

What is claimed is:

1. A cartridge for use with an instrument, comprising:

digital microfluidics comprising a plurality of electrowetting electrodes operative to perform droplet operations on a liquid droplet in a droplet operations gap; and

a fiber optic probe projecting into the droplet operations gap into proximity with a set of two or more of the electrowetting electrodes such that a droplet situated atop any electrode of the set of two or more electrodes contacts the fiber optic probe.
2. A cartridge for use with an instrument, the cartridge comprising:

a digital microfluidics substrate comprising a plurality of electrowetting electrodes operative to perform droplet operations on a liquid droplet in a droplet operations gap;

a top plate separated from the digital microfluidics substrate to form a droplet operations gap and comprising openings for flowing liquids into the droplet operations gap; and

a fiber assembly comprising a fiber optic probe projecting into the droplet operations gap and having a sensing end situated in proximity with one or more of the electrowetting electrodes.
3. The cartridge of any one of claims 1-2, wherein a fiber optic probe projecting into the droplet operations gap is situated in proximity with a set of two or more of the electrowetting electrodes such that a droplet situated atop any electrode of the set of two or more electrodes will contact the fiber optic probe.
4. The cartridge of any one of claims 1-3 wherein, the probe comprises a ligand.
5. The cartridge of any one of claims 1-4, further comprising:

a droplet controllable by the electrowetting electrodes to contact the fiber optic probe.
6. The cartridge of any one of claims 1-5, further comprising:

a low viscosity oil filling the gap.
7. The cartridge of any one of claims 1-6, wherein the top plate comprises two or more grooves or openings each aligning a fiber optic probe from the fiber assembly.
8. The cartridge of any of claims 1-7, wherein the sensing end comprises a nanoparticle sensor surface.

9. A method of conducting an assay, comprising:
 - providing a fiber optic probe comprising a ligand;
 - providing a droplet having a volume which is less than about 1000 nL and comprising an analyte potentially having an affinity for the ligand; and
 - contacting the droplet with the end of the probe and oscillating the droplet without removing the droplet from contact with the probe.
10. The method of claim 9, wherein the oscillation ranges from about 0.5 to about 15 Hz.
11. The method of any one of claims 9-10, wherein the oscillation ranges from about 4 to about 10 Hz.
12. The method of any one of claims 9-11, wherein the droplet has a volume which is less than about 900 nL.
13. The method of any one of claims 9-11, wherein the droplet has a volume which is less than about 800 nL.
14. The method of any one of claims 9-11, wherein the droplet has a volume which is less than about 700 nL.
15. The method of any one of claims 9-11, wherein the droplet has a volume which is less than about 600 nL.
16. The method of any one of claims 9-11, wherein the droplet has a volume which is less than about 500 nL.
17. The method of any one of claims 9-11, wherein the droplet has a volume which is less than about 400 nL.
18. The method of any one of claims 9-17, further comprising:
 - measuring a signal from the droplet via the fiber optic probe and using a computer to calculate a response curve from the signal.
19. The method any one of claims 9-18, wherein the fiber optic probe comprises multiple ligands and the droplet comprises multiple analytes.

20. The method of any one of claims 9-19, wherein the providing operation further comprises providing multiple fiber optic probes and multiple droplets and contacting each of the multiple droplets with a corresponding fiber optic probe and oscillating each of the multiple droplets in contact with the corresponding fiber optic probe.
21. The method of any one of claims 9-20, wherein the oscillation is mediated by electrowetting electrodes.
22. The method of claim 21, wherein each fiber optic probe is aligned so that the end is adjacent to an electrowetting electrode.
23. The method of any one of claims 21-22, wherein each fiber optic probe is aligned so that the end is in proximity to an edge of an electrowetting electrode.
24. The method of any one of claims 9-23, wherein the oscillation is mediated by electrowetting electrodes in a droplet operations gap of a digital microfluidics (DMF) cartridge.
25. The method of any one of claims 9-24, wherein the oscillation is substantially at a right angle to a line extending along a length of the fiber optic probe.
26. The method of any one of claims 9-24, wherein the oscillation is substantially in line with a line extending along a length of the fiber optic probe.
27. The method of any one of claims 9-24, wherein the oscillation is multidirectional.
28. The method of claim 27, wherein the oscillation is multidirectional in a plane parallel to a line extending along a length of the fiber optic probe.
29. The method of any one of claims 9-28, wherein the oscillation is conducted using an elongated droplet.
30. The method of claim 29, wherein the elongated droplet is a 2X droplet.
31. The method of claim 29, wherein the elongated droplet is a 3X droplet.
32. The method of any one of claims 9-31 wherein the assay is selected from the following: molecular library screening assays, binding kinetics assays, affinity determination assays, binding site mapping assays, thermodynamics studies, sandwich assays, competition analysis assays, specificity determination assays, and characterizations of antibody binding, and combinations thereof.
33. A DMF system, the system comprising:

a cartridge, comprising:

digital microfluidics comprising a plurality of electrowetting electrodes operative to perform droplet operations on a liquid droplet in a droplet operations gap, and

a fiber optic probe projecting into the droplet operations gap into proximity with a set of two or more of the electrowetting electrodes such that a droplet situated atop any electrode of the set of two or more electrodes will contact the fiber optic probe;

a controller operationally coupled to the electrowetting electrodes and the fiber optic probe;

an illumination source arranged to illuminate one or more droplets in the droplet operations gap; and

an optical measurement device optically coupled to the fiber optic probe and arranged to receive signal from the fiber optic probe.

34. A digital microfluidics (DMF) cartridge, comprising:

a first substrate comprising one or more electrowetting electrodes for conducting droplet operations;

a second substrate offset from the first substrate;

a droplet operations gap defined between the first substrate and the second substrate, wherein the one or more electrowetting electrodes are operative to perform droplet operations on a liquid droplet in the droplet operations gap; and

a sensing region in the droplet operations gap for contact with the liquid droplet, and

a fiber optic probe that provides excitation light from a primary illumination source to the sensing region and emission light from the sensing region to a primary optical measurement device.

35. The DMF cartridge of claim 34, wherein the sensing region comprises a sensor surface disposed on a terminal surface portion of the fiber optic probe.

36. The DMF cartridge of any one of claims 34-35, wherein the sensing region is disposed in the droplet operations gap in proximity to the one or more electrowetting electrodes such that the liquid droplet will contact the sensing region.

37. The DMF cartridge of any one of claims 34-36, wherein the fiber optic probe extends through the first substrate to dispose the sensing region in the droplet operations gap .
38. The DMF cartridge of any one of claims 34-37, wherein the fiber optic probe extends through the second substrate to dispose the sensing region in the droplet operations gap.
39. The DMF cartridge of any one of claims 34-38, wherein the fiber optic probe extends into the droplet operations gap between the first and second substrate substantially parallel to the first substrate and the second substrate to dispose the sensing region in the droplet operations gap.
40. The DMF cartridge of any one of claims 34-39, wherein at least one of the first substrate or the second substrate comprises at least one opening for introduction of a liquid into the droplet operations gap.
41. The DMF cartridge of any one of claims 34-40, wherein the sensing region comprises a ligand.
42. The DMF cartridge of any one of claims 34-41, wherein the sensing region comprises a nanoparticle sensor surface.
43. The DMF cartridge of any one of claims 34-42, wherein the fiber optic probe comprises one or more optical elements at the terminal surface portion.
44. The DMF cartridge of any one of claims 34-43, wherein the droplet operations gap contains a filler substance that is immiscible with the liquid droplet.
45. The DMF cartridge of any one of claims 34-44, wherein the first substrate and the second substrate comprise a material sufficiently transparent to allow excitation light from a secondary illumination source to pass through the first substrate to the sensing region and emission light from the sensing region to pass through the second substrate onto a secondary optical measurement device.
46. A digital microfluidics (DMF) system comprising:

a DMF cartridge according to any one of claims 34-45;
one or more illumination sources, wherein the one or more illumination sources supplies the excitation light to the sensing region of the DMF cartridge via the fiber optic probe; and
one or more optical measurement devices, wherein the one or more optical measurement devices receives and processes the emission light from the sensing region via the fiber optic probe.

47. The DMF system of claim 48, further comprising:

a controller in operative communication with the one or more electrowetting electrodes to control the conducting of the droplet operations by the one or more electrowetting electrodes.