A NEW MILP VARIABLE RESOURCE CONSTRAINED SCHEDULING MODEL FOR THE TESTING OF PHARMACEUTICALS AND AGROCHEMICALS

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Abstract

In highly regulated industries, such as agrochemical and pharmaceutical, new products have to pass a number of regulatory tests to gain FDA approval. If a product fails one of these tests it cannot enter the market place and the investment in previous tests is wasted. Depending on the nature of the products, testing may last up to 15 years, and the scheduling of tests should be made with the goal of minimizing the time to market and the cost of the testing. The various optimization models that have been proposed consider a set of candidate products for which the cost, duration and resource requirements of the tests are given. An important assumption in these approaches is that each test has pre-specified resource requirements. In reality, however, there is often a choice on the type and amount of resources that can be allocated to a test, which in turn determines the cost and duration of that test. Furthermore, new resources may be installed or purchased, if needed, during the course of the testing. In this work we propose a new scheduling MILP model that addresses three issues. More specifically, the model (i) handles resource allocation as a decision variable with the possibility of outsourcing, (ii) handles cost and duration of tests as functions of the type and amount of resources assigned to each test, (iii) allows for installation of new resources during the course of testing.

Keywords

New Product Development, Scheduling, Mixed-Integer Programming

Introduction

The problem of scheduling testing tasks in new product development has been studied by several authors. Schmidt and Grossmann (1996) proposed various MILP optimization models for the case in which no resource constraints are considered. The basic idea in this model is to use a discretization scheme in order to induce linearity in the cost of testing. Jain and Grossmann (1999) extended these models to account for resource constraints. Honkomp et al. (1997) addressed the problem of scheduling R&D projects, which is very similar to the one of scheduling testing tasks for new products. Subramanian et al. (2001) proposed a simulation-optimization framework that takes into account uncertainty in duration, cost and resource requirements. Papageorgiou et al. (2001) developed a model for finding the optimal investments needed for the production of new products, and Maravelias and Grossmann (2001) proposed an MILP model that integrates the scheduling of tests with the design and production planning decisions. An assumption made in all these approaches is that the cost and the duration of each

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test do not depend on the level of resources allocated to each test. In other words, the cost and the duration of a test are independent of the resources. In reality, however, the decision maker often has the option of allocating more resources to some tests in order to reduce the length of the critical path that dominates the duration of the testing process. Moreover, the cost of a test depends on the type and the level of resources assigned to it, and thus, it is also a variable. Another common assumption is that throughout the testing period the available resources are constant. It is common, though, for a company to decide to hire more scientists or build more laboratories if the number of potentially new products entering the company's R&D pipeline is larger than in the past.

In this work we propose a MILP optimization model that extends the model proposed by Jain and Grossmann (1999) and refined by Maravelias and Grossmann (2001), which addresses the above issues. Specifically, the assumption that each test has pre-specified resource requirements is relaxed. Instead, the type and level of resources assigned to a test is a decision variable, and as a result, the cost and the duration of each test are variables. As more resources are allocated to a test, its duration is reduced and its cost increases. The proposed model also allows for "installation" of new resources (building of new labs, hiring of new scientists) during the course of testing. The option of outsourcing is also included, as in Jain and Grossmann (1999). The main trade-off is between the higher cost of testing (caused by the utilization of more resources, the use of outsourcing or the "installation" of additional resources) and the higher income from sales due to shorter completion times.

Problem Statement

Given are a set of potential products that are in various stages of the company's R&D pipeline. Each potential product is required to pass a series of tests. Each test has a probability of success that is assumed to be known a priori. The duration and the cost of each test are known functions of resource allocation. Only limited resources are available to complete the testing tasks. If needed, a test may be outsourced at a higher cost, and in that case none of the internal resources are used. Resources can also be installed at a known cost. Resources are discrete in nature (e.g. labs and technicians), and tests are assumed to be non-preemptive. Due to technological precedences some tests can only be performed after the completion of other tests. There are four main decisions regarding the testing of new products: (a) the sequencing ($y_{kk'} = 1$ if test k must finish before test k') and timing (s_k = start time of test k) of tests, (b) the amount of resources allocated to a test (N_{rk} = number of resource units of category r allocated to test k), (c) the assignment of resource units to tests ($x_{kq} = 1$ if resource unit q is assigned to test k), and (d) the decision to buy a resource unit ($w_q = 1$ if resource q is "installed", b_q = time of installation). The objective is to maximize the Net Present Value (NPV) of multiple projects, i.e. the income from sales minus the cost of testing.

Model

Timing and Sequencing Constraints

Constraint (1) ensures that the testing completion time, T_j, of product j is greater than the completion time of any task k required for product j. Constraints (2) fix sequencing binaries $y_{kk'}$ for pairs (k,k') for which a technological precedence exists. Time sequencing is enforced through constraints (3) and (4), where U is a valid upper bound. Constraint (5) ensures that if the new resource unit $q \in QN$ is assigned to test k, then the starting time of k is larger than the installation time of q:

$$s_k + d_k \le T_j \quad \forall j, \forall k \in K(j) \tag{1}$$

$$y_{kk'} = 1, \quad y_{k'k} = 0 \quad \forall (k,k') \in A \tag{2}$$

$$s_k + d_k \le s_{k'} \quad \forall (k,k') \in A \tag{3}$$

$$s_k + d_k \le s_{k'} + U(1 - y_{kk'}) \quad \forall (k,k') \notin A \tag{4}$$

$$s_k \ge b_q - U(1 - x_{kq}) \quad \forall k, \forall q \in QN \tag{5}$$

Resource Constraints

The number of resources allocated to a test, N_{kr}, is bounded through constraint (6), and calculated through constraint (7). Constraint (8) ensures that there is a precedence between tests k and k' if they are both assigned to resource unit q. Constraint (8) is expressed for existing ($q \in QE$) and potentially new ($q \in QN$) resource units, but not for the dummy resource units ($q \in QD$) that represent the outsourcing option. The duration of test k, d_k, is calculated in equation (9) as a function of resource assignment decisions. The logical condition that a potentially new unit $q \in QN$ cannot be assigned if it is not installed is expressed by constraint (10):

$$N_{kr}^{MIN} \le N_{kr} \le N_{kr}^{MAX} \quad \forall k, \forall r \tag{6}$$

$$\sum_{q \in Q(r)} x_{kq} = N_{kr} \quad \forall k, \forall r \tag{7}$$

$$x_{kq} + x_{k'q} - y_{kk'} - y_{k'k} \le 1 \quad \forall q \in (QE \cup QN), \forall k \in K(q), \forall k' \in K(q) \tag{8}$$

$$d_k = d_k^{MAX} - \sum_q x_{kq} \delta_{kq} \quad \forall k \tag{9}$$

$$x_{kq} \le w_q \quad \forall k, \forall q \in QN \tag{10}$$

Testing Cost Constraints

The cost of testing consists of three elements: (1) a fixed cost for each task, (2) a cost associated with the use of particular resource units, and (3) the cost of resource installation. For all three cost elements a discounting factor r has been used. Thus, a piece-wise linearization scheme with weight factors is used to approximate the exponential discounting function. Grid points a_n are used with weights λ^1_{kn}, λ^2_{kqn} and λ^3_{qn}, respectively. The linearization factors are activated through equations (11), (12) and (13) and calculated through equations (14), (15) and (17). Since the RHS of constraint (16) is always non-zero the slack variable sl_{kq} has been added. This variable is non-zero only when $x_{kq} = 0$ (constraint 16):

$$\sum_n \lambda^1_{kn} = 1 \quad \forall k \tag{11}$$

$$\sum_n \lambda^2_{kqn} = x_{kq} \quad \forall k, \forall q \tag{12}$$

$$\sum_n \lambda^3_{qn} = w_q \quad \forall q \in QN \tag{13}$$

$$\sum_n \lambda^1_{kn} \alpha_n = -r \cdot s_k + \sum_{k' \in KK(k)} \ln(p_k) y_{k'k} \quad \forall k \tag{14}$$

$$\begin{aligned} &\sum_n \lambda^2_{kqn} \alpha_n - sl_{kq} = \\ &-r \cdot s_k + \sum_{k' \in KK(k)} \ln(p_k) y_{k'k} \quad \forall k, \forall q \end{aligned} \tag{15}$$

$$sl_{kq} \le U(1 - x_{kq}) \quad \forall k, \forall q \tag{16}$$

$$\sum_n \lambda^3_{qn} \alpha_n = -r \cdot b_q \quad \forall q \in QN \tag{17}$$

Objective Function Calculations

The three types of testing costs are calculated through constraints (18)-(20) and the income is calculated through constraints (21) and (22). The objective is to maximize NPV, equation (23).

$$CT1 = \sum_j \sum_{k \in K(j)} cf_k \sum_n \lambda^1_{kn} e^{a_n} \tag{18}$$

$$CT2 = \sum_j \sum_{k \in K(j)} \sum_q cq_{kq} \sum_n \lambda^2_{kqn} e^{a_n} \tag{19}$$

$$CT3 = \sum_{q \in QN} cb_q \sum_n \lambda^3_{qn} e^{a_n} \tag{20}$$

$$u_{jm} \ge T_j - b_{jm} \quad \forall j, \forall m \tag{21}$$

$$INC_j = INC_j^{MAX} - \sum_m f_{jm} u_{jm} \quad \forall j \tag{22}$$

$$\min NPV = \sum_j INC_j - CT1 - CT2 - CT3 \tag{23}$$

The prposed model consists of constraints (1) to (23). Details of some of these constraints can be found in Maravelias and Grossmann (2001).

Example

A small example with one new product, ten tests, 1 to 10, and two resource categories, *A* and *B*, is solved. For each resource category we assume that there are two existing units (1 and 2 of type A, 5 and 6 of type B), and that the company can install one additional unit for each category: unit 3 of type A at a cost of $50,000 and unit 7 of type B at a cost of $40,000. We also assume that at most one test can be outsourced at any time for each category. Dummy resource units 4 and 8 are used for representing the outsourcing option; i.e. resource constraint (8) is not expressed for units 4 and 8, and their utilization cost is higher. Income data are given in Table 1, and testing data in Table 2. The durations d_k^{MAX} and δ_{kr} are in months, and the costs cf_k and cq_{kq} are in $\$10^3$.

Table 1. Income data

m	b_{jm}	f_{jm}	
1	0	10	$r = 0.0075$
2	24	10	$INC^{MAX} = \$2,000,000$
3	48	10	

This example is first solved assuming that each test requires a single unit of each resource category ($N_{rk}^{MIN} = N_{rk}^{MAX} = 1,\ \forall r,k$) and without the option of installing new resources (case 1). It is next solved assuming that multiple resource units can be allocated to each test, but without the option of installing new resources, (case 2). Finally it is solved allowing both variable allocation and installation of new resources (case 3). The completion time, the income from sales, the testing costs and the objective value for the three cases are reported in Table 3. The Gantt charts for the resources are depicted in Figure 1.

By comparing the solutions of cases 1 and 2 we see that allowing for more resources to be allocated to a test results in higher test expenditures. However, the shortening of testing time (79 to 71 to 64 months) results in higher income that outweighs the additional testing costs. The comparison of case 3 with the previous cases shows that the installation of new resource units leads to smaller testing completion time (due to shorter durations) and thus in higher income that outweighs the increase in testing costs. The Gantt charts of Figure 1 show how more resources are allocated to a certain test as we move from case 1 to case 3, resulting in shorter individual testing durations, and consequently, to a shorter completion time.

Table 2. Testing data

Test	d_k^{MAX}	δ_{kr}		p_k	cf_k	cq_{kq}								N_{rk}^{MIN}		N_{rk}^{MAX}		Precedences
		A	*B*			*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*A*	*B*	*A*	*B*	
1	16	2	2	1	20	5	5	4	10	6	6	5	10	1	1	1	1	
2	18	3	2	1	25	4	5	3	8	5	5	5	10	1	1	2	1	1
3	20	2	1	0.95	30	6	6	5	12	3	3	2	5	1	1	2	2	2
4	24	2	3	1	50	10	10	8	25	2	2	2	3	1	1	2	2	2, 3
5	30	3	3	1	80	3	3	2	4	5	5	5	15	1	1	1	3	
6	24	2	3	0.9	60	8	8	7	15	10	12	10	20	1	1	1	3	
7	22	3	4	1	100	5	5	5	5	3	3	2	5	1	1	2	2	
8	20	3	2	1	50	8	9	8	12	6	6	5	15	1	1	2	1	3, 6
9	18	2	3	0.85	20	2	2	2	5	4	5	5	12	1	1	3	1	4, 5
10	22	4	2	1	40	4	4	3	6	5	5	4	8	1	1	1	2	7, 8

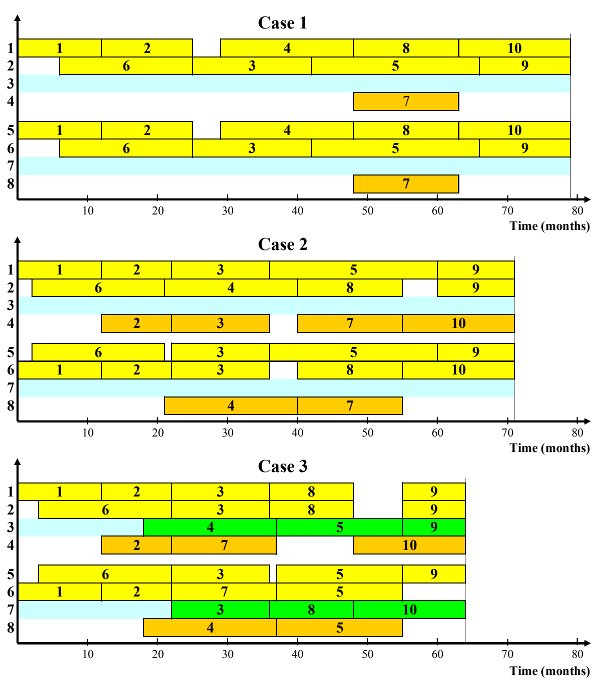

Figure 1. Resource Gantt charts of Example

Table 3. Income, Testing Costs and NPV

	Case 1	Case 2	Case 3
Completion Time	79	71	64
Income ($\$10^3$)	350	590.0	800.0
CT1 ($\$10^3$)	330.6	345.0	364.9
CT2 ($\$10^3$)	78.3	103.5	115.6
CT3 ($\$10^3$)	0	0	77.7
NPV ($\$10^3$)	-58.9	141.5	241.8

Conclusions

A new MILP optimization model for the scheduling of testing tasks in new product development has been proposed in this paper. The proposed model handles the level of resources allocated to tests as a decision variable, allowing for variable test durations and costs. It also allows for installation of new resources during the course of testing. The proposed model represents real-world situations closer than the previously reported models, and allows the construction of more flexible schedules.

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