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Stochastics and Statistics

R&D pipeline management: Task interdependencies and risk management

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ABSTRACT

Maintaining a rich research and development (R&D) pipeline is the key to remaining competitive in many industrial sectors. Due to its nature, R&D activities are subject to multiple sources of uncertainty, the modeling of which is compounded by the ability of the decision maker to alter the underlying process. In this paper, we present a multi-stage stochastic programming framework for R&D pipeline management, which demonstrates how essential considerations can be modeled in an efficient manner including: (i) the selection and scheduling of R&D tasks with general precedence constraints under pass/fail uncertainty, and (ii) resource planning decisions (expansion/contraction and outsourcing) for multiple resource types. Furthermore, we study interdependencies between tasks in terms of probability of success, resource usage and market impact. Finally, we explore risk management approaches, including novel formulations for value at risk and conditional value at risk.

1. Introduction

The goal of this paper is the development of a stochastic programming framework for resource-constrained project scheduling and resource planning in a research and development (R&D) pipeline context. This framework is designed to handle considerations such as task interdependency and risk management. While the focus is on the planning of R&D activities, the modeling techniques and theoretical results presented in this paper are directly applicable to a broader class of challenging but less-studied optimization problems under uncertainty, namely **ST**ochastic **O**ptimization problems under e**X**ogenous **U**ncertianty with **EN**dogenous **O**bservations (STOXUNO) (Bent and Van Hentenryck, 2004; Mercier and Van Hentenryck, 2008).

The development of new products can be a long, expensive and risky process. Of particular interest in the literature is the pharmaceutical industry, where it generally takes more than ten years from discovery of a compound to gaining regulatory approval by the Food and Drug Administration (FDA), while it costs on average more than $900 million to develop a drug (DiMasi et al., 2003). Furthermore, the development of new products is highly risky because not only are projects subject to overrunning budgets, missing deadlines or underperforming in the market, but there is also the chance of a project failing a development activity, resulting in spent resources without any return.

To remain competitive in the current environment, therefore, firms have to *optimize* their R&D activities, from the emergence of promising ideas to the timely performance of feasibility studies, and from the planning of resources for product and process development to the planning of manufacturing capacity. However, this is a challenging task due to the large number of decisions and the complex trade-offs among them, the long planning horizons that must be considered, and, most importantly, the highly stochastic nature of the R&D activities. Accordingly, the goal of this paper is the development of a systematic framework that addresses the aforementioned challenges.

1.1. Research and development overview

Clearly, the planning of R&D activities is similar to a stochastic version of the well-studied resource-constrained project scheduling problem (RCPSP): each product can be viewed as a project consisting of a number of (deterministic or stochastic) tasks with given processing times and resource requirements, subject to precedence and resource constraints. Nevertheless, existing methods are not well suited to address the problem at hand for the following reasons:

- **(a)** The focus in RCPSP has been on the development of methods for instances with many activities (tasks). The number of tasks however in the problem we consider in this paper is typically small. What makes this problem hard is the stochastic nature of the underlying process and the fact that the decision-maker can alter this process.
- **(b)** Most stochastic approaches to RCPSP consider uncertainty in the duration and/or resource requirements of tasks; however, in this problem, there is also major uncertainty in the outcome of a task. If a task fails, then a new, and often very different, schedule must be developed.

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Nomenclature

Indices and sets

$i, i' \in \mathbf{I}$	Projects under development
$j, k \in \mathbf{J}$	Tasks to be performed
$r \in \mathbf{R}$	Resources
$s, s' \in \mathbf{S}$	Scenarios
$t \in \mathbf{T}$	Stages

Subsets

$\mathbf{P}_{ij}$	Immediate prerequisites for task (i,j)
$\mathbf{R}^R/\mathbf{R}^C$	Renewable/consumable resources
$\mathbf{S}_t^m$	Maximal set of scenarios that are indistinguishable in stage t
$\mathscr{S}_t$	Family of maximal scenario subsets that are indistinguishable at stage t
$\mathscr{S}_t^2$	Family of pairs of scenarios that are indistinguishable in stage t
$\mathscr{S}_t^E$	Family of maximal subsets of scenarios that are indistinguishable in t due to *earliness*.

Parameters

c_{ij}	Cost of task (i,j)
$c_{rt}^E/c_{rt}^C/c_{rt}^O$	Discounted cost to expand/contract/outsource resource r at stage t
est_{ij}	Earliest stage task (i,j) can start
$\bar{p}_{ij}^n$	Probability of outcome n for task (i,j)
p_s	Probability of scenario s
α	Maximum percentage of scenarios with *NPV* bellow threshold γ
β	Bound on downside risk
γ	Fixed threshold in calculating risk measures
ξ_T	Random variable–outcome of task T
ρ_{ijr}	Requirement of resource r for task (i,j)
τ_{ij}	Duration of task (i,j)
ω	Weighting factor for (conditional) value at risk in the objective
$\theta_{ii'}$	Correlation of revenues of projects i and i'

Binary variables

X_{ijts}	=1 if task (i,j) starts at stage t in scenario s
$U_{ii't}$	=1 if projects i and i' with interdependent revenue are completed in scenario s
Y_s/Z_s	Indicator variables for risk management approaches

Continuous variables

E_{rts}	Availability of resource r at stage t in scenario s
$E_{is}^C/E_{is}^E/E_{is}^O$	Contraction/expansion/outsourcing for resource r at stage t in scenario s
NPV_s	Net present value of scenario s
$NNPV_s$	Auxiliary variable for calculation of *NPV* below threshold associated with scenario s
VRT/VUT	Variable threshold used in calculating the (conditional) value at risk

(c) RCPSP formulations often assume the resource level is known and fixed at the beginning of the time horizon. With development projects spanning multiple years, the ability to adjust resource levels can be as important as the timing of development tasks.

Accordingly, the focus of the present paper is the development of a formulation that accounts for the stochasticity of the process while considering all aforementioned aspects. Finally, we remark that the uncertainty in the development of new products can be classified into: (i) market uncertainty, which includes prices and demand (market share); and (ii) technical uncertainty, which includes task durations and resource requirements, and task outcomes. This work focuses on the technical uncertainty, primarily in task outcome. All other sources of uncertainty can in theory be addressed using the proposed framework, however prohibitively large formulations can result.

1.2. Literature review

The *static* selection of R&D projects has been the topic of extensive research (Souder and Mandakovic, 1986; Steele, 1988). Heuristic methods for the RCPSP, which is NP hard (Blazewicz et al., 1983), can be generally categorized as genetic algorithms (Hartmann, 1998), local search methods including simulated annealing and tabu search (Mika et al., 2005; Bouleimen and Lecocq, 2003), ant colony optimization (Merkle et al., 2002), and forward–backward improvement (Tormos and Lova, 2001; Valls et al., 2005) as well as numerous task prioritization techniques. An extensive overview of computation results for a large number of specific heuristics and meta-heuristics for standard test sets can be found in Kolisch and Hartmann (2006) and an overview of RCPSP can be found in Brucker et al. (1999). The RCPSP has also been extended to include ideas such as uncertain duration (Herroelen and Leus, 2005), partially renewable resources (Bottcher et al., 1999), and maximizing net present value rather than minimizing makespan (Neumann and Zimmermann, 2000). As far as R&D planning is concerned, the problems of portfolio selection in the pre-clinical trials section (Charalambous and Gittins, 2008), and the planning of R&D activities with technical failure without resource constraints (De Reyck and Leus, 2008) have been addressed. Also, a normative model for structuring R&D pipelines under uncertainty is discussed in Ding and Eliashberg (2002). Van Hentenryck and Mercier develop an anticipatory algorithm for the stochastic RCPSP (Mercier and Van Hentenryck, 2008). Finally, Solak et al. (2010) present a comprehensive mixed-integer programming (MIP) model for R&D portfolio optimization that accounts for endogenous uncertainty as well as technological interdependencies between tasks, and a sample average approximation solution approach.

A number of approaches have also been presented in the process systems engineering (PSE) literature. Grossmann and coworkers proposed deterministic MIP models that account for uncertainty through outsourcing while optimizing the expected net present value (Schmidt and Grossmann, 1996; Jain and Grossmann, 1999) and a deterministic model with outsourcing, resource expansion, and project crashing ideas (Maravelias and Grossmann, 2004). Pekny, Reklaitis and co-workers presented a simulation–optimization framework that accounts for uncertainty in task duration, resource requirements, and outcomes (Subramanian et al., 2001; Subramanian et al., 2003) and a probabilistic network method for portfolio selection (Blau et al., 2004). Choi et al. proposed a dynamic programming approach (Choi et al., 2004), while Maranas and co-workers presented a real-options strategy (Rogers et al., 2002; Gupta and Maranas, 2004). Shah, Papageorgiou and coworkers have worked on the related problem of capacity planning in the pharmaceutical sector (Gatica et al., 2003; Levis and Papageorgiou, 2004), while Mustafa et al. developed software to aid decision-making (Mustafa et al., 2005). An overview of methods for pharmaceutical R&D planning can be found in Shah (2004), while general discussions on the development of new products