

**SEBIOT-SBS: Current Challenges in Biomolecular Screening
Madrid, 13-14 November 2003**

Oral presentation on Friday 15th

Session 5: From Proteins to Cells: Accelerating Cell Biology

Solutions for the Challenges in High-throughput Cell Based Screening

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High information content screening (HICS) is a widely interpreted concept.

Minimalistically, HICS can be defined as screening campaigns in which 'more than one' endpoint is being recorded per assay entity. With microscopic readers, HICS became the process of automated image acquisition, image segmentation and the reduction of images to quantitative data.

Today's more ambitious view for HICS, is that of a technology that allows reading and quantifying the *full complexity of biological phenomena* such as proteins being expressed and transported to their 'workplace' to follow their interactions inside organelles and cells. To quantifying the multiple signalling pathway components that control and execute cell division, cell death, gene expression, cell motility, cell positioning in tissue, plant or animal models and ultimately, quantifying the modulating effects of drug candidates on the aforementioned events.

This trend from simple, single endpoint to complex multi-endpoint reading of a wider variety of features in cells or multi-cellular models has lead to a need for microscopic readers with better integration of the dimensions space and time with a novel blend of precision, sensitivity, flexibility and speed.

In this presentation, we will focus on microscopic reader technologies for fast reading of very weak fluorescent signals without induction of photo-toxicity, to achieve automated image acquisition for multiple *brightfield and fluorescent microscopy modes* assays in parallel and/or over time.

Examples will be given of the following enabling image acquisition and analysis software applications. Background-independent object identification in brightfield images of live cells that are distorted by air-liquid meniscus effects in the well, for automated quantification of monolayer confluency, cell-cell adhesion and neurite formation in *unlabeled live cell based assays*.

Robust object-based auto-focusing on subcellular structures that contain extremely weak fluorescent signals, as an alternative for 'hard autofocus' at an off-set above the plate bottom. Robust object identification and signal quantification in 'low-light' images with low signal to noise ratio.

Finally, we will address integration solutions that allow fast transition from 'hands-on' reading for assay development to 'plate stack to database ready' level automation in one work environment for genomics, cytomics, cytochemistry and drug discovery.