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Stanford group creates miniature self-contained fluorescence microscope

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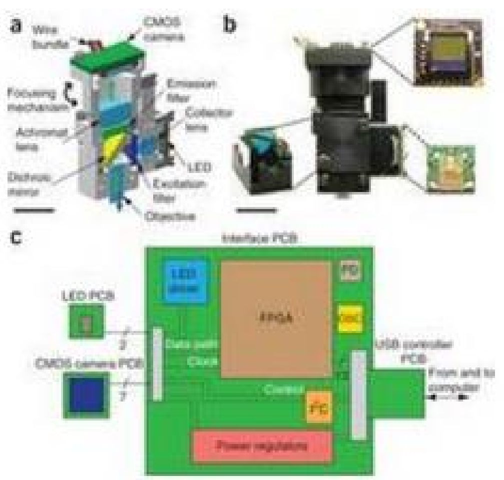

Design and fabrication of an integrated fluorescence microscope. Image: NPG, *Nature Methods* (2011) doi:10.1038/nmeth.1694

(PhysOrg.com) -- A team of researchers working at Stanford University have devised a means for building the smallest self-contained fluorescence microscope ever. Weighing just under 2 grams and slightly larger than the end of a pencil, the new microscope is small enough to attach to a mouse head, which means researchers can watch the mouse brain in a natural setting. Led by Mark Schnitzer and Abbas El Gamal, the team describes its findings in *Nature Methods.*

Till now, most brain researchers have had to use so-called bench-top microscopes, which are what they sound like; microscopes that sit on a bench. This requires that specimens be brought to the microscope (and held still) for examination. This new microscope turns that whole process around in that it allows the microscope to be brought to the specimen, allowing researchers to study the brain in ways that have not been possible before. The team reports that they have already discovered new capillary dilation properties in mouse brains.

The fluorescence microscope differs from traditional microscopes in that it looks at material that has a fluorescence property, i.e. is fluorescent (the emission of light by a material when exposed to radiation). To take advantage of this property specimens must be either naturally fluorescent (such as certain proteins) or stained with a fluorescent material. The approach is similar to that seen when a black-light is used to illuminate semen or blood samples at crime scenes. The light sources used in a fluorescence microscope are typically xenon arc or mercury-vapor lamps.

The miniaturized microscope developed by the team is comprised of mass produced parts, which the team says will allow for it to be mass produced at a much lower cost than standard bench-microscopes, opening the door to research at places that have up till now lacked the funds to purchase the more expensive equipment.

Researcher Mark Schnitzer demonstrates the microscope's tiny size and weight.

One downside to the new microscope is that its resolution isn’t quite as good as standard bench models; 2.5 microns as opposed to 0.5. But it does have a larger field of view, which means that most serious labs would likely want to have both types of microscopes, depending on what is being studied.

While it’s difficult to say what new discoveries might be made with a microscope that allows researchers to watch a mouse brain in action (on a computer screen) as the mouse goes about its normal activities, it’s probably safe to say, that many of them are likely to be quite illuminating.

Schnitzer and some of his colleagues have founded a company they call Inscopix to develop the new microscope and bring it to market, thought they can't say yet, when that might be.

More information: Miniaturized integration of a fluorescence microscope, *Nature Methods* (2011) doi:10.1038/nmeth.1694

Abstract
The light microscope is traditionally an instrument of substantial size and expense. Its miniaturized integration would enable many new applications based on mass-producible, tiny microscopes. Key prospective usages include brain imaging in behaving animals for relating cellular dynamics to animal behavior. Here we introduce a miniature (1.9 g) integrated fluorescence microscope made from mass-producible parts, including a semiconductor light source and sensor. This device enables high-speed cellular imaging across ~0.5 mm2 areas in active mice. This capability allowed concurrent tracking of Ca2+ spiking in >200 Purkinje neurons across nine cerebellar microzones. During mouse locomotion, individual microzones exhibited large-scale, synchronized Ca2+ spiking. This is a mesoscopic neural dynamic missed by prior techniques for studying the brain at other length scales. Overall, the integrated microscope is a potentially transformative technology that permits distribution to many animals and enables diverse usages, such as portable diagnostics or microscope arrays for large-scale screens.