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Model-based approach for optimizing the storage management of bio-repositories

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ABSTRACT

Systematically collected samples of human tissue and fluids (e.g. blood, urine) play a key role in biomedical research. Biomaterial banks aim at collecting such biomaterials systematically and providing long-term availability of samples, which have to be kept constantly frozen at low temperatures. Therefore, storage management has to meet critical constraints in order to maintain high quality of the samples. The project aims at supporting the application of optimization and simulation algorithms for storage management. The approach has to provide means for adapting the algorithms flexibly and systematically to different or changing settings of biomaterial management and, therefore, aims at implementing a model-based framework to specify and run the algorithms.

The process of establishing an optimization/simulation model for a given Biomaterial bank supported by the project starts with acquiring separately a model (1) of biomaterial handling and (2) of the optimization or simulation approach. The models for specific situations are derived from generic ontologies. A subsequent model mapping step assigns components representing aspects of biomaterial handling and storage to roles in a suitable optimization or simulation scheme. The mapping then enables the semi-automatic generation of optimization and simulation code. In the case of offline optimization problems, the framework produces program code that can be processed by an existing generic solver for mixed integer optimization programs (Zuse Institute Mathematical Programming Language code to be processed by the solver Solving Constraint Integer Programs). In the case of online problems, i.e., problems with an ongoing production of new information relevant for the optimization, the approach generates Java code suitable for processing by an existing simulation kernel (SimKit).

The mapping module has been verified by reproducing a given solution for the Capacitated Facility Problem. Preliminary results of simulation runs show antagonistic effects of sorting bio-specimens by sample type: Sorting decreases the number of freezer opening operations while it increases fragmentation. The project is the first to adopt ontology-based modeling and model mapping for systematically exploring optimization and simulation approaches to biomaterial storage management. The results of simulation runs not only demonstrate the feasibility of the approach, but yield first practical insights (e.g. the effect of sorting samples).

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1. Introduction

1.1. Background

Systematically collected human biomaterials of high quality will play a key role in future biomedical research, especially in the context of molecular research performed to further develop personalized medicine [1]. While the long-term cryopreservation of biomaterial, i.e. the systematic collection and storage of biomaterial (e.g. blood or tissue) at very low temperature (typically −80 °C), is a costly effort, the adoption of algorithmic optimization for storage management is a promising but nonetheless challenging approach that can be supported by domain ontologies and model mapping.

Biobanks combine freezer facilities for long-term cryopreservation of biomaterial with data management and information processing necessary for sample management and data analyses. Human biomaterial is often collected in the context of clinical studies including patients and healthy individuals or in the context of clinical treatment. In the context of treatment, the samples are first examined and diagnosed by pathologists to generate the required pathology report. In cases where no immediate processing is required or possible, the laboratory staff prepare the sample for temporary cryopreservation according to predefined steps of standard operating procedures.

Fig. 1 shows the standard processing in incoming biomaterial samples: The steps normally include splitting the sample into aliquots to be used independently for different examinations, assessing the sample quality (partly by molecular tests), filling the aliquots in suitable containers, and documenting the samples' pre-analytical history. If informed consent of the donors allows the research usage of the samples, they are selected for long-term preservation and eventually moved from temporary to long-term freezer locations. Pseudonymized clinical and patient data associated with the bio-specimens allow suitable samples to be found for a given research project afterwards: Researchers send a request for sample delivery to the biobank. The request contains selection criteria for the samples. If the biobank provides access to a search interface, the researchers will already be able to identify samples suitable for their project. If the request is approved by the biobank, the positions of the samples will be retrieved, the respective aliquots will be taken out of the long-term storage (''cherry-picking''), controlled for quality, and moved to transportation boxes. The samples and associated anonymized data are then delivered to the researcher. There are many variations of the delivery process, some including additional sample processing and testing.

Tubes containing samples are often arranged in matrix-like positions of container boxes. Depending on the organization of the biomaterial bank, a large variety of configurations is possible. Apart from the variety of organizational and technical solutions, there are common aspects of biomaterial processing: Samples need to be preprocessed, temporarily stored, moved to long-term storage positions, checked regularly for quality and rearranged, and of course retrieved and delivered for research purposes. Biobanks have to meet challenging requirements concerning sample retrieval, high quality of associated data, data exchange between biobanking information systems [2] and maintenance of exactly defined storage conditions (e.g. constant temperature, rapid sample access, protection against chemical influences, handling of infectious material) [3]. Aliquots delivered for research purposes are –in general– irreversibly modified or destroyed and cannot be used for additional investigations. Thus, if incoming samples did not use storage positions held by withdrawn samples before, storage capacity would be wasted, but filling the gaps with new samples could cause increased fragmentation or an inefficient structure of the bio-repository.

While biobank management systems maintain an index of storage positions, it is possible, in principle, to apply methods of algorithmic optimization to bio-repository storage management. There are reasons for considering such an approach a

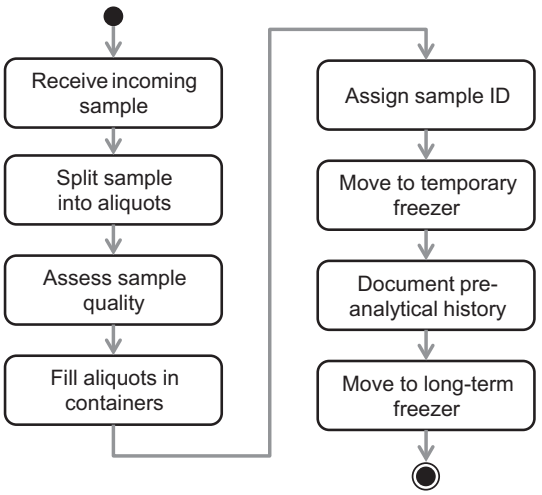

Fig. 1. Standard processing of incoming biomaterial samples (aliquots are only generated, if the size/volume of the sample allows splitting).