

# STSM REPORT by Paolo Tubertini

## 1 Introduction

In collaboration with Professor Ana Gomes Viana from INESC TEC we aim at discussing hybrid approach techniques to tackle and solve planning problems. The main goals of the SMST were to address the integration between simulation and optimization techniques so as to model the dynamic behaviour of real systems and solve the related planning problems with exact approaches. Both simulation and optimization techniques have been addressed.

The research period has been focused on analyzing the possible integration of simulation and optimization techniques to Kidney Exchange Problem (KEP).

The report is organized as follows, in Section 2 an overview of the above-mentioned simulation techniques is reported, in Section 3 an in-depth analysis of simulation-based techniques applied to KEP is reported. Finally Section 4 reports the proposed simulation-optimization integrated approach to KEP.

## 2 Literature review

### 2.1 System Dynamics

System dynamics is a simulation method invented by MIT professor Jay Forrester in the fifties. More accurately system dynamics is a computer-aided approach to policy analysis and design. It applies to dynamic problems arising in complex social, managerial, economic, or ecological systems literally any dynamic systems characterized by interdependence, mutual interaction, information feedback, and circular causality. Mathematically, the basic structure of a formal system dynamics computer simulation model is a system of coupled, nonlinear, first-order differential (or integral) equations. Simulation of such systems is easily accomplished by partitioning simulated time into discrete intervals of length  $dt$  and stepping the system through time one  $dt$  at a time. Conceptually, the feedback concept is at the heart of the system dynamics approach. Diagrams of loops of information feedback and circular causality are tools for conceptualizing the structure of a complex system and for communicating model-based insights. The loop concept underlying feedback and circular causality by itself is not enough, however. The explanatory power and insightfulness of feedback understandings also rest on the notions of active structure and loop dominance. The concept of endogenous change is fundamental to the system dynamics approach. It dictates aspects of model formulation: exogenous disturbances are seen at most as triggers of system behavior; the causes are contained within the structure of the system itself. The system dynamics approach emphasizes a continuous view. The continuous view strives to look beyond events to see the dynamic patterns underlying them. Moreover, the continuous view focuses not on discrete decisions but on the policy structure underlying decisions. Events and decisions are seen as surface phenomena that ride on an underlying tide of system structure and behavior. Case studies related to energy management can be found in [1] and in [2].

### 2.2 Discrete Event Simulation

Discrete event modeling is the process of depicting the behavior of a complex system as a series of well-defined and ordered events and works well in virtually any process where there is variability, constrained or limited resources or complex system interactions. Common applications of DES include stress testing, evaluating potential financial investments, and modeling procedures and processes in various industries, such as manufacturing and healthcare. The core concepts of DES are entities, attributes, events, resources, queues, and time. Entities are objects that have attributes, experience events, consume resources, and enter queues, over time. Entities can be created at the start or whenever it is appropriate to the problem. The time of relevance to an entity may be a subset of the simulation time (i.e., individual entities can enter and leave a model between model start and end times). Attributes are features specific to each entity that allow it to carry information. These values may be used to determine how an entity responds to a given set of circumstances (e.g., timing and type of past events may influence the likelihood and timing of subsequent events). Attribute values may be modified at any time during the simulation, aggregated with those of other entities, or analyzed further outside the simulation (e.g., to estimate mean cost and effect). Events are broadly defined as things that can happen to an entity

or the environment. Events can occur, and recur, in any logical sequence. A resource is an object that provides a service to an entity. This may require time. DES represents resource availability at relevant points in time. In representing resources, DES can capture spatial factors allowing layout analysis. If a resource is occupied when an entity needs it, then that entity must wait, forming a queue. A fundamental component of DES is time itself. An explicit simulation clock (initiated at the start of the model run) keeps track of time. Referencing this clock makes it possible to track of interim periods. The discrete handling of time means that the model can efficiently advance to the next event time, without wasting effort in unnecessary interim computations. Case studies related to energy management can be found in [3] and in [4].

### 2.3 Agent Based Simulation

Agent-based modelling and simulation (ABMS) is a relatively new approach to modelling complex systems composed of interacting, autonomous agents. Agents have behaviours, often described by simple rules, and interactions with other agents, which in turn influence their behaviours. By modelling agents individually, the full effects of the diversity that exists among agents in their attributes and behaviours can be observed as it gives rise to the behaviour of the system as a whole. By modelling systems from the ground up agent-by-agent and interaction-by-interaction self-organization can often be observed in such models. Patterns, structures, and behaviours emerge that were not explicitly programmed into the models, but arise through the agent interactions. The emphasis on modelling the heterogeneity of agents across a population and the emergence of self-organization are two of the distinguishing features of agent-based simulation as compared to other simulation techniques such as discrete-event simulation and system dynamics. Agent-based modelling offers a way to model social systems that are composed of agents who interact with and influence each other, learn from their experiences, and adapt their behaviours so they are better suited to their environment. A typical agent-based model has three elements: (i) a set of agents, their attributes and behaviours, (ii) a set of agent relationships and methods of interaction, and (iii) the agents environment (i.e. agents interact with their environment in addition to other agents). Case studies related to energy management can be found in [5] and in [6].

## 3 Dynamic kidney exchange: state-of-the-art

In their simplest format, kidney exchange programs evolve as a sequence of static problems. When a patient in need of a transplant finds a potential living donor who, although willing to donate one kidney, is blood-type and/or tissue incompatible with the patient, that pair can join a pool composed of similarly incompatible pairs. At pre-specified moments during a year, a matching algorithm will select for transplant pairs in the pool, such that compatible donors are assigned to patients. The selection is done in such a way that a given criterion is optimized (usually, the number of transplants is maximized). Other criteria, such as maximizing the number of blood type identical transplants or minimizing the length of the longest cycle, have also been addressed [7].

A KEP pool can be represented by a graph. Let  $G = (V, A)$  be a directed graph, where the set of vertices  $V$  consists of all incompatible patient-donor pairs in the pool, and  $A$  is the set of arcs  $(i, j)$  connecting vertices  $i, j \in V$  iff the patient in pair  $j$  is compatible with the donor in pair  $i$ . To each arc  $(i, j) \in A$  is associated a (typically unitary) weight  $w_{ij}$ .

The KEP optimization problem can then be stated as follows: find a maximum-weight set of vertex-disjoint cycles over graph  $G(V, A)$ , such that each cycle has length at most  $k$ . The parameter  $k$  sets the maximum number of pairs that can be involved in a cycle.

Static modeling of KEPs cannot address questions such as:

- *What is the best matching interval in order to reduce waiting times and dropouts?*
- *Which policies should be used to protect blood type O patients, and how do they affect the other patients?*
- *What is the impact of including different types of pairs in the overall performance of the KEP?*

To provide an answer to such questions, the evolution of a KEP pool over time must be studied; several dynamic approaches based on simulation techniques have been developed for this. Existing simulators can be classified according to the characteristics of the pool they are modeling, and to the performance indicators addressed.

Patients' and donors' blood type compatibility is taken into consideration in [8, 9]. Both articles consider pools with incompatible pairs only. The first proposes efficient dynamic matching mechanisms for 2-way and multi-way exchanges, and aims at maximizing the discounted exchange surplus. The latter considers only 2-way exchanges, and tries to maximize the overall number of transplants by adjusting the time interval between matches.

An improvement in terms of pool representation can be found in two articles taking into consideration virtual tissue type incompatibility between patients and donors; the analysis is based on data generated in [10]. First, [11] takes into consideration 2-way exchanges and the maximization of the number of transplants, weighted by the quality of the transplant and the waiting time. The method allows suggesting when a patient should enter a kidney paired donation program, or, alternatively, choose a desensitization treatment. Later, [12] exploits the potential of 3-way cycles, aiming at maximizing the overall number of transplants.

The probability of transplant failure due to patients' withdrawal or other viability issues is taken into consideration in [13]; here, 3-way exchanges are analyzed by incorporating fall-back positions, which can be implemented when the primary choice does not lead to a completed set of exchanges. The proposed approach tries to maximize the expected utility, which is related to transplant quality (zero antigen mismatches) and to logistic issues (having donor and candidate in the same transplant center).

Initial kidney exchange programs were composed exclusively of incompatible pairs; however, programs have been evolving, and nowadays may include donors without an associated patient, who are willing to donate a kidney for no return. The impact of allowing altruistic donor chains in a KEP is studied in [14, 15, 16]. The first article evaluates the impact of chains (of length at most equal to three) and aims at maximizing the expected utility. The two others aim instead at maximizing the number of transplants, in weighted (considering vertex potentials) and standard versions. An evolution of this approach can be found in [17], where a branch-and-price approach is proposed to solve large scale problems.

## 4 Simulation-optimization approach for KEP

We propose a KEP simulator that takes into consideration the wide variety of actors found in practice (incompatible pairs, altruistic donors, and compatible pairs) and handles different matching policies. In addition to the functionality of state-of-the-art on KEP simulators, we include the possibility of evaluating the impact of positive crossmatch of a selected transplant as well as dropouts in a dynamic environment. Furthermore, a procedure to estimate the general population Panel Reactive Antibody (PRA) should be implemented, allowing the policy maker to use the proposed framework with diverse data sets (*e.g.*, from different countries). A complete information IP model, providing an upper bound on the number of transplants — that would be achieved in case of having available all the information, including future events — completes the proposed approach. Its main components, as well as the interactions between them, are shown in Figure 1.

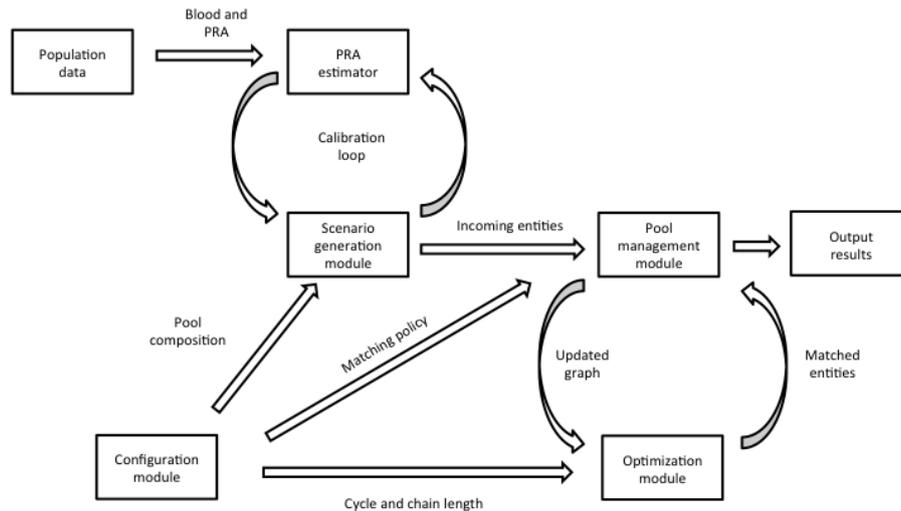


Figure 1: Component interaction in the proposed simulation-optimization tool.

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