CellH5: a format for data exchange in high-content screening

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ABSTRACT

Summary: High-throughput microscopy data require a diversity of analytical approaches. However, the construction of workflows that use algorithms from different software packages is difficult owing to a lack of interoperability. To overcome this limitation, we present CellH5, an HDF5 data format for cell-based assays in high-throughput microscopy, which stores high-dimensional image data along with inter-object relations in graphs. CellH5Browser, an interactive gallery image browser, demonstrates the versatility and performance of the file format on live imaging data of dividing human cells. CellH5 provides new opportunities for integrated data analysis by multiple software platforms.

Availability: Source code is freely available at www.github.com/cellh5 under the GPL license and at www.bioconductor.org/packages/release/bioc/html/hdf5.html under the Artistic-2.0 license. Demo datasets and the CellH5Browser are available at www.cellh5.org. A Fiji importer for cellh5 will be released soon.

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1 INTRODUCTION

Recent advancements in microscope automation enable high-content screening at unprecedented throughput and spatio-temporal resolution. Cell-based assays typically involve segmentation of individual objects (cells) within the imaging field, followed by quantification of cell morphologies (Conrad and Gerlich, 2010). Powerful algorithms have been developed for learning-based segmentation (Sommer et al., 2011) and quantification and classification of cell morphologies (Boland and Murphy, 2001; Carpenter et al., 2006; Eliceiri et al., 2012; Held et al., 2010; Walter et al., 2010). Application of any of these methods to large-scale biological data requires sophisticated workflow management and efficient batch processing, for which different software platforms have been developed (Carpenter et al., 2006; Eliceiri et al., 2012; Held et al., 2010; Jones et al., 2008). In practice, the analysis often asks for the combination of methods that are available in distinct software platforms. Integration by re-implementation into a single platform is inefficient and error prone. A preferable approach is integration by interoperability of tools. Here, we propose a versatile data format for serialization, disk-based storage and exchange of high-content screening data and processing results. This provides a flexible and sustainable solution for the development of integrated analysis pipelines based on multiple software platforms.

To facilitate the exchange of microscopy image data, the Open Microscopy Environment project (OME) has developed a standardized file format, OME-TIFF (Linkert et al., 2010), which can store raw microscopy images along with experimental meta-information (Supplementary Table S1). Semantically typed data hypercubes (Millard et al., 2011) have been proposed to store multi-dimensional high-content screening data in a hierarchical fashion based on Extensible Markup Language and the HDF5 data model, which is optimized for efficient storage and rapid access of large-scale multi-dimensional data. However, complex object relationships, as, for example, lineage trees of dividing cell populations that can comprise millions of cells objects, cannot be efficiently processed when stored in textual data formats such as Extensible Markup Language used in OME-TIFF and semantically typed data hypercubes.

Object relations are represented by network graphs, following standard formats such as GraphML (Brandes et al., 2001) and GraphViz (Ellson et al., 2002). These text-based formats, however, are designed mainly for visualization of graphs and cannot be efficiently enriched with high-dimensional binary data. An integrated data format representing both machine-readable graph structures and multivariate object features has not been reported in the field of bioimaging. With CellH5, we introduce an efficient mechanism, representing both object relations in graphs along with high-dimensional object data.

2 FORMAT SPECIFICATIONS

CellH5 contains four major components: images, objects, object relations and features (Fig. 1, Supplementary Figs S1–S3). Objects of different categories, e.g. cells or cell organelles like nuclei or vesicles, are initially derived by segmentation within the original images. Relations between these objects then define higher-level objects, e.g. cell organelles, which can be related to define cells, or cell objects can be related across time frames to define lineage trees. The resulting object graphs are stored by adjacency list in HDF5 datasets for fast index access.

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object features (Supplementary Table S2) and comprises convenient high-level access to object graphs and associated implemented in the cellh5 module of CellH5, which provides 2010) and CellH5. The Application Programming Interface is within the open-source frameworks CellCognition (Held et al., 2010) and visualized as series of single cell images with overlaid segmentation contours and class annotations (Supplementary Fig. S4). We further exploited the versatility of CellH5 to investigate the fate of dividing cells on perturbation of mitotic regulators (Supplementary Fig. S5). Cell trajectory plots indicated that RNA interference (RNAi)-mediated depletion of the mitotic motor protein KIF11 frequently induced prolonged prometaphase followed by mitotic cell death, whereas depletion of the mitotic checkpoint protein Mad2 led to a short mitosis, often followed by cell death in the subsequent interphase. These observations are consistent with the known phenotypes, indicating the feasibility of accurate cell fate profiling based on CellH5.

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