A „Tudomány Ünnepe 2010” rendezvénysorozat keretében
a Gábor Dénes Főiskolán, 2010. november 8.

Automatizált sejttenyésztő-rendszer tervezése

Kopácsi Sándor, Nacsa János

kopacsi@gdf.hu, nacsa@sztaki.hu

GDF, MTA SZTAKI

GÁBOR DÉNES FŐISKOLA

MTA SZTAKI
MAGYAR TUDOMÁNYOS AKADÉMIA
SZÁMÍTÁSTECHNIKAI ÉS
AUTOMATIZÁLÁSI KUTATÓINTÉZET

EU funded research project

- funded by the Seventh Framework Programme (FP7) for research and technological development
- this is the European Union's chief instrument for funding research over the period 2007 to 2013
- It brings together all research-related EU initiatives under a common roof playing a crucial role in reaching the goals of growth, competitiveness and employment

Project partners

- Fraunhofer IPA (Germany)
- ABO Akademy (Finland)
- Primacyt GmbH (Germany)
- Chip-Man Technologies (Finland)
- MTA Automation (Switzerland)
- Hochschule Regensburg (Germany)
- MTA SZTAKI (Hungary)
- Advanced Clean Production IT (Germany)
- AFT Automation (Germany)

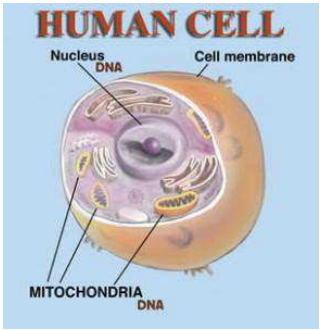
Targets

To develop an automated modular manufacturing platform for flexible and patient-specific cell production

- Enlarged application areas for personalised medicine
  - Compliance tests
  - Medication screening
  - Regenerative medicine therapies
- Examples
  - Cancer therapy (chemotherapy)
  - Cardiovascular therapy
  - Diabetes neurodegenerative diseases
  - Chronic liver failure

State-of-the-Art:

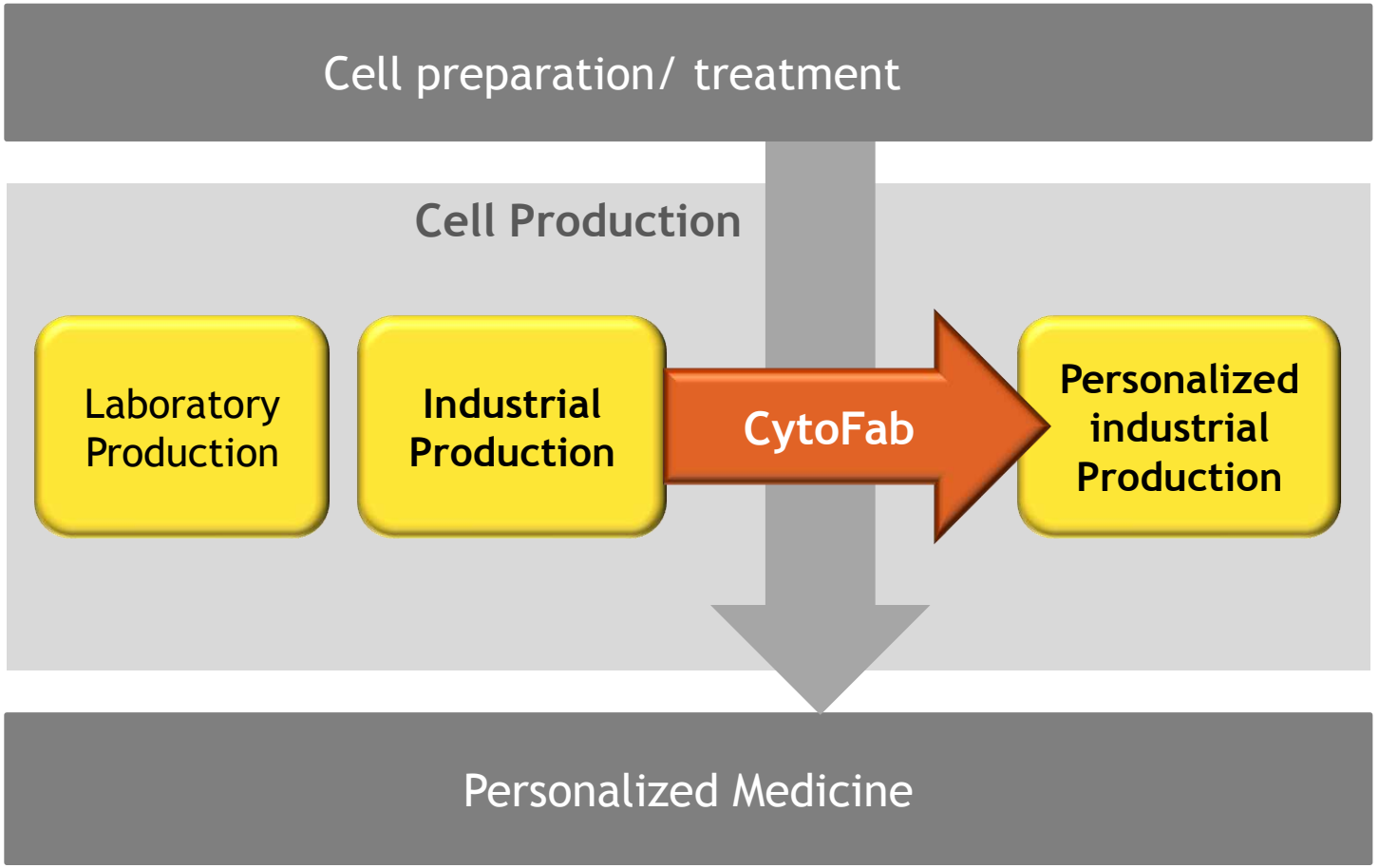
- Patient-specific production of cells on laboratory scale
- Automated production of cells only for “standard” cells



Conditions for automation of patient-specific cell production:

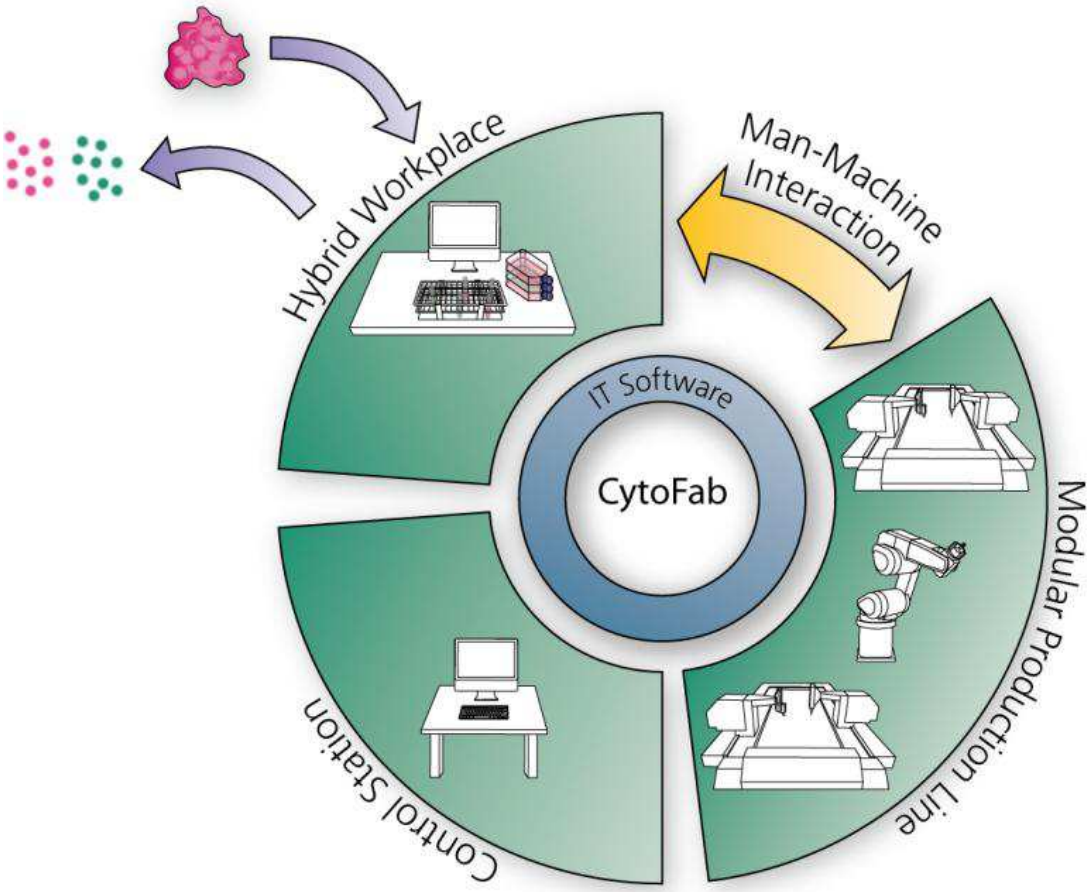
- Flexible processing of cell types / cell cultures due to their individual behaviour
- Avoidance of cross-contamination (especially among cell cultures)

Cytofab Concept



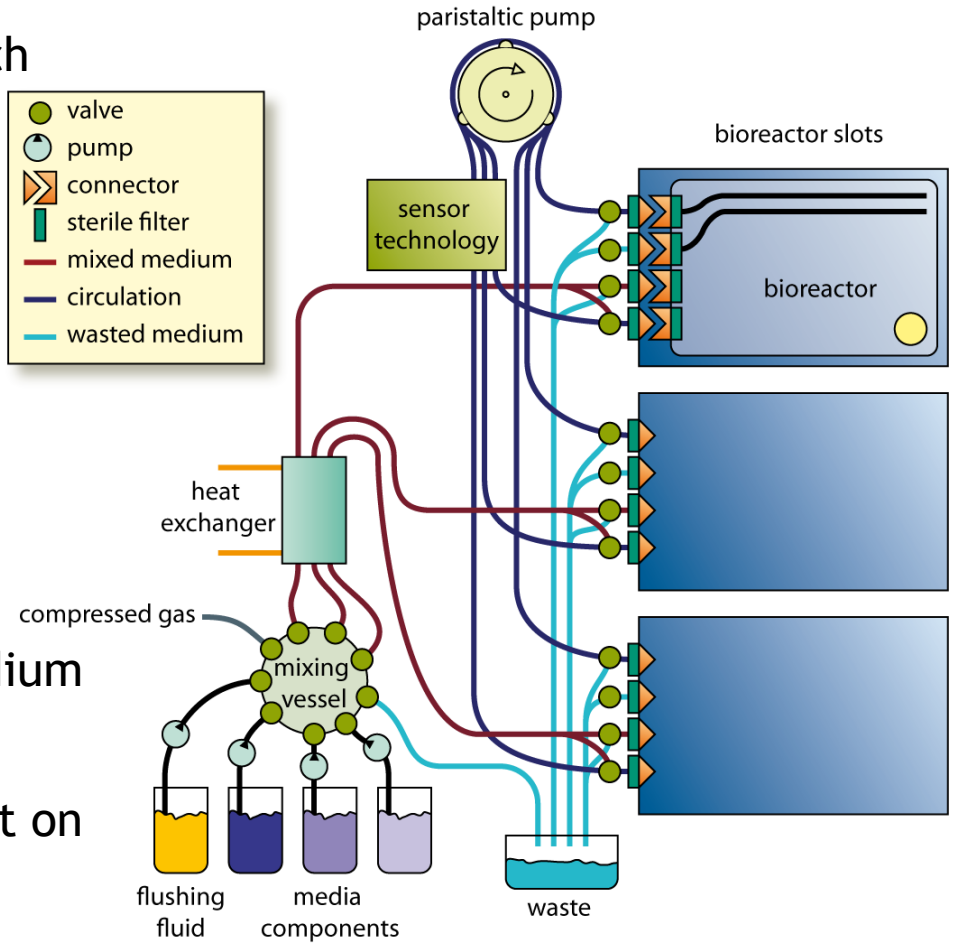
Main components

- Hybrid Workplace
- Modular production Line
  - Incubation
  - Liquid Handling
  - Monitoring
- Control Station
- SW: Manufacturing Execution System



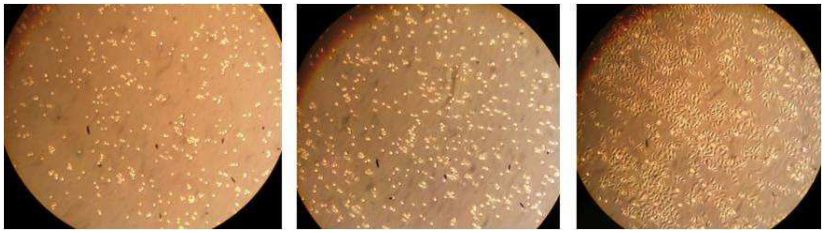
Incubation and Liquid Handling

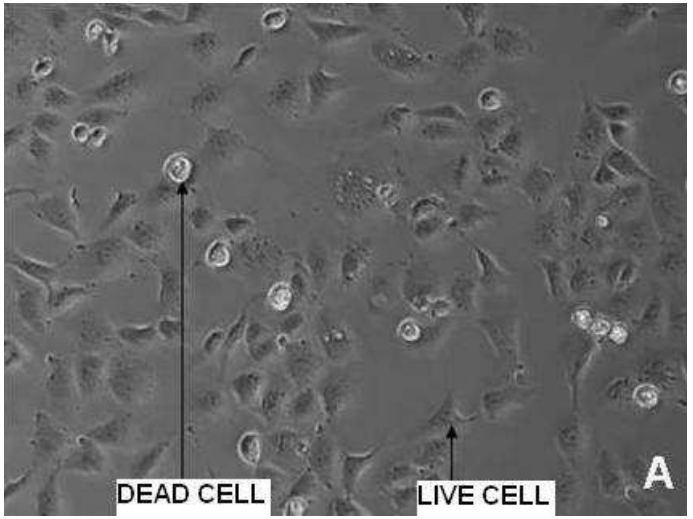
- Cell growth takes place within incubator
  - Separated process chambers for each bioreactor
  - Heating elements for temperature regulation
  - Liquid handling plugs for culture medium exchange
- Liquid handling system for culture mediums
  - Flexible composition of culture medium (for each bioreactor / cell culture)
  - Focus not on accuracy of volume but on accuracy of mixing ratio



Cell monitoring

- Optical:
  - measurement of cell number (analysis of cell culture growth)





  - measurement of cell status (live/stressed/dead)

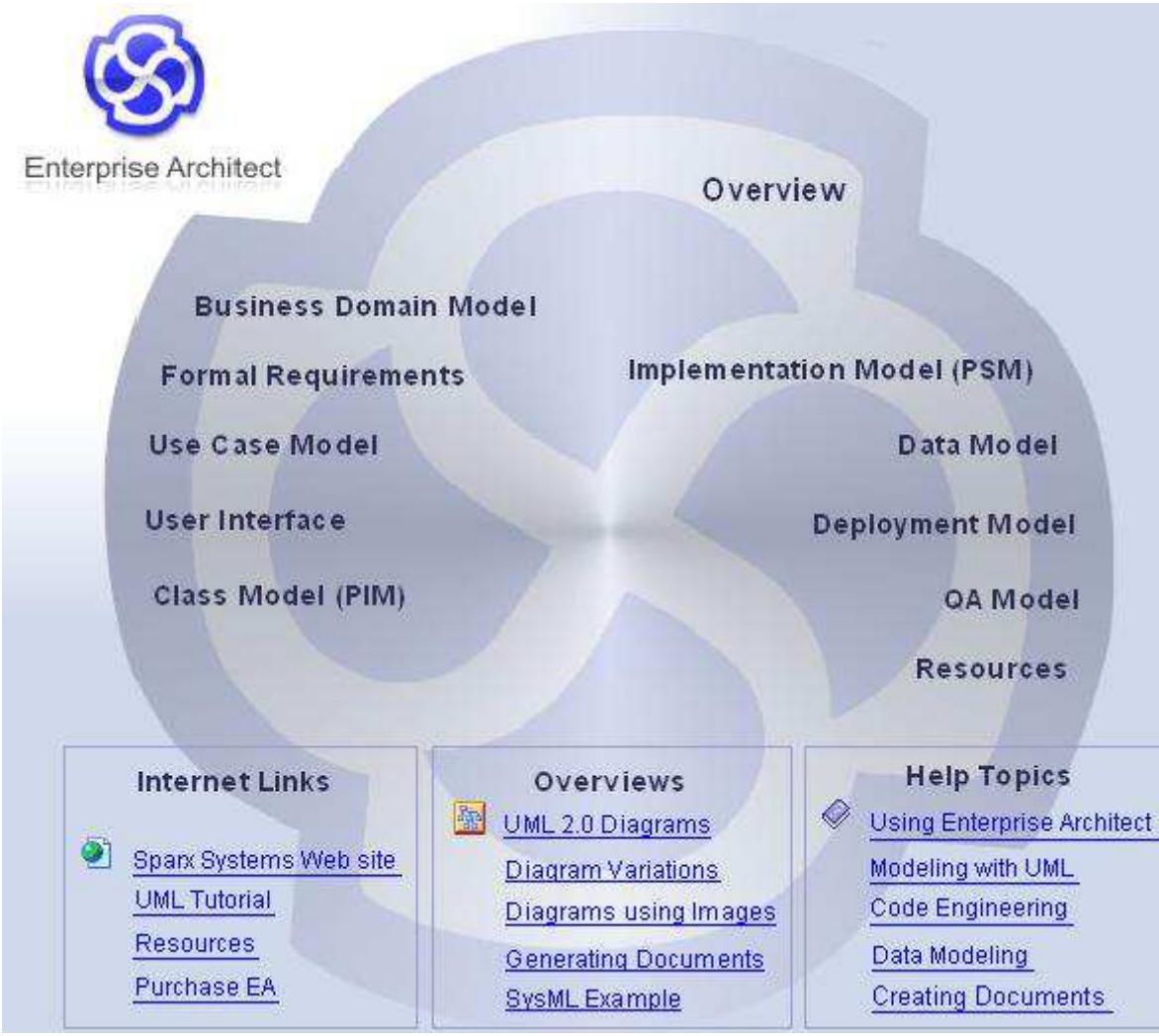
- Biochemical:
  - measurement of factors (e.g. impedance) which allow analysis of cell death, cell stress or cell growth

Way of work with the requirements in the project

- Software Tool: SPARX Systems' Enterprise Architect (EA)
  - UML tool with free viewer – can be used for the entire project
  - Correct price
  - Build a common EA model that includes requirement model
  - Version control sw. is running at IPA and easy to integrate with EA
  - Document generation, xml export/import
- Templates (requirements + use cases)
  - These templates are used :
    1. to confirm elicited requirements and use cases by the experts
    2. to gather new requirements from the experts
    3. to formulize their know-how about the details of the processes

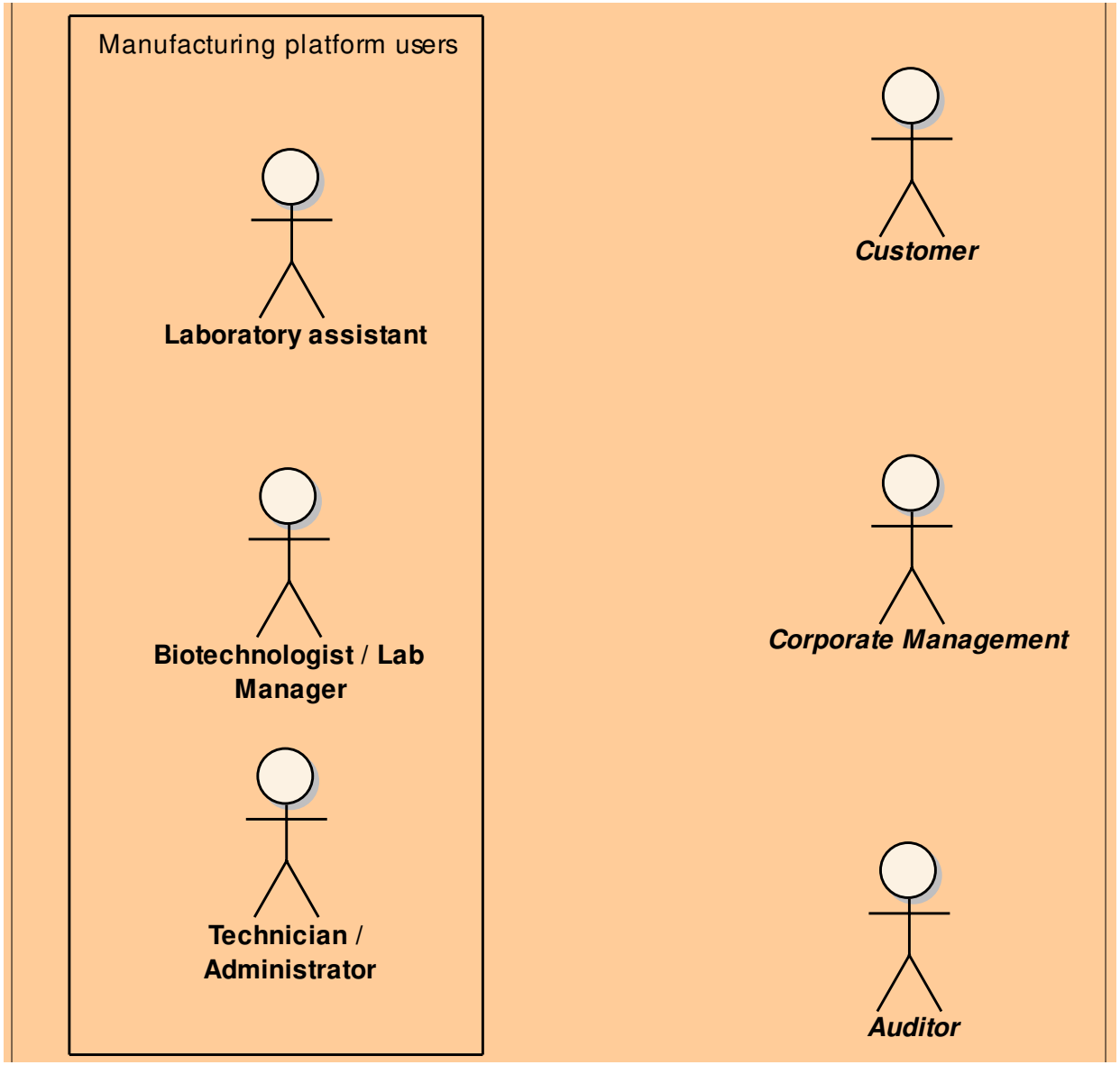
Main elements of the EA requirement model

- Business Process Model
  - Actors
  - Topology
  - Business workflows
- Requirement Model
  - Features
  - Non-functional requirements
  - Functional requirements
- Use Cases

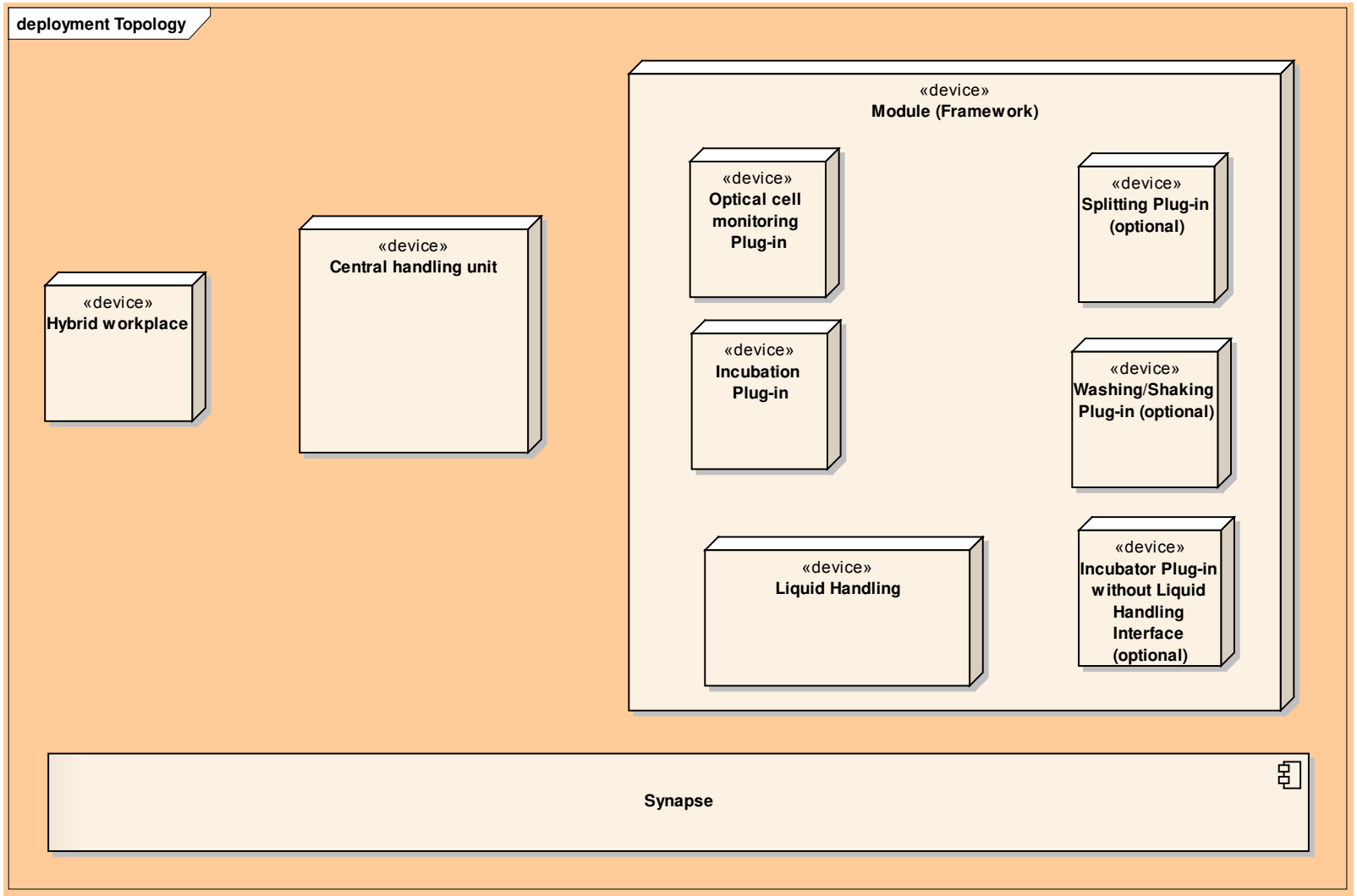


Actors

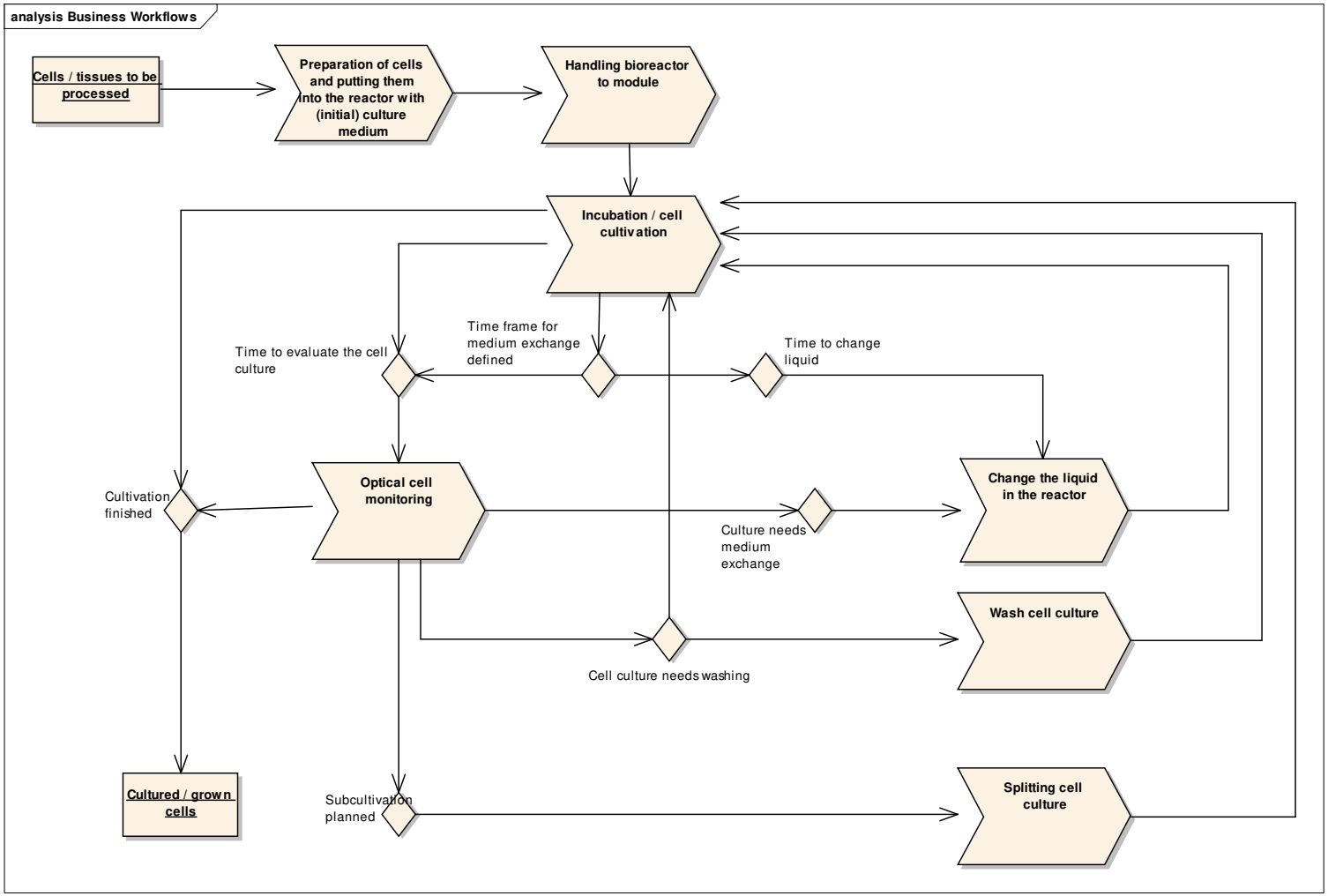
Stakeholders



Topology

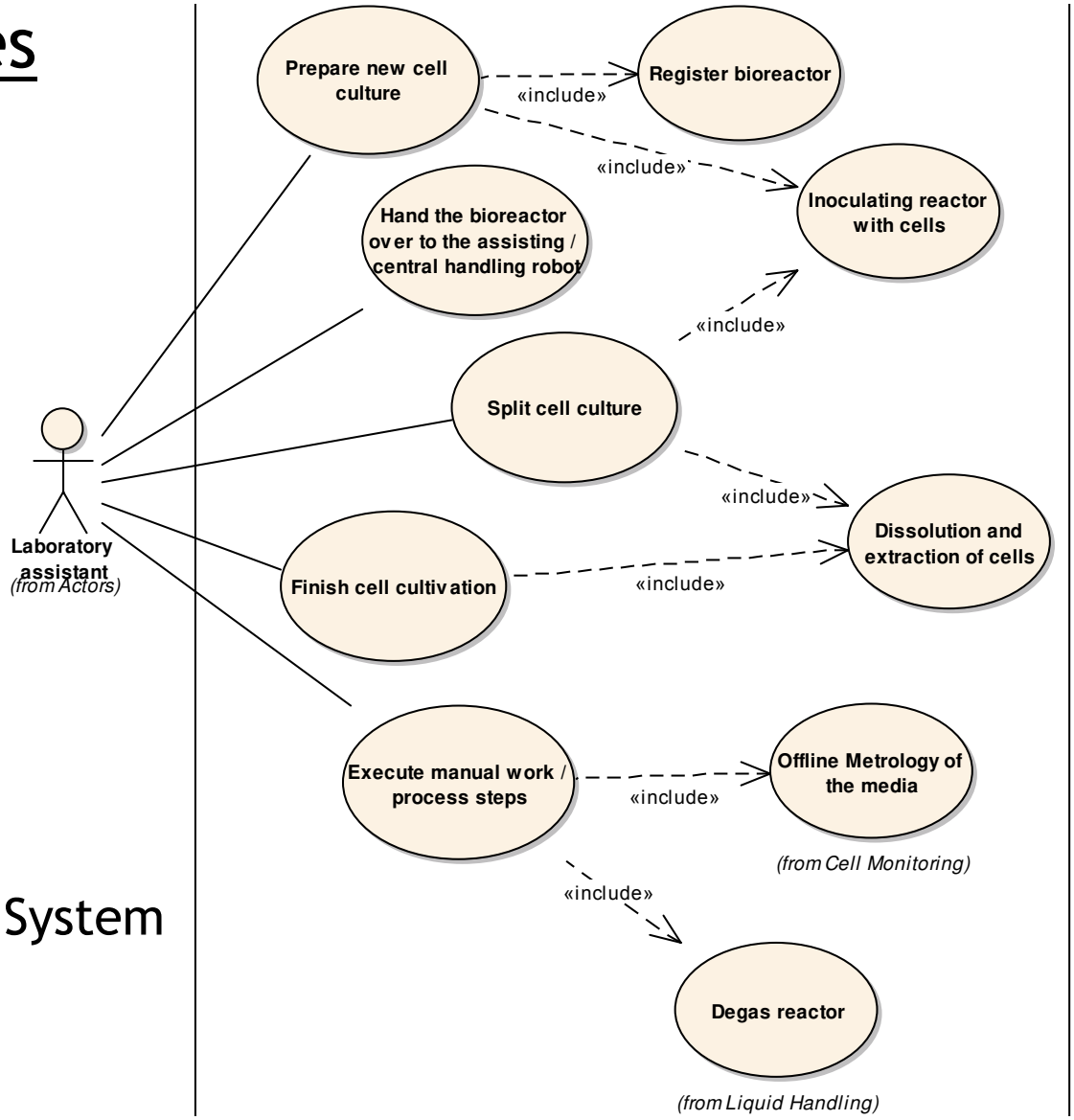

deployment Topology
«device»
Module (Framework)
«device»
Optical cell monitoring Plug-in
«device»
Splitting Plug-in (optional)
«device»
Hybrid workplace
«device»
Central handling unit
«device»
Incubation Plug-in
«device»
Washing/Shaking Plug-in (optional)
«device»
Liquid Handling
«device»
Incubator Plug-in without Liquid Handling Interface (optional)
Synapse

Main business workflow: cell cultivation



Groups of Use Cases

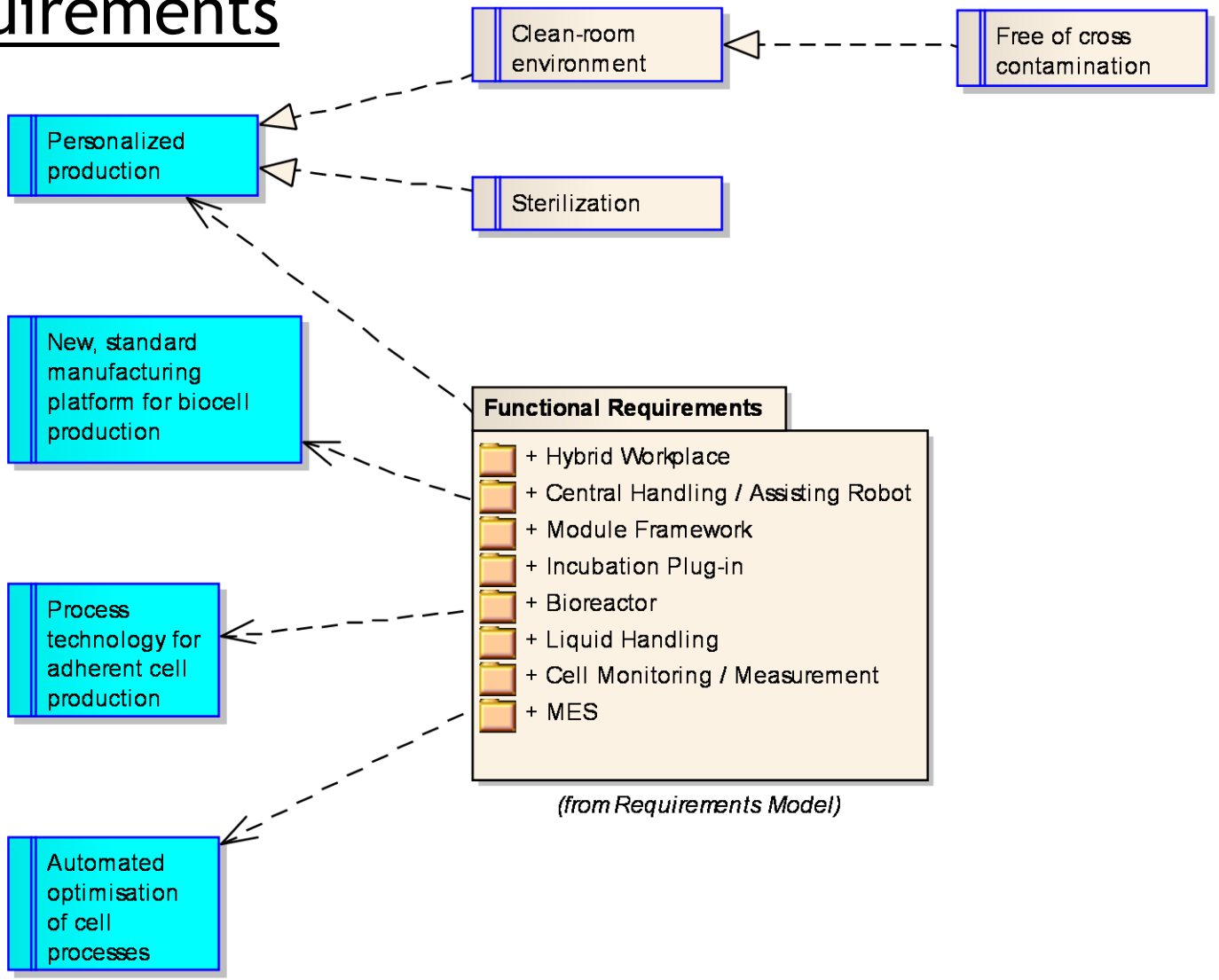
- Hybrid Workplace
- Central Handling
- Module Framework
- Incubation Plug-in
- Bioreactor
- Liquid Handling
- Cell Monitoring
- Manufacturing Execution System



Requirements in Enterprise Architect

- Strongly structured requirement graph
- Types:
  - Features tends to be a “higher-level” objective than a requirement - and is usually more focused on business needs rather than implementation.
  - Functional requirements specify actions that a system must be able to perform, without taking physical constraints into consideration
  - Non-functional requirements describe only attributes of the system or its environment, e.g. usability, reliability, performance (as efficiency, availability, throughput, response time), testability, maintainability, configurability etc.

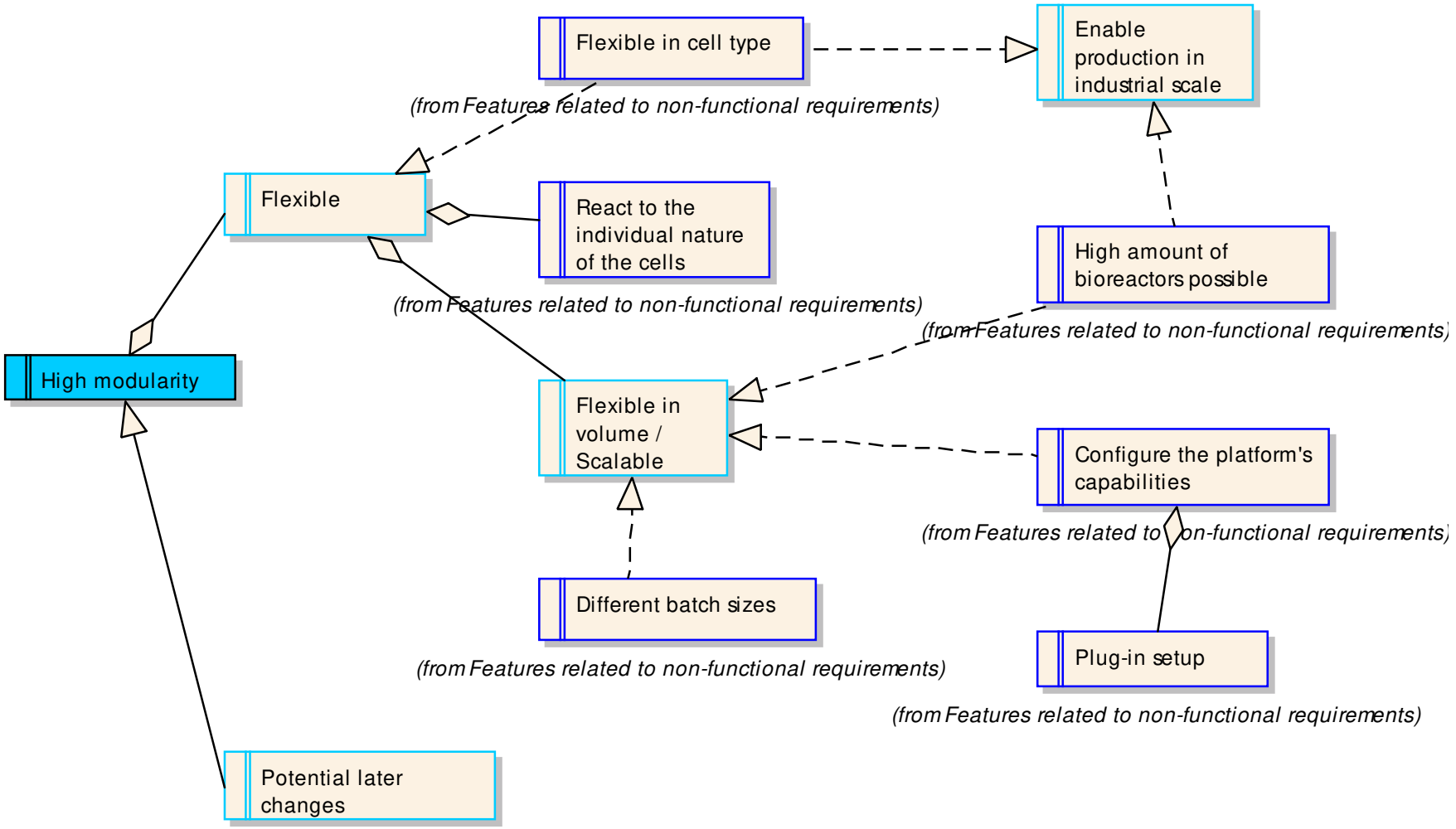
Features collecting different functional requirements



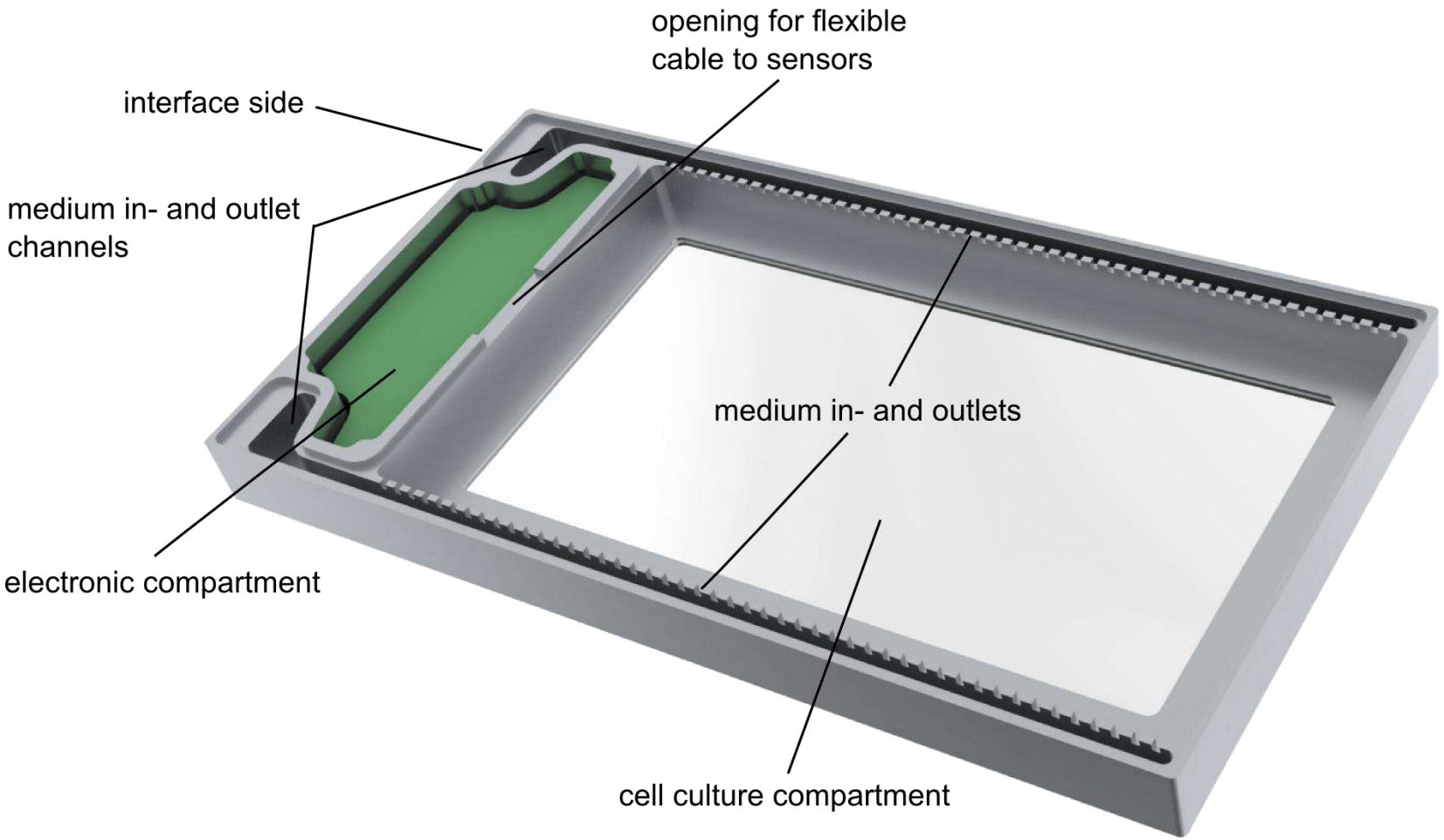
Features related to non-functional requirements

- surface modification
- Reduce rejection
- IPA_5.3 Cost efficiency
- Flexible in cell type
- React to the individual nature of the cells
- High amount of bioreactors possible
- Configure the platform's capabilities
  - Plug-in setup
- Different batch sizes
- Traceability
- Keep Good Manufacturing Practice
  - Assure consistent execution
- High reproducibility
- IPA_5.1 Standard manufacturing technologies
  - IPA_5.2 Standard tools

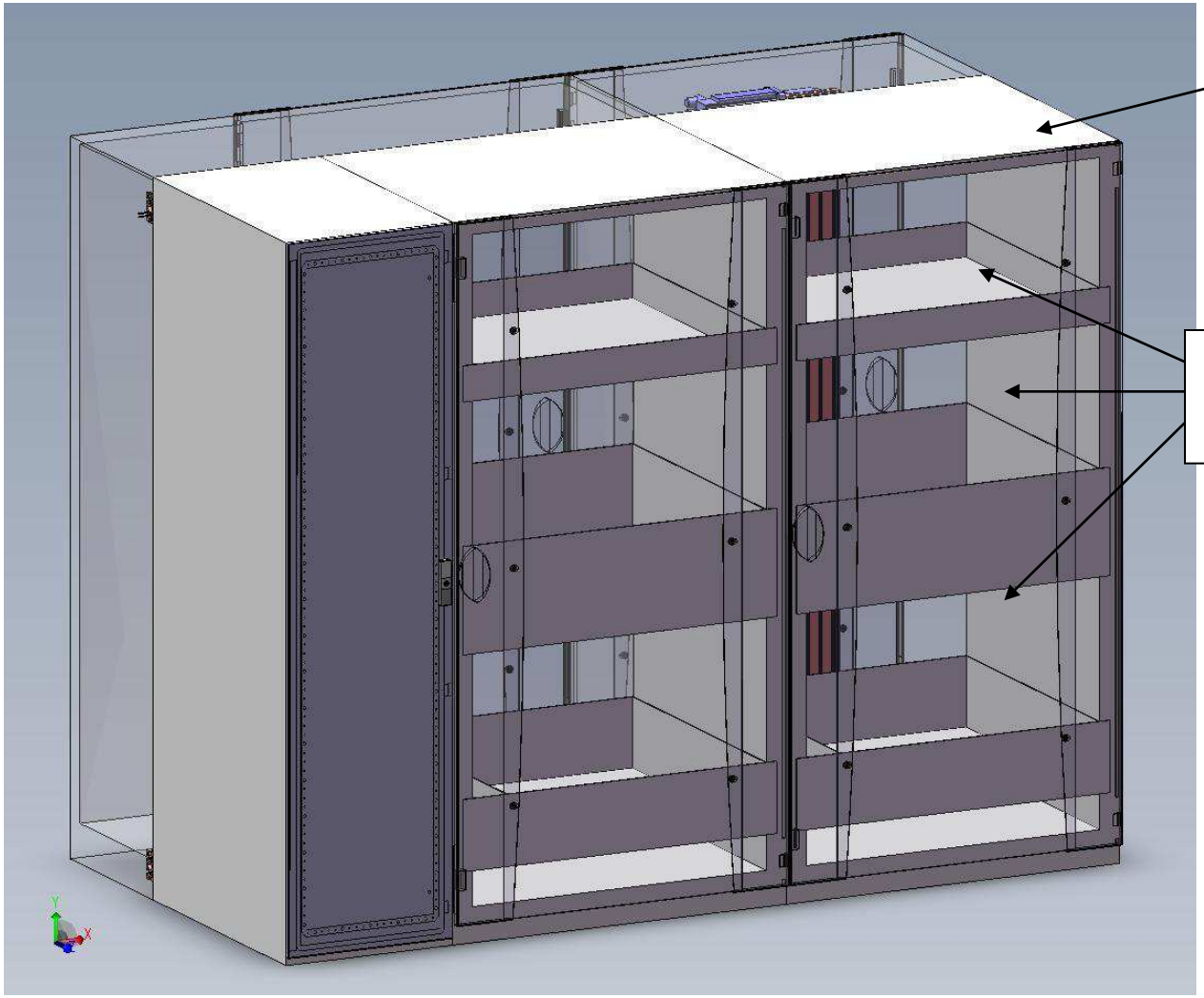
Example of a non-functional requirement



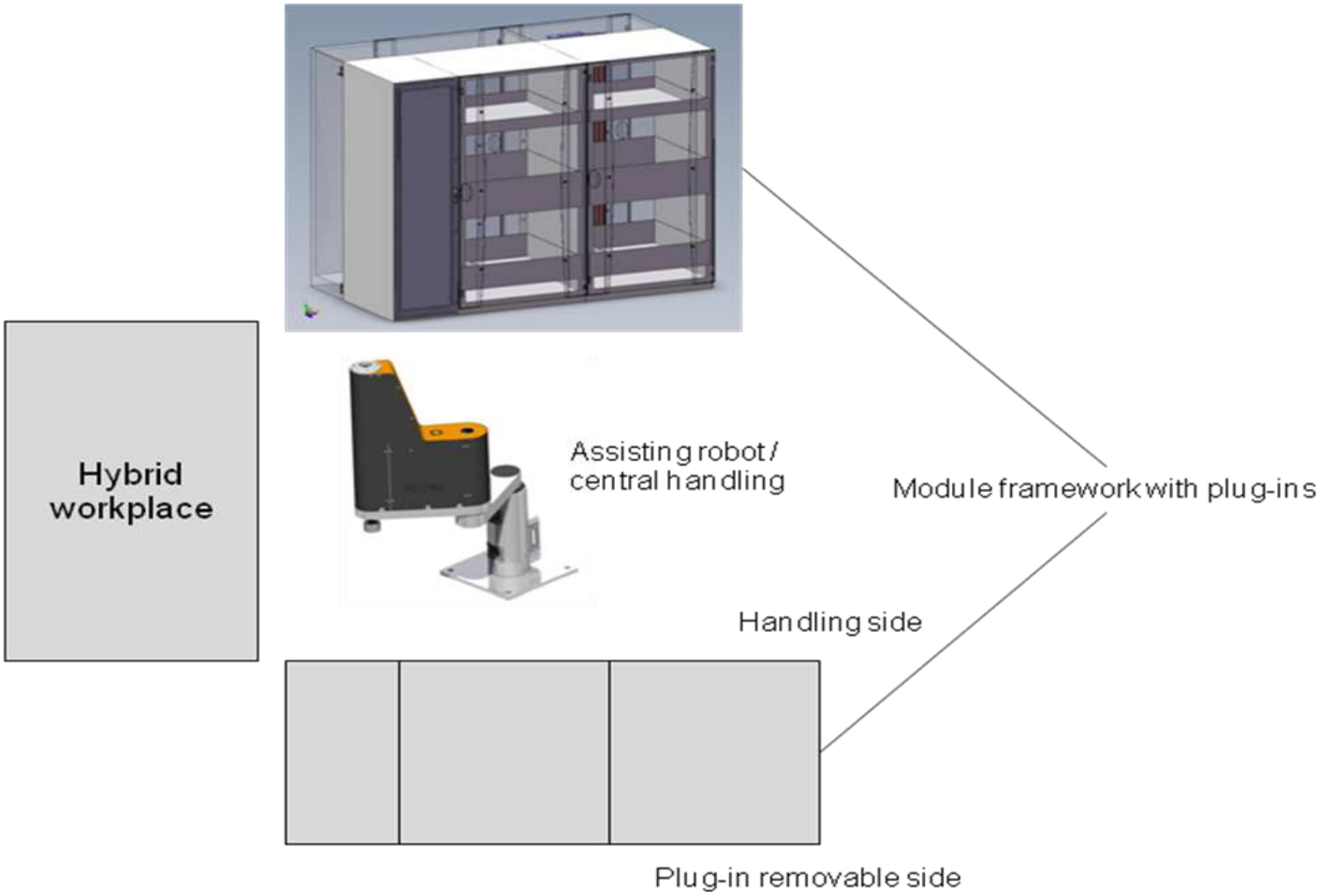
Early results: bioreactor



Early results: module workplace



Early results: Overall platform structure



Early results: liquid handling system