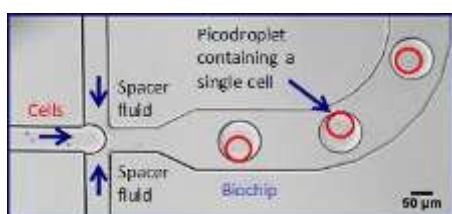




ESI-Mine™: high-throughput, miniaturised mass spectrometry using picodroplets

Technology Description:

Sphere Fluidics has developed unique, patented technology for **high-throughput miniaturised electrospray injection mass spectrometry (ESI-MS)**. The technology involves the use of novel microfluidics in biochips which control and process hundreds of thousands of small volume (pL to nL) stabilised, aqueous droplets called picodroplets (see image below). Each 500 pL picodroplet compartmentalises the sample - enabling analysis of > 200,000 per day.



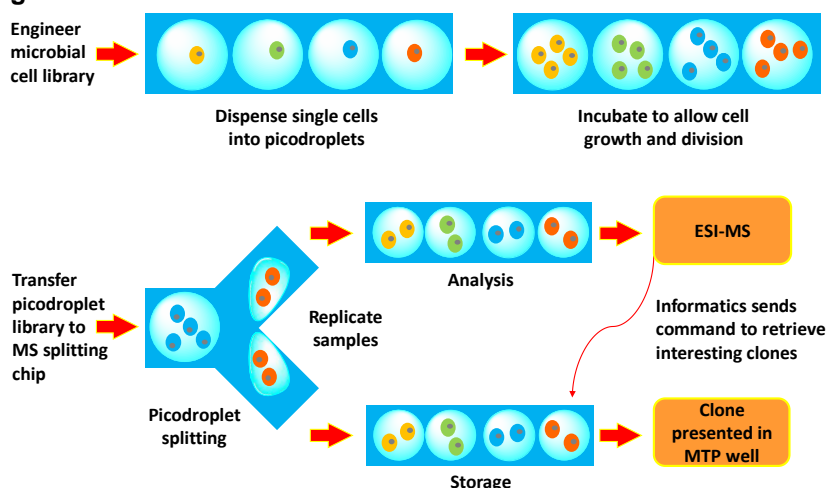
Applications:

- **Synthetic biology:**
 - Facilitates study of valuable molecules produced by libraries of engineered microbes.
- **Bioprocessing:**
 - Enables analysis and identification of microbial clones that are high expressors of, e.g. Active Pharmaceutical Ingredients.
- **Drug and molecular interaction studies:**
 - Measure drug or drug fragment interaction with soluble proteins for improved structure-activity relationship studies.
- **Enzyme evolution/Site-directed mutagenesis:**
 - Determine efficiency of engineered enzymes on their native substrates.

New Developments:

Sphere Fluidics is developing a brand new analytical platform (ESI-Mine™) that will allow **Rapid ESI-MS Screening of Cell Libraries**. The system will compartmentalise individual microbes in a picodroplet and incubate them to enable growth. The picodroplets are then automatically split, one daughter picodroplet sent for MS analysis, the other (replicate) stored on a biochip. When picodroplets that generate a 'hit' in the MS are identified, the user can retrieve the corresponding stored 'hit' replicate for further analysis. The hit replicates are then isolated by dispensing into individual microtitre plate (MTP) wells (see workflow image below). The system will be fully automated, have specialised consumables and software, and be compatible with most popular ESI-MS models.

Cell Library Screening:



Technology Comparison:

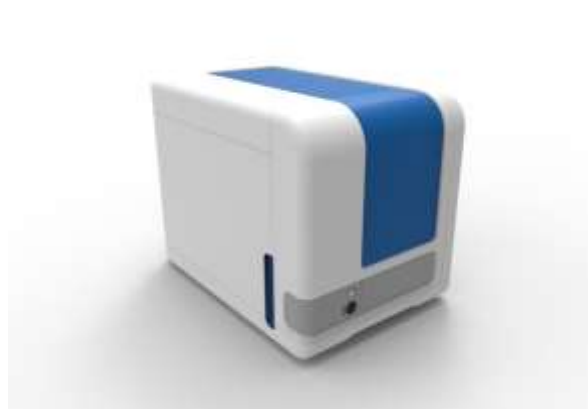
| Key challenge | Current technology | ESI-Mine™ |
|------------------------------|--------------------|---------------|
| Sample assay time | 5 - 10 sec | 0.4 sec |
| Throughput per day | 8,000 - 16,000 | > 200,000 |
| Sample test volume | 1,000 ml | 0.5 ml |
| Total test volume | 40 - 80 ml | 0.02 - 0.4 ml |
| Sample splitting and storage | No | Yes |
| Sample retrieval and testing | No | Yes |
| Screening of vast libraries | No | Yes |
| Reagent cost per test | High | Very Low |

Corporate:

Sphere Fluidics Limited is an established, Life Sciences company, based near Cambridge (UK) which has developed unique products for use in single cell analysis and characterisation and provides collaborative R&D services in this area. The Company has 59 patents (13 patent families with 34 patents being granted) and over 200 international customers.

Technology Access Program:

Sphere Fluidics is also developing Cyto-Mine™ - a Single Cell Analysis and Monoclonality Assurance System. Cyto-Mine™ is an automated system which (using proprietary, picodroplet technology and microfluidics) performs novel functional and binding assays on single cells, cell-cell and cell-biomolecule combinations. This instrument is specially designed for the biopharmaceutical discovery and development market. In a few hours, the platform can analyse Ab production from over one million primary B-cells or hybridomas. It can also isolate single cells that produce the most specific or highest yield of Ab. The platform also delivers significant savings in consumable costs with greater statistical accuracy in rare cell recovery.



Services:

➤ Research projects:

Example: in 1-3 months, assess use of picodroplets to analyse novel synthetic biology libraries by ESI-Mine™.

➤ Development programs:

Example: in 6-9 months, develop a novel biochip and workflow for cell:cell co-incubation assays.

➤ Discovery collaborations:

Example: in 9-12 months, engineer 10 specific proteins, transfect cells and isolate cDNAs for the best ones secreted from a vast library of millions of transformed single cells.



CONTACT US TO DISCUSS YOUR SPECIFIC NEEDS

Management:

Frank F. Craig PhD MBA (Chief Executive Officer). Frank is an experienced, serial entrepreneur who was a co-Founder of Aurora Biosciences (San Diego, USA), which had a peak market capitalization of £1.8 billion five years after formation. He was also a co-Founder and CEO of Smart Holograms (Cambridge, UK) - once the UK's Fastest Growing Company, a Vice-President of R&D at Amersham Biosciences and a Senior Scientist at GlaxoSmithKline.

Rob Marchmont PhD (Commercial Director). Rob brings more than 25 years' experience in the Life Sciences industry with a proven track record in business development and marketing; gained from GE Healthcare, NanoInk and NonLinear Dynamics.

Marian Rehak PhD (R&D Director). Marian has over 20 years' experience in Life Sciences R&D. After post-doctoral research at the University of Tokyo, the Weizmann Institute and the University of Cambridge, Marian has held a number of senior R&D roles at several biotechnology companies, such as Akubio, Unipath and DxTech.

Board of Directors:

Andrew Mackintosh PhD (Chairman). Previously, Chief Executive of the Royal Society Enterprise Fund and the CEO of Oxford Instruments PLC.

Frank F. Craig PhD MBA (Chief Executive Officer). See biography to left.

Ian Gray BCom. Chartered Accountant, member of the 24Haymarket angel syndicate and previously Managing Director of Candover. Ian was an early investor and long-serving Board member of Inveresk Research, which later sold for over £600 million.

Amanda Wooding PhD. Deputy Head of Life Sciences at Cambridge Enterprise and an expert in spin-out creation.

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