA)	Cancer Genomics Binary Classification
Algorithms for Embedding	Algebraic Geometry Integer Programming	D-Wave D-Wave
Photonic Ising Machines (Hardware)	Time Multiplexed (TMCIM) Spatial (SPIM)	Max-Cut Number Partitioning

Figure 1. Some computational quantum annealing initiatives at Quantum Technology Group (QTG).

20 At Carnegie Mellon University's Quantum Technologies Group (QTG), we have been working on several
21 initiatives¹ related to computational aspects of quantum annealing. See Figure 1.

- 22 1. While unconstrained optimization problems expressed as QUBO can be directly passed to an annealer
23 solver, it is also of practical interest to develop scalable decomposition methods that solve general non-
24 linear constrained optimization problems. We describe a novel quantum-classical algorithm, Graver
25 Augmented Multiseed Algorithm (GAMA) (Alghassi et al., 2019a,b) for solving such optimization
26 problems, building on previous work on the use of algebraic geometry for Integer Optimization with
27 a linear objective function (Tayur et al., 1995). GAMA is motivated by test sets, and (a) uses partial
28 Graver bases (Graver, 1975) instead of the complete Graver basis and (b) many feasible solutions as
29 starting points (rather than just one) for augmentation. Both the partial Graver basis and a number of
30 feasible solutions are obtained from the constraint equation expressed as QUBOs (that is solved by an
31 annealer). A particular advantage of this algorithm is that it separates the constraints from the objective
32 function, allowing us to tackle situations where the computation of objective function value may need
33 an oracle call (such as a simulation).
- 34 2. Many devices such as D-Wave have limited coupling connectivity between qubits. For a dense problem
35 graph, it is therefore necessary to develop a mapping - minor embedding - to the sparse hardware
36 graph. We have developed two methods, based on algebraic geometry and Integer Programming (Dridi
37 et al., 2018a; Bernal et al., 2020).
- 38 3. Building fully connected Ising hardware is another exciting area of current research. We have re-
39 constructed (with some refinements) two Photonic Ising Machines (PIM), building on the time
40 multiplexed coherent Ising machine (TMCIM) (Böhm et al., 2019) and the spatial multiplexed Ising
41 machine (SPIM) (Pierangeli et al., 2020). We have studied the performance of the annealers on
42 Max-Cut and Number Partitioning Problem with D-Wave (McGeoch, 2014) and Gurobi (Gurobi
43 Optimization, LLC, 2023).

44 The rest of the review is organized as follows. In Section 2, we describe GAMA. In Section 3, we illustrate
45 the application of the GAMA on identifying altered pathways in cancer genomics as a proof-of-principle
46 and recover known results. An algebraic geometry based embedding algorithm and its Integer Programming
47 reformulation are outlined in Section 4 and compared to the default heuristic that is used by D-Wave. The
48 performance of two Photonic Ising Machines is discussed in Section 5. We conclude in Section 6.

2 GRAVER AUGMENTED MULTISEED ALGORITHM (GAMA)

49 We begin with three definitions, taken verbatim from (Alghassi et al., 2019b).

50 **DEFINITION 1.** *A set $S \in \mathbb{Z}^n$ is a Test Set or an optimality certificate, if for every non-optimal, feasible*
51 *solution, x_0 , there exists $t \in S$ and $\lambda \in \mathbb{Z}_+$ such that $f(x_0 + \lambda t) < f(x_0)$. The vector, t is called the*
52 *augmenting direction.*

53 The following partial order is defined on \mathbb{R}^n .

54 **DEFINITION 2.** *Given $x, y \in \mathbb{R}^n$, we define x is conformal to y , written as $x \sqsubseteq y$, if $x_i y_i \geq 0$ (x and y lie*
55 *in the same orthant), and $|x_i| \leq |y_i|, \forall i \in \{1..n\}$. A sum $u = \sum_i v_i$ is called conformal if $v_i \sqsubseteq u, \forall i$.*

¹ QTG is also engaged in theoretical research on understanding speed up in adiabatic quantum computing (Dridi et al., 2018b, 2019a), and other connections between algebraic geometry and Ising models (Dridi et al., 2019b), topics not covered here.

56 For a matrix $A \in \mathbb{Z}^{m \times n}$, define the lattice

$$L^*(A) = \{x | Ax = 0, x \in \mathbb{Z}^n, A \in \mathbb{Z}^{m \times n}\} \setminus \{0\}. \quad (1)$$

57 DEFINITION 3. The Graver basis, $\mathcal{G}(A) \subset \mathbb{Z}^n$, of an integer matrix A is defined as the finite set of \square
58 minimal elements in $L^*(A)$.

59 The Graver basis (Graver, 1975) of an integer matrix, $A \in \mathbb{Z}^{m \times n}$ is known to be a test set for integer
60 linear programs. Graver basis is also a test set for certain non-linear objective functions including Separable
61 convex minimization (Murota et al., 2004), Convex integer maximization (De Loera et al., 2009), Norm p
62 minimization (Hemmecke et al., 2011), Quadratic (Lee et al., 2010; Murota et al., 2004) and Polynomial
63 minimization (Lee et al., 2010). It has also been shown that for these problem classes, the number of
64 augmentation steps needed is polynomial (Hemmecke et al., 2011; De Loera et al., 2009). Graver basis can
65 be computed (only for small size problems) using classical methods such as the algorithms developed by
66 Pottier (1996) and Sturmfels and Thomas (1997).

67 At QTG, we are exploring (a) the effectiveness of computing partial Graver basis using annealers by
68 solving a QUBO (for kernel elements), and, (b) instead of relying on just one feasible solution as the seed
69 for augmentation, using multiple feasible solutions (that are also obtained via annealing, by solving a
70 second QUBO), as parallel starting points. The GAMA heuristic (Alghassi et al., 2019a,b) thus aims to find
71 good solutions to constrained non-linear optimization problems of the form in Equation 2, using multiple
72 seeds as starting points for augmentation, with partial Graver basis elements as the augmenting directions:

$$(IP)_{A,b,l,u,f} = \begin{cases} \min f(x) \\ Ax = b & l \leq x \leq n \quad x, l, u \in \mathbb{Z}^n \\ A \in \mathbb{Z}^{m \times n} \quad b \in \mathbb{Z}^n \end{cases} \quad (2)$$

73 where $f : \mathbb{R}^n \rightarrow \mathbb{R}$ is a real valued function.

74 2.1 QUBO for kernel calculation

75 In order to find a sample of the kernel elements for the constraint matrix A , we solve the Quadratic
76 Unconstrained Integer Optimization (QUIO), given by

$$\begin{aligned} \min \quad & x^T Q_I x, \quad Q_I = A^T A, \quad x \in \mathbb{Z}^n \\ & x^T = [x_1, x_2 \dots x_n], x_i \in \mathbb{Z}. \end{aligned} \quad (3)$$

77 Since the inputs to the annealer are binary variables, we create a binary encoding of the integer variable.
78 Writing

$$x = L + EX, \quad (4)$$

79 with L as the lower bound vector and E as the encoding matrix, the QUIO is equivalent to the QUBO

$$\begin{aligned} \min \quad & X^T Q_B X, \quad Q_B = E^T Q_I E + \text{diag}(2L^T Q_I E), \\ & X \in \{0, 1\}^{nk}, Q_I = A^T A. \end{aligned} \quad (5)$$

80 The above QUBO is solved by an annealer to obtain kernel elements. A partial Graver basis can be
 81 obtained from the kernel elements in a classical post processing step by \square -minimal filtering (Alghassi
 82 et al., 2019a).

83 2.2 QUBO for feasible solutions

84 Similar to the kernel sampling, the $Ax = b$ constraint can be expressed in the QUBO form as

$$\begin{aligned} \min \quad & x^T Q_I x - 2b^T A x \\ & Q_I = A^T A, x \in \mathbb{Z}^n. \end{aligned} \quad (6)$$

85 After binary encoding, we get the QUBO given by

$$\begin{aligned} \min \quad & X^T Q_B X, \quad Q_B = E^T Q_I E + 2diag[(L^T Q_I - b^T A)E] \\ & X \in \{0, 1\}^{nk}, Q_I = A^T A. \end{aligned} \quad (7)$$

86 The above QUBO can be solved by an annealer to obtain a sample of feasible solutions.

3 AN APPLICATION OF GAMA: CANCER GENOMICS

87 As a proof-of-principle testing of GAMA, we describe an application (Alghassi et al., 2019) to identify
 88 cancer pathways de novo (Vogelstein and Kinzler, 2004; Haber and Settleman, 2007; Ciriello et al., 2012;
 89 Vandin et al., 2012a,b; Zhao et al., 2012) from mutation co-occurrence and mutual exclusivity (Leiserson
 90 et al., 2013; Weinberg and Weinberg, 2013).

91 Data from The Cancer Genome Atlas (TCGA) are now available for a variety of cancers providing
 92 information about which genes are mutated for which patient for any given cancer. With this, we can create
 93 a matrix. The rows of the matrix are patients, the columns are the genes, and the elements of the matrix
 94 (row i , column j) are zero or one (so this is a binary matrix), where “one” in (row i , column j) means that
 95 gene j is mutated for patient i .

96 However, not all mutations matter. The mutations that do not matter are called passengers. Those
 97 mutations that matter are called drivers. We want to isolate drivers from passengers. (Most mutations are
 98 passengers.) Furthermore, the same cancer can manifest itself due to different driver mutations, because
 99 different mutated driver genes can impact different cellular signaling and regulatory pathways. This
 100 mutational heterogeneity complicates efforts to identify drivers solely by their frequency of occurrence.

101 A pathway is a collection of genes. To find k pathways means finding k different collections of genes.
 102 Each collection of genes can be of a different size. To make the discovery of these pathways computationally
 103 manageable, we also make two commonly accepted simplifications:

104 **Simplification 1:** A pathway has at most one mutated driver gene. This is because driver genes are quite
 105 rare. Thus, two different pathways will not likely share a common driver gene. This is called (mutual)
 106 exclusivity.

107 **Simplification 2:** A pathway should apply to many patients. This is called coverage. The important thing
 108 to note is that even though two patients share a pathway, they can have a different mutated gene from that
 109 shared pathway as an explanatory reason for their cancer.

110 Another complexity that we need to handle is that real data are noisy because of measurement errors
 111 and passenger mutations. This means that we cannot impose exclusivity as a hard constraint. Instead, we
 112 allow for some overlap or “approximate exclusivity” and this is a parameter in our formulation. Similar
 113 considerations force a modification of Simplification 2 as well, in the sense that we now can only reasonably
 114 hope that most patients have at least one mutation in a pathway. Recall that mutual exclusivity problems
 115 even without the modification above are NP-hard (Karp, 1972).

116 3.1 Multiple-Pathway QUBO formulation for GAMA

117 Alghassi et al. (2019) developed a novel formulation tailored for GAMA to discover the cancer pathways.
 118 Consider a hypergraph $H_g = (V_g, E_p)$ with incidence matrix B , where each gene (g_i) is represented by
 119 a vertex $v_i \in V_g, i = 1, 2, \dots, n$ and the mutation list of each patient P_i is represented by a hyperedge
 120 $e_i \in E_p, i = 1, 2, \dots, m$.

121 The incidence matrix is mapped to its primal graph (G). This is a graph with the same vertices as that of
 122 the hypergraph and with edges between all pairs of vertices contained within the same hyperedge. The
 123 primal graph can be expressed in terms of the (positive) Laplacian matrix:

$$L^+(G) = BB^T = D(G) + A(G). \quad (8)$$

124 The weighted adjacency matrix $A = [a(i, j)]^{n \times n}$ is symmetric and has zero as the diagonal elements. The
 125 number of patients that have gene pairs (g_i, g_j) mutated is given by $a(i, j)$. The number of patients with
 126 gene g_i mutated is given by the element, d_i in the degree matrix, $D = \text{diag}\{d_1, d_2, \dots, d_n\}$, where d_i is the
 127 degree of the vertex v_i in the primal graph.

128 A k -pathway QUBO formulation simultaneously finds k pathways in a single optimization run. The
 129 solution vector is represented by the binary vector $x_i = [x_{i1}, x_{i2}, \dots, x_{in}]^T, i = 1, 2, \dots, k$ where, each
 130 element x_{ij} indicates if a vertex v_j belongs to the i^{th} pathway. Let $\mathbf{X} = [x_1, x_2, \dots, x_k]^T$. The QUBO
 131 formulation is given by the following (where $L = (D - A)$ is the negative Laplacian matrix).

$$\begin{aligned} \min \mathbf{X}^T (\mathbf{Q}_{main} + \alpha \mathbf{Q}_{orth}) \mathbf{X} \\ \mathbf{Q}_{main} &= -I_k \otimes L \\ \mathbf{Q}_{orth} &= (J_k - I_k) \otimes I_n \end{aligned} \quad (9)$$

132 Note that I_k and I_n are $k \times k$ and $n \times n$ identity matrices. J_k is the $k \times k$ matrix with all entries equal to 1.

133 Rewriting the system of equations(9) as

$$\begin{aligned} \min \mathbf{X}^T \mathbf{Q} \mathbf{X} \\ (\mathbf{1}_k^T \otimes I_n) \mathbf{X} &\leq \mathbf{1}_n \\ \mathbf{Q} &= -I_k \otimes L \end{aligned} \quad (10)$$

134 brings it in the form suitable for GAMA (Alghassi et al., 2019a).

135 This is a non-linear (quadratic) non-convex integer problem and of a Quadratic Semi Assignment Problem
 136 (QSAP) form. We can alternatively extract Graver basis and generate feasible solutions systematically in
 137 this case (Alghassi et al., 2019a) instead of solving QUBOs on a quantum annealer.

138 3.2 Numerical Results

139 GAMA algorithm is used to solve k-pathway problem using the mutation data of 33 genes for Acute
 140 Myeloid Leukemia (AML) for 200 patients (Network, 2013). By construction, the number of binary
 141 variables required is lower than available methods (?). For $k = 3$, the pathways discovered by GAMA are
 142 consistent with those reported by the TCGA authors. For $k = 6$, three additional pathways are discovered
 143 by GAMA albeit with lower coverage.

4 EMBEDDING ALGORITHMS

144 If an annealer hardware is not fully connected (e.g. the D-Wave system), it is necessary to map the logical
 145 graph, Y associated with the optimization problem into the processor graph, X (Boothby et al. (2016),
 146 Choi (2011)). We describe embedding algorithms² based on algebraic geometry (Dridi et al., 2018a).

147 **DEFINITION 4.** *Let X be a hardware graph. A minor-embedding of the graph, Y is a map, $\phi :$
 148 $Vertices(Y) \rightarrow connectedSubtrees(X)$ such that, $\forall (y_1, y_2) \in Edges(Y)$, there exists at least one edge
 149 connecting the subtrees, $\phi(y_1)$ and $\phi(y_2)$.*

150 Given an embedding of a logical graph, Y into a physical graph, X , the Y minor is a subgraph of X
 151 given by

$$\phi(Y) = \cup_{y \in Vertices(Y)} \phi(y) \quad (11)$$

152 This is the input graph to the quantum processor. The information regarding the mapping of each logical
 153 qubit is stored in a hash map,

$$id \times \phi : Vertices(Y) \times Vertices(Y) \rightarrow Vertices(Y) \times Subtrees(X) \quad (12)$$

154 which can be used to unembed desired solution returned by the processor.

155 4.1 Algebraic Geometry method

156 The set of embeddings can be viewed as an algebraic variety, which is the set of zeros of a system
 157 of polynomial equations (Cox et al., 2007). Given an embedding the mapping, $\pi : Vertices(X) \rightarrow$
 158 $Vertices(Y) \cup \{0\}$, where the pre-image (fiber) $\pi^{-1}(y) = \phi(y)$, $\forall y \in Vertices(Y)$ has the form:

$$\pi(x_i) = \sum_j \alpha_{ij} y_j$$

$$\text{with } \sum_j \alpha_{ij} = \beta_i, \alpha_{ij}(\alpha_{ij} - 1) = 0 \quad (13)$$

$$\alpha_{ij_1} \alpha_{ij_2} = 0, \text{ for } j_1 \neq j_2$$

159 where $\beta_i \in \{0, 1\}$ is equal to 1, if the physical qubit x_i is used, and 0 otherwise. Now, the conditions
 160 on the embedding ϕ in Definition 4 along with a limit on the number of usable physical qubits can be
 161 translated into a system of polynomial constraints on α_{ij} and β_i . This system defines an algebraic ideal \mathcal{I} ,
 162 and the embeddings can be obtained using the Groebner basis of \mathcal{I} .

² Note that X can be any graph in general, not just the hardware graph, which is the focus here.

163 4.2 Integer Programming (IP) method

164 An IP formulation of the embedding algorithm (Bernal et al., 2020) is developed by expressing the
165 polynomial conditions in Dridi et al. (2018a) as linear constraints involving integer variables. This
166 formulation includes constraints for *Minimum and Maximum size*. Embeddings are obtained by optimizing
167 the *Embedding size* within the feasible region. A decomposition approach, iterating between a qubit
168 assignment master problem and a fiber condition checking subproblem is also developed.

169 Bernal et al. (2020) tested these methods using random graphs that vary in structure, size and density.
170 The results are compared with the the D-Wave default heuristic, *minorminer* (Cai et al., 2014). The
171 IP-based approaches are found to be slower whenever the heuristic can find an embedding. However, it is
172 possible to obtain infeasibility proofs and bounds on solution quality with the IP methods, but not from the
173 heuristics. The decomposition approach outperforms the monolithic IP approach.

5 HARDWARE

174 Two fully connected Coherent Ising Machines (CIM) - the Temporal Multiplexed Coherent Ising Machine
175 (TMCIM) (based on (Böhm et al., 2019, 2021)) and the Spatial Photonic Ising Machine (SPIM) (an
176 enhancement of that of Pierangeli et al. (2019)) - were built by collaborators at IIT-Madras (Prabhakar
177 et al., 2023).

178 5.1 Temporal Multiplexed Ising Machine

179 The TMCIM was tested on the Max-Cut problem (Karp, 1972) and the results on various instances are
180 compared with Gurobi run on Intel Core i3 processor and also with a D-Wave machine. The graph instances
181 for the problem are generated using *rudyl* (Rendl et al., 2010). See Prabhakar et al. (2023) for details.

182 First, at a fixed graph size (100 nodes), and varying density, TMCIM performed better than Gurobi up
183 to a graph density of 40%. However, above 50%, the performance of TMCIM degraded. Next, the results
184 with a fixed graph density of 40% and varying size of the graph from 100 to 1000 were obtained. For larger
185 graphs, the performance of TMCIM was found to be considerably lower than Gurobi.

186 Second, the results are compared with the D-Wave Advantage 1.1 (DWA) annealer with the graph size
187 varying from 20 to 100 nodes and the graph density fixed at 10%. For all the graph sizes, TMCIM is able
188 to always give a Max-Cut value which is at least 96% of the value obtained using Gurobi (See Figure 6 in
189 Prabhakar et al. (2023)). A solution accuracy of 99% can be attained up to 30 nodes. For DWA, the solution
190 accuracy degrades beyond 20 nodes. This can be attributed to the limited connectivity of its Pegasus graph.

191 5.2 Spatial Photonic Ising Machine

192 The SPIM was tested on Number Partitioning Problem (NPP) with instance sizes varying from 16 to
193 16384 variables. The performance of the SPIM was compared with that of Gurobi and DWA. See Tables
194 3 and 4 in Prabhakar et al. (2023). For DWA, the number of variables that can be embedded is limited
195 to 11×11 fully connected graph and is not competitive. For problem sizes up to 1024 variables, Gurobi
196 performs better than SPIM. However, Gurobi is unable to find solutions as the problem size gets larger
197 while SPIM can handle up to 16384 variables.

6 CONCLUSION

198 We have developed GAMA (Graver Augmented Multi-seed Algorithm), a novel hybrid quantum-classical
199 algorithm for non-linear constrained integer optimization. As an application, we have explored a new
200 formulation for the the discovery of de-novo cancer pathways. This tailored formulation is found to require
201 fewer binary variables when compared with existing methods, and the pathways detected have been found
202 to be consistent with previously published results.

203 For minor embedding that is usually required in Ising hardware that does not have an all-to-all connectivity,
204 we have developed algebraic geometry and IP based algorithms. The IP algorithm is found to perform well
205 for highly structured source graphs, when compared with the currently employed heuristic, `minorminer`
206 and the Groebner basis method. While slower overall when compared with the heursitic, the algorithm can
207 detect instance infeasibility and obtain bounds on solution quality.

208 We have built two photonic Ising machines, TMCIM and SPIM. We have studied their performance
209 on Max-Cut and NPP problems, respectively, by comparing with D-Wave and Gurobi. For the Max-Cut,
210 TMCIM gave better results than Gurobi at smaller graph size (< 100 nodes) and lower densities ($< 40\%$),
211 while its accuracy is lower for larger problems. However, the performance is better than D-Wave, which
212 can be attributed to better connectivity. SPIM can solve NPP problems up to 16384 spins, which is larger
213 than the problem sizes solved by D-Wave and Gurobi. Gurobi's performance is better at smaller sizes, but
214 cannot exceed more than 1024 spins.

215 We conclude by noting some current work in quantum annealing. We are testing GAMA³ against state-of-
216 the-art classical approaches for an application in disaster preparation, in collaboration with researchers at
217 Koc University, as part of an initiative of the Turkish Ministry of Transportation and Infrastructure, focused
218 on probable earthquake in Istanbul. As noted earlier, the performance of the annealers depends crucially on
219 connectivity in the hardware. We are in the process of building another fully connected annealer, based on
220 Floquet Theory, collaborating with researchers at Cornell University and Raytheon BBN Technologies, that
221 is implemented using superconducting circuits (Onodera et al., 2020), adding to a growing set of devices
222 with all-to-all connectivity being developed on other technologies (such as trapped ions or cold Rydberg
223 atoms, such as QuEra processor). Nevertheless, we expect that the size of complete connectivity in any
224 hardware in the foreseeable future to be limited. It is therefore necessary to develop additional decomposition
225 techniques for efficiently partitioning (and then recombining) large scale optimization problems, an area of
226 active algorithmic research at QTG.

CONFLICT OF INTEREST STATEMENT

227 The authors declare that the research was conducted in the absence of any commercial or financial
228 relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

229 S. Tayur: Conceptualization, Supervision, Writing - review and editing. A. Tenneti: Writing- initial draft.

³ A parallel article in this issue explores GAMA for Binary Classification of X-ray images via Support Vector Machine (SVM) to detect pneumonia (Guddanti et al., 2023).

FUNDING

230 S. Tayur and A. Tenneti are supported by a DARPA Grant (through Raytheon BBN Technologies) on an
231 AFRL Contract entitled GLIMPSE.

ACKNOWLEDGMENTS

232 Dr. Hedayat Alghassi (IBM) and Dr. Raouf Dridi (QCI) were part of QTG and co-developed content
233 described in sections 2-4. Dr. David Bernal (Purdue) and researchers at NASA QuAIL collaborated on
234 research in Section 4.2. Faculty (Dr. A. Prabhakar and Dr. N. Chandrathoodan) and students (P. Shah, U.
235 Gautham, V. Natarajan, and V. Ramesh) at IIT-Madras collaborated on the photonic devices discussed in
236 Section 5.

REFERENCES

- 237 Alghassi, H., Dridi, R., Robertson, A. G., and Tayur, S. (2019). Quantum and Quantum-inspired methods
238 for de novo discovery of altered cancer pathways. *bioRxiv* doi:10.1101/845719
- 239 Alghassi, H., Dridi, R., and Tayur, S. (2019a). GAMA: A Novel Algorithm for Non-Convex Integer
240 Programs. *arXiv e-prints*, arXiv:1907.10930doi:10.48550/arXiv.1907.10930
- 241 Alghassi, H., Dridi, R., and Tayur, S. (2019b). Graver Bases via Quantum Annealing with Application to
242 Non-Linear Integer Programs. *arXiv e-prints*, arXiv:1902.04215doi:10.48550/arXiv.1902.04215
- 243 Bernal, D. E., Booth, K. E., Dridi, R., Alghassi, H., Tayur, S., and Venturelli, D. (2020). Integer
244 programming techniques for minor-embedding in quantum annealers. In *Integration of Constraint*
245 *Programming, Artificial Intelligence, and Operations Research: 17th International Conference, CPAIOR*
246 *2020, Vienna, Austria, September 21–24, 2020, Proceedings 17* (Springer), 112–129
- 247 Böhm, F., Vaerenbergh, T. V., Verschaffelt, G., and Van der Sande, G. (2021). Order-of-magnitude
248 differences in computational performance of analog Ising machines induced by the choice of nonlinearity.
249 *Communications Physics* 4, 149
- 250 Böhm, F., Verschaffelt, G., and Van der Sande, G. (2019). A poor man's coherent Ising machine based on
251 opto-electronic feedback systems for solving optimization problems. *Nature communications* 10, 3538
- 252 Boothby, T., King, A. D., and Roy, A. (2016). Fast clique minor generation in Chimera qubit connectivity
253 graphs. *Quantum Information Processing* 15, 495–508
- 254 Cai, J., Mcready, W. G., and Roy, A. (2014). A practical heuristic for finding graph minors. *arXiv preprint*
255 *arXiv:1406.2741*
- 256 Choi, V. (2011). Minor-embedding in adiabatic quantum computation: II. Minor-universal graph design.
257 *Quantum Information Processing* 10, 343–353
- 258 Chou, J. B., Bramhavar, S., Ghosh, S., and Herzog, W. (2019). Analog coupled oscillator based weighted
259 Ising machine. *Scientific Reports* 9
- 260 Ciriello, G., Cerami, E., Sander, C., and Schultz, N. (2012). Mutual exclusivity analysis identifies
261 oncogenic network modules. *Genome Research* 22, 398–406. doi:10.1101/gr.125567.111
- 262 Cox, D. A., Little, J., and O'Shea, D. (2007). *Ideals, Varieties, and Algorithms: An Introduction to*
263 *Computational Algebraic Geometry and Commutative Algebra* (Berlin, Heidelberg: Springer-Verlag)
- 264 De Loera, J., Hemmecke, R., Onn, S., Rothblum, U., and Weismantel, R. (2009). Convex integer
265 maximization via Graver bases. *Journal of Pure and Applied Algebra* 213, 1569–1577. doi:https:
266 //doi.org/10.1016/j.jpaa.2008.11.033. Theoretical Effectivity and Practical Effectivity of Gröbner Bases

- 267 Dridi, R., Alghassi, H., and Tayur, S. (2018a). A Novel Algebraic Geometry Compiling Framework for
268 Adiabatic Quantum Computations. *arXiv e-prints*, arXiv:1810.01440doi:10.48550/arXiv.1810.01440
- 269 Dridi, R., Alghassi, H., and Tayur, S. (2018b). Homological Description of the Quantum Adiabatic
270 Evolution With a View Toward Quantum Computations. *arXiv e-prints*, arXiv:1811.00675doi:10.48550/
271 arXiv.1811.00675
- 272 Dridi, R., Alghassi, H., and Tayur, S. (2019a). Enhancing the efficiency of adiabatic quantum computations.
273 *arXiv e-prints*, arXiv:1903.01486doi:10.48550/arXiv.1903.01486
- 274 Dridi, R., Alghassi, H., and Tayur, S. (2019b). Minimizing polynomial functions on quantum computers.
275 *arXiv e-prints*, arXiv:1903.08270doi:10.48550/arXiv.1903.08270
- 276 Glover, F. W., Kochenberger, G. A., and Du, Y. (2018). Quantum Bridge Analytics I: a tutorial on
277 formulating and using QUBO models. *4OR* 17, 335 – 371
- 278 Graver, J. E. (1975). On the foundations of linear and integer linear programming I. *Mathematical*
279 *Programming* 9, 207–226
- 280 Guddanti, S. S., Padhye, A., Prabhakar, A., and Tayur, S. (2023). Pneumonia Detection by Binary
281 Classification: Classical, Quantum and Hybrid Approaches for Support Vector Machine (SVM).
282 *Submitted (Frontiers)*
- 283 Gurobi Optimization, LLC (2023). Gurobi Optimizer Reference Manual.
- 284 Haber, D. A. and Settleman, J. (2007). Cancer: drivers and passengers. *Nature* 446, 145–146. doi:10.1038/
285 446145a
- 286 Harris, R., Sato, Y., Berkley, A. J., Reis, M., Altomare, F., Amin, M. H., et al. (2018). Phase transitions in
287 a programmable quantum spin glass simulator. *Science* 361, 162–165. doi:10.1126/science.aat2025
- 288 Hauke, P., Katzgraber, H. G., Lechner, W., Nishimori, H., and Oliver, W. D. (2020). Perspectives
289 of quantum annealing: methods and implementations. *Reports on Progress in Physics* 83, 054401.
290 doi:10.1088/1361-6633/ab85b8
- 291 Hemmecke, R., Onn, S., and Weismantel, R. (2011). A polynomial oracle-time algorithm for convex
292 integer minimization. *Mathematical Programming* 126, 97–117
- 293 Karp, R. M. (1972). *Reducibility among Combinatorial Problems* (Boston, MA: Springer US). 85–103.
294 doi:10.1007/978-1-4684-2001-2_9
- 295 King, A. D., Carrasquilla, J., Raymond, J., Ozfidan, I., Andriyash, E., Berkley, A., et al. (2018). Observation
296 of topological phenomena in a programmable lattice of 1,800 qubits. *Nature* 560, 456–460
- 297 Lee, J., Onn, S., Romanchuk, L., and Weismantel, R. (2010). The quadratic Graver cone, quadratic integer
298 minimization, and extensions. *Mathematical Programming* 136, 301–323
- 299 Leiserson, M. D. M., Blokh, D., Sharan, R., and Raphael, B. J. (2013). Simultaneous Identification of
300 Multiple Driver Pathways in Cancer. *PLOS Comput Biol* 9. doi:10.1371/journal.pcbi.1003054
- 301 Lucas, A. (2014). Ising formulations of many NP problems. *Frontiers in Physics* 2. doi:10.3389/fphy.2014.
302 00005
- 303 McGeoch, C. C. (2014). *Adiabatic Quantum Computation and Quantum Annealing* (Kenfield, CA:
304 MorganClaypool)
- 305 McMahan, P. L., Marandi, A., Haribara, Y., Hamerly, R., Langrock, C., Tamate, S., et al. (2016). A
306 fully programmable 100-spin coherent Ising machine with all-to-all connections. *Science* 354, 614–617.
307 doi:10.1126/science.aah5178
- 308 Mohseni, N., McMahan, P. L., and Byrnes, T. (2022). Ising machines as hardware solvers of combinatorial
309 optimization problems. *Nature Reviews Physics* 4, 363–379
- 310 Murota, K., Saito, H., and Weismantel, R. (2004). Optimality Criterion for a Class of Nonlinear Integer
311 Programs. *Oper. Res. Lett.* 32, 468–472. doi:10.1016/j.orl.2003.11.007

- 312 Network, C. G. A. R. (2013). Genomic and epigenomic landscapes of adult de novo acute myeloid
313 leukemia. *New England Journal of Medicine* 368, 2059–2074
- 314 Onodera, T., Ng, E., and McMahon, P. L. (2020). A quantum annealer with fully programmable all-to-all
315 coupling via Floquet engineering. *npj Quantum Information* 6, 48. doi:10.1038/s41534-020-0279-z
- 316 Pierangeli, D., Marcucci, G., Brunner, D., and Conti, C. (2020). Noise-enhanced spatial-photonic Ising
317 machine. *Nanophotonics* 9, 4109–4116
- 318 Pierangeli, D., Marcucci, G., and Conti, C. (2019). Large-scale photonic Ising machine by spatial light
319 modulation. *Physical review letters* 122, 213902
- 320 Pottier, L. (1996). The Euclidean Algorithm in Dimension n . In *Proceedings of the 1996 International*
321 *Symposium on Symbolic and Algebraic Computation* (New York, NY, USA: Association for Computing
322 Machinery), ISSAC '96, 40–42. doi:10.1145/236869.236894
- 323 Prabhakar, A., Shah, P., Gautham, U., Natarajan, V., V. R., N, C., et al. (2023). Optimization with photonic
324 wave-based annealers. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and*
325 *Engineering Sciences* 381, 2241. doi:10.1098/rsta.2021.0409
- 326 Rendl, F., Rinaldi, G., and Wiegele, A. (2010). Solving Max-cut to optimality by intersecting semidefinite
327 and polyhedral relaxations. *Mathematical Programming* 121, 307–335
- 328 Smelyanskiy, V. N., Rieffel, E. G., Knysh, S. I., Williams, C. P., Johnson, M. W., Thom, M. C., et al. (2012).
329 A Near-Term Quantum Computing Approach for Hard Computational Problems in Space Exploration.
330 *arXiv e-prints*, arXiv:1204.2821doi:10.48550/arXiv.1204.2821
- 331 Sturmfels, B. and Thomas, R. R. (1997). Variation of cost functions in integer programming. *Mathematical*
332 *Programming* 77, 357–387
- 333 Tanahashi, K., Takayanagi, S., Motohashi, T., and Tanaka, S. (2019). Application of Ising Machines and
334 a Software Development for Ising Machines. *Journal of the Physical Society of Japan* 88, 061010.
335 doi:10.7566/JPSJ.88.061010
- 336 Tayur, S. R., Thomas, R. R., and Natraj, N. R. (1995). An algebraic geometry algorithm for scheduling in
337 presence of setups and correlated demands. *Math. Program.* 69, 369–401. doi:10.1007/BF01585566
- 338 Vandin, F., Clay, P., Upfal, E., and Raphael, B. J. (2012a). Discovery of mutated subnetworks associated
339 with clinical data in cancer. *Pacific Symposium on Biocomputing. Pacific Symposium on Biocomputing*,
340 55–66
- 341 Vandin, F., Upfal, E., and Raphael, B. J. (2012b). De novo discovery of mutated driver pathways in cancer.
342 *Genome Research* 22, 375–385. doi:10.1101/gr.120477.111
- 343 Vogelstein, B. and Kinzler, K. W. (2004). Cancer genes and the pathways they control. *Nature Medicine*
344 10, 789–799. doi:10.1038/nm1087
- 345 Wang, T. and Roychowdhury, J. (2019). Oim: Oscillator-based Ising machines for solving combinatorial
346 optimisation problems. In *Unconventional Computation and Natural Computation: 18th International*
347 *Conference, UCNC 2019, Tokyo, Japan, June 3–7, 2019, Proceedings* (Berlin, Heidelberg: Springer-
348 Verlag), 232–256. doi:10.1007/978-3-030-19311-9_19
- 349 Wang, Z., Marandi, A., Wen, K., Byer, R. L., and Yamamoto, Y. (2013). Coherent Ising machine based on
350 degenerate optical parametric oscillators. *Phys. Rev. A* 88, 063853. doi:10.1103/PhysRevA.88.063853
- 351 Weinberg, R. A. and Weinberg, R. A. (2013). *The Biology of Cancer* (New York: Garland Science), 2
352 edition edn.
- 353 Zhao, J., Zhang, S., Wu, L.-Y., and Zhang, X.-S. (2012). Efficient methods for identifying mutated driver
354 pathways in cancer. *Bioinformatics (Oxford, England)* 28, 2940–2947. doi:10.1093/bioinformatics/
355 bts564
- 356 3106 words