Technical University Munich

Quantum Entrepreneurship Lab

QUEST

QUantum-Enabled SustainabiliTy

Franz von Silva-Tarouca
Cristian Emiliano Godinez Ramirez
Benjamin Classen
Yiyun Tong

Contents

1 Project Context

Quantum Entrepeunirship Lab (QEL) is a master-level course taught at the Technical University of Munich from a joint collaboration between PushQuantum Munich and the Tum Venture Lab Quantum. The main goal of the course is to explore possible commercial applications of quantum computing, by pairing a challenge partner together with a diverse group made up of business, software and quantum specialists.

In our case, our challenge partner was the healthcare/pharmaceutical company Merck. Together, we developed a realistic and comprehensive business model that leverages the power of quantum computing to solve an optimisation problem. In particular, we used a heuristic variation of the Quantum Approximate Optimisation Algorithm (QAOA) to solve the knapsack problem implemented to help companies find the optimal way to ramp up production with profitability and sustainability goals of the company in mind.

2 Business model

2.1 Problem and Product Scope

Looking at a pharmaceutical product, or a drug formulation, it goes through 3 stages in its product life cycle.There's 10-15 years of research and development in search for a new compound and running trials to find an effective medicine. Following approval for distribution, the drug is produced in high volume to make up for the cost of successful and unsuccessful R&D. After the patent expires, the drug is produced as a generic. The process between finalising drug formulation and production ramp-up is where Quest comes in to inform relevant stakeholders such as process chemists, production engineers and account managers to plan for the optimal way to ramp up production with profitability and sustainability goals of the company in mind.

We have found that the full potential of sustainability optimisation lies at the product level. The specific problems Quest addresses have been gathered through expert interviews with pharmaceutical researchers, industry experts and relevant partner company contacts.These are

- Lack of data dimension outside emissions for sustainability goals.
- Lack of reporting throughout the value chain in the industry.
- Lack of transparency in supply chain for prices and sustainability metrics.
- Long lead-time for supplier onboarding and production planning.
- Difficulty to determine optimal production quantity by weighing both profits and sustainability impact

2.2 Value proposition and key benefits

Quest is a platform that consolidates and analyses end-to-end production metrics in the pharmaceutical industry from suppliers and producers to drive sustainability, cost-effectiveness, and transparency in the product value chain through optimisation. The overview of its business model can be seen below.

The value proposition lies in the optimisation potential through which a fundamental shift in our pharmaceutical supply chain is enabled. This provides opportunities for pharmaceutical companies to not only optimise operations internally, but also provide customers with sustainability metrics that

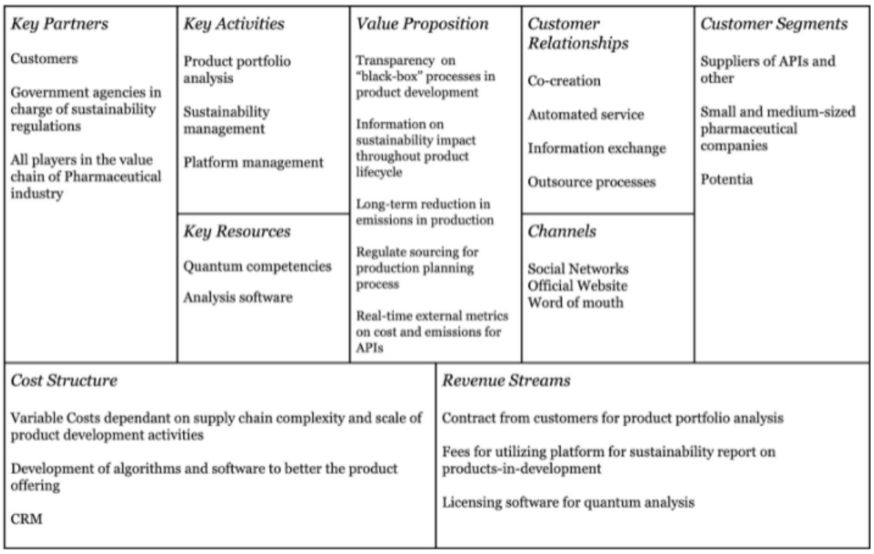


Figure 1: Quest Business Model Canvas

weren't available before. By introducing transparency in what can be described as analog sourcing process, this allows for cost savings and planning for optimised sustainability impact. For producers of pharmaceutical products, product development gains a clear overview of the choices they have for choosing alternative ingredients for their products with a clear timeline in relation to volume. Product life cycle analysis for their current product portfolio and products about to launch improves to include sustainability analysis on a product level.

2.3 Target customer groups (esp. payer vs. user)

The platform serves both sides of the pharmaceutical supply chain: suppliers and producers. We see both sides as the consumer and the customer as both benefit from the QUEST platform.

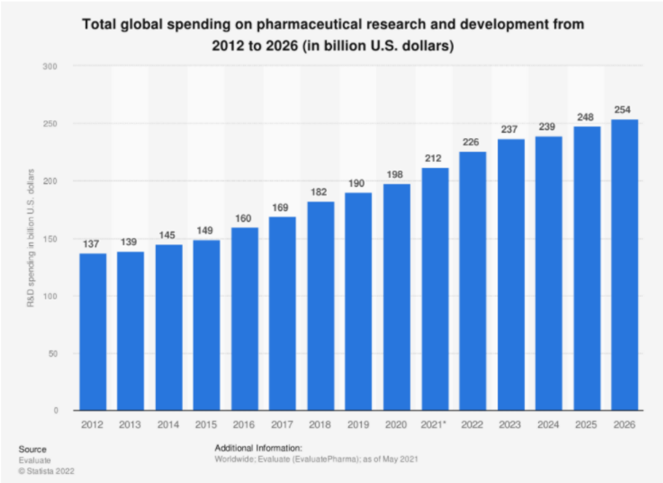
Suppliers want to compete and win contracts with large pharmaceutical companies (e.g. Merck, Pfizer) to provide APIs or biologics for them. There are clear benefits to an early commitment for business for planning purposes to potentially optimise resources and guarantee cash flow. In addition, the focus on and shift towards sustainability through relevant governmental regulations, such as increasing carbon tax drives the transformation of the suppliers in the supply chain. The suppliers need to be able to provide cost-effective and environmentally-friendly products in order to stay competitive in the marketplace and maintain the relationship with producers.

The users of the suppliers would be sales, production engineers and logistics personnel. In addition, employees responsible for green initiatives and sustainability should be involved in the usage of the platform. These roles determine how products are produced, sold, and delivered which is why the market analysis and demand prediction offered at a competitive price is crucial to the success of their goals.

On the producers' side, the sustainability team needs aggregated data product level sustainability in order to better optimise operations to continuously develop and report their sustainability efforts. Changes in the regulations on sustainability-related reporting push pharmaceutical companies to track and plan their production in costs and sustainability metrics especially in regards to the Scope 3 emissions. Sourcing is difficult and oftentimes time-intensive due to the inherent complexity of the supply chain for the pharmaceutical industry. Drug development would benefit from information on production costs and sustainability metrics in the later stages of the product development process.

2.4 Market Size

We believe that there's a market for the product, as confirmed by our industry partner as well as feedback from our interview partners. For the market analysis, we had broken it down into 3 levels as below.



1. **Serviceable Obtainable Market** (SOM):
   Serviceable Obtainable Market is most useful for businesses to determine short-term growth targets. We believe that by saving cost in procurement and production setup and proposing sustainable production strategies, we can help the pharma sell better, cheaper products. By having Merck as a potential first customer, we aim to integrate the data from both the supplier side and producer side, seeing that Merck acting as both simultaneously in the industry, and help improve the production ramp-up of excipients for products. The financial impact from both a cost-saving perspective and reduction in carbon taxes can realistically be around 100 million euros in the first 10 years.

2.5 Financials

2.5.1 Revenue streams

As described in the business model canvas, the revenue streams include companies paying to utilize the platform to create individual report and view performance dashboards that influences the decision-making in respect to his/her role, access to the dataset that is obtained and processed by QUEST and optimization jobs after integrating with existing product lifecycle analysis and process chemistry processes.

2.5.2 Pricing strategy

We have chosen to pursue different pricing strategies for both sides of the platform. For producers, a subscription model with individual pricing based on factors depending on volume, complexity of supply chain, detail of analysis, calculation speed. This allows for maximum flexibility as the producers could differ in size of their operations and technical capabilities. As an example, Merck sources in multiple locations with differing regulations on transportation to produce in multiple locations which introduces exponential complexity.

For suppliers, we want to connect with them on a freemium model so we can onboard them to the platform in a hassle free way. This means that we would provide tools that help with carbon-tax compliance-related reporting.

2.5.3 Consideration of profitability

With the advancements in quantum technology, quantum computers will get less and less expensive for the optimisation jobs of pharmaceutical production planning. The more players join the platform, the synergy of data allows for more accurate optimisation without spending costly time and resources to obtain and process previously unavailable data.

2.6 Go-to-market strategy

We have a look-alike prototype and a working functional prototype, we plan to combine the two in the foreseeable future and continuously pitch our idea to bring us closer to minimum viable product. From that point on, we will continuously iterate and test the product to improve the product offering, provide the best possible solutions to the user requirements and validate the business case. This should take form in a pilot project with a company like Merck where the focus is put on source materials such as excipients in generics or packaging materials, while benefiting from a high volume which leads to a high potential in optimisation. The validated business model then would then move on to determing the pricing and onboard early adopters of the platform. Given the B2B nature of the business model, it will follow a sales-intesive strategy. The ultimate goal is to be the go-to marketplace of raw materials in the pharmaceutical industry and is the golden standard in production planning and optimisation.

2.7 Competitor analysis

There are no competitors in the field that fulfills a role of a facilitator, a marketplace and an analyst for pharmaceutical companies in the domain of optimizing production rampup of pre-launch products while taking extensive sustainabilitity goals into account. Quest fills a gap in the market by providing the platform and analysis for both sides of the pharmaceutical industry. There are companies such as Tanso, whom we interviewed, that assists with reporting across industries on sustainability targets. There are also Merck internal tools that calculate costs and product lifecycle. But none of them could provide the same benefits to both sides as QUEST could, nor positions themselves in the market as an interface between suppliers and producers

3 User Journey

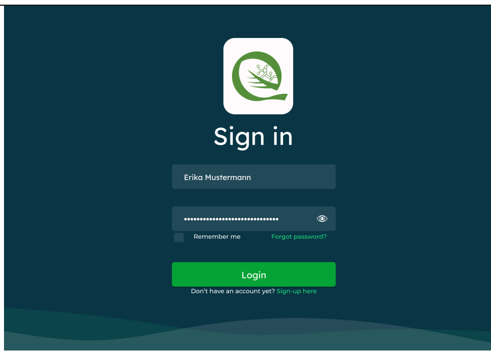
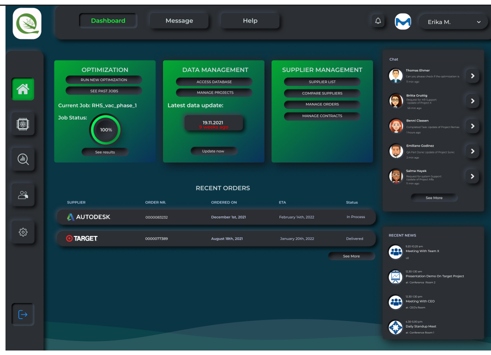
Quest principal end users consist of relevant stakeholders, such as process chemists, production engineers, and account managers, that want to ramp up the production of their company. Particularly, Quest aids these users to achieve their sustainability goals while maximising their profitability according to the specific needs of each company. In this section we describe an instance of a user journey including the doing, feeling and thinking of each stage.'

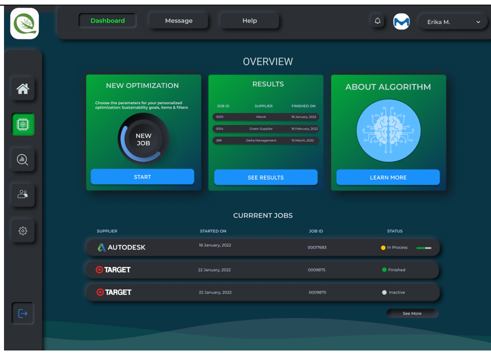
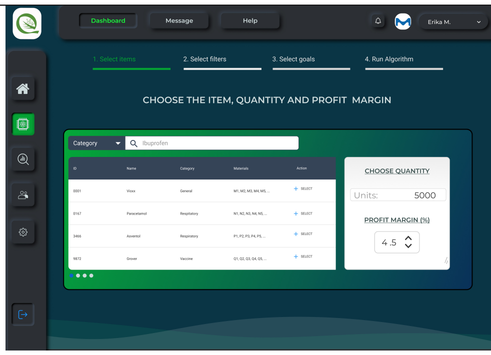
Let's imagine a user in Ms. Mustermann, a process chemist at an international pharmaceutical company. Her management board has decided to drive the company to comply with the upcoming regulations and achieve the 2030 agenda. To attain this, Erika wants to optimise the path of production of one of the products in their portfolio to improve their sustainability metrics while staying within a previously established profit variance.

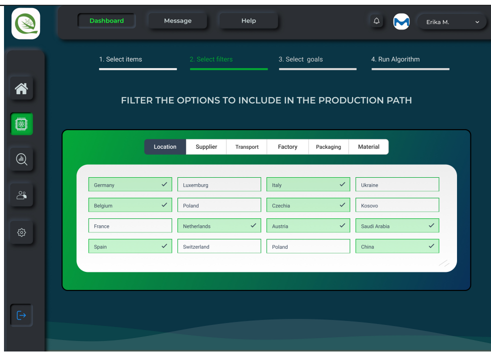
Erika Mustermann wants to:

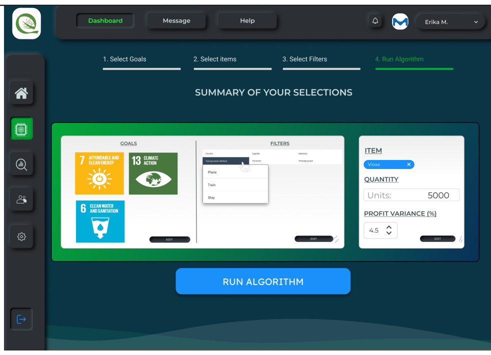
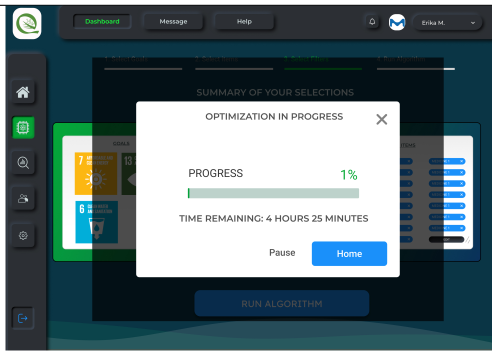
- Comply with the sustainability goals of her company by increasing the sustainability metrics of her portfolio

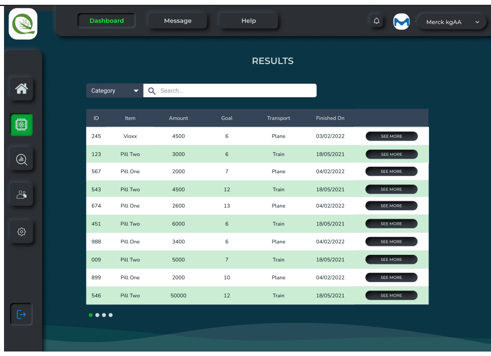
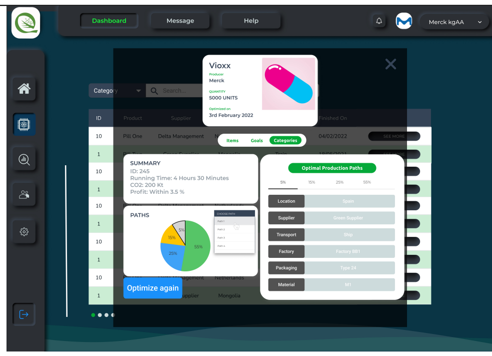
- Do so while staying within a reasonable, and previously established, profit variance

Stage	Access the Quest platform
UI	 
Doing	Log in to Quest Platform Head to the Optimization
Thinking	What product and parameters can be chosen to obtain the best outcome
Feeling	Enthusiastic about the possibilities the platform offers

Stage	Optimization: start new work and select items
UI	 
Doing	Start a new optimization work Include 5000 units of Vioxx Choose a 4.5% profit variance
Thinking	What other items she could have included in the optimization Whether the profit margin can vary slightly
Feeling	Pleased by how easy it is to choose the items from her database

Stage	Optimization: select production path filters and sustainability goals
UI	 
Doing	Choose the different options available to include in each of the 6 steps of the production path Choose sustainability goals 6, 7, 13, 14, and 15
Thinking	Could the company obtain information to implement other goal
Feeling	Excited to increase the sustainability metrics in the different areas available

Stage	Optimization: review options and submit job
UI	 
Doing	Review selections and edit them if necessary Start optimization
Thinking	Can a different set of parameters change significantly the results
Feeling	Eager to find out the outcome of the optimization

Stage	Check results and analyze optimization
UI	 
Doing	Access details of results section Select the last order corresponding to Vioxx and analyze the results of the optimization Evaluate the 4 different paths and the corresponding combination of options for each of the production path steps.
Thinking	Need to decide the feasibility for the outcome distribution of the total volume of Vioxx, corresponding to the 4 paths Does the increase in sustainability achieved justifies the profit margin Are all the outcome routes feasible Need to show these results to the other members of the team for a thorough review of applicability
Feeling	Glad such a comprehensive tool is available to make her and the company's goals achievable Reflective about the outcome, particularly on the components that are directly applicable Which of these components need a further optimization or second review

4 Putting the "Q" in the QUEST for sustainability

Let us now take an in-depth look at what our optimisation aims to achieve and how we approach creating a quantum algorithm for this task.

Figure 2 depicts a simplified model of the production steps for a pharmaceutical product. We will refer to the sum of all production steps as the "life" of the pill. At each of the points in the figure a decision to be made: Which supplier do we choose? Which mode of Transportation? And so on.

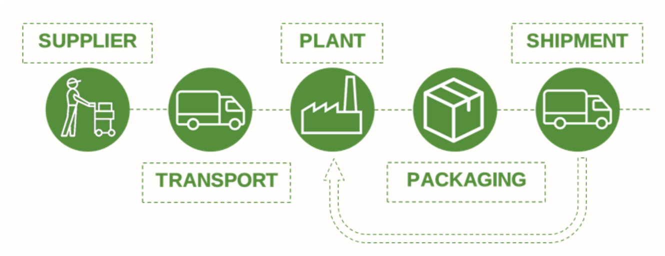


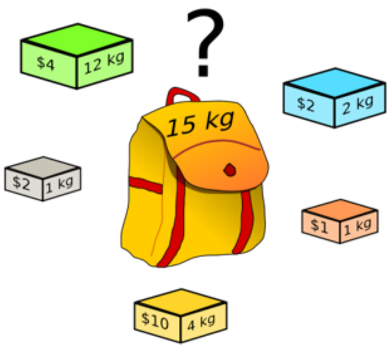
Figure 2: The life of a pill

The goal of our optimisation will be to make these decision such that the pharmaceutical product is produced in the most sustainable way, while staying within a certain profit range defined by our customer. To formulate an algorithm for this task, we express this optimisation as a well known combinatorial problem: The Knapsack problem.

4.1 Optimising the life of a pill using Knapsack

As illustrated in figure 3, the Knapsack generally deals with the following optimisation task:

Given a set of items, each with a value and a weight: Pick a subset such that the value is maximum and the maximum weight the knapsack can hold is not exceeded.



To apply the Knapsack formalism to our problem, we need to find a way to map real life quantities to the items, values and weights of the general Knapsack formulation.

Recall that there are several points in the life of a pill, where a decision needs to be made. In our case, each decision option resembles an item to put in our Knapsack. Putting it into our Knapsack, means choosing a certain option. Moreover, each option will perform differently in terms of how sustainable and profitable it is. Therefore, we choose as the value, which we will optimise a parameter which captures how this option performs in terms of fulfilling the sustainability goals the customer selects. We call this the sustainability score, S. As our weight, we assign the decision options a profit loss score, P. Exceeding the maximum weight, would mean exceeding the maximum profit loss that our customer

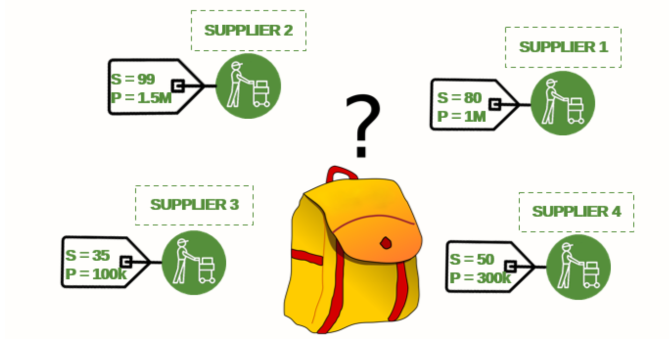


Figure 3: Illustration of the Knapsack problem applied to optimising which suppliers to choose from.

defines.This ensures that the company is optimally sustainable within their defined profit margins. Figure **??** illustrates this process.

Of course, in a real life scenario, there are many more options to choose from. For example our first customer Merck has around 60000 suppliers alone. To handle these large problem sizes efficiently Quest leverages the power of quantum computing. Concretely, we use an extension of the Quantum Approximation Optimization Algorithm (QAOA) as the basis of our Knapsack algorithm.

4.2 Extending QAOA to fit the Knapsack problem

While an optimisation function can be mapped organically to the QAOA algorithm, this is different with the Kapsack inherent constraint. In practice a common procedure is to introduce penalisation through additional qubits and thus prevent solutions with unacceptable total weight. Here an alternative approach is taken. This approach is taken from paper[1]. In this approach, each item of the knapsack is resembled by one qubit without adding qubits to deal with the maximum-weight constraint. This constraint is instead taken account of by post-processing the results which are obtained after measuring the quantum cirquit. There, invalid solutions are dismissed. Then however, measures have to be taken to prevent this from leading to many invalid solutions being output inefficient guessing. Since QAOA can be regarded as a random-walk algorithm, the core idea is to nudge the search to subspaces where the probability of finding valid solutions is higher. How this is achieved is explained in the following.

Tailoring the search space of qubit configurations

The aim of the modified QAOA variant is to restrict the search space in such a way that solutions that do not violate the total weight restriction are detected with increased probability. The following basic idea is implemented for this: the possible items are not contained in the Knapsack with uniform probability. Items that have a better profit-to-weight ratio than others are more profitable and therefore more likely to be included. To encode this in the QAOA setup, a non-homogeneous input state is used in contrast to the original QAOA. This state is of the form

$$|p\rangle = |p_1\rangle \otimes |p_2\rangle \otimes ... \otimes |p_n\rangle \tag{1}$$

where each of the states $|p_i\rangle$ is of the form

$$|p_i\rangle = \sqrt{1-p_i}\,|0\rangle + \sqrt{p_i}\,|1\rangle \tag{2}$$

The values p_i are obtained from classical heuristics. The lazy greedy algorithm is primarily used for this. Here, the items are sorted in descending order according to the profitability index r_i with $r_i = p_i/w_i$, the ratio of profit to weight. Starting with the most profitable item, the Knapsack is filled until the weight capacity is exhausted. Items that are contained in the Knapsack are marked with 1, others with 0. Subsequently, the values p_i are generated according to the formula

$$p_i = \frac{1}{1 + Ce^{-k(r_i - r^*)}} \tag{3}$$

where r^* corresponds to the lowest-but-still-taken profitability index. C and k are degrees of freedom which can later be optimised.

Generating the QAOA algorithm

The QAOA algorithm is defined by the sequential execution of time evolutions according to one energy and one mixing Hamiltonian. While the energy-corresponding unitary can be constructed according to the linear profit function,

$$U^C = U^{v_1}(\gamma) \otimes ... \otimes U^{v_n}(\gamma) \tag{4}$$

where $U^{v_i} |x_i\rangle = e^{-i\gamma v_i x_i}$ with v_i corresponding to the $i_t h$ item's profit, the mixing Hamiltonian is derived from the condition that the single-qubit states $|p_i\rangle$ are the mixing Hamiltonian H_{p_i}'s eigenvectors with minimal eigenvalue.

$$H_{p_i} |p_i\rangle = -|p_i\rangle \text{ and } H_{p_i} \left|p_i^\perp\right\rangle = \left|p_i^\perp\right\rangle \tag{5}$$

From that follows the corresponding time-evolution operator as

$$U^M(\beta) = \prod_{i=1}^{n} e^{-i\beta H_{p_i}^{(i)}} \tag{6}$$

Further encoding of classical heuristics

In addition to the profitability index, other useful heuristics can be used. It turns out that the success of the algorithm can be further increased by introducing correlations between qubits. These correlations are achieved by using an mixing hamiltonian which has eigenstates of the form

$$|p_{ij}\rangle = \sum_{x \in \{0,1\}^2} \sqrt{p_{ij}(x_i, x_j)}\, |x_i x_j\rangle \tag{7}$$

and is defined via

$$H_{p_{ij}} |p_{ij}\rangle = -2\, |p_{ij}\rangle\,; \langle p_{ij}|\, H_{p_{ij}}\, |p_{ij}\rangle \geq 0 \tag{8}$$

While coupling arbitrary qubits results in very complex time-evolution operators, promising results are already obtained by coupling neighbouring qubits negatively. The qubits are treated as being placed on a ring, meaning also the first and last qubit are coupled. The corresponding time-evolution operator is given by

$$\tilde{U}^M(\beta) = e^{-i\beta H_{p_{1,n}}} \left(\prod_{i=1}^{n} e^{-i\beta H_{p_{i+1,i+2}}} \right) \left(\prod_{i=1}^{n} e^{-i\beta H_{p_{i,i+1}}} \right) \tag{9}$$

Translating the operators into quantum circuits

Since in our setup only involves operations with one or two qubits, the individual mixing- and energy-hamiltonians can be expressed using single-qubit-rotations and controlled-operations. Because of space reasons, for details we refer to chapter 3 of .

4.2.1 The algorithm

Now everything is ready to assemble the algorithm. The algorithm can be divided into 4 different stages:

1. Deciding on the mixing-hamiltonian, i.e. whether correlations are introduced or not.
2. create the corresponding quantum circuit for general values of the free parameters, e.g. β and γ
3. for all possible values for the free parameters (i.e. discretising and doing grid-searching), run the circuit n times and each time output the optimal solution, where invalid solutions are disregarded
4. output the overall best solution

For a more mathematically concise definition, we refer to

4.2.2 Results

For testing the validity of the algorithm we followed the approach in and tested on different types of knapsack-instances. As described in instances with higher correlation between the profits and weights of the items tend do be harder to solve classically It was on those instances that our algorithm performed particularly well.

The results were obtained by creating almost 200 instances similar to the ones describe in For more details, we refer to the GitHub-Repository handed in alongside this report.

4.2.3 Comparison with classical solutions

As we can see in 4, the quantum algorithm outperforms its classical greedy counterparts in a substantial amount of instances. Note that for real-life applications dynamic programming takes too long and is therefore not taken into consideration. This is particularly interesting as the instances in which the quantum algorithm outperforms the classical ones are the ones where greedy algorithms tend to struggle finding optimal solutions This implies a real benefit for using the quantum algorithm and developing it further. Another major advantage of using the quantum approach can be found in the algorithm's runtime. In its current implementation it is linear in the number of qubits n, i.e. linear in the number of items, with constant circuit-depth. This is a significant speed-up to the classical greedy algorithms which run in time $O(nlog(n))$.

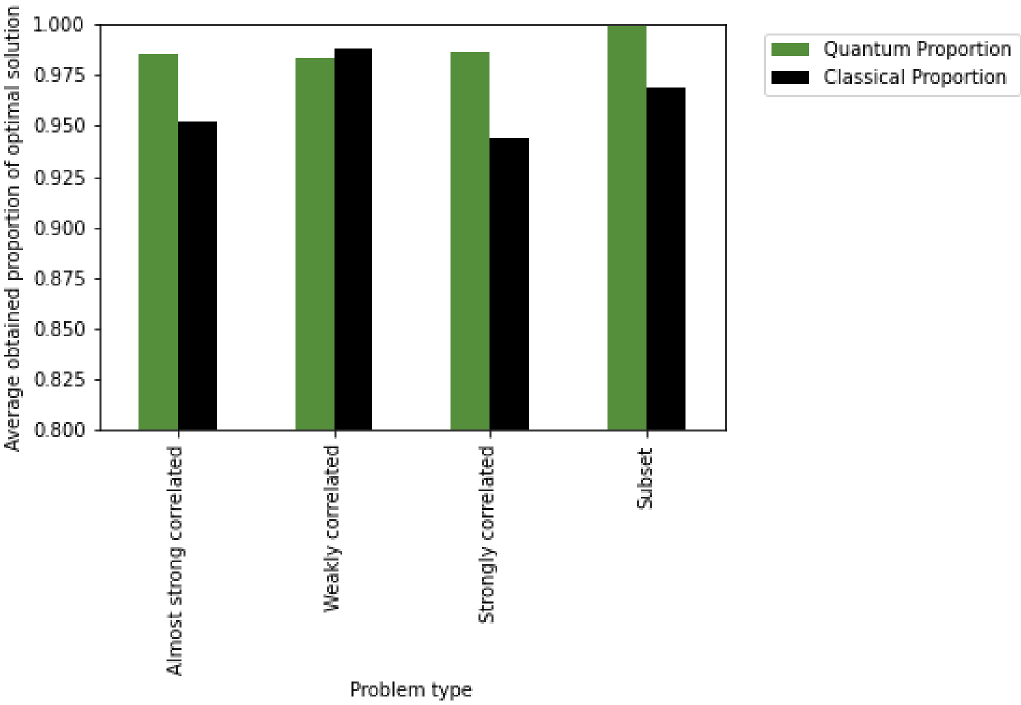


Figure 4: The results when running the algorithm for different Knapsack instance type. On the y-axis the proportion of the obtained total value to the optimal value is displayed.

4.2.4 Complexity

The runtime of the algorithm is highly flexible as the circuit-length in itself is constant. Following the proceeding in all testing was done using a circuit of length $p = 1$ and using n shots, where n is the number of items in the knapsack, resulting in a linear-in-n-runtime. It is up for future research to find out how much the algorithm can be improved by using larger quantum circuits, however we have seen that already with $p = 1$ the algorithm is quite successful. Since the algorithm's runtime in its current implementation would grow exponentially with p, certain adaptations would have to be made. It will most likely be a trade-off between accuracy and runtime when choosing the right circuit length.

5 References:

[1] Evaluate. Total global spending on pharmaceutical research and development from 2012 to 2026 (in billion U.S. dollars) In Statista. Retrieved March 02, 2022, from , July 30, 2021: https://www-statista-com.eaccess.ub.tum.de/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/

[2] IQVIA. Revenue of the worldwide pharmaceutical market from 2001 to 2020 (in billion U.S. dollars). In Statista. Retrieved March 02, 2022, from https://www-statista-com.eaccess.ub.tum.de/statistics/263102/pharmaceutical-market-worldwide-revenue-since-2001, April 28, 2021

[3] Wikipedia, 2021 [Graph] Retrieved March 02, 2022 from https://en.wikipedia.org/wiki/Knapsack$_{p}roblem$

[4] David Pisinger, Where are the hard Knapsack problems?, Computers and Operations Research 2005: https://doi.org/10.1016/j.cor.2004.03.002

[5] Wim van Dam, Karim Eldefrawy, Nicholas Genise, Natalie Parham,Quantum Optimization Heuristics with an Application to Knapsack Problems, Arxiv 2021: https://arxiv.org/abs/2108.08805