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Progetto standard co-finanziato dal Fondo europeo di sviluppo regionale
Standardni projekt sofinancira Evropski sklad za regionalni razvoj

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01

3. SCIENTIFIC AND RESEARCH REPORTS

High Content Analysis (HCA) - Use in Biotechnology

High-content analysis systems, also known as high-content screening systems, address a range of research applications from basic science to drug discovery screening. Paired with advanced analysis software, HCA systems provide high quality 3D imaging for enhanced live cell analysis. Examples are high-content screening system with the built-in incubator that lets you analyse extended live cell responses, highest quality confocal images and extended live cell imaging. HCA systems are accompanied with powerful machine learning functions analysis software that provides researchers with advanced insights into their HCA experiments such as label-free analysis.

In the context of the TRAIN project, HCA was used to evaluate several factors, including cell composition, cell viability, migration, angiogenesis, hypertrophy. HCA was used to evaluate cell composition, proliferation, apoptosis, viability, angiogenesis, fibrosis through myofibroblast activation and collagen secretion (GFP RFP mice), cardiomyocyte hypertrophy. Cell composition was evaluated using cell-specific antibodies CD31 or ERG for endothelial cells. Vimentin for fibroblasts and Troponin for cardiomyocytes cells can be
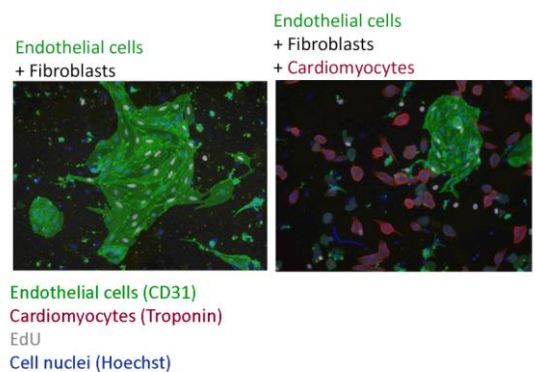

Figure 1: Cell proliferation and cell position as seen with the HCA system in the TRAIN project.

isolated from transgenic mice expressing cell type-specific fluorescent reporters expression of green or red fluorescent protein (GFP, RFP) for example under the control of a collagen promoter to identify fibroblasts or under the control of a PDGF promoter to identify endothelial cells.

Project resource - Report on HCA for 2D culture of heterogeneous culture

Other examples of use

In recent years a substantial development has been made in the field of cell-based screening, such as the emergence of stem cell technologies, micro tissues, organoid models and organ-on-a-chip platforms. With the relevance of 3D cell model systems and associated technologies, such systems may enable important advances in drug discovery and fundamental biology of the future as the example shows below.
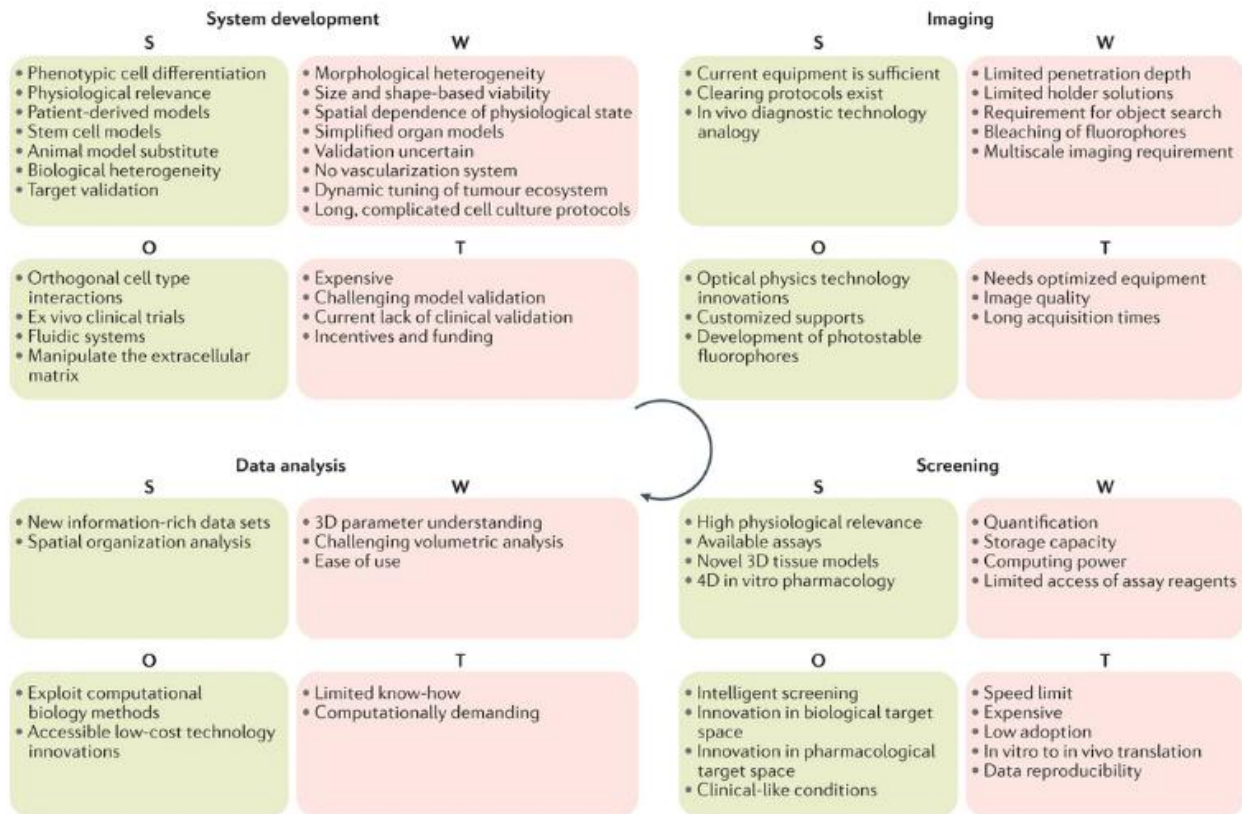
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Figure 2: Concerns, challenges and promises of high-content analysis of 3D cellular models (Carragher et al., 2018)

Another example of use of High Content Analysis is current state of the art phenotypic screening in cells. This scientific article describes approaches to cell-based high-content screening, the design and execution of screening experiments, data analysis and exploration. It highlights advances in fluorescence-labeling techniques and opportunities to use genome engineering to create novel markers for image-based screens.
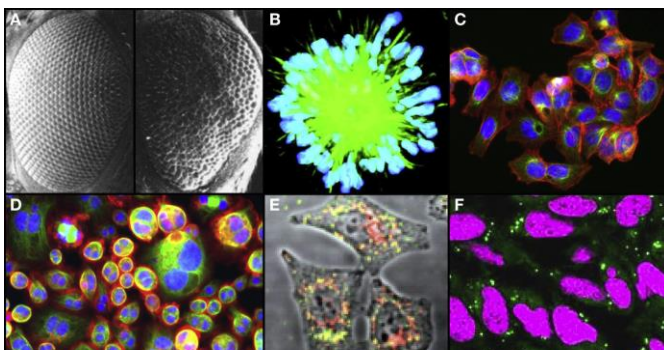

Figure 3: Cell based high content screening (Cell, Issue 6, 2015)

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VR TRAIN – a Virtual Reality simulation

The VR TRAIN virtual reality simulation was developed by Technology park Ljubljana in collaboration with [TovarnaTech](#) (Vrooooom produkcija) for the purposes of the project TRAIN, Interreg Italia-Slovenia. The aim of the simulation was to interactively and demonstrate how drugs for the treatment of heart disease are developed. The simulation starts with a presentation of laboratory procedures and equipment needed for finding molecules with therapeutic activity, using the method of high throughput screening. It also offers a view into the microscopic realm, where the user can see different effects of drug molecules on heart cells such as proliferation of heart cells, formation of blood vessels and degradation of fibrotic tissue. In the end, the user can cure a patient with heart disease using drugs that were developed beforehand. The simulation opens a door into the virtual world where it provides a rich and educational experience to gain insight into scientific research and build awareness regarding heart disease.

VR TRAIN simulation can be viewed at the following [link](#). It was also presented at several events related to TRAIN (Trieste NEXT 2019, Meet in Italy for Life Sciences 2019).

Big Data Analytics (BDA)

Big data analytics (BDA) is exciting new technology for mining big and complex data. BDA can handle different aspects of complexity, different types of structured outputs such. Big data and data streams, partially annotated data, network data and the so called deep learning can produce accurate and understandable models. Machine learning is the core of Artificial Intelligence and its focus is gaining knowledge from data also known as Data Mining and Data Science. Some examples are shown below.

Predictive modelling

Predictive modelling is a process that uses [data mining](#) and [probability](#) to forecast outcomes. Each model is made up of a number of predictors, which are variables that are likely to influence future results. Once data has been collected for relevant predictors, a statistical model is formulated. The model may employ a simple linear equation, or it may be a complex neural network, mapped out by sophisticated software. When additional data becomes available, the [statistical analysis](#) model can be validated or revised.

Predictive modelling has many applications in business and elsewhere. Example shown below is applied in medical diagnostics such as for predicting neurodegenerative diseases i.e. Alzheimer's disease. Predictive models focus on a target variable and predict its value from the values of input variables organised in a decision tree as shown in the example below:
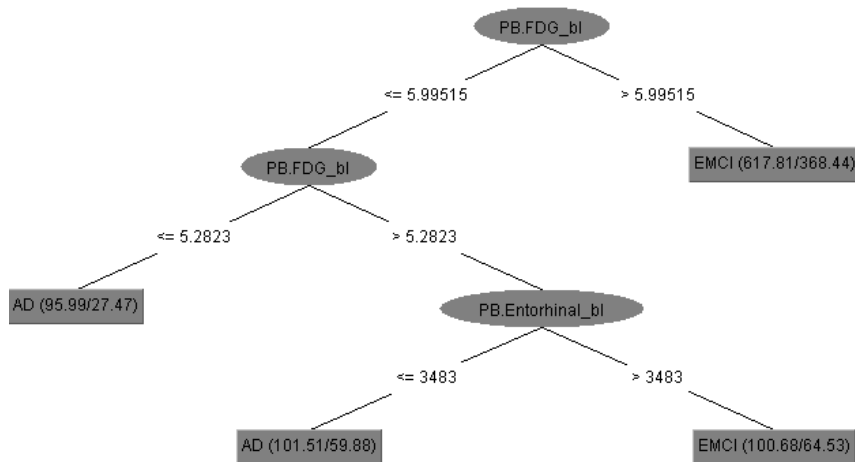
Figure 4: Decision tree for diagnosis

The decision tree takes as input values of attributes / independent variables. Researchers follow branches according to the values of these variables until one reaches a leaf. An example of using predictive modelling in medical diagnostic is a decision tree for diagnosing Neurodegenerative diseases where possible values are:

1. CN-Cognitively Normal

2. SMC-Significant Memory Concern

3. EMCI-Early Mild Cognitive Impairment

4. LMCI-Late Mild Cognitive Impairment

5. AD-Alzheimer's Disease

Other Life sciences examples with BDA were presented in the project TRAIN such as: Habitat modelling with Slovenian rivers, Soil micro arthropods in Danish farm soil, Vegetation in Victoria Australia, Predicting gene functions In model organisms *Arabidopsis thaliana, Saccharomyces cerevisiae*, Multi-Target Prediction for Virtual Compound Screening, *Mus musculus*, in bacterial genomes.

Detailed description of the applications of the predictive modelling in medical diagnostic and other domains can be found in video lectures and presentations provided in the scope of the TRAIN project.

Project resources:

- [Research profile of JSI](#)

- [Report on IT services of JSI](#)

- Machine learning for environmental and life sciences (Lecture by Sašo Džeroski PhD), TRAIN Seminar, Ljubljana, April 2019 (Videolecture, ppt)

- Multi-Target Prediction with Trees and Tree Ensembles (Lecture by Sašo Džeroski PhD), TRAIN Workshop, Bled, May 2019 (Videolecture, ppt)