Deliverable D2.2 – Definition of HoloZcan System Architecture

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Version 1.0	Paul Claassen	17 Dec 2021	First version
Version 2.0	Paul Claassen, Béla Mihalik	22 Dec 2021	Updated after review

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EXECUTIVE SUMMARY

The architecture of the HoloZcan Systems is described. Two separate models are defined, namely the Advanced Lab Setup and the Functional Prototype. The context and purpose of these models is given, followed by a specification of their functions as well as interfaces. A decomposition of both models is given into their key hardware components. For the Functional Prototype, the software functionality is given as well accompanied with a decomposition of software building blocks and a database description.

Although care is given to give an accurate high level description of the architecture, new insights and external factors can always lead to deviations of the actual hardware to this document.

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INTRODUCTION

Purpose of this document

This document describes the high level architecture of the HoloZcan holographic microscope systems used throughout the project. The system architecture description involves:

- description of system scope and context,
- functional and performance specifications,
- non-functional specifications,
- schematic decomposition of the system hardware and software,
- description of interfaces.

These topics are addressed in the following Sections in this document and projected on two distinct platforms.

This document is created with the best knowledge available at the moment of writing. The details however are subject to change, during the course of the HoloZcan project additional knowledge may become available throughout the process of experiment and development. Furthermore, external influences may require interfaces to change and can lead to new specifications.

Scope

As described in [1], the process towards the final system is iterative and involves multiple models. The scope of this document involves two separate models with distinct purposes. These models are called Advanced Lab Setup and Functional Prototype throughout this document, with their purposes given in Table 1.

Table 1 Definition of platforms

Model	Purpose
Advanced Lab Setup	Early prototype to develop the best optimized optical concept for the microscope via a series of experiments with flexible hardware. A subset of this setup is used to start building of an image database for algorithm development with the definite hardware concept.
Functional Prototype	A robust and fully functional microscope based on advanced lab setup for detection of details in biological samples. Refine image database for further algorithm improvement.

Only the hardware of the two mentioned models is described, a set of mechanical, optical and electrical components which can be used to generate holographic images of prepared samples. The supportive control software is included as well, needed to operate the system.

This document does *not* include the following topics:

- any processing of the images by means of (machine learned) algorithms
- preparation of the samples

Context

Due to their different purposes, the two models will be used in a somewhat different context, as shown in Figure 1 and Figure 2. The Advanced Lab Setup will be used by an optical developer who is fully aware of the model's functions and limitations. Samples are prepared and supplied by laboratory personnel and used by or under the supervision of the optical developer to create sets of raw (holographic) images. Those images are then used by an algorithm developer to create a first version of an algorithm that can be used offline for testing purposes.

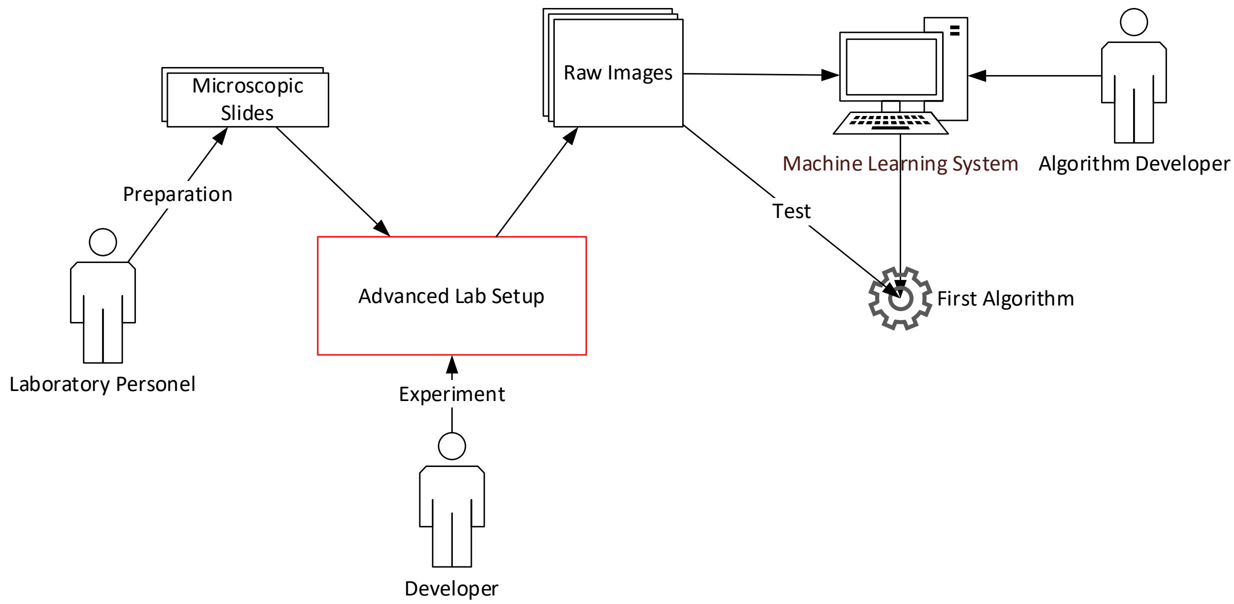

Figure 1 Context of Advanced Lab Setup

The Functional Prototype can have multiple types of users, e.g. directly by the laboratory personnel, field testers or any stakeholder. More images can be created with the purpose of improving the detection algorithm to a next level on a machine learning system by the algorithm developer. Those algorithms can also be actually used on the Functional Prototype to directly output results.

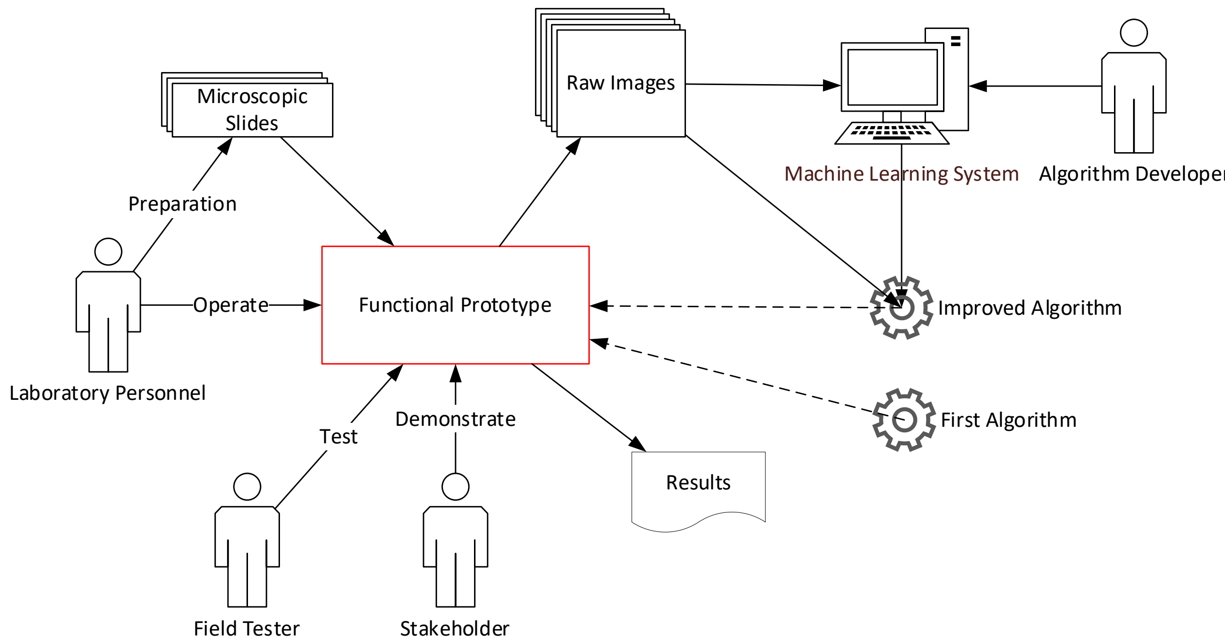

Figure 2 Context of Functional Prototype

SYSTEM SPECIFICATIONS

Both the system requirements and the system specifications go hand-in-hand as they both describe what the system does and upto what level it performs. Commonly, a requirement is defined on beforehand and is used to make a proper design that leads to specifications. A properly designed system has specifications that at least fit to the requirements, but may also include non-required behavior. For some cases, it is not clear and not always relevant whether a specification is required on beforehand or the result of design and then becoming a requirement in a later stage. Because of the technological uncertainties that exist and the level of research (within the design) that must be carried out for this project, the requirements may to some extent be influenced by the specifications.

This Chapter gives the system specifications, some of which could be interpreted as requirement as well. Specifications are given for both models simultaneously with differences clearly indicated, such that a comparison can be easily made.

Functional specifications

Functions of the models are listed in Table 2.

Table 2 Functional Specifications

Function	Adv. Lab Setup	Func. Prototype
Insert microscopic slide	Manually	Semi-automated
Remove microscopic slide	Manually	Semi-automated
Make image(s)	Semi-automated	Fully automated
Store and retrieve image(s)	No	Yes
Classify Sample	No	Yes

Sample specifications

The samples that are to be used in the models are described in Table 3.

Table 3 Sample Specifications

Subject	Specification
Sample carrier	Borosilicate microscopic slide 75x25x1 mm Borosilicate cover glass 0.14 mm thickness

Subject	Specification
Bulk material	Water
Sample spatial distribution	Individual particles and particle clusters
Short-time stability (<5 min)	No morphological or structural changes

Performance requirements

The product must be designed such that it fits in a roadmap to become useable for CBRN-purposes. This means that there are no applicable performance requirements for any of the models described in this document, but for a final CBRN product the following requirements will apply, in order of importance:

1. Usability requirements
2. Robustness requirements
3. Accuracy requirements

Non-functional specifications

Table 4 Non-functional Specifications

Specification	Adv. Lab Setup	Func. Prototype
Footprint	<1000 x 1000 mm	<600 x 800 mm
Height		<800 mm
Mass including packaging		<25 kg
Safe for transportation	No	Yes

Interface specifications

Table 5 Non-functional Specifications

<table>
<tr><th>Specification</th><th>Adv. Lab Setup</th><th>Func. Prototype</th></tr>
<tr><td>Power usage</td><td colspan="2">220VAC 50Hz grounded plug
Max 2000 W</td></tr>
<tr><td>Environment requirement</td><td colspan="2">Cleanroom class 6 or flowbench
20°C – 25°C</td></tr>
</table>

HARDWARE DECOMPOSITION

The hardware decomposition for both models are subsequently described below. These models are based on an Digital Inline Holographic Microscope (DIHM) architecture, as proposed in [1] and fits the goal of a robust, high performance and easy to use microscopic system.

Advanced Lab Setup

The Hardware Decomposition of the Advanced Lab Setup is described using the functional overview shown in Figure 3. The setup is not static however, which means that the components can be exchanged, repositioned, removed, added and connected in a flexible manner making use of off-the-shelf laboratory components.

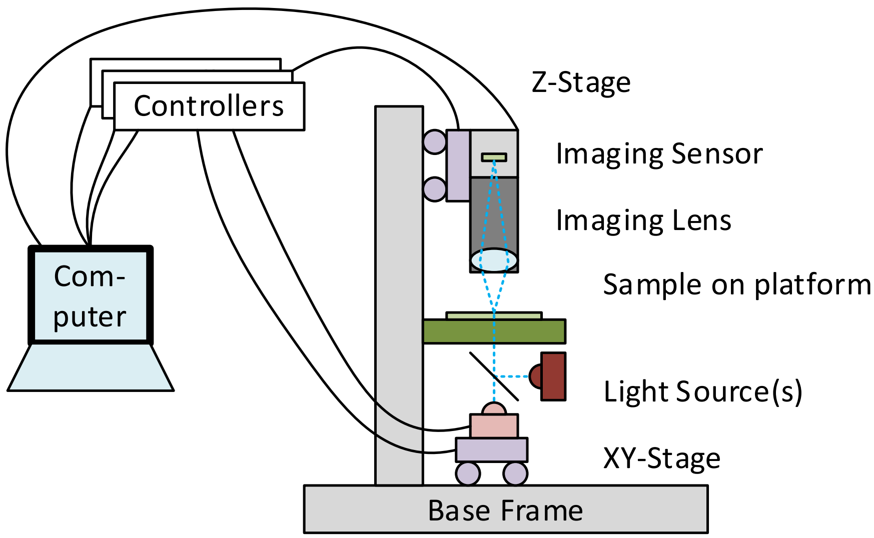

Figure 3 Functional Overview of Advanced Lab Setup

The following options are available for the components indicated in the sketch:

- Base frame
    - Optical breadboard for easy horizontal mounting of parts
    - Post for easy vertical mounting of parts
- Stages
    - Servomotor controlled horizontal (XY) stage for source(s)
    - Servomotor controlled vertical (Z) stage for imaging sensor
    - Optional encoders for accurate position reporting
- Source(s)
    - LD (Laser Diode), LED or SLD (Super Luminescent Diode)
    - One or more, combined with a beam splitter or hot/cold mirror
    - Multiple wavelength options ranging from UV to NIR
    - Mirror at 45 degrees to direct light towards the sample
    - Optional pinhole with different sizes
    - Optional focusing lens

  - Optional collimating lens
  - Optional bandpass filter(s)
- Sample platform
  - Platform for reproducible positioning of sample
  - Manual horizontal position (XY) control
- Imaging Lens
  - Microscope or machine vision lens with several magnification and resolution options
  - Option for lensless
- Imaging Sensor
  - Monochrome/color
  - Pixel size, array size
- Controller
  - Programmable controllers for servomotors and light source(s)
- Computer
  - Flexible computer to acquire sequences of images while controlling light and stages.

Functional Prototype

The Functional Prototype is not flexible in its setup like the Advanced Lab Setup, but fixed instead to the structural decomposition given in Figure 4. A functional overview is shown in Figure 5.

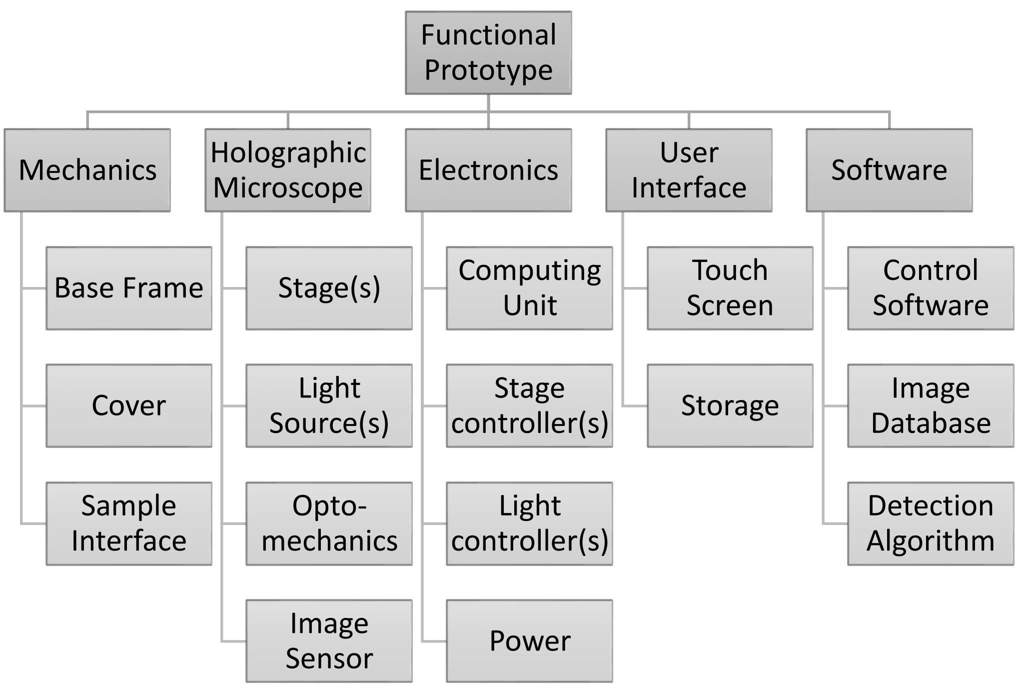

Figure 4 Structural Decomposition of Functional Prototype

At the highest level, the Functional Prototype consists of:

- Holographic Microscope
  The heart of the machine which involves optics and mechanics to make the actual images. The subcomponents will be defined by experiments with the Advanced Lab Setup.
- Mechanics
  - Base with handlebars and vibration isolation
    Supports microscope, allows it to be transported and protects it from external vibrations
  - Sample in Sample holder
    The sample is placed in a Sample holder to facilitate insertion and removal of the sample in the proper location.
  - Cover
    The cover protects the microscope and electronics from light, dust and other mechanical disturbances.
- Electronics
  - Controller
    Electronically controls the stages, illumination and camera inside the Holographic Microscope.
  - Computing Unit
    Controls the system, supports human interfacing and storage.
- User Interface
  - Touchscreen
    A human interface device
  - Storage
    Removable storage to transport images
- Software
  - Control software
    Software necessary to enable acquisition of holographic images
  - Image Database
    Information storage containing metadata of images
  - Detection Algorithm
    Machine learned algorithm that can use holographic images to detect biological matter.

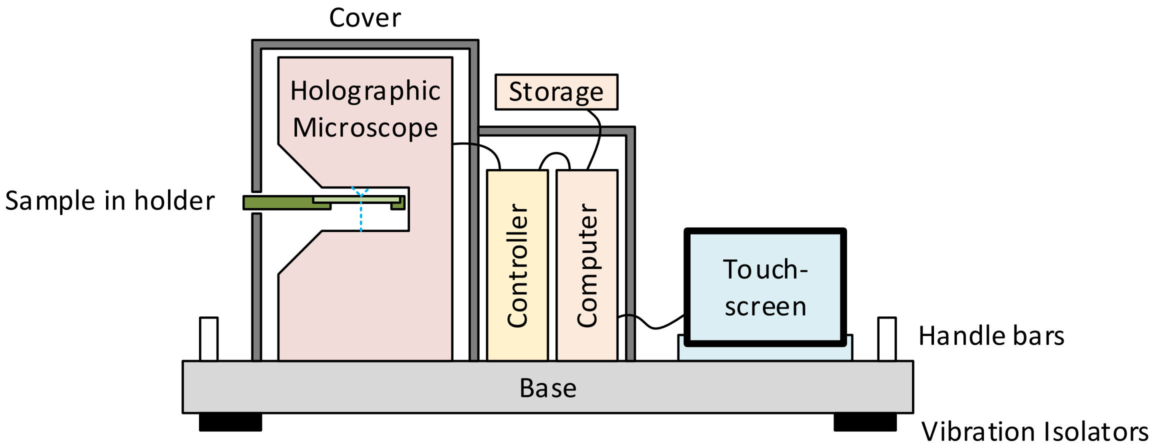

Figure 5 Architectural Overview of Functional Prototype

For reference, the initially proposed decomposition of hardware is shown in Figure 6. The decomposition defined in this document is missing the following aspects:

- The sampling system (above the red dashed line) is not part of the Functional Prototype. Interfacing of samples is via a microscopic slide.
- Supplementary Optical Sensor is not defined and might be excluded.

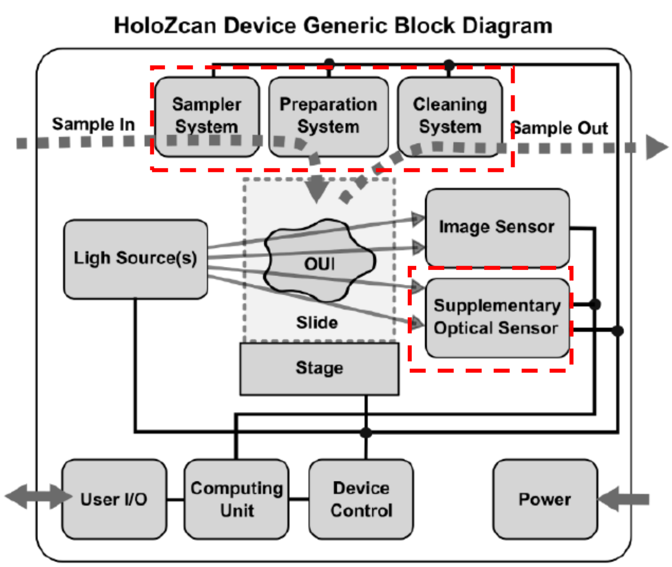

Figure 6 HoloZcan initial proposed Architecture as reported in Grant Agreement (Part B, page 25)

SOFTWARE DECOMPOSITION

The decomposition described in this Chapter applies to the Functional Prototype only. The Advanced Lab Setup can be used to further develop the software and may have a subset of the functions described here at different moments in time.

Software Functions

This Section describes the functions that the software must fulfill and which are available for a user to control the apparatus. User controllable items are:

- Sample loading/unloading
- Adjusting imaging parameters
  - Source ID
  - Z-range
  - Z-step size (number of images)
  - XY steps[1]
- Adjusting metadata
  - Configure current date/time
  - Set Operator name[2]
  - Set Environment/Location
  - Set Sample identification
- Start making images
- Interrupt taking images
- Skip step in taking images
- View images live and from storage
- Delete images from storage
- Copy images between local storage and removable storage
- Storage loading/unloading
- Create annotations (for database building purpose)
  - mark center and area (square, circular)
  - tagging (predefined list of IDs + possibility to extend)
  - free text notes
- Maintenance mode for adjusting:
  - Source current
  - Exposure time
  - Stage speed
  - Wait/settling times
  - Source wavelengths

[1] If applicable

[2] Allow for quick selection of previous input

A graphical user interface via a touchscreen will be included in the Functional Prototype. The following feedback is available:

- Sequence number of images being taken
- Total image count
- Show raw image being taken live
- Show raw image from storage
- Storage available
- Show raw image parameters (live and from storage)
    - Source Wavelength
    - Image X/Y/Z position
    - Time image taken
- Show sample metadata (from storage)
    - Sample identification
    - Operator name
    - Environment/location

Data Processing Flow

Images (matrices and vectors) are the input of HoloZcan system. The images are taken by the microscope and optional supplementary modalities and are preprocessed by adaptive filters. Reconstruction algorithms calculate physical parameters and/or features of particles found in the sample and final logic calculates a warning level by monitoring these characteristics. The HoloZcan data processing flow is illustrated in Figure 7. The blocks are explained in the next subsections.

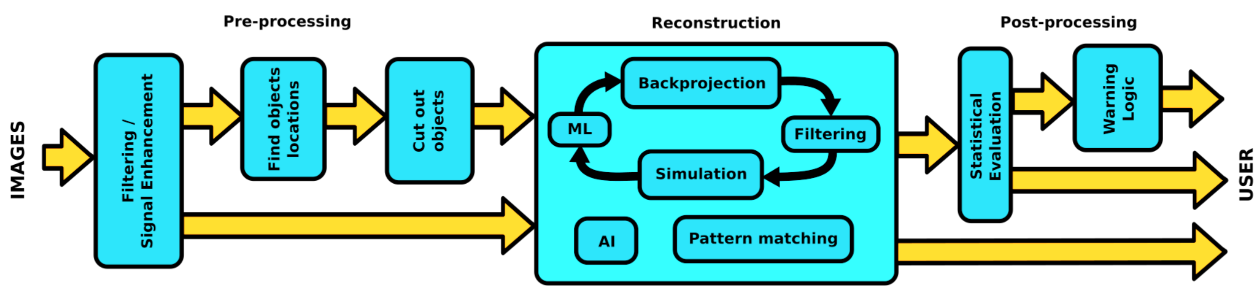

Figure 7 Data processing flow

Pre-processing

- **Filtering / Signal Enhancement** - camera error corrections, background corrections, frequency filters
- **Find objects locations** - identification of particle centres on image
- **Cut out objects** - identification of hologram size belonging to particle and create sub-matrix of data containing only relevant pixels

The pre-processing step can be bypassed by deep learning algorithms.

Reconstruction

- **Backprojection** - planar back-projection of interference pattern to object plane
- **Filtering** - regularization algorithms to enforce priori assumptions
- **Simulation** - planar light-field propagation from reconstructed object plane to image plane
- **ML** - maximum likelihood (or error minimalization) loop condition check and propagation of error into measurement data
- **AI** - artificial intelligence based reconstruction or classification algorithm
- **Pattern matching** - vector or matrix correlation based algorithm for parametric reconstruction

Post-processing

- **Statistical Evaluation** - parametric and classification data is statistically analysed both in function of time and distribution
- **Warning Logic** - the current measurement will be compared with normal levels and gradual alert levels (taking into account environmental and individual modifying parameters)

Post-processing step may be bypassed if used request image view

Warning-Logic may be bypassed in statistical visualization

Software Architecture

The apparatus contains microcomputer(s) as control unit – with personal computer level performance – running operating system and software components. The main blocks of the software system are: Device Control, Image Storage, Reconstruction, Server, and UI (User Interface). Device Control keeps connection with opto-electro-mechanical parts of apparatus, while UI keeps connection with the user. Server behaves as middleware between hardware and user, while it manages reconstruction and data analysis tasks. All parts rely on the Image Storage. User could have a direct connection to the image files via standard interfaces of operating system. The system is described in Figure 8. The blocks are explained in the following subsections.

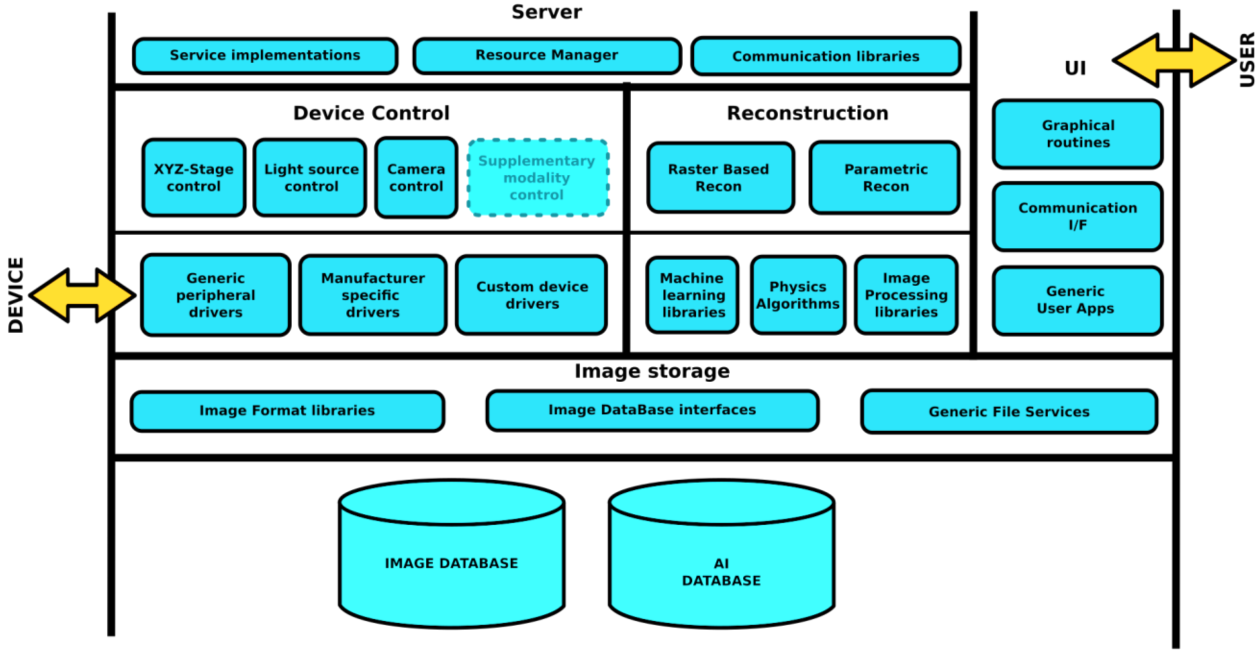

Figure 8 Software Decomposition

Device Control

- **XYZ-Stage control** - routines to handle three-axis actuator
- **Light source control** - routines to handle set of illumination sources
- **Camera control** - routines to request and save pictures from image sensor
- **Supplementary modality control** - to be defined
- **Generic peripheral drivers** - system level peripheral drivers (like USB, Serial)
- **Manufacturer specific drivers** - driver toolkit components and modules shipped with specific devices (like high-resolution camera control library)
- **Custom device drivers** - hardware interfaces implemented in HoloZcan project or by consortium partner

Reconstruction

- **Raster Based Recon** - algorithms used to reconstruct the object's bright-field (non-holographic) image on a pixel-matrix
- **Parametric Recon** - algorithms used to reconstruct only basic parameters of the analyzed object (like size, shape, refraction ratio)
- **Machine learning libraries** - set of third-party and custom components used for machine learning and running (like TensorFlow)
- **Physics Algorithms** - implemented physical equations to calculate image of analyzed object, or properties of object, based on theoretical laws
- **Image Processing libraries** - generic third party image processing and math libraries

Server

- **Service implementations** - functional routines performed at given user requests
- **Resource Manager** - command queue, thread starter, error handling, memory and disk space check
- **Communication libraries** - internal structure and protocol specifications, functions to send data between system units

UI

- **Graphical routines** - user interface components defined by the system or the development environment
- **Communication I/F** - subset of communication protocols and structures used only by UI and defined in perspective of UI
- **Generic User Apps** - generic applications, part of the operating system or environment, or installed by user to display images and perform scientific analysis

Image storage

- **Image Format libraries** - third party and self-implemented image I/O routines, to read and write pictures on disk
- **Image DataBase interfaces** - special codes to keep data in strict accessible way (access functions for a flat file system, connector to external database manager)
- **Generic File Services** - file sharing possibilities (FTP, SMB)

Database Architecture

The hierarchy of the database is borrowed from DICOM standard (dicomstandard.org). It allows system (in later developments) to be easily integrated with civil infrastructure of image archives while enabling users to use exiting scientific visualization, post-processing and analysis software. Basically images are intended to be stored as files in structured folders, where each folder represents a study, and image files are tagged with required information. Database contains SAMPLE, STUDY, SERIES and IMAGE levels. At each level records have its own ID, and can contain arbitrary number of lower level records, while lower level records have back reference to their parents.

Figure 9 shows the database hierarchy while the tables and fields are explained in the following subsections.

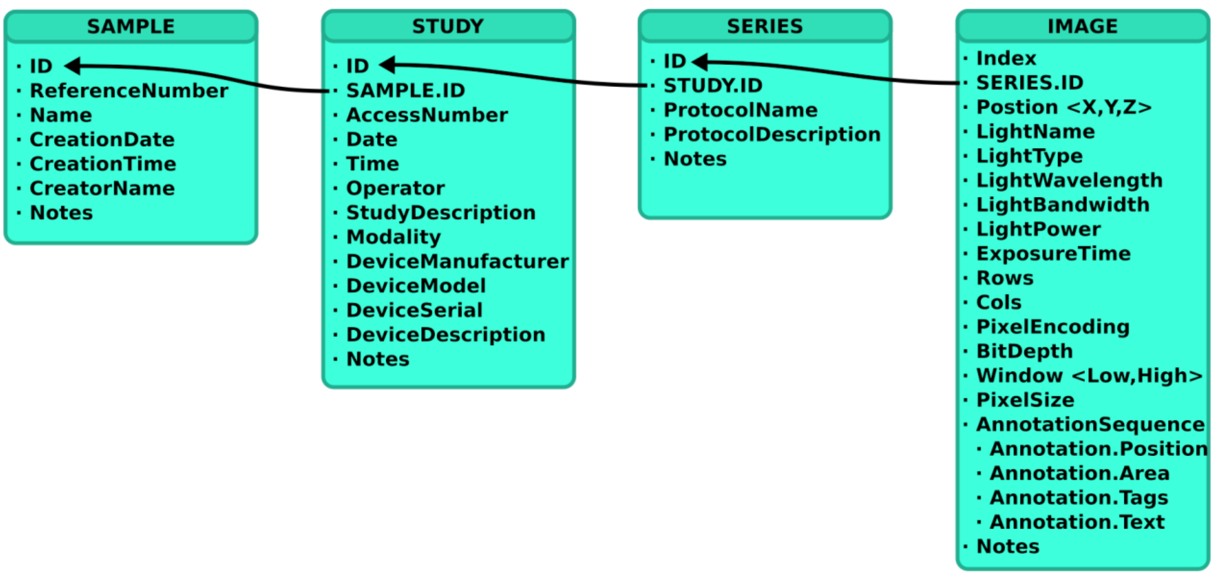

Figure 9 Database Scheme

Note that adaptations to this structure and its implementation might be required to comply with the Data Management Plan [2]. Furthermore, insights during the database building process can lead to new insights and may have impact on the structure as well as on the DMP.

SAMPLE

Represents a fixed of temporary prepared microscope slide

- **ID** - unique ID of sample is database
- **ReferenceNumber** - creator's reference number (for example access number in biobank)
- **Name** - short name of sample
- **CreationDate** - sample creation date (year, month, day)

- **CreationTime** - sample creation time (hour, minutes, seconds, subseconds)
- **CreatorName** - name of person who prepared the sample
- **Notes** - arbitrary text notes about the sample

STUDY

Represents a session of examination

- **ID** - unique ID of study in database
- **SAMPLE.ID** - the identifier of parent entry to which this STUDY belongs
- **AccessNumber** - reference number of this study in institute's register (if applicable)
- **Date** - start date of study (year, month, day)
- **Time** - start time of study (hour, minutes, seconds, subseconds)
- **Operator** - name of person who take the pictures
- **StudyDescription** - free textual description of study about
- **Modality** - what type of modality used (DHM, LIF, BF, etc.)
- **DeviceManufacturer** - manufacturer name of device used for study
- **DeviceModel** - model name of device used for study
- **DeviceSerial** - serial number of device used for study
- **DeviceDescription** - other free textual description of device used for study
- **Notes** - arbitrary text notes about the study

SERIES

Represents a sequence of pictures taken by mostly automated mechanism

- **ID** - unique ID of series in database
- **STUDY.ID** - the identifier of parent entry to which this SERIES belongs
- **ProtocolName** - Textual key identifier of protocol used to collect images (like wavelength scan, area scan)
- **ProtocolDescription** - Free text description of protocol
- **Notes** - arbitrary text notes about the series

IMAGE

Represents only one image taken at given position on given wavalength

- **ImageNumber** - image sequential index number inside the series
- **SERIES.ID** - the identifier of parent entry to which this IMAGE belongs
- **Postion<X,Y,Z>** - spatial position of the middle point of image (top surface of slide center is 0,0,0), can be approximated
- **LightName** - device dependant key-name of light source used to take picture
- **LightType** - type of light source (LD, LED, SLD ...)
- **LightWavelength** - central wavelength of light source [in micrometers]
- **LightBandwidth** - FWHM of light source [in micrometers]
- **LightPower** - power level of light source (defined in device dependent way)
- **ExposureTime** - time of exposure in seconds

- **Rows** - number of rows on image
- **Cols** - number of columns on image
- **PixelEncoding** - encoding mode of pixels (RGB, CMYK, Gray ...)
- **BitDepth** - number of bits per color components
- **Window<Low,High>** - proposed colorspace window thresholds for display image
- **PixelSize** - physical size of one pixel [in micrometers]
- **AnnotationSequence** - series of annotation made by operator
    - **Annotation.Position** - position of label
    - **Annotation.Area** - area size of identified object
    - **Annotation.Tags** - key tags for identified object
    - **Annotation.Text** - free text notes about identified object
- **Notes** - arbitrary text notes for image

REFERENCES

[1] HoloZcan Grant Agreement, number 101021723 (H2020-SU-SEC-2018-2019-2020).

[2] HoloZcan Deliverable D1.3, Data Management Plan

Security Sensitivity Assessment

Objective

This form is related to the Security Sensitivity Assessment procedure which will assure that no sensitive information will be included in the publications and deliverables of the HoloZcan project.

Security sensitive information means here all information in whatever form or mode of transmission that is classified by Council Decision on the security rules for protecting EU classified information (2011/292/EU) and all relevant national laws and regulations. The information can be already classified, or such that it should be classified.

In practice the following criteria is used:

- Information is already classified
- Information may describe shortcomings of existing safety, security or operating systems
- Information is such, that it might be misused.
- Information that can cause harm to
    - European Union
    - a Member State
    - society
    - industry and companies
    - third country
    - citizen or an individual person of a country

Document Information

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Assessment form for the main author

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List the results developed and presented in the publication/deliverable:
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The draft publication

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This publication does not include any data or information that could be interpreted as security sensitive. ☒ True ☐ No ☐ Not sure

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