Analytical Imaging System and Process

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SUMMARY
This invention was made by Dr. Robert Silver of the Marine Biological Laboratory in Woods Hole, MA. It provides for observation of living cells using a light microscope equipped with a beam splitter such that one beam is used to provide a standard visual image and the second beam is manipulated to yield only light of a given wavelength, degree of polarization or orientation. This second beam can be used to provide information on specified cellular processes such as calcium release and movement as indicated by an ionsensitive potonic reporter such as aequorin. The separate images from the two beams can be simultaneously recorded and subsequently combined and otherwise analyzed. This invention is covered by U.S. Patent #6,078,681 that issued 6/20/2000.

TECHNOLOGY
Living cells and tissues perform and coordinate hundreds to thousands of individual processes and control the location, orientation, and state of assembly of many structural components in the course of normal life. These processes are usually performed by specialized groups and classes of molecules. Biologists have used light microscopes to study these processes, both in living cells and in cells that have been preserved at particular points in the cells' lives. Study of these processes or structures involves the detection of molecules or reactions as signals that are often processed and analyzed to help the biologist learn and understand the particular process or structure. Such detection typically relies on a characteristic interaction of light with the molecules responsible for the process or structure that is subject to study. Because the molecules of interest are dynamic in living cells and interact with similar and dissimilar components, it is desirable to study the relationship of a component with one or more components in a cell.

The present invention includes an image processing system and process for imaging a specimen during an activity, such as biological, physical, or chemical activity, to analyze the specimen during the activity. The system receives and records different spectral images, preferably a visible image and a low intensity photonic image, and synchronously records them, preferably in real time on an image-recording disk recorder. These images can be displayed later in juxtaposition or in superposition and processed for further analysis.

In preferred embodiments, the system includes an image receiving device that includes a microscope with at least one beam-splitter. One output from the beam-splitter provides a visual image, while another output is filtered to pass only photons of a characteristic wavelength, phase, or orientation as a result of the activity. These images are preferably recorded with cameras with frame sampling times and rates synchronized by a common timing device. The cameras may operate at the same video field and frame rates or at integral multiples of such video field or frame rates to achieve increased temporal resolution for a given spectral band or other optical property of the specimen being observed. The image at the back focal plane of the objective lens may be directed to any camera

in the system with a Bertrand lens or similar device to provide the diffraction image of the specimen.

The data is digitized and then processed and analyzed by an image processing system that may be at the site of the activity or remote. The image processing system is programmed to analyze the image data, and to store and classify signals to establish spatial and temporal signatures of the observed activity. These signatures are accumulated and stored together to provide a library of signatures. The observed activity can be displayed on-line and an also be continuously compared with the signatures stored in the library to determine a correspondence or correlation as an activity is progressing. Variables that affect the activity, such as chemicals or other conditions such as heat or light can be modified to control that activity while the specimen is under observation.

In an exemplary application of this system and process, a visible image is that of a reproductive division (mitosis) produced by a microscope (e.g. with a signal influenced by changes in the localized refractive index as revealed through the use of polarized light or through methods of phase contrast enhancement, such as phase contrast, differential interface contrast, or modulation contrast optics). Another image indicates an interaction of specific ions or other compounds, such as calcium, with an ion-sensitive photonic reporter or other suitable means. Thus, a spatial-temporal image of photons attributable to and indicative of the presence of particular ions or other components at a characteristic concentration is recorded during mitosis.

INVENTOR(S):
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