CLAIMS:

1. A microscope comprising:

a fiducial image mask (110) that is capable of being illuminated on one surface and that is positioned a focal length from a fiducial lens (108);

an objective lens (112) that is positioned on an axis that is common to a detector lens (104);

a beam splitter (106) that is positioned between the objective lens (112) and the detector lens (104), wherein the beam splitter (106) is capable of receiving optical energy from the fiducial lens (108) and capable of directing the optical energy to the objective lens (112); and a detector (102) that is positioned a focal length from the detector lens (104) and that is capable of receiving optical energy that is reflected from a plurality of partially reflective surfaces, wherein the reflected optical energy is directed through the objective lens (112), the beam splitter (106), and the detector lens (104),

characterized in that the fiducial image mask (110) comprises an array of lines or circles, the array of lines forms a checkerboard pattern.

2. A microscope comprising:

a flow cell having a substantially planar inner surface region, wherein the flow cell has a fluidic channel (120) that is operative to carry a fluid; a fiducial image mask (110) capable of producing a collimated beam and coupled to a beam splitter (106) that is capable of directing the collimated beam to an objective lens (112) and onto a substantially planar region of the fluidic channel (120) that is located at an adjustable distance from the objective lens (112); a detector lens (104) that is on a common optical axis with the objective lens (112) and capable of receiving reflected optical energy from the substantially planar region, wherein the reflected optical energy is capable of passing through the beam splitter (106), and thereafter to a detector lens (104) and a fiducial detector that is positioned a detector-lens focal length from the detector lens (104); an optical source for exciting fluorescent labels in the flow cell; and one or more fluorescent-label optical paths coupled to fluorescent label optical energy in the common optical axis, wherein each fluorescent-label optical path is capable of directing a particular range of wavelengths to an associated fluorescent

label detector;

wherein the adjustable distance from the objective lens (112) to the substantially planar region is operative to provide a focused image of a fiducial pattern onto the fiducial detector; and

wherein the one or more detectors of each fluorescent-label optical path is operative to provide a focused image of fluorescent labels attached to a surface of the fluidic channel (120) when the optical source is enabled,

characterized in that the fiducial image mask (110) comprises an array of lines or circles, the array of lines forms a checkerboard pattern.

3. The microscope as claimed in 2, wherein the detector is capable of receiving optical energy that is reflected from a plurality of partially reflective surfaces, wherein the reflected optical energy is directed through the objective lens (112), the beam splitter (106), and the detector lens (104).

4. The microscope as claimed in 1 or 3, wherein

the plurality of partially reflective surfaces comprise a fluidic channel (120) having at least one planar region.

5. The microscope as claimed in 1 or 3, wherein

at least one of the plurality of partially reflective surfaces has an index of refraction that is at least 1% greater or smaller than an index of refraction of a different partially reflective surface.

6. The microscope as claimed in 1 or 3, wherein

at least one partially reflective surface is formed by a fluidic channel (120) that has a substantially planar inner surface.

7. The microscope as claimed in 1 or 3, wherein the detector is a 2D array of photodetector cells that are operative to form (a) 2D images of reflected fiducial optical energy and also (b) 2D images of direct fluorescent label energy from at least one of the plurality of partially reflective surfaces.

8. The microscope as claimed in 1 or 2, wherein the beam splitter (106) is positioned at an approximately 45 degree angle with respect to an axis of the

objective lens (112) and the detector lens (104).

9. The microscope as claimed in 2, wherein

the fiducial detector controls the adjustable distance to form a focused image at the fiducial detector; or

the substantially planar region of the fluidic channel (120) is an upper surface of the fluidic channel (120); or

each fluorescent-label optical path comprises a dichroic reflector, a detector lens (104), and a detector; or

a fluidic path has a change in index of refraction of at least 10% in a region perpendicular to the substantially planar region.

10. A method for imaging fluorescent labels in a fluidic channel (120) having a reflective interface adjacent to the fluidic channel (120),

wherein the method is operative in a microscope having an objective lens (112) that is an adjustable distance from the reflective interface, a fiducial pattern generator capable of coupling a collimated fiducial pattern through the objective lens (112) and onto the reflective interface, a detector lens (104) and fiducial detector that are capable of receiving optical energy that is reflected from the reflective interface and capable of forming an image at the fiducial detector, and one or more fluorescent-label optical paths capable of receiving optical energy from the fluorescent labels at the reflective interface,

the method comprising:

(a) activating the fiducial pattern generator;

(b) adjusting the distance from an objective lens (112) to the reflective interface until a focused image is present at the fiducial detector;

(c) applying a fluorescent label optical source to cause the fluorescent labels to fluoresce; and

(d) forming a focused image of fluorescent labels at each fluorescent label detector of a respective fluorescent-label optical path;

characterized in that the step of adjusting the distance from the objective lens (112) to the reflective interface step is performed with an alternating checkerboard fiducial pattern, wherein the alternating checkerboard is formed using a series of fine lines and large gaps, wherein the fiducial detector causes the distance from the objective lens (112) to the reflective interface to be varied until the fiducial detector senses a focused image that is based on resolving the alternating checkerboard pattern, wherein the fiducial detector causes the distance from the objective lens (112) to the reflective interface to be varied in the same direction until individual lines of the checkerboard are focused.

11 The method as claimed in 10, wherein the fiducial pattern generator is not enabled when the fluorescent label optical source is enabled.

12. The method as claimed in 10, wherein the fluidic channel (120) has an upper surface and wherein the reflective interface is adjacent to the upper surface of the fluidic channel (120).

13. The method as claimed in 10, wherein each fluorescent-label optical path comprises a dichroic reflector that is operative to reflect a particular range of wavelengths and to pass other wavelengths, wherein each dichroic reflector is directing a particular range of wavelengths to a respective detector lens (104) and to a respective fluorescent label detector.

14. The method as claimed in 10, wherein the fiducial detector uses a change in a width of fiducial features and a change in a peak-to-peak amplitude to determine whether to increase or decrease the distance between the objective lens (112) and the reflective interface.