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A large-scale cryoelectronic system for biological sample banking

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ABSTRACT

We describe a polymorphic electronic infrastructure for managing biological samples stored over liquid nitrogen. As part of this system we have developed new cryocontainers and carrier plates attached to Flash memory chips to have a redundant and portable set of data at each sample. Our experimental investigations show that basic Flash operation and endurance is adequate for the application down to liquid nitrogen temperatures. This identification technology can provide the best sample identification, documentation and tracking that brings added value to each sample. The first application of the system is in a worldwide collaborative research towards the production of an AIDS vaccine. The functionality and versatility of the system can lead to an essential optimization of sample and data exchange for global clinical studies.

1. Introduction

The first application of our large-scale cryoelectronic system is in the GHRC project (Global HIV Vaccine Research Cryorepository). The project provides a central storage facility for AIDS related material to be used in worldwide collaborative research (CAVD – Collaboration for AIDS Vaccine Discovery supporting the GHAVE – Global HIV/AIDS Vaccine Enterprise [1]) towards the production of a vaccine. The quality of documentation and strict adherence to ideal storage conditions are of prime importance. CAVD is a network of thirteen HIV vaccine discovery consortia and five central service facilities. There are 89 institutions involved spread over 22 countries. One of these institutions is the Fraunhofer-IBMT, coordinating a network that is developing the GHRC, one of the central service facilities [2]. The GHRC will be a new and unique facility that is not limited in the type of material collected. The specimens are preserved, stored and documented in the centralized facility and provided to other CAVD institutions for vaccine research.

The availability of high quality biological specimens for vaccine research purposes requires the development of standardised methods for collection, long-term storage, retrieval and distribution of specimens that will enable their future use [3]. Global collaborative research requiring worldwide sample exchange and comparison of results puts even larger demands on the quality, safety and documentation of precious samples. Standardization and optimized data exchange in the collection and storage of biological information associated with biological samples is thus a key issue for collaborative research and for biobanks today [4].

Considering these objectives it is obvious that there is a great need for electronic circuits and subsystems to be placed and operated in the cold storage environment. The aim is the reliable coupling of precious HIV (Human Immunodeficiency Virus) collections to cryo-tolerant electronics, particularly Flash memory chips holding data about the origin and type of the specimen, identification, lab processing and documentation near liquid nitrogen temperatures. We present: (1) the basic organisation of the large-scale cryoelectronic infrastructure, (2) the principle design and first prototypes of electronic system modules including electronic cryovials, (3) results for the cold Flash endurance screening and for the reliability of mechanical parts at liquid nitrogen temperatures and (4) important aspects for the system integration.

2. System organisation

The basic organisation is hierarchical with well-defined interfaces between the levels of the hierarchy. Not only the cryostorage area but also the laboratory working area is included in the system hierarchy. All workstations are connected to a supervisory machine having connection to the facilities database system. Each station is equipped with a sample reader and many are connected to laboratory equipment. Some of the stations control cold working areas and some of them control the cryotank systems. Each storage rack in a cryotank will be equipped with backplane electronics containing a microcontroller and several swing-out 'wings', each of which may hold samples directly or in sub-containers. The controller drives a bus running up the spine of the rack and connecting with the wings. The bus carries analog as well as digital data.

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The samples are stored in containers of various sizes equipped with Flash memory chips. The memory chips contain information about sample, container and processing. They plug into the next 'layer' of the system, which also has memory recording, among other things, the number and layout of its sample positions and the strategy for accessing them. This principle that each device has information identifying itself and giving its characteristics is repeated at higher levels so the resulting system is polymorphic. New types of sample containers and the physical and electronic infrastructure to support them can be easily added and mixed with existing types. Fig. 1 gives an overview of the system organisation in the entire facility.

3. System modules

Based on the hierarchical system organisation we have developed various system modules. This section describes: (A) the principle design and first prototypes of electronic cryovials for various sample volumes, (B) a dedicated laboratory workflow management system (WfMS) called 'ChameleonLab' for reproducible and standardised sample processing, and (C) the cryoelectronic infrastructure for sample storage tanks.

3.1. Development of electronic cryovials

The smallest system modules we have developed are HIV cryovials (made from polypropylene). These have securely attached serial Flash memory chips. For added security the containers also carry barcodes and low-temperature RFID tags (radio frequency identification tag). All identifiers can be injection moulded during manufacture of the vial to avoid the risk of loss. Screw capped containers (of various volumes) for the biological samples are coupled to a base holding the Flash memory chip. The base is also a plug connecting to a socket on special carrier plates. The Flash memory chip can store the identifier and additional sample description, legal constraints, data format and publication data as well as the complete parameter set for operating the laboratory workflow. First injection-moulded prototypes are available for sample volumes of 100 µl, 500 µl and 2 ml. Fig. 2 shows the principle design (Fig. 2a) and photographs (Fig. 2b) of injection-moulded prototypes. The prototypes are currently under extensive evaluation

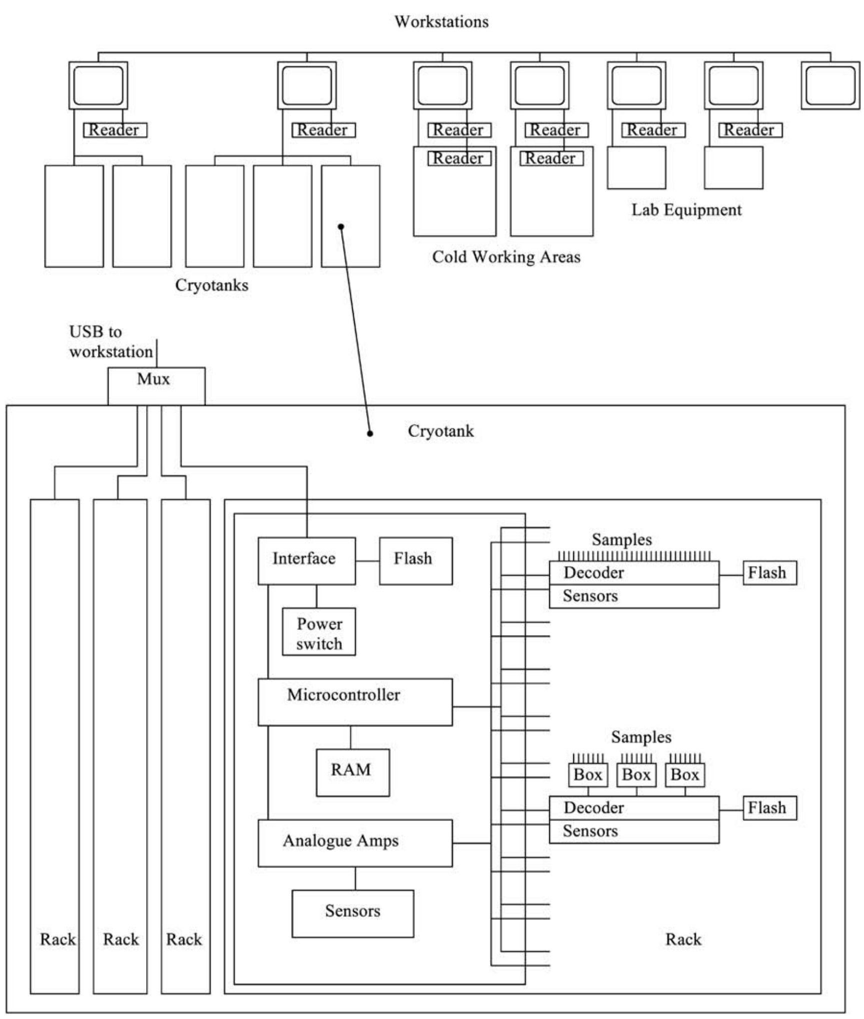

Fig. 1. The system consists of a number of workstations connected to a supervisory machine. Each station is equipped with a sample reader and many are connected to laboratory equipment. Each cryotank holds four racks and each rack has its own microcontroller that can communicate with the host workstation. Every rack has Flash memory to identify it and store data such as inventory. Into the rack plug swing-out 'wings' that, directly or indirectly, hold samples. Different wings are of different design to accommodate samples of various sizes but all share the same physical and logical interface and so can be mixed in a single rack. Each wing carries a Flash memory that identifies the wing and its type. Each sample also has Flash memory for identification and storing sample-related data. In some cases, samples are stored in intermediate containers. These boxes are also equipped with memory.