Microfluidic Microwell and Microcapillary Biochips

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Synopsis

1. We describe: novel, low cost, disposable biochips based on FiberOptic MicroSlide™ technology.

2. FiberOptic MicroSlides are uniquely suited for microarray applications involving moderate-resolution bottom viewing.

3. They enable ‘direct contact imaging’ allowing signals to be directly coupled to a detector without additional optics.

4. They are compact and have excellent light-gathering power.

5. The MicroSlide surface can be etched or patterned to form microwell arrays, or microfluidic structures suitable for genomic and proteomic analysis, cell migration and other studies.

6. We will also introduce low-cost microcapillary array plate technology.
FiberOptic MicroSlides are composed of millions of optical fibers that have been fused together:
MicroSlide Manufacture

1. Cane Draw
2. Multi Draw
3. Multi-Multi Draw
4. Mold Load
5. Pressing
6. Slicing

Core glass rod is inserted into clad glass tube and drawn into cane.
MicroSlide Optical Performance

Conventional glass offers no means of confining the light for bottom viewing.

A FiberOptic MicroSlide uses total internal reflection to guide light from the source to the detector without requiring any additional focusing.

‘Image plane transfer’ eliminates optical problems encountered when viewing through the thickness of the substrate.

The MicroSlide performs like a “zero thickness optic”
Resolution depends on the dimensions and numerical aperture of the MicroSlide fibers.

(L) A light source located on the surface is captured and confined by the contacting fiber and propagates to the opposite surface.

(R) A light source suspended above (air, liquid etc) the surface illuminates multiple fibers but then propagates to the opposite face without appreciable spreading.
MicroSlide Attributes for Bottom Viewing Microarray Applications

Enhanced resolution

10,000 X light collection efficiency

Chromatic dispersion significantly reduced

Focusing problems eliminated

Optical cross talk between 'spots' eliminated.

A conventional microscope slide refracts blue light more than red, resulting in chromatic dispersion.
Imaging: Resolution of two point sources:

The ability to resolve two point sources separated by distance ‘L’, at height “d” may be important for some applications.

\[(L)\] Two points can be laterally resolved if the source separation is about 2.5 times greater than the elevation above the MicroSlide. \[(R)\] The same sources cannot be resolved if their height is doubled and separation is fixed.
MicroWell Arrays for Genomic Analysis

- Formed by selective removal of core glass vs. clad glass.
- ‘Test tube bottoms’ coupled directly to a CCD, to optically interrogate reactions occurring in the wells.
- 42.5µΦ typical for genomic analysis
  - 75 picoliters ($10^{-12}$) or one DNA fragment per well
  - 300,000 wells on a 1” X 3” slide more than 1,000,000 on a larger size
- Each well interrogated by a single optical fiber.
454 Life Science: Genome Sequencer 20 System,
Selected Projects:

- Bacteria
- Fungi
- Human/mouse/plant.

N.Y., Jan. 3 (GenomeWeb News)

- Scientists announced the first genome sequences from a wooly mammoth, which became extinct about 10,000 years ago.
Patterned FOI Microwells

A microwell array formed by depositing a photolithographically patterned polymer on the surface of a FiberOptical MicroSlide.
Patterned FOI Microwells

120µ Φ, 160µ pitch
55µ depth

1,323 X 3µ Φ fibers/ well
MicroFluidic Biochip

- The analysis zone is optically interrogated through fused fiber optics that form the MicroSlide substrate.
- Well suited for ‘direct contact’ CCD counting applications or monitoring with inverted microscopy
- Applications include flow cytometry or biochips for biohazard detection.
Fluorescent Excitation

- Light incident within the acceptance cone is captured and propagated (except for a small fraction that is reflected or absorbed).
- Light used to excite a fluorescent reaction originating outside of the acceptance cone is not transmitted.
- A dichroic filter on the MicroSlide bottom or the CCD faceplate filters out any excitation wavelengths.
FiberOptical Bottom Plate

These microtiter plates feature thousands of coherent optical fibers interrogating each well.

Controlled N.A. (acceptance angle) and imbedded optically absorbing glass insure high signal-to-noise ratios while eliminating cross-talk between reactions.

Left – Available with standard 96 or 384 well plastic upper. Right - Optical isolation between adjacent fibers allows resolution of closely spaced ‘spot’ reactions on the bottoms of each well.
Microcapillary Array

- Comprised of thousands of uniform-diameter hollow 'flow through' capillaries.
- Applications:
  - Chemical analysis
  - Industrial sensing
  - Precision filtration
  - Biological and genetic testing
  - Bio-terrorism sensing
Microcapillary Array Structure

(Left) Low magnification and (right) close-up view of capillaries showing excellent uniformity of Incom’s advanced process.
Conclusions

**MicroSlides:**
1. Eliminate substrate ‘thickness’ problems
2. Significantly improve resolution
3. Provide 10,000 X light collection efficiency
4. Reduce chromatic dispersion
5. Enable direct coupling to a CCD
6. Eliminates focusing & optical cross talk
7. Enables economical microarray reader designs that are high speed, compact, robust and potentially portable.

**Microcapillary Arrays:**
1. A high-density flow-through platform for massively parallel testing
2. Large area arrays are available without regard to thickness vs. diameter constraints
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