The production and stability of microbubbles for drug delivery

Microbubbles are gas cores surrounded by a surfactant shell. Microfluidics is used to produce bubbles with a very high level of control over their size and production rate. Using multiple inlets, bubbles can be loaded with drug at specific concentrations.

Since they are gas filled and compressible, microbubbles are very strong ultrasound contrast enhancing agents. Their compressibility also means that they can be ruptured site specifically by ultrasound, releasing any encapsulated drug only where it is required.

1. Basics of bubble production

Activity

By hand, students control liquid flow and gas pressure by pushing gas syringes, in order to pinch off bubbles at the chip nozzle.

For a given gas pressure, varying the liquid flow rate has a large impact on the size of bubbles produced. For medical use, bubbles must remain < 8 μm diameter.

2. Variables of production

There are many variables that effect bubble production size, monodispersity, and production rate, including: flow rates, chip geometry, liquid viscosity, surfactant concentration, etc.

Here (b) an increase in gas pressure and flow rate, with an additional pressure drop region in the outlet leads to a higher concentration and higher production rate sample, but with a lower monodispersity and control on bubble size.

Increasing the viscosity of the solution leads to a more monodisperse sample, but slows down production.

3. Bubble shell composition

A) Hydrophobic drug carrier

B) Hydrophilic drug carrier

Bubble shells can be engineered to:
- carry drugs
- live longer
- be stiffer
- etc

C) Stronger shelled bubbles

Cross-linking molecules in the bubble shell stiffens the shell, increasing bubble lifetime.

4. Other outreach

Students build a physical representation of a drug delivery bubble, tasked with combatting one of four diseases.

Elements of bubble design to consider:
- Size ranges
- Gas core
- Targeting chemistry
- Production method
- Drug loading
- Costs

Students blow bubbles from water and soap, with and without glycerol in solution. Glycerol slows water evaporation, giving a longer lasting shell, increasing bubble lifetime.