**[Plug] Isolated Liquids**

- Why Isolated Liquids?
  - Isolated liquids under defined conditions for
    - Chemical reactions
    - Bio Assays
    - etc.
  - High-throughput screening
  - Need for small volumes
  - Handling massive parallel isolated liquid compartments
    - Microwell plates are the classical way

- Microtiter Plates
  - 96-well plate: 400 μL (pitch size: 9 mm)
  - 384-well: 105 μL (pitch size: 4.5 mm)
  - 1536-well: 12 μL (pitch size: 2.25 mm)
  - 6144-well: 1 μL (pitch size: 1.125 mm)
  - ...

- [Plug] Microtiter Plates and Plug-based Microfluidics

  - A comparison of screening in microtiter plates and screening with preloaded cartridges.
    - (a) To set up the screen in microtiter plates, robotics is required to dispense nanoliters of both the reagents and the substrate. Solutions in the microwells may evaporate.
    - (b) With preloaded cartridges, the reagents are confined in nanoliter plugs. When the flow is induced, defined nanoliter aliquots of the substrate solution are spontaneously dispensed into the plugs of reagents. Plugs of the reagents and the products are confined in capillaries and are surrounded by an impermeable fluorinated carrier fluid, preventing evaporation.

- [Plug] Plugs as Isolated Liquids

  - Advantages
    - Small reactant volumes
    - Surface tension keeps liquid compact
      - No Taylor Dispersion
      - Order of plugs liquid is held constant
      - No cross mixing
    - Separation and isolation by secondary phase (air, oil)
      - No diffusion through low solubility in embedding fluid of reactants
    - Accurate volume definition
    - Long term stability of conditions in the isolated compartments

  - Isolated Liquids
    - Plug-based microfluidics: immiscible-fluid flows (water and oil)
    - Droplet-based microfluidics: programmable planar LOC
[Plug] Isolated Liquids

**Plug-based Microfluidics**
- Actuation
  - with flow (pressure gradient)
- Movement with flow through channels in one direction
- Closed channel systems
- Immiscible-fluid flows (water and oil)

**Drop-based Microfluidics**
- Actuation
  - SAW (by surface acoustic waves: Lecture 15)
  - EWOD (by electrowetting: Lecture 14)
- Programmable planar LOC
- In two directions (arbitrary) movable

[Plug] Plug Formation (T-Junction)

**Immiscible Two-Phase Flow**
- Water-in-Oil plugs
- Liquid 'squeezed' between immiscible phases

**T-Junction**
- Shear flow of different phases with different flow rates - velocities
- Contraction of flow
- Rayleigh instability in contraction
- Pressure drop accumulation
  - by channel clogging
  - shear pressure drop along plug
- Plug detachment

[Plug] Plug Formation (Shear Focusing)

**Immiscible Two-Phase Flow**
- Aqueous-in-Lipid
- Liquid 'squeezed' between immiscible phases

**Hydrodynamic Shear Focusing**
- Shear flow of different phases with different flow rates - velocities
- Contraction — neck interface
- Rayleigh instability in neck
- And/or pressure drop accumulation over contraction
- Plug detachment
**Multiple Plug Formation**
- Plug in plug
- Bubble in plug
- Series of T-Junctions
- Soap Bubble Principle
  - Thin film of fluid around non-mixable phase

**Single Cells in Plug**
- Aqueous-in-oil plug
  - Selective encapsulation of single cells and subcellular organelles into picoliter- and femtoliter-volume droplets

**Functions**
- Sample Loading
- Plug formation
- Metering
- Transporting
  - Mixing
  - Merging
  - Splitting
  - Switching
  - Incubation
- Reaction
- Separation
- Detection

**Water Immiscible Perfluorodecaline (PFD)**
[Plug] Functions

- All functions are possible

  - Sample Loading
    - Plug formation
  - Metering
  - Transporting
    - Mixing
    - Merging
    - Splitting
    - Switching
    - Incubation
  - Reaction
    - Separation
    - Detection

Controlling surface chemistry in plug-based microfluidic devices with surfactants at the aqueous-fluorous interface. (a, b) Schematic of surfactant molecules at the interface of an aqueous plug of protein in a microfluidic channel. RF-COOH surfactant provided a noninert interface prone to protein adsorption. RF-OEG surfactant provided an inert, biocompatible interface (nonspecific protein adsorption).

[Plug] Strengths / Challenges

**Strengths**
- High-throughput screening
- Handling massive parallel isolated liquid compartments
- Small reactant volumes (~ 1 nL)
- No cross contamination between plugs
- Accurate volume definition
- Real-time in-situ reaction
- Long term stability of conditions in the isolated compartments
- A lot of applications
  - Chemical emulsion process
  - Nanoparticle formation
  - Protein crystallization
  - Drug discovery
  - LOC
  - ...

**Challenges**
- Residual plugs on the surfaces might contaminate the following plugs.
- Volume variation of plugs
- Extra carrier liquids (oils)
- Miniaturization of external periphery is difficult
  - Pressure-driven setup is required.

**SAW** SAW-based Microfluidics

- Surface Acoustic Waves (SAW)
  - Mechanical waves traveling along surface of bodies
  - Amplitude decreases exponentially with depth

- SAW excitation in microsystems
  - Piezoelectric substrate
  - Comb like electrodes on surface (interdigital transducer)
  - Electric stimulation excites wave
  - Wavelength depends only on geometry of electrodes
  - Wavelength depends not on stimulation period – used for filters in μ-electronics

- SAW-based Microfluidics
  - Droplets are moved on surface by IDT (InterDigitated Transducer)
[SAW] SAW-based Microfluidics

To see is to believe

- Demo 1: Programmable Biochips Animation
- Demo 2: Programmable Biochips Device
- Demo 3: Mixing by SAW
- Demo 4, 5, 6

4. Non diffusive mixing of smallest volumes
   1 microliter containing polystyrole beads
   animated gif, 196 kB, QT Movie, 3.3 MB

5. Actuation of single droplets:
   real time, volume ca. 50 nl
   animated gif, 560 kB, QT Movie, 2.3 MB

6. Nano chemistry:
   Chemoluminescence (Luminol) using two 50 nl droplets
   animated gif, 168 kB, QT Movie, 624 kB