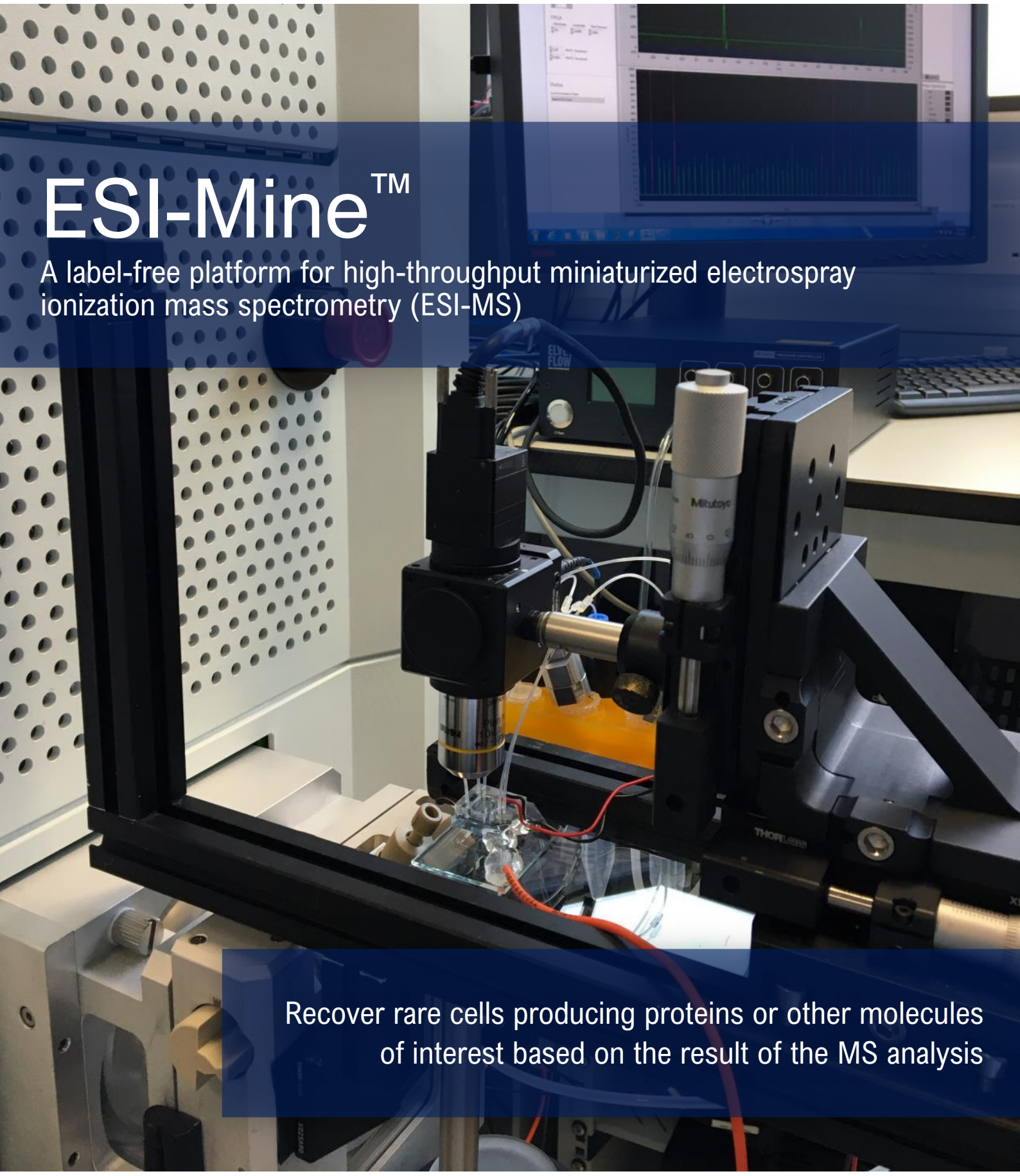
Sphere Fluidics

ESI-Mine™

A label-free platform for high-throughput miniaturized electrospray ionization mass spectrometry (ESI-MS)



Recover rare cells producing proteins or other molecules of interest based on the result of the MS analysis

www.spherefluidics.com

ESI-Mine™

ESI-Mine™ is a high-throughput, label-free platform for MS-based screening. It uniquely allows live clone retrieval of rare cells producing proteins or other molecules of interest based on the result of concurrent MS analysis.

Using our proprietary picodroplet (picolitre volume droplet) technology, ESI-Mine™ can test up to 200,000 biomolecular samples (e.g. peptides, enzymes, antibodies, metabolites and small molecules) per day in miniaturized volumes of 500-700pL (picodroplets) facilitating more efficient screening and analysis in bioproduction or synthetic biology processes.

Applying this novel approach, researchers can screen a large library of picodroplets containing microorganisms producing proteins or small molecules of interest. One major drawback of using MS in analysis is that samples are usually destroyed and cannot be retrieved. To overcome this total sample destruction by ESI-MS, we have developed a unique microfluidic workflow where picodroplets are split into two replicate streams with identical clones, one stream is analyzed by ESI-MS, and the second stream is subsequently 'held' and only those 'hit' daughter picodroplets sorted and retrieved based on the result of the MS analysis.

ESI-Mine™ Platform

Applications

ESI-Mine™ is suitable for several applications including:

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: Accurately measures drug or drug fragment interaction with soluble proteins for improved structure-activity relationship (SAR) studies.

Enzyme Evolution/Site-Directed Mutagenesis: Helps determine the efficiency of engineered enzymes on their native substrates.

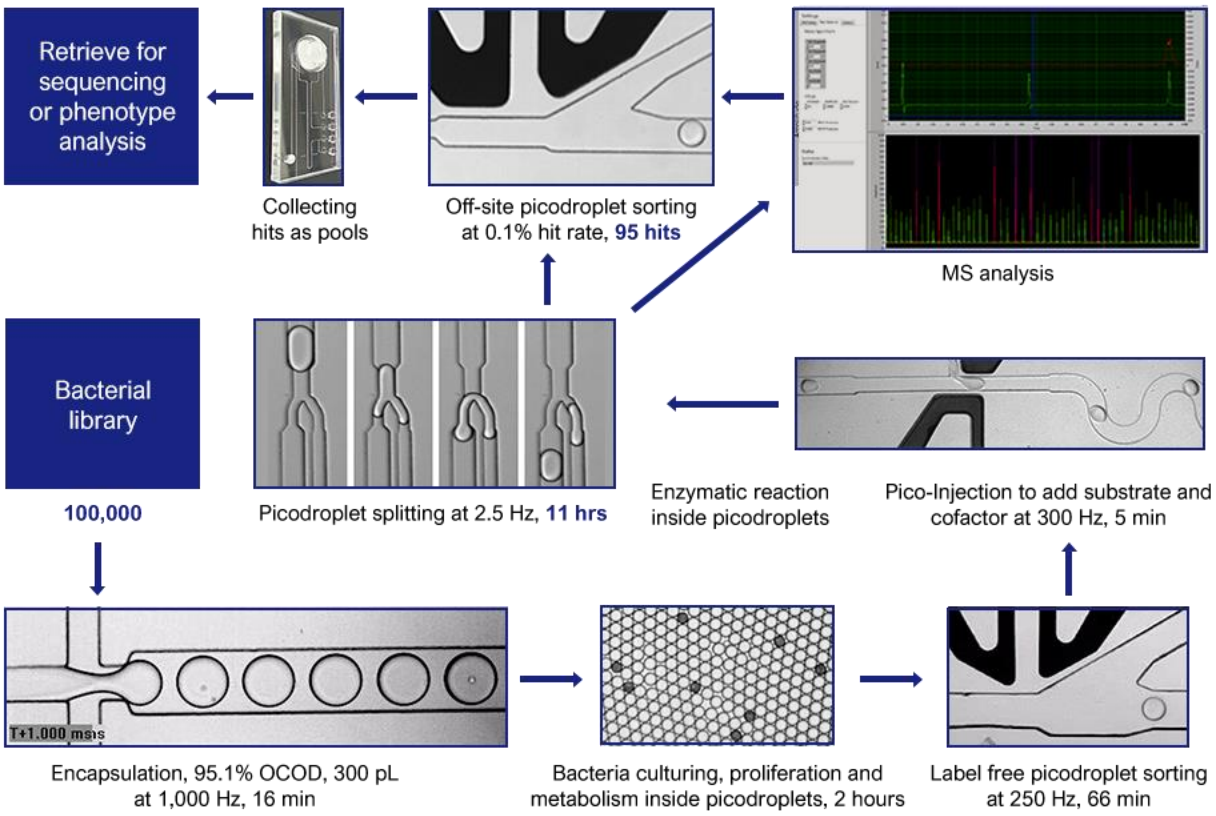
The Technology

MS offers label-free detection of the presence, absence, and abundance of multiple, specific molecules with high sensitivity and selectivity. However, it is relatively low-throughput and sample destruction during the analysis prevents the direct sorting of 'hit' molecules or samples of interest.

The microfluidic-based workflow of ESI-Mine™ addresses the main challenges in ESI-MS while offering advantages in high speed, increased sample throughput and lower cost over existing solutions.

Cells are encapsulated into picodroplets in a one-droplet-one-cell (OCOD) manner, creating a library of picodroplets that can express and retain novel proteins and/or other hydrophilic entities. The picodroplets are incubated to enable cell growth, protein expression and metabolic processes to occur and are then reinjected into the proprietary microfluidic emitter biochip on the ESI-Mine™ platform for label-free screening followed by real-time sorting based on MS analysis results. At this stage, each picodroplet is asymmetrically split, producing two daughter picodroplets from the same parent picodroplet. The larger daughter picodroplet is analyzed by ESI-MS. Its smaller sibling picodroplet is processed through microfluidic channels and sorted based on the MS signal. Hits are then collected as a pool for further downstream analysis.

Complete workflow of single cell analysis and sorting on ESI-Mine™ platform



Benefits

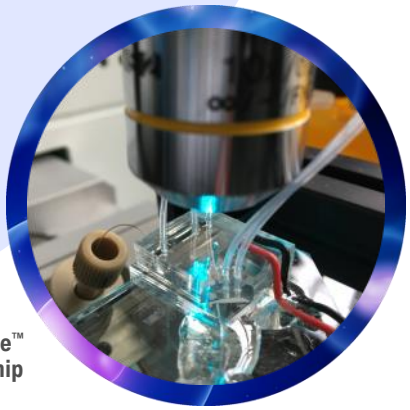
Recover Rare Variants
ESI-Mine™ uniquely allows live clone retrieval of rare cells producing proteins or other molecules of interest based on the result of the MS analysis.

High Throughput
ESI-Mine™ can selectively sort up to 200,000 biomolecular samples per day for efficient and high-throughput analysis of large cell libraries.

Miniaturization
Using picodroplets, the amount of media required is significantly reduced, further reducing costs.

Flexibility
We offer a range of customizable microfluidic biochips enabling the development of complex workflows on a single microfluidic device and interfacing to different MS instrument models

Versatility
ESI-Mine™ enables a broad range of novel microfluidic workflows and applications.



ESI-Mine™ Biochip

High-throughput and cost-effective bioprocessing

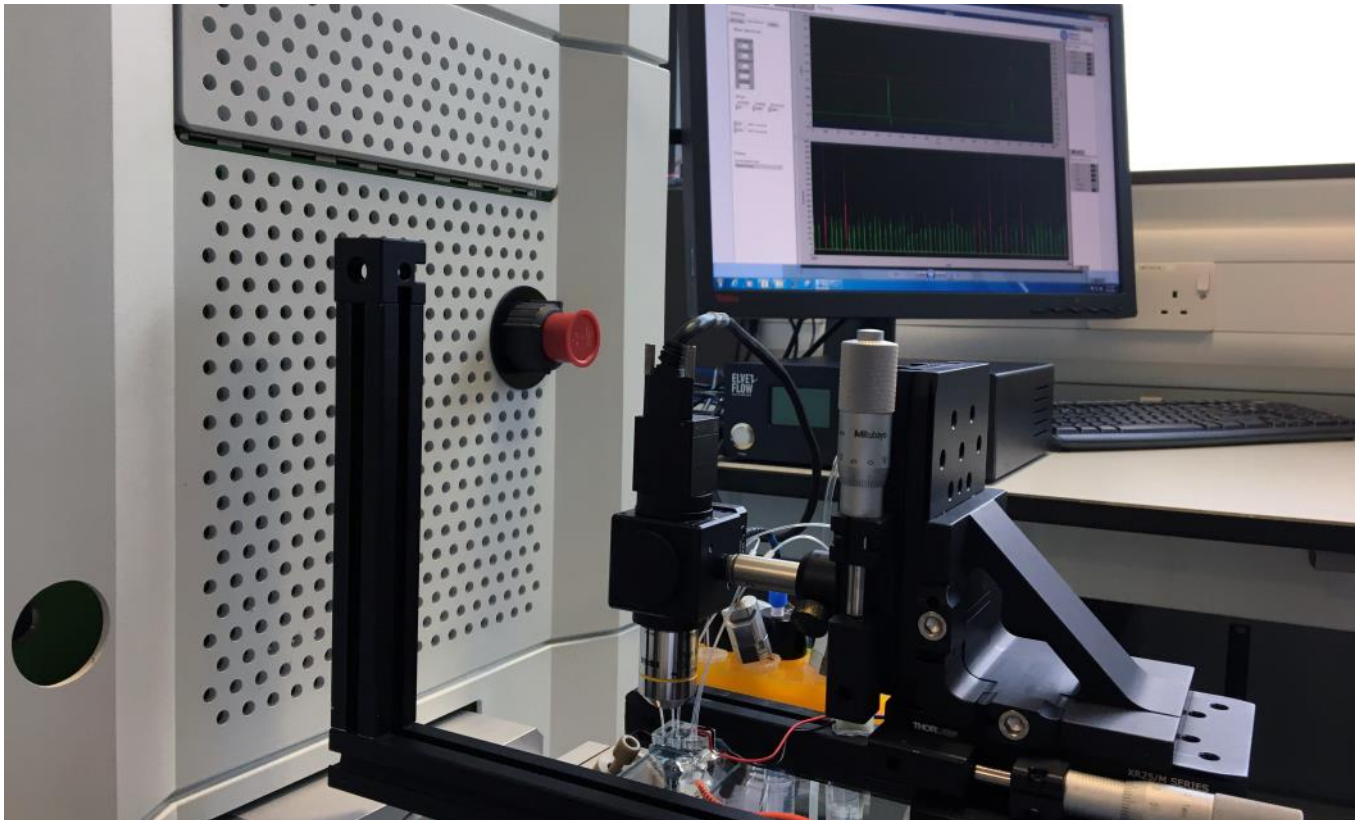
The table below summarises the substantial cost savings that can be achieved with the implementation of picodroplet technologies compared to a microplate format approach.

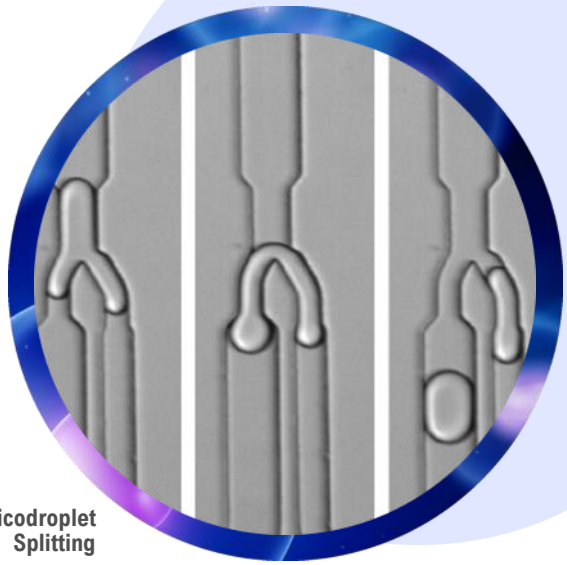
Parameter	Microplate	Picodroplet
Throughput samples/day	10^2 - 10^3 (LC-MS) 10^4 (RF-MS)	10^5 - 10^6
Reagent volume (to screen 1M mutants)	100 L (*e.g.* £500,000 for 10 mM NADPH)	1 mL (*e.g.* £5 for 10 mM NADPH)
Equipment	• Qpix colony picker • Multi-plate Incubators • Centrifuges • FX/Tecan liquid handling robots • LC-MS or RF-MS • MTPs (£20,000-£50,000)	• Syringe or air pressure pumps • Fabricated chips • Mass Spec • Biochip (£500).

Specifications

Run Specifications	
Sample input method	Loaded into single-use disposable Picodroplet Reinjection & MS Emitter microfluidic biochip
Sample input format	Picodroplet
Workflows (operation modes)	Synthetic Biology; Enzyme Evolution; Drug Screening
Containment and sterility	Requires biological safety lab
Detection	
Detection system	TOF MS and Laser-Induced Fluorescence (*e.g.* fluorophores)
Excitation wavelengths	488 nm
Fluorescent wavelengths *	Below 506nm and 524-634nm
Camera	High-speed CMOS
PC	
Computer	Embedded internally as part of the TOF MS; Control PC
PC operating system	Microsoft Windows 10 Professional
Monitor	Colour LCD (24")
Software Specifications	
System control software	TOF MS Driver; ESI-Mine™ Studio; Elveflow® ESI Pressure control software; StreamPix 6; Coherent Connection
Data tracking	On screen data point
Work Environment	
Clearance	30 cm
Humidity	30 - 80%
Operating temperature	16°C - 26°C
Site preparation	See the ESI-Mine™ System Site Requirements Guide
Consumables	
Microfluidic biochips	Picodroplet Reinjection & MS Emitter microfluidic biochip; Picodroplet Reinjection, Splitting, MS Emitter & Sorting microfluidic biochip
Specialist chemicals	Picodroplet Oil; Picodroplet Reinjection Oil; Picodroplet Spacing Oil

Implementation Example: ESI-Mine™ Linked to a Perkin Elmer Axion 2





Picodroplet Splitting

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Code	Product Ordering Information
S004	ESI-Mine™

Notes:

ISO 9001

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